# Antimicrobial drug resistance among clinically relevant bacterial isolates in sub-Saharan Africa: a systematic review

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**Background:** Little is known about the prevalence of antimicrobial resistance (AMR) amongst bacterial pathogens in sub-Saharan Africa (sSA), despite calls for continent-wide surveillance to inform empirical treatment guidelines.

**Methods:** We searched PubMed and additional databases for susceptibility data of key pathogens for surveillance, published between 1990 and 2013. Extracted data were standardized to a prevalence of resistance in populations of isolates and reported by clinical syndrome, microorganism, relevant antimicrobial drugs and region.

**Results:** We identified 2005 publications, of which 190 were analysed. Studies predominantly originated from east sSA (61%), were hospital based (60%), were from an urban setting (73%) and reported on isolates from patients with a febrile illness (42%). Quality procedures for susceptibility testing were described in <50% of studies. Median prevalence (MP) of resistance to chloramphenicol in Enterobacteriaceae, isolated from patients with a febrile illness, ranged between 31.0% and 94.2%, whilst MP of resistance to third-generation cephalosporins ranged between 0.0% and 46.5%. MP of resistance to nalidixic acid in *Salmonella enterica* Typhi ranged between 15.4% and 43.2%. The limited number of studies providing prevalence data on AMR in Gram-positive pathogens or in pathogens isolated from patients with a respiratory tract infection, meningitis, urinary tract infection or hospital-acquired infection suggested high prevalence of resistance to chloramphenicol, trimethoprim/sulfamethoxazole and tetracycline and low prevalence to third-generation cephalosporins and fluoroquinolones.

**Conclusions:** Our results indicate high prevalence of AMR in clinical bacterial isolates to antimicrobial drugs commonly used in sSA. Enhanced approaches for AMR surveillance are needed to support empirical therapy in sSA.

Keywords: antimicrobial resistance, antimicrobial susceptibility testing, surveillance, empirical treatment, bacterial infections

## Introduction

Effective empirical therapy of bacterial diseases requires knowledge of local antimicrobial resistance (AMR) patterns, acquired through up-to-date surveillance. Recently, alarming reports on the prevalence of (multi)drug-resistant bacteria in low- and middle-income countries in Asia, particularly the Indian subcontinent, have been published.<sup>1</sup>

Very little is known about current resistance patterns of common pathogenic bacteria in sub-Saharan Africa (sSA) where surveillance capacity is minimal.<sup>2</sup> In sSA, the relative burden of infectious diseases is high.<sup>3</sup> Recent studies show that the consumption of antimicrobials is rising in sSA;<sup>4</sup> however, often only a small repertoire of (poor-quality) antimicrobials is available, which may be sold over the counter without proper diagnostic guidance.<sup>5</sup> Inadequate hygiene and infection control in hospitals may increase the spread of (multi)drug-resistant pathogens.<sup>6</sup> In the absence of continent-wide surveillance of drug resistance in sSA, as recommended by the WHO,<sup>7</sup> and while awaiting further implementation of effective surveillance programmes in sSA, few analyses and reviews have been done describing increasing AMR in the region.<sup>8,9</sup> Other review studies have either focused on a certain subregion,<sup>10</sup> specific age group,<sup>11</sup> class of antibiotics<sup>12</sup> or clinical syndrome.<sup>13,14</sup>

This review aims to give a broader and updated overview of AMR in sSA (excluding South Africa) between 1990 and 2013. Common bacterial pathogens for this region were included, classified by the WHO as key pathogens for surveillance, causing community- as well as hospital-acquired infections.

## Methods

### Search strategy

We searched PubMed for articles published in English, French, German or Dutch between 1990 and 2013 using a dedicated search string

© The Author 2014. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com (see the Supplementary methods, available as Supplementary data at JAC Online). Additional searches were performed in the online database of the Cochrane Database of Systematic Reviews and in African Journals Online using the search terms 'antimicrobial drug resistance', 'antimicrobial susceptibility' and 'Africa'. Reference lists of relevant articles were scanned for additional titles (see the Supplementary methods).

### Study selection criteria

Studies were included in this systematic review if they were published between January 1990 and January 2013 and reported *in vitro* resistance levels to relevant antibiotics in key pathogens for surveillance, determined for at least 10 unique isolates which were cultured from patients with corresponding clinical syndromes, in sSA. We included studies reporting on samples from both sterile as well as non-sterile sites taken from patients of all age groups.

The selection of clinical syndromes, pathogens and antibiotics was based on the WHO recommendations published in the 2002 Surveillance Standards for Antimicrobial Resistance<sup>7</sup> (Table 1). In addition to the list recommended by WHO, the following pathogens were added based on their clinical relevance: non-typhoidal Salmonella species,<sup>15</sup> Shigella flexneri and Shigella sonnei (designated Shigella non-dysenteriae), Vibrio cholerae, Pseudomonas aeruginosa, Klebsiella pneumoniae and Staphylococcus aureus (Table 1). For patients with a febrile illness, key pathogens isolated from any clinical sample were included. The selection of relevant antibiotics was broadened based on expert opinion and included narrow-spectrum and extended-spectrum  $\beta$ -lactams (with or without  $\beta$ -lactamase inhibitor), aminoglycosides, macrolides, (fluoro)quinolones, chloramphenicol, tetracyclines, trimethoprim/sulfamethoxazole (co-trimoxazole) and nitrofurantoin (Table S1, available as Supplementary data at JAC Online).

The selection of countries in sSA was based on the composition of the geographical region of sSA as defined by the United Nations Statistics Division<sup>16</sup> (2011; Figure 1). The Republic of South Africa was excluded based on the premise that a disproportionate amount of data would be available in comparison to the other included countries.<sup>13</sup> Distinction was made between hospital-acquired and community-acquired

infections, with the former being defined as new clinical infections in patients who had been admitted for  ${\geq}48$  h in a hospital setting.

### Selection procedure

The titles and abstracts of all search results were listed per country and were reviewed by at least two investigators (S. J. L., H. T., C. S. and F. v. L.) to identify papers for full-text review. Abstract-based selection was done using predefined inclusion and exclusion criteria. When selection of articles on the basis of abstracts remained inconclusive, full texts were retrieved. Disagreement about selection of abstracts was resolved by the independent review of a third investigator. Names of authors from articles in the search results were not blinded before or during abstract and full-text review. When papers were selected for full-text review after abstract review, retrieval of the full-text version was attempted through PubMed, institutional web sites, the medical library of the University of Amsterdam, the Royal Tropical Institute (Amsterdam), HINARI (Geneva) or by personal communication with study authors. Full-text review was performed by two investigators (S. J. L. and H. T.) using a pre-specified checklist.

Studies were required to fulfil all selection criteria and none of the exclusion criteria. None of the papers selected for full-text review was excluded based on *a priori* set quality criteria given the absence of such criteria for AMR surveys or laboratory-based studies (see the Supplementary methods).

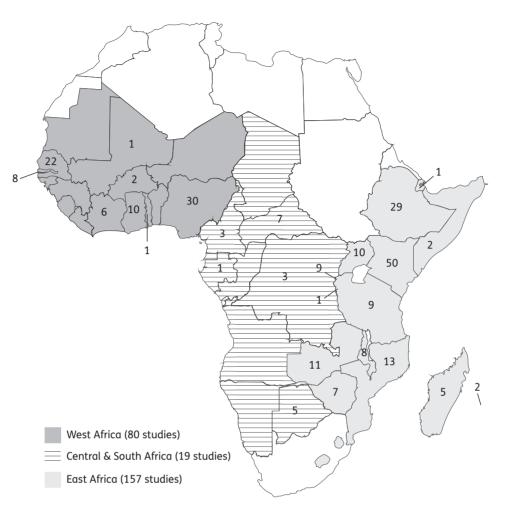
Discrepancies between the two reviewers on inclusion or exclusion of an article for analysis were independently resolved by a third investigator. Reports on specific subgroups such as patients infected with HIV/AIDS; or reports on isolates which were analysed in a laboratory outside the region but obtained from patients in one of the predefined countries, were included.

### Data extraction

A database was created in which the study period and the year of publication, study location, clinical syndrome and pathogen(s) tested were recorded. In addition, we recorded the age group, study and laboratory setting, sample type, culture methods, susceptibility testing methods,

 Table 1. Predefined list of clinical syndromes, pathogens and included publications

Clinical syndrome	Syndromes included	Pathogen	References
Acute diarrhoea	dysentery, gastrointestinal tract infection, diarrhoea, enteritis	Shigella dysenteriae, Shigella non-dysenteriae, non-typhoidal Salmonella, Vibrio cholerae, Escherichia coli	28-70
Acute respiratory infection	acute otitis media, upper respiratory tract infection, lower respiratory tract infection, pneumonia	Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus	71-80
Febrile illness/ septicaemia	febrile illness, typhoid fever, bacteraemia, septicaemia, invasive pneumococcal disease, neonatal infection	S. pneumoniae, H. influenzae, S. aureus, Neisseria meningitidis, Salmonella enterica Typhi, non-typhoidal Salmonella, E. coli, Shigella non-dysenteriae, Pseudomonas aeruginosa, Klebsiella pneumoniae	54,78,81-154
Hospital-acquired infection	hospital acquired: UTI, acute diarrhoea, septicaemia, bacteraemia, surgical wound infection, acute respiratory infection	S. aureus, E. coli, P. aeruginosa, K. pneumoniae	107,155-159
Meningitis	pyogenic meningitis, meningitis	N. meningitidis, S. pneumoniae, H. influenzae, S. aureus	160-172,146,173-175
UTI Urethral/vaginal discharge	urethritis, cystitis, pyelonephritis gonorrhoea, urethral discharge, vaginal discharge, sexually transmitted infection	E. coli, K. pneumoniae, P. aeruginosa, S. aureus Neisseria gonorrhoeae	159,176-193 194-214
Wound infection	burn wound, wound infection, skin infection	S. aureus, P. aeruginosa	215-217



**Figure 1.** Composition of geographical subregions of Africa. The selection of countries in Africa was based on the composition of geographical regions as defined by the United Nations Statistics Division. We included all countries in the western, central, eastern and southern regions of the African continent except for the Republic of South Africa. Data from Central and South Africa were combined for analysis. The entire region of northern Africa (Algeria, Egypt, Libya, Morocco, South Sudan, Sudan, Tunisia and Western Sahara) was not included. Numbers in countries indicate the number of studies included in the analysis for the country in which the number appears. The total number of studies (256) exceeds the number of publications (190) because publications could include multiple studies (see the Methods section).

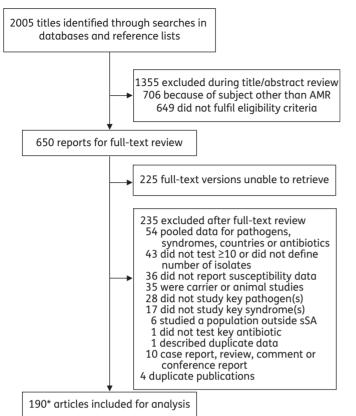
type of guideline used for susceptibility testing and whether quality control was done and breakpoints were reported. Quantitative data included the population size, sample size, number of isolates tested and the number of resistant strains per pathogen. Susceptibility data were recorded for each pathogen individually for a range of pre-specified antibiotics. The investigators recorded resistance data by extracting the percentages or numbers of susceptible, intermediate and resistant strains when available, based on the interpretation used in the original articles.

### Analysis approach

The extracted data were standardized to a prevalence of resistance, defined as the percentage of isolates being resistant out of the total number of isolates tested for the specific drug. Intermediate susceptible strains were categorized as resistant. Susceptibility data obtained by determination of the MIC were only included if prevalence of resistance could be determined and were combined with resistance estimates obtained using disc diffusion for a given pathogen. We report the prevalence of resistance as the median with the corresponding IQR by clinical syndrome, microorganism and most relevant antimicrobial drugs.

For publications that reported on a single clinical syndrome but for separate independent periods of data collection or from different independent study populations, e.g. community-acquired and hospital-acquired infections, we considered each independent dataset as a separate study. A single study could report on multiple syndromes, resulting in the number of syndromes reported being larger than the number of studies included, which in turn is larger than the number of publications extracted.

We did not pursue a meta-analysis of AMR to antimicrobial drugs of particular interest, after initial meta-regression showed an unacceptably large heterogeneity between the studies at the level of geographical region. A meta-analysis within each of the geographical regions was considered but rejected on the basis of having too few studies for most of the pathogen–antimicrobial drug combinations per region. For selected clinical syndromes and microorganisms, we show individual study data of resistance estimates to give insight into the spread and precision of individual studies. In addition, attempts were made to analyse time trends of resistance to relevant antimicrobial drugs for these microorganisms. CIs were based on the binomial distribution with an Agresti adjustment if needed.<sup>17</sup> All analyses were performed using STATA version 12 (STATA, College Station, TX, USA).



**Figure 2.** Flow chart of article selection procedure. \*The total number of studies (256) exceeds the number of publications (190) because publications could include multiple studies (see the Methods section).

# Results

### Characteristics of studies included in the analysis

Our search generated 2005 articles. During abstract review, 1355 articles were excluded because they did not meet the inclusion criteria. Six hundred and fifty articles were identified for full-text review, of which 190 were included in the final analysis (Figure 2), yielding a total of 256 studies. Eighty studies originated from west sSA (WA), 19 from central or southern sSA (CSA) and 157 from east sSA (EA). Two out of 8 (25%) countries in WA (Nigeria and Senegal) accounted for 65% of studies from this region, whilst 2 of 14 (14%) countries (Ethiopia and Kenya) accounted for 50% of studies from EA (Figure 1).

A total of 256 studies were included in the analysis, of which a majority of 154 (60%) reported on data obtained in hospitalbased clinical studies. Seventy-three percent of the studies were derived from an urban setting. The laboratories where antimicrobial susceptibility data were generated were based in clinical hospitals in 190 (74%) studies. The use of guidelines for antimicrobial susceptibility testing (AST) was reported in 197 (77%) studies. However, only 116 (45%) studies reported which breakpoints were used to define susceptibility and resistance of the isolates tested, while 120 (47%) studies reported on the application of guality controls when performing AST.

The 256 studies provided 259 estimates for the included clinical syndromes. Four publications reported on both community-acquired

and hospital-acquired infections. The number of studies per clinical syndrome varied widely, with a low number of studies including bacterial meningitis (20; 8%) and urinary tract infection (UTI) (24; 9%) isolates, compared with studies including isolates associated with diarrhoea (54; 21%) and febrile illness (109; 42%).

The study period in which data were collected was not reported in the majority of the studies, precluding analysis of time trends.

# Pathogens isolated from patients with a community-acquired febrile illness

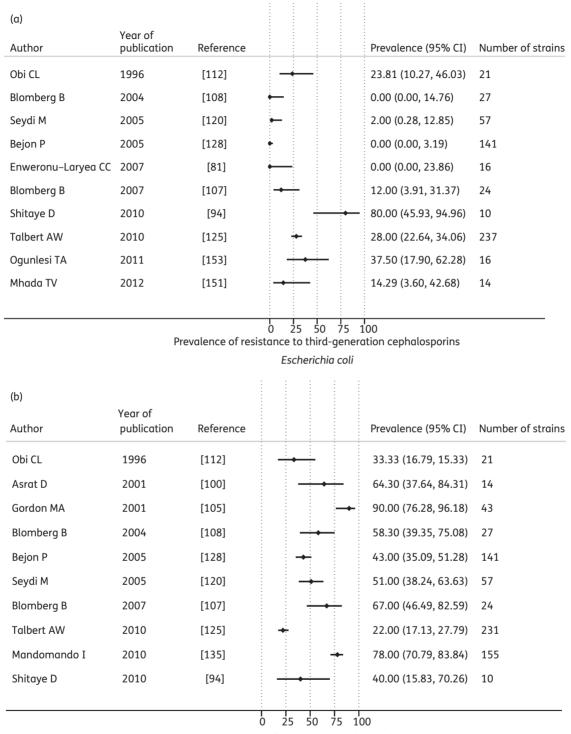
The median prevalence of resistance to ampicillin and cotrimoxazole for the Enterobacteriaceae, isolated from patients with febrile illness, ranged between 55.6% and 96.7% and between 51.0% and 86.7%, respectively. The median prevalence of resistance to chloramphenicol, including for Salmonella enterica Typhi, ranged between 31.6% and 94.2% for WA and between 31.0% and 70.2% for EA, whilst a study from CSA showed a prevalence of 41.3% in Salmonella Typhi. The median prevalence of resistance to third-generation cephalosporins ranged between 0.0% and 46.5% in WA, between 6.0% and 15.4% in CSA and between 0.0% and 22.0% in EA (Table S2, available as Supplementary data at JAC Online). Fluoroquinolone resistance prevalence was generally low. However, the median prevalence of resistance to nalidixic acid in Salmonella Typhi, indicative of reduced susceptibility to fluoroquinolones, ranged between 34.8% in EA, 15.4% in ČSA and 43.2% in WA. Data on azithromycin resistance in any of the Enterobacteriaceae was only found in one study on Salmonella Typhi from CSA reporting a 1% resistance prevalence.<sup>154</sup> Individual study data of chloramphenicol, thirdgeneration cephalosporins and fluoroguinolone resistance prevalence in Escherichia coli and Salmonella Typhi, combining all sSA regions, are presented in Figure 3. The median prevalence of gentamicin resistance ranged between 16.0% and 35.0% for E. coli and 28.6% and 47.0% for K. pneumoniae (Table S2).

Data for *Streptococcus pneumoniae* isolated from patients with a febrile illness indicated high levels of resistance to co-trimoxazole and tetracycline (Table S3, available as Supplementary data at *JAC* Online). Resistance to erythromycin showed a consistently low prevalence whilst the median prevalence of resistance to amoxicillin was 3.6% in WA and 15.8% in EA. There was an equally striking difference in the median prevalence of resistance reported to thirdgeneration cephalosporins of 0% in WA and 22.1% in EA, in the absence of data from CSA (Table S3). In contrast, the median prevalence of resistance to chloramphenicol was similar in both regions with 8.0% in WA and 7.1% in EA.

The median prevalence of resistance to oxacillin in *S. aureus* isolated from patients with a febrile illness was 13.4% for WA and 8.0% for EA, in the absence of data from CSA. The median prevalence of resistance to tetracycline, erythromycin, chloramphenicol and co-trimoxazole in *S. aureus* ranged from 21.4% for erythromycin to up to 80.0% for co-trimoxazole (Table S3).

# Pathogens isolated from patients with community-acquired acute diarrhoea or UTI

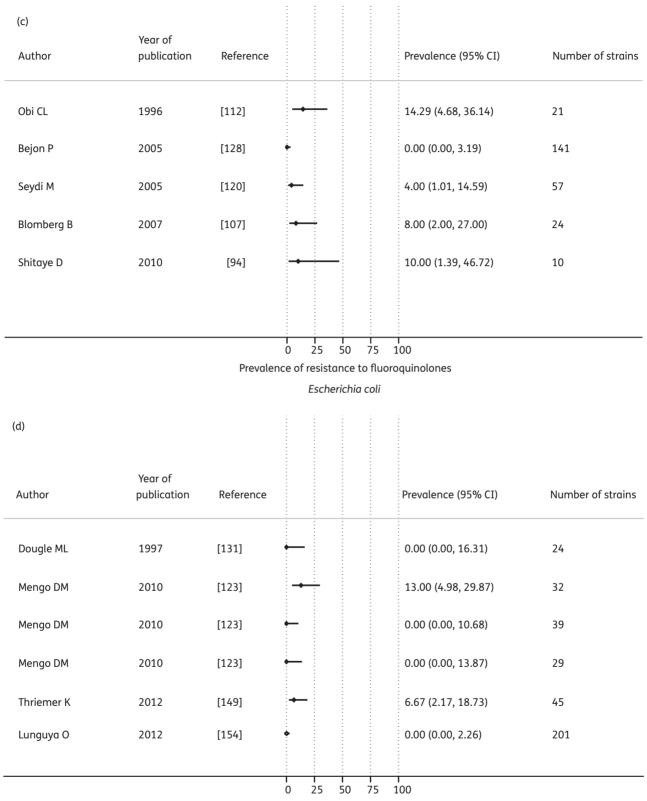
The median prevalence of resistance to ciprofloxacin and third-generation cephalosporins in Enterobacteriaceae isolated from patients with diarrhoea was low (Table S4, available as Supplementary data at JAC Online). Data on resistance to third-



Prevalence of resistance to chloramphenicol

Escherichia coli

**Figure 3.** Point prevalence estimates of resistance in *E. coli* and *Salmonella* Typhi isolated from patients with a community-acquired febrile illness. Summary chart of point prevalence estimates of individual studies presenting prevalence data on resistance to third-generation cephalosporins (a and d), chloramphenicol (b and e) and fluoroquinolones (c and f) of *E. coli* (a-c) and *Salmonella* Typhi (d-f) isolated from patients with a community-acquired febrile illness, combining all sub-Saharan African regions. A publication that appears with multiple entries reported on separate independent periods of data collection or on different independent study populations, each of which was considered a separate study.



Prevalence of resistance to third-generation cephalosporins

Salmonella enterica Typhi

Figure 3. Continued

Author	Year of publication	Reference					Prevalence (95% CI)	Number of strains
	•							
Dougle ML	1997	[131]	-				4.00 (0.56, 23.58)	24
Walsh AL	2000	[106]					0.00 (0.00, 23.86)	15
Gordon MA	2001	[105]	•	-			0.00 (0.00, 28.20)	12
Mengo DM	2010	[123]			-	+	81.00 (63.70, 91.20)	32
Mengo DM	2010	[123]	-	-	—	-	76.00 (57.50, 88.11)	29
Mengo DM	2010	[123]	-	-		-	67.00 (51.06, 79.80)	39
Gross U	2011	[150]					0.00 (0.00, 23.86)	15
Gross U	2011	[150]	-	-		-	88.30 (77.42, 94.32)	59
Thriemer K	2012	[149]		_	•		53.33 (38.89, 67.24)	45
Lunguya O	2012	[154]		-			41.30 (34.70, 48.23)	201
(0			-	onella				
	Year of publication	Reference		-			Prevalence (95% CI)	Number of strains
Author		Reference [131]					Prevalence (95% CI) 0.00 (0.00, 16.31)	Number of strains
Author Dougle ML	publication		÷					
Author Dougle ML Mengo DM	publication	[131]	÷				0.00 (0.00, 16.31)	24
Author Dougle ML Mengo DM Mengo DM	publication 1997 2010	[131] [123]	<b>←</b>				0.00 (0.00, 16.31) 19.00 (8.80, 36.30)	24 32
Author Dougle ML Mengo DM Mengo DM Mengo DM	publication 1997 2010 2010	[131] [123] [123]	• -+				0.00 (0.00, 16.31) 19.00 (8.80, 36.30) 14.00 (5.36, 31.87)	24 32 29
Author Dougle ML Mengo DM Mengo DM Gross U	publication 1997 2010 2010 2010	[131] [123] [123] [123]					0.00 (0.00, 16.31) 19.00 (8.80, 36.30) 14.00 (5.36, 31.87) 18.00 (8.83, 33.21)	24 32 29 39
(f) Author Dougle ML Mengo DM Mengo DM Gross U Gross U Thriemer K	publication 1997 2010 2010 2010 2011	[131] [123] [123] [123] [150]	÷				0.00 (0.00, 16.31) 19.00 (8.80, 36.30) 14.00 (5.36, 31.87) 18.00 (8.83, 33.21) 0.00 (0.00, 23.86)	32 29 39 15

Prevalence of resistance to fluoroquinolones Salmonella enterica Typhi

Figure 3. Continued

generation cephalosporins of *E. coli* and *K. pneumoniae* isolated from patients with UTIs were only available for WA and indicated a median prevalence of resistance of 5.0% and 4.3%, respectively (Table S5, available as Supplementary data at *JAC* Online). Data on resistance in Enterobacteriaceae isolated from urinary culture indicated high levels of resistance to co-trimoxazole and ampicillin, similar to isolates from patients with diarrhoea (Tables S4 and S5), leaving nitrofurantoin and ciprofloxacin for oral therapy (Table S5). Individual study data of co-trimoxazole, fluoroquinolone and nitrofurantoin resistance rates of *E. coli* and *K. pneumoniae*, isolated from patients with a community-acquired UTI combining all sSA regions, are presented in Figure 4.

# Pathogens isolated from patients with community-acquired acute respiratory tract infection

A limited number of studies reported on resistance in respiratory isolates of *S. pneumoniae* and *Haemophilus influenzae* (Table S6, available as Supplementary data at *JAC* Online). The median prevalence of resistance to erythromycin was consistently low for *S. pneumoniae* and ranged between 0% and 5.9%. The median prevalence of resistance to tetracycline was high for both *S. pneumoniae* (42.7%) and *H. influenzae* (100%) in WA, but much lower in EA (13% and 0%, respectively). Similarly, the median prevalence of resistance to co-trimoxazole appeared much higher in WA than in EA for both pathogens.

# Pathogens isolated from patients with other clinical syndromes

The number of studies reporting on isolates of *S. pneumoniae*, *H. influenzae* and *Neisseria meningitidis* from patients with meningitis (not related to outbreaks) for which resistance data were reported was small. However, data indicated a high median prevalence of resistance to chloramphenicol and ampicillin for *H. influenzae* isolates (Table S7, available as Supplementary data at JAC Online). Very few studies reported data on resistance to third-generation cephalosporins in these pathogens. The median prevalence of resistance reported was 0% for *S. pneumoniae*, between 0% and 6.0% for *H. influenzae* and 6.5% for *N. meningitidis* (Table S7).

*Neisseria gonorrhoea*, isolated from patients with urethral or vaginal discharge, showed a high median prevalence of resistance to penicillin and tetracycline. The median prevalence of resistance to ciprofloxacin and ceftriaxone was 0%, except for ceftriaxone resistance in CSA for which a median of 11.6% was reported (Table S8, available as Supplementary data at JAC Online).

We found very few studies on hospital-acquired infections in sSA and the available studies reported on small numbers of isolates. Data from EA suggested that methicillin-resistant *S. aureus* is prevalent in hospitals. Data on isolates obtained from wound infections provided similar limited information (Tables S9, S10, S11 and S12, all available as Supplementary data at JAC Online).

## Discussion

AMR is rapidly increasing across the globe. Given the importance of bacterial infections in the aetiology of febrile illness and other clinical syndromes in sSA, empirical treatment of these clinical syndromes should include antimicrobial therapy guided by the local epidemiology of AMR.<sup>14,18,19</sup> Unfortunately, as our results show, data on the prevalence of resistance to commonly used antimicrobial drugs in major bacterial pathogens based on systematic prospective surveillance of AMR in sSA are still limited or absent.

Our results indicate that the majority of the available data for sSA included in the analysis come from a limited number of countries and settings. There is a paucity of data from CSA countries. In addition to the introduction of bias, this geographical distribution of included studies indicates a virtual absence of recent information on AMR in clinical pathogens, outside of outbreak settings, in the majority of sSA countries. The median prevalence of resistance reported to chloramphenicol, which is inexpensive and therefore commonly used, was high across the different clinical syndromes and throughout sSA and chloramphenicol should not be recommended for use without availability of susceptibility test results. The median prevalence of resistance to thirdgeneration cephalosporins in E. coli and K. pneumoniae, presumably largely due to the production of extended-spectrum β-lactamases, and the median prevalence of resistance to gentamicin, the main representative of the aminoglycosides reported, were also considerable. Taken together, these data present a worrisome picture of AMR in Enterobacteriaceae in sSA, currently leaving third-generation cephalosporins and the fluoroquinolones as the main drugs of choice for empirical treatment of febrile illness and the carbapenems as an alternative (Table S13, available as Supplementary data at JAC Online).

Strikingly few studies reported on resistance rates in Enterobacteriaceae isolated from patients with UTI. This observation is surprising as bacterial culture of urine is relatively easy, in contrast to culture of faeces, blood or CSF, and AST results can provide clues into the prevalence of AMR in the community. In addition, empirical treatment of UTIs is likely to contribute heavily to community-based antimicrobial drug usage, thus contributing to AMR. A high median prevalence of resistance to co-trimoxazole, ampicillin and amoxicillin/clavulanic acid in *E. coli* and *K. pneumoniae* was reported. The main remaining options for oral therapy are nitrofurantoin and fluoroquinolones. However, nitrofurantoin may not be available in all countries in sSA.

As was also reported by other investigators,<sup>13</sup> there is a staggering lack of data on resistance in pathogens causing bacterial meningitis, outside of outbreak settings. The development of rapid diagnostic tests (RDTs) to improve diagnostic capacity for bacterial meningitis is extremely valuable for diagnostic practice, but enhanced efforts in clinical bacteriology will be needed to provide data on penicillin resistance in isolates of *S. pneumoniae* and *N. meningitidis* which RDTs currently do not provide.<sup>20,21</sup> The latter notion also applies to *N. gonorrhoea* and resistance to fluoroquinolones and third-generation cephalosporins. Data on AMR in nosocomial infections are equally lacking and there is an urgent need for better insight into AMR prevalence in hospitals, particularly in intensive care settings.<sup>20</sup>

There are a number of methodological considerations related to the studies included in our review. The majority of studies were urban hospital-laboratory based and therefore reflected AMR prevalence in a biased study population with potentially higher resistance prevalence than population-based studies or studies from rural areas would have yielded. In addition, reporting of technical performance of susceptibility testing suggests that quality

Author	Year of publication	Reference				Prevalence (%) (95% CI)	Number o strains
Adeyemo AA	1994	[178]				0.00 (0.00, 20.67)	18
Obi CL	1996	[187]				99.00 (96.09, 99.75)	192
Wolday D	1997	[184]		÷ ∔		75.00 (68.54, 80.51)	201
Moges F	2002	[183]				60.30 (49.11, 70.51)	78
Dromigny JA	2002	[191]				59.00 (52.58, 65.12)	234
Dromigny JA	2002	[191]		+	÷	61.60 (55.48, 67.37)	255
Musa–Aisien AS	2003	[177]	-	•		60.00 (34.81, 80.82)	15
Dromigny JA	2003	[190]		+		60.90 (54.49, 66.96)	233
Hima-Lerible H	2003	[180]			+ [	85.00 (78.88, 89.58)	174
Brown BJ	2003	[176]	←			0.00 (0.00, 21.63)	24
Adjei O	2004	[179]	-		-	13.33 (3.36, 40.54)	15
Dromigny JA	2005	[189]			-	67.80 (60.44, 74.37)	171
Dromigny JA	2005	[189]		+		71.10 (62.14, 78.67)	114
Dromigny JA Tessema B	2005	[189]		- <b>-</b>	-	64.60 (55.38, 72.85)	113
Randrianirina F	2007 2007	[182] [186]		$\pm T$		76.50 (69.45, 82.33) 73.10 (69.43, 76.48)	166 607
Sire JM	2007	[188]		14 T	-	58.50 (52.73, 64.04)	289
Sire JM	2007	[188]		÷.	÷	71.90 (66.75, 76.53)	323
Sire JM	2007	[188]		÷.	-	72.10 (65.61, 77.78)	207
Assefa A	2008	[181]			-	13.60 (4.45, 34.72)	22
	2009	[192]	1 1			95.00 (82.10, 98.75)	41
Aboderin UA	2009	[1]2]				JJ.00 (02.10, J0.7J)	
	2011	[159]	ice of resi		e to d	80.60 (69.86, 88.16) 0 co-trimoxazole	72
Aboderin OA Muvunyi CM (b)		[159]	ice of res		e to d	80.60 (69.86, 88.16) 0 co-trimoxazole	
Muvunyi CM		[159]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole	72 Number o
Muvunyi CM (b) Author	2011 Year of	[159] Prevaler	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole	72 Number o
Muvunyi CM (b) Author Adeyemo AA	2011 Year of publication	[159] Prevaler Reference	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI)	72 Number o strains
Muvunyi CM (b) Author Adeyemo AA Obi CL	2011 Year of publication 1994	[159] Prevaler Reference [178]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67)	72 Number of strains
Muvunyi CM (b) Author Adeyemo AA Obi CL Moges F Hima-Lerible H	2011 Year of publication 1994 1996	[159] Prevaler Reference [178] [187] [183] [180]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67) 0.00 (0.00, 2.36) 0.00 (0.00, 2.72) 10.00 (6.31, 15.49)	72 Number of strains 18 192
Muvunyi CM (b) Author Adeyemo AA Obi CL Moges F Hima-Lerible H Tessema B	2011 Year of publication 1994 1996 2002 2003 2007	[159] Prevaler Reference [178] [187] [183] [180] [182]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67) 0.00 (0.00, 2.36) 0.00 (0.00, 2.72) 10.00 (6.31, 15.49) 12.70 (8.43, 18.69)	72 Number of strains 18 192 78 174 166
Muvunyi CM (b) Author Adeyemo AA Obi CL Moges F Hima-Lerible H Tessema B Randrianirina F	2011 Year of publication 1994 1996 2002 2003 2007 2007	[159] Prevaler Reference [178] [187] [183] [180] [182] [186]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67) 0.00 (0.00, 2.36) 0.00 (0.00, 2.72) 10.00 (6.31, 15.49) 12.70 (8.43, 18.69) 16.40 (13.67, 19.56)	72 Number of strains 18 192 78 174 166 607
Muvunyi CM (b) Author Adeyemo AA Obi CL Moges F Hima–Lerible H Tessema B Randrianirina F Sire JM	2011 Year of publication 1994 1996 2002 2003 2007 2007 2007	[159] Prevaler Reference [178] [187] [183] [180] [182] [182] [186] [188]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67) 0.00 (0.00, 2.36) 0.00 (0.00, 2.36) 0.00 (0.00, 2.72) 10.00 (6.31, 15.49) 12.70 (8.43, 18.69) 16.40 (13.67, 19.56) 9.70 (6.78, 13.69)	72 Number of strains 18 192 78 174 166 607 289
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Muvunyi CM (b) Author Adeyemo AA Obi CL Moges F Hima-Lerible H Tessema B Randrianirina F Sire JM Sire JM	2011 Year of publication 1994 1996 2002 2003 2007 2007 2007 2007 2007 2007	[159] Prevaler Reference [178] [187] [183] [180] [182] [182] [188] [188] [188] [188]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67) 0.00 (0.00, 2.36) 0.00 (0.00, 2.72) 10.00 (6.31, 15.49) 12.70 (8.43, 18.69) 16.40 (13.67, 19.56) 9.70 (6.78, 13.69) 15.40 (11.87, 19.75) 22.10 (16.97, 28.25)	72 Number of strains 18 192 78 174 166 607 289 323 207
Muvunyi CM (b) Author Adeyemo AA Obi CL Moges F Hima-Lerible H Tessema B Randrianirina F Sire JM Sire JM	2011 Year of publication 1994 1996 2002 2003 2007 2007 2007 2007	[159] Prevaler Reference [178] [187] [183] [180] [182] [186] [188] [188]	ice of res	istance	e to d	80.60 (69.86, 88.16) 0 co-trimoxazole Prevalence (%) (95% CI) 0.00 (0.00, 20.67) 0.00 (0.00, 2.36) 0.00 (0.00, 2.72) 10.00 (6.31, 15.49) 12.70 (8.43, 18.69) 16.40 (13.67, 19.56) 9.70 (6.78, 13.69) 15.40 (11.87, 19.75)	72 Number of strains 18 192 78 174 166 607 289 323

### 0 25 50 75 100

Prevalence of resistance to fluoroquinolones

Escherichia coli

**Figure 4.** Point prevalence estimates of resistance in *E. coli* and *K. pneumoniae* isolated from patients with a community-acquired UTI. Summary chart of point prevalence estimates of individual studies presenting prevalence data on resistance to trimethoprim/sulfamethoxazole (co-trimoxazole) (a and d), fluoroquinolones (b and e) and nitrofurantoin (c) of *E. coli* (a-c) and *K. pneumoniae* (d and e) isolated from patients with a community-acquired UTI, combining all sub-Saharan African regions. A publication that appears with multiple entries reported on separate independent periods of data collection or on different independent study populations, each of which was considered a separate study.

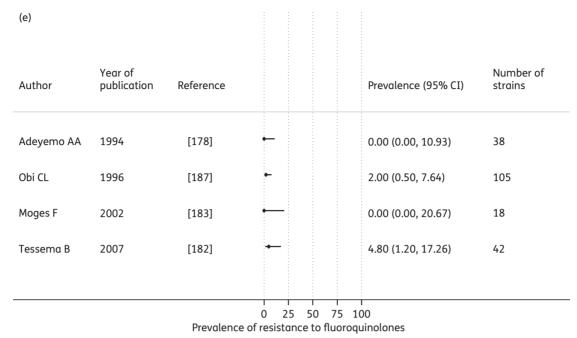
Author	Year of publication	Reference			F	Prevalence (95% CI)	Number of strains
Adeyemo AA	1994	[178]	+	-	٤	8.00 (1.14, 39.52)	18
Obi CL	1996	[187]	+		Ź	28.60 (22.66, 35.39)	192
Wolday D	1997	[184]	+		5	5.00 (2.71, 9.04)	201
Brown BJ	2003	[176]		•		37.50 (20.80, 57.82)	24
Adjei O	2004	[179]			- 6	56.67 (40.60, 85.40)	15
Sire JM	2007	[188]	+		g	9.50 (6.60, 13.49)	289
Sire JM	2007	[188]	+		1	11.00 (7.42, 16.01)	207
Sire JM	2007	[188]	+		1	10.00 (7.16, 13.80)	323
Assefa A	2008	[181]	←		(	0.00 (0.00, 17.55)	22
Aboderin OA	2009	[192]	-		2	20.00 (10.35, 35.12)	41
	2011	[159]	-	-	ź	26.40 (17.52, 37.73)	72
Muvunyi CM					5 100 o nitro	furantoin	
(d)			ce of resis	tance t	5 100 o nitro		Number o
_	Year of publication		ce of resis	tance t	5 100 o nitro		Number o strains
(d)	Year of	Prevalen	ce of resis	tance t	is 100 so nitro coli	furantoin	
(d) Author	Year of publication	Prevalen	ce of resis	tance t	5 100 o nitro coli	furantoin Prevalence (95% CI)	strains
(d) Author Adeyemo AA	Year of publication 1994	Prevalent Reference [178]	ce of resis	tance t	5 100 conitro coli	furantoin Prevalence (95% CI) 97.00 (81.60, 99.58)	strains 38
(d) Author Adeyemo AA Obi CL	Year of publication 1994 1996	Prevalent Reference [178] [187]	ce of resis	tance t	5 100 conitro coli	furantoin Prevalence (95% CI) 97.00 (81.60, 99.58) 97.20 (91.68, 99.09)	strains 38 105
(d) Author Adeyemo AA Obi CL Wolday D	Year of publication 1994 1996 1997	Prevalent Reference [178] [187] [184]	ce of resis	tance t	5 100 co nitro coli	furantoin Prevalence (95% CI) 97.00 (81.60, 99.58) 97.20 (91.68, 99.09) 83.00 (75.71, 88.44)	strains 38 105 134
(d) Author Adeyemo AA Obi CL Wolday D Moges F	Year of publication 1994 1996 1997 2002	Prevalent Reference [178] [187] [184] [183]	ce of resis	tance t	5 100 co nitro coli	furantoin Prevalence (95% CI) 97.00 (81.60, 99.58) 97.20 (91.68, 99.09) 83.00 (75.71, 88.44) 72.20 (48.08, 87.93)	strains 38 105 134 18
(d) Author Adeyemo AA Obi CL Wolday D Moges F Dromigny JA	Year of publication 1994 1996 1997 2002 2002	Prevalent Reference [178] [187] [184] [183] [191]	ce of resis	tance t	5 100 co nitro coli	furantoin Prevalence (95% CI) 97.00 (81.60, 99.58) 97.20 (91.68, 99.09) 83.00 (75.71, 88.44) 72.20 (48.08, 87.93) 48.50 (36.92, 60.24)	strains 38 105 134 18 68

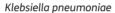
Prevalence of resistance to co-trimoxazole Klebsiella pneumoniae

#### Figure 4. Continued

control and quality assurance procedures were in place in only a limited number of laboratories. The poor reporting of breakpoints used to assign strains to a susceptible, intermediate resistance (where applicable) or resistance category suggests that a

heterogeneous set of cut-offs may have been used, which may have changed over time. However, in a sensitivity analysis we observed a similar median prevalence of resistance to the most commonly reported antimicrobial drugs in *E. coli*, *S. aureus* and





#### Figure 4. Continued

Salmonella Typhi, stratified by region (EA and WA), in studies reporting breakpoints compared with studies not reporting breakpoints (data not shown). Previous reviews on bacterial AMR in sSA, which were limited to certain regions<sup>10</sup> or antibiotic class,<sup>12</sup> reported similar issues. Clearly, there is a need for not only standardized performance of laboratory procedures but also for standardized reporting of the results obtained in the international literature.

A considerable proportion of publications identified for full-text review could not be retrieved despite our access to major online databases and medical libraries through multiple research institutes. Publications in highly accessed journals were therefore more likely to be retrieved for analysis. We only included studies reporting AMR data that could be related to a relevant clinical syndrome. With this approach we minimized case-mix and allowed ourselves to describe AMR data with relevance to a clinical setting and empirical treatment strategies. We therefore excluded articles that did not describe any clinical syndrome, in which a clinical syndrome or patient population could not be linked to the pathogens studied or in which a combined resistance was reported for pathogens isolated from different clinical syndromes. Due to these selection criteria, certain potentially highly relevant resistance data may have been excluded from the analysis, including e.g. data on non-typhoidal Salmonella species and data reported in carrier studies. Information on the year of isolation of the reported pathogens was often missing and therefore it was impossible to analyse trends of AMR over time. Despite these drawbacks, our results suggest high prevalence of AMR in clinical bacterial isolates to antimicrobial drugs that are commonly used in sSA. This finding warrants adjustment of empirical treatment guidelines towards recommendations including antimicrobial drugs for which resistance prevalence appears low to moderate, including, for example, nitrofurantoin for uncomplicated UTI and vancomycin for treatment of methicillin-resistant *S. aureus* infections. Unfortunately, such drugs are often not available in local hospitals or pharmacies.

The WHO recommends continent-wide surveillance of AMR as a health systems approach for containment,<sup>22</sup> of which the relevance has been underlined by others.<sup>23,24</sup> The implementation of surveillance programmes in low- and middle-income countries was shown to be challenging because human and financial resources and microbiology expertise are insufficient,<sup>25,26</sup> particularly if adequate sample sizes are to be reached. Clearly, novel approaches to AMR surveillance are needed, which may depend on smaller sample sizes and can provide locally relevant knowledge of AMR patterns, allowing for appropriate empirical antimicrobial therapy.<sup>27</sup>

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The study was carried out as part of our routine work.

### **Transparency declarations**

None to declare.

#### Author contributions

C. S. conceived the study. C. S., F. v. L. and S. J. L. designed the study. S. J. L. and H. T. searched published work, reviewed published papers and made the primary selection of eligible papers. C. S. and F. v. L. resolved disagreements regarding the eligibility of papers. S. J. L., H. T. and F. v. L. compiled the data. F. v. L. and C. S. analysed the data. All authors contributed to the writing of the report and have seen and approved the final version.

## Supplementary data

Supplementary methods and Tables S1 to S13 are available as Supplementary data at JAC Online (http://jac.oxfordjournals.org/).

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