Supplement

Table A - **List Of Countries Included In The Review Based On The World Bank Classification Of Economies (1)**

Low- and middle-income countries	High income countries
Albania	Australia
Azerbaijan	Denmark
Bangladesh	France
Bosnia and Herzegovina (including Republic of Srpska)	Germany
Botswana	Iceland
Brazil	Kuwait
Bulgaria	Netherlands
China	New Zealand
Ethiopia	Norway
Ghana	Qatar
India	Singapore
Iraq	Slovenia
Jordan	Spain
Kenya	Sweden
Kosovo	Taiwan
Lebanon	United Kingdom
Malawi	United States of America
Malaysia	
Mexico	
Mongolia	
Namibia	
Nigeria	
Pakistan	
Poland	
South Africa	
Sri Lanka	
Swaziland	
Syria	
Thailand	
Vietnam	
Zambia	
Zimbabwe	

Table B: Epidemiology of URTIs across Countries.

Country	Epidemiology
High income countries	
Australia	Respiratory tract infections were the most common reason for patients to visit their general practitioner (GP) (2, 3).
UK	Most people in the UK will develop an acute respiratory tract infection every year, with these infections seen as the commonest acute problem dealt with in primary care (4)
USA	• There were an estimated 14.4 million ambulatory care visits among all ages for influenza between 1997 and 2001 (5) • Overall, approximately 25 million cases of URTIs are managed annually by family physicians in the US, resulting in approximately 20-22 million days of absence from work or school each year (6)
Lower- and Middle-income countries	
Botswana	Excluding neonatal conditions, unspecified acute respiratory infections accounted for 3.5% of the outpatient childhood morbidity in 2010 (7).
Ethiopia	Results from the 2011 Ethiopian Demographic and Health Survey conducted among 11,645 children under five years of age and their mothers showed a prevalence rate of 7% for ARIs (8)
Ghana	The annual age-dependent incidence for URTIs varied from 7.9% to 8.3% between 1995 and 2000 (9).
Greenland	Among the Sisimiut population, the incidence of URTIs was 1.6 episodes per 100 days at risk in this population <2 years old (10).
India	• Among 3498 urban and rural patients, 8.2% had an URTI (11) • In another study in India among children from the urban slums in Gulbarga city, acute respiratory infections were seen among 27.25% of children with URTIs predominating (12) • In a separate study among children aged 0 to 10 in a rural north Indian community, the incidence of ARI was 5.9 (5.8-6.0) per child-year with minimal gender differences (13) • In one Indian hospital, 20-40% of outpatient visits and 12-35% of inpatients were because of an URTI, with most of these infections due to respiratory viruses (14, 15)
Malaysia	Out of a total of 123,524 prescriptions analysed in patients attending ambulatory care clinics in Malaysia, 5.8% of patients were diagnosed with an URTI (16).
Malawi	Among infants below 5 years of age, the yearly frequency of acute respiratory infections including URTIs was 32.6%, with a point prevalence of 8.3% (17).
Nigeria	Results from the 2013 Nigerian National Demographic and Health Survey revealed that 2% of children had symptoms suggestive of acute respiratory tract infections around whilst 13% of children had fever which is a major sign of an ARI (18)
Vietnam	The number of new cases for ARI among children was 623 per 100,000 inhabitants in 2008 (19).

NB: ARI = Acute respiratory tract infection; URTI = Upper respiratory tract infection

Table C: Physician prescribing Practices for Patients with Respiratory Tract Infections across among high income countries

Country	Antibiotic utilization
Australia	• In a survey conducted in 2014, 56.5% of general practitioners stated they would very often, often or sometimes prescribe an antibiotic for an URTI to meet patient expectations (3) • In a study published in 2016, 47% of patients diagnosed with an acute URTI were prescribed an antibiotic. This was despite guidelines indicating an acceptable range of between 0% - 20% for prescribing an antibiotic (20)
Denmark	Antibiotics prescribed were for URTIs in approximately 20% of encounters in ambulatory care (21).
European Union	Over 50% of patients presenting in ambulatory care with an acute cough among EU countries are currently prescribed antibiotics (range from just over 20% to 80%) whereas the appropriate figure should be only 10% (22-24).
Germany	Antibiotics were prescribed in 41% of consultations in ambulatory care for acute lower respiratory tract infections (25, 26).
Italy	• Antibiotics were prescribed in 67.3% of the consultations between physicians in local health units in Southern Italy and patients with acute respiratory tract infections (pharyngitis, bronchitis, influenza, and sinusitis) • Macrolides were the most frequently prescribed antibiotics followed by amoxicillin with clavulanic acid and the fluoroquinolones (27).
Netherlands	27% to 29% of patients visiting their family doctor were prescribed antibiotics for their acute respiratory tract infections (28).
Norway	27% of patients visiting their family doctor were prescribed antibiotics for their acute respiratory tract infections (29).
Taiwan	In children younger than 18, only 7% of patients received an antibiotic for a URTI between 2000 and 2009 (30), with an overall reduction in the prescribing of antibiotics for acute tonsillitis in children following greater awareness of likely causes (31).
UK	An appreciable number of patients presenting in ambulatory care with an acute uncomplicated RTI still received an antibiotic prescription – with many doctors and patients believing that this is the right thing to do (4)
USA	• Among commercial health plans between 2008 and 2012, 77% of children in healthcare plans in the US with pharyngitis tested for group A *Streptococcus* (strep) and received an antibiotic, with avoidance of antibiotic treatment for adults with bronchitis was 24%. It was estimated that the proportion of children that were not prescribed antibiotics for their URTI did not change – ranging from 83.4% to 85% in 2011 (32). • In another study conducted among ambulatory care practices between 2011 and 2012, it was estimated that approximately two-thirds of ambulatory care visits for acute respiratory tract infections may not be appropriate for antibiotic management (33) • In a third study conducted among patients attending the Cleveland Clinic Health System between 2011-2012, 54.8% of patients with a respiratory tract infection received an antibiotic (34) • In a fourth study published by Vaz et al in 2014, among children in 3 commercial health plans, RTIs accounted for a high percentage of all antibiotics prescribed (75%) with pharyngitis was the most common diagnosis associated with an antibiotic in children 6 to <12 years (35) • Overall, the prescribing of antibiotics for patients with acute respiratory infections in the US has decreased from 175 prescriptions per 1000 people in 2000 to 102 in 2010 (36) • In a more recent study, conducted between 2013 and 2015, 41% of 14 987 patients presenting in ambulatory care with an acute respiratory infection were prescribed an antibiotic. Among these 6136 patients, 41% had diagnoses for which antibiotics were not appropriate, with 84% seen as having a viral URTI or bronchitis (37)

Table D: Prevalence of Non-Prescription sales of antibiotics particularly for URTIs among LMICs

Country	Extent of self-purchasing
Bangladesh - 2014 and 2018	A) First study - 2014 (38): • Cross-sectional survey among 1300 patients • 26.69% had self-medicated with antibiotics • Perceived symptoms to purchase antibiotics was dysentery, diarrhoea and food poisoning (36.02%) followed by URTIs - cold, cough and fever (28.24%) B) Second study - 2018 (39): • Cross-sectional, questionnaire-based study among 250 undergraduate pharmacy students • 15.6% of students self-medicated with antibiotics for predominantly minor illnesses including URTIs • Greater use of antipyretics (58.4%) and analgesics (59.2%) for a range of predominantly minor illnesses
Bulgaria – 2014 (40)	• Observational cross-sectional study analyzing patient opinions and attitudes on self-medication with antibiotics including respiratory tract infections (1050 patients) • Self-medication rate with antibiotics was 43% • 24.2% of the patients had started taking antibiotics for a high temperature or fever and 24% for a sore throat and cough
China – 2014, 2017 and 2019	A) First study - 2014 (41): • Cross-sectional study conducted in vaccination clinics in rural counties in China among primary caregivers (typically parents) • 79% of caregivers thought antibiotics could cure viral infections, and half of the caregivers believed antibiotics could shorten the duration of URTIs resulting in 62% of the parents self-medicating their children with antibiotics B) Second study - 2017 (42): • Multicentre cross-sectional study among 256 pharmacists using simulated patients presenting with a URTI • 77.7% of staff dispensed an antibiotic without a prescription despite such practices being banned since 2004, greatest after simulated patient insistence • Pharmacists were only available in 14.8% of community pharmacies, with lower rates of non-prescription sales of antibiotics (but not significant) C) Third study – 2019 (43) • Simulated client method study among 2423 community pharmacies in six provinces in China • Non-prescription sales of antibiotics were observed during 70.1% adult URTI interactions
Ethiopia – 2015, 2017 and 2018	A) First study - 2015 (44) • Comparative cross sectional study design conducted in both urban and rural areas involving 1082 participants • Inappropriate use of antibiotics was 30.9% - self medication at 18.0% and 12.9% coming from family members • Amoxicillin most commonly used antibiotic - urban (67.3%) and rural (62.3%) communities followed by ampicillin • Respiratory tract symptoms were the most common reason for antibiotic use (74.6%) B) Second study - 2017 (45): • Community based cross-sectional survey conducted among 650 participants • Nearly half (48.5%) of participants in the survey had taken antibiotics in the previous year, with 36.8% of respondents obtaining their antibiotics from community drug retail outlets without a prescription • Respiratory tract infections (40.9%) the most common reason for which antibiotics were taken C) Third study - 2018 (46)

	• 2 phase mixed-methods study using simulated patients (50 patients) and in-depth interviews among community pharmacists in Ethiopia • 92% of simulated patients were dispensed an antibiotic without a prescription for a URTI, with the most common antibiotics dispensed being amoxicillin and amoxicillin-clavulanic acid • The interviews confirmed that the dispensing of antibiotics for URTIs was a common occurrence enhanced by financial gain and patient expectations
Ghana – 2012 and 2018	A) First study - 2012 (47): • Descriptive cross-sectional study involving face-to-face interviews with 600 tertiary students • Overall, considerable self-purchasing of antibiotics among tertiary level students (70%); however, significantly lower among medically inclined students • The most common antibiotic used was amoxycillin, and the majority of antibiotics were purchased for colds, coughs and fevers B) Second study – 2018 (48): • Twice-weekly visits to 12 households in three rural communities over 8 weeks • Most (65%) medicine-use events involved self-treatment w40% of medicine-use events involving antibiotics often without a prescription • Penicillins were the most commonly dispensed antibiotic The ease of access to antibiotics in pharmacies makes reducing AMR in Ghana a challenge. This is likely to change in the future with the recent launch of the national action plan in Ghana to reduce AMR (49, 50)
India - 2014 and 2015	A) First study - 2014 (51): • Community based cross sectional study aiming to gather information about the prevalence of self-medication with any treatment among 600 respondents • 16.7% purchased antibiotics, with self-purchasing of NSAIDs (25.3%), GI medication (20.8%) and antihistamines (19.7%) more common • Fever was the second most common ailment (14.5%) followed by respiratory problems and asthma (11.7%), with coughs and colds at 7% B) Second study - 2014 (52): • Prospective cross-sectional survey based study involving 781 members of the general population aged between 18 to 55 years • Prevalence of self-medication with antibiotics was 39.1% • Colds and fever were the most common reasons for antibiotic use (male 47.6%, female 36.7%), with use also for coughs and a sore throat (male 12%, female 8.15) C) Third study - 2015 (53): • Cross-sectional study involving simulated clinical scenarios among 261 pharmacies including URTIs • Antimicrobial drugs were obtained without prescription in 66.7 % pharmacies for 2 indications • Overall, antibiotics were dispensed without a prescription in 71.3% of simulated patients with URTIs
Indonesia - 2011 (54)	• Cross-sectional population-based survey self-administered to 625 randomly selected respondents over 18 years old, with 599 analysed • Self medication with antibiotics during the month prior to the study was 7.3%, with amoxicillin the most requested antibiotic (77%) • The common cold including a cough and a sore throat were the most common symptoms leading to self-medication
Iraq – 2014	A) First study (55): • Cross-sectional survey involving 348 patients were ≥ 15 years old • Influenza or the common cold were the commonest indications for self-medication • Antibiotics were the commonest medicines used for self-medication (74.7%) B) Second study (56):

	• Cross-sectional pilot exploratory study with simulated patients among 20 pharmacists with simulated patients asking the pharmacist about the strongest antibiotic for common cold • 45% of community pharmacists dispensed an antibiotic for a common cold usually in conjunction with symptomatic treatment • Amoxicillin was the most common antibiotic dispensed (44.4%) followed by amoxicillin/clavulanate (22.2%) The purchasing of antibiotics without a prescription takes place despite the legal position, and overall occurs in almost 100% of pharmacies for various conditions in addition to URTIs. This includes all common classes of antibiotics
Jordan - 2015 (57)	• Prospective study involving simulated women of childbearing-age with five different clinical scenarios visiting a total of 202 pharmacies • The clinical scenarios included a sore throat, otitis media, acute sinusitis, diarrhoea or a urinary tract infection • The percentage of pharmacies dispensing antibiotics without a prescription included: sore throat (97.6%), urinary tract infection (83.3%), diarrhoea (83%), otitis media (68.4%) and acute sinusitis (48.5%)
Lebanon – 2015 (58)	• Descriptive cross-sectional study involving 100 pharmacists in both high and low socioeconomic areas • 71% of pharmacists would prescribe an antibiotic for adults suffering from sore throat and fever, with 43% doing the same for children • Overall, 64% of pharmacists would prescribe antibiotics for adults with a sore throat, high fever and exudation in the absence of cough, 44% would prescribe antibiotics for adults with a cough and fever, and 46% for a cough, fever, chest pain and shortness of breath • Pharmacists working in lower socio-economic areas where more likely to prescribe antibiotics
Malaysia - 2013 and 2014	A) First Study - 2013 (59): • Cross sectional study involving simulated patients with symptoms of a common cold visiting 20 GP clinics and 50 Pharmacies • Antibiotics were dispensed in 32% of community pharmacies without a prescription – lower that the rate see among physicians (65%) • Greater dispensing of antihistamines (76%) and expectorants/ mucolytics/ antitussives (73%) B) Second study - 2014 (60): • Cross-sectional exploratory design with simulated patients with symptoms of a common cold involving 140 visits - 100 visits to 50 pharmacies and 40 visits to 20 GP Clinics • A greater number of GPs (65%) prescribed and dispensed antibiotics than community pharmacists (32%) for symptoms of a common cold • Amoxicillin and co-amoxiclav were the principle antibiotics prescribed/ dispensed
Mongolia - 2010 (61)	• Community-based cross-sectional survey involving 503 participating caregivers • 42.3% of children were given non-prescribed antibiotics in the past six months. Commonly treated symptoms with antibiotics were coughs (84%), a fever (66%), a nasal discharge (65%) or a sore throat (60%) • Amoxicillin was the most commonly used antibiotic (58%) followed by ampicillin (25%)
Nigeria – 2014, 2016 and 2018	A) First study - 2014 (62): • Prevalence study with 423 mother-child pairs • The prevalence of unprescribed (self-purchased) antibiotics in children with URTIs aged <5 years was 75.9% • Antibiotic abuse was commoner in older children with URTIs and among mothers with higher educational attainment B) Second study - 2016 (63):

	• Cross-sectional survey among 1,150 randomly patients attending 25 Primary Health Centers • The prevalence of antibiotics self-medication was common (82.2%) • Ampicillin/ cloxacillin combinations (24.1%) and ampicillin (20.3%) were the most common antibiotics for self-medication • A cough with productive mucus (30.1%) and a sore throat (23.7%) were the most frequent indications for self-medication C) Third study - 2018 (64): • Cross-sectional study evaluating the extent of self-medication with antibiotics and knowledge of antibiotic resistance among 1230 undergraduate students and community members • Frequency of antibiotic use among undergraduate students was 43% weekly and 26% weekly among community participants • Amoxicillin/clavulanic acid was the most common antibiotic for self-medication • Greater use of antibiotics for malaria, typhoid and dysentery than ear and throat pain D) Fourth study - 2018 (65): • Cross sectional community-based study using a semi-structured and self-administered questionnaire among 400 participants • Non-prescribed antibiotics were taken for asthma (5.7% of participants), sore throat (13.8%), a cold and cough (42.7%), and fever (16%) • Penicillin (58%) was the most regularly taken antibiotics followed by the quinolones (22%)
Pakistan - 2012 and 2016	A) First study - 2012 (66): • Cross-sectional study among 371 pharmacies using simulated patient to collect information on potential management of patients with acute respiratory tract infections • 82.2 % (n = 305) were dispensed medicines with 7.3 % referred to a physician • 57.4 % were dispensed an antibiotic, 12.8 % an antihistamine and 29.7% a NSAID B) Second study - 2016 (67): • Cross sectional study evaluating the use of antibiotics for URTIs among pharmacy and non-pharmacy university students • 87.8% of pharmacy students self-medicated with antibiotics versus 71.4% of non-pharmacy students. Both also used symptomatic treatments – higher in pharmacy students (88.4%) vs. non-pharmacy students (47.2%) • Self-purchased antibiotics included the beta-lactams (45.9%) and macrolides (26.5%)
Sri Lanka – 2019 (68)	• Cross-sectional survey among a random sample of community pharmacies (369) across all nine provinces in Sri Lanka using a self-administered questionnaire with 320 responding (pharmacists and pharmacy staff) • One in three pharmacy staff stated they had dispensed antibiotics without a prescription following patients' request rising to half of the pharmacy staff when the patient was known to them • Approximately 30% of surveyed pharmacists reported to have supplied antibiotics for minor infections in the week prior to the survey
Syria – 2011 (69)	• Cross-sectional study involving simulated patients visiting 200 pharmacies with symptoms of URTIs and requesting an antibiotic (despite non-prescription sales prohibited by law) • 87% of pharmacists sold antibiotics without insistence, 10% after insistence, and 3% refused to sell an antibiotic without a prescription • The most common antibiotic sold was co-amoxiclav (50.4% - 2 strengths) followed by amoxicillin (23.1%)

Tanzania – 2013 (70)	• Cross-sectional explorative study with simulated patients visiting 145 different pharmacy stores in Tanzania with up to 9 different cases which include symptoms of a URTI • Up to 79% of pharmacy stores sold antibiotics without a prescription including patients with URTIs
Thailand – 2014 (71)	• Cross-sectional descriptive research to assess knowledge, attitudes, and practices regarding antibiotics use among 396 adults • 37.4% stated that they sometimes take antibiotics every time they start to feel unwell • 18 – 19% stated they would buy the same antibiotics that worked in the past to save time and money
Uganda - 2016	A) First study (72): • Cross-sectional survey design study collecting qualitative and quantitative data from 200 households • 43% of children under 5 were being self-medicated with an antibiotic for an acute respiratory tract infection • Penicillins (43%) and sulphonamides (40%) were the most self-prescribed classes of antibiotics for respiratory tract infections B) Second study (73): • Cross sectional study visiting 170 drug stores using interviewees discussing children under 5 including those with severe URTIs • 93.5% of stores prescribed and sold antibiotics for patients with signs/ symptoms of severe URTIs • Amoxicillin (89.4%) and cotrimoxazole (95.6%) were the most dispensed antibiotics
Vietnam – 2011 and 2014	A) First study - 2011 (19): • Caregivers among 828 household were interviewed using a structured questionnaire about actual antibiotic use for children under five with acute respiratory infections in their household • 62% of children had been given antibiotics and 63% of antibiotic courses were used for mild acute respiratory tract infections during a 28-day period. This included both prescribed and non-prescribed antibiotics • Extended spectrum antibiotics such as ampicillin or amoxicillin were the most commonly used antibiotics (49%), followed by cephalosporins (27%) B) Second study - 2014 (74): • Cross sectional study observing all medicine sales among 30 private pharmacies (15 Urban and 15 Rural) coupled with semi-structured, in-depth interviews among pharmacists and drug sellers • Antibiotics were the most commonly sold medicines in community pharmacies, with most antibiotics sold without a prescription (88% to 91% of situations) • A cough was the most frequent reason for buying an antibiotic among urban patients (32%) and a fever among rural patients (22%)
Zambia – 2016 (75)	• Structured, interviewer-administered questionnaire among 73 pharmacy personnel (one in each of 73 community pharmacies). Questionnaire included simulated case of a paediatric patient with a respiratory tract infection • All community pharmacies dispensed antibiotics without a prescription • Commonly requested and dispensed antibiotics without a prescription included amoxicillin (52%) and cotrimoxazole (25%) • 74% of community pharmacists would dispense an antibiotic without a prescription for a child with a respiratory tract infection

NB: Most acute respiratory tract infections (ARIs) are URTIs (Upper respiratory tract infections) rather than lower respiratory tract infections. However, reported as ARIs in the Table if the authors had not distinguished between the different types of ARI (17, 76)

Table E: Summary of activities among high income countries/ internationally to reduce inappropriate antibiotic prescribing among physicians especially for patients with acute respiratory tract infections

Country	Initiative and outcome
International/ US (77-79)	A) AHRQ (US Agency for Healthcare Research & Quality) • Point-of-care testing generally reduces the overprescribing of antibiotics for patients with acute respiratory tract infections, with the addition of rapid streptococcal antigen testing decreasing overall antibiotic prescribing by 20% to 52% and decreasing inappropriate prescribing by 33% over usual care • Procalcitonin testing has reduced antibiotic prescribing in adults by 12% to 72%, but increased by 22% antibiotic prescriptions in children • C-reactive protein testing has also reduced antibiotic prescribing by 1.9% to 33.5%; however, this has been associated with an increase in hospitalizations at one month (1.1% vs. 0.2% of those who received usual care) B) Review of McDonagh et al • Twenty-six interventions were evaluated regarding their effectiveness to reduce inappropriate prescribing of antibiotics for patients with acute respiratory tract infections • Four interventions had moderate-strength evidence of improved prescribing; these were: o Parent education: 21% reduction in antibiotic prescribing, no increase in return visits o Combined patient/clinician education: 7% reduction in antibiotic prescribing, no change in complication or satisfaction rates o Procalcitonin testing for adults: 12%–72% reduction in antibiotic use, no increased adverse consequences o Electronic decision support systems: 24%–47% improvement in appropriate prescribing, 5%–9% reduction in inappropriate use of antibiotics, no increase in complication rates
Pan-European (80)	• Multinational, cluster, randomised, factorial, controlled trial involving 246 GP (family medicine) practices with patients with respiratory tract infections including URTIs • Internet training in communication skills and point-of-care testing achieved important reductions in antibiotic prescribing for acute RTIs across European countries with different languages and cultural boundaries • The combined intervention achieved the greatest reduction in the prescribing rate of antibiotics (combined risk ratio 0·38, 0·25–0·55, p<0·0001).
Australia (20)	• A series of comprehensive educational as well as advertising campaigns were undertaken with general practitioners and consumers across Australia between 2009 and 2015 with the aim of reducing antibiotic prescriptions for patients with URTIs • A Bayesian structural time series model was used to forecast dispensing volumes if the interventions had not taken place and compared with actual volumes • Overall, there was a 14% reduction in dispensed prescriptions after the multifaceted interventions
France (81)	• A multifaceted educational programme was instigated among 7 paediatric emergency departments in France between November 2009 to October 2014 • The programme consisted of local protocol implementation, education sessions, and feedback • The intervention resulted in a significant change in the rate of antibiotic prescriptions per 1000 PED visits (-0.4% per 15-day period, P = .04) with the cumulative effect estimated to be an overall 30.9% reduction in antibiotic prescriptions
Netherlands (82)	• A pragmatic, cluster-randomized intervention trial in 88 Dutch primary care practices involving interventions to improve the management of patients with respiratory tract and ear infections (respiratory tract infections)

	• The intervention was physician education and audit/feedback on the quantity and quality of their antibiotic prescribing • The number and types of antibiotics prescribed were analysed from 1 year prior to the intervention to 2 years after the intervention • Overall, the over prescribing of antibiotics for respiratory tract infections decreased from 44% of prescriptions to 28% following the intervention
Norway (83)	• Cluster randomised controlled study comprising 382 general practitioners to help improve antibiotic prescribing in patients with acute respiratory tract infections • The intervention groups had two visits by academic detailers including feedback reports on each GP's antibiotic prescribing profile the preceding year • There was a reduction (odds ratio 0.72, 95% confidence interval 0.61 to 0.84) in the prescribing of antibiotics for acute respiratory tract infections in the intervention compared with control groups
Spain (84)	• Cross-sectional before/after study carried out in one Region of Spain involving multiple training sessions with GPs on national guidelines to improve the use of antibiotics in ambulatory care including patients with acute respiratory tract infections • Appropriate antibiotic prescribing in patients increased from 36% of prescriptions in 2009 to 57 % in 2012 ($p<0.001$) • The greatest improvement was seen with beta-lactam antibiotics and in the treatment of respiratory and skin infections
United Kingdom (85)	• Randomised, 2 × 2 factorial trial involving 1581 GP practices in England • Every GP in the intervention group was sent a letter from England's Chief Medical Officer accompanied by a leaflet on appropriate antibiotics for use with patients. The letter stated that their GP practice was prescribing antibiotics at a higher rate than 80% of GP practices in the locality • The rate of antibiotic items dispensed per 1000 population decreased from 131.25 in the control group to 126·98 in the intervention group. This decrease of 4·27 (3·3%; $p<0·0001$), representing an estimated 73,406 fewer antibiotic items dispensed for limited cost • The authors concluded that social norm feedback from a senior governmental source indicating high prescribing of antibiotics significantly reduced antibiotic prescribing at low costs
USA	A) First Study (2013) (86) • Three-arm, cluster-randomized trial among 33 primary care practices belonging to an integrated health care system regarding the management of acute bronchitis • The printed intervention arm received decision support print-based management plan, the computerized intervention group received decision support through an electronic medical record-based strategy, with the third group as the control arm. Both intervention groups also received educational input, feedback on their prescribing practices, and education brochures to use with patients • Compared with the baseline period, the % of patients prescribed antibiotics for acute bronchitis decreased from 80.0% to 68.3% in physicians receiving printed material, decreased from 74.0% to 60.7% in those physicians with computerized intervention sites but increased slightly 72.5% to 74.3% among the control group B) Second Study (2015) (87) • Retrospective time series study among 118 providers at seven sites to assess the impact of interventions to reduce prescribing of antibiotics for uncomplicated acute respiratory infection. The main outcome measures included a potential reduction in antibiotic prescribing and physician visits avoided • Data were collected from January 2010 to November 2013, with the interventions occurring in March 2012

	• The intervention included academic detailing, auditing of prescribing with additional coaching for high prescribers. In addition, established patients who called to schedule a physician visit for acute respiratory infection related symptoms were offered a nurse phone care instead • The intervention was associated with a 16.5% absolute decrease in the antibiotic prescribing rate and 8.3% episodes did not require any provider visit C) Third Study (2016) (88) • Prospective study involving three behviousal interventions among physicians in 47 ambulatory care practices in Boston and Los Angeles to reduce inappropriate prescribing for acute respiratory infections • Intervention implemented alone or in combination and included (i) suggested alternatives in electronic order sets suggesting for instance non-antibiotic treatments for these infections; (ii) accountable justification - prompting clinicians to enter free-text justifications for prescribing any antibiotic for these infections; (iii) peer comparisons with "top performers" • Mean antibiotic prescribing rates decreased from 22.1% (18 months pre-intervention) to 6.1% for suggested alternatives 18 months post intervention; from 23.2% to 5.2% for accountable justification; and from 19.9% to 3.7% for peer comparison

Table F: Antibiotic Public Awareness Campaigns and their influence especially in High Income Countries

Country	Details
Europe - 2013 (89)	• Comparable data on systemic antibiotics administered among 21 European countries combined with data on national campaigns from the public health literature • Public campaigns significantly reduced ambulatory care antibiotic utilisation by 1.3 to 5.6 DIDs equating to a mean reduction of 6.5 to 28.3 % on pre-intervention levels
European Commission – 2009 and 2013 (90)	• The Eurobarometer surveys showed there was an increase in the number of people who responded that antibiotics do not kill viruses and are not effective against influenza and colds between 2009 and 2013 • This was seen as encouraging since the key messages of European Antibiotic Awareness Day campaigns were to reduce unnecessary requests and use of antibiotics for such infections
England – 2015 (91, 92)	• Sustained regional multimodal campaign in the north of England targeting patients and physicians centring around Moxy Malone, a cartoon character developed for use in campaign materials, including posters, television, radio coupled with prescribing support over 2 years • This resulted in a 5.8% reduction in prescription rates, equivalent to 21.7 fewer items prescribed per 1000 population
France 2009, 2011 and 2014	A) First study – 2009 (93) • Nationwide study evaluating antibiotic utilisation in France following a sustained national campaign aimed at patients as well as parents of children to reduce ambulatory care antibiotic prescribing principally among children with viral respiratory tract infections • Overall antibiotic utilisation decreased by 26.5% post the sustained campaign compared to the preintervention period • The greatest decline (- 35.8%) was seen among young children aged 6–15 years, with a significant reduction (-45%) in patients with flu-like syndromes receiving an antibiotic B) Second study – 2011 (94) • Evaluating antibiotic prescriptions and consultation rates for respiratory tract infections following yearly public antibiotic campaign since 2002 • Between 2001 and 2009, a 33% in reduction in prescriptions for respiratory tract infections was observed alongside a 23% reduction in physician consultations for respiratory tract infections • The proportion of consultations resulting in antibiotic prescriptions also decreased from 58% to 46% C) Third study – 2014 • Nationwide study with an interrupted time series design • Compared to the precampaign (2000-2002) period, antibiotic prescriptions decreased during campaign periods until the winter of 2006 to 2007 (-30%). Subsequently, they stabilized except for individuals >60 years of age in whom prescriptions rose to precampaign levels • During the warm months (April to September) there was no appreciable change in antibiotic utilisation patterns, although seniors had an increasing trend in their utilisation
Singapore 2017 (95)	• Study assessing the influence of a patient-targeted education via discussions and pamphlets among 914 patients in reducing antibiotic prescriptions for URTIs among adults attending private ambulatory care facilities • The intervention did not significantly reduce antibiotic prescriptions except in patients of Indian ethnicity • A positive association between the intervention and the view that antibiotics were not needed most of the time for URTIs was also restricted to the Indian subgroup
USA	A) First study 2005 (96)

	• This study was launched in 1999 to educate physicians and the public about the appropriate use of antibiotics especially for respiratory tract infections • Public education included advertisements on radio and TV, posters, pamphlets, and presentations at childcare centres • Overall antibiotic prescribing declined between 19.8% to 20.4% in the two settings from 1998 to 2003 B) Second study (97) • Multifaceted intervention campaign to try and reduce inappropriate prescribing of antibiotics for patients with URTIs involving both health care professionals and patients • There was a 15.6% decrease in the number of patients who received antibiotics for URTIs during the intervention period in the targeted group versus a 1.5% decrease in the control group (P=.006)

NB: URTI = upper respiratory tract infection

Box A: General Indicators That Have Been Used To Assess The Quality Of Antibiotic Prescribing In Ambulatory Care (98-105)

- Utilisation of penicillins (J01C) as a % of total antibiotic use
- % utilisation of combination penicillins such as co-amoxiclav as a percentage of amoxycillin use
- The proportion of amoxicillin users (amoxicillin index)
- The ratio between users of amoxicillin to broad-spectrum penicillins, cephalosporins and macrolides (*A*/*B* ratio)
- % utilisation of cephalosporins ((J01D) as a % vs. total antibiotics
- % utilisation of third- and fourth-generation cephalosporins vs first and second generation cephalosporins
- % utilisation of macrolides (J01F) as a % vs. total antibiotics
- % utilisation of quinolones (J01M) as % vs. total antibiotic use
- % broad to narrow-spectrum penicillins, cephalosporins and macrolides (B/N ratio)

Box B: Examples of Current Quality Indicators for Antibiotics in Slovenia

A) General QIs for general practitioners:

- Prevalence of prescribing of antibiotics (Number of patients/1000 who get at least 1 prescription per year)
- The ratio broad versus narrow spectrum antibiotics as well as the ratio of quinolones and cephalosporins compared with all antibiotics

B) Every GP has on the social insurance website their own data regarding their QIs as well as a table documenting for every patient prescribed an antibiotic during the year:

- Number of patients
- Number of prescriptions
- Number of antibiotic DDDs
- Share of antibiotics versus total medicines prescribed (DDD basis)

C) For Paediatricians:
Prevalence of prescribing of antibiotics (No. of patients/1000 who get at least 1 prescription per year and standardised by age)

- % of antibiotics in all prescriptions (DDD basis)
- % of patients who are prescribed another antibiotic within 14 days after the first one
- % of topical antibiotics in DDDs in all prescriptions
- The ratio broad/narrow spectrum antibiotics prescriptions
- The ratio of amoxicillin vs co-amoxyclav prescriptions

NB: DDD = Defined Daily Dose, QIs = Quality indicators

Box C: HEDIS Datasets - Specific Indicators for Patients with URTIs (32)

- Appropriate testing for children with pharyngitis, i.e. % of children 2 to 18 years of age diagnosed with pharyngitis, prescribed an antibiotic and received a group A *Streptococcus* (strep) test. The mean performance across all health plans in the US in 2012 was 80% (range 2–97%) versus a goal of 100%
- Appropriate treatment for children with URTIs, i.e. of children 3 months to 18 years of age, with URTIs not prescribed antibiotics on or three days after the episode date. Mean performance in the US in 2012 was 83% (range 45–99%) versus a goal of 100%
- Avoidance of antibiotics in adults with acute bronchitis, i.e. % of adults diagnosed with acute bronchitis not dispensed an antibiotic. Mean performance in 2012 was 23% (range 7-72%) versus a goal of 100%.
- These findings have resulted in advice from the American College of Physicians in the US that clinicians should not initiate antibiotics in patients with bronchitis unless pneumonia is suspected
- Patients with symptoms suggestive of group A streptococcal pharyngitis should have a rapid antigen detection test or culture, and only be treated with antibiotics if they have confirmed streptococcal pharyngitis
- Clinicians should reserve antibiotics for acute rhinosinusitis only prescribe them for patients presenting with persistent symptoms, onset of severe symptoms, signs of a high fever, have a purulent nasal discharge or facial pain, or worsening of symptoms
- Clinicians should not prescribe antibiotics for a common cold (106)

NB: URTIs = Upper respiratory tract infections

Box D: Protocol for Testing Suggested QIs for Managing Patients with URTIs in ambulatory care (Adapted From (107))

Necessity/ Clarity/ Acceptability

- Assessment of current indicators, e.g. Boxes 1 and 2, and their applicability in the pertinent LMIC before developing potential new QIs
- The wording of any new QI developed/used must be clear and precise with unambiguous language
- The indicators used/developed must be within the control of the ambulatory care physicians that will be assessed and acceptable to them/aligned with their professional values

Content validity

- The (new/ existing) indicator represents agreed high quality care and is consequently a valid indicator of the quality of prescribing.
- There is sufficient evidence/ professional consensus to support new/ existing QIs (building on necessity) with clear benefits to the patient (patient values)
- Each indicator is underpinned by a published evidence base
- Adherence to the indicator (new/ existing) should be based on ambulatory care physicians adhering to the indicator providing a higher quality of care than currently provided

Technical feasibility and reliability of data extraction / data availability

- Ability to write and integrate data into current health information systems
- Ability to produce reports assessing the quality of prescribing within a reasonable time frame and budget

Implementation and monitoring

- Any new indicator/ existing indicator used must be able to discriminate between physicians in terms of the quality of care provided
- Any new indicator developed must also be sensitivity to change (addressed through a potential pilot project)
- Clinical staff must be able to interpret any instigated indicator – and act upon the findings
- Before implementing any indicator:
- Changes required to implement any indicator including for instance any physical capital/staffing changes or changes to regulation, policies and education, must be fully assessed before implementation
- Workload implications of implementing any indicator must also be fully assessed before implementation
- Potential barriers among different stakeholder groups to the implementation of any indicator must also be assessed and addressed before implementation

- There must also be continual monitoring in case of any unintended consequences to the implementation any indicator (positive or negative) as these must also be addressed for the future

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