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Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Guillermo A Zabala ,[1,2,3,4] Khonsavath Bellingham ,[1,2,4] Vayouly Vidhamaly ,[1,2,4] Phonepasith Boupha ,[1,2,4] Kem Boutsamay ,[1,2,4] Paul N Newton ,[1,2,4] Céline Caillet [1,2,4]

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GAZ and KB are joint first authors.

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For numbered affiliations see end of article.

Correspondence to
Dr Céline Caillet;
celine.caillet@ndm.ox.ac.uk

ABSTRACT

Objectives Antimicrobial resistance (AMR) is a significant global health threat with substandard and falsified (SF) antibiotics being neglected contributing factors. With their relationships poorly understood, more research is needed in order to determine how interventions to reduce SF antibiotics should be ranked as priorities in national AMR action plans. We assessed the evidence available on the global prevalence of SF antibiotics, examined the quality of the evidence and discussed public health impact.

Materials/Methods We searched PubMed, Embase, Google and Google Scholar for publications on antibiotic quality up to 31 December 2020. Publications reporting on the prevalence of SF antibiotics were evaluated for quantitative analysis and assessed using the Medicines Quality Assessment Reporting Guidelines.

Results Of the 10 137 screened publications, 648 were relevant to antibiotic quality. One hundred and six (16.4%) surveys, published between 1992 and 2020 and conducted mainly in low-income and middle-income countries (LMICs) (89.9% (480/534) of the data points), qualified for quantitative analysis. The total number of samples tested for quality in prevalence surveys was 13 555, with a median (Q1–Q3) number of samples per survey of 47 (21–135). Of the 13 555 samples, 2357 (17.4%) failed at least one quality test and the median failure frequency (FF) per survey was 19.6% (7.6%–35.0%). Amoxicillin, sulfamethoxazole-trimethoprim and ciprofloxacin were the most surveyed antibiotics, with FF of 16.1% (355/2208), 26.2% (329/1255) and 10.4% (366/3511), respectively. We identified no SF survey data for antibiotics in the WHO 'Reserve' group. The mean Medicine Quality Assessment Reporting Guidelines score was 11 (95% CI 10.1 to 12.2) out of 26.

Conclusions SF antibiotics are widely spread with higher prevalence in LMICs. The quality of the evidence is poor, and these data are not generalisable that 17.4% of global antibiotic supply is SF. However, the evidence we have suggests that interventions to enhance regulatory, purchasing and financial mechanisms to improve the global antibiotic supply are needed.

PROSPERO registration number CRD42019124988.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Substandard and falsified (SF) antibiotics worsen clinical outcomes, lead to adverse drug reactions, economic loss and diminish public confidence in health systems, but there is limited evidence on their prevalence, although they are also hypothesised to be locally key drivers of antimicrobial resistance (AMR).

WHAT THIS STUDY ADDS

⇒ One hundred and six prevalence surveys were identified, including a total of 13 555 samples, and 17.4% of those failed at least one quality test.

⇒ Samples mainly failed because they did not contain the correct amount of active pharmaceutical ingredient or failed dissolution testing, risking reduced bioavailability.

⇒ There are major gaps in the evidence, with geographical disparities, and no data for many antibiotics important for public health and AMR.

⇒ These data are not generalisable to suggest that 17.4% of the global antibiotic supply are SF.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The quality of antibiotics, especially in supply chains in countries without stringent medicine regulation, requires urgent attention.

⇒ Further research is needed to assess the quality of antibiotics worldwide and its link to AMR, to inform policy to combat this serious health threat.

INTRODUCTION

Eight months after evidence supporting sulfanilamide use as an antibiotic in the USA in 1937, at least 105 patients died due to a toxic excipient.[1] This disaster led directly to the strengthening of the US Food and Drug Administration and requirement for evidence of safety before new medicine approval. The following decades saw the rapid spread of antibiotic use globally and an increasing number of agents available. The antibiotic market reached a total value of ~US$45 billion in 2018.[2]

Bacterial pathogens are still killing people in large numbers, with higher burdens in low-income and middle-income countries (LMICs).[3] With global economic development, antibiotic demand and consumption are growing; between 2000 and 2015, global antimicrobial medicines consumption (AMC) increased by 65% and is projected to increase up to 200% by 2030.[4 5] Compromised access is compounded by substandard and falsified (SF) antibiotics. Falsified medicines are those that 'deliberately/fraudulently misrepresent their identity, composition or source'.[5] Substandard medicines are 'authorised medical products that fail to meet either their quality standards or their specifications, or both'.[5] These may result from gross negligence/unintended errors during the manufacturing process or degradation through inappropriate storage/transport within the supply chain. Both may contain low, high, no or wrong active ingredients or impaired dissolution and can prolong illness duration and lead to death, loss of income, increased spending on healthcare and sow public mistrust.[6]

Within 5 years of its first clinical use, a large trade in falsified penicillin developed.[7] The problems persist; recently, a child's death in Uganda was associated with substandard ceftriaxone containing <50% of the stated active pharmaceutical ingredient (API).[8] WHO estimated that the prevalence of SF medicines is ~10% in LMICs, and antibiotics are the second most frequent class of SF medical products reported to the WHO Global Surveillance and Monitoring System.[9] Mathematical modelling suggested that 72 430 childhood pneumonia deaths per year are attributable to SF antibiotics.[10]

Subtherapeutic antibiotic concentrations promote antimicrobial resistance (AMR),[11–13] and one of the likely mechanisms for this is the consumption of SF medicines containing lower than the stated antibiotic concentrations, poor dissolution and/or adulteration with subtherapeutic amounts of unstated, cryptic, antibiotics.[14–18] For example, the high prevalence of substandard chloramphenicol and sulfamethoxazole-trimethoprim in Myanmar may have contributed to the high typhoid antibiotic resistance prevalence.[19 20]

Understanding the relationship between the prevalence of SF medicines and AMR using field data is impaired because of poorly understood time intervals between bacterial exposure to antibiotics and rise in AMR prevalence. Also, areas with high SF antibiotic prevalence are also likely to have other sympatric AMR drivers such as poor patient adherence, antibiotic misuse and inappropriate prescriptions, confounding relationships.[21 22] The WHO AWaRe (Access, Watch, Reserve) classification helps optimise antibiotic use and guides policies on access to quality antibiotics as contributors to Universal Health Coverage and the Sustainable Development Goals to reduce the risk of AMR.[23]

Research on the impact of SF antibiotics on AMR is neglected despite multiple passing references,[24 25] with AMR studies commonly omitting SF antibiotics as potential drivers.[22 26–36] Here, we review the epidemiology of SF antibiotics, discuss their potential impact on AMR and provide evidence to inform interventions.

METHODS

Search strategy

PubMed and Embase databases were searched in English, and Google and Google Scholar searched in English and French, without an inclusion start date, up to 31 December 2020. Search terms included the WHO terminology for medicine quality and other commonly used terms (eg, "substandard", "falsified", "counterfeit") and all antibiotic API listed in the Anatomical Therapeutic Chemical classification.[5 9 37] Different spelling and naming variations were included, such as British approved names (BAN) and alternative spellings (eg, cephalexin and cefalexin). Google and Google Scholar search terms were adapted for the character limit (online supplemental file 1). The results from PubMed, Embase and the first 20 pages (200 reports) of Google Scholar and Google were exported to Mendeley Desktop citation manager. After removal of duplicates, titles and abstracts were screened and full texts of the identified articles were assessed for eligibility. Manual searches of the reference lists in the included articles, and of the websites of Medicines Regulatory Agencies (MRA) and other organisations involved in medicine quality were performed. Relevant articles discovered in previous work by our group, but not captured by our search, were also included. Articles in Spanish and French resulting from our search were also included after translation by native speakers. This review was registered with the National Institute for Health Research International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42019124988).

Eligibility criteria

Scientific and grey literature articles evaluating or discussing the quality of antibiotics in English, Spanish or French, irrespective of whether they contained empirical data or not, were included. General discussions (eg, on the regulatory framework surrounding SF antibiotics) and reviews of the literature on various aspects of antibiotics' quality (eg, review of the literature on antibiotic recalls) were included. We included studies that surveyed the quality of antibiotics in one or more locations (hereafter 'prevalence surveys'), that compared the pharmaceutical equivalence of different brands of a given antibiotic (hereafter 'equivalence studies'), reports of adverse events that brought into question the quality of the antibiotics used, studies describing assay techniques to determine the quality of antibiotics (hereafter 'analytical technique studies'), publications discussing sampling methodology and pharmaceutical legislation, reports on seizures and recalls by pharmaceutical companies or MRA and case reports on antibiotic quality in the scientific or lay press (online supplemental file 2).

Antibiotics which are primarily used for the treatment of tuberculosis (rifampicin, isoniazid, ethambutol, pyrazinamide, bedaquiline, pretomanid, ethionamide, prothionamide, cycloserine and para-aminosalicylic acid) were not included. For the quantitative analysis, only publications that provided data on results for chemical and/or physical quality test results were included.

Definitions

Further to the discussion of key definitions given in the 'Introduction' section,[9] evidence to distinguish poor quality medicines resulting from errors within the factory or subsequent degradation in the supply chain due to heat, humidity or light exposure is sparse. It is not possible to accurately classify a medicine as substandard or falsified without packaging analysis. Products that failed at least one quality testing without information on packaging authenticity are thus defined as 'substandard or falsified' (SorF).[38] This term is not mandated by the WHO definitions, but we suggest that it enhances understanding for samples with incomplete evidence. Samples without packaging analysis that contained an API other than the stated or no API were assumed to be falsified. There is a risk of misclassification of such samples as falsified when they are substandard due to severe manufacturing errors.

Pharmaceutical analysis relies on compendial tests described in pharmacopoeial monographs. For finished medicines, monographs commonly include the identification and quantification of API content (using sophisticated standardised techniques such as liquid chromatography coupled with various detectors), dissolution testing, detection of specific levels of predetermined impurities/related substances, uniformity of dosage units and additional attributes depending on the formulation of the product (eg, tablet friability). In many studies included here, not all pharmacopoeial analyses were conducted and a variety of non-pharmacopoeial assays were used, for example, for investigating specific contaminants or unstated APIs. Assay details were not always provided making it difficult to standardise the definition of a 'failed sample'. Consequently, we define a failed sample as one for which at least one quality analysis test performed by the investigators gave a fail result, irrespective of the number and type of assays used. We relied on the authors conclusions as to whether a sample was genuine, falsified/counterfeit and substandard and did not reinterpret them.

We define 'failure frequency' (FF) as the proportion of samples included in a prevalence survey that failed at least one quality test described in the report. A 'data point' is a specific location where medicines were collected for quality analysis, at a given time during a given study (online supplemental file 2).

Data collection

Information within each publication was manually extracted into the 'Online Medicine Quality Data Manager', an online database developed by the Infectious Diseases Data Observatory (IDDO) Informatics team and the Medicine Quality Research Group (MQRG). Publication type (eg, report, original research article), year of publication, publisher, sampling type, location (country and city, where available) and type of outlet where samples were collected, total number of samples collected, API/API combination name, number of samples failing medicine quality test(s), quality defect and the techniques used to analyse samples were entered. In stability studies, only data on the quality test results of medicines before being submitted to stress conditions were included. In cases where the threshold used for the consideration of the sample as 'pass' or 'fail' was unclear, we did not include the data in the analysis.

Analysis and reporting

Data were extracted using FlySpeed SQL Query (V.3.5.4.2) and Microsoft Excel 365 and RStudio V.0.99.486 were used for data analysis and creation of figures and tables, including polynomial trend lines. Statistical analyses were carried out using Microsoft Excel 365 (means, medians and quartiles), FFs and Stata V.17.0. Qualitative variables were expressed as numbers and percentages (n (%)). Quantitative variables were expressed as the median and first and third quartiles (Q1–Q3) or mean (95% CI) where appropriate. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (online supplemental file 3).

Risk of bias assessment

Articles in which the primary objective was to estimate the prevalence of SF antibiotics were reviewed using the Medicine Quality Assessment Reporting Guidelines (MEDQUARG).[39] Only the prevalence surveys published as original articles in scientific journals or following the Introduction/Methods/Results/Discussion or similar style and published as reports, MSc or PhD thesis, were assessed. Two reviewers (GZ, KBe) blinded to each other's scores appraised each article independently, and a third (CC), blinded to colleagues' individual scores, resolved discrepancies. Since there are no standardised methods to assess equivalence, analysis technique, lay press and case reports publications, their risk of bias was not addressed.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Types of publications and studies

A total of 10 137 publications were identified through database searches. After removal of 2300 duplicates, 7837 remaining publications were screened by title and abstract, and 475 articles were eligible (online supplemental file 4). Non-academic Google and medicine

quality website searches yielded an additional 126 articles, and 68 publications with data on antibiotic quality previously identified in the MQRG scientific literature database were also included. Twenty-one studies were excluded due to being in languages not included in our review, or the full text not being available, resulting in a total of 648 included publications (online supplemental file 5). Four hundred and ninety-eight publications were original research publications from scientific journals, with 34 short communications, 33 public alerts, 32 lay press publications, 28 institutional reports, 17 theses, 3 articles discussing drug regulation/supply and 2 book/book chapters. The United States Pharmacopoeia Medicines Quality Database (https://www.usp.org/global-public-health/medicines-quality-database) was considered as a single 'publication'.

Of the 498 original research articles published in scientific journals, 225 described analytical techniques, 89 were prevalence surveys, 101 were equivalence studies, 51 were reviews, 14 were stability studies and 11 postmarketing surveillance studies. Five were case reports of falsified antibiotics or their deleterious effects on patients, one article studied tetracycline bioavailability as a surrogate for its quality[40] and one article studied how substandard antibiotics could affect AMR by using different concentrations of antibiotics.[41]

All data are mapped in the IDDO Quality Surveyor (https://www.iddo.org/mqsurveyor/#antibiotics) and can be freely downloaded .

Prevalence surveys

Characteristics of prevalence surveys

Data from 106 prevalence surveys were included in the quantitative analysis as one paper with aggregated data was excluded from analysis.[42] Eighty-nine (84.0%) papers were published as original research articles, eight (7.5%) were institutional reports, four (3.8%) short communications and five (4.7%) were theses. Of the 106 surveys, 76.4% (81/106) were published in peer-reviewed journals. Publication dates ranged between 1992 and 2020, but more than half (62.3%, 66/106) were published between 2010 and 2020 (figure 1). In total, 13555 samples, originating from 67 different countries, were tested for quality in prevalence surveys (online supplemental file 6). Seventy (66.0%, 70/106) of the included studies used convenience sampling, 30 used random sampling (28.3%, 30/106), 1 study used a combination of both, 4 did not disclose the sampling method and 1 study piloted Lot Quality Assurance Sampling.[43]

Antibiotic failure frequency

Of the 13555 samples included in the analysis, 2357 (17.4%) failed at least one quality test. Of those, 336 (14.3%) samples were substandard, 195 (8.3%) falsified and authenticity was not investigated for 1826 (77.5%) and are therefore considered SorF. We did not find any samples identified as 'degraded'. The proportions of SorF, substandard and falsified medicines from prevalence surveys were thus 13.5%, 2.5% and 1.4%, respectively (figure 2). The median (Q1–Q3) number of samples collected per survey was 47 (21–135) and the median FF (at least one quality test failing) per survey was 19.6% (7.6%–35.0%). Thirteen (12%) surveys found no SF antibiotics (online supplemental file 6).

Failure frequency—geographical distribution

Of the 534 data points, 267 (50.0%) were from Africa, 185 (34.6%) from Asia, 31 (5.8%) from the Americas,

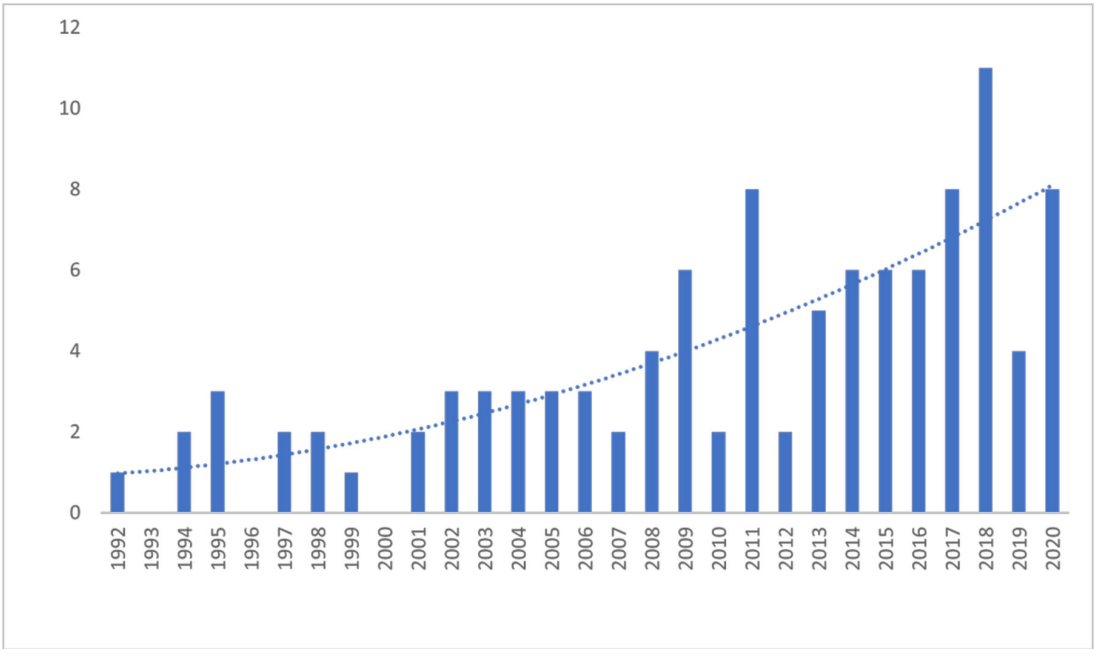

Figure 1 Number of prevalence surveys (y-axis) pertinent to antibiotic quality published per year (x-axis). A second-order polynomial trendline is represented as the blue dotted line.

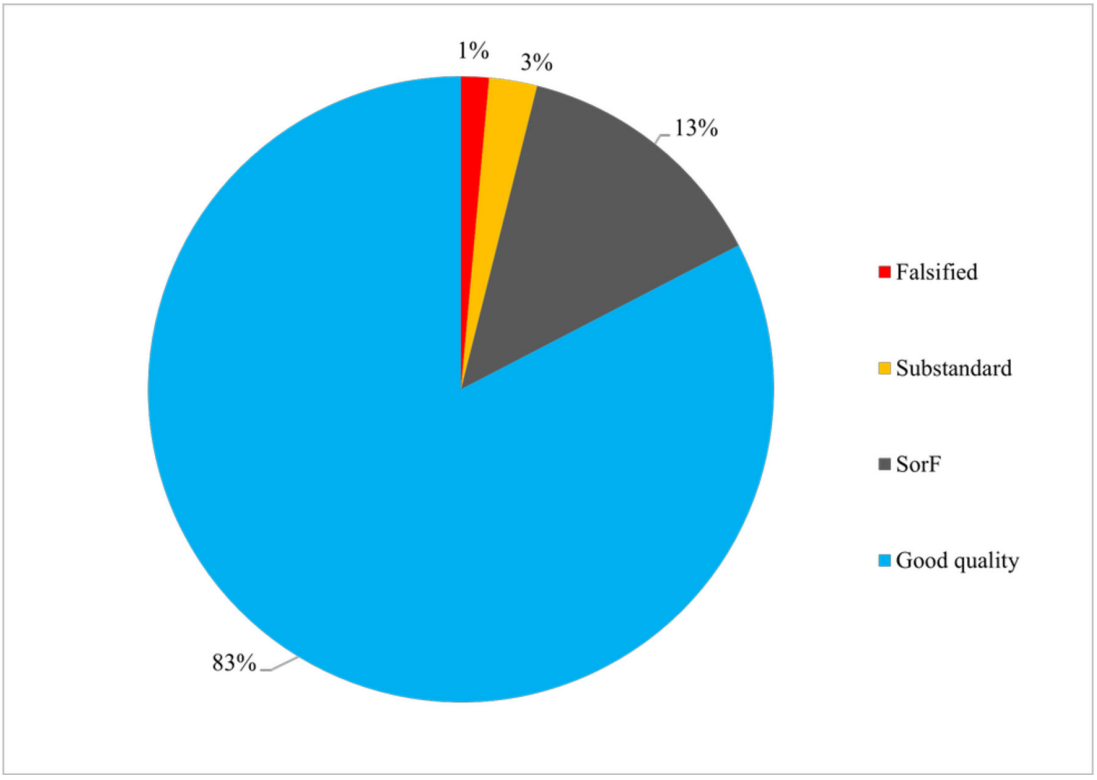

Figure 2 Quality categories of samples from antibiotic quality prevalence studies. Samples are classed as of 'good quality' if they passed all the tests performed by the investigators of a given study, which often do not cover the full pharmacopoeial specifications. Substandard and falsified samples are those who have failed at least one of the tests performed by the investigators. SorF, substandard or falsified.

9 (1.7%) from Europe and 14 (2.6%) from Oceania (online supplemental file 7). There were 28 (5.2%) 'unknown' data point locations, with the FF not broken down by geography. Most samples were collected in sub-Saharan Africa (n=3825, 28.2%), South-East Asia (n=3555, 26.2%) and South Asia (n=1388, 10.2%). The highest observed antibiotic FF was in Africa (28.4%, 1090/3836), followed by Asia, Oceania, Americas and Europe at 15.2% (943/6210), 15.0% (15/100), 12.5% (112/898) and 7.7% (5/65), respectively.

The median (Q1–Q3) number of samples tested per country was 56 (15–180). The five countries with the most samples reported were the Lao People's Democratic Republic (n=1334), Cambodia (n=1208), India (n=1055), Mongolia (n=1053) and Nigeria (n=632), with FF of 22.3%, 19.6%, 8.2%, 9.7% and 47.2%, respectively. Due to data aggregation, it was not possible to identify the country for 18.5% (2511/13 555) of samples. Sample numbers and FF per country are presented in figure 3, showing the disparity in the origin of the evidence, and potential 'hotspots' for SF antibiotics. Furthermore, 19.5% (2643/13 555) of the samples originated from low-income countries (LICs), 54.3% (7355/13 555) from LMICs, 3.6% (486/13 555) from upper-middle-income countries and 3.9% (524/13 555) from high-income countries (HICs). Due to data aggregation, it was not possible to identify the country-level income for 18.8% (2547/13 555) of samples.

Antibiotic failure frequency by AWaRe classification

Twenty-one (43.8%) APIs of the 48 included in the 2019 WHO AWaRe Access group and 16 (14.5%) of the 110 in the Watch group were investigated in prevalence surveys, with no Reserve group or carbapenems included.[23] We found data for two APIs not included in the AWaRe classification (nalidixic acid, sulfamethoxazole). The antibiotics with the highest number of samples collected were ciprofloxacin (n=3511, 25.9%), amoxicillin (n=2208, 16.3%), sulfamethoxazole-trimethoprim (n=1255, 8.6%), tetracycline (n=1191, 9.3%) and ampicillin (n=1010, 5.5%). The overall FF for these APIs were 10.4% (366/3511), 16.1% (355/2208), 26.2% (329/1255), 12.1% (144/1191) and 20.9% (211/1010), respectively. Antibiotics in the Access group had an overall FF of 19.5% (1633/8354) and those in the Watch group 13.8% (718/5191) (online supplemental file 8).

Techniques used and quality defects of samples

More than one quality test was conducted in 67.9% (72/106) of the prevalence surveys and the median (range) number of analysis techniques per survey was 3 (1–5). API content analysis was performed in 79.2% (84/106) of prevalence surveys, with 76.0% (10 307/13 555) of the samples tested and an FF of 16.5% (1701/10 307) (table 1). Of the samples tested for API content against the amount stated on the label and pharmacopoeial limits, 6.4% (662/10 307) were found to contain

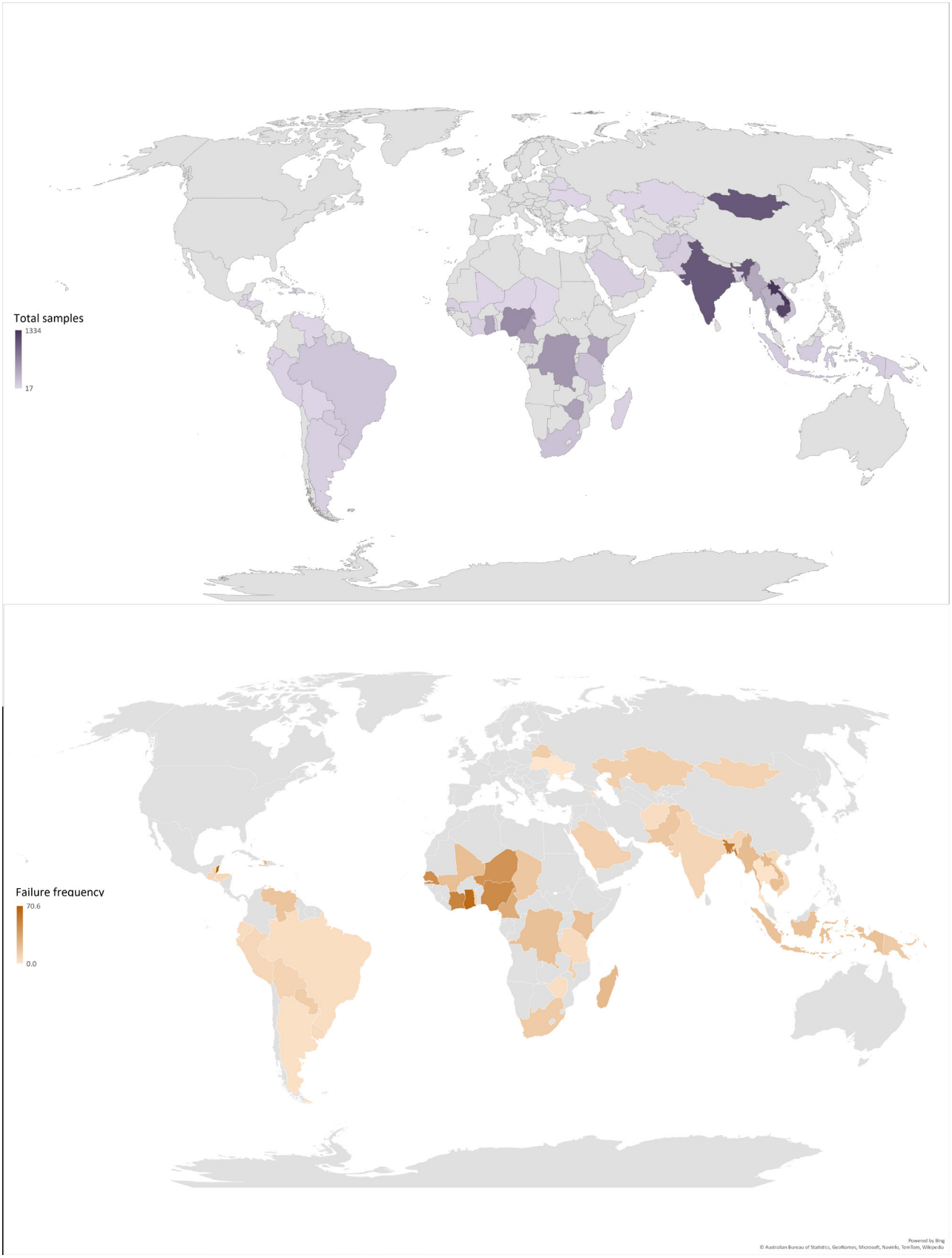

Figure 3 Global distribution of the evidence on antibiotics quality: total number of samples included in prevalence surveys (A) and failure frequency (B); countries with <15 samples have been greyed out. Caution must be exercised when drawing conclusions from these graphs. Samples from a given country may originate from a study sampling a single small urban or rural area, authorised or illicit outlets only (or a mix), etc and are not representative of medicine quality in the whole country. See online supplemental file 6 for further details.

Table 1 Percentage of failing samples per type of quality analysis in the prevalence studies

Quality component	FF % (n/N)
API content	16.5 (1701/10 307)
Dissolution	9.1 (296/3261)
API ID and semi-quantitation	7.5 (210/2783)
Impurity/Contaminant/Related substance	3.5 (12/346)
Packaging/Label/Physical appearance inspection	2.8 (129/4612)
Other chemical tests*	4.4 (187/4212)
Other physical tests†	2.2 (71/3290)

One sample may have been tested for more than one quality test.
*API identification, degradation products, pH and other undeclared chemical tests.
†Includes disintegration, friability, hardness, thickness, wetting time and water absorption testing.
API, active pharmaceutical ingredient; FF, failure frequency.

lower API, 1.3% (131/10 307) contained no API and 2.4% (249/10 307) contained higher API content. For 6.4% (659/10 307) of samples some dosage units contained lower API, and some contained higher API than stated, or samples were reported as having the incorrect API amount without further details given.

Dissolution testing was performed in 34/106 (32.1%) of surveys; 9.1% samples (296/3261) failed, making this the second most common defect found. Packaging analysis/visual inspection of dosage units were the third most frequently performed analyses, included in 31/106 (29.2%) of surveys, with a failure of 2.8% (129/4612) of those tested. Some APIs showed signals of concern for specific tests. Of all those that failed, flucloxacillin had an FF for API content of 85.7% (18/21), azithromycin of 65.6% (21/32), erythromycin of 48.3% (28/58), ampicillin-cloxacillin of 41.7% (80/192) and chloramphenicol 31.7% (40/126). Of samples that failed, dissolution failures were 69.2% (9/13) for erythromycin, 29.7% (19/64) for levofloxacin, 29.8% (17/57) for roxithromycin and 28.4% (25/88) for clarithromycin (online supplemental file 9).

Failure frequency by source

Outlets where antibiotics had been collected were reported for 48.9% (6624/13 555) of samples in prevalence surveys (table 2). In total, 6616/13 555 (48.8%) samples from 33 countries (255 different data points) were collected in outlet combinations, without breakdown by outlet type. The overall FF for such aggregated samples was 18.3% (1211/6616). Four studies did not contain explicit information on the outlets where samples were collected.[44–47]

Table 2 Failure frequency of antibiotics by outlet type in prevalence surveys

Outlet/Source	Failure frequency % (n/N)	Data points	Countries
Combination of outlets*	18.3% (1211/6616)	255	Afghanistan, Armenia, Azerbaijan, Belarus, Belize, Cambodia, Cameroon, Chad, Democratic Republic of the Congo, Estonia, Ghana, India, Indonesia, Kazakhstan, Kenya, Lao People's Democratic Republic, Madagascar, Malawi, Mongolia, Myanmar, Niger, Nigeria, Papua New Guinea, Russian Federation, Rwanda, Senegal, Sudan, Tanzania, Thailand, UK, Uzbekistan, Viet Nam, Zimbabwe
Government clinics/depots	22.1% (44/199)	8	Cambodia, Cameroon, Myanmar, South Africa
Hospitals/Health centres	4.8% (26/543)	16	Cameroon, India, Kazakhstan, Kenya, Tanzania, Ukraine, Zimbabwe
Internet	4.3% (11/255)	5	India, USA
Private pharmacies	15.7% (707/4510)	120	Argentina, Bangladesh, Bolivia, Brazil, Cambodia, Cameroon, China, Ecuador, Ethiopia, Ghana, Guatemala, Honduras, India, Kenya, Lao People's Democratic Republic, Malawi, Mexico, Nigeria, Pakistan, Papua New Guinea, Paraguay, Peru, Saudi Arabia, Sierra Leone, South Africa, Tanzania, Thailand, Togo, USA, Uruguay, Venezuela
Unknown†	16.2% (51/315)	12	Bangladesh, Cambodia, Cameroon, Ethiopia, Lao People's Democratic Republic, Thailand
Unregistered/Unlicensed outlets‡	34.3% (210/613)	36	Cameroon, Côte d'Ivoire, India, Kenya, Nigeria, Pakistan, Senegal, Thailand
Wholesalers/Distributors	19.3% (97/504)	82	Burkina Faso, Democratic Republic of the Congo, Germany, Kazakhstan, Kenya, Madagascar, Mali, Nepal, Nigeria, South Africa, Tajikistan, Tanzania, Uganda, Viet Nam, Zimbabwe

*Nearly half of the surveys described several types of outlets where medicines were collected in the methods but did not present their results broken down by individual types of outlets.
†Four studies did not explicitly mention the outlets where samples were sourced.
‡Includes unlicensed/unregistered market stalls, shops, ambulant sellers, etc.

When authors reported the results by outlet type, private pharmacies were the most commonly sampled, representing 33.3% (4510/13 555) of the samples collected in 31 different countries (120 data points), with an FF of 15.7% (707/4510). The type of outlet with the highest FF was unregistered/unlicensed, with samples collected in eight countries, and an FF of 34.3% (210/613). Samples from hospitals/health centres were collected in 7 countries with an FF of 4.8% (26/543), wholesalers/distributors from 15 countries, with FF of 19.3% (97/504) and internet pharmacies with data from 2 countries and an FF of 4.3% (11/255). The FF in government facilities was 22.1% (44/199), with samples from four countries.

Reporting bias assessment

Eighty-two prevalence surveys met the inclusion criteria for appraisal using MEDQUARG. Fifty-four (65.9%) were published after MEDQUARG publication in 2009; eight (14.8%) of those stated that they used this. Over the 82 surveys, the number (%) of MEDQUARG items reported ranged from 2/26 (7.7%) to 23/26 (88.5%), with a mean score of 11 (95% CI 10.1 to 12.2) and a mean proportion of agreement of 42.3% (online supplemental file 9). Scores were significantly higher for surveys published after 2009 with a mean difference of concordance of 4.5 (95% CI 2.4 to 6.5, t-test, p<0.001) (online supplemental file 10).

Fifty-six prevalence surveys out of 82 (68.3%) were identified as such in their titles, and their abstract included sufficient details of methods (figure 4). Quality of medicines definitions were provided in 47 (57.3%) studies. Eight studies (9.8%) specified the time frame for samples collection and analysis, eight (9.8%) provided information on how outlets were selected and how sample size was determined. Thirty-three (40.2%) studies reported whether sampling was conducted by covert shoppers or not and the reason the shopper gave to the seller for the purchase. Twenty-one (25.6%) studies clearly categorised the samples as genuine, falsified, substandard, other equivalent terminology or provided reasons for not having done so. The MRA of the country where samples were collected was either involved in conducting the survey or was stated as informed of the results in 27 (32.9%) studies.

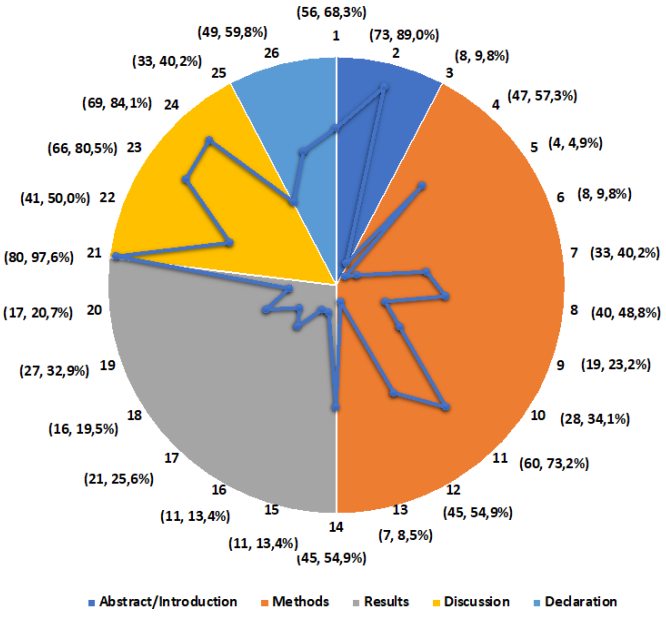

Figure 4 Frequency and proportion of prevalence surveys (out of 82) by individual Medicine Quality Assessment Reporting Guidelines checklist items reported.

Equivalence studies

One hundred and five publications assessed the quality of different antibiotic brands containing the same API(s) (online supplemental file 11). A total of 1090 samples, with a median of 9 (95% CI 5 to 12) samples per study, were collected in 51 countries (174 data points). These included 32 API/API combinations, 12 belonging to Access and 20 to Watch classes. The API/API combinations with the greatest number of studies were ciprofloxacin (n=32), metronidazole (n=17) and amoxicillin or amoxicillin-clavulanic acid (n=16). The overall FF was 25.9% (282/1090) and the median FF per study was 4.5% (95% CI 0.0% to 40.0%). The median number of techniques used to test the quality of each sample was 5 (95% CI 2 to 6). The tests most commonly failed were the API identification and semi-quantitation (15.2% (34/223)), API content (12.4% (155/1251)), dissolution (9.6% (59/616)) and impurities/contaminants/related substances (8.2% (8/98)).

Seizures, recalls and case reports

Sixty-six publications described recall/warning/alerts (n=41), seizures (n=18) and case reports (n=7) of antibiotics with quality issues, published between 1991 and 2020, in 24 countries (online supplemental file 12). In total, 120 API/API combinations were listed, 71 belonging to Access, 48 to Watch classes; one was not included in the AWaRe classification, and four articles did not state the API. Articles mostly described instances of SorF (n=41) and falsified antibiotics (n=27); 14 articles described substandard products, 4 of products unregistered in the country they were marketed in and 5 with unspecified details. Out-of-specifications API content and identification test failures were most commonly described (n=39); 11 contained no API, 5 contained lower API than stated, 4 contained wrong API(s) and in 19 cases no such details were given.

DISCUSSION

The quantitative analysis of 106 prevalence surveys from 67 different countries and 13555 samples tested for quality, resulted in an overall FF of 17.4%. Most samples were from LICs and LMICs in Africa and Asia. The majority were antibiotics from the Access group, a small proportion from the Watch group and none from the Reserve group. Sulfamethoxazole-trimethoprim had the highest FF, followed by ampicillin, amoxicillin, ciprofloxacin and tetracycline. Limited tests were used to assess

the quality of samples, with a focus on API content and, to a lesser extent, dissolution and packaging analysis. The survey methodology and reporting were of low quality, many surveys were of small sample size, and samples often collected using convenience sampling. These data cannot and should not be interpreted that 17.4% of the global supply of antibiotics are SF but they do point to severe focal issues necessitating interventions to improve the global antibiotic supply.

Similar to results from previous reviews,[6 48 49] most samples were collected in Asia and Africa, with many fewer samples from elsewhere. The highest FFs were found in Africa, followed by Asia. A review from 14 years ago also found the proportion of reported SF antibiotics to be highest in these regions but was lower in Africa than Asia at 18.7% and 33.6%, respectively.[50] This shift, also described in a recent review,[51] could be caused by the increasing research output from Africa, expansion of pharmaceutical supply, increased access and demand and an early stage regulatory environment in comparison with many Asian countries.

Quality assessment surveys have focused on the AWaRe Access class, representing more than three-fifths of samples included in prevalence surveys identified here. The remainder were Watch class antibiotics, with more than two-thirds of these samples being ciprofloxacin. Of concern, no data for Reserve class antibiotics were found, which may in part result from these antibiotics being relatively rarely used in Africa and Asia.[52] No surveys on vancomycin or antipseudomonal penicillins' quality were identified.

API content defects were the most frequently encountered. The most striking examples were from a survey in Bangladesh, which reported cephadrine and ciprofloxacin samples containing 1% and 1.5% of the stated amounts, respectively.[38] A study in the Western Pacific Islands identified cloxacillin tablets containing 6.9% of the stated amount.[39] In Kenya, parenteral ampicillin were found to contain 190% of the stated amount,[40] and in India azithromycin tablets contained 160% of the stated amount.[41] Lower API amount than stated on the label was found for >6% of all samples tested for API content. Dissolution failure was also observed in almost one-tenth of samples tested. These findings show that SF antibiotics may expose patients to subtherapeutic levels and risk the selection and spread of resistant bacteria.[14] There is a lack of evidence to what degree quality defects will translate in impaired antibiotic bioavailability. Would an 85% API content antibiotic, when the pharmacopoeial lower limit is set to 90%, have clinically significant effects on patient outcome and AMR for different bacterial pathogens? Pharmacodynamic-pharmacokinetic modelling to understand the relationship between quality defect(s), such as low API content or impaired dissolution, to clinical outcomes are needed.

Aggregate results of prevalence surveys were reported for combinations of outlet types for more than half of samples, similar to the WHO findings, making it difficult to assess the sources of SF antibiotics.[9] When outlet types were specified, private registered pharmacies were the most reported, with a 15.7% FF. The highest FF of 34.3% was for samples from unregistered and unlicensed outlets, but data points were few.

Combining AMC data with the prevalence of SF antibiotics could be a novel, although crude, method to assess population risk of consumption of SF antibiotics. This could allow policy makers to focus their efforts on agents with high AMC in relation to their quality issues and provide insights into SF antibiotics-AMR relationships. We paired global AMC data with the SF antibiotic data summarised here, multiplying median AMC and FF.[52 53] However, AMC reporting countries were mostly MIC or HIC. Beta-lactams and penicillins had the highest index (online supplemental file 13). Future SF prevalence surveys also collecting sympatric AMC or antimicrobial use (AMU) data could be a useful approach for estimating risk of SF antibiotics in supply chains and hence risk of SF antibiotics on both patient outcomes and AMR. Improved AMC and AMU reporting (eg, in Laos https://www.youtube.com/watch?v=QELwHIPsKw4) is needed in order to rank the local importance, or otherwise, of SF antibiotics as drivers of AMR and allow targeted policymaking.

The overall FF in prevalence surveys observed here is higher than estimates in other recent reviews such as that by Ozawa *et al*, who focused on 11 studies and reported an FF of 12.4%.[49] Comparison with the WHO 2017 review[10] is difficult because the antimicrobials category also included 'other anti-infective products' (FF of 7.2%). Great caution is needed when interpreting the findings, as the higher FF in our review may be influenced by the inclusion of studies with smaller sample sizes. Half of the surveys included <47 samples; these had a median FF of 22.8%.

Results are strongly influenced by the heterogeneity, and the low methodological quality of studies included, as mirrored by the low MEDQUARG scores. Gaps in the quality of the methods and results reporting were evident, such as poor sampling design or lack of packaging analysis. Two-thirds of all studies used convenience sampling, risking bias and misestimation of SF antibiotic prevalence.[10 16 49 54] We are further limited by the inclusion of studies published only in English, French and Spanish and by medicine regulatory authority and the pharmaceutical industry datasets mostly not being in the public domain.[10 16 38 49 54]

Most studies performed less than five tests to assess adherence to the different pharmacopoeial properties, budgetary constraints being a common hurdle encountered.[55–57] Difficulties in collecting sufficient dosage units required, especially in remote areas and when sampling using a 'mystery shopper' approach are also barriers. This has important implications since samples are classed as of good quality if they pass the reduced battery tests conducted instead of full pharmacopoeial standards. Therefore, an antibiotic could be reported as being of

good quality due to having a within-range amount of API but may actually be SF due to other key aspects not being tested for. Such underestimation of the prevalence of SF antibiotics is supported by the higher FF found in bioequivalence studies in which the median number of quality tests performed per sample was higher than in prevalence surveys.

Accurate data on the epidemiology of SF antibiotics are key to understanding the problem and planning and prioritising interventions. The true prevalence of SF medicines can only be known from good quality evidence. The MEDQUARG and subsequent WHO guidelines and checklists provide a framework for better quality field surveys and reporting of medicine quality studies.[39 58] Key features include randomised sampling of medicines with appropriate sample size; 'mystery shopper' sampling to mimic real-life procurement of medicines; minimised timing between collection and analysis and appropriate storage in-between collection and analysis; following pharmacopoeia monographs to test the quality of medicines, or at a minimum API identity and content compared with recommended, and dissolution rate. Packaging analysis is also important to differentiate between SF medicines but this is often difficult as genuine packaging should be obtained from pharmaceutical companies, some being hard to reach and committing to the requirement. Calculation of the required sample size is also vital. Due to the costs associated with pharmacopoeial analysis and randomised sampling, and in light of the severe implications SF antibiotics carry, more funding is needed to support such studies and allow access to a wider range of chemical analysis methods.

These data show reasons for global concern as SF antibiotics risk increased morbidity, mortality, patient health expense, decline in confidence in health systems, economic harm to societies, governments and the pharmaceutical industry and AMR. SF antibiotics in the Watch and Reserve classes could severely impact patient outcomes in sub-Saharan Africa, Oceania and Asia, where sepsis incidence and sepsis-related mortality are highest.[59] Poor antibiotic quality appears to affect all antibiotic classes, especially those which are most consumed and in countries facing greater socioeconomic challenges.[52] Furthermore, unlicensed outlets seem to be particularly affected by this public health threat. SF antibiotics are likely to impede achieving the Sustainable Development Goals and controlling AMR in pathogens of key global importance such as those included in the WHO Global Antimicrobial Resistance Surveillance System initiative.[56 60] Lastly, with increasing access to antibiotics and higher AMC, failure to tackle quality problems will inevitably lead to higher absolute numbers of SF antibiotics reaching the population, causing direct harm and engendering further AMR.

The relationship between SF antibiotics and AMR is tangled as SF antibiotics are likely to be found where poor adherence and prescribing are sympatric, and there is little understanding of the delay between bacterial communities being exposed to subtherapeutic antibiotic concentrations and rising AMR prevalence being observed. In a recent study, the abundance and diversity of resistance genes was mainly correlated to sanitation and population health at local and national levels, without including an assessment of the impact of antibiotic quality.[61] The highest predicted diversity of AMR genes was found in Africa, which was also the region with the highest concentration of antibiotics in urban sewage, and where the highest FF was observed here.[14 61] Whether SF AMC contributes disproportionately, in comparison to good quality AMC, to AMR gene diversity at an individual level, which then spreads horizontally in regions with poor sanitation, leading to worsened health outcomes which then affect AMC in a vicious cycle, needs exploring.

In addition to global efforts to promote responsible use of antibiotics in humans and in animal feed, interventions as recommended in the WHO's SF 'Prevent, Detect, Respond' strategy and enhanced regulatory oversight of antibiotic manufacture are needed without waiting for better evidence.[49 62] A comprehensive effort to alleviate this public health issue must include policy interventions to ensure access to good quality antibiotics and control of AMR.

CONCLUSION

Antibiotic quality epidemiology remains a poorly understood and neglected topic, as shown in recent analyses of the AMR situation that did not include medicine quality as a potential driver.[63] Logically SF antibiotics will increase the risk of adverse patient outcomes, cause economic harms and drive AMR. These data argue that nations and international organisations should assess and prioritise interventions to enhance regulatory, purchasing and financial mechanisms to improve the global antibiotic supply.[64] How interventions to reduce SF antibiotics should be ranked as priorities in national AMR action plans is unclear. WHO Prevent, Detect and Respond strategies are key,[62] and portable, affordable screening devices offer hope for empowering drug inspectors for postmarket surveillance of antibiotic quality.[65]

Author affiliations
[1]Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit, Medicine Quality Research Group, Laboratory of Microbiology, Mahosot Hospital, Vientiane, Lao People's Democratic Republic
[2]Nuffield Department of Medicine, Medicine Quality Research Group, University of Oxford Centre for Tropical Medicine and Global Health, Oxford, UK
[3]Clinical Infection Unit, Saint George's University Hospital NHS Foundation Trust, London, UK
[4]Nuffield Department of Medicine, Infectious Diseases Data Observatory (IDDO)/WorldWide Antimalarial Resistance Network (WWARN), Medicine Quality Research Group, University of Oxford, Oxford, UK

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ORCID iDs
Guillermo A Zabala http://orcid.org/0000-0001-8382-7748
Khonsavath Bellingham http://orcid.org/0000-0001-6162-2098
Vayouly Vidhamaly http://orcid.org/0000-0003-1941-8944
Phonepasith Boupha http://orcid.org/0000-0002-2094-7512
Kem Boutsamay http://orcid.org/0000-0001-8152-0523
Paul N Newton http://orcid.org/0000-0003-0734-2022
Céline Caillet http://orcid.org/0000-0002-5554-2603

REFERENCES

1 Wax PM. Elixirs, diluents, and the passage of the 1938 federal food, drug and cosmetic act. *Ann Intern Med* 1995;122:456–61.
2 Antibiotics Market Size, Share & Trends Analysis Report By Action Mechanism (Protein, DNA, RNA, Cell Wall Synthesis Inhibitors), By Drug Class (Penicillin, Cephalosporins, Fluoroquinolones), And Segment Forecasts, 2019 - 2026. 2019:1–119. Available: https://www.grandviewresearch.com/industry-analysis/antibiotic-market [Accessed 29 July 2022].
3 World Health Organization. The top 10 causes of death, 2020. Available: http://www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death [Accessed 28 May 2021].
4 Klein EY, Van Boeckel TP, Martinez EM, *et al*. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A* 2018;115:E3463–70.
5 World Health Organization. Member State mechanism on substandard / spurious / falsely - labelled / falsified / counterfeit medical products Report by the Director - General. *WHO Technical Report Series* 2017;20:1–42.
6 Kelesidis T, Falagas ME. Substandard/counterfeit antimicrobial drugs. *Clin Microbiol Rev* 2015;28:443–64.
7 Newton PN, Timmermann B. Fake penicillin, the third man, and operation Claptrap. *BMJ* 2016;355:i6494.
8 Nickerson JW, Attaran A, Westerberg BD, *et al*. Fatal Bacterial Meningitis Possibly Associated with Substandard Ceftriaxone--Uganda, 2013. *MMWR Morb Mortal Wkly Rep* 2016;64:1375–7.
9 World Health Organization. Global surveillance and monitoring system for substandard and Falsified medical products. 2017:1–73. Available: https://www.who.int/publications/i/item/9789241513425 [Accessed 24 Jul 2022].
10 World Health Organization. A study on the public health and socioeconomic impact of substandard and falsified medical products. 2017:1–77. Available: https://apps.who.int/iris/handle/10665/331690 [Accessed 24 Jul 2022].
11 Abdul-Aziz MH, Lipman J, Mouton JW, *et al*. Applying pharmacokinetic/pharmacodynamic principles in critically ill patients: optimizing efficacy and reducing resistance development. *Semin Respir Crit Care Med* 2015;36:136–53.
12 Gullberg E, Cao S, Berg OG, *et al*. Selection of resistant bacteria at very low antibiotic concentrations. *PLoS Pathog* 2011;7:1–9.
13 Lipsitch M, Levin BR, . The population dynamics of antimicrobial chemotherapy. *Antimicrob Agents Chemother* 1997;41:363–73.
14 Pisani E. Antimicrobial resistance: what does medicine quality have to do with it? 2015:1–45. Available: http://amr-review.org/sites/default/files/ElizabethPisaniMedicinesQualitypaper.pdf [Accessed 24 Jul 2022].
15 Taylor RB, Shakoor O, Behrens RH. Drug quality, a contributor to drug resistance? *Lancet* 1995;346:122.
16 Newton PN, Green MD, Fernández FM, *et al*. Counterfeit anti-infective drugs. *Lancet Infect Dis* 2006;6:602–13.
17 Nayyar GML, Breman JG, Newton PN, *et al*. Poor-Quality antimalarial drugs in Southeast Asia and sub-Saharan Africa. *Lancet Infect Dis* 2012;12:488–96.
18 Videau JY. Acces pour tous aux medicaments de qualité. *Med Trop* 2002;62:396–400.
19 World Health Organization. Counterfeit and substandard drugs in Myanmar and Viet Nam. 1999:1–19. Available: https://apps.who.int/iris/handle/10665/66032 [Accessed 10 Nov 2020].
20 Shwe TN, Nyein MM, Yi W, *et al*. Blood culture isolates from children admitted to medical unit III, Yangon children's Hospital, 1998. *Southeast Asian J Trop Med Public Health* 2002;33:764–71.
21 Wafula F, Dolinger A, Daniels B, *et al*. Examining the quality of medicines at Kenyan healthcare facilities: a validation of an alternative post-market surveillance model that uses standardized patients. *Drugs - Real World Outcomes* 2017;4:53–63.
22 Newton PN, Caillet C, Guerin PJ. A link between poor quality antimalarials and malaria drug resistance? *Expert Rev Anti Infect Ther* 2016;14:531–3.
23 World Health Organization. Who releases the 2019 aware classification antibiotics, 2019. Available: https://www.who.int/medicines/news/2019/WHO_releases2019AWaRe_classification_antibiotics/en/ [Accessed 28 May 2021].
24 Tschida S. A systematic review on antibiotic quality, 2016. Available: https://paperzz.com/download/8601990
25 Holmes AH, Moore LSP, Sundsfjord A, *et al*. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet* 2016;387:176–87.
26 Okeke IN, Aboderin OA, Byarugaba DK. Growing problem of multidrug-resistant enteric pathogens in Africa.: discovery service for Ghana. *Emerg Infect Dis*2007;13:1640.
27 Hadi U, van den Broek P, Kolopaking EP, Gardjito W, *et al*. Cross-Sectional study of availability and pharmaceutical quality of antibiotics requested with or without prescription (over the counter) in Surabaya, Indonesia. *BMC Infect Dis* 2010;10:203.
28 Khuluza F. In-Vitro evaluation of the quality of paracetamol and co-trimoxazole tablets used in Malawi based on pharmacopoeial standards. *Malawi Med J* 2014;26:38–41.
29 Haider SS, Nasrin N, Apu AS. Accelerated stability and antimicrobial sensitivity studies of amoxicillin dry suspensions marketed in Bangladesh. *J Appl Pharm Sci* 2011;01:51–5.

30 Tie Y, Vanhee C, Deconinck E, *et al*. Development and validation of chromatographic methods for screening and subsequent quantification of suspected illegal antimicrobial drugs encountered on the Belgian market. *Talanta* 2019;194:876–87.
31 Hajjou M, Krech L, Lane-Barlow C, Lukulay PH, El-Hadri L, Raymond C, *et al*. Monitoring the quality of medicines: results from Africa, Asia, and South America. *Am J Trop Med Hyg* 2015;92:68–74.
32 Nagaraj A, Tambi S, Shravani G, *et al*. Counterfeit medicines sale on online pharmacies in India. *J Res Pharm Pract* 2014;3:145–6.
33 Zachariah R, Harries AD, Spielmann MP, *et al*. Changes in Escherichia coli resistance to co-trimoxazole in tuberculosis patients and in relation to co-trimoxazole prophylaxis in Thyolo, Malawi. *Trans R Soc Trop Med Hyg* 2002;96:202–4.
34 Okeke IN, Lamikanra A. Quality and bioavailability of tetracycline capsules in a Nigerian semi-urban community. *Int J Antimicrob Agents* 1995;5:245–50.
35 Okeke IN, Lamikanra A. Quality and bioavailability of ampicillin capsules dispensed in a Nigerian semi-urban community. *Afr J Med Med Sci* 2001;30:47–51.
36 Kamuhabwa AAR, Saifuddin MH, Maganda B. Quality of co-trimoxazole tablets used for management of opportunistic infections in HIV/AIDS patients. *Int J Pharm Res* 2011;3:79–84.
37 Anatomical therapeutic chemical (ATC) classification system. who collaborating centre for drug statistics methodology, 2020. Available: https://www.whocc.no/atc_ddd_index/ [Accessed 20 Dec 2020].
38 Saraswati K, Sichanh C, Newton PN, *et al*. Quality of medical products for diabetes management: a systematic review. *BMJ Glob Health* 2019;4:e001636.
39 Newton PN, Lee SJ, Goodman C, *et al*. Guidelines for field surveys of the quality of medicines: a proposal. *PLoS Med* 2009;6:0252–7.
40 Santosh KK, Raghuram TC, Krishnaswamy K. Bioavailability of different brands of tetracycline in undernourished subjects. *Int J Clin Pharmacol Ther Toxicol* 1992;30:13–17.
41 Weinstein ZB, Zaman MH. Evolution of rifampin resistance in Escherichia coli and Mycobacterium smegmatis due to substandard drugs. *Antimicrob Agents Chemother* 2019;63:e01243–18.
42 Phanouvong S, Raymond C, Krech L, *et al*. The quality of antimalarial medicines in Western Cambodia: a case study along the Thai-Cambodian border. *Southeast Asian J Trop Med Public Health* 2013;44:349–62.
43 Khojah HMJ, Pallos H, Yoshida N, *et al*. The Quality of Medicines in Community Pharmacies in Riyadh, Saudi Arabia: A Lot Quality Assurance Sampling (LQAS)-Based Survey. *Pharm. Pharmacol.* 2013;04:511–9.
44 Ononna HF, ASMM alH, Ganguly A. Potency determination of essential drug samples manufactured by small and medium pharmaceutical industries in Bangladesh. *Bangladesh Med Res Counc Bull* 2017;43:87–93.
45 Hand RM, Senarathna SMDKG, Page-Sharp M, *et al*. Quality of benzathine penicillin G: a multinational cross-sectional study. *Pharmacol Res Perspect* 2020;8:1–7.
46 Wang T, Hoag SW, Eng ML, *et al*. Quality of antiretroviral and opportunistic infection medications dispensed from developing countries and Internet pharmacies. *J Clin Pharm Ther* 2015;40:68–75.
47 Phanouvong S, Reiss S, Smine A. Why be concerned about the quality of antimalarial and ARV drugs? In: *Seventh International Congress on AIDS in Asia and the Pacific*. Kobe, Japan: United States Pharmacopeia Drug Quality and Information Program (USP DQI), 2005.
48 Almuzaini T, Choonara I, Sammons H, Imti Choonara HS T. Substandard and counterfeit medicines: a systematic review of the literature. *BMJ Open* 2013;3:370–1.
49 Ozawa S, Evans DR, Bessias S, *et al*. Prevalence and estimated economic burden of substandard and Falsified medicines in low- and middle-income countries: a systematic review and meta-analysis. *JAMA Netw Open* 2018;1:e181662.
50 Kelesidis T, Kelesidis I, Rafailidis PI, *et al*. Counterfeit or substandard antimicrobial drugs: a review of the scientific evidence. *J Antimicrob Chemother* 2007;60:214–36.
51 McManus D, Naughton BD. A systematic review of substandard, falsified, unlicensed and unregistered medicine sampling studies: a focus on context, prevalence, and quality. *BMJ Glob Health* 2020;5:e002393.
52 World Health Organization. Who report on surveillance of antibiotic consumption: 2016-2018 early implementation. 2018:1–127. Available: https://www.who.int/publications/i/item/9789241514880 [Accessed 24 Jul 2022].
53 Klein EY, Milkowska-Shibata M, Tseng KK, *et al*. Assessment of who antibiotic consumption and access targets in 76 countries, 2000-15: an analysis of pharmaceutical sales data. *Lancet Infect Dis* 2021;21:107–15.
54 Tabernero P, Fernández FM, Green M, *et al*. Mind the gaps - the epidemiology of poor-quality anti-malarials in the malarious world - analysis of the WorldWide Antimalarial Resistance Network database. *Malar J* 2014;13:1–14.
55 Khurelbat D, Dorj G, Bayarsaikhan E, *et al*. Prevalence estimates of substandard drugs in Mongolia using a random sample survey. *Springerplus* 2014;3:709.
56 Aminu N, Sha'aban A, Abubakar A, *et al*. Unveiling the peril of substandard and Falsified medicines to public health and safety in Africa: need for All-Out war to end the menace. *Med Access Point Care* 2017;1:maapoc.0000023–54.
57 Chikowe I, Bliese SL, Lucas S, *et al*. Amoxicillin quality and selling practices in urban pharmacies and drug stores of Blantyre, Malawi. *Am J Trop Med Hyg* 2018;99:233–8.
58 Organization WH. Guidelines on the conduct of surveys of the quality of medicines. who expert Committee on specifications for pharmaceutical preparations (fiftieth report), 2016. Available: https://digicollections.net/medicinedocs/#d/s22404en [Accessed 24 Jul 2022].
59 Rudd KE, Johnson SC, Agesa KM, *et al*. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the global burden of disease study. *Lancet* 2020;395:200–11.
60 World Health Organization. Global antimicrobial resistance surveillance system (glass) report: early implementation 2016-2017. 2017:1–164. Available: https://apps.who.int/iris/bitstream/handle/10665/259744/9789241513449-eng.pdf [Accessed 3 Jun 2021].
61 Hendriksen RS, Munk P, Njage P, *et al*. Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage. *Nat Commun* 2019;10:1124.
62 World Health Organization. WHO's work in emergencies: prepare, prevent, detect and respond. 2018:1–41. Available: https://www.who.int/publications/i/item/who-s-work-in-emergencies-prepare-prevent-detect-and-respond [Accessed 24 Jul 2022].
63 The Center for Disease Dinamycs Economics and Policy. The state of the world' S antibiotics 2021, 2021. Available: https://cddep.org/blog/posts/the-state-of-the-worlds-antibiotics-report-in-2021/#:~:text=Researchers at CDDEP have released,www.resistancemap.org)%2C [Accessed 6 Feb 2021].
64 Pisani E, Nistor A-L, Hasnida A, *et al*. Identifying market risk for substandard and falsified medicines: an analytic framework based on qualitative research in China, Indonesia, turkey and Romania. *Wellcome Open Res* 2019;4:70.
65 Vickers S, Bernier M, Zambrzycki S, *et al*. Field detection devices for screening the quality of medicines: a systematic review. *BMJ Glob Health* 2018;3:e000725.

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 1. Search terms.

PUBMED

(substandard OR falsified OR counterfeit OR fake OR spurious OR degraded OR "falsely labelled" OR "drug* qualit*" OR "medicine* qualit*" OR "pharmaceutical* qualit*" OR "poor qualit*") AND (antibacterial* OR antibiotic* OR antimicrobial* OR anti-infective* OR demeclocycline OR doxycycline OR chlortetracycline OR lymecycline OR metacycline OR oxytetracycline OR tetracycline* OR minocycline OR rolitetracycline OR penimepicycline OR clomocycline OR omadacycline OR tigecycline OR eravacycline OR sarecycline OR chloramphenicol OR thiamphenicol OR ampicillin OR pivampicillin OR carbenicillin OR amoxicillin OR carindacillin OR bacampicillin OR epicillin OR pivmecillinam OR azlocillin OR mezlocillin OR mecillinam OR piperacillin OR ticarcillin OR metampicillin OR talampicillin OR sulbenicillin OR temocillin OR hetacillin OR aspoxicillin OR benzylpenicillin OR phenoxymethylpenicillin OR propicillin OR azidocillin OR pheneticillin OR penamecillin OR clometocillin OR "benzathine benzylpenicillin" OR "procain* benzylpenicillin" OR "benzathine phenoxymethylpenicillin" OR dicloxacillin OR cloxacillin OR methicillin OR oxacillin OR flucloxacillin OR nafcillin OR sulbactam OR tazobactam OR avibactam OR sultamicillin OR cefalexin OR cefaloridine OR cefalotin OR cefazolin OR cefadroxil OR cefazedone OR cefatrizine OR cefapirin OR cefradine OR cefacetrile OR cefroxadine OR ceftezole OR cefoxitin OR cefuroxime OR cefamandole OR cefaclor OR cefotetan OR cefonicid OR cefotiam OR loracarbef OR cefmetazole OR cefprozil OR ceforanide OR cefminox OR cefbuperazone OR flomoxef OR cefotaxime OR ceftazidime OR cefsulodin OR ceftriaxone OR cefmenoxime OR latamoxef OR ceftizoxime OR cefixime OR cefodizime OR cefetamet OR cefpiramide OR cefoperazone OR cefpodoxime OR ceftibuten OR cefdinir OR cefditoren OR cefcapene OR cefteram OR cefepime OR cefpirome OR cefozopran OR ceftolozane OR aztreonam OR carumonam OR meropenem OR ertapenem OR doripenem OR biapenem OR tebipenem OR imipenem OR panipenem OR "ceftobiprole medocaril" OR "ceftaroline fosamil" OR "faropenem" OR trimethoprim OR brodimoprim OR iclaprim OR sulfaisodimidine OR sulfamethizole OR sulfadimidine OR sulfapyridine OR sulfafurazole OR sulfanilamide OR sulfathiazole OR sulfathiourea OR sulfamethoxazole OR sulfamoxole OR sulfadiazine OR sulfadimethoxine OR sulfalene OR sulfametomidine OR sulfametoxydiazine OR sulfamethoxypyridazine OR sulfaperin OR sulfamerazine OR sulfaphenazole OR

sulfamazone OR erythromycin OR spiramycin OR midecamycin OR oleandomycin OR roxithromycin OR josamycin OR troleandomycin OR clarithromycin OR azithromycin OR miocamycin OR rokitamycin OR dirithromycin OR flurithromycin OR telithromycin OR solithromycin OR clindamycin OR lincomycin OR pristinamycin OR quinupristin OR dalfopristin OR streptomycin OR streptoduocin OR tobramycin OR gentamicin OR kanamycin OR neomycin OR amikacin OR netilmicin OR sisomicin OR dibekacin OR ribostamycin OR isepamicin OR arbekacin OR bekanamycin OR plazomicin OR ofloxacin OR ciprofloxacin OR pefloxacin OR enoxacin OR temafloxacin OR norfloxacin OR lomefloxacin OR fleroxacin OR sparfloxacin OR rufloxacin OR grepafloxacin OR levofloxacin OR trovafloxacin OR moxifloxacin OR gemifloxacin OR gatifloxacin OR prulifloxacin OR pazufloxacin OR garenoxacin OR sitafloxacin OR tosufloxacin OR delafloxacin OR rosoxacin OR nalidixic acid OR piromidic acid OR pipemidic acid OR oxolinic acid OR cinoxacin OR flumequine OR nemonoxacin OR vancomycin OR teicoplanin OR telavancin OR dalbavancin OR oritavancin OR colistin OR "polymyxin B" OR "fusidic acid" OR metronidazole OR tinidazole OR ornidazole OR azanidazole OR propenidazole OR nimorazole OR secnidazole OR nitrofurantoin OR nifurtoinol OR furazidin OR fosfomycin OR xibornol OR clofoctol OR spectinomycin OR methenamine OR "mandelic acid" OR nitroxoline OR linezolid OR daptomycin OR bacitracin OR tedizolid OR lefamulin OR macrolide* OR tetracycline* OR Beta-Lactam* OR Sulfonamide* OR lincosamide* OR aminoglycoside* OR *quinolone* OR glucopeptide* OR lipopeptide OR cephalosporin* OR "penicillin V" OR penicillin OR "penicillin G" OR co-amoxiclav OR Co-fluampicil OR Co-trimoxazole OR cephalexin OR cephaloridine OR cephalothin OR cephazolin OR cephapirin OR cephradine OR cephacetrile)

EMBASE

(substandard OR falsified OR counterfeit OR fake OR spurious OR degraded OR "falsely labelled" OR "drug quality" OR "medicine quality" OR "pharmaceutical quality" OR "poor quality") AND (antibacterial OR antibiotic OR antimicrobial OR anti-infective OR demeclocycline OR doxycycline OR chlortetracycline OR lymecycline OR metacycline OR oxytetracycline OR tetracycline OR minocycline OR rolitetracycline OR penimepicycline OR clomocycline OR omadacycline OR tigecycline OR eravacycline OR sarecycline OR chloramphenicol OR thiamphenicol OR ampicillin OR pivampicillin OR carbenicillin OR amoxicillin OR carindacillin OR bacampicillin OR epicillin OR pivmecillinam OR azlocillin OR mezlocillin OR mecillinam OR piperacillin OR ticarcillin OR metampicillin OR talampicillin OR sulbenicillin OR temocillin OR hetacillin OR aspoxicillin OR benzylpenicillin OR phenoxymethylpenicillin OR propicillin OR azidocillin OR pheneticillin OR penamecillin OR

clometocillin OR "benzathine benzylpenicillin" OR "procain benzylpenicillin" OR benzathine phenoxymethylpenicillin OR dicloxacillin OR cloxacillin OR methicillin OR oxacillin OR flucloxacillin OR nafcillin OR sulbactam OR tazobactam OR avibactam OR sultamicillin OR cefalexin OR cefaloridine OR cefalotin OR cefazolin OR cefadroxil OR cefazedone OR cefatrizine OR cefapirin OR cefradine OR cefacetrile OR cefroxadine OR ceftezole OR cefoxitin OR cefuroxime OR cefamandole OR cefaclor OR cefotetan OR cefonicid OR cefotiam OR loracarbef OR cefmetazole OR cefprozil OR ceforanide OR cefminox OR cefbuperazone OR flomoxef OR cefotaxime OR ceftazidime OR cefsulodin OR ceftriaxone OR cefmenoxime OR latamoxef OR ceftizoxime OR cefixime OR cefodizime OR cefetamet OR cefpiramide OR cefoperazone OR cefpodoxime OR ceftibuten OR cefdinir OR cefditoren OR cefcapene OR cefteram OR cefepime OR cefpirome OR cefozopran OR ceftolozane OR aztreonam OR carumonam OR meropenem OR ertapenem OR doripenem OR biapenem OR tebipenem OR imipenem OR panipenem OR "ceftobiprole medocaril" OR "ceftaroline fosamil" OR faropenem OR trimethoprim OR brodimoprim OR iclaprim OR sulfaisodimidine OR sulfamethizole OR sulfadimidine OR sulfapyridine OR sulfafurazole OR sulfanilamide OR sulfathiazole OR sulfathiourea OR sulfamethoxazole OR sulfamoxole OR sulfadiazine OR sulfametrole OR sulfadimethoxine OR sulfalene OR sulfametomidine OR sulfametoxydiazine OR sulfamethoxypyridazine OR sulfaperin OR sulfamerazine OR sulfaphenazole OR sulfamazone OR erythromycin OR spiramycin OR midecamycin OR oleandomycin OR roxithromycin OR josamycin OR troleandomycin OR clarithromycin OR azithromycin OR miocamycin OR rokitamycin OR dirithromycin OR flurithromycin OR telithromycin OR solithromycin OR clindamycin OR lincomycin OR pristinamycin OR quinupristin OR dalfopristin OR streptomycin OR streptoduocin OR tobramycin OR gentamicin OR kanamycin OR neomycin OR amikacin OR netilmicin OR sisomicin OR dibekacin OR ribostamycin OR isepamicin OR arbekacin OR bekanamycin OR plazomicin OR ofloxacin OR ciprofloxacin OR pefloxacin OR enoxacin OR temafloxacin OR norfloxacin OR lomefloxacin OR fleroxacin OR sparfloxacin OR rufloxacin OR grepafloxacin OR levofloxacin OR trovafloxacin OR moxifloxacin OR gemifloxacin OR gatifloxacin OR prulifloxacin OR pazufloxacin OR garenoxacin OR sitafloxacin OR tosufloxacin OR delafloxacin OR rosoxacin OR nalidixic acid OR piromidic acid OR pipemidic acid OR oxolinic acid OR cinoxacin OR flumequine OR nemonoxacin OR vancomycin OR teicoplanin OR telavancin OR dalbavancin OR oritavancin OR colistin OR polymyxin B OR fusidic acid OR metronidazole OR tinidazole OR ornidazole ornidazole OR azanidazole OR propenidazole OR nimorazole OR secnidazole OR nitrofurantoin OR nifurtoinol OR furazidin OR fosfomycin OR xibornol OR clofoctol OR spectinomycin OR methenamine OR "mandelic acid" OR nitroxoline OR linezolid OR daptomycin OR bacitracin OR tedizolid OR lefamulin OR macrolide OR tetracycline OR Beta-Lactam OR Sulfonamide OR lincosamide OR aminoglycoside OR fluorquinolone OR quinolone OR glucopeptide OR lipopeptide OR cephalosporin OR penicillin V OR penicillin OR

penicillin G OR co-amoxiclav OR Co-fluampicil OR Co-trimoxazole OR cephalexin OR cephaloridine OR cephalothin OR cephazolin OR cephapirin OR cephradine OR cephacetrile)

Google and Google Scholar (sorted by relevance, selected first 200 for each search)

English language searches

1. (substandard OR falsified OR counterfeit OR fake OR spurious OR “drug quality” OR “medicine quality” OR “pharmaceutical quality”) AND (antibacterial OR antibiotic OR antimicrobial OR aminoglycoside OR Quinolone OR macrolide OR Beta-Lactam)
2. (substandard OR falsified OR counterfeit OR fake OR spurious OR “drug quality” OR “medicine quality” OR “pharmaceutical quality”) AND (Tetracyclines OR penicillin OR Cephalosporin)

French language searches

3. (sous-standard OR falsifié OR contrefaçon OR faux OR "médicament fallacieux" OR "qualité des médicaments" OR “qualité pharmaceutique”) AND (antibactérien OR antibiotique OR antimicrobien OR aminoside OR quinolone OR macrolide OR béta-lactamine)
4. (sous-standard OR falsifié OR contrefaçon OR faux OR "médicament fallacieux" OR "qualité des médicaments" OR “qualité pharmaceutique”) AND (tétracycline OR pénicilline OR céphalosporine)

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 2: Types of studies included in the review and definitions

Scientific reports	Quality control	Study in which samples were collected to be analyzed in routine post marketing surveillance by a MRA or a laboratory mandated by a MRA
	Prevalence survey	Study in which samples were collected within the pharmaceutical supply chain to assess their quality, in order to describe the prevalence of circulating SF medicines
	Equivalence study	Study to assess the quality of different marketed brands of the same API(s) assuming that the results of the collected samples would represent the quality of the brand as a whole and not an estimate of the frequency of individual samples of different quality
	Analysis technique development/validation	Study in which samples are assembled in a laboratory to answer a chemical, rather than an epidemiological question (mostly for the development of a new quality technique)
	Stability study	Study in which quality test is performed on medicines subjected to various storage conditions
	Bioavailability study	Study of the *in vivo* bioavailability, i.e. testing for adequate body tissue concentration including the rate and extent to which drug reaches the body tissue compartment
Other reports	Recall/warning/alert	Recall/Warning/Alert of products by manufacturers via MRA or by MRAs directly, or by WHO rapid alert
	Case reports	Patients not responding to medicines or adverse drug reaction where the quality of the medicine was suspected as the cause. Also includes samples analyzed for quality not included in a scientific study.
	Seizure	Confiscations by police or MRA

Note: API, Active Pharmaceutical Ingredient; MRA, Medicines Regulatory Agency; WHO, World Health Organization

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 3: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	10-11
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	11
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	11

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 3: PRISMA Checklist

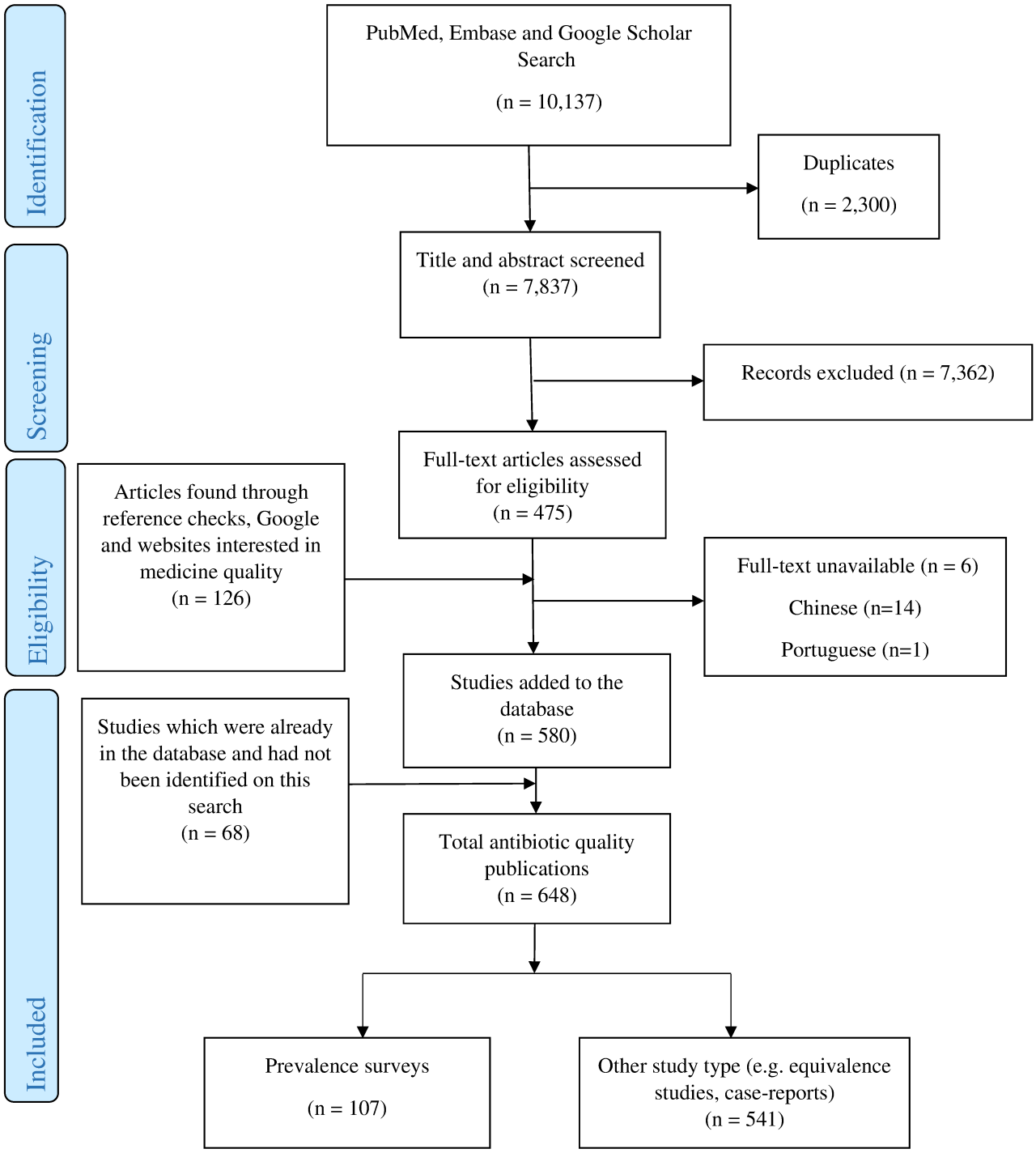
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not done
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11-12
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13 and suppl file 5, 10, 11
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	16 and suppl file 9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	15-18
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not done
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	16-17
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not done
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	18-20
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20-21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 4. PRISMA flow diagram of the selection process of the publications on antibiotic quality.



Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 5. Papers excluded post eligibility assessment of full text or unable to obtain full text

Unable to obtain full text

1. Agom JK, Akanni AO, Dawodu TO. Quality of ampicillin/cloxacillin preparations on the Nigerian market. Nig J Pharmacol 1990; 21: 36-38.
2. Hailu GS, Gutema GB, Hishe HZ, et al. Comparative in vitro bioequivalence evaluation of different brands of amoxicillin capsules marketed in Tigray, Ethiopia. Int J Pharm Sci Nanotech 2013; 6(1): 1966-1971.
3. Mukhtar MD, Maryam IA, Adoum AO. Quality assessment of some brands of ampicillin oral formulations on sale in some parts of Kano by thin layer chromatography and microbiological techniques. Journal of Research in Biosciences. 2006; 2(1).
4. Secco G, Sachetti C, Rossato-Grando LG, et al. Quality of vancomycin for injection formulations in Brazil. Current Pharmaceutical Analysis 2019; 15(3): 280-285
5. Tariq S, Rasheed H, Rasheed MA, Ashraf M 2012, 'Quality evaluation of different brands of ceftriaxone', M.Phil Thesis, University of Veterinary and Animal Sciences, Lahore, Pakistan.
6. Usman S, Alam A, Suleiman R, et al. Evaluation of dissolution testing for ciprofloxacin (500mg) tablets: post market surveillance of different brands available in Ras al Khaimah (UAE). Int J Biopharm 2014; 5: 65-72.

Study reported in other languages not included in the review

7. Bonfilio R, Santos OMM, Novaes ZR, et al. Controle de qualidade físico-químico e microbiológico em 2347 amostras manipuladas em 2010 e 2011. Revista de ciências farmacêuticas básica e aplicada 2013; 34(4): 527-535.
8. Cao FQ, Li D, Yan ZY. Determination of Norfloxacin by its enhancement effect on the fluorescence intensity of functionalized CdS nanoparticles. Guang Pu Xue Yu Guang Pu Fen Xi 2009; 29(8): 2222-2226.
9. Du Y. Study on the determination of metronidazole and amoxicillin in Bijiaxilin tablet by HPLC. Chinese Pharmaceutical Journal 2001; 36(2): 115-117.
10. Kan J, Qu J. HPLC determination of the contents in compound roxithromycin tablets. Chinese Journal of New Drugs 2009; I2: 171-173.
11. Li N, Shen J, Jia Y, et al. The inspection of amoxicillin medicines studied by the terahertz time-domain spectroscopy technique. Spectroscopy and Spectral Analysis 2007; 27(9): 1692-1695.
12. Lei DQ, Feng YC, Hu CQ. Using Near-infrared Spectroscopy correlation coefficient method monitoring drug quality in the circulation field. Chinese Pharmaceutical Journal 2010; 45(14): 1097-1103.

13. Liu L. Improvement of the TLC method of limit test for related substances in doxycycline hydrochloride. Chinese Journal of Pharmaceutical Analysis 1993; 13(5): 318-320.
14. Mei D, Du XL, Li DK. Pharmaceutical evaluation of different sterile ceftriaxone sodium products. Chinese Pharmaceutical Journal 2004; 39(6): 463-466.
15. Mei D, Zhao W, Fu Q, et al. Quality evaluation of different cefradine capsules. Chinese Journal of Antibiotics 2002; 27(1): 31-32, 62.
16. Shao-liang C, Lie L. Thermal analysis of the quality of chloramphenicol tablets. Chinese Journal of Antibiotics 2004; 29(1): 26-28.
17. Wu Y, Guo CM, Zhang SQ. Quality control of spectinomycin hydrochloride by HPLC/ELSD. Journal of China Pharmaceutical University 2005; 36(1):40-43.
18. Xie J, Zhang Y, Zeng Z, et al. Determination of clindamycin liposome by HPLC. Pharmaceutical Biotechnology 2008; 15(4): 299-301.
19. Yu T, Zhao RS, Zhou Y, et al. Quality evaluation of vancomycin hydrochloride for injection. Chinese Pharmaceutical Journals 2009; 44(21): 1662-1665.
20. Zarapkar SS, Halkar UP, Rane SH. Reverse phase high-performance liquid chromatographic determination of Ampicillin and Probenecid in capsules. Indian Drugs 200; 37(4): 200-203.
21. Zhang ZF, Yang GL, Liang GJ, et al. Quality study of cefoperazone sodium and sulbactam sodium for injection by HPLC. Chinese Pharmaceutical Journal 2003; 38(6): 462-464.

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 6. Main characteristics of prevalence surveys of antibiotic quality in order of date of publication

Reference	Journal/Publisher	Sampling method	Countries	Active Pharmaceutical Ingredients (API) Sampled	Data points	Failed samples n/N (%)
Iwuagwu, 1992[1]	International Journal of Pharmacy Practice	Convenience	Nigeria	Ampicillin	1	3/13 (23.1 %)
Muritu, 1994[2]	Journal of Pharmaceutical and Biomedical Analysis	Convenience	Kenya	Tetracycline	1	0/50 (0 %)
Okeke, 1995[3]	International Journal of Antimicrobial Agents	Convenience	Nigeria	Tetracycline	1	6/7 (85.7 %)
Taylor, 1995[4]	The Lancet	Convenience	Nigeria	Amoxicillin	1	5/9 (55.6 %)
Reseau Medicament et Developpement, 1995[5]	The World Health Organization	Convenience	Cameroon, Chad, Madagascar	Amoxicillin, Ampicillin, Chloramphenicol, Metronidazole, Penicillin-unspecified, Sulfamethoxazole-Trimethoprim, Tetracycline	21	47/180 (26.1 %)
Nazerali, 1996[6]	WHO Action Programme on Essential Drugs	Convenience	Zimbabwe	Amoxicillin, Ampicillin, Benzylpenicillin (penicillin G), Doxycycline, Phenoxymethylpenicillin (penicillin V), Tetracycline	13	9/299 (3.0%)
Gimenez, 1997[7]	Medecine et Maladies Infectieuses	Convenience	Cambodia	Amoxicillin, Chloramphenicol, Metronidazole, Sulfamethoxazole-Trimethoprim, Tetracycline	5	23/82 (28.0 %)
Shakoor, 1997[8]	Tropical Medicine and International Health	Convenience	Nigeria, Thailand	Amoxicillin, Ampicillin-Cloxacillin, Sulfamethoxazole-Trimethoprim, Tetracycline	12	21/59 (35.6 %)
Kibwage, 1998[9]	East and Central African Journal of Pharmaceutical Sciences	Convenience	Kenya	Sulfamethoxazole-Trimethoprim	2	14/37 (37.8 %)
Nazerali, 1998[10]	The British Medical Journal (BMJ)	Convenience	Zimbabwe	Ampicillin	1	2/10 (20.0 %)
Wondemagegnehu, 1999[11]	The World Health Organization	Random	Myanmar, Viet Nam	Amoxicillin, Ampicillin, Chloramphenicol, Metronidazole, Sulfamethoxazole-Trimethoprim, Tetracycline	15	46/313 (14.7 %)
Kamau, 2001[12]	East and Central African Journal of Pharmaceutical Sciences	Convenience	Kenya	Ampicillin	1	11/45 (24.4 %)
Taylor, 2001[13]	The Lancet	Random	Nigeria	Amoxicillin, Ampicillin, Ampicillin-Cloxacillin, Benzylpenicillin (penicillin G), Cloxacillin, Doxycycline, Metronidazole, Streptomycin, Sulfamethoxazole-Trimethoprim	9	136/273 (49.8 %)
Kolawole, 2002[14]	Nigerian Journal of Pharmaceutical Science	Convenience	Nigeria	Ampicillin	1	14/31 (45.2%)

Prazuck, 2002[15]	Sexually Transmitted Diseases	Combination *	Myanmar	Benzylpenicillin (penicillin G), Ceftriaxone, Chlortetracycline, Ciprofloxacin, Doxycycline, Erythromycin, Sulfamethoxazole-Trimethoprim	7	7/19 (36.8 %)
Sow, 2002[16]	International Journal of Infectious Disease	Convenience	Senegal	Ampicillin, Oxytetracycline, Phenoxymethylpenicillin (penicillin V), Sulfamethoxazole-Trimethoprim	4	27/47 (57.4 %)
Ahmed, 2003[17]	Journal of Biological Sciences	Random	Bangladesh	Metronidazole	1	9/40 (22.5%)
Kamau, 2003[18]	East and Central African Journal of Pharmaceutical Sciences	Convenience	Kenya	Amoxicillin	1	4/57 (7.0 %)
Risha, 2003[19]	Ghent University Faculty of Pharmaceutical Sciences	Convenience	Tanzania	Amoxicillin, Ciprofloxacin, Metronidazole, Sulfamethoxazole-Trimethoprim	4	2/25 (8.0 %)
Basco, 2004[20]	The American Journal of Tropical Medicine and Hygiene	Convenience	Cameroon	Sulfamethoxazole-Trimethoprim	1	0/1 (0.0 %)
Kayumba, 2004[21]	Journal of Clinical Pharmacy and Therapeutics	Convenience	Rwanda, Tanzania	Amoxicillin, metronidazole, sulfamethoxazole-trimethoprim	6	4/25 (16.0%)
Syhakhang, 2004[22]	Pharmaceutical World Science	Random	Lao People's Democratic Republic	Ampicillin, Tetracycline	4	124/356 (34.8 %)
Legris, 2005[23]	Universite Henri Poincare – Nancy I	Random	Ivory Coast	Ampicillin, amoxicillin, metronidazole, sulfamethoxazole-trimethoprim	4	33/65 (50.8%)
Phanouvong, 2005[24]	United States Pharmacopeia (USP)	Convenience	Cambodia, Lao People's Democratic Republic, Thailand	Tetracycline	3	3/168 (1.8 %)
Weir, 2005[25]	British Journal of Ophthalmology	Convenience	India	Ciprofloxacin	1	30/30 (100.0 %)
Lon, 2006[26]	Transactions of the Royal Society of Tropical Medicine and Hygiene	Convenience	Cambodia	Tetracycline	1	34/128 (26.6 %)
Obodozie, 2006[27]	Journal of Clinical Pharmacy and Therapeutics	Convenience	Nigeria	Ampicillin-Cloxacillin	2	23/40 (57.5 %)
Vijaykadga, 2006[28]	The Southeast Asian Journal of Tropical Medicine and Public Health	Convenience	Thailand	Tetracycline	1	0/19 (0.0 %)
Okoro, 2007[29]	Research Journal of Pharmacology	Convenience	Nigeria	Ampicillin	1	5/10 (50.0 %)
Sheth, 2007[30]	South East Asian FIP-WHO Forum of Pharmaceutical Associations	Convenience	India	Amikacin, Amoxicillin, Amoxicillin-Clavulanic acid, Ampicillin-Cloxacillin, Cefadroxil, Cefalexin, Cefotaxime, Ceftazidime, Cefuroxime, Ciprofloxacin, Erythromycin, Gentamicin, Roxithromycin	14	8/195 (4.1%)

Camara, 2008[31]	Ministere de l'Education Nationale, Universite de Bamako	Convenience	Mali	Erythromycin, gentamicin, tetracycline	3	6/30 (20.0%)
Kyriacos, 2008[32]	Journal of Clinical Pharmacy and Therapeutics	Random	Egypt, Jordan, Lebanon, Saudi Arabia	Amoxicillin	5	14/32 (43.8 %)
Meos, 2008[33]	Drug Development Research	Convenience	Estonia, Russian Federation	Doxycycline	2	2/8 (25.0 %)
Pouillot, 2008[34]	Bulletin de la Societe de Pathologie exotique	Convenience	Cameroon, Niger	Amoxicillin, Ampicillin, Chloramphenicol, Gentamicin, Metronidazole, Norfloxacin, Oxacillin, Sulfamethoxazole-Trimethoprim, Tetracycline	11	45/102 (44.1 %)
Bate, 2009[35]	PLoS ONE	Convenience	India	Ciprofloxacin, Erythromycin	4	17/220 (7.8 %)
Central Drug Standard Control Organisation, 2009[36]	Central Drugs Standard Control Organisation CDSCO, India	Convenience	India	Amoxicillin, Ciprofloxacin, Sulfamethoxazole-Trimethoprim	3	0/165 (0.0 %)
Diop, 2009[37]	Medecine Tropicale	Unknown	Senegal	Amoxicillin, Ampicillin, Ciprofloxacin, Erythromycin, Phenoxymethylpenicillin (penicillin V)	5	10/34 (29.4 %)
Mak, 2009[38]	Universite de la mediterranee aix-marseille II	Random	Cambodia	Amoxicillin	6	3/39 (7.7%)
Obaid, 2009[39]	Pakistan Journal of Pharmaceutical Sciences	Convenience	Pakistan	Ceftriaxone	1	16/96 (16.7 %)
Zaheer, 2009[40]	Pakistan Journal of Scientific and Industrial Research	Unknown	Pakistan	Ciprofloxacin, Levofloxacin, Ofloxacin	3	1/12 (8.3 %)
Hadi, 2010[41]	BMC Infectious Diseases	Convenience	Indonesia	Amoxicillin, Chloramphenicol, Ciprofloxacin, Sulfamethoxazole-Trimethoprim, Tetracycline	5	19/104 (18.3 %)
Khan, 2010[42]	Tropical Medicine and International Health	Random	Cambodia	Metronidazole	1	1/79 (1.3 %)
Bate, 2011[43]	Journal of Health Economics	Convenience	Democratic Republic of the Congo	Ciprofloxacin, Erythromycin	2	34/304 (11.2 %)
Haider, 2011[44]	Journal of Applied Pharmaceutical Science	Convenience	Bangladesh	Amoxicillin	1	3/10 (30.0 %)
Idries, 2011[45]	University of Khartoum	Convenience	Sudan	Amoxicillin, Ceftriaxone, Ciprofloxacin, Metronidazole	4	1/11 (9.1 %)
Kamuhabwa, 2011[46]	International Journal of Pharmaceutical Research	Convenience	Tanzania	Sulfamethoxazole-Trimethoprim	1	4/17 (23.5 %)
Nair, 2011[47]	Journal of Pharmaceutical Sciences	Random	Papua New Guinea	Amoxicillin	1	8/8 (100.0 %)
Seear, 2011[48]	Journal of Clinical Pharmacy and Therapeutics	Convenience	India	Ciprofloxacin	1	9/100 (9.0 %)

World Health Organization, 2011[49]	The World Health Organization	Convenience	Armenia, Azerbaijan, Belarus, Kazakhstan, Ukraine, Uzbekistan	Ofloxacin	6	6/50 (12.0 %)
Yusuf, 2011[50]	Management Sciences for Health		Afghanistan	Amoxicillin, Ceftriaxone, Ciprofloxacin, Gentamicin	4	5/125 (4.0%)
Karlage, 2012[51]	Drug Development and Industrial Pharmacy	Random	Mexico, United States	Amoxicillin, Ampicillin, Ciprofloxacin, Sulfamethoxazole-Trimethoprim	6	7/11 (63.6 %)
Patel, 2012[52]	BMC Health Services Research	Convenience	South Africa	Amoxicillin	3	0/46 (0 %)
Akinkunmi, 2013[53]	Annals of Tropical Medicine and Parasitology	Convenience	Nigeria	Chloramphenicol, Gentamicin	2	0/2 (0 %)
Khan, 2013[54]	BMC Pharmacology and Toxicology	Random	Cambodia	Amoxicillin-Clavulanic acid	1	26/59 (44.1 %)
Khojah, 2013[55]	Pharmacology & Pharmacy	Lot Quality Assurance Sampling	Saudi Arabia	Amoxicillin	1	9/83 (10.8%)
Phanouvong, 2013a[56]	The Southeast Asian Journal of Tropical Medicine and Public Health	Random	Thailand	Tetracycline	1	1/242 (0.4 %)
Phanouvong, 2013b [57]**	The Southeast Asian Journal of Tropical Medicine and Public Health	Random	Cambodia	Tetracycline	1	unknown (5.0%)
Ramachandran, 2013[58]	Tropical Medicine and International Health	Convenience	India	Levofloxacin	1	9/67 (13.4 %)
Food and Drug Quality Control Center (Lao PDR), 2014[59]	Ministry of Health, Lao PDR	Random	Lao PDR	Amoxicillin, Cloxacillin	11	0/15 (0%)
Hetzel, 2014[60]	PLoS ONE	Random	Papua New Guinea	Amoxicillin, Doxycycline	2	1/59 (1.7 %)
Khuluza, 2014[61]	Malawi Medical Journal	Random	Malawi	Sulfamethoxazole-Trimethoprim	1	5/11 (45.4 %)
Khurelbat, 2014[62]	SpringerPlus	Random	Mongolia	Amoxicillin, Ampicillin, Doxycycline, Metronidazole, Sulfamethoxazole-Trimethoprim	10	55/699 (7.8 %)
Nagaraj, 2014[63]	Journal of Research in Pharmacy Practice	Convenience	India	Amoxicillin, Cefuroxime, Ofloxacin	3	0/10 (0.0 %)
Yoshida, 2014[64]	BMC Pharmacology and Toxicology	Random	Cambodia	Cefixime, Clarithromycin, Sulfamethoxazole-Trimethoprim	3	32/190 (16.8 %)

Bate, 2015[65]	Journal of Economics & Management Strategy	Convenience	Angola, Brazil, China, Democratic Republic of the Congo, Egypt, Ethiopia, Ghana, India, Kenya, Mozambique, Nigeria, Russia, Rwanda, Tanzania, Thailand, Turkey, Uganda, Zambia	Ciprofloxacin	1	142/1437 (9.9 %)
Boadu, 2015[66]	Medicinal Chemistry	Convenience	Ghana	Amoxicillin, Cloxacillin, Flucloxacillin	3	23/54 (42.6 %)
Fadeyi, 2015[67]	The American Journal of Tropical Medicine and Hygiene	Convenience	Ghana, Nigeria, United Kingdom	Amoxicillin, Sulfamethoxazole-Trimethoprim	6	15/35 (42.8 %)
Tshilumba, 2015[68]	Pan African Medical Journal	Convenience	Democratic Republic of the Congo	Amoxicillin, Ampicillin, Ciprofloxacin, Metronidazole	4	14/47 (29.8 %)
Wang, 2015[69]	Journal of Clinical Pharmacy and Therapeutics	Convenience	China, Ethiopia, Lao People's Democratic Republic, Mexico, Nigeria, South Africa, Thailand, United States	Sulfamethoxazole-Trimethoprim	10	2/42 (4.8 %)
World Health Organization, 2015[70]	The World Health Organization	Convenience	Burkina Faso, Kenya, Madagascar, Nepal, Nigeria, Tajikistan, Tanzania, Uganda, Viet Nam, Zimbabwe	Amoxicillin, Ampicillin, Ceftriaxone, Gentamicin, Procaine benzylpenicillin (penicillin G)	49	23/106 (21.7 %)

Kaale, 2016[71]	PLoS ONE	Random	Tanzania	Amoxicillin, Sulfamethoxazole-Trimethoprim	2	0/124 (0 %)
Khan, 2016[72]	International Journal of Pharmacy and Pharmaceutical Sciences	Convenience	India	Amoxicillin	1	13/46 (28.3 %)
Nga, 2016[73]	International Journal of Innovation and Applied Studies	Random	Cameroon	Sulfamethoxazole-Trimethoprim	3	27/37 (73 %)
Osei-Safo, 2016[74]	International Journal of Pharmaceutical Sciences and Research	Convenience	Ghana, Nigeria	Azithromycin, Clindamycin, Erythromycin	6	36/45 (80.0 %)
Tshilumba, 2016[75]	International Journal of Pharmacy and Pharmaceutical Sciences	Random	Democratic Republic of the Congo	Metronidazole	1	4/15 (26.7 %)
Wafula, 2016[76]	Drugs - Real World Outcomes	Convenience	Kenya	Amoxicillin, Amoxicillin-Clavulanic acid, Erythromycin, Metronidazole, Sulfamethoxazole-Trimethoprim	5	2/21 (9.5 %)
Alhedethe, 2017[77]	Archives in Chemical Research	Convenience	Sierra Leone	Amoxicillin	1	0/9 (0.0%)
Bate, 2017[78]	Safe Medicines Coalition	Convenience	The Internet	Ciprofloxacin	1	11/244 (4.5 %)
Islam, 2017[79]	Journal of International Health	Convenience	Cambodia	Ceftriaxone, Cefuroxime, Ciprofloxacin, Clarithromycin, Gentamicin, Levofloxacin, Nalidixic acid, Ofloxacin, Phenoxymethylpenicillin (penicillin V), Roxithromycin, Sulfamethoxazole-Trimethoprim	11	115/590 (19.5 %)
Islam, 2017[80]	Graduate School of Medical Science & Technology Kanazawa University	Convenience	Myanmar	Ceftriaxone, Cefuroxime, Gentamicin	3	37/167 (22.2 %)
Khuluza, 2017[81]	The American Journal of Tropical Medicine and Hygiene	Random	Malawi	Amoxicillin, Amoxicillin-Clavulanic acid, Cefuroxime, Chloramphenicol, Ciprofloxacin, Phenoxymethylpenicillin (penicillin V)	6	3/23 (13.0 %)
Nabirova, 2017[82]	The International Journal of Tuberculosis and Lung Disease	Random	Kazakhstan	Amoxicillin-Clavulanic acid, Levofloxacin, Moxifloxacin, Ofloxacin	4	1/8 (12.5 %)
Ononna, 2017[83]	Bangladesh Medical Research Council Bulletin	Random	Bangladesh	Amoxicillin, Azithromycin, Cefixime, Cephradine, Ciprofloxacin, Metronidazole	6	36/39 (92.3 %)
Petersen, 2017[84]	PLoS ONE	Convenience	Democratic Republic of the Congo	Amoxicillin, Amoxicillin-Clavulanic acid, Ampicillin, Ampicillin-Cloxacillin, Azithromycin, Cefalexin, Cefixime, Ceftriaxone, Cefuroxime, Chloramphenicol, Ciprofloxacin, Clarithromycin, Cloxacillin, Doxycycline, Erythromycin, Levofloxacin, Metronidazole, Moxifloxacin, Ofloxacin, Phenoxymethylpenicillin (penicillin V), Sulfamethoxazole, Sulfamethoxazole-Trimethoprim, Tetracycline	23	5/426 (1.2 %)

Bate, 2018[85]	The B.E. Journal of Economic Analysis & Policy	Convenience	Argentina, Bolivia, Brazil, Ecuador, Guatemala, Honduras, Paraguay, Peru, Uruguay, Venezuela	Ciprofloxacin	10	48/687 (7.0 %)
Chikowe, 2018[86]	The American Journal of Tropical Medicine and Hygiene	Convenience	Malawi	Amoxicillin	1	0/42 (0.0 %)
Ernest, 2018[87]	International Journal of Recent Innovations in Academic Research	Convenience	Cameroon	Metronidazole	3	2/10 (20.0%)
Frimpong, 2018[88]	Journal of Tropical Medicine	Random	Ghana	Amoxicillin, Cefuroxime, Ciprofloxacin, Flucloxacillin, Metronidazole, Sulfamethoxazole-Trimethoprim	6	21/29 (72.4 %)
Joda, 2018[89]	lfe Journal of Science	Random	Nigeria	Ciprofloxacin	1	4/16 (25.0 %)
Lehmann, 2018a[90]	Journal of Pharmaceutical Sciences	Random	South Africa	Amoxicillin, Amoxicillin-Clavulanic acid	2	25/138 (18.1 %)
Lehmann, 2018b[91]	Journal of Pharmacy and Pharmacology	Convenience	Germany, South Africa	Amoxicillin-Clavulanic acid	2	0/2 (0.0 %)
Nga, 2018[92]	Health Sciences and Diseases	Random	Cameroon	Sulfamethoxazole-trimethoprim	2	21/81 (25.9%)
Schafermann, 2018[93]	PLoS ONE	Convenience	Togo	Amoxicillin, Amoxicillin-Clavulanic acid, Ciprofloxacin, Doxycycline, Metronidazole, Phenoxymethylpenicillin (penicillin V), Sulfamethoxazole-Trimethoprim	25	6/64 (9.4 %)
Schiavetti, 2018[94]	The American Journal of Tropical Medicine and Hygiene	Random	Democratic Republic of the Congo	Amoxicillin	1	9/80 (11.2 %)
Tshilombo, 2018[95]	American Journal of Analytical Chemistry	Convenience	Democratic Republic of the Congo	Amoxicillin, Amoxicillin-Clavulanic acid	2	55/200 (27.5%)
Lawal, 2019[96]	Asian Journal of Pharmaceutical Research and Development	Convenience	Nigeria	Ampicillin-Cloxacillin, Amoxicillin, Amoxicillin-Clavulanic acid, Ciprofloxacin, Metronidazole, Sulfamethoxazole-Trimethoprim	6	43/112 (38.4%)
Myers, 2019[97]	Analytical Methods	Convenience	Kenya	Amoxicillin, Amoxicillin-Clavulanic acid, Ampicillin	3	46/189 (24.3 %)

Scrimgeour, 2019[98]	Journal of Pharmacy Practice and Research	Convenience	Papua New Guinea, Solomon Islands, Vanuatu	Amoxicillin, Ampicillin, Benzylpenicillin (penicillin G), Ceftriaxone, Cloxacillin, Doxycycline, Erythromycin, Flucloxacillin, Metronidazole, Phenoxymethylpenicillin (penicillin V), Sulfamethoxazole-Trimethoprim	11	6/33 (18.2 %)
Tabernero, 2019[99]	Journal of Antimicrobial Chemotherapy	Random	Lao People's Democratic Republic	Amoxicillin, Ampicillin, Ceftriaxone, Ciprofloxacin, Doxycycline, Ofloxacin, Sulfamethoxazole-Trimethoprim, Tetracycline	8	129/905 (14.3%)
Bekoe, 2020[100]	Tropical Medicine and International Health	Convenience	Ghana	Ampicillin, Amoxicillin, Amoxicillin-Clavulanic acid, Benzylpenicillin, Cefuroxime, Ceftriaxone, Ciprofloxacin, Erythromycin, Gentamicin, Metronidazole, Phenoxymethylpenicillin, Sulfamethoxazole-Trimethoprim, Tetracycline	13	231/342 (67.5%)
Hand, 2020[101]	Pharmacology Research and Perspectives	Unknown	Unknown	Benzathine Benzylpenicillin	1	0/35 (0.0%)
Husaini, 2020[102]	PLoS ONE	Random	Belize	Amoxicillin, Ciprofloxacin, Sulfamethoxazole-Trimethoprim	3	12/17 (70.6%)
Jean-Baptiste, 2020[103]	MDPI	Random	Haiti	Amoxicillin, Amoxicillin-Clavulanic acid, Azithromycin, Ciprofloxacin, Clarithromycin, Cloxacillin, Erythromycin, Metronidazole, Sulfamethoxazole-Trimethoprim, Tetracycline	10	45/180 (25.0%)
Khurelbat, 2020[104]	BMC Public Health	Random	Mongolia	Amoxicillin, Ciprofloxacin, Metronidazole	3	47/354 (13.3%)
Koech, 2020[105]	Hindawi BioMed Research International	Convenience	Kenya	Amoxicillin, Amoxicillin-Clavulanic acid	2	4/53 (7.6%)
Sakuda, 2020[106]	Pharmacy (MDPI)	Unknown	Myanmar	Ciprofloxacin, Levofloxacin	2	20/86 (23.3%)
Schafermann, 2020[107]	The Journal of Tropical Medicine and Hygiene	Random	Cameroon, Democratic Republic of the Congo	Amoxicillin, Amoxicillin-Clavulanic acid, Ciprofloxacin, Doxycycline, Metronidazole, Phenoxymethylpenicillin, Sulfamethoxazole-Trimethoprim	14	45/348 (12.9%)
*** Combination of convenience and randomized**						
**** Number of samples unknown**						

References

1 Iwuagwu MA, Onyeonwu N. In vitro assessment of ampicillin capsules marketed in Nigeria. *Int J Pharm Pract* 1992;**1**:167–71.

2 Muritu JW, Kibwage IO, Maitai CK, *et al.* Evaluation of tetracycline raw materials and finished products found on the Kenyan market. *J Pharm Biomed Anal* 1994;**12**:1483–8. doi:10.1016/0731-7085(94)00105-7

3 Okeke IN, Lamikanra A. Quality and bioavailability of tetracycline capsules in a Nigerian semi-urban community. *Int J Antimicrob Agents* 1995;**5**:245–50. doi:10.1016/0924-8579(94)00064-2

4 Taylor RB, Shakoor O, Behrens RH. Drug quality, a contributor to drug resistance? *Lancet* 1995;**346**:122.

5 Reseau Medicament et Developpement. La qualite des medicaments sur le marche pharmaceutique africain: etude analytique dans trois pays - Cameroun, Madagascar, Tchad. Geneva: 1995.

6 Nazerali H, Muchemwa T, Hogerzeil H. Stability of essential drugs in tropical climates (Zimbabwe). Geneva: 1996. http://apps.who.int/medicinedocs/pdf/s2206e/s2206e.pdf

7 Gimenez F, Bruneton C, Narong Rith DY. Etude de la qualite des medicaments vendus et dispenses au Cambodge. *Med Mal Infect* 1997;**27**:541–4.

8 Shakoor O, Taylor RB, Behrens RH. Assessment of the incidence of substandard drugs in developing countries. *Trop Med Int Heal* 1997;**2**:839–45. doi:10.1046/j.1365-3156.1997.d01-403.x

9 Kibwage IO, Ondari CO, Mureithi IG, *et al.* Analysis of Co-trimoxazole products on the Kenyan market. *East Cent African J Pharm Sci* 1998;**1**:34–8.

10 Nazerali H, Hogerzeil H V. The quality and stability of essential drugs in rural Zimbabwe: controlled longitudinal study. *BMJ* 1998;**317**:512–3. doi:10.1136/bmj.317.7157.512

11 Wondemagegnehu E. Counterfeit and Substandard Drugs in Myanmar and Viet Nam. Geneva: 1999. doi:10.1016/j.scispo.2006.06.006

12 Kamau FN, Thoithi GN, Kibwage IO. Quality of Ampicillin Preparations on the Kenyan Market. *East Cent African J Pharm Sci* 2001;**4**:25–9.

13 Taylor RB, Shakoor O, Behrens RH, *et al.* Pharmacopoeial quality of drugs supplied by Nigerian pharmacies. *Lancet* 2001;**357**:1933–6.

14 Kolawole JA, Olorunfemi PO, Okeniyi SO, *et al.* Quality and availability of ampicillin products (capsules and suspensions) in Nigeria. *Niger J Pharm* 2002;**33**:27–41.

15 Prazuck T, Falconi I, Morineau G, *et al.* Quality control of antibiotics before the implementation of an STD program in Northern Myanmar. *Sex Transm Dis* 2002;**29**:624–7. doi:10.1097/00007435-200211000-00002

16 Sow PS, Gueye TSN, Sy E, *et al.* Drugs in the parallel market for the treatment of urethral discharge in Dakar: epidemiologic investigation and physicochemical tests. *Int J Infect Dis* 2002;**6**:108–12. doi:10.1016/s1201-9712(02)90070-6

17 Ahmed F, Das AK, Karmakar UK, *et al.* Quality of marketed metronidazole preparations in Bangladesh - An analytical overview. *J Biol Sci* 2003;**3**:940–50.

18 Kamau FN, Thoithi G., Ngugi JK, *et al.* Quality of amoxycillin preparations on the Kenyan market. *East Cent African J Pharm Sci* 2003;**6**:57–60.

19 Risha PG. *Quality of essential drugs on the Tanzanian market: influence of tropical climate on in vitro dissolution and bioavailability*. 2003.

20 Basco LK. Molecular epidemiology of malaria in Cameroon. XIX. Quality of antimalarial drugs used for self-medication. *Am J Trop Med Hyg* 2004;**70**:245–50.

21 Kayumba PC, Risha PG, Shewiyo D, *et al.* The quality of essential antimicrobial and antimalarial drugs marketed in Rwanda and Tanzania: influence of tropical storage conditions on in vitro dissolution. *J Clin Pharm Ther* 2004;**29**:331–8. doi:10.1111/j.1365-2710.2004.00568.x

22 Syhakhang L, Lundborg CS, Lindgren B, *et al.* The quality of drugs in private pharmacies in Lao PDR: a repeat study in 1997 and 1999. *Pharm World Sci* 2004;**26**:333–8. doi:10.1007/s11096-004-0558-3

23 Legris C. *La détection des médicaments contrefaits par investigation de leur authenticité: Étude pilote sur le marché pharmaceutique illicite de Côte d'Ivoire*. 2005.

24 Phanouvong S, Reiss S, Smine A. Why be concerned about the quality of antimalarial and ARV drugs? Maryland: : United States Pharmacopeia 2005.

25 Weir RE, Zaidi FH, Charteris DG, *et al.* Variability in the content of Indian generic ciprofloxacin eye drops. *Br J Ophthalmol* 2005;**89**:1094–6. doi:10.1136/bjo.2004.059519

26 Lon CT, Tsuyuoka R, Phanouvong S, *et al.* Counterfeit and substandard antimalarial drugs in Cambodia. *Trans R Soc Trop Med Hyg* 2006;**100**:1019–24. doi:10.1016/j.trstmh.2006.01.003

27 Obodozie OO, Mustapha KB, Ebeshi BU, *et al.* A comparative study on the prevalence of substandard ampicillin/cloxacillin preparations in the Nigerian market: Mid 1990's and present. *J Phytomedicine Ther* 2006;**11**:1–8. doi:10.4314/jopat.v11i1.48619

28 Vijaykadga S, Cholpol S, Sitthimongkol S, *et al.* Strengthening of national capacity in implementation of antimalarial drug quality assurance in Thailand. *Southeast Asian J Trop Med Public Health* 2006;**37 Suppl 3**:5–10.

29 Okoro IA, Ejike EN. Quality control assay of ampicillin brands of capsules in Onitsha market, Southeastern Nigeria. *Res J Pharmacol* 2007;**1**:9–11.

30 Sheth PD, Siva Prasada Reddy M V, Regal B, *et al.* Extent of Spurious (Counterfeit) Medicines in India. New Delhi: 2007.

31 Camara I. *Étude de la qualité des médicaments génériques DCI achetés par la Pharmacie Populaire du Mali dans le cadre des appels d'offres de 2002 à 2005*. 2008.

32 Kyriacos S, Mroueh M, Chahine RP, *et al.* Quality of amoxicillin formulations in some Arab countries. *J Clin Pharm Ther* 2008;**33**:375–9. doi:10.1111/j.1365-2710.2008.00926.x

33 Meos A, Paap M, Matto V, *et al.* Comparative evaluation of quality of doxycycline formulations registered in Estonia to those registered in the Russian Federation. *Drug Dev Res* 2008;**69**:58–68. doi:10.1002/ddr.20228

34 Pouillot R, Bilong C, Boisier P, *et al.* Le circuit informel des médicaments à Yaoundé et à Niamey : étude de la population des vendeurs et de la qualité des médicaments distribués. *Bull la Soc Pathol Exot* 2008;**101**:113–8.

35 Bate R, Tren R, Mooney L, *et al.* Pilot study of essential drug quality in two major cities in India. *PLoS One* 2009;**4**:e6003. doi:10.1371/journal.pone.0006003

36 Central Drugs Standard Control Organization. Report on countrywide survey for spurious drugs. New Delhi: 2009.

37 Diop A, Sarr SO, Diop YM, *et al.* Contrôle de la qualité de quelques molécules antibiotiques utilisées au Sénégal. *Med Trop* 2009;**69**:251–4.

38 Mak S. *Evaluation de la qualite de l'amoxicilline au Cambodge*. 2009.

39 Obaid A. Quality of ceftriaxone in Pakistan: reality and resonance. *Pak J Pharm Sci* 2009;**22**:220–9.

40 Zaheer M, Rahman S, Mahmood S, *et al.* In vitro analysis and data comparison of market brands of ciprofloxacin, ofloxacin and levofloxacin. *Pak J Sci Ind Res* 2009;**52**:186–90.

41 Hadi U, van den Broek P, Kolopaking EP, *et al.* Cross-sectional study of availability and pharmaceutical quality of antibiotics requested with or without prescription (Over The Counter) in Surabaya, Indonesia. *BMC Infect Dis* 2010;**10**:1–10. doi:10.1186/1471-2334-10-203

42 Khan MH, Okumura J, Sovannarith T, *et al.* Prevalence of counterfeit anthelminthic medicines: A cross-sectional survey in Cambodia. *Trop Med Int Heal* 2010;**15**:639–44. doi:10.1111/j.1365-3156.2010.02494.x

43 Bate R, Zhe Jin G, Mathur A. Does price reveal poor-quality drugs? Evidence from 17 countries. Massachusetts: : National Bureau of Economic Research 2011. doi:10.1016/j.jhealeco.2011.08.006

44 Haider SS, Nasrin N, Apu AS, *et al.* Accelerated stability and antimicrobial sensitivity studies of amoxicillin dry suspensions marketed in Bangladesh. *J Appl Pharm Sci* 2011;**01**:51–5.

45 Idries A. Incidence of substandard medicines in Khartoum, Sudan in 2009-2010: Results of medicines quality monitoring survey. Khartoum: 2011.

46 Kamuhabwa AA. R, Saifuddin MH, Maganda B, *et al.* Quality of co-trimoxazole tablets used for management of opportunistic infections in HIV/AIDS Patients. *Int J Pharm Res* 2011;**3**:79–84.

47 Nair A, Strauch S, Lauwo J, *et al.* Are counterfeit or substandard anti-infective products the cause of treatment failure in Papua New Guinea? *J Pharm Sci* 2011;**100**:5059–68. doi:10.1002/jps.22691

48 Seear M, Gandhi D, Carr R, *et al.* The need for better data about counterfeit drugs in developing countries: a proposed standard research methodology tested in Chennai, India. *J Clin Pharm Ther* 2011;**36**:488–95. doi:10.1111/j.1365-2710.2010.01198.x

49 World Health Organization. Survey of the quality of anti-tuberculosis medicines circulating in selected newly independent states of the former Soviet Union. Geneva: 2011. https://digicollections.net/medicinedocs/#d/s19053en

50 Yusuf I, Lee D, Fatehzada Z, *et al.* Afghanistan Medicines Sampling and Testing – A Quantitative Survey. Virginia: 2011.

51 Karlage KL, Franklin SJ, Mufich WC, *et al.* Comparative evaluation of pharmaceutical products obtained in Mexico: Augmenting existing scientific data. *Drug Dev Ind Pharm* 2012;**38**:808–14. doi:10.3109/03639045.2011.628678

52 Patel A, Gauld R, Norris P, *et al.* Quality of generic medicines in South Africa: perceptions versus reality - a qualitative study. *BMC Health Serv Res* 2012;**12**:1–8. doi:10.1186/1472-6963-12-297

53 Akinkunmi EO. An evaluation of the pharmaceutical quality and antimicrobial effectiveness of some frequently used eye drop products available for sale in Nigeria. *Ann Trop Med Public Heal* 2013;**6**:221–6. doi:10.4103/1755-6783.116509

54 Khan MH, Hatanaka K, Sovannarith T, *et al.* Effects of packaging and storage conditions on the quality of amoxicillin-clavulanic acid - an analysis of Cambodian samples. *BMC Pharmacol Toxicol* 2013;**14**:1–7.

55 Khojah HMJ, Pallos H, Yoshida N, *et al.* The quality of medicines in community pharmacies in Riyadh, Saudi Arabia: A Lot Quality Assurance Sampling (LQAS)-based survey. *Pharmacol Pharm* 2013;**04**:511–9. doi:10.4236/pp.2013.47074

56 Phanouvong S, Dijiba Y, Vijaykadga S, *et al.* The quality of antimalarial medicines in Eastern Thailand : a case study along the Thai-Cambodian border. *Southeast Asian J Trop Med Public Health* 2013;**44**:363–73.

57 Phanouvong S, Raymond C, Krech L, *et al.* The quality of antimalarial medicines in Western Cambodia : a case study along the Thai-Cambodian border. *Southeast Asian J Trop Med Public Health* 2013;**44**:349–62.

58 Ramachandran G, Chandrasekaran V, Hemanth Kumar AK, *et al.* Estimation of content of anti-TB drugs supplied at centres of the Revised National TB Control Programme in Tamil Nadu, India. *Trop Med Int Heal* 2013;**18**:1141–4. doi:10.1111/tmi.12158

59 Food and Drug Quality Control Center. Comparative study of the quality , availability, and source of antimalarial medicines in Cambodia, Laos, Thailand, and Vietnam in PQM-MQM covered and non-covered areas in Mekong Sub-Region. Vientiane: 2014.

60 Hetzel MW, Page-Sharp M, Bala N, *et al.* Quality of Antimalarial Drugs and Antibiotics in Papua New Guinea: A Survey of the Health Facility Supply Chain. *PLoS One* 2014;**9**:e96810. doi:10.1371/journal.pone.0096810

61 Khuluza F. In-vitro evaluation of the quality of paracetamol and co-trimoxazole tablets used in Malawi based on pharmacopoeial standards. *Malawi Med J* 2014;**26**:38–41.

62 Khurelbat D, Dorj G, Bayarsaikhan E, *et al.* Prevalence estimates of substandard drugs in Mongolia using a random sample survey. *Springerplus* 2014;**3**:1–10. doi:10.1186/2193-1801-3-709

63 Nagaraj A, Tambi S, Shravani G, *et al.* Counterfeit medicines sale on online pharmacies in India. *J Res Pharm Pract* 2014;**3**:145–6. doi:10.4103/2279-042X.145397

64 Yoshida N, Khan MH, Tabata H, *et al.* A cross-sectional investigation of the quality of selected medicines in Cambodia in 2010. *BMC Pharmacol Toxicol* 2014;**15**:1–8. doi:10.1186/2050-6511-15-13

65 Bate R, Jin GZ, Mathur A. Falsified or Substandard? Assessing Price and Non-price Signals of Drug Quality. *J Econ Manag Strateg* 2015;**24**:687–711. doi:10.1111/jems.12114

66 Boadu RF, Agyare C, Adarkwa-Yiadom M, *et al.* In vitro activity and evaluation of quality of some selected penicillins on the Ghanaian market using developed HPLC methods. *Med Chem (Los Angeles)* 2015;**5**:1–14. doi:10.4172/2161-0444.1000235

67 Fadeyi I, Lalani M, Mailk N, *et al.* Quality of the antibiotics—amoxicillin and co-Trimoxazole from Ghana, Nigeria, and the United Kingdom. *Am J Trop Med Hyg* 2015;**92**:87–94. doi:10.4269/ajtmh.14-0539

68 Tshilumba PM, Amuri SB, Kaghowa ER, *et al.* Enquête sur la contrefaçon de quelques anti-infectieux administrés per os commercialisés dans la ville de Lubumbashi. *Pan Afr Med J* 2015;**22**. doi:10.11604/pamj.2015.22.318.7302

69 Wang T, Hoag SW, Eng ML, *et al.* Quality of antiretroviral and opportunistic infection medications dispensed from developing countries and internet pharmacies. *J Clin Pharm Ther* 2015;**40**:68–75. doi:10.1111/jcpt.12226

70 World Health Organization. Medicines for women and children: quality and availability of selected life-saving reproductive health medicines in developing countries. *WHO Drug Inf* 2015;**29**:324–33.

71 Kaale E, Manyanga V, Chambuso M, *et al.* The quality of selected essential medicines sold in accredited drug dispensing outlets and pharmacies in Tanzania. *PLoS One* 2016;**11**:e0165785. doi:10.1371/journal.pone.0165785

72 Khan AN, Khar RK, Udayabanu M. Quality and affordability of amoxicillin generic products: A patient concern. *Int J Pharm Pharm Sci* 2016;**8**:386–90.

73 Nga EN, Tabi Ombga YLT, Kidik Pouka MC, *et al.* Evaluation de la qualité du cotrimoxazole 480mg comprimé générique vendu dans la ville de Douala (Cameroun). *Int J Innov Appl Sci* 2016;**15**:926–35.

74 Osei-Safo D, Egbo HA, Nettey H, *et al.* Evaluation of the quality of some antibiotics distributed in Accra and Lagos. *Int J Pharm Sci Res* 2016;**7**:1991–2000. doi:10.13040/IJPSR.0975-8232.7(5).1991-00

75 Tshilumba PM, Duez P, Ndoumba JBK. Preliminary survey of counterfeiting of albendazole and metronidazole marketed in Lubumbashi. *Int J Pharm Pharm Sci*

2016;**8**:282–7.https://innovareacademics.in/journals/index.php/ijpps

76 Wafula F, Dolinger A, Daniels B, *et al.* Examining the quality of medicines at Kenyan healthcare facilities: A validation of an alternative post-market surveillance model that uses standardized patients. *Drugs - Real World Outcomes* 2016;**4**:53–63. doi:10.1007/s40801-016-0100-7

77 Alhedethe A, Alhudaithy K, Zloh M. An evaluation of prevalence of low quality of medicines in Saudi Arabia and factors associated an analytical comparative study. *Arch Chem Res* 2017;**02**:1–18. doi:10.21767/2572-4657.100014

78 Bate R. Web pharmacies and ciprofloxacin: a field study. Safe Med. Coalit. 2017;:1–2.http://safemedicinescoalition.org/ (accessed 17 Mar 2021).

79 Islam R, Yoshida N, Tsuboi H, *et al.* Four-year survey of the quality of antimicrobial medicines in Cambodia. *J Int Heal* 2017;**32**:233–42. doi:10.11197/jaih.32.233

80 Islam R. *Investigations of the quality medicines distributed in Myanmar and Cambodia, through different surveys*. 2017.

81 Khuluza F, Kigera S, Heide L. Low prevalence of substandard and falsified antimalarial and antibiotic medicines in public and faith-based health facilities of Southern Malawi. *Am J Trop Med Hyg* 2017;**96**:1124–35. doi:10.4269/ajtmh.16-1008

82 Nabirova D, Schmid G, Yusupova R, *et al.* Assessment of the quality of anti-tuberculosis medicines in Almaty, Kazakhstan, 2014. *Int J Tuberc Lung Dis* 2017;**21**:1161–8. doi:10.5588/ijtld.17.0074

83 Ononna HF, Al Hossain ASMM, Ganguly A, *et al.* Potency determination of essential drug samples manufactured by small and medium pharmaceutical industries in Bangladesh. *Bangladesh Med Res Counc Bull* 2017;**43**:87–93. doi:10.3329/bmrcb.v43i2.35195

84 Petersen A, Held N, Heide L. Surveillance for falsified and substandard medicines in Africa and Asia by local organizations using the low-cost GPHF Minilab. *PLoS One* 2017;**12**:e0184165. doi:10.1371/journal.pone.0184165

85 Bate R, Mathur A. Corruption and medicine quality in Latin America: a pilot study. *BE J Econ Anal Policy* 2018;**18**. doi:10.1515/bejeap-2017-0076

86 Chikowe I, Bliese SL, Lucas S, *et al.* Amoxicillin quality and selling practices in urban pharmacies and drug stores of Blantyre, Malawi. *Am J Trop Med Hyg* 2018;**99**:233–8. doi:10.4269/ajtmh.18-0003

87 Ernest D, Gislaine N, Michel TJ. Contrôle de qualité des imidazolés antiparasitaires distribués a Bafoussam: albendazole, mebendazole et metronidazole. *Int J Recent Innov Acad Res* 2108;**2**:79–90.

88 Frimpong G, Ofori-Kwakye K, Kuntworbe N, *et al.* Quality assessment of some essential children's medicines sold in licensed outlets in Ashanti region, Ghana. *J Trop Med* Published Online First: 2018. doi:10.1155/2018/1494957

89 Joda AE, Tayo F, Aina BA. Quality assessment of ciprofloxacin tablets obtained from community pharmacies in Lagos, Nigeria. *Ife J Sci* 2018;**20**:155–68. doi:10.4314/ijs.v20i1.16

90 Lehmann A, Katerere DR, Dressman J. Drug quality in South Africa: a field test. *J Pharm Sci* 2018;**107**:2720–30. doi:10.1016/j.xphs.2018.06.012

91 Lehmann A, Hofsäss M, Dressman J. Differences in drug quality between South Africa and Germany. *J Pharm Pharmacol* 2018;**70**:1301–14. doi:10.1111/jphp.12985

92 Nga EN, Tanga RT, Lobe VS, *et al.* Évaluation de la Stabilité du Cotrimoxazole 240 mg/5 ml Suspension Commercialisé dans les Circuits Formel et Informel de la Ville de Douala. *Heal Sci Dis* 2018;**19**:66–71.

93 Schäfermann S, Wemakor E, Hauk C, *et al.* Quality of medicines in southern Togo: Investigation of antibiotics and of medicines for non-communicable diseases from pharmacies and informal vendors. *PLoS One* 2018;**13**:e0207911. doi:10.1371/journal.pone.0207911

94 Schiavetti B, Wynendaele E, De Spiegeleer B, *et al.* The quality of medicines used in children and supplied by private pharmaceutical wholesalers in Kinshasa, Democratic Republic of Congo: A prospective survey. *Am J Trop Med Hyg* 2018;**98**:894–903. doi:10.4269/ajtmh.17-0732

95 Tshilombo NK, Hamuli PC, Mbinze JK, *et al.* Investigation of the quality of antibiotics-based amoxicillin for monitoring of some different medicine markets of Democratic Republic of Congo. *Am J Anal Chem* 2018;**9**:366–85. doi:10.4236/ajac.2018.98029

96 Lawal MG, Mukhtar MD, Magashi AM. Quality assessment of antibiotic oral drug formulations marketed in Katsina State, Nigeria. *Asian J Pharm Res Dev* 2019;**7**:6–10. doi:10.22270/ajprd.v7i6.615

97 Myers NM, Maina MW, Were PM, *et al.* Lab on paper: assay of beta-lactam pharmaceuticals by redox titration. *Anal Methods* 2019;**11**:4741–50. doi:10.1039/C9AY01547G

98 Scrimgeour S, Nunan M, Sanburg ALC, *et al.* Pharmaceutical quality of antibiotics in Small Island Nations in the Western Pacific region: a pilot survey. *J Pharm Pract Res* 2019;**49**:426–32. doi:10.1002/jppr.1540

99 Tabernero P, Swamidoss I, Mayxay M, *et al.* A random survey of the prevalence of falsified and substandard antibiotics in the Lao PDR. *J Antimicrob Chemother* 2019;**74**:2417–25. doi:10.1093/jac/dkz164

100 Bekoe SO, Ahiabu M-A, Orman E, *et al.* Exposure of consumers to substandard antibiotics from selected authorised and unauthorised medicine sales outlets in Ghana. *Trop Med Int Heal* 2020;**25**:962–75. doi:10.1111/tmi.13442

101 Hand RM, Senarathna SMDKG, Page-Sharp M, *et al.* Quality of benzathine penicillin G: A multinational cross-sectional study. *Pharmacol Res Perspect* 2020;**8**:e00668. doi:10.1002/prp2.668

102 Husaini DC, Kishan UJV, Wu C-Y, *et al.* Field-based screening of selected oral antibiotics in Belize. *PLoS One* 2020;**15**:e0234814. doi:10.1371/journal.pone.0234814

103 Jean-Baptiste T, Carpenter JF, Dahl K, *et al.* Substandard quality of the antimicrobials sold in the street markets in Haiti. *Antibiotics* 2020;**9**:407. doi:10.3390/antibiotics9070407

104 Khurelbat D, Dorj G, Sunderland B, *et al.* A cross-sectional analysis of falsified, counterfeit and substandard medicines in a low-middle income country. *BMC Public Health* 2020;**20**:1–9.

105 Koech LC, Irungu BN, Ng'ang'a MM, *et al.* Quality and brands of amoxicillin formulations in Nairobi, Kenya. *Biomed Res Int* Published Online First: 2020. doi:10.1155/2020/7091278

106 Sakuda M, Yoshida N, Takaoka T, *et al.* Substandard and falsified medicines in Myanmar. *Pharmacy* 2020;**8**. doi:10.3390/pharmacy8010045

107 Schäfermann S, Hauk C, Wemakor E, *et al.* Substandard and falsified antibiotics and medicines against noncommunicable diseases in Western Cameroon and Northeastern Democratic Republic of Congo. *Am J Trop Med Hyg* 2020;**103**:894–908. doi:10.4269/ajtmh.20-0184

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 7. Failure frequency of antibiotics by country, region and AWaRe group in prevalence surveys included in the review*.

Country/Region	Income	AWARE group	AMC**[1]	Data points	Failed samples	Total samples	% FF
Africa				**267**	**1,090**	**3,836**	**28.4**
Burkina Faso	LIC	*ACCESS*	10.4	3	2	7	28.6
		WATCH	3.3	1	0	3	0.0
Cameroon	LMIC	*ACCESS*	Not available	24	136	436	31.2
		WATCH	Not available	1	2	25	8.0
Chad	LIC	*ACCESS*	Not available	7	3	19	15.8
		WATCH	Not available	n/a	n/a	n/a	n/a
Côte d'Ivoire	LMIC	*ACCESS*	8.8	4	33	65	50.8
		WATCH	1.7	n/a	n/a	n/a	n/a
Democratic Republic of the Congo	LIC	*ACCESS*	Not available	13	96	495	19.4
		WATCH	Not available	2	6	43	14.0
Ethiopia	LIC	*ACCESS*	Not available	2	0	2	0.0
		WATCH	Not available	n/a	n/a	n/a	n/a
Ghana	LMIC	*ACCESS*	Not available	19	202	332	60.8
		WATCH	Not available	8	88	119	74.0
Kenya	LMIC	*ACCESS*	Not available	16	83	430	19.3
		WATCH	Not available	2	1	6	16.7
Madagascar	LIC	*ACCESS*	Not available	10	14	59	23.7
		WATCH	Not available	1	0	3	0.0
Malawi	LIC	*ACCESS*	Not available	6	8	70	11.4
		WATCH	Not available	2	0	6	0.0
Mali	LIC	*ACCESS*	Not available	2	2	20	10.0
		WATCH	Not available	1	4	10	40.0
Niger	LIC	*ACCESS*	Not available	8	14	32	43.8
		WATCH	Not available	1	0	1	0.0

Nigeria	LMIC	*ACCESS*	Not available	37	252	544	46.3
		WATCH	Not available	6	46	88	52.3
Rwanda	LIC	*ACCESS*	Not available	3	1	8	12.5
		WATCH	Not available	n/a	n/a	n/a	n/a
Senegal	LMIC	*ACCESS*	Not available	7	31	69	44.9
		WATCH	Not available	2	6	12	50.0
Sierra Leone	LIC	*ACCESS*	Not available	1	0	9	0.0
		WATCH	Not available	n/a	n/a	n/a	n/a
South Africa	UMIC	*ACCESS*	Not available	7	25	186	13.4
		WATCH	Not available	n/a	n/a	n/a	n/a
Sudan	LIC	*ACCESS*	23.1	2	0	6	0.0
		WATCH	6.1	2	1	5	20.0
Tanzania	LMIC	*ACCESS*	15.3	12	10	182	5.5
		WATCH	6.1	2	0	11	0.0
Togo	LIC	*ACCESS*	Not available	21	3	51	5.9
		WATCH	Not available	4	3	13	23.1
Uganda	LIC	*ACCESS*	Not available	6	2	12	16.7
		WATCH	Not available	1	0	3	0.0
Zimbabwe	LMIC	*ACCESS*	Not available	19	16	450	3.6
		WATCH		2	0	4	0.0
Americas				**31**	**112**	**898**	**12.5**
Argentina	UMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	1	2	75	2.7
Belize	LMIC	*ACCESS*	Not available	2	7	12	58.3
		WATCH	Not available	1	5	5	100.0
Bolivia	LMIC	*ACCESS*	15.1	n/a	n/a	n/a	n/a
		WATCH	4.4	1	3	34	8.8
Brazil	UMIC	*ACCESS*	14.7	n/a	n/a	n/a	n/a
		WATCH	6.7	1	6	157	3.8
Ecuador	UMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	1	2	43	4.7
Guatemala	UMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a

		WATCH	Not available	1	4	52	7.7
Haiti	LMIC	*ACCESS*	Not available	6	28	153	18.3
		WATCH	Not available	4	17	27	63.0
Honduras	LMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	1	3	45	6.7
Mexico	UMIC	*ACCESS*	Not available	4	6	9	66.7
		WATCH	Not available	1	0	2	0.0
Paraguay	UMIC	*ACCESS*	8.7	n/a	n/a	n/a	n/a
		WATCH	10.3	1	14	111	12.6
Peru	UMIC	*ACCESS*	7.2	n/a	n/a	n/a	n/a
		WATCH	3.0	1	4	56	7.1
United States	HIC	*ACCESS*	Not available	3	1	3	33.3
		WATCH	Not available	n/a	n/a	n/a	n/a
Uruguay	HIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	1	4	78	5.1
Venezuela	N/A	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	1	6	36	16.7
Asia				**185**	**932**	**6,202**	**15.0**
Afghanistan	LIC	*ACCESS*	Not available	2	2	74	2.7
		WATCH	Not available	2	3	51	5.9
Armenia	UMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	2	1	24	4.2
Azerbaijan	UMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	2	0	10	0.0
Bangladesh	LMIC	*ACCESS*	Not available	5	31	69	44.9
		WATCH	Not available	3	17	20	85.0
Cambodia	LMIC	*ACCESS*	Not available	19	125	697	17.9
		WATCH	Not available	9	106	502	21.1
		Non-AWARE	Not available	1	6	9	66.7
China	UMIC	*ACCESS*	Not available	1	0	3	0.0
		WATCH	Not available	n/a	n/a	n/a	n/a
India	LMIC	*ACCESS*	Not available	11	17	380	4.5

		WATCH	Not available	16	69	675	10.2
Indonesia	LMIC	*ACCESS*	Not available	4	19	85	22.4
		WATCH	Not available	1	0	19	0.0
Kazakhstan	UMIC	*ACCESS*	Not available	1	0	3	0.0
		WATCH	Not available	6	4	32	12.5
Lao People's Democratic Republic	LMIC	*ACCESS*	Not available	22	289	1242	23.3
		WATCH	Not available	3	8	92	8.7
Mongolia	LMIC	*ACCESS*	46.2	12	85	935	9.1
		WATCH	18.1	1	17	118	14.4
Myanmar	LMIC	*ACCESS*	Not available	11	28	193	14.5
		WATCH	Not available	7	57	202	28.2
Nepal	LMIC	*ACCESS*	Not available	5	2	8	25.0
		WATCH	Not available	1	0	3	0.0
Pakistan	LMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	4	17	108	15.7
Saudi Arabia	HIC	*ACCESS*	Not available	1	9	83	10.8
		WATCH	Not available	n/a	n/a	n/a	n/a
Tajikistan	LMIC	*ACCESS*	Not available	3	2	9	22.2
		WATCH	Not available	1	0	3	0.0
Thailand	UMIC	*ACCESS*	Not available	8	3	331	0.9
		WATCH	Not available	n/a	n/a	n/a	n/a
Uzbekistan	LMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	2	0	15	0.0
Viet Nam	LMIC	*ACCESS*	Not available	10	12	177	6.8
		WATCH	Not available	4	0	6	0.0
Unknown***		*ACCESS*	Not available	5	12	32	43.8
		WATCH	Not available	n/a	n/a	n/a	n/a
Europe				**9**	**5**	**65**	**7.7**
Belarus	UMIC	*ACCESS*	9.8	n/a	n/a	n/a	n/a
		WATCH	6.3	2	3	24	12.5
Estonia	HIC	*ACCESS*	6.7	1	0	4	0.0
		WATCH	3.6	n/a	n/a	n/a	n/a

Germany	HIC	*ACCESS*	5.7	1	0	1	0.0
		WATCH	3.0	n/a	n/a	n/a	n/a
Russian Federation	UMIC	*ACCESS*	7.1	1	2	4	50.0
		WATCH	6.5	n/a	n/a	n/a	n/a
Ukraine	LMIC	*ACCESS*	Not available	n/a	n/a	n/a	n/a
		WATCH	Not available	2	0	23	0.0
United Kingdom	HIC	*ACCESS*	13.2	2	0	9	0.0
		WATCH	4.2	n/a	n/a	n/a	n/a
Oceania				14	15	100	15.0
Papua New Guinea	LMIC	*ACCESS*	Not available	3	9	67	13.4
		WATCH	Not available	n/a	n/a	n/a	n/a
Unknown****		*ACCESS*	Not available	10	5	30	16.7
		WATCH	Not available	1	0	3	0.0
Unknown***		*ACCESS*		12	6	257	2.3
		WATCH		15	189	2188	8.6
		Non-AWARE		1	0	1	0.0

HIC: High income, LIC: Low income, UMIC: Upper middle income, LMIC: Lower middle

* Due to the limited number of samples tested for quality in the studies included in this review, the figures should not be interpreted as representative of the prevalence of specific SF antibiotics (please refer to the discussion section of the article for more details).

** Median Antimicrobial Consumption (AMC) between 2016-2018, in Defined Daily Doses per 1,000 inhabitants per day (DID).

*** Multicountry study (Egypt, Jordan, Lebanon, Saudi Arabia) with no breakdown of the results by country

**** Multicountry study (Papua New Guinea, Solomon Islands, Vanuatu) with no breakdown of the results by country

***** Aggregated data without further details of continent and/or countries

Source of AMD data = World Health Organization. WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation. 2018;:1–127.https://www.who.int/medicines/areas/rational_use/oms-amr-amc-report-2016-2018/en/ (accessed 8 Sep 2019).

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 8. Antibiotic quality failure frequency by WHO AWaRe groups.

WHO group/API	DID *[1]	Median FF (%)	IQR FF (%)	No. samples	No. SF	Median N° samples per data point	IQR N° Samples per data point	Data points	Countries
ACCESS	5.6-12.4	10	0.0-40.0	8,354	1,633	8	3-25	394	
Amikacin		0	N/A	17	0	17	N/A	1	India
Amoxicillin		3	0.0-8.3	2,208	355	25	5-52	91	Afghanistan, Bangladesh, Belize, Cambodia, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ghana, Haiti, India, Indonesia, Kenya, Lao People's Democratic Republic, Madagascar, Malawi, Mexico, Mongolia, Myanmar, Nepal, Niger, Nigeria, Papua New Guinea, Rwanda, Saudi Arabia, Senegal, Sierra Leone, South Africa, Sudan, Tajikistan, Tanzania, Thailand, Togo, Uganda, United Kingdom, United States, Unknown, Viet Nam, Zimbabwe
Amoxicillin-Clavulanate		21.3	5.8-38.6	437	130	13	5-42	21	Cambodia, Cameroon, Democratic Republic of the Congo, Germany, Ghana, Haiti, India, Kazakhstan, Kenya, Malawi, Nigeria, South Africa, Togo, Unknown

Ampicillin	5	2.0-9.0	1,010	211	19	9-45	44	Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ghana, Kenya, Lao People's Democratic Republic, Madagascar, Mexico, Mongolia, Myanmar, Nepal, Niger, Nigeria, Senegal, Tajikistan, Tanzania, Uganda, Unknown, Viet Nam, Zimbabwe
Ampicillin - Cloxacillin	6.5	1.3-19.3	110	62	12	8-32	8	India, Nigeria, Unknown
Cefadroxil	0	N/A	14	0	14	N/A	1	India
Cefalexin	0	N/A	21	0	10	N/A	2	India, Unknown
Cephadrine	100	N/A	6	6	6	N/A	1	Bangladesh
Chloramphenicol	1.5	0.0-5.8	132	32	13	4-24	11	Cambodia, Cameroon, Chad, Indonesia, Madagascar, Malawi, Myanmar, Niger, Nigeria, Unknown, Viet Nam
Clindamycin	83.3	N/A	6	5	6	N/A	2	Ghana, Nigeria
Cloxacillin	2.5	0.5-3.0	54	13	7	4-9	10	Ghana, Haiti, Lao People's Democratic Republic, Nigeria, Unknown
Doxycycline	1	0.0-8.5	347	73	12	9-35	18	Cameroon, Democratic Republic of the Congo, Estonia, Lao People's Democratic Republic, Mongolia, Myanmar, Nigeria, Papua New Guinea, Russian Federation, Togo, Unknown, Zimbabwe
Flucloxacillin	100	90.6-100.0	21	18	4	3-10	3	Ghana, Unknown

Gentamicin	1	0.0-3.0	226	27	22	10-35	21	Afghanistan, Burkina Faso, Cambodia, Ghana, India, Kenya, Madagascar, Mali, Myanmar, Nepal, Niger, Nigeria, Tajikistan, Tanzania, Uganda, Viet Nam, Zimbabwe
Metronidazole	3.5	0.3-7.8	838	166	21	10-42	38	Bangladesh, Cambodia, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ghana, Haiti, Kenya, Madagascar, Mongolia, Myanmar, Niger, Nigeria, Rwanda, Sudan, Tanzania, Togo, Unknown, Viet Nam
Oxacillin	0	N/A	2	0	2	N/A	1	Niger
Penicillin G (IV/IM)	0	0.0-3.0	209	17	6	5-28	13	Burkina Faso, Ghana, Madagascar, Myanmar, Nigeria, Tanzania, Uganda, Unknown, Zimbabwe
Penicillin V (PO)	0	0.0-1.0	230	43	8	3-41	12	Cambodia, Cameroon, Democratic Republic of the Congo, Ghana, Malawi, Senegal, Togo, Unknown, Zimbabwe
Penicillin-unspecified formulation	1	0.5-1.5	20	2	10	8-12	4	Cameroon, Chad, Madagascar, Senegal

Co-trimoxazole		5	2.0-12.0	1,255	329	20	6-44	62	Belize, Cambodia, Cameroon, Chad, China, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, Haiti, India, Indonesia, Kenya, Lao People's Democratic Republic, Madagascar, Malawi, Mexico, Mongolia, Myanmar, Niger, Nigeria, Rwanda, Senegal, South Africa, Tanzania, Thailand, Togo, United Kingdom, United States, Unknown
Tetracycline		1	0.0-6..0	1,191	144	22	11-101	30	Cambodia, Cameroon, Chad, Ghana, Haiti, Indonesia, Kenya, Lao People's Democratic Republic, Madagascar, Mali, Myanmar, Niger, Nigeria, Senegal, Thailand, Unknown, Viet Nam, Zimbabwe
WATCH	1.3-6.1	8.2	0.0-30.0	5,191	718	12	3-43	138	
Azithromycin		3.5	2.5-7.8	61	27	16	6-25	5	Bangladesh, Ghana, Haiti, Nigeria, Unknown
Cefixime		6	3.0-6.5	104	13	37	22-49	3	Bangladesh, Cambodia, Unknown
Cefotaxime		0	N/A	21	0	21	N/A	1	India
Ceftazidime		0	N/A	7	0	7	N/A	1	India

Ceftriaxone	2	0.0-6.5	309	49	26	3-42	24	Afghanistan, Burkina Faso, Cambodia, Ghana, Kenya, Lao People's Democratic Republic, Madagascar, Myanmar, Nepal, Nigeria, Pakistan, Sudan, Tajikistan, Tanzania, Uganda, Unknown, Viet Nam, Zimbabwe
Cefuroxime	2.5	0.0-13.5	188	71	11	6-44	8	Cambodia, Ghana, India, Malawi, Myanmar, Unknown
Ciprofloxacin	3	0.0-8.0	3,511	366	19	8-57	47	Afghanistan, Argentina, Bangladesh, Belize, Bolivia, Brazil, Cambodia, Cameroon, Democratic Republic of the Congo, Ecuador, Ghana, Guatemala, Haiti, Honduras, India, Indonesia, Lao People's Democratic Republic, Malawi, Mexico, Mongolia, Myanmar, Nigeria, Pakistan, Paraguay, Peru, Senegal, Sudan, Tanzania, Togo, Unknown, Uruguay, Venezuela
Clarithromycin	6	0.8-11.8	102	26	26	3-49	4	Cambodia, Haiti, Unknown
Erythromycin	3.5	0.8-9.8	345	66	12	4-23	14	Ghana, Haiti, India, Kenya, Mali, Myanmar, Nigeria, Senegal, Unknown
Kanamycin	0.5	0.3-0.8	70	1	35	19-51	7	Armenia, Azerbaijan, Belarus, Kazakhstan, Ukraine, Uzbekistan
Levofloxacin	5	0.3-12.8	185	42	26	6-56	6	Cambodia, India, Kazakhstan, Myanmar, Pakistan, Unknown
Moxifloxacin	0	0.0-0.0	5	0	3	2-3	2	Kazakhstan, Unknown

Norfloxacin		0	N/A	1	0	1	N/A	1	Niger
Ofloxacin		1	0.0-6.0	192	26	7	3-55	12	Armenia, Azerbaijan, Belarus, Cambodia, India, Kazakhstan, Lao People's Democratic Republic, Pakistan, Ukraine, Unknown, Uzbekistan
Roxithromycin		10.5	7.3-13.8	71	21	36	25-46	2	Cambodia, India
Streptomycin		52.7	N/A	19	10	19	N/A	1	Nigeria
RESERVE	Not available								
No data									
Antibiotics not in AWaRe	Not available	33.3	16.7-50.0	10	6	5	3-7	2	
Nalidixic acid		66.7	N/A	9	6	9	N/A	1	Cambodia
Sulfamethoxazole (without trimethoprim)		0	N/A	1	0	1	N/A	1	Unknown (Africa and Asia)

*Median Antimicrobial Consumption (AMC) in 2015 in LMIC and HIC, respectively, as Defined Daily Doses per 1,000 inhabitants per day (DID).

1 Klein EY, Milkowska-Shibata M, Tseng KK, *et al.* Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: an analysis of pharmaceutical sales data. *Lancet Infect Dis* 2021;**21**:107–15. doi:10.1016/S1473-3099(20)30332-7

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 9. Failure frequency per type of quality test by API in prevalence surveys of antibiotic quality*.

Colour gradient: grey (no data), orange (<20% FF), light red (21-40% FF), red (41-70% FF), brown (>70% FF).

	Type of defect % (n/N)							
API name	**API Content**	**API ID & Semi-quantitation**	**Dissolution**	**Impurities/ contaminant/related substance**	**Uniformity of units**	**Packaging/ label/physical appearance inspection**	**Other physical analysis*** **	**Other chemical analysis**** **
Total	16.5 (1,701/10,307)	7.5 (210/2,783)	9.1 (296/3,261)	3.5 (12/346)	6.5 (255/3,916)	2.8 (129/4,612)	2.2 (71/3,290)	4.4 (187/4,212)
Amikacin	0 (0/17)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Amoxicillin	14.7 (268/1,829)	8.3 (3/36)	6.7 (31/461)	17.7 (3/17)	2.8 (16/581)	2.1 (13/609)	0.2 (1/541)	0.8 (5/599)
Amoxicillin-Clavulanic acid**	26.6 (98/369)	0 (0/22)	14.3 (62/432)	n/a	4.5 (13/292)	8.4 (12/143)	0 (0/82)	4.8 (4/84)
Ampicillin	12.0 (114/951)	4.2 (1/24)	0 (0/147)	30.8 (8/26)	9.6 (50/522)	23.3 (27/116)	0.5 (1/198)	9.4 (43/459)
Ampicillin-Cloxacillin**	41.7 (80/192)	0 (0/2)	n/a	n/a	n/a	n/a	0 (0/2)	0 (0/2)
Azithromycin	65.6 (21/32)	0 (0/25)	0 (0/20)	n/a	n/a	0 (0/25)	0 (0/25)	10.7 (3/28)
Benzylpenicillin (penicillin G)	13.1 (14/107)	n/a	n/a	0 (0/11)	n/a	0 (0/3)	0 (0/31)	0 (0/1)
Cefadroxil	0 (0/14)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Cefalexin	0 (0/10)	0 (0/11)	n/a	n/a	n/a	n/a	0 (0/11)	0 (0/11)
Cefixime	15.2 (10/66)	0 (0/37)	5.6 (3/54)	n/a	0 (0/55)	n/a	0 (0/37)	0 (0/37)
Cefotaxime	0 (0/21)	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Ceftazidime	0 (0/7)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Ceftriaxone	16.5 (47/284)	0 (0/26)	n/a	0 (0/35)	12.4 (18/145)	0 (0/38)	n/a	0.7 (1/149)
Cefuroxime	28.3 (51/180)	0 (0/8)	8.7 (10/115)	n/a	26.6 (30/113)	n/a	0 (0/8)	8.3 (1/12)
Cephradine	100 (6/6)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Chloramphenicol	31.7 (40/126)	18.2 (2/11)	14.3 (1/7)	n/a	0 (0/27)	0 (0/1)	5.3 (2/38)	12.1 (4/33)
Ciprofloxacin	14.8 (116/783)	8.3 (152/1,836)	1.1 (3/276)	n/a	5.5 (12/220)	1.0 (18/1,808)	2.4 (13/538)	3.2 (10/311)
Clarithromycin	5.1 (5/98)	0 (0/3)	28.4 (25/88)	n/a	8.6 (8/93)	n/a	0 (0/3)	25.0 (1/4)
Clindamycin	66.7 (4/6)	n/a	16.7 (1/6)	n/a	n/a	0 (0/6)	n/a	n/a
Cloxacillin	40 (10/25)	0 (0/26)	0 (0/5)	n/a	0 (0/7)	28.6 (2/7)	0 (0/31)	8.8 (3/34)
Doxycycline	20.1 (68/339)	0 (0/10)	1.8 (4/217)	0 (0/8)	3.1 (8/255)	0 (0/182)	1.3 (2/157)	0.6 (1/180)
Erythromycin	48.3 (28/58)	8.4 (13/154)	69.2 (9/13)	n/a	0 (0/5)	5.0 (1/20)	5.8 (9/154)	18.6 (8/43)
Flucloxacillin	85.7 (18/21)	n/a	n/a	n/a	n/a	0 (0/1)	n/a	0 (0/4)
Gentamicin	9.8 (22225)	n/a	0 (0/1)	n/a	0 (0/1)	0 (0/30)	0 (0/1)	1.9 (3/157)
Kanamycin	0 (0/67)	33.3 (1/3)	n/a	n/a	n/a	0 (0/67)	n/a	0 (0/67)
Levofloxacin	14.7 (26/177)	0 (0/12)	29.7 (19/64)	n/a	n/a	0 (0/2)	6.3 (1/16)	0 (0/10)
Metronidazole	19.7 (146/741)	0 (0/40)	5.5 (15/274)	n/a	8.4 (36/430)	1.2 (5/416)	3.0 (11/363)	0.6 (2/351)
Moxifloxacin	n/a	0 (0/5)	n/a	n/a	n/a	0 (0/2)	0 (0/5)	0 (0/3)
Nalidixic acid	0 (0/9)	n/a	66.7 (6/9)	n/a	0 (0/9)	n/a	n/a	n/a
Norfloxacin	0 (0/1)	n/a	0 (0/1)	n/a	0 (0/1)	n/a	0 (0/1)	0 (0/1)
Ofloxacin	10.7 (20/187)	0 (0/8)	14.9 (15/101)	1.9 (1/53)	18.0 (16/89)	0 (0/54)	8.3 (1/12)	0 (0/20)
Oxacillin	0 (0/2)	n/a	0 (0/2)	n/a	0 (0/2)	n/a	0 (0/2)	0 (0/2)
Penicillin - unspecified formulation	7.1 (1/14)	0 (0/6)	n/a	n/a	7.1 (1/14)	0 (0/6)	5.0 (1/20)	0 (0/14)

Phenoxymethylpenicillin (penicillin V)	19.8 (43/217)	0 (0/11)	1.0 (1/103)	n/a	0 (0/3)	2.4 (1/42)	0 (0/45)	0 (0/44)
Procaine Benzylpenicillin (penicillin G) - intramuscular	2.9 (3/102)	n/a	n/a	0 (0/5)	0 (0/5)	0 (0/5)	n/a	0 (0/10)
Roxithromycin	5.6 (4/71)	n/a	29.8 (17/57)	n/a	0 (0/57)	n/a	n/a	n/a
Streptomycin	52.6 (10/19)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Sulfamethoxazole-Trimethoprim**	19.9 (397/2,093)	4.8 (4/84)	12.9 (72/558)	0 (0/180)	0.5 (4/774)	1.6 (10/647)	2.4 (19/781)	5.8 (75/1,286)
Sulfamethoxazole-Uncombined	n/a	0 (0/1)	n/a	n/a	n/a	n/a	0 (0/1)	0 (0/1)
Tetracycline	3.4 (29/842)	6.3 (24/382)	0.8 (2/250)	0 (0/11)	19.9 (43/216)	10.5 (40/382)	5.4 (10/187)	9.1 (22/242)

* Samples are often subjected to more than one test technique within each category. Numbers represent testing events per API sample
** Combination antibiotics were usually tested twice for API content, once for each ingredient. However, some authors analysed only one of the APIs or an uneven number of them
*** Includes disintegration, friability, hardness, thickness, wetting time and water absorption testing
**** Includes API identification, degradation products, pH, and other undeclared chemical tests

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 10. Concordance with the 26 items of the MEDQUARG checklist of the prevalence surveys of antibiotics quality.

Item	Description	Iwuagwu, 1992	Okeke et al, 1995	Gimenez et al, 1997	Shakoor et al, 1997	Kibwage et al, 1998	Stenson et al, 1998	Wondemagegnehu (WHO), 1999	Kamau et al, 2001
1	Identify as MQ paper with abstract of what was done and found, describing survey and analytical methods	N	Y	N	Y	N	Y	Y	N
2	Background and objectives	Y	Y	Y	Y	Y	Y	Y	Y
3	Survey details (when and where collected & analysed)	N	N	N	N	N	N	N	N
4	Definitions (Substandard, falsified...)	N	N	Y	Y	N	Y	Y	N
5	Outlets and outlet size indicator (sales, turnover, etc.)	N	N	N	N	N	N	N	N
6	Sampling design, size calculation, definition of sample	N	N	N	N	N	N	N	N
7	Samplers and method of randomization	N	N	N	Y	N	N	Y	N
8	Statistical methods	N	N	N	N	N	N	N	N
9	Ethical issues	N	N	N	N	N	N	N	N
10	Packaging and reference standard	N	N	N	N	N	N	Y	N
11	Chemical analysis SOPs, location of laboratory and reference standards	Y	Y	N	N	N	Y	Y	Y
12	Method validation against reference or study	N	N	N	Y	Y	Y	Y	N
13	Blinding between chemistry analysis and packaging	N	N	N	N	N	N	N	N
14	Outlets: details of outlets actually sampled	N	N	Y	Y	N	N	N	N
15	Missing samples (ie why an outlet did not procure samples, lost, etc.)	N	N	N	N	N	N	N	N
16	Packaging & chemistry results and correlation. Include details of products sampled	N	N	N	N	N	N	N	N
17	Category of poor-quality medicine (stating if SF in results)	N	N	N	N	N	N	Y	N
18	State company and address as given on packaging	N	N	N	N	Y	N	N	Y
19	Sharing data with MRA	N	N	Y	N	N	Y	Y	N
20	Dissemination: packaging features that allows ID of falsified?	N	N	N	N	N	N	N	N
21	Key results in relation to objectives	Y	Y	N	Y	Y	Y	Y	Y
22	Limitations	N	N	Y	N	N	N	N	N
23	Interpretation in conjunction with prior studies and in relation to public health	N	Y	N	Y	N	Y	N	N
24	Intervention	Y	Y	N	Y	Y	Y	Y	N
25	Conflict of interest	N	N	N	N	N	N	N	N
26	Funding	N	N	Y	N	Y	Y	Y	N

Y= Reported; N=Not reported

Item	Taylor et al, 2001	Kolawole et al, 2002	Sow et al, 2002	Prazuck et al, 2002	Ahmed et al, 2003	Kamau et al, 2003	Risha, 2003	Basco, 2004	Syhakhang et al, 2004	Weir et al, 2005	Lon et al, 2006	Obodozie et al, 2006
1	Y	N	Y	Y	N	N	Y	Y	Y	Y	Y	N
2	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y
3	N	N	N	N	N	N	N	N	N	N	N	N
4	Y	Y	Y	N	N	N	N	Y	N	N	N	N
5	N	N	N	N	N	N	N	N	N	N	N	N
6	N	N	N	N	N	N	N	N	N	N	N	N
7	Y	N	Y	N	N	N	N	Y	Y	N	Y	N
8	N	Y	Y	N	N	N	Y	N	Y	N	Y	N
9	N	N	N	N	N	N	N	N	Y	Y	N	N
10	N	N	N	N	N	N	N	N	N	N	Y	N
11	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12	Y	N	N	N	N	N	Y	Y	Y	Y	Y	Y
13	N	N	N	N	N	N	N	N	Y	N	N	N
14	Y	N	Y	N	N	N	N	Y	N	N	Y	Y
15	N	N	N	N	N	N	N	N	N	N	N	N
16	N	N	N	N	N	N	N	N	N	N	Y	N
17	N	N	N	N	N	N	N	Y	N	N	Y	N
18	N	N	N	Y	N	Y	Y	N	N	N	N	N
19	N	N	N	N	N	N	N	N	Y	N	Y	N
20	N	N	N	N	N	N	N	N	N	N	Y	N
21	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
22	N	N	N	Y	N	N	N	N	Y	Y	Y	Y
23	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y
24	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
25	N	N	N	N	N	N	N	N	Y	Y	Y	N
26	Y	N	N	N	N	N	Y	Y	Y	N	Y	N

Y= Reported; N=Not reported

Item	Vijaykadga et al, 2006	Meos et al, 2008	Kyriacos et al, 2008	Pouillot et al, 2008	Bate et al, 2009	Obaid, 2009	Zaheer et al, 2009	Hadi et al, 2010	Khan et al, 2010	Yoshida et al, 2010	Bate et al, 2011	Haider et al, 2011	Kamuhabwa et al, 2011
1	Y	Y	Y	N	Y	N	N	Y	Y	Y	Y	N	Y
2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
3	N	N	N	N	Y	N	N	N	N	Y	N	N	N
4	Y	Y	Y	N	N	Y	N	Y	Y	Y	Y	N	N
5	N	N	N	N	N	N	N	N	N	N	N	N	N
6	N	N	N	N	N	N	N	N	N	Y	N	N	N
7	Y	N	N	N	Y	N	N	Y	N	N	Y	N	N
8	N	N	N	N	N	N	N	Y	Y	Y	Y	N	N
9	N	N	N	N	N	N	N	Y	N	N	N	N	N
10	Y	N	N	N	N	N	N	N	Y	Y	Y	N	N
11	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	N	N
12	Y	N	Y	N	Y	N	N	Y	N	Y	Y	N	N
13	N	N	N	N	N	N	N	N	N	N	N	N	N
14	Y	N	N	N	Y	N	N	Y	Y	Y	Y	N	N
15	N	N	N	N	N	N	N	Y	N	N	N	N	N
16	N	N	N	N	N	N	N	N	N	N	N	N	N
17	Y	N	Y	N	N	N	N	Y	Y	N	N	N	N
18	N	Y	N	N	N	N	N	Y	N	N	N	N	N
19	Y	N	N	N	N	N	N	N	Y	Y	N	N	N
20	N	N	N	N	N	N	N	N	N	Y	N	N	N
21	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
22	Y	Y	N	N	N	N	N	Y	Y	Y	N	N	N
23	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y
24	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
25	N	N	N	N	Y	N	N	Y	N	Y	N	N	N
26	Y	Y	N	N	Y	N	N	Y	Y	Y	Y	N	N

Y= Reported; N=Not reported

Item	Nair et al, 2011	Karlage et al, 2012	Akinkunmi, 2013	Egbo, 2013	Khan et al, 2013	Phanouvong et al, 2013a	Phanouvong et al, 2013b	Ramachandran et al, 2013	Hetzel, 2014	Khurelbat et al, 2014	Khuluza, 2014
1	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y
2	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
3	N	N	N	N	N	N	N	N	N	N	N
4	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y
5	N	N	N	N	N	N	N	N	N	N	N
6	N	N	N	N	N	Y	Y	Y	N	N	N
7	Y	N	N	N	Y	Y	Y	N	Y	Y	N
8	N	N	N	Y	Y	N	Y	Y	Y	Y	Y
9	N	N	N	N	Y	N	N	N	Y	Y	N
10	Y	N	N	Y	Y	Y	Y	N	N	Y	N
11	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
12	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y
13	N	N	N	N	N	N	N	Y	Y	N	N
14	Y	N	Y	N	Y	Y	Y	N	Y	Y	Y
15	N	N	N	N	N	N	N	N	N	N	N
16	Y	N	N	Y	Y	N	N	N	N	N	N
17	Y	N	N	N	Y	N	N	N	N	Y	N
18	Y	Y	N	Y	N	N	N	N	Y	N	N
19	N	N	N	N	Y	N	Y	N	N	Y	N
20	Y	N	Y	Y	N	N	N	N	Y	N	N
21	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
22	Y	Y	Y	N	Y	Y	Y	N	Y	Y	N
23	Y	N	Y	N	Y	Y	N	Y	Y	Y	Y
24	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
25	N	Y	Y	N	Y	N	N	N	Y	Y	N
26	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N

Y= Reported; N=Not reported

Item	Bate et al, 2015	Boadu et al, 2015	Fadeyi, 2015	Tshilumba et al, 2015	Wang et al, 2015	Khan et al, 2016	Kaale et al, 2016	Mwamba et al, 2016	Nga et al, 2016	Osei-Safo et al, 2016	Islam, 2017	Islam et al, 2017	Khuluza et al, 2017
1	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y
2	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3	N	N	N	N	N	N	N	N	N	N	N	N	N
4	Y	Y	N	Y	Y	Y	N	N	N	Y	N	N	Y
5	N	N	N	N	N	N	N	N	N	N	N	N	N
6	N	N	N	N	N	N	N	N	N	N	N	N	N
7	Y	N	N	N	N	N	Y	N	N	Y	N	Y	Y
8	N	Y	N	N	N	Y	Y	Y	Y	N	Y	Y	Y
9	N	N	Y	N	N	N	N	N	N	N	N	N	Y
10	Y	N	Y	Y	N	N	N	Y	N	N	Y	Y	Y
11	Y	Y	Y	N	Y	N	N	Y	N	Y	Y	N	Y
12	Y	Y	Y	N	N	Y	N	N	N	Y	Y	N	Y
13	N	N	N	N	N	N	N	N	N	N	N	N	N
14	N	N	N	Y	Y	N	Y	Y	Y	N	Y	Y	Y
15	N	N	N	N	N	N	N	N	N	N	N	N	Y
16	N	N	N	N	N	N	N	N	N	N	N	N	Y
17	Y	N	Y	N	N	N	N	N	N	Y	N	N	Y
18	N	N	Y	N	Y	N	N	N	N	N	N	N	N
19	N	Y	N	N	N	N	Y	Y	N	N	Y	Y	Y
20	Y	N	N	Y	N	N	Y	Y	N	N	Y	N	Y
21	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
22	Y	N	Y	N	N	N	N	Y	N	N	Y	N	Y
23	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y
24	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y
25	N	N	N	Y	Y	Y	Y	Y	Y	N	N	Y	N
26	N	N	Y	N	Y	N	Y	Y	N	N	N	Y	Y

Y= Reported; N=Not reported

Item	Nabirova et al, 2017	Ononna et al, 2017	Petersen et al, 2017	Schiavetti et al, 2018	Bate et al, 2018	Ernest et al, 2018	Frimpong et al, 2018	Islam et al, 2018	Joda et al, 2018	Lehmann et al, 2018a	Lehmann et al, 2018b	Schafermann et al, 2018	Tshilombo et al, 2018
1	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N
2	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
3	Y	N	N	N	N	N	N	N	N	Y	N	N	N
4	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
5	Y	Y	N	Y	N	N	N	N	N	N	N	N	N
6	Y	N	N	Y	N	N	N	N	N	N	N	Y	N
7	N	N	Y	Y	Y	Y	N	Y	N	Y	N	Y	Y
8	Y	N	N	Y	N	N	N	Y	Y	Y	Y	Y	Y
9	Y	N	N	Y	N	N	N	Y	N	N	N	N	N
10	Y	N	Y	Y	Y	N	N	Y	N	Y	N	N	N
11	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
12	Y	N	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y
13	N	N	N	Y	N	N	N	N	N	Y	N	N	N
14	Y	N	N	Y	N	Y	Y	Y	N	Y	Y	Y	N
15	Y	N	Y	Y	Y	N	N	N	N	Y	N	Y	N
16	Y	N	N	Y	N	N	Y	N	N	Y	N	Y	N
17	N	N	Y	Y	N	N	Y	Y	N	N	N	Y	N
18	Y	N	Y	N	N	N	N	N	N	N	N	N	N
19	Y	N	Y	Y	N	N	N	Y	N	N	Y	N	N
20	Y	N	Y	Y	N	N	N	N	N	N	N	N	N
21	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
22	N	N	Y	Y	Y	N	N	Y	Y	Y	N	Y	N
23	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
24	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
25	Y	N	Y	N	N	N	Y	Y	N	N	N	Y	Y
26	Y	N	Y	Y	Y	N	Y	Y	N	N	N	Y	Y

Y= Reported; N=Not reported

Item	Lawal et al, 2019	Scrimgeour et al, 2019	Tabernero et al, 2019	Bekoe et al, 2020	Jean-Baptiste et al, 2020	Hand et al, 2020	Husaini et al, 2020	Koech et al, 2020	Khurelbat et al, 2020	Schafermann et al, 2020	Sakuda et al, 2020
1	N	N	Y	N	N	Y	N	Y	Y	N	N
2	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
3	N	N	Y	Y	Y	N	N	N	Y	N	N
4	N	N	Y	Y	N	N	N	N	Y	Y	N
5	N	N	N	Y	N	N	N	N	N	N	N
6	N	N	N	N	N	N	N	N	Y	N	N
7	N	N	Y	N	Y	N	N	N	N	Y	N
8	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y
9	N	Y	Y	Y	N	Y	N	Y	Y	Y	Y
10	N	N	Y	N	N	N	N	N	Y	N	Y
11	N	N	Y	Y	N	N	Y	N	Y	Y	N
12	N	N	Y	N	N	Y	Y	N	N	N	N
13	N	N	Y	Y	N	N	N	N	N	N	N
14	N	Y	Y	Y	Y	N	N	N	Y	Y	Y
15	N	Y	Y	N	N	N	N	N	N	Y	N
16	N	N	N	N	N	N	N	N	N	Y	N
17	N	N	Y	Y	N	N	N	N	N	N	N
18	N	N	Y	N	N	N	N	N	N	N	N
19	N	Y	Y	N	N	N	N	N	Y	Y	Y
20	N	N	N	N	N	N	N	N	N	Y	Y
21	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
22	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
23	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
24	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
25	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y
26	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y

Only the prevalence surveys published as original articles in scientific journals or following the Introduction/Methods/Results/Discussion or similar style and published as reports, MSc or PhD thesis, were appraised.

Y= Reported; N=Not reported

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 11. Main characteristics of equivalence studies on the quality of antibiotics

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Mouton, 1979[1] Netherlands	Cefadrine Cefamandole Cefalotin Cefazolin Cefotaxime Cefoxitin Cefuroxime	Unspecified	Manufacturer	Unspecified	API content - Microbiological assay	0/7 (0.0%)
Van der Bijl, 1988[2] Unknown	Ampicillin	Famicillin, Penbritin, Petercillin	Unknown	Unspecified	API identification - HPLC-MS, microbiological assay, related substances	0/10 (0.0%)
Kibwage, 1991[3] Kenya	Metronidazole	Flagyl, Unknown	Manufacturer Wholesaler	BP	API content - UV-Spectroscopy, crushing strength, disintegration, dissolution, friability, mass uniformity	6/11 (54.5%)
Sakolchai, 1991[4] Thailand	Metronidazole Ampicillin Co-trimoxazole	Unknown	Hospital/Health centre, Private pharmacy	USP	API content - HPLC, dissolution, mass uniformity	6/14 (42.9%)
Antony, 1999[5] Tanzania	Co-trimoxazole Metronidazole	Bactrim, Flagyl, Unknown	Distributor Pharmacy	BP, USP	API content – TLC and UV-Spectroscopy, disintegration, dissolution, friability	3/6 (50.0%)
Nightingale, 2000a[6] Israel, Poland, Slovakia, Slovenia	Clarithromycin	Fromilid, Karin	Unknown	USP, Manufacturer's standard	API content - HPLC, dissolution, impurity	6/11 (54.6%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Nightingale, 2000b[7] Brazil, Chile, China, Colombia, Costa Rica, El Salvador, Guatemala, India, Indonesia, Pakistan, Peru, Turkey, Uruguay	Clarithromycin	Bicrolid, Clacine, Clambiotic, Clamicin, Clamycin, Claribac, Claricide, Clarimax, Clarimicin, Clarion, Clarithro-250, Claritrobac, Claritrol, Claritromicina, Claritromicina MK, Comtro, Crixan, Dicupal, Infex, Klarid, Klarolid, Klaromin, Klax, Limaixian, Macrol, Macrolien, Mus, Pre-Clar, Synclar	Unspecified	USP	API content – HPLC, dissolution, impurity – HPLC, visual inspection	34/40 (85.0%)
Mei, 2002[8] China	Cephradine	Unknown	Unknown	Chinese Pharmacopeia	API content – HPLC, dissolution	1/13 (7.7%)
Lambert, 2003[9] United Kingdom	Ceftriaxone	Axon, Broadced, Cefaxona, Cefaxone, Ceftrex, Ceftriaxon, Ceftriaxona GI, Ceftriaxona Sodium, Ceftriaxone Cef 3, Ceftriaxone, Cerixon, Desfin, Elpicef, Keptrix, KGE Ceftriaxone, LGP Ceftriaxone, Mercefex, Novocef, Oframax, Titan, Tpnakcoh, Triceft, Trixone, Unocef, Ventraxin, Zeftrox	Unknown	European Pharmacopoeia, USP	API content - HPLC, impurity - HPLC, pH, sterility	10/34 (29.4%)
Iqbal, 2004[10] Pakistan	Ofloxacin	Albact, Avocin, Bacivid, Ciof, Curitol, Eracin, Exact, Flovix, Floxy, Geoflox, Gyrasid, Gyrex,	Unknown	National Committee for Clinical Laboratory Standards	API content - In-vitro antibacterial susceptibility	15/34 (44.1%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
		Kapcin, Korvid, Loxat, Oflamac, Oflobid, Oflobiotic, Ofloxin, Ofloquin, Oflox, Oftab, Oxil, Quinox, Rutix, Tabroxacin, Tariflox, Tarivid, Wiloxin				
Mei, 2004[11] China	Ceftriaxone	Unknown	Unregistered outlets	BP, European Pharmacopoeia, USP	API content - HPLC	0/17 (0%)
Nightingale, 2005[12] Argentina, Cyprus, Greece, Hong Kong, India, Indonesia, Malaysia, Mexico, Morocco, Pakistan, Palestine, Republic of Korea, Singapore, Slovenia, Spain, Uruguay	Clarithromycin	Adel, Berafen, Bicrolid, Binoclar, Clacin, Clamont, Clari, Clarion, Claripen, Claritek, Clarithro, Clarithromycin A, Claritromicina Alter, Claritromicina Bexal, Claritromicina, Geminis, Claritromicina Kern, Claromycin, Claros, Clarytas, Cleron, Crixan, E-Clar, Ezumycin, Fromilid, Hammi, Iset, Klaribact, Klaricare, Klermed, Neo-Klar, Pathocin, Ulcecure	Unspecified	USP	API content – HPLC, dissolution, impurity – HPLC, visual inspection	9/65 (13.9%)
Semde, 2005[13] Burkina Faso	Amoxicillin, Ampicillin, Metronidazole, Phenoxymethylpenicillin (Penicillin V), Sulfamethoxazole + Trimethoprim	Amoxicilline, Ampicilline, Bactrim Adultes, Clamoxyl, Co-trimoxazole, Flagyl, Metronidazole, Penicilline V, Starpen, Totapen	Wholesalers/ importer/ distributors	BP, European Pharmacopoeia, USP	API content – UV/Visible spectrophotometry, disintegration, dissolution, friability, hardness	0/20 (0%)
Adegbolagun, 2007[14] Nigeria	Ciprofloxacin	Unknown	Private pharmacy	BP, USP	API content – TLC, hardness, disintegration	4/10 (40.0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Bamiro, 2007[15] Nigeria	Metronidazole	Unknown	Retail outlets - undefined	BP	API content – Titrimetry, disintegration, dissolution, friability, tablet hardness, mass uniformity	2/7 (28.6%)
Ibezim, 2008[16] Nigeria	Metronidazole	Unknown	Unregistered outlet, patent medicine vendor, hospital, private pharmacy	BP, USP	API content – UV/Visible spectrophotometry	9/10 (90.0%)
Mu'az, 2009[17] Nigeria	Ciprofloxacin	Unknown	Manufacturer	BP, USP	API content - LC, disintegration, dissolution, friability, hardness	0/7 (0%)
Nazir Mughal, 2009[18] Pakistan	Ciprofloxacin	Axcin, Ciproxin, Cyrocin, Mercip	Unknown	Unknown/Not specified.	API content - In-vitro antibacterial susceptibility	0/8 (0%)
Ngwuluka, 2009[19] Nigeria	Ciprofloxacin	Cipro-J, Ciprobon, Ciprogem, Ciproval, Ivacip, Vitapro	Private pharmacy	BP, USP	API content - UV-visible spectrophotometry, disintegration, dissolution, friability test, tablet hardness, mass uniformity	3/6 (50.0%)
Shahnaz, 2009[20] Pakistan	Cefixime	Unknown	Private pharmacy	BP, USP	API content – HPLC and microbiological assay, disintegration, dissolution, mass uniformity	0/6 (0%)
Wei, 2009[21] China	Cefteram	Unknown	Unknown	Unknown/Not specified	API content - HPLC	0/2 (0%)
Awofisayo, 2010[22] Nigeria	Ofloxacin	Asflovid, Drovid, Floxan, Floxavid, Gaxin, Oflomed, Tarivid, Traflox, Zanocin	Private pharmacy	USP	API content – UV-Spectroscopy, disintegration, dissolution, friability, tablet hardness, mass uniformity	9/9 (100.0%)
Nayak, 2010[23] India	Ciprofloxacin	Unknown	Private pharmacy	Indian Pharmacopeia, USP	API content – UV-spectrophotometry, disintegration, dissolution, friability, tablet hardness, mass uniformity	0/7 (0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Silva, 2010[24] Colombia	Meropenem, Piperacillin-tazobactam	Unknown	Hospital/Health centres	Colombia National Formulary, United States Pharmacopeia	API content – microbiological assay	0/39 (0%)
Arshad, 2011[25] Pakistan	Gatifloxacin	Unknown	Private pharmacy	BP, USP	API content - HPLC-UV, disintegration, dissolution, tablet hardness, size variability, thickness, mass uniformity	0/5 (0%)
Bano, 2011[26] Pakistan	Levofloxacin	Unknown	Private pharmacy	BP, USP	API content - UV-visible spectrophotometry and In-vitro antibacterial susceptibility, disintegration, dissolution, friability, tablet hardness, thickness, mass uniformity	0/6 (0%)
Diaz, 2011[27] Colombia	Vancomycin	Unknown	Hospital/Health centres	USP	API content - In-vitro antibacterial susceptibility and microbiological assay	0/23 (0%)
Hailu, 2011[28] Ethiopia	Sulfamethoxazole-Trimethoprim	Bactrim, Bisepton, Cotreich, Cotri, Cotrimoxazole, Deprim	Manufacturer	BP, USP	API content – HPLC, disintegration, dissolution, friability, tablet hardness, thickness, mass uniformity	0/6 (0%)
Singal, 2011[29] India	Ciprofloxacin	Ciprobid	Private pharmacy	Indian Pharmacopeia	API content – HPLC and UV-Spectroscopy, API identification – IR spectroscopy, dissolution, mass uniformity	0/20 (0%)
Akpabio, 2011[30] Nigeria	Ciprofloxacin	Cefroden, Cipox, Ciprocare, Cipronol	Manufacturer	USP	API content – Titrimetry, disintegration, dissolution, friability, mass uniformity	1/4 (25.0%)
Mikre, 2011[31] Ethiopia	Amoxicillin	Unknown	Private pharmacy	BP, USP	API content- UV-visible spectrophotometry, API identification-TLC, dissolution, pH, mass uniformity, water content-Karl-Fischer titration	2/13 (15.4%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Musa, 2011[32] Nigeria	Metronidazole	Unknown	Hospital, Patent medicine vendor, Private pharmacy	BP	API content – unknown, dissolution, friability, tablet hardness, mass uniformity	10/15 (66.7%)
Omari, 2011[33] Jordan	Ciprofloxacin	Unknown	Manufacturer	US FDA, USP	API content - HPLC	0/2 (0%)
Singhal, 2011[34] India	Ciprofloxacin	Ciprobid, Ciproral	Private and public outlet - undefined	Indian Pharmacopeia	API content and identification – HPLC, content uniformity, mass uniformity	0/2 (0%)
Ashraful Islam, 2012[35] Bangladesh	Ciprofloxacin	Unknown	Private pharmacy	USP	API content – HPLC, disintegration, dissolution, friability, tablet hardness, mass uniformity	0/6 (0%)
Olanrewaju, 2012[36] Nigeria	Amoxicillin plus Clavulanic acid	Unknown	Private pharmacy	BP, USP	API content – HPLC, disintegration, dissolution, friability, tablet hardness, mass uniformity	3/6 (50.0%)
Onanuga, 2012[37] Nigeria	Ciprofloxacin, Gentamicin	Cenox, Cifran, Cipro-J, Ciprotab, Ciproxamed, Cyplox, Depmax, Elcees, Gentamicin Sulphate, Gentaven, Glogent, Paulio, Siprosan, Taman, Tivagenta, Unknown, Vitrapro	Combination of outlets, Private pharmacy	Unknown/Not specified	API content-in-vitro antibacterial susceptibility	11/17 (64.7%)
Nambiar, 2012[38] USA	Vancomycin	Unknown	Wholesaler/ Importer/ distributors	BP	API content and impurity – HPLC	0/6 (0%)
Hadwiger, 2012[39] United States of America	Vancomycin	Unknown	Manufacturer	BP, USP	API content - UHPLC, impurity - UV-MS	0/6 (0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Qureshi, 2012[40] Pakistan	Ciprofloxacin	Unknown	Unknown	Unknown/Not specified	API content- HPLC	1/11 (9.1%)
Kahaliw, 2013[41] Ethiopia	Metronidazole	Amrizole, Camezol, Giardyl-125, Metazole, Metrogyl, Metrolag, Metronidazole	Private pharmacy	BP, Indian Pharmacopeia, USP	API content – HPLC, disintegration, dissolution, friability, tablet hardness, mass uniformity, sedimentation, viscometer	1/10 (10.0%)
Rahim, 2013[42] Pakistan	Cefadroxil	Unknown	Retail – undefined, Wholesaler	USP	API content – HPLC, disintegration, dissolution, tablet hardness, mass uniformity, tablet thickness	0/7 (0%)
Hussain, 2013[43] Pakistan	Ciprofloxacin	Unknown	Private pharmacy	USP	API content – UV spectroscopy, disintegration, dissolution, tablet hardness, mass uniformity	1/12 (8.3%)
Birhanu, 2013[44] Ethiopia	Erythromycin	Erycin, Erythromycin, Etocin, Rythro	Drug retail outlets – undefined	BP, USP	API content – unknown, disintegration, dissolution, tablet hardness, identity, mass uniformity	1/4 (25.0%)
Akhtar, 2013[45] Pakistan	Levofloxacin	Cravit, Farleo, Feelix, Lecord, Levodin, Levofin, Levoflox, Levosafe, Qevo	Unknown	BP, USP	Disintegration, dissolution, friability, tablet hardness, mass uniformity	8/9 (88.9%)
Kassaye, 2013[46] Ethiopia	Amoxicillin	Unknown	Unknown	USP	Dissolution	0/8 (0%)
Pais, 2013[47] India	Amoxicillin	Unknown	Government outlets	USP	API content-alkalimetry test and in-vitro antibacterial susceptibility, moisture content-drying oven method, pH, sedimentation test	4/12(33.3%)
Naveed, 2014[48] Pakistan	Doxycycline	Doxycycline, Doxyn, Vibramycin	Unknown	BP, USP	Disintegration, dissolution, mass uniformity	0/3 (0%)
Khamis, 2014[49] Gulf region	Metronidazole	Amrizole, Metrolags, Negazole, Nidazol	Private pharmacy	USP	API content – UV-spectroscopy, disintegration, friability, tablet hardness, mass uniformity	0/4 (0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Al-Tahami, 2014[50] Yemen	Amoxicillin plus Clavulanic acid	Unknown	Private pharmacy	USP	API content – HPLC, pH	0/4 (0%)
Arnet, 2014[51] China, Myanmar	Ceftriaxone	Becef, Cefaxone, Cefin, Ceftriaxon, Incept, Oframax, Triacef	Wholesalers/ importer/ distributors	Manufacturer	API content – HPLC, API identification – NIR, impurity – HPLC, pH, physical appearance, sterility	8/8 (100.0%)
Aliyu, 2014[52] Nigeria	Metronidazole	Bonagyl, Emgyl, Jugyl, Lemetro, Loxagyl, Metrotab, Metrozam, Metrozo, Palagyl, Stargyl, Unigyl, Vamis	Private pharmacy	BP	API content – UV-spectroscopy, disintegration, dissolution, friability, tablet hardness, mass uniformity	7/12 (58.3%)
Humayoon, 2014[53] Pakistan	Doxycycline	Generic	Private pharmacy	BP	API content- UV-visible spectrophotometry, disintegration, dissolution, mass uniformity	0/6 (0%)
Idries, 2014[54] Sudan	Ceftriaxone	Unknown	Unknown	Unknown	API content - microbiological assay	1/2 (50.0%)
Fahmy, 2014[55] United Arab Emirates	Ciprofloxacin	Unknown	Private pharmacy	USP	Bioavailability, dissolution	0/6 (0%)
Fayyaz, 2014[56] Pakistan	Levofloxacin	Unknown	Unknown	USP	API content – HPLC, disintegration, dissolution, tablet hardness, mass uniformity	1/6 (16.7%)
Hamam, 2014[57] Sudan	Ciprofloxacin	Unknown	Unknown	USP	API content – HPLC, disintegration, friability, mass uniformity, tablet thickness	0/4 (0%)
Malele, 2014[58] Tanzania	Ciprofloxacin	Unknown	Combination of outlets	Unknown/Not specified	API content - In-vitro antibacterial susceptibility	4/9 (44.4%)
Nettey, 2014[59] Ghana	Amoxicillin-Clavulanic acid	Unknown	Private pharmacy	BP	API content – HPLC and in-vitro antibacterial susceptibility, disintegration, dissolution	29/38 (76.3%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Jaman, 2015[60] Bangladesh	Ciprofloxacin	Unknown	Unknown	USP	API content – UV spectroscopy, disintegration, dissolution, tablet hardness, mass uniformity, tablet thickness	0/5 (0%)
Aljohani, 2015[61] Egypt, India, Jordan, Morocco, United Kingdom, United States	Azithromycin	Unknown, Zithromax	Hospital/health centres, private pharmacy	US FDA, USP	API content - HPLC	5/19 (26.3%)
Bashir, 2015[62] Pakistan	Levofloxacin	Bexus, Cravit, Dynaquin, Effiflox, Floxolev, Glit, Lazer, L-cyn, Lecin, Leflox, Levo, Levocil, Levocure, Levoday, Levomerc, Levoscot, Levotar, Levotas, Levovis, Locus, Mclevo, Protektin, Qumic, Spectrix, Tavanic, Vizor, Voksec, Voxiquin, Xeflox	Unknown	National Committee for Clinical Laboratory Standards	In-vitro antibacterial susceptibility	0/29 (0%)
Bendari, 2015[63] Oman	Metronidazole	Flazole, Klont, Metrolag, Negazole, Nidazole, Suprazole	Unknown	USP	Disintegration, dissolution- UV-visible spectrophotometer, friability, tablet hardness, mass uniformity	2/6 (33.3%)
El Attug, 2015[64] Libya	Amoxicillin-clavulanic acid	Unknown	Unknown	USP	API content – LC and in-vitro antibacterial susceptibility, API ID – LC and FTIR, disintegration, dissolution, tablet hardness, tablet thickness, mass uniformity	0/5 (0%)
Alzomor, 2016[65] Yemen	Sulfamethoxazole plus trimethoprim	Amirtrim, Balkatrim, Batrim, Cotrix, Farcotrim, Omtran, Septram, Septrim, Shatrim, Sinotrim	Unregistered	BP, USP	API content – HPLC, disintegration, dissolution, friability, tablet hardness	2/10 (20.0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Shraim, 2016[66] State of Palestine	Cefuroxime	Unknown	Unregistered	USP	API content – HPLC, dissolution, mass uniformity	0/3 (0%)
Idrees, 2016[67] Pakistan	Amoxicillin	Acamoxil, Amoxascot, Amoxicillin, Effimox, Glomox, HMC, Lapmox, Maxil, Medimox, Namoxil, Werrimox	Unknown	Unspecified	API content – HPLC and capillary electrophoresis	1/11 (9.1%)
Israr, 2016[68] Pakistan	Cefuroxime	Unknown	Manufacturer	USP	API content – HPLC, disintegration, dissolution, mass uniformity, thickness	0/4 (0%)
Osonwa, 2016[69] Nigeria	Ciprofloxacin	Unknown	Private pharmacy	BP	API content - UV-visible spectrophotometry, disintegration, dissolution, friability, Monsanto tablet tablet hardness, mass uniformity	1/15 (6.7%)
Pathak, 2016[70] India	Amoxicillin-clavulanic acid	Unknown	Private pharmacy	Unknown/Not specified	API content - In-vitro antibacterial susceptibility	2/6 (33.3%)
Adeniyi, 2017[71] Nigeria	Ciprofloxacin	Unknown	Private pharmacy	BP	API content - In-vitro antibacterial susceptibility, mass uniformity	0/5 (0%)
Al-Tabakha, 2017[72] United Arab Emirates	Amoxycillin plus Clavulanic acid	Unknown	Private pharmacy	USP	API content – HPLC, dissolution, friability, mass uniformity	0/5 (0%)
Uddin, 2017[73] Bangladesh	Ciprofloxacin	Unknown	Private pharmacy	BP, USP	API content – UV spectroscopy, disintegration, dissolution, friability, tablet hardness, mass uniformity	4/10 (40.0%)
Manani, 2017[74] Kenya	Clarithromycin	Unknown	Private pharmacy	USP	API content – HPLC, dissolution	0/16 (0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Noor, 2017[75] Bangladesh	Metronidazole	Unknown	Private pharmacy	BP, USP	API content – UV/Visible spectrophotometry, disintegration, dissolution, friability, tablet hardness, mass uniformity, tablet thickness and diameter	0/9 (0%)
Gberindyer, 2017[76] Nigeria	Gentamicin	Unknown	Private pharmacy	USP	API content – HPLC-UV	0/14 (0%)
Fatima, 2017[77] Pakistan	Metronidazole	Unknown	Unknown	USP	Disintegration, dissolution, tablet hardness, mass uniformity, tablet thickness and diameter	2/3 (66.7%)
Alyahawi, 2018[78] Yemen	Ciprofloxacin	Unknown	Private pharmacy	BP, USP	API content - UV spectrophotometry, disintegration, dissolution, friability Roche friabilator, tablet hardness, mass uniformity	0/5 (0%)
Hasin, 2018[79] Bangladesh	Cefuroxime	Unknown	Private pharmacy	BP	API content – HPLC, disintegration, dissolution, friability, tablet hardness, mass uniformity, tablet thickness and diameter	0/3 (0%)
Gogoi, 2018[80] India	Ciprofloxacin	Unknown	Private pharmacy	Indian Pharmacopeia	API content and identification – HPLC, dissolution, mass uniformity	0/2 (0%)
Shaibu, 2018[81] Nigeria	Ciprofloxacin	Unknown	Private pharmacy	BP	API content – UV/Visible - Spectrophotometry, disintegration, friability, impurity, mass uniformity	3/20 (15.0%)
Thamer, 2018[82] Iraq	Cefotaxime	Cefotaxime LDP, Cefotaxime LG, Fortax, Kon-SEFATAX, Loraxime 1000	Private pharmacy	USP	API content – HPLC, API identification – NIR, impurity, pH, physical appearance	0/5 (0%)
Obarisiagbon, 2018[83] Nigeria	Erythromycin	Althrocin-S 500, Donythrocin-500, Enthrox-500, Erotab-500, Eryfast-500 Erythromycin, Erymycin,	Unknown	USP	Disintegration, dissolution, friability, tablet hardness, mass uniformity	5/12 (41.7%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
		Erythrocin-500, Erythromycin, Erythromycin 500mg, Icethrocin, Labcin-500, Rycin Erythromycin, Zin zine				
Thambavita, 2018[84] Sri Lanka	Metronidazole	Flagyl, Metrogyl	Private pharmacy	BP, USP	API content and Identification- UV-Vis Spectrophotometry disintegration, dissolution, tablet hardness, mass uniformity	0/2 (0%)
Ukwueze, 2018[85] Nigeria	Azithromycin	Unknown	Private pharmacy	BP, USP	API content – UV/Visible spectrophotometry, disintegration, dissolution, friability, tablet hardness, mass uniformity	1/9 (11.1%)
Igboasoiyi, 2018[86] Nigeria	Ciprofloxacin	Unknown	Private pharmacy	BP USP	API content – Titrimetry and UV/Visible spectrophotometry, disintegration, dissolution, friability, tablet hardness, mass uniformity	3/10 (30.0%)
Rafiq, 2018[87] Pakistan	Ofloxacin, Ciprofloxacin	Unknown	Government outlet, Private pharmacy	BP, USP	Disintegration, dissolution-UV/Visible spectrophotometer, friability, tablet hardness, thickness, mass uniformity	0/4 (0%)
Ogochukwu, 2018[88] Nigeria	Azithromycin Clarithromycin	Klabax, Zithromax, Unknown	Private pharmacy	USP	API content – microbiological assay and UV Spectrophotometry, disintegration, dissolution, friability, tablet hardness	0/9 (0%)
Bagbi, 2018[89] Nigeria	Cefuroxime	Axacef, Donacef-500, Kadnat, Microcef-500, Sefzitil, Spizef, Zinnat	Private pharmacy	BP USP	API content – UV/Visible spectrophotometry, disintegration, dissolution, friability, tablet hardness, mass uniformity	3/7 (42.9%)
Anah, 2019[90] Nigeria	Ciprofloxacin	Unknown	Private pharmacy	BP USP	API content – Titrimetry and UV spectrophotometry, disintegration, dissolution, friability, tablet hardness, mass uniformity	11/15 (73.3%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Avianto, 2019[91] Indonesia	Amoxicillin	Unknown	Hospital/Health centres	Indonesia Pharmacopoeia (Farmakope Indonesia)	API content - microbiological assay	0/5 (0%)
Pereira dos Anjos, 2019[92] Brazil	Amoxicillin, Azithromycin	Unknown	Government outlets - others	Unknown/Not specified	Impurities - LC-MS	1/2 (50.0%)
Rahman, 2019[93] Bangladesh	Ciprofloxacin	Unknown	Private pharmacy	BP, USP	API content - UV spectrophotometry, disintegration, dissolution, tablet hardness, mass uniformity	0/5 (0%)
Shah, 2019[94] Pakistan	Moxifloxacin	Unknown	Private pharmacy	BP, USP	API content – HPLC, disintegration, dissolution, friability, tablet hardness, mass uniformity	0/5 (0%)
Sharif, 2019[95] Pakistan	Azithromycin	Azomin, Ery-Pack, Unknown	Unknown	Unknown/Not specified	API content - Ouchterlony Double Immune Diffusion Technique	1/3 (33.3%)
Uwambajineza, 2019[96] Rwanda	Amoxicillin, Metronidazole	Unknown	Unknown	USP	Disintegration, dissolution, friability, HPLC-DAD, visual inspection, mass uniformity	1/14 (7.1%)
Hambisa, 2019[97] Ethiopia	Norfloxacin	Asnor, Gyrablock, Negaflox, Norbek, Norcin, Norfen, Norflox, Trizolin, Uriflox	Hospital/ Health centres, Private pharmacy	USP	API content – HPLC, dissolution, friability, tablet hardness, mass uniformity	2/9 (22.2%)
Agudelo, 2019[98] Columbia	Imipenem plus cilastatin	Inem, Tienam	Private pharmacy	USP	API content – HPLC-UV and microbiological assay	1/2 (50.0%)
Badulla, 2020[99] Yemen	Ciprofloxacin	Unknown	Unknown	BP	API content - Spectrophotometry-no detail	0/9 (0%)
Desta, 2020[100] Ethiopia	Ciprofloxacin	Unknown	Private pharmacy	USP	API content – HPLC, disintegration, dissolution - UV-visible spectrophotometer, mass uniformity	0/6 (0%)

Reference / country of collection	Active pharmaceutical ingredient (s) (API)	Brand name	Outlet	Reference standard	Test(s) performed and analytical technique for API content/Impurities	Failure rate n/N (%)
Hobeika, 2020[101] Lebanon	Amoxicllin, Amoxicillin-Clavulanic acid, Ciprofloxacin	Unknown	Private Pharmacy	USP	API content - HPLC	6/13 (46.2%)
Leficho, 2020[102] Ethiopia	Doxycycline	Doxy denk, Doxycad, Doxycap,Doxylagap, Doxyleb, Epadoxine, Medomycin, Miraclin, Remycin 100, Teradoxin	Private pharmacy	USP	API content and identification - HPLC, dissolution, friability, tablet hardness, visual inspection, mass uniformity	3/10 (30.0%)
Oli, 2020[103] Nigeria	Ciprofloxacin, Metronidazole	Unknown	Private pharmacy	BP	API content - UV-visible spectrophotometry, particulate matter, pH, sterility	12/16 (75.0%)
Rahman, 2020[104] Bangladesh	Metronidazole	Antipro, D-Metro, Filmet, Flagyl, Metryl	Combination of outlets	USP	API content - UV-visible spectrophotometry, disintegration, dissolution, friability, mass uniformity, size variability, tablet hardness, tablet thickness	0/5 (0%)
Tolentino-Hernandez, 2020[105] Mexico	Ciprofloxacin	Cipro XR, Ciproflox DM	Unknown	European Medicines Agency	API content - HPLC	0/2 (0%)

Note: FTIR - Fourier Transform Infrared Spectrometry, HPLC – High performance liquid chromatography, IR – infrared spectroscopy, LC – DAD - Liquid chromatography-diode array detection, NIR – near-infrared spectroscopy, TLC – Thin liquid chromatography, UHPLC – Ultra high-performance liquid chromatography, UV-MS – UV mass spectrometry

References

1 Mouton RP, Bongaerts GPA, Van Gestel M. Comparison of activity and beta-lactamase stability of cefotaxime with those of six other cephalosporins. *Antimicrob Agents Chemother* Published Online First: 1979. doi:10.1128/AAC.16.6.757

2 Van Der Bijl P, Seifart HI, Parkin DP, *et al.* Oligomeric substances in ampicillin preparations. A comparison of Penbritin, Famicillin and Petercillin. *South African Med J* 1988;**73**:453–5.

3 Kibwage IO, Thuranira J, Migosi D. Quality performance of metronidazole tablet products on the Kenyan market. *East Afr Med J* 1991;**68**:365–71.

4 Sakolchai S, Chaiyakum A, Wiyakrutta S, *et al.* A Survey on Qualities of Drugs Commercially Avilable in Thailand. 2010;**6**.

5 Antony PGR, Temu-Justin M, P.G.R. Antony MT-J. The Quality of Drugs Manufactured in Tanzania. *East Cent African J Pharm Sci* 1999;**2**:45–9.

6 Nightingale CH. A survey of the quality of generic clarithromycin products manufactured in Slovenia and Israel. *Adv Ther* 2000;**17**:167–78. doi:10.1007/BF02853159

7 Nightingale CH. A survey of the quality of generic clarithromycin products from 13 countries. *Clin Drug Investig* 2000;**19**:293–305. doi:10.2165/00044011-200019040-00007

8 Mei D, Zhao W, Qiang F, *et al.* Quality evaluation of different cefradine capsules. *Chinese J Antibiot* 2002;**1**.

9 Lambert PA, Conway BR. Pharmaceutical quality of ceftriaxone generic drug products compared with Rocephin®. *J Chemother* 2003;**15**:357–68. doi:10.1179/joc.2003.15.4.357

10 Iqbal M, Hakim ST, Hussain A, *et al.* Ofloxacin: Laboratory evaluation of the antibacterial activity of 34 brands representing 31 manufacturers available in Pakistan. *Pakistan J Med Sci* 2004;**20**:349–56.

11 Mei D, Du X, Li D. Pharmaceutical evaluation of different sterile ceftriaxone sodium products. *Chinese Pharm J* 2004;**39**:463–6.

12 Nightingale CH. A survey of the quality of generic clarithromycin products from 18 countries. *Clin Drug Investig* 2005;**25**:135–52.

13 Semdé R, Ouédraogo HW, Guissou IP, *et al.* Évaluation in vitro de la bio-équivalence de quelques formes génériques d'antibactériens. J. Pharm. Belg. 2005;**60**:51–5.

14 Adegbolagun OA, Olalade OA, Osumah SE. Comparative evaluation of the biopharmaceutical and chemical equivalence of some commercially available brands of ciprofloxacin hydrochloride tablets. *Trop J Pharm Res* 2007;**6**:737–45. doi:10.4314/tjpr.v6i3.14654

15 Bamiro OA, Odeniyi MA, Osonuga OA. Brand variations in the physicochemical properties of metronidazole tablets. *Nig Q J Hosp Med* 2007;**17**:22–5. doi:10.4314/nqjhm.v17i1.12536

16 Ibezim EC, Attama AA, Obitte NC, *et al.* In vitro prediction of in vivo bioavailability and bioequivalence of brands of metronidazole tablets in Eastern Nigerian drug market. *Sci Res Essay* 2008;**3**:552–8.

17 Mu'az J, Gazali LK, Sadiq GU, *et al.* Comparative in vitro evaluation of the pharmaceutical and chemical equivalence of multi-source generic

ciprofloxacin hydrochloride tablets around Maiduguri metropolitan area. *Niger J Pharm Sci* 2009;**8**:102–6.

18 Nazir Mughal MS, Asghar MT, Zia MA, *et al.* Comparison of the antibacterial activities of different brands of Ciprofloxacin. *Rev Científica UDO Agrícola* 2009;**9**:700–4.

19 Ngwuluka NC, Lawal K, Olorunfemi PO, *et al.* Post-market in vitro bioequivalence study of six brands of ciprofloxacin tablets/caplets in Jos, Nigeria. *Sci Res Essay* 2009;**4**:298–305.

20 Shahnaz G, Arshad HM, Shyum NSB, *et al.* Pharmaceutical Evaluation of Commercial Brands of Cefixime 400MG Capsules Marketed in Karachi (Pakistan). *J Pharm Res* 2009;**8**:98–104. doi:10.18579/jpcrkc/2009/8/2/79774

21 Wei F, Zhu R, Zhao W, *et al.* Pharmacokinetics and bioequivalence studies of cefteram pivoxil in healthy Chinese volunteers. *Eur J Drug Metab Pharmacokinet* 2009;**34**:157–62. doi:10.1007/BF03191167

22 Awofisayo SO, Awofisayo OA, Eyen N, *et al.* Comparative assessment of the quality control measurements of multisource ofloxacin tablets marketed in Nigeria. *Dissolution Technol* 2010;**17**:20–5. doi:10.14227/DT170210P20

23 Nayak AK, Pal D. Comparative in vitro bioequivalence analysis of some ciprofloxacin HCl generic tablets. *Int J Pharm Sci Res* 2010;**1**:51–7.

24 Silva E, Díaz JA, Arias MJ, *et al.* Comparative in vitro study of the antimicrobial activities of different commercial antibiotic products for intravenous administration. *BMC Clin Pharmacol* 2010;**10**:1–13. doi:10.1186/1472-6904-10-3

25 Arshad H, Shoaib M, GHAYAS S, *et al.* Pharmaceutical quality control studies on gatifloxacin 200 mg tablets available in the Pakistani market. *Lat Am J Pharm* 2011;**30**:1922–6.

26 Bano R, Gauhar S, Naqvi SBS, *et al.* Pharmaceutical evaluation of different brands of levofloxacin tablets (250 mg) available in local market of Karachi (Pakistan). *Int J Curr Pharm Res* 2011;**3**:15–22.http://www.ijcpr.org/

27 Diaz JA, Silva E, Arias MJ, *et al.* Comparative in vitro study of the antimicrobial activities of different commercial antibiotic products of vancomycin. *BMC Clin Pharmacol* 2011;**11**:1–10. doi:10.1186/1472-6904-11-9

28 Hailu GS, Gutema GB, Asefaw AA, *et al.* Comparative assessment of the physicochemical and in-vitro bioavailability equivalence of co-trimoxazole tablets marketed in Tigray, Ethiopia. *Int J Pharm Sci Res* 2011;**2**:3210–8.

29 Singal G, Nanda A, Kotwani A. A comparative evaluation of price and quality of some branded versus branded-generic medicines of the same manufacturer in India. *Indian J Pharmacol* 2011;**43**:131–6. doi:10.4103/0253-7613.77344

30 Akpabio E, Jackson C, Ugwu C, *et al.* Quality control and in vitro bioequivalence studies on four brands of ciprofloxacin tablets commonly sold in Uyo Metropolis, Nigeria. *J Chem Pharm Res* 2011;**3**:734–41.

31 Mikre W, Mekonnen N. Assessment on the quality and influence of tropical storage conditions on amoxicillin formulations marketed in Ethiopia. *East Cent African J Pharm Sci* 2011;**14**:23–32.

32 Musa H, Sule YZ, Gwarzo MS. Assessment of physicochemical properties of metronidazole tablets marketed in Zaria, Nigeria. *Int J Pharm Pharm Sci* 2011;**3**:27–9.

33 Omari DM, Johary D, Salem II, *et al.* Bioequivalence of two oral extended release formulations of ciprofloxacin tablets in healthy male volunteers under fed and fasting conditions. *J Bioequivalence Bioavailab* 2011;**3**:038–42. doi:10.4172/jbb.1000055

34 Singhal GL, Kotwani A, Nanda A. Jan Aushadhi stores in India and quality of medicines therein. *Int J Pharm Pharm Sci* 2011;**3**:204–7.

35 Ashraful Islam S., Dewan I, Shahriar M, *et al.* Validation and application of a simple HPLC method for the comparative in vitro dissolution study of some multisource ciprofloxacin tablets. *IJPI ' s J Anal Chem* 2012;**2**:1–12.

36 Olanrewaju OJ, Paul AC, Olusola AM. Quality assessment of amoxicillin-clavulanate potassium tablets in Lagos, Nigeria. *J Chem Pharm Res* 2012;**4**:5032–8.

37 Onanuga A, Eboh DD. Biological Activities of Ciprofloxacin tablets and Gentamicin injections commonly used in. *J Pharm Biomed Sci* 2012;**14**:1–6.

38 Nambiar S, Madurawe RD, Zuk SM, *et al.* Product quality of parenteral vancomycin products in the United States. *Antimicrob Agents Chemother* 2012;**56**:2819–23. doi:10.1128/AAC.05344-11

39 Hadwiger ME, Sommers CD, Mans DJ, *et al.* Quality assessment of U.S. marketplace vancomycin for injection products using high-resolution liquid chromatography-mass spectrometry and potency assays. *Antimicrob Agents Chemother* 2012;**56**:2824–30. doi:10.1128/AAC.00164-12

40 Qureshi MN, Rahman IU, Marwat GA. Comparative analysis of ciprofloxacin in different pharmaceutical products by high performance liquid chromatograph. *Sci Technol Dev* 2012;**31**:69–73.

41 Kahaliw W, Ashenef A. Comparative quality evaluation of some metronidazole tablets and metronidazole benzoate oral suspensions available in retail outlets of Addis Ababa, Ethiopia. *Int J Pharm Sci Res* 2013;**4**:1384–91.

42 N. Rahim, S. Baquir Shyum Naqvi, E. Iqbal, S. Nesar, U. Abdul Khaliq SKH. Investigation on Pharmaceutical Quality of Different Brands of Cefadroxil Monohydrate Available in Karachi, Pakistan. *Indo Am J Pharm Res* 2013;**3**:4557–84.

43 Hussain A, Hanif M, Shoaib M, *et al.* Comparative studies of ciprofloxacin 250 mg tablets available in pakistani market. *Lat Am J Pharm* 2013;**32**:484–9.http://www.latamjpharm.org/

44 Birhanu G, Kassa F, Hymete A, *et al.* Comparative in-vitro quality evaluation of erythromycin stearate tablets marketed in Addis Ababa, Ethiopia. *Int J Pharm Sci Res* 2013;**4**:378–85.http://www.ijpsr.com/

45 Akhtar MS, Malik A, Bashir S, *et al.* Pharmaceutical evaluation of different brands of Levofloxacin tablets (500MG) available in Pakistan. *Int J Curr Pharm Res* 2013;**5**:42–5.

46 Kassaye L, Genete G. Evaluation and comparison of in-vitro dissolution profiles for different brands of amoxicillin capsules. *African Heal Sci* 2013;**13**:369–75. doi:10.4314/ahs.v13i2.25

47 Pais KP, Panchmal GS, Shenoy R, *et al.* Comparison of medicine quality of the generic formulation of amoxicillin provided by the government of Karnataka with marketed brands - a public health perspective. *Int J Pharm Sci Rev Res* 2013;**23**:37–42.

48 Naveed S, Waheed N. Comparative study of three different brands of doxycycline capsules available in Karachi. *Open Access Libr J* 2014;**1**:1–7. doi:10.4236/oalib.1100458

49 Khamis ANR, Khan SA. Comparative in-vitro pharmaceutical evaluation of four brands of Metronidazole tablets marketed in gulf region. *Jordan J Pharm Sci* 2014;**7**:144–52. doi:10.12816/0027235

50 Al-Tahamani K. Quality and stability of co-amoxiclav products in Yemeni market. *J Chem Pharm Res* 2014;**6**:565–9.

51 Arnet I, Altermatt M, Roggo Y, *et al.* Pharmaceutical quality of eight generics of ceftriaxone preparation for injection in Eastern Asia. *J Chemother* 2015;**27**:337–42. doi:10.1179/1973947814Y.0000000208

52 Aliyu S. *Comparative bioequivalence studies of some brands of metronidazole tablets marketed in Zaria, Nigeria*. 2014.

53 Humayoon R, Razvi N, Anjum F, *et al.* Quality control testing and equivalence of Doxycycline Hyclate (100 mg) capsule brands under biowaiver conditions. *J Pharm Drug Deliv Res* 2014;**03**. doi:10.4172/2325-9604.1000124

54 Idries AM, Ibrahim KE. Microbiological Assay of Two Selected Products of Ceftriaxone Powder for Injection from Pharmaceuticals' Market in Sudan. *Sudan J Med Sci* 2014;**9**:251–8.

55 Fahmy S, Abu-Gharbieh E. In vitro dissolution and in vivo bioavailability of six brands of ciprofloxacin tablets administered in rabbits and their pharmacokinetic modeling. *Biomed Res Int* Published Online First: 2014. doi:10.1155/2014/590848

56 Fayyaz M, Yousuf RI, Shoaib MH, *et al.* Quality evaluation and in vitro interaction studies between levofloxacin 250mg and diclofenac sodium 50mg tablets. *Pak J Pharm Sci* 2015;**28**:119–28.

57 Hamam SBH. Comparative in vitro evaluation of generic ciprofloxacin hydrochloride tablets. *World J Pharm Pharm Sci* 2014;**3**:388–96.

58 Malele R., Mwambete K., Hassanali L. Antibacterial effects of nine brands of ciprofloxacin tablets available in Dar es Salaam. *East Cent African J Pharm Sci* 2014;**17**:10–7.

59 Nettey H, Allotey-Babington GL, Debrah P, *et al.* The quality and in vitro efficacy of amoxicillin/clavulanic acid formulations in the central region of Ghana. *Pharmacol Pharm* 2014;**5**:49–60. doi:10.4236/pp.2014.51009

60 Jaman M, Chowdhury AA, Rana AA, *et al.* In vitro evaluation of Ciprofloxacin Hydrochloride. *Bangladesh J Sci Ind Res* 2015;**50**:251–6. doi:10.3329/bjsir.v50i4.25833

61 Aljohani BA. *Pharmaceutical bioequivalence studies: Ensuring safety, effectiveness and high quality*. 2015.

62 Bashir S, Nasir SR, Usman F, *et al.* Comparative in-vitro evaluation of antibacterial activity of levofloxacin brands available in Pakistan. *Adv Life Sci* 2015;**2**:165–70.

63 Bendari A, Al-shehi B, Ahuja A. Comparison of pharmaceutical properties of different marketed brands of metronidazole tablets available in Oman. *Int J Pharm Arch* 2015;**4**:9–21.

64 El Attug MN, Ammar A, Tunsi S, *et al.* Pharmaceutical evaluation of an Augmentin brand manufactured in different countries. *Am J Pharm Pharmacol* 2015;**2**:35–44.

65 Alzomor AK, Al-Madhagi Y, Noman NM, *et al.* Quality Assessment of Ten Co-trimoxazole Brands as Tablet Compared to the Original Brand in

Yemeni Market. *Int J Biol Pharm Allied Sci* 2016;**5**:2746–56.

66 Shraim N, Zaid AN, Malkieh N, *et al.* Investigation of the interchangeability between cefuroxime axetil tablets marketed in Palestine. Is there a quality reason behind the price? *Palest Med Pharm J* 2016;**1**:7–14.

67 Idrees M. *Analysis of amoxicillin in counterfeit antibiotics from the Subcontinent and the Middle East*. Unplished MSc by Res. Thesis. 2009.

68 Israr F, Mahmood ZA, Hassan F, *et al.* Pharmaceutical evaluation of cefuroxime axetil tablets available in drug market of Pakistan. *Indian J Pharm Sci* 2016;**78**:17–26. doi:10.4103/0250-474X.180242

69 Osonwa UE, Abali SO, Chukwu KI, *et al.* Quality assessment of fifteen different brands of ciprofloxacin hydrochloride tablets marketed in Anambra State, Nigeria. *African J Pharm Res Dev* 2016;**8**:1–8.

70 Pathak P, Dawane J. In vitro comparison of generic and branded preparations of amoxicillin with potassium clavulanate. *J Clin Diagnostic Res* 2016;**10**:FC07–9. doi:10.7860/JCDR/2016/20009.8466

71 Adeniyi BA, Ayolabi CI, Ukonu EJ. Comparative antimicrobial activity of five brands of ciprofloxacin sold in Lagos state. *J Nat Sci Eng Technol* 2016;**15**:21–32.

72 Al-Tabakha MM, Fahelelbom KMS, Obaid DEE, *et al.* Quality attributes and in vitro bioequivalence of different brands of amoxicillin trihydrate tablets. *Pharmaceutics* 2017;**9**:1–11. doi:10.3390/pharmaceutics9020018

73 Uddin S, Mamun A Al, Hossain S, *et al.* In vitro quality evaluation of leading brands of ciprofloxacin tablets available in Bangladesh. *BMC Res Notes* 2017;**10**:1–9. doi:10.1186/s13104-017-2507-y

74 Manani RO, Abuga KO, Chepkwony HK. Pharmaceutical equivalence of clarithromycin oral dosage forms marketed in Nairobi County, Kenya. *Sci Pharm* 2017;**85**. doi:10.3390/scipharm85020020

75 Noor S, Salam FBA, Hima HN, *et al.* Comparative in-vitro quality evaluation of some brands of metronidazole tablet available in Bangladesh. *Int J Appl Res* 2017;**3**:753–8.

76 Gberindyer FA, Abatan MO, Wiesner L. Composition of gentamicin C components in gentamicin sulphate generics commonly used in small animal practice in Nigeria. *J Pharm Pharmacol* 2017;**5**:20–5. doi:10.17265/2328-2150/2017.01.005

77 Fatima S, Jamil S, Gauhar S, *et al.* In-vitro dissolution testing for therapeutic equivalence of metronidazole immediate release tablets available in Karachi, Pakistan. *Int J Pharm Sci Res* 2017;**8**:3133–7. doi:10.13040/ijpsr.0975-8232.8(7).3133-37

78 Alyahawi A, Alsaifi A. Quality control assessment of different brands of ciprofloxacin 500mg tablets in Yemen. *Univers J Pharm Res* 2018;**3**:29–33. doi:10.22270/ujpr.v3i4.180

79 Hasin F, Hossain M, Ghosh KK, *et al.* Pharmaceutical quality evaluation of cefuroxime axetil tablets available in drug market of Bangladesh. *World J Pharm Pharm Sci* 2018;**7**:1589–99. doi:10.20959/wjpps20181-10886

80 Gogoi B, Baishya H, Bordoloi R, *et al.* Quality control parameters of two different brands of ciprofloxacin tablets IP available commercially as per Indian Pharmacopoeia. *World J Pharm Res* 2018;**7**:1203–11. doi:10.20959/wjpr20182-10794

81 Shaibu AN, Audu AA. Physico-chemical and metal impurity assessment of some brands of ciprofloxacin hydrochloride tablets marketed in Kano Metropolis, Nigeria. *ChemSearch J* 2018;**9**:65–75.

82 Thamer HA, Haddad NS, Jawad AM. Analysis of drug contents of cefotaxime formulations available in the local market and the effect of storage conditions. *Int J Med Pharm Sci* 2018;**8**:11–8. doi:10.24247/ijmpsapr20183

83 Obarisiagbon AJ, Ogunlowo OP. Erythromycin Stearate Tablets: Quality Assurance Assessment. UK Essays. 2018.https://www.ukessays.com/essays/chemistry/erythromycin-stearate-tablets-quality-assurance-4970.php?vref=1 (accessed 24 May 2021).

84 Thambavita D, Fernando S, Galappatthy P, *et al.* Application of biowaiver methodology for a post-marketing study of generic and brand name metronidazole tablets. *Dissolution Technol* 2018;**25**:34–8. doi:10.14227/DT250218P34

85 Ukwueze S, Nwachukwu IP, Ezealisiji K. Ultraviolet spectrophotometric evaluation of different brand of azithromycin dihydrate tablets and capsules sold in Nigeria. *Eur J Pharm Med Res* 2018;**5**:80–4.

86 Igboasoiyi AC, Offor AC, Egeolu AP. Quality assessment of various brands of ciprofloxacin hydrochloride tablets sold in Uyo Metropolis. *Niger J Pharm Appl Sci Res* 2018;**7**:89–93.

87 Rafiq M, Khan TR, Iftikhar S, *et al.* Comparative quality control tests for different medicines supplied by medical store depot to health facilities and similar generics available in the market. *Indo Am J Pharm Sci* 2018;**5**:4914–9. doi:10.5281/ZENODO.1286148

88 Ogochukwu U, Christianah I, Marlene E, *et al.* Quality assessment of some brands of clarithromycin and azithromycin tablets using the concept of dissolution efficiency and similarity factor. *Int J Pharm Sci Res* 2018;**9**:5401–10. doi:10.13040/IJPSR.0975-8232.9(12).5401-10

89 Bagbi BM, Alagala MB, Ovwenahaye O, *et al.* Product quality assessment of brands of cefuroxime axetil tablets marketed in southern and western Nigeria. *Pharma Innov J* 2018;**7**:84–9.

90 Anah VU, Ebong AS, Charles GE, *et al.* Quantitative and qualitative analysis of some brands of ciprofloxacin tablets sold in Uyo metropolis, Akwa Ibom State, Nigeria. *Niger J Pharm Appl Sci Res* 2019;**8**:15–22.

91 Avianto P, Mahfudz M, Suharjono S, *et al.* In vitro equivalence of generic and branded amoxicillin tablet by microbiological assay method. *J Basic Clin Physiol Pharmacol* Published Online First: 2019. doi:10.1515/jbcpp-2019-0247

92 Pereira dos Anjos J, Sherratt S, Viana JD, *et al.* Detection of impurities in anti-infective generic drugs in Brazil by Liquid Chromatography-Mass Spectrometry. *J Bioeng Technol Appl to Heal* 2019;**2**:36–46. doi:10.34178/jbth.v2i2.55

93 Rahman M, Haque MA, Fahim NF. Comparative quality evaluation of different brands of ciprofloxacin tablets available in pharmaceutical market of Bangladesh. *Pharmacol Online* 2019;**1**:43–9.

94 Shah MR, Nasiri MI, Anwer S, *et al.* Pharmaceutical quality assessment of different brands of moxifloxacin 400 mg tablets available in Pakistan. *RADS J Pharm Pharm Sci* 2019;**7**:2–8.

95 Sharif H, Sharif S, Diwan H. Direct analysis of substandard antibiotics sensitivity pattern against common isolates of pathogens via modified Outerlony technique-A vitro study in Karachi. *Int J Curr Sci Multidiscip Res* 2019;**2**:126–34.

96 Uwambajineza T, Tuyishime F, Mugwiza E, *et al.* A survey of the quality of selected antibiotics in Kigali. Academia. 2019.https://www.academia.edu/38187916/A_SURVEY_OF_THE_QUALITY_ON_SELECTED_ANTIBIOTICS_IN_KIGALI_pdf (accessed 24 May 2021).

97 Hambisa S, Belew S, Suleman S. In vitro comparative quality assessment of different brands of norfloxacin tablets available in Jimma, Southwest Ethiopia. *Drug Des Devel Ther* 2019;**13**:1241–9. doi:10.2147/DDDT.S189524

98 Agudelo M, Rodriguez CA, Zuluaga AF, *et al.* Nontherapeutic equivalence of a generic product of imipenem-cilastatin is caused more by chemical instability of the active pharmaceutical ingredient (imipenem) than by its substandard amount of cilastatin. *PLoS One* 2019;**14**. doi:10.1371/journal.pone.0211096

99 Badulla WFS, Al-Omary YST, Ali KS. In vitro antimicrobial activity evaluation for different pharmaceutical dosage forms of ciprofloxacin Aden-Yemen. *Electron J Univ Aden Basic Appl Sci* 2020;**1**:93–9.

100 Desta HK, Teklehaimanot TT. In vitro quality evaluation of generic ciprofloxacin tablets available in community pharmacies of Dessie town, Northeast Ethiopia. *J Generic Med* 2020;**0**:1–8. doi:10.1177/1741134320921929

101 Hobeika E, Farhat J, Saab J, *et al.* Are antibiotics substandard in Lebanon? Quantification of active pharmaceutical ingredients between brand and generics of selected antibiotics. *BMC Pharmacol Toxicol* 2020;**21**:1–12. doi:10.1186/s40360-020-0390-y

102 Leficho AW, Lambore AH, Olbemo KS, *et al.* In-Vitro comparative quality assessment of different brands of doxycycline hyclate finished dosage forms: capsule and tablet in Jimma Town, South West Ethiopia. Reprints. 2020. doi:10.20944/preprints202004.0070.v1

103 Oli AN, Ibeabuchi MU, Enweani IB, *et al.* Pharmaceutical quality of selected metronidazole and ciprofloxacin infusions marketed in South Eastern Nigeria. *Drug Healthc Patient Saf* 2020;**12**:103–12. doi:10.2147/DHPS.S246050

104 Rahman M, Jahan FI, Fahim NF, *et al.* In vitro comparative quality evaluation of leading brands of metronidazole tablets available in Bangladesh. *Pharmacol Online* 2020;**2**:63–72.

105 Tolentino-Hernández SJ, Cruz-Antonio L, Torres-Roque I, *et al.* Bioequivalence of two oral ciprofloxacin extended-release formulations in healthy Mexican volunteers. *Lat Am J Clin Sci Med Technol* 2020;**2**:85–90. doi:10.34141/ljcs1055083

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 12: Seizures/Recalls/Alerts/Case-reports of substandard and falsified antibiotics

Country	API/combination of APIs	Year	No. Batch/ Case	Quality test failure	Report Type	Ref
Cameroon	Metronidazole	Mar-2015	Unstated	Falsified-"Traffic de médicaments: 35 millions FCFA de médicaments contrefaits détruits dans la ville de Bafoussam […] Entre autres médicaments détruits, l'on a pu dénombrer du Métronidazole intraveineux Metlife 500mg/100ml […]"	Seizure	[1]
	Amoxicillin, Ampicillin	2016	Unstated	Falsified–no API	Recall/Warning/Alert	[2]
	Phenoxymethylpenicillin (Penicillin V)	Nov-2017	1	Falsified–wrong API (tablet contained paracetamol 50mg)	Recall/Warning/Alert	[3]
	Amoxicillin-Clavulanic acid	Mar-2018	1	Falsified–"[…] packaging appears to be a close imitation of the genuine product but GlaxoSmithKline confirmed they did not manufacture it."	Recall/Warning/Alert	[4]
Cambodia	Antibiotics-unspecified	Nov-2018	Unstated	SorF-"[…] illegal goods and substandard medication […] included […] antibiotics"	Seizure	[5]
Canada	Ampicillin, Doxycycline	Sept-2015	Unstated	Unregistered - seized at "Taste of Ukraine" in Burnaby	Seizure	[6]
	Amoxicillin, Ampicillin	May-2018	Unstated	Unregistered - seized from Gigi's Market, Ottawa	Seizure	[7]
Costa Rica	Ceftriaxone	Feb-2018	1	Falsified–contains cefazolin and a low concentration of unidentified contaminants.	Recall/Warning/Alert	[8]
Democratic Republic of Congo	Chloramphenicol, Sulfamethoxazole-Trimethoprim	2012	46	Falsified-"cotrimoxazole bought at illicit points of sale is the main etiology of fixed drug eruption"	Case report	[9]
	Amoxicillin, Ampicillin	Oct-2015	1	Falsified–no API	Recall/Warning/Alert	[10]
	Nalidixic acid	Jan-2016	Unstated	Falsified–no API ("30,000 false tablets")	Recall/Warning/Alert	[11]
	Cefixime	Jan-2018	2	Falsified–one batch contained no API and another batch contain 2.5% cefixime	Recall/Warning/Alert	[12]
Dominican Republic	Antibiotics-unspecified	2014	Unstated	Falsified-"Among the drugs seized there are […], antibiotics and […]"	Seizure	[13]
	Amoxicillin, Ampicillin	Oct-2015	3	Falsified-"List of the 22 falsified medicines: [….] Amoxicillin 500mg capsules, Amoxicillin 1000mg capsules, Ampicillin 1000mg capsules […]"	Recall/Warning/Alert	[14]
El Salvador	Ampicillin, Nitrofurantoin, Sulfamethoxazole-Trimethoprim	Jan-1991	1	Falsified – "[…] Scanprin tablets 400mg + 80mg score narrower and tablet is 1 mm higher than Scanpharm's; Furinamine s/c tablet 100mg weight approximately 560mg whereas Scanpharm's tablets weight approximately 460mg, colour brighter blue than Scanpharm's tablets; Ampiscan capsules 500mg capsule size 00 without snap fit whereas Scanpharm's capsules are size 0 E with snap fit."	Recall/Warning/Alert	[15]
France	Amoxicillin-Clavulanic Acid	Jan-2019	4	Substandard-labelling with incorrect administration instruction	Recall/Warning/Alert	[16]

Germany	Gentamicin	Jul-1997	1	Substandard-visible particulates	Recall/Warning/Alert	[17]
Guatemala	Gentamicin	Aug-2013	Unstated	Falsified–"A fake version of Gentamicina MK, injection solution 80mg […] under the name Gentamicina MIC"	Recall/Warning/Alert	[18]
Haiti	Ciprofloxacin	Apr-2001	1	SorF-"[…] unclear whether the ciprofloxacin he received in Haiti was substandard, his previous prompt response to quinolones alone suggested that it was."	Case report	[19]
India	Ampicillin, Cefalexin	2003	Unstated	Falsified-"[…] two antibiotics have been identified as Ampoxin-500 and Sporidex-500."	Seizure	[20]
	Amoxicillin-Clavulanic acid	Apr-2013	Unstated	Falsified–no API	Seizure	[21]
	Amoxicillin-dicloxacillin, ofloxacin	Jul-2014	Unstated	SorF–"Karnataka DC dept seizes 20 out-of-std quality drugs from pharmacies […] Staph-AC with amoxicillin and dicloxacillin […] Offmark-Oz containing ofloxacin and ornidazole […] Dorflox-OR (ofloxacin and ornidazole) […] Dibaymox which contains amoxicillin with dicloxacillin […]"	Seizure	[22]
	Ciprofloxacin	Nov-2014	13	SorF-contaminant	Case report	[23]
	Ciprofloxacin	Mar-2015	Unstated	SorF–API contents (not detailed)	Seizure	[24]
	Azithromycin	Jul-2015	1	SorF-visual inspection	Recall/Warning/Alert	[25]
	Cefixime	Jul-2015	1	SorF-API content and identification, dissolution, mass uniformity	Recall/Warning/Alert	[25]
	Erythromycin	Jul-2015	1	SorF-API content and identification, mass uniformity, water content	Recall/Warning/Alert	[25]
	Meropenem	Jul-2015	1	SorF-loss on drying	Recall/Warning/Alert	[25]
	Metronidazole	Jul-2015	1	SorF-dissolution	Recall/Warning/Alert	[25]
	Ceftazidime-Tazobactam	Oct-2015	1	SorF-impurity	Recall/Warning/Alert	[26]
	Clindamycin	May-2016	1	SorF-water content	Recall/Warning/Alert	[27]
	Norfloxacin	May-2016	1	SorF-dissolution	Recall/Warning/Alert	[27]
	Erythromycin	Aug-2016	2	SorF–API content (not detailed)	Seizure	[28]
	Amoxicillin, Cefixime, Ciprofloxacin, Ofloxacin	Dec-2016	Unstated	Falsified –"Koshia told TOI seized drugs included fake amoxicillin, ciprofloxacin, ofloxacin and even high-power antibiotics like cefixime."	Recall/Warning/Alert	[29]
	Gentamicin, Ofloxacin	Jun-2017	Unstated	SorF-"[…] found to be not of standard quality are […] Gentarid fo rIM/IV use which is gentamycin injection […] Lifobid-200 which are ofloxacin tablets […]"	Seizure	[30]
	Levofloxacin	Jul-2018	1	Substandard–low API, failed dissolution test	Case reports	[31]

Amoxicillin-Clavulanic acid	Apr-2019	2	SorF-API content, API identification and particulate matter	Recall/Warning/Alert	[32]
Cefpodoxime	Apr-2019	1	SorF-API content and disintegration	Recall/Warning/Alert	[32]
Ciprofloxacin	Apr-2019	2	SorF-dissolution	Recall/Warning/Alert	[32]
Gentamicin	Apr-2019	1	SorF-particulate matter	Recall/Warning/Alert	[32]
Amikacin	Jun-2019	Unstated	Falsified-"[…] nearly 10,000 fake antibiotic vials of amikacin injection worth Rs 7 lakh were recovered in Agra."	Seizure	[33]
Ceftriaxone	Nov-2019	1	SorF-dissolution	Recall/Warning/Alert	[34]
Amoxicillin-Clavulanic acid	Dec-2019	1	SorF-API content, content uniformity	Recall/Warning/Alert	[35]
Azithromycin, Cefadroxil, Cefuroxime, Ciprofloxacin, Erythromycin, Norfloxacin	Dec-2019	6	SorF-dissolution	Recall/Warning/Alert	[35]
Azithromycin, Neomycin-Polymyxin, Tobramycin	Dec-2019	3	SorF-API content (not detailed)	Recall/Warning/Alert	[35]
Cefixime	Dec-2019	1	SorF-API content, pH, water content	Recall/Warning/Alert	[35]
Cloxacillin	Dec-2019	1	SorF-description, API identification	Recall/Warning/Alert	[35]
Amoxicillin, Amoxicillin-Clavulanic acid, Clindamycin	Feb-2020	3	SorF-API content (not detailed)	Recall/Warning/Alert	[36]
Erythromycin, Metronidazole	Feb-2020	2	SorF-dissolution	Recall/Warning/Alert	[36]
Oxytetracycline	Feb-2020	1	SorF-water content	Recall/Warning/Alert	[36]
Amoxicillin-Clavulanic acid	Apr-2020	1	Substandard-API content (not detailed)	Recall/Warning/Alert	[37]
Cefotaxime	Apr-2020	1	Substandard-impurity	Recall/Warning/Alert	[37]
Cefuroxime, Ofloxacin	Apr-2020	2	Substandard-API content	Recall/Warning/Alert	[37]
Cefpodoxime, Chloramphenicol, Norfloxacin	Apr-2020	4	Substandard-dissolution	Recall/Warning/Alert	[37]
Cefpodoxime, Ciprofloxacin	May-2020	2	SorF-dissolution	Recall/Warning/Alert	[38]
Ofloxacin	May-2020	1	SorF-API identification	Recall/Warning/Alert	[38]
Amoxicillin-Clavulanic acid	Jun-2020	1	SorF-API content (not detailed)	Recall/Warning/Alert	[39]
Cefotaxime	Jun-2020	1	SorF-"water"	Recall/Warning/Alert	[39]
Doxycycline	Jun-2020	2	SorF-API content, mass uniformity	Recall/Warning/Alert	[39]

	Nitrofurantoin	Jun-2020	1	SorF-dissolution	Recall/Warning/Alert	[39]
	Polymyxin B-Chloramphenicol-Dexamethasone	Jun-2020	1	SorF-API content (not detailed)	Recall/Warning/Alert	[39]
	Ciprofloxacin	Jul-2020	1	SorF-API content, dissolution	Recall/Warning/Alert	[40]
Indonesia	Antibiotics-unspecified	Mar-2009	Unstated	Falsified- "Counterfeit products included antibiotics…"	Seizure	[41]
Ireland	Gentamicin-Prednisolone eyedrops	Oct-2001	Unstated	Substandard-preservative efficacy	Recall/Warning/Alert	[42]
Kenya	Amoxicillin-Clavulanic acid	Aug-2019	1	Falsified–no API	Recall/Warning/Alert	[43]
Lao PDR	Tetracycline	Oct-2004	Unstated	SorF-API content	Case report	[44]
Mali	Amoxicillin	Mar-2014	Unstated	Falsified-"[…] district police of Bamako seized 192 cartons of counterfeit medicines. The boxes consisted […] amoxicillin."	Seizure	[45]
Nepal	Amoxicillin	Mar-2004	Unstated	Falsified–no API	Seizure	[46]
Niger	Amoxicillin	Oct-2014	1	Falsified–"[…] the following lots have been identified and confirmed as falsified Amoxycillin B.P 250mg […]"	Recall/Warning/Alert	[47]
Nigeria	Sulfamethoxazole-Trimethoprim	Feb-1993	Unstated	Falsified–wrong API	Recall/Warning/Alert	[48]
	Ampicillin-Cloxacillin, Lincomycin, Sulfamethoxazole-Trimethoprim	Jun-2010	Unstated	Falsified-"The fake drugs intercepted are […] lincomycin capsule 500, ampicillin/cloxacillin 500mg, trimethoprime 80mg/sulfametoxazol 400mg […]"	Recall/Warning/Alert	[49]
	Ampicillin-Cloxacillin, Chloramphenicol	Oct-2011	Unstated	Falsified-API identification	Recall/Warning/Alert	[50]
	Sulfamethoxazole-Trimethoprim	Oct-2011	Unstated	Unregistered-"Banned product"	Recall/Warning/Alert	[50]
	Amoxicillin-Clavulanic acid, Ampicillin-Cloxacillin, Bacitracin-Neomycin, Sulfamethoxazole-Trimethoprim	Jan-2014	Unstated	Falsified-"[…] the seized fake drugs […] Septrin suspension, Cicatrin powder, Ampiclox suspension, Augmentin syrup […]"	Seizure	[51]
Republic of the Philippines	Amoxicillin-Clavulanic acid, Cefdinir, Cefuroxime, Clindamycin, Gentamicin	Mar-2015	Unstated	Unregistered	Recall/Warning/Alert	[52]
	Clarithromycin	May-2015	Unstated	Falsified–no API, visual inspections	Recall/Warning/Alert	[53]
	Amoxicillin-Clavulanic acid	Jul-2015	Unstated	Substandard-Low API content	Recall/Warning/Alert	[54]

Tanzania	Amoxicillin, Ampicillin, Betamethasone-Clotrimazole-Gentamicin	Sep-2005	Unstated	Falsified-visible particulates, related substances, no API	Recall/Warning/Alert	[55]
	Betamethasone-Clotrimazole-Gentamicin	Sept-2005	Unstated	Falsified-low API, wrong API	Recall/Warning/Alert	[55]
Uganda	Tetracycline	Nov-2008	Unstated	Falsified–no API, wrong API (soya flour)	Seizure	[56]
	Ceftriaxone	Jan-2016	1	SorF-low API	Case report	[57]
	Amoxicillin-Clavulanic acid	Aug-2019	1	Falsified–no API	Recall/Warning/Alert	[43]
United Kingdom	Amoxicillin	Jul-2004	Unstated	SorF-low API	Recall/Warning/Alert	[58]
	Chloramphenicol eyedrops	Apr-2019	18	Substandard-incorrect PIL and labelling	Recall/Warning/Alert	[59]
United States of America	Tetracycline	Apr-1963	3	SorF-degraded "[…]patients suffering from Fanconi syndrome with suspicions that it was caused by a degradation product of tetracycline[…]"	Case report	[60]
	Clindamycin	Jun-2017	7	Substandard-microbial contamination	Recall/Warning/Alert	[61]
	Ceftriaxone	Jan-2019	42	Substandard-visual particulate in reconstituted vials	Recall/Warning/Alert	[62]
	Piperacillin-Tazobactam	Jul-2018	2	Substandard-presence of particulates identified as glass and silicone material	Recall/Warning/Alert	[63]
	Tetracycline	Apr-2020	8	SorF-dissolution	Recall/Warning/Alert	[64]
	Ceftazidime	May-2020	1	Substandard-stability	Recall/Warning/Alert	[65]
Unknown	Antibiotics-unspecified	Jun-2013	Unstated	Falsified-"[…] fake medicines seize during Pangea VI were antibiotics."	Seizure	[66]

REFERENCES

1 Donko P. Cameroon - Drug trafficking: 35 million FCFA of counterfeit drugs destroyed in the city of Bafoussam. Cameroon-Info.net. 2015.http://www.cameroon-info.net/article/cameroun-traffic-de-medicaments-35-millions-fcfa-de-medicaments-contrefaits-detruits-dans-la-ville-241500.html (accessed 7 Jun 2021).

2 Tchundju B. Sante : Amoxicillin 250 mg interdit de vente au Cameroun. Camersenat.info. 2016.http://www.camersenat.info/ (accessed 2 Sep 2017).

3 WHO. Medical Product Alert N° 4/2017: Falsified Penicillin V circulating in Cameroon. 2017.https://www.who.int/medicines/publications/drugalerts/drug_alert4-2017/en/ (accessed 1 Oct 2018).

4 WHO. Medical Product Alert N° 2/2018: Falsified 'Augmentin' circulating in Cameroon. 2018.https://www.who.int/medicines/publications/drugalerts/drug_alert2-2018/en/ (accessed 28 Sep 2019).

5 Sovuthy K. Authorities net more than 40 tonnes of counterfeit medicines - Khmer Times. Khmer Times. 2018.https://www.khmertimeskh.com/552535/authorities-net-more-than-40-tonnes-of-counterfeit-medicines/ (accessed 7 Jun 2021).

6 Health Canada. Three unauthorized health products labelled with prescription drug names seized at 'Taste of Ukraine' in Burnaby, B.C. - Recalls and safety alerts. Recalls Saf. alerts. 2015.https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2015/54918a-eng.php (accessed 1 Oct 2018).

7 Health Canada. Advisory - Unauthorized prescription antibiotic drugs seized from Gigi's Market in Ottawa, ON, may pose serious health risks. Cision Canada. 2018.https://www.newswire.ca/news-releases/advisory---unauthorized-prescription-antibiotic-drugs-seized-from-gigis-market-in-ottawa-on-may-pose-serious-health-risks-683078011.html (accessed 1 Oct 2018).

8 Ministerio de Salud Republica de Costa Rica. Deteccion De Medicamento Falso Rocephin 1 Gramo En Costa Rica. Alerta por Prod. en el Merc. 2018.https://registrelo.go.cr (accessed 1 Oct 2018).

9 Ognongo-Ibiaho AN, Atanda HL. Epidemiological study of fixed drug eruption in Pointe-Noire. *Int J Dermatol* 2012;**51**:30–1. doi:10.1111/j.1365-4632.2012.05561.x

10 Minilabs save lives. Minilabs save lives: Falsified antibiotics found in DRC. Minilabs save lives. 2015.https://web.facebook.com/minilab/photos/a.194864549665.125350.182507359665/10153694583429666/?_rdc=1&_rdr (accessed 4 Mar 2019).

11 Minilabs save lives. Falsified nalidixic acid with no active ingredient in DR-Congo. Facebook. 2016.https://www.facebook.com/minilab/posts/10154299278734666:0 (accessed 7 Jun 2021).

12 WHO. Medical Product Alert N° 1/2018: Falsified cefixime products circulating in the Democratic Republic of the Congo. 2018.https://www.who.int/medicines/publications/drugalerts/drug_alert1-2018/en/ (accessed 1 Oct 2018).

13 Anonymous. Health authorities seize counterfeit medicines in Santiago. Dominic. Today. 2014.https://dominicantoday.com/dr/local/2014/7/5/Health-authorities-seize-counterfeit-medicines-in-Santiago/ (accessed 7 Jun 2021).

14 Anonymous. The Dominican Republic Recalls 22 Batches Of Falsified Medicines. Int. Inst. Res. Against Counterfeit Med. 2015.http://www.iracm.com/en/2015/10/the-dominican-republic-recalls-22-batches-of-falsified-medicines/ (accessed 11 Jun 2018).

15 WHO. WHO Alert: Four counterfeit products recalled in El Salvador. 1991.https://www.who.int/

16 Sandoz Inc. Rappel de lots Amoxicilline Acide Clavulanique Sandoz Nourrissons et Enfants Document d ' information pour les patients. 2019.https://www.sandoz.fr/

17 WHO. Alert No. 60: Gentamicin ampoules defective product recall Helm Pharmaceuticals GMBH. 1997.https://www.who.int/

18 International Institute of Research Against Counterfeit Medicines (IRACM). Guatemala: Health Alert on Fake Medicines. Int. Inst. Res. Against Counterfeit Med. 2013.http://www.iracm.com/en/2013/08/guatemala-health-alert-on-fake-medicines/ (accessed 30 Oct 2018).

19 Reidenberg MM, Conner BA. Counterfeit and substandard drugs. *Clin Pharmacol Ther* 2001;**69**:189–93. doi:10.1067/mcp.2001.114672

20 India Express (New Delhi). Bad medicine: Sacks full of fake antibiotics seized. India Environ. Portal. 2003.http://www.indiaenvironmentportal.org.in/content/161624/bad-medicine-sacks-full-of-fake-antibiotics-seized/ (accessed 7 Jun 2021).

21 Hamid PA. Government hospitals in Indian-administered Kashmir supplied spurious antibiotics. Kashmir Newz. 2013.https://www.kashmirnewz.com/n000430.html (accessed 7 Jun 2021).

22 Bureau O. Karnataka DC dept seizes 20 not-of-std quality drugs from pharmacies, cos asked to withdraw stocks. Pharmabiz.com. 2014.http://www.pharmabiz.com/NewsDetails.aspx?aid=82889&sid=1 (accessed 7 Jun 2021).

23 Algar J. Rat poison in antibiotic pills may have killed at least 13 women in India. Tech Times. 2014.https://www.techtimes.com/articles/20314/20141116/shocking-rat-poison-chemical-in-antibiotic-pills-may-have-killed-at-least-13-indian-women-during-sterilization-drive.htm (accessed 12 Jun 2021).

24 Vijay N. Karnataka DC dept seizes 51 not-for-standard qlty drugs; cautions hospitals, public to not to use. Pharmabiz.com. 2015.

25 Central Drugs Standard Control Organization. Drug Alert list for month of July 2015. Notifications-Alerts.

2015.https://cdsco.gov.in/opencms/opencms/en/Notifications/Alerts/ (accessed 7 Jun 2021).

26 Central Drugs Standard Control Organization. Drug Alert list for month of October 2015. Notifications-Alerts. 2015.

27 Central Drugs Standard Control Organization. Drug Alert for the month of May 2016. Notifications-Alerts. 2016.

28 Vijay N. Karnataka DC seizes 11 NSQ drugs, cautions hospitals, public. Pharmabiz.com. 2016.

29 TNN. Fake antibiotics worth Rs 51 lakh seized. The Times of India. 2016.

30 Vijay N. Karnataka drugs control dept detects 16 NSQ drugs, alerts cos and pharmacies. Pharmabiz.com. 2017.http://www.pharmabiz.com/NewsDetails.aspx?aid=102744&sid=1 (accessed 8 Jun 2021).

31 Srinagar. Sale of substandard drugs continues unabated in Kashmir, alleges DAK. United News India. 2018.http://www.uniindia.com/sale-of-substandard-drugs-continues-unabated-in-kashmir-alleges-dak/states/news/1291562.html (accessed 8 Jun 2021).

32 Central Drugs Standard Control Organization. Drug Alert for the month of April 2019. Notifications-Alerts. 2019.

33 TNN. Nearly 10,000 fake antibiotic vials worth Rs 7 lakh recovered in Agra, 4 held. The Times of India. 2019.

34 Central Drugs Standard Control Organization. Drug Alert list for month of November 2019. Notifications-Alerts. 2019.https://cdsco.gov.in/opencms/opencms/en/Notifications/Alerts/ (accessed 8 Jun 2021).

35 Central Drugs Standard Control Organization. Drug Alert list for month of December 2019. Notifications-Alerts. 2019.

36 Central Drugs Standard Control Organization. Drug Alert for the month of February 2020. Notifications-Alerts. 2020.

37 Central Drugs Standard Control Organization. Drug Alert list for month of April 2020. Notifications-Alerts. 2020.

38 Central Drugs Standard Control Organization. Drug Alert for the month of May 2020. Notifications-Alerts. 2020.

39 Central Drugs Standard Control Organization. Drug Alert for the month of June 2020. Notifications-Alerts. 2020.

40 Central Drugs Standard Control Organization. Drug Alert for the month of July 2020. Notifications-Alerts. 2020.

41 Sagita D, Rachman A. Raids uncover counterfeit drugs. Jakarta Globe. 2009.

42 WHO Quality Assurance and Safety of Medicines Team. Alert No. 104: Rapid Alert Notification of a Quality Defect in Prednisolone- Gentamicin (Pred-G) Eye Drops. Rapid Alert Notif. a Qual. Defect. 2001.https://www.who.int/

43 WHO. Medical Product Alert N° 9/2019: Falsified Augmentin found in Uganda and Kenya. World Heal. Organ. 2019.https://www.who.int/medicines/publications/drugalerts/drug_alert-9-2019/en/ (accessed 3 Sep 2019).

44 Jähnke RWO. Counterfeit medicines and the GPHF-Minilab for rapid drug quality verification. *Fachthemen pharmind* 2004;**66**:1187–93.

45 International Institute of Research Against Counterfeit Medicines (IRACM). Mali: Seizure of counterfeit medicines. Media post. 2014.

46 Rai D. Which is real, and which is fake? Nepali Times. 2004.http://archive.nepalitimes.com/news.php?id=3765#.YL8guzb7RpR (accessed 8 Jun 2021).

47 WHO. Alert No. 132: Falsified Medicines west and central Africa. Drug Alert. 2014.https://www.who.int/medicines/publications/drugalerts/Alert_132_FalsifiedMedicinesWestandCentralAfricav2.pdf (accessed 19 Jun 2020).

48 WHO. Alert No. 33: Counterfeit Bactrim (Trimethoprim/sulfamethoxazole) syrup containing Valium (Diazepam). 1993.https://www.who.int/

49 Udoh F. Nigeria: NAFDAC Impounds consignments of fake drugs valued at N500 million. All Africa. 2010.

50 Yinka Oladoyinbo A. NAFDAC raises alarm over circulation of adulterated drugs in Ondo. Niger. Trib. 2011.

51 Adebowale S. Federal Operations Unit of Customs seizes fake drugs worth N12.5m. The Eagle Online. 2017.

52 Uy JR. FDA warns vs 20 unregistered drugs | Inquirer News. Inquirer.net. 2015.https://newsinfo.inquirer.net/680618/fda-warns-vs-20-unregistered-drugs (accessed 8 Jun 2021).

53 Solon A. Solon seeks probe on fake antibiotics. Phillipine Star. 2015.https://newsinfo.inquirer.net/739973/fda-warns-on-fake-antibiotics-for-kids-defective-anti-tb-drug-recalled (accessed 30 Jun 2017).

54 Jaymalin M. Substandard antibiotic recalled from market. Phillipine Star. 2015.http://www.philstar.com/headlines/2015/07/13/1476377/substandard-antibiotic-recalled-market (accessed 6 Jun 2017).

55 Ndomondo-Sigonda M. Counteracting Counterfeiting: Strategies for Improving the Integrity of the Medicinal Marketplace in Tanzania. Tanzania Food Drugs Auth. 2005.

56 Bagala A. 3 held over fake malaria drugs. Dly. Monit. 2008.

57 Nickerson JW, Attaran A, Westerberg BD, *et al.* Fatal Bacterial Meningitis Possibly Associated with Substandard Ceftriaxone — Uganda, 2013. *Morb Mortal Wkly Rep* 2016;**64**:1375–7. doi:10.15585/mmwr.mm6450a2

58 Anonymous. Amoxicillin injection recall. Pharm. J. 2004;**273**:105.

59 Medicines and Healthcare products Regulatory Agency. Class 4 Medicines Defect Information: Chloramphenicol 0.5% W/V Antibiotic Eye Drops (MDR 105-03/19). Drug Alert. 2019.https://www.gov.uk/drug-device-alerts/class-4-medicines-defect-information-chloramphenicol-0-5-w-v-antibiotic-eye-drops-mdr-105-03-19 (accessed 31 May 2019).

60 Frimpter GW, Timpanelli AE, Eisenmenger WJ, *et al.* Reversible 'Faconi syndrome' caused by degraded tetracycline. *JAMA - J Am Med Assoc* 1963;**184**:111–3. doi:10.1001/jama.1963.03700150065010

61 US Food & Drug Administration. Alvogen issues voluntary nationwide recall of clindamycin injection due to a potential for a lack of sterility assurance. Recalls, Mark. Withdrawals, Saf. Alerts. 2017.https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/alvogen-issues-voluntary-nationwide-recall-clindamycin-injection-due-potential-lack-sterility (accessed 8 Jun 2021).

62 US FDA. Lupin Pharmaceuticals, Inc. Issues Voluntary Recall of Ceftriaxone for Injection USP, 250mg, 500mg, 1g and 2g | FDA. Recalls, Mark. Withdrawals, Saf. Alerts. 2019.https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/lupin-pharmaceuticals-inc-issues-voluntary-recall-ceftriaxone-injection-usp-250mg-500mg-1g-and-2g (accessed 25 Jan 2019).

63 US FDA. AuroMedics Pharma LLC Issues Voluntary Nationwide Recall of Piperacillin and Tazobactam for Injection 3.375 grams per Vial, Due to Presence of Particulates Identified as Glass and Silicone Material | FDA. Recalls, Mark. Withdrawals, Saf. Alerts. 2018.https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/auromedics-pharma-llc-issues-voluntary-nationwide-recall-piperacillin-and-tazobactam-injection-3375 (accessed 10 Aug 2018).

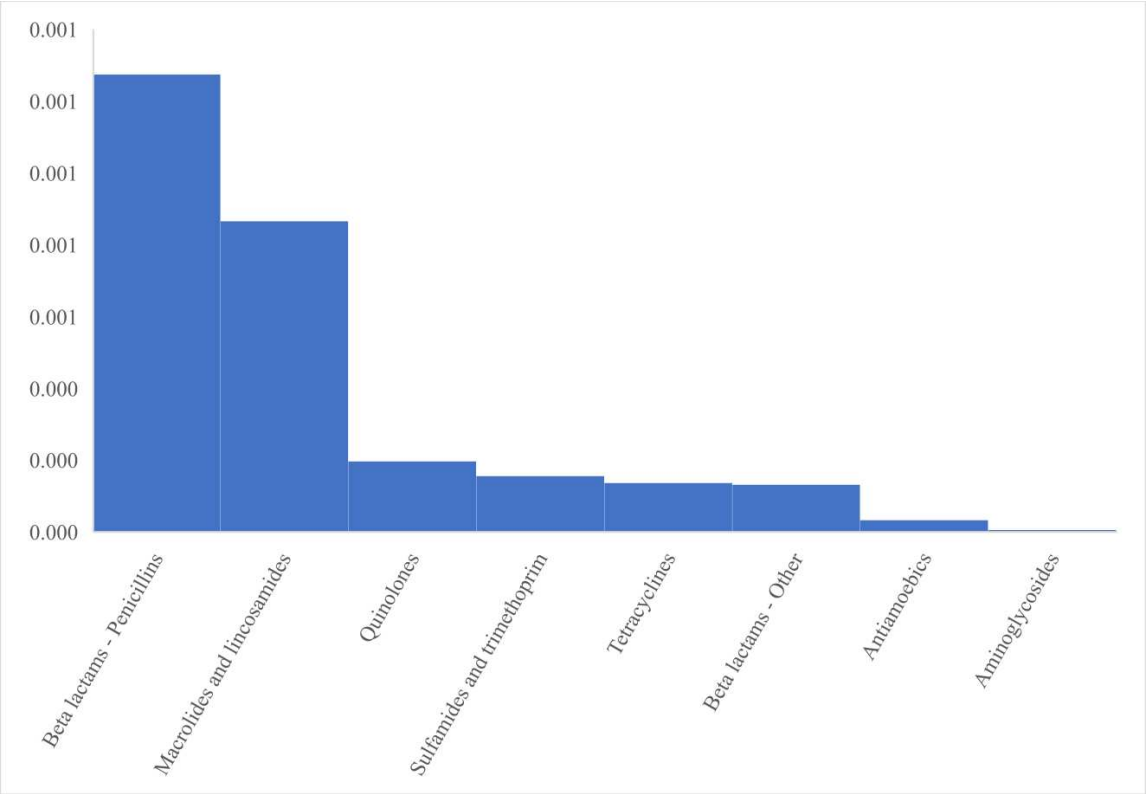
64 US Food & Drug Administration. Avet Pharmaceuticals Inc. issues voluntary nationwide recall of tetracycline HCl capsules USP, 250mg and 500mg due to failed dissolution specifications. Recalls, Mark. Withdrawals, Saf. Alerts. 2020.

65 US Food & Drug Administration. Ceftazidime injection by B. Braun: Recall - due to Out-of-Specification results for high molecular weight polymers. MedWatch. 2020.https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/b-braun-medical-inc-issues-voluntary-nationwide-recall-one-1-lot-ceftazidime-injection-usp-and (accessed 8 Jun 2021).

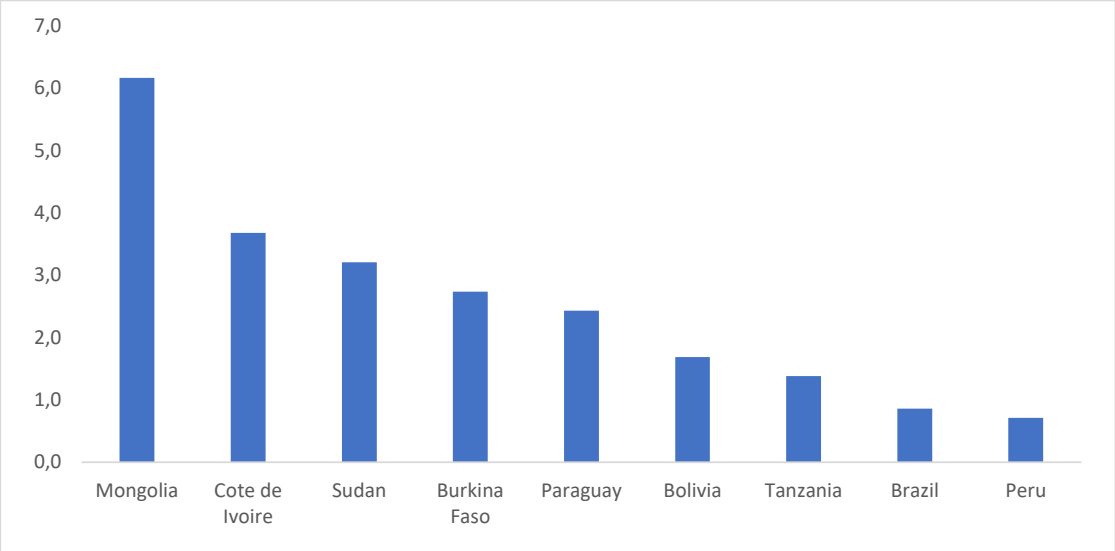
66 Taylor P. Pangea VI swoop nets $41m-worth of fake medicines. Secur. Ind. 2013.

Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?

Supplementary file 13. Index of substandard and falsified antibiotic consumption.



Global median SF antibiotic consumption measured in Defined Daily Doses per 1,000 inhabitants per day (Y axis), for different antibiotic groups. Calculated by multiplying global FF times global AMC



Median SF antibiotic AMC (in DDD per 1,000 inhabitants per day) (Y axis) for countries in which the WHO AMC report and our review had matching data.[1]

1 World Health Organization. WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation. 2018;:1–127.https://www.who.int/medicines/areas/rational_use/oms-amr-amc-report-2016-2018/en/ (accessed 8 Sep 2019).