

G OPEN ACCESS

Citation: Monk EJM, Jones TPW, Bongomin F, Kibone W, Nsubuga Y, Ssewante N, et al. (2024) Antimicrobial resistance in bacterial wound, skin, soft tissue and surgical site infections in Central, Eastern, Southern and Western Africa: A systematic review and meta-analysis. PLOS Glob Public Health 4(4): e0003077. https://doi.org/ 10.1371/journal.pgph.0003077

Editor: Janelisa Musaya, Kamuzu University of Health Sciences, MALAWI

Received: October 16, 2023

Accepted: March 15, 2024

Published: April 16, 2024

Copyright: © 2024 Monk et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Database of extracted data will be included as a <u>supplementary file</u>.

Funding: The authors received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

RESEARCH ARTICLE

Antimicrobial resistance in bacterial wound, skin, soft tissue and surgical site infections in Central, Eastern, Southern and Western Africa: A systematic review and meta-analysis

Edward J. M. Monk^{1,2}, Timothy P. W. Jones³, Felix Bongomin⁴, Winnie Kibone⁴, Yakobo Nsubuga⁶, Nelson Ssewante⁵, Innocent Muleya⁶, Lauryn Nsenga⁷, V. Bhargavi Rao^{6,8°}, Kevin van Zandvoort^{1°}

 Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom, 2 Infection Care Group, St George's University Hospitals NHS Foundation Trust, London, United Kingdom, 3 Nuffield Department of Medicine, Jenner Institute, University of Oxford, Oxford, United Kingdom, 4 Faculty of Medicine, Department of Medical Microbiology and Immunology, Gulu University, Gulu, Uganda, 5 Child and Health Development Centre, College of Health Sciences, Makerere University, Kampala, Uganda, 6 The Mason Unit, MSF UK, London, United Kingdom, 7 School of Medicine, Kabale University, Kabale, Uganda, 8 Department of Global Health and Development, London School of Hygiene and Tropical Medicine, London, United Kingdom

So These authors contributed equally to this work.

* kevin.van-zandvoort@lshtm.ac.uk

Abstract

Antimicrobial resistance (AMR) is a major global threat and AMR-attributable mortality is particularly high in Central, Eastern, Southern and Western Africa. The burden of clinically infected wounds, skin and soft tissue infections (SSTI) and surgical site infections (SSI) in these regions is substantial. This systematic review reports the extent of AMR from sampling of these infections in Africa, to guide treatment. It also highlights gaps in microbiological diagnostic capacity. PubMed, MEDLINE and Embase were searched for studies reporting the prevalence of Staphylococcus aureus, Eschericheria coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Acinetobacter baumannii in clinically infected wounds, SSTI and SSI in Central, Eastern, Southern or Western Africa, and studies reporting AMR from such clinical isolates. Estimates for proportions were pooled in meta-analyses, to estimate the isolation prevalence of each bacterial species and the proportion of resistance observed to each antibiotic class. The search (15th August 2022) identified 601 articles: 59 studies met our inclusion criteria. S. aureus was isolated in 29% (95% confidence interval [CI] 25% to 34%) of samples, E. coli in 14% (CI 11% to 18%), K. pneumoniae in 11% (CI 8% to 13%), P. aeruginosa in 14% (CI 11% to 18%) and A. baumannii in 8% (CI 5% to 12%). AMR was high across all five species. S. aureus was resistant to methicillin (MRSA) in >40% of isolates. E. coli and K. pneumoniae were both resistant to amoxicillin-clavulanic acid in \geq 80% of isolates and resistant to aminoglycosides in 51% and 38% of isolates respectively. P. aeruginosa and A. baumannii were both resistant to anti-pseudomonal carbapenems (imipenem or meropenem) in ≥20% of isolates. This systematic review found that a large proportion of the organisms isolated from infected wounds, SSTI and SSI in

Africa displayed resistance patterns of World Health Organisation (WHO) priority pathogens for critical or urgent antimicrobial development.

Introduction

Antimicrobial resistance (AMR) is recognised by the World Health Organization (WHO) as a major global health threat to humanity, estimated to lead to 10 million deaths annually by 2050 [1–3]. In a recent systematic review of the global burden of AMR on health, four subregions of Africa were all found to have rates of death attributable to bacterial AMR higher than any other global sub-region: Central, Eastern, Southern and Western Africa each had a AMR-attributable mortality rate of over 75/100,000 [4]. In their review, Murray et al found that six main pathogens contribute to AMR burden in these African sub-regions: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Of these, all but *S. pneumoniae* are recognised as common pathogens of wound infections, skin and soft tissue infections (SSTI) or surgical site infections (SSI) [5,6].

Globally, bacterial infections of the skin and subcutaneous tissues are the sixth highest infectious syndrome causing AMR-attributable death: only lower respiratory tract infections (LRTI), bloodstream infections, intra-abdominal infections, urinary tract infections and tuberculosis have higher AMR-attributable mortality. In Africa the burden is particularly high, reflected by SSTI leading to an estimated 16.2% of all adult inpatient antibiotic prescriptions for systemic use; the highest of proportion of any global region [7]. Versporten and colleagues found Africa to be the only regional setting where SSTI inpatient antibiotic prescriptions estimates exceed those for inpatient pneumonia/LRTI (10.3%), doing so by over 50%.

To date, the vast majority of microbiological data for infected wounds, SSTI and SSI in Africa are from small, single-centre cross-sectional studies. This systematic review and metaanalysis of proportions synthesises the data available from Central, Eastern, Southern and Western Africa over a ten-year period. It aims to report the extent of AMR in *S. aureus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii* to the antibiotic classes commonly used in clinical practice for empiric and targeted treatment.

Materials and methods

Literature search

The literature search was designed to understand: "what proportion of *S. aureus, E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii* isolates from infected wounds (including infected chronic wounds and ulcers), SSI and SSTI have been reported to be antimicrobial resistant in Central, Eastern, Southern and Western Africa in the last ten years?". This question was summarised into three key concepts, restricted to publication from 1st January 2012: Concept 1) Wounds, surgical sites, skin infections, burns and trauma; Concept 2) Antimicrobial resistance; and Concept 3) Central, Eastern, Southern and Western Africa.

The search was conducted in PubMed, MEDLINE and Embase to capture data from general patient populations (S1 Text). Duplicate articles were removed prior to further screening and assessment. The WHO's African Index Medicus (AIM) was searched separately, using the search terms for the antimicrobial resistance concept alone, for additional eligible articles.

Inclusion and exclusion criteria for studies

Study. Data from cross-sectional, cohort or case-control study designs were eligible for inclusion. Results from randomised controlled trials (RCT) were also included if they reported data from a control group or an intervention that did not impact upon bacterial isolate prevalence or resistance reporting. Case reports and case series were excluded to avoid the introduction of reporting bias. Studies had to be published between 1st January 2012 and 15th August 2022, conducted in a healthcare facility within Central, Eastern, Southern or Western Africa, and available in English.

Population. There were no individual-level patient inclusion or exclusion criteria outside of the requirement for there to be a recorded clinical suspicion of wound infection, SSI or SSTI. Patients could be of any age and from any aspect of the healthcare system (primary, secondary or tertiary care as inpatients or outpatients). Data from cases of osteomyelitis were excluded, as this clinically distinct group of patients was not the focus of this review.

Outcomes. Studies had to report on 1) the prevalence of *S. aureus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa* or *A. baumannii* in samples taken from infected wounds (including chronic wounds and ulcers), SSI and SSTI, and/or 2) the proportion of these isolates showing AMR to a prespecified list of agents within antibiotic classes (S2 Text) [8]. Species identification methods had to be described for all included studies. To be included for resistance data, phenotypic antibiotic sensitivity testing (manual or automated) or sensitivity testing methods using mass spectrometry had to be reported. Resistance mechanism data from genetic testing methods were not included.

Screening assessment. All identified articles were initially screened by title and abstract. Full-texts of successfully screened articles were then formally assessed to confirm suitability for inclusion. For both stages of screening and assessment, two authors considered articles independently, and a third author was consulted if consensus could not be reached.

Data extraction and handling. Study, patient and microbiological characteristics were extracted from all eligible studies. For each included organism of interest, the prevalence of isolation (stratified by type of infection) and the proportion of reported AMR was recorded. AMR definitions were species-specific, with antibiotic agents and classes chosen to reflect those used by the European Centre for Disease Control (ECDC) during the observation period of this review to determine multidrug resistance (MDR) [8].

Risk of bias assessment. All included studies were assessed for risk of bias according to the National Institutes of Health (NIH) Study Quality Assessment Tool for observational cohort and cross-sectional studies [9]. The five categories of potential bias were 1) population definition, 2) inclusion/exclusion clarity, 3) patient selection methods, 4) case establishment and 5) outcome establishment. Every study was assessed on each of these categories as low, medium or high risk of bias [10].

Determination of resistance within antibiotic classes. Resistance within an antibiotic class was defined as the proportion of non-susceptibility (isolates reported within studies as resistant, intermediate or non-susceptible) to at least one agent within the class [8]. Where non-susceptibility was reported within a single study to more than one agent within an antibiotic class, the agent with the higher proportion was used for further analysis. The proportions reported by studies were cross-referenced against the presented numerator and denominators where available: discrepant data were excluded from analysis.

Meta-analysis. Meta-analyses for proportions were performed using Stata version 15.1, to estimate the prevalence of each of the bacterial species of interest from infection samples. Analyses were stratified by infection type (infected wound, infected chronic wound/ulcer, SSI or SSTI). Analyses for the proportion of resistance observed within each antibiotic class were

stratified by country. A sensitivity analysis was performed between prospective cohort studies and cross-sectional studies reporting data from SSI.

As studies reporting no resistance (0%) and complete resistance (100%) to an antibiotic class were included, a Freeman-Tukey double arcsine transformation was applied to each analysis in order to stabilise variances [11]. The 95% score confidence interval (CI) was used to calculate the CI of individual studies. A random-effects model with random-effects applied at the study-level was used to produce pooled estimates, with inverse-variance weighting used to account for differences in precision of individual study estimates. Pooled 95% CIs were calculated using the Wald method. A random-effects model was chosen over a fixed-effects model, given the expected variability of proportions between studies due to microbiological, population, and facility-level influences that could not be adjusted for by sub-group stratification.

Results

Results of the search

The database search, conducted on 15th August 2022, identified 601 unique articles (PubMed: 413, MEDLINE: 281, Embase: 446) that met the search criteria. No additional articles were found from the AIM search. After initial screening on title and abstract, the full-text of 161 articles were assessed for eligibility: 101 of these were subsequently excluded (Fig 1). The most common reasons for exclusion include: i) data were from patients without a clinical suspicion of infection (39/101: 39%), ii) data were from patients with infected wounds, SSI or SSTI not separated from other sample types (33/101: 33%), and iii) data were not presented to allow calculation of prevalence or antibiotic non-susceptibility (15/101: 15%). The remaining 60 articles reported data from 59 studies and are included in this review. Two articles reported data from the same study, these were extracted separately where the articles reported different aspects of the study, but data that was repeated was only recorded once [12,13].

Included studies. The study design, geographical, population and outcome reporting characteristics of the 59 studies included in this systematic review are summarised in Table 1 [12–71].

Types of study

The most common study design was cross-sectional (48/59: 81%), whilst the remaining 11 studies were prospective cohort studies. Of the cross-sectional studies, 46/48 (96%) recruited patients directly from clinical settings, whereas two studies utilised samples from laboratory storage which were specifically reported to have come from patients with clinical signs of an infected wound, SSI or SSTI.

Time period and geographical location

Of the 58 studies that reported their dates and duration of observation, the median start date of observation was 2017 (interquartile range [IQR] 2013–2019), with a median observation duration of six months (IQR 4–9.5).

Studies included data from 11 countries, including countries from Central Africa (Central African Republic [n = 1] and Rwanda [n = 2]), Eastern Africa (Eritrea [n = 2], Ethiopia [n = 25], Sudan [n = 2], Tanzania [n = 6] and Uganda [n = 7]), Southern Africa (Mozambique [n = 1]) and Western Africa (Ghana [n = 5], Nigeria [n = 7] and Sierra Leone [n = 1]).



Fig 1. Literature search PRISMA flowchart.

https://doi.org/10.1371/journal.pgph.0003077.g001

Population and sampling site

Of the studies included, 35/59 (59%) reported on data from both children and adults. Fourteen studies (24%) only included adults and one study (2%) only children. The remaining studies (9/59: 15%) did not report age. Of the 27 studies declaring their population's rural/urban distribution, 6/27 (30%) had an entirely rural population and 1/27 (5%) entirely urban: 13/20 (65%) of studies with a mixed population were predominantly rural. Study-specific inclusion criteria or wound characteristics are shown in Table 1.

Outcome measures reported

Universally, samples were processed in the same laboratories which provided the routine microbiology diagnostics for the recruiting healthcare facility, using local culture procedures and methods for direct sensitivity testing (S1 Table). Techniques for species identification

Study characteristics			Patient characteristics					Outcome reporting				
Study	Country	Study Design	First data collection (total months)	Age	Rural/ urban residence	Type of infection	Specific characteristics	SA	EC	KP	РА	AB
Abayneh 2022 [14]	Ethiopia	Prospective cohort	2021 (4)	Not reported	Mixed (52%/48%)	SSI		Prev Sens	Prev Sens	-	Prev Sens	-
Abosse 2020 [<u>15]</u>	Ethiopia	Cross- sectional	2019 (5)	Adults and children	Mixed (58%/42%)	SSI		Prev Sens	Prev Sens	-	Prev Sens	Prev Sens
Adeyemo 2021 [<u>16]</u>	Nigeria	Cross- sectional	2016 (10)	Adults	Not reported	Chronic wounds/ ulcers	Diabetic foot ulcers	Prev Sens	Prev -	-	Prev -	-
Akinloye 2021 [17]	Nigeria	Cross- sectional	2017 (13)	Adults	Not reported	Wounds		Prev -	Prev -	-	Prev Sens	-
Alebel 2021 [<u>18]</u>	Ethiopia	Cross- sectional	2020 (5)	Adults and children	Mixed (51%/49%)	Wounds	Patients in ITU	-	Prev -	Prev -	Prev -	-
Alelign 2022 [<u>19]</u>	Ethiopia	Cross- sectional	2021 (11)	Not reported	Mixed (57%/43%)	SSI	Orthopaedic surgery	Prev Sens	Prev Sens	Prev Sens	Prev Sens	Prev Sens
Bediako-Bowan 2020 [<u>20]</u>	Ghana	Prospective cohort	2017 (22)	Not reported	Not reported	SSI		Prev Sens	Prev Sens	Prev Sens	Prev Sens	Prev Sens
Bitew Kifilie 2018 [<u>21]</u>	Ethiopia	Cross- sectional	2016 (5)	Adults [†]	Mixed (22%/78%)	SSI	Caesarean section and episiotomy	Prev Sens	Prev Sens	Prev Sens	Prev Sens	-
De Nardo 2016 [<u>22]</u>	Tanzania	Prospective cohort	2013 (3)	Adults [†]	Not reported	SSI	Caesarean section	Prev Sens	Prev -	-	Prev -	-
Desalegn 2020 [<u>23]</u>	Ethiopia	Cross- sectional	2019 (-)	Adults and children	Mixed (30%/70%)	SSTI	Dermatology outpatients	Prev Sens	-	-	-	-
Dessie 2016 [<u>24]</u>	Ethiopia	Prospective cohort	2013 (6)	Adults and children	Mixed (54%/46%)	SSI		Prev Sens	Prev Sens	Prev Sens	Prev Sens	-
Egyir 2021 [<u>25]</u>	Ghana	Cross- sectional	2018 (6)	Adults and children	Not reported	SSI		Prev Sens	-	-	-	-
Garoy 2019 [<u>26]</u>	Eritrea	Cross- sectional	2017 (4)	Adults and children	Not reported	SSTI and wounds		Prev Sens	-	-	-	-
Garoy 2021 [<u>27]</u>	Eritrea	Cross- sectional	2016 (4)	Adults and children	Not reported	SSI		Prev Sens	Prev Sens	-	-	-
Gemechu 2021 [<u>28]</u>	Ethiopia	Cross- sectional	2015 (9)	Adults	Not reported	SSI		Prev Sens	Prev Sens	Prev Sens	Prev -	-
George 2018[<u>29]</u>	Uganda	Cross- sectional	2015 (5)	Adults and children	Rural	SSI		Prev Sens	Prev Sens	-	Prev Sens	-
Hope 2019[<u>30]</u>	Uganda	Cross- sectional	2015 (3)	Adults and children	Not reported	SSI		Prev Sens	Prev Sens	-	-	-
Janssen 2018[<u>31]</u>	Ghana	Cross- sectional	2014 (5)	Adults and children	Rural	Wounds		Prev Sens	Prev Sens	Prev Sens	Prev Sens	Prev Sens
Kabanangi 2021[<u>32]</u>	Tanzania	Cross- sectional	2017 (10)	Children	Not reported	Wounds	Patients with burns	-	Prev Sens	-	Prev Sens	-
Kahsay 2014[<u>33]</u>	Ethiopia	Cross- sectional	2011 (4)	Adults	Mixed (65%/35%)	SSI		Prev Sens	-	-	-	-
Kalayu 2019[<u>34]</u>	Ethiopia	Prospective cohort	2016 (13)	Adults and children	Not reported	SSI		Prev Sens	Prev Sens	-	-	-
Kassam 2017[<u>35]</u>	Tanzania	Cross- sectional	2013 (12)	Adults and children	Not reported	Wounds		Prev Sens	Prev Sens	Prev Sens	Prev Sens	-
Kazimoto 2018[<u>36]</u>	Tanzania	Cross- sectional	2012 (9)	Adults and children	Not reported	SSTI		Prev Sens	Prev -	Prev Sens	Prev Sens	Prev -
Khalim 2021[37]	Uganda	Cross- sectional	2020 (3)	Adults and children	Not reported	Chronic wounds/ ulcers		Prev -	-	-	Prev -	-

Table 1. Study, patient and outcome reporting characteristics of the studies included in this systematic review.

Table 1. (Continued)

Study characteristics			Patient characteristics					Outco	me rep	eporting				
Study	Country	Study Design	First data collection (total months)	Age	Rural/ urban residence	Type of infection	Specific characteristics	SA	EC	КР	PA	AB		
Krumkamp 2020[<u>38</u>]	Ghana	Cross- sectional	2016 (11)	Adults	Rural	Chronic wounds/ ulcers		Prev Sens	Prev -	Prev Sens	Prev -	-		
Lakoh 2022[<u>39]</u>	Sierra Leone	Prospective cohort	2021 (6)	Adults	Urban	SSI		-	Prev -	Prev -	-	Prev -		
Mama 2014[<u>40]</u>	Ethiopia	Cross- sectional	2013 (5)	Adults and children	Not reported	Wounds		Prev Sens	Prev Sens	Prev Sens	Prev Sens	-		
Mama 2019[<u>41]</u>	Ethiopia	Cross- sectional	2017 (3)	Adults and children	Mixed (40%/60%)	SSI and wounds		Prev Sens	-	-	-	-		
Manyahi 2014 <u>[42]</u>	Tanzania	Cross- sectional	2011 (5)	Adults	Not reported	SSI		Prev Sens	Prev Sens	Prev Sens	Prev Sens	Prev Sens		
Mekonnen 2021[<u>43]</u>	Ethiopia	Cross- sectional	2020 (3)	Adults and children	Mixed (62%/38%)	SSI		-	-	-	Prev -	-		
Mengesha 2014 [44]	Ethiopia	Cross- sectional	2012 (6)	Adults	Not reported	SSI		Prev Sens	Prev Sens	-	Prev Sens	-		
Misha 2021 [<u>45]</u>	Ethiopia	Prospective cohort	2019 (5)	Adults	Mixed (73%/27%)	SSI		Prev Sens	Prev Sens	-	Prev Sens	-		
Moges 2019 [<u>46]</u>	Ethiopia	Cross- sectional	2017 (5)	Adults and children	Mixed (59%/41%)	Wounds		-	-	Prev Sens	-	Prev Sens		
Mohammed 2013 [47]	Nigeria	Cross- sectional*	2010 (3)	Not reported	Mixed (63%/37%)	Wounds		Prev Sens	Prev Sens	-	Prev Sens	-		
Mohammed 2017 [<u>48]</u>	Ethiopia	Cross- sectional	2014 (3)	Adults and children	Not reported	Wounds		Prev Sens	Prev Sens	-	Prev Sens	-		
Monnheimer 2021 [<u>49]</u>	Ghana	Cross- sectional	2017 (8)	Not reported	Rural	SSI and acute/ chronic wounds			-	-	-	Prev -		
Moremi 2019 [<u>50]</u>	Tanzania	Prospective cohort	2014 (10)	Not reported	Not reported	SSI		Prev Sens	-	-	-	-		
Motbainor 2020 [<u>51</u>]	Ethiopia	Cross- sectional	2018 (4)	Adults and children	Mixed (47%/53%)	SSI		-	-	-	Prev -	Prev -		
Muhindo 2021 [<u>52]</u>	Uganda	Cross- sectional	2016 (9)	Not reported	Not reported	SSI		- Sens	- Sens	- Sens	- Sens	-		
Mukagendaneza 2019 [<u>53]</u>	Rwanda	Prospective cohort	2017 (4)	Adults	Not reported	SSI		Prev -	Prev -	-	-	-		
Nwankwo 2014 [54]	Nigeria	Cross- sectional	2009 (24)	Adults and children	Not reported	SSI		Prev Sens	Prev Sens	Prev Sens	Prev Sens	-		
Oladeinde 2013 [55]	Nigeria	Cross- sectional	2006 (48)	Adults and children	Rural	Wounds		Prev Sens	Prev Sens	-	Prev Sens	-		
Omer 2020 [56]	Sudan	Cross- sectional	2016 (1)	Not reported	Not reported	Chronic wounds/ ulcers	Patients with diabetes	-	-	-	Prev Sens	-		
Pondei 2013 [57]	Nigeria	Cross- sectional*	2020 (4)	Adults and children	Not reported	Wounds		Prev Sens	Prev Sens	-	Prev Sens	-		
Rafai 2015 [58]	Central African Republic	Cross- sectional	2011 (13)	Adults and children	Not reported	SSI		Prev Sens	Prev -	Prev -	Prev Sens	Prev Sens		
Seni 2013 [<u>12,13]</u>	Uganda	Cross- sectional	2011 (8)	Adults and children	Not reported	SSI		Prev Sens	Prev Sens	-	Prev Sens	-		
Shakir 2021 [59]	Ethiopia	Prospective cohort	2020 (1)	Adults and children	Mixed (48%/52%)	SSI		Prev -	Prev -	-	-	-		
Shimekaw 2020 [60]	Ethiopia	Cross- sectional	2019 (5)	Adults and children	Mixed (55%/45%)	Wounds		Prev Sens	Prev Sens	Prev Sens	Prev Sens	-		

Study characteristics			Patient characteristics					Outcome reporting				
Study	Country	Study Design	First data collection (total months)	Age	Rural/ urban residence	Type of infection	Specific characteristics	SA	EC	КР	PA	AB
Tadesse 2018 [<u>61]</u>	Ethiopia	Cross- sectional	2013 (7)	Adults and children	Not reported	SSI		Prev Sens	-	-	-	-
Tambuwal 2020 [<u>62]</u>	Nigeria	Cross- sectional	2014 (6)	Adults and children	Not reported	SSTI		- Sens	-	-	-	-
Tefera 2021 [<u>63]</u>	Ethiopia	Cross- sectional	2020 (3)	Adults and children	Mixed (71%/29%)	SSI		Prev Sens	-	-	-	-
Tilahun 2022 (1) [<u>64]</u>	Ethiopia	Cross- sectional	2021 (7)	Adults and children	Mixed (61%/39%)	Wounds			-	-	Prev -	-
Tilahun 2022 (2) [<u>65]</u>	Ethiopia	Cross- sectional	2021 (11)	Adults and children	Mixed (24%/76%)	SSI		Prev Sens	Prev Sens	Prev Sens	-	-
Tsige 2020 [<u>66]</u>	Ethiopia	Cross- sectional	2016 (3)	Adults and children	Mixed (23%/77%)	Wounds		Prev Sens	-	-	-	-
Van der Meeren 2013 [<u>67]</u>	Mozambique	Cross- sectional	2010 (10)	Adults and children	Not reported	SSTI and wounds		Prev Sens	-	-	-	-
Velin 2021 [<u>68]</u>	Rwanda	Prospective cohort	2019 (6)	Adults [†]	Rural	SSI	Caesarean section	Prev Sens	Prev Sens	Prev Sens	Prev Sens	Prev Sens
Wangoye 2022 [<u>69]</u>	Uganda	Cross- sectional	2020 (3)	Not reported	Not reported	Chronic wounds/ ulcers		Prev -	-	-	Prev -	-
Wekesa 2020 [70]	Uganda	Cross- sectional	2017 (6)	Adults [†]	Not reported	SSI	Caesarean section	Prev Sens	Prev Sens	-	Prev Sens	-
Yagoup 2019 [71]	Sudan	Cross- sectional	2016 (19)	Adults and children	Not reported	Wounds		-	-	-	Prev	-

Table 1. (Continued)

*Cases selected from laboratory samples, rather than from patient cohort. [†]Women of childbearing age. ITU = intensive care unit, SSI = surgical site infections, SSTI = skin and soft tissue infections, SA = *Staphylococcus aureus*, EC = *Eschericheria coli*, KP = *Klebsiella pneumoniae*, PA = *Pseudomonas aeruginosa*, AB = *Acinetobacter baumannii*, Prev = prevalence, Sens = sensitivity.

https://doi.org/10.1371/journal.pgph.0003077.t001

included a combination of colony morphological interpretation, Gram stain and various biochemical tests according to local practices in the majority (56/59: 95%) of studies. Of these, eight (14%) used an API system, MALDI biotyper (Bruker Daltronics, Bremen, Germany) or VITEK 2/VITEK 2 Compact (*bioMerieux*, Marcy l'Etoile, France) to confirm indeterminate/all isolates and five (9%) included them in their methods but not systematically. In three studies (5%), morphological interpretation, Gram stain and biochemical tests were not performed and identification was established with a MALDI biotyper or VITEK 2/VITEK 2 Compact system only.

The prevalence of *S. Aureus* was reported in 47/59 (80%) studies and resistance within an antibiotic class of importance was reported in 44/59 (75%): for *E. coli*, 38/59 (64%) studies reported prevalence and 29/59 (49%) reported resistance; for *K. pneumoniae*, 19/59 (32%) studies reported prevalence and 17/59 (29%) reported resistance; for *P. aeruginosa*, 38/59 (64%) studies reported prevalence and 28/59 (47%) reported resistance; and for *A. baumannii*, 12/59 (20%) studies reported prevalence and 8/59 (14%) reported resistance.

Funding

Local funding was reported for a significant proportion of studies: 17/59 (29%) of studies were funded by affiliated universities and 3/59 (5%) were funded by the local Ministry of Health. Bilateral donors funded 8/59 (14%) of studies and 2/59 (3%) of the studies were funded by



Fig 2. Risk of bias assessment summary.

https://doi.org/10.1371/journal.pgph.0003077.g002

multilateral donors (NGOs). 13/59 (22%) studies received no funding, whilst 16/59 (27%) did not state

Risk of bias assessment

We classed most studies as having low or moderate overall risk of bias (Fig 2). The most substantial risk of bias identified across all studies was from patient selection methods, with 24/59 (41%) determined as having a high risk, followed by the inclusion and exclusion criteria reported in the studies (16/59 [27%]). The category of potential bias in which the studies performed the best was how outcomes were established, with 58/59 (98%) studies having a low risk (S3 Text).

Prevalence of organisms isolated from samples

When considering all relevant samples from contributing studies through pooled meta-analysis of proportions, *S. aureus* was isolated in 29% (95% confidence interval [CI] 25% to 34%: 47 studies) of samples, *E. coli* in 14% (CI 11% to 18%: 38 studies), *K. pneumoniae* in 11% (CI 8% to 13%, 19 studies), *P. aeruginosa* in 14% (CI 11% to 18%: 38 studies) and *A. baumannii* in 8% (CI 5% to 12%: 12 studies) (Fig 3).

S. aureus was the most commonly isolated organism across all types of infection: prevalence was highest in SSTI (69%, CI 65% to 74%: four studies) and similar in all remaining types of infection: 32% in infected wounds (CI 26% to 37%: 12 studies), 34% in infected chronic wounds and ulcers (CI 28% to 40%, four studies) and 24% in SSI (CI 20% to 28%: 30 studies). Of the Gram negative bacilli, *P. aeruginosa* was more commonly isolated from infected wounds (21%, CI 15% to 28%: 13 studies) than *E. coli* (12%, CI 9% to 15%: 11 studies) or *K. pneumoniae* (9%, CI 5% to 14%: six studies).

Antimicrobial resistance estimates

The rates of resistance observed to agents within the antibiotic classes of interest in isolates of *S. aureus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii* are presented in Table 2. Regional AMR estimates are included in the Supporting Information (S2 Table).

Staphylococcus aureus

Average pooled anti-staphylococcal beta-lactam/cephamycin resistance (cefoxitin, methicillin or oxacillin), suggesting methicillin-resistant *S. aureus* (MRSA), was 48% (CI 35% to 61%: 32 studies). Regional differences in resistance were observed across a number of antibiotic classes



Fig 3. Proportion of samples positive for *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, according to infection type (with 95% confidence intervals) in Central, Eastern, Southern and Western Africa. Bars represent pooled proportions and error-bars the 95% confidence intervals.

https://doi.org/10.1371/journal.pgph.0003077.g003

for *S. aureus*. Anti-staphylococcal beta-lactam/cephamycin resistance, indicating MRSA, was lower in studies conducted in Western Africa (23%, CI 9% to 41%: six studies) compared to Eastern Africa (58%, CI 41% to 73%: 23 studies). A higher resistance to lincosamides was also observed in Eastern Africa (32%, CI 17% to 49%: 16 studies) compared to other regions (9%, CI 5% to 16% in Central Africa: one study; 2%, CI 1% to 7% in Southern Africa: one study; and 6%, CI 1% to 13% in Western Africa: four studies).

Enterobacteriaceae

In *E. coli*, AMR was estimated to be higher than 40% for all antibiotic classes apart from carbapenems (6%, CI 0% to 19%: 13 studies). A similar pattern of resistance was seen in *K. pneumoniae*, which had a pooled estimate of over 30% resistance to all antibiotic classes apart from carbapenems (8%, CI 0% to 24%: nine studies). Significant variation was seen between regions for carbapenem resistance, which was high in Eastern Africa (10%, CI 0% to 28% for *E. coli*: 10 studies, and 31%, CI 5% to 64% for *K. pneumoniae*: four studies) and low in all other regions.

Pseudomonads

The pooled rates of resistance observed to agents within the antibiotic classes of interest in isolates of *P. aeruginosa* and *A. baumannii* were all 20% or greater, apart from aminoglycosides for *P. aeruginosa* (19%, CI 9% to 32%: 25 studies) and anti-pseudomonal penicillins with betalactamase inhibitors for *A. baumannii* (3%, CI 0% to 17%: two studies). Significant variation was seen between regions for resistance to anti-pseudomonal penicillins with beta-lactamase

Table 2. Pooled estimates of antimicrobial resistance in wound, skin, soft tissue and surgical site infections in Central, Eastern, Southern and Western Africa.

Antibiotic class (agents)	Resistance	95% Confidence Interval	Data source	I ²
Staphylococcus aureus				
Aminoglycosides	0.24	0.15 to 0.34	1422 samples	94%
(Gentamicin)			(29 studies)	
Ansamycins	0.08	0.00 to 0.28	183 samples	87%
(Rifampin)			(3 studies)	
Anti-staphylococcal beta-lactams/cephamycins	0.48	0.35 to 0.61	1611 samples	96%
(Cefoxitin, methicillin or oxacillin)			(32 studies)	
Fluoroquinolones	0.19	0.13 to 0.26	1485 samples	89%
(Ciprofloxacin)			(23 studies)	
Folate synthesis inhibitors	0.53	0.37 to 0.70	1432 samples	97%
(Trimethoprim-sulphamethoxazole)			(27 studies)	
Glycopeptide	0.03	0.00 to 0.09	750 samples	89%
(Vancomycin)			(16 studies)	
Lincosamides	0.24	0.12 to 0.37	1159 samples	95%
(Clindamycin)			(22 studies)	
Macrolides	0.44	0.33 to 0.56	1353 samples	94%
(Erythromycin)			(27 studies)	
Oxazolidinones	0	N/A	33 samples	N/A
(Linezolid)			(1 study)	
Phenicols	0.36	0.16 to 0.60	1023 samples	98%
(Chloramphenicol)			(17 studies)	_
Phosphoric acids	0	NA	31 samples	N/A
(Fosfomycin)			(1 study)	
Tetracyclines	0.54	0.40 to 0.67	1392 samples	96%
(Doxycycline or tetracycline)			(26 studies)	_
			i	
Aminoglycosides	0.51	0.42 to 0.60	600 complos	720/
Aminogiycosides	0.51	0.42 10 0.60	(22 studies)	/ 3%
(Amikacin or gentamicin)	0.40	0.27 to 0.70		200/
(Dimenseillin tenchestern)	0.48	0.27 10 0.70	(4 studies)	89%
(Piperaciiiii-tazobactaiii)	0.06	0.00 to 0.10	(4 studies)	0.00/
	0.06	0.00 10 0.19	(12 studies)	90%
(Impenem or meropenem)	0.72	0.59.4-0.95	(13 studies)	(20)
(Cofeening on coference)	0.72	0.58 to 0.85	215 samples	02%
	0.74	0.501.0.05	(6 studies)	010/
(Coforing a fotoring a fotorial line on a fotorial)	0.74	0.60 to 0.86	/2/ samples	91%
(Cerepime, cerotaxime, certazidime or certriaxone)	0.52	0.22 += 0.71	(25 studies)	710/
	0.52	0.32 to 0.71	131 samples	/1%
	0.54		(5 studies)	
riuoroquinoiones	0.54	0.40 to 0.66	831 samples	91%
		0.50	(24 studies)	
Folate pathway inhibitors	0.83	0.73 to 0.92	732 samples	86%
(1 rimethoprim-sulphamethoxazole)			(20 studies)	
Penicillins	0.93	0.88 to 0.98	764 samples	75%
(Ampicillin)			(22 studies)	1

Table 2. (Continued)

Antibiotic class (agents)		95% Confidence Interval	Data cource	I ²
Antibiotic class (agents)	Resistance	55% confidence interval	Data source	1
Penicillins with beta-lactamase inhibitors	0.8	0.66 to 0.92	729 samples	92%
(Amoxicillin-clavulanic acid)			(18 studies)	
Phenicols	0.51	0.33 to 0.68	387 samples	91%
(Chloramphenicol)			(15 studies)	
Tetracyclines	0.81	0.71 to 0.91	403 samples	79%
(Doxycycline or tetracycline)			(17 studies)	
Klebsiella pneumoniae				
Aminoglycosides	0.38	0.20 to 0.57	201 samples	85%
(Amikacin or gentamicin)			(12 studies)	-
Anti-pseudomonal penicillins with beta-lactamase inhibitors	0.58	0.44 to 0.71	57 samples	1%
(Piperacillin-tazobactam)			(3 studies)	-
Carbapenems	0.08	0.00 to 0.24	262 samples	90%
(Imipenem or meropenem)			(9 studies)	-
First/second generation cephalosporins	0.66	0.23 to 0.98	102 samples	95%
(Cefazolin or cefuroxime)			(5 studies)	
Third/fourth generation cephalosporins	0.61	0.41 to 0.80	256 samples	88%
(Cefepime, cefotaxime, ceftazidime or ceftriaxone)			(14 studies)	
Cephamycins	0.43	0.10 to 0.79	57 samples	86%
(Cefoxitin)			(3 studies)	
Fluoroquinolones	0.32	0.15 to 0.52	254 samples	89%
(Ciprofloxacin)			(13 studies)	
Folate pathway inhibitors	0.78	0.62 to 0.90	261 samples	84%
(Trimethoprim-sulphamethoxazole)			(14 studies)	
Penicillins with beta-lactamase inhibitors	0.85	0.69 to 0.96	180 samples	81%
(Amoxicillin-clavulanic acid)			(9 studies)	
Phenicols	0.51	0.28 to 0.74	99 samples	80%
(Chloramphenicol)			(6 studies)	
Tetracyclines	0.69	0.51 to 0.85	143 samples	78%
(Doxycycline or tetracycline)			(10 studies)	
Pseudomonas aeruginosa				
Aminoglycosides	0.19	0.09 to 0.32	590 samples	88%
(Amikacin or gentamicin)			(25 studies)	
Anti-pseudomonal carbapenems	0.21	0.02 to 0.49	404 samples	97%
(Imipenem or meropenem)			(15 studies)	
Anti-pseudomonal cephalosporins	0.41	0.22 to 0.61	600 samples	94%
(Cefepime or ceftazidime)			(20 studies)	
Antipseudomonal fluoroquinolones	0.26	0.14 to 0.42	670 samples	92%
(Ciprofloxacin)			(25 studies)	
Anti-pseudomonal penicillins with beta-lactamase inhibitors	0.28	0.02 to 0.64	57 samples	86%
(Piperacillin-tazobactam)			(3 studies)	
Monobactams	0.88	0.81 to 0.93	122 samples	0%
(Aztreonam)			(2 studies)	
Polymyxins	0.25	0.16 to 0.36	69 samples	NA
(Polymyxin B)			(1 study)	

Table 2. (Continued)

Antibiotic class (agents)	Desistance	95% Confidence Interval	Data source	I ²	
	Resistance				
Acinetobacter baumannii					
Aminoglycosides	0.57	0.37 to 0.76	70 samples	57%	
(Amikacin or gentamicin)			(6 studies)		
Anti-pseudomonal carbapenems	0.2	0.09 to 0.34	81 samples	40%	
(Imipenem or meropenem)			(7 studies)		
Anti-pseudomonal fluoroquinolones	0.45	0.30 to 0.60	47 samples	0%	
(Ciprofloxacin)			(5 studies)		
Anti-pseudomonal penicillins with beta-lactamase inhibitors	0.03	0.00 to 0.17	29 samples	0%	
(Piperacillin-tazobactam)			(2 studies)		
Extended-spectrum cephalosporins	0.7	0.17 to 1.00	71 samples	93%	
(Cefepime, cefotaxime, ceftazidime or ceftriaxone)			(7 studies)		
Folate pathway inhibitors	0.67	0.39 to 0.90	15 samples	0%	
(Trimethoprim-sulphamethoxazole)			(2 studies)		
Tetracyclines	0.49	0.08 to 0.90	62 samples	46%	
(Doxycycline or tetracycline)			(5 studies)		

https://doi.org/10.1371/journal.pgph.0003077.t002

inhibitors, which was high in Eastern Africa (45%, CI 29% to 60% for *P. aeruginosa*: two studies, and 50%, CI 19% to 81% for *A. baumannii*: one study) and low in Western Africa (10%, CI 3% to 30% for *P. aeruginosa*: one study, and 0%, CI 0% to 14% for *A. baumannii*: one study).

Sensitivity analysis

The impact of the potential bias introduced by selective sampling of more critically ill patients was explored in a sensitivity analysis, comparing the AMR reported in SSI prospective cohort studies, which assessed for the development of SSI in well patients prior to starting antibiotics, and cross-sectional SSI studies, which were more likely to include patients failing treatment. Similar patterns of AMR were estimated between these two types of study (S3 Table).

Discussion

This review reports the isolation of *S. aureus, E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii* from the majority of swabs taken from clinically infected wounds, skin, soft tissue and surgical sites in Central, Eastern, Southern and Western Africa: *S. aureus* was the most commonly isolated organism, particularly in SSTI. AMR was high across all five species: of particular note, *S. aureus* was resistant to methicillin (MRSA) in >40% of isolates; *E. coli* and *K. pneumoniae* were both resistant to amoxicillin-clavulanic acid in \geq 80% of isolates and resistant to aminoglycosides in 51% and 38% of isolates respectively; and *P. aeruginosa* and *A. baumannii* were both resistant to anti-pseudomonal carbapenems (imipenem or meropenem) in \geq 20% of isolates. All of these resistant isolates have the potential to represent priority pathogens requiring critical (extended spectrum beta-lactamase [ESBL]-producing or carbapenem-resistant *A. baumannii*) or urgent (MRSA) development of new antibiotics according to the WHO [72]. It is essential however, that plans for antimicrobial development are accompanied by policies that ensure equitable access once available.

The majority of the current literature considering wound infections in Africa is summarised in two recent systematic reviews from Ethiopia by Chelkeba et al. [5,6]. They found similar results in wound infections to our systematic review, with *S. aureus* being the bacterial pathogen most commonly isolated (36%) and *E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii* all contributing to a smaller proportion of infections (8–17%). Our systematic review covers a larger geographical area, stratifies by types of infection (clinically infected wounds, SSTI, and SSI), and focusses on clinically relevant isolates only. Other systematic reviews of AMR in Africa, not restricted to wound infection, SSI and SSTI, reported similar levels of MRSA amongst isolates, but much higher levels of vancomycin resistance [73,74], whereas our systematic review suggested a pooled vancomycin resistance estimate of only 3% (CI 0% to 9%: 16 studies). This may be due to previous reviews including samples taken to screen for carriage of resistant organisms in healthy individuals.

Compared to Murray et al's recent review on global AMR burden, we found higher third generation cephalosporin resistance in *E. coli*, similar to that reported in Southeast Asia where resistance is almost uniformly over 50% [4]. This might reflect the proportion of patients with surgical site infections in our review and the use of ceftriaxone in surgical prophylaxis, selecting out isolates resistant to third generation cephalosporins. Our results were consistent to those estimates by Murray and colleagues with respect to the proportion of MRSA amongst *S. aureus* isolates, levels of third generation cephalosporin resistance in *K. pneumoniae*, and carbapenem levels of resistance across the Gram negative organisms [4].

This systematic review also highlights the microbiological diagnostic gaps in many African clinical settings. A recent review found Africa to be the global region with the lowest proportion of available AMR national action plans (NAPs) [75]. This may explain why we only found data for 11 countries in Central, Eastern, Southern and Western Africa, albeit using English search terms: whilst very few studies where screened out due to language, our search may have missed articles published in other languages and therefore under-represent non-anglophone communities.

Sustainable, coordinated funding is an essential component of research and development, and it is notable that the funding for the studies included in this review were rarely awarded by international grants or large organisations: when obtained, the vast majority were supported by local universities attached to a tertiary healthcare facility, while over 20% of the included studies reported that they received no dedicated funding. AMR surveillance, diagnostic stewardship and targeted infection treatment would all benefit from strengthening local capacity with funding support, which would create an opportunity for local and regional standardisation, external quality assessment and reporting protocols, strengthening research and improving data quality [76]. In 2018, the WHO published it's model list of essential in vitro diagnostics (EVD) that, much like its model list of essential medications, allows an objective analysis of knowledge gaps and provides a benchmark for laboratory practice [77,78]. These diagnostics are still lacking in many African healthcare settings [79].

Our review comprehensively collected clinical, microbiological and study design characteristics, allowing a detailed reporting of *S. aureus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa* and A. *baumannii* AMR using data from almost 5,000 significant isolates from over 26,000 clinical samples. We also only included studies that presented data from patients with clinical signs of infection. Whilst contamination of samples from clinically infected wounds, skin, soft tissue or surgical sites is difficult to exclude, these methods will have increased the yield of clinically significant microbiological reporting.

One of the limitations of this review is that in settings with constrained microbiology resources, sampling might be limited to the most critically ill patients who are not responding to empirical treatment, applying selection pressure for resistant organisms that could lead to

AMR over-reporting. However, our sensitivity analysis comparing prospective (following up all patients regardless of illness severity) and cross-sectional analyses did not find a difference. Another potential impact of limited resources is that access to reliable and timely microbiological reporting allows for improved antimicrobial stewardship, surveillance and infection prevention control. These might explain the disparities in MRSA prevalence between countries in this review.

The proportion of resistance reported to each antibiotic was not at isolate-level. Antibiograms, and thus resistance mechanisms and rates of multi-drug resistance (MDR), were not able to be established. Each study reported AMR to various antimicrobial agents/categories according to local protocols or the study design, rather than a standardised list. Therefore, the data presented cannot be used to establish optimal empirical therapies. They can, however, be used to estimate an approximate risk of failure of commonly used antimicrobial antibiotics.

Finally, the clinical settings included in this review varied by geography, time and patient characteristics, likely contributing to considerable heterogeneity. Whilst some of that heterogeneity could be explained by infection type and African sub-region, study-level population differences persisted in our sub-group analyses, indicated by high I^2 statistics. It is also important to note that a large number of included studies were conducted in Ethiopia, and therefore potentially skewed by any prescribing practices, clinical guidelines or diagnostic access specific to the country.

Conclusion

The prevalence of AMR in *S. aureus, E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii* isolates from clinically infected wounds, skin, soft tissue and surgical sites in Central, Eastern, Southern and Western African healthcare settings was high. In particular, a large proportion of these organisms display resistance patterns with critical or urgent WHO priority for antimicrobial development. We highlight significant gaps in microbiological testing capacity in Africa, with contributions from only 11 countries: a strong signal that we are far from diagnostic equity and the WHO's EVD goals. Achieving reliable, timely testing and reporting of microbiological samples is essential to 1) benefit patient care through more informed empiric treatments regimens and more frequently targeted therapy, 2) improve surveillance, 3) support diagnostic stewardship practices and 4) allow standardisation for quality assurance and academic dissemination of higher quality, comparable data.

Supporting information

S1 Checklist. PRISMA checklist. (DOCX)

S1 Text. Literature search terms. (DOCX)

S2 Text. Antibiotic agents and classes of interest according to species. (DOCX)

S3 Text. Study-level risk of bias assessment. (DOCX)

S1 Table. Methods of bacterial species identification and susceptibility testing. (DOCX)

S2 Table. Regional AMR estimates. (DOCX)

S3 Table. SSI prospective cohort study versus cross-sectional study sensitivity analysis. (DOCX)

Author Contributions

Conceptualization: Edward J. M. Monk, V. Bhargavi Rao, Kevin van Zandvoort.

Data curation: Edward J. M. Monk, Timothy P. W. Jones, Felix Bongomin, Winnie Kibone, Yakobo Nsubuga, Nelson Ssewante.

Formal analysis: Edward J. M. Monk.

Investigation: Edward J. M. Monk.

Methodology: Edward J. M. Monk, Timothy P. W. Jones.

Project administration: Edward J. M. Monk.

Supervision: V. Bhargavi Rao, Kevin van Zandvoort.

Visualization: Edward J. M. Monk.

Writing - original draft: Edward J. M. Monk.

Writing – review & editing: Edward J. M. Monk, Timothy P. W. Jones, Felix Bongomin, Winnie Kibone, Yakobo Nsubuga, Nelson Ssewante, Innocent Muleya, Lauryn Nsenga, V. Bhargavi Rao, Kevin van Zandvoort.

References

- 1. World Health Organization. Antimicrobial resistance. 2021. Available at: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance (accessed 26th August 2023).
- O'Neill J. Tackling drug-resistant infections globally: final report and recommendations London: the review on antimicrobial resistance. 2016. Available at: https://amr-review.org/sites/default/files/ 160518_Final%20paper_with%20cover.pdf (accessed 26th August 2023).
- O'Neill J. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. London: review on antimicrobial resistance. 2014. Available at: https://amr-review.org/sites/default/files/AMR% 20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth% 20of%20nations_1.pdf (accessed 26th August 2023).
- Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022; 399(10325):629–55. https://doi.org/10.1016/S0140-6736(21)02724-0 PMID: 35065702
- Chelkeba L, Melaku T. Epidemiology of staphylococci species and their antimicrobial-resistance among patients with wound infection in Ethiopia: a systematic review and meta-analysis. J Glob Antimicrob Resist. 2022; 29:483–98. https://doi.org/10.1016/j.jgar.2021.10.025 PMID: 34801740
- Chelkeba L, Melaku T, Mega TA. Gram-Negative bacteria isolates and their antibiotic-resistance patterns in patients with wound infection in Ethiopia: a systematic review and meta-analysis. Infect Drug Resist. 2021; 14:277–302. https://doi.org/10.2147/IDR.S289687 PMID: 33542636
- Versporten A, Zarb P, Caniaux I, Gros M-F, Drapier N, Miller M, et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Lancet Glob Health. 2018; 6(6):e619–e29. <u>https://doi.org/10.1016/S2214-109X(18)</u> 30186-4 PMID: 29681513
- Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012; 18(3):268–81. https://doi.org/ 10.1111/j.1469-0691.2011.03570.x PMID: 21793988
- National Institutes of Health. Study Quality Assessment Tools. 2021. Available at www.nhlbi.nih.gov/ health-topics/study-quality-assessment-tools (accessed 26th August 2023).

- Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E, et al. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. BMC Med Res Methodol. 2021; 21(1):189. https://doi.org/10.1186/s12874-021-01381-z PMID: 34544368
- 11. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health. 2014; 72(1):39. https://doi.org/10.1186/2049-3258-72-39 PMID: 25810908
- Seni J, Bwanga F, Najjuka CF, Makobore P, Okee M, Mshana SE, et al. Molecular characterization of Staphylococcus aureus from patients with surgical site infections at Mulago Hospital in Kampala, Uganda. PLoS One. 2013; 8(6):e66153. https://doi.org/10.1371/journal.pone.0066153 PMID: 23840416
- Seni J, Najjuka CF, Kateete DP, Makobore P, Joloba ML, Kajumbula H, et al. Antimicrobial resistance in hospitalized surgical patients: a silently emerging public health concern in Uganda. BMC Res Notes. 2013; 6:298. https://doi.org/10.1186/1756-0500-6-298 PMID: 23890206
- Abayneh M, Asnake M, Muleta D, Simieneh A. Assessment of bacterial profiles and antimicrobial susceptibility pattern of isolates among patients diagnosed with surgical site infections at Mizan-Tepi University Teaching Hospital, Southwest Ethiopia: a prospective observational cohort study. Infect Drug Resist. 2022; 15:1807–19. https://doi.org/10.2147/IDR.S357704 PMID: 35444431
- Abosse S, Genet C, Derbie A. Antimicrobial resistance profile of bacterial isolates identified from surgical site infections at a referral hospital, Northwest Ethiopia. Ethiop J Health Sci. 2021; 31(3):635–44. https://doi.org/10.4314/ejhs.v31i3.21 PMID: 34483621
- Adeyemo AT, Kolawole B, Rotimi VO, Aboderin AO. Multicentre study of the burden of multidrug-resistant bacteria in the aeitiology of infected diabetic foot ulcers. Afr J Lab Med. 2021; 10(1):a1261. https://doi.org/10.4102/ajlm.v10i1.1261 PMID: 33824857
- Akinloye AO, Adefioye JO, Adekunle CO, Anomneze BU, Makanjuola OB, Onaolapo OJ, et al. Multidrug-resistance genes in pseudomonas aeruginosa from wound infections in a tertiary health institution in Osogbo, Nigeria. Infect Disord Drug Targets. 2021; 21(1):90–8. https://doi.org/10.2174/ 1871526520666200117112241 PMID: 31957616
- Alebel M, Mekonnen F, Mulu W. Extended-Spectrum beta-Lactamase and carbapenemase producing Gram-negative bacilli infections among patients in intensive care units of Felegehiwot Referral Hospital: a prospective cross-sectional study. Infect Drug Resist. 2021; 14:391–405. <u>https://doi.org/10.2147/IDR.</u> S292246 PMID: 33564247
- Alelign D, Tena T, Tadesse D, Tessema M, Seid M, Oumer Y, et al. Bacteriological profiles, antimicrobial susceptibility patterns, and associated factors in patients undergoing orthopedic surgery with suspicion of surgical site infection at Arba Minch General Hospital in Southern Ethiopia. Infect Drug Resist. 2022; 15:2427–43. https://doi.org/10.2147/IDR.S367510 PMID: 35592104
- Bediako-Bowan AAA, Kurtzhals JAL, Molbak K, Labi AK, Owusu E, Newman MJ. High rates of multidrug resistant gram-negative organisms associated with surgical site infections in a teaching hospital in Ghana. BMC Infect Dis. 2020; 20(1):890. <u>https://doi.org/10.1186/s12879-020-05631-1</u> PMID: 33238903
- Bitew Kifilie A, Dagnew M, Tegenie B, Yeshitela B, Howe R, Abate E. Bacterial profile, antibacterial resistance pattern, and associated factors from women attending postnatal health service at University of Gondar Teaching Hospital, Northwest Ethiopia. Int J Microbiol. 2018:3165391. https://doi.org/10. 1155/2018/3165391 PMID: 29681942
- De Nardo P, Gentilotti E, Nguhuni B, Vairo F, Chaula Z, Nicastri E, et al. Post-caesarean section surgical site infections at a Tanzanian tertiary hospital: a prospective observational study. J Hosp Infect. 2016; 93(4):355–9. https://doi.org/10.1016/j.jhin.2016.02.021 PMID: 27125664
- Desalegn M, Befekadu A, Tegene B, Million Y. Antibiotic susceptibility pattern and associated factors of methicillin-resistant Staphylococcus aureus among dermatological patients at the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia: a prospective cross-sectional study. Clin Lab. 2020; 66(11). https://doi.org/10.7754/Clin.Lab.2020.200236 PMID: 33180444
- 24. Dessie W, Mulugeta G, Fentaw S, Mihret A, Hassen M, Abebe E. Pattern of bacterial pathogens and their susceptibility isolated from surgical site infections at selected referral hospitals, Addis Ababa, Ethiopia. Int J Microbiol. 2016:2418902. https://doi.org/10.1155/2016/2418902 PMID: 27446213
- 25. Egyir B, Bentum J, Attram N, Fox A, Obeng-Nkrumah N, Appiah-Korang L, et al. Whole genome sequencing and antimicrobial resistance of Staphylococcus aureus from surgical site infections in Ghana. Pathogens. 2021;10(2). https://doi.org/10.3390/pathogens10020196 PMID: 33673230
- 26. Garoy EY, Gebreab YB, Achila OO, Tekeste DG, Kesete R, Ghirmay R, et al. Methicillin-resistant Staphylococcus aureus (MRSA): prevalence and antimicrobial sensitivity pattern among patients—a multicenter study in Asmara, Eritrea. Can J Infect Dis Med Microbiol. 2019:8321834. <u>https://doi.org/10. 1155/2019/8321834</u> PMID: 30881532

- Garoy EY, Gebreab YB, Achila OO, Tecklebrhan N, Tsegai HM, Hailu AZ, et al. Magnitude of multidrug resistance among bacterial isolates from surgical site infections in two national referral hospitals in Asmara, Eritrea. Int J Microbiol. 2021:6690222. https://doi.org/10.1155/2021/6690222 PMID: 33727929
- Gemechu MM, Tadesse TA, Takele GN, Bisetegn FS, Gesese YA, Zelelie TZ. Bacterial profile and their antimicrobial sensitivity patterns in patients admitted at MaddaWalabu University Goba Referral Hospital, Ethiopia: a cross sectional study. Afri Health Sci. 2021; 21(2):513–22. https://doi.org/10.4314/ahs. v21i2.5 PMID: 34795703
- 29. George M, Iramiot JS, Muhindo R, Olupot-Olupot P, Nanteza A. Bacterial aetiology and antibiotic susceptibility profile of post-operative sepsis among surgical patients in a tertiary hospital in rural Eastern Uganda. Microbiol Res J Int. 2018; 24(2). https://doi.org/10.9734/MRJI/2018/41690 PMID: 30370374
- Hope D, Ampaire L, Oyet C, Muwanguzi E, Twizerimana H, Apecu RO. Antimicrobial resistance in pathogenic aerobic bacteria causing surgical site infections in Mbarara Regional Referral Hospital, Southwestern Uganda. Sci Rep. 2019; 9(1):17299. <u>https://doi.org/10.1038/s41598-019-53712-2</u> PMID: 31754237
- Janssen H, Janssen I, Cooper P, Kainyah C, Pellio T, Quintel M, et al. Antimicrobial-resistant bacteria in infected wounds, Ghana, 2014. Emerg Infect Dis. 2018; 24(5):916–9. https://doi.org/10.3201/ eid2405.171506 PMID: 29664368
- 32. Kabanangi F, Joachim A, Nkuwi EJ, Manyahi J, Moyo S, Majigo M. High level of multidrug-resistant Gram-negative pathogens causing burn wound infections in hospitalized children in Dar es Salaam, Tanzania. Int J Microbiol. 2021:6644185. https://doi.org/10.1155/2021/6644185 PMID: 34306091
- Kahsay A, Mihret A, Abebe T, Andualem T. Isolation and antimicrobial susceptibility pattern of Staphylococcus aureus in patients with surgical site infection at Debre Markos Referral Hospital, Amhara Region, Ethiopia. Arch Public Health. 2014; 72(1):16. <u>https://doi.org/10.1186/2049-3258-72-16</u> PMID: 24949197
- Kalayu AA, Diriba K, Girma C, Abdella E. Incidence and bacterial etiologies of surgical site infections in a public hospital, Addis Ababa, Ethiopia. The Open Microbiology Journal. 2019; 13(1):301–7. https:// doi.org/10.2174/1874285801913010301
- Kassam NA, Damian DJ, Kajeguka D, Nyombi B, Kibiki GS. Spectrum and antibiogram of bacteria isolated from patients presenting with infected wounds in a tertiary hospital, Northern Tanzania. BMC Res Notes. 2017; 10(1):757. https://doi.org/10.1186/s13104-017-3092-9 PMID: 29262867
- 36. Kazimoto T, Abdulla S, Bategereza L, Juma O, Mhimbira F, Weisser M, et al. Causative agents and antimicrobial resistance patterns of human skin and soft tissue infections in Bagamoyo, Tanzania. Acta Trop. 2018; 186:102–6. https://doi.org/10.1016/j.actatropica.2018.07.007 PMID: 30006029
- Khalim W, Mwesigye J, Tungotyo M, Twinomujuni SS. Resistance pattern of ected chronic wound isolates and factors associated with bacterial resistance to third generation cephalosporins at Mbarara Regional Referral Hospital, Uganda. PLOS One. 2021; 16(12):e0261264. <u>https://doi.org/10.1371/journal.pone.0261264</u> PMID: 34914757
- Krumkamp R, Oppong K, Hogan B, Strauss R, Frickmann H, Wiafe-Akenten C, et al. Spectrum of antibiotic resistant bacteria and fungi isolated from chronically infected wounds in a rural district hospital in Ghana. PLoS One. 2020; 15(8):e0237263. https://doi.org/10.1371/journal.pone.0237263 PMID: 32764812
- Lakoh S, Yi L, Sevalie S, Guo X, Adekanmbi O, Smalle IO, et al. Incidence and risk factors of surgical site infections and related antibiotic resistance in Freetown, Sierra Leone: a prospective cohort study. Antimicrob Resist Infect Control. 2022; 11(1):39. <u>https://doi.org/10.1186/s13756-022-01078-y</u> PMID: 35189952
- 40. Mama M, Abdissa A, Sewunet T. Antimicrobial susceptability pattern of bacterial isolates from wound infection and their sensitivity to alternate topical agents at Jimma University University Hospital, South-West Ethiopia. Ann Clin Microbiol Antimicrob. 2014; 13:14. <u>https://doi.org/10.1186/1476-0711-13-14</u> PMID: 24731394
- Mama M, Aklilu A, Misgna K, Tadesse M, Alemayehu E. Methicillin- and inducible clindamycin-resistant Staphylococcus aureus among patients with wound infection attending Arba Minch Hospital, South Ethiopia. Int J Microbiol. 2019: 2965490. https://doi.org/10.1155/2019/2965490 PMID: 31065270
- 42. Manyahi J, Matee MI, Majigo M, Moyo S, Mshana SE, Lyamuya EF. Predominance of multi-drug resistant bacterial pathogens causing surgical site infections in Muhimbili National Hospital, Tanzania. BMC Res Notes. 2014; 7(7):500. https://doi.org/10.1186/1756-0500-7-500 PMID: 25100042
- 43. Mekonnen H, Seid A, Molla Fenta G, Gebrecherkos T. Antimicrobial resistance profiles and associated factors of Acinetobacter and Pseudomonas aeruginosa nosocomial infection among patients admitted at Dessie Comprehensive Specialized Hospital, North-East Ethiopia. A cross-sectional study. PLoS One. 2021; 16(11):e0257272. https://doi.org/10.1371/journal.pone.0257272 PMID: 34780494

- Mengesha RE, Kasa BG-S, Saravanan M, Berhe DF, Wasihun AG. Aerobic bacteria in post surgical wound infections and pattern of their antimicrobial susceptibility in Ayder Teaching and Referral Hospital, Mekelle, Ethiopia. BMC Res Notes. 2014; 7:575. <u>https://doi.org/10.1186/1756-0500-7-575</u> PMID: 25164127
- 45. Misha G, Chelkeba L, Melaku T. Bacterial profile and antimicrobial susceptibility patterns of isolates among patients diagnosed with surgical site infection at a tertiary teaching hospital in Ethiopia: a prospective cohort study. Ann Clin Microbiol Antimicrob. 2021; 20(1):33. https://doi.org/10.1186/s12941-021-00440-z PMID: 33971896
- 46. Moges F, Eshetie S, Abebe W, Mekonnen F, Dagnew M, Endale A, et al. High prevalence of extended-spectrum beta-lactamase-producing Gram-negative pathogens from patients attending Felege Hiwot Comprehensive Specialized Hospital, Bahir Dar, Amhara region. PLoS One. 2019; 14(4):e0215177. https://doi.org/10.1371/journal.pone.0215177 PMID: 30986262
- Mohammed A, Adeshina GO, Ibrahim YK. Incidence and antibiotic susceptibility pattern of bacterial isolates from wound infections in a tertiary hospital in Nigeria. Tropical Journal of Pharmaceutical Research. 2013; 12(4). https://doi.org/10.4314/tjpr.v12i4.26
- Mohammed A, Seid ME, Gebrecherkos T, Tiruneh M, Moges F. Bacterial isolates and their antimicrobial susceptibility patterns of wound infections among inpatients and outpatients attending the University of Gondar Referral Hospital, Northwest Ethiopia. Int J Microbiol. 2017:8953829. <u>https://doi.org/10.</u> 1155/2017/8953829 PMID: 28386280
- Monnheimer M, Cooper P, Amegbletor HK, Pellio T, Gross U, Pfeifer Y, et al. High prevalence of carbapenemase-producing Acinetobacter baumannii in wound infections, Ghana, 2017/2018. Microorganisms. 2021; 9(3). https://doi.org/10.3390/microorganisms9030537 PMID: 33807838
- 50. Moremi N, Claus H, Vogel U, Mshana SE. The role of patients and healthcare workers Staphylococcus aureus nasal colonization in ocurrance of surgical site infection among patients admitted in two centers in Tanzania. Antimicrob Resist Infect Control. 2019; 8:102. <u>https://doi.org/10.1186/s13756-019-00554-</u>V
- Motbainor H, Bereded F, Mulu W. Multi-drug resistance of blood stream, urinary tract and surgical site nosocomial infections of Acinetobacter baumannii and Pseudomonas aeruginosa among patients hospitalized at Felegehiwot Referral Hospital, Northwest Ethiopia: a cross-sectional study. BMC Infect Dis. 2020; 20(1):92. https://doi.org/10.1186/s12879-020-4811-8 PMID: 32000693
- Muhindo AB, Aliero AA, Odoki M, Ntulume I, Eilu E, Mutebi J, et al. Antibiotic-resistant profiles of bacteria isolated from cesarean and surgical patients from Kasese District Hospitals Western Uganda. Borneo Journal of Pharmacy. 2021; 4(2):145–56. https://doi.org/10.33084/bjop.v4i2.1948
- 53. Mukagendaneza MJ, Munyaneza E, Muhawenayo E, Nyirasebura D, Abahuje E, Nyirigira J, et al. Incidence, root causes, and outcomes of surgical site infections in a tertiary care hospital in Rwanda: a prospective observational cohort study. Patient Saf Surg. 2019; 13:10. <u>https://doi.org/10.1186/s13037-019-0190-8</u> PMID: 30820247
- 54. Nwankwo EO, Mofolorunsho CK, Akande AO. Aetiological agents of surgical site infection in a specialist hospital in Kano, North-Western Nigeria. Tanzan J Health Res. 2014; 16(4):289–95. https://doi.org/10. 4314/thrb.v16i4.5 PMID: 26891518
- Oladeinde BH, Omoregie R, Olley M, Anunibe JA, Onifade AA. A 5-year surveillance of wound infections at a rural tertiary hospital in Nigeria. Afr Health Sci. 2013; 13(2):351–6. https://doi.org/10.4314/ ahs.v13i2.22 PMID: 24235935
- 56. Omer THS, Mustafa SAM, Mohamed SOO. Extended spectrum beta-lactamase-mediated resistance and antibiogram of Pseudomonas aeruginosa isolates from patients attending two public hospitals in Khartoum, Sudan. Int J Microbiol. 2020:2313504. https://doi.org/10.1155/2020/2313504 PMID: 33163076
- 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. Trop Med Health. 2013; 41(2):49–53. https://doi.org/10.2149/tmh.2012-14 PMID: 23874138
- Rafai C, Frank T, Manirakiza A, Gaudeuille A, Mbecko JR, Nghario L, et al. Dissemination of IncF-type plasmids in multiresistant CTX-M-15-producing Enterobacteriaceae isolates from surgical-site infections in Bangui, Central African Republic. BMC Microbiol. 2015; 15:15. <u>https://doi.org/10.1186/s12866-015-0348-1</u> PMID: 25648151
- 59. Shakir A, Abate D, Tebeje F, Weledegebreal F. Magnitude of surgical site infections, bacterial etiologies, associated factors and antimicrobial susceptibility patterns of isolates among post-operative patients in Harari region public hospitals, Harar, Eastern Ethiopia. Infect Drug Resist. 2021; 14:4629–39. https://doi.org/10.2147/IDR.S329721 PMID: 34764659
- Shimekaw M, Tigabu A, Tessema B. Bacterial profile, antimicrobial susceptibility pattern, and associated risk factors among patients with wound infections at Debre Markos Referral Hospital, Northwest,

Ethiopia. Int J Low Extrem Wounds. 2020; 21(2):182–92. https://doi.org/10.1177/1534734620933731 PMID: 32594808

- Tadesse S, Alemayehu H, Tenna A, Tadesse G, Tessema TS, Shibeshi W, et al. Antimicrobial resistance profile of Staphylococcus aureus isolated from patients with infection at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. BMC Pharmacol Toxicol. 2018; 19(1):24. <u>https://doi.org/10.1186/s40360-018-0210-9 PMID: 29784040</u>
- Tambuwal SH, Iliyasu G, Dayyab FM, Habib ZG, Tiamiyu AB, Liman HM, et al. Clinical and microbiologic profile of patients with Staphylococcus aureus infection. Infect Dis Clin Pract. 2020; 28:78–83. https://doi.org/10.1097/IPC.0000000000816
- 63. Tefera S, Awoke T, Mekonnen D. Methicillin and vancomycin resistant Staphylococcus aureus and associated factors from surgical ward inpatients at Debre Markos Referral Hospital, Northwest Ethiopia. Infect Drug Resist. 2021; 14:3053–62. https://doi.org/10.2147/IDR.S324042 PMID: 34408449
- 64. Tilahun M, Gedefie A, Bisetegn H, Debash H. Emergence of high prevalence of extended-spectrum beta-lactamase and carbapenemase producing Acinetobacter species and Pseudomonas aeruginosa among hospitalized patients at Dessie Comprehensive Specialized Hospital, North-East Ethiopia. Infect Drug Resist. 2022; 15:895–911. https://doi.org/10.2147/IDR.S358116 PMID: 35299856
- 65. Tilahun M. Multi-drug resistance profile, prevalence of extended-spectrum beta-lactamase and carbapenemase-producing Gram negative bacilli among admitted patients after surgery with suspected of surgical site nosocomial infection North East Ethiopia. Infect Drug Resist. 2022; 15:3949–65. <u>https:// doi.org/10.2147/IDR.S376622 PMID: 35924020</u>
- 66. Tsige Y, Tadesse S, T GE, Tefera MM, Amsalu A, Menberu MA, et al. Prevalence of methicillin-resistant Staphylococcus aureus and associated risk factors among patients with wound infection at referral hospital, Northeast Ethiopia. J Pathog. 2020:3168325. https://doi.org/10.1155/2020/3168325 PMID: 32566311
- 67. Van der Meeren BT, Millard PS, Scacchetti M, Hermans MH, Hilbink M, Concelho TB, et al. Emergence of methicillin resistance and Panton-Valentine leukocidin positivity in hospital- and community-acquired Staphylococcus aureus infections in Beira, Mozambique. Trop Med Int Health. 2014; 19(2):169–76. https://doi.org/10.1111/tmi.12221 PMID: 24205917
- Velin L, Umutesi G, Riviello R, Muwanguzi M, Bebell LM, Yankurije M, et al. Surgical site infections and antimicrobial resistance after cesarean section delivery in rural Rwanda. Ann Glob Health. 2021; 87 (1):77. https://doi.org/10.5334/aogh.3413 PMID: 34430227
- Wangoye K, Mwesigye J, Tungotyo M, Twinomujuni Samba S. Chronic wound isolates and their minimum inhibitory concentrations against third generation cephalosporins at a tertiary hospital in Uganda. Sci Rep. 2022; 12(1):1195. https://doi.org/10.1038/s41598-021-04722-6 PMID: 35075152
- 70. Wekesa YN, Namusoke F, Sekikubo M, Mango DW, Bwanga F. Ceftriaxone- and ceftazidime-resistant Klebsiella species, Escherichia coli, and methicillin-resistant Staphylococcus aureus dominate caesarean surgical site infections at Mulago Hospital, Kampala, Uganda. SAGE Open Med. 2020; 8. https:// doi.org/10.1177/2050312120970719 PMID: 35154757
- Yagoup MA, Taha AA, Mubarak AK, Abdalla AE, Ournasseir ME, Abosalif KOA, et al. Drugs-resistant Pseudomonas aeruginosa isolated from various clinical specimens in Khartoum, Sudan. PJMHS. 2019; 13(2):441–4.
- World Health Organization. WHO publishes list of bacterias for which new antibiotics are urgently needed. 2017. Available at: https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteriafor-which-new-antibiotics-are-urgently-needed (accessed 26th August 2023).
- 73. Abubakar U, Sulaiman SAS. Prevalence, trend and antimicrobial susceptibility of methicillin resistant Staphylococcus aureus in Nigeria: a systematic review. J Infect Public Health. 2018; 11(6):763–70. https://doi.org/10.1016/j.jiph.2018.05.013 PMID: 29933910
- 74. Berhe DF, Beyene GT, Seyoum B, Gebre M, Haile K, Tsegaye M, et al. Prevalence of antimicrobial resistance and its clinical implications in Ethiopia: a systematic review. Antimicrob Resist Infect Control. 2021; 10(1):168. https://doi.org/10.1186/s13756-021-00965-0 PMID: 34861894
- 75. Charani E, Mendelson M, Pallett SJC et al. An analysis of existing national action plans for antimicrobial resistance—gaps and opportunities in strategies optimising antibiotic use in human populations. Lancet Glob Health. 2023; 11(3):e466–e474. <u>https://doi.org/10.1016/S2214-109X(23)00019-0</u> PMID: 36739875
- World Health Organization. Overview of external quality assessment (EQA). 2009. Available at https:// www.who.int/publications/m/item/overview-of-external-quality-assessment-eqa (accessed 26th August 2023).
- World Health Organization. Second WHO model list of essential in vitro diagnostics. 2019. Available at: https://www.who.int/publications/i/item/WHO-MVP-EMP-2019.05 (accessed 26th August 2023).

- 78. Yusuf E, Hamers RL. What the WHO's list of essential diagnostics means for clinical microbiology laboratories and antimicrobial stewardship practice worldwide. Clin Microbiol Infect. 2019; 25(1):6–9. https://doi.org/10.1016/j.cmi.2018.08.013 PMID: 30145402
- 79. Yadav H, Shah D, Sayed S, Horton S, Schroeder LF. Availability of essential diagnostics in ten lowincome and middle-income countries: results from national health facility surveys. Lancet Glob Health. 2021; 9(11):e1553–e1560. https://doi.org/10.1016/S2214-109X(21)00442-3 PMID: 34626546