Inappropriate supply of antibiotics for common viral infections by community pharmacies in Vietnam: A standardised patient survey

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Summary

Background This study aimed to evaluate the appropriateness of antibiotic dispensing of private pharmacies in Vietnam.

Methods Standardised patient surveys were conducted in randomly selected community pharmacies across 40 districts in Vietnam. Four clinical scenarios were represented by patient actors: (a) an adult requesting treatment for a sibling with a viral upper respiratory tract infection (URTI), (b) a parent requesting treatment for a child with acute diarrhoea, (c) an adult making a direct antibiotic request, and (d) an adult presenting with an antibiotic prescription. We calculated the proportion of interactions that resulted in inappropriate supply of antibiotics and patient advice. Predictors of inappropriate antibiotic supply were assessed.

Findings Patient actors attended 949 pharmacies, resulting in 1266 clinical interactions. Antibiotics were inappropriately supplied to 92% (291/316) of adults requesting treatment for URTI symptoms, 43% (135/316) for children with acute diarrhoea symptoms and to 84% (267/317) of direct request for antibiotics. Only 49% of pharmacies advised patients regarding their antibiotic use. Female actors were more likely to be given antibiotics than male actors for URTI (aOR 2·71, 1·12−6·60) but not for diarrhoeal disease. Pharmacies in northern Vietnam were more likely than those in southern Vietnam to supply antibiotics without a prescription: for adult URTI (aOR=5·8, 95% CI: 2·2−14·9) and childhood diarrhoea (aOR=3·5, 95% CI: 2·0−6·0) symptoms, but less likely to dispense for direct antibiotics request.

Interpretation Inappropriate antibiotic supply was common in Vietnamese private pharmacies. Multifaceted measures are urgently needed to achieve WHO's global action plan for the optimal use of antimicrobials.

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Keywords: Antibiotics; Standardised patients; Vietnam; Viral infections; Pharmacy; Antimicrobial resistance; Diarrhoea; Upper respiratory tract infection

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Research in context

Evidence before this study

Antimicrobial resistance (AMR) is a major threat to global public health. Inappropriate use of antibiotics amplifies AMR. Pharmacists have an important role to reduce inappropriate antibiotic use in the community.

To understand the previous research on this area, we searched PubMed and Google Scholar for articles published from 31st January 2000 to 30th March 2019 using the terms "standardised patients" ("pseudo patient", "mystery shoppers", "simulated client", or "patient actor"), "antibiotic" ("antimicrobial", "antibacterial", "pharmacy" ("drug counter", "chemist", or "pharmacist"), "diarrhoea" and "viral infection" "Upper respiratory Tract Infection" with and without the key word "Vietnam". The articles published in English were considered.

A limited number of studies had used standard patient survey methods to assess appropriate antibiotic dispensing in the western pacific region. In most studies, private pharmacies responded to self-reported surveys or qualitative interviews, which may not reflect their actual practice and prone to recall bias, social desirability bias and Hawthorne effect. Studies found that inappropriate dispensing of antibiotics in the region is common problem, which contributes to underdiagnosis of infections, delay hospital admission and AMR. The AMR compromise the effectiveness of antibiotics both locally and globally and impose unnecessary healthcare costs on patients. The World Health Organisation prioritises optimal use of antibiotics to combat AMR.

There are still major gaps in understanding of the magnitude and causes of the problem in resource-limited community settings in the western pacific region. The extent to which private pharmacies represent the main source of antibiotics, contribute to inappropriate antibiotic use is yet to be characterised across Vietnam and the region. We found no national representative evidence estimating the magnitude of inappropriate antibiotic supply from private pharmacies in rural and urban community settings in Vietnam using standardised patient surveys in last 20 years.

Added value of this study

Our multi-centre, geographically representative study estimated that the inappropriate supply of antibiotics was widespread for presumed viral infections in the private pharmacy settings in Vietnam. Our findings are comparable to other similar socio-economic settings in the region. Gender of the patient and regional variation impacted antibiotic dispensing practice.

Implications of all the available evidence

This study demonstrates the importance of strengthening enforcement of local regulations relating to antibiotic dispensing. It also demonstrates the need for interventions to improve the appropriateness of dispensing by private pharmacists; continuing pharmacy education for private practitioners and strengthened training on antimicrobial stewardship for pharmacists may help in long-term improvement of pharmacy practice. Improving of public awareness of antimicrobial stewardship is also vital. Finally, efforts to ensure access to affordable medical care should be improved particularly in the rural settings

Introduction

Antimicrobial resistance (AMR) is a major and complex global public health problem.[1] If no action is taken, by the middle of the century, the annual mortality due to AMR is predicted to exceed ten million people and the cumulative cost to the global economy is forecast to exceed US$100 trillion.[2,3] The inappropriate use of antimicrobials is a major driver of AMR.[4,5] Antibiotics are commonly given inappropriately to patients with self-limiting infections, such as viral upper respiratory tract infections (URTIs)[6] and acute diarrhoea,[7] instead of more appropriate symptomatic remedies.[8,9] Community pharmacies remain a major source of antibiotic supply in most low and middle income countries (LMICs) or where access to medical services may be limited, and access to pharmacies is more convenient or barriers related to cost prevent patients from accessing legal prescriptions.[6,10,11]

The Vietnamese health sector was reformed in the late 1980s by introducing market-oriented mechanisms. As a result, government health expenditure declined, while out-of-pocket health spending has become the main form of health finance.[12] This has particularly affected the rural poor, deterring them from accessing health care due to poverty and their health seeking behaviour towards private pharmacies.[13] Hence, private pharmacies have become the dominant medicine supplier in the market, representing 60% of the market share on pharmaceutical sales resulted weaknesses in drug regulations.[13,14] Pharmacies are widely accessible in Vietnam, particularly in urban areas, with long opening hours – typically 7 am to 8.30 pm.[15] However, concerns have been raised regarding the quality of patient counselling when medications are dispensed[16] and inappropriate supply of antibiotics.[17]

A recent meta-analysis estimated the pooled proportion of antibiotic sales in community pharmacies without a prescription was 62% (95% CI 53–72%) worldwide, and 65% (95% CI 54–76%) in Asia.[6] A previous standardised patient survey of pharmacies in southern Vietnam, conducted in 2003 found that patient actors with symptoms of viral URTIs and acute diarrhoea were given antibiotics inappropriately in 99% and 75% of cases, respectively.[18] The inappropriate supply of antibiotics contributes to the emergence and spread of resistant bacteria, compromising the effectiveness of antibiotics both locally and globally.[19,20] It can also mask the diagnosis of infections, delay hospital admission, and impose unnecessary healthcare costs on patients.[21] For this reason, The World Health Organisation (WHO) has developed a global action plan for the optimal use of antibiotics.[2]

It recommends that antibiotics only be given rationally, defined as the delivery of the correct medicine to the right patient for the correct duration, in the required dosage and quantity.[22] Many LMICs have developed national action plans to combat AMR. In Vietnam, community pharmacies are the leading source of antibiotic supply,[12] and national laws to mandate prescription only medicines[23] and Good Pharmacy Practice (2007) standards have been introduced to improve the quality of pharmacy service.[12]

Major gaps remain in understanding of the magnitude and causes of the inappropriate use of antibiotics in LMICs.[10,24] The extent to which private pharmacies represent the main source of medicine including antibiotics and, contribute to inappropriate antibiotic use is yet to be characterised across Vietnam.

Previous self-reported surveys and qualitative studies have shown that self-medication with antibiotics is common, and that antibiotic supply by private pharmacies in Vietnam is frequently inappropriate.[25–27] Limitations of previous research include a lack of blinding of the pharmacists – potentially contributing to social desirability bias[28] – as well as possible recall bias.[29] Standardised patient surveys (SPS) can overcome these forms of bias, by evaluating the performance of pharmacy staff in real life scenario. The approach uses trained actors to imitate patients, allowing a consistent clinical scenario to be evaluated across multiple pharmacies.[30]

This study aimed to evaluate antibiotic dispensing practices of pharmacy staff within the private sector in Vietnam using the SPS methodology.

Methods

Study design and setting

We performed a cross-sectional standardised patient survey across 40 districts in the northern (Hanoi and Thanh Hoa provinces) and southern Mekong Delta (Ca Mau and An Giang provinces) provinces of Vietnam, between April and November 2019. Districts located less than two hours' drive or less than 150 km from provincial centres were included. Within each district, a geographical cluster comprising approximately one quarter of the total population was selected by simple random sampling.

We identified all private retail pharmacies, drug counters, and pharmacies located in the private clinics where antibiotics were sold, within the selected clusters. Pharmacies comprised either drug counters or private pharmacies. According to Vietnamese law, 'private pharmacies' in urban areas must be managed by a university graduate pharmacist and 'drug counters' may are typically managed by a pharmacist with a college level diploma.[23] All pharmacies within selected clusters were mapped using door-to-door visits by study staff. Facilities only selling traditional medicines, wholesalers and pharmacies located within hospitals were excluded (Supplementary Appendix). Pharmacies were classified as either registered (with a registration ID displayed on a signboard) or unregistered (no ID displayed).

Description of scenarios

Four clinical scenarios were developed in collaboration with clinicians, pharmacists, public health experts and researchers from Vietnam and Australia, with reference to similar studies conducted in other resource-limited settings.[31,32] The scenarios reflected a range of common clinical interactions within private pharmacies in Vietnam and other similar settings,[10,33] and common conditions associated with inappropriate antibiotic use in resource-limited settings.[7,29] The four scenarios comprised: (1) an adult requesting treatment for a sibling with an URTI; (2) an adult requesting four tablets of an antibiotic by showing an old medicine packaging; (3) a parent describing acute diarrhoea symptoms in their child (the child not present); (4) an adult presenting a valid prescription from a physician to the pharmacy. Table 1 describes the opening statements, the rationale, and the expected outcomes of each clinical scenario.

We adapted the scenarios to the local context in consultation with clinical pharmacy lecturers, community pharmacists and clinicians. Scenarios were piloted in 20 pharmacies in northern and southern Vietnam prior to implementation.

The purpose of pilot was to ensure the feasibility of the research methods, and to obtain feedback regarding the scenarios.

The pilot activities revealed that: 1. Implementing the study in urban and rural settings was feasible; 2. The actors were not detected by pharmacists; 3. Actors required additional training to ensure the interaction was reproduced reliably- and additional training was provided. 4. Antibiotic availability varied, requiring minor modifications to the script.

The pilot work enabled us to appropriately staff the study and determine the average time to conduct a pharmacy visit. Accordingly, following this process we made necessary changes made in the prescription scenario and further training on acting to overcome above mention challenges.

We used "third-person scenarios"[34,35] meaning that the health condition of a sick person was reported by a healthy patient actor to pharmacy staff, this was to minimise possible scepticism of pharmacy staff when a healthy actor presented as a sick patient.[35] Approximately 60% of the interactions were performed by female patient actors, to reflect that in Vietnam, female members of the household are commonly responsible for family healthcare needs.

Recruitment and training of patient actors

Local residents were recruited to be patient actors, and trained using pre-determined scripts that were adapted

Approach	Scenario description	Presentation	Rationale
Symptoms based antibiotic request	**Scenario 1** Antibiotic request by reporting symptoms of viral URTI in a family member with two days cough, runny nose, slight fever and occasional sneezing.	"My sister, who is 20 years old, has been suffering from a cough, runny nose, slight fever and occasional sneezing. The symptoms have been going for two days. Can I get some medicine for her please?"	Symptoms of self-limiting viral infections are very common and does not require antibiotic treatment. Only symptomatic treatment should be advised for viral URTIs. It has not been documented how frequently inappropriate antibiotics are supplied by private community pharmacies for this indication in Vietnam.
Direct antibiotic product request	**Scenario 2** Antibiotic direct product request for viral URTI in a family member with two days cough, runny nose, slight fever and occasional sneezing.	Can I have four tablets of this medication please (showing an old strip of amoxycillin/clavulanic acid)?	Previous studies suggested that amoxycillin or amoxycillin/clavulanic acid tablets are easily obtained from private pharmacies without a prescription in Vietnam. This has not been tested in a standardised patient survey, or in patients presenting with common URTI symptoms in both rural and urban settings of our study regions
Symptoms based antibiotic request	**Scenario 3** Antibiotic request by reporting symptoms of acute diarrhea of a child with abdominal pain and watery diarrhea about 3 to 4 times a day for the last two days	"My 5-year old son has had abdominal pain and watery diarrhoea about 3 to 4 times a day for 2 days. Can I get some medicine for him please?"	Acute watery diarrhoea in children is common and self-limiting; the only treatment required is fluid (preferably oral rehydration solution) to prevent dehydration. It has not been documented how frequently inappropriate antibiotics are supplied by private community pharmacies for this indication in Vietnam.
Prescription based antibiotic request	**Scenario 4** An antibiotic request by a parent presenting a doctor prescription. The prescription included azithromycin 200mg/5 ml, which required dry powder reconstitution to make a suspension that should be kept in the room temperature or in the refrigerator.	Can I get the medicine on this prescription?	The appropriate advice provided by private community pharmacy staff in Vietnam on the appropriate reconstitution, storage and use of antibiotics has not been studied (patient advice).

***Table 1*: Standardised patient scenario descriptions and rationale.**
URTI – Upper Respiratory Tract Infection

to Vietnamese local accents. The training was conducted over four days by a researcher with experience implementing SPS in other settings. Training involved interactive discussions, role playing and pilot visits to private pharmacies using training modules that had been used previously when implementing the SPS Method in private community pharmacies in India[36] and Sri Lanka.[32] Patient actors' performances were assessed against a checklist to ensure that they were convincing and consistent (Supplementary Appendix).

Procedure during pharmacy visits

One patient actor and an observer visited each selected pharmacy during business hours. Each actor and observer couple had a randomly assigned scenario. The observer was identified to pharmacy staff as a friend and listened to the interaction, but did not participate in the clinical interaction. Immediately after each visit, the patient actor and observer jointly completed a data collection sheet and made a structured audio recording of 2, 3 min, describing the visit. The recording included the number of customers present in the shop, the number of staff present, the behaviour of the staff, and the layout of the pharmacy.

Either a research coordinator or the trainer performed monthly independent quality assessment visits to pharmacies to ensure each patient actor's adherence to the scenario and interaction guide provided to them (Supplementary Appendix). Pharmacies visited with scenario 1 were revisited with scenario 2 in two weeks apart.

Levels of antibiotic request

The willingness with which pharmacy staff dispensed antibiotics was evaluated for the two scenarios in which patient actors reported symptoms of viral respiratory illness (Scenario 1) and acute diarrhoea (Scenario 3). For a 'Level 1 request', patient actors asked for a medicine to alleviate their symptoms without specifying that an antibiotic be provided. If an antibiotic was not provided during that initial interaction, the actor asked for a stronger medicine "can you give me any stronger medicine?" (Level 2 request). If the staff did not provide an antibiotic upon this request, the patient actor then explicitly requested an antibiotic "I want an antibiotic" (Level 3 request). This allowed for an assessment of the threshold at which antibiotics would be supplied in response to different levels of consumer demand.[11,34,37] A team of three study pharmacists identified the antibiotics and other medicines received and coded them according to their therapeutic mode of action (Supplementary Appendix).

Outcome measures

We measured the appropriateness of dispensing practice based on WHAAMM[38] and What-Stop-Go protocols[39] and the Vietnam Good Pharmacy Practice guide.[12] These are described in the Supplementary Appendix.

The primary outcomes were 1) the proportion of pharmacies in which antibiotics were provided (Scenarios 1–3), and 2) the proportion of pharmacies in which the patient actors were advised appropriately how to use antibiotics (Scenario 4).

Secondary outcomes included the proportion of pharmacy staff who asked patient actors for additional information regarding the reported scenario (Supplementary Appendix), the proportion of pharmacies providing advice to patient actors regarding medication use (Scenarios 1–3), and the proportion of patients recommended to attend to medical services if symptoms did not improve.

Sample size and statistical issues

The study was powered to measure the proportion of pharmacy interactions in which antibiotic supply was inappropriate. The expected proportion of inappropriate antibiotic dispensing of 50%, based on studies from comparable settings[32,36] with a precision of +/- 5% and an alpha of 0·05 (i.e. 95% confidence limits), assuming that half of clusters were urban, we estimated to sample 318 pharmacy interactions across all four included provinces for each scenario – a total of 1272 interactions. This estimation was derived using the Schlesselmann formula for proportions.[40] Although it is possible that clustering occurred at the level of the province, we considered it more likely that the level of variation would be greatest at the level of the individual pharmacy. Pharmacies had no more than two interviews conducted, and therefore we considered intraclass correlation at this level to be limited. Therefore, the sample size estimate was not adjusted for intraclass correlation.

Study outcomes were presented using descriptive statistics, including median with interquartile range (IQR) for continuous variables, or frequencies and percentages for categorical data. We assessed the relationship between independent variables (socio-demographic characteristics of the pharmacy and the patient actors) and the study outcome (antibiotic supply without a prescription). Multivariable regression with backwards elimination (for covariates where $P > 0{\cdot}10$) was used in the comparative analysis (SPSS v24, IBM Corp). Results were presented as adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs). Model fit was evaluated using the chi-square likelihood ratio test, pseudo R-square values, and the Hosmer-Lemeshow chi-square test statistics. Multilevel logistic regression models were performed to assess cluster specific random effect on regression models.

Ethical considerations

Ethical approval was provided by the National Institute of Hygiene and Epidemiology Vietnam (HDDD-41/2018), and the University of Sydney Human Research Ethics Committee (2018/2020). Approval from the relevant provincial Departments of Health was obtained. A waiver of consent was granted by both ethics committees, allowing the identity of the patient actors to be masked from pharmacy staff.

Role of the funding source

No funding bodies had any role in the study design, data collection, analysis or decision to publish.

Results

A total of 1266 interactions took place in 949 private pharmacies (Table 2). The majority of the pharmacies were drug counters (90·3%), and 84·6% were located in rural settings. In 81·3% of interactions pharmacy staff were female. No concerns were raised by any pharmacy staff regarding the actors.

Upper respiratory tract infection scenarios

Antibiotic supplies. Antibiotics were supplied without a prescription in 558 [88·2% (95% CI 85–91%)] of

Characteristics	Different scenarios			
	Viral upper respiratory tract infection n (%)	Child with acute watery diarrhoea symptoms n (%)	Valid prescription presented n (%)	Overall n (%)
Scenario number	Scenario 1 and 2*	Scenario 3	Scenarios 4	
Total	316 (100%)	316 (100%)	317 (100%)	949 (100%)
Type of private drug seller				
Pharmacy[a]	28 (8·9%)	31 (9·8)	33 (10·4)	92 (9·7)
Drug counter[b]	288 (91·1%)	285 (90·2)	284 (89·3)	857 (90·3)
Pharmacy registration status				
Registered[c]	193 (61·1)	183 (57·9)	172 (54·3)	548 (57·7)
Unregistered	122 (38·6)	129 (40·8)	144 (45·4)	395 (41·6)
Unknown	1 (0·3)	4 (1·3)	1 (0·3)	6 (0·6)
Setting				
Rural	269 (85·1)	263 (83·2)	271 (85·5)	803 (84·6)
Urban	47 (14·9)	53 (16·8)	46 (14·5)	146 (15·4)
Region				
Northern region	*200 (63·3)*	*200 (63·3)*	*200 (63·1)*	*600 (63·2)*
Hanoi	130 (41·1)	130 (41·1)	130 (41·1)	390 (41·1)
Thanh Hoa Province	70 (22·2)	70 (22·2)	70 (22·2)	210 (22·1)
Southern region	*116 (36·7)*	*116 (36·7)*	*117 (36·9)*	*349 (36·8)*
An Giang Province	72 (22·8)	72 (22·8)	73 (23·0)	217 (22·9)
Ca Mau Province	44 (13·9)	44 (13·9)	44 (13·9)	132 (13·9)
Gender of pharmacy staff attending the patient actor	*N* = 633*			*N* = 1266**
Male	104 (16·4)			237 (18·7)
Female	529 (83·6)	66 (20·9)	67 (21·1)	1029 (81·3)
		250 (79·1)	250 (78·9)	
Gender of patient actor	*N* = 633*			*N* = 1266**
Male	254 (40·1)	128 (40·5)	127 (40·1)	509 (40·2)
Female	379 (59·9)	188 (59·5)	190 (59·9)	757 (59·8)

***Table 2*: Characteristics of pharmacies visited by patient actors.**

[a] Pharmacies are established in urban centers, mostly registered under university graduate pharmacist.
[b] Drug counters are mostly in rural communes, registered under a College Pharmacist (without B.Pharm).
[c] Assessed based on registration number displayed on the signboard of the pharmacy.
* Same pharmacies interacted twice; (1) symptom-based scenario interaction (2) product-based scenario interaction
** The same pharmacies interacted twice were added together.

interactions where symptoms of a viral URTI were reported (Table 3). The proportion of pharmacies that offered antibiotics for the reported symptoms of viral URTIs was 92·1% (95% CI 88–95%), which was higher than for direct product request 84·2% (95% CI 80–88%). The most common reason for not supplying any antibiotics in response to a direct antibiotic product request was the unavailability of the requested antibiotic (86·0%; 43/50). Oral cephalosporins, penicillins, and fluoroquinolones were the most frequently supplied antibiotics for the reported symptoms of URTI. Usually where antibiotics were supplied, they were provided at only the first level of request (97·3%; 283/291) (Table 3).

Other medicines supplied. A total of 1569 individual medicines (including antibiotics) were supplied for the symptoms of URTIs interactions (median 5 medicines, IQR 4–6 medicines). Many tablets included formulations containing two or more different active ingredients including antihistamines, analgesics and/or vitamins (14·9%). The types of other medicines supplied were identical when comparing pharmacies that supplied antibiotics and those that did not (Table 3).

Patient clinical history taking and advice. Table 4 describes the communication behaviour of pharmacy staff when interacting with patient actors. Few interactions resulted in pharmacy staff requested an antibiotic prescription in the URTIs scenarios, reporting respiratory symptoms (3/316, 1%) or requesting an antibiotic product (9/317, 3%). A few pharmacy staff collected a clinical history, this was higher during symptoms-based

Variables	Viral upper respiratory tract infection *n* (%)	Direct product request *n* (%)	Child with acute watery diarrhoea symptoms *n* (%)
Scenario	Scenario 1	Scenario 2	Scenario 3
Total number of visits	316 (100)	317 (100)	316 (100)
Antibiotic offered at any level of requests*			
Yes	291 (92·1)	267 (84·2)	135 (42·7)
No	25 (7·9)	50 (15·8)	181 (57·3)
Number of different medicines supplied			
0	2 (0·6)	50 (15·8)	0
1-2	2 (0·6)	253 (79·8)	122 (38·6)
3-4	97 (30·7)	11 (3·5)	147 (46·5)
5-6	190 (60·1)	3 (0·9)	44 (13·9)
≥7	25 (7·9)	0	3 (0·9)
Median number of medicines [IQR]	5 [4—6]	1 [1—1]	3 [2—4]
Categories of medicines dispensed			
Total number individual types of medicines received	1569	313	962
Unlabelled medicines	494 (31·5)	7 (2·2)	209 (21·7)
Antibiotics	255 (16·3)	267 (85·3)	115 (12·0)
Antidiarrheals	0	0	262 (27·2)
Analgesics/ antipyretics	46 (2·9)	3 (1·0)	3 (0·3)
Antihistamines	107 (6·8)	5 (1·6)	1 (0·1)
Antitussives	199 (12·7)	9 (2·9)	0
Steroids/ NSAIDS	100 (6·4)	5 (1·6)	0
Vitamin Supplements	32 (2·0)	0	191 (19·9)
Medications containing 2 or more drugs Others	234 (14·9) 102 (6·5)	13 (4·2) 4 (1·3)	2 (0·2) 179 (18·6)
Level of demand required to obtain antibiotic	*n* = 291	Not Applicable	*N* = 135
Level 1	283 (97·3)		111 (82·2)
Level 2	3 (1·0)		3 (2·2)
Level 3	4 (1·4)		21 (15·6)
Missing data	1 (0·3)		
Types of antibiotics supplied **	*n* = 255	*n* = 267	*n* = 115
Penicillins	52(20·4)	248 (92·9)	5 (4·3)
Tetracyclines	1(0·4)	0	3 (2·6)
Cephalosporins	118 (46·3)	16 (6·0)	3 (2·6)
Fluoroquinolones	45(17·6)	1 (0·4)	3 (2·6)
Lincomycins	5 (2·0)	0	0
Macrolides	24 (9·4)	1 (0·4)	2 (1·7)
Sulfonamides	4(1·6)	0	73 (63·5)
Unknown antibiotics	5(1·6)	1(0·4)	18 (15·7)

***Table 3*: Medications supplied by private community pharmacies according to different scenarios.**

* Reported by patient actor (prior to study pharmacist verification)

** Purchased medicines verified by study pharmacist

interactions (44%) than for direct antibiotic product requests (6%).

Over two thirds of the pharmacy staff advised the patient actors on how to use and how often to use antibiotics during symptoms-based interactions. A minority of pharmacy staff advised on when to stop taking antibiotics (11%). Nevertheless, during the antibiotic product requests, few attending pharmacy staff advised the patient actors on antibiotic use. In both cases, 6% of the pharmacy staff recommended patient actors to seek medical advice if the symptoms did not improve (Table 4).

Diarrhoea scenario

Medicines supplied. Table 3 shows the types of medicines supplied by pharmacy staff for the reported symptoms of acute diarrhoea. Antibiotics were offered without a prescription in 135 interactions [42·7% (95% CI 37—48%)]. Sulfonamides were the most common class of antibiotics supplied (63.5%). These antibiotics were offered to the majority of patient actors at the first level of request (82.2%; 111/135). A total of 962 individual medicines were supplied by pharmacy staff

Behaviours of pharmacy staff	Antibiotic supplied			Antibiotics not supplied			Prescription presented n (%) *N* = 317
	Viral upper respiratory tract infection n (%)	Direct product request n (%)	Child with acute watery diarrhoea symptoms n (%)	Viral upper respiratory tract infection n (%)	Direct product request n (%)	Child with acute watery diarrhoea symptoms n (%)	
Scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Total	291	267	135	25	50	181	317
Request antibiotic prescription							N/A
Yes	2 (0·7)	6 (2·2)	3 (2·2)	1 (4·0)	3 (6·0)	178 (98·3)	
Additional clinical history taken by pharmacy staff							N/A
Yes[a]	131 (45·0)	18 (6·7)	56 (41·5)	7 (28·0)	1 (2·0)	56 (31·8)	
Advised to seek medical care if symptoms persist or worsen							N/A
Yes	11 (3·8)	3 (1·1)	6 (4·4)	23 (92·0)	0	19 (10·5)	
Gave instructions about how to take medication				N/A	N/A	N/A	*n* = 273[b]
Yes	219 (75·3)	56 (21·0)	115 (85·2)				133 (48·7)
Gave instructions about frequency of use				N/A	N/A	N/A	*n* = 273[b]
Yes	201 (69·1)	45 (16·9)	122 (90·4)				145 (53·1)
Provided advice on duration of therapy				N/A	N/A	N/A	*n* = 273[b]
Yes	32 (11·0)	17 (6·4)	44 (32·6)				87 (31·9)
Instructions given about preparation	N/A	N/A	N/A	N/A	N/A	N/A	*n* = 273[b]
of medication Yes							10 (3·7)
How to store dry powder suspension	N/A	N/A	N/A	N/A	N/A	N/A	*n* = 273[b]
Yes							0
Duration of the interaction in minutes							*N* = 317
Median [IQR]	3 [3–4]	2 [1·5–3]	4 [3–5]	3 [2–3]	1·7 [1–2]	4 [3–5]	4 [3–5]

***Table 4*: Behaviour of private community pharmacy staff according to their decision to supply antibiotics.**
N/A – Not applicable
[a] Possible history taken by attended pharmacy staff in relation to reported symptoms.
[b] Pharmacies those who filled the antibiotic prescriptionIQR – Inter quartile Range.

(including antibiotics) during the interactions (median 3 medicines, IQR 2–4). Other than antibiotics, the most commonly supplied medicines were anti-diarrheal (27·2%) and vitamin supplements (19·9%). One fifth of medicines were unlabelled.

Patient clinical history taking and advice. Table 4 describes the communication behaviour of pharmacy staff when interacting with patient actors. Pharmacy staff requested a prescription for antibiotic supply in 57·3% (181/316) of interactions, and 98·3% of pharmacy staff who requested a prescription, did not supply an antibiotic without a prescription. Overall, 112 (35·4%) pharmacy staff inquired about symptoms of the children. Though high proportion pharmacy staff advised patient actors on antibiotic use, only a few staff (7·9%) advised them when to seek medical attention.

Prescription based scenario. Table 4 shows the proportion of pharmacy staff providing counselling to patient actors. Approximately half of the pharmacy staff who dispensed antibiotics with a prescription, advised the patient actors on how to (48·7%) and when to (53·1%) use the antibiotic. A minority of staff advised the patient actors on when to stop taking the antibiotic (3·9%). A small proportion of staff gave advice on how to prepare an antibiotic suspension from the prescribed dry powder (3·7%). No patient actors were advised about how to store the prepared suspension.

Factors associated with antibiotic supply for an UTRI and acute diarrhoea. Female patient actors were more likely than males to obtain antibiotics for URTI for both symptom-based (aOR=2·7, 95% CI: 1·1–6·6), and direct product requests (aOR=3·4, 95% CI: 1·6–7·1), however there was no difference for the child diarrhoeal scenario. Staff who spent more time interacting with patient actors were more likely to sell antibiotics without a prescription for both symptom-based and (aOR=1·6, 95% CI: 1·0–2·4) and product-based requests (aOR=2·1, 95% CI: 1·5–3·2). Pharmacies in northern provinces were more likely to dispense antibiotics without a prescription for reported symptoms of presumptive viral URTIs and acute diarrhoea than in the south, but less likely to dispense for direct antibiotic request (Table 5). There was no interaction found between the interaction time in the pharmacy and medical history taking, and geographical location and region in all three multivariable regression models. There was no significant variability in the intercept suggest that there is no substantial cluster effect on our data (Appendix Table 2).

Discussion

This standardised patient survey of 1266 patient actor interactions at private pharmacies across northern and southern Vietnam revealed that pharmacy supply of antibiotics without a prescription was widespread for presumed viral infections. Female actors were more likely to receive antibiotics than male actors for scenarios with viral respiratory infections. Regional variation in antibiotic dispensing practices was also observed. Overall, a substantial proportion of pharmacies dispensed antibiotics without a clear clinical indication.

This SPS demonstrated that a high proportion of pharmacies supplied antibiotics without a prescription for presumed viral URTIs. Our finding that 92% of patient actors with viral URTIs were given antibiotics was lower than a previous study in which 99% interactions resulted in antibiotic dispensing in one of the southern provinces in Vietnam 18 years earlier.[18] However, antibiotic dispensing without a prescription was substantially higher than estimates globally (67%, 95% CI 55–79%) and in Asia (65%, 95% CI 54–76%).[6] Together, these findings demonstrate limited change in antibiotic sales without a prescription in Vietnam over the last two decades.

Practices observed in this study contrast with the regulatory framework in Vietnam, which mandate prescription-only use of antibiotics in the community.[23] Such inappropriate use of antibiotics for viral infections contributes to AMR,[41,42] limiting the choice of antibiotics in the treatment of common infections and increases the risk of morbidity and mortality.[41] Therefore, further efforts are required to enforce current regulations and improve the understanding of appropriate antimicrobial use within the private pharmacy sector.

Worryingly, a high proportion of antibiotics inappropriately supplied to the patient actors were broad spectrum antibiotics, including higher generation cephalosporins and fluoroquinolones. A similar trend was observed in presumptive tuberculosis SPS scenarios in the same settings.[17] These antibiotics have been classified by WHO as "critically or highly important antimicrobials,"[43] indicating that their use should be preserved for certain severe infection such severe *Salmonella and Escherichia coli* infections, especially in children.[43] The unwarranted use of fluoroquinolones for patients with respiratory symptoms due to *Mycobacterium tuberculosis* may also drive the emergence of tuberculosis that is resistant to this important second-line antibiotic.

There are several factors that may explain inappropriate antibiotic supply. These include but may not limited to, lack of knowledge among pharmacy staff, profit motives and lack of state intervention and/or regulation.[10] A previous review noted that drivers of inappropriate medicine use in Vietnam were a lack of knowledge among both suppliers and patients and weak regulation.[44] A previous qualitative study in Vietnam also revealed that perceived pressure from customers and fear of losing customers resulted in inappropriate antibiotic supply.[45] In contrast, we found

Predictors	Viral upper respiratory tract infection (Scenario 1) Odds of antibiotic being supplied without a prescription		Direct product request (Scenario 2) Odds of antibiotic being supplied without a prescription		Child with acute watery diarrhoea symptoms (Scenario 3 Odds of antibiotic being supplied without a prescription	
	Unadjusted OR (95% CI)	**Adjusted OR (95% CI) * *N* = 315**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)** *N* = 316**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI) *** *N* = 312**
Pharmacy characteristics						
Region	*N* = 316		*N* = 317		*N* = 316	
South	Ref	Ref	Ref	Ref	Ref	Ref
North	5·06 (2·05–12·53)	5·79 (2·25–14·93)	0·76 (0·40–1·45)	0·35 (0·16-·78)	2·62(1·61–4·27)	3·47(2·02–5·96)
Geographical location	*N* = 316		*N* = 317		*N* = 316	
Rural	Ref	Ref	Ref	Ref	Ref	-
Urban	1·31 (0·37–4·55)	2·86 (0·76–10·72)	5·26(1·24–22·40)	3·28(0·70–15·38)	0·42(0·22–0·81)	
Registration status	*N* = 315		*n* = 316		*n* = 312	
Not registered	Ref	-	Ref	-	Ref	-
Registered	0·47 (0·18–1·22)		1·41(0·77–2·60)		0·71 (0·45–1·11)	
Type of the pharmacy	*N* = 316	-	*N* = 317	-	*N* = 316	-
Pharmacy	Ref		Ref		Ref	
Drug store	1·45 (0·41–5·19)		0·37(0·08–1·61)		1·64(0·75–3·61)	
Staff and patient actor characteristics						
Gender of attended pharmacy staff	*N* = 316	-	*N* = 317	-	*N* = 316	-
Male	Ref		Ref		Ref	
Female	1·15 (0·41–3·20)		0·92(0·39–2·20)		1·19 (0·68–2·07)	
Gender of the patient actor	*N* = 316		*N* = 317		*N* = 316	-
Male	Ref	Ref	Ref	Ref	Ref	
Female	2·88 (1·23–6·75)	2·71(1·12–6·60)	1·62(0·88–2·97)	3·40 (1·63–7·07)	0·98(0·62–1·55)	
Medical history taken	*N* = 316	-	*N* = 317	-	*N* = 316	
No	Ref		Ref		Ref	
Yes	2·10 (0·85–5·19)		3·54 (0·46–27·15)		1·39 (0·88–2·21)	
Interaction time (Minutes)	*N* = 316	1·56(1·03–2·36)	*N* = 317	2·15 (1·47–3·16)	*N* = 316	-
	1·63 (1·06–2·51)		1·76 (1·28–2·43)		1·06(0·92–1·23)	
Population-based factors						
Number of Pharmacies	*N* = 316	-	*N* = 317	0·97 (0·94–1·00)	*N* = 316	-
(per additional 10,000 population)	1·00 (0·96–1·04)		0·99 (0·96–1·01)		0·98(0·96–1·01)	
Commune population density (per additional	*N* = 316	-	*N* = 317	1·11 (1·04–1·19)	*N* = 316	0·95 (0·92–0·99)
population per hectare (pph)	1·03 (0·98–1·09)		1·05 (1·00–1·10)		0·98 (0·95–1·01)	

***Table 5*: Factors associated with inappropriate antibiotic supply.**
URTI: Upper Respiratory Tract Infection
*Model accuracy and fit: Model 1: Percentage accuracy in classification (PAC) = 92·1%; Omnibus chi-square test for the model <0·001 and Hosmer and Lemeshow chi-square test for the model = 0·628.
**Model: PAC = 86·1%; Omnibus chi-square test for the model <0·001 and Hosmer and Lemeshow chi-square test for the model = 0·121.
***Model : PAC = 63·5%; Omnibus chi-square test for the model <0·001 and Hosmer and Lemeshow chi-square test for the model = 0·728. Ref = Reference category; aOR = Adjusted odds ratio; CI = 95% confidence interval Other variables adjusted in the models: Gender of attended staff, registration status of the pharmacy, type of pharmacy, and commune pharmacy density.
-Not predicted in the dimension of final model produced using backward deletion method using the SPSS default *P* value 0·1 as a condition to remove variables from the model.
pph= Number of people per hectare.

that almost all antibiotics were supplied with minimal pressure from the customer. Our findings are consistent with findings of a SPS conducted in Sri Lanka[11] and China[34] where a high proportion of pharmacies supplied antibiotics on their own (a 'Level 1' request) without demand from the client. This suggests that reforms relating to antibiotic use must involve working with pharmacists to improve clinical practice, not just education of the general public.[10].

Interestingly, we observed that patient and contextual factors influenced the decision to dispense medications. Women were more likely than men to be given antibiotics. This reflects local cultural practice that women are more commonly care-givers for their families, and hence their opinions may be more highly valued by pharmacists. Secondly, sites in the north of the country were more likely to dispense medication for viral respiratory and diarrhoeal infections, but less likely to do so when antibiotics were directly requested. This reflects the importance of local norms relating to antimicrobial use in the community, and may reflect differing local regulatory practices, business models, and the community expectations. Further research is required to understand how local factors can be addressed through improved regulation and public health campaigns.

This study has important policy and public health implications. First, it demonstrates the importance of strengthening enforcement of local regulations relating to antibiotic sales. Other studies have shown a positive effect on antibiotic supply through strict government regulations,[46–48] this is likely to be beneficial in Vietnam. Second, our results also demonstrate the need for interventions to improve the appropriateness of dispensing by private pharmacists. Continuing pharmacy education for private practitioners, and strengthened training about antimicrobial stewardship for diploma pharmacy trainees may help in the long-term improvement of pharmacy practice.[49] Improvement of public awareness regarding antimicrobial stewardship (AMS) is also vital. Further, efforts to ensure access to affordable medical care should also be improved particularly in the rural settings. Expanding the number of physicians in rural areas will enable patients to access expert advice regarding antimicrobial use, avoiding the need for direct-to-consumer sales of antibiotics. Finally, our study indicates the need for ongoing oversight of dispensing practices in the private sector. Computer-based reporting of drug dispensing may assist local health authorities to identify pharmacies in which antimicrobial supply is excessive, and deliver additional training for pharmacists.

This study has number of strengths. This is a large-scale study included 40 districts across four provinces from northern and southern regions in Vietnam, encompassing urban and rural areas. We randomly allocated scenarios to the pharmacies within each cluster. Therefore, this is representative of a range of regions within Vietnam and possibility other countries with similar settings. Second, the SPS method enabled us to overcome a Hawthorne effect, avoiding an effect of social desirability bias. By recruiting local actors, and using third person scenarios,[35] we were able to avoid detection and ensure our findings accord with daily practice in the community.

There were also several limitations. Firstly, the study did not involve direct clinical assessment of sick patients by pharmacists. This may have altered their willingness to give antibiotics. Secondly, we were unable to evaluate the reasons pharmacists gave antibiotics. Further qualitative research is required to evaluate the perspectives of pharmacy staff and members of the community. As we did not directly interview pharmacy staff, we were unable to determine whether their level of pharmacy training influenced their behaviour. Thirdly, we acknowledge that the number of included interactions was 0.5% less than planned in the sample size. This is unlikely to affect the power of the study substantially. As we found that the low intra-class correlation coefficient (ICC) for the primary outcome was 0·26 for scenario 1, ICC=0·03 for scenario 2 and ICC=0·06 for scenario 3, indicating that intra cluster correlation substantially low (Appendix Table 2). Finally, as we restricted study sites to those within 150 km of provincial centres, the findings may not be generalisable to very remote sites. However, by including four provinces in the north and south of the country, with both urban and rural provinces, the findings are relevant to the majority of the Vietnamese population (Table 5).

In conclusion, inappropriate dispensing of antibiotics for self-limiting viral infections remains common practice in private pharmacies in Vietnam. These practices are likely to contribute to the high rates of AMR observed in Vietnam.[50,51] Further research is required to evaluate the effect of stronger regulation and community-based interventions to reduce inappropriate antibiotic dispensing in the private pharmacy sector. More effective antibiotic stewardship will ensure that the potency of antibiotics can be preserved for patients with serious infections, and contribute to the realisation of the WHO global action plan for optimal use of antibiotics.[2]

Authors' contribution

GF, TA, JB, DDA, SZ, JN, SB, KV, CHT, DD, SJ, THH, PTTV, NTS, BM and GM were responsible for conception and study design.

SZ, HL, TA, LMT, HTTM, NNV and NTT were responsible for data curation.

SZ and HL accessed and verified the data.

HL coordinated study activities across the sites with a supervision of TA.

SZ led the data analysis with a supervision of GF.

SZ drafted the manuscript with a supervision of GF.

All authors contributed to the final version of the manuscript and approved the submission.

All authors had full access to all the data in the study, and the corresponding author had final responsibility to submit for publication.

Data sharing statement

Data may be available according to data sharing policy of the local partners and ethics committees upon request to the corresponding author.

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Declaration of interests

The authors declare that they have no conflict interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lanwpc.2022.100447.

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