



# Facility Report:

## Central Regional Referral Hospital, Bhutan

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### March 2023



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## Part I: General Introduction

### Aim

This report has been prepared by the CAPTURA team to share apparent findings and observations from the project metadata and AMR/U data shared by your facility. It also provides feedback and recommendations on data management and quality based on the experiences of the in-country team.

### Introduction

Capturing data on Antimicrobial Resistance Patterns and Trends in Use in Regions of Asia (CAPTURA) fosters a two-fold aim:

- To increase the volume of available data on antimicrobial resistance (AMR), antimicrobial use (AMU), and antimicrobial consumption (AMC)
- To illustrate data availability and capacity of laboratories generating those data

Local governments and facilities in 10 South or Southeast Asian countries were engaged. Among these, AMR, AMU, and/or AMC data were collected from 8 countries, including Bangladesh, Bhutan, Laos, Nepal, Pakistan, Papua New Guinea, Sri Lanka, and Timor-Leste. The collated data are analysed to paint a local overview and to understand data availability in regional and inter-regional contexts wherever possible. CAPTURA's findings may inform future initiatives in bolstering awareness, policy, and interventions to combat the urgent global threats of spreading AMR and antimicrobial misuse.

CAPTURA is funded by the Fleming Fund Regional Grant.

### Description of data activities

To meet CAPTURA's two-fold aim, two distinct types of data were collected: namely, source data and project metadata. The source data includes AMR, AMU, and AMC data, which were collected/generated by local facilities (microbiology laboratories, pharmacies, or central government procurement and distribution agencies). The project metadata constitutes all information collected directly by the CAPTURA consortium, via questionnaires developed specifically for the purpose of CAPTURA. These include Laboratory/Pharmacy Questionnaires and Rapid Laboratory Quality Assessment (RLQA).

To optimize the data collection process, extensive mapping activities took place by engaging local governments and data-holding facilities. Laboratory capacities as well as the quality of data from each facility were assessed, which were also used to identify areas for quality improvement at an individual-facility level. Data collection primarily focused on a four-year timeframe between 1 January 2016 and 31 December 2019, but also included data from 2020 and 2021 for certain sites.

Throughout the project, capacity-building activities have taken place to help facilities collate and curate data in a standardized format. These capacity-building activities also extend the aims of CAPTURA to help improve local data management practices.

### Engagement with CRRH

Central Regional Referral Hospital (CRRH) was introduced to the CAPTURA consortium during the initial scoping visit via the liaison of the Bhutan Ministry of Health. Through signing the Data Transfer Agreement (DTA), the laboratory agreed to isolate level AMR data sharing and to allowing the data to be shared with Health Care and Diagnostic Division, Department of Medical Services, Ministry of Health. CAPTURA formed an in-country team who mediated communications with sites, engaged local stakeholders, and collected data during the project period.

## Part II: AMR Data Analysis

The microbiology laboratory at CRRH shared its isolate level susceptibility data for the time frame of January 2017 to December 2019. The CAPTURA in-country team led the efforts to digitize the AMR records from the and entering the data into the WHONET software. CAPTURA's in-country microbiologist conducted a thorough review to identify typos and errors in the data, after which Dr. John Stelling and the WHONET team conducted a review to understand the quality of data. Before sharing data with CAPTURA, patient identifiers were removed (e.g., patient name) and encrypted (e.g., patient ID). The data files were then uploaded to the CAPTURA Warehouse. The facility also participated in project's metadata activities, including the Rapid Laboratory Quality Assessment and Laboratory Questionnaire.

### *Data Analysis disclaimer*

*The dataset can be analysed using the 'Data Analysis' and 'Quick Analysis' features in the WHONET software. The Quick Analysis feature allows both the Epidemiological and Data Quality reports to be exported in a word document. The interpretation and graphical representation in this report is, however, a combined outcome of the WHONET software and CAPTURA AMR Data Visualization Tool. Additional curation (e.g., combining sub-species, reassigning categories to ensure alignment with WHONET software) and interpretation were conducted by the CAPTURA Data Team to provide the facility a detailed report. Therefore, the reports will not be identical to those generated from WHONET software alone.*

# Epidemiology Report

## 1 Data Volume

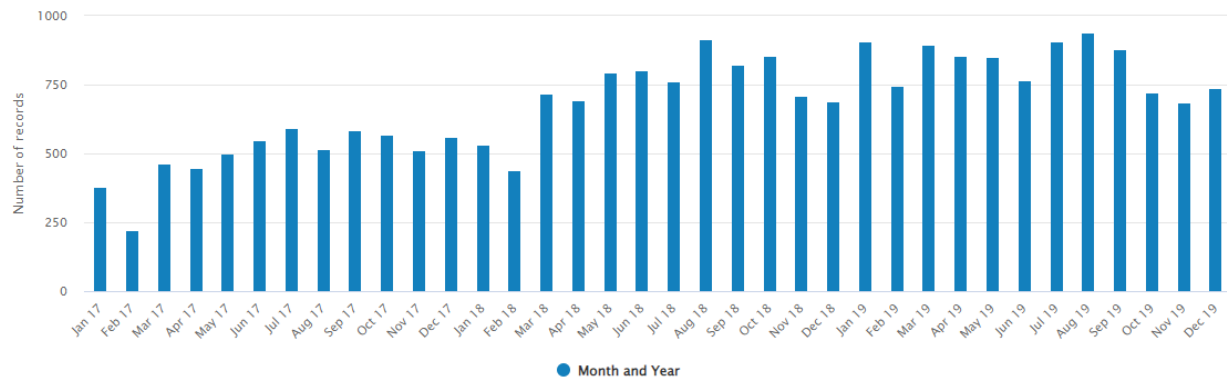
CRRH has shared bacteriological culture records, with a total of 24,517 observations over the period of January 2017 to December 2019 (Figure 1). Of these observations, 11,463 had bacterial growth reported as positive cultures. The shared dataset includes all variables considered essential to a complete AMR dataset, except for the Patient Location and Sex variables.

**Table 1.** List of expected variables included or missing in the shared dataset. Expected variables are variables that CAPTURA considered essential to a complete AMR dataset.

| Expected Variables included in the dataset | Expected Variables NOT included in the dataset |
|--|--|
| Patient Identification number              | Patient Location (Ward/Clinic)                 |
| Age  | Sex  |
| Specimen Number                            |  |
| Specimen Type                              |  |
| Specimen date                              |  |
| Organism                                   |  |
| Department                                 |  |

**Table 2.** The number of culture records over time. For each year, the number indicates the number of culture records, including bacterial growth and no growth results.

| Data volume overview |            |      |      |      |      |      |      |      |
|----------------------|------------|------|------|------|------|------|------|------|
|                      | Cumulative | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | NULL |
| Number of records    | 24517      | 0    | 5895 | 8734 | 9888 | 0    | 0    | 0    |
| Bacterial Growth     | 11463      | 0    | 2954 | 3877 | 4632 | 0    | 0    | 0    |
| No Growth            | 13054      | 0    | 2941 | 4857 | 5256 | 0    | 0    | 0    |



**Figure 1.** The distribution of the number of culture records over time, including negative results.

Documenting the volume of testing performed by a laboratory is useful for monitoring changes in sampling practices over time and for comparing the workloads between laboratories. One may also identify time periods where data entry is incomplete; for instance, many laboratories experienced a significant decrease in bacteriological testing in April-May 2020 with the arrival of COVID-19.

## 2 Patient Demographics and Sample Details

### 2.1 Sex and Age

The AMR dataset from CRRH has the distribution of patients by sex and age group as follows:

- **Sex:** Female: 0, Male: 0
- **Median age group:** No results found.

In many countries, the number of samples from female patients exceeds the number of samples from male patients for the following reasons:

- 1) A large proportion of laboratory samples are often from urinary tract infections in women.
- 2) Women may seek medical assistance more frequently than men.
- 3) In many countries, women have a longer lifespan than men. The age distribution will reflect the patient population served by the laboratory.

The CRRH dataset did not include any information on gender and age groups, and thus no comment could be made on the distribution of sex and age groups in the clinical samples. This could be due to issues related to data management but needs to be verified by comparing the existing lab and/or patients records at CRRH with the shared dataset. As CRRH is a referral hospital, we presume that the number of samples from female patients would be higher than the male patients, as urine is the most frequently processed sample for culture, and samples tend to be from females of reproductive age.

No results found.

**Figure 2.** Distribution of the number of patients by sex and age group for all records.

### 2.2 Location

The location variable generally refers to the specific location where samples originated from. For the CRRH microbiology laboratory, this would include the ward or department information, such as "Neurology", or "Diabetes clinic".

Location type is a category of location such as "inpatient" or "outpatient". It will be beneficial to use standard WHONET codes to standardize the dataset across laboratories and facilitate the comparison of results between laboratories, but this is not an absolute necessity.

Keeping information on the origin of the samples will help a facility to understand the types and volume of samples being processed at each location and help facilities plan logistics required at the department. Moreover, it allows the facilities to understand the resistance patterns of the pathogens being isolated in the clinics and allows the clinicians/researchers/public health experts to identify local outbreaks within the facility and take appropriate actions.

**Table 3.** The distribution of samples and patients by location type. The location codes are those used by the laboratory to identify the specimen collection site. The abbreviations indicated here are location codes provided by the laboratory. It is recommended to accompany abbreviations with a data dictionary for interpretation.

| Location type | Number of samples | (%)  | Number of patients | Samples per patient |
|---------------|-------------------|------|--------------------|---------------------|
| out           | 18,391            | 75   | 14,510             | 1.3                 |
| in            | 4,039             | 16.5 | 2,691              | 1.5                 |
| eme           | 1,089             | 4.4  | 955                | 1.1                 |
| icu           | 998               | 4.1  | 539                | 1.9                 |

### **Q. Why care about “Isolates per patient”?**

**A.** This metric quantifies the average number of records available from patients over time. In low-resource settings, this number is typically low, between 1.1 and 1.5 records per patient. A low number of samples per patient may indicate that there are few patients for which multiple samples were collected. It is recommended to provide a unique patient identification number to confirm this observation. If a dataset is missing a link between a patient and samples collected from that patient, it suggests that there are no meaningful patient identification numbers that can be used to track patients over time. A higher number may suggest issues, such as 1) patient identification numbers are reused for different patients over time; and 2) there may be a problem in the data export from a laboratory information system or in the BacLink configuration. CLSI recommends analysing the first isolate per species in the time period.

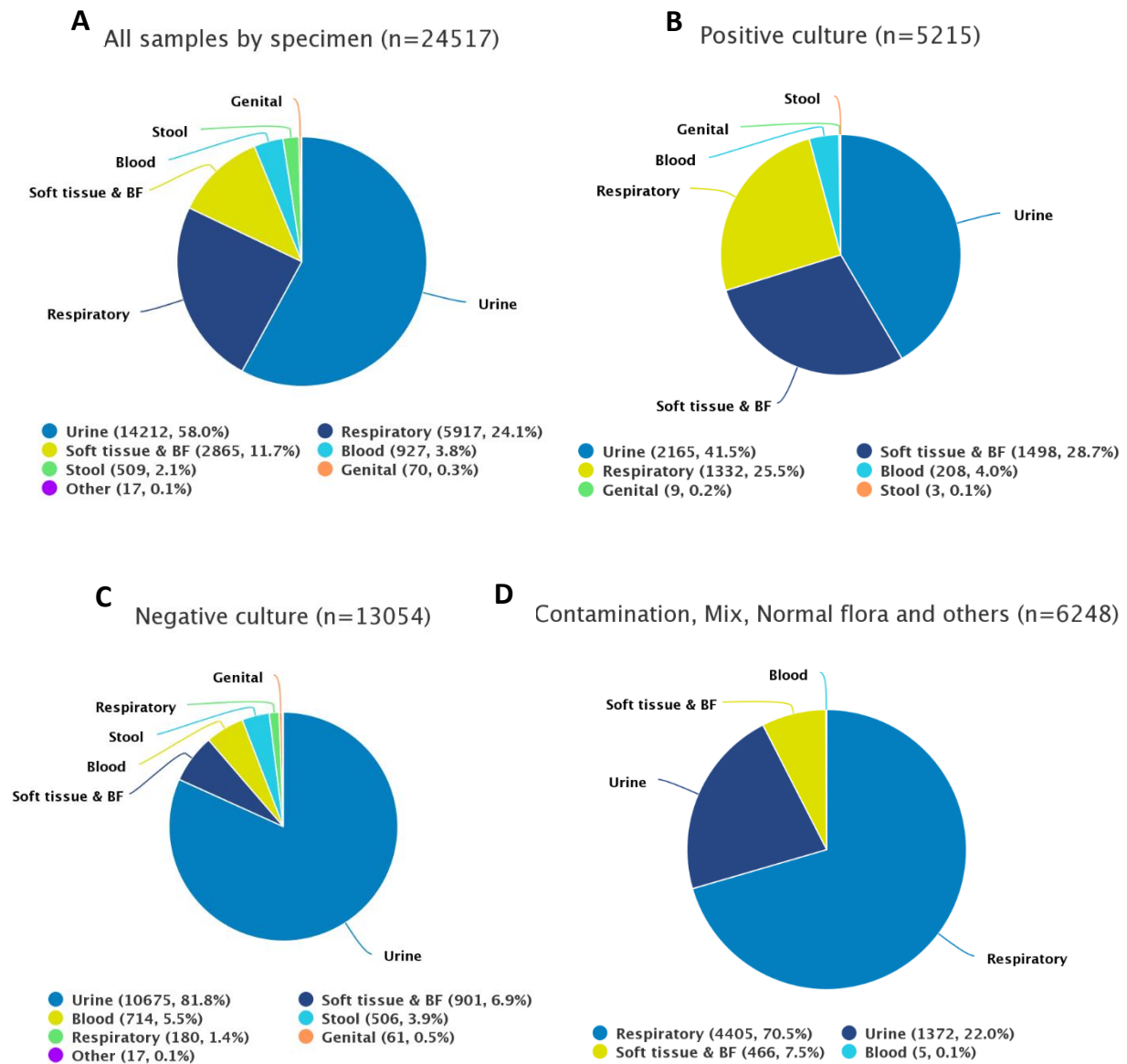
### **2.3 Sample Details**

WHONET categorizes specimen types into eight broad categories: Blood, Genital, Respiratory, Soft tissue and bodily fluids, Stool, Urine, Other, and Unknown. In the secondary curation conducted by the CAPTURA team, the Other and the Unknown categories were combined under Other.

Urine was the most common specimen subjected to the bacterial culture at CRRH, followed by respiratory and soft tissue and bodily fluids specimens (Figure 3). When a subset of samples that showed growth was further analysed, the order changed to urine, then soft tissue and bodily fluids, and then respiratory specimens.

It is a normal observation in laboratories with microbiological culture facilities to have a relatively large number of urine samples, as it is the most frequently processed sample for culture. Additionally, it is a regular observation that samples are obtained from females, as the number of female patients tends to be higher. It is an important practice to include gender and age information in the AMR records in order to better understand the needs of different groups within the patient demographic.

Culture positivity rate of blood culture is usually low (range 3-25%) in most regular clinical laboratories as the isolation rate depends on various factors including the clinical condition, ambulatory or hospitalized state, length of hospital stay, age of the patient, and several other factors. Thus, the change in the order when only samples with bacterial growth were analysed is a normal finding. However, in the context of CRRH, the order of blood samples remained unchanged and with a blood culture positivity rate of 22.4%, which is towards the upper limit of normal range.



**Figure 3.** The number of culture records stratified by specimen category. Cumulative records including both culture positive and negative finding (A). Showing only those with significant growth of true pathogens (B). Showing only culture negative results (C). Showing growth with contamination/normal flora/mixed flora and others (D).



### 3 Organism Statistics

#### 3.1 Organism Frequencies

Looking into the most frequently isolated organisms in all samples, *Escherichia coli*, *Klebsiella* sp., *Pseudomonas* sp., *Staphylococcus aureus* ss *aureus*, and coagulase-negative *Staphylococcus* were the top five most isolated organisms found in the CRRH dataset (Figure 4).

This correlates well with the fact that most common sample in the dataset was urine, as *Escherichia coli* is often the most frequently reported pathogen in urine cultures (Figure 5). It is also worth noting that pathogens such as *Klebsiella* spp., *Pseudomonas* spp., and *Staphylococcus aureus* were other frequently isolated organisms in this setting. As the time of patient admission and onset of disease variables were not recorded, it is not possible to comment on whether these pathogens were from hospital acquired infections or community settings. However, these organisms are potential nosocomial pathogens that are mostly MDR and are associated with high mortality and morbidity in hospitalized patients. It is thus essential that the hospital strictly follow infection control practices to prevent the spread of these organisms in hospital as well as community settings.

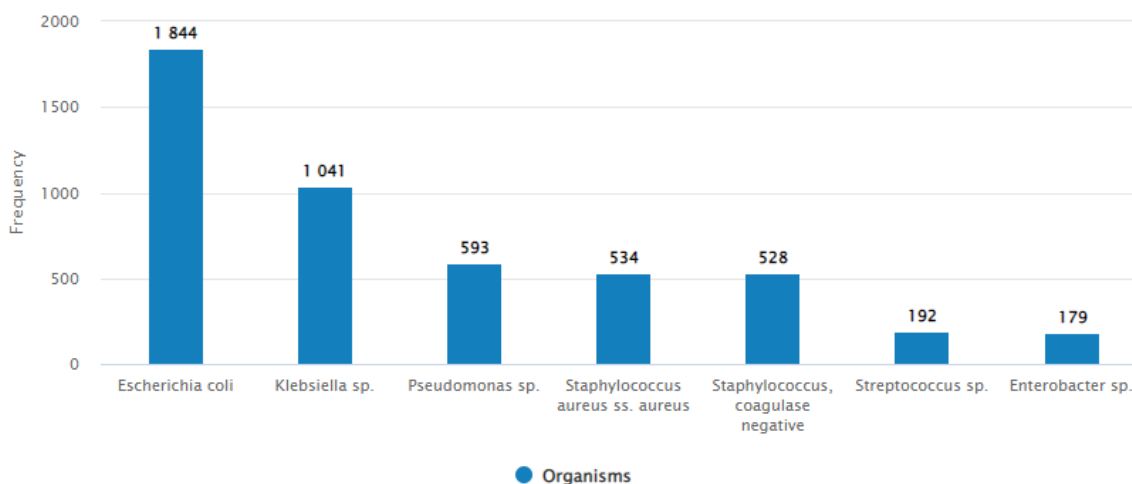


Figure 4. Most common organisms isolated from all samples over the reported period.

WHONET has categorized some pathogens as "important species". Such pathogens are considered important for public health because of their potential for outbreaks and thus often included in national disease control programs.

Table 4. Public health alerts - important species.

| Organisms                     | Number of isolates | Priority        |
|-------------------------------|--------------------|-----------------|
| <i>Neisseria gonorrhoeae</i>  | 1                  | High priority   |
| <i>Pseudomonas aeruginosa</i> | 188                | Medium priority |

One isolate of high priority pathogen *Neisseria gonorrhoeae* was identified in the CRRH dataset. This is consistent with the fact that gonorrhoea is an important public health problem in Bhutan; a recognized public health threat, *Neisseria gonorrhoeae* is progressively developing AMR to all therapeutic antibiotics. Identification and careful monitoring for early diagnosis and treatment of patients will help prevent its spread. If possible, it is recommended to preserve these high priority isolate/s for future studies. Many samples also yielded medium priority pathogen *Pseudomonas aeruginosa*, which is responsible for hospital-associated infections and shows a high level of MDR. It is therefore necessary to closely monitor for any associated outbreaks with this pathogen.



**Figure 5.** Most common organisms by specimen category. Urine, Respiratory, Soft tissue, Blood, Stool, and Genital.

**Q. Why is it important to understand organism frequencies?**

**A.** Understanding temporal changes in pathogen diversity in a given geographic area will help develop local/regional policies and guidelines for case management. It will also help public health experts to monitor the disease occurrence/spread and changes in the resistance pattern in the pathogen of concern. The frequency of organisms seen in a microbiology laboratory may change over time for different reasons:

- Microbial factors
  - Long-term changes in organism epidemiology related to organism dissemination, virulence factors, and disease prevention measures such as vaccination and improved sanitation.
  - Short-term changes suggestive of disease outbreaks. Statistical algorithms for automated outbreak detection are described in a separate section.
- Non-microbial factors
  - Healthcare services provided and patient populations.
  - Sampling practices.
  - Laboratory capacity and practices for organism identification.

Long-term changes in organism frequency with simple linear regression of organism counts over time is shown in Table 5. The column “slope” in the table indicates increase (if positive value) or decrease (if negative value) in the isolation frequency.

**Table 5.** Organisms with statistically significant increases in organism frequency over time using simple linear regression,  $p < 0.05$ . The slope indicates the estimated change in the number of isolates by quarter.

| Organism                                   | Q1-17 | Q2-17 | Q3-17 | Q4-17 | Q1-18 | Q2-18 | Q3-18 | Q4-18 | Q1-19 | Q2-19 | Q3-19 | Q4-19 | Slope |
|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| <i>Escherichia coli</i>                    | 66    | 95    | 154   | 121   | 121   | 159   | 156   | 146   | 154   | 170   | 179   | 110   | 5.6   |
| <i>Klebsiella pneumoniae ss pneumoniae</i> | 39    | 58    | 59    | 53    | 54    | 78    | 78    | 66    | 79    | 87    | 85    | 71    | 3.3   |
| Mixed bacterial species present            | 17    | 62    | 101   | 69    | 33    | 75    | 103   | 106   | 102   | 154   | 168   | 106   | 9.5   |
| <i>Pseudomonas aeruginosa</i>              | 4     | 10    | 9     | 7     | 3     | 8     | 21    | 23    | 19    | 27    | 21    | 17    | 1.8   |
| <i>Staphylococcus aureus ss aureus</i>     | 25    | 25    | 38    | 29    | 25    | 34    | 57    | 35    | 41    | 32    | 71    | 66    | 3.3   |
| No growth                                  | 490   | 658   | 715   | 706   | 891   | 1,179 | 1,146 | 954   | 952   | 1,001 | 1,130 | 905   | 42.7  |

**Table 6.** Organisms with statistically significant decreases in organism frequency over time using simple linear regression,  $p < 0.05$ . The slope indicates the estimated change in the number of isolates by quarter.

| Organism                                | Q1-17 | Q2-17 | Q3-17 | Q4-17 | Q1-18 | Q2-18 | Q3-18 | Q4-18 | Q1-19 | Q2-19 | Q3-19 | Q4-19 | Slope |
|---|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| There was no sufficient data available. |       |       |       |       |       |       |       |       |       |       |       |       |       |

**4 Antimicrobial Statistics**

**4.1 Antimicrobial Resistance Patterns and Trends**

CAPURA analysis includes presentation of the cumulative resistance pattern of key organisms over the reported years, as well as the resistance trends over the same period for key organisms for a set of antimicrobials. In the context of CRRH, no patterns and trends analyses are presented due to the low availability of information in the shared datasets.

Understanding antimicrobial patterns helps clinicians in routine case management, whereas monitoring antimicrobial trends is important from public health perspectives.

## 4.2 Gram-positive and Gram-negative Antibiograms

The appendix contains the cumulative antimicrobial susceptibility test statistics for Gram-positive and Gram-negative bacteria, typically known as an "antibiogram". The number of isolates tested is greater than or equal to 20. The official recommendation from the CLSI M39 document and others is at least 30 isolates, but a limit of 20 is still useful, especially in a low-resource setting with smaller data volumes and for organisms of clinical importance.

Policymakers must be aware of problems in laboratory test quality and different types of bias due to patient presentation, sampling practices, and laboratory test practices. Routine microbiology laboratory data typically underestimates the incidence of microbial disease but overestimates the proportion of resistance.

## 4.3 Isolate alerts - Important Resistance

WHONET has built-in public health alerts that signal when high and medium priority "important resistance" has been recorded. These public health alerts are identified by WHONET. We recommend that the laboratory confirm these test results to ensure that there is no error in the organism identification or antimicrobial susceptibility test. A separate section in this report lists out the "Global Priority List of Antimicrobial Resistant Bacteria" defined by the WHO.

**Table 7.** The distribution of public health high priority and medium priority important resistance from CRRH identified by WHONET.

| Organisms                              | Alert   | Number of isolates | Priority        |
|--|---|--------------------|-----------------|
| <i>Enterobacteriaceae</i>              | carbapenems = non-susceptible   | 26                 | High priority   |
| <i>Streptococcus</i> , beta-haemolytic | penicillins = non-susceptible   | 3                  | High priority   |
| <i>Enterobacteriaceae</i>              | amikacin = non-susceptible  | 7                  | Medium priority |
| <i>Enterobacteriaceae</i>              | ESBL-producing <i>Enterobacteriaceae</i>  | 12                 | Medium priority |
| <i>Enterobacteriaceae</i>              | Possible ESBL-producing <i>Enterobacteriaceae</i>   | 880                | Medium priority |
| <i>Staphylococcus aureus</i>           | methicillin-resistant <i>Staphylococcus aureus</i>  | 129                | Medium priority |
| <i>Streptococcus pneumoniae</i>        | penicillin-non-susceptible <i>Streptococcus pneumoniae</i> : penicillins or cephalosporin III = non-susceptible | 1                  | Medium priority |

## 4.4 Multidrug Resistance: (following ECDC definitions of MDR/XDR/PDR)

In a 2012 publication, the European Centre for Disease Prevention and Control (ECDC) proposed definitions for common bacterial pathogens resistant to multiple antimicrobials. MDR refers to multidrug resistance, XDR to extensive drug resistance, and PDR to pan-drug resistance. It is, however, important to note that WHONET/CAPTURA does not confirm the pathogens as truly XDR and PDR due to the limited number of antimicrobials tested. Thus, we report possible XDR/PDR on the assumption derived from the groups of antimicrobials tested and analysed by the application. Further, defining MDR, XDR, and PDR according to the local context of available antibiotics is more important than following the ECDC definitions. It is recommended that labs maintain a repository of the isolates that shows a PDR profile, and to periodically verify it with reference laboratories by sharing their results and isolates.

The CRRH dataset showed frequent isolation of organisms exhibiting MDR and possible XDR and PDR, with more than 25% of *Escherichia coli* being MDR and possible XDR. *Acinetobacter* spp. exhibited the highest frequency of MDR (29%), possible XDR (29%), and PDR (10%). If correct, this is alarming and a matter of concern for the facility. We recommend using the WHONET program to periodically monitor these findings. Similarly, we also recommend ensuring proper infection control practices and antimicrobial stewardship to prevent the emergence and spread of these strains.

**Table 8.** Summary of MDR, possible XDR, and possible PDR results.

| Organism                      | Number of isolates | MDR       | Possible XDR | Possible PDR |
|-------------------------------|--------------------|-----------|--------------|--------------|
| <i>Staphylococcus aureus</i>  | 534                | 127 (24%) | 91 (17%)     | 4 (1%)       |
| <i>Acinetobacter</i> sp.      | 51                 | 15 (29%)  | 15 (29%)     | 5 (10%)      |
| <i>Escherichia coli</i>       | 1,844              | 481 (26%) | 481 (26%)    | 77 (4%)      |
| <i>Klebsiella pneumoniae</i>  | 882                | 76 (9%)   | 76 (9%)      | 21 (2%)      |
| <i>Pseudomonas aeruginosa</i> | 188                | 8 (4%)    | 8 (4%)       | 5 (3%)       |

#### Q. Why we need antibiotic resistance profiles?

Antibiotic resistance profiles can be used for cluster analysis and other several applications:

- Phenotypic strain tracking facilitates the monitoring of distinct microbial subpopulations, greatly improving the recognition of 1) new strains, and 2) hospital and community outbreaks. Clusters identified by phenotypic tracking could be investigated by molecular typing to confirm clonality.
- The study of cross-resistance is useful in the development of treatment guidelines, including 1) the determination of recommended "first-line" and "second-line" treatment options, and 2) estimating the value of combination therapy on local pathogens.
- Predicting resistance mechanisms based on the results from antimicrobials within a specific antimicrobial class or subclass or related classes.
- Exploring potential errors in laboratory test practices. For example, the finding of isolates of *Escherichia coli* susceptible to ampicillin but resistant to imipenem is unlikely as imipenem belongs to a higher class of beta-lactam antibiotics and has a greater potency and antibacterial activity than ampicillin. This may be due to a testing error, such as using imipenem disks that have lost their disk potency.

#### 4.5 WHO Global Priority List of Antibiotic-Resistant Bacteria

WHO defines the following list of organisms in its Global Priority List of Antibiotic-Resistant Bacteria. Priority pathogens are critical, as WHO identifies that these pathogens organisms are rapidly developing resistance to existing antibiotics and thus urgently require newer antibiotics. If any such findings are observed, labs should conduct confirmation testing to ensure that there is no error in the organism identification or in the antimicrobial susceptibility test. It is, however, important for each country to come up with its own priority list that fits the unique epidemiologic context.

Here, it is again important for the facility to confirm these results by testing again, and to keep a biorepository of these isolates. These isolates should be sent to a reference lab to confirm the findings.

**Table 9.** WHO Global priority list of antibiotic-resistant bacteria.

| Priority | Organism                        | Antibiotic results                        | Number (%)      |
|----------|---------------------------------|---|-----------------|
| Critical | <i>Acinetobacter</i> spp.       | carbapenem-resistant                      | 0/2 (0%)        |
|          | <i>Pseudomonas aeruginosa</i>   | carbapenem-resistant                      | 1/1 (100%)      |
|          | <i>Escherichia coli</i>         | cefotaxime-resistant                      | 73/240 (30%)    |
|          | <i>Escherichia coli</i>         | ceftriaxone-resistant                     | 494/1,625 (30%) |
|          | <i>Escherichia coli</i>         | meropenem-resistant                       | 0/2 (0%)        |
| High     | <i>Enterococcus faecium</i>     | vancomycin-resistant                      | -               |
|          | <i>Staphylococcus aureus</i>    | methicillin-resistant (MRSA)              | 106/472 (22%)   |
|          | <i>Staphylococcus aureus</i>    | vancomycin-resistant                      | 0/476 (0%)      |
|          | <i>Staphylococcus aureus</i>    | vancomycin-intermediate                   | 0/476 (0%)      |
|          | <i>Helicobacter pylori</i>      | clarithromycin-resistant                  | -               |
|          | <i>Campylobacter</i> spp.       | fluoroquinolone-resistant                 | -               |
|          | <i>Salmonella</i> spp.          | fluoroquinolone-resistant (ciprofloxacin) | -               |
|          | <i>Neisseria gonorrhoeae</i>    | third generation cephalosporin-resistant  | -               |
|          | <i>Neisseria gonorrhoeae</i>    | fluoroquinolone-resistant                 | -               |
| Medium   | <i>Streptococcus pneumoniae</i> | penicillin non-susceptible                | 0/1 (0%)        |
|          | <i>Haemophilus influenzae</i>   | ampicillin-resistant                      | -               |
|          | <i>Shigella</i> spp.            | fluoroquinolone-resistant                 | 3/3 (100%)      |

### **Key Highlights from AMR Epidemiology Report**

- CRRH collects a basic set of variables necessary for the culture report, but patient related information is missing. Culture report and patient information variables, if collected and maintained, will allow multiple analyses that will be helpful for the development of institutional and national guidelines and policies.
- The isolation of priority pathogens of public health importance that are MDR/possible XDR and PDR is alarming. This needs to be verified and closely monitored to prevent their spread.
- Facilities should introduce tests for screening important resistance (ESBL, MRSA, VISA/VRSA, VRE etc.) which will support RIS interpretations and supplement AST reports.
- A high level of resistance in common organisms, along with frequent isolation of pathogens associated with HAI, is a matter of concern.
- The facility should ensure testing of recommended antibiotics consistently according to standard guidelines.

## Quality Report

The WHONET Quality report addresses the issue of data quality from several perspectives. The analyses include several indicator metrics that can be used to identify priority areas for improvement, to monitor improvement over time, and to compare results from different laboratories.

- **Data entry and data management:** Completeness and accuracy of data entry, antibiotic configuration, use of recommended WHONET codes
- **Laboratory results:** Organism identification, antimicrobial susceptibility test practices, quality control results

### 5 Data Entry and Management

#### 5.1 Data Volume

From a data quality perspective, some of the main considerations include the below:

- **Are there any results from outside of the expected date ranges?** This may suggest an error in data entry.
- **Are there any time periods where the number of records is lower or higher than expected?** This may suggest incomplete data entry or double data entry. Data entry practices may change over time. For example, some laboratories only enter positive results when they begin to use WHONET, but over time they may expand to include both positive and negative results.

#### 5.2 Completeness and Validity of Data Entry

**Table 10.** Data entry completeness and quality metrics.

| Data Field            | % Completed |
|-----------------------|-------------|
| Age                   | 100%        |
| Organism              | 100%        |
| Identification number | 98%         |
| Sex                   | 100%        |
| Specimen type         | 100%        |
| Specimen date         | 100%        |
| Location              | 100%        |
| Location type         | 0%          |

### 6 Quality Control Testing

The regular testing of standard quality control strains such as ATCC 25922 *Escherichia coli* and ATCC 25923 *Staphylococcus aureus* is highly recommended to ensure the reliability of test results. The user can enter the results of these standard strains into WHONET.

No quality control results were found in the CRRH dataset shared with CAPTURA, and the practice of testing quality control was not further verified by the project. In general, it is recommended that the hospital introduce and practice internal quality control program and maintain records of such IQC activity to validate the results.

## 7 Organism Results

This section provides information on the capacity of lab to speciate an isolated organism. This provides valuable insights into a laboratory's capacity for isolating and identifying organisms. Broadly, this section, generated from WHONET, describes how the lab identifies organisms using general terms such as "Gram negative enteric organism," or whether the laboratory can identify organisms to the genus, species, subspecies, or serotype level such as "*Klebsiella* sp." or "*Klebsiella pneumoniae*". It also assesses whether the laboratory isolates fastidious organisms such as *Haemophilus influenzae*, *Campylobacter* sp., or anaerobic organisms.

### 7.1 Capacity for Organism Identification

There are many important microbes that are usually identified to the species level, for example, *Escherichia coli* and *Staphylococcus aureus*. For other microbes, it depends on the resources, capacity, expertise, and practices of the laboratory, especially for laboratories using manual identification methods.

**Table 11.** Level of organism identification for aerobic bacteria. *Staphylococcus aureus* and *Escherichia coli* have been excluded as most laboratories routinely identify these organisms to the species level. CRRH has demonstrated capacity for bacterial isolation and identification for most pathogens up to species level, except for *Enterococcus* sp.

| Organism                | % Speciated          |
|-------------------------|----------------------|
| <i>Enterococcus</i> sp. | / 21 (0%)            |
| <i>Klebsiella</i> sp.   | 1,041 / 1,041 (100%) |
| <i>Pseudomonas</i> sp.  | 188 / 593 (32%)      |
| Overall                 | 1,229 / 1,655 (74%)  |

### 7.2 Capacity for Isolation and Identification of Fastidious Organisms

Some bacteria are difficult for laboratories to isolate or identify for several reasons:

- Organisms may not be viable when the specimen arrives in the laboratory
- Special medium required for the organism to grow
- Special incubation conditions
- Special reagents required for organism identification
- Advanced knowledge and experience required by laboratory staff

Examples include *Haemophilus* sp., *Campylobacter* sp., *Helicobacter* sp., *Streptococcus pneumoniae*, *Neisseria* sp., *Mycobacteria* sp., and anaerobic organisms. From the CRRH dataset, very few fastidious organisms were isolated over the reported years. It is recommended to address this issue to avoid missing important pathogens from clinical samples. Further, a diagnostic laboratory should also consider the clinical relevance of reporting unusual organisms and their associated impact on patient management.

**Table 12.** Results for fastidious organisms.

| Organism                        | Number of isolates | (%)  | Number of patients | Isolates per patient |
|---------------------------------|--------------------|------|--------------------|----------------------|
| <i>Clostridium cochlearium</i>  | 1                  | 11.1 | 1                  | 1                    |
| <i>Neisseria gonorrhoeae</i>    | 1                  | 11.1 | 1                  | 1                    |
| <i>Streptococcus pneumoniae</i> | 7                  | 77.8 | 7                  | 1                    |



## 8 Antimicrobial Susceptibility Test Practices

Clinicians and public health authorities depend on microbiology laboratories to provide reliable antimicrobial susceptibility test results. To this end, laboratories must decide which antimicrobials to test for different organism groups and by which test method. For disk diffusion tests, the laboratory must also select an appropriate disk potency. These decisions should be based primarily in recommendations from CLSI or EUCAST guidelines.

It is important to explore two aspects of antimicrobial susceptibility test practices:

- Appropriateness of antimicrobial selected:** Many laboratories test antimicrobials that have no validated CLSI or EUCAST breakpoints. For example, there are no breakpoints for cephradine and there are no breakpoints for imipenem and *Staphylococcus aureus*.
   
**Regularity of testing:** Laboratories often test antimicrobials inconsistently, for reasons such as stock outages of required disks or changes in purchases over time. There is often insufficient appreciation of the importance of consistent testing for clinical reporting and antimicrobial resistance surveillance.

### 8.1 Antibiotic Configuration

Antimicrobials with no results in the data files analysed are also indicated. If there were no plans to enter and analyse results from these antimicrobials, they were removed from the laboratory configuration.

**Table 13.** Antibiotics defined by the laboratory, configured on the WHONET specifically for CRRH Laboratory.

| Guidelines | Test method    | Number of antibiotics | Antibiotics  |
|------------|----------------|-----------------------|--|
| CLSI       | Disk diffusion | 34                    | amikacin, amoxicillin, ampicillin, cefazolin, cefotaxime, cefotaxime/clavulanic acid, ceftazidime, ceftazidime/clavulanic acid, ceftriaxone, cefuroxime, cephalothin, chloramphenicol, ciprofloxacin, clarithromycin, clindamycin, doxycycline, erythromycin, gentamicin, imipenem, meropenem, nalidixic acid, nitrofurantoin, norfloxacin, novobiocin, ofloxacin, oxacillin, penicillin G, piperacillin, polymyxin B, tetracycline, tobramycin, trimethoprim/sulfamethoxazole, vancomycin |
| CLSI       | MIC            | 3                     | cefotaxime, penicillin G, vancomycin   |
| CLSI       | Etest          | 3                     | cefotaxime, penicillin G, vancomycin   |

### 8.2 Antibiotic Tests without Validated Breakpoints

The following antibiotics from CRRH dataset have no breakpoints for any organism.

**Table 14.** Antibiotics tested at the laboratory that have no breakpoints for any organism in the dataset.

|  |
|--|
| amoxicillin_CLSI_Disk_25                     |
| cefotaxime/clavulanic acid_CLSI_Disk_30/10µg |
| ceftazidime/clavulanic acid_CLSI_Disk_30/4µg |
| cephalothin_CLSI_Disk_30µg                   |
| novobiocin_CLSI_Disk_5µg                     |

CRRH reports few antibiotics tested that do not have breakpoints for *Staphylococcus aureus* and *Escherichia coli*. Testing these combinations is not a standard practice and thus not recommended by existing testing guidelines. The facility should stop testing these and frequently run WHONET reports to get updated results and recommendations.

**Table 15.** Invalid tests performed for *Staphylococcus aureus*.

| Test method    | Antibiotic | Number tested |
|----------------|------------|---------------|
| Disk diffusion | vancomycin | 476           |

**Table 16.** Invalid tests performed for *Escherichia coli*.

| Test method    | Antibiotic  | Number tested |
|----------------|-------------|---------------|
| Disk diffusion | amoxicillin | 67            |
| Disk diffusion | cephalothin | 1,551         |
| Disk diffusion | vancomycin  | 1             |

The most common reasons for invalid antibiotic tests include:

- The laboratory is testing incorrect antimicrobials (e.g., cephalexin), and they should be encouraged to switch to a similar antimicrobial with validated breakpoints (e.g., cephalothin).
- There is a mistake in the WHONET laboratory configuration, for example, choosing the wrong antimicrobial agent or choosing an incorrect disk potency.

In both circumstances, corrective action is indicated. If there is a mistake in the WHONET or BacLink configuration, this should be corrected. If the laboratory is performing incorrect testing, then education and review of purchasing and test practices would be indicated.

There are a few circumstances in which antimicrobials without validated clinical breakpoints would not be considered a testing mistake:

- The laboratory may be aware of published acceptable vendor-specific breakpoints that have not been evaluated by CLSI or EUCAST. In these cases, the user should manually enter the vendor-specific breakpoints into WHONET.
- The antimicrobial is tested for reasons that do not require clinical breakpoints; e.g., novobiocin or optochin are used for species identification, while ceftriaxone/clavulanic acid is used for ESBL confirmation.
- The laboratory may test an appropriate antibiotic, such as cefoxitin with *Staphylococcus aureus*, to predict the findings of another antibiotic that may be used in clinical therapy, such as methicillin or nafcillin. This has been described as proxy testing or surrogate testing.
- The laboratory is working collaboratively with CLSI or EUCAST to develop new breakpoints.
- The laboratory may not have sufficient resources to perform MIC testing when it is recommended, so the disk diffusion method is used instead to screen for resistance, for example *Staphylococcus aureus* and the vancomycin disk test. However, such results should not be considered reliable.

### 8.3 Antimicrobial Susceptibility Test Measurements

Measuring, recording, and analysing antimicrobial susceptibility test measurements, such as the disk diffusion, zone diameter and the MIC value are very important for the following reasons:

- To provide the correct test interpretation to the clinician.
- To compare old results with new results if the breakpoints change.
- To provide more detailed characterization of resistance mechanisms associated with high, moderate, and low levels of resistance.
- To conduct improved strain tracking.
- To assess the quality of laboratory test reagents and the quality of laboratory test performance.

The CRRH laboratory does not record the zone diameter, though it is recommended that facilities measure and record the zone diameter.

## 9 Quality Control Alerts

WHONET offers four different quality control alerts to facilitate the recognition of possible deficiencies in test performance. It is important to note that a quality control alert does not necessarily indicate that a result is incorrect. Therefore, repeat testing and confirmation are recommended before reporting these findings.

WHONET addresses four types of quality control alert:

- **Intrinsic resistance:** The organism is lacking a resistance characteristic typical of the species, for example *Klebsiella pneumoniae* susceptible to ampicillin.
- **Discordant test results:** In some cases, the results are biologically implausible, such as an *Escherichia coli* susceptible to ampicillin but resistant to ampicillin/sulbactam. In other cases, the results may be correct, but are relatively rare. For example, most isolates of *Escherichia coli* resistant to amikacin will also be resistant to gentamicin. However, in South America, there are many isolates have been confirmed to be amikacin resistant but gentamicin susceptible.
- **Rare resistance:** Resistance to some antimicrobials is extremely rare for some species and may suggest an error in the organism identification or in the antimicrobial susceptibility test result, such as *Staphylococcus aureus* resistant to vancomycin.
- **Incorrect test method:** There are some organisms and some organism-antibiotic combinations that should not be tested by certain test methods. For example, *Neisseria meningitidis* should always be tested by the MIC method. *Staphylococcus aureus* should not be tested with the oxacillin or vancomycin disk, and *Streptococcus pneumoniae* should not be tested by the oxacillin disk.

**Table 17.** Quality control alerts for unlikely and infrequent findings observed in the CRRH dataset shared with CAPURA.

| Organisms                       | Alert   | Number of isolates | Priority        | CRH |
|---------------------------------|---|--------------------|-----------------|-----|
| All organisms                   | quinolones and fluoroquinolones = discordant results                            | 10                 | Medium priority | 10  |
| <i>Citrobacter</i> sp.          | cephalosporin III = susceptible   | 18                 | Low priority    | 18  |
| <i>Citrobacter</i> sp.          | penicillins or cephalosporin I or cephalosporin II or cephamycins = susceptible | 18                 | Low priority    | 18  |
| <i>Enterobacter</i> sp.         | cephalosporin III = susceptible   | 113                | Low priority    | 113 |
| <i>Enterobacter</i> sp.         | penicillins or cephalosporin I or cephalosporin II or cephamycins = susceptible | 26                 | Low priority    | 26  |
| <i>Enterobacteriaceae</i>       | cephems = discordant results  | 6                  | Medium priority | 6   |
| <i>Klebsiella</i> sp.           | penicillins = susceptible   | 12                 | Low priority    | 12  |
| <i>Proteus</i> sp.              | nitrofurantoin = susceptible  | 1                  | Medium priority | 1   |
| <i>Proteus vulgaris</i>         | penicillins or cephalosporin I or Cephalosporin II = susceptible                | 8                  | Low priority    | 8   |
| <i>Pseudomonas aeruginosa</i>   | penicillins or cepems = susceptible   | 28                 | Low priority    | 28  |
| <i>Serratia</i> sp.             | cephalosporin III = susceptible   | 1                  | Low priority    | 1   |
| <i>Streptococcus pneumoniae</i> | beta-lactams = tested by disk diffusion   | 1                  | Medium priority | 1   |
| <i>Streptococcus viridans</i>   | penicillin or ampicillin = tested by disk diffusion                             | 1                  | Low priority    | 1   |

### Key Highlights from AMR Quality Report

- A limited number of CAPURA essential variables are completely collected at CRRH.
- No quality control results were found in the CRRH dataset shared with CAPURA. It is recommended that the hospital verifies the internal quality control program in place and ensures a record of such IQC activity to validate the results.
- Isolation of very few fastidious organisms at the facility over the reported years was observed. This observation identifies a big gap in the laboratory's capacity, as some pathogens of public health importance are missing and not reported from the clinical samples processed at the facility. Advanced microbiology training, with provision for access to additional laboratory supplies/resources, may be required at the laboratory.
- CRRH tests few antibiotics that do not have CLSI/EUCAST breakpoints for *Staphylococcus aureus* and *Escherichia coli*. Testing these combinations is not a standard practice and thus not recommended by existing testing guidelines.
- Antibiotics are not being tested consistently in CRRH. The frequency of antibiotic testing for *Staphylococcus aureus* and *Escherichia coli* displays huge gaps. This makes it difficult to analyse the AMR patterns and trends over a time period.
- Many unlikely and infrequent resistance results have been identified in the dataset. These are highlighted as quality control alerts and require retesting/confirmation.

## Metadata: Laboratory Questionnaire and RLQA

### 10 Laboratory Questionnaire

The Laboratory Questionnaire (also known as the AMR Questionnaire) captured basic information about the facility — including their capacity, availability of data and data capture/storage practices. The questionnaires helped the in-country team and the CAPTURA consortium to identify relevant facilities for further engagement.

The Laboratory Questionnaire completed in April 2020 indicated that the laboratory does cultures for blood, cerebrospinal fluid (CSF), respiratory, soft tissue and bodily fluids, stool, and urine. The disk diffusion method is most often used for antimicrobial susceptibility testing (AST), and, on average, approximately 51-100 ASTs have been reported to be performed monthly. The laboratory holds 3 years of AST results in the record, in paper (logbook) format. Collected variables are reported as the following (Table 18).

**Table 18.** List of variables collected as answered in the laboratory questionnaire. Please note that actual data collected at CRRH may contain different information.

| CAPTURA Priority variables  |  | Variables Collected |
|---|--|---------------------|
| Sample Origin   |  | Collected           |
| Date of Birth/Age   |  | Collected           |
| Sex   |  | Collected           |
| Patient Location (Ward/Clinic)  |  | Collected           |
| Healthcare Facility Admission Date (if in-patient)  |  | Collected           |
| Healthcare Facility Admission Date of Visit (if out-patient)  |  | Collected           |
| Specimen Date   |  | Collected           |
| Specimen Type   |  | Collected           |
| Culture Result  |  | Collected           |
| AST Interpretation  |  | Collected           |
| AST Measurement   |  | Collected           |
| Specialized/Targeted variables (Optional CAPTURA Variables)   |  |                     |
| Antibiotics Prescribed After Specimen Collection  |  | Collected           |
| Diagnosis (after laboratory results provided)   |  | Collected           |
| Patient Outcome   |  | Collected           |
| Date and Cause of Death (if applicable)   |  | Collected           |
| Additional/Recurrent Isolates/Infections  |  | Collected           |
| Additional Patient Information (e.g., change in initial therapy, date of discharge, comorbidities, date of discharge) |  | Collected           |

### 11 Rapid Laboratory Quality Assessment

Rapid Laboratory Quality Assessment (RLQA) was used to assess the capacity and quality of laboratories generating AMR data. RLQA is NOT a validated tool for assessing laboratory, but a tool developed by the project for project purposes: to gauge the quality of data and laboratory and assist in facility prioritisation for data collection.

RLQA consists of eight sections that sums up to 126 questions. The first seven sections include human resources, equipment availability, status of supplies, and quality control standards implemented while the last section requires a visual inspection to verify some of the responses provided. The responses of RLQA are now electronically stored, and each complete RLQA was scored via an automated scoring scheme. Summaries of scores and observations made in the RLQA are found in Table 19 and Figure 6.

**Table 19.** Summary of scores in RLQA with description of each section.

| The microbiology laboratory at CRRH participated in the RLQA on May 23, 2020. The total score was 60.5, while the country median taken from 4 facilities across the country was 66.9. Facility section scores are shown below, with country median scores indicated in brackets for reference. <i>Country median scores have been calculated from laboratories that participated in CAPTURA RLQA; they do not accurately represent the national medians.</i> |   |             |
|--|---|-------------|
| Equipment  | The Equipment section assesses the laboratory's access to the necessary equipment for conducting identification, antimicrobial susceptibility testing (AST), and performing internal quality control (IQC) over the past 3 years. | 58.3 (72.9) |
| Staffing   | The Staffing section evaluates the number of staff working in the laboratory, the level of qualification of senior staff, and the training that bench staff receives.   | 40.0 (57.5) |
| Media  | Media section examines the type, source, and quality of the media used specifically for AST.  | 55.6 (76.8) |
| Identification   | The Identification section examines how pathogens are tested, identified, and reported.   | 70.0 (72.5) |
| AST  | The AST section assesses the laboratory's AST practices to understand which AST guidelines are followed, how closely current breakpoint guidance is adhered to, and how the laboratory captures AST data.                         | 73.1 (73.5) |
| IQC  | The IQC section assesses the laboratory's internal procedures for ensuring test validity and the reliability of equipment.  | 84.4 (76.2) |
| EQA  | The EQAS section examines the laboratory's involvement in various EQAS and resulting scores.  | 33.3 (33.3) |

## RLQA Summary

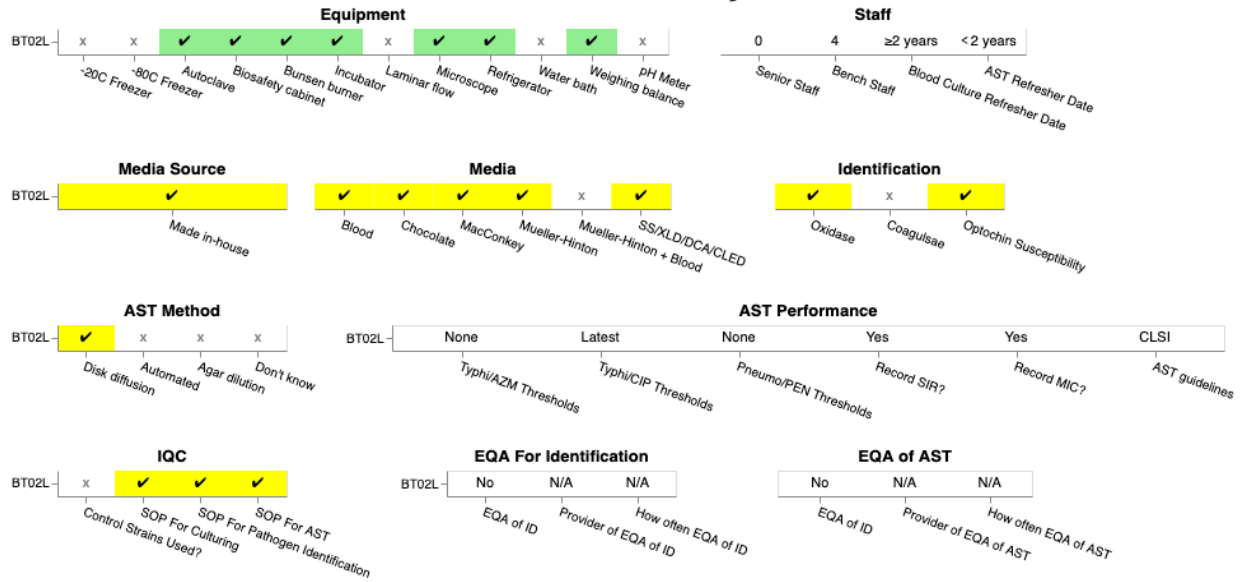


Figure 6. Summary of observations from RLQA conducted on May 23, 2020.

### Key takeaway

As RLQA is not a validated tool, we suggest that the scores and observations presented above to be used as a cursory reference, and not for determining current quality and capacity of the laboratory. Please note that both Questionnaire and RLQA may now include outdated or inaccurate information, as laboratory improvements and strengthening activities may have taken place in between now and then. Upon the collection of the information, the project was also not able to validate the responses due to the limited time and resources available. We suggest using a validated assessment tool to verify and validate the observations presented above, and regarding the RLQA scores as a “quick snapshot” of the capacity noted by the project at the start of engagement.

Importantly, going forward, we recommend the facility to treat this experience with CAPTURA as a starting point to initiate a periodic collection of AMR metadata, which can be defined as, a set of data providing information about AMR data. AMR metadata, such as lab assessments, can be useful in understanding the data and systems in which the data was generated and collated. A comprehensive collection of AMR metadata ultimately provides contextual information, which in turn helps to curate/clean data and interpret analyses accurately.

## Appendix. Antibigrams

### Gram-positive and Gram-negative Antibigrams

The antibiogram shows the cumulative antimicrobial susceptibility test statistics for Gram-positive and Gram-negative bacteria. The number of isolates tested is greater than or equal to 20. The official recommendation from the CLSI M39 document and others is at least 30 isolates, but 20 is still useful, especially in a low-resource setting with smaller data volumes, and for organisms of clinical importance.

Policymakers must be aware of problems in laboratory test quality and different types of bias due to patient presentation, sampling practices, and laboratory test practices. Routine microbiology laboratory data typically underestimates the incidence of microbial disease but overestimates the proportion of resistance.

**Table 20.** Gram-positive antibiogram. The numbers indicate % Susceptible.

| Organism                                 | Number of patients | AMP | FOX | CHL | CIP | DOX | ERY | GEN | NIT | PEN | SXT | VAN |
|--|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| <i>Staphylococcus aureus</i>             | 478                |     | 78  |     | 56  | 97  |     | 92  |     | 4   | 81  |     |
| <i>Streptococcus pyogenes</i>            | 179                |     |     | 89  |     | 92  | 91  |     |     | 99  |     | 100 |
| Coagulase-negative <i>Staphylococcus</i> | 170                |     | 22  |     | 63  | 75  |     | 95  |     | 1   | 59  |     |
| <i>Staphylococcus epidermidis</i>        | 31                 |     | 55  |     | 64  |     |     | 93  |     | 3   | 48  |     |
| <i>Staphylococcus saprophyticus</i>      | 25                 |     | 16  |     | 96  | 96  |     |     | 100 |     | 96  |     |
| <i>Enterococcus sp.</i>                  | 21                 | 70  |     |     |     |     |     |     |     |     |     | 100 |

**Table 21.** Gram-positive organisms tested against the following antimicrobials were included in the antibiogram.

| Code | Antibiotic      | Code | Antibiotic     | Code | Antibiotic                    |
|------|-----------------|------|----------------|------|-------------------------------|
| AMP  | ampicillin      | DOX  | doxycycline    | PEN  | penicillin G                  |
| FOX  | cefoxitin       | ERY  | erythromycin   | SXT  | trimethoprim/sulfamethoxazole |
| CHL  | chloramphenicol | GEN  | gentamicin     | VAN  | vancomycin                    |
| CIP  | ciprofloxacin   | NIT  | nitrofurantoin |      |                               |

**Table 22.** Gram-negative organisms tested against the following antimicrobials were included in the antibiogram.

| Organism                      | Number of patients | AMK | AMP | CZO | CTX | CAZ | CRO | CEP | CIP | GEN | IPM | NAL | NIT | NOR | PIP | SXT |
|-------------------------------|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| <i>Escherichia coli</i>       | 1,630              |     | 24  | 25  |     |     | 68  |     |     | 92  |     | 32  | 98  | 58  |     | 55  |
| <i>Klebsiella pneumoniae</i>  | 806                |     | 1   | 30  | 81  |     | 78  |     | 89  | 96  |     | 79  | 62  | 83  |     | 67  |
| <i>Pseudomonas sp.</i>        | 380                |     |     |     |     | 77  |     |     | 91  | 98  |     |     |     |     |     |     |
| <i>Enterobacter sp.</i>       | 170                |     | 12  | 10  | 58  |     | 66  |     | 77  | 85  |     | 61  | 82  | 82  |     | 75  |
| <i>Pseudomonas aeruginosa</i> | 167                |     |     |     |     | 80  |     |     | 94  | 94  |     |     |     |     | 63  |     |
| <i>Klebsiella oxytoca</i>     | 154                |     | 2   | 27  | 78  |     | 75  |     | 87  | 94  |     | 55  | 80  | 72  |     | 58  |
| <i>Proteus mirabilis</i>      | 119                |     | 58  | 24  | 97  |     | 95  |     | 84  | 96  |     | 59  |     | 76  |     | 61  |
| <i>Acinetobacter sp.</i>      | 49                 | 50  | 3   |     | 4   | 10  | 14  |     | 53  | 59  | 80  |     |     |     |     |     |
| <i>Proteus vulgaris</i>       | 37                 |     | 20  | 7   |     |     | 95  |     |     | 92  |     | 65  |     | 91  |     | 74  |

**Table 23.** Gram-negative antibiogram. % Susceptible, first isolate per patient.

| Code | Antibiotic  | Code | Antibiotic    | Code | Antibiotic                    |
|------|-------------|------|---------------|------|-------------------------------|
| AMK  | amikacin    | CRO  | ceftriaxone   | NAL  | nalidixic acid                |
| AMP  | ampicillin  | CEP  | cephalothin   | NIT  | nitrofurantoin                |
| CZO  | cefazolin   | CIP  | ciprofloxacin | NOR  | norfloxacin                   |
| CTX  | cefotaxime  | GEN  | gentamicin    | PIP  | piperacillin                  |
| CAZ  | ceftazidime | IPM  | imipenem      | SXT  | trimethoprim/sulfamethoxazole |

**-End of report-**