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Review

Interventions to improve dispensing of antibiotics at the community level in low and middle income countries: a systematic review

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ABSTRACT

Objectives: Inappropriate antibiotic dispensing is one of the key drivers of antibiotic resistance. This review documents the effectiveness of interventions aimed at improving antibiotic dispensing practices at the community level by drug dispensers in low- and middle-income countries (LMIC).
Methods: We conducted a systematic search in PubMed, EMBASE, Cochrane Central Register of Controlled Trials and Web of Science (11 November 2019). Studies were included if they reported data on the outcome measure: appropriate dispensing of medicine including antibiotics. The effectiveness of studies was assessed based on quantitative results reported in the studies included.
Results: A total of 1158 articles were screened. Thirteen studies from Asia (six), Africa (five) and South America (one) and one study from both Africa and Asia were included in this review. Nine (69.2%) studies reported significant effectiveness of interventions on all or more than 50% of antibiotic-related outcomes. Cochrane Effective Practice and Organization of Care interventions frequently applied were educational meetings (9/13), distribution of educational materials (7/13), educational outreach meetings (7/13), reminders (6/13), local consensus processes (6/13), distribution of supplies (6/14) and clinical practice guidelines (4/14), Nine studies reported on stakeholder involvement.
Conclusion: This review shows that it is possible to improve antibiotic dispensing practices at the community level in LMIC. Stakeholders' involvement was key in the design and implementation of interventions.

1. Introduction

Globally, antimicrobial resistance is a major public health challenge, particularly in low- and middle-income countries (LMIC) [1–3]. Antimicrobial resistance is largely attributed to inappropriate antibiotic access and use [1,2,4]. Community health posts (CHPs), over-the-counter medicine sellers (OTCMSs) and community pharmacies are important sources of healthcare in LMIC, especially in rural and hard-to-reach communities [5–7]. In Ghana, about 80% of medicine outlets in rural communities are OTCMSs [8]. Similarly, community pharmacies in some Asian countries are major sources of healthcare for common illness in rural areas [9–11]. CHPs, OTCMSs and community pharmacies supply treatment for malaria [12–18], sexually transmitted infections and acute respiratory infections [9,10,19,20], among others.

In many LMIC, CHPs, OTCMSs and community pharmacies dispense 'prescription only' medicines including antibiotics, which is against regulations [12]. Efforts by regulators to supervise and prevent especially OTCMSs from dispensing antibiotics have not produced the desired result. Dispensing of antibiotics and other essential medicine by CHPs, OTCMSs and community pharmacies is a pharmaceutical regulatory issue that creates tension between

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regulators and dispensers [21]. Regulation enforcement is interpreted by OTCMSs as interference in their market space and is met with resistance and evasion [12].

Considering the inadequacies in health service delivery, proper dispensing of antibiotics (according to guidelines) by CHPs, OTCMSs and community pharmacies is crucial in the fight against antibiotic resistance (ABR) as they are closest to the communities [21]. This underscores the need to develop evidence-informed interventions that equip CHPs, OTCMSs and community pharmacies to dispense antibiotics appropriately [21]. To inform future public health policies and to make recommendations on such interventions to governments and stakeholders in LMIC, synthesized data on the effectiveness of studies previously performed to improve dispensing practices of CHPs, OTCMSs and community pharmacies on antibiotic dispensing and other essential medicines are important.

This systematic review documents (i) the effectiveness of interventions to improve the dispensing of antibiotics by CHPs, OTCMSs and community pharmacies in LMIC and (ii) the determinants of success or failure of these interventions.

2. Methods

2.1. Search strategy

We searched PubMed, Embase, Cochrane Central Register of Controlled Trials and Web of Science for papers on the effectiveness of interventions to improve antibiotics dispensing by CHPs, OTCMSs and community pharmacies in LMIC, published from January 1990 up to 11 November 2019 (Supplementary Appendix S1). We also used keywords/phrases (antibiotic dispensing, appropriate antibiotic dispensing, interventions to improve antibiotic dispensing and LMIC) to conduct web searching in Google and Google Scholar for grey literature. EndNote X7 was used to aggregate search results. Duplicate studies were removed. All titles and abstracts were screened by one author (SAA) and 25% were independently screened by another author (MAA). The full texts of all potentially relevant articles were assessed by both authors for eligibility. Any disagreement was resolved through discussion. We also reviewed reference lists of included studies/papers to identify relevant papers.

2.2. Inclusion and exclusion criteria

We included studies that reported on the effectiveness of interventions to improve dispensing of medicines including antibiotics by CHPs, OTCMSs and community pharmacies in a LMIC setting according to the definition of the World Bank [22]. First, titles and abstracts were screened (Table 1). Next, a full-text review was performed to determine whether the studies met all inclusion criteria (Table 1). We included both randomised controlled trials (RCTs) and observational studies. We excluded case reports, narrative reviews, discussion papers, conference papers, letters to the editor and editorials.

2.3. Data extraction

Data were extracted from included studies with a standardised form to obtain information on participants (number and type of persons, setting, country), study design, intervention elements (as described by the authors and as categorised by the authors), methods of data collection, follow-up duration and outcome measures. We also extracted data on the effectiveness of interventions on outcomes reported, stakeholder involvement (yes or no), determinants analysis performed for developing interventions (yes or no) and reported determinants of success or failure of interventions. We extracted effectiveness data as reported in the papers (i.e., percentages, *P*-values). To categorise intervention elements, the Cochrane Effective Practice and Organization of Care (EPOC) Taxonomy was used [23]. Two authors (SAA and MH) independently extracted data from one paper and outcomes were discussed. Data from another paper were extracted by SAA and MAA for comparison. Data from the remaining papers were extracted by SAA and were fully checked for accuracy by MAA. Discrepancies identified were resolved through discussion. For this systematic review we followed the PRISMA criteria (Supplementary Appendix S4), and the study protocol was registered at PROSPERO (CRD42018116526).

Table 1
Summary of inclusion criteria.

Criteria	Include if
Stage 1: title/abstract review	
Year of publication	Study was published in 1990 and later
Study site	Study was conducted in a LMIC
Intervention	Study evaluates an intervention to improve dispensing practices of CHPs, OTCMSs and community pharmacies
Stage 2: full-text review	
Primary study	Study assesses primary outcome of interest at CHPs, OTCMSs and community pharmacies in the LMIC
Evaluates an intervention	Study evaluates effectiveness of interventions to improve dispensing of medicines including antibiotics
Description of intervention	Intervention is clearly described
Effectiveness	Study reports original data on the effectiveness of intervention

2.4. Methodological quality

The quality of randomised controlled studies was assessed using the Cochrane Risk of Bias tool for randomised controlled trials. Bias was assessed as a judgement (high, low or unclear) based on seven indicators. The quality of non-randomised studies was assessed with the Newcastle-Ottawa Quality Assessment Scale for non-randomised controlled trials. We evaluated each study based on five indicators. We assessed whether the studies fulfilled the descriptive characteristics for each indicator. Studies were considered to be of higher quality if they explicitly described the characteristics for each element. For each indicator, studies were assigned a yes (met criteria), partial (met half of criteria) or no (failed to meet criteria) (Table 2). The risk of bias of studies was assessed by SAA and verified by MAA.

2.5. Data synthesis and analysis

The effectiveness of studies was assessed based on quantitative results reported for all study outcomes. Most studies reported unique outcome parameters. To facilitate comparisons, we developed a study 'summary of effectiveness score' (i.e., number of significant outcomes/total number of outcomes measured $\times$ 100) to determine the overall effectiveness of interventions. These scores were categorised: intervention showed statistically significant effects on all study outcomes, $\geq$50% of study outcomes and $<$50% of study outcomes. We also summarised the interventions performed in the included studies using EPOC categorisation [23]. Information on stakeholder involvement in intervention development, determinants analysis performed for developing intervention and reported determinants of success or failure of intervention were analysed thematically.

Table 2
Characteristics of 13 studies, 15 papers.

Author, publication year [reference]	Topic	Participants, setting, country	Units of analysis	Study design (cRCT, ITS etc)	Description of intervention (I)/Comparison (C)	Methods of data collection and follow-up duration	Predefined endpoints (see Appendix S1 (all endpoints) and Table 3 (antibiotic endpoints only) for detailed information)	Study quality
1. Adu-Sarkodie et al., 2000 [19]	Syndromic management of urethral discharge in pharmacies	-100 Drug sellers at pharmacy/over-the-counter medicine shops (50 intervention, 50 control) -Private -Ghana	Pharmacy/over-the-counter medicine shops	Cluster RCT with after intervention measurement	I: * Training C: No training (routine care)	*Trained simulated clients visits pharmacy/drug shops *Structured questionnaire completed for each pharmacy staff encounter *Follow-up duration: intervention was assessed for 1 months after 8 months of implementation	-Total of all outcomes: 14 -Antibiotic related outcomes: 6	Random sequence generation, low risk; Allocation concealment, unclear; Blinding of participants and personnel, unclear; Blinding of outcome assessment, low risk; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, unclear
2. Awor et al., 2014 [28]	Integrated management of malaria, pneumonia and diarrhoea	-3759 household interviews with caretakers of children less than 5 years (1604 before/2155 after) - 943 exit interviews with caretakers of children less than 5 years (163 before/780 after)-Private-Uganda	Caretakers of children less than 5 years	Quasi-experimental study (one intervention and one non-intervention) with before-after measurement	I: * Provision of dose specific pre-packaged and subsidized drugs and diagnostics to registered drug shops drugs * Training of drug shop attendants * A community awareness campaign. **C:** Usual care/current practices	*Structured questionnaire/exit interviews with clients at drug shops -Household interviews with care takers/mothers *Direct observation at drug shops *Follow-up duration: interventions were assessed for 2 months after 8 months of implementation	-Total of all outcomes: 18 -Antibiotic related outcomes: 7	Population of interest, yes; Outcomes assessed and reported, yes; Measurement same for all subjects, yes; Confounding controlled, yes; Intervention, yes
3. Chalker, 2001 [20]	Antibiotic prescribing	- Community health workers in 217 community health stations-Public -Vietnam	Record of patients	Longitudinal time series	**I**: * Conditional equipment donation *Standard treatment guideline * Regular supervision * Workshops **C**: Routine care at baseline	*Records from outpatients book at community health stations *Follow-up duration: interventions were assessed through monthly supervision for 6 to 24 months	-Total of all outcomes: 2-Antibiotic related outcomes: 2	Population of interest, no; Outcomes assessed and reported, yes; Measurement same for all subjects, partial; Confounding controlled, partial; Intervention, yes

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Table 2 (*continued*)

Author, publication year [reference]	Topic	Participants, setting, country	Units of analysis	Study design (cRCT, ITS etc)	Description of intervention (I)/Comparison (C)	Methods of data collection and follow-up duration	Predefined endpoints (see Appendix S1 (all endpoints) and Table 3 (antibiotic endpoints only) for detailed information)	Study quality
4. Chalker et al., 2002 [9], Chalker et al., 2005 [10] & Chuc et al., 2002 [24]	Dispensing practices at private pharmacies regarding antibiotics and steroids	**Vietnam** Drug sellers in 68 pharmacies (34 intervention and 34 control) -Private	**Pharmacies**	**Hanoi** Cluster RCT with before and after measurement	**Hanoi I:*** Regulation enforcement * Educational visits: * Peer influence: peer review **C:** Routine care	**Hanoi** simulated clients methods- trained clients visited pharmacies to assess pharmacy worker performance	**Hanoi and Bangkok** Total of all outcomes: 29 -Antibiotic related outcomes: 8	Random sequence generation, low risk; Allocation concealment, low risk; Blinding of participants and personnel, low risk; Blinding of outcome assessment, low risk; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, low risk
		Thailand * Drug sellers in 78 pharmacies (39 intervention and 39 control) -private	**Pharmacies**	**Bangkok** Cluster RCT with before and after measurement	**Bangkok I:** * Regulation enforcement * Educational visits and seminars * Peer influence; peer review with peer facilitators **C:** Usual services	**Bangkok** Simulated clients methods- trained clients visited pharmacies to assess pharmacy worker performance*Follow-up duration: each interventions were assessed for 3 months after 3 months of implementation		
5. Chowdhury et al., 2018 [29]	Antibiotic dispensing practices	*Drug sellers in 100 pharmacies *Private -Bangladesh	**Pharmacies**	Before and after study	**I:*** Development of treatment guidelines for drug sellers.* Educational intervention (training manuals, posters, leaflet on ARI treatment algorithm)	*Structured questionnaire was administered to drug sellers *Simulated clients-trained simulated clients visited pharmacies to assess pharmacy worker performance *Follow-up duration: interventions were assessed for 1 year after 6 months of implementation	-Total of all outcomes: 29-Antibiotic related outcomes: 7	Population of interest, yes; Outcomes assessed and reported, yes; Measurement same for all subjects, yes; Confounding controlled, yes; Intervention, yes
6. Garcia et al., 2003 [25]	Recognition, management, and prevention of STDs	-Pharmacy workers in 24 districts (Intervention:220 and Control :220) -Private -Peru	Pharmacy workers	Cluster RCT with repeated after measurements (at one, three, and six months)	**I:*** Seminars/Training* Provision of merchandise and educational materials* Referral Networks * Monthly follow-up visits **C:** * One day seminar on treatment of diarrhoea	* Simulated clients methods-trained simulated clients visited pharmacies to assess pharmacy worker performance *Follow-up duration: interventions were assessed for 6 months after 2 months of implementation	-Total of all outcomes: 36-Antibiotic related outcomes:9	Random sequence generation, low risk; Allocation concealment, low risk; Blinding of participants and personnel, low risk; Blinding of outcome assessment, low risk; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, low risk

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Table 2 (*continued*)

Author, publication year [reference]	Topic	Participants, setting, country	Units of analysis	Study design (cRCT, ITS etc)	Description of intervention (I)/Comparison (C)	Methods of data collection and follow-up duration	Predefined endpoints (see Appendix S1 (all endpoints) and Table 3 (antibiotic endpoints only) for detailed information)	Study quality
7. Kafle et al., 1998 [26]	Safe Dispensing, Correct Advice, and Appropriate Referral for Diarrhoea, ARI, and Pregnancy	-342 drug retailer -Private-Nepal	Drug retailers	Cluster RCT with before and after measurement	**I-1:** * Small group training *Reinforcement materials **I-2:** * Audit and feedback **I-3:** * Mailed printed educational materials **C:** Routine care	*Simulated client method-trained simulated clients visited drug retailers to assess their performance * Structured questionnaire for exit interviews with patients *Follow-up duration: interventions were assessed for two months after five months of implementation	-Total of all outcomes: 68 -Antibiotic related outcomes:5	Random sequence generation, low risk; Allocation concealment, low risk; Blinding of participants and personnel, low risk; Blinding of outcome assessment, low risk; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, unclear
8. Kafle et al., 2001 [33]	Prescribing practices for acute diarrhoea, Pneumonia, acute respiratory infection; scabies, pyrexia of unknown origin and antibiotics prescribing	80 prescribers in health post -public -Nepal	Health post	Cluster RCT with before and after measurement	**I:** * Action-oriented, small group, face-to-face training * Reinforcement educational materials * Peer group discussion using self-assessment findings **C:** Routine care	*Carbon copies of prescription pads collected monthly from health post *Follow-up duration: interventions were assessed for 2 months after 6 months of implementation	-Total of all outcomes: 32 -Antibiotic - related outcomes:17	Random sequence generation, low risk; Allocation concealment, low risk; Blinding of participants and personnel, low risk; Blinding of outcome assessment, low risk; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, unclear
9. Kitutu et al., 2017 [30]	Integrated community case Management of paediatric febrile illness (pneumonia, malaria, diarrhoea) by drug sellers	*84 drug shops (61 intervention, 23 control) *553 care-seeker exit interviews (285 intervention and 268 control)-Private -Uganda	Care-seekers encounters	Before and after study	**I:** (1) selection, training and work activities of drug sellers, (2) provision of information, education, information and communication, (3) supply mechanism by study team in partnership with pharmaceutical wholesalers for diagnostics (malaria RDT and respiratory rate counters) and medicines (ACT, amoxicillin dispersible tablets (DT) and zinc sulphate/ORS), (4) monthly support supervision done by study field supervisor	* Structured questionnaire for exit interviews with care seekers Follow-up duration: interventions were assessed for 2 months after 14 months of implementation	-Total of all outcomes: 16 -Antibiotic related outcomes:5	Population of interest, yes; Outcomes assessed and reported, yes; Measurement same for all subjects, yes; Confounding controlled, yes; Intervention, yes

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Table 2 (*continued*)

Author, publication year [reference]	Topic	Participants, setting, country	Units of analysis	Study design (cRCT, ITS etc)	Description of intervention (I)/Comparison (C)	Methods of data collection and follow-up duration	Predefined endpoints (see Appendix S1 (all endpoints) and Table 3 (antibiotic endpoints only) for detailed information)	Study quality
10. Mandal, 2013 [31]	Rational use of Medicines in the Community	-10 Community pharmacies-30 prescriptions each from the same 10 pharmacies before and after intervention-stakeholders in healthcare system -Private-India	Prescriptions records in community pharmacies	Before and after study	**I:*** Workshop/seminars	Collection of prescriptions forms from community pharmacies Follow-up duration: not reported	-Total of all outcomes: 6 -Antibiotic related outcomes:1	Population of interest, no; Outcomes assessed and reported, no; Measurement same for all subjects, yes; Confounding controlled, no; Intervention, yes
11. Nsimba, 2007 [32]	Management of malaria and other childhood illnesses	-40 drugstores (20 intervention, 20 control) -Private-Tanzania	Drug sellers	Cluster RCT with before and after measurement	**I:** * Educational interventions (posters, individual information and a one-to-one training sessions) **C:** * Only posters	*Simulated clients methods-trained simulated clients completed records forms after each encounter with drug sellers *Structured questionnaire for exit interviews with care seekers Follow-up duration: interventions were assessed for 1 month after 6 months of implementation	-Total of all outcomes: 15-Antibiotic related outcomes:3	Random sequence generation, low risk; Allocation concealment, low risk; Blinding of participants and personnel, unclear; Blinding of outcome assessment, unclear; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, low risk

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Table 2 (*continued*)

Author, publication year [reference]	Topic	Participants, setting, country	Units of analysis	Study design (cRCT, ITS etc)	Description of intervention (I)/Comparison (C)	Methods of data collection and follow-up duration	Predefined endpoints (see Appendix S1 (all endpoints) and Table 3 (antibiotic endpoints only) for detailed information)	Study quality
12. Ross-Degnan et al., 1996 [27]	Diarrhea treatment in pharmacies	**Kenya** * 90 pharmacist and 162 counter attendants in 107 private Pharmacies. Group 1- 58 received training. In phase I, Group 2- 24 acted as control in phase I but were trained in phase II. Group III-25 received no training and acted as control throughout * 128/109 pharmacy attendants before and after training. -Private	Pharmacies, pharmacist and counter attendants	**Kenya** Controlled before after design	**Kenya I**: * Educational material * Interactive training sessions **C:** Routine care	**Kenya** *Surveys/interviews with pharmacy owners, pharmacist and counter attendants * Simulated clients methods-Trained simulated clients posed as mothers *FGD with pharmacist and counter attendants Follow-up duration: interventions were assessed for 1 month after 1 month of implementation	**Kenya and Indonesia** -Total of all outcomes: 16 -Antibiotic related outcomes:2	Random sequence generation, high risk; Allocation concealment, low risk; Blinding of participants and personnel, low risk; Blinding of outcome assessment, low risk; Incomplete data outcome, low risk; Selective reporting, unclear; Other bias, unclear
		Indonesia * 87 private pharmacies (intervention=43, control=44)- Private	Pharmacies, pharmacist and counter attendants	**Indonesia** Controlled before after design	**Indonesia I**: * Printed educational material **C:** Routine care	**Indonesia** *Surveys/interviews with pharmacy owners, assistant pharmacist and counter attendants * Simulated clients methods-trained clients posed as mothers *FGD with pharmacist and counter attendants follow-up duration: interventions were assessed for 1 month after 1 month of implementation		
13. Valimba et al., 2014 [3]	Antimicrobial use	-124 accredited dispensers, 84 healthcare providers and 8 health management team members - public and private -Tanzania	Drug dispensers in accredited drug dispensing outlet and customers	Before and after study	**I:** * Job aids and educational materials * Sensitization seminars * Training and on-site supervisory monitoring visits	-Exit interviews with drug shop clients -Direct observation of clients at drug shops -Review of dispensing records at drug shops Follow-up duration: interventions were assessed for 1 month after 11 months of implementation	-Total of all outcomes: 21 -Antibiotic related outcomes:8	Population of interest, yes; Outcomes assessed and reported, yes; Measurement same for all subjects, partial; Confounding controlled, no; Intervention, yes

NOTE: Chalker et al., 2002 and Chuc et al., 2002 are two papers from the same study but reported on different outcomes.

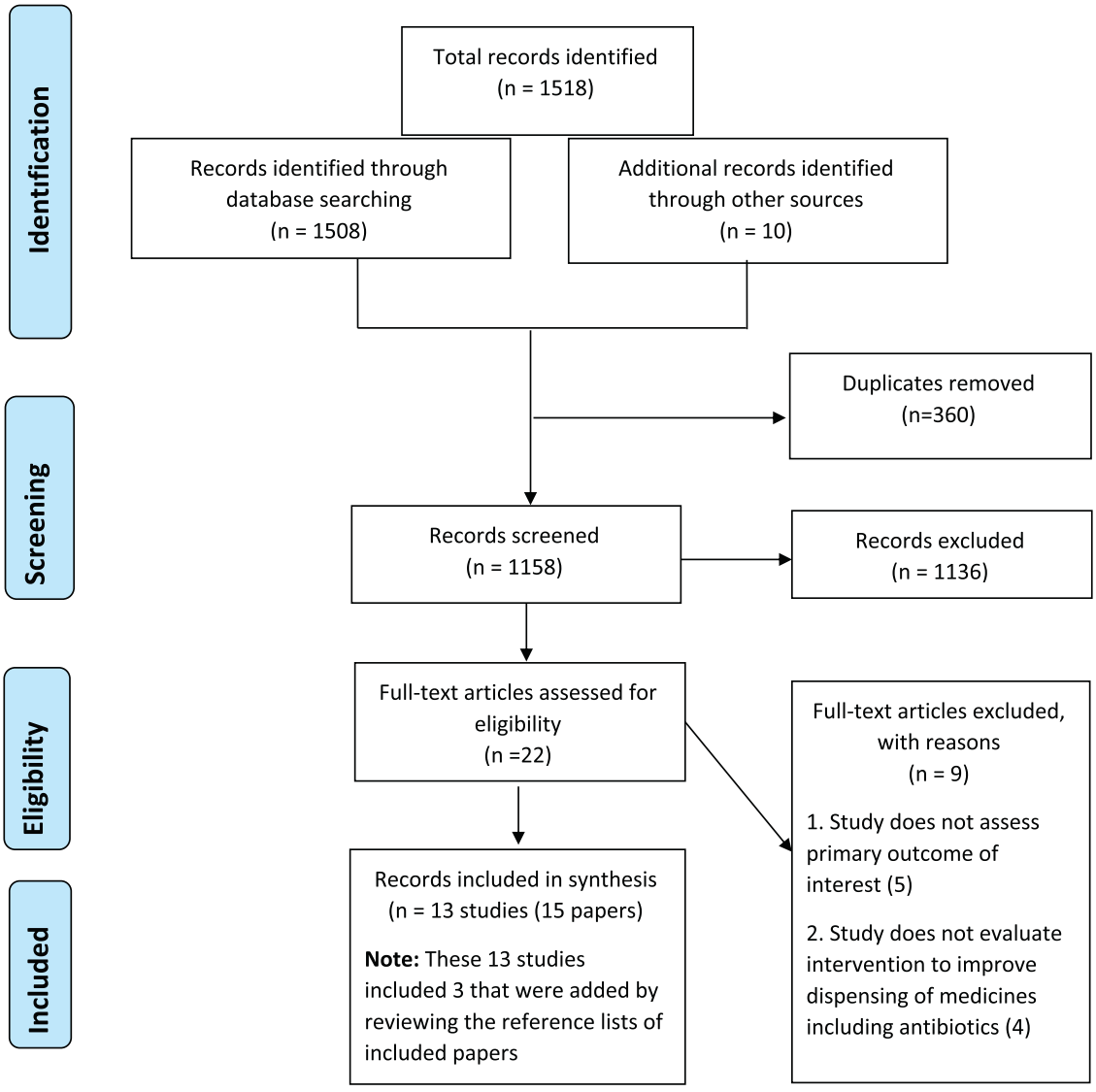

Fig. 1. PRISMA flow diagram.

3. Results

3.1. Search results

A total of 1508 papers were initially identified through the database searches. In addition, 10 papers we identified through the Google search. After removing duplicates, 1158 papers remained for screening. Following screening of titles and abstracts, 22 potentially relevant studies were selected for full-text screening, out of which 13 studies (15 papers) met the inclusion criteria (Fig. 1).

3.2. Characteristics of studies

Studies in this review (Table 2) were conducted in Asia (Vietnam (n=1), Vietnam and Thailand (n=1), Nepal (=2), Bangladesh (n=1), India (n=1)), Africa (Ghana (n=1), Tanzania (=2), Uganda (n=2)) and South America (Peru (n=1)). One study was conducted in both Africa (Kenya) and Asia (Indonesia). Out of the 13 intervention studies, 10 were conducted in private OTCMS shops or community pharmacies [9,10,19,24–32], two were conducted in public CHPs among community health workers [20,33], and one was conducted in both private OTCMS shops and public/private CHP settings [3] (Table 2). Seven out of the 13 studies [9,10,19,24–27,32,33] were RCTs and generally rated as 'good quality', which shows that the trials/studies largely reported low risk of bias for relevant study indicators. Six were observational studies [3,20,28–31] including three pre and post studies, two quasi-experimental studies and one longitudinal time series. Three of the six observational studies were rated as poor-quality studies with high risk of bias [3,20,31].

3.3. Outcome measures and effectiveness of studies

3.3.1. Appropriate dispensing of antibiotics

All the 13 studies included in this review focused on outcomes that are related to appropriate dispensing of medicine including antibiotics. The number of predefined endpoints per study varied between 2 [20] and 68 [26] outcomes, with antibiotic-related outcomes varying between 1 [31] and 17 [33]. Table 3 provides results as reported in the included studies and the summary of effectiveness scores for antibiotics dispensing related outcomes only. All studies reported positive effects following intervention. Four (30.8%) out of the 13 studies reported statistically significant effect of the intervention on all outcomes measured [9,10,20,24,27,28].

Table 3
Summary of results on antibiotic related outcomes reported in studies.

Author, publication year [reference] and topic	Outcome measure related to antibiotic use	Intervention group (Before and after where applicable)	Control group (Before and after where applicable)	Statistic	Overall effectiveness
1. Adu-Sarkodie et al., 2000 [19]	*Appropriateness of treatment offered for urethral discharge				1 out of 6 predefined antibiotic use endpoints (16.7%) improved after intervention Interventions were effective on <50 of outcomes
Syndromic management of urethral discharge in Ghanaian pharmacies	1. Total correct drug dose	27%	13%	NS	
	2. Total acceptable drug provision	39%	18%	$P < 0.05$	
	*Appropriateness of treatment offered for gonorrhoea				
	3. Total correct drug dose	41%	31%	NS	
	4. Total acceptable drug provision	76%	64%	NS	
	*Appropriateness of treatment offered for chlamydia				
	5. Total correct drug dose	32%	23%	NS	
	6. Total acceptable drug provision	41%	31%	NS	
2. Awor et al., 2014 [28] Increased Access to Care and Appropriateness of Treatment at Private Sector Drug Shops with Integrated Management of Malaria, Pneumonia and Diarrhoea	*Management of children with cough and fast breathing (pneumonia)				7 out of 7 predefined antibiotic use endpoints (100 %) improved after intervention Interventions were effective on all outcomes Note: PR is the prevalence ratio
	1. Amoxicillin dispensed	0%, 75.3%	0%, 26.7%	$P < 0.0001$	
	2. Respiratory timer used and amoxicillin dispensed	0%, 49.3%	0%, 0%	$P < 0.000$	
	*Treatment using antibiotics, ACTs and ORS/zinc				
	3. Children with pneumonia treated with amoxicillin (5–7 days)	0%, 75.3%	0%, 26.7%	PR-2.8 (2.0–3.9)	
	4. Children with pneumonia treated with cotrimoxazole	79.2%, 2.7%	37.5%, 24.4%	PR- 0.07 (0.01–0.39)	
	5. Overall antibiotic use	45.0%, 60.0%	65.1%, 73.5%	PR- 0.82(0.69–0.97)	
	6. Cotrimoxazole treatment	43.5%, 21.0%	65.2%, 55.8%	PR- 0.45 (0.27–0.74)	
	7. Amoxicillin treatment	31.5%, 25.6%	30.8%, 28.7%	PR- 0.82 (0.58–1.2)	
3. Chalker 2001 [20] Improving antibiotic prescribing	**1. Patients receiving an antibiotic as part of their prescription**	69%	43%	$P < 0.05$	2 out of 2 predefined antibiotic use endpoints (100%) improved after intervention interventions were effective on all outcomes
	2. Patients who received in adequate dose	30%	98%	$P < 0.01$	

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Table 3 (*continued*)

Author, publication year [reference] and topic	Outcome measure related to antibiotic use	Intervention group (Before and after where applicable)	Control group (Before and after where applicable)	Statistic	Overall effectiveness
4. Chalker et al., 2002 [9], Chalker et al., 2005 [10] and Chuc et al., 2002 [24] Multi component intervention to improve private pharmacy dispensing practices	**Hanoi (all interventions)** Sexually transmitted disease: Urethral discharge				8 out of 8 predefined antibiotic use endpoints (100 %) improved after intervention Interventions were effective on all outcomes
	*Treatment				
	1. Antibiotics	16%, 9%	11%, 36%	***P* = 0.02**	
	2. Traditional medicine	5%, 57%	14%, 23%	***P* = 0.03**	
	*Sell cefalexin with no prescription				
	3. Sell antibiotics	57%, 20%	45%, 61%	***P* = 0.02**	
	*ARI case management				
	4. Antibiotics dispensed	45%, 30%	39%, 42%	***P* = 0.023**	
	*Cefelexin request				
	5. Cefalexin dispensed	95%, 56%	94%, 89%	***P* = 0.002**	
	6. Prescription request	0%, 21%	0%, 2%	***P* = 0.009**	
	7. Received requested antibiotics	Baseline- 99%	Baseline- 97%	$P = 0.1625$	
		Post regulatory 98%	Post regulatory-98%	$P = 0.7389$	
		Post educational 69%	Post educational 90%	***P* = 0.0471**	
		Post peer review 71%	Post peer review 95%	***P* = 0.0125**	
	8. Ask no questions gave no advice for low-dose antibiotic request	Baseline: 70%	Baseline: 73%	$P = 0.6027$	
		Post regulatory 77%	Post regulatory 77%	$P = 0.9597$	
		Post educational 45%	Post educational 71%	***P* = 0.0025**	
		Post peer review 51%	Post peer review 81%	***P* = 0.0028**	
	Bangkok (all interventions)				
	*Received requested antibiotics	Baseline- 76%	Baseline- 75%	$P = 0.8925$	
		Post regulatory- 58%	Post regulatory-67%	$P = 0.3770$	
		Post educational-92%	Post educational-95%	$P = 0.4795$	
		Post peer review- 88%	Post peer review -92%	$P = 0.5525$	
	*Ask no questions gave no advice for low-dose antibiotic request	Baseline- 82%	Baseline- 86%	$P = 0.4165$	
		Post regulatory- 89%	Post regulatory-91%	$P = 0.5526$	
		Post educational- 87%	Post educational- 87%	$P = 0.9447$	
		Post peer review - 72%	Post peer review 81%	$P = 0.1927$	
5. Chowdhury, 2018 [29] Effectiveness of an educational intervention to improve antibiotic dispensing practices	* Antibiotic dispensing and referral for acute respiratory infections (ARI)				5 out of 7 predefined antibiotic use endpoints (71.4%) improved after intervention interventions were effective on ≥50% of outcomes
	1. Children with uncomplicated ARI	30%, 21%	-	***P* = 0.04**	
	2. Children with complicated ARI	15%, 17%	-	$P = 0.06$	
	3. Adults with uncomplicated ARI	48%, 40%	-	$P = 0.1$	
	4. Adults with complicated ARI	44%, 78%	-	***P* = 0.01**	
	* Drug sellers' advice on ARI				
	5. Recommended advice in ARI guidelines	5%, 29%	-	***P* = 0.01**	
	6. Take antibiotics according to physician's prescription	11%, 0%	-	***P* = 0.01**	
	7. Take antibiotics if not cured after initial treatment	39%, 7%	-	***P* = 0.001**	

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Table 3 (*continued*)

Author, publication year [reference] and topic	Outcome measure related to antibiotic use	Intervention group (Before and after where applicable)	Control group (Before and after where applicable)	Statistic	Overall effectiveness
6. Garcia et al., 2003 [25] Training pharmacy workers in recognition, management, and prevention of STDs	Pilot evaluation of pharmacy workers on adherence to guidelines				5 out of 9 predefined antibiotic use endpoints (55.6%) improved after intervention
	*Urethral discharge				
	1. Adequate management of the syndrome	82.5%, 25%	-	**$P < 0.001$**	interventions were effective on ≥50% of outcomes
	*Genital ulcer				
	2. Recognition of STD symptoms	95%, 53.8%	-	**$P < 0.001$**	
	3. Adequate management of the syndrome	67.5%, 20.8%	-	**$P < 0.001$**	
	*Vaginal discharge				
	4. Adequate management of the syndrome	40%, 20%	-	**$P = 0.001$**	
	*Pelvic inflammatory disease				
	5 Adequate management of the syndrome	50%, 9.7%	-	**$P < 0.001$**	
	Main evaluation of pharmacy workers				
	*Urethral discharge				
	6. Adequate management of the syndrome	80%, 30%	-	NR	
	*Genital ulcer				
	7. Adequate management of the syndrome	80%, 25%	-	NR	
	*Vaginal discharge				
	8. Adequate management of the syndrome	70%, 24%	-	NR	
	*Pelvic inflammatory disease				
	9. Adequate management of the syndrome	70%, 20%	-	NR	
7. Kafle et al., 1998 [26] Action-Oriented Training and/or Mailed Print Material on Retailer Practices	*Dispensing practices for diarrhoea				1 out of 5 predefined antibiotic use endpoints (20.0%) improved after intervention interventions were effective on <50% of outcomes
	1. Antimicrobial product dispensed	55.8%, 45%	59.3%, 30%	NS	
	2. Single antimicrobial dispensed	45.3%, 54.0%	45.3%, 30%	NS	
	3. Multiple antimicrobials dispensed	10.5%, 3.8%	14%, 3.8%	NS	
	*Dispensing practices for pneumonia				
	4. Antibacterials	18.6%, 28.8%	32%, 17.5%	**$P = 0.003$**	
	5. Co-trimoxazole	8.1%, 17.5%	7.0%, 8.8%	NS	
8. Kafle et al., 2001 [33] Test of strategies for implementing STS in improving use of drugs	*Prescribing practices for diarrhoea in children				**3 out of 17 predefined antibiotic use endpoints (17.6%) improved after intervention interventions were effective on <50% of outcomes**
	1. ORS + Antimicrobials	53.6%, 28.6%	61.4%, 75%	P = NS	
	2. Antimicrobials + other drugs	28.6% 3.6%	11.4%, 18.3%	P = NS	
	*Prescribing practices for pneumonia in children				
	3. Cotrimoxazole alone	5.3%, 10.9%	25.7%, 0%	**$P = 0.016$**	
	4. Cotrimoxazole + Paracetamol	31.6%, 58.9%	37.1%, 63.6%	**$P = 0.043$**	
	5. Cotrimoxazole + other drugs	5.3% 7.8%	8.6%, 9.1%	P = NS	
	6 Amoxycillin alone	0%, 0%	2.9%, 0%	P = NS	
	7. Amoxycillin + Paracetamol	15.8%, 6.2%	0%, 4.5%	P = NS	
	8. Amoxycillin + other drugs	5.3%, 3.9%	0%, 4.5%	P = NS	
	9. Antibiotics other than Amoxycillin and co-trimoxazole	36.8%, 12.4%	25.7%, 18.2%	P = NS	
	*Practices for no pneumonia in children				
	10. Antibiotics	92.9%, 37.5%	60%, 54.5%	P = NS	
	*Prescribing practices for scabies				
	11. Benzylbenzoate alone	12.5%, 23.2%	14.8%, 5.3%	**$P = 0.007$**	
	12. Benzylbenzoate + antibiotic	34.1%, 21.1%	36.3%, 40.7%	P = NS	
	13. Antibiotics + other drugs	17.1%, 16.8%	26.8%, 26%	P = NS	
	*Prescribing practices for pyrexia of unknown origin				
	14. Antibiotics alone	5.9%, 0%	0%, 3.6%	P = NS	
	15. Antibiotics + other drugs	47.1%, 13.3%	66.7%, 77.6%	P = NS	
	16. Antimalarial + Antibiotics	0%, 0%	6.7%, 14.1%	P = NS	
	*Average number of drugs and percentages of antibiotics				
	17. Encounters receiving antibiotic	54%, 54%	56%, 67%	P = NS	

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Table 3 (*continued*)

Author, publication year [reference] and topic	Outcome measure related to antibiotic use	Intervention group (Before and after where applicable)	Control group (Before and after where applicable)	Statistic	Overall effectiveness
9. Kitutu, 2017 [30] Integrated community case management by drug sellers	*Provision of ACTs, amoxicillin and diarrhoea treatment				3 out of 5 predefined antibiotic use endpoints (60.0%) improved after intervention interventions were effective on ≥50 of outcomes
	1. Provision of DT amoxicillin for suspected pneumonia symptoms	4.8%, 93.2%	3.1%, 0%	**$P < 0.001$**	
	* Integrated community case management on antimicrobial medicine use linear trend				
	2. DT amoxycillin	54%, 50%	-	**$P = 0.001$**	
	3. Either ACTs, DT amoxycillin or both	80%, 70%	-	**$P < 0.001$**	
	Nonlinear trend				
	4. DT amoxycillin	56%, 33%	-	$P = 0.587$	
	5. Either ACTs, DT Amoxycillin or Both	81%, 50%	-	$P = 0.769$	
10. Mandal, 2013 [31] Improving use of medicines in the community through Interventions for Cost effective treatment	1. Percentage of prescriptions for antibiotics	54.33%, 34.66%	-	$P =$ not reported	Authors reported that the outcome improved 'significantly', the exact *P*-value was not reported
11. Nsimba, 2007 [32] Assessing the impact of educational intervention	*Knowledge on medicines dispensed				2 out of 3 predefined antibiotic use endpoints (66.7%) improved after intervention interventions were effective on ≥50% of outcomes
	1. Give cotrimoxazole for all types of diarrhoea	20%	55%	**$P < 0.01$**	
	2. Give ampicillin syrup for simple cough	40%	55%	**$P < 0.01$**	
	3. Give any antibiotics for colds	55%	60%	$P =$ NS	
12. Ross-Degnan, 1996 [27] The impact of face-to-face educational outreach on diarrhoea treatment	**Kenya and Indonesia**				2 out of 2 predefined antibiotic use endpoints (100%) improved after intervention interventions were effective on all outcomes
	*Impact of training on knowledge				
	1. Signs of bacterial aetiology	1.54, 1.72	-	**$P < 0.05$**	
	2. Antibiotics useful only to treat diarrhoea	0.34, 0.54	-	**$P < 0.01$**	
13. Mainous et al., 2014 [3] Engaging the private sector to improve antimicrobial use	*Appropriate treatment of common health conditions				7 out of 8 predefined antibiotic use endpoints (87.5%) improved after intervention interventions were effective on ≥50% of outcomes
	1. Did not dispense antibiotics for non-bloody diarrhoea	63%, 88%		**$P = 0.0002$**	
	2. Did not dispense antibiotics for acute upper respiratory infection	73%, 89%	-	**$P = 0.0088$**	
	* Listing factors contributing to antimicrobial resistance				
	3. Incomplete course	88%, 100%	-	**$P < 0.05$**	
	4. Insufficient amount of medicine	66%, 89%	-	**$P < 0.05$**	
	5. Poor quality of medicine	49%, 74%	-	**$P < 0.05$**	
	6. Wrong medicine	44%, 91%	-	**$P < 0.05$**	
	7. Nonadherence	7%, 3%	-	NR	
	8. Take someone else's medicine	6%, 94%	-	**$P < 0.05$**	

In one of such studies, patients who received antibiotics in adequate dose increased from 30% to 98% as a result of interventions to improve the use and dosage of antibiotics prescribed at community health stations in Vietnam [20]. Five (38.5%) studies reported significant effect of the interventions on 50% or more of the outcomes measured [3,25,29,30,32]. For example, dispensing of cotrimoxazole for all types of diarrhoea and ampicillin syrup for simple cough reduced from 55% to 20% and 55% to 40%, respectively, following interventions to improve the management of malaria and other childhood illnesses in Tanzania [32]. Also, three (23%) studies reported effectiveness of interventions on less than 50% of the outcomes measured [19,26,33]. In one study (7.7%), though the level of significance was not reported, prescriptions for antibiotics reduced from 54.33% to 34.66% as a result of interventions to improve rational use of medicines in India [31] (Table 3).

Supplementary Appendix S2 shows the dispensing of all medicines including antibiotic-related outcomes. Similarly, all studies reported positive effects following intervention with slightly different summary of effectiveness scores. Out of the 13 studies, one (7.7%) reported statistically significant effect of the interventions on all outcomes measured [20]. Seven studies (50%) reported significant effect of the interventions on 50% or more than half of the outcomes measured [3,9,10,24,25,27,28,30,32], and four (28.6%) reported effectiveness of interventions on less than half of the outcomes measured [19,26,29,33]. One study did not report the level of significance for the effect of intervention on outcomes measured [31].

3.4. Single and multiple interventions to improve antibiotic dispensing practices

Table 4 provides an overview of the 14 different interventions performed in the 13 included studies according to the EPOC taxonomy [34]; only two studies tested a similar, single intervention [19,31]. Interventions frequently applied were educational meetings (9/13), distribution of educational materials (7/13), educational outreach meetings (7/13), reminders (6/14), procurement and distribution of supply (6/13), clinical practice guideline (4/13) and local consensus processes (4/13). There does not seem to be a relation between number of interventions implemented and degree of effectiveness.

Two studies applied a similar single intervention, i.e., an educational meeting (EPOC). The first study, conducted in India, sought to improve rational use of drugs including antibiotics [31]. This was a before-and-after comparison study among 10 community pharmacies using a workshop/seminar. In this study, the reported proportion of prescriptions of antibiotics reduced from 54.3% to 34.7%. Another study conducted in Ghana involved the training of pharmacy workers and OTCMSs in the syndromic management of sexually transmitted infections [19]. This was a randomised controlled study with after-intervention measurements among 50-intervention and 50-control pharmacy workers and OTCMSs. The intervention was effective on less than 50% of outcomes measured (1/6, 16.7%) (Table 3).

Twelve out of the 13 included studies applied multiple interventions to improve antibiotic-dispensing practices. The number of interventions that were combined and evaluated ranged from two to eight per study (Table 4). A study conducted in Vietnam applied eight EPOC strategies: a clinical practice guideline, educational meetings, local consensus process, monitoring of performance, procurement and distribution of supplies, mass media campaign-community and audit and feedback [20]. This study reported effectiveness of interventions on all the outcomes measured (2/2, 100%) (Table 4). Another study conducted among drug-dispensing outlets in Tanzania applied seven EPOC interventions including a clinical practice guideline, educational meetings, distribution of educational materials, educational outreach visits, monitoring of performance, procurement and distribution of supplies and reminders [3]. This study also reported effectiveness of the interventions on almost all outcomes measured (7/8, 87.5%) (Table 4).

3.5. Stakeholder involvement in intervention development

Eight out of 13 studies reported on stakeholder involvement in the development of study interventions, with four studies reporting antibiotic-related summary of effectiveness scores of 100% [9,10,20,24,27,28], five studies reporting scores varying between 55% and 87% [3,25,29,30,32] and three studies reporting scores varying between 16% and 20% [19,26,33]; one study did not report a *P*-value for the 'significant' improvement [31] (Table 3). Stakeholders involved in the various studies included international organisations, health system personnel (from the national to district levels), professional associations, academics, health trainees and OTCMS associations.

3.6. Analysis performed for developing intervention

Four studies indicated that an analysis was performed to inform the development of the interventions with effectiveness scores varying between 18% and 100% [3,27,29,33] (Supplementary Appendix S3). The development of interventions was premised mainly on stakeholder consultation/engagement and baseline studies/assessment. A study from Nepal used qualitative findings from a formative study to develop intervention materials [33]. In Tanzania, findings from a baseline study were also used to develop training programs [3].

3.7. Determinants of success or failures of interventions

Only one study conducted in Vietnam and Thailand performed a subgroup analysis to explore determinants of success or failure [9,10,24] (Supplementary Appendix S3). In Thailand, participation in the peer review (one of the three intervention components) was voluntary. Staff from 18 of the intervention pharmacies took part, and 16 did not. The analysis was done for the whole intervention group and separately for the participants. Comparing the whole intervention group to the control group, there were no differences or significant improvements in the two antibiotic-related outcomes following the three components' intervention. Looking only at the intervention group that participated in the peer review and comparing them to controls, there was a significant effect for asking questions and giving advice, one of the two antibiotic-related outcomes.

Three studies described determinants that positively influenced the success of study interventions [9,10,20,24,27]. The main reported determinant of success revolved around the involvement of stakeholders including study participants in the design and implementation of interventions. For example, one of the studies conducted in Kenya and Indonesia reported stakeholders' involvement contributed to the positive effect of study interventions [27]. Another study, showing overall effect in Vietnam but not in Thailand, specified the baseline level of knowledge of study participants as the determinant of relative effectiveness of the educational intervention component in Vietnam [9,10,24] (Supplementary Appendix S3).

On the other hand, two studies reported reasons that might explain why interventions were not effective on some of the study outcomes. A study conducted in Bangladesh reported that interventions were effective on less than half of outcomes measured possibly because drug sellers did not follow the dispensing guidelines developed by the study. Drug sellers feared that referring customers could affect the business and relationship with customers

Table 4
EPOC interventions applied in included studies.

→ EPOC strategies (n=14) ↓ Studies/papers (n=14 studies, 15 papers)	Managerial supervision (n=1)	Clinical practice guideline (n=4)	Educational materials (n=7)	Educational meeting (n=9)	Educational outreach visits (n=6)	Local consensus processes (n=4)	Monitoring of performance (n=3)	External funding (n=3)	Procurement and distribution of supplies (n=6)	Reminders (n=6)	Referral systems (n=1)	Continuous quality improvement (n=1)	Mass media campaign , community (n=2)	Audit and feedback (n=2)	**Effectiveness of interventions on antibiotic related outcomes reported in studies**
Adu-Sarkodie et al, 2000[19]				■											Interventions were effective on < 50 of outcomes (16.7%)
Mandal, 2013[31]				■											Level of significance were not reported
Nsimba, 2007[32]					■					■					Interventions were effective on ≥ 50% of outcomes (66.7%)
Awor et al, 2014[28]				■				■					■		Interventions were effective on all of outcomes (100 %)
Kafle et al, 2001[33]			■			■				■					Interventions were effective on < 50% of outcomes (17.6%)
Kitutu, 2017[30]	■			■					■						Interventions were effective on ≥ 50% of outcomes (60.0%)
Ross-Degnan, 1996[27]			■		■				■	■					Interventions were effective on all of outcomes100%)
Chowdhury, 2018 [29]		■	■	■		■				■					Interventions were effective on ≥ 50% of outcomes (71.4%)
Kafle et al, 1998[26]			■		■				■	■				■	Interventions were effective on < 50% of outcomes (20.0%)
Garcia et al, 2003[25]			■	■	■			■	■		■				Interventions were effective on ≥ 50% of outcomes (55.6%)
Valimba et al, 2014[3]		■	■	■	■		■		■	■					Interventions were effective on ≥ 50% of outcomes (87.5%)
Chalker et al, 2005[10], Chalker et al, 2002[9] & Chuc et al, 2002[24] (Three papers from one study)		■	■	■	■	■	■					■			Interventions were effective on all outcomes (100%)
Chalker, 2001[20]		■		■		■	■	■	■				■	■	Interventions were effective on all of outcomes (100 %)

as they were unable to meet customer demands for antibiotics [29]. Another study—showing overall effect in Vietnam but not in Thailand—attributed the failure to less focused interventions in the Thailand study settings [9,10,24] (Supplementary Appendix S3).

3.8. Study follow-up duration

In 11 out of the 14 studies, interventions were followed up for 1–6 months after 2–14 months of implementation. The follow-up period for one of the studies was not reported. In one study, the interventions were followed up throughout the study period for 6–24 months, and data collected after a year showed that the intervention effects were stable for 17 months after the study had ended. In another study, the interventions were followed up for one year after six months of implementation (Table 2).

4. Discussion

This review shows that it is possible to improve the dispensing of medicines including antibiotics at the community level in LMIC. With regard to only antibiotics dispensing related outcomes, 9 (69.2%) of 13 studies reported significant effects of interventions on all (30.8%) or ≥50% (38.4%) of the outcomes measured. Similarly, for the dispensing of all medicines including antibiotics, 8 (61.5%) of 13 studies reviewed reported significant effects of the intervention on all (7.7%) or ≥50% (53.8%) of the outcomes measured. Various interventions ranging from a single educational intervention to multiple interventions consisting of as many as eight components were effective. It is therefore important to note that it is not possible to select a magic bullet that will most certainly work, hence the need for tailoring to context.

Nine intervention studies evaluated educational meetings including workshops and training [34] with the focus of improving dispensing practices. Educational and training interventions are largely proven to be effective strategies for improving the practices of professionals/non-professionals in diverse fields, with larger effects with higher attendance rates and interactive components, and smaller effects for complex behaviours [35]. Some reviewed studies concluded that educational and training interventions have the potential of improving the dispensing practices of informal medicine sellers including the sale of antibiotics without prescription, which is against regulations in LMIC [25,27,28,30]. In LMIC where there is inadequate supervision and regulatory enforcement, educational interventions for OTCMSs and community pharmacies could be useful when sustained beyond the research phase [21].

There was no evidence to suggest that multiple interventions were more effective than single interventions. Other interventions that emerged from our review include distribution of educational materials, educational outreach meetings, reminders, clinical practice guidelines, local consensus processes, procurement and distribution of supply and monitoring of performance. When selecting interventions, context should be taken into account by tailoring the intervention to local barriers, available resources and other practical considerations [35]. These interventions are worth considering for implementation in LMIC where weak regulation is a structural challenge to the sale of non-prescription medicines including antibiotics [21,36].

There is the need for follow-up to check on sustainability of intervention effects and to consciously roll out these interventions into policy. Follow-up to evaluate the long-term effectiveness of interventions is important because it enables implementers to know whether the interventions have met their objectives and to evaluate the determinants of success or failure of interventions [37,38]. It is therefore important to consider the study context and intervention types vis-à-vis the duration of follow-up to determine the effectiveness of interventions. The interventions in two of the included studies were followed up for a year or more. The follow-up period for the remaining studies was less than a year, which is generally considered inadequate [39]. An assessment of intervention relatively soon after implementation may show positive effects but dwindles after a long time as participants may return to their usual practices, though sometimes it takes a lot of time to change performance.

Our review highlights the importance of stakeholders' engagement in the development of interventions to improve dispensing practices and as a determinant of effectiveness of intervention studies. The involvement of stakeholders helps to contextualise interventions and gives a sense of ownership to potential implementers within the health system. The involvement of stakeholders at all levels is therefore likely to ensure the sustainability of interventions especially beyond the research phase [40]. The involvement of study participants in the implementation of interventions promotes acceptance and the willingness to participate [3].

5. Limitations

This review is a synthesis of evidence based on reported findings in the included studies. A meta-analysis was not conducted as results from reviewed studies could not be statistically analysed due to substantial differences in strategies implemented and outcomes used. Included studies evaluated unique interventions while using different numbers and types of outcome measures. This review therefore also shows the need for using similar outcome measures across studies to make results of intervention studies comparable and reproducible. Such standardisation will aid the synthesis of evidence to inform the future design and implementation of interventions to improve access to essential medicines. Although the studies were heterogeneous (addressed different strategies and outcomes), similarities in study settings indicate high feasibility of adaptation of study methods and procedures across these LMIC contexts. We also acknowledge that the 'summary of effectiveness score' (number of significant outcomes/total number of outcomes measured ×100) has its shortcomings.

The relatively small number of studies included in this review was mainly because our focus was largely on interventions that improved antibiotic dispensing at the lower levels. The scope of this review was therefore limited to interventions that were conducted to improve antibiotic dispensing in community health posts, over-the-counter medicine sellers' shops and community pharmacies. Also, due to the existence of regulations that prevent the dispensing of antibiotics by community health posts, over-the-counter medicine sellers' shops and community pharmacies in LMIC, interventions that targets antibiotic dispensing at the community level may be rare.

6. Conclusion

This review shows that it is possible to improve antibiotic-dispensing practices at the community level in LMIC. Our review contributes to the knowledge on the effectiveness of previous studies performed to improve dispensing practices of CHPs, OTCMSs and community pharmacies in LMIC. Interventions frequently applied in this review showed different levels of effectiveness on the outcomes measured, but all improved the dispensing behaviour of dispensers. It is important to involve relevant stakeholders to facilitate the design and successful implementation of interventions. There is the need to ensure the long-term sustainability of interventions beyond the research phase and provide recommendations on how long follow-up should take. This review also shows the need for standardisation in the conduct of intervention aimed at improving medicine dispensing at the community level.

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Competing interests

All authors declare no competing interests.

Ethics approval

This was a systematic review and does not require ethics approval. All papers reviewed were publicly available.

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Supplementary materials

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References

[1] Holloway K, Van Dijk L. The world medicines situation 2011. Rational use of medicines. Geneva: WHO; 2011.
[2] Mendelson M, Røttingen J, Gopinathan U, Hamer DH, Wertheim H, Basnyat B, et al. Maximising access to achieve appropriate human antimicrobial use in low-income and middle-income countries. Lancet 2016;387:188–98. doi:10.1016/S0140-6736(15)00547-4.
[3] Valimba R, Liana J, Joshi MP, et al. Engaging the private sector to improve antimicrobial use in the community: experience from accredited drug dispensing outlets in Tanzania. J Pharm Policy Pract 2014;7:11. doi:10.1186/2052-3211-7-11.
[4] Holmes AH, Moore LSP, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. Lancet 2016;387:176–87. doi:10.1016/S0140-6736(15)00473-0.
[5] Peters DH, Bloom G. Health care: order health systems in developing world. Nature 2013;495:47. doi:10.1038/495047c.
[6] Smith F. The quality of private pharmacy services in low and middle-income countries: a systematic review. Pharm World Sci 2009;31:351–61. doi:10.1007/s11096-009-9294-z.
[7] WHO. Drug seller initiatives 2012. http://www.apps.who.int/medicinedocs/documents/s19609en/s19609en.pdf [accessed 28 March 2020].
[8] Gyansa-Lutterodt, M. Antibiotic Policy in Ghana; the way forward. 2015. http://studylib.net/doc/9590107/antibiotic-policy-in-ghana [accessed 20 January 2018].
[9] Chalker J, Chuc NTK, Falkenberg T, Tomson G. Private pharmacies in Hanoi, Vietnam: a randomized trial of a 2-year multi-component intervention on knowledge and stated practice regarding ARI, STD and antibiotic/steroid requests. Trop Med Int Health 2002;7:803–10. doi:10.1046/j.1365-3156.2002.00934.x.
[10] Chalker J, Ratanawijitrasin S, Chuc NT, et al. Effectiveness of a multi-component intervention on dispensing practices at private pharmacies in Vietnam and Thailand: a randomized controlled trial. Soc Sci Med 2005;60:131–41. doi:10.1016/j.socscimed.2004.04.019.
[11] Khan M, Grübner O, Krämer A. Frequently used healthcare services in urban slums of Dhaka and adjacent rural areas and their determinants. J Public Health 2012;34:261–71. doi:10.1093/pubmed/fdr108.
[12] Goodman C, Brieger W, Unwin A, Mills A, Meek S, Greer G, et al. Medicine sellers and malaria treatment in sub-Saharan Africa: what do they do and how can their practice be improved? Am J Trop Med Hyg 2007;77(6 Suppl):203–18 PMCID: PMC2657822.
[13] Abuya T, Fegan G, Rowa Y, et al. Impact of ministry of health interventions on private medicine retailer knowledge and practices on anti-malarial treatment in Kenya. Am J Trop Med Hyg 2009;80:905–13 PMID: 19478247.
[14] Abuya TO, Mutemi W, Karisa B, et al. Use of over-the-counter malaria medicines in children and adults in three districts in Kenya: implications for private medicine retailer interventions. Malar J 2007;6:57. doi:10.1186/1475-2875-6-57.
[15] Ansah EK, Narh-Bana S, Affran-Bonful H, et al. The impact of providing rapid diagnostic malaria tests on fever management in the private retail sector in Ghana: a cluster randomized trial. BMJ 2015:350. doi:10.1136/bmj.h1019.
[16] Cundill B, Mbakilwa H, Chandler C, et al. Prescriber and patient-oriented behavioural interventions to improve use of malaria rapid diagnostic tests in Tanzania: facility-based cluster randomised trial. BMC Med 2015;13. doi:10.1186/s12916-015-0346-z.
[17] Ikwuobe JO, Faragher BE, Alawode G, et al. The impact of rapid malaria diagnostic tests upon anti-malarial sales in community pharmacies in Gwagwalada, Nigeria. Malar J 2013;12:380. doi:10.1186/1475-2875-12-380.
[18] Maloney K, Ward A, Bonnie Krenz B, et al. Expanding access to parasite-based malaria diagnosis through retail drug shops in Tanzania: evidence from a randomized trial and implications for treatment. Malar J 2017;16:6. doi:10.1186/s12936-016-1658-y.
[19] Adu-Sarkodie Y, Steiner M, Attafuah J, Tweedy K. Syndromic management of urethral discharge in Ghanaian pharmacies. Sex Transm Infect 2000;76:439–42. doi:10.1136/sti.76.6.439.
[20] Chalker J. Improving antibiotic prescribing in Hai Phong Province, Viet Nam: the 'antibiotic-dose' indicator. Bull World Health Org 2001;79:313–20.
[21] Afari-Asiedu S, Kinsman J, Boamah-Kaali E, et al. To sell or not to sell; the differences between regulatory and community demands regarding access to antibiotics in rural Ghana. J Pharm Pol Pract 2018;11:30. doi:10.1186/s40545-018-0158-6.
[22] Worldbank. World Bank Country and Lending Groups. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups [accessed 24 June 2020].
[23] EPOC. EPOC Taxonomy. 2015. https://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/taxonomy/epoc_taxonomy.pdf [accessed 11 November 2019].
[24] Chuc NT, Larsson M, Do NT, Diwan VK, Tomson GB, Falkenberg T, et al. Improving private pharmacy practice: a multi-intervention experiment in Hanoi, Vietnam. J Clin Epidemiol 2002;55:1148–55. doi:10.1016/s0895-4356(02)00458-4.
[25] Garcia P, Hughes J, Carcamo C, Holmes KK. Training pharmacy workers in recognition, management, and prevention of STDs: District-randomized controlled trial. Bull World Health Org 2003;81:806–14.
[26] Kafle KK. Impact of action-oriented training and/or mailed print material on retailer practices: safe dispensing, correct advice and appropriate referral for diarrhoea, ARI and pregnancy. ARI and Pregnancy 1998.
[27] Ross-Degnan D, Soumerai SB, Goel PK, et al. The impact of face-to-face educational outreach on diarrhoea treatment in pharmacies. Health Policy Plan 1996;11:308–18.
[28] Awor P, Wamani H, Tylleskar T, Jagoe G, Peterson S. Increased access to care and appropriateness of treatment at private sector drug shops with integrated management of malaria, pneumonia and diarrhoea: a quasi-experimental study in Uganda. PLoS One 2014;9(12):e115440. doi:10.1371/journal.pone.0115440.
[29] Chowdhury F, Sturm-Ramirez K, Mamun AA, et al. Effectiveness of an educational intervention to improve antibiotic dispensing practices for acute respiratory illness among drug sellers in pharmacies: a pilot study in Bangladesh. BMC. Health Serv Res 2018;18:676. doi:10.1186/s12913-018-3486-y.
[30] Kitutu FE, Kalyango JN, Mayora C, Selling KE, Peterson S, Wamani H. Integrated community case management by drug sellers influences appropriate treatment of paediatric febrile illness in South Western Uganda: a quasi-experimental study. Malaria J 2017;16:425. doi:10.1186/s12936-017-2072-9.
[31] Mandal SC, Mandal M. Improving use of medicines in the community through interventions. Value Health 2011;14:A340.
[32] Nsimba SE. Assessing the impact of educational intervention for improving management of malaria and other childhood illnesses in Kibaha District-Tanzania. East Afr J Public Health 2007;4:5–11 PMID: 17907754.
[33] Kafle K, Shrestha A, Karkee S. Test of strategies for implementing STS in improving use of drugs. Report to the RPM Project, 2001.
[34] Effective Practice and Organisation of Care (EPOC). EPOC Taxonomy; 2015 . Available at: https://epoc.cochrane.org/epoc-taxonomy.
[35] Grimshaw JM, Eccles MP, Lavis JN, Hill SJ, Squires JE. Knowledge translation of research findings. Implement Sci 2012;7:50. doi:10.1186/1748-5908-7-50.
[36] Gebretekle GB, Serbessa MK. Exploration of over the counter sales of antibiotics in community pharmacies of Addis Ababa, Ethiopia: pharmacy professionals' perspective. Antimicrob Resist Infect Control 2016;5:2. doi:10.1186/s13756-016-0101-z.
[37] Eisen M, Zellman GL, McAlister AL. A health belief model approach to adolescents' fertility control: Some pilot program findings. Health Educ Q 1985;12:185–210.
[38] Eisen M, Zellman GL, AL McAlister AL. A health belief model-social learning theory approach to adolescents' fertility control: findings from a controlled field trial. Health Educ Q 1992;19:249–62.
[39] Bourbonnais R, Brisson C, Vinet A, Vézina M, Abdous B, Gaudet M. Effectiveness of a participative intervention on psychosocial work factors to prevent mental health problems in a hospital setting. Occup Environ Med 2006;63:335–42. doi:10.1136/oem.2004.018077.
[40] O'Cathain A, Croot L, Sworn K, et al. Taxonomy of approaches to developing interventions to improve health: a systematic methods overview. Pilot Feasibility Stud 2019;5:41. doi:10.1186/s40814-019-0425-6.