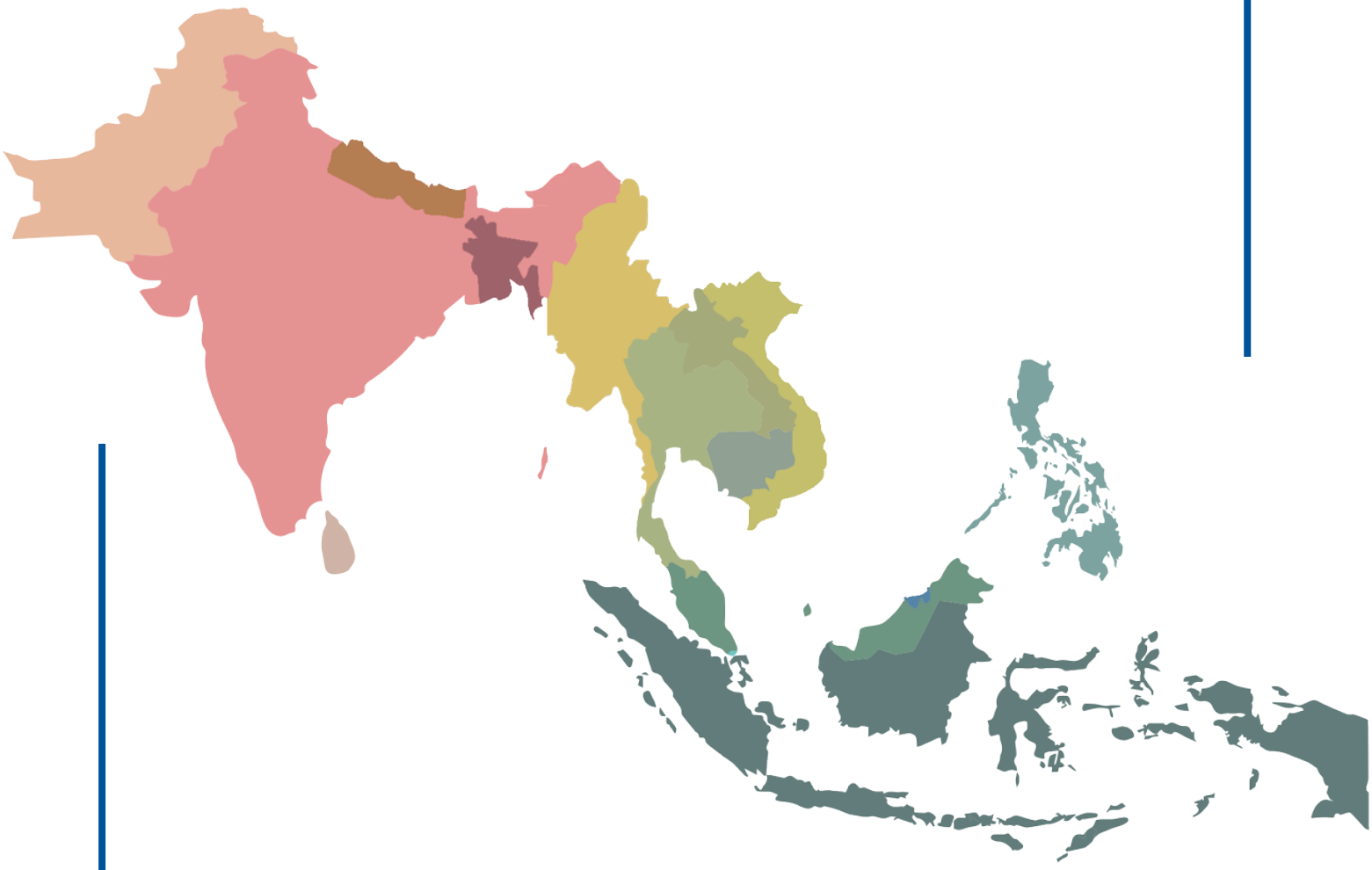
Roadmap for Pathogen Genomics in Asia

Results from a Multi-Country Assessment (2023)



Asia Pathogen Genomics Initiative

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Executive Summary

Asia remains the region of the world most vulnerable to new and emerging disease threats. During the COVID-19 pandemic, pathogen genomic surveillance using next generation sequencing (NGS) has proven to be a powerful tool to detect novel pathogens, track emerging variants, investigate outbreak clusters and provide insights to global genomic epidemiology.

The Asia Pathogen Genomics Initiative (Asia PGI) is a multi-country coordination and capacity development platform established to accelerate the application of NGS within existing infectious disease surveillance efforts among low- and middle-income countries (LMICs).

To assess the current state of pathogen genomic surveillance in the region, we conducted a cross-sectional survey with national partners supporting pathogen genomic surveillance efforts across 13 countries in south and southeast Asia between June 2022 and March 2023. The survey explored national partnerships, financing, policy and guidelines, procurement and supply chains, laboratory capacity, quality assurance, bioinformatic capability and data sharing.

Findings suggest that all 13 Asian countries are conducting in-country pathogen genomic sequencing with capacity extending across multiple sectors, including national public health laboratories (NPHLs), private and academic partners. Pathogens prioritised for genomic surveillance included SARS CoV-2, tuberculosis, antimicrobial resistant bacteria, arboviruses and influenza. Furthermore, many countries have applied NGS to detect unknown pathogens (metagenomics) in humans with roughly half also investigating unknown pathogens in animals or the environment.

Financing for genomic surveillance of infectious diseases remains heavily reliant on external donor support. While few countries have a national strategic plan and national guidelines that includes pathogen genomic surveillance, most have expert panels to advise policy makers on the use of pathogen genomic data.

NGS platforms deployed in Asia include Illumina and Oxford Nanopore Technologies (ONT), followed by ThermoFischer and MGI/BGI. Supply chain challenges were identified as a major barrier with countries reporting long lead-times for purchasing and equipment repair, with median re-supply times for reagents and consumables reaching 8 weeks. The regional median time between sample collection and sequencing generation/reporting was estimated at 18 days. While laboratory guidelines and protocols for pathogen sequencing exist, few laboratories have been accredited by national or international bodies and external quality assurance is largely absent. Majority of the countries are sharing over 75% of pathogen genomic data on publicly available platforms. However, the in-country capacity for the analysis of genomic data remains a challenge and reproducibility of results is uncertain.

Despite all countries in Asia having established national systems to support early pathogen detection using advances in genomics, more coordinated regional efforts are required to optimise cost-efficient system-design for public health impact. Pivoting the capacity built during COVID-19 towards novel, emerging and endemic pathogens is a priority. A series of recommendations (**Table 1**) are outlined to respond to challenges identified with the aim of accelerating adoption and scale in the region.

Table 1. Recommendations to accelerate pathogen genomic surveillance in Asia

	Key constraints	Recommendations
Financing	Insufficient and unsustainable domestic financing; over-reliance on donors/external partners	• Develop national investment cases for pathogen genomic surveillance • Prioritise genomic surveillance in country applications to global financing mechanisms (The Global Fund, the Pandemic Fund) • Pooled procurement support for genomic surveillance commodities through established global procurement catalogues
Policy and guidelines	Few LMICs in Asia have updated comprehensive national strategic plans that integrate pathogen genomics into wider surveillance efforts	• Establish multi-partner national coordination mechanisms that leverage capacity between national public health institutions, academic bodies and other stakeholders • Define where pathogen genomics should take place in routine systems vs research • Develop pragmatic decision tree tools to assist countries in designing cost-efficient approaches to pathogen genomic surveillance plans that optimise public health impact • Design integrated monitoring frameworks for One Health surveillance that include targets for genomic surveillance • Document regional learning, emerging best practices and use-cases on the value proposition of pathogen genomic surveillance
Supply chain	Procurement, supply and distribution bottlenecks for NGS equipment, consumables and reagents limit the timeliness of response and impact of pathogen genomic surveillance	• Enhance regional supply chains to support regional manufacturing, warehousing and distribution of genomics commodities • Track procurement lead-times • Address customs/tax-exemption challenges through coordinated national engagement • Establish mechanisms for supply chain problem solving between manufacturers and country partners
Laboratory infrastructure	Pathogen genomics remains a novel and rapidly evolving technology with on-going training needs. Timeliness of sequencing and reporting remains constrained among most LMICs in Asia.	• Coordinate multi-platform hubs for laboratory training in genomic sequencing for endemic and novel pathogens • Facilitate joint capacity development efforts between human and animal laboratories • Design, test and share system-level innovations that reduce the time between specimen collection, pathogen sequencing and reporting
Quality assurance	Laboratories undergo limited national/ international accreditation and are not undergoing External Quality Assessments (EQA)	• Define national accreditation standards for pathogen genomics • Establish low-cost regional EQA • Link EQA efforts to forward looking capacity development efforts
Bio-informatics and data sharing	Bioinformatics capacity remains limited. Data quality standards need to be strengthened to ensure high utility of sequences shared regionally and globally.	• Enhance in-country bioinformatics capacity • Work with global partners to develop and implement meta-data standards for samples used in pathogen genomic surveillance • Support efforts to integrate human and animal surveillance systems • Work with service providers to recommend system resources that address computing and storage needs as well as security concerns

Background

Asia is particularly prone to emerging infectious disease outbreaks. A dense population with high rates of mobility, abundant wildlife with frequent human-animal interaction, climate stress and a rapidly changing environment combined have placed the region at very high risk of infectious disease outbreak and transmission[1]. Therefore, cross-country efforts to strengthen infectious disease surveillance remain a central pillar of regional outbreak preparedness.[2]

NGS for pathogen genomic sequencing has been identified as a powerful tool to detect novel pathogens[3, 4]. During the COVID-19 pandemic NGS had an important role of contributing to the initial identification of SARS-CoV-2 and allowing for detection and monitoring of new variants of concern.[5] Technical analyses of SARS-CoV-2 sequences, along with supporting population level data, allowed public health officials and policy makers to understand geographic and temporal spread within and across borders, providing critical evidence to inform timely public health interventions[6,7]. In addition, the availability of genomic data is crucial for the development of outbreak response and prevention tools, such as diagnostics and vaccines (including tailored seasonal influenza and SARS-CoV-2 vaccines)[8-10].

While NGS for surveillance of pathogens within humans is well-established, translation to animal and environmental surveillance are increasingly important complementary strategies for detecting early signals of outbreak risk[11, 12]. In Asia, NGS has been used for pathogen detection in domestic and wild animal reservoirs in order to identify and confirm zoonotic transmission and locate the source of outbreak[13, 14]. During the COVID-19 pandemic, NGS was also used for pathogen tracking in wastewater and other environmental samples to better monitor and understand community infection dynamics, to assess the effectiveness of existing control measures and to serve as an early warning strategy[15, 16].

Although NGS has been employed for several years as an infectious disease surveillance tool in high-income settings, major global disparities exist in its application among low- and middle-income countries (LMICs)[17, 18]. During the COVID-19 pandemic, high income countries submitted 10-fold more sequences per COVID-19 case than LMICs[19]. While NGS for pathogen sequencing has also been established in resource-constrained countries, it has primarily been used to support ad hoc outbreak investigation and research, with limited integration into routine surveillance systems[20-23]. The World Health Organisation (WHO) Global Genomic Surveillance Strategy (2022-2032)[24] highlights common challenges faced by low resourced countries, including limited government commitment and funding, low capacity for bioinformatics and data analysis, weak public health infrastructure and laboratory capacity, and the lack of standardised sequencing methods and practices[25].

Accelerating the application of genomic sequencing in infectious disease surveillance to enhance outbreak preparedness among LMICs in Asia is an urgent priority. In these contexts, NGS is a relatively recent arrival, with much of the experience and capacity for pathogen genomic surveillance built during the SARS CoV-2 outbreak. While the cost of NGS has fallen dramatically with parallel increases in sequencing output, the technology remains relatively expensive in low-resource settings[26]. Pivoting existing SARS-CoV-2 sequencing capacity towards priority endemic pathogens, accelerating the adoption of integrated rapid cost-efficient approaches to surveillance, and facilitating cross-country data sharing are central to wider regional health security efforts. Additional support will be required in demonstrating the value proposition of NGS, exploring NGS use-cases for public health impact, and translating the WHO Global Strategy into costed national surveillance plans for

tackling novel, emerging and endemic pathogens.

The Asia Pathogen Genomics Initiative (Asia PGI) was established in 2021 as a multi-country collaboration and capacity development platform with the aim of accelerating the application of NGS to infectious disease surveillance. The initiative builds on learning from a parallel effort, the Africa PGI, which was established in 2018 as a platform for partnerships to effectively implement and translate pathogen genomics into public health action[27]. As the regional landscape for pathogen genomic sequencing in Asia has evolved substantially in recent years, generating a deeper understanding of the current state of pathogen genomic surveillance in Asia alongside country priorities are essential to inform national strategic planning, technical support needs, global financing, and resource allocation.

This roadmap presents the status of pathogen genomic surveillance across Brunei and 12 LMIC countries in South and Southeast Asia. Brunei was included in Asia PGI due to their only recent adoption of NGS for pathogen surveillance, and therefore their need for technical support. The present assessment focuses on documenting national partnerships; enabling factors including financing, policies, guidelines, and regulatory systems; NGS capacity for pathogen surveillance, the major NGS and bioinformatics platforms utilised; challenges and bottlenecks experienced by countries; and key priorities moving forward. Findings from this assessment inform a regional road map to assist the development of integrated national genomics strategies and facilitate multi-sectorial, cross-country technical support and resource allocation that accelerate adoption and scale.

Methods

A cross-sectional survey was rolled-out across 13 countries in south and southeast Asia: Bangladesh, Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Nepal, Pakistan, Philippines, Sri Lanka, Thailand and Vietnam. The survey tool, or Landscape Assessment, is a semi-quantitative questionnaire containing over 90 questions. Partners from participating sites across all countries self-administered the survey between June 2022 to March 2023 supported through virtual and on-site consultations. Respondents included representatives from major national public health institutions and research entities engaged in pathogen genomic surveillance at a national level. Perspectives from stakeholders including advisors to policy makers, laboratory managers, and bioinformaticians were required to complete the different sections of the survey. Countries and their partner institutions involved in the landscape assessment are highlighted below (**Figure 1**).

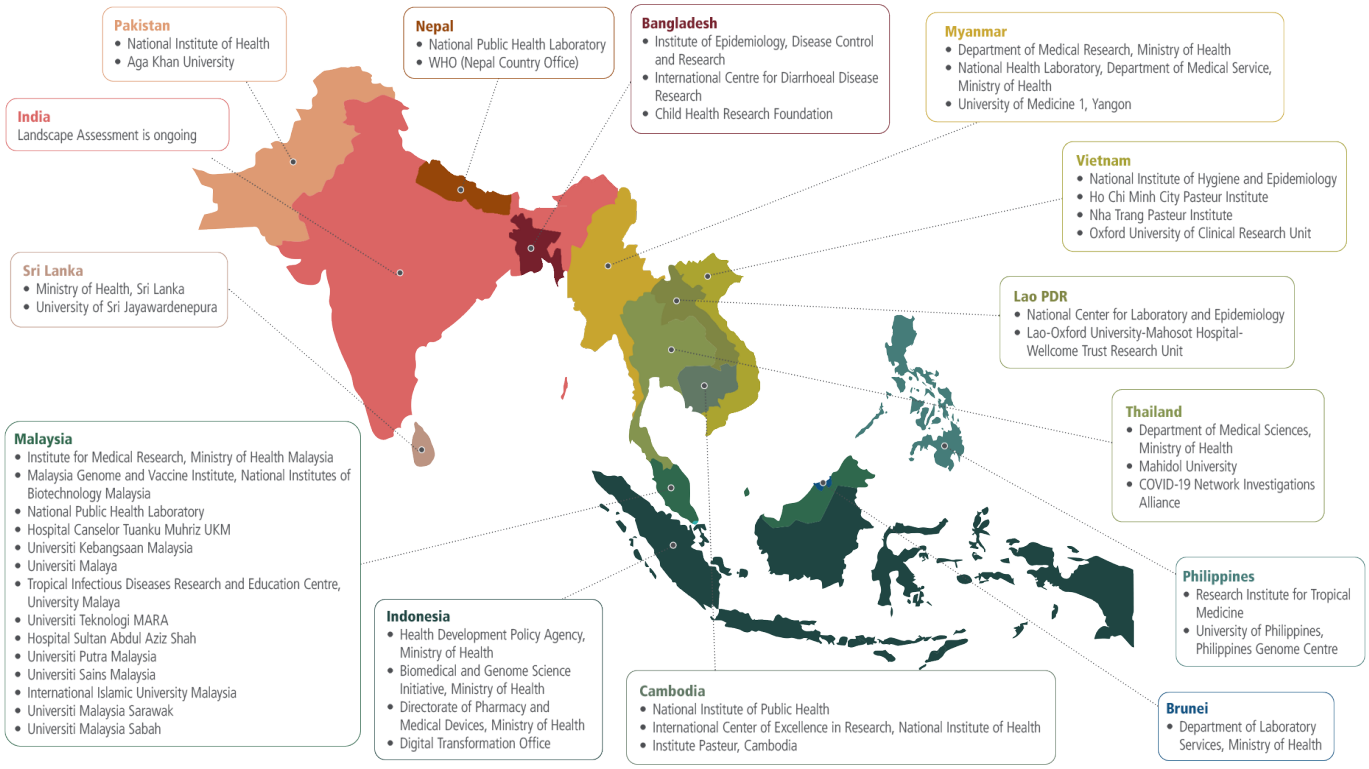

***Figure 1**. Asia PGI country partners*

Framework development

Expert consultations were held with a reference group of global and regional experts in pathogen genomic surveillance to identify thematic focus areas which led to the development of a guiding framework for the Landscape Assessment (**Figure 2**). This guiding framework was composed of three main sections, i.e. i) enabling environment, ii) capacity, iii) quality assurance and data sharing, which together captured 25 key indicators of pathogen genomic surveillance.

Landscape assessment tool

A scoping of existing tools for pathogen genomic surveillance assessment (such as tools developed by the UK Health Security Agency, World Health Organization, US-Centre for Disease Control, and others) was conducted between February and March 2022 (**Annex 1**). To facilitate alignment with prior research and NGS assessments, selected questions and recommendations from these tools were used as a reference for the development of the landscape survey tool. The survey (**Annex 2**) was structured to capture an end-to-end assessment of pathogen genomic surveillance at the national level. The questionnaire was further refined from April – May 2022 following consultations with country partners and the Asia PGI reference group (which included representatives from the WHO, FIND, the Bill and Melinda Gates Foundation, the Africa Pathogen Genomics Initiative and others). The final landscape questionnaire with over 90 questions was rolled out using anelectronic word document format.

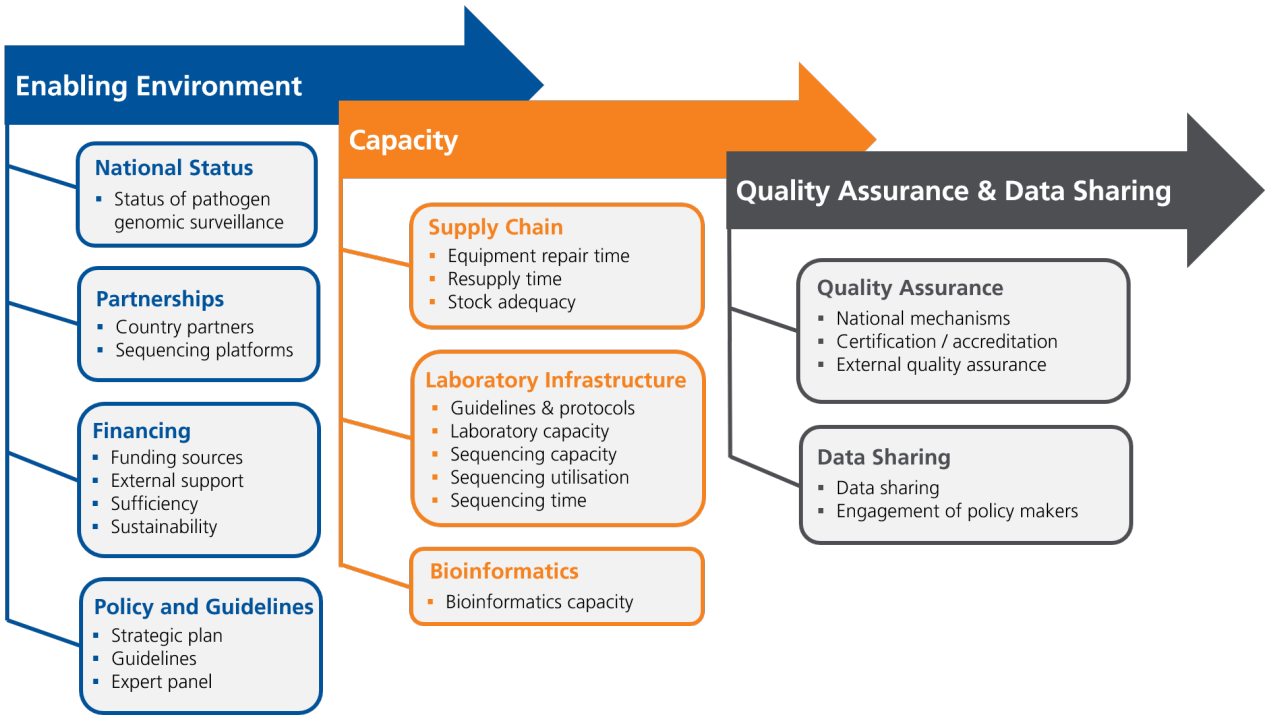

Figure 2. *Landscape assessment framework for pathogen genomic surveillance*

Regional partner institution recruitment

Relevant country partners were identified through consultations with national public health institutions and related research entities involved in pathogen genomic surveillance. Participation was voluntary and a list of the 42 participating institutions across the 13 countries is included in **Annex 3**. Responding institutions represented a range of different sectors including government, academia, public/private laboratories, and NGOs directly involved in pathogen genomic sequencing efforts. The study was exempted from full Institutional Review Board due to minimal risk to subjects.

Data collection and validation

The research team held introductory sessions with country respondents to introduce the objectives, format, and content of the survey. Country respondents were given approximately four weeks to complete the survey, which was conducted through self-assessment either jointly or separately by reporting agencies. Survey data were then entered into Microsoft Excel using double-data entry for all response fields to ensure the integrity of data transcription.

Initial findings were summarised and presented back to the country respondents virtually for data verification and validation. In cases where multiple surveys were completed per country, responses were merged and then validated by country teams. Inconsistencies or missing quantitative responses that required further clarification were discussed in detail during the validation calls. Participants had the opportunity to elaborate on their open-text responses to provide qualitative insights on challenges and bottlenecks. Country summaries, comprised of data from completed questionnaires and validated calls, were prepared for each country and shared with country teams for validation. Data were compiled for cross-country analysis and data visualisation using the software, Tableau 2023.1.

Data analysis and summary indicators

Using survey responses, a total of 25 cross-country summary indicators were calculated to assess the regional status of pathogen genomic surveillance, partnerships, financing, policy and guidelines, supply chain, laboratory capacity, quality assurance, bioinformatics and data sharing (**Table 2**). Responses to survey questions were captured as Likert scores (scale of 1 – 5), binary (Yes/No), or continuous data. Likert data are shown as proportions of countries scoring above an indicated threshold (e.g., score of 4 – 5 on the Likert scale), with higher values on the scale reflecting higher scores. Data are presented as cross-country averages or medians based on summary responses as appropriate. Continuous data are displayed as a cross-country means for normally distributed data, or as cross-country medians for non-normally distributed data.

Results

Between June 2022 and March 2023, the survey was completed by 42 responding institutions from 13 Asian countries. **Table 2** displays cross-country summary findings. More detailed country-level data are presented in individual country profiles (**Annex 4**).

Priority pathogens: Pathogens are listed in order of their median Likert score (3 = medium priority, 4 = high priority, 5 = high priority). Coronaviruses, tuberculosis, anti-microbial resistance (AMR) bacteria, influenza viruses, and arboviruses were reported as the highest priority pathogens across countries in the region. Followed by polio, RSV, measles, rubella, viral hemorrhagic fevers, HIV and malaria which were ranked as medium priority. Countries also reported on the use of NGS in pathogen surveillance in the last 5 years, captured by type of surveillance activity, such as routine, outbreak or research purposes, and by surveillance context including human or environment (**Figure 3**). Across all pathogens, country responses consistently indicated the use of pathogen genomics in human surveillance as being more prevalent than environmental surveillance.

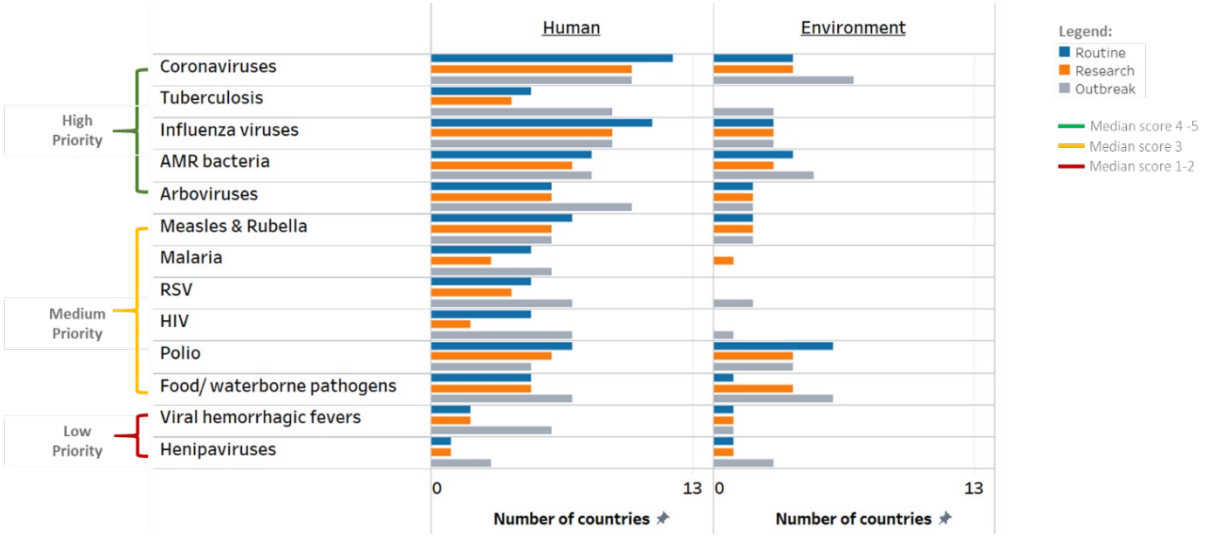

Figure 3. *Pathogens prioritised for genomic surveillance in the past 5 years by surveillance type and context*

National Status: All countries (13/13) have applied NGS for routine pathogen surveillance over the previous two years. Additionally, most countries (11/13) are using metagenomic NGS to detect unknown pathogens in humans, while approximately half of countries have applied NGS for environmental surveillance (7/13) or animal surveillance (7/13).

Partnerships: A range of formal and informal partner coordination mechanisms had been established, with pathogen genomic surveillance capacity residing across the public sector (43%), academic institutions (39%) the private sector (6%) and other partners (12%). The main NGS platforms being utilised across countries are Illumina, Oxford Nanopore Technologies, Thermo Fisher and MGI/BGI.

Financing: Resources to support pathogen genomic sequencing partnerships are derived primarily from donors and external partners (57%) followed by contributions from the public sector (328%), academic institutions (6%) and private (4%). Most countries in the region have indicated that the over-reliance on external funders is a major barrier for pathogen genomic surveillance. Only very few countries perceive that they have secured sufficient (2/13 countries) or sustainable (1/13 countries) funding for pathogen genomics in the coming five-year period.

Policy and guidelines: 7/13 countries have a national strategic plan that integrates genomics into pathogen surveillance. 6/13 had developed guidelines for genomic surveillance of pathogens and 9/13 had established expert panels to advise policy makers and program managers on the use of pathogen genomic data for decision making.

Supply chain: Supply chain challenges are a major concern. Long lead-times were highlighted in purchasing equipment, reagents and consumables. Equipment repair times and stock outs of consumables and reagents were identified as challenges, with median resupply times reaching 8 weeks.

Laboratory capacity: Over 130 laboratories were reported as contributing towards pathogen genomic surveillance across the 13 countries assessed. These represent a median of 0.12 labs per million population, which together contribute a median of 6.8 pathogen sequences per million population each month. 9/13 countries reported having developed laboratory guidelines and protocols for NGS. Countries reported utilising only 51% of their maximum monthly sequencing capacity in the past year. Additionally, the median time between sample collection and sequence generation/reporting was 18 days.

Bioinformatics: Bioinformatics is largely reliant on proprietary software or solutions provided by NGS manufacturers. 6/13 countries reported utilising published workflows or in-house pipelines to conduct genomic data analysis.

Quality assurance: While governance mechanisms for ensuring national laboratory quality exists in most countries (9/13), few laboratories conducting pathogen genomic sequencing have been certified or accredited by any local or internationally recognised programs, or have participated in external quality assurance programs for pathogen sequencing.

Data sharing: Most countries (9/13) reported data sharing using publicly available platforms for at least 75% of pathogen samples sequenced. Similarly, most countries (10/13) reported regularly sharing genomic data to policymakers to inform decision making.

Barriers and priorities: Countries were asked to rank major barriers and future priorities for genomic surveillance (**Figure 4**). The most commonly identified barriers were related to financing constraints. These were followed by constraints in human resources, availability of reagents and consumables, and computing power and storage. The most commonly reported future priorities for pathogen genomics included training on bioinformatics and data analysis, improving availability and lead time for sequencing reagents and equipment, and increasing and improving calibration, service and maintenance of laboratory and sequencing equipment.

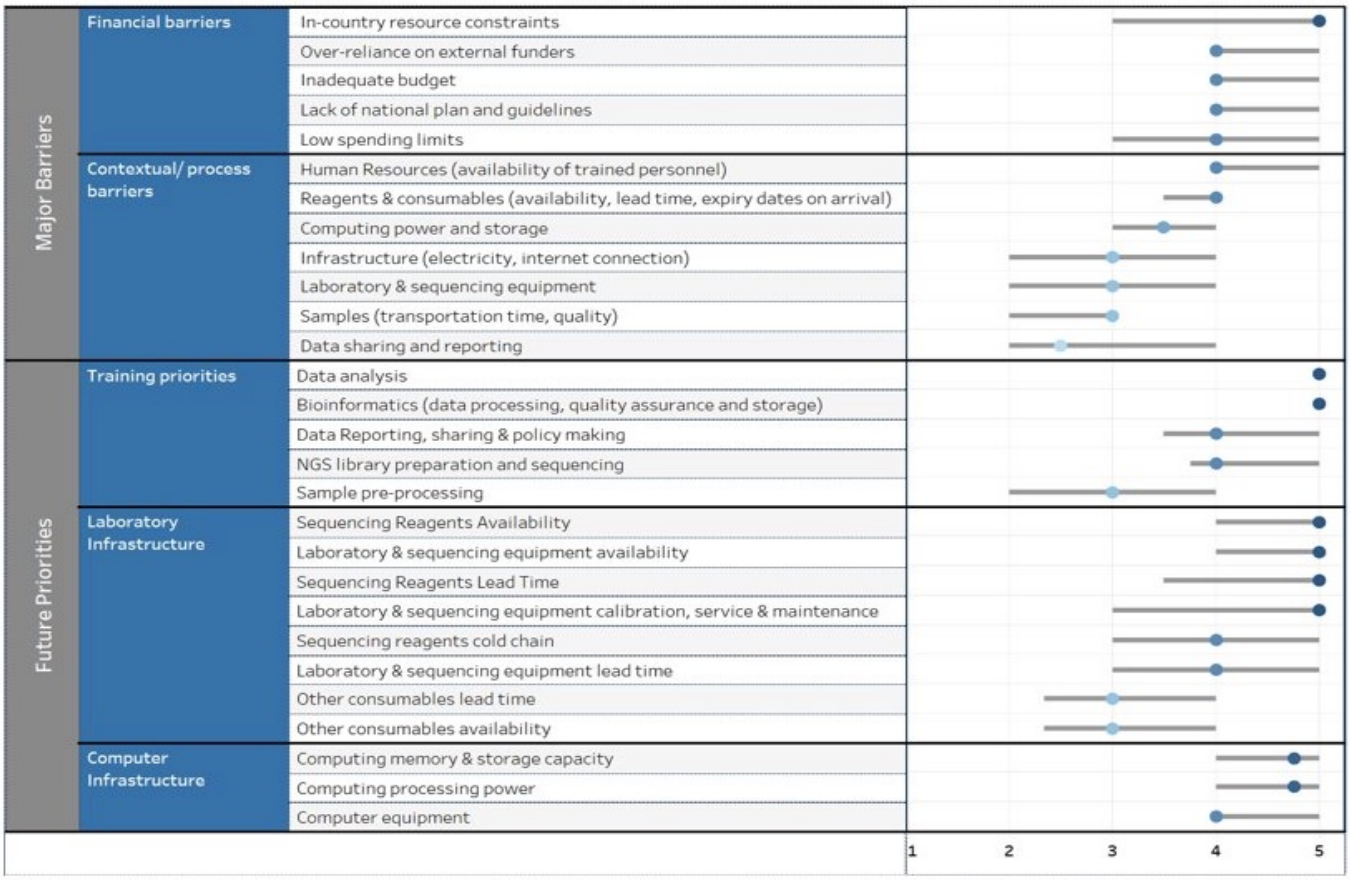

Figure 4. *Major Barriers and Future Priorities for pathogen genomic surveillance across 13 countries (Median Likert Score 1-5)*

Country context: In addition to the quantitative findings presented above, key themes emerged from country consultations and data validation exercises with country partners. Illustrative points regarding the country context for NGS application to infectious disease surveillance are highlighted below (**Figure 5**).

Bangladesh

- Pathogen specific consortiums exist along with a national coordination group that was established in 2021.
- Sequencing is centralised at the capital city, Dhaka. Samples from states across the country take ~2 weeks to reach the capital.
- Efforts are underway to move to a more decentralised system for sequencing.

Brunei

- In-country pathogen genomics for public health surveillance were built in response to the COVID-19 pandemic and were largely supported by donations in the past year.
- Sequencing is centralised within the public health laboratory.
- Long-term sustainability planning and wider integration into national surveillance of other pathogens are currently being discussed.

Cambodia

- Three public laboratories in Cambodia are engaged in strengthening local sequencing capacity and genomic epidemiology expertise.
- They now use genome-sequencing technology bought during the COVID-19 pandemic to sequence other pathogens, like in February with H5N1 Bird Flu.

Indonesia

- Established its first national integrated biomedical program, the Biomedical and Genome Science Initiative (BGSI) to support the National Genome Project. Human genomics efforts may be leveraged to build capacity for pathogen genomics surveillance.
- While funding may not be the most pressing issue, limited sequencing capacity is a major barrier.

Laos

- Despite growing interest to establish genomic surveillance, there is a shortage of trained laboratory staffs due to lack of training and financing opportunities.
- There are significant challenges in the pricing and supply chain that hamper sustainability and cost-effectiveness of genomic surveillance.

Malaysia

- Unlike most other countries, two ministries - Ministry of Health (MOH) and the Ministry of Science, Technology and Innovation (MOSTI) work together to support sequencing in Malaysia.
- Private laboratories have the capacity to support so that the total output can be expanded when needed.

Myanmar

- NGS capacity for Pathogen genomic surveillance lies in the academic sector. Current funding mechanism mainly involves the public sector and WHO equally.
- Main barriers relate to shortage of trained personnel and reagents and consumables. Inadequate budget and lack of national plan and guidelines were also highlighted as common barriers.

Nepal

- In-country sequencing capacity was built only during the COVID-19 pandemic. While a third of the samples are sequenced in-country, remaining are still shipped overseas for sequencing.
- Data from private institutions is limited. Only National Public Health Laboratory (Nepal) perspective is captured here.

Pakistan

- Vertical programs and plans exist for specific pathogens, such as Polio, TB and SARS-CoV-2, but a single comprehensive plan is still pending.
- While funding from donors is helpful to ramp up the capacity in the short term, sustainability of funding for the long-term is still uncertain.

Philippines

- Philippines is gearing up to integrate WGS for influenza as part of The Philippines National Influenza Centre.
- There are procurement issues with respect to supply chain management, it takes 12 weeks of resupply time for reagents and consumables.

Sri Lanka

- Ongoing economic crisis is leading to severe funding shortages. Plans for sustainable sources of funding are still uncertain.
- Despite local interest in expanding genomic surveillance, the unstable economic situation is leading to a shortage of trained personnels due to emigration or 'Brain Drain'.

Thailand

- One of the few countries where the majority of NGS funding (75%) and NGS capacity for genomic surveillance (75%) are located in the public sector.
- Although Ministry of Public Health is responsible for pathogen genomic surveillance, other independent consortiums also conduct NGS, raising issues of coordination and verticalisation of NGS efforts in country.

Vietnam

- The NGS and pathogen genomic surveillance capacity exists among multiple partners and sectors. This study may not have captured the full capacity in the country, especially those represented by the private sector.
- Training priorities for Data analysis, and Computer infrastructures are the pressing needs in term of future priorities.

Figure 5. *Country context of NGS application to infectious disease surveillance.*

Table 2. *Findings from a landscape assessment of pathogen genomics across LMICs in Asia*

THEME	INDICATOR	DEFINITION	VALUE
National status	Status of pathogen genomic surveillance	Proportion of countries with NGS capacity to support pathogen genomic surveillance in past 2 years	13/13 (100%)
	NGS for unknown pathogens	Proportion of countries using NGS to detect *unknown pathogens*	Human = 11/13 (85%) Animal = 7/13 (54%) Environment = 7/13 (54%)
Partnerships	Country partners	Average proportion of NGS capacity for pathogen genomic surveillance, by sector	Public = 43% Academic = 39% Private = 6% Others = 12%
	Sequencing platform	Proportion of countries using platform for genomic surveillance, by manufacturer	ONT = 11/13 (85%) Illumina = 11/13 (85%) ThermoFischer = 4/13 (31%) MGI/BGI = 2/13 (15%)
Financing	Funding sources	Average proportion of funds provided for pathogen genomic surveillance in the past year, by funding source	External = 57% Public = 32% Academic = 6% Private = 4%
	External support	Proportion of countries where over-reliance on external support is low/ no barrier for NGS	3/13 (23%)
	Sufficient funding	Proportion of countries who perceive sufficient funding for pathogen genomic surveillance systems over the coming 5 year cycle	2/13 (17%)
	Sustainable funding	Proportion of countries who perceive sustainable funding for genomic surveillance systems for the coming 5 year cycle	1/13 (8%)
Policy and guidelines	Strategic plan	Proportion of countries where a national strategic plan exists that includes pathogen genomic surveillance	7/13 (54%)
	Guidelines	Proportion of countries where national guidelines exist for pathogen genomic surveillance	6/13 (46%)
	Expert panel	Proportion of countries where a national expert panel or technical advisory group exists to advise government interpretation/use of pathogen genomic surveillance data	9/13 (69%)
Supply chain	Equipment repair lead time	Proportion of countries who perceive equipment repair lead time as low/ no barrier to sequencing capacity	6/13 (46%)
	Resupply time length	Median re-supply time between order and receipt of reagents and consumables	8 weeks
	Stock adequacy - reagents and consumables	Proportion of countries reporting no stock out of reagents / consumables in the past 6 months	10/13 (77%)
Laboratory capacity	Laboratory guidelines and protocols	Proportion of countries where laboratory guidelines and protocols exist for pathogen genomic sequencing	9/13 (69%)
	Laboratory capacity	Median number of laboratories in country performing NGS for public health surveillance, per million population	0.12 /million pop
	Sequencing capacity	Median monthly pathogen sequences generated in the past year, per million population	6.8 /million pop
	Sequencing utilisation	Average monthly sequencing output relative to maximum monthly sequencing capacity for the past year	51%
	Sequencing time	Median estimated time required for NGS surveillance between specimen collection, sequence generation and reporting	18 days

THEME	INDICATOR	DEFINITION	VALUE
Bioinformatics	Bioinformatics capacity	Proportion of countries with in-country bioinformatics expertise (defined as the ability to utilise published workflows (containerised or locally installed) or in-house pipelines for >75% of genomic data analysis)	6/13 (46%)
Quality assurance	National quality assurance mechanism	Proportion of countries where national quality assurance mechanisms exist for governance of national laboratory quality	9/13 (69%)
	Laboratory certification or accreditation	Proportion of countries where > 75% of laboratories conducting NGS have been certified or accredited by any local or internationally recognised body	1/13 (8%)
	External quality assurance	Proportion of countries where >75% of laboratories have participated in any proficiency testing or external quality assurance audits for NGS	2/13 (15%)
Data sharing	Data sharing	Proportion of countries reporting > 75% of total sequences are shared on public databases	9/13 (69%)
	Engagement of policymakers	Proportion of countries reporting regularly sharing genomic data to policymakers to inform decision making	10/13 (77%)

Discussion

While the utility of pathogen genomic sequencing in public health is well recognised, its application to infectious disease surveillance efforts among many high-risk countries in Asia has been limited. In this region during the SARS-CoV-2 pandemic, there was an upsurge in NGS capacity and its utilisation in SARS-CoV-2 surveillance[7]. In the current study conducted from June 2022 to March 2023, we assessed the status of pathogen genomic surveillance across 13 countries in South and Southeast Asia. Findings suggest all countries are conducting genomic sequencing of pathogens, although large variations in laboratory capacity and application of pathogen genomics in surveillance exist between countries. While NPHLs have the mandate for surveillance efforts,[28] a substantial portion of national pathogen genomic sequencing capacity sits within research bodies, academic institutions, and the private sector.

Securing adequate domestic and external financing are essential for accelerating and sustaining pathogen genomic surveillance for early detection in emerging economies. The relatively high cost of sequencing remains a barrier to adoption and scale among low resource countries in Asia. Countries remain heavily reliant on external partner support and donations, which account for the bulk of financing for pathogen genomic surveillance. Leveraging global financing mechanisms such as The Global Fund and The World Bank's Pandemic Fund are imperative to provide additional, long-term financing to address critical gaps among LMICs[29]. Despite a projected 1% increase in GDP invested into national government health spending on pandemic preparedness, developing national investment cases that coordinate resource streams between domestic and external sources is crucial[30]. Furthermore, a recent market assessment suggests LMICs are paying up to ten-fold more per sequence than high-income countries[26]. Opportunities for cost-reductions could be realised through more efficient system-design, and listing key equipment, reagents and consumables on global supply catalogues (The Global Fund, UNICEF Supply Division), to create pooled-procurement opportunities and linking procurement support to global financing. Clear volume estimates of country demand would be a pre-requisite, as would backing by external partner financing.

Financing would need to be informed by the development of comprehensive national surveillance plans that integrate pathogen genomics as an early detection strategy. Pivoting capacity built during COVID-19 towards routine surveillance of endemic pathogens is essential to sustain regional surveillance capability. Findings from this assessment suggest countries have prioritised a range of endemic pathogens for genomic surveillance, including coronaviruses, tuberculosis, anti-microbial resistance (AMR) bacteria, influenza, and arboviruses. Surveillance system-level design, planning and decision making is required to highlight the value-proposition of pathogen genomics to policy makers and program managers and to inform the development of context-relevant and pathogen-specific approaches. Integrated multi-pathogen One Health approaches to genomic surveillance of infectious diseases will allow for more cost-efficient system-design that maximises public health impact. To support these efforts, countries should leverage the full range of partnerships and identify where pathogen genomics should be positioned within NPHLs for routine surveillance, to complement the currently ongoing targeted research conducted by academic institutions and research partners. Linking national plans to clear guidelines and key performance metrics is essential. Finally, integration of pathogen sequencing with new surveillance approaches, such as environmental surveillance, may allow for cost-efficiency, rapid screening of multiple pathogens (polio, cholera, AMR) and outbreak prediction. Given the rapid pace of innovation in this space, documenting country experience around successful use-cases with active cross-country knowledge sharing has the potential to accelerate adoption and scale with maximum public health impact.

While many LMICs in Asia have established a diversity of sequencing platforms to support pathogen genomic surveillance, major procurement and supply chain barriers have presented major delays. Long lead times for procurement of reagents and consumables and equipment repair were identified as a common constraint by countries. During discussions, major manufacturers have reported some of the causes of long lead-times and price disparities as being due to local customs clearance and taxation on genomics commodities. In response to supply chain challenges, manufacturers are working to establish regional manufacturing and distribution hubs, with systems to track repair and procurement lead-times. Coordinated efforts with national ministries will be required to advocate for listing of equipment and commodities required for pathogen genomics as essential commodities for pandemic preparedness and to explore options for expedited import.

Issues of laboratory capacity and quality assurance were identified as major challenges by country respondents. These challenges were similar in the context of developing clinical metagenomics in LMICs[31]. The number of laboratories conducting pathogen genomic surveillance across LMICs in Asia remains comparatively limited, with additional infrastructure and training highlighted as a key priority. While laboratory guidelines and protocols for pathogen genomics exist, few facilities were certified or accredited and external quality assurance (EQA) for pathogen genomics is largely absent. Within the region, efforts are ongoing to support coordinated multi-platform capacity development hubs for laboratory training. Working with national bodies to develop accreditation standards for laboratories conducting pathogen sequencing and developing low-cost regional providers of EQA testing is essential to ensure a high level of quality assurance in pathogen genomic surveillance in the region.

Finally, improving regional bioinformatics capacity remains a pressing challenge. Countries remain reliant on bioinformatics tools provided by NGS manufacturers and expensive proprietary software. The lack of in-country bioinformatics expertise presents issues with adaptability and scalability of analysis. Although countries included in this assessment share sequencing data on publicly accessible sites (such as NCBI, EBI, GISAID), wide variations exist across countries. Global data indicates that during the SARS-CoV-2, sequencing far outpaced data sharing[32]. In addition, although countries report having technical committees to feedback the results of genomic surveillance to decision makers, the 18 day time horizon between sample collection and reporting limits the utility of pathogen sequencing to inform public health responses in real-time. National concerns regarding adequate computing resources for comprehensive data analysis, reporting and storage will need to be addressed. Linking pathogen genomic data to metadata, such as clinical and epidemiological information, is essential for real-time decision making. This will require establishment of meta-data standards for pathogen genomic surveillance[19] alongside efforts to bridge monitoring systems between human, animal and environmental health.

A key limitation of this study has been the focus on partner institutions that conduct pathogen surveillance mainly within the human health sector. There is potential to expand future work to agencies conducting pathogen surveillance in animal and environmental health, including those supported by national environmental agencies, the World Organisation for Animal Health (WOAH), and the UN Food and Agricultural Organization (FAO). The study methodology utilises a cross-sectional survey tool to capture respondent perceptions which is limited to the knowledge of the participants. The challenge with a quantitative survey tool is the lack of depth and full appreciation and explanation of local country context, which could be supplemented by future in-depth qualitative work. Moreover, many participants have responded with SARS-CoV-2 in mind, which may reduce applicability of results to other priority pathogens. However, the advantage to this methodology has been the

rapid collection of data that has allowed for a comprehensive cross-country assessment and dialogue. Repeat longitudinal assessments will be important to assess change over time and compare country capacities, barriers and priorities for pathogen genomic surveillance.

Conclusion

In summary, the application of pathogen genomic sequencing to infectious disease surveillance among LMICs in Asia remains at an early stage. The findings from this assessment inform a set of recommendations (**Table 1**) and road map for accelerating early pathogen detection through genomic surveillance across the region. The recommendations respond to challenges identified including the need for sustainable financing, strengthening national surveillance planning, addressing procurement and supply chain issues, improving laboratory capacity and quality assurance, and supporting advances in bioinformatics and cross-country data sharing. Coordinated efforts that draw from the full range of national partners, leverage the expertise of regional and global partners, and optimise support from manufacturers will be essential for advancing regional health security.

Annex 1: Reference tools for landscape assessment development

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***Annex 2**: Landscape assessment tool*

Click here to download and view the questionnaire used for the landscape assessment.

Annex 3: List of participating countries and institutions

Country	Institution	Percentage of total SARS-CoV-2 sequences submitted to GISAID (Jan – Dec 2022)
Bangladesh	1. Child Health Research Foundation (CHRF)	71%
	2. Institute of Epidemiology, Disease Control and Research (IEDCR, Bangladesh)	
	3. International Centre for Diarrhoeal Disease Research (icddr,b)	
Brunei	4. Department of Laboratory Services, Ministry of Health	100%
Cambodia	5. Institute Pasteur Cambodia (IPC)	100%
	6. International Center of Excellence in Research (ICER), National Institutes of Health	
	7. National Institute of Public Health (NIPH)	
Indonesia	8. Health Development Policy Agency, Ministry of Health	82%*
	9. Biomedical and Genome Science Initiative (BGSI), Ministry of Health	
Lao PDR	10. Lao-Oxford University-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU)	100%
	11. National Centre for Laboratory and Epidemiology (NCLE)	
Myanmar	12. Department of Medical Research, Ministry of Health	2%**
	13. National Health Laboratory (NHL) Department of Medical Service, Ministry of Health	
Malaysia	14. Malaysia Genome and Vaccine Institute (MGVI), National Institutes of Biotechnology Malaysia (NIBM)	84%
	15. Institute for Medical Research (IMR), Ministry of Health Malaysia	
	16. Hospital Canselor Tuanku Muhriz UKM (HCTM)	
	17. Universiti Kebangsaan Malaysia (UKM)	
	18. Universiti Malaya (UM)	
	19. Tropical Infectious Diseases Research and Education Centre (TIDREC), University Malaya	
	20. Universiti Teknologi MARA (UiTM)	
	21. Hospital Sultan Abdul Aziz Shah (HSAAS)	
	22. Universiti Putra Malaysia (UPM)	
	23. Universiti Sains Malaysia (USM)	
	24. International Islamic University Malaysia (IIUM)	
	25. Universiti Malaysia Sarawak (UNIMAS)	
	26. Universiti Malaysia Sabah (UMS)	
	27. National Public Health Laboratory	
Nepal	28. WHO (Nepal Country Office)	68%
	29. National Public Health Laboratory	

Country	Institution	Percentage of total SARS-CoV-2 sequences submitted to GISAID (Jan – Dec 2022)
Pakistan	30. National Institute of Health (NIH)	85%
	31. Aga Khan University (AKU, Pakistan)	
Philippines	32. Research Institute for Tropical Medicine (RITM)	100%
	33. Philippine Genome Centre (PGC), University of the Philippines	
Sri Lanka	34. Ministry of Health	92%
	35. University of Sri Jayewardenepura	
Thailand	36. Department of Medical Sciences, Ministry of Health	86%
	37. Mahidol University	
	38. COVID-19 Network Investigations Alliance	
Vietnam	39. National Institute of Hygiene and Epidemiology (NIHE)	73%
	40. Oxford University Clinical Research Unit	
	41. Institute Pasteur, Ho Chi Minh City (IP HCMC)	
	42. Institute Pasteur,Nha Trang (IP Nha Trang)	

Annex 4: Country profiles

Click here to download and view each of the country profiles.

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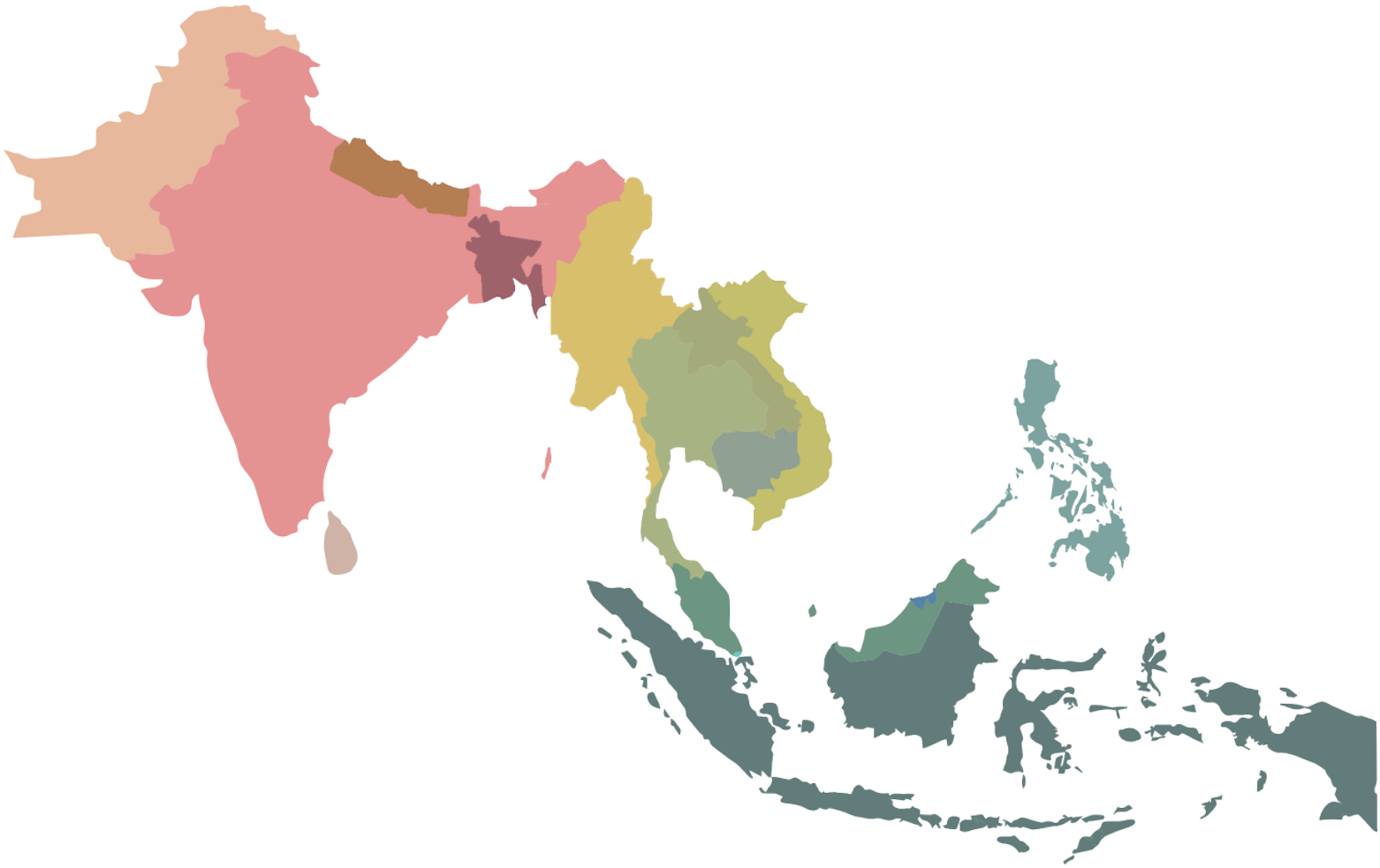

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