CAPTURA Country Report: Nepal

September 2022



Government of Nepal Ministry of Health and Population







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CAPTURA Consortium

The CAPTURA consortium is led by the International Vaccine Institute (IVI), and includes as partners, the Public Health Surveillance Group (PHSG), Harvard Medical School's Brigham & Women's Hospital (BWH) and Oxford University's Big Data Institute (BDI).









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CAPTURA also extends its gratitude to our country coordinators, consultant microbiologists and entire team for supporting data collection and effective liaison with in-country stakeholders.

Use of Document

This is the final report summarizing CAPTURA engagements and activities conducted in Nepal. It is written to help inform planning future investments in combatting AMR in the Asian Region and beyond. As such, it is aimed at any individual or organization interested and/or active in the field of antimicrobial resistance (AMR) surveillance and research, funding of AMR initiatives including policy and regulatory decision-making, and infectious disease prevention and control programs in Nepal, the Asian region and beyond. This covers sectors such as academia, government, philanthropy, the private sector, supranational organizations, and the general public.

The findings presented in this report have been generated based on data collected directly as part of the CAPTURA project as well as on previously generated original data shared based on the agreement between individual laboratories, Ministry of Health and Population, and the International Vaccine Institute. The use and/or reproduction of data or other report contents without agreement of the International Vaccine Institute and the Government of Nepal (as relates to original data contents) is not permitted.

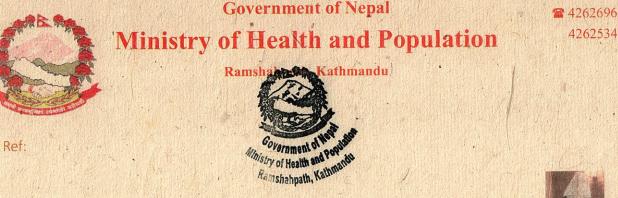
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Message



The specter of Antimicrobial Resistance (AMR) is a mounting global health concern, and its burgeoning impact on our nation, Nepal, is a significant challenge that we are committed to address. Our shared experience with COVID-19 has further underscored the criticality of having robust health care responses to such threats, which are only set to grow in complexity and scale.

Recognizing this, Nepal's dedicated efforts to endorse the National Action Plan (NAP), despite not being officially endorsed yet, represent our commitment to this cause. This plan, backed by a robust financing strategy, serves as a roadmap to guide our multi-sectoral approach towards tackling AMR.

At this juncture, I would like to extend our warmest congratulations to the team at the CAPTURA consortium led by International Vaccine Institute (IVI) funded by Fleming Fund for the comprehensive CAPTURA Country Report: Nepal they have compiled. Their meticulous work offers crucial insights into the AMR landscape, providing essential data to guide our future efforts. The Ministry of Health and Population (MoHP) has been delighted to agree with IVI's plan, providing the necessary support throughout this endeavor.

The success of this initiative testifies to the power of multi-country coordination. The rich data accumulated through this project is an invaluable resource that will significantly shape our future planning and actions in the healthcare sector.

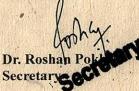
It brings me great pleasure to share that through this collaborative effort, we have successfully generated clean data across all 28 facilities, a substantial achievement that places us in a strong position moving forward. This data is now with the sites themselves, marking a significant step forward in our fight against AMR.

As we continue to combat AMR, I implore all stakeholders to make optimum use of this invaluable resource. The insights we gain from this data will be key to informing our policy-making and could greatly enhance our public health response strategies.

I would like to take this opportunity to reassure all our partners of the Ministry's commitment to providing any necessary support to foster collaboration among all agencies in this shared mission. Our goal remains steadfast: to not only combat AMR, but to strengthen our healthcare sector's ability to proactively address future public health challenges.

Finally, our deepest gratitude goes to the CAPTURA consortium led by International Vaccine Institute funded by Fleming Fund. Their unwavering support and invaluable contributions have been instrumental to the success of this initiative.

Our collective vision is clear: a healthier future for our population, free from the threat of AMR. It's a challenging path ahead, but I remain confident that through our collective dedication and efforts, we will succeed.





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Foreword

Ith issue, and its implications for ou

Antimicrobial Resistance (AMR) represents a considerable global health issue, and its implications for our nation, Nepal, are significant. To address this, we have been steadfast in our efforts and determination, navigating the complexities of this issue with the support of dedicated stakeholders involved.

Despite being in the final stages of endorsement, our National Action Plan (NAP) bears witness to our nation's commitment to this cause. This comprehensive plan, complemented by a robust financing strategy, has been central to our multi-sectoral approach in the battle against AMR.

It is in this context that I am pleased to introduce a milestone in our AMR containment efforts - the comprehensive CAPTURA Country Report: Nepal. The document, a result of meticulous efforts of the CAPTURA consortium led by International Vaccine Institute (IVI) funded by Fleming Fund, presents a detailed overview of our existing AMR landscape, highlighting areas of success, and elucidating the challenges that lie ahead. It is a testament to the power of collaboration and dedication in addressing critical health issues.

The Quality Standards and Regulation Division had approved this project, extending complete support to CAPTURA's comprehensive plan. The international, multi-country coordination that we have witnessed is remarkable and has culminated in the creation of a rich dataset.

This data, now housed with the 28 participating facilities, is a significant achievement. This clean, wellcurated data set will be instrumental in informing our future strategies in the ongoing battle against AMR. As we strive forward in this fight, I urge all stakeholders to make the maximum use of this valuable data

repository. The insights we derive from this data will be essential in informing our strategies, influencing policy-making, and shaping our public health response.

I assure all partners of our commitment to fostering collaboration and providing the necessary support to bring together all agencies in this shared mission. Our vision extends beyond AMR; we aim to strengthen our healthcare sector's capacity to respond to future public health challenges.

Finally, I wish to extend our deepest gratitude to the CAPTURA consortium led by International Vaccine Institute funded by Fleming Fund. Their unwavering support and significant contributions have been pivotal in the success of this initiative.

We are united in our vision: to secure a healthier future for our population, free from the threat of AMR. Despite the challenges ahead, I remain confident that through our shared dedication and combined efforts, we will prevail.

MA

Dr. Madan Kumar Upadhyaya Chief, Quality Standards and Regulation Division

Executive Summary

As part of the large Fleming Fund (FF) portfolio of grants funded by the Government of the United Kingdom and established as a response to the global problem of AMR, in 2019 the CAPTURA project was awarded with the specific objective of expanding the volume of historical data on antimicrobial resistance (AMR), consumption (AMC), and use (AMU) in the human health care sector across 12 countries in South and Southeast Asia, including Nepal.

AMR context in Nepal

AMR is a growing threat for Nepal with high level resistance to commonly used antimicrobials in the country. The AMR-National Action Plan (2018-2022) has identified several challenges to be addressed for achieving its objectives to guide various sectors to ensure a coherent, multi-sectoral approach towards combatting AMR. Nepal has a well-established AMR surveillance system, which is being expanded over time to incorporate new surveillance of emerging resistance and pathogens of interest for the country. Data generated through the network is routinely being shared within the country and externally different mechanisms.

The government and private sector players provide Healthcare in Nepal. The Ministry of Health and Population (MoHP), along with multinational development agencies and external partners in the country, are working closely to upgrade the existing infrastructures and technologies to generate standardized quality data. In addition, they are also providing trainings to prepare future leaders to champion the AMR containment efforts.

The authority to regulate production, import, sales and prescription of antimicrobials in the country lies with the Department of Drug Administration (DDA). The government has already made efforts to ban over-the-counter sales of antibiotics and their use in animal feed, and has been monitoring the import, production, and sales of antimicrobial agents. But, due to resource limitations, the endeavor has not been highly effective, and a large number of unregistered facilities selling drugs has posed a great challenge. Consolidated antimicrobial production, procurement, and distribution data is not available and there is an urgent need to collect it in a systematic way. With Nepal joining the GLASS-AMC, establishing a future data collection network following the GLASS methodology will enable the country to analyze, use, and share AMC data at both the local and global levels in the coming years.

To generate data on antimicrobial use, antimicrobial audits are currently piloted with support from FF Country Grant and is planned to be extended across the country's major hospitals.

The continued collection of national AMR/C/U data will allow Nepal to further establish its national surveillance system as well as to implement evidence-based approaches for treating and managing infectious diseases, tracking AMR trends, and formulating AMR containment strategies.

CAPTURA experience

CAPTURA's early engagement with the AMR stakeholders and subsequent effective coordination between the project team and the MoHP led to an expedited approval and work initiation. Although early progress was slowed down by the COVID-19 pandemic, CAPTURA was able to successfully achieve its objectives of identifying and assessing existing microbiology capacity, collecting and analyzing retrospective AMR data, and providing WHONET trainings to technical laboratory staff from both the human and animal health sectors. Further, a subset of AMU data was collected and analyzed as part of a piloting exercise.

CAPTURA findings

CAPTURA activities in Nepal have enabled capacity building within data management and analysis for future AMR and AMU surveillance efforts. In this report, we present a summary of findings from the scoping and analytical work conducted by CAPTURA in collaboration with the MoHP since 2019. The data content for this final report was selected after discussions with the CAPTURA in-country team and AMR stakeholders at the MoHP. Comprehensive analytical outputs and visualization tools will be shared with the National AMR program, QSRD, NPHL, and data owners before the closure of the project.

The main utility of the retrospective data collected on AMR and AMU through the CAPTURA project in Nepal has been to identify the data sources and establish a preliminary data baseline. It is our hope that it can be a useful contribution to planning future investments in combatting AMR in Nepal and the Asian region.

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Acronyms

AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMRTWG	AMR Technical Working Group
AMRCSC	AMR Containment Multisectoral Steering Committee
AMU	Antimicrobial Use
AST	Antimicrobial Susceptibility Test
AWaRe	Access, Watch and Reserve
CA / DTA	Collaborative Agreement / Data Transfer Agreement
CAPTURA	Capturing data on Antimicrobial resistance Patterns and Trends in Use in Regions of Asia
CG	Country Grant
CIP	Country Implementation Plan
CLSI	Clinical & Laboratory Standards Institute
CONS	Coagulase Negative Staphylococci
DD	Disk Diffusion
DDA	Department of Drug Administration
EQA	External Quality Assurance
FF	Fleming Fund
GLASS	Global Antimicrobial Resistance Surveillance System
HAI	Hospital Acquired Infection
IQC	Internal Quality Control
МІС	Minimum Inhibitory Concentration
MoHP	Ministry of Health and Population
MRSA	Methicillin Resistant Staphylococcus aureus
NAP	National Action Plan
NACM	Nepalese Association of Clinical Microbiologists
NCC	National Coordinating Center
NEML	National Essential Medicine List
NPH	National Public Health Laboratory
PPS	Point Prevalence Survey
RIS	Resistant Intermediate Susceptible
RLQA	Rapid Laboratory Quality Assessment
SOP	Standard Operating Procedure



section 01

CAPTURA Overview

Introduction

The Capturing data on Antimicrobial resistance Patterns and Trends in Use in Regions of Asia (CAPTURA) consortium was awarded the Fleming Fund (FF) Regional Grants Round 1 for the South and Southeast Asian regions. These FF grants, funded by the Government of the United Kingdom, were established as a response to the global problem of AMR. The aim of the Round 1 grants is to expand the volume of historical and current data on AMR, AMC, and AMU from the human health sector.

The CAPTURA project takes place in 12 countries, six of which are in South and Southeast Asia. The project includes collecting four years' worth of deidentified retrospective AMR/C/U data, assessing the quality of datasets and laboratories where data were collected, and analyzing data, which then can be used by the countries to make evidence-based policies and practices. Additionally, collaborative efforts with country stakeholders can foster capacity building opportunities and strengthen advocacy for improved data quality and submission to regional and/or national repositories. It is our hope that the CAPTURA project can assist in improving surveillance, containment, and awareness of AMR in local, regional, and global contexts.

The CAPTURA project was executed in several phases in Nepal (Figure 1).

1.Initial country visit for project introduction and key informant interviews 2. Draft Country Implementation Plan, identify in-country consultants and receive approval for project activities

3. Collect metadata and AMR/U data and provide technical support on WHONET 4. Map out data sources and their capacities. Curate and analyse/visualise shared data

Implementation Phase

5. Conduct feedback meetings with data-providers and generate Final Report

Planning Phase

Figure 1. CAPTURA's scope of work in Nepal



AMR Context

Nepal, situated in the Himalayas, is a nation of nearly 30 million inhabitants. AMR is a growing threat in the country, especially given its location in South Asia. In the 1990s, most healthcare was delivered through public facilities, but rapid economic liberalization resulted in the expansion of the private sector. Today, private facilities offer a majority of facilities and healthcare expenditure.¹ Most private facilities are based in major cities and advanced ones are concentrated in the Kathmandu Valley, while public facilities more widely dispersed.²

Nepal's AMR sector is relatively mature. The surveillance of bacterial pathogens was established in 1999 with nine hospitals. In the early years, the network was supported by the International Centre for Diarrhoeal Disease Research, Bangladesh (Icddr,b), and the US Centers for Disease Control (CDC). Currently, support is provided by WHO.³

In 2011, Nepal signed the Jaipur Declaration, recognizing the seriousness of AMR and committing to safeguard the efficacy of antimicrobial drugs.⁴ In 2015, a situational analysis of antibiotic use and resistance was developed. The current WHOsupported National Antimicrobial Resistance Containment Action Plan (2016) identified several AMR challenges. These included: less than rational use of antimicrobials; weak surveillance and monitoring of AMR and AMU; insufficient education and awareness among specialists and the public; suboptimal prescribing practices by healthcare providers and pharmacies; and inclusion of antibiotics in animal feeds.⁵ Though the NAP is yet to be endorsed by the cabinet, a substantial effort has already been made over the last three years through the support of the Fleming Fund.

The NAP has five pillars:

- "Improve awareness and understanding of AMR through effective communication, education and training.
- 2. Strengthen the knowledge and evidence base through research and surveillance.
- 3. Reduce the incidence of infection through effective hygiene and infection prevention measures.
- 4. Optimize the use of antimicrobial medicines in human and animal health.
- Develop the economic case for sustainable investment that takes account of the needs of all countries, as well as the need for investment in new medicines, diagnostic tools, vaccines and other interventions."⁶

Nepal's key human health stakeholders include the Ministry of Health and Population (MoHP), especially the Quality Standards Regulatory Division (QSRD), National Public Health Laboratory (NPHL), Department of Drug Administration (DDA), AMR Containment Multisectoral Steering Committee (AMRCSC), and AMR Technical Working Group (AMRTWG). The AMRCSC is a multisectoral group that includes the AMRTWG.

Nepal has adopted a One Health approach to combatting AMR. This approach includes stakeholders from the Ministry of Agriculture, especially the Department of Food Technology and Quality Control, Ministry of Agriculture and Livestock Development, and is supported by WHO, OIE, and FAO country offices.⁷

According to the most recent WHO GLASS report, Nepal's national AMR surveillance system includes 26 sites. They all perform antimicrobial susceptibility testing, participate in NEQAS, and are committed voluntarily to share data to GLASS.⁸ The

⁸ Conversation with FHI360 country grantee on 2 March 2022.



¹ Mishra, Shiva Raj et al. "National health insurance policy in Nepal: challenges for implementation." Global health action vol. 8 28763. 21 Aug. 2015, doi:10.3402/gha.v8.28763

² WHO, "Resource mobilisation for AMR: Getting AMR into plans and budgets of government and development partners - Nepal country report", Sept 2018.

³ Mott MacDonald Fleming Fund Country Assessment for Nepal, 10 May 2017.

⁴ "One Health approach to tackle antimicrobial resistance in Southeast Asia." BMJ (Clinical research ed.) vol. 358 j3625. 5 Sep. 2017, doi:10.1136/bmj.j3625

⁵ Nepal National Antimicrobial Resistance Containment Action Plan (2016) (https://1doxu11lv4am2alxz12f0p5jwpengine.netdna-ssl.com/wp-

content/uploads/3d9bf4b7ab190c600921a99cf1803059.pdf). ⁶ Nepal National Antimicrobial Resistance Containment Action Plan (2016) (https://1doxu11lv4am2alxz12f0p5jwpengine.netdna-ssl.com/wp-

content/uploads/3d9bf4b7ab190c600921a99cf1803059.pdf). ⁷ Nepal Country page, Fleming Fund

⁽https://www.flemingfund.org/countries/nepal/).

National Reference Lab in Nepal uses the CLSI standard and has been participating regularly in external quality assurance programs.⁹

In December 2020, Nepal enrolled in GLASS's AMC module. As of 2021, Nepal is enrolled and implementing the ESBL *E. coli* Tricycle project, as well as conducting surveillance in HIV drug resistance, drug-resistant tuberculosis, Malaria Therapeutic Efficacy Studies, and One Health.¹⁰

The Fleming Fund has invested heavily in Nepal beyond CAPTURA. The Fleming Fund country grantee, FHI360, has focused on sustaining AMR surveillance in human and animal health and expanding surveillance to the environmental sector. They have also supported in carrying out major laboratory renovations; provided training in the One Health approach on bacteriology, biorepository, data analysis, WHONET and AMR data management, QA/EQAS, among others; and strengthened the active surveillance system for AMR in poultry. The Fleming Fund also supports 12 fellowships in Nepal, covering AMR, AMU, and AMC surveillance and policy across human and animal health. All fellows are supported by the Doherty Institute. Nepal participates in the EQASIA project, supported by the Fleming Fund, in implementing a comprehensive EQA program for AMR across all One Health sectors. Additionally, the RADAAR project identified Nepal as one of the countries to implement the EVIP-NET pilot, while the Ending Pandemics project supported the standardization of data collection and analysis through the use of common protocols. Lastly, Nepal is a contributor and beneficiary of the global AMR burden research conducted by the Global Research on AMR (GRAM),

(https://1doxu11lv4am2alxz12f0p5j-wpengine.netdnassl.com/wp-

content/uploads/9a2d7826679c36ed6ff72a3260032621.pdf). ¹² Acharya, J.; Zolfo, M.; Enbiale, W.; Kyaw, K.W.Y.; Bhattachan, M.; Rijal, N.; Shrestha, A.; Shrestha, B.; Madhup, S.K.; Raghubanshi, B.R.; Kattel, H.P.; Rajbhandari, P.; Bhandari, P.; Thakur, S.; Sharma, S.; Singh, D.R.; Jha, R. Quality Assessment of an Antimicrobial Resistance Surveillance System in a Province of

Nepal. Trop. Med. Infect. Dis. 2021, 6, 60.

as well as grants led by OIE, WHO, and South Centre.¹¹

Recent research on AMR has yielded insights into human and animal health. An assessment of nine AMR surveillance sites in 2021 found that only five had been providing regular reports.¹² The same year, an assessment of a private hospital (Nepal Mediciti in Lalitpur) found antibiotic resistance in *P. aeruginosa* occurring with all 19 AWaRe group antibiotics tested.¹³ Earlier, a 2019 review had summarized existing resistance in the human and animal sectors.¹⁴

Recent research on AMU and AMC is limited. However, a cross-sectional study at Patan Hospital in 2021 found that the total DDD of parenteral antibiotics increased by 23% from 2017 to 2019.¹⁵ An older assessment in 2017 found that 79% of 324 participants (selected from the public) purchased antibiotics over the counter and 43% of the participants understood that fever could be treated with antibiotics. The same study interviewed 33 private pharmacies, 23% of whom responded that antibiotics could be used to treat viral diseases.¹⁶

Within animal health, a 2020 publication examined poultry rectal swabs and urine from patients visiting Kantipur Hospital in Kathmandu. It found multidrug resistance in 80% of *E. coli* from poultry and 79% from clinical specimens.¹⁷ In 2018, an assessment of 150 commercial poultry farmers gave insight to farmers' knowledge, attitudes, and practices. Notably, antimicrobial use for growth promotion was employed by 13% of producers, among whom 35% were using colistin.¹⁸

https://doi.org/10.1186/s41256-021-00187-2.

⁹ WHO-GLASS 2021 report.

¹⁰ WHO-GLASS 2021 report.

¹¹ Nepal Country Brief, Fleming Fund

https://doi.org/10.3390/tropicalmed6020060

 ¹³ Mahto, M. & Shah, A. & Moses, F. & Stewart, A.. (2021).
 Pseudomonas aeruginosa in Nepali hospitals: poor outcomes amid 10 years of increasing antimicrobial resistance. Public Health Action. 11. 58-63. 10.5588/pha.21.0048.

¹⁴ Acharya KP and Wilson RT (2019) Antimicrobial Resistance in Nepal. Front. Med. 6:105. doi: 10.3389/fmed.2019.00105.

 ¹⁵ Baral P, Hann K, Pokhrel B, Koirala T, Thapa R, Bijukchhe SM, Khogali M. Annual consumption of parenteral antibiotics in a tertiary hospital of Nepal, 2017-2019: a cross-sectional study.
 Public Health Action. 2021 Nov 1;11(Suppl 1):52-57. doi: 10.5588/pha.21.0043. PMID: 34778016; PMCID: PMC8575388.
 ¹⁶ Rijal, K.R., Banjara, M.R., Dhungel, B. et al. Use of antimicrobials and antimicrobial resistance in Nepal: a nationwide survey. Sci Rep 11, 11554 (2021). https://doi.org/10.1038/s41598-021-90812-4.

¹⁷ Muktan, B., Thapa Shrestha, U., Dhungel, B. et al. Plasmid mediated colistin resistant mcr-1 and co-existence of OXA-48 among Escherichia coli from clinical and poultry isolates: first report from Nepal. Gut Pathog 12, 44 (2020). https://doi.org/10.1186/s13099-020-00382-5

¹⁸ Lambrou, A.S., Innes, G.K., O'Sullivan, L. et al. Policy implications for awareness gaps in antimicrobial resistance (AMR) and antimicrobial use among commercial Nepalese poultry producers. glob health res policy 6, 6 (2021).

section 02

CAPTURA Experience

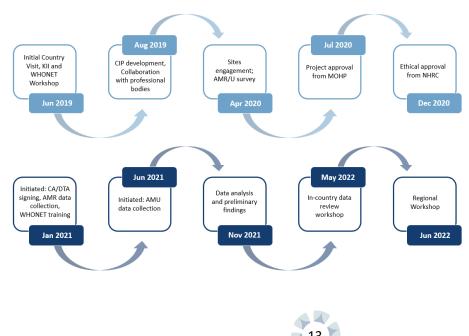
Planning and Implementation

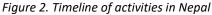
In May 2019, a meeting was held with the AMRCSC Member Secretary to introduce the CAPTURA project. A proposal was made by CAPTURA to organize an incountry consultation workshop in the following month with Nepal's AMR stakeholders. Prior to the workshop, a meeting was held with the AMRTWG members to explain the project in detail. The workshop was held on 18 June 2019 at the Yak and Yeti Hotel in Kathmandu. At the event, the AMRTWG participated and invited additional stakeholders, such as FHI360 (Fleming Fund's country grantee) and WHO Country Office. During the workshop the CAPTURA team had the opportunity to meet with a large group of AMR stakeholders, to discuss collaborations and to learn about the country's efforts to strengthen AMR surveillance.

When the event concluded, the CAPTURA team initiated key informant interviews (KII) and began planning for the in-country approval process. The KIIs were conducted with the NPHL, WHO Country Office, Patan Hospital Microbiology Lab, Tribhuvan University Teaching Hospital (TUTH), DDA, and Center for Molecular Dynamics Nepal (CMDN). They provided information on the availability of AMR/C/U data and background to understand the situation in Nepal. After the initial country visit, the CAPTURA team created a Country Implementation Plan (CIP) in August 2019. It outlined the proposed scope, objectives, and timeline of the work in Nepal. The CIP was presented to the MoHP for review and approval. However, approval was delayed for several reasons: changes in AMRCSC and AMRTWG leadership, the COVID-19 pandemic, and shifts in methodology on site selection. In July 2020, approval was finally granted. It came with a letter of support from the MoHP to CAPTURA, as well as a letter for the cooperation of collaborating facilities.

Additionally, CAPTURA sought approval from the Nepal Health Research Council (NHRC) to conduct research and data collection. The NHRC granted approval for one year starting December 2020.

IVI on behalf of CAPTURA also entered a Memorandum of Understand with the Nepalese Association of Clinical Microbiologists (NACM) with the objective of "research and capacity building in activities focused on surveillance, containment and awareness of AMR and contribute to the shared goals of uplifting and advancing health sector in Nepal." The body facilitated CAPTURA's entry into laboratories that have NACM members in different posts.





The CAPTURA project strategy and coordination of activities was led centrally by the International Vaccine Institute (IVI) with specific technical input and support from the consortium partners. The Public Health Surveillance Group (PHSG) supported all incountry implementation activities, including the development and monitoring of data collection tools. The BWH/WHONET supported AMR data collection through the use of the WHONET software and also led capacity building activities. The BDI oversaw data warehousing and provided analytical and visualization support.

The IVI and PHSG assigned each a country lead to ensure continuity and dedicated attention throughout the project. In addition, an in-country team carried out the project's core activities, including traveling to project sites for meetings, training sessions, and data collection. They enabled the success of the project by having people embedded locally to develop relationships with the MoHP and other stakeholders.

Though in-country activities were delayed due to the COVID-19 pandemic, the overall implementation proceeded in a smooth manner. Approval requests was promptly reviewed by the MoHP, and the incountry team quickly gathered metadata and AMR/U data.

A summary of the timeline for CAPTURA implementation is provided in Figure 2.



Capacity Building Activities

CAPTURA supported numerous WHONET trainings (on-site and virtual) as part of its capacity building efforts. Trained Nepali WHONET users trained laboratory staff in-person using the Nepali language and their own datasets. This was the first time such a method had been used in WHONET training in the country.

As a result, several laboratory staff at facilities sharing data with CAPTURA have now been trained in the use of WHONET. Subsequently, these staff became involved in data digitization and processing tasks, prior to sharing data with CAPTURA. The following trainings were provided in Nepal.

Table 1. List of WHONET Trainings

Nepal Medical CollegeJuly 2020Kist Medical CollegeOct 2020Lumbini Medical CollegeOct 2020Lumbini Provincial HospitalNov 2020Koshi Zonal HospitalDec 2020Nobel Medical CollegeDec 2020Birat Medical CollegeDec 2020/Jan 2021Bheri HospitalFeb 2021Dadeldhura HospitalFeb 2021Manmohan Memorial Teaching HospitalApr 2021National Trauma CentreApr 2021Chitwan Medical CollegeApr 2021Bharatpur HospitalApr 2021Sahid Gangalal Heart CentreJun 2021Om Hospital and Research CentreJul 2021United Mission HospitalAug 2021	Participating Facilities	Training date
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Om Hospital and Research Centre Jul 2021	Vayodha Hospital	Jun 2021
	Sahid Gangalal Heart Centre	Jun 2021
United Mission Hospital Aug 2021	Om Hospital and Research Centre	Jul 2021
	United Mission Hospital	Aug 2021



section 03

CAPTURA Findings

Results

In the following section we present a summary of findings from the scoping and analytical work conducted by CAPTURA in Nepal since 2019.

A majority of the analysis and visualizations for the project were carried out using electronic visualization tools. The data presented in this report are primarily excerpts from these.

Comprehensive analytical outputs and visualization tools have been shared directly with stakeholders at the MoHP. The data content of this final report has been selected after discussion with the AMR technical working group and relevant technical staff considering reliability in terms of data quality and value of data sharing.

Data Types

To identify relevant data holding facilities and to ensure data quality, assessments of facilities were conducted through facility questionnaires and visits before data sharing agreements were made. As a result, two levels of information are available and presented here:

- CAPTURA metadata, which constitutes all the information collected directly by and as part of the CAPTURA project from questionnaires and interviews
- CAPTURA AMR/U/C data, which are the identified retrospective source data generated in facilities between 1 January 2016 and 31 December 2019 (and sometimes beyond). The definitions and more detailed descriptions can be found in the Appendix.

The overall approach to the selection of facilities, collation and analysis of different data sources is illustrated below (Figure 3). See Appendix for more detailed information on the methods.

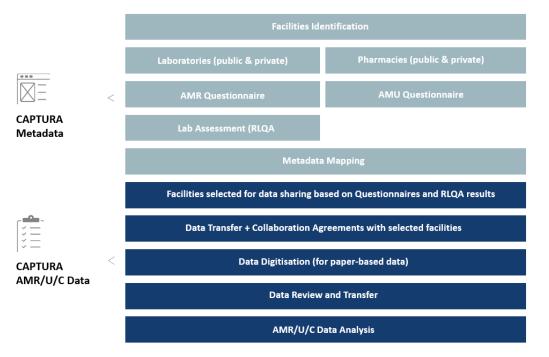


Figure 3. Approach to data identification and mapping



Facility Identification

In Nepal, healthcare (preventive, curative, traditional) is provided by both the public and private sector healthcare centers. Access to the private sector is limited to those that can afford the services and focused in urban areas. The public sector is readily accessible to all but restricted due to limited facilities and resources, including specialized human resources. During the initial desktop review, the CAPTURA team identified 91 laboratories potentially generating AMR data (Figure 4). Following the scoping visit to the country and subsequent communication with government AMR stakeholders, 56 (private and public) out of the 91 facilities were shortlisted for surveys, laboratory assessment, and data sharing.

Each major hospital in the country has its own pharmacy. In addition, numerous private pharmacies have been operating in the vicinity of the hospitals. They sell medical supplies, including antimicrobial agents, to both out- and in-patients. As per the law, it is essential to have a prescription before dispensing antibiotics and regulated drugs. However, due to weak monitoring and aggressive competition among the pharmacies, these drugs are freely available over the counter. This is more prevalent in rural areas where patients often visit nearby pharmacies prior to going to a hospital.

Very few pharmacies maintain proper digital sales and/or patient records. Those that maintain records in logbooks keep them for their financial audits or inventory maintenance. These data are either incomplete or with no key variables useful for AMU/C analysis. CAPTURA, through a convenient sampling technique, first selected 30 pharmacies for the AMU survey. Once it was ascertained that data found at these pharmacies could not be used for AMU/C analysis, a different approach had to be adopted. Four major tertiary care hospitals, two public and two private, were selected for the collection of prescription data (hospital in-patient data). Then, an exemplar AMU analysis was performed on the collected data.

The DDA with the support of WHO-CO in Nepal collected AMC data for 2017-18. To avoid duplication of the activity, the CAPTURA team held numerous consultation meetings with the DDA and offered technical assistance/capacity building activities. Though there was an initial hesitancy to collaborate, following an in-country data review meeting held in May 2022, an interest for collaboration has been

noted. As the project in the current scope of work is coming to a close, the CAPTURA team recommends such collaborative opportunities to be considered in future activities. This could be an opportunity to support the establishment of a mechanism for prospective AMU/C surveillance in the country.

An overview of all the facilities surveyed are provided in Table 2 and 3.

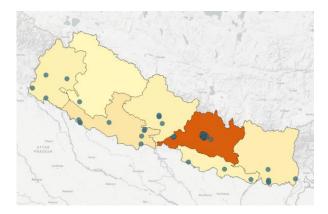


Figure 4. Map of facilities identified

AMR Metadata

Thirty nine out of 41 laboratories responding to CAPTURA's AMR survey indicated to conduct bacterial culture and AST. The laboratories were mostly hospital-based (36/39) and public healthcare facilities (20/39). The disk diffusion method was the predominant method employed by most laboratories (36/39) with four labs conducting the MIC method (one automated MIC). The survey findings also indicated good record-keeping practices with 29 facilities using an electronic LIS for recording AST data and 10 having three years to a decade of e-records on AST. The volume of samples being processed varied from less than 100 to more than 1000 samples per month.

Twenty one out of 39 laboratories processed a complete set of sample types, including blood, stool, cerebrospinal fluid (CSF), sputum, soft tissue and bodily fluids, urine, and genital specimens for bacteriological culture. All labs had good records of specimen, pathogen culture, and AST information. However, zone diameters (6/36) and associated clinical information (3/36) for diagnosis were uncommon.

Laboratories within the existing AMR surveillance network were regularly sharing data with the NPHL. A descriptive summary of the laboratory selection process for the AMR survey and its findings are presented in pages 19-20. The findings include the locations and affiliations of the laboratories, methods employed by the laboratories for AST, volume of susceptibility tests performed, and availability of records.

Rapid laboratory quality assessment (RLQA) was conducted at 36 laboratories across Nepal. Nineteen of the 36 laboratories were privately owned and 33 were associated with hospitals. In general, all the laboratories were equipped and staffed to perform basic Microbiology assays.

A basic set of in-house made media is used by most of Nepal's laboratories. Gaps were identified particularly in pathogen identification capacity, AST performance, and internal and external quality assurance programs. A common Standard Operating Procedure (SOP) for microbiological processes and technical support for implementing the set standard will help generate quality data. In addition, the survey found gaps in provisions of refresher training on blood culture.

Table 2. Overview of facilities surveyed on data availability (AMR)

Name of Hospitals	AMR	Danid Laboratory
Name of Hospitals	Questionnaire	Rapid Laboratory Quality Assessment
Bayalpata Hospital, Achham	V	√
Koshi Hospital, Biratnagar	√	√
Patan Academy of Health Sciences, Kathmandu	1	✓
Kathmandu Model Hospital, Kathmandu	✓	√
KIST Medical College, Lalitpur	V	V
Sukraraj Tropical & Infectious Disease Hospital. Kathmandu	√	√
Manipal Teaching Hospital, Pokhara	✓	√
United Mission Hospital, Palpa	√	√
Lumbini Provincial Hospital, Butwal	√	√
Bheri Regional Hospital, Nepalgunj	√	✓
Kanti Children's Hospital, Kathmandu	√	✓
Mid Western Provincial Hospital, Surkhet	1	✓
Seti Regional Hospital, Dhangadi	1	✓
Mechi Hospital, Bhadrapur	x	✓
Paropakar Maternity & Women's Hospital, Kathmandu	√	✓
Vayodha Hospital, Kathmandu	√	✓
National Reference Laboratory, Kathmandu	√	√
Sahid Gangalal National Heart Centre, Kathmandu	√	V
Grande International Hospital, Kathmandu	√	V
Om Hospital and Research Centre, Kathmandu	✓	√
Dadeldhura Hospital, Dadeldhura	√	√
Chitwan Medical College, Bharatpur	√	√
Bharatpur Hospital. Bharatpur	√	√
College of Medical Sciences, Bharatpur	√	√
Bir Hospital, Kathmandu	√	√
Birat Medical College, Birathnagar	✓	√



Nobel Medical College, Birathnagar	√	√
Nepal Medical College, Kathmandu	√	√
Siddhi Poly Path Lab, Kathmandu	1	√
Lumbini Medical College, Palpa	1	V
National Trauma Centre, Kathmandu	√	√
Manmahona Memorial Teaching Hospital, Kathmandu	1	√
National Public Health Laboratory, Kathmandu	√	V
Nepalgunj Medical College, Nepalgunj	√	V
Kathmandu Medical College, Kathmandu	√	√
B.P. Koirala Memorial Cancer Hospital, Bharatpur	√	V
G P Koirala National Respiratory Center, Tanahu	1	V
Gandaki Medical College, Pokhara	√	х
Trivubhan University Teaching Hospital, Kathmandu	1	x
Sushil Koirala Prakhar Cancer Hospital, Nepalgunj	√	x
Sahid Dharma Bhakta Organ Transplantation Centre, Bhaktapur	√	х

AMU Metadata

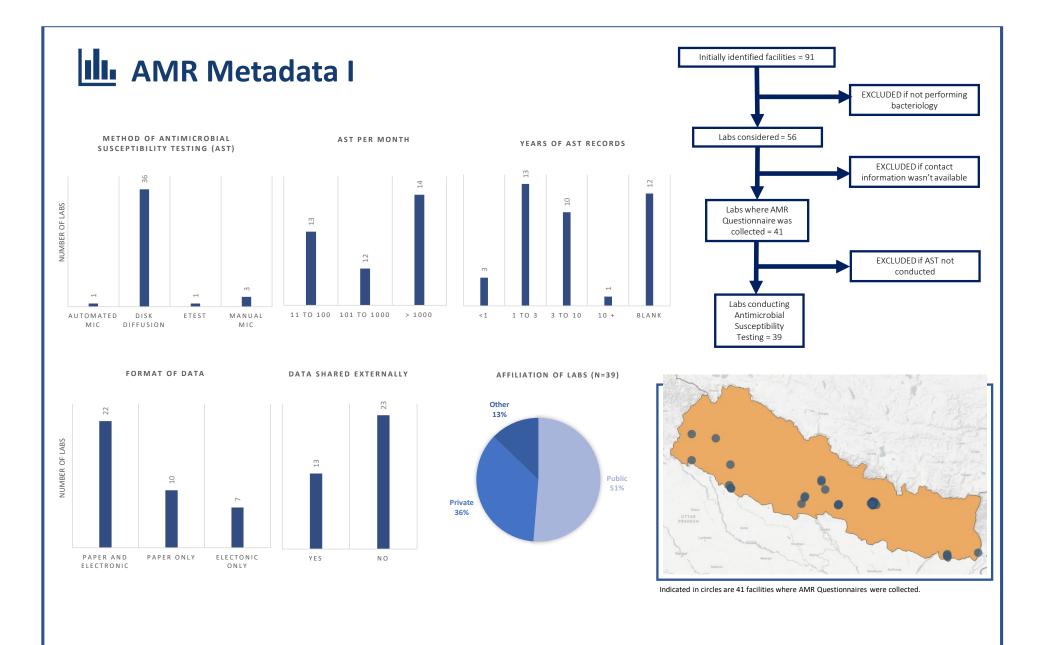
Of the 34 surveyed facilities (30 pharmacies and four hospitals), 30 were dispensing antimicrobials. Of the 30, 17 were maintaining records of the dispensed drugs. Similarly, most of the pharmacies responded that they required prescriptions for dispensing antimicrobial agents. However, retaining copies of prescriptions was not a common practice. The survey responses indicated that a majority of the prescriptions did not include a diagnosis, and access to relevant laboratory records were not available to the pharmacies. The sales records were being maintained either in electronic or manual format or using both methods. One pharmacy reported having maintained more than 10 years of records in its database while some (n=9) reported maintaining records up to five years.

Moreover, a majority (85%) of the surveyed pharmacies were privately owned and did not receive supplies from the government warehouses but rather through a parallel supply chain. Dispensing and stocking drugs using available guidelines was followed by some, but periodic training on the guidelines were not regularly provided.

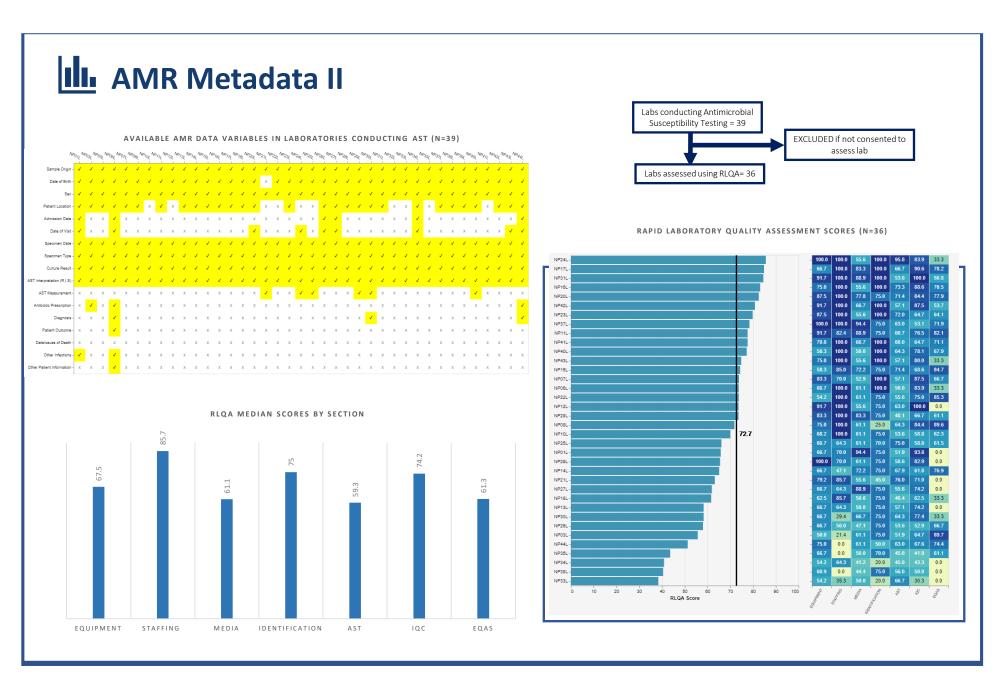
Nam	e of Pharmacy Completing AMU Questio	nnaire
Uddharya Pharma	Kalas Pharmacy	Siles Pharmacy
Bindabasini Pharmacy	Filisiya Pharmacy	IMO Medical Hall (M.V. Polyclinic)
Omtara Pharmacy	Mediholic Pharmacy	24*7 Pharmacy, Metro Hospital
Hami Sabaiko Pharmacy	Manmohan Hospital Pharmacy	Kathmandu Medical College- KMC Hospital
Daju Bhai Pharmacy	Hopewell Pharmacy	Gyankul Pharmacy
Shankarapur Hospital	Karthabya Pharmacy	Medimart Pharma
Best Buy Pharmacy	Sarovar Pharmacy	SNH Pharmacia
Ganga Jamuna Pharmacy	Jenin Pharmacy	Hamro Sambandha Medical Hall
Nepal National Hospital Pharmacy	Pabitra Progress Pharmacy (Bir Hospital)	Chemmart Pharmacy
Jagat Aama Pharmacy	Jamakatel Pharmacy	Boje Pokhari Pharmacy

Table 3. Overview of facilities surveyed on data availability (AMU)

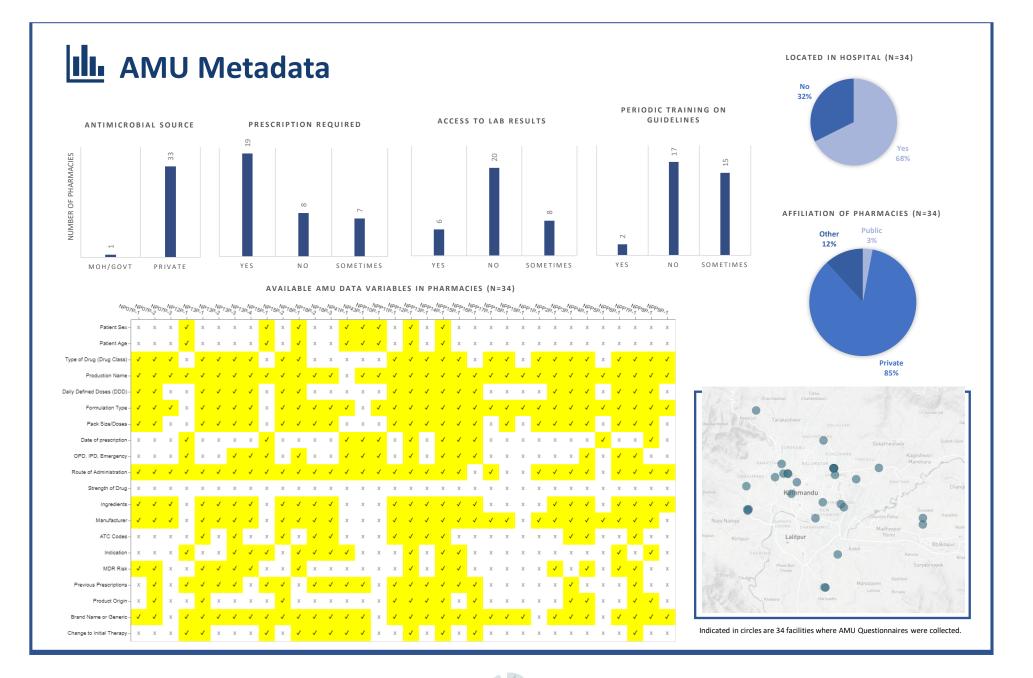












AMR data findings

Epidemiology

Nepal provided 28 datasets with microbiological culture records from 28 laboratories. After combining all datasets, a consolidated WHONET report (Epidemiology and Quality Report) was prepared to generate the findings included in this report.

The period between 2017 to 2020 had 662,201 culture records. Of these, 477,225 were reported as no growth or negative results, and 184,976 (approx. 27.9%) reported bacterial growth. Among the records with bacterial growth, 68,435 (~37%) reported no significant findings or did not yield a pathogen (no significant growth, normal flora, mixed bacterial species, no pathogens found, among others.). AST results were available for most records where true pathogen was isolated.

The majority of the records were generated between 2017-2020 with a stark noticeable drop in numbers in 2020, possibly due to the impact of the COVID-19 pandemic. Of the total (records with growth and no growth findings), urine (51.3%) comprised the highest number of samples tested, followed by blood (24.9%), respiratory (9.9%), soft tissue and body fluid (9.3%), and a nearly equal volume of genital and stool samples (1.8%). This reflects a normal/common observance in any diagnostic microbiology lab, where nearly half the samples tested are urine. A descriptive data summary is presented in pages 27-28. They include details on the number of samples processed, number of isolates, as well as patient and sample demographics.

Organism statistics:

The most common bacteria isolated in the obtained datasets were 'Escherichia coli' (nearly 37.51% of positive records) followed by Staphylococcus aureus, Klebsiella spp., Pseudomonas spp., Acinetobacter spp., coagulase negative Staphylococci and Enterococcus spp. (14.05%, 12.34%, 6.16%, 5.91%, 5.68%, 2.73%, respectively). Infrequent isolation of important public health priority pathogens like Vibrio cholerae, Yersinia pestis, Neisseria gonorrhoeae, Neisseria meningitidis, etcetera, warrants close monitoring to prevent the development of resistance and outbreaks.

Positivity among urine samples was highest (51.2%), corresponding proportionally with the number of samples tested. *E. coli* (59.98%, n=35,807 of the total positive urine samples) was found to be the most

frequently isolated organism from this sample as well as in the aggregated analysis. *Klebsiella spp.*, *Pseudomonas spp.*, *Staphylococcus aureus* and *Enterococcus spp.*, constituted the top five pathogens isolated from the urine samples.

In most settings, only 5-13% of blood culture will turn out to be positive, with nearly half of those representing contaminants among the positives. The analyzed dataset had similar findings with blood culture positivity at 10%. Coagulase negative staphylococci, which is a part of normal skin flora, was reported as the second frequently isolated organism in blood culture from the Nepal dataset. It is important that such observation is monitored across the laboratories as there are chances of over reporting contaminants/normal flora as pathogen. The high percentage of contaminants in positive culture is not only seen in cases of blood culture but also in other samples, especially those that pass through highly contaminated surfaces during collection (e.g., sputum, stool etc.), and reporting such results requires a high level of technical expertise. It is also worth noting that in-addition to pathogens like Staphylococcus aureus, Acinetobacter spp. and E. coli, high public health priority pathogens like Salmonella Typhi was also among the top five frequently isolated pathogens from blood culture in the Nepal dataset. As mentioned above, it is essential for the lab to ensure quality assured results to correctly identify true pathogens and monitor their susceptibility patterns for the effective containment of AMR.

Similarly, known diarrheal agents like Salmonella spp., Shigella spp., and E. coli, were the top pathogens in stool culture. Isolation of these pathogens viz. Salmonella spp. including Typhi, Shigella spp. from blood and stool, highlights the fact that Enteric fever, Salmonellosis and Shigellosis are still endemic in the country. It also highlights the need for targeted intervention for elimination, including WASH and vaccination. Further, identifying and reporting E. coli as the most frequently isolated intestinal pathogen from stool warrants further confirmatory tests. It is important to do so as *E. coli* also exist in normal gut flora and only certain strains are diarrheagenic. Thus, reporting this pathogen without confirmatory testing/evidence for diarrheagenic E. coli may lead to inappropriate treatment (misuse of antimicrobials), further contributing to the development of AMR.

From 2017 to 2019, there were statistically significant increases in isolation of *Acinetobacter, Klebsiella spp., Pseudomonas* and *Enterococcus*. As the dataset shared

with CAPTURA was retrospectively collated and was not complete in-terms of essential variables, we were not able to categorize the isolates as communityacquired or hospital-associated. It was not possible to comment on the increase in isolation rates of these pathogens. But a gradual rise was observed in testing over the period, and it may contribute to the increase seen in the country. Nevertheless, an increase in the frequency of isolation of pathogens associated with hospital-associated infections requires close monitoring as they are usually associated with high levels of AMR.

Antimicrobial results:

Detailed analyses of resistance profiles on the isolated pathogens, including Gram-positive and Gramnegative antibiograms, have been generated and will be shared with the laboratories. Resistance rates were also determined for the WHO Global priority list of resistant bacteria, with a number of critical priority bacteria, including carbapenem resistant Acinetobacter spp. (43%) and ceftriaxone/cefotaxime resistant E. coli (up to 56%). Similarly, isolation of high priority pathogens like MRSA and fluoroquinolone resistant Neisseria gonorrheae and Salmonella spp. (Ciprofloxacin resistant) is a matter of concern for Nepal. Meanwhile, reporting VRSA based on disc diffusion test poses a question on reliability and data quality. Furthermore, the observance of high-level resistance in WHO GLASS pathogens, particularly the SDG indicator for blood isolates of Staphylococcus aureus (%MRSA) = 35%) and E. coli (% third generation cephalosporin resistance = 54%), is an alarming finding.

Multidrug resistance (MDR), extensively drug resistance (XDR) and pan drug resistance (PDR) profiles need to be followed up closely over time for several reasons. These include outbreak detection, development of treatment guidelines, characterization of resistance mechanisms, and/or recognition of possible errors in laboratory testing. Confirmation of XDR/PDR requires testing using all classes of antimicrobials. This is not commonly practiced in diagnostic labs, thus WHONET identifies possible XDR/PDR based on the antimicrobials tested. Table 4 lists the frequency of isolation of MDR, possible XDR and PDR in the dataset received from Nepal.

Table 4. Summary of MDR, XDR, PDR

Organism				
Staphylococcus aureus	16,379	5,913 (36%)	4,008 (24%)	587 (4%)
Enterococcus faecalis	590	36 (6%)	35 (6%)	16 (3%)
Enterococcus faecium	22	8 (36%)	8 (36%)	
Escherichia coli	43,715	11,933 (27%)	8,107 (19%)	844 (2%)
Klebsiella pneumoniae	10,700	4,052 (38%)	3,005 (28%)	487 (5%)
Pseudomonas aeruginosa	5,201	1,361 (26%)	1,223 (24%)	74 (1%)
Acinetobacter sp.	6,893	3,435 (50%)	2,833 (41%)	301 (4%)

While resistance rates and profiles are valuable in monitoring resistance trends and in developing treatment guidelines, policymakers must be aware of laboratory test quality and different types of biases (due to patient presentation, sampling practices, and laboratory test practices).

Test practices and quality report

This section addresses the issue of "quality" from several perspectives. The analyses include several indicator metrics that could 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

Data entry:

Data completeness of the core data available variables was satisfactory (75%). However, patient ages were absent in a large number of records (n=36,356). A few records with missing organisms (n=616) were also observed and were subsequently excluded during data curation. Issues were identified in recording information related to patient identification numbers (only 50% complete), sample locations (only 26% complete), and location types (only 40%). Patient identification numbers are valuable for tracking and counting individuals with repeated samples over time. Similarly, identifying the sample location supports additional analysis of data and adds value for the descriptive epidemiological analysis of the samples.



Table 5. Data entry completeness and quality matrix

Data Field	% Completed	% Use of standard codes
Total completeness	75%	83%
Age	95%	
Organism	100%	100%
Identification number	50%	
Sex	98%	98%
Specimen type (Numeric)	100%	100%
Specimen date	91%	
Location	26%	
Location type	40%	35%

It is recommended that quality control strains are used at regular intervals to ensure the reliability of test results. The maintenance of such records is also part of a good documentation practice. None of the analyzed datasets contained data related to the testing of quality control strains.

Organism identifications:

Other than *E. coli* and *Staphylococcus aureus*, the laboratories were able to identify nearly 74% of organisms up to the genus level. The laboratories were mostly able to identify Gram negative organisms at a greater rate (e.g., 88% of *Klebsiella*, 72% of *Pseudomonas*) compared to Gram positive organisms (19% of *Enterococcus*). The ability to identify several fastidious organisms, as seen in the dataset shared with CAPTURA (important ones include *Moraxella catarrhalis, Streptococcus pneumoniae, Neisseria gonorrhoeae, Hemophilus influenzae*), is an indicator of the laboratory's capacity to receive, process, isolate, and identify samples with special growth characteristics or reagent needs.

AST practices:

All laboratories performed disk diffusion testing following CLSI guidelines, which was also followed by the laboratories that performed MIC.

An important observation made during the analysis was the inconsistent and irregular testing against commonly recommended sets of antimicrobials. It was not possible for us to generate a list of regularly tested core antimicrobials from the dataset. We would recommend adopting a standard set of antimicrobials to be promoted within and among laboratories, both to support routine clinical decisions and to improve comparability of findings over time and between facilities.

Furthermore, there were results of several antimicrobials for which validated breakpoints do not exist. This could either be due to the testing of

incorrect antimicrobials or a mistake in laboratory configuration of WHONET. Corrective action is needed in both circumstances. If there is a mistake in the WHONET or BacLink configuration, it should be immediately rectified. In the case of incorrect testing, education/training and review of purchasing and test practices should be conducted as soon as possible.

Additionally, although test interpretations (RIS) were recorded, the inhibition zone diameters were missing. In the future, we would recommend the recording of disk diffusion zone diameters to improve the assessment of data quality and recognition and tracking of microbial sub-populations. Moreover, such measurement permits data re-analysis even if breakpoints change.

Isolate alerts:

WHONET generated a number of isolate-level alerts. From a public health perspective, some of the more important ones included high-priority important species: *Neisseria gonorrhoeae*, *Neisseria meningitidis*, and *Salmonella* Typhi. From a quality perspective, alerts facilitate the recognition of possible deficiencies in test performance. Isolation of colistin or polymyxin non-susceptible *Acinetobacter*, *Citrobacter*, *Escherichia coli*, *Klebsiella*, among others, need confirmation as quality control alerts do not necessarily indicate that a result is incorrect. Results are validated through repeat testing and confirmation.

In summary, this study noted a few key issues in pathogen identification and susceptibility test practices. These include: 1. Irregular testing practice, 2. Not testing quality control strains on a routine basis "OR" recording the findings if such a practice is in place, 3. Testing of antimicrobials for which there are no validated Clinical Laboratory Standard Institute (CLSI) interpretative criteria, 4. Not recording disk diffusion zone diameters, which is typical of most databases.

In the future, we recommend that the laboratories in the country address these issues as a priority. We believe it will contribute to reliability of clinical reports, quality assessment, and epidemiological monitoring.



AMU data findings

The antimicrobial usage data in this report was collected through a piloting exercise. The CAPTURA and the in-country team collaborated to create a template, which was based on both the WHO protocol on surveillance of antimicrobial consumption¹⁹ as well as adaptations from the WHO protocol on Point Prevalence Surveys²⁰.

Due to limitations in the initial dataset generated from this pilot, the analysis presented in this report is preliminary and primarily meant to serve as an initial evaluation of the collection tool before further development and broader implementation. All curation, analysis, and visualizations were performed using the R statistical software. The summary of AMU data can be found on pages 31-32.

Data sources

Antimicrobial use data were extracted from paperbased medical records of admitted in-patients at four facilities located in Kathmandu:

- Bir Hospital (Public, Central Tertiary Care Hospital)
- Sukraraj Tropical Hospital (Public, Central Infectious Disease Super Specialty Hospital)
- Nepal Medical College (Private, Tertiary Care Academic Hospital)
- Vayodha Hospital (Private, Specialty Hospital)

These facilities were selected as per convenience and their willingness to share data.

Data were collected from the general medical wards at all four facilities, with the addition of data from the Intensive Care Unit (ICU) at one facility. Trained enumerators with nursing backgrounds entered the AMU data into the SurveyCTO data server using a tablet-based data-entry software developed by the incountry team. All personal patient information, such as patient ID and ages over 70, were encrypted before performing any analysis.

The data contained the following information on prescriptions: generic name, trade name, form, route of administration, strength, treatment start and stop date, frequency, indication, infection site, and diagnosis. In addition, specimen collection and It is important to note that antimicrobial use in all of the surveyed hospitals is likely to be disproportionally higher than in others around the country because all hospitals in the capital are tertiary level/specialized hospitals and serve as referral centers for lower-tier hospitals across Nepal. As such, the surveyed hospitals cater to more serious cases or patients requiring specialized treatment, often necessitating more and broader spectrum antimicrobials. The results, therefore, cannot be generalized for the entire country.

Data overview and preliminary results

Initial curation on the aggregated data from all four facilities resulted in the retention of 62,523 individual prescriptions. As expected, patients had more than one prescribed antibiotic. Thus, the total number of patients included in the collected dataset was 22,102.

The most prescribed antibiotic group were other betalactams (comprising of beta-lactam antibacterials, other than penicillin and cephalosporins), followed by beta-lactam antibacterials (including penicillin). Macrolides and quinolones were also frequently prescribed. In terms of individual agents, ceftriaxone, azithromycin, and cefixime were among the most prescribed antibiotics.

Overall, most antibiotic prescriptions were written for the management of primary infection (84.7%, N = 52,930), followed by prophylaxis (14.5%, N = 9069). The relatively significant proportion of prophylactic use is typically only observed in hospitals where it is used for deliveries as well as surgeries. It was not possible to determine if the prophylactic use was mostly appropriate. Very few hospital-acquired infections were reported (~0%, N = 27), but this is likely due to a lack of related surveillance.

In medical wards, a majority of the treatment was for patients with primary infections. Within primary infections, the lower respiratory tract (39.7%, N = 21,030) and the gastro-intestinal tract (25.0%, N = 13,222) were the two most common types of infection for which antibiotics were prescribed. Antibiotic use for the treatment of primary infection follows the same pattern as the overall prescription pattern

microbiology laboratory data for a subset of prescriptions were collected from two facilities.

¹⁹ World Health Organisation. WHO methodology for a global programme on surveillance of antimicrobial consumption v1.0

²⁷

 ²⁰ (WHO) World Health Organisation. WHO Methodology for Point
 Prevalence Survey on Antibiotic Use in Hospitals v1.1. Geneva, 2018.

where other beta-lactam subgroup comprises the majority among the prescribed drugs.

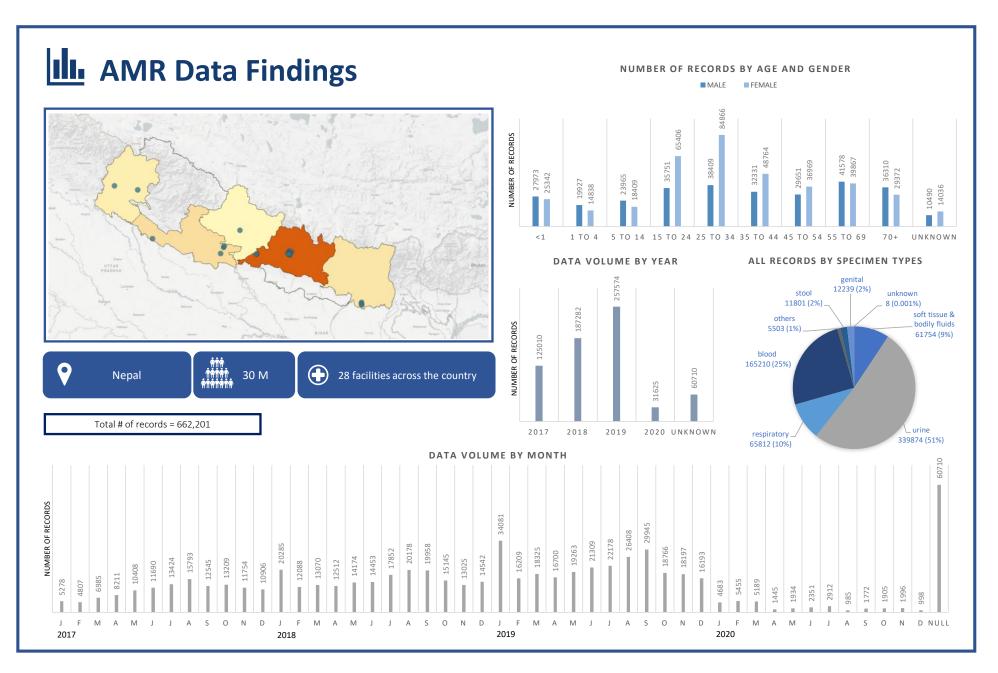
Obtaining cultures prior to starting antibiotic therapy is an important practice that can help clinicians confirm the pathogen of concern, their susceptibility patterns, and ensure the appropriateness of the treatment. In the Nepal aggregate dataset, a biological sample was only seldom obtained. Roughly 17.7% of prescriptions had records of laboratory investigation for bacteriological culture before an antibiotic was prescribed. Even if bacteriological culture was performed, it was often not recorded in patient files for future reference. For prescriptions for which samples were obtained, the lower-respiratory tract infection was the most common (49%, n = 5,468), followed by gastrointestinal tract infection (21.0%, n = 2,326).

Analysis by the WHO AWaRe classification gives a good insight into the appropriateness of prescribing or dispensing patterns. It also helps set benchmarks based on WHO's target to use at least 60% of antibiotics consumed to come from the 'Access' category. In our analysis, the 2021 WHO AWaRe Classification²¹ was used to understand the prescription practice in the datasets. Across all four hospitals, a very high use of 'Watch' antibiotics (60% or higher in relative distribution of antibiotics prescription) was observed. These observations may seem to show that the facilities did not meet the global target of 60% of antibiotic consumption to come from the 'Access' category. However, these numbers are not unexpected in tertiary/specialty care facilities. Nevertheless, the high proportions of not recommended or uncategorized antimicrobials being used for treatment must be noted as a point for further investigation.

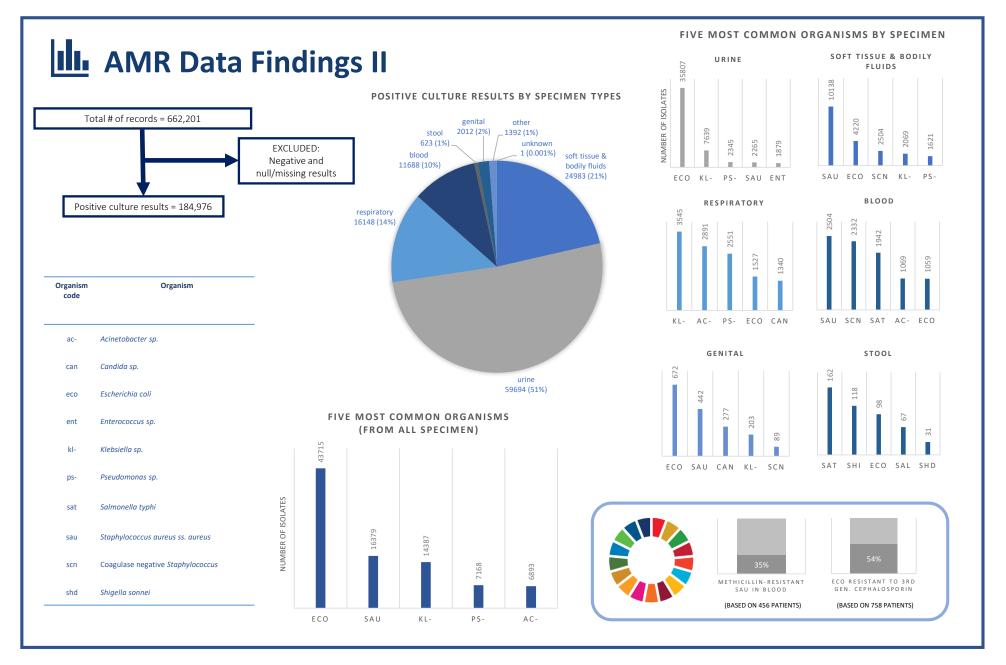
Importantly, the AMU findings presented here should not be interpreted as a complete picture of the state of AMU in Nepal. The AMU findings here are aggregated from four facilities that serve different roles in their respective communities, which is reflected in the differences in prescribing patterns between facilities. Further, the volume of data shared by each facility widely varies, which limits generalization of the findings to other facilities. The findings here are thus preliminary and mainly meant to be used for informing updates to the prospective data collection and analysis efforts planned in Nepal.

²¹ World Health Organisation. 2021 AWaRe classification





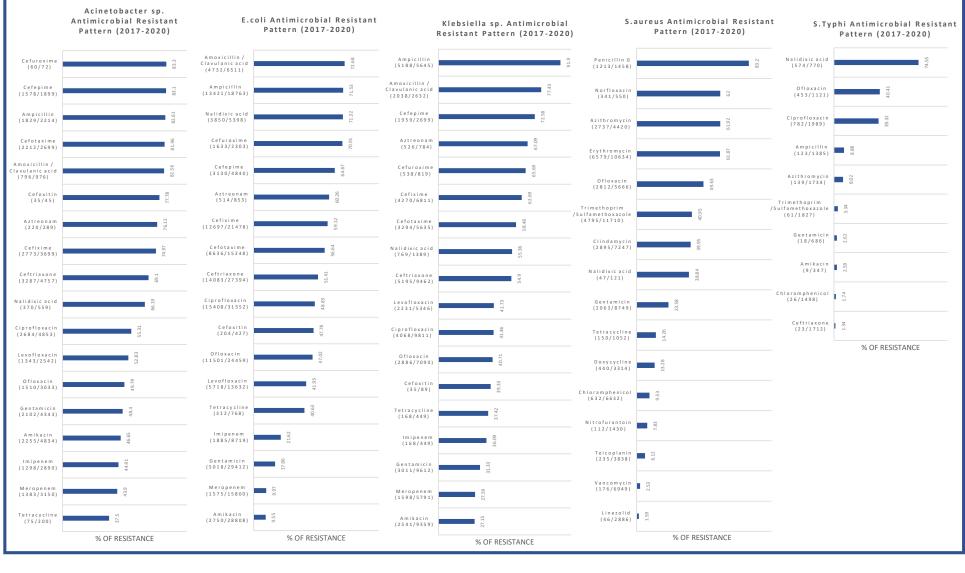






III. AMR Data Findings III

Antimicrobial RESISTANCE patterns of the five most important pathogens, tested against relevant antimicrobials. (number of resistant test results / total tests conducted)

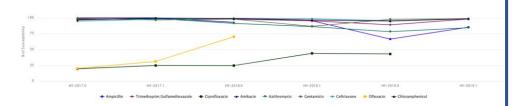




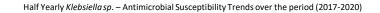
III. AMR Data Findings IV

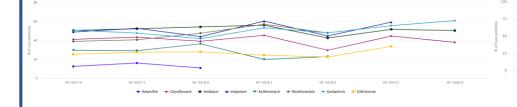
Half Yearly S. Typhi-Antimicrobial Susceptibility Trends over the period (2017-2020)

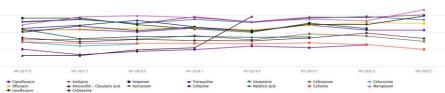
Half yearly **antimicrobial SUSCEPTIBILITY trends** of the five most important pathogens, tested against relevant antimicrobials.



Half Yearly Acinetobacter sp. – Antimicrobial Susceptibility Trends over the period (2017-2020)

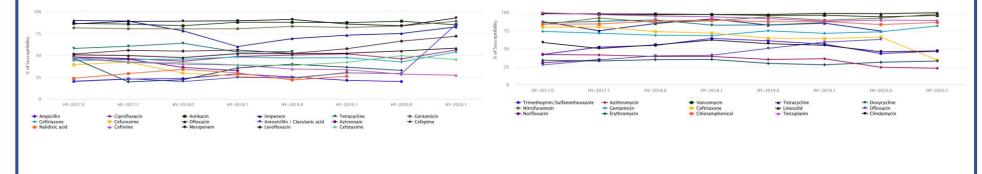


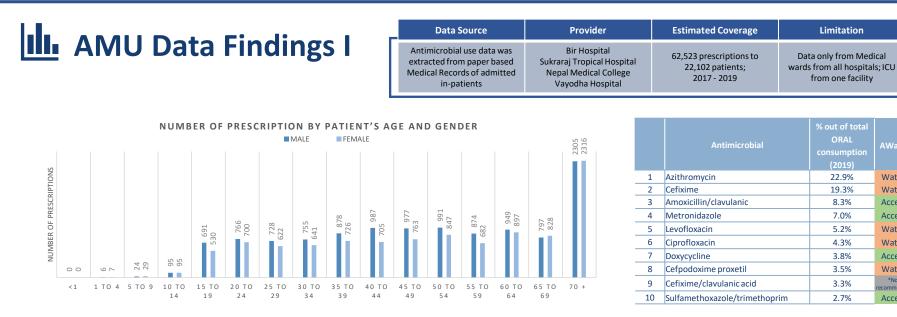




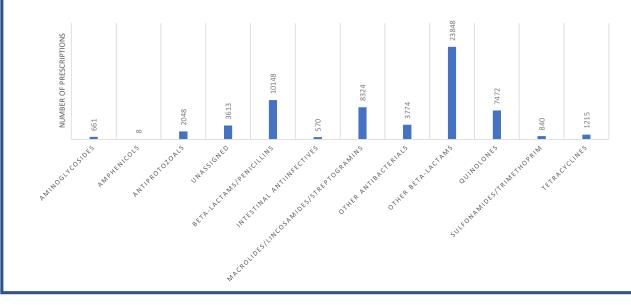
Half Yearly E. coli – Antimicrobial Susceptibility Trends over the period (2017-2020)

Half Yearly S. aureus – Antimicrobial Susceptibility Trends over the period (2017-2020)





NUMBER OF PRESCRIPTIONS BY PHARMACOLOGICAL SUBGROUP



	Antimicrobial	% out of total PARENTERAL consumption (2019)	AWaRE
1	Ceftriaxone	35.6%	Watch
2	Piperacillin/tazobactam	11.6%	Watch
3	Metronidazole	8.8%	Access
4	Amoxicillin/clavulanic acid	6.9%	Access
5	Levofloxacin	5.3%	Watch
6	Ciprofloxacin	4.5%	Watch
7	Ceftriaxone/tazobactam	3.9%	*Not recommended
8	Cefuroxime	3.3%	Watch
9	Cefotaxime	3.3%	Watch
10	Clindamycin	2.3%	Access

22.9%

19.3%

8.3%

7.0%

5.2%

4.3%

3.8%

3.5%

3.3%

2.7%

Watch

Watch

Access

Access

Watch

Watch

Access

Watch

*Not

commende

Access

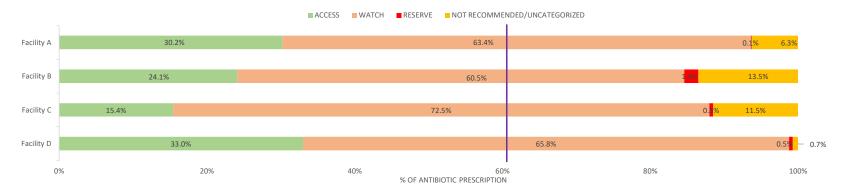
Top 10 oral (top) and parenteral (bottom) use of antimicrobials, 2017-2019

*Not recommended as per the 2019 WHO AwaRe classification

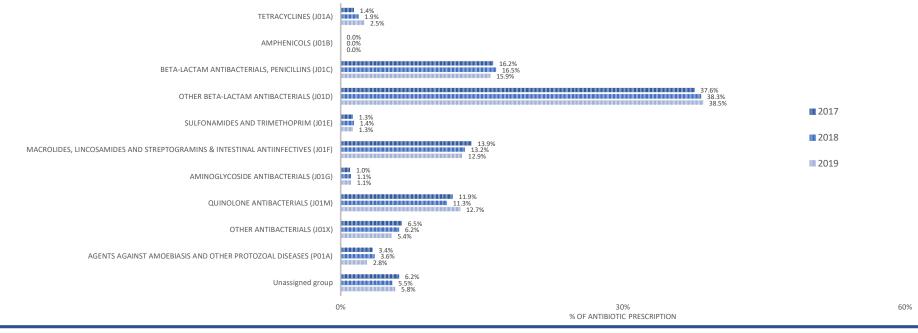


III. AMU Data Findings II

ANTIMICROBIAL CONSUMPTION BY AWARE CATEGORY



PROPORTIONS OF PHARMACOLOGICAL GROUPS IN ALL ANTIBIOTIC PRESCRIPTION BY YEAR





section 04

Conclusion

This final country report has served to summarize the experiences made through the in-country implementation of CAPTURA activities in Nepal between June 2019 and June 2022. It presents the summary findings from the initial AMR and AMC/U data identification, assessment, and analysis.

As noted above, most of the analysis and visualizations for the project were done using electronic visualization tools. Comprehensive analytical outputs and the visualization tools will be shared directly with the QSRD, MoHP, GON. The final data content of this report has been selected after discussions with and feedback from data owners and relevant technical staff in the country, considering both reliability in terms of data quality as well as value of data sharing.

It is important to note that we believe the main utility of the data collected on AMR and AMU through the CAPTURA project in Nepal is to help establish a preliminary data baseline, and that the activities primarily have enabled capacity building within data management and analysis for future AMR surveillance efforts.

AMR - limitations and recommendations

CAPTURA's findings demonstrate the availability of bacteriological culture and AST capacity in at-least 56 facilities across the country, but the information needs to be verified through detailed scoping surveys. It is important for a country to have a list of all facilities generating AMR data, and to update it periodically to understand the country's capacity and prepare policies based on existing strengths. CAPTURA identified major gaps in terms of QC (IQC and EQA), AST testing, and data management capacity. Having a strong quality management system at the laboratory will ensure report and data validity, which leads to acceptability of the findings by clinicians and researchers for its use in their respective domains. Hence, Nepal needs to initiate appropriate measures to enhance the capacity and quality of microbiology diagnostic services across the country focusing on IQC and EQA.

This study observed that laboratory staff have been maintaining AST data where and as it is available, and through CAPTURA, the technical staff involved in data generation and management have been trained on the use of WHONET. Additionally, standardized testing procedures are in place and designated NRLs are regularly providing training on common testing protocol. Therefore, it is possible for the country to strengthen and potentially expand the existing AMR surveillance network. Efforts should also be made towards long-term sustainability of the network using available local resources and development of a robust data sharing mechanism designed for the country context (for uninterrupted local data sharing for continuous monitoring and tracking of AMR trends and patterns as well as sharing findings at the international level).

A process to digitize AMR data with the support of CAPTURA has been initiated in facilities where laboratory management systems were not in place. Additionally, to ensure standardized data generation across all facilities, training on the use of WHONET/BacLink software was provided to the sites. This effort can be continued prospectively for proper data recording and management for future use. The NPHL, designated as NRL, has the capacity to process all types of samples and specimens concerning public health and continues to provide quality oversight to the laboratories under its AMR surveillance network. With further capacity building and technical support, this oversight can be extended to newly identified facilities. Though it is not an absolute necessity, recording AST findings with zone diameters should help in the future use of the data if the susceptibility breakpoints change over time. Furthermore, we would recommend the adoption of a standard set of antimicrobials to be promoted among laboratories, both to support routine clinical decisions and to improve comparability of findings over time within and between facilities. Equally important is to have uninterrupted supplies of reagents at the laboratory to ensure quality controlled outcomes and results.

Though the NPHL has been participating in EQAs and providing its own NEQAS for a long time, the unavailability of quality control strain test results in the surveillance data shared with CAPUTRA allows a question to be raised on the quality of data being generated. It is recommended to maintain such records to validate the AST data generated by each laboratory. Further development and implementation of a more robust Quality Management System (QMS) for ensuring consistent quality performance should be prioritized. Similarly, regular participation in an EQA program on both ID and AST by the NRL should continue as a routine practice. NRLs should identify such programs to enroll and upon establishment of microbiology capacity at referral sites, strengthening of a national proficiency testing program for bacterial

culture, pathogen identification and AST is encouraged.

AMU – limitations and recommendations

Similar to CAPTURA's experience across other countries in the region, Nepal also has very limited information readily available on antimicrobial use at the patient level. Though PPS methodology for AMU has been recently introduced with the support of the FFCG, enhanced effort is required for an AMU surveillance to start in the country.

The CAPTURA-obtained antimicrobial use data was limited to piloting collection of digitized prescriptions and medical record data from four hospitals located in Kathmandu. Although limited in amount, the AMU data collected from Nepal was unique in that it allowed for more detailed analysis at the individual patient level, which is crucial to inform and evaluate antimicrobial stewardship interventions. If such data can be prospectively gathered across multiple facilities in a standardized manner, including consistent linkage to clinical and AMR data, it will truly represent a distinctive example of national AMU surveillance in the region.

To further enable the establishment of this system, CAPTURA supported Nepal AMR stakeholders by sharing the EXCEL AMU data collection tool and minimal list of variables required for AMU analysis. This can be introduced throughout the country after customization across major hospitals/pharmacies. For this purpose, CAPTURA specifically recommends the following:

1) Adopt a framework at the national level on AMU/AMC surveillance. It should clearly define surveillance protocols and roles and responsibilities of hospitals participating in AMU/AMC.

2) Hospitals should prioritize electronic prescription data capture wherever possible.

3) Ensure that prescriptions include information on:

- basic patient and department demographics
- treatment duration and indication
- link to clinical diagnosis (and outcomes) as well as relevant lab information.

This will allow a more granular assessment of use quantities and, most importantly, assessment of appropriateness of antimicrobial use.

AMC – limitations and recommendations

Since CAPTURA was unable to collect AMC data or support analysis of already collected data, specific recommendations could not be provided. But it is evident that AMC monitoring has not been done in a systematic manner in Nepal. It is, therefore, important to acknowledge that the DDA-led activity is continued prospectively, and the findings of the work are shared with key stakeholders for planning future efforts. Nepal is encouraged to collect and compare data across several years by establishing a robust AMC surveillance system to monitor antibiotic consumption over time. Specifically, it is advised to ensure that future data collection is done at a national level using the WHO methodology.

CAPTURA developed a freely available data template and visualization tool, which has been shared with the QSRD, MoHP. This will allow monitoring of trends and eventually contribute to a systematic and quality AMC data to GLASS AMC module. Early detections of changes in antibiotic consumption patterns merits further exploration, which may have policy implications and/or lead to stewardship interventions.



SECTION

05

Appendix

1. CAPTURA's data definitions

Project metadata constitutes all the information collected directly by and as part of the CAPTURA project. This data includes:

- information collected by landscape- and desktopreviews, and from interviews on the names, function, and location of facilities etc.
- information collected to identify, quantify, and prioritize data sources
- information collected to assess the quality and relevance of data sources or facilities generating data

Most of the project meta-data is collected by questionnaires generated for the purpose of and administered by the CAPTURA project.

Project facility data is the actual retrospective source data from the identified facilities, which has been identified and prioritized for collection. This data includes historical AMR, AMU or AMC data already collected in the facilities.

Antimicrobial resistance (AMR):

AMR data refers to microbiology laboratory data with a special focus on antimicrobial susceptibility test results of WHO priority pathogens²¹ (excl. TB). This data may or may not include characteristics of the person from whom the sample was drawn. Examples of AMR data may be isolate level test results from microbiology labs or aggregate data on AMR testing from hospitals such as antibiograms.

Antimicrobial use (AMU):

AMU data refers to records of dispensed antibiotics to individual patients (e.g., prescription data including patient information and potentially also information on indication or diagnoses). Examples of AMU data, for the purpose of CAPTURA project, include pharmacy-level records on dispensed antibiotics to patients/customers and hence differentiated into the individual prescription level.

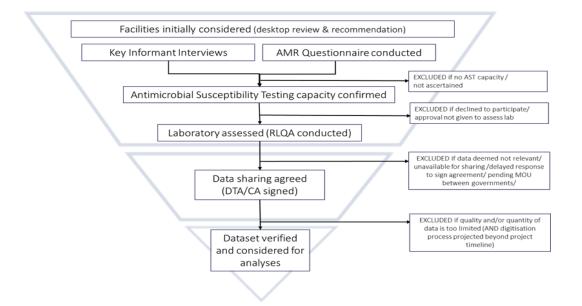


2. Metadata methodology

The AMR Questionnaire assisted CAPTURA and MoHP to collect information on AMR data available at each facility, the methods used to collect it, format of the stored data, and additional indicators prior to collection of AMR datasets from each laboratories selected (see overview of variables in the next page).

A 'Rapid Laboratory Quality Assessment Tool for AMR' (RLQA) was used to rapidly assess selected quality indicators of laboratories' pathogen identification and antibiotic susceptibility testing for the past 3 years. The information was collected from a person who had access to the historical records, necessary information regarding the laboratory and adequate knowledge about the microbiology processes done at the laboratory for at least the past three years. The RLQA assesses seven sections: Equipment, Staffing, Media, Pathogen Identification, Antimicrobial Susceptibility Testing (AST), Internal Quality Control (IQC), and External Quality Assurance (EQA). It is important to note that the RLQA tool and the associated scores do not represent a comprehensive and validated microbiology lab assessment.

The AMU Questionnaire assisted CAPTURA and MoHP to understand the antimicrobial use (AMU) data available at each facility, the methods used to collect it, format of the stored data, and additional indicators in prioritizing the facilities to be considered for future AMU surveillance (see overview of variables in the next page).





CAPTURA AMR Metadata and Priority Variables

Facility Location
Public or private facility
Type of culturing conducted
Ability to conduct Antimicrobial Susceptibility Testing (AST)
How AST performed (automated or manual)
Average number of AST per month
AST data format (paper or electronic)
Number of years of available AST data
Presence of Laboratory Information System
Presence of internet connectivity at facility
Priority and Specialized Variables
Sample Origin (Human/Animal/Food)
Date of Birth/ Age
Sex
Patient Location (ward/clinic)
Healthcare Facility Admission Date (if inpatient)
Healthcare Facility Date of Visit (if outpatient)
Specimen Date
Specimen Type
Culture Result (organism isolated)
AST Interpretation (R, I, S)
AST Measurement (disk diffusion zone diameter/MIC value)
Antibiotics Prescribed After Specimen Collection
Diagnosis (after laboratory results provided)
Patient Outcome
Date and Cause of Death (if applicable)
Additional/Recurrent Isolates/Infections
Additional Patient Information
(e.g., change in initial therapy, date of discharge,
comorbidities, date of discharge, etc.)

CAPTURA AMU Metadata and Priority Variables

Metadata
Facility Location
Public or private facility
Located within a hospital/health center
In-patient ward, Out-patient ward, Emergency Department
Number of staff working at facility and qualifications
Source of antimicrobials
Antimicrobial distribution data format (public or private)
Number of years of recorded data
Data format (e.g., paper or electronic)
Type of software used
Prescription linked to patient diagnosis
Ability to conduct data analysis
Presence of internet connectivity at facility
Priority and Specialized Variables
Patient Age
Patient Sex
Date of Prescription
Department (OPD, IPD, ED)
Type of Drug (Drug Class)
Ingredients
Strength of Drug
Formulation Type
Route of Administration
Product Name
Manufacturer
Pack Size Unit /Number of Doses Distributed
Daily Defined Doses (DDD)
Indication for Prescription / Diagnosis
MDR Risk
Product Origin
Brand Name or Generic
Previous Antimicrobial Prescriptions
Change to Initial Therapy



3. Contents of CAPTURA's WHONET AMR reports for facilities

Epidemiology Report
1. Data volume
2. Patient and sample details
2.1 Patient demographics
2.2 Location details
2.3 Sample details
3. Organism statistics
3.1 Organism frequencies
3.2 Organism frequencies by specimen categories
3.3 Organism trends
4. Antimicrobial statistics
4.1 Gram-positive and Gram-negative antibiograms
4.2 Isolate alerts - Important resistance
4.3 Multidrug resistance: ECDC definitions of MDR/XDR/PDR
4.4 Multidrug resistance: Resistance profiles
5. Reporting to the World Health Organization and the United Nations
5.1 WHO Global Priority List of Antibiotic-Resistant Bacteria
5.2 WHO GLASS results
5.3 United Nations Sustainable Development Goals
6. Cluster detection
6.1 Cluster detection by species
6.2 Cluster detection by resistance profile
Appendix A. Antibiograms
Test practices and quality report
1. Data entry and management
1.1 Data volume
1.2 Completeness and validity of data entry
2. Quality control testing
3. Organism results
3. Organism results 3.1 Capacity for organism identification
3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms
3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms 3.3 Blood culture results
3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms 3.3 Blood culture results 4. Antimicrobial susceptibility test practices
 3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms 3.3 Blood culture results 4. Antimicrobial susceptibility test practices 4.1 Antibiotic Configuration
3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms 3.3 Blood culture results 4. Antimicrobial susceptibility test practices
 3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms 3.3 Blood culture results 4. Antimicrobial susceptibility test practices 4.1 Antibiotic Configuration 4.2 Antibiotic tests without validated breakpoints 4.3 Regularity of antimicrobial testing
3. Organism results 3.1 Capacity for organism identification 3.2 Capacity for the isolate of fastidious organisms 3.3 Blood culture results 4. Antimicrobial susceptibility test practices 4.1 Antibiotic Configuration 4.2 Antibiotic tests without validated breakpoints



4. Glimpses of CAPTURA activities in Nepal (2019-22)

Pictures from CAPTURA's visit to MoHP, May 2019



Pictures from CAPTURA's AMR and AMU Data Review Meeting in Kathmandu, May 2022





Pictures from CAPTURA's Dissemination Workshop in Kathmandu, May 2022





