BMJ Open

Identifying key influences on antibiotic use in China: a systematic scoping review and narrative synthesis

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To cite: Coope C, Schneider A, Zhang T, *et al*. Identifying key influences on antibiotic use in China: a systematic scoping review and narrative synthesis. *BMJ Open* 2022;**12**:e056348. doi:10.1136/bmjopen-2021-056348

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-056348).

Received 11 August 2021
Accepted 15 February 2022

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ABSTRACT

Introduction The inappropriate use of antibiotics is a key driver of antimicrobial resistance. In China, antibiotic prescribing and consumption exceed recommended levels and are relatively high internationally. Understanding the influences on antibiotic use is essential to informing effective evidence-based interventions. We conducted a scoping review to obtain an overview of empirical research about key behavioural, cultural, economic and social influences on antibiotic use in China.

Methods Searches were conducted in Econlit, Medline, PsycINFO, Social Science citation index and the Cochrane Database of Systematic Reviews for the period 2003 to early 2018. All study types were eligible including observational and intervention, qualitative and quantitative designs based in community and clinical settings. Two authors independently screened studies for inclusion. A data extraction form was developed incorporating details on study design, behaviour related to antibiotic use, influences on behaviour and information on effect (intervention studies only).

Results Intervention studies increased markedly from 2014, and largely focused on the impact of national policy and practice directives on antibiotic use in secondary and tertiary healthcare contexts in China. Most studies used pragmatic designs, such as before and after comparisons. Influences on antibiotic use clustered under four themes: antibiotic prescribing; adherence to antibiotics; self-medicating behaviour and over-the-counter sale of antibiotics. Many studies highlighted the use of antibiotics without a prescription for common infections, which was facilitated by availability of left-over medicines and procurement from local pharmacies.

Conclusions Interventions aimed at modifying antibiotic prescribing behaviour show evidence of positive impact, but further research using more robust research designs, such as randomised trials, and incorporating process evaluations is required to better assess outcomes. The effect of national policy at the primary healthcare level needs to be evaluated and further exploration of the influences on antibiotic self-medicating is required to develop interventions that tackle this behaviour.

Strengths and limitations of this study

- The scoping review design facilitated the inclusion of a wide range of evidence using varied study designs and enabled a comprehensive summary of the extent and nature of the evidence base concerning influences on antibiotic use in China.
- This scoping review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews guidelines.
- A narrative synthesis was additionally undertaken to enhance the accessibility of the results for policymakers, practitioners, and consumers, facilitating uptake of evidence-based practice.
- A limitation of the scoping review method is that a quality assessment of the evidence is not conducted and therefore the relative robustness of the evidence is not systematically reported.
- The review used English search terms and searched databases of literature published predominantly in English, therefore, evidence published only in Chinese is not included in this review.

INTRODUCTION

Antimicrobial resistance (AMR) is widely regarded as an increasing threat to global health and well-being. The overuse and misuse of antibiotics has been identified as a key driver of AMR.[1] In China, studies have shown that both antibiotic prescribing and consumption exceed recommended levels, and are higher than in many other countries.[2–5] For instance, at Community Health Institutions across China prescriptions for antibiotics were double WHO recommended levels.[2 6] An investigation of antibiotic consumption from 2000 to 2010 across 17 countries found a 36% global increase, of which 76% was accounted for by an increase in five countries, including China.[4]

Improving our understanding of the drivers of inappropriate antibiotic prescribing and consumption are key to informing the development of evidence-based policy and practice. Much of the available evidence on which current policy and practice are informed

emanates from European and North American countries. This evidence suggests that diverse, and multilevel factors operate at individual, societal, organisational and policy levels to influence suboptimal antimicrobial use.[7 8] Although some influences may be common across different countries and populations, cultural and structural differences need to be identified and responded to within specific settings. A better understanding of variation between countries is necessary to design interventions that are context and target group specific, in order to reduce health and care inequalities.

Since the late 1970s China has undergone far-reaching economic change with a rapidly expanding market-oriented economy,[9] resulting in the weakening of the community health and medical system that was developed under Mao Zedong. A consequence of these changes has been the need for myriad healthcare reforms that aim to provide all citizens with access to basic medical care.[10] Primary healthcare is delivered through community health centres (CHC) and stations (CHS) in urban areas and through township health centres (THC) and village clinics (VCs) in rural areas. CHC, CHS and THC are all part of the state healthcare system, whereas VC are run by independent practitioners, although VC are contracted to deliver some public health services and are to some extent overseen by THC.[11] Practitioners at THC all have some biomedical training, whereas practitioners in VC may have trained principally in Traditional Chinese Medicine (TCM) and have only minimal biomedical training. TCM is widely available within the state system, with over 90% of CHC and THC providing both TCM and biomedical treatments.[12] The costs of most health services provided by both state run and VC will be reclaimed from one of the three major Government run health insurance scheme (for rural residents, urban employed or non-working urban residents such as children, elderly and disabled).[13] The provider–payment mechanisms introduced to ensure universal access to primary care in China unintentionally introduced incentives that led to over utilisation of medicines and services.[14]

The overuse of antibiotics was inadvertently incentivised by some of these reforms. For instance, government subsidies for public hospitals sharply declined from 60% of total hospital revenue in the early 1980s to less than 25% by 2008, while remuneration mechanisms for clinicians allowed a 15% markup on biomedical pharmaceuticals from initial wholesale cost to retail price, thus incentivising drug prescribing.[15 16] Other hypothesised influences on antibiotic overuse and misuse include patient expectations and beliefs about antibiotics and a lack of access to laboratory diagnostics for village practitioners.[11 17–19] However, the extent and scope of the available evidence concerning key influences on antibiotic use in China has not been collated or synthesised, to our knowledge. We address this gap through a systematic scoping review of the evidence that aims to answer the following question: What is the evidence concerning key behavioural, cultural, economic and social predictors for, and explanations of, antibiotic use in humans in China?

METHODS

A systematic scoping review was undertaken to explore and map the evidence base in this broad and complex area.[20] The review protocol was published on the Open Science Framework[21] prior to conducting the database searches. We drew on an established framework to guide the methodology and adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews.[22] The volume, nature and characteristics of the primary research were mapped in order to identify evidence gaps, which can be further examined in subsequent research. A narrative synthesis of a large and wide-ranging body of research sought to make the results accessible to policy-makers, practitioners and consumers, facilitating uptake of evidence-based practice.

Eligibility criteria

To systematically develop an inclusive review approach, the SPICE framework was used to define its scope[23]:

- Setting: Chinese hospitals, health clinics, pharmacies and the community.
- Population: humans of all ages.
- Phenomenon of interest: factors associated with antibiotic use including prescribing.
- Comparison: any or no comparator.
- Evaluation: no restriction (all study types included).

All study types including quantitative descriptive and intervention studies, qualitative, mixed-methods and systematic reviews were eligible for inclusion. In the category of intervention studies, we included both experimental research (eg, randomised controlled trials (RCTs)) and non-experimental studies (eg, studies analysing secondary data in order to examine the effects of real-world policy changes).

We excluded studies from countries other than China, abstracts, commentaries and letters.

Search strategy

Searches were conducted in Econlit, Medline, PsycINFO, Social Science citation index and the Cochrane Database of Systematic Reviews chosen to cover a range of disciplines including anthropology, economics, medicine, politics, psychology and sociology. The search period was from 1 January 2003 to 28 February 2018. A start date of 2003 was chosen as this was the year the New Rural Co-operative Medical System was introduced in China; a voluntary health insurance programme for rural residents that is subsidised by central, provincial and county governments and seeks to improve rural access to healthcare.[24] A list of key English search terms were compiled based on existing antibiotic reviews,[5 17 25] using the SPICE framework and checking and reviewing the abstract of relevant articles for commonly used terms. Database searches were combined with Boolean search commands (see online

supplemental file 1) for search terms. Records were stored and managed in Endnote V.X9.

Study selection

Twenty per cent of all titles and abstracts were independently screened by two reviewers (AS and CCo or AS and PK) to check inter-rater reliability. Reviewers discussed their inclusion decisions until consensus could be reached. Having checked that the inclusion criteria were understood and implemented properly, one reviewer (AS) screened all remaining studies. Six of the studies reviewed, in Mandarin, were assessed for eligibility by a Mandarin-speaking coauthor (RF) who was familiar with the review process. During the screening of these six studies, English language versions were identified for five of these and, four studies were assessed as eligible for inclusion (CCo). Full texts of all studies included at screening were reviewed for eligibility and reasons for exclusion were documented. The included studies were grouped into two main types during the selection stage: (1) intervention and (2) descriptive/non-intervention studies.

Data extraction

A data extraction form was developed and incorporated details on the source, study design, behaviour related to antibiotic use, influences on behaviour and intervention effect (see online supplemental file 2). Data were extracted by one reviewer (CCo). Ten per cent of studies underwent double-data extraction (CCa) to check for internal consistency of the process. Where discrepancies occurred, these were discussed and resolved by consensus.

Patient and public involvement

There was no formal involvement of patients or the public in this scoping review.

Collating, synthesising and reporting results

The extracted data were quantified by study characteristics using Excel and Stata (V.15).[26] Summary information included year of publication, study design, economic region of China,[27] study context, population sampled or type of data, and main focus of the study including the type of intervention assessed in the case of intervention studies.

For the descriptive/non-intervention studies, a narrative synthesis was conducted to facilitate the organisation and summary of the data.[28] We used the Behaviour Change Wheel system for further characterising intervention types into nine intervention functions and eight policy categories (see table 1).[29]

RESULTS

Description of included studies

After removal of duplicates, the initial electronic searches identified 2305 potentially eligible records. Screening identified 75 studies matching the inclusion criteria (figure 1).

Table 1 Definitions of interventions and policies described by the behaviour change wheel

Interventions	Definition
Education	Increasing knowledge or understanding
Persuasion	Using communication to induce positive or negative feelings or stimulate action
Incentivisation	Creating expectation of reward
Coercion	Creating expectation of punishment or cost
Training	Imparting skills
Restriction	Using rules to reduce the opportunity to engage in the target behaviour (or to increase the target behaviour by reducing the opportunity to engage in competing behaviours)
Environmental restructuring	Changing the physical or social context
Modelling	Providing an example for people to aspire to or imitate
Enablement	Increasing means/reducing barriers to increase capability or opportunity*
Policies	
Communication/ marketing	Using print, electronic, telephonic or broadcast media
Guidelines	Creating documents that recommend or mandate practice. This includes all changes to service provision
Fiscal	Using the tax system to reduce or increase the financial cost
Regulation	Establishing rules or principles of behaviour practice
Legislation	Making or changing laws
Environmental/social planning	Designing and/or controlling the physical or social environment
Service provision	Delivering a service

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*Capability beyond education; opportunity beyond environmental restructuring.

A summary of key study characteristics is presented in table 2 and additional details of intervention studies in table 3. Intervention studies made up nearly two-thirds of the included studies (44/75) (table 2). Overall, few studies were published from 2003 to 2009 (5/75), while the 1-year period from 2014 to 2015 accounted for 31 studies and the latter period (2016–February 2018) 21 studies. Over half of studies were conducted in East or Central China. Almost half of the descriptive studies (15/31) were conducted in community settings, and of those conducted in clinical settings none were conducted in tertiary or teaching hospitals. All intervention studies were conducted in clinical settings, of which 36% were conducted in primary care or CHC (16/44). Intervention

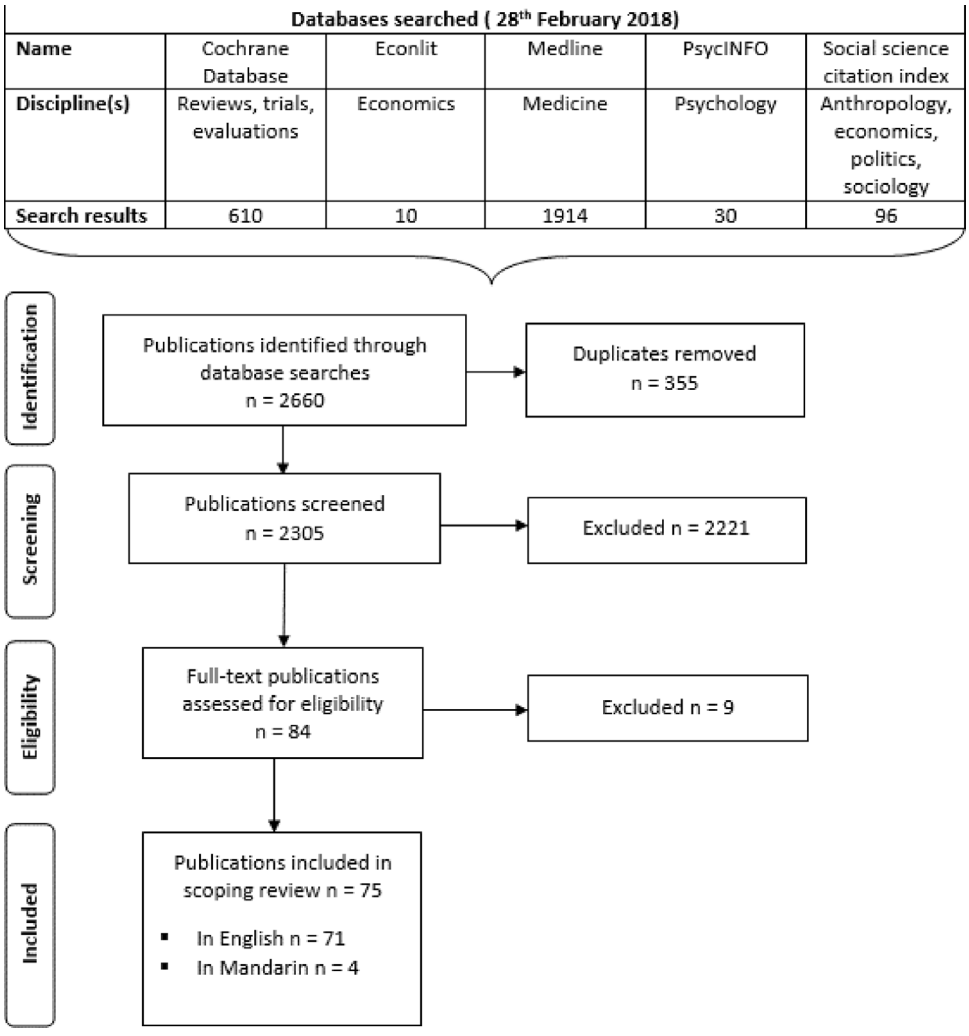

Figure 1 Flow diagram of the selection process for publications included in the scoping review.

study populations included adult and child in-patients, physicians, other healthcare workers and community members (table 3). Primary outcomes were antibiotic use (n=17) and antibiotic prescribing (n=19). Most of the intervention studies used a comparator group design (n=39). National policy guidance made up many interventions evaluated (n=20) while other interventions included public reporting of antibiotic prescribing, pharmacist interventions with local antibiotic stewardship, performance related pay, medical insurance and educational or other interventions. In respect to behaviour change intervention and policy categories, only the primary category is presented, although it was common for interventions to incorporate more than one intervention and policy category.

Summary of key behaviours and influences

A synthesis of the findings from included studies was based on study type (intervention/descriptive) and key behaviours relating to antimicrobial use including antibiotic prescribing, adherence to antibiotics, self-medicating with antibiotics and the sale of antibiotics without a prescription (table 4). Details of the studies and their key findings are presented in online supplemental file 3 (descriptive studies) and online supplemental file 4 (intervention studies).

Antibiotic prescribing

Fourteen descriptive studies identified influences on antibiotic prescribing (online supplemental file 3),[15 17 18 30–42] which included: clinical assessment, healthcare practitioners' skills, knowledge and training, patients' knowledge and expectations concerning antibiotics, external or environmental factors and financial incentives (table 4). Most intervention studies (42/44) focused on antibiotic prescribing or consumption as a key outcome measure (online supplemental file 4).[43–84]

Clinical presentation

Clinical assessment, incorporating both symptoms and patient characteristics, was a key factor influencing prescribing decisions. Greater severity of illness and the presence of certain disease related symptoms predicted antibiotic prescribing.[34 38] Symptoms that favoured antibiotic prescribing for acute cough included confusion (delirium) (aOR 6.8), cough (aOR 3.7), wheeze (aOR

Table 2 Description of all studies included in the scoping review (n=75)

Characteristics of studies	All studies n=75		Intervention n=44		Descriptive n=31	
	n	%	n	%	n	%
Year of publication						
2003–2009	5	6.7	3	6.8	2	6.5
2010–11	6	8.0	2	4.6	4	12.9
2012–13	8	10.7	2	4.6	6	19.4
2014–15	31	41.3	20	45.5	11	35.5
2016–2018*	25	33.3	17	38.6	8	25.8
Study design						
Before and after	24	32.0	24	54.5	–	–
RCT/cluster RCT	6	8.0	6	13.6	–	–
Time series	4	5.3	4	9.1	–	–
Case–control	2	2.7	2	4.6	–	–
Evaluation	2	2.7	2	4.6	–	–
Routine data analysis	6	8.0	4	9.1	2	6.5
Systematic review	3	4.0	2	4.6	1	3.2
Cross-sectional survey	17	22.7	–	–	17	54.8
Qualitative	4	5.3	–	–	4	12.9
Mixed-method	3	4.0	–	–	3	9.7
Audit study	3	4.0	–	–	3	9.7
Prospective cohort	1	1.3	–	–	1	3.2
Health Bureau region						
East	18	24.0	12	27.3	6	19.4
Central	14	18.7	11	25.0	3	9.7
West	12	16.0	8	18.2	4	12.9
Northeast	1	1.3	–	–	1	3.2
2–3 regions	7	9.3	3	6.8	4	12.9
All regions	10	13.3	7	15.9	3	9.7
International plus China	2	2.7	1	2.3	1	3.23
Hong Kong, Macao, Taiwan	6	8.0	–	–	6	19.4
Not specified	5	6.7	2	4.6	3	9.7
Main study context						
Clinical	59	78.7	44	100	15	48.4
Community	14	18.7	–	–	14	45.2
Clinical and community	2	2.7	–	–	2	6.5
Details of clinical contexts (n=59)						
Tertiary/specialist hospital	7	11.9	7	15.9	–	–
Teaching hospital	4	6.8	4	9.1	–	–
City/county hospital	5	8.5	1	2.3	4	26.7
Township hospital	2	3.4	2	4.6	–	–
Primary care	17	28.8	13	29.6	4	26.7
Community health centre	5	8.5	3	6.8	2	13.3
Inpatients	2	3.4	2	4.6	–	–
Outpatients	7	11.9	5	11.4	2	13.3
Various hospitals/clinic	6	10.2	4	9.1	2	13.3
Inpatients and outpatients	3	5.1	3	6.8	–	–

Continued

Table 2 Continued

Characteristics of studies	All studies n=75		Intervention n=44		Descriptive n=31	
Other	1	1.7	–	–	1	6.7
Details of community contexts (n=14)						
Preschool/school	1	7.1	–	–	1	7.1
Pharmacy	1	7.1	–	–	1	7.1
Village	3	21.4	–	–	3	21.4
University	5	35.7	–	–	5	35.7
Other community	4	28.6	–	–	4	28.6

*1January 2016 –28 February 2018.
RCTs, randomised controlled trials.

3.2), shortness of breath (aOR 2.9), sputum production (aOR 2.7), feeling unwell (aOR 1.9) and muscle pain (aOR 1.6).[12 38] For patients with diarrhoea, presence of abdominal pain increased odds of antibiotic prescribing (aOR 7.6), as did taking antibiotics prior to consulting with a hospital physician (aOR 4.07).[34]

Physicians' knowledge, skills and training

Healthcare providers' knowledge and skills were identified as important factors in antibiotic prescribing.[17] Doctors having a higher academic degree compared with an undergraduate degree (*b* 0.08 v 0.18 p=0.03), and being an internist compared with a surgeon or obstetrician (*b* 0.06 v 0.16 p=0.30 or 0.21 p=0.014) were associated with a lower level of antibiotic prescribing.[37] A lower level of clinical competency in village practitioners compared with paediatricians, including a lack of knowledge of the association between the length of treatment and antibiotic resistance, the meaning of AMR,[15] and the correct treatments for children[39] was associated with a higher level of antibiotic prescribing.[35] Village practitioners acknowledged they were unsure about prescribing antibiotics for very young children (under 3 years) in respect to dose and type of antibiotics to use.[39] Uncertainty of treatment coupled with more severe illness in children resulted in village practitioners referring children to county or township hospitals.[35 39] Other factors related to differences in healthcare providers' antibiotic prescribing practices included recency and extent of their medical training, their knowledge of the latest antibiotics and whether they felt they had adequate knowledge and skills to prescribe antibiotics correctly, particularly for children.[15 17 18 35] The prescribing competency of physicians varied from hospitals to primary care.[36]

Interventions aimed at influencing physician antibiotic prescribing

Antibiotic-related training reduced the proportion of clinicians who prescribe antibiotics incorrectly for common cold (14% vs 29% in control).[18] Within the hospital setting, clinical pharmacy services providing education and recommendations to physicians on antibiotic use influenced antibiotic prescribing,[44] including a reduction in the rate of use of antibiotics from 100% to 7.3%.[49]

National guidelines and regulations on clinical use of antibiotics aimed at physicians, can be helpful in improving appropriate antibiotic prescribing.[46–48 53 66] In one study, village practitioners highlighted an absence of authoritative national clinical prescribing guidelines.[15] Since the National Guideline for Antimicrobial Use in Clinical Practice was launched in late 2004 antibiotic use has decreased. For instance, a study of five large children's hospitals identified a 23% reduction in antibiotic use from 2005 to 2006.[53]

Complex antibiotic stewardship interventions that incorporated both guidelines and training for physicians indicated a positive influence on antibiotic practices,[51 61 68 80] including a decrease in use of certain classes of antibiotics (ie, second and third-generation cephalosporins) and in antibiotic use overall in a paediatric intensive care units,[80] as well as decreases in the percentage of antimicrobial prescriptions and the proportion of prescriptions containing restricted antimicrobials in hospital.[68]

Patients' knowledge and expectations about antibiotics

Patients' lack of knowledge about antibiotic use appeared to be a key factor influencing the inappropriate use of antibiotics in China.[17] Patients who demonstrated better knowledge about the appropriate use of antibiotics and the association between antibiotic use and resistance were less likely to be prescribed antibiotics compared with patients who did not display strong antibiotic knowledge (aOR 0.47).[32 38] Patients requested specific antibiotics from village practitioners if they had been prescribed them previously for similar symptoms, demonstrating the important influence of past experience on patients' treatment expectations.[85] In Hong Kong, patients who self-identified as usually seeking help from a TCM practitioner rather than a biomedical doctor were slightly more knowledgeable about antibiotics (average knowledge score of 4.1 vs 3.9), preferred doctors who rarely prescribed antibiotics (aOR 1.29) and were less likely to accept antibiotics from a biomedical doctor when offered (aOR 0.38).[86] In contrast, while medical students'

Table 3 Characteristics specific to intervention studies included in the scoping review (n=44)

Characteristics of intervention studies	n	%
Focus of study (as defined by authors)		
Antibiotic use—treatment	17	38.6
Antibiotic prescribing	19	43.2
Antibiotic use—prophylaxis	3	6.8
Antibiotic costs	4	9.1
Other	1	2.3
Type of intervention evaluated		
National policy guidance	20	45.5
Public reporting of antibiotic prescribing	7	15.9
Educational	2	4.6
Medical Insurance Scheme	3	6.8
Performance pay	2	4.6
Pharmacist Intervention	4	9.1
Local antibiotic stewardship	2	4.6
Other*	4	9.1
Research population or data type†		
Prescription data	17	38.6
Adult inpatient	10	22.7
Child inpatient	3	6.8
Patient records	3	6.8
Physician	1	2.3
Other healthcare worker	1	2.3
Community members	2	4.6
Hospital	2	4.6
Other healthcare facility	1	2.3
Systematic reviews	2	4.6
Other	2	4.6
Comparator group used		
No	4	8.9
Yes	39	86.7
Not applicable	2	4.4
Reported evidence of desired effect		
No	2	4.4
Yes	39	86.7
Not applicable	4	8.9
BCW intervention type (primary)		
Education	24	54.6
Incentivisation	4	9.1
Coercion	8	18.2
Restriction	4	9.1
Environmental restructuring	1	2.3
Enablement/resources	3	6.8
BCW policy type (primary)		
Fiscal	4	9.1
Communication/marketing	8	18.2
Service provision	4	9.1
Regulation	3	6.8
Guidelines	24	54.6
Environmental/social planning	1	2.3

*Electronic Medical Records system; change from a hospital affiliated to self-governing model for CHCs; hypothetical scenarios to distinguish high and low performing physician; adopting procalcitonin testing among patients with acute respiratory infections.
†Data type given where population not specified.
CHCs, community health centres.

antibiotics knowledge score was higher than non-medical students,[87 88] they were significantly more likely to ask a doctor to prescribe antibiotics (19% vs 12%).[87] Physicians often perceived pressure from patients to prescribe antibiotics,[17 31] and this had a strong influence on prescribing: patients' expectation (aOR 5.1), anticipation (aOR 5.1) and direct request (aOR 15.7).[38]

Only two studies concerned educating patients. One multicomponent antimicrobial stewardship intervention providing brief caregiver education indicated a significant absolute risk reduction of 29% in the antibiotic prescribing rate.[61] Evidence from a systematic review on the impact of clinical pharmacy services, including delivery of education to outpatients and inpatients, showed some evidence of a positive influence on the appropriate use of antibiotics.[44]

External or environmental factors

The type and organisational structure of a health facility setting appears to influence antibiotic prescribing,[18 40] such as in the difference in the proportion of prescriptions for common cold between county hospitals (47%), township (44%) and VCs (71%).[18] Focus groups with directors of health institutions pointed to an extremely high antibiotic prescription rate, up to 80%–90%, at township and village level facilities compared with the national target of 20% set by China's Ministry of Health.[39] A change of governance structure in CHC (from hospital-affiliated model to a self-managed independent model) resulted in a significant decrease in antibiotic prescribing, including a 9.2% decrease in the proportion of patients receiving an antibiotic injection and a 7.3% decrease in the proportion receiving two or more antibiotics.[74] Primary care practitioners working in the private, rather than public, sector had a higher odds of prescribing antibiotics (aOR 9.7).[89]

The following external factors were highlighted as barriers to effective antibiotic prescribing: limited access to diagnostic testing (blood tests and laboratory diagnostic and antibiotic sensitivity tests are not available in

Table 4 Main categories and subcategories from the narrative analysis of the descriptive studies (n=31)

Main themes	Subthemes	Details	No of studies
Antibiotic prescribing	Clinical assessment of patient	Illness type and severity[51 52 54 56 121]; Patients having self-treated with antibiotics[56]; Patient's age[45 50 71]	8
	Patient knowledge/ expectations of antibiotics	Patient antibiotic beliefs, expectations and demands[50 54 66]; Patient's knowledge about appropriate use and antibiotics resistance[51 61 66 68]	7
	Physician knowledge	Level of education and medical specialty; level of knowledge of antibiotics and resistance[43 56 61 63]; training – primary vs secondary/tertiary care[63]	5
	External/environmental factors	Type of health facility and setting[43 45 54]; Work environment incl. access to laboratory testing and career opportunities[43]; Unclear or ineffective National guidance[56 61 66]; Environmental/financial barriers to help-seeking; quality of health service; Doctors high workload[53 56]	8
	Financial incentives	Drug sales as a source of income for hospitals and practitioners[54–58 70];Inducements from pharmaceutical companies[61 70]; Patient insurance[44];	8
Compliance with antibiotic therapy	Patient characteristics	Higher average antibiotic knowledge score; patient gender and age[47 66]; educational level[47 66]; relation to child[72]	3
	External/environmental factors	Country[72]	1
Self-medicating behaviour: university students	Student characteristics	Knowledge of antibiotics (better and worse)[52 60 65]; gender	3
	Topic and level of study	Being a medical student[62 65]; level of course	2
	External/environmental factors	Coming from a rural area[62]; Monthly income (higher and lower)[60]; available at pharmacies[47 66]	4
Self-medicating behaviour: parents/carers	External/environmental factors	Having a family member in the healthcare sector[72]; Purchasing antibiotics without prescription[46]; Living in a rural village[46]; City[71]	3
	Financial	Having child health insurance[72]; cost saving	1
	Attitudes	Caregiver being supportive of self-medicating for children[72]; good adherence to physician's advice[46]	2
	Facilitative behaviours	Storing antibiotics at home[46]; prior surplus	1
	Family/child factors	Raising more than one child[46]; age of child[72]	2
Sale of antibiotics without a prescription	Staff factors	Presence of a licensed pharmacist[71]	1
	External/environmental factors	City[71]	1

VCs),[15 39] lack of ambulance transport between villages and townships, and patients being unable to afford costs of transportation and hospital care.[35] Transportation was a specific problem in some villages during the rainy season when road travel becomes difficult .[35] Other external barriers to improved antibiotic prescribing included poor quality health services, pressure from high workloads on doctors, and the lack of effective control and regulatory mechanisms on medicine.[17]

Several intervention studies identified reductions in antibiotic prescribing attributed to the impact of regulatory mechanisms at national level,[17 46–50 66 78 81] or local level.[68 70 75 77] For example, following the introduction of National Special Rectification Scheme on Clinical Use of Antibiotics in 2011, various antibiotic consumption measures in hospitals nationwide showed significant reductions including prophylactic use for type 1 incision operations,[47] proportion of antibiotic use in inpatients,[46 66]

and outpatients,[66] and defined daily doses per 100 inpatient days[46]; in addition to a significant decrease in annual antibiotic consumption from 2009 to 2013 in one individual hospital.[48]

Financial incentives

Financial influences on antibiotic prescribing include: drug sales as a source of income for hospitals and practitioners[17 31 35 39]; inducements from pharmaceutical companies[15]; patient's insurance status[17 40]; and incentives/ gifts from patient to prescriber.[33] A systematic review identified economic incentives as the most frequently mentioned factor (30% of 67 reviewed studies in China) influencing inappropriate drug use in China, including antibiotics.[17] Health workers described financial incentives from pharmaceutical companies to prescribe antibiotics with profit splitting of the mark-up on drug sales.[15] Village practitioners commented that to make a living they needed to supplement their low salaries with activities such as injections, which generated additional payment[35] and they feared losing patients and associated income if they did not prescribe antibiotics.[39] Conversely, an audit study found that gifts given by patients to physicians resulted in a reduced proportion of physicians prescribing antibiotics to patients (50%–33.8%).[33] Another study found that the antibiotic prescribing rate dramatically increased from 10% to 55% when antibiotics were bought from hospital pharmacies rather than elsewhere (implying an internal financial incentive to prescribe), and further increased from 14% to 85% when coupled with patients requesting them.[31]

In addition to financial factors that directly influenced physicians' prescribing behaviours, economic incentives at the health system level were also associated with antibiotic prescribing. Increased government health funding in China may be associated with improvements in doctors' antibiotic prescribing behaviours; for example, the proportion of prescriptions containing antibiotics in urban CHC gradually decreased from 45% to 31% with the increase of government health funding between 2007 and 2011.[45] Similarly, a change in health financing from a fee-for service to capitation with pay-for-performance system was associated with 15%–16% reductions in antibiotic prescriptions among THC and VCs, respectively.[43 55] Patient insurance status was also a factor influencing antibiotic prescribing,[17 40 65 76] with evidence that patients enrolled in the township applied cooperative medical scheme, compared with those who were not, were more likely to be prescribed antibiotics (OR=1.80).[76]

Adherence to antibiotic therapy

Seven descriptive studies identified influencing factors associated with compliance with antibiotic therapy (online supplemental file 3).[85–87 90–93]

Patient characteristics

In adult outpatients, one study found that a higher average antibiotic knowledge score among patients was associated with better adherence to antibiotic instructions (B=0.481),[90] while in an international survey of antibiotic compliance, younger age was associated with non-compliance in China.[92] Residents in Hong Kong noted that recovery before the end of full course and concerns about side-effects were the main reasons for non-compliance with the full antibiotic course,[94] while being male, younger than 40 years old, having primary education or less, being in a low or middle income, and being a user of TCMs were associated with reduced likelihood of finishing a course of antibiotics (aOR 0.67).[86 95] In parents and care givers of young children (0–7 years) a lower adherence to a prescribed antibiotic regimen was associated with being a parent, rather than being a grandparent or carer, and with parents being younger and better educated.[91] A study among students found that medical students score more poorly on a composite score measuring appropriateness of antibiotic behaviour/practice than non-medical students.[87]

Self-medication with antibiotics

Nine descriptive studies identified factors associated with self-medicating with antibiotics in different populations including community members in Hong Kong,[94 95] clinicians (primary care clinicians (general practitioners and pulmonologists),[96] university students[88 89 97 98] and parents of young children (online supplemental file 3).[99 100]

Studies of populations from mainland China living in Hong Kong found evidence of an association between lower levels of self-medication with antibiotics and an awareness of the potential harm of this practice (OR 0.47).[95] Higher levels of self-medication were associated with having leftover antibiotics (aOR 6.03 among local-born; aOR 5.51 among recent immigrants),[94] and recent immigration status (aOR 2.37). Hong Kong residents commented on how expensive it was to see a clinician and that buying antibiotics was less expensive and "worked fine".[95]

Among parents and caregivers, factors influencing self-medication with antibiotics included: having a family member in the healthcare profession (aOR 1.38)[100]; having child health insurance (aOR 1.30); caregiver having a positive attitude towards self-medicating children (aOR 2.66); being a female carer (aOR 1.25); storing antibiotics at home (aOR 2.79/6.25)[99 100]; (29, 22) living in a rural location (aOR 1.64)[99]; (29) raising more than one child (aOR 2.17); purchasing antibiotics without prescription (aOR 6.26) and higher age of the child (aOR 1.15). In contrast, factors associated with not self-medicating with antibiotics included: knowledge that antibiotics should only be sold with a prescription (aOR 0.77)[100] and good adherence to physician's advice (aOR 0.64).[99]

Sale of antibiotics without a prescription

Only one descriptive study was identified, a cross-sectional survey that aimed to identify factors associated with the sale of antibiotics without prescription (online

supplemental file 3).[42] This study sampled urban community pharmacies in three cities across China and focused on the sale of antibiotics for two discrete problems, paediatric diarrhoea and adult respiratory problems. Sale of antibiotics without a prescription varied significantly by city, with proportions reported as 58%, 37% and 74% in the case of paediatric diarrhoea and 61%, 81% and 96% in adult respiratory problems in Nanjing, Changsha and Xi'an, respectively. The proportion of inappropriate antibiotic sales was lower in pharmacies where a licensed pharmacist was present (34% vs 60%).

DISCUSSION

Between 2003 and 2018, there was an increase in the number of studies on key influences on antibiotic use in China published in English language journals. This scoping review identified 31 descriptive studies (quantitative and qualitative) and 44 intervention studies. The increase in the latter study type, particularly between 2014 and 2015, may reflect the introduction of widescale antibiotic policy and healthcare reforms in China[95]; over half of the interventions evaluated were national policy guidelines with before-and-after designs. A small number were RCTs/cluster RCTs, none of which included qualitative or mixed-method process evaluations.

In general, higher rates of antibiotic prescribing were associated with more severe clinical presentation, lower levels of clinical training (both antibiotic specific and general), patient preference for antibiotic treatment, lower level of the healthcare system or private health facilities, and financial incentives built into the system. Antibiotics were sold without prescription by community retail pharmacies but sales without a prescription were lower in those pharmacies with a licensed pharmacist on site. Self-medication with antibiotics was widespread among the studies and higher rates of self-medication were associated with greater access (health professional relative, supply of left-over antibiotics, health insurance, higher income), populations where higher antibiotic use was the norm (rural, medical students, mainland China vs Hong Kong), preference for antibiotic treatment, and low awareness of the potential harms, such as antibiotic resistance, from excessive antibiotic use.

There is evidence that the introduction of policies to reduce the overuse of antibiotics in China may have had a positive impact. Reforms to China's rural healthcare provision and 15% mark-up policy introduced new mechanisms for compensation for village and higher-level hospital health practitioners including user fees, especially from drug sale revenues,[101] which contributed to overprescribing and prescribing of expensive drugs by health practitioners.[102 103] With more recent National Essential Medicines and Zero Mark-up policies that removed these financial incentives, our review indicates a decrease in the proportion of prescriptions containing antibiotics at both national and local levels. Similar financial policies, such as pay-for performance, that separate practitioners' income from drug sales have also led to reductions in antibiotic prescribing in the UK and Taiwan.[104 105] However, government efforts to restrict the use of antibiotics in China have not dealt with the issue of low pay for village practitioners who experience pressure to subsidise their income. Indirect financial incentives remain that include additional compensation for clinical services, including administration of intravenous antibiotics which are frequently prescribed by village practitioners.

Higher rates of antibiotic prescribing were associated with less clinical training, lower-level health facilities and rural areas. These factors are linked as rural areas are served by VCs, which are staffed by practitioners who have more limited training than hospital doctors and may not possess a medical degree and have limited access to diagnostic testing.[12] In China, most qualified health practitioners are concentrated in large hospitals and urban areas, with lower-level township hospitals in the more rural areas usually staffed with practitioners with the more limited training.[106] This review found evidence that antibiotic focused training for clinicians was associated with reduced errors and reduced prescribing rates.[39 44 55 56 63 71 73 78] Antibiotic prescribing training or guideline introduction are common components of successful antimicrobial stewardship interventions in clinical settings in low-income and middle-income countries (LMIC).[107 108] However, the effectiveness of clinically specific guidelines or training may be reduced if the practitioners themselves have a very limited medical education. These inherent weaknesses in the rural primary care system in China contribute to the problem of overuse of antibiotics and may constrain the impact of national guidelines.[12]

Patient preference or expectation for antibiotic treatment was associated with higher antibiotic prescribing rates and with higher rates of self-medication. Patient expectations (perceived and actual) of antibiotic treatment is a known influence on antibiotic prescribing.[109–111] Evidence-based educational interventions directed at changing patient knowledge, beliefs and attitudes towards antibiotics can reduce antibiotic treatment expectations, but it is not clear whether patient education can affect antibiotic prescribing in the absence of an intervention aimed at clinicians.[112] Patient beliefs about when antibiotic treatment is needed are based on experiences of being prescribed antibiotics for certain symptoms, and the way in which clinicians link antibiotic prescription to these symptoms in the clinical encounter.[113 114] High rates of antibiotic prescribing create expectations of antibiotic treatment, practitioners' anticipation of patient antibiotic expectations mean antibiotics are more likely to be prescribed, thus creating a positive feedback loop that supports a norm of high antibiotic use.[19] This review found evidence that higher rates of antibiotic prescribing were seen in populations where norms of high antibiotic use might be expected, such as in rural areas[18 88 99] and in patients who usually attend biomedical rather than

TCM practitioners.[86 95] In order to reduce patient antibiotic expectations as well as practitioner willingness to pre-empt such expectations by prescribing antibiotics, particularly within areas or populations where high use is the norm, interventions that target both patient beliefs and clinician prescribing are needed.

Self-medication with antibiotics, bought from retail pharmacies or obtained from family and friends, is common across LMICs,[115] even when prohibited by law.[116] This review found evidence of higher rates of self-medication by medical students,[87 88] which may seem counter-intuitive, since their medical education might be expected to lead to more appropriate use. Higher use of antibiotics has been observed in university students studying a range of clinical sciences.[115] It may be that students undergoing biomedical training have a positive attitude towards antibiotics, perhaps viewing them as safe and effective, which may be a more important influence than knowledge of clinical guidance on use. Self-medication with antibiotics is higher in LMICs where health systems are weaker and people purchase antibiotics from retail pharmacies because they are more accessible than formal healthcare services.[115] The sale of antibiotics without prescription was prohibited in China in 2003 and the National Action Plan to Curb Bacterial Resistance 2016–2020[117] introduced a series of educational and monitoring initiatives aimed at reducing non-prescription antibiotic sales. Such multifaceted interventions are likely to be more effective, particularly if they target both pharmacy workers and customers.[118]

Strengths and limitations

The scoping review design facilitated the inclusion of a wide range of evidence using varied study designs. This enabled a comprehensive summary of the extent and nature of the evidence base concerning influences on antibiotic use in China. A limitation of the scoping review method is that a quality assessment of the evidence was not conducted. Hence, we are not able to comment on the robustness of the evidence reported here. A further limitation is that the review used English search terms and searched databases of literature published predominantly in English, which means that evidence published only in Chinese will not have been included in this review.

Gaps in the literature

The evidence base is dominated by studies with relatively weak designs (observational or before and after intervention studies), which focus mainly on secondary and tertiary level hospital settings. Many of the interventions evaluated were policies or guidelines and there may have been differences in the way these are interpreted and implemented at provincial, city, town, and village healthcare level, but none of the intervention studies had integrated process evaluations, so there is no evidence on variation in implementation or effectiveness. None of the studies explicitly used behavioural theory to develop interventions, although the influences on antibiotic use and prescribing behaviours are complex and operate at multiple levels.[23 105] The lack of evidence regarding the impacts of national policy interventions on antibiotic use at a rural level is linked to a lack of reliable surveillance data from rural primary care.[119] Although, national surveillance systems exist, such as the China Antimicrobial Resistance Surveillance System and Centre for Antibacterial Surveillance, that provide national standardised data on AMR and the clinical use of antibiotics, most data come from tertiary hospitals. Similar gaps in the evidence have been found for evaluations of antibiotic stewardship programmes in LMICs and from Asia at the rural hospital and community level.[96 97]

CONCLUSIONS

This scoping review has described the extent, nature and characteristics of the primary research on the influences on antibiotic use in China. The results of this scoping review highlight key gaps in the evidence and can inform future research directions.

For instance, although evidence suggests that China's legislative reforms aimed at reducing the overuse of antibiotics are having some positive effects, all of the supporting evidence emanates from urban healthcare contexts and evidence of their impact at the rural health facility level is lacking and therefore urgently required. This is particularly important as we found evidence that inequalities within the Chinese health system relating to context, including inadequately trained village practitioners, low-quality care in rural areas,[12 106 120] and poor accessibility to urban healthcare, appear to interact to drive high antibiotic prescribing rates. Thus, within the rural context, high antibiotic use is the norm and fuelled by widespread self-medication with antibiotics, often purchased without prescription from retail pharmacies. As evidence suggests that the drivers of inappropriate antibiotic use in China are multifaceted increased knowledge of this context is required in order design and deliver effective antimicrobial stewardship programmes. In urban contexts where evidence exists there is a need for more robust evaluations.

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Contributors AS, PK, RF, HL, DW, IO, SM and CCo contributed to the conception or design of the work and CC, AS, PK, CCa and TZ were involved in the acquisition, analysis, or interpretation of data. CMo, TZ and CCa were involved in drafting the manuscript and AS, PK, RF, HL, DW, IO, SM and CCo critically revised the manuscript. All authors gave final approval of the submitted manuscript, and all authors agreed to be accountable for all aspects of the work,with CCa acting as guarantor.

Funding Newton Fund (UKRI and NSFC) the National Natural Science Foundation of China (NSFC) supported this study under the UK-China AMR Partnership Initiative, grant number MR/P00756/1 and 81661138001. The funding source had no role in study design, analysis or in the decision to submit the manuscript for publication. CLC and IO and CMC acknowledge support from the NIHR Health Protection Research Unit in Evaluation of Interventions at the University of Bristol.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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Supplement 1 Search Terms

Econlit, Medline, PsycINFO, Social Science citation index

(Antibiotic* OR antimicrobial* OR antibacterial* OR bacterial* OR anti-infective)
AND (Use OR Utilisation OR Utilization OR Consum* OR prescri* OR therapy OR medication OR self-medication OR treatment OR purchas* OR sale OR sell* OR pay* OR supply OR remuneration OR regulation OR policy)
AND (China OR Chinese) NOT (pathology OR etiology OR aetiology OR livestock OR agricultur* OR Food OR Water OR environment*)

Supplement 2 Data extraction template

Category	Details (including examples)
Data extraction	▪ Name (person extracting data) ▪ Date
Source details	▪ Authors ▪ Title ▪ Source (i.e. research article, review, book chapter) ▪ Year of publication ▪ Type of publication (i.e. descriptive or intervention evaluation or review)
Study details	▪ Aims / research questions ▪ Methodology (i.e. quantitative, qualitative or mixed-methods, including methodological details such as experiment description or type of qualitative study) ▪ Study population (i.e. healthcare providers, physicians, any other prescribers, patients, community, pharmacists, medicine shop owners and employees, pharma representatives) and sample size (if applicable) ▪ Location (i.e. county or province where study was conducted) ▪ Setting / context (i.e. patients' home, village clinics or village health care centres, township hospitals, city hospitals, pharmacies or medicine shops, local and national policy context) ▪ Year(s) of data collection
Behaviours related to antibiotic consumption	▪ Behaviours (i.e. patient consumption, treatment seeking, antibiotic purchasing and storage, health care professionals' prescribing or treatments (e.g. IV), healthcare professions' claiming, pharmacist or medicine shop selling and supplying) ▪ Influences on behaviours according to capabilities, opportunities and motivation to engage in the behaviour (i.e. knowledge, skills, social / professional role and identity, beliefs about capabilities, optimism, beliefs about consequences, reinforcement, intentions, goals, memory / attention / decision processes, environmental context and resources, social influences, emotion, behavioural regulation) ▪ References to inappropriate prescribing or consumption (including details what this is based on, i.e. national or local policies, other references or authors' own views)
For intervention studies only:	▪ Intervention type and comparator (i.e. other treatment options such as traditional Chinese medicine) ▪ Theory used (if applicable) ▪ Intervention effect ▪ Related patients' safety aspects

Supplement 3 Summary of evidence of factors influencing antibiotic use, non-intervention studies (n=31)

(Study ID) Author, year	Study objective/research question(s)	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
ANTIBIOTIC PRESCRIBING / CONSUMPTION					
(1) Chen, 2014[30]	Was there a tendency of prescribing high-priced drugs among physicians? What were the underlying factors of physician prescription preferences?	Routine data analysis 2000 to 2008	Clinical – Hospital data on antibiotic use, prices and volumes used of penicillin and cephalosporin's (beta-Lactam agents) at hospitals in Shanghai including tertiary (n=21), secondary (n=20) and primary (n=6).	Antibiotic consumption	A greater volume of higher priced penicillin and cephalosporin's were administered each year from 2000 to 2008 Availability of a range of penicillin and cephalosporin drugs that differ by trade name and price only i.e., chemical name, dosage and specification are the same
(2) Currie, 2014[31]	To examine the effect of removing financial incentives, and to try to separate out the effects of patient demand. To investigate the effects of reducing financial incentives to prescribe, and to distinguish between the effects of financial incentives and the effects of other competing explanations for overuse of antibiotics.	Experimental audit: University students acted as simulated patients with identical mild flu-like symptoms and; Scenario 1 – did not request antibiotics; Scenario 2 – requested antibiotics; Scenario 3 - requested antibiotics but indicated they would purchase the drug elsewhere Scenario 4 - included 2 & 3 October 2011 to June 2012	Clinical –outpatient visits at a large city hospital (n=1); hospital physicians (n=200); young University students acted as simulated patients	Antibiotic prescribing	Inverse association with: Antibiotic prescribing rate compared to Scenario 1 - Antibiotics not requested by patient (reference group); Scenario 2- Antibiotics requested by patient, [0.85 p=0.04]; Scenario 3 - Antibiotics requested but patient indicated they would purchase the drug elsewhere, [0.10 p=0.03]; Scenario 4 - Includes 2 & 3, [0.14 p=0.04]
(3) Currie, 2011[32]	To examine the effect of patient knowledge on health care utilization and service quality.	Experimental audit: University students acted as simulated patients with identical mild flu-like symptoms and: A – showcased knowledge of antibiotics, or B – did not; Jan 2008 to Mar 2008 and Nov 2008 to Feb 2009	Clinical – outpatient visits at hospitals (n=16) in 2 city locations and 1 rural location; Hospital physicians; University students acted as simulated patients (n=8)	Antibiotic prescribing	Significant difference in antibiotic prescribing rate by: Patient knowledge of antibiotic prescribing [A 39%, B 64% p=<0.01] Urban/rural hospital [City 65%, Rural 55% p=<0.01]

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(4) Currie, 2013[33]	Does gift exchange generate externalities for people outside of the bilateral relationship between the gift giver and recipient and is the nature of this relationship affected by social networks.	Experimental audit: College students were paired and trained to simulate similar complaints (slight dizziness, poor appetite, coughing, worsened this am) with one A giving a small gift and B not. Plus, both suggested an unwillingness to take antibiotics. A third scenario included introduction of a friend. May to August 2012	Clinical – hospital outpatient clinics / large city; college students (n=32) visited physicians (n=160).	Antibiotic prescribing	*Significant difference* in antibiotic prescribing rate by: Gift giving versus control [A 0.34, control 0.50 p=<0.05]
(5) Ke, 2012[34]	To understand diagnostic and treatment practices for patients with acute diarrhoea.	Cross-sectional survey 2009	Clinical – physicians (n=237) from hospitals (n=22) in one province	Antibiotic prescribing	*Positive association* with prescribing of antibiotics for last outpatient seen with acute diarrhoea and: Patient has abdominal pain [Adj. OR 7.57, 95% CI 3.36, 17.05]; Patient took antibiotics before seeing the physician [Adj. OR 4.07, 95% CI 2.08, 7.97]; *Inverse association* with prescribing of antibiotics for last outpatient seen with acute diarrhoea and: Physician works in paediatric unit [Adj. OR 0.31, 95% CI 0.16, 0.60]
(6) Moa, 2015[17]	To assess the landscape of irrational use of medicines in each of the two countries. Specifically, it aims to (1) describe the situation of irrational use of medicines in each country and (2) examine and analyse influential factors.	Systematic review Eligible studies from 1993 to 2013 in Chinese, English and Vietnamese	Clinical - Studies of irrational drug use in China (n=69) and Vietnam (n=29) in tertiary and secondary hospitals, primary healthcare, outpatients' clinics and pharmacies.	Antibiotic prescribing	*Influencing factors of the inappropriate use of medicines in China:* Healthcare providers' lack of skills and knowledge [13%] Pressure from patients' demand [2%] Economic incentive and profits from prescribing medicines [30%] Patients' lack of knowledge [21%] Poor quality of health services [3%] Pressure from heavy patient load [3%] Insurance status of patients [6%] Lack of effective control and regulatory mechanisms on medicines use [5%]

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(7) Li, 2012[35]	To assess the current situation of the health system of rural health care and evaluating the clinical competency of village doctors in management of childhood illnesses prior to implementing IMCI programme in remote border rural areas.	Mixed-method study – survey, focus-group discussions, and observations. 2010	Clinical – village doctors (n=154) in one border province	Antibiotic prescribing for childhood illnesses	*Health service system:* Previously supported by county and township hospitals until reforms of 1980's. Village doctors are unconfident in treating children; "We cannot deal with children with severe diseases since we are inexperienced. For somewhat severe cases, we will refer them to the county hospital" *Clinical competency of village doctors on IMCI checklist:* Paediatrician versus village doctors prescribing: 73% of village doctors determined antibiotics were necessary compared with 14% of paediatricians. 57% village doctors versus 5% of paediatrics deemed injectable medicine was required, of which 98% were antibiotics *Financial mechanisms:* "Our salary is too low. It is not enough even for our transportation". "When the government set the rule of zero profit for selling drugs, my income diminished. I really don't want to be a village doctor. If I could find another job, I could earn more money"; ".. .. .., we have to get some money from injection fee" Patients refusing to be referred to hospital because of their inability to pay; "They often could not go because they could not afford the costs of transportation and relatives' accommodation and food." Environmental barriers - "In the rainy season, no vehicle can get out of our village. The road is very boggy, making it difficult for vehicles to go through". Only two township hospitals have ambulances and so patients have to find their own way; "There is no referral transportation between village and township hospitals" Superstition: "Some severely ill patients think that they have insulted ghosts or spirits, so they just practise certain rituals to gain their pardon instead of going to the hospital"
(8) Su, 2012[36]	To understand the level of knowledge, diagnosis procedures, and usage habits for medication concerning the common cold among physicians from all hospital tiers.	Cross-sectional survey 2010	Clinical – physicians (n=1001) from hospitals and primary care across 10 cities.	Antibiotic prescribing	In-patient versus hospital doctors: Proportion who chose the correct treatment regimen was lower than that of doctors in other roles Proportion who opted to prescribe antimicrobials was higher than that of doctors in other roles

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(9) Reynolds, 2009[15]	To assess knowledge, attitudes, and practices in relation to the use of antibiotics.	Qualitative study – semi-structured interviews and focus group discussion 2005	Clinical and community - patients (n=24), village doctors (n=11), health workers (n=26), key informants (n=7). Plus, validation interviews (n=9).	Antibiotic prescribing / use	Doctor's views: Concerned to avoid long courses of antibiotics (few were aware that courses that were too short might facilitate resistance). Frequency with which national guidance was issued, with no single authoritative documentary source available. No clinical guidelines could be identified at any level of the system, from the village to the provincial hospital. Treating colds (self-limiting viral infection) with antibiotics results in apparently successful cure leading to recommendations by patients and a cycle of over-treatment. Younger doctors start with newest antibiotics for profit or to demonstrate swift effect. Non-prescription use of antibiotics. "Many patients abuse antibiotics before they come to hospital and have already developed drug resistance before they arrive. Thus, each antibiotic course is 3 days, but the overall treatment is usually of longer duration." Laboratory confirmation and testing for antibiotic sensitivity is rare, reflecting a lack of access in villages and affordability in cities. Financial incentives from pharmaceutical companies that split profits with prescribers (illegally), plus entitlement to 15% profit on sales of antibiotics to fund services
(10) Sun, 2015[18]	Attitudes towards, and prescribing behaviour antibiotics for common cold	Cross-sectional survey and retrospective analysis of prescription data 2012	Clinical – doctors (n=188) working at health facilities (n=30) (village clinics, township health centres, county hospitals) in three counties of one province.	Antibiotic prescribing	Description of differences in knowledge of antibiotic prescribing guidance by: Healthcare institution (village 17%, township 2%, county hospital 0%, [p=<0.001]). Significant difference in antibiotic prescribing for common cold by: Had not attended training (29% vs. 14%, p < 0.001) Health care institution worked (county hospital 23%, township 12%, village clinic 13% [p= < 0.05]) Significant difference in proportion who said they had encountered resistant bacteria by: Attending training on antibiotic use (79% vs 47% [p=<0.001]). Of prescriptions for common cold those from village clinics are more likely to contain a prescription for an antibiotic (village 71%, township 44%, county hospital 47%, [p=<0.001])
(11) Wang, 2013[37]	To investigate prescription patterns and influencing factors in Chinese county hospitals.	Cross-sectional survey and retrospective analysis of prescription data 2011 to 2012	Clinical – doctors (n=337) from country hospitals (n=10) in one province, prescriptions (n=5099)	Antibiotic prescribing	Lower percentage of antibiotics prescribed significantly associated with having a higher academic degree [p=0.004] Higher percentage of antibiotic prescribed significantly associated with being a surgeon or obstetricians/ gynaecologists compared to paediatricians [p=0.03, p=0.14]

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(12) Wong, 2016[38]	To explore (1) symptoms and duration of acute cough, (2) patient perception and expectations for antibiotics and (3) antibiotic prescription and associated factors. for acute cough in Chinese primary care population.	Prospective observational study of case reports and patient diaries 2011 to 2014	Clinical – public and private primary care clinics in Hong Kong, primary care physicians (n=19) recruited adult patients presenting with acute cough (n=455)	Antibiotic prescribing	*Positive association* with antibiotic prescribing for acute cough by: Clinicians assessment of symptom severity (following symptoms); cough [Adj.OR 3.73, 95% CI 1.94, 7.17], sputum [Adj.OR 2.70, 95% CI 1.59, 4.60], short of breath [Adj.OR 2.85, 95% CI 1.85, 4.38], wheeze [Adj.OR 3.23, 95% CI 2.00, 5.22], muscle aching [Adj.OR 1.56, 95% CI 1.08, 2.27], feeling unwell [Adj.OR 1.85, 95% CI 1.23, 2.77], confusion [Adj.OR 6.80, 95% CI 1.73, 26.65] and overall severity score [Adj.OR 1.11, 95% CI 1.02, 1.22 Private primary care clinician [Adj.OR 9.70, 95% CI 2.05, 46.04] Clinicians perceptions including: Patients want me to prescribe antibiotics [Adj.OR 3.26, 95% CI 2.03, 5.26]; Patients are satisfied with the consultation [Adj.OR 3.51, 95% CI 1.02, 10.23]; Antibiotics will help getting better quickly [Adj.OR 25.95, 95% CI 2.05,101.14] Patient perceptions including: Expecting antibiotics [Adj.OR 5.11, 95% CI 1.74, 11.57] Anticipating antibiotics [Adj.OR 5.06, 95% CI 1.68, 15.02] Requesting antibiotics [Adj.OR 15.75, 95% CI 5.02, 49.39] Believing antibiotics are necessary [Adj.OR 2.50, 95% CI 1.33, 5.16] *Negative association* with antibiotic prescribing by: Patients' opinions on antibiotics as follows; I believe antibiotics use will increase resistance [Adj.OR 0.47, 95% CI 0.29, 0.83]
(13) Zhang, 2016[39]	To explore the knowledge, attitudes, and practices of village doctors regarding the prescribing of antibiotics for children under 15 years with upper respiratory tract infections (URTIs) in rural China.	Qualitative – focus-group discussions (n=12) 2014	Clinical – primary health care stakeholders including village doctors (n=35), parents (n=11), directors of township hospitals and county level health departments (n=17)	Antibiotic prescribing	Over-prescribing of antibiotics by village doctors: "According to the requirements of China's Ministry of Health, antibiotics prescription and consumption should be less than 20% for outpatients. But as we know, it was up to 80–90% (it is high) both in the township and village level." (Director, male, FGD5). Knowledge regarding the use of antibiotics for treatment of URTIs in children: "I am not sure how to prescribe antibiotics to children with URTIs; under 3 years particularly." (Village doctor, male, FGD6). Attitudes toward antibiotic prescribing decisions*: Fear of complications* - "I think it's viral, but because of the lack of blood testing, no one knows if it may re-infect or turn out to be bacterial. In this case, we would prescribe antibiotics to them to prevent complications, and also maintaining the parents' peace of mind." (Village doctor, female, FGD7). *Primary caregivers' pressure* – "Most parents don't know when and how to use antibiotics nor the consequences of AMR. Besides, they want an instant cure, so they ask village doctors to prescribe antibiotics." (Director, male, FGD5). *Patient retention and financial considerations*: "As we all know, the URTIs will self-recover in 5–7 days. But if you give antibiotics, the child will be better in 2–3 days. If I don't prescribe antibiotics, the patient will visit another doctor who prescribes antibiotics. Then I have lost a patient." (Village doctor, male, FGD3).

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(14) Zhang, 2017[40]	To assess the condition of antibiotic use at health facilities at county, township and village levels in rural Guangxi, China.	Retrospective observational study 2014	Clinical – Outpatient prescription data from county hospitals (n=4), township hospitals (n=8) and village clinics (n=8) in one province/ antibiotic prescriptions for children aged 2-14 years old with upper respiratory tract infection (URTI) (n=9,340)	Antibiotic prescribing	*Positively associated* with antibiotic prescribing: Older age of child (6-14 versus 2-5 years old) [Adj.OR 1.3, 95% CI 1.2, 1.5]; URTI involving a single versus multiple anatomical site [Adj.OR 7.7, 95% CI 6.2, 9.5] Receiving care at a township versus county hospital [Adj.OR 5.0, 95% CI 4.1, 6.0] *Inversely association* with antibiotic prescribing: Having insurance co-payment versus those fully paid out-of-pocket [Adj.OR 0.8, 95% CI 0.7, 0.8]
ANTIBIOTIC COMPLIANCE / REQUEST					
(15) Ding, 2015[91]	To describe caregivers' KAP in a rural province in eastern China, and to identify socio-demographic factors associated with inappropriate antibiotic use.	Cross-sectional survey 2014	Community – 12 villages in one province / primary caregivers (n=172) of children aged 0-7 years	Antibiotic use/adherence (self-reported)	*Descriptive results focused on characteristics associated with knowledge of: p*rescription-only regulation on antibiotic sales by: Higher than primary level education, aged over 30 years, being a grandparent [p=<0.01]; suboptimal antibiotic use and risk of resistance by: Higher than primary level education, aged over 30 years, being a grandparent [p=<0.01]; and expectation of being prescribed antibiotics by: Child's age group, < 3 years versus 3 and over [p=0.02] *Where information about antibiotics was obtained from, either b*ooks or magazines and the internet by: Education level of high school or above compared with a lower level [books and magazines - 15 vs. 4.8 %, p < 0.001], [internet - 21.7 vs. 6.8 %, p < 0.001]. Reported low adherence to antibiotic regimen prescribed, versus high differed significantly by: age of caregiver [p=0.000]; sex of caregiver [p=0.034]; educational level [p=0.003]; relation to child [p=0.000].
(16) Huang, 2013[87]	To analyse the present status of Chinese medical (MS)- and non-medical (NS) students' KAP on the use of antibiotics and examine the influence of Chinese medical curriculum on the appropriate usage of antibiotics among medical students.	Cross-sectional survey Publication 2013 – no date for survey	Community – 3 Universities in north-eastern China / University students – medical (n=1236) and non-medical (n=852)	Request antibiotic prescription (self-reported)	*Descriptive results focused on characteristics associated with knowledge of:* Antibiotic use (e.g., Can antibiotics cure bacterial infections (yes)); better knowledge for final year medical compared with final year non-medical students [80% versus 94% p=<0.0001]; behaviour towards use of antibiotics (score) (e.g., Asked doctors to prescribe antibiotics when you catch a common cold (yes)) poorer for final year medical compared with non-medical student [30% versus 12% p=<0.0001]. Attitude to antibiotic use and public education (e.g., abuse of antibiotics has become the main cause leading to bacterial resistance (agree)); higher score for final year medical versus non-medical students [81% versus 55% p=<0.0001].

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(17) Jin, 2011[85]	To examine notions of antibiotics as a category of drug, their uses, patient preferences and strategies for managing risk by accessing what were seen as 'better' antibiotics.	Qualitative study – 12 focus group discussions, in-depth interviews 2008	Community – villagers from two provinces including village committee members, poor and wealthier householders, men and women (n=28)	Request antibiotic prescription; buy antibiotics without a prescription; use antibiotics prophylactically	*Qualitative description of:* *Perceptions and practices of antibiotics and antimicrobial resistance:* Antibiotics are not framed as a specific class of drug; "Xiaoyanyao is antibiotics, for example, amoxicillin and cephalosporin for common cold". (HB1-6) Some awareness of the concept of antimicrobial resistance (mainly wealthier villagers). Widespread belief in a never-ending line of antibiotics. *Patterns of antibiotic use:* Villagers sometimes request specific antibiotics. Antibiotics may be used as prophylactics. Villagers often succeed in buying antibiotics in pharmacies rather than clinics, without requiring a prescription; "They will sell to you any drug that you request (in the pharmacy)". (HB2-7) *Perception of provider's antibiotics prescribing:* Village doctors are using a large frequency of drips and increasingly so; "They (village doctor) always prescribe drips for both adults and children when we go there. It was not like this before – it has happened just in the past two years". (HB1-7) Doctors prescribe later generations of antibiotics than before. Villagers are aware of the doctor's profit incentives and complained about the lack of care for those unable to afford it.
(18) Pechere, 2007[92]	To determine those factors that influence non-compliance and the psychographic profile of the non-compliant patient in 11 different countries from four continents.	Cross-sectional survey 2005	Community – adult patients aged ≥18 years who had taken a self-administered antibiotic as an outpatient within the past 12 months / across 11 countries including China (n=284)	Non-compliance with antibiotics	Described a significantly higher lack of awareness of correct antibiotic use in China versus other countries [China 53% versus 30% others; p=<0.0001]; *Significantly higher* admitted non-compliance associated with: Younger versus older age [younger Chinese respondents were especially non-compliant, 57% versus 30%; p=<0.0001] In China respondents reporting a three or more times a day regimen [62% p=<0.0001] In China versus other countries (p=<0.0001)
(19) Wun, 2014[86]	To compare Traditional Chinese Medicine (TCM) attenders with the western medicine (WM)-attenders in Hong Kong about their knowledge, attitude and practice (KAP) with antibiotics.	Cross-sectional telephone survey 2010	Community – adult residents of Hong Kong (n=2,471) made up of Traditional Chinese Medicine (TCM) attenders (n=270) and Western Medicine (WM) attenders (n=2092)	Antibiotic knowledge/ use/adherence (self-reported)	TCM-attenders compared with WM attenders: had a higher average antibiotic knowledge score than WM attenders [4.1 versus 3.9, p=0.0119]; were less likely to agree that antibiotics are useful for common cold [Adj.OR 0.68, 95% CI 0.50, 0.91]; were less likely to accept antibiotics when offered [Adj.OR 0.38, 95% CI 0.25, 0.61]; were more likely to agree that antibiotics had side-effects [Adj.OR 2.03, 95% CI 1.29, 3.37]; were more likely to agree antibiotic resistance was a serious problem [Adj.OR 2.07, 95% CI 1.38, 3.22]; prefer doctors who rarely prescribe antibiotics [Adj.OR 1.29, 95% CI 1.12, 1.49]; were less likely to always finish a course of antibiotics [Adj.OR 0.67, 95% CI 0.48, 0.93]

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(20) Ye, 2017[93]	To explore knowledge, attitudes, and practice (KAP) towards antibiotic use in the general public in eastern, central, and western China.	Cross-sectional survey 2015	Community – adults (n=1,204) living in three cities of China	No behaviour reported	Identified significant differences in antibiotic attitude score by: city, age-group, educational level, employment status, having health insurance and health status. Identified significant differences in antibiotic knowledge score by: city, age-group, educational level and employment status.
(21) Chen, 2015[90]	To describe adherence to antibiotic treatment regimens among outpatients suffering from acute infection, and explore factors influencing patient adherence when using antibiotics.	Cross-sectional survey 2013	Clinical – adult outpatients being treated for a bacterial infection (n=162) at a medical centre in Taiwan	Adherence to antibiotic therapy	A higher antibiotic knowledge score was significantly associated with better adherence to antibiotic adherence instructions
SELF-MEDICATION WITH ANTIBIOTICS					
(22) Chang, 2018[100]	To assess knowledge, attitudes, and practices (KAP) regarding antibiotics use among caregivers in urban China	Cross-sectional survey; conducted Nov 2013 to May 2014	Community – urban, three cities across China. Parents, grand-parents, caregivers (n=4,200) of pre-school children under 7 years	Self-medication with antibiotics for children	Positive association with: Having a family member or relative working in the health [Adj. OR 1.38, 95% CI 1.14, 1.66]; Agreement caregivers can self-medicate child with antibiotics [Adj. OR 2.66 95% CI 2.21, 3.19]; being a female carer [Adj. OR 1.25 95% CI 1.06, 1.47] as opposed to male Having children's' health insurance [Adj. OR 1.30 95% CI 1.14, 1.61]; always keeping antibiotics at home [Adj. OR 6.25 95% CI 4.73, 8.26] Inverse association with: Acknowledgement of prescription-only regulation on antibiotic sales [Adj. OR 0.77, 95% CI 0.66, 0.91] Being from Shanghai [Adj. OR 0.34 95% CI 0.28, 0.42] and Changsha [Adj. OR 0.78 95% CI 0.65, 0.96] compared with Xi'an
(23) Davies, 2014[96]	To explore clinicians' views on antibiotic and/or steroid 'rescue packs' used as self-treatment for patients with exacerbations of COPD.	Qualitative study – focus group discussions (n=3) in China Mar 2011 to Mar 2012	Clinical – 7 countries including China (Hong Kong)/ primary care clinicians (GPs) and pulmonologists	Self-medication with antibiotics for patients with COPD exacerbation	*Choosing the right patient* - ''Exactly, this requires not only familiarity, but a very good patient - physician relation….trust on both sides'' [Pulmonologist R9] *Perceived benefits and risks* - ''Prednisolone and antibiotic are short (high dose) treatments, both are two kinds of medications which have consequences concerning comorbidity'' [GP4] *Enabling patients to use the self-treatment* – "the consultation time for COPD cases is short, but if we use rescue pack, we have to explain it very clearly and in detail, instead of just prescribe it for the patients. . . and it takes time'' [GPA]

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(24) Lv, 2014[88]	To evaluate the knowledge, attitude and behaviours of university students on the use of antibiotics.	Cross-sectional survey 2013	Community – one University / undergraduate University students (n=731)	Self-medicating with antibiotics	Antibiotic knowledge score was *significantly associated* with College level (Freshman to Intern) and medical versus non-medical students [p=<0.001]. Antibiotic attitudes and beliefs score were *significantly associated* with College level (Freshman to Intern) [p=0.005], medical versus non-medical students [p=<0.001] and gender [p=0.027]. *Positive association* with self-medication with antibiotics by: Students college (non-medical versus medical) [OR 1.62, 95% CI 1.19, 2.18] Students hometown (rural versus urban) [OR 1.62, 95% CI 1.19, 2.18]
(25) Pan, 2012[98]	To evaluate knowledge and behaviours of university students and risk factors concerning self-medicating with antibiotics.	Online cross-sectional survey 2011	Community – one University / University students (n=1,300)	Self-medicating with antibiotics	*Positive association* with self-medication with antibiotics and: Higher educational level of study - versus undergraduate [Masters: OR 2.65, 95% CI 2.05, 3.42; PhD: OR 10.23, 95% CI 3.03, 34.55] Higher allowance - versus <500 RMB/month [500-1,000: OR 1.73, 95% CI 1.37, 2.17; 1,001-2,000: OR 2.54, 95% CI 1.54, 4.20; >2,000: OR 6.20, 95% CI 1.30, 29.45] Hometown - versus Guangdong [Shandong: OR 12.43, 95% CI 4.89, 31.58; Anhui: OR 5.02, 95% CI 2.16, 11.68; others: OR 1.65, 95% CI 1.20, 2.25]
(26) Wang, 2017[89]	(I) to explore knowledge and antibiotic use behaviours of university students from across China; (ii) determine the association between this knowledge and healthcare-seeking behaviours in relation to antibiotic use; and (iii) examine the contributions of these behaviours to the overall use of antibiotics.	Cross sectional survey 2015	Community – University students (n=11,192) across six universities each representing one province situated in each of the six regions of China	Self-medicating with antibiotics and being prescribed antibiotics	*Significant association* between a higher knowledge score (5-9 or 10-13 respectively vs 0-4) and a lower odds of: Self-treating with antibiotics [Adj. OR 0.53, 95% CI 0.39, 0.72 or 0.36, 95% CI 0.24, 0.54] Taking antibiotics prophylactically [Adj.OR 0.64, 95% CI 0.57, 0.72 or 0.35, 95% CI 0.30, 0.41] Being prescribed antibiotics [Adj. OR 0.58, 95% CI 0.39, 0.87 or 0.46, 95% CI 0.27, 0.76] *Significant association* between a higher knowledge score (5-9 vs 0-4) and an increased odds of keeping antibiotics at home [Adj. OR 1.29, 95% CI 1.15, 1.45]
(27) Wun, 2013[95]	To examine the public's perspectives on antibiotic resistance in our study of the public's knowledge, attitude and practice with antibiotics.	Mixed-method – focus group discussions (n=8) and cross-sectional survey 2009 to 2010	Community – Hong community centre members (n=56); random households', adult members, for telephone survey (n=2471)	Self-medicating with antibiotics	Self-medication with antibiotics (acquiring non-prescription antibiotics) was significantly lower among those who agreed there was potential harm of this practice compared with those who disagreed [OR 0.47, 95% CI 0.34, 0.65] Financial barriers: "*I had urinary problems years ago. You know, seeing the urologist was expensive, so this time, I was smart enough to keep one tablet of each medication and later bought them from the drug store. It worked fine*." (FG2_P1.p26, middle-aged housewife)

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
(28) Wun, 2015[94]	To study whether recent-immigrants from mainland China to Hong Kong would have KAP with antibiotics different from the local born after moving to live in a community with many differences in daily life.	Mixed-method – focus group discussions (n=8) and cross-sectional survey 2010	Community – Community centre members including Cantonese speaking first generation Chinese immigrants to Hong Kong (n=56); random households', adult members, for telephone survey (n=2471)	Self-medicating with antibiotics	Knowledge of antibiotics did not vary by; Local-born or recent immigrant status: "I am quite confused with antibiotics and anti-inflammatory drugs. Are they of the same kind?" (local, secondary school teacher) "[Antibiotics were for] killing bacteria and anti-inflammation." (local; and immigrant) Acquiring non-prescription antibiotics was associated with: Keeping left-over antibiotics [local-born Adj.OR 6.03, 95% CI 3.46, 10.27; recent immigrants Adj.OR 5.51, 95% CI 1.35, 21.65] Recent immigrants were more likely to: keep left over antibiotics [Adj.OR 2.37, 95% CI 1.29, 4.15] and acquire antibiotics without prescription [Adj.OR 2.37, 95% CI 1.28, 4.15]
(29) Yu, 2014[99]	To investigate parents' perceptions of antibiotic use for their children, interactions between parents and physicians regarding treatment with antibiotics, and factors associated with parents self-medicating children with antibiotics.	Cross-sectional survey 2012	Community – parents visiting vaccination clinics with their child (n=854), in two rural counties of one province	Self-medicating with antibiotics	Better knowledge of the uses of antibiotics was significantly associated with higher educational level [p=<0.05]. Parents self-medicating their child was associated with: Higher age of child [Adj.OR 1.15, 95% CI 1.04, 1.27]; Having more than one child [Adj.OR 2.17, 95% CI 1.49, 3.18] Parents' good adherence to physicians' advice (Adj. OR 0.64, 95% CI: 0.45, 0.91) Living in a village [Adj.OR 1.64, 95% CI 1.11, 2.44] Having ever purchased antibiotics without a prescription (Adj. OR 6.26, 95% CI: 4.14, 9.47) Having stored antibiotics at home (Adj. OR 2.79, 95% CI: 1.96, 3.98)
(30) Zhu, 2016[97]	1) to investigate self-medication with antibiotics behaviours and risk factors; 2) to explore the association between self-medication practices and adverse drug events.	Cross sectional survey 2011	Community - University; students (n=660) from one University	Self-medication with antibiotics	Positive association of self-medication with: Knowledge of antibiotics acquired via lectures [Adj.OR 2.26, 95% CI: 1.59,3.22] Reasons for self-medicating with antibiotics: Cost saving [Adj.OR 2.02, 95% CI: 1.12, 3.64]; Fever symptom [Adj.OR 1.66, 95% CI: 1.00, 2.78]; own experience [Adj.OR 1.82, 95% CI: 1.08, 3.08] Positive association of self-medication with: female gender (Adj.OR 1.44, 95% CI: 1.01, 2.05); older age (Adj.OR 1.25, 95% CI: 1.12. 1.38)

Author, year	Study objective	Study type and description	Setting or context & population	Antibiotic use / consumption behaviour	Key findings/Evidence of influencing factors on antibiotic use/consumption behaviour
SALE OF ANTIBIOTICS WITHOUT A PRESCRIPTION					
(31) Chang, 2017[42]	To quantify the proportion of antibiotics sales without a prescription and to assess the quality of pharmacy services provided when dispensing these drugs in urban China.	Cross-sectional survey; conducted May 2015 to June 2015	Community – urban, community pharmacies in (n=256) in three cities across China Pharmacy staff including licensed and non-licensed pharmacists	The sale of antibiotics at community pharmacies for paediatric diarrhoea or adult respiratory infection	<u>For Paediatric diarrhoea</u> Significant difference by: Whether a licensed pharmacist was in the pharmacy [Yes 34%, No 60%, p=0.004] City [Nanjing 58%, Changsha 37%, Xi'an 74% p=<0.001] No significant difference by: Pharmacy size [p=0.418] Gender or age of pharmacy staff [p=0.583 and p=0.279 respectively] <u>For AURI</u> Significant difference by: City [Nanjing 61%, Changsha 81%, Xi'an 96% p=<0.001] No significant difference by: Pharmacy size [p=0.262] Gender or age of pharmacy staff [p=0.416 and p=0.282 respectively]

Supplement 4 Summary of intervention functions using the COM-B model (n=44)

(Study ID) Author, year	Main behaviour studied / type of study /setting and population / year(s) of study	Intervention description	BCW - INTERVENTION	BCW - POLICIES	Main outcome measures [antibiotic related outcomes in bold]	Results for antibiotic related outcomes only [evidence of effect in bold]
(32) Chao, 2018[84]	Rational use of drugs Before and after study using retrospective prescription data (n=3400) Clinical – primary care health institutions (n=17) in three cities in one province January 2010 and January 2014	National Essential Medicines Policy (NEMP). Launched in August 2009.	Restriction	Regulation	WHO Core Drug Use Indicators as follows: 1) % of drugs prescribed from the EML; 2) average number of drugs per prescription; **3) prescription percentage of antibiotics;** 4) prescription percentage of injections; 5) average cost per prescription	3) City A 2010 42%, 2014 45% p=0.061; City B 2010 40%, 2014 42% p=0.614; City C 2010 39%, 2014 38% p=0.854;
(33) Chen, 2014a[83]	Prescribing patterns Before and after study using retrospective prescription data (before n=8,258, after n=8,278) Clinical – primary care health institutions (n=83) nationwide (intervention=60; control=23) 2007 and 2010	National Essential Medicines Policy (NEMP). Launched in 2009. Core aim was to eliminate primary care provider's economic incentives to overprescribe or prescribe unnecessary expensive drugs.	Restriction	Regulation	1) average number of medicines prescribed (including Western and traditional Chinese); **2) proportion of prescriptions containing two or more antibiotics (urban and rural);** 3) prescription expenditure; **4) proportion of antibiotics, infusion, hormones, and injectable used in primary healthcare facilities**	2) Urban: 2007 Intervention (I) 12%, Control (C) 16%, 2010 I 10% C 10%; Rural: 2007 I 19%, C 13%, 2010 I 16% C 16%; 4) Bronchitis. Urban: 2007 I 70% C 92% 2010 I 62% C 70%; Rural: 2007 I 83%, C 90%, 2010 I 84% C 81%; Upper respiratory tract infection. Urban: 2007 I 61% C 90% 2010 I 60% C 68%; Rural: 2007 I 77%, C820%, 2010 I 76% C 71%; Antibiotics were also prescribed for non-infectious disease.
(34) Chen, 2014b[82]	Health workers management of viral infections-KAP & prescribing Cluster-randomized controlled trial in township health centres (n=100) in one province Health workers (control=487, intervention=490) including family physicians (approximately 50%) 2011	Communication of clinical recommendations to health workers. Intervention group - sent text messages on the management of viral infections affecting the upper respiratory tract and otitis media, and the control group was given the same messages in the context of a regular continuing medical education programme (a one-day training programme delivered by two senior physicians).	Education	Communi-cation/ marketing	**1)Percentage point change in average test score (knowledge of disease management for five acute respiratory conditions),** **2)Percentage point difference in average number of antibiotic and steroid prescriptions issued by family physicians**	**1) Post intervention: Control 0.32, Intervention 0.47, Difference 0.16 (95% CI 0.157, 0.163)** 2) Post intervention: Control 67% Difference +17%; Intervention 68% Difference 0%

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(35) Ding, 2016[81]	Prescribing patterns Before and after study using retrospective prescription data (n=2899) Township hospitals (n=29) from six counties in three provinces 2008 and 2013	2009 health reforms including National Essential Medicines Policy (NEMP) and medical insurance system for primary care institutions.	Restriction / Enablement	Regulation / Fiscal	WHO/ International Network for Rational Use of Drugs prescribing indicators: **1) % of prescriptions requiring antibiotics (PPA)**; 2) % of prescriptions requiring adrenal corticosteroids (PPC); 3) % of prescription requiring injections (PPI); 4) average number of medicines per prescription; **5) % of prescriptions combining antibiotics and adrenal corticosteroids (PPA&C)**	**1) PPA: 2008 58% 2013 38% [p=0.000];** **5) PPA&C: 2008 17%, 2013 6% [p=0.000]**
(36) Ding, 2008[80]	Use of antibiotics & prescribing Before and after study: retrospective review of clinical records (n=180) and antibiotic usage One children's hospital, paediatric intensive care unit (PICU) January 2002 to December 2006	Intervention included (1) educating the paediatricians on antibiotics prescribing, (2) applying an antimicrobial spectrum chart, and (3) controlling the prescription of specific antibiotics with the use of a guideline.	Education/ restriction	Guidelines / regulation	**1) % of total number of admitted patients that received antibiotics; 2) indication of antibiotic usage (%) [empiric, therapeutic, prophylactic];** **3) patterns of usage (%);** **4) antibiotic type usage (%)**	% before v after 1) 99% v 94% [NS]; **2) Empiric use: 83% v 67% [p<0.01];** **Therapeutic use:12% v28% [p=<0.01];** Prophylactic: 5% v 5% [NS]; 3) Patterns of usage [NS]; **4)Penicillin's: 4% v 3% [NS]; b-Lactam/b-lactamase inhibitors: 1% v 10% [p=<0.01]; 2nd-Generation cephalosporins:13% v 48% [p=<0.01]; 3rd-Generation cephalosporins: 53% v 17% [p=<0.01]; 4th-Generation cephalosporins: 1% v 1% [p=<0.05]; Macrolides: 20% v 12% [p=<0.01];** Glycopeptides: 4% v 4% [NS]; Carbapenems: 3% v 4% [NS]
(37) Gong, 2016[79]	Antibiotic prescribing Before and after study: retrospective prescription data analysis Nationwide (35 cities), outpatient prescriptions (n=376,700) from primary care providers (CHCs - community health centres; community health stations) 2007 to 2011	China's National Essential Medicines Policy (NEMP) 2009. NEMP has four active elements: an essential drugs list (n~307) for primary care providers; centralized purchasing and distribution of drugs; zero-mark up policy; stipulates insurers payment for essential drugs listed.	Coercion/ restriction	Guidelines / regulation	Six prescribing indicators: 1) average number of drugs prescribed per prescription; 2) average expenditure per prescription; **3)% prescriptions with antibiotics;** **4) % prescriptions with injections;** **5 % prescriptions with two or more antibiotics;** 6) % prescriptions with two or more corticosteroids.	**Before versus after NEMP and NEMP with NON_NEMP for difference in difference (DID):** **% prescriptions with antibiotics L: DID -7, R^2=0.06.** **4) % prescriptions with injections DID -2, R^2=0.13** **5 % prescriptions with two or more antibiotics: DID -2, R^2=0.06**

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(38) Guo, 2015[78]	Antibiotic consumption & prescribing Retrospective time series study Antibiotic use data from a city teaching hospital 2008 to 2013	Enhanced 3-year nationwide antimicrobial stewardship campaigns launched in 2011. Consists of: strengthening regulations on antibiotic use; clarifying responsibilities of hospital management staff; legal penalties; targets for antibiotic management; classification management of antibiotics; antibiotic surveillance networks; and establishing antibiotic stewardship departments in hospitals.	Coercion / restriction	Guidelines / regulation	**Total annual antimicrobial agent consumption**; **trends in: ciprofloxacin-resistant isolates and fluoroquinolones consumption; ceftazidime-resistant K pneumoniae and third-generation cephalosporins consumption; imipenem-resistant A baumannii and carbapenem consumption**	**Total antimicrobial agent consumption: decreasing trend over 6 years (p<0.001). Ciprofloxacin-resistant isolates [*E coli; K. pneumoniae; A baumannii; P aeruginosa*] and fluoroquinolones consumption [correlation coefficients of 0.41 (P = .05), 0.39 (P = .07), 0.41 (P = .05), and 0.48 (P = .02)]; Ceftazidime-resistant *K pneumoniae* and third-generation cephalosporins consumption [correlation coefficient of 0.45 (P = .03)];** **Imipenem-resistant *A baumannii* and carbapenem consumption [correlation coefficient of 0.44 (P = .06)].**
(39) Hou, 2014[77]	Antibiotic consumption Before and after study: retrospective antibiotic use data One tertiary teaching hospital ICU department October 2010 to March 2011 and October 2011 to March 2012.	Antimicrobial stewardship strategy in ICU (emanating from Ministry of Health Policy 2011) including: formulary restriction; preauthorization; perioperative quinolone restriction; control of total antibiotic consumption	Coercion / restriction	Guidelines / regulation	**Total antibiotic consumption in the ICU; initial use of no antibiotics or of a single antibiotic; use of two antibiotics in combination**	**Total antibiotic consumption: defined daily doses (DDDs) per 100 patient-days decreased from 197.65 to 143.41;** **Initial use of no antibiotics or of a single antibiotic significantly increased (p=0.001);** **Use of two antibiotics in combination significantly decreased (p=0.001)**
(40) Jiang, 2011[76]	Antibiotic use Before and after study: retrospective data analysis Healthcare records from four healthcare facilities (county hospitals, township health clinics, village clinics) Period 1: January 1997 - July 2000; Period 2: August 2000 - September 2003; Period 3: October 2003 - December 2006	The new cooperative medical system (CMS)	Incentivisation	Fiscal	**Use of antibiotics; prescribed antibiotics; prescription costs**	**Use of antibiotics: 36.5% (period 1), 48.6% (period 2) and 50.0% (period 3);** Prescribed antibiotics in the intervention township: 60.1% of patients during the intervention and for 61.0% postintervention; **Prescription costs: median prescription costs for the intervention site increased in the THC from 19.4 yuan (period 1) to 30.0 yuan (intervention) and 45.7 yuan (postintervention).**

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(41) Li, 2013[75]	Antibiotic use Before and after study: retrospective data analysis Patient antibiotic use records [before, n=202,560; after, n=182,215] Group 1 before: April to October 2010; Group 2 after: April to October 2011	Electronic Medical Records (EMR) system to improve treatment management and track antibiotic prescriptions (April 2011).	Environmental restructuring / restriction	Guidelines / regulation	**Antibiotic consumption measured as defined daily dose (DDD) (1) total consumption of all antibiotics; (2) total consumption of each type of antibiotic**; (3) patient information (sex and age); (4) information on each antibiotic (level of antibiotic, price, and route of administration); and (5) information on hospitalization (charge type, days in hospital, days in CCU, emergency treatment times, surgery times, etc.)	**DDD per 1,000 patient days: Group 1-727 versus Group 2-480 (p=0.001);** Total consumption of each type of antibiotic – descriptive information only.
(42) Liang, 2014[74]	Antibiotic use Before and after study: interrupted time-series analysis Outpatient electronic medical records for children <5 years treated for AURI (n=23,4810), community health centres in one province June 2008 to May 2010	Change from an hospital-affiliated to self-managed independent model for CHCs regarding finance, personnel and employee compensation.	Enablement	Environ-mental / social planning / service provision	**Proportion of antibiotic use; proportion of patients receiving an antibiotic injection; proportion of patients receiving >1 antibiotic conditional on receiving an antibiotic; average per patient cost of prescribed antibiotic;** average number and average cost of medications per patient, and proportion of each antibiotic class.	proportion of patients receiving an antibiotic injection [decreased by 9.2% P<0.01]; proportion of patients receiving >1 antibiotic conditional on receiving an antibiotic [decreased by 7.3% =<0.05]; monthly average cost of antibiotics prescribed per patient decrease over time [p<0.05]
(43) Liu, 2017[73]	Patients choice of healthcare provider & prescribing Evaluation survey Adults (n=515) from three provinces	Six aspects of public reporting of comparative performance information (PRCPI); As follows: Star rating; numerical information; simplified information; insufficient information; too much information; disordered information; ranking	Education / persuasion	Commun-ication / marketing	**Choosing high-performance physicians in antibiotics; Distinguishing low-performance physicians in antibiotics; Choosing high-performance physicians in injections;** Distinguishing low-performance physicians in injections; Choosing high-performance physicians; Distinguishing low-performance physicians; Participants fully understanding and correctly usage	**Numerical information: significantly increased participants' ability to distinguish low-performance physicians (OR=2.573, P=.029), low-performance physicians in antibiotics (OR=2.974, P=.031) and low performance physicians in injections (OR=2.369, P=.035). Disordered information: impeded participants differentiating low-performance physicians (OR=0.491, P=.039) and low-performance physicians in injections (OR=0.440, P=.016).**

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(44) Liu, 2015[72]	Antibiotic prescribing Before and after; segmented regression analysis Primary care institutions (n=10) in one province, outpatient prescriptions (n=326,655) September 2012 to September 2013 and October 2013 to August 2014	Public reporting of comparative performance information (PRCPI) (October 2013)	Education / persuasion	Communication / marketing	**% prescriptions requiring antibiotics;** **% prescriptions requiring injections;** average expenditure of patients	**After PRCPI: downward trends from baseline on antibiotic use (coefficient =−0.64, P = 0.004); combined use of antibiotics (coefficient =−0.41, P < 0.001); and injections (coefficient =−0.5957, P = 0.001)**; temporary increase in average expenditure of patients (coefficient = 2.20, P = 0.307) but slowed down the ascending trend (coefficient =−0.45, P = 0.033)
(45) Liu, 2016[71]	Antibiotic prescribing Matched pair cluster-randomized trial Primary care institutions (n=20) in one province, outpatient prescriptions (n=748,632) September 2012 to September 2013 and October 2013 to August 2014	Public reporting of comparative performance information (PRCPI) (October 2013)	Education / persuasion	Communication / marketing	**1. Whether antibiotic is used or not in a patient prescription.** **2. Whether combined antibiotics are used or not in a patient prescription.** **3. Whether injection is used or not in a patient prescription.** 4. Average expenditure of patients (including consultations, diagnostic tests, and prescriptions).	**After PRCPI: Slight increase in prescriptions requiring antibiotics (OR=1.089, P<0.001, 95%CI: 1.067–1.110) or injections (OR=1. 258, P<0.001, 95%CI: 1.234–1.283).** **Reduction in the use of combined antibiotics (odds ratio [OR]=0.870, P<0.001)** and slowed the average expenditure increase of patients (coefficient= 0.051, P<0.001).
(46) Ma, 2016[70]	Antibiotic use Before and after study One hospital ICU patients (n=978) June 2010 to May 2011 and June 2012 to May 2013	Antimicrobial stewardship strategy in ICU (emanating from Ministry of Health Policy 2011)	Coercion / restriction	Guidelines / regulation	**Monthly mean Defined Daily Dose (DDD) per 100 occupied bed-days; proportion of patients colonized or infected with MDRO;**	**Monthly mean DDD decreased from 96 ± 7 to 65 ± 6 (p < 0.001);** **Proportion of patients colonized / infected with MDRO decreased from 36 to 13% at ICU admission and declined from 48 to 29% at ICU discharge (both p < 0.001).**

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(47) Shen, 2011[69]	Antibiotic use Prospective case-control study Two independent respiratory wards at one tertiary teaching hospital, all adult inpatients (n=354; 178 controls, 176 intervention) July 2009 to April 2010	Clinical pharmacist intervention, including: (1) indication: antibiotics used only when indication was adequate; (2) choice: appropriate choice of antibiotics; (3) dosage: appropriate dosage of antibiotics; (4) dosing schedule: appropriate interval between doses; (5) duration: appropriate treatment duration for antibiotic therapy; (6) conversion: timely conversion from intravenous to oral therapy.	Education / training	Service provision	Total cost of hospitalization; cost of antibiotics; length of hospital stay; 6 items of suboptimal antibiotic use (including indication, choice, dosage, dosing schedule, duration and conversion)	Intervention versus control: Total costs of hospitalization: intervention were significant lower ($1442.3 ± 684.9 vs. $1729.6 ± 773.7, P= 0.001); cost of antibiotics was significantly lower ($832.0 ± 373.0 vs. $943.9 ± 412.0, P = 0.01); patients required shorter length of hospital stay (14.2 ± 6.2 vs. 15.8 ± 6.0 days, P = 0.03); 6 items of suboptimal antibiotic use were all lower in the intervention group compared with the control group.
(48) Song, 2014a[68]	Antibiotic use Before and after; retrospective data analysis One University hospitals outpatients department / outpatient prescriptions for one-year March 2012 to March 2013	The Joint Commission International (JCI) accreditation standards including: formulary adjustment; classification management; motivational, information technological educational and organizational measures.	Education / Restriction / Environmental restructuring	Guidelines / regulations	**% of antibacterial prescriptions;** **% prescriptions containing restricted antibacterials;** **% of oral versus all antibacterial prescriptions;** **Rate of DRPs (drug-related problems);** **Total expenditure on antibacterials for outpatients.**	**% of antibacterial prescriptions significantly decreased (12.7% versus 9.9%, P < 0.01).** **% prescriptions containing restricted antibacterials decreased [44.7% in the first, 30.4% in second phase (P < 0.01)].** **% of oral versus all antibacterial prescriptions increased (94.0% to 100%, P < 0.01).** **Rate of DRPs decreased from 13.6% to 4.0% (P < 0.01), with a larger decrease seen in surgical clinics (surgical: 19.5% versus 5.6%; internal medicine: 8.4% versus 2.8%, P < 0.01).** **Total expenditure on antibacterials for outpatients decreased by 34.7% after the intervention**

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(49) Song, 2014b[67]	Antibiotic use Before and after; retrospective data analysis Primary healthcare facilities (n=146 township healthcare centres) in four provinces of China / outpatient prescriptions (n=28,651) 2010 and 2011	China's National Essential Medicines Policy (NEMP) 2009.	Coercion/ restriction	Guidelines / regulation	1.Average number of drugs per prescription 2. Percentage of drugs prescribed from the EDL **3. Average number of antibiotics per prescription** **4. Percentage of prescriptions including an antibiotic** **5. Percentage of prescriptions including an injection** 6. Percentage of prescriptions including adrenal corticosteroid	**Percentage of prescriptions including antibiotics decreased from 60.3 to 58.5% (p < 0.01); Prescriptions for injections decreased to 40.3%.**
(50) Stojanovic, 2017[122]	Cost of care Economic evaluation One hospital / inpatients admitted for acute respiratory infection (n=16,405) 2015	Procalcitonin (PCT) testing among patients with acute respiratory infections (ARI) to aid/inform antibiotic stewardship.	Enablement	Service provision	**Total antibiotic-related costs by setting** (hospital ward, hospital ICU, or clinic/ED) (typical daily dosage multiplied by the wholesale acquisition cost)	**PCT-guided care versus usual care: Costs: 1.1 million Yuan versus 1.8 million Yuan; overall annual net savings of PCT-guided care was nearly 3.4 million Yuan.**
(51) Sun, 2015[66]	Antibiotic use Before and after; interrupted times series analysis Nationwide / tertiary hospitals (n=35) / antibiotic clinical and prescription outpatient (OP) and inpatient (IP) data March 2005 to December 2012	Nationwide intervention on antimicrobial clinical use and its implementation strategy (2011) and Administrative regulations for clinical use of antibacterial agents (2012). Measures include: setting targets; strengthening accountability; auditing clinical indications for antibiotic use; building capacity of infection control; prescribing recommendations; restricting the number of agents prescribed; antimicrobial resistance monitoring and alerts of multi-resistance; guideline training; monthly OP prescription and IP medical record audit;	Education / persuasion / training / restriction / enablement	Guidelines / regulation / service provision	% of OP prescriptions with antibiotic; % of OP prescriptions with parenteral antibiotic; % of IP medical records with antibiotic; % of IP medical records with parenteral antibiotic; % of antibiotic prophylaxis before incision; % of antibiotic prophylaxis duration >24 h	**Before and after change: % of OP prescriptions with antibiotic [β_{2*} =−4.7, p=0.03]**; % of OP prescriptions with parenteral antibiotic [β_2 =−0.7, p=0.5]; **% of IP medical records with antibiotic [β_2 =−7.3, p=0.04]; % of IP medical records with parenteral antibiotic [β_2 =−8.6, p=0.03];** % of antibiotic prophylaxis before incision [β_2 =5.0, p=0.4]; % of antibiotic prophylaxis duration >24 h [β_2 =-8.6, p=0.003] *β_2-immediate effect of the intervention

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(52) Sun, 2016[65]	Antibiotic prescribing / healthcare utilization and expenditure Before and after study; descriptive and times series analysis One province / administrative data from all health facilities (n=636) and a subset of primary care facilities affiliated for CD/OP benefit (n=46) August 2008 to July 2012	Municipal Health Insurance 'common primary care disease outpatient benefit' (CD/OP), available as an opt in for insured individuals (2009); CD/OP benefit covers all diagnostics and treatments (including medicines) as listed by the insurance programmes for primary care services; an annual capitated provider payment replaced the fee-for-service system	Enablement	Service provision	**Quality of medication prescribing (proportions of CD/OP visits during which at least one antibiotic and injectable was prescribed)**; healthcare utilization and expenditure.	**Trend in proportion of CD/OP visits with at least one antibiotic prescribed dropped slightly in August 2009 (P = 0.76) and reversed into a significant increasing trend afterwards (P = 0.02).** **Trend in proportion of CD/OP visits with at least one injectable prescribed dropped by 7.4% (P = 0.03) in August 2009, then continued a downward trend (P = 0.06).**
(53) Tang, 2016[64]	Antibiotic prescribing Randomized controlled trial One province / urban and rural primary care institutions (n=20; 10 intervention, 10 control); routinely collected prescription data for bronchitis (n=36,121), gastritis (n=14,849)) and hypertension (n=18,376) March 2013 to August 2014	Public reporting on antibiotic and injection prescriptions in urban and rural primary care settings	Education / persuasion	Communication / marketing	**% prescriptions containing antibiotics;** **% prescriptions containing two or more antibiotics;** % prescriptions containing injections; **% prescriptions containing antibiotic injections;** **% average prescription cost**	**Difference in difference analyses: % prescriptions containing antibiotics:** Bronchitis [0.02%, p=0.964]; **Gastritis [-12.7%, p<0.001]; Hypertension [2.0%, p=0.008];** **% prescriptions containing two or more antibiotics: Bronchitis [-3.8%, p=0.005];** Gastritis [-0.1%, p=0.898]; Hypertension [0.4%, p=0.073]; **% prescriptions containing antibiotic injections:** Bronchitis [-0.08%, p=0.939]; **Gastritis [-10.7%, p<0.001];** Hypertension [-0.2%, p=0.569]; **% average prescription cost: Bronchitis [-7.9%, p<0.001]; Gastritis [-5.7%, p=0.005];** Hypertension [-1.7%, p=0.388];
(54) Tang, 2018[121]	Antibiotic procurement Interrupted time-series analysis One province / urban and rural health centres (n=1,430), monthly procurement data May 2011 to November 2013	Province administrative rules for clinical use of antibiotics; including: (1) antibiotics are categorized into three groups— non-restricted, restricted and controlled; (2) administrative restrictions; (3) penalties for violation of rules August 2012	Restriction / coercion	Guidelines / regulation	**Procurement volume of parenteral administered restricted antibiotics; cost of parenteral administered restricted antibiotics;** **procurement cost of non-restricted oral antibiotics**	**Trends:** **procurement volume of parenteral administered restricted antibiotics [– 0.038 million DDDs per month, p = 0.05]; cost of parenteral administered restricted antibiotics [– 0.28 million Yuan per month, p = 0.019];** **procurement cost of non-restricted oral antibiotics [– 0.36 million Yuan per month, p = 0.029]**

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(55) Tang, 2017[63]	Antibiotic prescribing Before and after study; cluster randomized-controlled trial A city in one province / primary care institutions (n=20), prescriptions for upper respiratory tract infection (URTI) (n=31,460) Pre-intervention 2013, intervention March to September 2014	Monthly publicly reported prescription indicators including: (1) percentage of prescriptions containing antibiotics; (2) percentage of prescriptions containing injections; and (3) average expenditure per prescription; prescribers were categorised as high, average or low prescribers.	Education / persuasion	Communication / marketing	% reduction in URTI antibiotic prescribing attributed to intervention; % reduction in combined antibiotic prescribing attributed to intervention	% reduction in antibiotic prescribing: **2.82% [95% CI, −4.09, −1.54%, P<0.001];** % reduction in antibiotic prescribing in low prescribers (−1.41%, 95% CI, −3.81, 0.99%, P=0.249); % reduction in antibiotic prescribing in average **prescribers (−5.01%, 95% CI, −6.94, −3.07%, P<0.001)**. % reduction in all antibiotics prescribing: **3.81% (95% CI, −5.23, −2.39%, P<0.001);** % reduction in antibiotic prescribing in low prescribers **(−2.42%, 95% CI, −4.39, −0.45%, P=0.016);** % reduction in antibiotic prescribing in average **prescribers (−5.01%, 95% CI, −7.47, −2.56%, P<0.001).**
(56) Wang, 2015[62]	Prophylactic antibiotic prescribing Before and after study A city in one province / tertiary hospital, obstetrics and gynaecology / elective caesarean section patients (n=394; before n=197, after n=197) Pre-intervention: June to August 2012, post-intervention: October to December 2012	Clinical pharmacist intervention including: obstetrician education, real-time monitoring of clinical records and making recommendations to obstetricians on prophylactic antibiotic prescription	Education / enablement	Service provision	The evaluation criteria included: 1. choice of antibiotic; 2. dosing; 3. administration route; 4. timing of administration of first pre-operative dose; 5. need for additional dose during surgery; 6. duration of prophylaxis; 7. need for combination of antibiotics.	% change pre- and post-intervention: Correct choice of antibiotics 4% versus 94%; plus dose 4% versus 94%; plus correct timing 3% versus 93%, **plus correct duration 0% versus 19% (p<0.001)**
(57) Wei, 2017a[61]	Antibiotic prescribing Pragmatic, cluster-randomised controlled trial Two counties within one province / primary care township hospitals (n=25; 12 intervention, 13 control)/ children aged 2-14 years attending outpatients and diagnosed with upper respiratory tract infection (URTI) July 2015 to March 2016	Complex antimicrobial stewardship intervention including: clinician guidelines and training on appropriate prescribing, monthly prescribing peer-review meetings, and brief caregiver education.	Education / training / enablement	Guidelines / regulation / service provision	**Antibiotic prescribing rate in children attending the hospitals**	Pre- and post-implementation: Antibiotic prescription rate at the individual level decreased from 82% (1936/2349) to 40% (943/2351) in the intervention group, and from 75% (1922/2548) to 70% (1782/2552) in the control group. **Absolute risk reduction in antibiotic prescribing of −29% (95% CI −42 to −16; p=0·0002).**

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(58) Wei, 2017b[60]	Antibiotic prescribing Mixed-method – retrospective cohort data and qualitative interviews Two counties within one province / outpatient and inpatient records from two county hospitals / children aged 2-14 years attending outpatients and diagnosed with upper respiratory tract infection (URTI) 2011 to 2014	National essential medicines scheme and zero-mark-up policy (2009)	Coercion/ restriction	Guidelines / regulation	**Antibiotic prescribing rate (APR) in children attending the hospitals**	**2011, APR intervention, 30% and comparison hospital 88%.** **2014, APR intervention reduced by 21% (95% CI: 23%, 18%, p<0.001), intravenous infusion by 58% (95% CI: 64%, 52%, p<0.001) and prescription cost by 31 USD (95% CI: 35, 28, p=<0.001), compared with the controls.**
(59) Yang, 2013[39]	Antibiotic prescribing Quasi-intervention time-series analysis One province / primary care organisations (n=18) / prescription data (n=55,800) January 2009 to July 2011	National essential medicines policy (NEMP) (2009)	Coercion/ restriction	Guidelines / regulation	Percentage of drugs prescribed from the EML; average number of medicines per prescription; average expenditure per prescription; percentage of prescriptions requiring antibiotics; and percentage of prescriptions requiring injections.	38 151 prescriptions (68%) included antibiotics, and no evidence of reductions were found after the NEMP interventions. Average cost per prescription declined significantly post NEMP (¥ 44.67 vs ¥ 26.67 CNY, P<0.03).
(60) Yang, 2014a[58]	Antibiotic prescribing Matched-pair cluster-randomized trial A city in one province / primary care institutions (n=20) / outpatient prescriptions for upper respiratory tract infection (URTI)(n=34,815) Pre-intervention: March to May 2013; post-intervention: March to May 2014	Public reporting (PR) on antibiotic prescribing for URTIs (October 2013: monthly prescription statistics were disclosed to patients, health authorities and health workers (intervention); identical training on appropriate prescribing to intervention and control.	Education / persuasion	Communication / marketing	Reduction in antibiotic prescribing rates	PR resulted in: **9% (95% CI −17 to −1) reduction in the use of oral antibiotics (adjusted RR =39%, p=0.027);** Unchanged use of injectable antibiotic; **7% (95% CI −14 to 0; adjusted RR =36%, p=0.049) reduction in combined use of antibiotics;**

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(61) Yang, 2014b[57]	Antibiotic use Case-control study A city / one university hospital / surgical wards / patients undergoing selected operations (n=1543; n=778 controls, n=765 cases) September to December 2012	Drug Rational Usage Guidelines System (DRUGS): clinical practice guidelines embedded in a computerised surgeon order system includes pop-up information for clinicians	Education / enablement	Guidelines / service provision	**Antibiotic administrative categories; time of initial dose; duration of administration; length of stay; costs of antibiotics**; SSIs and adverse drug reactions (ADR).	Controls versus cases: **average length of hospital stay 7 days versus 2.5 days; dose within 24 hours 91% versus 15%; average cost of antibiotics ¥3481 versus ¥1693;** no significant differences in the incidence of SSIs and ADR between two groups
(62) Yao, 2015[56]	Antibiotic prescribing Before and after study: retrospective analysis of routine data One province / primary care facilities (n=192) (urban and rural) / prescription data (n=22,973) 2009 to 2010	National Essential Medicines Scheme (NEMS) (introduced January 2010)	Coercion/ restriction	Guidelines / regulation	1. average number of drug types per prescription; **2. percentage prescriptions containing antibiotics;** 3. percentage prescriptions containing injections; and 4. percentage EML drugs	Before versus after stratified by urban/rural: average antibiotic prescription incidence in urban facilities (62% versus 63 %) and rural facilities (67 % versus 66 %).
(63) Yip, 2014[55]	Antibiotic prescribing Matched-pair cluster-randomized experiment One province / all New Cooperative medical Scheme enrolees (n=440,473) 2009 to 2011	Capitated budget policy versus pay-for-performance	Incentivisation	Fiscal	**Percentage change in visits with antibiotic prescription**	Capitation versus pay-for performance: **visits with antibiotic prescription; township health centre -6.6%, p<0.05; village posts -6.0%, p<0.05**

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(64) Zhang, 2014a[54]	Prophylactic antibiotic use Before and after study: retrospective cohort One province / a tertiary hospital urology surgical department / records of surgical patients (n=370; pre-intervention (n=196, post-intervention (n=174)) Pre-intervention: January to June 2011; post-intervention: January to June 2012	A clinical pharmacist intervention including: real-time monitoring of medical records and controlling prescriptions of prophylactic drugs against criteria	Education / restriction	Guidelines / service provision	**Total number of cases administered prophylactic antibiotics; mean number of antibiotics used; mean antibiotics cost; mean duration of prophylaxis**	Pre versus post-intervention: **total % of cases administered prophylactic antibiotics [100% versus 77%, p<0.001]; mean number of antibiotics used [1.7 versus 1.3, p<0.001]; mean antibiotics cost (USD) [339 versus 99, p<0.001]; mean duration of prophylaxis (days) [8 versus 3, p<0.001]**
(65) Zhang, 2008[53]	Antibiotic use Before and after study: retrospective cohort data Four cities (in separate provinces) / large children's tertiary hospitals (n=5) / antibiotic prescriptions for all in-patients aged 0-18 years 2002 to 2006	National Guidelines for Antibacterial Use in Clinical Practice (2004) and subsequent local implementation	Education / restriction	Guidelines	**Percentage of antibiotic use; overall antibiotic use by hospital and year (defined daily doses/100 bed-days - DDD)**	**In 2006, overall antibiotic use decreased by 22.6% (P= 0.042).** **2002 versus 2006 DDD antibiotic use by hospital (B, SA, SB, C, G): B 41 versus 45; SA 98 versus 39; SB 49 versus 39; C 81 versus 57; G 106 versus 69**
(66) Zhang, 2014b[52]	Antibiotic prescribing Before and after study: retrospective analysis of routine data One province and city / township hospitals (n=22) / doctors (n=274) Before: July to October 2013; After: November 2013 to February 2014	Monthly public medicine use information to patients and doctors (intervention): including the values and rankings of average expenditure per prescription, percentage of prescriptions requiring antibiotics, and percentage of prescriptions requiring injections for each hospital and each doctor prescribing medications	Education / persuasion	Communication / marketing	Prescription costs; **antibiotics use**; and injection use	Pre versus post intervention: average prescription cost 43 versus 47 Yuan; **% prescriptions containing antibiotics 63 versus 61%;** % prescription containing injections 71 versus 66 %.

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(67) Zhang, 2007[51]	Antibiotic use Before and after study: cross-sectional survey All counties / township hospitals and village health centres (n=419; pre-intervention n=345, post intervention n=74)/ mothers of sick children (n=678, pre-intervention n=542, post-intervention n=136) Before: April to June 2004; After: April to June 2006	Integrated Management of Childhood Illness (IMCI) strategy which includes three components: improving health worker's skills; improving family and community practice; improving the health system	Education	Guidelines	**Rational use of drugs**; provision of basic equipment; drug supplies to both township and village facilities	Before and after suboptimal use of drugs significantly decreased: **injection/IV (43.6% to 2.7%), antibiotics (59.3% to 6.2%)** and hormones (4.9% to 0)
(68) Zhang, 2017[50]	Antibiotic prescribing Retrospective analysis of trends in routine data One city in one province / data from medical insurance information system / adult (over 18 years) inpatients with medical insurance of urban workers (UEBMI) (2003: n=18,505; 2014: n=92426) 2003 to 2014	Guidelines for antimicrobial use in clinical practice (Ministry of Health of China, 2004). National antimicrobial stewardship action plan (Ministry of Health of China, 2011, 2012, 2013)	Education / restriction	Guidelines / regulation	Trends in: **antimicrobial prescription rates; proportion of inpatients used one antimicrobial; proportion of inpatients used three or more antimicrobials; bacterial culture rate**	Trends in: **antimicrobial prescription rates: 2003 to 2014 [79% to 44%; adj. OR 0.21; 95% CI 0.29, 0.21]; proportion of inpatients used one antimicrobial: 2003 to 2014 [26% to 47%]; proportion of inpatients used three or more antimicrobials: 2003 to 2014 [47% to 24%]; bacterial culture rates: 2003 to 2014 [20% to 37%; adj. OR 2.25; 95% CI 2.15, 2.35]**
(69) Zhou, 2015[49]	Antibiotic use Retrospective analysis of routine data One city in one province / tertiary hospital urological department / data on antibiotic use for all patients undergoing clean urological surgery 2010 to 2013	National special rectification scheme on clinical use of antibiotics (2011). Pharmacist participation in antibiotic management (June 2011) including: establishment of an antibiotic management working group in the hospital; monthly statistical analysis of antibiotic use of the whole hospital.	Education / restriction / enablement	Guidelines / regulation / service provision	Number of discharged patients; hospitalization days; **antibiotic use density (AUD); antibiotic use rate**; total drug cost; **antibiotic cost**	Change from 2010 to 2013**: AUD decreased by 59%; average antibiotic cost decreased by 246.94 dollars; cost of antibiotics (percentage of total drug cost) decreased by 28%; rate of use of antibiotics decreased from 100% to 7.3%.**

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(70) Zou, 2015[48]	Antibiotic consumption Time series analysis One city in one province / University tertiary hospital / hospital, pharmacy and laboratory data / inpatients 2009 to 2013	National special rectification scheme on clinical use of antibiotics (2011).	Education / restriction	Guidelines / regulation	Annual antibiotic consumption; antibiotic resistance rates;	**Annual antibiotic consumption from 2009 to 2013: decreased from 62 to 28 DDDs (defined daily dose) /100 PDs (patients per day) (β =−10.50, p=0.022)**
(71) Zhou, 2016[47]	Prophylactic antibiotic use Before and after study: cross-sectional survey 30 provinces / secondary and tertiary hospitals (n=244) / in patient (n=36,600) and outpatient (n=29,280) prescription data 2011 (before) and 2012 (after)	National special rectification scheme on clinical use of antibiotics (2011): included regulation and quality assurance, rational use, human resources and education, monitoring and evaluation of the antibiotics.	Education / restriction	Guidelines / regulation	percentage of microbiology testing; antibiotic prophylactic use for type 1 incision operations (T1IO);	**2011 versus 2012: percentage of microbiology testing [30% versus 50-80%]; antibiotic prophylactic use for T1IO [60% versus 44%, p<0.001**]
(72) Zou, 2014[46]	Antibiotic use Before and after study: retrospective analysis of routine data 30 provinces / secondary and tertiary hospitals (n=244) / in patient (n=33,900; before n=15,750, after n=18,150) and outpatient (n=27,120; before n=12,600, after n=14520) prescription data 2011 (before) and 2012 (after)	National special rectification scheme on clinical use of antibiotics (2011). Included regulation and quality assurance, rational use, human resources and education, monitoring and evaluation of the antibiotics.	Education / restriction	Guidelines / regulation	Antibiotic use: defined daily doses (DDDs) per 100 inpatient days; percentage of antibiotic use in outpatient prescriptions; percentage of antibiotic use in inpatient cases	2011 versus 2012: **DDD/100 inpatient days [39% versus 27%, p<0.001]**; percentage of antibiotic use in outpatient prescriptions [24% versus 19%, p=0.109**]**; **percentage of antibiotic use inpatient cases [65% versus 60%, p=0.006]**

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(73) Sun, 2017[45]	Prescribing behaviours Retrospective analysis of prescription data National / cities (n=36) / urban community health institutions / prescription data (n=442,100) 2007 to 2011	Government health funding (GHF)	Incentivisation	Fiscal	Average number of drugs per prescription; % of prescriptions with injections; **% of prescriptions with antibiotics; % of prescriptions with 2 or more antibiotics**	2007 versus 2011: **% of prescriptions with antibiotics [45% versus 31%]; % of prescriptions with 2 or more antibiotics [14% versus 8%]**
	SYSTEMATIC REVIEWS					
(74) Penm, 2014[44]	Impact of clinical pharmacy services on use of medicines, including antimicrobials Systematic review National / studies included inpatient (n=51), outpatient (n=20) and both (n=4) / different therapeutic areas 2005 to 2012	Clinical pharmacy services in hospitals: inpatient interventions included pharmacists educating doctors and patients, evaluating and monitoring hospital policies and/or reviewing medications on the ward. Outpatient interventions included educating patients. 33 included a multimodal approach i.e. an additional intervention alongside clinical pharmacy services.	Education / restriction	Guidelines / service provision	Clinical and humanistic and economic measures	China has implemented clinical pharmacy services in a range of inpatient and outpatient settings. Nearly all studies reported that clinical pharmacy services positively influenced clinical and humanistic outcomes by increasing appropriate use of medication, patient knowledge, quality of life, adherence and reducing patient length of stay. Two studies found no significant effect of clinical pharmacy services on surrogate markers in the outpatient setting on patients with diabetes.
(75) Yuan, 2017[43]	Antibiotic prescribing Systematic review International studies (n=21) including China (n=1) / outpatient primary care and mental health facilities 1927 to 2016	Three payment comparisons.1) Pay for performance (P4P) plus existing payment method versus existing payment method. 2) Capitation combined with P4P versus fee-for-service (FFS). 3) capitation versus FFS.	Incentivisation	Fiscal	Various	Capitation combined with a pay-for-performance system targeted at reducing antibiotic use probably slightly reduces antibiotic prescriptions when compared to a fee-for-service system. One study from China is included in this scoping review