Antimicrobial resistance in Africa: a systematic review

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Abstract

Background: Antimicrobial resistance (AMR) is widely acknowledged as a global problem, yet in many parts of the world its magnitude is still not well understood. This review, using a public health focused approach, aimed to understand and describe the current status of AMR in Africa in relation to common causes of infections and drugs recommended in WHO treatment guidelines.

Methods: PubMed, EMBASE and other relevant databases were searched for recent articles (2013–2016) in accordance with the PRISMA guidelines. Article retrieval and screening were done using a structured search string and strict inclusion/exclusion criteria. Median and interquartile ranges of percent resistance were calculated for each antibiotic-bacterium combination.

Results: AMR data was not available for 42.6% of the countries in the African continent. A total of 144 articles were included in the final analysis. 13 Gram negative and 5 Gram positive bacteria were tested against 37 different antibiotics. Penicillin resistance in Streptococcus pneumoniae was reported in 14/144 studies (median resistance (MR): 26.7%). Further 18/53 (34.0%) of Haemophilus influenza isolates were resistant to amoxicillin. MR of Escherichia coli to amoxicillin, trimethoprim and gentamicin was 88.1%, 80.7% and 29.8% respectively. Ciprofloxacin resistance in Salmonella Typhi was rare. No documented ceftriaxone resistance in Neisseria gonorrhoeae was reported, while the MR for quinolone was 37.5%. Carbapenem resistance was common in Acinetobacter spp. and Pseudomonas aeruginosa but uncommon in Enterobacteriaceae.

Conclusion: Our review highlights three important findings. First, recent AMR data is not available for more than 40% of the countries. Second, the level of resistance to commonly prescribed antibiotics was significant. Third, the quality of microbiological data is of serious concern. Our findings underline that to conserve our current arsenal of antibiotics it is imperative to address the gaps in AMR diagnostic standardization and reporting and use available information to optimize treatment guidelines.

Keywords: Antimicrobial resistance, Africa, Bacteria, Systematic review

Background

Internationally, there is a growing concern over antimicrobial resistance (AMR) which is currently estimated to account for more than 700,000 deaths per year worldwide [1]. If no appropriate measures are taken to halt its progress, AMR will cost approximately 10 million lives and about US$100 trillion per year by 2050 [1]. In contrast to some other health issues, AMR is a problem that concerns every country irrespective of its level of income and development as resistant pathogens do not respect borders [1, 2].

Despite the threat presented by AMR, the 2014 World Health Organization (WHO) and the recent O’Neill report describe significant gaps in surveillance, standard methodologies and data sharing [1, 2]. The 2014 WHO report identified Africa and South East Asia as the regions without established AMR surveillance systems [2]. This lack of quality data is problematic often leading to treatment guidelines that are not adequate for the local
situation. The gap in public health capacity is also an issue given the changing resistance mechanisms and the emergence of multidrug-resistant bacteria that can only be detected through systematic screening in quality assured microbiology laboratories [3, 4].

One factor contributing to AMR is misuse of antibiotics. Improved malaria diagnostics and the recognition that malaria transmission is decreasing globally has highlighted the lack of tests for other infections and many patients who test negative for malaria are treated with antibiotics indiscriminately [5–7]. Clinical treatment algorithms like the Integrated Management of Neonatal and Childhood Illnesses (IMNCI) and Integrated Management of Adolescent and Adulthood Illnesses (IMAI) guidelines implemented by the WHO have tried to optimize antibiotic prescription in resource-limited settings, however overuse of antibiotics is still happening [8–11]. Following these guidelines amoxicillin or sulfamethoxazole/trimethoprim are the first line drugs for urinary tract infections (UTI) or acute respiratory tract infections. A combination of ampicillin and gentamicin or ceftriaxone are the drugs of choice for treating blood stream infections (BSI) and sulfamethoxazole/trimethoprim or ciprofloxacin are recommended for the treatment of dysentery [8, 9, 12].

A number of recent reviews summarized AMR data in Africa, most recently Leopold et al. (2014) which focused on Sub-Saharan Africa. The authors found a high level of resistance to the commonly used antibiotics in the sub-Saharan African region. For example, 90% of Gram negatives were resistant to chloramphenicol, a commonly used antibiotic. In contrast, resistance to third-generation cephalosporins (like ceftriaxone) was less common, recommending this group for use [13].

To design suitable local and global interventions, it is important to understand the current status of AMR and identify knowledge gaps. The purpose of this review is to summarize the available information about the occurrence of AMR on the entire African continent and describe laboratory methods currently in use, to identify knowledge gaps and highlight diagnostic needs.

Methods
Search strategy
PubMed, EMBASE, Science Daily, the Cochrane Database for Systematic Reviews, African Journals Online Library and Free-text Web Searches using Google Scholar were searched for articles published in English from January 1, 2013 through January 31, 2016. Literature before January 2013 was covered in previous reviews [13, 14]. Reference lists of relevant articles were checked for additional titles for inclusion in the review. Key words used for the search were “Antimicrobial Resistance”, “Antimicrobial Susceptibility”, “Surveillance”, “Diagnostic”, “Africa” and specific names of all African countries.

The detailed search strategy, as well as details of the article quality assessment can be found in Additional file 1.

Selection criteria
Articles reporting AMR prevalence, availability of AMR surveillance systems or diagnostic needs of antibiotic resistance in the whole African region were included. Based on the abstract, articles of all types with any data on etiology and antibiotic susceptibility pattern were included for further screening. Studies were included or excluded following predefined criteria.

Inclusion:
- Reports on AMR in humans from the African region
- Abstracts and full text available in English
- Drug sensitivity testing done in a laboratory setting with defined cutoffs for drug susceptibility testing
- The denominator as total isolates clearly described for population based studies
- Case reports and case series

Exclusion:
- Reports published before 2013
- Studies only focused on malaria, HIV or tuberculosis without AMR information
- Studies without information on total studied isolates

Selection procedure
Titles and abstracts of all the articles retrieved through the search were screened. In the event of uncertainty as to whether articles met the criteria for study inclusion they were discussed with two co-authors. Articles selected for full text review were obtained using PubMed, WHO GIFT access, HINARI, institutional websites or by contacting the authors directly. Names of authors from articles in the search results were not blinded for abstract or full-text review.

Data extraction
Data extraction was done using a predesigned and pretested database, developed for the purposes of this review using Microsoft Excel 2013. Information extracted included article information (PMID, first author, year of publication, duration of data collection and country), study design (sample size, age group, hospital acquired or community acquired, number of specimens collected, and clinical syndrome), pathogen identification and antimicrobial susceptibility testing methodology, laboratory accreditation information and antibacterial resistance data.

Article quality assessment
The quality of each article was assessed using a tool modified for the purposes of this study from criteria
published by Omulo et al. and the Cochrane guidelines for assessing bias in observational studies. Since a limited number of articles was available, results of the quality assessment were not used for inclusion/exclusion. The quality criteria included 26 items to assess the design, details of sample collection, processing and storage, reporting on AMR methodologies and quality assurance strategies.

Data analysis
We calculated prevalence, median resistance (MR) and inter quartile range (IQR) of resistance for each bacterium-antibiotic combination to calculate a standardized measure from the collected data. Pediatric age was considered less than 18 years and neonatal age less than 28 days. Meta-analysis was not conducted because of the large variability in AMR methodology, geography and the small number of articles available per country. Since the number of studies from hospital/in-patient settings was small, they were combined and median percentages with interquartile ranges were generated. Statistical analyses and visualization were performed using Microsoft Excel 2013, STATA v14 (STATA, College Station, TX, USA) and R-software 3.3.1.

Results

Data and study characteristics
In total, 1704 articles were identified. Of those, 144 studies met the inclusion criteria and were included in the final analysis (Fig. 1). Samples from a total of 149,733 patients were analyzed in the selected studies. The majority of the studies were from East Africa (59/144, 40.9%) while the smallest number of studies were from the South African region (6/144, 4.2%) (Fig. 2). No suitable report was identified from 23/54, 42.6% countries. While the articles were published between 2013 and 2016, the reported data were collected from 1995 to 2015 with the majority from before 2013 (98/144, 68.1%). Most of the studies (92/144, 63.9%) were cross sectional studies or case series (Table 1). Similar numbers of studies were published with susceptibility data for isolates from blood culture (25/144, 17.4%), urine culture (25/144, 17.4%), wound discharge/pus isolates (22/144, 15.3%); and multiple sample types (21/144, 14.6%). More than 80% of the studies fulfilled more than half of the quality parameters (121/144, 84.0%) used to score the articles (Additional file 1). Among the different studies, four different methods for susceptibility testing and five different interpretation guidelines were used (Table 1).

Microbial resistance patterns
The most commonly reported bacterium was *Escherichia coli* (87/144, 60.4%) with the most frequent susceptibility data for gentamicin (77/144, 53.5%), ciprofloxacin (71/144, 49.3%) and sulfamethoxazole/trimethoprim (68/144, 47.2%) (Table 2). In total, 13 Gram negative opportunistic pathogens were tested against 37 antibiotics (Table 3, Additional file 2). Overall resistance to commonly used drugs [8, 9, 12], like amoxicillin (MR 72.9%,
IQR 9.1%–87.3%) and trimethoprim/sulfamethoxazole (MR 75.0%, IQR 49.5%–92.3%) was high. Low to moderate resistance was found to gentamicin (MR 22.1%, IQR 2.0%–45.0%), ciprofloxacin (MR 16.7%, IQR 0%–38.5%) and ceftriaxone (MR 17.2%, IQR 0%–45.0%). Gentamicin resistance in *Klebsiella* spp., which is naturally resistant to ampicillin, was reported in 1031/2715, 38.0% of tested isolates. Resistance to either ceftriaxone or cefotaxime, which is suggestive of extended-spectrum beta lactamase (ESBL) production was reported in 593/2963, 20.0% and 1051/5395, 19.5% of *E. coli* as well as 545/1594, 34.2% and 560/1199, 46.7% of the *K. pneumoniae* isolates, respectively. Imipenem, a drug rarely available in rural Africa, was investigated in 21/144 (14.6%) of the studies and showed the lowest overall MR (MR 3.0%, IQR 0%–26.6%) (Table 3). Of the *Acinetobacter* isolates reported in three studies, 32.3% (10/31) were resistant to meropenem. Ciprofloxacin resistance in *S. Typhi* was reported rarely (MR 0%, IQR 0%–11.7%) while ampicillin resistance in *Haemophilus influenzae* was high (MR 100%, IQR 76.6%–100%). There was no documented ceftriaxone resistance in *N. gonorrhoeae* but ciprofloxacin resistance was reported in 37.5% (IQR 30.7%–83.9%) of the isolates.

In the Gram positive group, Coagulase Negative *Staphylococcus* spp. (CoNS), *S. aureus*, *Streptococcus pneumoniae* and Group A streptococcus were the most commonly investigated bacteria (Table 4). Methicillin resistant *S. aureus* (MRSA) was reported in 7/79 (8.9%) of the studies, however as cefoxitin is typically used to screen for MRSA, the MRSA rate is likely underestimated [15]. Erythromycin resistance in *S. aureus* was found in 33.9% (IQR 13%–46.4%). Methods used to assess penicillin susceptibility in *S. pneumoniae* varied: median oxacillin resistance was reported in 40.7% (IQR 0%–55.7%) compared to 26.7% (IQR 8.4%–33.6%) for penicillin and 22.5% (IQR 20%–32.5%) for amoxicillin.

Vancomycin showed the lowest resistance pattern for all the tested Gram positive bacteria (Table 4). In the reviewed literature, *E. coli* was commonly isolated from patients with BSI (17/87, 19.5%), UTI (17/87, 19.5%) and wound infection (16/87, 18.4%). *Citrobacter* spp. were reported most commonly among patients with UTIs (7/19, 36.8%), followed by BSI (5/19, 26.3%). Two (2/19, 10.6%) [16, 17] of the studies which reported on *Citrobacter* spp. were from HAIs; five (5/19, 26.3%) from community acquired infections of which three (3/5)
Table 1: Characteristics of the articles included in the systematic review

| Characteristic                        | Frequency (%) | References |
|---------------------------------------|---------------|------------|
| **Publication Year**                  |               |            |
| 2013                                  | 67 (46.5)     | [17, 19, 26, 43–99] |
| 2014                                  | 39 (27.1)     | [13, 16, 18, 22, 24, 27, 45, 100–138] |
| 2015                                  | 35 (24.3)     | [20, 21, 23, 25, 139–172] |
| 2016                                  | 3 (2.1%)      | [173–175] |
| End of data collection                | NA            |            |
| Before 2010                           | 17 (11.8)     |            |
| Between 2010 and 2013                 | 81 (56.3)     |            |
| After 2013                            | 41 (28.5)     |            |
| Not mentioned                         | 5 (3.5)       |            |
| **Study Design**                      |               |            |
| Cross sectional/Case Series           | 92 (63.9)     | [16–23, 25, 26, 28, 30–32, 36, 38–40, 42, 43, 45, 46, 48–50, 53, 55–58, 60, 63, 67–71, 73–75, 77, 79, 82–85, 87, 89, 90, 92, 93, 95–100, 103–105, 108, 112–116, 119, 123–133, 137, 139–142, 144, 146, 151, 153, 154, 156, 157, 160, 176] |
| Case control                          | 3 (2.1)       | [59, 106, 150] |
| Prospective Cohort/Clinical Trial     | 11 (7.6)      |            |
| Retrospective                         | 18 (12.5)     | [44, 52, 56, 74, 76, 79, 80, 116, 126, 135, 153, 164] |
| Surveillance                          | 9 (6.3)       | [24, 27, 49, 50, 62, 91, 95, 103, 124, 125, 136, 149, 160, 163, 165, 167, 173] |
| Not Mentioned                         | 11 (7.6)      | [67, 69, 77, 81, 121, 132, 151, 158, 162] |
| Source of Data                        |               |            |
| In patient                            | 59 (41.0)     | [16, 17, 20, 22, 23, 26, 44–46, 53, 54, 56, 60–62, 64, 66, 68, 71, 72, 77, 80, 84, 88, 90–92, 95, 97, 99, 101, 104, 108, 112, 117–120, 123, 126–129, 132, 135, 136, 138, 147, 148, 153, 155, 158, 162, 164, 166, 167, 173] |
| Outpatient                            | 49 (30.0)     | [18–20, 24, 25, 43, 51, 52, 58, 59, 63, 70, 73–75, 78, 82, 85, 87, 94, 96, 100, 105–107, 111, 113, 116, 117, 131, 133, 134, 139, 140, 142, 150–152, 156, 157, 159, 170–172, 175, 176] |
| Both                                  | 12 (8.3)      | [50, 79, 83, 86, 130, 143, 149, 161, 163, 169, 177, 178] |
| Unknown                               | 24 (17.4)     | [27, 38, 49, 57, 65, 67, 76, 79, 81, 93, 103, 109, 110, 115, 121, 124, 125, 145, 146, 154, 165, 174] |
| Type of Infection                     |               |            |
| Hospital Acquired                     | 22 (15.3)     | [16, 17, 20, 23, 54, 60–62, 72, 80, 88, 90, 91, 97, 104, 119, 123, 127–129, 135, 147] |
| Community acquired                    | 58 (40.3)     | [18–20, 24, 25, 28, 36, 37, 43, 44, 48, 35, 58–60, 63, 67, 70, 72, 79, 81, 85, 90–92, 96, 98, 101, 102, 116, 118, 119, 124, 125, 127, 135–137, 141, 142, 144, 155–157, 160, 161] |
| Both                                  | 11 (7.6)      | [50, 55, 77, 79, 86, 95, 145, 162, 163, 166, 167] |
| Unable to say                          | 53 (37.5)     |            |
| AMR/Drug susceptibility methodology⁴  |               |            |
| Disk Diffusion                        | 118 (81.9)    | [38, 56, 63, 74, 81, 84, 86, 96, 104, 115, 140, 146, 148, 150] |
| VITEK                                 | 11 (7.6)      | [65, 77, 116, 121, 132, 155] |
| E-test                                | 2 (1.4)       |            |
| MIC                                   | 7 (4.9)       |            |
| Not mentioned                         | 6 (4.2)       |            |
| Laboratory Standard                   | NA            |            |
| BSAC                                  | 6 (4.1)       |            |
| CA-SFM/EUCAST                         | 15 (10.4)     |            |
| NCCLS/CLSI                            | 105 (72.9)    |            |
| Not Mentioned                         | 18 (12.5)     |            |
| Organism identification Method⁴       |               |            |
| Morphology                            | 95 (66.0)     | [16, 17, 19, 22, 24, 43–45, 50, 51, 53, 54, 56, 58, 62–64, 64, 67, 70, 71, 73, 75, 78, 81–83, 85–87, 89, 90, 92, 94, 95, 97, 98, 101, 103–106, 108, 110–113, 119, 120, 125–129, 131, 134, 138, 139, 142, 151, 152, 155, 157, 162, 164, 165, 169, 172, 174–176] |
| API⁴                                  | 17 (11.8)     |            |
| VITEK                                 | 6 (4.2)       |            |
came from pregnant women at antenatal care follow up [18–20] and two (2/5) had unknown risk factors [21, 22]. S. Typhi was most frequently reported from patients with BSI (13/28, 46.4%) followed by patients with diarrhea (6/28, 21.4%). It was also more commonly reported in children below 18 years (12/28, 48.9%) than in adults (2/28, 7.1%) (Table 2).

In the current review, the susceptibility results were taken at face value, however there were inconsistencies casting the credibility of several results in doubt. For example a study reporting more than 80% of Proteus isolates (n = 6) as resistant to imipenem also reported that 80% of them were susceptible to ceftriaxone and 50% were susceptible to vancomycin, a combination that is highly unusual [23]. There were other unverified reports of highly unusual resistance patterns from some centers, such as penicillin resistant S. pyogenes [24, 25] and vancomycin-resistant S. aureus [26, 27].

Regional antibiotic resistance patterns
Generally, a lower level of resistance of S. aureus, Klebsiella spp., E. coli and S. pneumoniae to carbapenems and fluoroquinolones was observed in all the regions as compared to the other antibiotic-bacterium combinations. However, Klebsiella spp. resistance to ciprofloxacin in West Africa was observed to be higher than in other regions. Resistance to the trimethoprim (MR: 33.9%–100%), ampicillin (MR: 7.9%–100%) and penicillin (MR: 0%–75%) was generally high in all regions (Fig. 3).

Discussion
The rise and spread of AMR threatens the effective control and treatment of various bacterial diseases worldwide [1, 2]. The achievements gained in reducing mortality and morbidity through early use of antibiotics based on empiric guidelines are in serious jeopardy if appropriate actions are not taken to control AMR [28, 29]. Availability of routine and research data on pathogen susceptibilities is an important step towards designing targeted strategies to tackle the global AMR crisis. The current review describes recently (2013–2016) published data on antibiotic drug susceptibility from Africa.

The lack of consistency in the measurement and reporting of susceptibility data makes it difficult to compare findings among different countries and laboratories, sometimes even within one country [30, 31]. To address this issue, high income countries have implemented harmonization efforts. For example, laboratories in Europe are encouraged to use the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standard over the Clinical and Laboratory Standards Institute, API Analytical profile index, NAAT Nucleic acid amplification tests, MALDI-ToF Matrix Assisted Laser Desorption/Ionization-Time of Flight, ISO International Organization for Standardization, EQA External Quality Assurance; ¥Polymerase Chain Reaction

*Studies might have used more than one method and they were counted more than once

Two studies mentioned a non-specific accreditation and National Accreditation; Hospital acquired infection (HAI) was defined as a new clinical infections in patients who had been admitted for ≥48 h in a hospital setting. Community acquired infection was defined as infection occurring in the community or within 48 h of hospital admission

| Table 1 Characteristics of the articles included in the systematic review (Continued) |
|----------------------------------|----------------------------------|
| Variable                          | Count (Percentage)               |
| NAAT                             | 3 (2.1)                          |
| MALDI-ToF                        | 2 (1.4)                          |
| Not mentioned                    | 21 (14.6)                        |
| Lab Accreditation/Quality assurance activities |                          |
| ISO                              | 5 (3.5)                          |
| EQA                              | 6 (4.2)                          |
| Not mentioned                    | 133 (92.3)                       |
| Age Group                        | NA                               |
| Adults                           | 42 (29.2)                        |
| Pediatrics and neonates\(^b\)    | 34 (23.6)                        |
| Both adults and pediatrics       | 42 (29.2)                        |
| Neonates only                    | 4 (2.8)                          |
| Unknown                          | 22 (15.3)                        |

NA not applicable, BSAC British Society for Antimicrobial Chemotherapy, CA-SFM Comité Antibio gramme – Société Française de Microbiologie (CA-SFM), EUCAST European Committee on Antimicrobial Susceptibility Testing, NCCLS National Committee for Clinical Laboratory Standards, CLSI Clinical and Laboratory Standards Institute, API Analytical profile index, NAAT Nucleic acid amplification tests, MALDI-ToF Matrix Assisted Laser Desorption/Ionization-Time of Flight, ISO International Organization for Standardization, EQA External Quality Assurance; ¥Polymerase Chain Reaction

\(^a\)Studies might have used more than one method and they were counted more than once

\(^b\)Two studies mentioned a non-specific accreditation and National Accreditation; Hospital acquired infection (HAI) was defined as a new clinical infections in patients who had been admitted for ≥48 h in a hospital setting. Community acquired infection was defined as infection occurring in the community or within 48 h of hospital admission
tracking. Furthermore, improved access to reference laboratories and EQA schemes are needed augmenting the current WHO initiative to scale up the global antimicrobial surveillance system (GLASS) based on country specific priority pathogens [34]. Currently, in the absence of a uniform laboratory methodology the GLASS goals will be very difficult to meet.

Comparing our findings with previous reviews in the region like Leopold et al. (2014), overall, we identify similarly high resistance to commonly used antibiotics [13]. The same review reported a high level of resistance of Enterobacteriaceae to ampicillin and co-trimoxazole which is in agreement with our findings. Similarly, resistance to co-trimoxazole and tetracycline by *S. pneumoniae* was reported to be high. However, discrepancies were observed in various antibiotic/bacterium combinations. For instance, our finding of resistance to chloramphenicol in *Salmonella* Typhi isolates is lower than that previously reported [13]. Resistance to oxacillin by *S. aureus* was also much higher in the current review than the review by Leopold et al. [13]. The observed differences between data published in 2014 and the current work could indicate a rising pattern in AMR in certain pathogens. However it could also be because of the differences in AMR testing methodologies underlying the need for harmonization of laboratory methods in the region.

A notable finding of this review was the high resistance rate of common causes of UTI to common first line regimes like amoxicillin and sulfamethoxazole/trimethoprim. In the presence of a failing treatment, patients with UTIs are at increased risk of developing renal damage and future risks of renal insufficiency or hypertension [35]. Similarly, given the resistance profiles in the current review, neonatal sepsis or BSI caused by *E. coli*, *K. pneumoniae* and *S. aureus* are not being effectively treated by first line drugs like ampicillin, aminoglycosides and cephalosporins, which will result in increased mortality in patients with life-threatening infections. The high levels of resistance to amoxicillin and penicillin in *S. pneumoniae* and *H. influenzae* are also concerning given that pneumonia is a leading cause of death in children [36, 37].

**Table 2** Bacteria reported as number of studies (% of all of studies) in different clinical syndromes

| Bacteria                   | No. Studies | HAI N (%) | BSI N (%) | UTI N (%) | AGE N (%) | WI N (%) | Carriage N (%) |
|----------------------------|-------------|-----------|-----------|-----------|-----------|----------|---------------|
| *S. aureus*                | 79          | 17 (21.5) | 17 (21.5) | NS        | NS        | 22 (27.8)| 10 (12.7)     |
| *S. pneumoniae*            | 24          | NA        | 8 (33.3)  | 1 (4.2)   | NS        | NS        | 4 (16.7)      |
| *E. coli*                  | 87          | 15 (17.2) | 17 (19.5) | 17 (19.5) | 7 (8)     | NS        | 2 (2.3)       |
| Enterobacter spp.          | 36          | 3 (8.3)   | 8 (22.2)  | 8 (22.2)  | 1 (2.8)   | NS        | NA            |
| Haemophilus influenza       | 7           | NA        | NA        | NS        | NS        | NS        | NA            |
| CoNSa                      | 27          | 9 (33.3)  | 6 (22.2)  | 5 (18.5)  | NS        | 9 (33.3)  | NA            |
| Citrobacter spp.           | 19          | 2 (10.5)  | 5 (26.3)  | 7 (36.8)  | NS        | NS        | NA            |
| S. Typhi                   | 28          | 2 (7.1)   | 13 (46.4) | 1 (3.6)   | 6 (21.4)  | NS        | 1 (3.6)       |
| Pseudomonas aeruginosa     | 60          | 17 (28.3) | 11 (18.3) | 8 (13.3)  | NS        | 20 (33.3)| 2 (3.3)       |
| Serratia spp.              | 7           | 1 (14.3)  | 2 (28.6)  | NA        | NS        | NS        | 1 (14.3)      |
| Klebsiella pneumoniae      | 75          | 15 (20)   | 21 (28)   | 15 (20)   | NS        | 16 (21.3)| 2 (2.7)       |
| Proteus spp.               | 46          | 10 (21.7) | 8 (17.4)  | 10 (21.7) | NS        | NS        | 1 (2.2)       |
| Acinetobacter spp.         | 17          | 5 (29.4)  | 7 (41.2)  | 1 (5.9)   | NS        | 4 (23.5)  | NA            |
| Neisseria meningitdis      | 1           | NA        | NA        | NS        | NS        | NS        | NA            |
| Shigella spp.              | 8           | NA        | NA        | 6 (75)    | NS        | NS        | NA            |
| Campylobacter spp.         | 3           | NA        | NA        | 1 (33.3)  | 3 (100)   | NS        | NA            |
| Group A Streptococcus      | 18          | 1 (5.6)   | 6 (33.3)  | NS        | NS        | 3 (16.7)| 2 (11.1)      |
| Group B Streptococcus      | 2           | NA        | NA        | NS        | NS        | NA        | NA            |
| Listeria monocytogenes     | 2           | NA        | 1 (50)    | 1 (50)    | NS        | NA        | NA            |
| Non-Typhoidal Salmonella spp.| 11        | 9 (81.8)  | NS        | 2 (18.2)  | NS        | NS        | NA            |
| Neisseria gonorhaoeae      | 11          | NS        | NA        | 2 (18.2)  | NS        | NS        | NA            |
| Moraxella spp.             | 2           | NS        | NA        | NS        | NS        | NS        | NA            |
| Streptococcus spp.         | 3           | NA        | NA        | 1 (33.3)  | 1 (33.3)  | 1 (33.3)| 1 (33.3)      |

HAI Hospital Acquired Infection, UTI Urinary Tract Infection, AGE Acute Gastroenteritis, WI Wound Infection, BSI Bloodstream Infections, NS Not significant since the bacterium is an unlikely cause of the infection etiology [180], NA Not applicable because data were not available for the specific combination aCoNS: Coagulase Negative Staphylococcus spp.
| Drugs | Acinetobacter spp (N Isolates) Median (IQR) | Carbofuran spp (N Isolates) Median (IQR) | Escherichia coli (N Isolates) Median (IQR) | Haemophilus influenzae (N Isolates) Median (IQR) | Nesiella gonorrhoeae (N Isolates) Median (IQR) | Proteus spp (N Isolates) Median (IQR) | Proteus vulgaris (N Isolates) Median (IQR) | Pseudomonas aeruginosa (N Isolates) Median (IQR) | Salmonella enteric (N Isolates) Median (IQR) | Shigella spp (N Isolates) Median (IQR) |
|-------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| Amikacin | (20) | 32.7(6.3) | 5.9(15.4) | 0(24.5) | NC | NC | NC | NC | NC | NC |
| Amoxicillin | NC | (71) | 78.5(95.8) | (5500) | 88.1(92.6) | NC | NC | NC | NC | NC |
| Ampicillin | (188) | 100(92.5–100) | (59) | 100(6.1–100) | (2951) | 86.7(96.7) | (18) | 100(76.6–100) | NC | NC |
| Amoxicillin and Clavulanic Acid | (56) | 94.1(15–100) | (53) | 34.8(100) | (6764) | 43.3(61.9) | (35) | 22.0(39.5) | NC | NC |
| Azithromycin | NC | NC | NC | NC | NC | NC | NC | NC | NC | NC |
| Cefotaxime | (205) | 90.9(17–100) | (58) | 29.2(7.1–72.8) | (5173) | 26.8(6.3–64.5) | NC | NC | NC | NC |
| Cefazolin | (260) | 81.5(3.9–100) | (60) | 45.9(78.6) | (2773) | 19.5(10.0–55.8) | NC | NC | NC | NC |
| Ceftriaxone | (69) | 74.2(33–100) | (116) | 25.3(77.2) | (2800) | 31.5(69.4–47.7) | (88) | 20.4(57.1) | (1547) | 47.2(52.6) |
| Cefuroxime | (31) | 75(45.8–100) | (3925) | 30.1(51.7–112) | (3947) | 51.9(35.8–83.2) | NC | NC | NC | NC |
| Cefoxitin | NC | NC | NC | NC | NC | NC | NC | NC | NC | NC |
| Cefepime | (79) | 50(75.2) | (95.7) | 21.8(8.2–42.5) | NC | NC | NC | NC | NC | NC |
| Cefalotin | NC | NC | NC | NC | NC | NC | NC | NC | NC | NC |
| Chloramphenicol | (47) | 100(60.4–100) | (88) | 70.8(18.8–91.7) | (2963) | 40.9(11.3–58.0) | (56) | 28.6(10.9–100) | (1046) | 62.8(48.9–91.5) |
| Ciprofloxacin | (47) | 29.9(12.1–74.9) | (147) | 100(31.2) | (7877) | 23.2(77.7–35.6) | (28) | 14.6(31.9–79.2) | (2473) | 24.3(7.8–35.4) |
| Trimethoprim/ Sulfamethoxazole | (133) | 80.4(54.5–100) | (122) | 85.7(64.3–100) | (7493) | 74.8(88.8–85.6) | (54) | 83.8(80–100) | (2093) | 67.8(60.5–93.0) |
| Doxycycline | NC | NC | NC | NC | NC | NC | NC | NC | NC | NC |
| Erythromycin | NC | NC | NC | NC | NC | NC | NC | NC | NC | NC |
| Gentamicin | (288) | 61.1(25–86) | (143) | 37.5(48.4) | (8282) | 29.8(44.5) | (35) | 59.4(8.9–100) | (2691) | 41.7(64.67) |
| Imipenem | (230) | 20(23) | (1613) | 0.2(5.5) | NC | NC | (100) | 0.3(1.3) | NC | NC |

Table 3: Median resistance with interquartile range of selected Gram negative bacteria to all tested antibiotics.
| Antibiotic     | NC       | NC   | (75.4) | 19.2(8.7–47.6) | NC       | (246) | 15.6(8.6–62.7) | NC       | (138) | 42.7(47.7–91.7) | (77) | 25.8(16.5–36.5) | NC       | NC   |
|---------------|----------|------|--------|---------------|----------|-------|----------------|----------|-------|----------------|------|----------------|----------|------|
| Levofloxacin  | NC       | NC   | (3402) | (751) | 0(0–5.7) | NC       | (711) | 3.6(0–11.7) | NC       | (154) | 10(1–1.6) | (138) | 15.8(0–32) | NC       | NC   |
| Meropenem     | (24)     | NC   | (39)   | (10–44.4) | NC       | (246) | 15.6(8.6–62.7) | NC       | (138) | 15.8(0–32) | NC       | NC   |
| Nalidixic Acid| NC       | NC   | (2960) | (751) | 36(12.7–53.8) | NC       | (507) | 35(14.8–53) | NC       | (1007) | 10.6(4.4–19.6) | (101) | 78.4(54.2–90.8) | (537) | 5.7(0.6–19.3) |
| Norfloxacin   | (2)      | NC   | (5.2)  | (24) | 40(0–44.4) | NC       | (3402) | 0(0–5.7) | NC       | (711) | 3.6(0–11.7) | (138) | 15.8(0–32) | NC       | NC   |
| Ofloxacin     | NC       | NC   | (876)  | (24) | 40(0–44.4) | NC       | (5087) | 14(4.5–25.1) | NC       | (257) | 24.0(13–54.7) | (151) | 76.5(65.9–80) | NC       | NC   |
| Oxacillin     | (39)     | NC   | (89)   | (63–86) | NC       | (2960) | 0(0–5.7) | NC       | (711) | 3.6(0–11.7) | (138) | 15.8(0–32) | NC       | NC   |
| Penicillin    | NC       | NC   | (1294) | (24) | 40(0–44.4) | NC       | (5107) | 31(5.6–43.6) | NC       | (1007) | 10.6(4.4–19.6) | (151) | 76.5(65.9–80) | NC       | NC   |
| Piperacillin  | (17)     | NC   | (43)   | (24) | 40(0–44.4) | NC       | (5.2)  | 40(0–44.4) | NC       | (246) | 15.6(8.6–62.7) | (138) | 15.8(0–32) | NC       | NC   |
| Piperacillin/ | (3)      | NC   | (89)   | (41–105) | NC       | (24) | 40(0–44.4) | NC       | (246) | 15.6(8.6–62.7) | (138) | 15.8(0–32) | NC       | NC   |
| Tazobactam    | (17)     | NC   | (43)   | (24) | 40(0–44.4) | NC       | (246) | 15.6(8.6–62.7) | NC       | (138) | 15.8(0–32) | NC       | NC   |
| Tetracycline  | (28)     | NC   | (72)   | (26–87.9) | NC       | (246) | 15.6(8.6–62.7) | NC       | (138) | 15.8(0–32) | NC       | NC   |
| Tobramycin    | NC       | NC   | (677)  | (24) | 40(0–44.4) | NC       | (246) | 15.6(8.6–62.7) | NC       | (138) | 15.8(0–32) | NC       | NC   |

Antibiotics which are routinely available and recommended as first or second line antibiotics according to IMNCI and IMAI empiric guidelines are highlighted in bold [8, 9].

NA Not Applicable: Bacterium is naturally resistant to agent
Antibiotic is not recommended for treatment of this bacterium since resistance is likely to be present.

* NC Not Calculated: MR and IQR not calculated because of a small number of studies for the specific combination.
| Antibiotics                  | CoNS (N Isolates) Median (IQR) | Group A Streptococcus (N Isolates) Median (IQR) | S. aureus (N Isolates)  Median (IQR) | S. pneumoniae (N Isolates) Median (IQR) |
|-----------------------------|---------------------------------|-----------------------------------------------|-------------------------------------|----------------------------------------|
| Amikacin                    | NC (228)                        | 10.4 (4.6–33.8)                               | NC (331)                           | 36.7 (25.8–54.2)                       |
| Amoxicillin                 | NC (96)                         | 28.1 (2.7–39.5)                               | NC (156)                           | 28.7 (6.5–38.5)                       |
| Amoxicillin and Clavulanic Acid | NC (142)                        | 23.5 (11.4–40.2)                              | NC (185)                           | 16.2 (0–13.2)                         |
| Ceftriaxone                 | (366)                           | 39.7 (27.5–49.3)                              | NC (155)                           | 24.1 (0–16.2)                         |
| Cefuroxime                  | (58)                            | 49.2 (32.5–62.6)                              | NC (144)                           | 20.7 (0.9–24.9)                       |
| Chloramphenicol             | (445)                           | 23.6 (21.4–25.8)                              | NC (144)                           | 26.7 (8.4–28.5)                       |
| Ciprofloxacin               | (588)                           | 60.4 (58.2–62.8)                              | NC (90)                            | 23.5 (11–26.8)                        |
| Clindamycin                 | NC (58)                         | 60.4 (58.2–62.8)                              | NC (113)                           | 24.1 (1.3–24.9)                       |
| Sulfamethoxazole/Trimethoprim| (496)                           | 66.6 (59.3–85.3)                              | NC (163)                           | 27.1 (10.4–26.8)                      |
| Doxycycline                 | NC (777)                        | 55.5 (40–79.9)                                | NC (3948)                          | 97.6 (71.4–98.6)                      |
| Erythromycin                | (476)                           | 24.1 (0–16.2)                                 | NC (197)                           | 25.5 (0–16.2)                         |
| Gentamicin                  | (748)                           | 16.0 (21.1–23.3)                              | NC (90)                            | 13.5 (4.1–70.1)                       |
| Imipenem                    | NC (58)                         | 67.4 (58.2–62.8)                              | NC (113)                           | 13.5 (4.1–70.1)                       |
| Levofloxacin                | NC (1148)                       | 55.5 (40–79.9)                                | NC (163)                           | 27.1 (10.4–26.8)                      |
| Nitrofurantoin              | (89)                            | 67.4 (58.2–62.8)                              | NC (90)                            | 13.5 (4.1–70.1)                       |
| Norfloxacin                 | NC (37)                         | 24.1 (0–16.2)                                 | NC (90)                            | 13.5 (4.1–70.1)                       |
| Ofloxacin                   | NC (1214)                       | 24.1 (0–16.2)                                 | NC (163)                           | 27.1 (10.4–26.8)                      |
| Oxacillin                   | (467)                           | 24.1 (0–16.2)                                 | NC (163)                           | 27.1 (10.4–26.8)                      |
| Penicillin                  | (275)                           | 24.1 (0–16.2)                                 | NC (163)                           | 27.1 (10.4–26.8)                      |
| Tetracycline                | (603)                           | 24.1 (0–16.2)                                 | NC (163)                           | 27.1 (10.4–26.8)                      |
| Vancomycin                  | (384)                           | 24.1 (0–16.2)                                 | NC (163)                           | 27.1 (10.4–26.8)                      |

Antibiotics routinely available and recommended as first or second line antibiotics according to IMNCI and IMAI empiric guidelines are highlighted in bold [8, 9].

NA Not Applicable: Bacterium is naturally resistant to agent
NC Not Calculated: MR and IQR not calculated because of a small number of studies for the specific combination
*The four most frequently isolated Gram positive bacteria were included in this table
rates were variable and doubts remain about reliability of identification at all sites which are confirmed by the findings of one Kenyan study which found that MRSA rates dropped dramatically after switching to an automated identification method [38].

Compared to reports from Asia, quinolone resistance in S. Typhi was rare and, reassuringly, there were no reports of ceftriaxone resistance in N. gonorrhoeae [39]. Less commonly prescribed antibiotics like imipenem and vancomycin also showed low level resistance and they should be preserved as alternative drugs in severe infections. Most of the imipenem resistance was described in isolates of P. aeruginosa which has been reported from other centers [33]. Oxacillin resistance should predict penicillin resistance in S. pneumoniae reliably [40, 41], however in the current review resistance to oxacillin was much higher than to penicillin, possibly because of the differences in the number of isolates tested for both antibiotics and the use of different cut-offs for meningitis and non-meningitis strains.

The results also yielded data on the susceptibility of less commonly described bacteria like Acinetobacter spp. and Citrobacter spp. Acinetobacter spp are especially important given their importance in clinical infections and the reported rising trend of resistance, further they have been included in the priority pathogens for global surveillance based on the GLASS initiative [42]. Citrobacter spp were reported from hospital and community settings, including in pregnant mothers and can cause UTI which puts pregnant women at risk of preterm labor. Our results would suggest that current frontline treatments are ineffective against most common uro-pathogens.

The limitations of the current review include the exclusion of non-English language reports, as articles from...
French speaking African countries might have been missed, biasing this review. The representativeness of the data is hard to assess as it is possible that the absence of resistance is not routinely reported and focus is given to reports of resistance. There were very few reports from South Africa, which has a better functioning health system than neighboring countries and better national AMR surveillance. These data were not accessible by our search and therefore larger AMR trends might have been missed. A further limitation is combining AMR results from different patient groups across different countries to compare the data. This approach might have leveled out peaks of resistance in different settings. However, given the observed trends, we believe that the resolution of the obtained data was sufficient to show general developments. Moreover, since case reports were not excluded with intention of capturing as much data as possible in the current review, the findings from the three case (3/144, 2.1% of the studies) might bias the resistance testing results as case reports tend to report on specific multi-drug resistant pathogens. Finally, resistance data obtained with different laboratory methodologies were combined for the purposes of this review. However, as the majority of studies used the disk diffusion method and CLSI guidelines, the impact of the variation in AMR methodology on the validity of the final results is thought to be minimal.

Conclusion
In summary, our review highlights three important findings: first, more than a third of the countries on the continent did not have recent AMR data published in the public domain and only a few of those were surveillance data. Second, a high level of drug resistance exists to commonly prescribed antibiotics in the African continent. Third, the standardization and quality of the microbiological identification and susceptibility testing methods needs to be improved to allow national and international organizations to monitor the extent of the AMR problem. All of the identified areas of concern need urgent attention by the global health community in order to halt the public health threat associated with spreading AMR.

Additional files

Additional file 1: Detailed Methodologies (DOCX 24 kb)
Additional file 2: Proportion of resistance of bacterial isolates to tested antibiotics by region and country (DOCX 263 kb)

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Ethics and consent to participate
Not applicable.

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Availability of data and materials
Data supporting our findings can be found through the corresponding author (email: birkenhiltahun@gmail.com) or the senior author (email: Sabine.Dittrich@finddr.org).

Authors’ contributions
BTT, IJG and SD conceived the idea, prepared the systematic review protocol and were involved in the literature search, screening and extraction of data. BTT performed the data analysis and developed the first draft of the manuscript. SD, IJG, SO, MW, JH, EA provided critical review of the manuscript and contributed to the final version. All the authors read and approved the final version of the manuscript.

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

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References
1. O'Neill J: Tackling Drug-Resistant Infections Globally: Final Report and Recommendations May 2016(http://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf).
2. WHO: Antimicrobial Resistance: In: Global Report on surveillance. Edited by WHO. Geneva, Switzerland; 2014.
3. Liu YY, Wang Y, Walsh TR, Yi LX, Zhang R, Spencer J, Doi Y, Tian G, Dong B, Huang X, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis. 2016;16(2):161–8.
4. Xavier BB, Lammens C, Ruhal R, Kumar-Singh S, Butaye P, Goossens H, Malhotra-Kumar S. Identification of a novel plasmid-mediated colistin resistance gene, mcr-2, in Escherichia Coli, Belgium, June 2016. Euro Surveill. 2016;21(27).
5. WHO: World Malaria Report. In. Edited by WHO, vol. http://apps.who.int/iris/bitstream/10665/200018/1/9789241565158_eng.pdf?ua=1. Switzerland, Geneva, 2015.
6. Harbarth S, Samore MH. Antimicrobial resistance determinants and future control. Emerg Infect Dis. 2005;11(6):794–801.
7. Do NT, Tran NT, Tran HM, Vu BT, Hoang LB, van Doorn HR, Vu DT, Cals JW, Chandna A, et al. Point-of-care C-reactive protein testing to reduce inappropriate use of antibiotics for non-severe acute respiratory infections in Vietnamese primary health care: a randomised controlled trial. Lancet Glob Health. 2016.
8. WHO: Integrated Management of Neonatal and Childhood Illnesses (IMNCI). Switzerland, Geneva 2014, http://apps.who.int/iris/bitstream/10665/104772/16/9789241506823_Chartbook_eng.pdf?ua=1.
9. WHO: Integrated Management of Adolescent and Adulthood Illnesses (IMAI). Switzerland, Geneva 2009, http://www.who.int/hiv/pub/imai/acute_care.pdf?ua=1.
bacterial resistance in living-donor liver transplantation: a multicenter epidemiologic study in Egypt. Transplant Proc. 2014;46:1444–7.

131. Maltu G, Beyene G, Zeynadin A. Prevalence of Shigella, salmonella and campylobacter species and their susceptibility patterns among under five children with diarrhea in Hawassa town, south Ethiopia. Ethiopia J Health Sci. 2014;24:101–8.

132. Phoha MF, De Boech H, Ifeka BB, Dawilli J, Lunguya O, Vanhoof R, Muyembe J-J, Van Geet C, Bertrand S, Jacobs J. Epidemic increase in salmonella bloodstream infection in children, Bwamanda, the Democratic Republic of Congo. European journal of clinical microbiology & infectious diseases: official publication of the European Society of Clinical Microbiology. 2014;33:79–87.

133. Randrianarasi R, Ratima EH, Rampanarison L, Randremanana R, Rakotondrainy HC, Andriamanetana T, Rakotonarison F, Rajatonirina S, Richard V, Talarmin A. Antimicrobial resistance of bacterial enteropathogens isolated from stools in Madagascar. BMC Infect Dis. 2014;14:104.

134. Moyo SJ, Aboud S, Blomberg B, Mkopi N, Kasubi M, Manji K, Lyamuya EF, Phoba M-F, De Boeck H, Ifeka BB, Dawili J, Lunguya O, Vanhoof R, Muyembe J-J. Multidrug resistance and extended-spectrum β-lactamases in bloodstream infection in children with Salmonella spp. bloodstream infection in a hospital in Gabon. BMC Infect Dis. 2014;14:2082–8.

135. Scherbaum M, Koster K, Murbeth RE, Ngoga UA, Kemsner PG, Bell L, Alabi A, M, S, K, K, R. E. M, et al. Incidence, patterns and resistance patterns of nosocomial infections at a rural hospital in Gabon. BMC Infect Dis. 2014, 14:124.

136. Swann O, Everett DB, Furyk JS, Harrison EM, Musuku MT, Hayderman RS, Molyneux EM. Bacterial meningitis in Malawian infants <2 months of age: etiology and susceptibility to World Health Organization first-line antibiotics. Pediatr Infect Dis J. 2014;33:560–5.

137. Vernet G, Mary C, Altmann DM, Dombou O, Morpeth S, Bhuta ZA, Klugman KP. Surveillance for antimicrobial drug resistance in under-resourced countries. Emerg Infect Dis. 2014;20(3):43–41.

138. Wondimeneh Y, Muluye D, Alemu AA, Atifanu A, Yitayew G, Gebrecherkos T, Berhanu Y. Antimicrobial susceptibility of bacteria causing bloodstream infections in children with meningitis in Ethiopia. J Neurosurg Pediatr. 2015;15:150–8.

139. Kalonji LM, Post A, Phoba M-F, Falay D, Ngbonda D, Muyembe J-J, Bertrand S, Ceyssens P-J, Mattheus W, Verhaegen J, et al. Invasive salmonella infections at multiple surveillance sites in the Democratic Republic of the Congo. 2015;S339–45.

140. Onwaesieze IA, Onok FE. Extended spectrum beta-lactamase producing uropathogens in asymptomatic pregnant women attending antenatal care in a urban community secondary health facility. Afr J Clin Exp Microbiol. 2015;16:49–53.

141. Iregbu KC, Eze SO. Pseudomonas Aeruginosaa infections in a tertiary hospital in Nigeria. Afr J Clin Exp Microbiol. 2015;16:33–6.

142. Kiyumwese R, Mutiza L, Kasangaki A, Kajumbula H, Rwemyonyi CM. Characteristics of pyogenic otorrhagia infection in patients attending Mulago hospital Uganda: A cross-sectional study. BMC Microbiology. 2015;14:546.

143. Kalonji LM, Post A, Phoba M-F, Falay D, Ngbonda D, Muyembe J-J, Bertrand S, Ceyssens P-J, Mattheus W, Verhaegen J, et al. Invasive salmonella infections among children from rural Mozambique, 2001–2014. Clin Infect Dis. 2015;61:S346–9.

144. Onwaesieze IA, Onok FE. Extended spectrum beta-lactamase producing uropathogens in asymptomatic pregnant women attending antenatal care in a urban community secondary health facility. Afr J Clin Exp Microbiol. 2015;16:49–53.

145. Kwambana-Adams B, Darboe S, Nabwera H, Foster-Nyarko E, Ikuamapay UN, Secka O, Betts M, Bradbury R, Wegmüller R, Lawal B, et al. Salmonella infections in the Gambia, 2005–2015. Clin Infect Dis. 2015;61:S354–62.

146. Kretz C, Alabi AS, Peters G, Becker K, Kemsner PG, Rossatanga EG, Mollmann A, Grobush MP, Zanger P, Schaumburg F. Co-detection of Panton-valentine leukocidin encoding genes and colistin resistance in Staphylococcus Aureus in Gabon: Implications for HIV-patients’ care. Front Microbiol. 2015;62.

147. Langendorf C, Le Hèllo S, Mounouni A, Gouali M, Mamaty A-A, Grais RF, Weill F-X, Page A-L. Enteric bacterial pathogens in children with diarrhea in niger: diversity and antimicrobial resistance. PLoS One. 2015;10:e0120755.

148. Mofoforonsho CK, Ochieni M, Omotola CA, Agieni AG. Staphylococcus Aureus prevalence and antibiotic susceptibility pattern in anyigba, north-central Nigeria. Am J Infect Dis. 2015;11:93–9.

149. Shehab El-Din EMR, El-Sokkary MMA, Bassiony MR, Hassan R. Epidemiology of neonatal sepsis and implicated pathogens: a study from Egypt. Biomed Res Int. 2015;2015.

150. Nwankwo EO, Magaji NS, Tijani J. Antibiotic susceptibility pattern of extended spectrum beta-lactamase (ESBL) producers and other bacterial pathogens in Kano, Nigeria. Trop J Pharm Res. 2015;14:1273–8.

151. Ilyasu G, Habib AG, Aminu MB. Antimicrobial susceptibility pattern of invasive pneumococcal isolates in north west Nigeria. J Global Infect Dis. 2015;7:70–4.

152. Tesfaw G, Kibru G, Melkonnen D, Abdissa A. Prevalence of group B β-haemolytic streptococcus among children with pharyngitis in Ethiopia. Eur Respir J. 2015;46.

153. Hamdan HZ, Kubbara E, Adam AM, Hassan OS, Sultuan SO, Adam I. Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum Sudan. Annals of clinical microbiology and antimicrobials. 2015;14:26.

154. Mandomando I, Bassat Q, Sigauqwe B, Massoro S, Quinto L, Acacio S, Nhampossa T, Vubil D, Garnire M, Macete E, et al. Invasive salmonella infections among children from rural Mozambique, 2001–2014. Clin Infect Dis. 2015;61:S346–95.

155. Onwaesieze IA, Onok FE. Extended spectrum beta-lactamase producing uropathogens in asymptomatic pregnant women attending antenatal care in a urban community secondary health facility. Afr J Clin Exp Microbiol. 2015;16:49–53.

156. Nitrenganya C, Manzi O, Muvunyimy CM, Ogbaru O. High prevalence of antimicrobial resistance among common bacterial isolates in a tertiary health care facility in Rwanda. Am J Trop Med Hyg. 2015;92:865–70.

157. Ochung N, Okechi T, Ferson S, Albright AL. Bacteria causing ventriculopontal fistula patients at Gondar University Hospital, Northwest Ethiopia. BMC Womens Health. 2014;14:12.

158. Nwankwo EO, Magaji NS, Tijani J. Antibiotic susceptibility pattern of extended spectrum beta-lactamase (ESBL) producers and other bacterial pathogens in Kano, Nigeria. Trop J Pharm Res. 2015;14:1273–8.

159. Onwaesieze IA, Onok FE. Extended spectrum beta-lactamase producing uropathogens in asymptomatic pregnant women attending antenatal care in a urban community secondary health facility. Afr J Clin Exp Microbiol. 2015;16:49–53.
171. Okoje-Adesomoju VN, Ifesanya JU, Alonge TO. Antimicrobial susceptibility pattern of oral microbial isolates among pregnant women in Ibadan south-east local government area, Nigeria. Afr J Biomed Res. 2015;18:29–35.

172. Mulu W, Yimer M, Zenebe Y, Abera B. Common causes of vaginal infections and antibiotic susceptibility of aerobic bacterial isolates in women of reproductive age attending at Felegehiwot referral hospital, Ethiopia: a cross sectional study. BMC Womens Health. 2015;15

173. Maina D, Omuse G, Revathi G, Adam RD. Spectrum of microbial diseases and resistance patterns at a private teaching Hospital in Kenya: implications for clinical practice. PloS One. 2016;11:e0147659.

174. Odetoyin BW, Hofmann J, Aboderin AO, Okeke IN. Diarrhoeagenic Escherichia coli in mother-child Pairs in Ile-Ife, South Western Nigeria. BMC Infect Dis. 2016.

175. Onanuga A, Selekele TL. Virulence and antimicrobial resistance of common urinary bacteria from asymptomatic students of Niger Delta University, Amassoma, Bayelsa state, Nigeria. Journal of Pharmacy and Bioallied Sciences. 2016;8:29–33.

176. Abdelaziz ZA, Ibrahim ME, Bilal NE, Hamid ME. Vaginal infections among pregnant women at Omdurman maternity Hospital in Khartoum, Sudan. Journal of Infection in Developing Countries. 2014;8:490–7.

177. Olorunmola FO, Kolawole DO, Lamikanra A. Antibiotic resistance and virulence properties in escherichia coli strains from cases of urinary tract infections. African Journal of Infectious Diseases. 2013;7:1–7.

178. Pondei K, Fente BG, Oladapo O. Current microbial isolates from wound swabs, their culture and sensitivity pattern at the Niger Delta University teaching hospital, Okolobiri, Nigeria. Tropical Medicine and Health. 2013;41:49–53.

179. Maina D, Makau P, Nyereea A, Revathi G. Antimicrobial resistance patterns in extended-spectrum ß-lactamase producing Escherichia Coli and Klebsiella Pneumoniae isolates in a private tertiary hospital, Kenya. Microbiology Discovery. 2013;1

180. Sanford Guide - Trusted infectious disease recommendations: http://www.sanfordguide.com/stewardship/.