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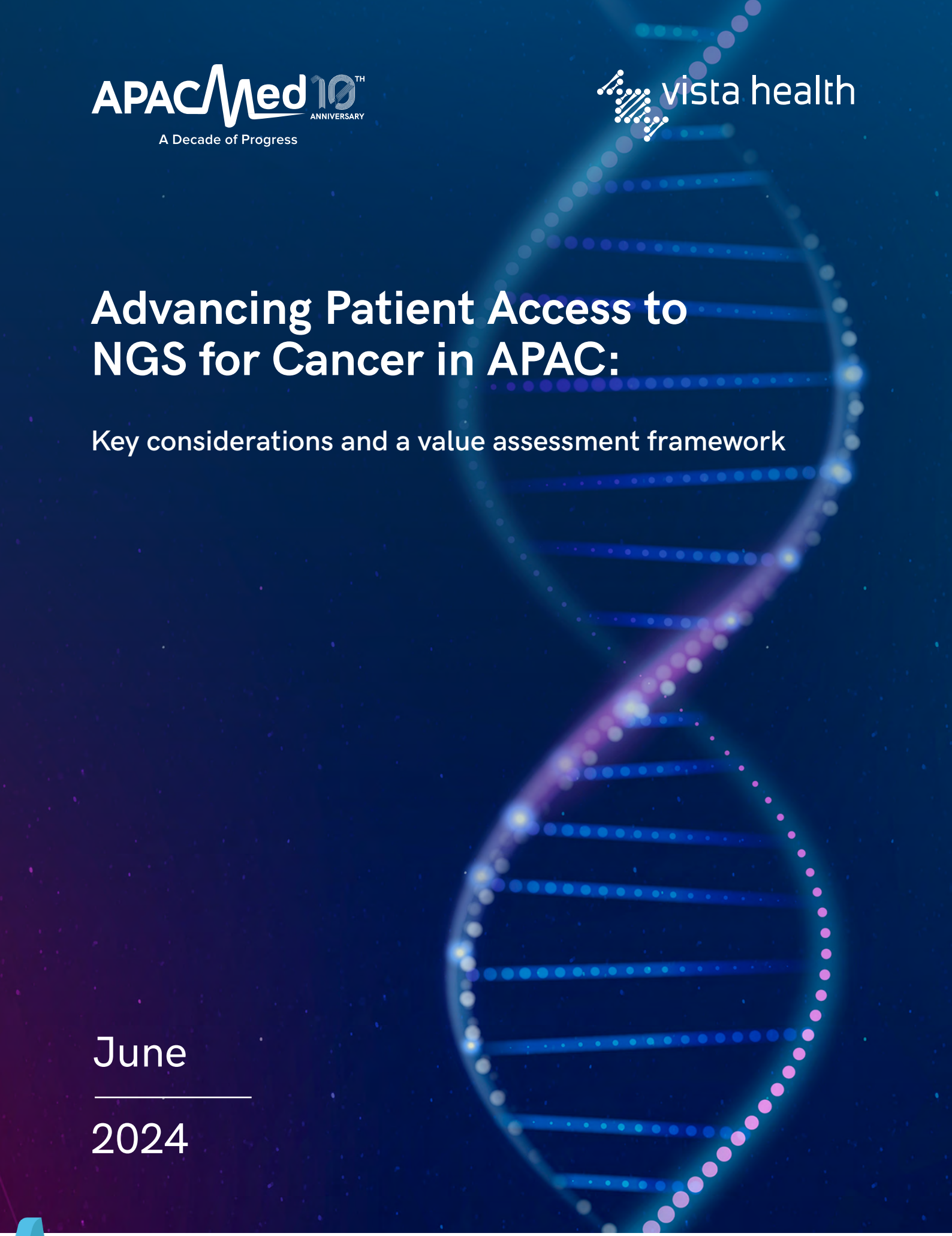
Advancing Patient Access to NGS for Cancer in APAC:

Key considerations and a value assessment framework



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GLOSSARY

ABBREVIATIONS	TERMS
ACE	Agency for Care Effectiveness
APAC	Asia Pacific
APCM	Advanced Precision Cancer Medicine
C-CAT	Center for Cancer Genomics and Advanced Therapeutics
cDx	Companion Diagnostics
CGP	Comprehensive Genomic Profiling
CGT	Clinical Genetic/Genomic Testing
CRC	Colorectal Cancer
DALY	Disability-Adjusted Life Years
DRUP	Drug Rediscovery Protocol
EMR	Electronic Medical Record
EU	Europe
ESMO	European Society for Medical Oncology
FDA	Food and Drug Administration
GDP	Gross Domestic Product
GEP	Genomics Education Programme
GMC	Genomic Medicine Centre
GMS	Genomic Medicine Service
HCP	Healthcare Professional
HIRA	Health Insurance Review and Assessment Service
HTA	Health Technology Assessment
IVD	In-Vitro Diagnostic
KPI	Key Performance Index
KPMNG	Korean Precision Medicine Networking Group
LDT	Laboratory-Developed Test
LIS	Laboratory Information System
MIR	Mortality-to-Incidence Ratio
MFDS	Ministry of Food and Drug Safety
MHLW	Ministry of Health, Labour and Welfare
MSAC	Medical Services Advisory Committee
MTB	Molecular Tumor Board
NCCP	National Cancer Control Plan
NECA	National Evidence-based Healthcare Collaborating Agency
NGP	National Genomic Platform
NGS	Next Generation Sequencing
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NSCLC	Non-Small Cell Lung Cancer
OS	Overall Survival
PAG	Patient Advocacy Group
PFS	Progression-Free Survival
PMI	Precision Medicine Initiative
PPM	Personalized and Precision Medicine
QALY	Quality-Adjusted Life Years
QoL	Quality of Life
RWE	Real-World Evidence
SGT	Single Gene Testing
TMB	Tumor Mutational Burden
UK	United Kingdom
VAF	Value Assessment Framework
WGS	Whole Genome Sequencing

FOREWORD

Harjit Gill
APACMed CEO

Over the past decade, we have witnessed rapid growth in genomic research and its applications in healthcare. In addition, there have been recent developments in Asia Pacific (APAC) to advance access to Next Generation Sequencing (NGS), driven forward by many of our members.

NGS has emerged as a potential game-changer, providing unparalleled insights that make a big impact on patient lives. In particular, NGS can revolutionize cancer care, unlocking better patient outcomes and building efficient and effective health systems.

The promise of NGS is undeniable but translating that potential into widespread patient benefit requires further action. This is driven by a range of challenges including mixed political commitment for NGS, incomplete infrastructure, funding gaps, and a perception of limited value. While some APAC territories are starting to make headway in addressing these challenges with the inclusion of NGS in national strategies and reimbursement for implementation in cancer care, it is often limited by cancer or technology type.

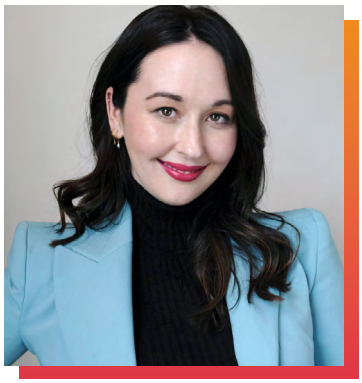
It therefore gives me great pleasure to present this white paper in collaboration with our valued NGS experts from across the APAC region. Building on the efforts of APACMed's previous publication "Unlocking the Value of Quality Next-Generation Sequencing in APAC", this paper presents an overview of the status of access to NGS-based cancer care in APAC and actions required to improve access, including a first-of-its-kind value assessment framework for NGS tailored to the regional context.

Sustained commitment and collaboration will be required from all stakeholders across the ecosystem to address political, clinical and reimbursement barriers to NGS access. These barriers will persist if we continue to silo efforts, but a concerted effort by all ecosystem stakeholders can undoubtedly overcome this challenge.

I would like to show my deep appreciation to all experts who helped develop this White Paper. I share their ambitious aspiration to break down barriers to NGS, and advance patient access to life-changing clinical care.

Harjit Gill

FOREWORD



Founder for Humanise Health & Genomic Advocate

Decades of medical research tell us that every person's cancer is unique, driven by a unique combination of genetic changes. Considering that the APAC region bears the heaviest burden of cancer worldwide, with ~10 million new patients every year, this leads us to deliberate the possibility that there are ~10 million unique cancers in APAC every year!

These unique genetic differences between cancers mean that each patient responds differently to the same treatment. Fortunately, we now have tools like NGS to analyze the genetic makeup of each patient's cancer and empower clinicians to personalize treatment plans that lead to the best outcomes. As someone who has watched generations of my family suffer from cancer, I was the first person in my family to access the true power of these tools.

Yet, for many cancer patients in APAC, access to NGS remains out of reach. I believe that this is driven by differences in the way the benefits of NGS are valued by stakeholders, leading to a lack of prioritization for system-wide implementation. As an advocate for patients, I recognize the potential of NGS to transform cancer care and continue to champion access to this technology. Nevertheless, I also acknowledge that there are other considerations and challenges for stakeholders to implement NGS at scale.

To address this, I call for all stakeholders to come together and shift their perspectives from the traditional valuation of healthcare technologies toward a broader understanding of the value that NGS can bring. The contents of this White Paper support this and is the first in APAC to propose a comprehensive framework for evaluating the value of NGS in cancer care and capturing the multifaceted benefits of NGS. This framework can help foster a deeper understanding of the value of NGS amongst all stakeholders in the healthcare ecosystem. Such recognition is crucial for informing decisions aimed at improving NGS access, like Australia's decision in November 2023 to fund small NGS panel testing for patients with non-squamous non-small cell lung cancer (NSLSC).

As we navigate this journey together, let this White Paper remind us of our shared commitment to ensure that no patient is left behind. Through our collective efforts, we can transform the landscape of cancer care in APAC, offering every patient the chance to fight cancer with the best tools at our disposal.

Together, we can harness the potential of NGS to create a future where cancer care is defined not by its challenges, but by its possibilities and the lives we can save.

Krystal Barter

EXECUTIVE SUMMARY

APAC region continues to witness an increase in the burden of cancer,[1] imposing clinical, societal, and economic burden on a region encompassing 60% of the world's population. **Cancer disease burden** measured in Disability Adjusted Life Years (DALY) **in APAC is still increasing** (Compound Annual Growth Rate (CAGR) = +1.81%), compared to other regions where the burden is decreasing such as Europe (CAGR = -0.43%). This trend is expected to worsen over the next few decades as incidence and mortality rates are expected to surge in APAC vs EU.

Despite existing efforts in APAC to address cancer through National Cancer Control Plans (NCCPs), **clinical outcomes for cancer in APAC still lag behind the West**, with estimated mortality-to-incidence ratio (MIR) of APAC (0.52) being much higher as compared to Western and Northern EU, and USA (0.32).[2] The implementation of specific, innovative measures across the cancer care continuum is required to improve outcomes and reduce burden.[3]

One such innovative measure is **implementing Next-Generation Sequencing (NGS) in cancer care** to enable the **delivery of personalized cancer care through tumor profiling**.[4] Specific genomic characteristics of tumors unique to each patient can thus be identified, enabling precise management of cancer.[4] Multiple studies in APAC territories have shown the real-world, **positive impact of NGS testing** on improving patient outcomes through shortening time to results, identifying more patients for matched therapies and clinical trials and decreasing diagnosis costs compared to current practice.[5,6,7] Hence, NGS is poised to help policymakers and all stakeholders in the healthcare ecosystem **achieve the shared goal of improving outcomes for cancer patients and reducing the economic and societal burden of cancer**.

However, **access to NGS-based tumor profiling is heterogeneous across the APAC region** due to diversity in healthcare infrastructure and access policies, local practice guidelines, and patients' socioeconomic status.[8] Adding to this complexity, conventional assessment methodologies that inform funding decisions do not appreciate the full value of NGS-based tumor profiling, resulting in low political commitment, lack of testing capabilities, and deprioritized financing.[9] While some APAC territories have made progress in reimbursing NGS-based tumor profiling to some extent *(e.g. Japan, Australia, South Korea, Hong Kong, and Taiwan[10])*, access barriers still exist in these mentioned territories.

To realize the benefits of NGS on patient outcomes, this paper proposes considerations for policymakers and other key stakeholders to improve access to NGS. These considerations have been validated through targeted literature reviews, roundtables and interviews with regional experts, including oncologists, pathologists, payer-advisors, payers, policymakers, and patient advocacy groups (PAGs).

Table 1 below summarizes the considerations where policymakers need to take the lead to improve NGS access:

Table 1: Policy considerations

1 **Include NGS for tumor profiling in national strategies/programs** *(e.g. genomic or precision medicine)* to enable improved clinical outcomes for cancer patients and optimize healthcare spend	2 **Ensure linkage between regulatory, reimbursement and clinical implementation policies**, to provide more timely and equitable patient access to both in-territory and overseas NGS testing	3 **Facilitate the use of digital technologies to enable multi-disciplinary collaboration** necessary for more efficient and productive NGS-based cancer care
4 **Develop a strong national genomics infrastructure** to enable the generation of local data, in order to validate effectiveness	5 **Invest in NGS-based drug trial programs** to increase patient access to matched therapies in the short term to improve local evidence generation and demonstrate clinical utility	6 **Establish a fit-for-purpose value assessment framework** that recognizes the **full value of NGS** in tumor profiling

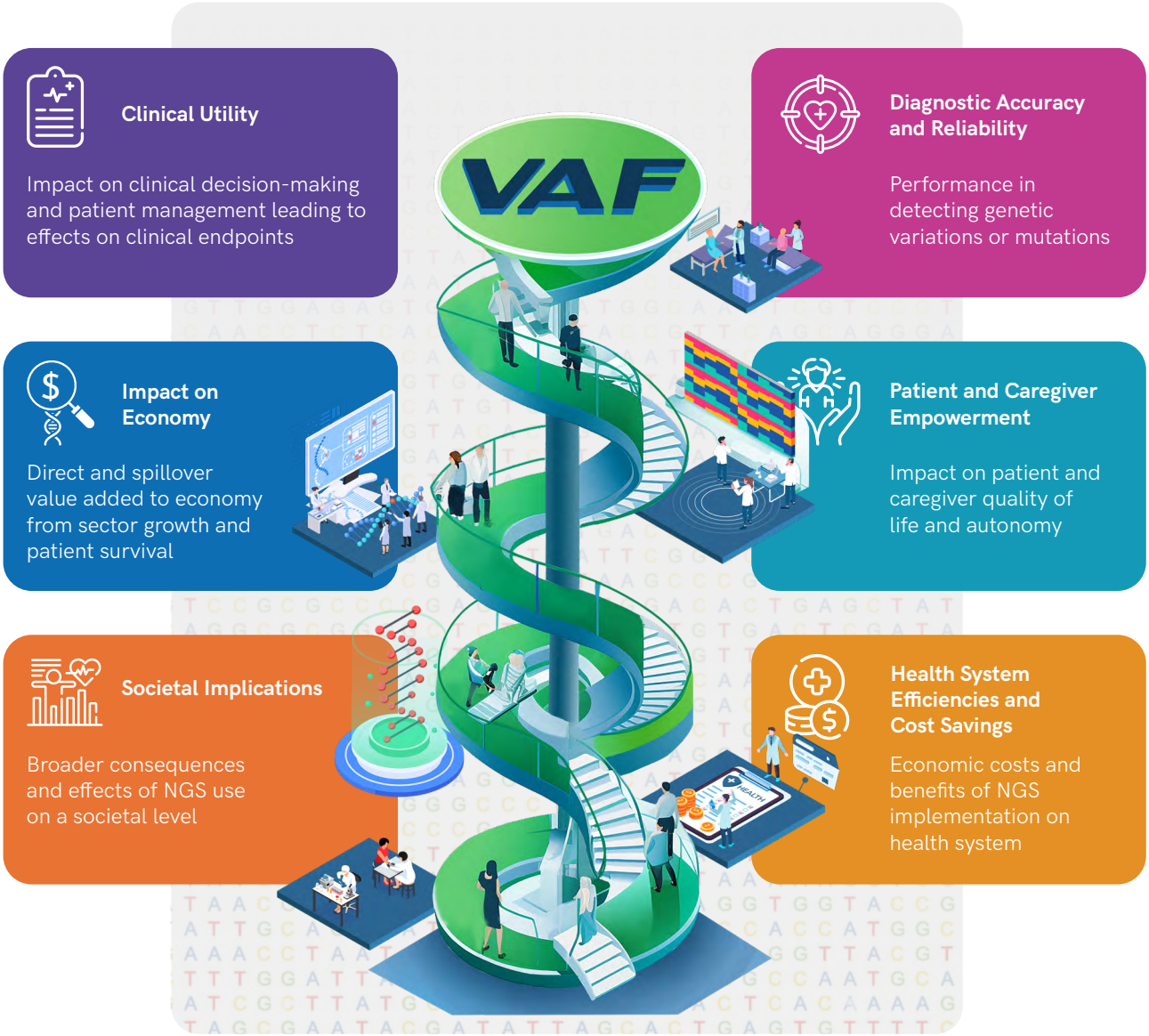
A **fit-for-purpose Value Assessment Framework (VAF) for NGS-based tumor profiling** is critical to comprehensively evaluate NGS. This report is the first APAC policy paper to propose a VAF as a practical tool to comprehensively assess the value of NGS-based tumor profiling while capturing all healthcare ecosystem stakeholder perspectives.

The proposed VAF **encompasses the benefits of NGS that extend beyond clinical domains, into economic and societal domains**. It also goes beyond the current Health Technology Assessment (HTA) frameworks for diagnostics, as these primarily focus on comparing costs and benefits linked to a single treatment or treatment class.[11] However, this presents a challenge for NGS, which is associated with multiple diseases and treatments. Therefore, the proposed VAF is key to help capture multi-stakeholder considerations when evaluating NGS, which includes value domains that may not be conventionally considered in payer assessments, to:

- Demonstrate the comprehensive value of NGS applicable to all stakeholders in the healthcare ecosystem
- Inform policy decisions on access for NGS-based tumor profiling
- Development or inclusion into formal assessment frameworks

This VAF encompasses a comprehensive set of six value domains across clinical, economic and societal / humanistic value types (Figure 1), going beyond clinical utility dependent on matched therapies and cost-effectiveness.[12,13]

Figure 1: Overview of the proposed NGS Value Assessment Framework



The benefits of the proposed policy considerations can be realized with **immediate and coordinated action** as territories strive to adopt NGS-based cancer care. Testing capabilities, processes, and investment policies need to be in place to deliver the benefits of NGS-based tumor profiling.

1. INTRODUCTION

This paper seeks to provide considerations on NGS access for policymakers to address the large and growing burden of cancer in the APAC region through NGS-based cancer care for patients. In this section, we discuss how NGS is a key tool that can help policymakers and all healthcare ecosystem stakeholders achieve the shared goal of improving outcomes for all cancer patients and reducing the burden and costs of cancer.

1.1 BURDEN OF CANCER IN APAC AND NGS'S ROLE IN ADDRESSING IT

The burden of cancer is growing in APAC and is a financial strain on healthcare systems in the region

Globally, cancer is a growing public health concern as the burden of cancer has a profound impact on individuals, health systems and societies.[14] In APAC, there is a significant financial burden on healthcare systems.

South Korea

Observed a surging economic cost of cancer, with medical cost due to cancer increasing from

US$1.2 billion in 2004 to **US$9.2 billion in 2023**[15]

Japan

Bears an annual economic burden of

~US$19.4 billion

as of 2023[16]

Despite existing efforts, the growth rate of the burden of cancer in APAC is accelerating compared to that in Europe **(Figure 2**[17]**)** and is expected to worsen over the next few decades as projections of incidence and mortality rates in APAC continue to surge **(Figure 3**[18]**)**.

Figure 2: Growth of disease burden of cancers in APAC and Europe from 2011 to 2019 in disability-adjusted life years[17] (DALY*)

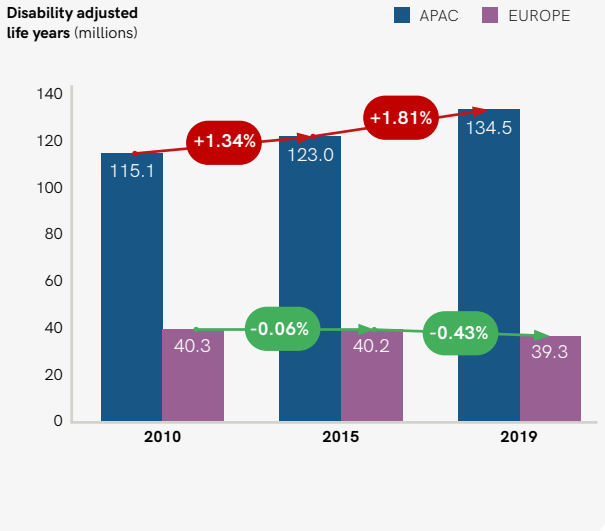


Figure 3: Cancer incidence and mortality rates in APAC and Europe from 2020 to 2040[18]

Incidence rate
projected to be an increment of
55.4% in APAC,
21.2% in Europe

Mortality rate
projected to be an increment of
67.8% in APAC,
29.2% in Europe

EFFORTS TO ADDRESS CANCER BURDEN

APAC territories are addressing this burden but are unable to keep up with its acceleration, there is a need for innovative measures to support existing efforts

APAC territories are working towards targets set to reduce cancer burden as set out in the World Cancer Declaration by the Union for International Cancer Control, targeting to reduce premature cancer deaths, improving Quality of Life (QoL) and cancer survival rates.

These efforts are being met through established NCCPs as seen in Table 2.

Table 2: Overview of NCCPs in the APAC territories

Taiwan	Australia	South Korea	Mainland China
Implemented 3 phases of its NCCP since 2005 and has adopted all of WHO's NCD targets for 2025[19]	Has several national/ state cancer plans, with the most recent plan launched in 2023[20]	Initiated its fourth NCCP in 2021[21]	Established a new national cancer prevention and control plan as a main component of the Health Mainland China 2020 Program[22]
Progress			
The cancer mortality rate in Taiwan saw a reduction in past decades from **53.38% in 2000** to **41.12% in 2020**[23]	The age-adjusted cancer mortality rates decreased from **255 deaths per 100,000 people in 2000** to an estimated **195 deaths per 100,000 people in 2023**[24]	The national cancer screening rate *(targeting stomach, liver, colorectum, breast, and cervix uteri cancers)* in Korea has increased to around 50%.[21] National health insurance coverage rate for cancer patients has also **improved from 49.6% in 2004 to 78.5% in 2019**[21,22]	The upward trend of cancer incidence and mortality has been limited in Mainland China. The territory's overall five-year cancer survival rate has increased from **40.5% in 2015 to 43.7% in 2022**[25]

THE ROLE OF NGS

Innovative technologies like NGS are invaluable tools to address these challenges and aid territories in achieving their targets

As seen in **Table 3**, in territories with limited NGS access for cancer testing, it is observed that the mortality-to-incidence ratios (MIR) are higher, compared to territories with greater NGS access.

Table 3: Mortality-to-incidence ratios of territories with and without NGS reimbursement[2]

MIR IN TERRITORIES WITH SOME LEVEL OF NGS REIMBURSEMENT			MIR IN TERRITORIES WITHOUT NGS REIMBURSEMENT
EUROPE	UNITED STATES	APAC	APAC
UK 0.39	**US** 0.25	**Japan** 0.41	**Singapore** 0.51
Denmark 0.40		**Australia** 0.24	**Philippines** 0.60
Sweden 0.39		**Korea** 0.38	**Thailand** 0.65
Germany 0.40			**Malaysia** 0.60
Finland 0.37			
Average 0.39	Average 0.25	Average 0.34	Average 0.59

- Although there is an absence of current studies establishing a causal relation between MIR and variations in NGS access, there have been studies highlighting the positive impact on patient outcomes after NGS reimbursement. This is evident in South Korea where advanced colorectal cancer (CRC) and NSCLC patients who opted for NGS testing experienced more favourable survival outcomes compared to those who did not.[26,27]
- However, many territories within APAC have not included NGS in their NCCPs, contributing to the lack of NGS access, which may potentially impede these territories' progress in improving cancer outcomes

TERRITORIES IN-FOCUS

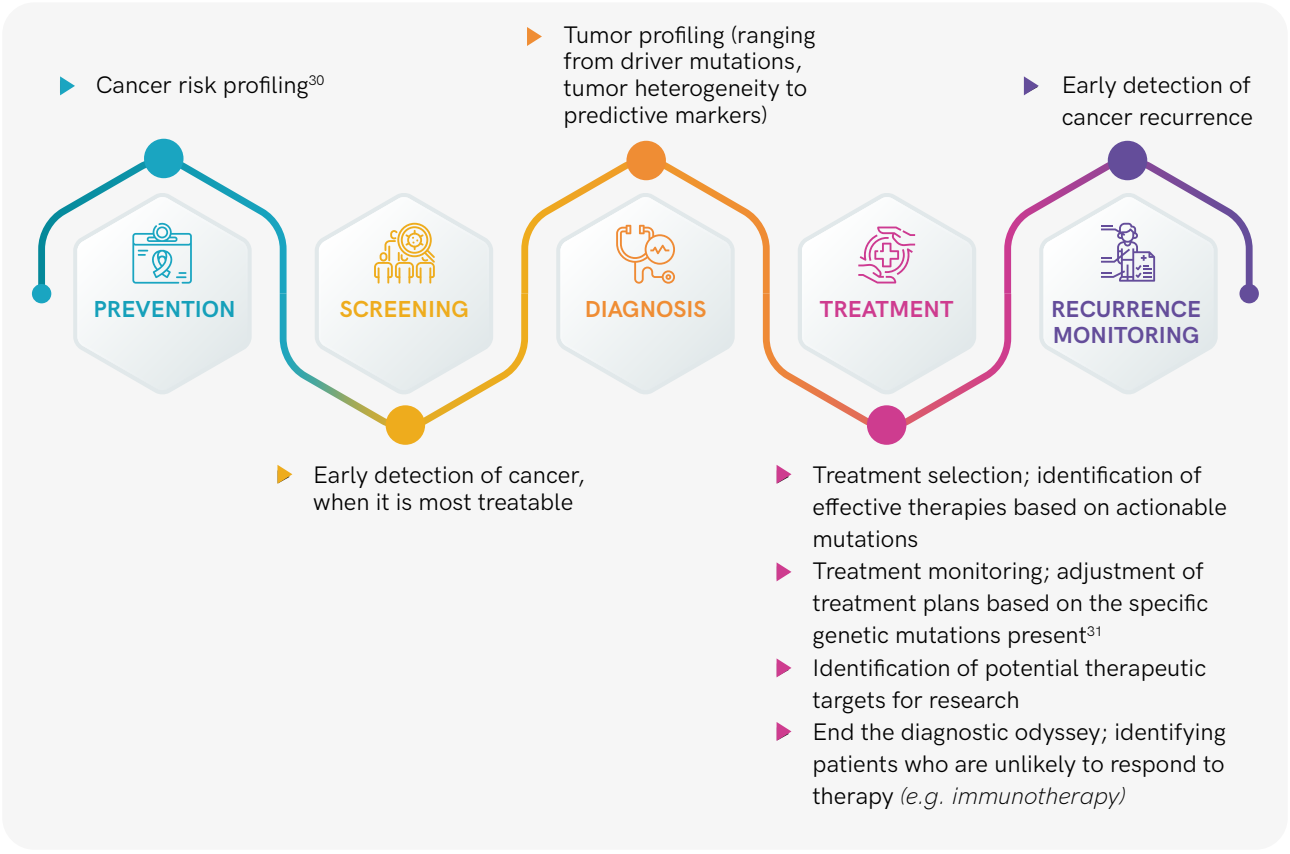
In this paper, we have opted to focus on territories that exhibit varying levels of health system maturities and possess economic readiness to improve the implementation of NGS-based cancer care and address the growing burden of cancer.

Australia | **Mainland China** | **Hong Kong** | **Japan** | **South Korea** | **Singapore** | **Taiwan**

1.2 BACKGROUND OF NGS AND ITS CLINICAL APPLICATIONS FOR CANCER CARE

NGS utilizes high-throughput technology and in-parallel processing to determine the sequence of DNA or RNA.[28] The clinical applications and benefits of NGS in oncology are both diverse and transformative across the cancer care continuum **(Table 4)**.[29] The benefits of NGS is most apparent in the diagnosis and treatment of cancers where tumor profiling using NGS has enabled a deeper understanding of the genomic characteristics of tumors, providing insights to inform care decisions.

Table 4: Applications of NGS across the cancer care continuum (prevention, screening, diagnosis, treatment, recurrence monitoring)



Unlike conventional single-gene testing which analyzes specific genes associated with known mutations, NGS offers a range of test types for tumor profiling, from smaller hotspot/targeted gene panels to larger comprehensive genomic profiling (CGP) tests. Small to mid-sized gene panels sequence specific segments of genes or the full exonic region of genes frequently implicated in cancer (typically encompassing ≤50 genes), while large NGS test types such as CGPs *(e.g. based on either tissue or liquid biopsies)* can detect both novel and known genetic variations, including genomic alterations *(base substitutions, insertions and deletions, copy number alterations and rearrangements)* and genomic signatures *(such as microsatellite instability-high [MSI-H] and tumor mutational burden [TMB])*. Multi-omics information *(e.g., genomic, epigenomic transcriptomic, fragmentomics etc.,)* from NGS tests provide a large range of insights in a single test, stretching from cancer screening, treatment decision-making, minimal residual disease testing, and recurrence monitoring purposes.

NGS tests can be processed locally (***in-territory NGS tests***) or out-of-territory (***overseas NGS tests***).

1.3 VALUE OF NGS FOR TUMOR PROFILING

Numerous global and APAC studies consistently highlight the clinical and economic benefits associated with NGS tumor profiling.[30,32-34] Along with humanistic and societal benefits, the key benefits of NGS are summarized in **Table 5**.[32] Further elaboration of the value of NGS tumor profiling can be found in the **Appendix: Section 1** of the paper.

Table 5 : Overview of key benefits of NGS for tumor profiling *(non-exhaustive)*

CLINICAL[6,35-41]	ECONOMIC[37,42-44]	HUMANISTIC AND SOCIETAL
BENEFITS		
Improvements to clinical endpoints *(e.g., overall survival, progression-free survival, health-related quality of life)* through reliable and accurate analysis of tumor genomic characteristics to inform clinical decision making. More informed management of tumors through effective risk stratification and prognosis, enabled through the help of NGS in pinpointing specific genetic changes that drive a tumor's growth.	Efficiencies and cost savings realized in health system through better utilization of resources and improved value delivery *(e.g., less delayed care)*.	Improvement to individuals and the society due to reduced waiting times for treatments and enhanced public health and care provision, resulting in lower cancer-related distress and better quality of life.[45,46]
EVIDENCE SHOWCASING BENEFITS		
In the United States, a study involving late-stage cancer patients showed that those who underwent NGS testing and were subsequently matched to targeted therapy **achieved a median overall survival of 52 weeks, double the 26 weeks observed in the control group.**[37]	In Korea, the cost per patient per year for advanced NSCLC and advanced colorectal cancer patients was found to be **~10% lower for those using NGS vs single gene tests.**[28]	A modelling study in Spain uncovered NGS testing could **add 1,188 quality-adjusted life years (QALYs)** to a target population of 9,734 advanced NSCLC patients compared with single-gene testing (SGT).[47]
ELABORATION		
▸ Matches patients to appropriate targeted therapies and clinical trials, leading to enhanced survival rates and improved quality of life ▸ Reduced need for tissue re-biopsy and tissue biopsy and timelier care management due to identification of more actionable biomarkers per test compared to sequential single gene testing. This is crucial for patients who exhausted standards of care	▸ Improve cost efficiencies in the healthcare system by identifying treatment-resistant mutations ▸ Costs avoided through clinical trial or hospice enrolment[48] ▸ Reduce hospitalization visits, length of stay in hospital due to adverse events or reactions, treatment costs, and/or wastage from use of ineffective therapies	▸ Promote health equity and social inclusion by providing information that enables the prompt delivery of the right care interventions to the right population[49] ▸ Provides 'value of knowing' that empowers patients and caregivers to make life-planning decisions *(e.g., cancer prognosis)*

1.4 OBJECTIVE OF THE WHITE PAPER

Considering the above evidence, there is a strong case to provide adequate patient access to fully realize benefits of NGS-based cancer care in APAC. However, as this paper explores, there are currently significant barriers to such access in the region which first need to be addressed.

This white paper aims to:

1. **Understand the barriers to access for NGS in APAC**

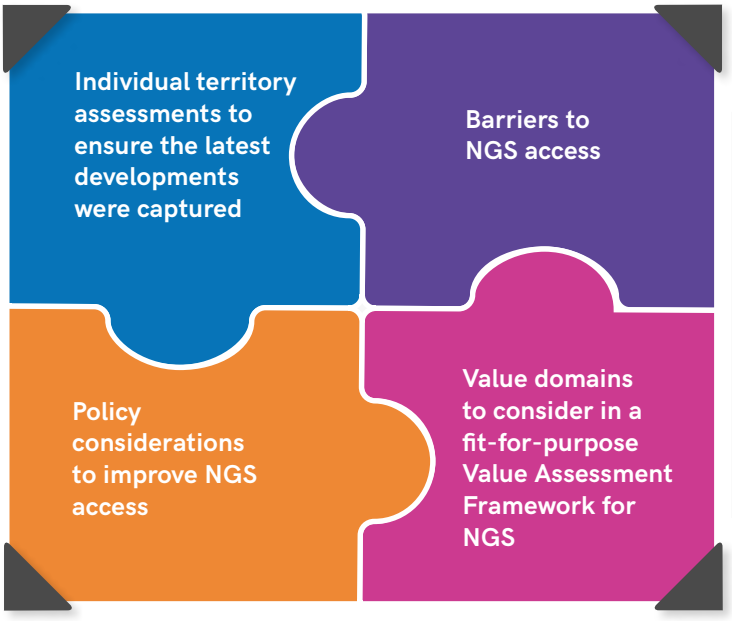
2. **Identify the opportunities and propose policy considerations to increase access to NGS in APAC**

3. **Propose a fit-for-purpose Value Assessment Framework for NGS**

4. **Provide implementation considerations and a call-to-action for policymakers**

1.5 OUR APPROACH

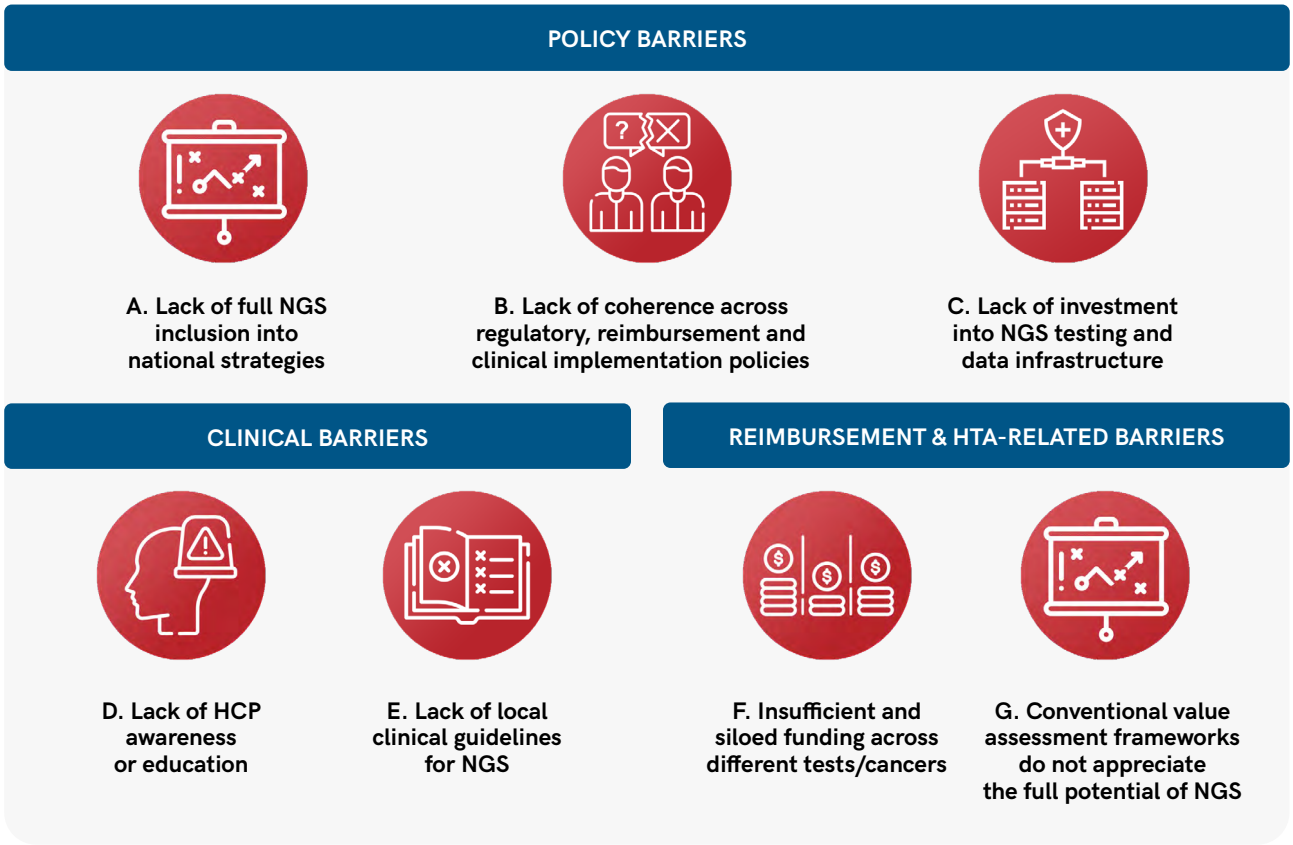
A targeted review of peer-reviewed publications, grey literature, and white papers was conducted to gather insights into the existing status of NGS access for tumor profiling in the APAC region. Key themes identified were broken down into sub-parameters and analysed. In-depth interviews and roundtable discussions with in-territory experts were conducted to further validate:



2. KEY BARRIERS TO NGS ACCESS ACROSS THE APAC REGION

Despite the known clinical and economic benefits of NGS, challenges to the uptake of NGS persist. The identified key barriers **(Figure 4)**, are classified into policy, clinical and reimbursement/HTA-related barriers, along with specific territory examples that will be explored in depth in this section.

Figure 4: Overview of key barriers of NGS



These barriers to access and reimbursement of NGS tumor profiling for patients exist across all territories in the APAC region, but the severity of barriers differs across territories based on current status and ongoing efforts to address them. The severity of barriers across the territories are outlined in a heatmap in **Figure 5** which have been evaluated based on a rubric found in **Figure 8** in the appendix.

Based on the barrier severity in **Figure 5** and rubric outlined in **Figure 8** in the Appendix, territories are classified into three archetypes that will serve as the basis for prioritizing policy considerations **(explored in Section 4)** for different landscapes:

Nascent archetype – limited access to NGS based cancer care, attributed to a lack of policies initiatives. Additionally, low clinical implementation, and limited reimbursement and HTA frameworks for NGS testing is observed.

Emerging archetype – improved access to NGS based cancer care through an observed shift in policies initiatives and funding decisions. However, there is still room for more policies that address the limited clinical implementation of NGS, and the absence of HTA frameworks specific to NGS.

Developing archetype – policy, clinical implementation, and funding initiatives to increase access to NGS based cancer care show the greatest maturity compared to prior archetypes. However, there is still potential for policymakers to expand reimbursement of NGS towards different cancer types and take the lead in implementing NGS-specific evaluation frameworks.

Although territories have been categorized into three archetypes based on the severity of access barriers, it is important to acknowledge that no territory aligns perfectly with a single archetype, and there are overlapping features which will be highlighted accordingly. Specific examples of NGS access barriers, sorted by archetype can be found in **Appendix: Section 2**.

Figure 5: Overview of NGS heatmap by territory

Archetypes	NASCENT	EMERGING			DEVELOPING		
Barriers	**Mainland China**	**Singapore**	**Hong Kong**	**Taiwan**	**Australia**	**South Korea**	**Japan**
A. Lack of full NGS inclusion into national strategies	NGS for tumor profiling lacks political prioritisation	Initiatives limited to implementing PGx testing; only for hereditary diseases	NGS is included in national strategies, with plans to expand existing capacity to cater for more NGS tests by early-2024	Despite lack of a formal national plan for NGS, discussions on NGS implementation strategies and NHIA reimbursement have taken place in 2024	Increasing investment in establishing government agencies/ departments for genomics, and discussions of NGS in the Cancer Plan 2030	Precision medicine designated a National Strategic Project since 2016 with some R&D projects, and plans to leverage genomics data in Fourth National Cancer Control Plan (2021-2025); discussions for a greater inclusion of NGS in cancer care	Major investment in a national framework to boost readiness for NGS
B. Lack of coherence across regulatory, reimbursement and clinical implementation policies	Decentralised reimbursement process for new medical devices such as NGS. Each local government (provincial / city) evaluates and makes decisions on reimbursement applications	Processes allow regulatory and reimbursement considerations for both local and overseas tests, however reimbursement policies for NGS still lacking		Lack of streamlined processes for approval and reimbursement of overseas LDTs	Overseas tests approved, but reimbursement framework does not consider overseas tests	Regulatory framework still follows "per indication" basis, and only local testing results eligible for reimbursement	Processes streamlined to consider approval and reimbursement of overseas tests
C. Lack of investment into NGS testing and data infrastructure	No plan to invest announced; implementation of infrastructure currently limited to research institutions	SG's STCC built on existing data infrastructure Health Data Grid	Currently expanding, but limited to academic institutions/centers of excellence	Recent initiatives to develop testing and data infrastructure and network	Expanding, especially in the private sector. However, lack of a federated system limits national integration	Expansive data and testing infrastructure available to support NGS testing, such as South Korea's K-MASTER clinical trial referral platform, and Japan's C-CAT genomic database	
D. Lack of HCP awareness or education	Low familiarity of NGS and strong preference for single gene testing	Low familiarity among surgeons/ oncologists, knowledge limited to centers of excellence	Growing, with recent recommendations to integrate NGS into CMEs and to establish MTBs	Clinical usage observed mainly in private sector (high OOP)	Low familiarity among surgeons/ oncologists, knowledge limited to centers of excellence	High awareness, but implementation constrained by long turnaround times for local tests	High awareness with knowledge sharing, but implementation limited by reimbursement constraints
E. Lack of local clinical guidelines for NGS	Guidelines available but lacks implementation due to low awareness	No local guidelines for NGS	Recent consensus statements outlines guiding principles for clinical implementation, and calls for the development of specific clinical guidelines and decision-making tools	No local guidelines for NGS	No specific guidelines, but likely following western guidelines	Local guidelines available	
F. Insufficient and siloed funding across different tests / cancers	Reimbursement of NGS is limited to some cities / provinces in China	Standard diagnostic reimbursement for all diagnostics, but amount insufficient for NGS	Reimbursement for small gene panels piloted in early 2023 for NSCLC patients	Reimbursement decision for NGS announced for May 2024, with 19 eligible cancer types and claimable once-per-lifetime for each cancer type	Reimbursement for local small gene panels commenced in Nov 2023 for limited selection of cancers	Reimbursement for small and large panels for solid and blood cancers is available. However, it has recently been reduced for non-NSCLC solid cancers	70-90% of CGP costs are reimbursed, but only for advanced metastatic cancers and claimable once per lifetime
G. Conventional value assessment frameworks do not appreciate the full potential of NGS	No specific methodologies for NGS but traditional methods have been applied to NGS. However, methods currently differ across provinces and cities resulting in discrepancies in reimbursement decisions across the territory	HTA evaluation methods for NGS not yet determined ; ACE assessed liquid biopsy NGS tests and recognized effectiveness but did not issue positive funding recommendation due to uncertainties over its cost-effectiveness	No specific methodologies for NGS have been developed, but traditional frameworks have been applied to NGS with announcements of pilot funding for Hong Kong, and reimbursement decisions for Taiwan		Recent HTA review did not consider additional advantages NGS have *(e.g. societal benefits)*; nonetheless NGS-specific methods are being developed	HTA agencies (NECA and HIRA) are looking into ways to refine existing frameworks that enable access to NGS.	No specific methodologies for NGS have been developed, but traditional frameworks have been applied to NGS with examples of positive recommendation. However, methods currently differ across provinces and cities resulting in discrepancies in reimbursement decisions across the territory

Abbreviations
CGP: *Comprehensive Genomic Profiling,* ***CME:*** *Continuing Medical Education,* ***HCP:*** *Healthcare Professionals,* ***HIRA:*** *Health Insurance Review & Assessment Service* ***MTB:*** *Molecular Tumor Board,*
NECA: *National Evidence-based Healthcare Collaborating Agency,* ***NSCLC:*** *Non-small Cell Lung Cancer,* ***OOP:*** *Out-of-Pocket,* ***PGx:*** *Pharmacogenomics,* ***STCC:*** *Singapore Translational Cancer Consortium*

Severity of barriers

2.1 POLICY BARRIERS TO NGS TESTING FOR TUMOR PROFILING

A. LACK OF FULL NGS INCLUSION INTO NATIONAL STRATEGIES

The lack of full NGS incorporation into national strategies (including any national plans for healthcare including genomics strategy, national cancer control plans, and guidelines) restricts the downstream nationwide implementation of NGS into clinical practice.[50]

Inclusion of NGS in national cancer surveillance, prevention programs and national precision medicine plans are pivotal for establishing NGS as a research priority, developing a market for molecular diagnostic tests, disseminating guidelines for oncologists, and creating reimbursement mechanisms and incentives.[51,52]

However, in several APAC territories, a lack of full inclusion of NGS in recent precision medicine strategy announcements has led to restricted access to NGS.[50]

Table 6: Lack of full NGS inclusion into national strategies by archetype

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	There is a lack of NGS inclusion into national strategies	There is inclusion of NGS in national strategies, but not with a tumor profiling focus	Initial discussions to include NGS for tumor profiling in national strategies, but yet to be formalized
Example of barrier by archetype	The absence of NGS in **Mainland China's** Precision Medicine Initiative (PMI) which was launched in 2016, has hindered accessibility of NGS. Post launch of the PMI, despite reports of testing rates for key biomarkers such as *EGFR* and *HER2* reaching 80-95%[53], only 15% is attributed to NGS testing due to its high costs and constrained availability	**Singapore's** National Precision Medicine (NPM) Initiative is a whole-of-government initiative which aims to generate precision medicine data and improve delivery of care.[54] However, projects under this initiative only focus on sequencing hereditary diseases rather than tumor testing	Despite **Taiwan** exhibiting Emerging archetype traits overall, NGS testing has been recognized as a key driver to implement precision health in existing care pathways, leading to impactful discussions such as The Advanced Precision Cancer Medicine (APCM) Forum in August 2023 to promote implementation of NGS. However, no formal plan has been published yet

B. LACK OF COHERENCE ACROSS REGULATORY, REIMBURSEMENT AND CLINICAL IMPLEMENTATION POLICIES FOR NGS

Across the APAC region, it is observed that access to NGS is hindered by fragmented regulatory, reimbursement, and clinical implementation policies. These individual bodies often function in silos, resulting in a lack of coherence across approval, reimbursement, and implementation policies for NGS. Reimbursement is more likely to occur for diagnostics that have established regulatory and implementation guidelines, hence ensuring the linkage of policies across the NGS landscape is important to enable NGS access.

Table 7: Lack of coherence across regulatory, reimbursement and clinical implementation policies for NGS across archetypes

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	There are discrepancies among policies, both within and across jurisdictions in the territory	There is a lack of coherence between regulatory, reimbursement and clinical implementation policies within the territory	Although policies are more adequate, there is scope to streamline further
Example of barrier by archetype	In **Mainland China**, despite the regulation of NGS tests by the National Medical Products Association (NMPA), existing Human Genetic Resources regulations restrict access to well-validated, U.S. FDA-approved overseas testing,[55] but allow local testing Additionally, local NGS tests are partially reimbursed through public insurance in selected cities, but not across other jurisdictions in Mainland China	Despite **South Korea** exhibiting Developing archetype traits overall, reimbursement for in-territory tests allow 'pan-cancer' indications, but regulatory approval is still done on a 'per indication' basis Additionally, no regulatory or reimbursement pathways exist for overseas tests	Despite **Taiwan** exhibiting Emerging archetype traits overall, pathways for approval of overseas lab developed tests exist. However, there is a lack of centralization with regulatory guidelines and clinical implementation policies, as individual applications are still required for each medical institution to implement NGS (as opposed to a single regulatory body *e.g., TFDA approving NGS IVDs used locally*)[56]

C. LACK OF INVESTMENT INTO NGS TESTING AND DATA INFRASTRUCTURE

The lack of investment into robust infrastructure to support scaling up NGS testing capacity and capability, coupled with siloed budgets for diagnostics and other hospital facilities, result in infrastructural limitations in data sharing and data storage infrastructure capabilities. These competing priorities and lack of the right capability and capacity limits access to NGS.

Additionally, the lack of harmonization of clinical infrastructure *(e.g., data capture through electronic health records and limited laboratory and analytic services)* contribute to gaps in evidence generation that decision-makers rely on to assess the clinical and cost-effectiveness of NGS, which is crucial for informing funding decisions.[51]

> *Generation of local evidence that demonstrates NGS' clinical utility and health system efficiencies and cost savings has implications on informing funding decisions, which can improve access to NGS. The inability to do so will be an obstacle in helping policymakers and payers recognize the value of NGS.*
>
> ***HCP KOL***

The extent of infrastructure available to support NGS testing varies across the APAC region, with gaps in infrastructure capabilities and capacities impairing territory ability to implement NGS and generate evidence to inform funding decisions.

Table 8: Lack of investment into NGS testing and data infrastructure across archetypes

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	There is insufficient investment in infrastructure, with no plans to do so yet	There are plans to invest in infrastructure to support NGS	There is existing infrastructural investment, but implementation is limited to Centers of Excellence / selected healthcare facilities
Example of barrier by archetype	In **Mainland China**, there is expert consensus calling for plans to improve web-based automated clinical decision support systems, which can enable Molecular Tumor Boards (MTBs) and improve the clinical implementation of NGS[57] More details on MTBs can be found in **Consideration D.1, under Section 4**	**Taiwan** announced the Cancer Precision Medicine and Biobank Consortium Collaboration Pilot Project in 2021[58] to establish the National Biobank Consortium of Taiwan (NBCT), a virtual biobank that expands Taiwan's genetic data management capabilities and enabled the setup of MTBs in participating hospitals	Despite **Singapore** exhibiting Emerging archetype traits overall, its setup of the Singapore Translational Cancer Consortium (STCC) and collaboration with industry partners in 2022 will increase patient access to targeted therapies using CGP, and enable the setup of MTBs in participating hospitals[59]

2.2 CLINICAL BARRIERS TO NGS TESTING FOR TUMOR PROFILING

D. LACK OF HCP AWARENESS OR EDUCATION

The widespread implementation of NGS in oncology first requires healthcare professionals (HCPs) to appreciate its value. As HCPs are a primary source of patient awareness for health knowledge, low HCP awareness of NGS translates to low patient awareness of NGS and its value in cancer care. Across the APAC region, it is observed that knowledge of NGS amongst HCPs and dedicated NGS workforce may be limited to centers of excellence where knowledge sharing activities and MTBs are likely implemented.[60] MTBs have been established as best practice to aid oncologists in integrating NGS into clinical practice, and serves as a platform for experts to harmonize and create consensus on treatment recommendations based on genomic results.[61] A lack of continuous education opportunities and less frequent MTBs may widen the gap between scientific development and clinical application, especially as more biomarkers and targeted therapies are discovered at a rapid pace.[61]

Table 9: Lack of HCP awareness or education across archetypes

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	There is a lack of awareness of NGS testing	Awareness of NGS testing is limited to centers of excellence, however awareness or education programs are yet to be in place	Growing awareness of NGS testing beyond centers of excellence, with plans to establish programs to increase awareness
Example of barrier by archetype	Based on expert opinion, clinicians in **Mainland China** lack exposure to NGS testing in cancer care, and thus strongly prefer traditional sequence testing and primarily treat based on experience	In **Singapore**, the broader HCP community does not receive sufficient ongoing education on NGS to keep pace with the advancing technology.[62] Awareness of NGS testing is limited to centers of excellence, primarily attributed to research initiatives and MTBs	While **Hong Kong** shows characteristics of Emerging archetypes and historically low HCP awareness of NGS testing, there are recent plans to incorporate NGS testing into continuous medical education programs and setting up MTBs to advance the awareness and delivery of NGS testing.[61] Additionally, in-house tests are being introduced in not just academic institutions but also high-volume community centers[8]

E. LACK OF LOCAL CLINICAL GUIDELINES FOR NGS

Absence of local clinical guidelines for NGS tumor testing and interpretation of results in local patient populations is a barrier to its implementation and clinician awareness of its clinical applications.[8] Guidelines provide a clear roadmap for the practical implementation of NGS in local clinical settings. However, other than South Korea[63], Japan[64] and Mainland China[65], other APAC territory guidelines are not updated with NGS testing.

Table 10: Availability of local NGS guidelines in the focus APAC territories

AVAILABILITY OF GUIDELINES			LACK OF GUIDELINES			
South Korea	**Japan**	**Mainland China** (but not uniformly adhered to nationwide)	**Australia**	**Singapore**	**Taiwan**	**Hong Kong**

Table 11: Lack of local clinical guidelines for NGS

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	No locally relevant clinical guidelines on NGS testing	Plans to develop locally relevant clinical guidelines on NGS testing	Local clinical guidelines on NGS testing available, with limited implementation
Example of barrier by archetype	While **Singapore** and **Taiwan** exhibit Emerging archetype traits overall, the lack of clinical guidelines to guide NGS use in local practice can lead to inconsistencies in clinical implementation of NGS testing within and across cancer indications[62]	While formal clinical guidelines remain a gap, **Hong Kong** has recently published consensus statements recommending these guidelines be established for local practice[61]	While **Mainland China** typically exhibits Nascent archetype traits, clinical guidelines for NGS testing in NSCLC have been published in 2020. Nevertheless, there is limited implementation in practice due to lack of dissemination[65]

2.3 REIMBURSEMENT & HTA BARRIERS OF NGS TESTING FOR TUMOR PROFILING

F. INSUFFICIENT AND SILOED FUNDING ACROSS DIFFERENT TESTS / CANCERS

Funding for NGS testing is essential to enable its access. Although the cost of NGS testing has reduced notably since its introduction, higher costs compared to traditional diagnostic methods such as single gene testing (SGT) may still be an affordability barrier for patients on the lower end of a territory's income distribution, and may deter payers from considering the technology. It should be noted, however, that some APAC territories have conducted preliminary studies showing exclusionary testing with NGS to be more cost effective than traditional SGT.[5]

> *Reduction in NGS testing costs may eventually reach a plateau due to ongoing labor costs associated with NGS testing, which are not anticipated to decrease in the future. This highlights the need for alternative funding models for NGS to ensure continued access to this technology.*
>
> ***HTA expert***

Variation in funding decisions across the APAC region contributes to inequitable access to NGS testing, where only patients with greater spending power (including private insurance) or select cancer indications have greater access to NGS.

> *Efforts to secure reimbursement for NGS-based tumor profiling is a challenge that experts across the region have attributed to concerns about the potential budget impact from downstream costs associated with high-cost matched therapies.*
>
> ***HCP KOL***

Table 12: Insufficient and siloed funding across different tests/cancers

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	There is no NGS-specific reimbursement	Reimbursement of NGS testing has been piloted, planned or ongoing but highly restricted to small set of cancer types and with strict eligibility criteria	Reimbursement still siloed but open to a wider set of cancer types with strict eligibility criteria
Example of barrier by archetype	In **Singapore**, despite being classified under the Emerging archetype, there is a withdrawal limit of S$600/year for all cancer diagnostics and cancer drug services through the national medical savings scheme (MediSave). This is typically exhausted during initial consultations, before NGS testing is suggested treatment selection is discussed[62]	In **Australia**, small NGS panels are funded since 2023, but is limited to a small set of cancers with strict eligibility criteria[66] Since early 2023, **Hong Kong** has piloted funding of NGS testing in clinical practice in NSCLC patients,[67] but official reimbursement remains to be announced	In **Japan**, 70-90% of CGP testing costs are reimbursed. However, reimbursement is only for patients with advanced cancers and can only be claimed once-per-lifetime[68] Despite **Taiwan** portraying Emerging archetype traits overall, NGS will be reimbursed for 19 cancer types, including in-territory and overseas testing, from May 2024; but can only be claimed once-per-lifetime for each cancer type[10,69]

G. CONVENTIONAL VALUE ASSESSMENT FRAMEWORKS DO NOT APPRECIATE THE FULL POTENTIAL OF NGS

Traditional HTA frameworks, originally designed for the evaluation of single biomarker tests or drugs targeting specific tumor types, face challenges with innovative technologies like NGS.[70]

Traditional frameworks evaluate the cost-benefits of a diagnostic by considering the value of associated matched therapies on a per-indication basis. This method does not sufficiently capture the value of NGS as a whole, as the technology can be applied to multiple indications with different treatments.

> *Clinicians shared that policymakers and payers might perceive clinical utility of NGS to be lacking as less than 5 to 10 percent of genomic information obtained through NGS is currently applicable or actionable in terms of guiding treatment decisions or identifying targeted therapies. Lack of structured evidence-based assessments capturing the broader benefits of NGS has led to payer uncertainties, temporary reimbursement decisions, and reductions in funding.*
>
> ***HCP KOL***

Although there are APAC territories with diagnostics evaluation frameworks in place, many lack specific frameworks tailored for NGS.[70] There is a need for all stakeholders in the healthcare ecosystem to recognize the diagnostic value of NGS beyond a tool to identify matched therapies, including the intrinsic value of NGS in guiding management decisions. This will underpin a shift in the healthcare delivery paradigm, analogous to the usage of MRIs for diagnosis and guiding a breadth of interventions.

> *Clinical experts have highlighted that the diagnostic value of NGS itself, which allows for a deeper understanding of tumor biology to inform tumor management pathways and chemotherapy-sparing strategies, is also an untapped opportunity to recognize NGS' value in clinical decision-making.*
>
> ***HCP KOL***

Therefore, there is a need for NGS evaluation frameworks to evolve beyond the confines of traditional assessments, through an assessment framework specific to NGS that is fit-for-purpose. Not only will it enable the broader benefits of NGS to be captured, it will also help policymakers' and payers' recognize the value of NGS.[51] This paper proposes a fit-for-purpose Value Assessment Framework (VAF) which will be covered in further detail in **Section 5**.

Table 13: Status of current evaluation frameworks used for NGS

	NASCENT	EMERGING	DEVELOPING
Barrier description by archetype	Traditional evaluation frameworks for diagnostics have been used to evaluate NGS with no success Low perception of clinical utility of NGS	Traditional evaluation frameworks for diagnostics have been used to evaluate NGS with limited success Low perception of clinical utility of NGS	There is existing HTA evaluation for diagnostics, with plans to establish/adapt for NGS Increasing perception of clinical utility of NGS, driven by initiatives to improve perception in short term *(e.g., clinical trials for matched therapies)*
Example of barrier by archetype	Despite showing Emerging archetype characteristics, **Singapore**, ACE assessed liquid biopsy tests for NSCLC patients but did not issue a positive funding / reimbursement recommendation despite recognizing its effectiveness in detecting driver mutations, citing uncertainty over cost-effectiveness[71]	According to expert opinion, **Mainland China** has reimbursed NGS for cancer in major cities with established HTA methods. However, these processes differ across provinces and cities, resulting in discrepant reimbursement decisions across the territory. Moreover, the HTA processes in Mainland China tend to favor drug evaluation rather than diagnostics According to expert opinion, **Hong Kong** has applied traditional frameworks to evaluate NGS, leading to a pilot funding scheme for NSCLC (yet to be formalized)	In **Australia**, the Medical Services Advisory Committee's (MSAC) recent HTA review process for small NGS panels included the consideration of extensive clinical and economic evidence, but did not consider the additional advantages these NGS tests may have, such as societal benefits.[66] Nonetheless, according to expert opinion, specific methods for NGS evaluation are currently being explored In **South Korea**, the HTA agencies (National Evidence-based healthcare Collaborating Agency (NECA) and the Health Insurance Review & Assessment Service (HIRA)) are looking into ways to refine existing frameworks that enable access to NGS.[70] However, according to expert opinion, recent decisions to reduce reimbursement for all gene panels other than non-NSCLC cancer underscore the repercussions of insufficient local evidence.

3. CASE STUDIES

3.1 OUTLINE OF CASE STUDIES

While barriers to NGS access across APAC have been observed, some territories have demonstrated success in addressing them. These case studies highlight potential learnings that can be leveraged to address barriers and improve access to NGS across healthcare system and reimbursement archetypes, though specific steps will need to be tweaked in application to account for variations in healthcare systems and reimbursement archetypes. In this section of the paper, case studies from Europe and APAC will be outlined in **Table 14** below, detailing the steps taken to address barriers and outcomes achieved in improving NGS access.

Table 14: Case studies of territories addressing NGS access barriers

TERRITORY	BARRIER	STEPS TAKEN TO ADDRESS BARRIER	OUTCOMES
United Kingdom	**A. Lack of full NGS inclusion into national strategies**	UK's Department of Health and Social Care had set the direction for genomics use in healthcare, delivered by NHS, which outlined key goals related to genomic testing in their 'NHS Long Term Plan'. Delivery of the goals were supported by NHS' new Genomic Medicine Service, which detailed the necessary strategic priorities and initiatives[72-74]	With clear articulation of the value of genomics and its incorporation into the NHS' Long Term Plans, political commitment is shown by pushing for improving genomic access and use in the territory
	D. Lack of HCP awareness or education	Genomic Education Programme (GEP) was launched by Health Education England, focusing on developing genomic education and training resources to upskill and develop the multi-professional workforce in genomic advances[75]	The implementation of GEP has led to the development of various educational resources as well as education and training leads across England to support workforce development
	F. Insufficient and siloed funding across different tests/cancers	A National Genomic Test directory was established by NHS, specifying genomic tests commissioned by them in England, along with an annual review process to update clinical indications of genomics tests[746]	The test directory currently includes 203 cancer clinical indications, out of which multi-target NGS panels cover 135 across 5 types of cancers, with constant processes to update clinical indications
Sweden	**A. Lack of full NGS inclusion into national strategies**	The Genomics Medicine Sweden (GMS) was set up through a bottom-up approach, enabling policymakers to recognise the value of NGS	Improvements in Sweden's capabilities to provide NGS testing in their healthcare system were observed, leading to actionable outcomes in a greater number of cancer patients
	C. Lack of investment into NGS testing and data infrastructure	The National Genomics Platform (NGP) was established by Genomics Medicine Sweden to enable seamless data sharing nationwide[77]	A unified infrastructure enables real-time sharing of genomics data on a national level, streamlining access and expanding testing capabilities
Japan	**A. Lack of full NGS inclusion into national strategies**	The Japanese government launched a range of policies to drive research and healthcare improvements, as part of their initiative to implement precision medicine in practice	Initiatives that strengthened Japan's infrastructure, Japan's hospitals' capability to utilize NGS testing and access to NGS have been enabled through the prioritization of NGS
	E. Lack of local clinical guidelines for NGS	A joint publication by three medical societies outlined clinical guidelines for NGS-based cancer testing[64]	Standard of care established for quality NGS testing, including the requirement of MTBs to provide necessary expertise in interpreting results

3.2 UK CASE STUDY

3.2.1 ACCELERATING GENOMIC MEDICINE IN THE NHS

BARRIER ADDRESSED:
A. LACK OF FULL NGS INCLUSION INTO NATIONAL STRATEGIES

The UK's Department of Health and Social Care has acknowledged the value of genomics in healthcare, setting the vision for the use of genomics in the future. The vision was actualized within the 'NHS Long Term Plan' in 2019, a strategy document that included genomics as a priority healthcare area. Their commitment to include genomics in healthcare delivery is supported by the Genomics Medicine Service (GMS), which outlines objectives and initiatives to incorporate genomics into the system.

IMPLEMENTATION/STEPS TAKEN:

In the plan, key goals for genomics include offering whole genome sequencing as part of routine care, providing extended access to molecular diagnostics and routinely offering genomic testing to all cancer patients for early detection and treatment.[72]

The plan's delivery was supported by NHS' GMS, which detailed the strategic priorities and necessary initiatives to accomplish these goals.[74]

GMS priorities include:

- Embedding genomics across the NHS, through a world-leading innovative service model from primary and community care through to specialist and tertiary care
- Delivering equitable genomic testing for improved outcomes in cancer, rare, inherited, and common diseases and in enabling precision medicine
- Enabling genomics to be at the forefront of the data and digital revolution, ensuring genomic data can be interpreted and informed by other diagnostic and clinical data
- Evolving the service through cutting-edge science, research and innovation to ensure that patients can benefit from rapid implementation of advances

RESULTS/OUTCOME:

The clear articulation of the value of genomics and its incorporation into the NHS' Long Term Plans has resulted in political commitment to:

- Work with medical associations to develop genomics training programs for HCPs
- Conduct annual reviews to update the provision of NGS testing in the National Genomic Test Directory for new clinical indications
- Develop shared data standards and infrastructure to support digital interoperability

LEARNINGS FOR POLICYMAKERS:

Policymakers can signal their commitment to the delivery of NGS-based care in oncology by incorporating genomic testing, such as NGS, as a priority area in national strategies. To drive this, clear objectives, initiatives, and relevant stakeholder responsibilities should be articulated to turn policy into implementation.

3.2.2 GENOMICS EDUCATION PROGRAM (GEP)

BARRIER ADDRESSED:
D. LACK OF HCP AWARENESS OR EDUCATION

With the integration of genomics in NHS care, healthcare professionals are required to be equipped with the essential skills for delivering genomics in care settings, such as its usage in clinical practice as well as supporting patients through genomic testing. To achieve this, Health Education England launched the Genomics Education Program in 2014, introducing a set of resources to improve genomics competency for healthcare professionals[78], including:

- Resources on application of genomics in specialties *(e.g., cardiology, oncology)* and functions *(e.g., nursing, midwifery)*
- Competency frameworks comprising 10 knowledge, skills and behaviors for HCPs to effectively communicate genomic results to patients *(e.g., consent conversation, result implication, support routes, test factors, clinical knowledge, etc.)*
- Knowledge hub with quick, concise information to help HCPs make the right decisions for every stage of the clinical pathway *(e.g., who can be offered a test, relevant conditions to offer, etc.)*

The program also developed various educational resources as well as education and training modules across England to support workforce development

IMPLEMENTATION/STEPS TAKEN:

All NHS healthcare professionals must possess a strong understanding of the relevance and potential of genomics to impact the diagnosis, treatment, and management of patients using the service.

- In 2014, a working group was formed among key genomic organizations to champion the integration of genomics into clinical practice[79]
- The group's efforts resulted in Health Education England launching a four-year £20 million GEP in 2014 *(and ongoing funding)* to ensure the NHS workforce has the knowledge, skills, and experience for applying genomics in healthcare[75]

OBJECTIVES OF GEP INCLUDE:

- **Prepare the workforce to deliver NHS GMS**
- **Support the completion of the landmark 100,000 Genomes Project**
- **Provide the best education opportunities in genomics for the NHS workforce**
- **Develop strategic collaborations to keep the UK at the forefront of genomics in healthcare**

RESULTS/OUTCOME:

- The GEP developed various educational resources incorporating a multidisciplinary perspective on genomics and its applications. More than 3,000 people across all professional groups in the NHS have studied at least one Master's module on genomics through the GEP[80]
- GEP funded education across England to support workforce development requirements for genomics, including educational workshops and training courses engaging with patients and the public to raise awareness on application of genomics in healthcare

LEARNINGS FOR POLICYMAKERS:

Healthcare professionals were educated on the benefits of genomic testing, such as NGS, and their application in clinical practice through a comprehensive genomics education program.

Policymakers can work with providers, medical associations, academia, and industry to support them in developing these programs so that healthcare professionals are aware of the value of NGS and are equipped with the essential skills to deliver its benefits in healthcare.

3.2.3 NATIONAL GENOMIC TEST DIRECTORY

BARRIER ADDRESSED:
F. INSUFFICIENT AND SILOED FUNDING ACROSS DIFFERENT TESTS/CANCERS

The UK launched the NHS Directory of Genetic Disorders/Genes for Diagnostic Testing in the 2000s, which only evaluated and recommended genomic tests for rare and inherited diseases. Cancer genomic testing was then introduced into the directory in 2018 through the launch of the National Genomic Test Directory, to ensure equity in access to various genomic tests. At present, over 200 cancer clinical indications are included, including NGS panels.

IMPLEMENTATION/STEPS TAKEN:

The National Genomic Test Directory contains genomic tests funded by NHS England for eligible patients, which includes NGS panels for cancer. Through the directory, the NHS aims to improve the effectiveness and equitability of genomic testing.[76]

An annual review process further supports the expansion of clinical indications for genomics testing and promote access to tests that benefit the health system. This review process includes:

- Horizon scanning process: Identify potential test additions to the directory, taking into consideration recommendations from institutions like NICE, as well as relevant policy changes, such as improvement of care management with NGS testing
- Fast track application system: Ensure that the directory can respond quickly to genomic developments across different tests and cancer types, allowing for accelerated inclusion of new NGS tests

RESULTS/OUTCOME:

- Currently, the test directory includes NGS panels covering 135 indications across five categories: solid tumors, neurological tumors, sarcomas, hematological and pediatric
- UK's National Genomic Test Directory is also a best practice example for other territories to model public test directories after

> *Currently, the UK National Genomic Test Directory is used as a case example to explore the feasibility of a Australian Genomic Test Directory[81] which would list the latest genomic tests available in Australia and the criteria for ordering (e.g., personnel, data interpretation required, genetic counselling needs).*
>
> ***Policy officer***

LEARNINGS FOR POLICYMAKERS:

The inclusion and funding of genomic tests across various indications, including cancer, was achieved through implementation of a forward-looking annual review process to help guide inclusion of new genomic tests.

Policymakers can encourage payers to adopt a similar review process to enhance their national test directory, tackling fragmented funding for clinical conditions.

3.3 SWEDEN CASE STUDY

3.3.1 GENOMICS MEDICINE SWEDEN

BARRIER ADDRESSED:
A. LACK OF FULL NGS INCLUSION INTO NATIONAL STRATEGIES

Prior to the establishment of Genomic Medicine Sweden (GMS) in 2017, Sweden had encountered challenges in developing a national strategy for NGS that further enabled its implementation in clinical practice. This challenge was brought about by Sweden's regionally-organized healthcare system.[82]

IMPLEMENTATION/STEPS TAKEN:

- In 2014, SciLifeLab, a national life-sciences infrastructure developed by academic stakeholders, launched a Clinical Genomics platform to enable the use of NGS testing in clinical research and diagnostics in Sweden.[82]
- Following this development, in 2017, academic and healthcare stakeholders collaborated to form Genomics Medicine Sweden, a national coordinating infrastructure for the implementation of precision medicine in Swedish healthcare systems.[82]
- Swedish policymakers began to signal their increased priority for precision medicine and NGS through funding support for the setup of Genomics Medicine Sweden.[83]

RESULTS/OUTCOME:

The successful setup of the SciLifeLab Clinical Genomics platform (in 2014) and Genomics Medicine Sweden (2017) has improved Sweden's capabilities in providing NGS testing in their health system and evidence generation.[82,83]

Additionally, political support for Genomics Medicine Sweden has increased access to NGS testing for tumor profiling in Sweden, benefitting patients with solid tumors and blood cancer.

- Compared to 2017 when Genomics Medicine Sweden was first setup, there was a 140% increase in cancer patients screened[84] *(majority of lung, colorectal and skin cancer patients)*
  - » Additionally, there had been a 480% increase in patients with blood cancer screened
- Additional government grants are currently supporting the pilot implementation of NGS in patients with other cancer types (including breast and ovarian) to support ongoing clinical studies[83,85]

Findings generated from NGS testing have led to actionable outcomes:

- A recently published study in June 2023 explored the clinical impact of whole genome sequencing (WGS) in 118 children with solid tumors[86]
- Potential treatment targets were found in 26% of patients, with targeted therapy administered to 13% of the treatment targets identified
- WGS is now being recommended by the Swedish Paediatric Association as a routine diagnostic test for all childhood cancer patients at the time of diagnosis, and is currently being implemented in routine clinical practice[87]

(Learnings for policymakers in the next page)

LEARNINGS FOR POLICYMAKERS:

This case study highlights that a bottom-up approach driven by academic and healthcare stakeholders in Sweden can also enable policymakers to recognise the need to accelerate the clinical implementation of NGS at scale.

Policymakers can look for support at a grassroots level from academics, clinicians and other ecosystem stakeholders to accelerate the clinical implementation of NGS.

BARRIER ADDRESSED: C. LACK OF INVESTMENT INTO NGS TESTING AND DATA INFRASTRUCTURE

Sweden's decentralized healthcare system is prone to forming information silos across non-interconnected systems,[88] hindering effective delivery of genomic testing. To address this, Genomics Medicine Sweden (funded by the Swedish government) introduced the National Genomics Platform (NGP) infrastructure in 2022 to facilitate seamless genomic data sharing nationwide. This enhances collaboration between healthcare institutions and research centers while laying the foundation for evidence generation in genomic research and healthcare.

IMPLEMENTATION/STEPS TAKEN:

The recent establishment of NGP enables seamless data sharing between the seven regional Genomic Medicine Centres (GMCs) in Sweden (similar infrastructure setup in UK in 2014).[77,89] These GMCs, strategically located across the territory to cover all healthcare regions, serve as primary points of contact for genomic sequencing, thereby creating an integrated network for both healthcare delivery and advanced medical research.

The NGP has three primary functions:

- Storing and sharing of genomic and associated clinical data across Sweden
- Indexing of data for swift retrieval and mobilization of genomic data
- Data processing and analysis to reveal insights into genetic patterns and diseases

RESULTS/OUTCOME:

- A unified infrastructure enables real-time sharing of genomics data on a national level[82], facilitating evidence generation for NGS-based tumor profiling
  - » Efficient sharing of resources and expertise further enhances the efficiency and reach of NGS services
- A common platform to consolidate and analyze genomic data can potentially increase diagnostic accuracy and expand testing capabilities
  - » Standardization of data structuring can be enforced, making it feasible for national analysis of genomic data

LEARNINGS FOR POLICYMAKERS:

Seamless data sharing across the nation is achievable through the implementation of a national infrastructure. This promotes collaborative efforts to enhance evidence generation in genomic medicine. Policymakers should thus introduce initiatives to establish digital tools and a unified genomics infrastructure to encourage data sharing and collaboration.

To gain a deeper understanding of current system readiness for NGS testing and identify further areas for investment, policymakers should also gather inputs from healthcare providers and medical associations.

3.4 JAPAN CASE STUDY

3.4.1 INCLUSION OF NGS INTO PRECISION MEDICINE INITIATIVES

BARRIER ADDRESSED:
A. LACK OF FULL NGS INCLUSION INTO NATIONAL STRATEGIES

The lack of full NGS incorporation into any national plans for healthcare *(e.g., genomics strategies and national cancer control plans)* restricts the nationwide downstream implementation of NGS into clinical practice and restricts access to NGS.[68]

IMPLEMENTATION/STEPS TAKEN:

- In 2015, Japan launched a precision medicine initiative focused on cancer genomics, recognizing the need for a comprehensive research framework
- The Japanese government initiated a concerted effort to foster the growth of Personalized and Precision Medicine (PPM) in Japan. Specifically, the Ministry of Health, Labor and Welfare (MHLW) was tasked to set key performance indicators (KPIs) and establish policies that drive research and healthcare improvements in cancer care, through the increased utilisation of advanced diagnostics such as NGS

RESULTS/OUTCOME:

- From 2018, as part of their PPM strategy, the Japanese government established the following initiatives
  1. Setup of the Centre for Cancer Genomics and Advanced Therapeutics (C-CAT) in 2018 to consolidate cancer genomic data and clinical information generated from NGS:
     - As of 2024, C-CAT is estimated to be collecting data from over 15,000 tests annually, hence propelling NGS use and PPM in clinical practice
  2. Designating 13 hospitals in Japan as primary centers for cancer genomic medicine
     - These hospitals were tasked with conducting NGS tests, managing in-house expert panels, and participating in matched therapy clinical trials while ensuring patient data is regularly and securely shared with C-CAT[90]
     - Expert panels in Japan are similar to MTBs, where the results of tumor sequencing are interpreted with clinical information, then recommended treatment and genetic information to be provided are determined[90]
  3. These initiatives also supported the implementation of NGS testing with the approval and reimbursement of multiple NGS assays in Japan with streamlined regulatory and reimbursement pathways for local and send-out tests **(refer to Barrier B on heatmap in Figure 5)**

LEARNINGS FOR POLICYMAKERS:

Creating a national precision medicine initiative and collaborating across government sectors to establish clear objectives and standards can lead to effective policies *(e.g., setting up of genomics infrastructure and enabling clinical implementation)* that improve access to precision medicine and advanced genomic technologies such as NGS.

3.4.2 FORMULATION OF CLINICAL GUIDELINES

BARRIER ADDRESSED:
E. LACK OF LOCAL CLINICAL GUIDELINES FOR NGS

The absence of adequate clinical guidelines in NGS testing can lead to inconsistencies *(e.g. variability in testing methodologies and result interpretation)*, compromising the overall reliability of NGS-based testing for cancer care. Establishment of guidelines can ensure a consistent standard of care, enable the provision of high-quality NGS testing, and serve as a tool for clinicians to better understand the various clinical applications of NGS.

IMPLEMENTATION/STEPS TAKEN:

To facilitate the widespread adoption of NGS-based cancer care in a safe manner, three Japanese medical societies came together in 2017 to issue a clinical guideline for NGS application in tumor profiling and treatment:

- The Japanese Society of Medical Oncology, the Japan Society of Clinical Oncology, and the Japan Cancer Association, jointly issued the *Guidance for Cancer Treatment Based on Gene Panel Testing Using Next-Generation Sequencers (1st edition) in 2017*
- To better develop the local clinical guidelines in Japan, global guidelines and definitions used by the European Union and the United States were referenced.[91] The Japanese guideline was later revised in 2020, following new developments surrounding cancer genomic medicine[64]

These clinical guidelines detailed:

- Selection of NGS tests, collecting and handling samples, disclosure of test results, etc
- Expert panels (EP), comprising medical oncology, genetics, pathology and bioinformatics experts need to be set up at designated core hospitals, offering appropriate expertise to interpret NGS-based tumor profiling results and providing guidance for appropriate treatment

RESULTS/OUTCOME:

- Guidelines ensured that high-quality NGS tumor profiling is accessible through a network of approximately 230 hospitals designated for cancer genomic medicine[92]
- The guidelines also established standard of care for NGS-based medicine by:
  - Ensuring quality and guiding interpretation of NGS testing
  - Discouraging unnecessary testing, positively contributing to health system efficiencies and cost savings for NGS-based cancer care

LEARNINGS FOR POLICYMAKERS:

Guidelines play a pivotal role in setting a standard of care for NGS-based medicine, ensuring that standardized NGS testing of high-quality are accessible nationally. With medical societies and providers being key stakeholders for the formulation of clinical guidelines, policymakers can collaborate and encourage them to implement NGS-based guidelines by referencing and adapting established global guidelines to fit local healthcare settings.

4. CONSIDERATIONS TO IMPROVE ACCESS TO NGS

The value of NGS-based tumor profiling has been well established, as detailed in the previous sections. There is growing demand and increasing awareness of the benefits for NGS technologies among healthcare stakeholders, evidenced by the increased investments seen in funding and developing the NGS testing ecosystem. Additionally, the utility of NGS is expected to increase as a growing number of biomarkers and associated therapies are identified. Addressing barriers to access now will unlock value for NGS in cancer care for the future.

To increase access to NGS for tumor testing in the APAC region, this paper proposes 11 considerations to address the key access barriers identified in **Section 2.** These considerations start from the top of the access 'funnel' to address upstream systemic barriers that will lay the groundwork necessary for VAF implementation and reimbursement downstream.

Table 15: Barriers and considerations to improve access to NGS for tumor profiling

	BARRIERS *(refer to Section 2 for details on barrier)*	CONSIDERATIONS TO IMPROVE ACCESS TO NGS FOR TUMOR PROFILING
A	**Lack of full NGS inclusion into national strategies**	**A.1** Include NGS for tumor profiling in national strategies/programs *(e.g. genomic or precision medicine)* to enable improved clinical outcomes for cancer patients and optimize healthcare spend
B	**Lack of coherence across regulatory, reimbursement and clinical implementation policies for NGS**	**B.1** Ensure linkage between regulatory, reimbursement and clinical implementation policies to provide more timely and equitable patient access to both in-territory and overseas NGS testing
C	**Lack of investment into NGS testing and data infrastructure**	**C.1** Facilitate the use of digital technologies to enable multi-disciplinary collaboration necessary for more efficient and productive NGS-based cancer care **C.2** Develop a strong national genomics infrastructure to enable the generation of local data, in order to validate effectiveness
D	**Lack of HCP awareness or education**	**D.1** Promote understanding of the impact of genomic information on patient outcomes and health system through education campaigns
E	**Lack of local clinical guidelines**	**E.1** Establish and promote national clinical guidelines, resources, and best practices for NGS-based cancer care management
F	**Insufficient and siloed funding across different tests/ cancers**	**F.1** Explore alternative funding models to broaden access to NGS testing in the short-term **F.2** Expand government-led funding and reimbursement for NGS testing equitably across the cancer patient population
G	**Conventional value assessment frameworks do not appreciate the full potential of NGS**	**G.1** Invest in NGS-based drug trial programs to increase patient access to matched therapies in the short term to improve local evidence generation and demonstrate clinical utility of NGS **G.2** Establish a fit-for-purpose VAF that recognizes the full value of NGS tumor profiling **G.3** Share local/ regional knowledge and experiences of best practices in value assessment frameworks for NGS

To account for nuances in the NGS landscape and address barriers across the territories in scope, considerations are also mapped to territory archetypes **(Figure 6)**, with different sets of takeaway actions for policymakers based on archetype detailed for each consideration. Given that no territory perfectly aligns with a predefined archetype, it is important to acknowledge that the considerations outlined in this paper may not apply to every territory.

Figure 6: Mapping of considerations to different territory archetypes

BARRIERS ADDRESSED	CONSIDERATIONS	NASCENT	EMERGING	DEVELOPING
Policy barriers	**A.1** Include NGS for tumor profiling in national strategies/programs *(e.g. genomic or precision medicine)* to enable improved clinical outcomes for cancer patients and optimize healthcare spend	✓	✓	✓
	B.1 Ensure linkage between regulatory, reimbursement and clinical implementation policies to provide more timely and equitable patient access to both in-territory and overseas NGS testing	✓	✓	
	C.1 Facilitate the use of digital technologies to enable multi-disciplinary collaboration necessary for more efficient and productive NGS-based cancer care	✓	✓ Investments to be tailored based on current infrastructure	
	C.2 Develop a strong national genomics infrastructure to enable the generation of local data, in order to validate effectiveness	✓	✓ Investments to be tailored based on current infrastructure	
Clinical barriers	**D.1** Promote understanding of the impact of genomic information on patient outcomes and health system through education campaigns	✓	✓	
	E.1 Establish and promote national clinical guidelines, resources, and best practices for NGS-based cancer care management	✓	✓	
Reimbursement/ HTA Barriers	**F.1** Explore alternative funding models to broaden access to NGS testing in the short-term	✓	✓	
	F.2 Expand government-led funding and reimbursement for NGS testing equitably across the cancer patient population	✓	✓	✓
	G.1 Invest in NGS-based drug trial programs to increase patient access to matched therapies in the short term to improve local evidence generation and demonstrate clinical utility of NGS	✓	✓	
	G.2 Establish a fit-for-purpose VAF that recognizes the full value of NGS tumor profiling	✓	✓	✓
	G.3 Share local/ regional knowledge and experiences of best practices in value assessment frameworks for NGS	✓	✓	✓
	TOTAL PRIORITY POLICY CONSIDERATIONS	11	9	4

For territories to achieve greater patient access for NGS-based cancer care, policymakers need to take on these considerations in a multi-stakeholder approach involving payers, providers, clinicians, pathologists, patient advocacy groups, industry and academics (Refer to **Table 16** in the next page).

Table 16: Call to action for stakeholders in the NGS-based tumor testing ecosystem

Barriers	Considerations	Payers	Policy-makers	Clinicians	Pathologists	PAGs	Industry	Providers	Academics
A. Lack of full NGS inclusion into national strategies	**A.1** Include NGS for tumor profiling in national strategies/ programs *(e.g. genomic or precision medicine)* to enable improved clinical outcomes for cancer patients and optimize healthcare spend		✓	✓	✓	✓	✓		✓
B. Lack of coherence across regulatory, reimbursement and clinical implementation policies	**B.1** Ensure linkage between regulatory, reimbursement and clinical implementation policies to provide more timely and equitable patient access to both in-territory and overseas NGS testing	✓	✓	✓	✓	✓	✓	✓	✓
C. Lack of investment into NGS testing and data infrastructure	**C.1** Facilitate the use of digital technologies to enable multi-disciplinary collaboration necessary for more efficient and productive NGS-based cancer care	✓	✓	✓	✓		✓	✓	✓
	C.2 Develop a strong national genomics infrastructure to enable the generation of local data, in order to validate effectiveness		✓	✓	✓		✓	✓	✓
D. Lack of HCP awareness or education	**D.1** Promote understanding of the impact of genomic information on patient outcomes and health system through education campaigns		✓	✓	✓	✓	✓	✓	✓
E. Lack of local clinical guidelines	**E.1** Establish and promote national clinical guidelines, resources, and best practices for NGS-based cancer care management		✓	✓	✓	✓	✓	✓	✓
F. Insufficient and siloed funding across different tests / cancers	**F.1** Explore alternative funding models to broaden access to NGS testing in the short-term	✓	✓ *where regulations permit			✓	✓		
	F.2 Expand government-led funding and reimbursement for NGS testing equitably across the cancer patient population	✓	✓	✓	✓	✓	✓	✓	
G. Conventional value assessment frameworks do not appreciate the full potential of NGS	**G.1** Invest in NGS-based drug trial programs to increase patient access to matched therapies in the short term to improve local evidence generation and demonstrate clinical utility of NGS		✓	✓	✓	✓	✓	✓	✓
	G.2 Establish a fit-for-purpose VAF that recognizes the full value of NGS tumor profiling	✓	✓	✓	✓	✓	✓	✓	✓
	G.3 Share local/ regional knowledge and experiences in value assessment frameworks for NGS	✓	✓				✓		✓

✓ **Lead Stakeholders**

✓ **Supporting Stakeholders**

Payers: Body responsible for reimbursement, funding and HTA evaluations informing funding decisions

Policymakers: Personnel from a range of different government bodies capable of suggesting, influencing and implementing policy changes *(e.g. Ministries of Health, Trade and Industry, Science and Technology, Finance, etc)*

Clinicians: Doctors having direct contact with patients and corresponding medical societies

Pathologists: Medical doctors with specialized training to diagnose medical conditions using laboratory tests and techniques and corresponding medical societies

PAGs: Patient advocacy groups are organizations that represent and support patients and their families with specific medical conditions societies

Industry: Medtech, pharma and private financing institutions *(e.g., insurers, banks)*

Providers: Health facilities (including hospitals, teaching / university hospitals, laboratories, clinics) that are licensed to provide health care diagnosis and treatment

Academics: Research and educational institutions conducting clinical or health economics research

The following sub-sections will further explore specific takeaway actions for each consideration by archetype, along with elaboration on:

- Requirement for consideration
- Description of best practice execution of consideration
- Actions required to execute consideration

CONSIDERATION A.1

Include NGS for tumor profiling in national strategies/programs *(e.g. genomic or precision medicine)* **to enable improved clinical outcomes for cancer patients and optimize healthcare spend**

LEAD STAKEHOLDER(S)

Policymakers

PAGs

SUPPORTING STAKEHOLDERS

Clinicians

Pathologists

Industry

Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Establish a national strategy that recognizes NGS as an enabler/ catalyst to meet cancer control goals with initiatives roadmap, supported by clear articulation of investments required, governance mechanisms (KPIs) and initiative owners *(e.g., executing stakeholders)*

EMERGING

Update existing national strategies to include NGS with a tumor profiling focus to advance delivery of NGS-based cancer care in the national agenda, supported by clear articulation of investments required, governance mechanisms (KPIs) and initiative owners *(e.g., executing stakeholders)*

DEVELOPING

Formalize the implementation of NGS for tumor profiling outlined in national strategies through establishing governance mechanisms (KPIs, accountability) with executing stakeholders to achieve national cancer objectives (with possibility for broadening indications)

WHY IS IT REQUIRED:

All territories need a clear, shared vision for the implementation of NGS-based cancer care to achieve equitable and improved patient care.

WHAT DOES GOOD LOOK LIKE:

A coordinated national strategy should address upstream barriers that impede access to NGS and lay the groundwork for universal implementation of NGS testing. Strategies should outline goals, initiatives, accountable stakeholders and measures for success.

WHAT NEEDS TO BE DONE: To achieve this, all stakeholders in the ecosystem need to be engaged to understand current barriers to access to efficiently co-create objectives of the national strategy, shape policies, and inform investment decisions required for NGS-based care. Policymakers need to show commitment to support NGS tumor testing through its inclusion in national health agendas, policies, and programs *(e.g. Genomic Medicine Sweden)* and establish relevant governance mechanisms to ensure the goals of the national strategy are met.[93]

- In Australia, the ongoing development of the Australian Cancer Plan 2023-2033 demonstrates their current commitment towards improving the quality and equity of cancer care throughout the territory[20]

Additionally, PAGs can represent patient voice and engage in grassroots advocacy for inclusion of NGS in policies.

> *Upon positive MSAC recommendation in AU, organizations such as Australian Genomics and PAGs work together to advocate for the inclusion of technologies such as NGS in national cancer plans, and develop guidelines and initiatives to support its full national rollout.*
>
> ***Policy officer***

CONSIDERATION B.1

Ensure linkage between regulatory, reimbursement and clinical implementation policies to provide more timely and equitable patient access to both in-territory and overseas NGS testing

LEAD STAKEHOLDER(S)

Policymakers

SUPPORTING STAKEHOLDERS

Payers, Clinicians, Pathologists, PAGs, Industry, Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Establish coherent and centralized pathways, and task relevant regulatory, reimbursement and clinical implementation stakeholders to review inconsistencies in policies, both within and across jurisdictions in the territory

EMERGING

Establish coherent pathways, and task relevant regulatory, reimbursement and clinical implementation stakeholders to review inconsistencies in policies, within the territory

WHY IS IT REQUIRED: Timely access to NGS testing requires harmonious regulatory, reimbursement and clinical implementation policies.

WHAT DOES GOOD LOOK LIKE: Upstream regulatory approval and reimbursement policies should be aligned on priority test types and cancer indications, along with clear pathways for timely approval. Processes should also be in place to update local clinical guidelines following global developments and local approval/reimbursement for timely implementation of NGS-testing.

WHAT NEEDS TO BE DONE: Policymakers should aim to design coherent pathways and task regulatory, reimbursement and clinical implementation stakeholders to initiate a review of policies to resolve inconsistencies. Industry, clinicians, pathologists and PAGs should be consulted to understand gaps in policies and pathways.

Where there is a lack of clear pathways to regulate overseas tests and LDTs, regulators can leverage international approvals from reference agencies such as US FDA and Japan's Ministry of Health, Labour and Welfare (MHLW) to establish a list of validated overseas NGS tests and labs recognized for local use.

Several territories like Singapore[94] and Taiwan[56] have published quality standards that are accepted for local and overseas testing. This ensures clarity on lab accreditations/certifications needed for regulatory and reimbursement decisions.

- However, the need for each medical institution in Taiwan planning to offer LDTs to submit individual applications poses an administrative burden. A unified application system, similar to IVD product registration processes, should be considered to streamline this process and increase access

> *There is a crucial need for alignment between regulatory and reimbursement processes of in-territory and overseas NGS tests South Korea. Reimbursement for in-territory tests allow 'pan-cancer' indications, but regulatory approval is still done on a 'per indication' basis.*
>
> *This involves updating regulatory pathways for NGS tests from 'per indication' to 'pan-cancer' to accommodate the emergence and reimbursement of pan-cancer treatments, such as those targeting TMB, Homologous Recombination Deficiency (HRD), and specific drugs like pembrolizumab, laparib, or niraparib. Additionally, pathways need to be set up for overseas NGS tests, which currently have no existing pathways.*
>
> *Harmonizing these processes will ensure a cohesive and streamlined approach to patient care enable timelier access to innovative therapies.*
>
> ***HCP KOL***

CONSIDERATION C.1

Facilitate the use of digital technologies to enable multi-disciplinary collaboration necessary for more efficient and productive NGS-based cancer care

LEAD STAKEHOLDER(S)

Policymakers

SUPPORTING STAKEHOLDERS

Payers

Clinicians

Pathologists

Industry

Providers

Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Update existing infrastructure development plans to expand or redirect existing healthcare technologies to support propagation of NGS testing workflows in clinical settings; with clear governance mechanisms *(e.g., KPIs)* and bodies to enforce implementation; secure funding for investment

EMERGING

Formalize expansion of infrastructure for NGS through establishing governance mechanisms *(e.g., KPIs)* with supporting stakeholders to monitor the implementation of relevant digital technologies into existing workflows, evaluating their downstream impacts on NGS access and assessing opportunities to further expand implementation of digital technologies nationwide

WHY IS IT REQUIRED: As territories work towards implementing NGS-based cancer care, workflows and referral systems supporting NGS tumor testing need to upgrade to meet current and future needs. Digital technologies will not only enhance accessibility of healthcare services and patient outcomes, but also the efficiency of the entire health system and its workflows to accelerate access to care. Digitizing processes will significantly improve efficiencies in the data collection and processing required for the multi-disciplinary collaboration fundamental to NGS-based cancer care.

WHAT DOES GOOD LOOK LIKE: Key enablers for collaborative cancer care are digital platforms and networks designed to be interoperable, connecting all stakeholders within the NGS ecosystem and streamlining associated workflows for effective care delivery and collaboration.

- **Effectiveness of care delivery:** Interoperable electronic medical records (EMRs) and laboratory information systems (LIS) will enhance data collection, sharing, and analysis. This is especially valuable where large amounts of cancer patient case data from various sources are required for decision-making, and cancer patients do not have time to wait[95]
- **Workforce efficiency:** Digital solutions have also been applied to MTBs to streamline the labor-intensive tasks required in the process *(e.g. literature search, establishing consensus, analysis reporting, etc)*[96-98]
- **Collaboration:** Increased connectivity will also improve accessibility of NGS-based care, especially benefiting patients in remote or underserved areas where physical access to specialized facilities may be limited.[99] Moreover, increased connectivity will allow MTBs to tap into expertise across geographies and specialties *(e.g., pathologists, bioinformaticians, specialists)* to increase capability and capacity for enable multi-disciplinary collaboration

In territories where geographical barriers (e.g. rural populations in Australia) or disease areas where patients' conditions (e.g. advanced cancer patients) may be an issue, digital networks to connect patients data across testing and consultation services will also be of greater value.

Policy officer

WHAT NEEDS TO BE DONE: Implementing digital solutions will require policymakers to establish or update healthcare infrastructure plans with the input of providers, clinicians and pathologists, along with clear governance mechanisms to enforce implementation. Provider, clinician and pathologist input will be important to direct investments into digital tools and platforms for the operational and clinical workflows that can benefit the most.

CONSIDERATION C.2

Develop a strong national genomics infrastructure to enable the generation of local data, in order to validate effectiveness

LEAD STAKEHOLDER(S)

Policymakers

Providers

SUPPORTING STAKEHOLDERS

Clinicians

Pathologists

Industry

Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Consult providers, academic and clinical stakeholders to develop a genomics infrastructure plan with goal of generating local data as an objective (in addition to other objectives of the plan), establishing goals, initiatives and investments required

EMERGING

Formalize integration of genomics infrastructure and evaluate impacts on NGS data interoperability and evidence generation capabilities, whilst exploring opportunities to expand infrastructure nationwide

WHY IS IT REQUIRED: Reimbursement decision making for NGS testing requires a good understanding of the relationship between genomic information and the clinical and economic outcomes from NGS tumor profiling. This requires a nationwide genomics infrastructure that supports the harmonization and integration of NGS data with other clinical and molecular data sources and contributes towards evidence generation.

There is a crucial need for peer-reviewed analyses on the cost-benefit of NGS testing that considers the diverse ethnic and disease profiles within local or regional populations. Local evidence generation serves as the cornerstone for ensuring that NGS is not only relevant but also cost effective in managing the diverse and unique healthcare needs of local patient populations.

HCP KOL

WHAT DOES GOOD LOOK LIKE: A robust national genomics infrastructure should include:

- **Data storage and processing infrastructure:** Connected and interoperable systems that enable large-scale capture and generation of NGS testing genomics data, enhancing analyses. This enables comprehensive studies of disease progression, treatment responses, and the emergence of resistance, contributing to a nuanced understanding of the clinical and economic implications of local genomic alterations and responses to treatments to inform policies and reimbursement decisions
- **Testing infrastructure:** Availability of NGS instruments and tests, HCPs and academics equipped with knowledge of NGS testing and application in cancer care
- **Other supporting infrastructure:** Supplementary facilities like biobanks, digital connectivity, HCP education on genomics that enable effective NGS testing

Successful models, such as Japan's SCRUM cancer genome screening project and the C-CAT genomic database,[100,10] and Korea's clinical trial referral platform K-MASTER[102] showcase comprehensive testing and data infrastructure for evidence generation and advancing the delivery of NGS-based cancer care.

WHAT NEEDS TO BE DONE: Policymakers will need to incorporate or establish a genomics infrastructure plan into existing national strategies with the inclusion of the generation of local data as a goal. Inputs from providers, clinicians, pathologists, and academics will be required to identify capabilities and corresponding investments required. Further governance mechanisms *(e.g., through KPIs and accountability)* will be required to ensure infrastructure is established and utilized to meet goals.

CONSIDERATION D.1

Promote understanding of the impact of genomic information on patient outcomes and health system through education campaigns

LEAD STAKEHOLDER(S)

- Clinicians
- Pathologists
- Providers

SUPPORTING STAKEHOLDERS

- Policymakers
- PAGs
- Industry
- Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Designate an institution for NGS tumor profiling thought leadership within the territory *(e.g., oncology centers of excellence, academic institution)* to develop education and awareness campaigns endorsed by policymakers, facilitating knowledge dissemination

EMERGING

Task medical/oncology societies to update and develop curriculum for current and future HCPs; endorse developed curriculum and mandate inclusion into HCP competency evaluations

WHY IS IT REQUIRED: Education campaigns to raise awareness of the benefits of NGS testing will empower patients and clinicians to realize the benefits from its use across the patient journey.

WHAT DOES GOOD LOOK LIKE: Awareness and education of the value of NGS testing should be raised for both new and existing healthcare professionals through a variety of initiatives, some examples listed:

New healthcare professionals:

- Education on NGS testing can be integrated into medical school curriculums to prepare future healthcare professionals.[62]

Existing healthcare professionals:

- Accredited seminars and workshops focused on NGS testing should be developed or integrated in existing Continuous Medical Education programs.[62]
  - In Singapore, the Ministry of Health has published a "Competency Framework for the Provision of Clinical Genetic/Genomic Testing (CGT) Services" framework to ensure healthcare professionals achieve competencies to provide NGS-based cancer care.
- Platforms for industry collaboration with medical societies can also enable the provision of NGS product training and increase awareness and best practices, such as that seen in Hong Kong.[103]
- Public education and awareness campaigns can also ensure that patients are well informed of the benefits of and open to NGS testing. Similar to the Genomic Education Program (GEP) initiative mentioned in **Section 3.2.2,** healthcare professionals can be empowered to engage and educate patients.

- MTBs also promote continuous medical education on NGS-based cancer care by serving as a platform to discuss complex cases[104,105] and translate new research advancements into clinical practice.
  - » In Taiwan, MTBs are conducted at least once a month at the Mainland China Medical University Hospital to discuss complex cases and guide treatment decisions, focusing on patients with unique NGS results that require further explanation by pathologists, bioinformaticians, laboratory technicians and clinicians.[60]

> *MTBs also provide a platform for discussions to keep pace with the growing knowledge of complex molecular alterations in patients with advanced solid cancer, allowing cancer experts such as medical oncologists and pathologists to share clinical insights and establish optimal treatment strategies with each other.*
>
> ***HCP KOL***

It is important for medical or pathology societies, and providers to develop awareness and education campaigns sharing the benefits of NGS testing in oncology. Policymakers and providers can designate institutions for NGS tumor profiling thought leadership to concentrate expertise and disseminate knowledge across the territory. Competency frameworks incorporating NGS should be developed by medical societies, endorsed by policymakers to be included in HCP evaluations with processes to regularly update guidelines.

WHAT NEEDS TO BE DONE: To achieve this, all stakeholders in the ecosystem need to be engaged to understand current barriers to access to efficiently co-create objectives of the national strategy, shape policies, and inform investment decisions required for NGS-based care. Policymakers need to show commitment to support NGS tumor testing through its inclusion in national health agendas, policies, and programs *(e.g. Genomic Medicine Sweden)* and establish relevant governance mechanisms to ensure the goals of the national strategy are met.[93]

CONSIDERATION E.1

Establish and promote national clinical guidelines, resources, and best practices for NGS-based cancer care management

LEAD STAKEHOLDER(S)

- Clinicians
- Pathologists
- Providers

SUPPORTING STAKEHOLDERS

- Policymakers
- PAGs
- Industry
- Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Initiate a policymaker endorsed taskforce with providers, HCPs and academics to develop and publish expert consensus on NGS testing in local oncology practice as a basis for development of local clinical guidelines (referencing global guidelines where necessary)

EMERGING

Endorse plans to develop guidelines and assign responsibility to relevant stakeholders *(e.g., medical society, provider systems)* with policymaker oversight *(e.g., ministerial liaison)* to ensure guidelines are developed and disseminated

WHY IT IS REQUIRED: Clear, evidence-based recommendations for NGS testing and results interpretation are essential for empowering clinicians to make cancer care management decisions confidently. This can only happen if clinicians are equipped with the right information and clinical decision support tools.

WHAT DOES GOOD LOOK LIKE: Global guidelines *(e.g. ESMO's Recommendations for the use of next-generation sequencing for patients with metastatic cancers)* provide strong recommendations that can be leveraged. However, local patient population and genomic profile differences will need to be considered. Territories should start by developing guidelines for the cancer indications most likely to benefit from NGS testing based on local settings and priorities. Guidelines should also detail when *(e.g. upfront or subsequent)* and which technologies *(e.g. small panel, CGPs, etc.)* to use, how to interpret and action results, and the clinical decision support tools available.[62,106] Multiple international guidelines have advocated for MTBs as best practice to provide structure to the multi-disciplinary decision making process central to NGS-based cancer care.[63]

- The Korean Precision Medicine Networking Group (KPMNG), in collaboration with the Korean Society of Pathologists, gathered expert consensus through collaboration between oncology specialists, pathologists, and bioinformaticians to develop more locally applicable recommendations on NGS for advanced solid cancer patients. Clinical trial databases and resources *(e.g. K-CAT scale)* were also provided as part of local recommendations.
- Australia has also developed TOPOGRAPH, a knowledge base for literature and evidence to guide clinicians specifically on targeted therapies based on genomic aberrations, while considering both local accessibility and maturity of a drug.[107]
- A Hong Kong based study demonstrated the value of MTB-guided treatment by demonstrating a significantly longer median OS than those who did not receive MTB-guided therapy *(12.7 months vs. 5.2 months, p = 0.0073)*.[61]

WHAT NEEDS TO BE DONE: To establish national clinical guidelines, HCPs, academics, and providers need to develop a consensus on NGS testing in local practice, and subsequently develop clear guidelines and recommendations. Policymakers can assign responsibility and oversight to the responsible stakeholder bodies *(e.g., medical associations)* to develop guidelines and endorse implementing them nationwide.

CONSIDERATION F.1

Explore alternative funding models to broaden access to NGS testing in the short-term

LEAD STAKEHOLDER(S)

Policymaker

Industry

SUPPORTING STAKEHOLDERS

PAGs

Payers

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Gather expert consensus on priority oncology areas and set up pathways for private partnerships *(e.g., risk sharing)* to enable NGS funding; whilst concurrently exploring more sustainable funding options

EMERGING

Gather expert consensus on priority oncology areas and set up pathways for private partnerships to enable NGS funding; whilst concurrently exploring more sustainable funding options

WHY IS IT REQUIRED: In territories where reimbursement is a long-term goal and not yet in place for NGS, there is often a heavy financial burden borne by patients and caregivers. Alternative funding models supplement payer funding gaps *(through private or other non-traditional public funding)* and alleviate patient financial burden in the short term while territories work on generating evidence and establishing more sustainable funding for NGS testing.

WHAT DOES GOOD LOOK LIKE:

Patient access programs (PAPs)

PAPs can be implemented for drugs and cDx technologies in the short term with industry funding to provide financial assistance to select patients who would not be able to afford innovative cancer care in the absence of sufficient government reimbursement.

- Expenditure cap models such as those developed by pharmaceutical and diagnostic companies can, for example, cap NSCLC patients' monthly treatment bills at a fixed level, after drawing from available government savings and reimbursement schemes.[108] On top of treatment subsidies, programs can also extend the expenditure cap model to its cancer genomic testing services (including NGS testing) that will enable patients greater access to these treatments
- However, such alternative access pathways provide access on a case-by-case basis and/or to only a small pool of patients and are not a sustainable means of providing access to NGS testing for the broader cancer patient population in the long term.

WHAT NEEDS TO BE DONE: To encourage healthcare ecosystem stakeholders to participate in alternative funding models in the short-term, policymakers should foster an environment *(e.g., platforms, pathways for application / discussion)* to enable public-private and private-private partnerships for alternative funding models (where regulations permit). Input from patient advocacy groups and payers could help inform and prioritize oncology areas requiring supplementary funding.

CONSIDERATION F.2

Expand government-led funding and reimbursement for NGS testing equitably across the cancer patient population

LEAD STAKEHOLDER(S)

Payers

SUPPORTING STAKEHOLDERS

Policymakers

Clinicians

Pathologists

PAGs

Industry

Providers

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT

Gather expert consensus to understand priority oncology areas most suitable for NGS; engage in discussions with payers to build initial reimbursement/ pilot funding models for NGS

EMERGING

Together with payers, ensure reimbursement schemes translate into tangible benefits *(e.g. increased clinical implementation resulting in improved clinical outcomes)*; formalize processes to review oncology areas that require NGS testing and funding

DEVELOPING

Together with payers, extend current reimbursement policy and processes to review a broader set of cancer indications requiring NGS testing and funding; introduce assessment methods that appreciate broader value of NGS beyond identification of matched therapies

WHY IS IT REQUIRED: While some APAC territories have made progress in providing some form of reimbursement for NGS testing, reimbursement is often limited to specific tests, panel types or cancer types *(e.g., NSCLC only)*. This fragmented reimbursement contributes significantly to inequities in NGS access, where other populations who may benefit from the technology are left without coverage.

- Japan's MHLW reimburses both hotspot panels and CGPs up to 70% of the cost, but only in advanced metastatic cancers. This constitutes a small subset of the patient population

It should be acknowledged that many APAC territories may be economically disadvantaged compared to Established territories *(e.g., UK, Nordics)* in providing funding for NGS profiling.[108,109] However, Established territories have also laid the groundwork necessary to support NGS reimbursement and are equipped with infrastructure and policy will to recognize the value of NGS.

WHAT DOES GOOD LOOK LIKE: Equitable reimbursement should encompass a broader spectrum of NGS tests and various cancer types, with mechanisms in place to evaluate and identify oncology areas where NGS has most utility.

> *This includes extending coverage to different cancers and stages that can also benefit from earlier NGS testing such as lung and colorectal cancer, and other NGS tests such as larger gene panels and CGPs.*
>
> ***Patient advocacy group representative***

Territories can draw references from reimbursement statuses in other territories such as the UK, to expand reimbursement of NGS testing to wider patient populations.

- The UK's NHS provides full reimbursement for various types of cancers, ranging from solid tumors, sarcoma to pediatric cancers. Those eligible will be able to take various NGS-based tests such as multi-target panels, hotspot panels and CGPs[76]
  - » This is supported by an annual review process that allows for ensuring that what is reimbursed meets the changing needs of the healthcare system

However, reimbursement challenges may persist in many territories as current evaluation processes fail to appreciate the full value of NGS testing (which often assess availability of matched therapies instead of the broader benefits).[106] Thus, assessment methods that appreciate the value of NGS should be introduced to provide payers with frameworks to prioritize funding for more cancer indications.

WHAT NEEDS TO BE DONE: Policymakers need to establish and prioritize oncology areas that require additional interventions (including NGS) to improve patient outcomes, and work with payers to initiate pilot funding or formalize processes to review and reimburse oncology areas requiring funding. To further enable expansion to a greater patient population, assessment methods that appreciate greater value of NGS need to be developed by payers.

CONSIDERATION G.1

Invest in NGS-based drug trial programs to increase patient access to matched therapies in the short term to improve local evidence generation and demonstrate clinical utility of NGS

LEAD STAKEHOLDER(S)

- Policymakers
- Industry
- Providers
- Academics

SUPPORTING STAKEHOLDERS

- Clinicians
- Pathologists
- PAGs

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT | **EMERGING**

Gather expert consensus to understand which priority oncology areas lack access to matched therapies; incentivize industries and relevant stakeholders to co-create relevant clinical trials in these areas *(e.g. grants for trial programs that utilize NGS, nationwide platforms or bodies to facilitate collaboration)*

WHY IS IT REQUIRED: The availability of matched therapies remains a key factor for payers to determine the utility of NGS technologies. However, current access to NGS-guided therapies is limited as payers are uncertain of the clinical benefits of novel treatments and value of biomarkers. NGS-based drug trial programs present an alternative means to increase access to matched therapies and help establish the value of NGS. Additionally, there are tangible benefits, including both direct economic growth within the sector and broader spillover effects on the economy, enabled by access to NGS.

WHAT DOES GOOD LOOK LIKE: The presence of a nationwide platform and guidelines recommending patients to participate in clinical trials based on NGS results will encourage approval and access to matched therapies and recognition of the value of NGS.

In South Korea, in cases where the drug recommended by the MTB lacks local approval or does not meet off-label use conditions, guidelines promote participation in clinical trials or engaging in the Expanded Access Program, all of which includes the use of in-territory NGS.[63]

- This program allows patients, who are ineligible for standard treatment or clinical trials, to use drugs still under development with approval from the Ministry of Food and Drug Safety (MFDS) as a last resort
- In return for government approval, adverse events, effectiveness and safety data of the Investigational New Drug (IND) must be reported to the IND provider.[110] This data is then shared with the MFDS as a way to increase the pool of evidence and manage uncertainties of the value of the biomarker and the new drug before official approval and funding decisions are made

The successes of Omico[111] in Australia as a platform for funding NGS-based trials *(through attracting foreign investment and collaboration)* are also testament to how territories can leverage trials to unlock greater access to new therapeutic options for thousands of patients.

> *In Emerging archetypes territories such as Singapore where NGS testing is still in its early stages, increased clinical implementation of NGS, particularly in the treatment of specific cancers such as NSCLC and colorectal cancer, is also largely attributed to clinical trials. Clinical trials are also highly appreciated as early access routes, especially in smaller territories where access is limited.*
>
> ***HCP KOL***

WHAT NEEDS TO BE DONE: Policymakers and industry partners can achieve this by prioritizing strategic investments in early access pathways and genomic-based clinical trials for targeted therapies.

Input from academics should also be considered to identify research topics and oncology areas that are a priority for clinical trials in the territory.

While trial programs provide avenues to increase patient access to NGS testing and matched therapies in the short term, government-led funding is still key for sustainable patient access to NGS technologies.

Public-private endeavors (be it PAPs or trials) can require multi-million dollar investments from industry partners, making them unsustainable as the primary method for providing broad access to NGS testing. In addition, access to NGS testing in research settings (e.g. clinical trials), as is often the case in 'Nascent and 'Emerging' archetypes, often depends on grants that expire upon the completion of a study.

HCP KOL

CONSIDERATION G.2

Establish a fit-for-purpose Value Assessment Framework that recognizes the full value of NGS tumor profiling

LEAD STAKEHOLDER(S)

- Policymakers
- Payers

SUPPORTING STAKEHOLDERS

- Clinicians
- Pathologists
- PAGs
- Industry
- Providers
- Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT	EMERGING	DEVELOPING
Shape healthcare ecosystem stakeholder consensus on the value of NGS; champion and monitor the adaptation of value assessment framework by payers		

WHY IS IT REQUIRED: To assess the value of NGS in these domains, a fit-for-purpose VAF for NGS is required that captures all value domains beyond conventional considerations like clinical utility and health system efficiencies (Refer to **Table 17** in the next page).

WHAT DOES GOOD LOOK LIKE: The proposed VAF should capture three types of value across clinical, economic, and humanistic / societal domains. In our subsequent section **(Section 5)**, this paper will delve into a detailed exploration of the proposed VAF and considerations for assessing value.

Table 17: Proposed value types and domains to capture in a fit for purpose VAF for NGS

Value Type	Value Domain	Description
Clinical	Health System Efficiencies and Cost Savings	Economic costs and benefits of NGS implementation on health system
	Clinical Utility	Impact on clinical decision-making and patient management leading to effects on clinical endpoints
Economic	Diagnostic Accuracy and Reliability	Performance in detecting genetic variations or mutations
	Impact on Economy	Direct and spillover value added to economy from sector growth and patient survival
Humanistic and societal	Patient and Caregiver Empowerment	Impact on patient and caregiver quality of life and autonomy
	Societal Implications	Broader consequences and effects of NGS use on a societal level

WHAT NEEDS TO BE DONE: Section 5.4 of the White Paper provides recommendations on how the VAF should be implemented, with policymakers and payers taking the lead to understand regional best practices of evaluating NGS, obtain expert consensus on the value domains relevant to NGS, and assess how the VAF can be implemented into existing evaluation frameworks.

CONSIDERATION G.3

Share local/regional knowledge and experiences of best practices in value assessment frameworks for NGS

LEAD STAKEHOLDER(S)

Payers

SUPPORTING STAKEHOLDERS

Policymakers, Industry, Academics

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT | **EMERGING** | **DEVELOPING**

Engage local and regional HTA bodies to share knowledge on existing assessment frameworks for diagnostics, and collectively build a new / adapted assessment framework for NGS

WHY IS IT REQUIRED: As territories in the APAC region continue to incorporate innovative technologies into clinical practice, they need to acknowledge that current processes are based on outdated models of evaluation.[4] The boundaries of conventional VAFs have continuously been challenged in recent years as advanced diagnostics and innovative therapies are developed and introduced.[112]

> *In order to make the necessary changes to deliver equitable healthcare in the future, there is an opportunity to share regional evidence and approaches for greater harmonization in value assessment.*
>
> ***HTA expert***

WHAT DOES GOOD LOOK LIKE: Multiple global and APAC HTA communities exist to accelerate the exchange of information and experiences, with aims to develop efficient national evaluation processes designed to inform decisions. Some examples of communities that can be engaged for local and regional knowledge sharing:

- World Health Organization (WHO)
- INAHTA
- Health Technology Assessment International (HTAi)
- Guidelines International Network (G-I-N)
- i-HTS
- EUnetHTA
- HTAsiaLink
- RedETSA
- ISPOR

WHAT NEEDS TO BE DONE: Sharing can be facilitated through participation of payers and policymakers in an APAC multi-stakeholder alliance, where all territories can benefit from established methodologies, avoid duplication of efforts, and learn from the knowledge and experience from others.[112] Policymakers may assist in engagement and facilitation of knowledge sharing between payer bodies across territories.

5. VALUE ASSESSMENT FRAMEWORK

5.1 AUDIENCE AND PURPOSE OF THE PROPOSED VAF

Value assessment frameworks (VAFs) act as tools to inform decision-making by outlining value domains to measure a healthcare service or intervention.

The paper is the first to propose a fit-for-purpose VAF for NGS in the APAC region and is targeted at capturing multi-stakeholder considerations when evaluating NGS. The value domains introduced in this section may not be conventionally considered in payer assessments but aim to:

- Demonstrate a comprehensive value of NGS applicable to all stakeholders in the healthcare ecosystem
- Inform policy decisions on access for NGS-based tumor profiling
- Serve as considerations for the development or adaptation into existing assessment frameworks

There are limitations in how formal assessments typically evaluate technologies such as NGS:[12,13]

Current HTA frameworks for diagnostics involve the comparison of the costs and benefits associated with using a diagnostic test to identify patients suitable for targeted treatment, compared with no testing and use of standard treatment.[11] While this is feasible for diagnostics linked to a single treatment or treatment class, it is a significant challenge for NGS which is often linked to multiple diseases and treatments.

Beyond individual clinical benefit, NGS testing may also provide personal utility *(e.g., enhanced prognosis and a sense of hope)* and systemic benefits *(e.g., efficiencies in health systems through reductions in time to diagnosis, and follow-up visits)*. None of these benefits are formally considered.[113-115]

- Indirect benefits arising from personal utility and the "value of knowing", are often overlooked in favor of cost-utility analyses that rely on incremental cost per Quality-Adjusted Life Year (QALY) gained

Thus, there is a need for NGS evaluation frameworks to evolve beyond the confines of conventional payer assessments, through a fit-for-purpose value assessment framework (VAF), which will capture:

- **Additional spillover benefits**, such as contributions to the economy and sector growth, which are typically not accounted for in existing frameworks
- **Societal implications**, such as equity of NGS access and future improvements in public health outcomes, which are also not often considered for NGS diagnostics. These implications are driven by knowledge generated from NGS tests

The VAF for NGS proposed in this paper:

- Is based on existing value assessment and HTA frameworks of similar diagnostics, and reflects value elements that have been validated by experts.[116-121] A detailed methodology on how the VAF was built can be found in the **Appendix: Section 3** of the paper
- Captures the broader benefits of NGS beyond its clinical utility and impacts on health system efficiencies and cost savings. Other value domains include, impacts on the wider economy, patient and caregiver outcomes, as well as societal implications
- Is also adaptable across the APAC region to account for heterogeneity in the access landscape for NGS

> *In Australia, the proposed VAF aligns harmoniously with existing policies and government strategies for the implementation of NGS. The value domains currently employed by MSAC are largely similar to the proposed VAF.*
>
> ***HTA expert***

There is strong support among experts for the inclusion of a comprehensive set of value domains in a VAF for NGS to capture all benefits **(Table 18)**.

Table 18: Domains of the proposed VAF for NGS

	Evaluation Considerations (non-exhaustive)
Health System Efficiencies and Cost Savings Economic costs and benefits of NGS implementation on health system	▸ Direct costs related to NGS testing ▸ Budget impact and cost savings for healthcare system[122] ▸ Workforce and workflow efficiencies ▸ Downstream healthcare resource utilization and cost savings (including estimated costs of delaying care[122]) from » Timelier diagnoses » Efficient treatment identification » Reduced need for invasive biopsies » Directing patients to clinical trials
Clinical Utility Impact on clinical decision-making and patient management leading to effects on clinical endpoints	**Leading indicators:** ▸ Cancer prognosis ▸ Prevention of adverse events ▸ Time to treatment ▸ Cancer outcome prediction **Lagging indicators:** ▸ Overall survival (OS) ▸ Progression-free survival (PFS) ▸ Quality of life ▸ Treatment response *(e.g., according to RECIST (Response Evaluation Criteria in Solid Tumors))*
Diagnostic Accuracy and Reliability Performance in detecting genetic variations or mutations	▸ Quality standards for NGS tests, *e.g.* » *Analytical validity* » *Clinical validity* » *Clinical utility*
Impact on Economy Direct and spillover value added to economy from sector growth and patient survival	▸ Impact on GDP ▸ Job creation ▸ Productivity benefits ▸ Identification of novel biomarkers and impact on drug development processes
Patient and Caregiver Empowerment Impact on patient and caregiver quality of life and autonomy	▸ Patient-reported outcomes *(e.g., using EORTC Questionnaires, SF-12 Health Survey, EQ5D)* ▸ Impact on patient mental state ▸ Value of knowing (prognostic indicators and outcome prediction) ▸ Value of "hope" *(patients/ caregivers looking forward to newer investigative treatments enabled by NGS)* ▸ Patient involvement in their own care ▸ Financial burden of overall cancer care
Societal Implications Broader consequences and effects of NGS use on a societal level	▸ Equity of NGS access *(estimated via rates of NGS testing within local/regional populations to identify testing disparities) (e.g., analyzing utilization demographics through electronic medical records / claims data)*[123] ▸ Improvements in public health outcomes, driven by knowledge generated from NGS tests

However, there is variance between stakeholders on the priority of value domains across different regions, highlighting the need for a comprehensive approach to assessing the value of NGS-based tumor profiling.

> *There are varied priorities amongst stakeholders across the region, with payers such as those in Taiwan, Japan, and South Korea expected to prioritize health system efficiencies and cost savings associated with NGS implementation, while pathologists in South Korea prioritizing diagnostic accuracy, and clinicians, clinical utility of NGS tests. Patients also tend to prioritize patient and caregiver empowerment outcomes. Nonetheless, there is agreement on the six domains across the board.*
>
> ***HCP KOL, HTA expert***

5.3 AUDIENCE AND PURPOSE OF THE PROPOSED VAF

While some value domains and evaluation considerations outlined in **Section 5.2** are already recognized in current value assessments, it is recommended that more evaluation considerations within each domain be taken into account to capture the full value of NGS. This section will elaborate on the respective value domains and share perspectives on how the value of NGS can be assessed.

5.3.1 HEALTH SYSTEM EFFICIENCIES AND COST SAVINGS

This domain relates to the economic costs and benefits of implementing NGS on health systems, including the measurement of direct and indirect costs linked to NGS testing, incremental budget impact, impacts on workforce and workflow efficiencies, as well as downstream healthcare resource utilization and cost savings.

- **Direct costs related to NGS testing**

  There is a wide variety of economic studies that have evaluated the cost-effectiveness of NGS. A study that estimated NGS costs from a Canadian public payer perspective found that NGS reduced testing costs per patient when compared to SGT due to a quicker initiation of treatment with matched therapies for oncology patients.[122]

- **Downstream healthcare resource utilization and cost savings (including estimated costs of delaying care[121])**

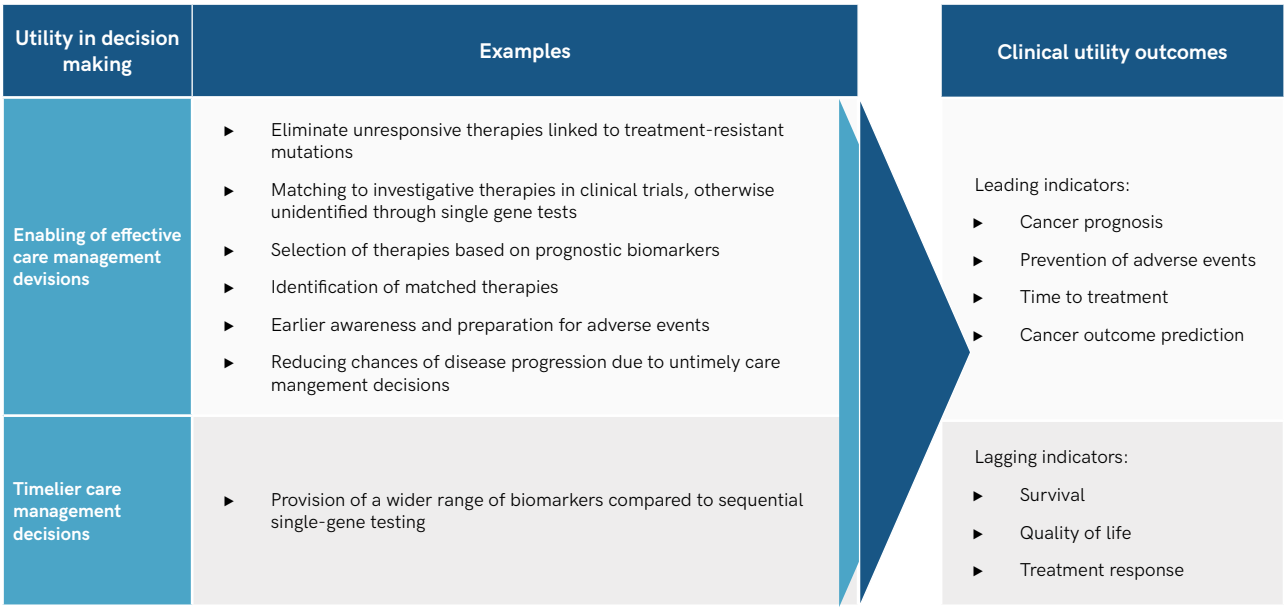
  Furthermore, a budget impact analysi s conducted in a US setting suggests that there are benefits to be realized from the implementation of NGS in hospitals.[46] These include a reduction in testing turnaround time, increase in the number of patients receiving matched therapy, and a positive budgetary impact of introducing NGS testing in hospitals. Similar findings emerged from a comparison of costs between NGS-based and SGT-based approaches in Italy, encompassing personnel, consumables, equipment, and overhead costs.[124]

> *When conducting evaluations, payers are interested in understanding the tangible cost savings of NGS testing, ranging from costs of the appropriate treatment to costs incurred from caregiving and medical transport. This is observed in certain territories such as Australia, South Korea and Taiwan.*
>
> *In Taiwan, since the National Health Insurance reimburses most diagnostic tests and drugs, they prioritise evaluations of health system efficiencies and cost savings. The Centre for Drug Evaluations, a HTA body in Taiwan, would be the responsible party in making these evaluations.*
>
> ***HCP KOL, HTA expert***

5.3.2 CLINICAL UTILITY

Clinical utility measures the ability of NGS to provide tumor profiling information that supports effective and more timely care management. This utility extends beyond the identification of matched therapies through its ability to pinpoint specific genetic changes that drive a tumour's growth. Consequently, this diagnostic information enables HCPs to make more informed clinical decisions for tumor management through effective risk stratification and prognosis **(Figure 7)**. This translates into faster time from sampling to treatment initiation[125] and improvements on clinical endpoints such as overall survival in terms of PFS and OS.[125] Additionally, as the quantity of actionable mutations and targeted therapies grow, the clinical utility of NGS is expected to increase over time.[62]

Figure 7: Clinical utility of NGS across leading and lagging indicators



The intrinsic clinical utility of NGS is highlighted through its potential in identifying a greater breadth of genes compared to sequential SGT. In Japan, medical societies are currently working on creating an appropriate 'scale' to assess the diagnostic value of NGS, in terms of:

- *Molecular diagnosis for disease prognosis and risk management*
- *Potential for chemotherapy-sparing and enhancements in patient well-being*

Payers in Australia and South Korea prioritize the current percentage of patients with matched therapies in their evaluation of NGS' clinical utility

- *Recent studies highlight that the percentage of patients with matched therapies may not be as low as payers perceive*
  - *For example, Australia's Rare Cancers Australia reported that an estimated 50% of all NSCLC patients fall into 10 molecular subtypes of cancer, in which there are matched therapies available*

HCP KOL, Policy officer

5.3.3 DIAGNOSTIC ACCURACY AND RELIABILITY

Another domain to evaluate the value of NGS is its ability to accurately report clinically relevant, actionable, and reproducible results. The implementation of high-quality NGS tests assures clinicians that NGS tests are accurate, reliable, and clinically relevant.[32]

The quality standards of NGS testing (also discussed in **APACMed's Unlocking the Value of Quality Next-Generation Sequencing in APAC**)[32] can be divided into three key areas:

ANALYTICAL VALIDITY

Refers to the ability of the test to predict the presence or absence of a particular gene or genetic change. Assessment of analytical validity involves the measurement of the test's performance over a set of predefined metrics, to demonstrate whether it is adequate for its indications of use. Key quality metrics for analytical validity pertain to accuracy, precision, and limit of detection of NGS tests.

CLINICAL VALIDITY

Refers to how well NGS tests can detect or predict a clinical condition associated with the genotype. Sensitivity, specificity, positive predictive value and negative predictive value are key measurements.

CLINICAL UTILITY

Explained in **Section 5.3.2**, refers to the usefulness of the results obtained from the NGS test, including whether they provide helpful information about disease diagnosis, treatment, management, and prevention.

> *This domain is important for pathologists, who rely on NGS tests to provide accurate diagnosis and tumor subtyping.*
>
> *This domain also drives NGS' intrinsic clinical utility; accurate diagnoses inform risk stratification and prognosis, contributing to more informed tumor management. Using accurate and reliable tests enables the understanding of the specific alterations driving the tumor. Subsequently, clinicians can identify alternative treatments other than matched therapies that may be more effective in treating the cancer.*
>
> ***HCP KOL***

5.3.4 IMPACT ON ECONOMY

The implementation of NGS also has implications on the wider economy beyond clinical and health system settings. This domain enables the creation of value in the economy through:

- **Growth of the NGS sector, leading to direct and spillover impact on GDP and job creation**

  Increased provision of quality NGS assays will lead to demand for products and services associated with the sector. This will lead to an increase in GDP and creation of jobs to support the sector *(e.g., research scientists, manufacturing, technology infrastructure, etc.)*

  The Australian government invested 61.2 million AUD from the Australian Government's Medical Products stream of the National Manufacturing Priority into PrOSPeCT, a public-private partnership that aims to bring in 525 million AUD of direct investment into local clinical trials and create 650 jobs in 2 years.[126]

- **Potential productivity benefits from improvement in patient outcomes**

  Oncology patients can now live longer, healthier, and productive lives as they receive the best care management informed through NGS. This enables patients and caregivers *(who may need to spend less time on caregiving)* to better contribute to the economy.

  These potential productivity benefits on the economy should be considered in VAFs to fully capture the spillover benefits of NGS.

- **New drug discovery and biopharma sector growth**

  The wealth of data that NGS testing provides can facilitate the identification of novel biomarkers and accelerates the drug discovery process, reducing the time and resources traditionally required to do so.

  Consequently, this streamlined approach to drug development not only expedites the introduction of innovative cancer treatments and growth in the biopharmaceutical sector.

> *The Australian government recognized that investing in OMICO's PrOSPeCT project could yield benefits extending beyond the enhancement of NGS access. The project was seen as a catalyst for driving growth in the healthcare sector, encompassing economic expansion, job creation, and the elevation of skills within the employed population engaged in clinical research in Australia.*
>
> *The advantages of this investment were not confined solely to the research sector; rather, they were contingent on collaborative efforts. It is through this collaborative venture that the full spectrum of economic benefits, including sectoral growth and the development of a skilled workforce contributing to clinical research, could be actualized in Australia.*
>
> ***HCP KOL, Policy officer***

5.3.5 PATIENT AND CAREGIVER EMPOWERMENT

This domain relates to individual utility provided by NGS testing beyond a patient's clinical state influencing their overall QoL and autonomy, along with the well-being of caregivers. All aspects of the patient journey are considered in this domain including emotional and social aspects, with benefits including:

- **Improvements in QoL**

  Improvements in QoL can be attributed to the ability to provide optimal care options, like preventing the selection of treatments that could lead to adverse events with minimal improvement in outcomes, which in turn, can lead to improvements in mental health and overall well-being. This is supported through a survey conducted among German respondents who validated that there are QoL benefits associated with NGS.[127]

- **The value of 'hope'**

  The value of 'hope' is also widely discussed in oncology, as patients may place greater value on treatment/care pathways that ultimately leads to an extended period of survival. NGS has intrinsic clinical utility in offering and even avoiding standard cancer treatments, through investigative drugs in clinical trials and chemotherapy-sparing respectively. By uncovering more treatment options with a single test, NGS testing instills confidence in individuals and society to manage cancer.[127]

- **The value of knowing**

  NGS testing in cancer care also confers a 'value of knowing' for patients and caregivers, a concept which encapsulates the effects of testing which may not immediately translate into health improvements but rather pertain to the potential benefits associated with knowledge of a prognosis or diagnosis. This can empower patients and caregivers to make informed life planning decisions based on their prognosis or relieve anxiety after obtaining information that aids diagnosis.

  Australia's MSAC also considers the 'value of knowing' aspect when evaluating health technologies including NGS. In addition to the established clinical utility of NGS, the MSAC examines non-health-related benefits and harms under the umbrella of the value of knowing.[128]

> *Personal utility of NGS testing in terms of QoL impacts is seen as the top priority for oncology patients, which extends to downstream benefits of NGS such as treatment sparing and mental health impacts*
>
> ***Policy officer***

5.3.6 SOCIETAL IMPLICATIONS

The societal implications of NGS testing refer to the broader consequences and effects that the widespread use of NGS has on society at large. These implications extend beyond healthcare settings and encompass social and ethical dimensions. Broader consequences/impacts include:

- **Ensuring equitable cancer care management**

  A consideration for NGS use includes ensuring equitable access to cancer care across diverse populations. Access to NGS has the potential to improve healthcare equity, as genomics data ensures that the most effective healthcare intervention is used on patients who need it the most, as opposed to relying on socioeconomic determinants such as affordability of testing.[49]

> *Equity of access is a crucial societal implication of NGS. Stakeholders in Australia are advocating for more centralized support for NGS testing to minimize inequities. Recognizing and addressing disparities in access to NGS is essential to ensure that the benefits of genomic advancements are accessible to all members of society, promoting fairness and inclusivity.*
>
> ***HTA expert***

- **Improvements in public health outcomes**

  There is also societal benefit from the wealth of data generated by NGS testing.[106] Firstly, NGS-generated data creates research opportunities, allowing the in-depth exploration of tumor profiles for the identification of novel biomarkers and therapeutic targets. This sets the stage for future targeted treatments, enhancing public health outcomes.

  Additionally, NGS data serves as a crucial resource for clinicians. A deeper understanding of genetic tumor profiles enables precise diagnostic and treatment planning. This personalized approach ensures oncology patients receive optimized care, contributing to better individual and collective health outcomes.

  As these advancements integrate into clinical practice, the healthcare system will become better equipped to address individual variations in disease susceptibility and treatment response.

5.4 STEPS TO IMPLEMENT VAF

Disclaimer: all inputs in this section are expert opinions

Implementing a VAF for NGS involves policymakers and payers taking lead roles, with support from stakeholders in the healthcare ecosystem (Refer to **Table 19** in the next page). In this section, we highlight the implementation steps required from a policymaker's perspective, the respective areas where other stakeholders can support collectively, and the drivers for successful VAF implementation.

Table 19: Overview of implementation for NGS-specific VAF

Note: Lead stakeholders will be responsible for enacting implementation steps with the support of other stakeholders in the ecosystem

Implementation steps		1 Horizon scanning	2 Gather expert consensus	3 Adapt VAF within current evaluation frameworks	4 Assess NGS with adapted evaluation frameworks
Roles that the ecosystem can play in implementing the VAF	Policymakers	**Lead stakeholder**		Continue to provide policy support to adapt VAF	Track impact of VAF adaptation on NGS access and measured value domains, with continuous adjustments and updates to meet needs
	Payers	Provide inputs on existing valuation framework for NGS/similar diagnostics	NGS Key Opinion Leaders to provide inputs based on VAF framework and domains on how NGS should be evaluated	**Lead stakeholder**	
	Academics			Provide advice and endorsement for VAF adaptation	Provide relevant data/participate in evidence-generation related activities, provide feedback on VAF impact on NGS access
	Clinicians	Provide inputs on how NGS is used in clinical practice and the current level of access		Advocate and champion adoption of VAF domains based on unmet needs	
	Pathologists				
	Providers			Adapt existing in-hospital HTA frameworks	
	PAGs	Provide inputs on current level of access		Provide consultation on HTA frameworks	Increase capacity and capability to provide evidence, provide feedback on VAF impact on NGS access
	Industry	Provide intelligence on regional level of access best practices for evaluation of NGS	Provide support in fostering multi-stakeholder collaborations to provide inputs on valuing NGS	Provide inputs and endorsement for VAF adaptation	Provide relevant data/participate in evidence-generation related activities, provide feedback on VAF impact on NGS access

STEP 01

Horizon scanning

Policymakers should first conduct a landscape scan to understand regional and local developments and best practices in the evaluation of NGS. The aims are to deepen understanding on current levels of NGS access, readiness of existing frameworks to value NGS and similar diagnostics, and the needs and priorities of local health systems.

Drivers for success include the analysis of best practices from territories that have achieved success in improving NGS access, *e.g., through reimbursement and implementation of VAFs for NGS*.

All territory archetypes in APAC typically reference European territories, including the UK and Nordic territories *(e.g, Sweden, Denmark)* or the US for best practices.

STEP 02

Gather multi-stakeholder expert consensus

Policymakers should work towards implementing a territory specific VAF, which can be guided through expert consensus on the value domains that should be implemented. Inputs from multi-stakeholder groups on frameworks and value domains for NGS should be considered to drive successful implementation of the VAF. Across the in-scope APAC territories, different stakeholder groups were prioritised based on territory landscape:

- Across all territories, the perspective of payers on territory specific priorities of value domains are important to obtain early on, especially in single-payer systems
- In South Korea, clinicians and pathologists' inputs are vital as they are key advisors to payers; inputs from providers, which have hospital level procurement and evaluation processes are also important
- In Japan, inputs from a group of providers *(a total of 13 hospitals who are key providers of NGS)* on value domains are highly valued
- Across Australia and Taiwan, input from patient advocacy groups *(especially in Australia where PAGs are invited to give inputs on HTA evaluations)* and clinician communities are important

STEP 03

Adapt the VAF's value domains for NGS within local existing evaluation frameworks

When the value domains proposed in an NGS specific VAF aligns or is recognized by policymakers and payers with existing evaluation frameworks for similar diagnostics devices, it is likely that the VAF will be accepted through adaptation into existing frameworks. At this stage, continued policy support and endorsement from policymakers to support the VAF's adaptation will be a driver for success.

STEP 04

Apply VAF domains to assess NGS with adapted evaluation frameworks

After the adaptation of the VAF, the evaluation frameworks will be used to assess NGS technologies to enable access.

It is recommended that the impact of the VAF on enabling NGS access be monitored at a policymaker level, with feedback continuously gathered from healthcare ecosystem stakeholders as inputs for updating and iterating on the VAF. The VAF can be further modified to address other applications of NGS in cancer care, as outlined in **Section 1.2 of the Introduction**.

Additionally, real world outcomes related to the value domains in the VAF should also be measured to understand if benefits match defined evaluation considerations. To drive this, baseline measurements pre-implementation of VAF should also be gathered by the relevant stakeholders *(e.g., clinical utility metrics collected by **providers** and **clinicians**)*

6. CALL TO ACTION

The expert consensus we have gathered through roundtables and interviews is that the integration of NGS into cancer care not only enhances patient and clinical outcomes but also confers additional societal and economic benefits. As a result, NGS can serve as a vital tool in addressing the clinical and economic challenges of increasing cancer burden in APAC. In order to realize these benefits, all healthcare ecosystem stakeholders need to work together to tackle access barriers, led and coordinated by national-level policymakers.

To realize the promise of NGS, we urge policymakers to spearhead a collective effort to address barriers limiting NGS access in the APAC region by:

- Establishing and implementing **a comprehensive and fit-for-purpose VAF for NGS,** to ensure that the full value of NGS is captured and realized in the entire healthcare ecosystem
- Placing **a larger emphasis on NGS** in national strategies for oncology
- Providing guidance to government agencies **to harmonize regulatory, reimbursement and clinical implementation** policies to both in-territory and overseas NGS testing
- Driving **collaboration and investment into infrastructure** to boost the existing clinical implementation and evidence generation of NGS
- Seeking ways to supplement and expand government-led **funding and reimbursement for NGS testing**
- Ensuring **equitable access to NGS** across a larger cancer patient population across a wider range of cancer types

The VAF captures the broader benefits of NGS beyond its clinical utility and impacts on health system efficiencies and cost savings, which includes additional spillover benefits to the economy, and societal implications. It is also adaptable across the APAC region to account for the heterogeneity in the access landscape for NGS.

However, to achieve these goals, support and leadership will also need to come from all stakeholders in the healthcare ecosystem, including payers, academics, clinicians, pathologists, providers, PAGs and industry. Inclusion of diverse perspectives will ensure that the considerations to access barriers are put in place that are adaptable within local healthcare settings.

Payers can:

- Lead the adaptation and assessment of the VAF for NGS into existing evaluation frameworks

Providers can:

- Support the digitisation of existing NGS capabilities and collaborate with other provider groups to establish national level networks
- Collaborate with industry to generate local evidence to substantiate the benefits of NGS

Clinicians and pathologists can support by:

- Developing national clinical guidelines and decision-making tools for NGS
- Advocating for inclusion of NGS in national strategies and plans by championing its value
- Educating other healthcare professionals, patients and caregivers on the benefits of NGS

Industry, inclusive of medtech, pharma and private financing institutions can:

- Provide and enable short-term access and affordability measures such as clinical trials and PAPs for NGS and matched therapies
- Collaborate with providers to generate local evidence to support and substantiate value assessment
- Collaborate with governments and other private parties such as institutional investors to find longer-term innovative funding solutions
- Empower PAGs to take up advisory roles in decisions that enable NGS access

Academics can support by:

- Providing guidance to policymakers on how to localize regional frameworks such as the VAF
- Guiding payers to adapt and implement VAF domains at a national level

Patient advocacy groups can:

- Champion the clinical and societal benefits of NGS
- Seek to play a greater involvement in decisions related to NGS access

In conclusion, we argue that improving access to NGS-based tumor profiling will tip the scales in favor of better care for oncology patients, efficient health systems and equitable healthcare. This starts with getting healthcare ecosystems to realize the value it brings to health systems, society, and most importantly, patients.

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Vista Health

Vista Health is the leading life sciences advisory in the Asia-Pacific region. Vista Health offers strategic consulting and tech enabled solutions across all corners of health care, building lasting partnerships with payers, providers, patients, and industry. For more information, visit: **https://vista.health/**

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APPENDIX

SECTION 1: ADDITIONAL INFORMATION ON NGS BENEFITS

1.3.1 CLINICAL BENEFITS OF NGS

Many studies have established the clinical value demonstrated by NGS-based diagnostics in oncology.[129,130] The value of NGS in delivering improved patient outcomes and cost efficiencies in the APAC region have also been reported in a recent APACMed report 'Unlocking the Value of Quality Next-Generation Sequencing in APAC.[32]

NGS enables oncologists to obtain a comprehensive genomic profile of a patient's tumor, allowing for more precise diagnosis and treatment planning. It provides insights into the specific genomic alterations driving cancer, potentially identifying emerging biomarkers and equipping clinicians with the knowledge needed to make informed decisions about patient management, including targeted therapies, chemotherapy-sparing, trial referrals, and other care decisions.[8]

NGS has also been shown to be versatile in cancer management across tumor types. Multiple studies have shown NGS enhances survival outcomes with chemoimmunotherapy and targeted therapies in specific cancer types like breast cancer, ovarian cancer, gastrointestinal cancer and non-small cell lung cancer (NSCLC).[62,131–133] One key retrospective study involving late-stage cancer patients in the United States showed those who underwent NGS testing and were subsequently matched to targeted therapy achieved a remarkable median overall survival of 52 weeks, double the 26 weeks observed in the control group.[37] Another study in Japan involved patients with metastatic castration-resistant prostate cancer who underwent CGP tests, with 22.2% of them treated with genotype-matched therapy and showed promising survival outcomes.[6]

Given the clinical benefits associated with NGS, clinical oncology organizations such as the American Society of Clinical Oncology (ASCO), the Japan Society of Clinical Oncology (JSCO) and the National Comprehensive Cancer Network (NCCN) have issued guidelines recommending the use of more NGS tests, such as hotspot panels and CGP, for specific cancer types such as advanced NSCLC.[64,134–136]

1.3.2 ECONOMIC BENEFITS OF NGS

In addition to its significant clinical value, NGS has also been shown to be cost-effective compared to traditional sequence testing.[122] This is driven by its ability to analyze multiple genes at once, reducing the need for multiple sequential tests and their associated costs. A study comparing total testing costs between NGS and single gene testing for NSCLC patients demonstrated cost savings for the NGS cohort.[122] Additionally, the results from NGS testing can lead to more efficient resource allocation by avoiding ineffective and potentially harmful treatments, lengthy hospitalizations, and directing patients to appropriate clinical trials.[137–139]

With the increasing HCP endorsement and use of NGS, evidence of the economic benefit of NGS tumor testing is beginning to emerge in territories reimbursing NGS *(e.g., partially in Korea, Taiwan and Japan)*.[26,27] Greater acceptance and implementation of NGS-based cancer care is anticipated to enable better management of cancers, enhance patient outcomes, and reduce healthcare costs for oncology.[37,43]

- In Korea, cost per patient per year for advanced NSCLC and advanced colorectal cancer patients was found to be ~10% lower for patients using NGS vs single gene tests[26,27]
- In Hong Kong, a clinical and economic impact study involving NSLSC patients showed that exclusionary testing *(SGT for EGFR and ALK followed by NGS for other alterations)* led to $4.6 million in cost savings and shortest time to results compared to the current practice of sequential testing[5]
- A cost-effectiveness study evaluated five molecular profiling strategies and found that a sequential tissue-plasma NGS approach is cost-effective, providing additional QALYs and monetary benefits, especially when considering a willingness-to-pay threshold of S$45,000/QALY[140]

1.3.3 HUMANISTIC AND SOCIETAL VALUE OF NGS

The value of NGS-based tumor profiling at the humanistic and societal level is often missed in current evaluation frameworks in APAC.[113] At the individual level, there is "value of knowing" the wide array of genomic information for patients and caregivers:

- **Relieve patient anxiety** due to quicker definite diagnoses compared to sequence testing, and provide hope for patients as better care options or treatments are identified[141]
- **Improved quality of life** from selecting optimal care options and sparing ineffective expensive options *(e.g., chemotherapy or immunotherapy in patients with certain targetable biomarkers who are unlikely to respond)*[141]
- Patients and caregivers are **empowered to make life-planning decisions** based on the prognosis information provided by NGS and have **access to life-changing investigational treatments**

A showcase of NGS value at the individual level could be found in Germany, where a study using in-house NGS testing reduced the testing turnaround time by an average of 10 days and increased the number of patients on targeted therapy by 3.38%, significantly reducing the waiting time for treatment.[46] Another study conducted in UK, compared the clinical utility of cell-free DNA next-generation sequencing (cfDNA-NGS) against routine standard-of-care (SOC) molecular tissue testing as commissioned by NHS England, in patients with advanced non-small cell lung cancer (aNSCLC). Median time from request-to-report was shorter for cfDNA-NGS versus SOC molecular tissue testing (8 versus 22 days) and halves time-to-treatment (16 versus 35 days).[125]

At a societal level, shortening or ending the diagnostic odyssey is likely to improve clinical management as well as economic benefits. A timelier diagnosis enables more appropriate treatment, and avoidance of unnecessary spend on potentially toxic therapy, and repeated testing costs. Moreover, the wealth of knowledge generated from NGS can drive improvements in public health outcomes through:

- Enabling faster more accurate diagnoses in a cancer patient population through a better understanding of tumor profiles
- Contributing to future improvements in healthcare by identifying drug candidates from tumor profiling

By leveraging genomic data, NGS testing also contributes to promoting health equity, ensuring that interventions are tailored to individuals based on their specific genetic makeup. The goal is to deploy the right intervention for the right person at the right time, thereby optimizing healthcare and fostering a more equitable health landscape.[49]

SECTION 2: ADDITIONAL TERRITORY EXAMPLES FOR NGS ACCESS BARRIERS, SORTED BY ARCHETYPE

Figure 8: Evaluation rubric for severity of barrier by archetype

ARCHETYPES	NASCENT	EMERGING	DEVELOPING
Policy barriers			
A. Lack of full NGS inclusion into national strategies	There is a lack of NGS inclusion into national strategies	There is inclusion of NGS in national strategies, but not with a tumor profiling focus	Initial discussions to include NGS for tumor profiling in national strategies, but yet to be formalized
B. Lack of coherence across regulatory, reimbursement and clinical implementation policies	There are discrepancies among policies, both within and across jurisdictions in the territory	There is a lack of coherence between regulatory, reimbursement and clinical implementation policies within the territory	Although policies are more adequate there is scope to streamline further
C. Lack of investment into NGS testing and data infrastructure	There is insufficient investment in infrastructure, with no plans to do so	There are plans to invest in infrastructure to support NGS	There is existing infrastructural investment, but implementation is limited to Centers of Excellence / selected healthcare facilities
Clinical barriers			
D. Lack of HCP awareness or education	There is a lack of awareness of NGS testing	Awareness of NGS testing is limited to centers of excellence, however awareness or education programs are yet to be in place	Growing awareness of NGS testing beyond centers of excellence, with plans to establish programs to increase awareness
E. Lack of local clinical guidelines for NGS	No locally relevant clinical guidelines on NGS testing	Plans to develop locally relevant clinical guidelines on NGS testing	Local clinical guidelines on NGS testing available, with limited implementation
HTA / reimbursement barriers			
F. Insufficient and siloed funding across different tests / cancers	There is no NGS-specific reimbursement	Reimbursement of NGS testing has been piloted, planned or ongoing but highly restricted to small set of cancer types and with strict eligibility criteria	Reimbursement still siloed but open to a wider set of cancer types with strict eligibility criteria
G. Conventional value assessment frameworks do not appreciate the full potential of NGS	Traditional evaluation frameworks for diagnostics have been used to evaluate NGS with no success Low perception of clinical utility of NGS	Traditional evaluation frameworks for diagnostics have been used to evaluate NGS with limited success Low perception of clinical utility of NGS	There is existing HTA evaluation for diagnostics, with plans to establish/ adapt for NGS Increasing perception of clinical utility of NGS, driven by initiatives to improve perception in short term *(e.g., clinical trials for matched therapies)*

A. LACK OF FULL INCLUSION OF NGS INTO NATIONAL STRATEGIES

Nascent archetype examples:

- The absence of NGS in Mainland China's Five-Year Plan, which encompasses the 15-year Mainland China Precision Medicine Initiative (PMI) launched in 2016, has hindered accessibility of NGS
  - Barriers include high costs, limited availability of NGS, and the lack of harmonization in treatment capacities, capabilities, and standards across different classes of hospitals
  - Consequently, NGS utilization is estimated at only 15%, despite reports that testing rates for key biomarkers such as *EGFR* and *HER2* can reach 80-95%[53]

Emerging archetype examples:

- Singapore's National Precision Medicine (NPM) Initiative is a whole-of-government initiative which aims to generate precision medicine data and improve delivery of care.[54] However, projects under this initiative only focus on sequencing hereditary diseases rather than tumor testing

Developing archetype examples:

- NGS testing has been recognized as a key driver to help Taiwan implement precision health in its existing care pathways, leading to impactful discussions such as The Advanced Precision Cancer Medicine (APCM) Forum in August 2023 to promote implementation of NGS[142]
- While this has led to announcements for reimbursement of NGS, policymakers have expressed a need to formulate policies addressing practical issues such as infrastructure and resource constraints, along with KPIs to measure progress[142]

B. LACK OF COHERENCE ACROSS REGULATORY, REIMBURSEMENT AND CLINICAL IMPLEMENTATION POLICIES FOR NGS

Nascent archetype examples:

- In Mainland China, despite the existing frameworks for NGS tests regulated by the National Medical Products Association (NMPA), Human Genetic Resources regulations restrict access to well-validated, U.S. FDA-approved overseas testing[55]
  - Additionally, local NGS tests are partially reimbursed through public insurance in selected cities, but not across other jurisdictions in the territory

Emerging archetype examples:

- In South Korea, while there is existing reimbursement for 'pan cancer' indications, its regulatory framework is still based on a 'per indication' basis

Developing archetype examples:

- In Taiwan, pathways for approval of overseas LDTs exist. However, there is a lack of centralization with regulatory guidelines and clinical implementation, as individual applications are still required for each medical institution to implement NGS (as opposed to a single regulatory body *e.g., TFDA approving NGS IVDs used locally*)[56]

C. LACK OF INVESTMENT INTO NGS TESTING AND DATA INFRASTRUCTURE

Nascent archetype examples:

- In Mainland China, there is expert consensus calling for improvements in web-based automated clinical decision support systems, which can enable MTBs and improve the clinical implementation of NGS.[57] More details on MTBs can be found in **Consideration D.1, under Section 4**

Emerging archetype examples:

- Taiwan announced the Cancer Precision Medicine and Biobank Consortium Collaboration Pilot Project in 2021[58] to establish the National Biobank Consortium of Taiwan (NBCT), a virtual biobank that expands Taiwan's genetic data management capabilities and enabled the setup of MTBs in participating hospitals

Developing archetype examples:

- In Australia, despite the establishment of infrastructure to support NGS testing, the challenge for nationwide integration persists due to the lack of a federated system
- Although Singapore exhibits Emerging archetype traits overall, its setup of the Singapore Translational Cancer Consortium (STCC) and its national clinic-genomic database initiative in 2020 will enhance NGS implementation in Singapore in the future[59]
- Hong Kong, another Emerging archetype territory, has recently established a Working Group on Laboratory Network for Genetic Testing was established, with aims to enhance collaboration and coordination of genetic testing services across Hong Kong[143]

D. LACK OF HCP AWARENESS OR EDUCATION

Nascent archetype examples:

Traditional sequential testing is still predominant and preferred in clinical practice, even in cancer indications shown to highly benefit from NGS-based tumor profiling *(e.g. NSCLC)*. Additionally, there is an unrealised opportunity to improve the general awareness and education of its benefits.

> *In Mainland China, clinicians primarily treat based on experience and traditional sequence testing, often overlooking the need for NGS-based diagnostics in their treatment approaches due to lack of exposure to NGS utility.*
>
> ***HTA expert***

Emerging archetype examples:

- Despite Australia portraying Developing archetype traits overall and a growing interest in NGS testing in cancer, surgeons and oncologists are still not familiar with cancer genomics and have limited experience with the latest methodologies in daily practice.[144,145]
- In Singapore, the general community of HCPs *(e.g., doctors and nurses)* do not receive sufficient ongoing education on NGS tests in their clinical practice to keep up with the rapid advancements in NGS-based diagnostics[62]

While molecular tumor boards (MTBs) can fill this educational gap, they are still a very nascent concept in Nascent and Emerging archetypes.[60] MTBs involve gatherings of multi-disciplinary experts to address complex patient cases, with a specific focus on molecular findings. These findings include NGS data and results from other relevant assays, and discussions involve how this information can guide treatment decision-making.

- However in Taiwan, MTBs are only conducted once or twice monthly due to limited availability of resources and expertise[146]

Developing archetype examples:

- While Hong Kong has generally shown trends characteristic of Emerging archetypes, there have been recent progress in advancing HCP awareness of NGS testing
  - Current late-stage delivery of public education on precision medicine may have resulted in low levels of the scientific community expressing interest in precision medicine careers leading to low awareness of the benefits of NGS tumor profiling[147]
  - However, it has recently recognized the need for and recommended continuous medical education (CME) programs in precision oncology be delivered to all oncologists to support integration of NGS testing in practice[148]
  - Furthermore, the Hong Kong Precision Oncology Society (HKPOS) has been set up to provide a platform for driving precision oncology, including education
  - The HKU-HKSH territory-wide, multicenter, pan-cancer MTB established in 2018 has also set a gold standard for other institutions to follow within the region[61]

E. LACK OF LOCAL CLINICAL GUIDELINES FOR NGS

Nascent archetype examples:

- While Singapore and Taiwan exhibit Emerging archetype traits overall, these territories lack clinical guidelines to guide NGS use in local practice
- This delays treatment for patients undergoing sequential testing, and potentially increases overall diagnostics and treatment costs for those on non-targeted treatments[62]

> *Although international guidelines offer guidance on NGS testing, guidelines catered to local patients and disease profiles are paramount to improving application of NGS, especially in the Asian context. These territory-specific guidelines are crucial for providing clear direction in the local context on how NGS testing should be optimally positioned to realize the benefits, considering the relevant cancer types and availability of matched therapies and trials.*
>
> ***HCP KOL***

Emerging archetype examples:

- In Hong Kong, Consensus Statements on Precision Oncology in the Mainland China Greater Bay Area *(inclusive of Guangdong, Hong Kong, Macau)* were recently published to harmonize the clinical integration of precision oncology by formulating a set of principles guiding clinical application, results interpretation, and reporting, with further recommendations on how to further optimize integration[148]
- While this shows recent efforts to support integration into local healthcare systems, the consensus statements also call for establishing a working group to develop local clinical practice guidelines, as that remains a gap to guide the clinical use of NGS panels

Developing archetype examples:

- While Mainland China typically exhibits Nascent archetype traits, the Chinese Society of Clinical Oncology recently published the Chinese Expert Consensus on Next Generation Sequencing Diagnosis for Non-small Cell Lung Cancer (2020 Edition)[65]
- However, these guidelines are not yet sufficiently promoted and disseminated among the medical community, resulting in a lack of awareness and implementation

F. INSUFFICIENT AND SILOED FUNDING ACROSS DIFFERENT TESTS / CANCERS

Nascent archetype examples:

- In Singapore, despite being classified under the Emerging archetype, there is only a blanket subsidy for cancer diagnostics through the national medical savings scheme (MediSave), and the amounts are currently insufficient to cover the costs of NGS-based diagnostics[62]

Emerging archetype examples:

- Since early 2023, the Hong Kong government has incorporated NGS tests into clinical practice to improve diagnostic services for NSCLC patients through a pilot funding programme.[67] However, there is still potential for pilot funding to be expanded into other cancer types which can benefit from NGS testing
- Although Mainland China is classified under the Nascent archetype, there is funding for NGS available. However funding is limited only to local public insurance schemes from major cities such as Beijing and Shanghai, leaving the majority of patients from other cities to self-finance[148]

Developing archetype examples:

- Despite Taiwan portraying Emerging archetype traits overall, NGS will be reimbursed for 19 cancer types, including in-territory and overseas testing, from May 2024; but can only be claimed once-per-lifetime for each cancer type[10,69]
- In Japan, reimbursement decisions had been announced for 6 CGP tests, however this funding is currently constrained only as a last resort measure, to patients with advanced cancers and can only be claimed once-per-lifetime[68]
- In Australia, funding for small gene panels had taken place in November 2023, but is limited to NSCLC patients[66]

G. CONVENTIONAL VALUE ASSESSMENT FRAMEWORKS DO NOT APPRECIATE THE FULL POTENTIAL OF NGS

Nascent archetype examples:

- Despite showing Emerging archetype characteristics, Singapore's ACE assessed liquid biopsy tests for NSCLC patients but did not issue a positive funding / reimbursement recommendation[71]

Emerging archetype examples:

> *While Mainland China has established HTA methods, these processes differ across provinces and cities, with more established procedures in major cities. Moreover, the HTA processes in Mainland China tend to favor drug evaluation rather than diagnostics.*
>
> ***HTA expert***

> *Similarly, in Taiwan and Hong Kong, traditional HTA frameworks have been applied successfully to evaluate NGS, leading to its recent support for NGS through the 2024 funding decision and pilot funding programme respectively.*
>
> ***HCP KOL***

Developing archetype examples:

- In Australia, the Medical Services Advisory Committee's (MSAC) recent HTA review process for small gene panels included the consideration of extensive clinical and economic evidence, but did not consider the additional advantages these NGS tests may have, such as societal benefits[66]

> *Following Australia's MSAC recommendation to fund small gene panels, specific methods for NGS evaluation are currently being explored.*
>
> *The "value of knowing", or the additional information that NGS provides which can contribute towards understanding of treatment responses, prognostic indicators, and adverse events, have also been recognised by payers as a growing consideration.*
>
> ***HTA expert***

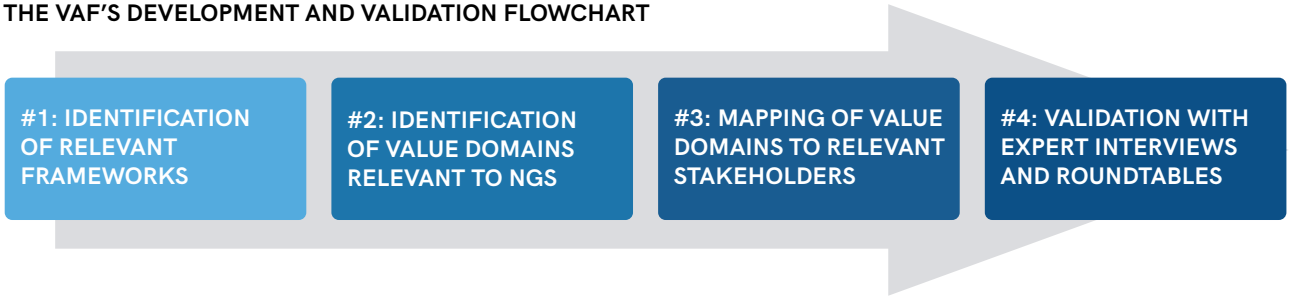
- In South Korea, the HTA agencies (National Evidence-based healthcare Collaborating Agency (NECA) and the Health Insurance Review & Assessment Service (HIRA)) are looking into ways to refine existing frameworks that enable access to NGS.[70] However, recent decisions to reduce reimbursement for non-lung cancers underscore the repercussions of insufficient evidence

> *The uncertainty regarding the clinical utility of NGS testing in local populations has led to these reimbursement reductions, as payers attribute the clinical utility of NGS to the availability of matched therapies, which is recognized to be less than 5% in all cancer types excluding lung cancers*
>
> ***HCP KOL***

SECTION 3: METHODOLOGY FOR THE FIT-FOR-PURPOSE VAF FOR NGS

The value domains that make up the NGS VAF were based on an extensive range of publications, with specific considerations given to publications that introduced frameworks and recommendations on the evaluation of advanced diagnostics. Following which, the value domains were validated through expert interviews and roundtable sessions.

THE VAF'S DEVELOPMENT AND VALIDATION FLOWCHART



#1: IDENTIFICATION OF RELEVANT FRAMEWORKS

An extensive list of publications that highlight the benefits of NGS was considered, to ensure that the benefits of NGS that extend beyond clinical domains, into economic and societal domains were captured in the fit-for-purpose VAF.

Table 20 below shows the relevant evaluation frameworks of similar diagnostics were considered.

Table 20: List of existing frameworks considered for NGS VAF

NO.	FRAMEWORKS	GEOGRAPHY	DEVELOPERS
1	**VODI in Cancer Care**[149]	Europe	MedTech Europe
2	**Strengthening Healthcare Systems Through the Critical Role of Diagnostics**[150]	APAC	APACMed
3	**VODI: VAF for In-Vitro Diagnostics in APAC**[151]	APAC	APACMed
4	**Evaluation of genomic applications in practice and prevention (EGAPP)**[118]	United States	Government office
5	**Blancquaert evaluation framework**[119]	Canada	Independent researchers
6	**EuroGentest evaluation model**[120]	Europe	Scientific associations
7	**Accelerating genomic medicine in the NHS [Genomics Unit at NHS England]**[152]	United Kingdom	HTA agency

#2: IDENTIFICATION OF VALUE DOMAINS RELEVANT TO NGS

Amongst the relevant evaluation frameworks considered, value domains relevant to NGS were identified in **Table 21** below.

Table 21: Mapping of relevant value domains to considered frameworks

Identified Value Domain	Framework 1	Framework 2	Framework 3	Framework 4	Framework 5	Framework 6	Framework 7
Diagnostic Accuracy and Reliability	✓	✓	✓	✓	✓	✓	
Clinical Utility	✓	✓	✓	✓	✓	✓	✓
Health System Efficiencies and Cost Savings	✓	✓	✓		✓		✓
Impact on Economy			✓		✓		✓
Patient and Caregiver Empowerment	✓	✓	✓	✓	✓		✓
Societal Implications	✓	✓	✓	✓	✓	✓	✓

#3: STAKEHOLDER MAPPING

The value domains were then mapped to key stakeholder groups to ensure that the proposed VAF is fit-for-purpose shown in **Table 22** below.

Table 22: Mapping of relevant value domains to key stakeholder groups

VALUE DOMAIN	DOMAINS TARGETED AT:				
	HEALTHCARE PROFESSIONALS	HEALTHCARE PROVIDERS	PATIENTS	PAYERS	POLICYMAKERS
Health System Efficiencies and Cost Savings	✓	✓	✓	✓	✓
Clinical Utility	✓	✓	✓	✓	✓
Diagnostic Accuracy and Reliability	✓	✓	✓	✓	
Impact on Economy	✓	✓	✓	✓	✓
Patient and Caregiver Empowerment	✓	✓	✓	✓	✓
Societal Implications		✓	✓		✓

#4: VALIDATION WITH EXPERT INTERVIEWS AND ROUNDTABLES

Following the development of the VAF, its value domains along with its evaluation considerations were presented and validated through a group of NGS experts. These validation processes were conducted through a range of interviews and roundtable sessions. There is strong support among experts for the inclusion of a comprehensive set of value domains in a VAF for NGS to capture all its benefits.

SECTION 4: POLICYMAKER TAKEAWAYS, BY ARCHETYPE

POLICYMAKER TAKEAWAY BY ARCHETYPE:

NASCENT	EMERGING	DEVELOPING
A.1 Include NGS for tumor profiling in national strategies/programs *(e.g. genomic or precision medicine)* to enable improved clinical outcomes for cancer patients and optimize efficient healthcare spend		
Establish a national strategy that recognizes NGS as an enabler/catalyst to meet cancer control goals with initiatives roadmap, supported by clear articulation of investments required, governance mechanisms (KPIs) and initiative owners *(e.g., executing stakeholders)*	Update existing national strategies to include NGS with a tumor profiling focus to advance delivery of NGS-based cancer care in the national agenda, supported by clear articulation of investments required, governance mechanisms (KPIs) and initiative owners *(e.g., executing stakeholders)*	Formalize the implementation of NGS for tumor profiling outlined in national strategies through establishing governance mechanisms (KPIs, accountability) with executing stakeholders to achieve national cancer objectives (with possibility for broadening indications
B.1 Ensure linkage between regulatory, reimbursement and clinical implementation policies to provide more timely and equitable patient access to both in-territory and overseas NGS testing		
Establish coherent and centralized pathways, and task relevant regulatory, reimbursement and clinical implementation stakeholders to review inconsistencies in policies, both within and across jurisdictions in the territory	Establish coherent pathways, and task relevant regulatory, reimbursement and clinical implementation stakeholders to review inconsistencies in policies, within the territory	
C.1 Facilitate the use of digital technologies to enable multi-disciplinary collaboration necessary for more efficient and productive NGS-based cancer care		
Update existing infrastructure development plans to expand or redirect existing healthcare technologies to support propagation of NGS testing workflows in clinical settings; with clear governance mechanisms *(e.g., KPIs)* and bodies to enforce implementation; secure funding for investment	Formalize expansion of infrastructure for NGS through establishing governance mechanisms *(e.g., KPIs)* with supporting stakeholders to monitor the implementation of relevant digital technologies into existing workflows, evaluating their downstream impacts on NGS access and assessing opportunities to further expand implementation of digital technologies nationwide	
C.2 Develop a strong national genomics infrastructure to enable the generation of local data, in order to validate effectiveness		
Consult providers, academic and clinical stakeholders to develop a genomics infrastructure plan with goal of generating local data as an objective (in addition to other objectives of the plan), establishing goals, initiatives and investments required	Formalize integration of genomics infrastructure and evaluate impacts on NGS data interoperability and evidence generation capabilities, whilst exploring opportunities to expand infrastructure nationwide	
D.1 Promote understanding of the impact of genomic information on patient outcomes and health system through education campaigns		
Designate an institution for NGS tumor profiling thought leadership within the territory *(e.g., oncology centers of excellence, academic institution)* to develop education and awareness campaigns endorsed by policymakers, facilitating knowledge dissemination	Task medical/oncology societies to update and develop curriculum for current and future HCPs; endorse developed curriculum and mandate inclusion into HCP competency evaluations	
E.1 Establish and promote national clinical guidelines, resources, and best practices for NGS-based cancer care management		
Initiate a policymaker endorsed taskforce with providers, HCPs and academics to develop and publish expert consensus on NGS testing in local oncology practice as a basis for development of local clinical guidelines (referencing global guidelines where necessary)	Endorse plans to develop guidelines and assign responsibility to relevant stakeholders *(e.g., medical society, provider systems)* with policymaker oversight *(e.g., ministerial liaison)* to ensure guidelines are developed and disseminated	*(Item F.1 to be continued in the next page)*

POLICYMAKER TAKEAWAY BY ARCHETYPE:

	NASCENT	EMERGING	DEVELOPING
F.1 Explore alternative funding models to broaden access to NGS testing in the short-term	Gather expert consensus on priority oncology areas and set up pathways for private partnerships *(e.g., risk sharing)* to enable NGS funding; whilst concurrently exploring more sustainable funding options	Gather expert consensus on priority oncology areas and set up pathways for private partnerships to enable NGS funding; whilst concurrently exploring more sustainable funding options	
F.2 Expand government-led funding and reimbursement for NGS testing equitably across the cancer patient population	Gather expert consensus to understand priority oncology areas most suitable for NGS; engage in discussions with payers to build initial reimbursement/ pilot funding models for NGS	Together with payers, ensure reimbursement schemes translate into tangible benefits *(e.g. increased clinical implementation resulting in improved clinical outcomes)*; formalize processes to review oncology areas that require NGS testing and funding	Together with payers, extend current reimbursement policy and processes to review a broader set of cancer indications requiring NGS testing and funding; introduce assessment methods that appreciate broader value of NGS beyond identification of matched therapies
G.1 Invest in NGS-based drug trial programs to increase patient access to matched therapies in the short term to improve local evidence generation and demonstrate clinical utility of NGS	Gather expert consensus to understand which priority oncology areas lack access to matched therapies; incentivize industries and relevant stakeholders to co-create relevant clinical trials in these areas *(e.g. grants for trial programs that utilize NGS, nationwide platforms or bodies to facilitate collaboration)*		
G.2 Establish a fit-for-purpose Value Assessment Framework that recognizes the full value of NGS tumor profiling	Shape healthcare ecosystem stakeholder consensus on the value of NGS; champion and monitor the adaptation of value assessment framework by payers		
G.3 Share local/regional knowledge and experiences of best practices in value assessment frameworks for NGS	Engage local and regional HTA bodies to share knowledge on existing assessment frameworks for diagnostics, and collectively build a new / adapted assessment framework for NGS