Systematic Reviews

RESEARCH

Open Access

Antimicrobial prescription pattern and appropriateness for respiratory tract infection in outpatients: a systematic review and meta-analysis

Gashaw Enbiyale Kasse[1,2*], Suzanne M. Cosh[3], Judy Humphries[1] and Md Shahidul Islam[1]

Abstract

Background Millions of people die every year as a result of antimicrobial resistance worldwide. An inappropriate prescription of antimicrobials (e.g., overuse, inadequate use, or a choice that diverges from established guidelines) can lead to a heightened risk of antimicrobial resistance. This study aimed to determine the rate and appropriateness of antimicrobial prescriptions for respiratory tract infections.

Methods This review was conducted in accordance with the PRISMA guidelines. Web of Science, PubMed, ProQuest Health and Medicine, and Scopus were searched between October 1, 2023, and December 15, 2023, with no time constraints. Studies were independently screened by the first author and the co-authors. We included original studies reporting antimicrobial prescription patterns and appropriateness for respiratory tract infections. The quality of included studies' was assessed via the Joanna Briggs Institute's Critical Appraisal Checklists for Cross-Sectional Studies. The assessment of publication bias was conducted using a funnel plot and Egger's regression test. A random effect model was employed to estimate the pooled antibiotic prescribing and inappropriate rates. Subgroup analysis was conducted by country, study period, data source, and age group.

Results Of the total 1220 identified studies, 36 studies were included in the review. The antimicrobial prescribing rate ranged from 25% (95% CI 0.24–0.26) to 90% (95% CI 0.89–0.91). The pooled antimicrobial prescription rate was 66% (95% CI 0.57 to 0.73). Subgroup analysis by region revealed that the antimicrobial prescription rate was highest in Africa (79%, 95% CI 0.48–0.94) and lowest in Europe (47%, 95% CI 0.32–0.62). Amoxicillin and amoxicillin-clavulanate antimicrobials from the Access group, along with azithromycin and erythromycin from the Watch group, were the most frequently used antimicrobial agents. This study revealed that the major reasons for antimicrobial prescription were acute bronchitis, pharyngitis, sinusitis, and the common cold. The pooled inappropriate antimicrobial prescription rate was 45% (95% CI 0.38–0.52). Twenty-eight of the included studies reported that prescribing antimicrobials without proper indications was the main cause of inappropriate antimicrobial prescriptions. Additionally, subgroup analysis by region showed a higher inappropriate antimicrobial prescription rate in Asia at 49% (95% CI 0.38–0.60). The result of the funnel plot and Egger's tests revealed no substantial publication bias (Egger's test: $p = 0.268$).

*Correspondence:
Gashaw Enbiyale Kasse
gkasse@myune.edu.au; Gashaw.enbiyale@uog.edu.et
Full list of author information is available at the end of the article

Conclusion The prescribing rate and inappropriate use of antimicrobials remain high and vary among countries. Further studies should be conducted to generate information about factors contributing to unnecessary antimicrobial prescriptions in outpatients.

Systematic review registration Systematic review registration: CRD42023468353.

Keywords Antimicrobial prescription, Antimicrobial resistance, Outpatient, Respiratory tract infections

Introduction

Antimicrobial resistance is an increasing public health concern worldwide, causing millions of deaths per year [1]. Recent studies reported approximately 5 million deaths worldwide in 2019 and this number is expected to double by 2050 [2, 3]. The misuse and overuse of antimicrobials contribute to the development of antimicrobial resistance. According to Klein, et al. [4], antibiotic consumption expressed in defined daily doses (DDDs) increased by 65% (21.1–34.8 billion DDDs) across 76 countries between 2000 and 2015. The rise of antimicrobial resistance has been further exacerbated by inadequate infectious prevention practices and limited access to healthcare facilities in various [5]. According to a report by the World Bank [6], antimicrobial resistance could lead to a significant economic burden, potentially costing the global economy up to $100 trillion by 2050 due to increased healthcare costs and lost productivity.

Acute respiratory tract infections are a major reason for outpatient visits and are frequently treated with antimicrobials [7]. A study in the USA reported that acute respiratory tract infection accounts for a significant proportion of all outpatient antimicrobial prescriptions [8]. However, it is important to note that antimicrobials provide limited benefits for such infections, and their excessive use contributes to the growing problems of antimicrobial resistance [9]. Viruses cause most upper respiratory tract infections, are self-limiting, and do not require antibiotic treatment [10, 11]. For example, a study highlighted that approximately 72% of primary healthcare visits for acute respiratory tract infections did not require antimicrobial prescriptions [12]. A study conducted by Smith, et al. [13] reported that antimicrobials are prescribed for upper respiratory tract infections in up to 60% of cases in primary healthcare settings, despite evidence indicating that such treatments do not improve outcomes. Inappropriate antimicrobial prescription practices including overuse, inadequate use, and improper selection of antimicrobials (where the choice diverges from established guidelines), may lead to diverse clinical outcomes and antimicrobial resistance [14]. Studies have shown that more than half of the antimicrobials taken globally are inappropriately prescribed, distributed, or marketed [15, 16]. Furthermore, a study found that the inappropriate use of antimicrobials was associated with increased healthcare costs and prolonged hospital stays [4].

Several surveillance studies have examined the appropriateness of antimicrobial prescriptions for outpatients with acute respiratory tract infections in terms of indications, frequency, and duration. For example, a study in Italy explored antimicrobial prescribing patterns for the upper respiratory tract in pediatric patients and reported that 27.4% of the prescribed antimicrobials were inappropriate [17]. Similarly, another study in Jordan found that antimicrobials were inappropriately prescribed at a high rate (71%) for respiratory tract infections in the outpatient setting [18]. Furthermore, research in Tunisia also investigated the appropriateness of antibiotic use for acute respiratory infections and found that 75% of antimicrobials were prescribed inappropriately in primary care settings [19]. These studies shed light on the importance of understanding prescribing patterns and the appropriate use of antimicrobials for respiratory tract infections in outpatient settings. A review of the available evidence on the use of antibiotics for respiratory tract infection is therefore critical to compacting antimicrobial resistance, as it helps to identify patterns of overuse and misuse, informs targeted interventions, and guides policy changes aimed at improving prescribing practice. This will contribute to achieving the World Health Organization's plan to compact antimicrobial resistance [20]. However, a systematic review and meta-analysis of existing quantitative evidence are lacking. This study aims to fill this gap by providing a concise summary of the available evidence regarding the patterns and appropriateness of antimicrobial prescriptions for respiratory tract infection in outpatients.

Materials and methods

Protocol and registration

This systematic review was conducted based on the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) 2020 guidelines [21]. The protocol was registered in the international Prospective Register of Systematic Reviews (PROSPERO) (CRD42023468353).

Eligibility criteria

The focus of the review was to examine quantitative studies reporting on antibiotic prescribing rates and

appropriateness for respiratory tract infections in outpatient settings. On the basis of this objective, the inclusion criteria for this review were (1) studies that assessed the appropriateness and/or patterns of antimicrobial prescriptions for respiratory tract infection, (2) original studies published in peer-reviewed journals in English, (3) conducted in outpatient settings, and (4) quantitative study designs. Systematic reviews, study protocols, studies not published in English, those not published in peer-reviewed journals, editorials, conference abstracts, qualitative studies, and case reports were excluded.

Information source and search strategy

A comprehensive literature search was performed in PubMed, Web of Science, ProQuest Health and Medicine, and Scopus from October 1 to December 15, 2023, without time constraints. A combination of keywords such as "antibiotic" "antimicrobial", "prescriptions", "respiratory tract infection", "appropriate", and "prescription patterns" were used in the search query. We used Boolean operators (AND, OR, *) to identify relevant findings and combine similar phrases/words. Furthermore, the Google Scholar search engine and reference lists from the included articles were used to retrieve relevant articles that might have been missed throughout the database searches. For the full search string seeSupplementary file 1.

Study selection

The search results were imported into EndNote 20 and duplicates were removed. The first author (GK) and co-authors (MSI, JH, and SC) independently screened all studies by title and abstract, with potentially relevant studies then subjected to full-text review. Any disagreements were resolved by discussion.

Data extraction

Data were extracted using prepared data extraction forms and included first author, publication year, objectives, study area (country), sample size, study design, data source, unit of analysis (patients or prescription), age group, healthcare settings, commonly prescribed antimicrobials, diagnosed respiratory tract infection, commonly used antibiotic class, rates of antimicrobial prescriptions and inappropriate use. Data extraction was conducted by the first author and co-authors (MSI, JH, and SC). Any disagreements were resolved through discussion.

Study quality assessment

The methodological quality of the included articles was critically appraised using the Joanna Briggs Institute's Critical (JBI) Appraisal Checklist for Cross-Sectional Studies [22]. This tool contains eight items to assess the quality of cross-sectional studies, with response options including "yes", "no", "unclear" and "not applicable". The first author and co-authors independently appraised the quality of all included articles. Any disagreement was resolved through discussion.

Data analysis and publication bias

RStudio version 4.1.2 was used to analyze the extracted data. The antibiotic prescribing rate and appropriateness of prescription were pooled using a random effect model with a 95% confidence interval (CI) [23]. Cochran's tau^2, Q, H^2, and I^2 were used to quantify heterogeneity. According to Higgins and Thompson [21] if the values of I^2 fall within the range of 0–25%, 25–50%, 50–75%, and above 75% the results were categorized as low heterogeneity, moderate heterogeneity, substantial heterogeneity, and high heterogeneity respectively. Subgroup analysis was performed to investigate whether the variability in effect sizes was explained by differences in the study characteristics. Subgroup analyses of the rate of antibiotic prescriptions were conducted on the basis of region, data source, study period, unit of analysis, and age group. The most prescribed antimicrobials in the selected studies were described using the Access, Watch, and Reserve (AWaRe) framework (WHO, 2021). Publication bias was assessed using a funnel plot. Egger's regression test was used to examine the asymmetry of the funnel plot. Sensitivity analysis was performed by identifying and excluding outliers and influencing studies.

Results

In total, 1220 studies were initially identified. Of these, 1170 articles were obtained through four electronic database searches: Web of Science ($n=250$), Scopus ($n=400$), PubMed ($n=370$), and ProQuest Health and Medicine ($n=150$). The remaining 50 articles were identified from Google Scholar and the reference lists of the included studies. After the removal of duplicates and screening of titles and abstracts, 210 studies were assessed for eligibility. Following the assessment against the inclusion criteria, 36 full-text articles were included in this meta-analysis (Fig. 1, Supplementary file 2).

Study characteristics

All included studies used a cross-sectional study design. The 36 studies included in this review were conducted between 2005 and 2023 across 23 countries, including the USA ($n=5$), China ($n=4$), Italy ($n=3$), Japan ($n=3$), UK ($n=2$) and one study each in the remaining countries ($n=17$) as shown in Table 1. One study was carried out across five countries (Denmark, Sweden, Russia, Argentina Spain, Lithuania) [24]. The included studies focused on the types of prescribed antimicrobials, rates

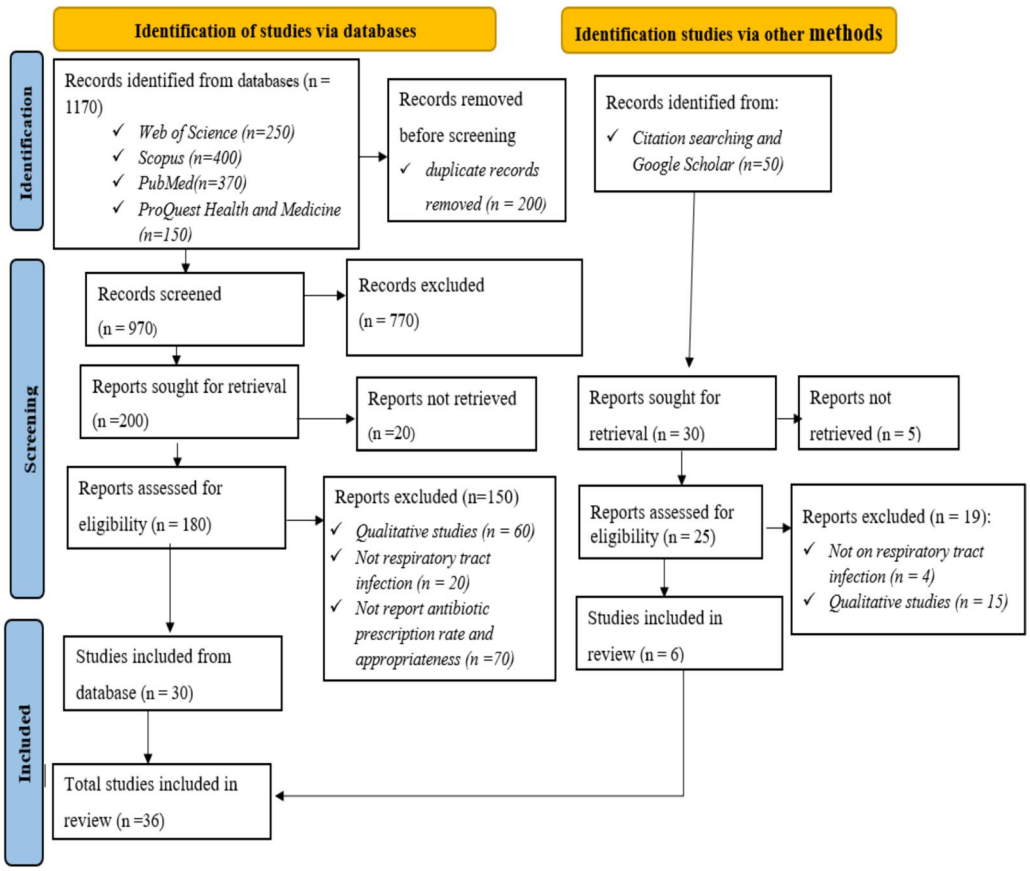

Fig. 1 Flow diagram of study selection (PRISMA 2020 model)

of antimicrobial prescriptions, and appropriateness. In terms of data sources, nine studies used surveys, five studies used prescription audits, and the remaining studies ($n=22$) used electronic medical records (Table 1). The age groups of the participants in the included studies varied; 26 studies considered all age groups, while six studies focused specifically on children, and the remaining four studies targeted adult participants. The unit of analysis in most studies was prescriptions ($n=24$), whereas the other 12 studies used patients as the unit of analysis. In terms of setting, four studies were conducted in both public and private healthcare services, while 30 studies focused on the public sector, and two studies focused on the private sector. From the included studies, six studies [13, 25–29] did not mention the overall antimicrobial prescription rate because their sample consisted of only patients who had received antibiotic prescriptions.

Quality of studies

According to the Joanna Briggs Institute's Critical Appraisal Checklist for cross-sectional studies, 20 studies met all the criteria, addressing the possibility of bias in their design, identifying confounding factors with clearly stated strategies, and conducting appropriate statistical analysis. On the other hand, 16 studies identified confounding factors but did not state strategies to address confounding factors.

Sensitivity analysis and publication bias assessment

There was no difference in the result of the sensitivity analysis. On the basis of the funnel plot, there was no asymmetrical distribution of the effects of the studies. Additionally, Egger's test revealed that there was no statistical evidence for publication bias ($b=0.4098$ CI − 0.1553–0.9750; $p=0.256$). When the outliers were removed, the results of Egger's test and the asymmetry of the funnel plot did not change significantly (seeSupplementary file 3).

Antimicrobial prescription patterns for respiratory tract infections

All included studies reported patterns of antimicrobial prescriptions for respiratory tract infections. As shown in Table 1 penicillin (44%), macrolides (20%), and cephalosporins (12%) were the three main classes of antimicrobials used for respiratory tract infection treatment. The

Table 1 Study characteristics

Author (year of publication)	Country	Sample size	Study design	Data source	Unit of analysis	Age group	Health sector	Prescribed antimicrobials N (%)	Inappropriate antimicrobial prescriptions N (%)	Two most commonly diagnosed infections (from most to least)	Three most commonly used antibiotic classes for RTI (from most to least)	The three most commonly used antibiotics for RTI (from most to least)
Wang, et al. [30]	China	162,742	Cross-sectional	Medical records	Prescriptions	All	Public	138,330 (85%)	63,438 (45.86%)	Acute sinusitis, acute pharyngitis	Cephalosporin, macrolides, penicillin	Penicillin v, ceftriaxone, Azithromycin
Bo, et al. [31]	Malaysia	205	Cross-sectional	Survey (full structured questionnaire)	Patients	All	Private	120 (58.50%)	68 (57.1%)	Acute pharyngitis, acute bronchitis	Macrolides, penicillin	Amoxicillin, azithromycin
Bianco, et al. [32]	Italy	1979	Cross-sectional	Survey (self-administered questionnaire)	Patients	All	Public	1332 (67.3%)	886 (66.5%)	Acute pharyngitis	Cephalosporins, macrolides	Amoxicillin, cefuroxime, azithromycin
Bianco, et al. [17]	Italy	565	Cross-sectional	Survey (face-to-face interview)	Patients	Children	Public	177 (31.3%)	50 (28%)	Pharyngotonsillitis, common cold	Cephalosporins, quinolone	Levofloxacin, ceftriaxone
Smith, et al. [13]	UK	4,574,373	Cross-sectional	Medical records	Prescriptions	All	Public	NA	2,172,827 (48%)	Common cold, acute bronchitis	Penicillin, macrolides	Ampicillin, azithromycin
Giuseppe, et al. [11]	Italy	311	Cross-sectional	Medical records	Patients	Adults	Public	216 (69.4%)	150 (69.4%)	Acute pharyngitis, influenzas	Penicillin, quinolone	Amoxicillin with clavulanic acid amoxicillin, azithromycin
Arnolda, et al. [33]	Australia	2621	Cross-sectional	Survey (questionnaire and observation)	Patients	Children	Both	2280.3 (87%)	1411 (62%)	Bronchitis, common cold	Cephalosporin, macrolides	Ceftriaxone, azithromycin
Alekaw, et al. [34]	Ethiopia	279	Cross-sectional	Medical records	Patients	Children	Public	248 (88.9%)	76 (30.8%)	Pneumonia, acute bronchitis	Penicillin, cephalosporin	Amoxicillin, ceftriaxone
Bagger, et al. [24]	Denmark, Sweden, Russia, Argentina Spain, Lithuania	15,022	Cross-sectional	Survey (self-administered questionnaire and observation)	Patients	All	Public	3755 (25%)	1690 (45%)	Acute sinusitis, pharyngitis	Penicillins, quinolones and macrolides	Amoxicillin, levofloxacin, clarithromycin

Table 1 (continued)

Author (year of publication)	Country	Sample size	Study design	Data source	Unit of analysis	Age group	Health sector	Prescribed antimicrobials N (%)	Inappropriate antimicrobial prescriptions N (%)	Two most commonly diagnosed infections (from most to least)	Three most commonly used antibiotic classes for RTI (from most to least)	The three most commonly used antibiotics for RTI (from most to least)
Bel Haj Ali, et al. [19]	Tunisia	9886	Cross-sectional	Survey (observation and structured questionnaire)	Patients	All	Public	6426 (65%)	1574 (24.5%)	Acute bronchitis, tonsillitis	Penicillin, tetracyclines	Amoxicillin, doxycycline,
Kumari Indira, et al. [35]	India	8910	Cross-sectional	Prescriptions audit	Prescriptions	All	Both	6183 (69.4%)	3092 (50%)	Common cold, pharyngitis	Penicillin, macrolides	Amoxicillin, erythromycin
Chandra Deb, et al. [36]	USA	10,592	Cross-sectional	Patient medical records	Prescriptions	All	Both	9342 (88.2%)	3942 (42.2%)	Acute bronchitis, pharyngitis	Penicillin, cephalosporin	Amoxicillin, ceftriaxone, doxycycline
Shaheen, et al. [37]	Saudi Arabia	908	Cross-sectional	Prescriptions audit	Prescriptions	All	Both	515 (56.7%)	247 (48%)	Common cold, bronchitis	Cephalosporin, macrolides, penicillin	Amoxicillin, ceftriaxone, azithromycin
Al Sous, et al. [38]	Syria	14,913	Cross-sectional	Medical records	Prescriptions	All	Public	13,422 (90%)	8053 (60%)	Acute tonsillitis, acute bronchitis	Cephalosporins, macrolides	Ceftriaxone, azithromycin
Fu, et al. [39]	China	10,678	Cross-sectional	Prescriptions audit	Prescriptions	All	Public	4752 (44.5%)	1473 (31%)	Acute bronchitis, common cold	Cephalosporins, macrolides	Cefuroxime, ceftriaxone, amoxicillin
Fu, et al. [40]	China	212,036	Cross-sectional	Prescriptions audit	Prescriptions	All	Public	159,027 (75%)	47,708 (30%)	Acute bronchitis, CAP	Cephalosporin, quinolone	Ceftriaxone, amoxicillin
Ababneh, et al. [41]	Jordan	5829	Cross-sectional	Survey (questionnaire- interview)	Patients	Children	Public	4570 (78.4%)	3162 (69.2%)	Influenzas, tonsillitis	Penicillin, macrolides	Amoxicillin-clavulanate azithromycin, clarithromycin
Nguyen, et al. [42]	Vietnam	193,010	Cross-sectional	Medical records	Prescriptions	All	Public	129,317 (67%)	58,193 (45%)	Acute pharyngitis, acute bronchitis	Penicillins, cephalosporins,	Vancomycin, cefuroxime, amoxapine

Table 1 (continued)

Author (year of publication)	Country	Sample size	Study design	Data source	Unit of analysis	Age group	Health sector	Prescribed antimicrobials N (%)	Inappropriate antimicrobial prescriptions N (%)	Two most commonly diagnosed infections (from most to least)	Three most commonly used antibiotic classes for RTI (from most to least)	The three most commonly used antibiotics for RTI (from most to least)
Gonzales, et al. [43]	USA	2270	Cross-sectional	Medical records	Prescriptions	All	Public	1430 (63%)	887 (62%)	Acute bronchitis, pharyngitis	Penicillins, cephalosporins,	Azithromycin, amoxicillin, ceftriaxone
Suttajit, et al. [44]	Thailand	4512	Cross-sectional	Medical records	Prescriptions	Adults	Public	2838 (63%)	1788 (63%)	Bronchitis, pharyngitis,	Penicillins, macrolides, fluoroquinolones,	Amoxicillin with clavulanic acidic, dicloxacillin
Barlam, et al. [45]	USA	4942	Cross-sectional	Medical records	Prescriptions	All	Public	3509 (71%)	1579 (45%)	Bronchitis, Acute pharyngitis	Macrolides, penicillin	Roxithromycin, ceftriaxone, amoxicillin
Ishida, et al. [46]	Japan	3940	Cross-sectional	Medical records	Prescriptions	Adults	Public	3546 (90%)	461 (13%)	Common cold, bronchitis	Penicillins, cephalosporins,	Azithromycin, amoxicillin
Moon, et al. [27]	Sierra Leone	777	Cross-sectional	Survey (questionnaire interview)	Patients	Children	Pubic	NA	218 (28%)	Bronchiolitis, pneumonia	Macrolides, penicillin	Ampicillin + gentamicin, ceftriaxone
Keohavong, et al. [47]	Japan	576	Cross-sectional	Medical records	Prescriptions	Children	Public	397 (68.8%)	269 (68%)	Common cold	Penicillin, macrolides	Amoxicillin, ampicillin, erythromycin,
Sánchez Choez, et al. [48]	Ecuador	1393	Cross-sectional	Medical records	Patients	All	Public	523 (37.5%)	471 (90%)	Common cold, acute tonsillitis	Cephalosporins, macrolides	Benzathine penicillin + Amoxicillin', Benzathinepenicillin + azithromycin'
Chang, et al. [26]	China	74,648	Cross-sectional	Medical records	Prescriptions	All	Public	NA	68,527 (91.8%)	Acute tonsillitis, acute pharyngitis	Penicillin, macrolides	Co-amoxiclav, amoxicillin, azithromycin
Alkhaldi, et al. [18]	Jordan	73,701	Cross-sectional	Medical records	Prescriptions	All	Public	20,133 (27%)	5795 (28.8%)	Tonsillitis	Cephalosporins, penicillins	Azithromycin, ceftriaxone, amoxicillin

Table 1 (continued)

Author (year of publication)	Country	Sample size	Study design	Data source	Unit of analysis	Age group	Health sector	Prescribed antimicrobials N (%)	Inappropriate antimicrobial prescriptions N (%)	Two most commonly diagnosed infections (from most to least)	Three most commonly used antibiotic classes for RTI (from most to least)	The three most commonly used antibiotics for RTI (from most to least)
Butt, et al. [25]	Qatar	75,733	Cross-sectional	Medical records	Prescriptions	All	Private	NA	34,080 (45%)	Acute pharyngitis, acute sinusitis	Macrolides, Fluoroquinolone	Roxithromycin, amoxicillin, levofloxacin
Dekker, et al. [49]	Netherlands	2724	Cross-sectional	Medical records	Prescriptions	All	Public	1035 (38%)	476 (46%)	Chronic sinusitis, pneumonia	Penicillin, macrolides cephalosporins	Amoxicillin
Gačina, et al. [50]	Croatia	709	Cross-sectional	Survey (structured questionnaire)	Patients	All	Public	231 (32.6%)	69 (30%)	-	Penicillin, cephalosporins fluoroquinolones	Ceftriaxone, amoxicillin, azithromycin,
Lakkis, et al. [51]	Lebanon	372	Cross-sectional	Medical records	Prescriptions	All	Public	328 (88%)	131 (40%)	Acute pharyngitis, acute bronchitis	Cephalosporins, macrolides penicillins	Amoxicillin-clavulanate ceftriaxone
Ji, et al. [52]	Japan	1,937,379	Cross-sectional	Medical records	Prescriptions	Adults	Public	813,699 (42%)	284,795 (35%)	Acute nasopharyngitis	Cephalosporins, macrolides, fluoroquinolones	Not mentioned
Rún Sigurðardóttir, et al. [53]	Denmark and Iceland	1428	Cross-sectional	Prescriptions audit	Prescriptions	All	Public	964 (67.5%)	155 (16%)	Acute sinusitis, acute pharyngotonsillitis	Penicillin, macrolides	Not mentioned
Nowakowska, et al. [28]	UK	1,151,105	Cross-sectional	Medical records	Prescriptions	All	Public	NA	444,902 (39%)	-	Penicillins, quinolones, and macrolides	Amoxicillin, ampicillin, Phenoxymethylpenicillin
Tobia, et al. [29]	USA	153	Cross-sectional	Medical records	Prescriptions	All	Public	NA	99 (65%)	Sinusitis, CAP	Fluoroquinolones cephalosporins	Ciprofloxacin, ceftriaxone, moxifloxacin

Table 1 (continued)

Author (year of publication)	Country	Sample size	Study design	Data source	Unit of analysis	Age group	Health sector	Prescribed antimicrobials N (%)	Inappropriate antimicrobial prescriptions N (%)	Two most commonly diagnosed infections (from most to least)	Three most commonly used antibiotic classes for RTI (from most to least)	The three most commonly used antibiotics for RTI (from most to least)
Vergidis, et al. [54]	USA	617	Cross-sectional	Medical records	Prescriptions	All	Public	352 (57%)	74 (24%)	Acute bronchitis, pneumonia	Penicillins, beta-lactam combination, macrolides	Amoxicillin, azithromycin, co-amoxiclav

NA Not applicable because their sample consisted only of patients who had received antibiotic prescription

studies conducted in Croatia, Tunisia, Saudi Arabia, Jordan, China, and India reported that the majority (74.8%, 58.8%, 53%, 52.75%, 51.5%, and 50% respectively) of antimicrobials prescribed were from the penicillin group [18, 19, 26, 35, 37, 50]. Similarly, studies conducted in Ecuador, Sierra Leone, Thailand, Jordan, the UK, and Saudi Arabia revealed that the most commonly prescribed antimicrobials were benzathine penicillin + amoxicillin (86.7%), ampicillin (75.8%), amoxicillin (70%), and amoxicillin-clavulanate (69.9%) [27, 28, 37, 41, 44, 48]. A study conducted in Ethiopia reported that Ceftriaxone was the main prescribed third-generation cephalosporin antibiotic, accounting for 84.9% of antimicrobial prescriptions [34].

In this review, we identified that the major reasons for antimicrobial prescription were acute bronchitis, pharyngitis, sinusitis, and the common cold. However, the frequency of these diagnoses varies from country to country. A study conducted in Syria [38] reported that 98.5% of antimicrobials were prescribed for acute tonsillitis. According to a study conducted by Chandra Deb in the USA [36], 74.4% of antimicrobials were prescribed for acute bronchitis. Another two studies conducted in Vietnam, and India reported that 66% and 63.5% of antimicrobials were prescribed for acute pharyngitis, and common cold diagnosis, respectively [35, 42]. A study conducted in Denmark and Iceland reported that 80% of antimicrobials were prescribed because of acute sinusitis [53].

Among the included studies, 19 reported the pattern of AWaRe antibiotic use (Table 2). The majority of prescriptions were from the Access group followed by the Watch group. However, studies conducted in Ethiopia and China reported that 64% of antimicrobials were prescribed from the Watch group [34, 39] (Table 2). Additionally, a study conducted in Vietnam reported that 2.8% of antimicrobials were prescribed to the Reserve group [42].

Antimicrobial prescription rates for respiratory tract infections

Among the included studies, 30 reported the antibiotic prescribing rate. In these studies, a total of 2,685,049 patients were analyzed, and 1,328,984 patients received antimicrobial prescriptions for various diagnoses related to respiratory tract infection. The range of antimicrobial prescription rates in these studies ranged from 25% (95% CI 0.24–0.26) to 90% (95% CI 0.89–0.91) [24, 38, 46]. The estimated pooled antimicrobial prescription rate was 66% (95% CI 0.57–0.73, $I^2 = 99.9\%$) (Fig. 2). There was a high degree of heterogeneity observed between studies.

Given the high degree of heterogeneity, subgroup analyses by region (Africa, Asia, Europe, North America, and Oceania), age group (adults, children, and all), unite of analysis (patients and prescriptions), and data source (survey, prescription audit and medical records), and study period (2000–2009, 2010–2019, and 2020–2023) were performed to understand the source of variability or heterogeneity with at least two studies in each group (seeSupplementary file 4) on the basis of the availability of information. Subgroup analysis by region revealed a high antimicrobial prescription rate in Africa at 79% (95% CI 0.48–0.94), with the lowest prescription rate reported in Europe at 47% (95% CI 0.32–0.62) using a random effect model with significant subgroup differences. Additionally, the subgroup analysis showed that the overall antimicrobial prescription rates in Asia and North America were 70% and 72% respectively (Fig. 3).

Based on the study period of the included studies, a higher pooled prevalence of antimicrobial prescriptions was observed for the period 2020–2023, with a rate of 77% (95% CI 0.60–0.88) compared with the other study periods (Table 3). The pooled prevalence of antimicrobial prescription rates from 2000 to 2009 was 57% (95% CI 0.45–0.68). In the subgroup analysis based on the data source, the pooled prevalence of antimicrobial prescriptions was 57% (95% CI 0.39–0.74) for questionnaire surveys, 70% (95% CI 0.59–0.79) for medical records, and 63% (95% CI 0.52–0.73) for prescription audits (Table 3). The subgroup analysis revealed that the proportion of patients receiving antimicrobials was greater for children than for adults, with rates of 74% (95% CI 0.51–0.89) and 69% (95% CI 0.44–0.86), respectively. Analysis of the 19 studies that used prescriptions as the unit of analysis also showed a high antimicrobial prescription rate for respiratory tract infections, with a pooled estimate of 69% (95% CI 0.59–0.77). There was no significant variation observed in the subgroup analysis based on sample size (see Supplementary file 4). Due to very few studies conducted solely in the private health sector, no comparison was made against the public sector.

Inappropriate antimicrobial prescriptions for respiratory tract infection

The included studies assessed the rationality of antimicrobial prescription or appropriateness in terms of indication, dosage, frequency, and route of administration. Thirty-four studies utilized national and international guidelines to measure the appropriateness of the prescription. The remaining two studies conducted in Tunisia and the USA utilized the Medication Appropriateness Index (MAI) in addition to international guidelines [19, 29]. Among the included studies, 28 reported that the main reason for inappropriate antimicrobial prescription was the prescription of antimicrobials without proper indications. For instance, a study conducted in Ethiopia revealed that the highest proportion

Table 2 AWaRe classification of antimicrobial prescription in a subset of studies included in the analysis (19 studies)

Study	Country	Two most commonly diagnosed infections (from most to least)	No. of antimicrobials prescribed	Access-group antimicrobials *N* (%)	Watch-group antimicrobials *N* (%)	Reserve-group antimicrobials *N* (%)
Bo, et al. [31]	Malaysia	Acute pharyngitis, acute bronchitis	120	76 (63.3%)	44 (36.7%)	0
Bianco, et al. [17]	Italy	Pharyngotonsillitis, common cold	177	1001 (57%)	76 (43%)	0
Giuseppe, et al. [11]	Italy	Acute pharyngitis, influenzas	216	162 (75%)	54 (25%)	0
Alekaw, et al. [34]	Ethiopia	Pneumonia, acute bronchitis	248	89 (35.7%)	159 (64.3%)	0
Bel Haj Ali, et al. [19]	Tunisia	Acute bronchitis, tonsillitis	6426	3746 (58.3%)	2679 (41.7%)	0
Kumari Indira, et al. [35]	India	Common cold, pharyngitis	6183	3091 (50%)	3091 (50%)	0
Shaheen, et al. [37]	Saudi Arabia	Common cold, bronchitis	515	314 (61%)	201 (39%)	0
Fu, et al. [39]	China	Acute bronchitis, common cold	4752	1711 (36%)	3041 (64%)	0
Ababneh, et al. [41]	Jordan	Influenzas, tonsillitis	4570	3702 (81%)	868 (19%)	0
Nguyen, et al. [42]	Vietnam	Acute pharyngitis, acute bronchitis	129,317	119 360 (92.3%)	7243 (5.6%)	3620 (2.8%)
Suttajit, et al. [44]	Thailand	Bronchitis, pharyngitis,	2838	2270 (80%)	568 (20%)	0
Sánchez Choez, et al. [48]	Ecuador	Common cold, acute tonsillitis	523	446 (85%)	78 (15%)	0
Moon, et al. [27]	Sierra Leone	Bronchiolitis pneumonia	777	591 (76%)	186 (24%)	0
Chang, et al. [26]	China	–	68,527	39,746 (58%)	28,781 (42%)	0
Alkhaldi, et al. [18]	Jordan	–	20,133	10,620 (52.75%)	9513 (47.25%)	0
Dekker, et al. [49]	Netherlands	Chronic sinusitis, pneumonia	1035	797 (77%)	238 (23%)	0
Gačina, et al. [50]	Croatia	–	709	530 (74.8%)	179 (25.2%)	0
Lakkis, et al. [51]	Lebanon	Acute pharyngitis acute bronchitis	328	197 (60%)	131 (40%)	0
Vergidis, et al. [54]	USA	Acute bronchitis, pneumonia	352	292 (83%)	60 (17%)	0

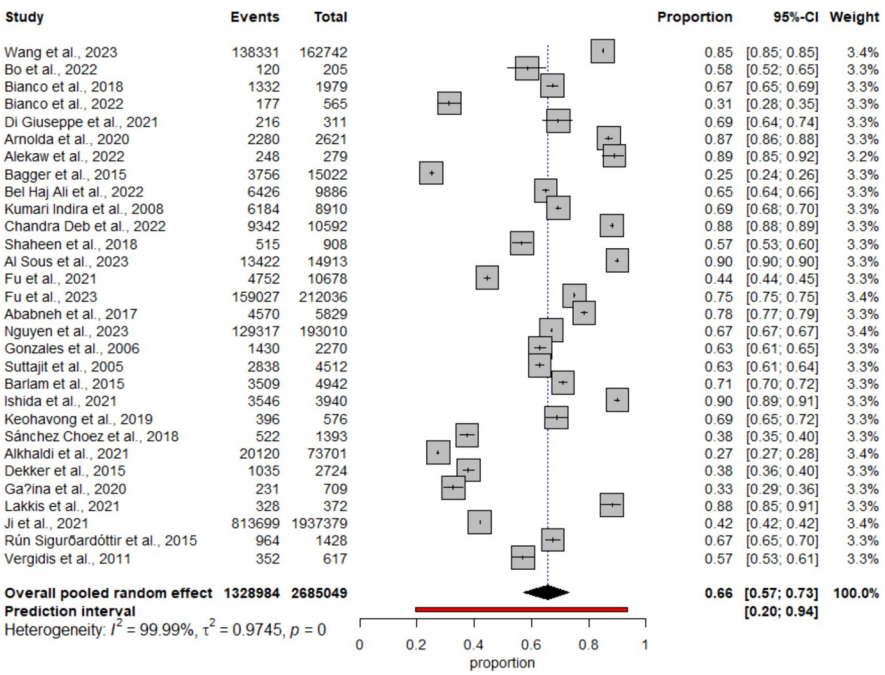

Fig. 2 Forest plot for antimicrobial prescription rate. *Note*: Events = antimicrobials, Total = sample size

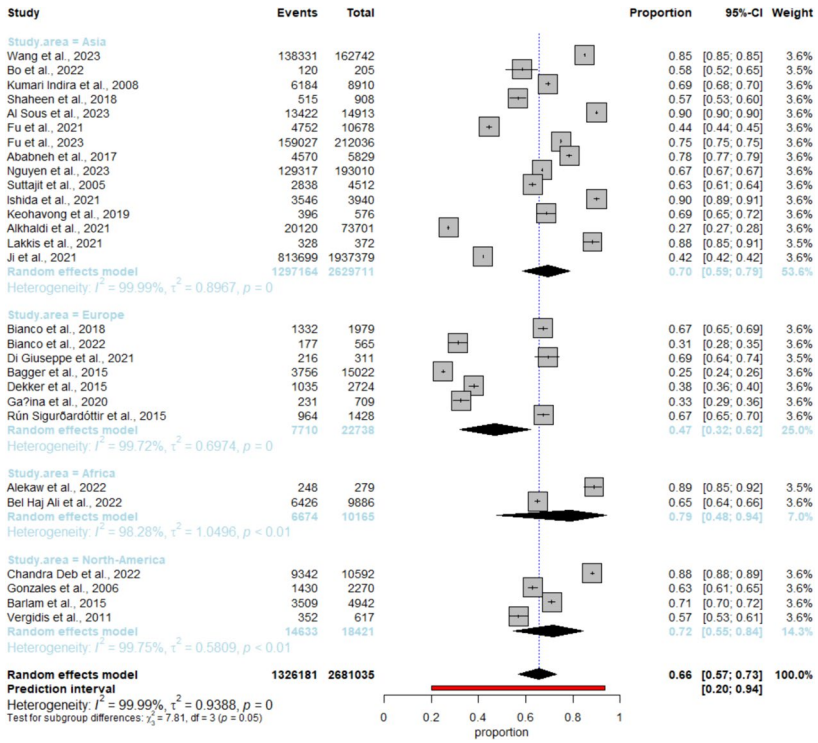

Fig. 3 Forest plot for subgroup analysis of antimicrobial prescription rates by study area. *Note:* Events = antimicrobials, Total = sample size

Table 3 Subgroup analysis of antimicrobial prescription rates

Subgroup	Categories	No. of studies	No. of examined	No. of antimicrobials prescribed	Pooled proportion % (95%CI)	^{2}%(*p*-value)
Study area or Region	Africa	2	25,187	10,429	79 (0.48–0.94)	98.2 (< 0.01)
	Asia	15	2,683,004	1,327,668	70(0.59–0.79)	99.9 (< 0.001)
	Europe	7	2,521,485	1,190,181	47(0.32–0.62)	99.72 (< 0.001)
	North America	4	2,482,529		72(0.55–0.84)	99.75(< 0.01)
Study period	2000–2009	8	40,425	20,067	57(0.45–0.68)	99.89 (< 0.001)
	2010–2019	19	2,643,458	1,308,057	67 (0.55–0.77)	99.9 (< 0.001)
	2020–2023	3	1166	860	77(0.60–0.88)	94.93 (< 0.01)
Data source	Questionnaire survey	8	36,816	18,891	57 (0.39–0.74)	99.9 (< 0.001)
	Medical records	17	2,414,273	1,138,651	70 (0.59–0.79)	99.9 (< 0.001)
	Prescription audit	5	233,960	171,441	63 (0.52–0.73)	99 (< 0.001)
Unit of analysis	Patients	11	38,799	19,878	60 (0.44–0.74)	99.8 (< 0.001)
	Prescription	19	2,646,250	1,309,106	69 (0.59–0.77)	99.9 (< 0.001)
Age group	Children	5	9,870	7671	74 (0.51–0.89)	99.4 (< 0.01)
	Adults	4	1,946,142	820,299	69 (0.44–0.86)	99.9 (< 0.00)
	All	21	729,037	501,013	63 (0.53–0.72)	99.9 (< 0.001)

of patients with inappropriate prescriptions (20.8%) received antimicrobials that were not appropriate for their condition or not indicated by guidelines [34]. Another study conducted in Tunisia similarly reported that antibiotic therapy was inappropriate in 75% of patients, with 40% of cases attributed to a lack of proper indications [19]. This review identified inappropriate routes of administration and dosages as additional reasons for inappropriate prescriptions. According to a study conducted in Qatar, out of 45% of inappropriate

prescriptions, 23% of antimicrobial prescriptions were administered improperly [25].

Among the 36 included studies, the proportion of inappropriate prescriptions exceeded 50% in 11 studies, whereas the remaining 25 studies reported a proportion below 50% (Table 1). The lowest level of inappropriate prescription was reported in a study conducted in Japan, in which 3546 prescribed antimicrobials were analyzed with a rate of 13% [46]. In contrast, the highest rate of inappropriate prescription reported in a study from Ecuador was 90.25% [48].

The overall pooled prevalence of inappropriate antimicrobial prescription was 45% (95% CI 0.38–0.52, PI 0.12–0.82, $I^2 = 99.9\%$) (seeSupplementary file 4). Subgroup analysis on the basis of study region showed a relatively high rate of inappropriate antimicrobial prescription in Asia at 49% (95% CI 0.38–0.60), followed by North America with 46% (95% CI (0.31–0.63) (Fig. 4) and Europe, 46% (95% CI 0.30–0.55). However, the subgroup analysis also revealed that the pooled prevalence of inappropriate antimicrobial prescriptions in Africa for respiratory tract infections was 27% (95% CI 0.24–0.31). The pooled prevalence of inappropriate prescriptions in Africa was lower than that in other regions, which may be due to the smaller number of studies conducted. The overall inappropriate antimicrobial prescription rate for respiratory tract infection did not vary by age group, study period, data source, and unit of analysis (see Supplementary file 4).

Discussion

This review aimed to provide a summary of the available evidence on the rate and appropriateness of prescribing antimicrobials for outpatients with respiratory tract infections. The results indicated that the antimicrobial prescription rate and inappropriateness are generally high but the rate varies by country. This variation may be due to the number of studies included in this review varying for each country. For instance, we have fewer studies from Africa than from Asia and Europe. This finding showed that countries were not at the same level regarding the research-based evidence of antimicrobial resistance patterns. There was a high rate of heterogeneity observed. In proportional meta-analyses, high heterogeneity is common due to the nature of proportional data (variation in time and place of included studies) even in small sample studies and it does not necessarily mean that the data are inconsistent [55]. However, it is important to interpret the results cautiously.

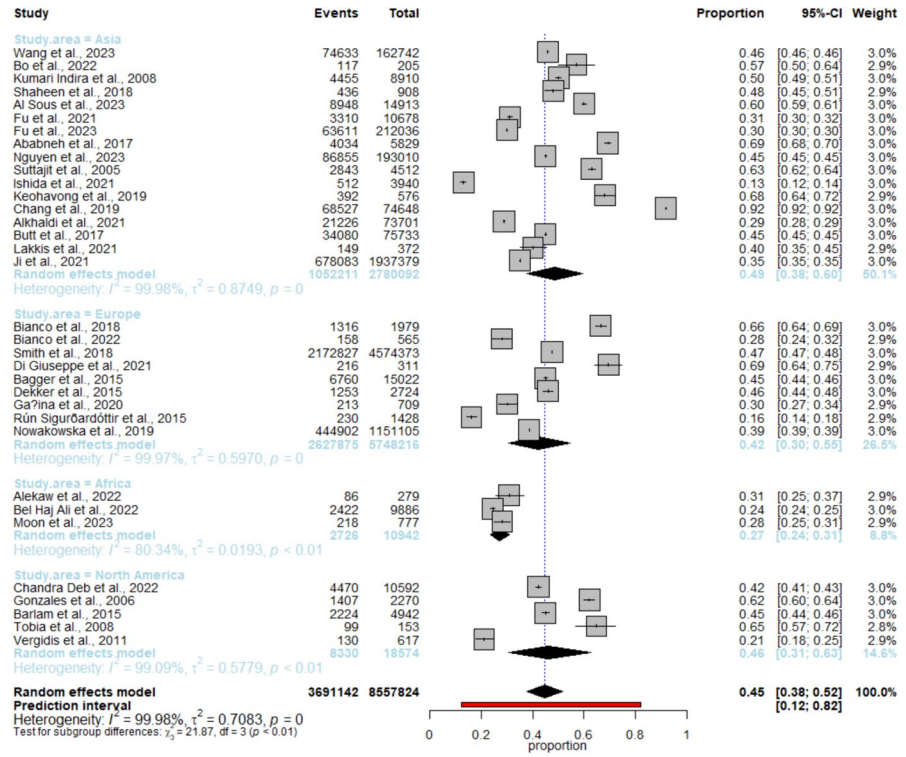

Fig. 4 Forest plot for subgroup analysis of inappropriate antimicrobial prescription rate per study area. *Note :* Events = antimicrobials, Total = sample size

The overall pooled prevalence of antimicrobial prescribing rate for outpatients with respiratory tract infection was 66% (95% CI 0.57–0.73 (Fig. 2), with considerable heterogeneity observed. Except for one study [24], the reported antibiotic prescribing rates in the other studies were higher than the WHO-recommended rate of 27% or less [56], suggesting inappropriate antibiotic use. The current result is lower than the 69.8% reported in a previous study of antibiotic use for respiratory tract infection among adults living in long-term care facilities Huang, et al. [57]. Conversely, our pooled rate is higher than the result of the previous study conducted by Acam, et al. [58] which reported 57%. This variation may be attributed to the fact that the previously reported rates were analyzed in both inpatients and outpatients, whereas this review focused solely on outpatients. Subgroup analysis by region revealed a high antimicrobial prescription rate in Africa 79% (95% CI 0.48–0.94), with the lowest prescription rate reported in Europe 47% (95% CI 0.32–0.62). This variation may be attributed to less adherence to the WHO recommendation rate and potentially exacerbated by the absence of stewardship for antimicrobial resistance management in African nations [58]. According to a systematic review conducted across Africa on the pattern of antimicrobial prescription, the overall prevalence of antimicrobial use among inpatients and outpatients with different infections ranged from 40.7 to 97.6% [59]. This is much higher than the 47% rate reported in Europe. In contrast, Europe has been shown to have more stringent antimicrobial stewardship programs and better regulatory mechanisms in place, which likely contribute to the lower prescription rates observed [4].

Furthermore, this review revealed a greater pooled prevalence of antimicrobial prescriptions for the period 2020–2023 (77%; 95% CI 0.60–0.88) than for the period 2000–2009 ((57%; 95% CI 0.45–0.68). This suggests an increasing trend in antimicrobial use in recent years. This increase could be attributed to several factors, including the COVID-19 pandemic, which has increased the use of antimicrobials due to concerns about secondary bacterial infections and the lack of specific treatments for viral infections [60]. The subgroup analysis based on data sources revealed varying antimicrobial prescription rates: 57% for questionnaire surveys, 70% for medical records, and 63% for prescription audits. These differences highlight potential biases and limitations inherent in each data collection method. There is a possibility that questionnaire surveys underreport prescriptions, due to recall bias or incomplete responses, whereas medical records and prescription audits can provide more accurate and thorough information, but they are still subject to recording methods and healthcare provider behavior.

The study revealed that children were prescribed antimicrobials at a higher rate (74%; 95% CI 0.50–1.89) than adults were (69%; 95% CI 0.40–40.86). This finding is consistent with prior research, which suggests that children are more commonly prescribed antibiotics due to the greater prevalence of respiratory diseases and other diseases in this age group, as well as parental expectations and healthcare provider concerns [57]. It is imperative to promote sensible antimicrobial use in pediatric populations, such as antimicrobial stewardship programs, to address this issue.

On the basis of our review, we found that antimicrobial prescription was most commonly associated with acute bronchitis, pharyngitis, sinusitis, and the common cold. Nevertheless, the frequency of these diagnoses varies from country to country. These differences may be due to differences in healthcare systems, diagnostic capabilities, and cultural expectations. For example, low-and middle-income countries often face challenges, such as over-the-counter antimicrobial sales and limited access to diagnostic tests, leading to higher rates of antimicrobial prescription [61]. Fleming-Dutra et al. (2016) reported that a significant proportion of antimicrobial prescriptions in the USA were for acute respiratory conditions, such as bronchitis and sinusitis, despite most of these illnesses being viral in origin and not requiring antimicrobials [8]. Another study conducted in the UK reported that the majority of antimicrobial prescriptions were for respiratory tract infections, including pharyngitis and the common cold [62]. This review found that amoxicillin, ampicillin, amoxicillin/clavulanate, azithromycin, and erythromycin were the most commonly prescribed antimicrobials. Similar observations were demonstrated by studies conducted in Nigeria and Tanzania which reported that amoxicillin and amoxicillin-clavulanate were the most commonly prescribed antimicrobials for respiratory tract infection in outpatients [63, 64]. This finding indicates that prescribers are using broad-spectrum antimicrobials, whereas it is recommended to maintain narrow-spectrum antimicrobials at $\geq$ 80% in cases where an antibiotic is prescribed [65, 66]. This may contribute to the increase in antimicrobial resistance.

In addition to the misuse of antimicrobials, therapeutic regimens may be inappropriate due to incorrect choice of antimicrobials, prescribed antimicrobials when not indicated, or use of incorrect dosages or durations. For example, a study conducted in Ethiopia reported that 14% of antimicrobials were prescribed inappropriate dosages [34]. This result is in line with a study conducted in India where 15% of antimicrobials were prescribed at inappropriate dosages [35]. As a result of this review, the overall pooled prevalence of inappropriate antimicrobial prescriptions was 45% (95% CI 0.38–0.52). This finding is

higher than the inappropriate prescription rate reported in a previous systematic review and meta-analysis for outpatients in high-income countries which was 31.5.% [67]. This variation may be attributed to the fact that our study focused exclusively on all age groups, whereas the previous study focused solely on children and focused on high-income countries. The broader inclusion criteria in the present study may also account for the higher overall rate of inappropriate antibiotic prescription.

Subgroup analysis by region indicated that Asia had the highest inappropriate antimicrobial prescription rate at 49% (95% CI 0.38–0.60), followed by North America with 46% (95% CI 0.31–0.63). On the other hand, our results showed that there is a lower inappropriate antimicrobial prescription rate in Africa at 27% (95% CI 0.24–0.31), which may be attributed to the smaller number of studies or less research from Africa analysis in this review. This result is in line with a study conducted by Donnelly, et al. [68] in America, which reported that in emergency department patients with respiratory tract infections, approximately 43% of antimicrobial prescriptions were inappropriate. The variation in the rate of inappropriateness could also be due to the types of infection and their prevalence across regions, as shown in Table 1. This is supported by [69], who reported that regional variation in inappropriate prescribing could be influenced by differences in patient characteristics, insurance systems, and clinical diagnosis. Further studies are needed to investigate the factors contributing to inappropriate antimicrobial prescriptions and compliance with the recommended guidelines.

Limitations

We employed thorough search strategies and performed a rigorous systematic review and meta-analysis; however, there are some limitations in this study. There was high heterogeneity between studies even in the subgroup analysis, which may be due to broader inclusion criteria. Q and its derivatives I^2 and H^2 increase rapidly with a larger sample size and are influenced by the nature of proportional data [55, 70]. Consequently, the results of this study should be interpreted with caution. Second, it is noteworthy that we included only published data in the English language. Third, a substantial portion of the data in the included studies were sourced from electronic medical records. These records are susceptible to underreporting, as not all diagnoses or antimicrobial prescriptions may be registered [71]. Fourth, our investigation focused solely on outpatients and excluded inpatients. Additionally, we did not explore the factors associated with high prescription rates and inappropriate prescriptions. Therefore, this review may not provide a general overview of antibiotic usage patterns for respiratory tract infections.

The implications of the results for practice, policy, and future research

Indeed, this review could serve as valuable information for shaping policies on stewardship programs and guiding future research on antimicrobial resistance. The results of this review revealed a high prescription rate of 66%. However, the WHO recommended that the rate of antimicrobial prescription should be less than 27%, and Access-group antimicrobials should constitute at least 60% of overall antibiotic use [56]. This suggests a potential issue with antibiotic prescribing that may need attention, considering the importance of responsible antibiotic use and the WHO recommendations to combat antibiotic resistance. Additionally, we observed that the rates of inappropriate antimicrobial prescriptions remain high (45%). This suggests that a significant portion of antimicrobial prescriptions are not aligned with guidelines or clinical standards. Achieving the necessary reduction in inappropriate antibiotic prescribing to combat antimicrobial resistance requires a paradigm shift in antibiotic stewardship and the transformation of policy into clinical practice. Furthermore, our investigation focused solely on the antimicrobial prescription rate and appropriateness, and further research is needed to explore the factors influencing antibiotic prescription and to provide suggestions for interventions to minimise inappropriate antibiotic prescribing.

Conclusion

This review investigated the pattern and appropriateness of antibiotic prescriptions for respiratory tract infections in outpatients. This highlighted a generally high antibiotic prescribing rate and inappropriate use of antimicrobials. The prevalence of high antimicrobial prescription rates varies across countries. This review found that antimicrobial prescribing was most commonly associated with acute bronchitis, pharyngitis, sinusitis, and the common cold. Furthermore, ampicillin amoxicillin and amoxicillin-clavulanate antimicrobials from the Access group, along with azithromycin and erythromycin from the Watch group, were the most frequently used antimicrobials. This result suggested that it is necessary to improve antimicrobial prescription practices improving antimicrobial stewardship programs for frequently used antimicrobials in outpatient treatment, to minimize unnecessary antibiotic use. Furthermore, this review suggests that further research is needed to investigate the factors contributing to inappropriate antimicrobial prescription.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-024-02649-3.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Acknowledgements
We would like to express our gratitude to the University of New England librarians for their support in developing the search strategy.

Authors' contributions
GEK: conceptualization, drafting, quality assessment, data extraction and analysis. SI, JM, and SC: conceptualization, quality assessment, data analysis, critical insights, and refinement of the manuscript. All authors read and approved the final manuscript.

Funding
This review has not received any funding.

Availability of data and materials
All the data generated or analyzed during this review are included in this manuscript and supplementary files.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Computing interests
The authors declare that they have no competing interests.

Author details
[1]School of Health, Faculty of Medicine and Health, University of New England, Armidale 2351, Australia. [2]Department of Clinical Medicine, College of Veterinary Medicine and Animal Science, University of Gondar, Gondar 196, Ethiopia. [3]School of Psychology, Faculty of Medicine and Health, University of New England, Armidale 2351, Australia.

Received: 3 February 2024 Accepted: 28 August 2024
Published online: 06 September 2024

References

1. WHO: Global online consultation: a people-centred framework for addressing antimicrobial resistance in the human health sector 2023. https://www.who.int/news-room/articles-detail/global-online-consultation-people-centred-framework-for-addressing-antimicrobial-resistance-in-the-human-health-sector. Accessed at 14 Oct 2023.
2. CDC: About Antimicrobial Resistance. 2022. https://www.cdc.gov/drugresistance/about.html. 3 Sept 2023.
3. de Kraker ME, Stewardson AJ, Harbarth S. Will 10 million people die a year due to antimicrobial resistance by 2050? PLoS Med. 2016;13(11):e1002184.
4. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, Goossens H, Laxminarayan R. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci. 2018;115(15):E3463–70.
5. Mendelsohn E, Ross N, Zambrana-Torrelio C, Van Boeckel TP, Laxminarayan R, Daszak P. Global patterns and correlates in the emergence of antimicrobial resistance in humans. Proc R Soc B. 2007;2023(290):20231085.
6. Bank W. Drug-resistant infections: a threat to our economic future. World Bank; 2017. https://documents1.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf.
7. Harris AM, Hicks LA, Qaseem A. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention. Ann Intern Med. 2016;164(6):425–34.
8. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM, Finkelstein JA, Gerber JS, Hyun DY, Linder JA. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010–2011. JAMA. 2016;315(17):1864–73.
9. WHO: Antimicrobial resistance and primary health care 2018 https://apps.who.int/iris/bitstream/handle/10665/326454/WHO-HIS-SDS-2018.56-eng.pdf. 29 Aug 2023.
10. Metcalfe S, Laking G, Arnold J. Variation in the use of medicines by ethnicity during 2006/07 in New Zealand: a preliminary analysis. N Z Med J. 2013;126(1384):14–41.
11. Giuseppe G, Lanzano R, Silvestro A, Napolitano F, Pavia M. Pattern and appropriateness of antimicrobial prescriptions for upper respiratory tract and dental infections in male prisoners in Italy. Antibiotics (Basel). 2021;10(11):2-10.
12. Renati S, Linder JA. Necessity of office visits for acute respiratory infections in primary care. Fam Pract. 2016;33(3):312–7.
13. Smith DR, Dolk FCK, Pouwels KB, Christie M, Robotham JV, Smieszek T. Defining the appropriateness and inappropriateness of antibiotic prescribing in primary care. J Antimicrobial Chemother. 2018;73(suppl_2):ii11–8.
14. Arnold FW, LaJoie AS, Brock GN, Peyrani P, Rello J, Menéndez R, Lopardo G, Torres A, Rossi P, Ramirez JA, et al. Improving outcomes in elderly patients with community-acquired pneumonia by adhering to national guidelines: community-acquired pneumonia organization international cohort study results. Arch Intern Med. 2009;169(16):1515–24.
15. Kotwani A, Bhanot A, Singal GL, Gandra S. Marketing and distribution system foster misuse of antibiotics in the community: insights from drugs wholesalers in India. Antibiotics (Basel). 2022;11(1):2–8.
16. Joda AE, Aderemi-Williams RI. A comparative study of prescribing patterns in two tertiary care teaching hospitals in Lagos, Nigeria. Int J Pharm Pharmacol. 2013;2(1):041–6.
17. Bianco A, Licata F, Nobile CG, Napolitano F, Pavia M. Pattern and appropriateness of antibiotic prescriptions for upper respiratory tract infections in primary care paediatric patients. Int J Antimicrob Agents. 2022;59(1):106469.
18. Alkhaldi SM, Yaseen NA, Bataineh EA, Al-Rawashdeh B, Albadaineh MA, Mubarak SM, Jaras RE, Taha HA. Patterns of antibiotic prescribing and appropriateness for respiratory tract infections in a teaching hospital in Jordan. Int J Clin Pract. 2021;75(6):e14113.
19. Bel Haj Ali K, Sekma A, Messous S, Trabelsi I, Ben Youssef J, Maghraoui H, Razgallah R, Walha A, Grissa MH, Beltaief K. Appropriateness of antibiotic treatment of acute respiratory tract infections in Tunisian primary care and emergency departments: a multicenter cross-sectional study. BMC Primary Care. 2022;23(1):295.
20. WHO. Global research agenda for antimicrobial resistance in human health. World Health Organization; 2023. https://www.who.int/publications/m/item/global-research-agenda-for-antimicrobial-resistance-in-human-health.
21. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58.
22. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K. Chapter 7: Systematic reviews of etiology and risk. Joanna briggs institute reviewer's manual. The Joanna Briggs Institute 2017; 5:217-269.
23. IntHout J, Ioannidis JP, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open. 2016;6(7):2–3.
24. Bagger K, Nielsen ABS, Siersma V, Bjerrum L. Inappropriate antibiotic prescribing and demand for antibiotics in patients with upper respiratory tract infections is hardly different in female versus male patients as seen in primary care. Eur J Gen Pract. 2015;21(2):118–23.
25. Butt AA, Navasero CS, Thomas B, Al Marri S, Al Katheeri H, Al Thani A, Al Khal A, Khan T, Abou-Samra A-B. Antibiotic prescription patterns for

upper respiratory tract infections in the outpatient Qatari population in the private sector. Int J Infect Dis. 2017;55:20–3.
26. Chang Y, Chusri S, Sangthong R, McNeil E, Hu J, Du W, Li D, Fan X, Zhou H, Chongsuvivatwong V, et al. Clinical pattern of antibiotic overuse and misuse in primary healthcare hospitals in the southwest of China. PLoS ONE. 2018;14(6):3–8.
27. Moon TD, Sumah I, Amorim G, Alhasan F, Howard LM, Myers H, Green AF, Grant DS, Schieffelin JS, Samuels RJ. Antibiotic prescribing practices for acute respiratory illness in children less than 24 months of age in Kenema, Sierra Leone: Is it time to move beyond algorithm driven decision making? 2023.
28. Nowakowska M, van Staa T, Mölter A, Ashcroft DM, Tsang JY, White A, Welfare W, Palin V. Antibiotic choice in UK general practice: rates and drivers of potentially inappropriate antibiotic prescribing. J Antimicrob Chemother. 2019;74(11):3371–8.
29. Tobia CC, Aspinall SL, Good CB, Fine MJ, Hanlon JT. Appropriateness of antibiotic prescribing in veterans with community-acquired pneumonia, sinusitis, or acute exacerbations of chronic bronchitis: a cross-sectional study. Clin Ther. 2008;30(6):1135–44.
30. Wang J, Li F, Chen Z, Guo Y, Liu N, Liu B, Xiao S, Yao L, Li J, Zhuo C. Antibiotic prescription patterns for acute respiratory infections in rural primary healthcare settings in Guangdong, China: Analysis of 162,742 Outpatient Prescriptions. Antibiotics. 2023;12(2):297.
31. Bo ZM, Tan WK, Chong CSC, Lye MS, Parmasivam S, Pang ST, Satkunanantha SE, Chong HY, Malek A, Al-Khazzan BAAM. Respiratory microorganisms in acute pharyngitis patients: identification, antibiotic prescription patterns and appropriateness, and antibiotic resistance in private primary care, central Malaysia. PLoS ONE. 2022;17(11): e0277802.
32. Bianco A, Papadopoli R, Mascaro V, Pileggi C, Pavia M. Antibiotic prescriptions to adults with acute respiratory tract infections by Italian general practitioners. Infect Drug Resist. 2018;11:2199–205.
33. Arnolda G, Hibbert P, Ting HP, Molloy C, Wiles L, Warwick M, Snelling T, Homaira N, Jaffe A, Braithwaite J. Assessing the appropriateness of paediatric antibiotic overuse in Australian children: a population-based sample survey. BMC Pediatr. 2020;20:1–8.
34. Alekaw H, Derebe D, Melese WM, Yismaw MB. Antibiotic prescription pattern, appropriateness, and associated factors in patients admitted to pediatric wards of Tibebe Ghion Specialized Hospital, Bahir Dar, North West Ethiopia. Infect Drug Resist. 2022;Volume 15:6659–69.
35. KS KI, Chandy SJ, Jeyaseelan L, Kumar R, Suresh S. Antimicrobial prescription patterns for common acute infections in some rural, urban health facilities of India. Indian J Med Res. 2008;128(2):165–71.
36. Chandra Deb L, McGrath BM, Schlosser L, Hewitt A, Schweitzer C, Rotar J, Leedahl ND, Crosby R, Carson P. Antibiotic prescribing practices for upper respiratory tract infections among primary care providers: a descriptive study. Open Forum Infect Dis. 2022;9(7):ofac302.
37. Shaheen M, Siddiqui M, Jokhdar H, Hassan-Hussein A, Garout M, Hafiz S, Alshareef M, Falemban A, Neveen A, Nermeen A. Prescribing patterns for acute respiratory infections in children in primary health care centers, Makkah Al Mukarramah, Saudi Arabia. J Epidemiol Glob Health. 2018;8(3–4):149.
38. Al Sous MMJ, Al Houri HN, Safiah MH, Alazrak SO, Akwan RR. Antibiotic prescription patterns for acute upper respiratory tract infections in an outpatient population with health insurance in Syria—a retrospective cross-sectional study. IJID regions. 2023;7:66–71.
39. Fu M, Wushouer H, Hu L, Li N, Guan X, Shi L, Ross-Degnan D. Outpatient prescribing pattern for acute bronchitis in primary healthcare settings in China. NPJ Prim Care Respir Med. 2021;31(1):24.
40. Fu M, Gong Z, Li C, Ling K, Zhu Y, Li H, Shi L, Guan X. Appropriate use of antibiotics for acute respiratory infections at primary healthcare facilities in China: a nationwide cross-sectional study from 2017 to 2019. Lancet Reg Health-Western Pac. 2023;40:100880.
41. Ababneh MA, Al-Azzam SI, Ababneh R, Rababa'h AM, Demour SA. Antibiotic prescribing for acute respiratory infections in children in Jordan. Int Health. 2017;9(2):124–30.
42. Nguyen NV, Do NTT, Vu DTV, Greer RC, Dittrich S, Vandendorpe M, Pham TN, Ta NTD, Pham TQ, Khuong VT. Outpatient antibiotic prescribing for acute respiratory infections in Vietnamese primary care settings by the WHO AWaRe (Access, Watch and Reserve) classification: an analysis using routinely collected electronic prescription data. Lancet Reg Health-Western Pac. 2023;30:30.
43. Gonzales R, Camargo CA Jr, MacKenzie T, Kersey AS, Maselli J, Levin SK, McCulloch CE, Metlay JP. Antibiotic treatment of acute respiratory infections in acute care settings. Acad Emerg Med. 2006;13(3):288–94.
44. Suttajit S, Wagner AK, Tantipidoke R, Ross-Degnan D, Sitthi-amorn C. Patterns, appropriateness, and predictors of antimicrobial prescribing for adults with upper respiratory infections in urban slum communities of Bangkok. Southeast Asian J Trop Med Public Health. 2005;36(2):489–97.
45. Barlam TF, Morgan JR, Wetzler LM, Christiansen CL, Drainoni M-L. Antibiotics for respiratory tract infections: a comparison of prescribing in an outpatient setting. Infect Control Hospital Epidemiol. 2015;36(2):153–9.
46. Ishida T, Hagiya H, Honda H, Nakano Y, Ogawa H, Obika M, Ueda K, Kataoka H, Hanayama Y, Otsuka F. Antimicrobial prescription practices for outpatients with acute respiratory tract infections: a retrospective, multicenter, medical record-based study. PLoS ONE. 2021;16(11): e0259633.
47. Keohavong B, Vonglokham M, Phoummalaysith B, Louangpradith V, Inthaphatha S, Kariya T, Saw YM, Yamamoto E, Hamajima N. Antibiotic prescription for under-fives with common cold or upper respiratory tract infection in Savannakhet Province. Lao PDR Trop Med Health. 2019;47:1–10.
48. Sánchez Choez X, Armijos Acurio ML, Jimbo Sotomayor RE. Appropriateness and adequacy of antibiotic prescription for upper respiratory tract infections in ambulatory health care centers in Ecuador. BMC Pharmacol Toxicol. 2018;19(1):1–11.
49. Dekker ARJ, Verheij TJM, van der Velden AW. Inappropriate antibiotic prescription for respiratory tract indications: most prominent in adult patients. Fam Pract. 2015;32(4):401–7.
50. Gačina A, Botica MV, Botica I, Hodžić AH, Žuti IB, Kobaš A. Antibiotic prescription rate for upper respiratory tract infections in general practice-a Croatian study. Medicinski Glasnik. 2020;17(1):2–4.
51. Lakkis NA, Alameddine R, Issa HG, Mahmassani D, Osman MH. Prescribing antibiotics in adults with respiratory tract infections in Lebanon. Int J Clin Pract. 2021;75(10):1–8.
52. Ji L, Yoshida S, Kawakami K. Trends and patterns in antibiotic prescribing for adult outpatients with acute upper respiratory tract infection in Japan, 2008–2018. J Infect Chemother. 2021;27(11):1584–90.
53. Rún Sigurðardóttir N, Nielsen ABS, Munck A, Bjerrum L. Appropriateness of antibiotic prescribing for upper respiratory tract infections in general practice: comparison between Denmark and Iceland. Scand J Prim Health Care. 2015;33(4):269–74.
54. Vergidis P, Hamer DH, Meydani SN, Dallal GE, Barlam TF. Patterns of antimicrobial use for respiratory tract infections in older residents of long-term care facilities. J Am Geriatr Soc. 2011;59(6):1093–8.
55. Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E, Munn Z. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. BMC Med Res Methodol. 2021;21:1–9.
56. Ofori-Asenso R. A closer look at the World Health Organization's prescribing indicators. J Pharmacol Pharmacother. 2016;7(1):51–4.
57. Huang Y, Wei WI, Correia DF, Ma BHM, Tang A, Yeoh EK, Wong SYS, Ip M, Kwok KO. Antibiotic use for respiratory tract infections among older adults living in long-term care facilities: a systematic review and meta-analysis. J Hosp Infect. 2023;131:107–21.
58. Acam J, Kuodi P, Medhin G, Makonnen E. Antimicrobial prescription patterns in East Africa: a systematic review. Syst Rev. 2023;12(1):18.
59. Okedo-Alex IN, Akamike IC, Iyamu I, Umeokonkwo CD. Pattern of antimicrobial prescription in Africa: a systematic review of point prevalence surveys. Pan Afr Med J. 2023;45:67.
60. Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, Satta G, Cooke G, Holmes A. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis. 2020;71(9):2459–68.
61. Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, Laxminarayan R. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. Lancet Infect Dis. 2014;14(8):742–50.
62. Gulliford MC, Dregan A, Moore MV, Ashworth M, Staa TV, McCann G, Charlton J, Yardley L, Little P, McDermott L. Continued high rates of antibiotic prescribing to adults with respiratory tract infection: survey of 568 UK general practices. BMJ Open. 2014;4(10):e006245.

63. Khalfan MA, Sasi PG, Mugusi SF. The prevalence and pattern of antibiotic prescription among insured patients in Dar es Salaam Tanzania. Pan Afr Med J. 2021;40(1):2–3.
64. Okoro RN, Nmeka C, Erah PO. Antibiotics prescription pattern and determinants of utilization in the national health insurance scheme at a Tertiary Hospital in Nigeria. Afr Health Sci. 2019;19(3):2356–64.
65. Adriaenssens N, Coenen S, Tonkin-Crine S, Verheij TJ, Little P, Goossens H. European Surveillance of Antimicrobial Consumption (ESAC): disease-specific quality indicators for outpatient antibiotic prescribing. BMJ Qual Saf. 2011;20(9):764–72.
66. Hong SY, Taur Y, Jordan MR, Wanke C. Antimicrobial prescribing in the USA for adult acute pharyngitis in relation to treatment guidelines. J Eval Clin Pract. 2011;17(6):1176–83.
67. Burvenich R, Dillen H, Trinh NT, Freer J, Wynants L, Heytens S, De Sutter A, Verbakel JY. Antibiotic use in ambulatory care for acutely ill children in high-income countries: a systematic review and meta-analysis. Arch Dis Child. 2022;107(12):1088–94.
68. Donnelly JP, Baddley JW, Wang HE. Antibiotic utilization for acute respiratory tract infections in US emergency departments. Antimicrob Agents Chemother. 2014;58(3):1451–7.
69. King LM, Bartoces M, Fleming-Dutra KE, Roberts RM, Hicks LA. Changes in US outpatient antibiotic prescriptions from 2011–2016. Clin Infect Dis. 2020;70(3):370–7.
70. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I 2 in assessing heterogeneity may mislead. BMC Med Res Methodol. 2008;8:1–9.
71. Sulis G, Adam P, Nafade V, Gore G, Daniels B, Daftary A, Das J, Gandra S, Pai M. Antibiotic prescription practices in primary care in low-and middle-income countries: a systematic review and meta-analysis. PLoS Med. 2020;17(6):e1003139.

Publisher's Note