Extended data 6

ACORN II study analysis plan

STATISTICAL ANALYSIS PLAN

Study Title:

A Clinically-Oriented Antimicrobial Resistance Surveillance Network – Phase 2

Short title:
Infection surveillance to improve understanding of antibiotic resistance

Version: 2.4

Date: 01 Sep 2022

Protocol number: **BAC21002**

Study Statistician: Sue J Lee
Email: sue@tropmedres.ac

Name and Function	Date *DD/MM/YYYY*	Signature
SAP Author		
Sue J Lee		
Chief Investigator(s)		
Paul Turner		
Elizabeth Ashley		
Rogier van Doorn		

CONFIDENTIALITY STATEMENT:

This document contains confidential information that must not be disclosed to anyone other than the authorised individuals from the University of Oxford, the Investigator Team, and members of the Oxford Tropical Research Ethics Committee (OxTREC) and relevant Local / National Ethics Committees, unless authorised to do so.

Table of contents

1 Introduction

This document describes the statistical analysis plan for the following project: “A Clinically-Oriented Antimicrobial Resistance Surveillance Network – Phase 2”.

1.1 Description of the study

Current antimicrobial resistance (AMR) surveillance systems are typically passive and pathogen-focused, based on routine antimicrobial susceptibility testing (AST) results alone, generated by clinical microbiology laboratories. These systems lack relevant patient-level metadata and clinical syndromic denominators to appropriately inform treatment guidelines and decision making (1), and, especially in low- and middle-income countries (LMIC), suffer from various biases, due to lack of diagnostic stewardship and underutilisation of diagnostic microbiology resources (2). Collection of samples for microbiologic testing is often not part of a standard diagnostic work-up for many clinical syndromes, it is more likely for samples to be collected only in more severe cases or in case of treatment failure.

The utility of integrated patient and laboratory-based surveillance, i.e. case-based surveillance, has been highlighted recently (3, 4). In addition, there are several key patient-level questions that may not be adequately answered by passive pathogen-focussed AMR surveillance:

- What is the impact and cost of a drug-resistant infection (DRI) at the patient level?
- What are the patient-level risk factors for DRI in a particular setting?
- Which AMR-syndrome combinations are associated with the poorest outcomes in particular patient groups?

High-quality patient-level surveillance data from LMICs are necessary to informmodels to determine the impact of AMR, using big datasets with key patient-level variables, and to identify opportunities for intervention (5). The concept of ACORN is operationally efficient case-based AMR surveillance that can be deployed in low resource settings to add value to existing laboratory capacity building efforts.

The current ACORN protocol (https://acornamr.net/#/) incorporates lessons learned during the pilot phase, including expansion of patients of interest and refinements in case capture procedures. Additionally, data will be collected to enable calculation of attributable mortality for BSI caused by resistant *Escherichia coli* and *Staphylococcus aureus* in accordance with the WHO-GLASS attributable mortality protocol (6).

1.2 Study aim

The aim of this project is to roll out clinical AMR surveillance as part of routine care in a network of hospitals in across Asia and Africa, and to collect microbiology and clinical data from 2,500 patients per site, that will expand on the sample-based approach of WHO GLASS and enable classification of infection syndromes, origin of infection and outcome.

1.3 Timing of the analysis

Prospective surveillance in at least 15 study sites in nine countries will continue for 24 months from time of site commencement. As the primary objective is to implement AMR surveillance with comprehensive data capture, summary level analysis will be available in real time throughout the study via a Shiny dashboard application, specific to each site. Via the dashboard, site investigators will have access to real time enrolment frequencies and patient demographics, follow up on clinical outcome and day 28 status, weekly active hospital-acquired infections (HAI) point prevalences, microbiology summaries, and antimicrobial susceptibility and resistance patterns.

Secondary outcomes characterising drug-resistant infections and calculating attributable mortality for extended spectrum beta-lactamase producing *E. coli* and methicillin resistant *S. aureus* bloodstream infection will be analysed at study completion in Sep2024. This document concentrates on the analysis of the secondary outcomes of ACORN.

2 Statistical hypotheses and methods

2.1 Primary outcome(s)

The primary outcome of the study is to implement clinical antimicrobial resistance (AMR) surveillance of hospitalised patients with suspected acute bacterial infections at up to 15 sites in nine countries. A comparison of the results from ACORN surveillance, with and without clinical denominators, against GLASS estimates will be compiled.

2.2 Secondary outcomes

The secondary outcomes include:

2.1. The characterisation of drug-resistant infections (DRI) by clinicalsyndrome, place of acquisition (CAI, HAI, HCAI), patient group (adult, paediatric, neonatal), sample type, and location (site, country, region). Target organisms will be the bloodstream infections (BSI) relevant WHO GLASS pathogens: *Streptococcus pneumoniae, Staphylococcus aureus, Salmonella* spp.*, Pseudomonas aeruginosa, Neisseria meningitidis, Klebsiella pneumoniae, Haemophilus influenzae, Escherichia coli,* and *Acinetobacter* spp. Pathogens will be described separately as well as in groups to facilitate analysis of small numbers: Enterobacterales (*E*. *coli* and *K. pneumoniae*), non-fermenting Gram negatives (*Acinetobacter* spp and *P. aeruginosa*) and vaccine preventable pathogens (*S. pneumoniae*, *N. meningitidis*, and *H*. *influenzae*).

2.2. The determination of attributable mortality for extended spectrum beta-lactamase producing *E. coli* and methicillin resistant *S. aureus* bloodstream infection
2.3. Determination of the major indications for prescribing parenteralantibiotics by patient group (adult, paediatric, neonatal), timing of prescription (day of admission versus >2 days after admission), and location (site, country, region)
2.4. Frequency of major empiric parenteral antibiotics used by clinical syndrome, place of acquisition (CAI, HAI, HCAI), patient group (adult, paediatric, neonatal), and location (site, country, region)
2.5. Length of stay (LoS) in hospital (days) estimated for resistant versus susceptible infections, pooled as well as by pathogen groups.
2.6. Mortality at discharge and at day 28, pooled as well as by pathogen groups, by country, place of acquisition (CAI, HAI, HCAI), resistance status, and by clinical syndrome.

3 Study population and analysis datasets

3.1 Criteria for eligibility, recruitment, withdrawal and follow-up

The surveillance population includes all hospitalised patients of any age with suspected infection enrolled in ACORN.

Inclusion for **CAI**: Patient with clinically suspected infection on admission to a surveillance ward (including those transferred directly from another facility), in whom the decision to start IV antibiotic treatment has been made, and willing to participate in the surveillance.

Inclusion for **HAI**: Patient resident on a surveillance ward during a scheduled point prevalence survey for HAI, willing to participate in the surveillance, and meeting the following criteria (adapted from the European Centre for Disease Prevention and Control definition (7)):

- Clinical suspicion of bacterial infection and prescription / commencement of a new IV antibiotic (but not escalation of antibiotic treatment for an existing suspected or proven infection)

AND

- Onset of infection syndrome at least Day 3 of admission (Day 1 = day of admission)

AND

- Infection syndrome was not active during the previous weekly review: i.e. onset at least one day following the most recent previous HAI point prevalence survey

There are no criteria for stopping or discontinuing, as this is not an interventional study. Withdrawal from surveillance will not result in exclusion of the data already collected for that participant from analysis, unless the participant does not permit this use.

The final follow-up of patients will be on day 28 (or next working day if day 28 falls on a weekend or public holiday) post enrolment to determine post-discharge health status (alive [fully recovered], alive [not fully back to normal activities], or dead) and date of death, if appropriate. If enrolled for >1 infection episode during an admission, then this assessment will occur 28 days following the final enrolment date.

3.2 Analysis datasets

Analysis will include all patients enrolled into surveillance with data. Minimum data for inclusion in the analysis of attributable mortality will be confirmation and date of bloodstream infection, admission date, resistance status, and outcome.

4 Description of statistical methods

4.1 General approach

4.1.1 Implementation

Site summary and surveillance staff assessment questionnaire data will be summarised in tables and graphs. Simple descriptive statistics will be used where appropriate to compare data within and across sites, countries, and regions. A logical framework defining goals, purpose and indicators will be set out in a separate document.

4.1.2 AMR surveillance data

Site-level data visualisation and analysis will be done onsite using the project specific R-Shiny app or online via the identical web app (https://acornamr.net). For the overall project, site surveillance datasets will be merged prior to analysis.

For all cases, clinical notes and electronic hospital information systems will be reviewed regularly to capture:

- Final categorisation of infection syndrome (or infection diagnosis rejected)
- Hospitalisation outcome (death, discharge, discharged moribund)
- Disposition (home, transfer to another healthcare facility, unknown)
- Number of days admitted to an intensive care unit

Key outcome variables will be:

Blood culture and other microbiology results (Dummy Table 1)

- Presence or absence of target pathogen
- Frequency of blood culture testing
- Antimicrobial susceptibilities
- Duration of hospitalisation

- Hospital discharge vital status
- Day-28 vital status

Data will be summarised in tables and graphs (Appendix). Categorical variables will be compared using Chi-squared or Fisher's exact test. Continuous variables will be compared using Student's t-test, one-way ANOVA, or their non-parametric equivalents. Alternatively or in addition to comparisons, associations may be quantified using univariate regression. While no formal correction for multiple comparisons will be made, p-values will be reported to the third decimal so results canbe assessed against a Bonferroni corrected p-value (i.e., significance level of alpha/m,where alpha = 0.05 and m = number of comparisons), if desired. Results will be stratified by:

- Clinical infection syndrome
- Participant age category (neonatal (<28 days), paediatric (1 month – 17 years), adult (≥18 years))
- Place of acquisition (CAI, HCAI, HAI)
- Location (site, country, region)

Patients who have a single admission with a single infection will be compared against those with multiple admissions or admissions with multiple infections, in particular with respect to underlying illness and comorbidities. Subsequent analysis may be modified depending on any key differences found, e.g., if neonates and elderly patients are found to be significantly more likely to have multiple infections when compared with all others, analysis may be stratified by age group.

4.1.2.1 Associations with resistance and mortality

Univariable and multivariable (see more on this below in section on Attributable Mortality) logistic regression models will be fitted to explore whether any clinical or microbiological variables are associated with the outcomes of resistance, mortality and discharged moribund. The unit of analysis will be admissions, with patient and site fitted as random effects.

4.1.2.2 Length of stay

Length of stay (LoS) will be summarised as median with inter-quartile range, by resistant versus susceptible infections, as well as by died versus survived to discharge. Overall LoS will be calculated from time of admission to hospital. Length ofstay will also be assessed from time of blood culture.

4.1.2.3 Antimicrobial susceptibility testing

For specimen- and isolate-based analyses, data will be deduplicated prior to calculation of infection and antimicrobial resistance rates, following WHO GLASS recommendations. For overall AST reporting, the first isolate of a given species per

participant per specimen type and place of acquisition (CAI, HCAI, HAI) will be analysed. Summaries will include:

- Incidence of target pathogen bloodstream infection, including drug resistant infections (denominator will be only those with a blood culture sample)

- The percentage of isolates resistant or susceptible to key antibiotics or treatment regimens

4.1.2.4 Attributable mortality

For *E. coli* and *S. aureus* BSI attributable mortality analyses, the survival model approach outlined in the WHO-GLASS protocol will be followed (6). Given the likely small numbers of BSI at each site, data from across the network will be combined. At each site, observed crude case fatality rates (survival data) will be compared between cohorts: patients with AMR BSI for selected pathogen-antimicrobial combination (cohort 1), patient with non-AMR BSI for selected pathogen-antimicrobial combination (cohort 2), or ACORN-enrolled patient from the same surveillance ward in whom *E. coli* and *S. aureus* were not isolated from blood cultures and who did not receive pre-culture antibiotics (cohort 3).

Cases of AMR *E. coli* or *S. aureus* bacteraemia (cohort 1) will be matched 1:1 retrospectively with cases of non-AMR *E. coli* or *S. aureus* bacteraemia (cohort 2). Optionally, randomly selected exposure density sampling plus additional matching criteria (age group and reason for admission) will be used to match 1:1 cohort 3 patients with cohort 1 and cohort 2 patients. Ideally, matching will be by age category, admission ward, month of infection, and clinical syndrome at enrolment, as well as by the time from admission to infection, i.e., uninfected patients admission should be at least as long as matched case time to infection. This will result in three groups of patients (infected – drug susceptible, infected – drug resistant, non-infected) to enable robust determination of attributable mortality under both “additive” and “replacement” scenarios.

The effect of antibiotic resistance on vital status will be estimated using cause-specific Cox proportional hazards models, assessing the competing events of mortality and discharge alive, from the time of infection. Admissions, rather than patients, will be used as the unit of analysis and only the first relevant infection episode will be considered. Multivariable models will include gender, ICU stay (y/n), surgery (y/n), Charlson comorbidity index score, age, type of admission and Pitt bacteraemia score as categorical (scores of 0-1, 2-3 and ≥4) or qSOFA score. A composite all-cause end-of-stay endpoint (either death or discharge alive) will also be assessed which may be interpreted as an indication of the daily hazard of a patient’s admission ending. All models will include adjustment for the time (days) between admission and infection. Proportional hazards assumptions will be checked using Schoenfeld residuals and visual inspection of log-log plots. Non-proportional hazards will be corrected using stratification. Separate models for CAI and HAI will be run, if numbers permit.

4.1.2.5 *Empiric treatment*

For empiric antibiotic analyses, drugs prescribed on the day of admission (CAI, HCAI) or symptom onset (HAI) will be classified according to the WHO AWaRe criteria (8). Concordance (i.e. cultured isolate was susceptible) or discordance (i.e. cultured isolate was resistant) with microbiology test results will be determined (Dummy Table 3).

To assess the impact of initial treatment on mortality another set of Cox proportional hazards models will be run, but for antibiotic resistance will be replaced by receipt of active initial therapy as the exposure of interest.

4.1.2.6 *Excess length of stay*

Excess length of stay in days will be calculated using multistate models. The difference in expected length of stay will be estimated between the resistant and susceptible states.

4.1.2.7 *Missing values*

In the case where key variables of interest have 20% or more missing values, missing values imputation will be considered, and results presented alongside the "complete case" analysis.

4.2 Baseline descriptive statistics

On the day of enrolment, baseline clinical data will be extracted from the patient clinical records / electronic hospital information systems and by brief interview of the patient:

- Date of birth or age
- Gender
- Date of admission and original hospitalisation (if transferred directly from another healthcare facility or ward)
- Admission type (emergency or elective)
- Primary reason for admission
- Co-morbidity status (modified Charlson comorbidity index) – for adults
- Healthcare exposure, hospitalisation, and surgery in the three months before admission

The following data will be collected about the infection episode:

- Surveillance category (CAI or HAI)
- Ward details
- Clinically suspected infection syndrome / reason for prescription
- Clinical severity signs on date of admission (CAI) or symptom onset (HAI)
    - qSOFA score for adults, ≥18 years (9)
    - Sepsis six recognition features or LqSOFA for children, <18 years (10)
    - General WHO severity signs for neonates, <28 days (6)
- Presence of medical devices / surgical procedures (HAI only)

- Microbiology
    - Blood culture collected within 24 hours of admission (CAI) or symptom onset (HAI)
    - Received ≥1 dose of a systemic antibiotic in the 24 hours before the blood culture collected
- Empiric antibiotic treatment details (all antibiotics prescribed on the day of admission (CAI) or symptom onset (HAI))

During hospitalisation, cases with confirmed *E. coli* or *S. aureus* BSI will have additional data collected for analysis:

- Admission ward details
- Immunosuppression status in the 48 hours prior to the blood culture
- Pitt BSI score on date of blood culture collection
- Empiric and targeted antibiotic treatment details, plus date of delivery of AST results to treating clinicians
- Likely source of infection
- Features of complicated infection (*S. aureus* only)

4.3 Analysis of the primary outcome(s)

Specific outcomes from the surveillance include:

4.3.1 Number of sites with successful implementation of surveillance defined as activity on at least three wards with upload of an .acorn data file at monthly intervals over at least 12 months

4.3.2 Numbers of patients enrolled by clinical syndrome, place of acquisition (community-acquired infection [CAI], hospital-acquired infection [HAI], healthcare associated infection [HCAI]), patient group (adult, paediatric, neonatal), and location (site, country, region)

4.3.3 Proportion of timely (within 48 hours) and correctly (i.e. syndrome-relevant specimens collected: blood culture (all patients), CSF specimen (CNS infection patients), lower respiratory tract specimens (pneumonia patients), urine specimen (urinary tract infection patients)) sampled patients per clinical syndrome, place of acquisition, and patient group by site, country, and region

4.3.4 Clinician and surveillance staff acceptability and ease of use survey results by site, country, and region

4.3.5 Comparison of the results, with and without clinical denominators, against GLASS estimates (including an assessment of how well aligned locally cultured organisms are with the GLASS pathogen list)

4.4 Analysis of the secondary outcome(s)

Drug-resistant infections (DRI) will be characterised by clinical syndrome, place of acquisition (CAI, HAI, HCAI), patient group (adult, paediatric, neonatal), and location (site, country, region) using estimates of:

4.4.1 Frequencies of resistant and susceptible infections for WHO GLASS target pathogens with isolate, specimen, and case level denominators by location.

4.4.2 Incidence of WHO GLASS target pathogen bloodstream infection for patients with blood culture specimen (per 1,000 patient episodes) by clinical syndrome, place of acquisition, patient group, and location

4.4.3 Weekly HAI point prevalence data by clinical syndrome, patient group, and location (with denominator being the number of patients resident on the ward at 8am on day of survey)

4.4.4 Duration of hospitalisation for DRI and non-DRI by clinical syndrome, place of acquisition, patient group, and location

4.4.5 Patient outcomes / mortality for DRI and non-DRI by clinical syndrome, place of acquisition, patient group, and location

4.4.6 Economic costs for DRI and non-DRI by clinical syndrome, place of acquisition, patient group, and location (Statistical analysis procedures reported in separate document)

Other secondary outcomes include:

4.4.7 Determination of attributable mortality for extended spectrum beta-lactamase producing *E. coli* and methicillin resistant *S. aureus* bloodstream infection using cause specific Cox models for death, discharge alive and a composite “all-cause” outcome.

4.4.8 Incidence of bloodstream infection by *E. coli* and *S. aureus* (per 1,000 patient episodes) by clinical syndrome, place of acquisition, patientgroup, CAI, HAI, and location for patients who have a blood culture collected

4.4.9 Frequencies of antimicrobial susceptibility (single and multi-drug resistance) of *E. coli* and *S. aureus* bloodstream infections by clinical syndrome, place of acquisition, patient group, and location

4.4.10 Patient outcomes / mortality for susceptible vs. resistant *E. coli* and *S. aureus* bloodstream infections by clinical syndrome, place of acquisition, patient group, and location. The impact of AMR on mortality and hospital length of stay will be assessed for ESBL-producing Enterobacteriaceae and MRSA. Patients infected with these two drug-resistant pathogens will be compared against patients infected with the same organisms but without the presence of ESBL or methicillin-resistance, respectively.

4.4.11 The effect of AMR on the probability of mortality will be estimated using a Cox Proportional Hazards model, with time from infection as the timescale. To account for competing outcomes, we will build two models (one for in-hospital mortality and one for discharge alive) and report cause-specific hazard ratios.

4.4.12 Major indications for prescribing parenteral antibiotics by patient group (adult, paediatric, neonatal), timing of prescription (day of admission versus >2 days after admission), and location (site, country, region)

4.4.13 Frequencies of the major empiric antibiotics used by clinical syndrome, place of acquisition (CAI, HAI, HCAI), patient group (adult, paediatric, neonatal), and location (site, country, region)

4.4.14 Excess length of stay will be calculated using multistate models with four states (admission, resistant, susceptible and discharged/died). The expected length of stay will be estimated for each day in the resistant and susceptible states using Aalen-Johansen estimators for transition probabilities. Difference in the length of stay will then be calculated

between resistant infections and sensitive infections, and then a weighted average estimated using the observed distribution of time to infection. Standard errors and 95% confidence intervals will be derived by bootstrapping.

5 Additional sub-group analyses

Subgroups to be considered include, but are not necessarily limited to:

- Place of acquisition
  - CAI (a subset of this group will be direct transfer patients)
  - HAI
  - HCAI

- Participant age category
  - Adult
  - Paediatric
  - Neonatal

- Location
  - Site
  - Country
  - Region

- Clinical infection syndrome

6 Sample size

Based on pilot data, and the revised enrolment criteria, the target number of enrolments per site will be 2,500 (estimated 37,500 infection episodes in total) over the 24-month surveillance period.

Assuming that 80% of enrolled patient episodes include a blood culture (pilot: 88% for Cambodia and 75% for Laos) and that 5% of blood cultures will yield a target organism (pilot: 4.9% for Cambodia and 7.4% for Laos), then the surveillance will yield 37,500 patient episodes, 30,000 blood culture results, and 1,500 target pathogen blood culture isolates with AST data. Non-blood culture specimen data, especially urine and pus / swabs, will be expected to increase the organism yield significantly (11).

7 Case definitions

For the purposes of this study, patients will be defined as having **susceptible** or **resistant** infections to received treatment and/or 1st and 2nd line empiric guideline regimens (ampicillin plus gentamicin, cefotaxime / ceftriaxone (3rd generation cephalosporins), or a carbapenem). For attributable mortality work, definitions are resistance to 3rd generation cephalosporins (cefotaxime, ceftriaxone, or ceftazidime) for *E. coli* and resistance to methicillin for *S. aureus*. For all pathogens, resistance will be described following the core WHO GLASS organism – antibacterial agent pairs (excluding tigecycline, colistin and 4th generation cephalosporins) (12):

Table 3. Pathogen–antimicrobial combinations on which GLASS will gather data

Pathogen	Antibacterial class	Antibacterial agents that may be used for AST[a,b]
Escherichia coli	Sulfonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Fourth-generation cephalosporins	Cefepime
	Carbapenems[c]	Imipenem, meropenem, ertapenem or doripenem
	Polymyxins	Colistin
	Penicillins	Ampicillin
Klebsiella pneumoniae	Sulfonamides and trimethoprim	Co-trimoxazole
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Fourth-generation cephalosporins	Cefepime
	Carbapenems[c]	Imipenem, meropenem, ertapenem or doripenem
	Polymyxins	Colistin
Acinetobacter baumannii	Tetracyclines	Tigecycline or minocycline
	Aminoglycosides	Gentamicin and amikacin
	Carbapenems[c]	Imipenem, meropenem or doripenem
	Polymyxins	Colistin
Staphylococcus aureus	Penicillinase-stable beta-lactams	Cefoxitin[d]
Streptococcus pneumoniae	Penicillins	Oxacillin[e]
		Penicillin G
	Sulfonamides and trimethoprim	Co-trimoxazole
	Third-generation cephalosporins	Ceftriaxone or cefotaxime
Salmonella spp.	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Third-generation cephalosporins	Ceftriaxone or cefotaxime and ceftazidime
	Carbapenems[c]	Imipenem, meropenem, ertapenem or doripenem

This list of pathogens and pathogen-antimicrobial combinations of interest will be updated according to the anticipated revised GLASS manual when released or, if publication is delayed, according to current insights into relevant pathogens and pathogen-antimicrobial combinations.

Healthcare associated infections (HCAI) will be defined as the subset of CAI, where the patient was known to have had exposure to healthcare facilities in the three months prior to admission.

For syndrome-based analyses, the **clinical syndrome** will be that which was recorded at enrolment. Discharge syndrome will be used to identify which patients should not be included in the analysis due to non-infection diagnosis.

8 Statistical software

The analysis will be performed using STATA, v17.0.

9 Document history

Version	Notes / Changes
1.0	Initial version
1.1	Updated after comments received from Paul Turner
1.2	Add length of stay as secondary endpoint (SJL)
1.3	Add detail for multiple comparisons, missing values and clarifications related to infection v. admission v. patient units (SJL)
1.4	Respond to queries/suggestions made by Rogier and Liz (SJL and PT)
2.0	Resolve queries and agree discussion points (RvD, EA, PT, JH, SJL)
2.1	Minor revisions for “final” review (SJL)
2.2	Tidy up of document after discussion/approval of attributable mortality methods with Barbara Tornimbene (WHO)
2.3	Incorporated/addressed final comments/concerns from Barbara Tornimbene (WHO) and chief investigators.
2.4	Added references (SJL), 1 Sep 2022

10 References

1. Ashley EA, Recht J, Chua A, Dance D, Dhorda M, Thomas NV, et al. An inventory of supranational antimicrobial resistance surveillance networks involving low- and middle-income countries since 2000. J Antimicrob Chemother. 2018;73(7):1737-49.
2. Rempel OR, Laupland KB. Surveillance for antimicrobial resistant organisms: potential sources and magnitude of bias. Epidemiol Infect. 2009;137(12):1665-73.
3. Seale AC, Hutchison C, Fernandes S, Stoesser N, Kelly H, Lowe B, et al. Supporting surveillance capacity for antimicrobial resistance: Laboratory capacity strengthening for drug resistant infections in low and middle income countries. Wellcome Open Res. 2017;2(91).
4. Ryu S, Cowling BJ, Wu P, Olesen S, Fraser C, Sun DS, et al. Case-based surveillance of antimicrobial resistance with full susceptibility profiles. JAC-Antimicrobial Resistance. 2019;1(3).
5. Hay SI, Rao PC, Dolecek C, Day NPJ, Stergachis A, Lopez AD, et al. Measuring and mapping the global burden of antimicrobial resistance. BMC medicine. 2018;16(1):78.
6. Global Antimicrobial Resistance and Use Surveillance System. GLASS method for estimating attributable mortality of antimicrobial resistant bloodstream infections Geneva: World Health Organization; 2020.
7. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals – protocol version 5.3. Stockholm: ECDC; 2016.
8. World Health Organization. Adopt AWaRe: Handle antibiotics with care 2019 [Available from: https://adoptaware.org/.]
9. Rudd KE, Seymour CW, Aluisio AR, Augustin ME, Bagenda DS, Beane A, et al. Association of the Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries. JAMA. 2018;319(21):2202-11.
10. Tong J, Plunkett A, Daniels R. G218(P) The Paediatric Sepsis 6 Initiative. Archives of Disease in Childhood. 2014;99:A93.
11. Vihta K-D, Gordon NC, Stoesser N, Quan TP, Tyrrell CSB, Vongsouvath M, et al. Antimicrobial resistance surveillance: can we estimate resistance in bloodstream infections from other types of specimen? medRxiv. 2020.10.12.20211243.
12. World Health Organization. Global Antimicrobial Resistance Surveillance System: Manual for Early Implementation. Geneva: World Health Organization; 2015.