

Supplementary Material

Table S1. Initiatives to improve antibiotic utilization among physicians in ambulatory care in LMICs.

Country, Year and Reference	Intervention	Impact
Malaysia, 2006 [90]	Principally education involving academic detailing from the resident family medicine specialist alongside an information leaflet	<ul style="list-style-type: none"> Reduction in general antibiotic prescribing rates from 14.3% of patients pre-intervention to 11.0% post-intervention (RR 0.77, 95% CI 0.72 to 0.83) Reduction in URTI-specific antibiotic prescribing rates from 27.7% and 16.6% post-intervention (RR 0.60, 95% CI 0.54 to 0.66) No significant change in prescribing habits among control physicians, i.e. those that did not participate in the study
Sudan, 2006 [91]	<ul style="list-style-type: none"> 20 health centers in Khartoum State were randomly assigned to receive either (a) no intervention; (b) audit and feedback; (c) audit and feedback + seminar; or (d) audit and feedback + academic detailing The targeted interventions involved audit and feedback alongside academic detailing 	<ul style="list-style-type: none"> There was a significant reduction in the mean number of physician encounters where an antibiotic was prescribed by 6.3 and 7.7 (p<0.001) at 1 and 3 months post-intervention, respectively The mean number of encounters where antibiotics were inappropriately prescribed was also significantly reduced post intervention (p<0.001)
Bangladesh, 2007 [92]	<ul style="list-style-type: none"> 3-arm study principally involving education divided into 3 groups: Group I – education surrounding current treatment guidelines and subsequent auditing of the prescribing of ARIs Group-II - Just education surrounding current treatment guidelines Group-III - Control group, i.e., no intervention) 	<ul style="list-style-type: none"> The prescribing of unnecessary antibiotics to treat ARIs was significantly reduced (p<0.01) compared to the pre-intervention period in Group I The average reduction in antibiotic prescribing (patient encounters) was 23.7% in Group I vs. 15.2% in Group II When factoring in the Control group (Group III), there was a 15.2% reduction in antibiotic prescribing in Group I and 6.9% in Group II
Nepal, 2009 [93]	<p>Principally educational initiatives:</p> <ul style="list-style-type: none"> Supervision/ monitoring via periodic visits by district supervisors to 41 primary health care (PHC) facilities Small-group training among prescribers followed by peer-group discussions as well as self-assessment of the data presented 	<ul style="list-style-type: none"> In children < 5 years, there was a significant improvement with respect to decreasing the prescribing of antimicrobials to treat children with diarrhea There was also a significant improvement in the prescribing of antibiotics for patients with URTIs without pneumonia
Thailand, 2014 [94]	<p>Principally education which included:</p> <ul style="list-style-type: none"> Training HCPs on the rational use of antibiotics Introduction of practice guidelines Potential for throat swabs (stool cultures for acute diarrhea) Printed brochures for patients/ relatives in waiting rooms. This included the potential harm associated with the overuse of antibiotics for URTIs and acute diarrhea 	<p>The multifaceted program resulted in:</p> <ul style="list-style-type: none"> Limited prescribing of antibiotics for URTIs (13.0%) and for acute diarrhea (19.1%) Clinical responses on day 3 among patients after receiving care revealed more than 97% of patients who received antibiotics/ those who did not receive antibiotics were cured or improved

Kenya 2017 [95]	<ul style="list-style-type: none"> • A comprehensive set of interventions to improve the management of URTIs, UTIs, STIs and childhood diarrhea in PHCs. <ul style="list-style-type: none"> • Interventions included: <ul style="list-style-type: none"> ○ Online educational programs explaining the clinical guidelines for these 4 conditions ○ 2-hour educational sessions ○ Monthly feedback meetings ○ Materials including posters and other material to remind prescribers of appropriate prescribing 	<ul style="list-style-type: none"> • Adherence to agreed clinical quality measures (CQM) increased from 41.4% to 77.1% for PHCs that took part in the intervention but dropped slightly from 26.5% to 21.8% in controls over the 6-month study period. This was greatest for UTIs • Adherence to CQMs significantly increased over the 6-month study period for the active intervention group <p>The interventions were well received by those operating in the PHCs</p>
India, 2018 [96]	<ul style="list-style-type: none"> • Principally education to reduce the rate of inappropriate prescribing of antibiotics for URTIs <ul style="list-style-type: none"> • Initiatives consisted of: <ul style="list-style-type: none"> ○ Repeated process of audit and feedback combined with interactive training sessions ○ One-to-one case-based discussions ○ Guideline development and broadcasting alongside coding updates 	<ul style="list-style-type: none"> • Antibiotic prescribing among 222 audited patients reduced from 62.6% of patients with URTIs prescribed antibiotics to 7.2% following the multiple interventions • This was combined with an increase in the documentation of examination findings from 52.7% to 95.6% of patients justifying the treatment approach
Malaysia, 2019 [97]	<p>Principally education involving educational toolkits included a training module for HCPs on URTI and acute diarrhea involving:</p> <ul style="list-style-type: none"> • One-hour educational sessions covering diagnostic criteria and treatment decision pathways • Educational posters in Malay and English hung in patient waiting areas and consultation rooms • Multimedia educational videos in the patient waiting areas • Physician reminders 	<p>Appreciable reduction in antibiotic prescribing:</p> <ul style="list-style-type: none"> • URTIs down from 29.1% to 13.7% • Acute diarrhea down from 11.2% to 6.7%

NB: ARIs = Acute Respiratory Tract Infections; HCPs: Healthcare Professionals; PHCs = Primary Healthcare Centers; STIs = Sexually Transmitted Infections; URTIs = Upper Respiratory Tract Infections; UTIs = Urinary Tract Infections

Table S2. - Summary of ASPs and other activities to reduce inappropriate dispensing of antibiotics without a prescription among LMICs and their impact.

Country and reference	Intervention and Aims	Impact of the Intervention
A) Successful Interventions		
Bangladesh [98]	<ul style="list-style-type: none"> • Drug sellers in Dhaka participated in 6 standardized role-playing scenarios • An ARI guideline was developed following the role-play coupled with a one-day educational course regarding the appropriate management of ARIs • The guidelines only recommended antibiotics for children with complicated ARI 	<p>Mixed results:</p> <ul style="list-style-type: none"> • In children, the dispensing of antibiotics for uncomplicated ARIs decreased (30% baseline vs. 21% post-intervention; $p = 0.04$) • However, drug sellers were equally likely to dispense antibiotics for complicated ARIs and referrals to physicians for complicated ARIs decreased (70% baseline vs. 58% post-intervention; $p = 0.03$) • For adults, the dispensing of antibiotics without a prescription remained similar for patients with uncomplicated ARI (48% baseline vs. 40% post-intervention; $p = 0.1$) but increased among those with complicated ARI (44% baseline vs. 78% post-intervention; $p < 0.001$)
China [99]	<ul style="list-style-type: none"> • Multiple initiatives were introduced in Shaanxi Province in China to reduce the purchasing of antibiotics without a prescription given rising concerns <ul style="list-style-type: none"> • These included: <ul style="list-style-type: none"> ○ Stricter regulations for dispensing antibiotics ○ Improved education of pharmacists <ul style="list-style-type: none"> ○ Stipulating there must be a qualified pharmacist's present to dispense antibiotics ○ Increased frequency of unannounced pharmacy inspections alongside punishments for abuse 	<ul style="list-style-type: none"> • These multiple measures resulted in: <ul style="list-style-type: none"> ○ Decreased antibiotic sales between 2011 and 2017 ○ Decreased dispensing of antibiotics without a prescription for a 5 year old child with diarrhoea between 2011 and 2017 - from 72.3% to 50.2% ($p < 0.0001$) among simulated patients ○ A reduction in the dispensing of antibiotics for simulated patients with URTIs – down from 95.8% to 69.5% ($p < 0.0001$)
Kenya [83,100-103]	<ul style="list-style-type: none"> • Multiple activities including: <ul style="list-style-type: none"> • Education among pharmacists linked to the Pharmacy undergraduate programme at the University of Nairobi (UoN) • Regular interaction with University staff and students regarding key issues surrounding antibiotics and AMR, especially inappropriate use <ul style="list-style-type: none"> • The University launched and implemented an AMS curriculum for undergraduate pharmacy students as part of its NAP to reduce AMR 	<ul style="list-style-type: none"> • Low level of dispensing of antibiotics without a prescription (94.1% of antibiotics dispensed with a valid prescription) in the study of Mukokinya et al. (2018) among pharmacies allied to the UoN – <ul style="list-style-type: none"> • Contrasts with pharmacies not allied to the university and are not supervised by pharmacists - in the study by Muloi et al. (2019), 52% of surveyed pharmacists not allied to the University had sold antibiotics without a prescription • In the study of Opanga et al. (2021) at the start of the COVID-19 pandemic, there was no purchasing of antimicrobials without a prescription among patients with actual or suspected COVID-19 among community pharmacies allied to the UoN. These community pharmacists typically recommended alternative treatments for ARIs

		<ul style="list-style-type: none"> This compares with the study of Kimathi et al. (2022) who found 23.4% of patients had self-medicated with antibiotics during the pandemic, 60.6% at the onset of COVID-19 symptoms before confirmatory tests, with 51.5% self-medicating more than once
Namibia [78, 104]	<ul style="list-style-type: none"> Education of pharmacists starting in universities and continuing post qualification Implementation of regulations banning the purchasing of antibiotics without a prescription <ul style="list-style-type: none"> Activities of community pharmacies regularly monitored 	<ul style="list-style-type: none"> In a survey among 100 households in Namibia, typically cold/flu medication, paracetamol, and decongestants were used to treat adults or their children with ARIs including for common colds and influenza. There was no purchasing of antibiotics without a prescription A similar situation was seen during the COVID-19 pandemic with no change in antibiotic utilization patterns early in the pandemic among 55 community pharmacies surveyed
Republic of Srpska [84,105]	<ul style="list-style-type: none"> Multiple interventions including: <ul style="list-style-type: none"> Education of pharmacists regarding the appropriate management of infectious diseases including ARIs Production of guidelines for the 42 most frequent diseases and conditions seen in everyday practice in community pharmacies Greater enforcement of the regulations of guidelines banning the dispensing of antibiotics without a prescription together with possible fines for violation of laws (Euro500–1500 for pharmacy directors and Euro500–750 for pharmacy technicians) Special attention given to the importance of adequate communication and skills among community pharmacists especially given their increasing importance 	<ul style="list-style-type: none"> The dispensing of antibiotics without a prescription decreased from 58% to 18.5% of pharmacies OTC therapy to alleviate symptoms was offered in 72.3% of pharmacies in 2015 - up from 67.2% in 2010 OTC medication dispensed included analgesics and antihistamines, throat and nasal sprays, decongestants and oral expectorants Significantly fewer pharmacies dispensed an antibiotic without a prescription where OTC medicines were offered Encouragingly, the most common reason for not dispensing an antibiotic to simulated clients with ARIs was that antibiotics cannot be dispensed without a prescription
Uganda [106]	<ul style="list-style-type: none"> Four-part intervention to improve the management of pediatric febrile illness among drug sellers. These included: <ul style="list-style-type: none"> Training and work activities Provision of information, education alongside communication Supply activities to drug sellers including diagnostics and medicines Monthly support supervision via supervisors trained in either pharmacy or clinical medicine 	<ul style="list-style-type: none"> The intervention increased the appropriate treatment of children with uncomplicated malaria, pneumonia symptoms and non-bloody diarrhoea by 80.2% (95% CI 53.2–107.2), 65.5% (95% CI 51.6–79.4) and 31.4% (95% CI 1.6–61.2) respectively versus the pre-intervention period Adherence to guidelines during the intervention phase was high without causing excessive prescribing of antimicrobial medicines
B) Interventions that failed to achieve the desired outcome		
Chile [107,108]	<ul style="list-style-type: none"> Introduction of a law in 2005 in Chile which banned the purchasing of antibiotics without a prescription Alongside this initial monitoring and enforcement 	<ul style="list-style-type: none"> The initial enforcement of the law had a modest impact on overall antibiotic sales in the first three years of its implementation (-1.00 DDDs/ 1000 inhabitants per day) However, a follow-up study five years after implementation found a high number of pharmacies

		(80.3%) were still not complying with the law due to lax monitoring
		<ul style="list-style-type: none"> • These findings prompted calls for a greater enforcement of the law to reduce the purchasing of antibiotics without a prescription in the country
Venezuela [107]	<ul style="list-style-type: none"> • The government implemented policies in an attempt to limit the dispensing of three antibiotic groups without a prescription • However, there were no public awareness campaigns and no real 'enforcement' as this was via government publications with no active campaigns to follow up of the regulations 	<ul style="list-style-type: none"> • As a consequence, there was no decrease in antibiotic utilization levels in the country following the implementation of these modest policies • In fact, the opposite was seen with an actual increase in antibiotic utilisation in the country despite the policies
Vietnam [86]	<ul style="list-style-type: none"> • There were strict regulations banning the dispensing of antibiotics without a prescription along with the monitoring of pharmacies • However, there were limited sanctions for community pharmacists when dispensing antibiotics without a prescription - a fine of only US\$15-25 per documented violation • However, going straight to community pharmacists is seen by patients as typically more convenient and does not waste time to see a physician, which may decrease daily wages • In addition, often limited monitoring of outlets in practice 	<ul style="list-style-type: none"> • 487 out of 1,626 participants taking part in the study involving community pharmacies and drug sellers were able to purchase antibiotics without a prescription • 81.7% were able to purchase antibiotics without a prescription involving 29 different antibiotics • In 86.4% of the situations, participants were prescribed antibiotics by drug sellers <p>Most antibiotics were sold to treat RTIs (61.4%)</p>

Supplementary Table S3: Questionnaire

Antimicrobials dispensing practices from community pharmacies/medical stores during COVID-19 in Punjab

Section 1 Information related to drug sale point

1. Name of division.....
2. Name of district.....
3. Name of tehsil.....
4. Code of pharmacy/medical store.....
5. Location of pharmacy/medical store
 - Urban
 - Rural
6. Presence of pharmacist/pharmacy technicians
 - Yes
 - No
7. Type of pharmacy/medical store
 - Chain
 - Independent
8. Number of encounters during study duration.....

Section 2 Demographic characteristics of the patients/customers

1. Age of patients in years
2. Gender

Male

Female

3. Category of AM dispensed

Antibiotics

Antiviral

Antifungal

Anthelmintics

Antiprotozoal

Section 3

Detail of AM dispensed

Name of agent (Non-proprietary)	Indication	Route of administration
Antibiotic		
Antiviral		
Antifungal		
Anthelmintics		
Antiprotozoal		

If antibiotics were dispensed then, detail of antibiotics as per the AWaRe class

1. Access
2. Watch
3. Reserve