APACMed
The voice of MedTech

Transforming Healthcare
Saving Lives

Strengthening Healthcare Systems Through the Critical Role of Diagnostics

Co-Creation Opportunity for Asia-Pacific Government & Payer Leaders

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An Initiative of the Digital Health and Government Affairs & Market Access Committees

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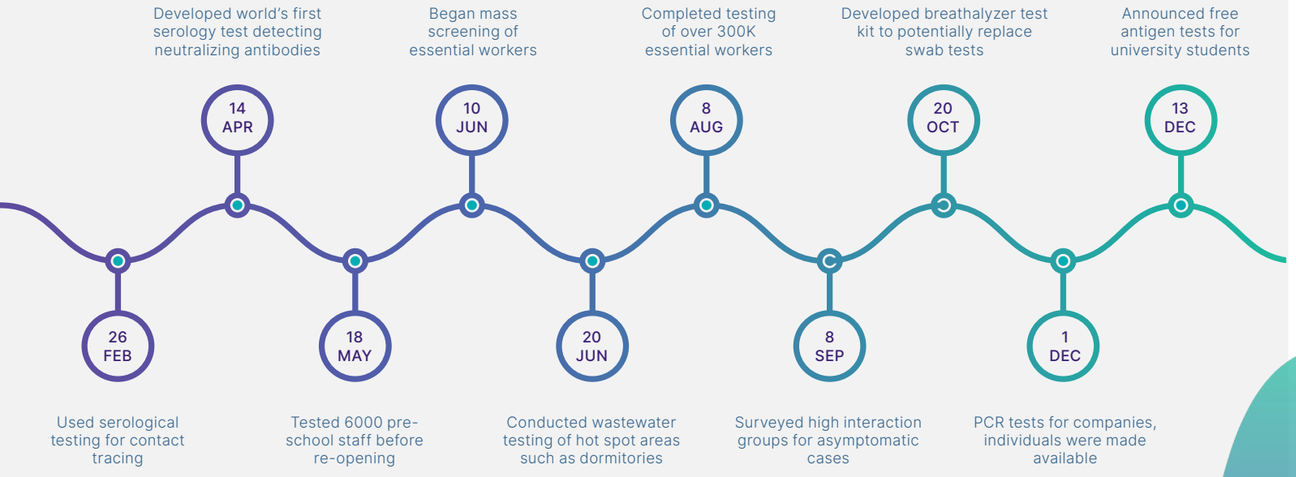
Paper Context and Summarized Call-to-Action

"Never waste a good crisis". These words were first uttered nearly 100 years ago, and here we find ourselves in similar circumstances during the modern pandemic. While, certainly, COVID-19 has caused devastation across various health, social, and economic levels, the crisis has been a wake-up call as to the demands for continued structural reforms to systems in the Asia-Pacific region. Indeed, whether it be infectious disease, cancer, or other serious health threats, the quest for solutions to these significant challenges starts with – and depends on – diagnostics.

The role of medical diagnostic technologies fit squarely into this mantra. Investments in Universal Health Coverage (UHC) in the Asia Pacific bring some USD 2.5 trillion into the region, which has traditionally underfunded access to high-quality technologies[1]. Equally, stakeholders from patients and healthcare practitioners through to government leaders and payers have observed, in action, the power of fast, accurate testing solutions. The Asia-Pacific Medical Technology Association (APACMed) published a report during COVID-19 about the role played by medical diagnostic technologies[2].

Case Study: Evolution of testing approaches in Singapore

As the pandemic progressed, Singapore adopted various testing strategies at different stages to minimize transmission whilst ensuring early re-opening of workplaces and educational institutions.



*First local transmission cluster reported on 4 Feb 2020

Figure 01
Excerpt case study from APACMed's "The Critical Role of Diagnostics in COVID-19 Management", highlighting how stakeholders were able to come together to drive testing innovation[2].

Now, the ambition is to take the topic further by calling for even greater recognition of the value that medical diagnostic technologies are delivering to governments and payers in the Asia Pacific. Beyond COVID-19, diagnostic technologies are used across the entire patient journey of multiple disease states, and provide the tools to prevent, detect, and monitor the required interventions. This new paper, a joint effort between the APACMed Digital Health and Government Affairs & Market Access committees, seeks to improve the value recognition of these solutions, in-line with the WHO's Essential Diagnostics List (ESL)[3] and augmented more recently by the Lancet Commission's landmark report about transforming access to diagnostic technologies[8]. The approach of this paper is educational in nature, providing real-world use cases as means to offer opportunities to co-create, across public and private sectors, the path ahead. In particular, the key recommended actions can be summarized as follows:

1. **Leverage COVID-19 momentum to properly measure whole-of-society diagnostics value.**
2. **Conduct a comparison analysis against the WHO and Lancet Commission frameworks.**
3. **Continue to harmonize technology review speeds, reliance, and data standards.**
4. **Right-size resourcing models to align to the critical role played by diagnostic solutions.**
5. **Tackle historic under prioritization of screening and diagnostics with fit-for-purpose strategies.**
6. **Drive transparent investment and coverage schemes aligned to the value of diagnostics.**

Roberta Sarno
Head of Digital Health
APACMed

We look forward to working together to ensure that the impacts of access to diagnostic technologies are felt are not just as a point-in-COVID-time, but rather ongoing for healthcare needs in the region.

03

APAC Health Ambitions, and the Role of Diagnostic Technologies

The pandemic has forever changed the healthcare landscape, including the needs and expectations of patients. These experiences have reinforced the critical role of access to modern testing, beyond just the clinical setting and into our everyday communities. Indeed, the heightened awareness and appreciation of diagnostics has fostered a renewed inspiration in the field[4].

APACMed, in conjunction with leading public and private sector collaborators, published a report during the pandemic which showcased the value that diagnostics are delivering. Ranging from monitoring disease transmissions to early identification of new viral strains to enablement of return-to-work programs, the report estimates that 95% of companies (large and small) have been able to resume operations in some fashion[2]. We feel the presence of diagnostic technologies at events and airports, a race against time which, now trending toward the winning side, exemplifies high quality through testing sensitivities and specificities at nearly 100% under ideal conditions[5]. Most importantly, diagnostic technologies are saving lives and livelihoods. For example, testing is seen as integral for disease eliminations programs like the WHO's Cervical Cancer Call-to-Action[21].

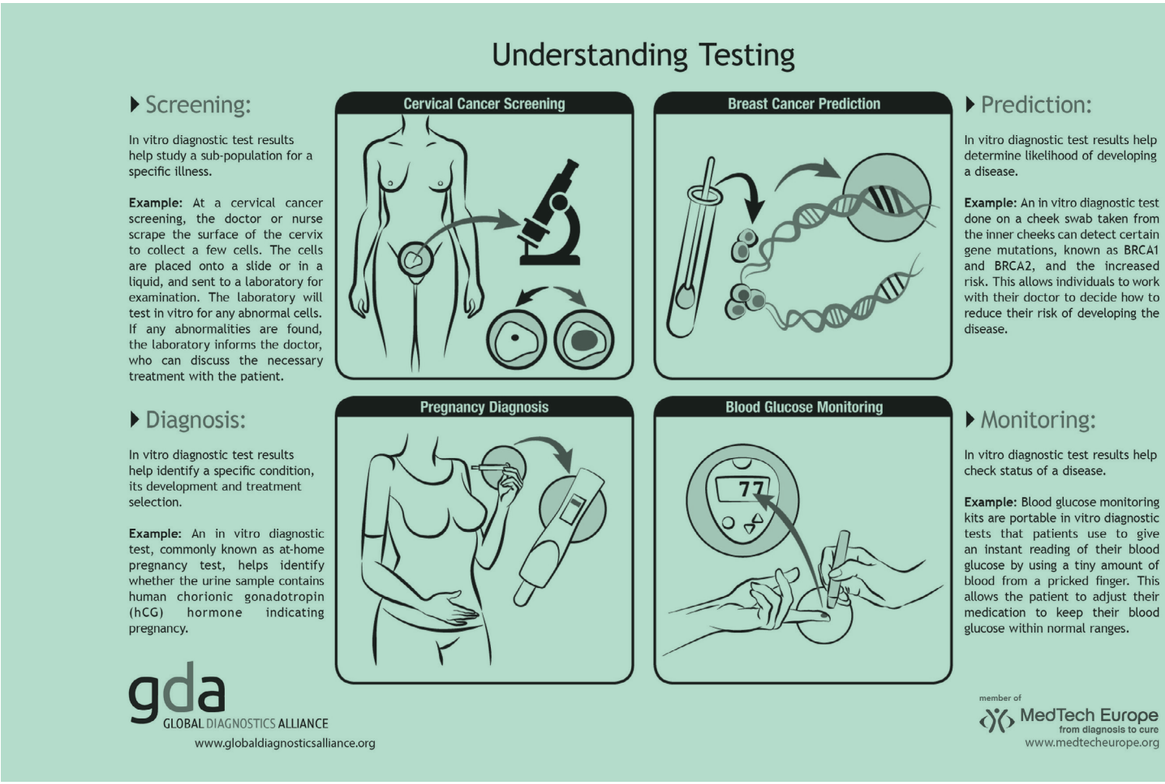


Figure 02
An explanation of the key forms of testing procedures, empowered by diagnostics technologies, as provided by the Global Diagnostics Alliance[6]. From APACMed perspective, ambitions should aim even higher as well in terms of access to innovations in genetic-based testing as a first-line standard of care[22].

The intertwine of diagnostic technologies and healthcare ambitions

Of course, diagnostics technologies play a much bigger role beyond pandemic response. Zooming out a bit more widely into our overarching Universal Health Coverage (UHC) ambitions in the Asia-Pacific region, since 2018 the World Health Organization (WHO) has published an annual Essential Diagnostics List (EDL) in order to address the lack of access to testing products and services in the countries. The EDL, which is essentially a basket of recommended diagnostic technologies that should be made more readily available so as to harness the potential efficiency and effectiveness gains, is the go-to evidence-based guide for testing recommendations based on global disease patterns[3].

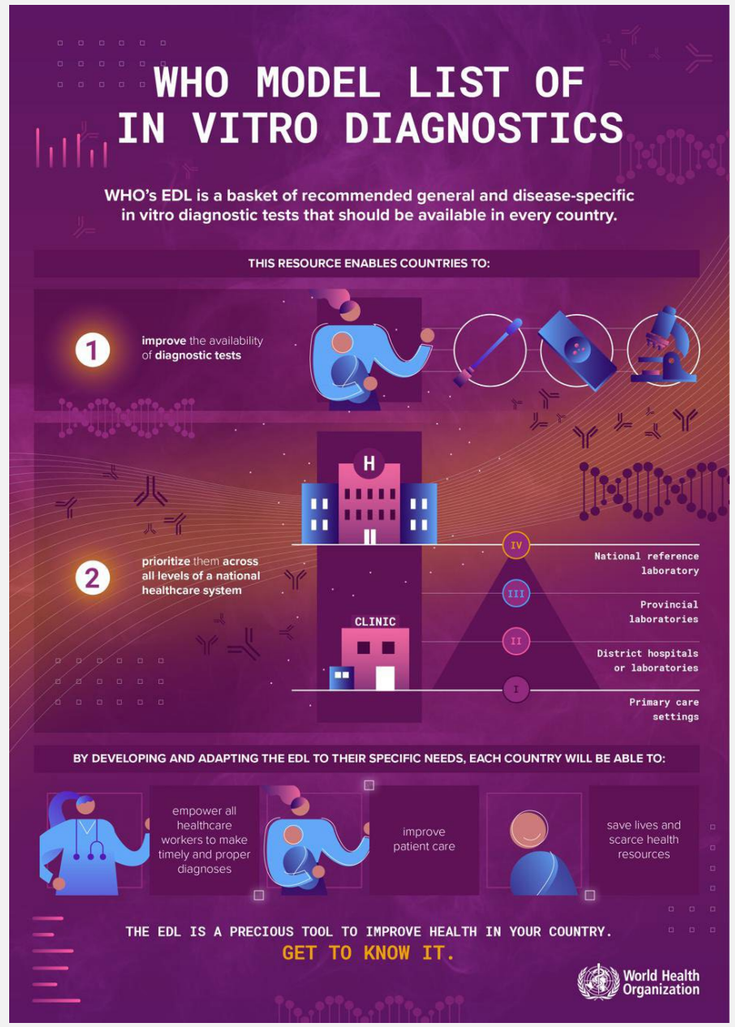


Figure 03
Infographic illustration of recent updates to the WHO EDL. "Access to quality tests and laboratory services is like having a good radar system that gets you where you need to go; without it, you're flying blind", said Dr. Tedros Adhanom Ghebreyesus, Director-General of the WHO. "All countries should pay particular attention to the diagnostics space, and use the essential list to promote better health, keep their populations safe, and serve the vulnerable."[3]

Some circles have even begun to proclaim the 2020s, on our march toward the United Nations' Sustainable Development Goals (SDGs) like #3 for UHC, to be the "Decade of Diagnostics"[7]. The Lancet Commission's landmark report in 2021 calls for a transformation in access schemes for diagnostics, the report of which forms a strong foundation for our APACMed paper and elevates the discussion beyond just the basic essentials. The impacts of diagnostic technologies can be felt at the systems as well as individual levels, enshrining confidence in patient journeys. A greater control of our collective well-being is awaiting. So, why then, do there remain lingering barriers to the value and access of diagnostic technologies in the Asia-Pacific region?

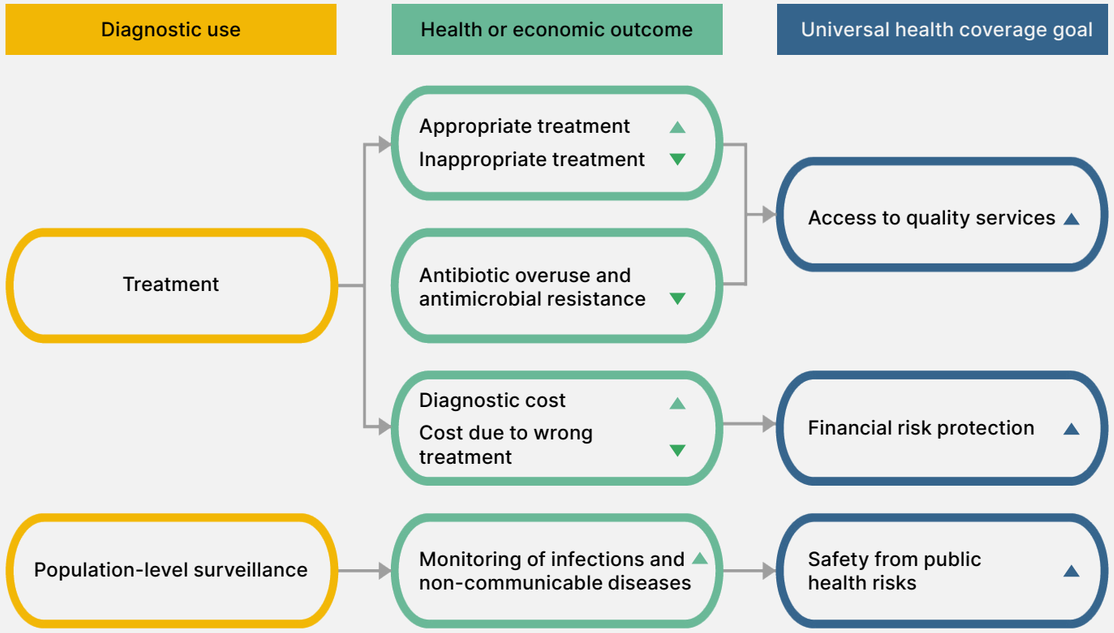


Figure 04
A schematic mapping of the role of diagnostic technologies as aligned to UHC principles, from Lancet Commission. We will further discuss the valuation approaches over the coming pages[8].

A new era of healthcare decentralization and democratization

In the ideals of UHC, access to safe, affordable healthcare products and services should be made available to everyone, everywhere in the Asia Pacific, even in the most hard-to-reach locations. A major trend of particular relevance to value and access of diagnostics, therefore, is the shift toward decentralized, democratized models of care.

Starting with decentralization, the trend can be very much enabled by technology, as we've observed in the case of Australia[23]. Decentralized point-of-care testing for COVID-19 was implemented in order to scale up response effort equity to the remote Aboriginal and Torres Strait Islander communities. Of interest for broader population health targets as a means to prioritize precious resources toward those most vulnerable, we've seen around the world how diseases like COVID-19 are disproportionately affecting certain communities, evidenced by higher diagnosis and hospitalization rates. These vulnerabilities are not limited to infectious disease, but moreover rising comorbidities like diabetes and cardiovascular issues too. In Australia, for example, people living in remote areas (which represents 20% of the total population) have up to four times the burden of disease as compared to others who reside in urban cities. Most importantly, access to testing and treatment is often too scarce.

Australia's COVID-19 experience with decentralized testing has subsequently led to updated national guidelines around handling of suspected health threat cases as well as enhanced testing, enabled by point-of-care technology. Strong governance, public-private collaboration, and sufficient resourcing models have been hailed as the success factors behind the Australia program. Equally, ongoing discussions continue around challenge themes such as supplier agreements, staff training, and the realities of managing the dynamism of various disease patterns.

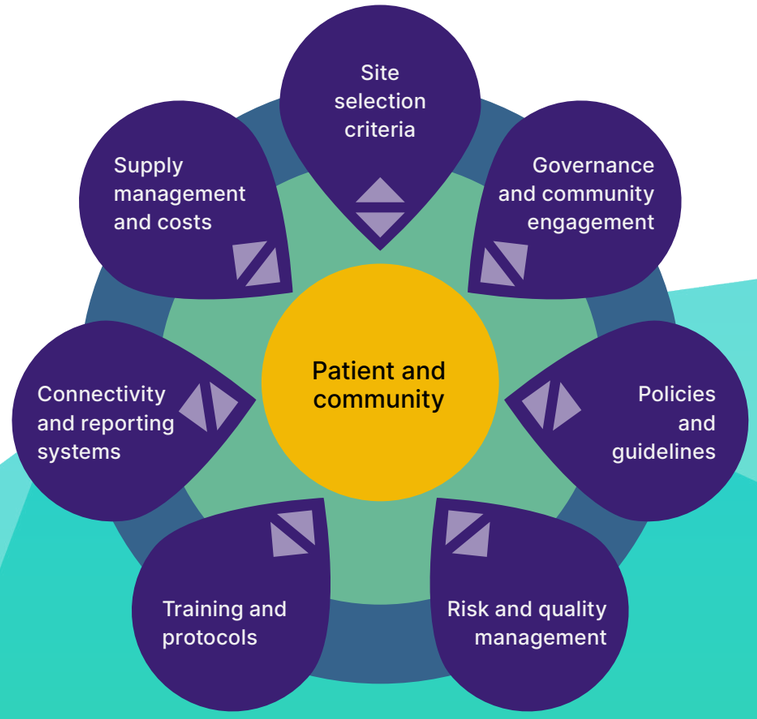


Figure 05
Framework for point-of-care (decentralized) testing models, as exemplified by Australia's response efforts during the COVID-19 pandemic for its remote, vulnerable populations[23].

Another case of testing decentralization comes from India, albeit with more of a policy angle[24]. India's inter-governmental response to COVID-19 exposed challenges with the highly centralized tendencies as well as lack of flexibility in planning and execution. At some point, like in many geographies globally, the impacts of 60+ days of mandated lockdown began to take their toll on the social and economic well-being of people. India initiated a phased re-opening process, which launched the transition of COVID-19 management to the state level.

Some states used the opportunity to evolve into a more decentralized healthcare model, such as in Odisha. The state suffers nearly 25% of India's natural disasters, and thus had already invested in advanced crisis management systems. Odisha became the first state to declare lockdown in India, yet concurrently ramped up decentralized testing capacities and incentivized people to engage in the grassroots effort. Additional strategies included engagement with the private sector, construction of medical camps at the village level, and forward disbursements of welfare resources to the neediest beneficiaries. Such a decentralized policy model for testing (and more) led to lower fatality rates and higher recovery/discharge throughput than the national average. The learning point is to leverage centralized governance for system-level design of health management and budgets, while empowering more localized leaders to take action with a degree of flexibility.

Coupled with these two examples of decentralization of diagnostic solutions, comes the trend toward democratization[25]. Many expect, and hope, that COVID-19 is the catalyst which ushers in a new era of greater access to diagnostic technologies, whether it be in centralized or decentralized testing models. This means engaging stakeholders, public and private sector alike, across all levels of care. The goal is not to undermine the role of pathway champions like laboratories; rather, the ambition is to enhance existing efforts by bringing optimized patient and provider experience into the loop. Such a move could stand to reduce pressure on ancillary health system services, harnessing the technologies available to facilitate place-based care and freeing up resources to focus on the more specialized demands. Decentralized and democratized testing goes hand-in-hand with broader and more personalized care models, the access to which still deserves greater recognition and value in the Asia Pacific.

Measuring the impact of diagnostic technologies, and the challenges ahead

A key takeaway for readers, is that the concept of value and how it is measured for diagnostic technologies is different than that of therapeutic medical devices or pharmaceuticals. Diagnostic technologies are complex interventions, which can provide information on a wide range of outcomes depending on the contextual factors and perspectives taken. To put things into view, **results of testing influence as many as 70% of clinical decisions, despite accounting for <1% of healthcare expenditures[9]**.

Upon completing a literature review for this paper, the following tend to be the most desired value-drivers for governments and payers, in the increased adoption of diagnostics technologies[9, 10, 11, 12]:

- **Economic savings through enablement of more fit-for-purpose, place-based care models**
- **Societal gains of early detection and prevention of disease progression (versus complications)**
- **Efficiencies in targeting toward the more at-risk sub-populations, increasingly in real time**
- **Improved disease management tools for providers, coupled with patients' "value of knowing"**
- **Reduced treatment trial-and-error, thereby decreasing adverse event costs**
- **Maximizing treatment effectiveness through more personalized population health data**
- **Fostering an innovation ecosystem through industry R&D and workforce contributions**

On the flip side, unrecognized value has implications too. Studies have shown that lingering access challenges to diagnostic technologies have been linked to thousands of avoidable adverse health events and deaths, to the tune of hundreds of millions of avoidable healthcare expenditures[12].

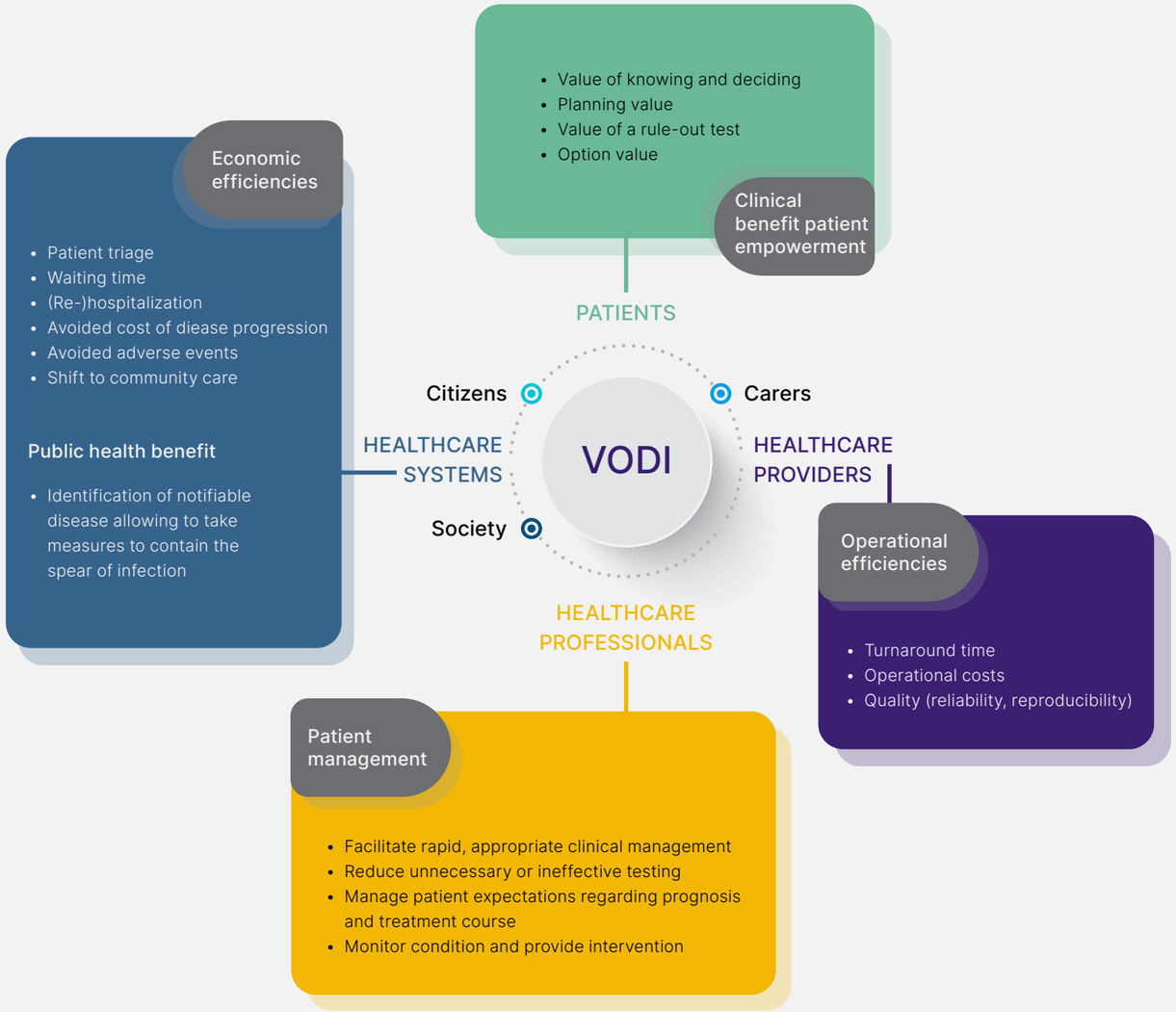


Figure 06
Visualization of the multifaceted Value of Diagnostic Information (VODI) delivered by diagnostic technologies across the healthcare ecosystem, as evidenced by research performed at Public Health Genomics[11].

Alluded above is the next great foray for UHC design in the Asia-Pacific region – more personalized, precise patient journeys. The drive to ensure healthcare spending is sustainable while providing equitable access to high-quality care, across a range of chronic and infectious disease profiles, has ignited the discussions about what value really means, down to the individual patient level. With billions of tests performed every year, the diagnostics industry has become one of the largest stewards of real-world data, which serves to be better leveraged for a "right patient, right intervention, right time" strategy. The deepening understanding of molecular science, together with new diagnostic technologies and sources of data, has sparked a revolution. On one hand, screening has the potential to identify changes in the body before the disease even occurs. On the other hand, when diagnoses are delayed, opportunities for providing optimal healthcare can be lost forever[7].

Despite the value potential of diagnostic technologies, a number of barriers prevent not only the innovations from being properly recognized, but also, moreover, unnecessarily limit access to the tools desired by patients and their care providers. Challenges facing the diagnostic industry at present pertain to a spectrum of regulatory-, funding and reimbursement-, market-, scientific/technical-, and societal-based dilemmas; however, our view is that these are really only symptoms of the underlying dearth of political will to prioritize screening and diagnostic solutions. Thanks to efforts such as the WHO EDL and Lancet Commission, diagnostic technologies are already recommended in more than half of the evidence-based clinical practice guidelines, and for 80% of the particularly burdensome disease conditions. And yet, a study conducted in the United States found that testing was still being underutilized 51% of the time (typically there is a misperception of the opposite, i.e. over-testing)[12].

Disease*	Quality Indicator*	Treated prevalence (per 100,000)*	Total health spendin (billions)*	Underuse (%)*
Asthma		4,610	$11.3	
	• Theophylline levels measured once per year for patients under constant medical management			100.0%
	• Theophylline levels measured after an asthma attack			62.4%
Heart disease		6,226	$56.7	
	• Newly diagnosed atrial fibrillation patients that received a thyroid test			81.4%
	• Newly diagnosed angina patients that receive hemoglobin test to detect diabetes			61.6%
	• Newly diagnosed congestive heart failure patients offered standard blood panel within 1 month of diagnosis			65.9%
	• Patients on ACE inhibitors with serum potassium checked annually			21.7%
Cancer	Colorectal cancer patients:	3,348	$38.9	
	• Patient offered colonoscopy within 3 months following positive FOBT result			72.1%
	Breast cancer patients:	13,290	$42.6	
	• Biopsy & cellular analysis performed within 6 weeks when mammography suggests malignancy			49.8%
	• Biopsy & cellular analysis or mammography performed within 3 months following detection of a palpable mass			10.9%
Diabetes	Diabetic patients:	4,260	$18.3	
	• Offered a HbA1c test every 6 months			76.1%
	• Urine protein test performed annually			76.4%
	• With documented serum and HDL tests			42.1%
Prenatal care		1,237	NA[5]	
	• African American or women with a history of sickle cell disease offered a sickle cell test			100.0%
	• Rh factor/antibody screen following first prenatal visit			5.9%
	• Women with abnormal glucose offered a glucose test			100.0%
Hip fracture	Initial laboratory tests include:	11,000	$2.9	
	• Preoperative coagulation tests			57.3%
	• Preoperative urinalysis			91.7%

Figure 07
Empirical study in the United States, demonstrating the consistent underutilization of diagnostic technologies vis-à-vis healthcare quality and cost parameters[12].

The lack of value recognition has further hurt the diagnostics industry through confusing payer coverage schemes. Examples range from variability in coding standards to creating a low-cost, low-benefit environment. Studies show that most countries have not even updated funding for diagnostic technologies to match general inflation, representing an actual reduction in resource allocation, in real terms, over recent decades[12].

Research has shown as well that the large majority of healthcare leaders desire to play a bigger role in supporting more sustainable health systems, and 95% of whom see diagnostics as leading the practice of healthcare analytics[5]. Put another way – the overall healthcare value chain is triggered when screening, or suspicion of disease, leads to the application of a diagnostic test[11]. The rest of the domino pieces fall from there, whether that be advantageous (in a high value system) or problematic (where value is not properly captured).

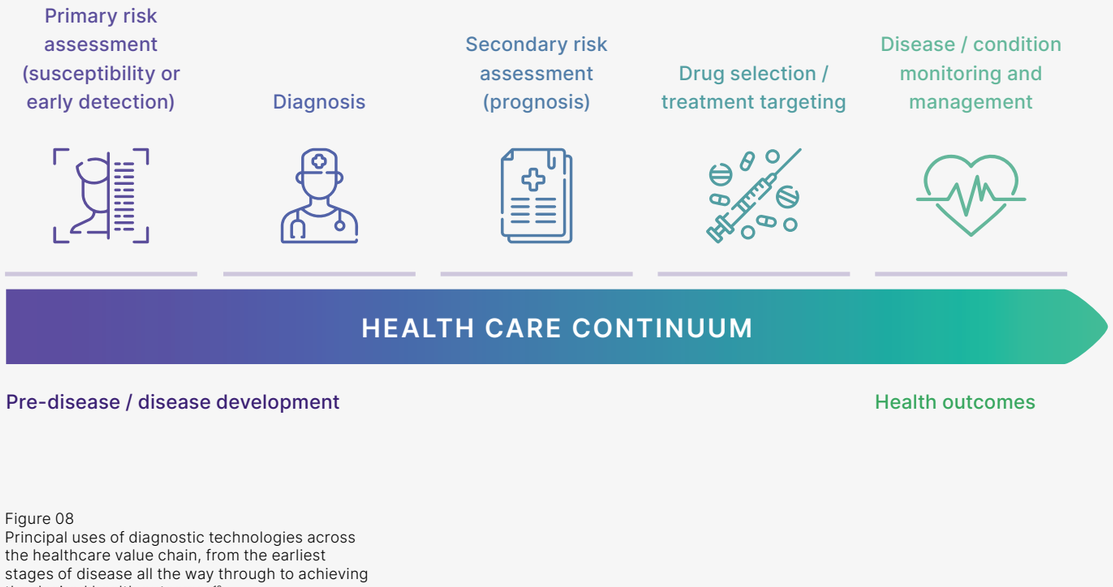


Figure 08
Principal uses of diagnostic technologies across the healthcare value chain, from the earliest stages of disease all the way through to achieving the desired health outcomes[12].

Next, let us observe how variations in health system designs for the value of diagnostics are manifesting themselves in the Asia-Pacific region. Thereafter, we will also provide use cases to illustrate the same.

04

Market Archetyping of Best Practices and Gaps

In the prior section, we highlighted the tremendous value that diagnostic technologies are already delivering to health systems in the Asia Pacific, yet the lack of appropriate recognition provided and therefore limitations on access and affordability for wider populations.

We will, as part of this paper, provide use cases and recommendations so as to frame the collaborative path ahead. However, given APACMed's experience in the region with building more fit-for-purpose policies, it is important to realize that not all markets are alike in terms of transformation need. Therefore, we have organized the below reflections by archetype.

The WHO says that diagnosis is the driver of patient, financial, and health system impact; in other words, a critical enabler of UHC and also the weakest link in the care cascade[3]. This is especially true in the typical design of UHC in the Asia Pacific (whether already achieved or still in process), which emphasizes the role of earlier, more localized intervention techniques. Therefore, a key differentiator in archetypes pertains to the degree of fragmentation of a market's testing system[4], akin to the opportunity to drive health equities through the more appropriate use of diagnostic technologies.

Archetype 1: Fragmented models, in route to achieving UHC 1.0

A large portion of markets in the Asia Pacific remain on the march toward Sustainable Development Goal (SDG) #3, in providing their populations with one of the greatest gifts of a generation – access to equitable, affordable healthcare. Of course, these markets also tend to be of the Low- to Middle-Income Country (LMIC) socioeconomic variety, meaning that testing models, as a function of the overall UHC design, are fragmented.

Lancet Commission has undertaken significant efforts on this theme, identifying access to diagnostic technologies in pathology, laboratory medicine, and imaging to be poor and inequitable in LMICs. The discussion is not new either – in 2008, the Maputo Declaration on Strengthening of Laboratory Systems called for action to address a confluence of factors facing diagnostic inequities, in terms of UHC insurance schemes, global health security, and the rising threat of Anti-Microbial Resistance (AMR). The Declaration fed into the eventual WHO EDL and, while the last 15 years have brought tremendous innovations in technology and informatics, many issues linger in the form of insufficient financial support, staff shortages, infrastructure deficiencies, low visibility, and, hence, low priority. To put the context for Archetype 1 into perspective[8]:

- **There is a diagnostic gap (proportion of population with undiagnosed conditions) of up to 62%, the largest such gap along the care pathway. Only 19% of people in LMICs have access to testing.**
- **1.1 million premature deaths in LMICs could be avoided annually by reducing the diagnostic gap for the high burden conditions (e.g. diabetes, hypertension, HIV, tuberculosis, antenatal care).**
- **The benefit-cost ratio of reducing the diagnostic gap is estimated to be as high as 24:1.**
- **Beyond the economic case, lack of access to testing particularly affects the rural and marginalized communities – this is an equity and social justice mission.**

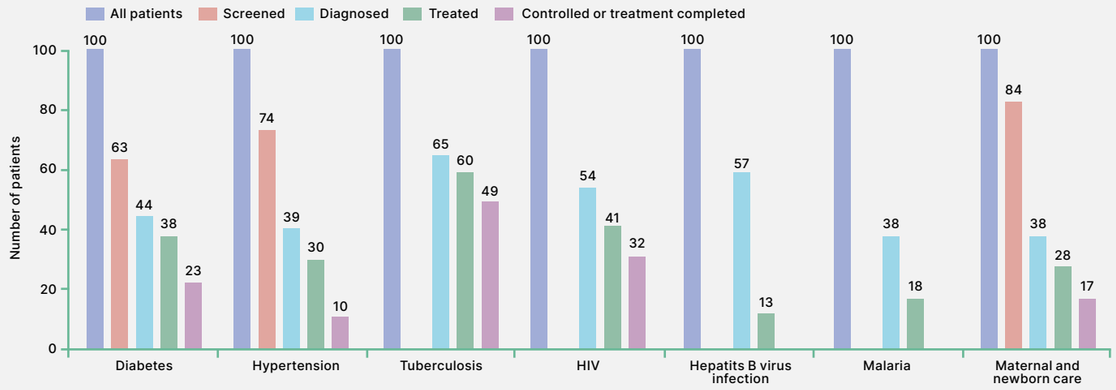


Figure 09
Visualization of the diagnostic gap in LMICs for the most pressing disease priorities, highlighting the danger of attempting to achieve UHC without addressing the testing challenge[8].

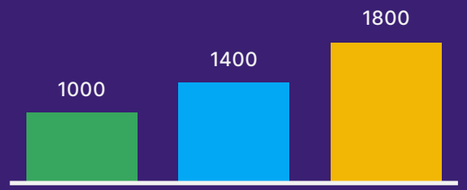
For example, India, a market archetype we will revisit shortly, has only 1,151 accredited laboratories as compared to 260,000 in the United States, at 25% of India's population size. Another estimate suggests it would take 400 years for LMICs to reach the same level of pathologists as the developed world; put simply, we must be cleverer in our strategy for Archetype 1[8]. DNA testing for HPV instead of Pap, as called out in the Figure 1 caption above and recommended by WHO[22], demonstrates the potential to harness diagnostic technology to bridge the human resource challenge and to leap ahead.

The diagnostic technologies access issues are not just about volumes, either. Misdiagnosis, due to poor quality diagnostic products and services in the region, has led to 38% of maternal deaths during pregnancy which could have been avoided. Malaria, the most commonly over-diagnosed disease in LMICs, has a typical error rate of more than 84%[8].

With more than 100,000 pathology sites in India, the industry is highly fragmented; no organized market player has more than 5% share of volumes. At the same time, price points of testing have not increased for years, despite overall average consumer index inflation growth of 30%. The Indian testing system operates at one of the lowest coverage models in the world, around one-eighth the resourcing of the United States and half that of New Zealand.

At the same time, the diagnostics industry employs nearly one million people in India, with 5x new jobs created in the country for each testing transformation initiative undertaken. What's more, testing contributes 80% of the objective data in the population's clinical records. The good thing, and for other Archetype 1 markets to take note, is that the transformation efforts in India are having an impact. Both in terms of the access to diagnostic technologies, as well as the novel mechanisms by which emerging UHC markets can use structural challenges to their advantage.

Increase in specialised test menu (2010-2018)[21]



Specialised tests

Molecular diagnostics, flow cytometry, genetics /cytogenetics and histopathology among others

National laboratories are moving towards high-end tests and advanced diagnostics and pathology

Archetype 1 illustration[13]

Mr. Ram stays in a tier 3/4 city in India. He is used to travel twice to the laboratory, in the morning to deposit the sample and in the evening or on the following day to collect his report:

- × Used to travel ***30-60km*** to get to high-end diagnostic tests done and collect his report
- × Used to spending ***3-4 hours*** and
- × ***INR 200-350*** on traveling
- × Used to incur a ***loss of daily wage***
- × Used to wait for ***24 hours for report collection***

Patient's home

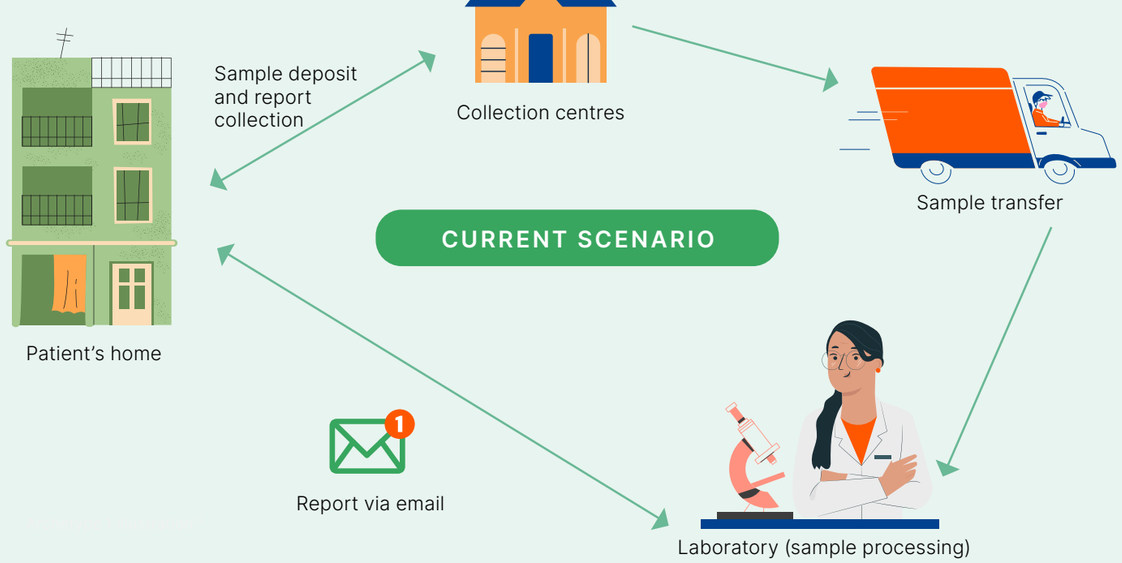
Morning - sample deposit

HISTORICAL SCENARIO

Evening - report collection

Laboratory (sample processing)

With the evolution of this industry, patients are able to get the same tests done with ease and convenience



Fortunately for Archetype 1, there are a number of multistakeholder initiatives and toolkits available to improve the situation by which the incoming UHC populations can have access to diagnostic technologies. For example, Lancet Commission, mentioned above, has produced an evidence-based template for a national EDLs in order to better integrate the testing models; the template is tied to the WHO EDL, and prioritizes the most pressing disease burdens for the LMIC cohort[8].

There is the International Medical Device Regulators Forum (IMDRF), which superseded the Global Harmonization Task Force in 2011, and includes specific provisions for diagnostic technologies approval pathways. The World Economic Forum, moreover, has stepped in to ensure a platform for public-private partnership on the same. An example of Archetype 1, provided by the Forum as part of their overall recommendation set for access to diagnostic technologies in LMICs (see Figure 9), is Egypt's "100 Million Healthy Lives" campaign. The campaign sought to detect and eradicate Hepatitis C, whereby public and private sectors partnered together to bring high-quality testing to populations in need, co-designing the multi-tier payment models and incentives aimed at delivering on wider socioeconomic goals[14].

Multi-tier model for affordable diagnostics

Government investment	Private investment	Employer investment	Donors
Universal coverage of diagnostics (screening, diagnoses, monitoring, surveillance)	Scalable and affordable technologies	Coverage for diagnostics	Establishment of a Global Alliance for Affordable Diagnostics (GAAD)
Public health infrastructure	Supply chain management	Wellness and prevention services	Foundation support for disease and diagnostics
Early stage innovation	Delivery and laboratory platforms	Disease management	NGO support for delivery
Commercialization programmes	Education / training platforms for healthcare professionals		

Figure 10
Framework proposed by the World Economic Forum, for improvements in access to affordable diagnostic technologies in Low- to Middle-Income Countries (Archetype 1) through the technique of public-private partnerships.

In closing on Archetype 1, the following are the most common recommendations for government leaders and payers to consider. These recommendations are coalesced around key empirical research, as well as reflecting APACMed members' own experiences in the Asia Pacific.

1. **Continue harmonization of approval requirements, including in alignment high-income countries.**
2. **Address practical barriers, like reference data requirements based on local population needs.**
3. **Overcome historical tendencies by raising the prioritization of screening and diagnostics.**
4. **Evolve procurement models to recognize the value that higher quality testing can deliver.**
5. **Enable training to build capacity of testing professionals for the adoption of advanced diagnostics.**

Archetype 2: Integrated models, for scale-up into UHC 2.0

Contrary to Archetype 1 in the Asia Pacific, Archetype 2 tends to feature a more integrated testing model. The model goes hand-in-hand with mature UHC states and more developed economic status. Launched in 2021 by the World Economic Forum, the notion of a "UHC 2.0" has emerged as a mechanism to derive maximum health system value over the next generational wave, especially in the face of ageing demographics and more complex epidemiological needs[15].

Certainly, Archetype 2 has its unique set of diagnostic technologies challenges to deal with too. Often, these challenges are the product of their inherent UHC design. For example, a study in the Netherlands found that the reference price for a multi-round regimen of amoxicillin is more than 4x cheaper than for a C-reactive protein test, essentially exacerbating the threat of AMR. Efforts are only beginning to better understand evaluation models for diagnostics (as compared to pharmaceuticals); for example, through the creation of the Diagnostics Expert Advisory Panel by the UK's NICE[16]. Archetype 2 markets are furthermore grappling with rebounding the balance of infectious with chronic disease management; in the UK, it is estimated that 3,000 additional deaths in the next five years (representing 60,000 years of life lost) will occur due to delayed diagnoses as a result of the COVID-19 pandemic[8].

Perhaps the greatest opportunity for Archetype 2 markets in the Asia Pacific, in line with UHC 2.0 ambitions, is to harness the deeper socioeconomic benefit of diagnostic technologies. As the Lancet Commission concurs, Archetype 2 markets must shift the conversation from a unit-based healthcare design (i.e. pricing per test) or related near-term cost control measures, to a conversation about the value that screening and diagnostic solutions are delivering to patients, care providers, and wider society. UHC 2.0 systems are primed for more modernized incentive structures for testing.

And things are happening in the region. In Taiwan, for example, a strong UHC design that covers 99% of the population has seen investments in critical testing capabilities such as Information & Communication Technology (ICT) and biobanking (35 in total), on the march toward realizing the vision of precision health. More recent efforts have included the integration of national medical databases (2.3 billion images), whole genome sequencing which represents the largest source of its kind for Han Chinese profiles, and launch of the Taiwan Precision Medicine Project (TPMP) for future research endeavors. What's more, there are strong collaborations with diagnostic technology industry players to push the access boundary even further into areas such as Artificial Intelligence (AI) for blood parameters, anthropometrics, and gut microbiota[26].

Singapore, likewise, has leaned into the value of diagnostics discussion. Following the Lancet Commission report, Singapore convened 300 local and international leaders (including the WHO) in February 2022 covering topics such as improved governance frameworks, upskilling of the healthcare workforce, and fostering an environment for diagnostic technologies to benefit whole of society. From pathology to radiology to laboratory medicine, commitments were made to adopt the Lancet Commission recommendations. As stated by Professor Fong Kok Yong, Deputy Group CEO of SingHealth: "Diagnostics is closely interlinked with almost every medical specialty and plays a defining role in every patient's journey. There is much value in the exchange of insights and perspectives through dialogue, that will enable us to work towards developing sustainable diagnostic solutions to achieve our shared vision of enhancing care for patients and our populations."[27]

Of course, there are then Archetype 2 situations like Japan, for which research bodies claim that the recognition of the value of diagnostics is on the decline[28]. Japan took an early lead on diagnostic technology adoption in the 1960s (similar to many aspects of their wider society), leading to noticeable improvements in patients' quality of life and integrating testing as part of the national health system. And yet, over time, reimbursement levels for diagnostic technologies have decreased through rounds of payer rate revisions. Stakeholders are calling for more active discussions in areas like linkages between the national health insurance rates and value assignments, improved access to diagnostic solutions, and public awareness programs about the value that diagnostics can deliver.

The concept of "value" in healthcare is no longer novel, and increasingly intertwined into the ideals of UHC 2.0. Traditionally, value in healthcare is defined by the outcomes achieved vis-à-vis the cost base (or resourcing model) used to deliver those results. In other words, focusing on the true value across health, social, and economic indicators.

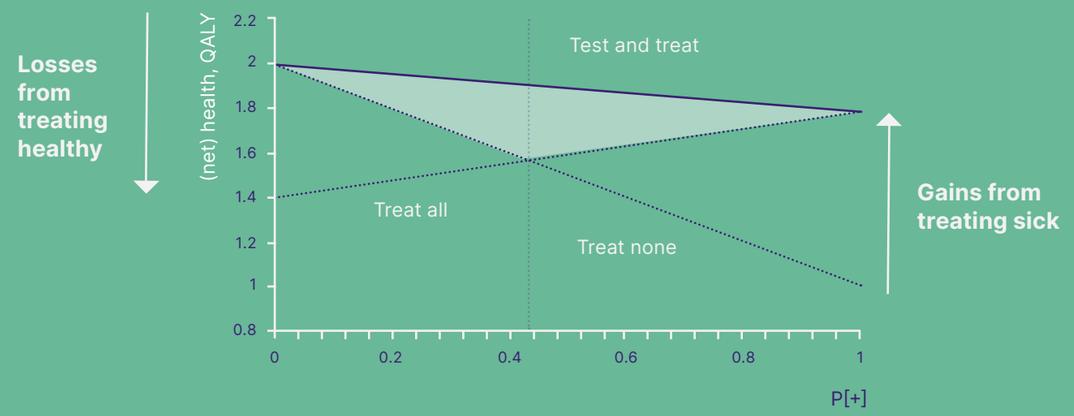
We are making headway in the adoption of value-based principles in healthcare, including regarding the unique nuances of sub-specialisms such as testing. We reference here a study undertaken in more developed markets about the role of diagnostic technologies in clinical decision-making and, therefore, the potential features of a value-based relationship.

Interestingly, while diagnostic technologies account for ~2% of healthcare expenditures in Archetype 2 markets, the majority of policymakers and payers believed that the figure was beyond 5%. On the positive side, the study found a high desire amongst stakeholders to rely on diagnostic technologies for patient journey routing, as well as increasingly for improved data sharing.

Unfortunately, investments in diagnostic technologies, respective to other areas of healthcare, have actually decreased over time in some mature UHC states. The Archetype 2 study concludes with a proposed equation for public and private sector dialogue to consider, on the evolving journey toward a more equitable, accessible model that is rooted in appropriate value schemes.

IVD value = [Technical accuracy / Turnaround time] x [Utility / Costs]

Put into practice, the mature measurement of value for diagnostic technologies can be thought of as identifying a targeted "test and treat" segment of the population. By tailoring treatment decisions to patients, the health outcomes of the population improve, thereby generating the desired value[19].



Archetype 2 illustration[18]

In looking more broadly at studies of other Archetype 2 markets around the globe, themes such as employment levels and R&D reinvestments can also be considered in the holistic value story of the industry. We will highlight further examples of the same in the use cases segment of the paper later.

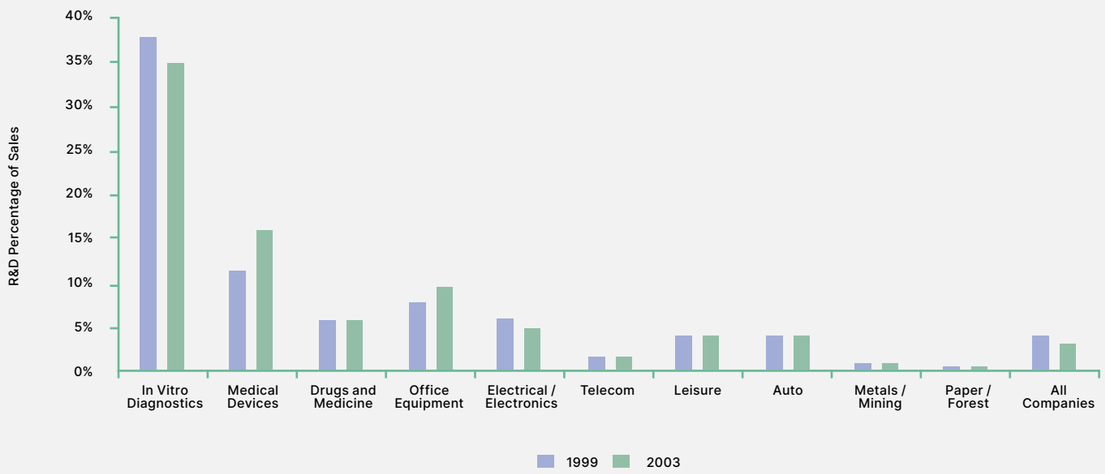


Figure 11
A more evolved way of viewing the positive influence of diagnostic technologies, for Archetype 2 markets, is to seek to better understand the wide socioeconomic benefit being delivered[12].

While such a mindset shift may sound logical, the transformation is in the details. One deep dive area of the value story for Archetype 2 lies in the design of UHC payer schemes. Often operating at loss ratios (sometimes as high as 85%), emphasis going forward will be on improved utilization management of healthcare products and services. Herein is an opportunity for the public and private sectors to work together on more value-oriented contracting models, centered around the critical role of testing. Another deep dive topic for the industry in the Asia Pacific is known as "code stacking", which has become a cumbersome process, for all parties involved, to navigate the spectrum of medical coding for diagnostic technologies instead of, say, a more fit-for-purpose, consolidated structure[17]. The US FDA, for example, has addressed these challenges by offering a bespoke testing regulation (called "Turbo 510(k)"), faster policy turnaround cycles, and frequent reviews of coding practices so as to iteratively make adjustments as the technologies and population needs evolve[12].

Lastly, advanced discussions for Archetype 2 may be had into areas such as cloud storage and federated data access. There needs to be open dialogue on the related themes of consent, privacy, and even AI. We point toward efforts like the Global Alliance for Genomics & Health's Framework for Responsible Sharing of Genomic and Health-Related Data, governing data standards, which is now available[14].

Figure 12
Greater access to diagnostic technologies for Archetype 2, on the march toward UHC 2.0, also means more advanced opportunities for informatics and analytics that can guide patient outcomes[8].

Wrapping up Archetype 2, the following are the most common set of recommendations for government leaders and payers to consider. Similar to Archetype 1, these recommendations are coalesced around key empirical research, as well as reflecting APACMed members' own experiences in the Asia Pacific.

1. **Aim to reduce approval timelines of technologies, adopting a recognition and reliance approach.**
2. **Co-create forward-looking clinical guidelines, coding, and standards for the testing pathway.**
3. **Related to the above, advance themes such as genetic testing, data consent/privacy, and AI.**
4. **Monitor the emergence of low-quality tools, which put consumer safety at risk.**
5. **Develop more fit-for-purpose value assessment frameworks for diagnostic technologies.**

05

Use Case Collection to Demonstrate the Value of Diagnostics

A chunk of the educational content of this paper comes through a combination of empirical global research and APACMed member experiences. For Section 5, the intention is to illustrate the concepts raised thus far through contribution of our own primary research in the form of live use cases. While, certainly, these real-world examples demonstrate the tremendous value that diagnostics technologies bring to Asia Pacific governments and payers, the use cases also highlight the gaps that remain.

The use cases cover a range of burdening disease states ranging from infections to chronic conditions, and including impacts observed during the COVID-19 pandemic. These use cases were selected based on their value in terms of lives saved, quality adjusted improvement indicators, and cost effectiveness, across Archetypes 1 and 2. Following the presentation of the use cases, Section 6, in closing, will summarize the holistic set of recommendations for progressive dialogue ahead.

Use case

The power of decentralized testing + digital enablement during COVID-19[29, 30, 31]

We touched prior on the trend toward decentralized testing, as accelerated during COVID-19. Many APACMed member companies worked hand-in-hand with Asia Pacific governments and stakeholders during the pandemic to design and roll out innovative point-of-care, data-driven diagnostic platforms, achieving a broader objective of digitizing and democratizing healthcare.

Abbott's COVID-19 Panbio self-test and companion reporting app, NAVICA, are on such example. These tools, approved on the WHO Emergency Use Listing and winners of the CES 2022 Innovation Award, provided patients and care providers with automated test results, as well as interpretation using the built-in AI features. Access to the diagnostics included urgent care clinics, physician offices, schools, workplaces, and even in the comfort of home. Exemplifying the type of collaboration recommended by this paper, Abbott engaged with the Council of Medical Research and the Central Drugs Standard Control Organisation in India to have open dialogue about regulatory frameworks and patient data security/consent. The goal being to equip the Indian government with real-time disease surveillance capabilities (15-min results with 95.7% sensitivity and 97.6% specificity, to be exact) to more effectively manage the pandemic. The "digital health pass" generated by NAVICA was moreover adopted by partners such as airlines, in order to progress toward economic reopening.

Early-stage patient identification and monitoring	Telehealth services	Post-acute care optimization/ management	Population health management services
Digital monitoring and therapeutics (e.g., Azumio's glucose monitoring app allows for early identification of prediabetes and has a platform for physicians to monitor and offer digital therapeutics)	Digital assistant (e.g., Teladoc Health connects patients with international health experts to review patient's case and identify the best medical centers for them)	Wound care management (e.g., 3M Negative Pressure Wound Therapy systems promote at-home wound care for patient self-medication and ambulatory care)	Digital testing management (e.g., Abbott NAVICA acts as a digital passport for COVID-19 test-taker by displaying a temporary encrypted digital pass with a QR code)

Figure 13
Solutions like Abbott's NAVICA fit nicely into the evolved testing value chain, enabling the digitalization ambitions of progressive healthcare systems around the world.

A related example is the roll-out of Abbott's AegisPOC solution in New Zealand, to support testing ambitions where connectivity and coordination were lacking at the local primary care and decentralized laboratory levels. The solution is a web-based platform that is able to connect results across multiple devices, including between the hospitals and clinics, in order to present an integrated test record in user-friendly format. In other words, AegisPOC supports the ambition of the lab to be the center of the value chain, in a digitalized model which can reach even the most vulnerable populations. At APACMed, we believe that a digitally connected, data-driven rapid diagnostics landscape can serve as a positive effect on public health management and enable the mission toward improved health outcomes. Particularly when frontline healthcare workers are overwhelmed and societies seek to return to a sense of normalcy, the time for access to these tools is now.

Use case

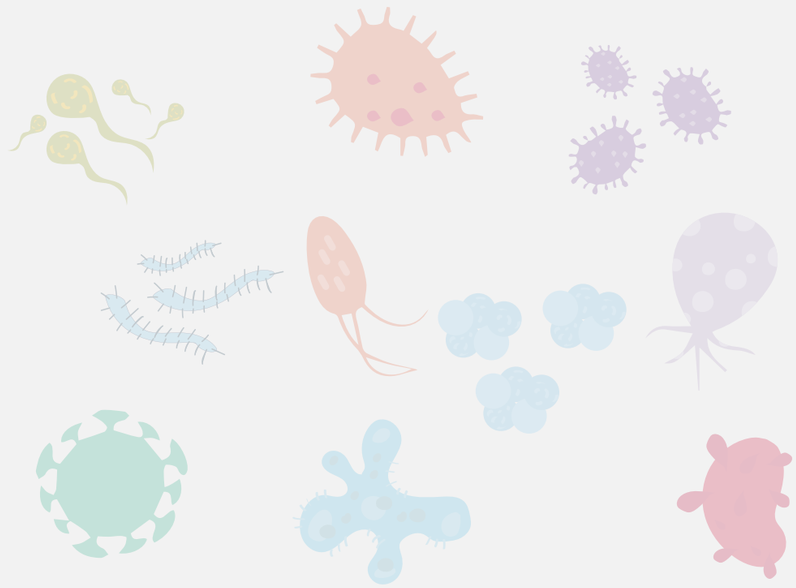
Getting more bang for the diagnostic buck with novel infection testing technology[29, 32, 33, 34, 35]

As COVID-19 reminded us, we cannot afford to solely focus on chronic diseases in our Asia Pacific populations; indeed, the threat of lingering infectious diseases remains omnipresent. An emerging technological trend in this space, mentioned above, is the concept of point-of-care testing. Point-of-care testing brings care closer to hard-to-reach patients and increases the likelihood that coordinated care teams can receive results faster, thereby leading to timelier clinical management decisions (which is key for infection control).

Figure 14
Illustrations of the value impact of PCR and rapid antigen point-of-care testing, particularly for infectious disease management.

An APACMed member use case comes from Cepheid, and their diagnostic technology suite known as Xpert® MTB/RIF. Conventional approaches to Tuberculosis (TB) diagnosis and resistance testing, such as microscopic examination of acid-fast-stained sputum smears, are slow and require specialized, trained technicians. The Xpert® MTB/RIF assay is an automated, molecular diagnostic assay for rapid TB diagnosis, offering results within two hours. The Xpert® MTB/RIF assay and system require minimal laboratory equipment, space, or technician time, and is highly sensitive and specific, providing rapid identification of rifampin resistance and allowing earlier treatment of drug-resistant TB. The concept being that a single sputum sample from suspected TB cases is able, through the Xpert® solution, to result in faster average time-to-diagnosis and to lower total healthcare expenditures (as compared to the traditional microscopy + culturing approach) as well as improved outcomes in the form of measurable Quality-Adjusted Life Years (QALYs). Given that TB is the leading cause of death by infection in the Asia Pacific (Southeast Asia is home to 26% of the global population yet 44% of the burden of TB incidence), studies have shown as much as 14 days decrease in average time-to-diagnosis (16.3 days for non-molecular versus 2.71 days for Xpert®), representing 6.32 QALYs, are gained from this form of advanced TB intervention.

The sensitivity of Xpert®, moreover, can be as high as 0.95, even for unconcentrated sampling procedures, thereby saving an average of 51 patient hours due to the improved efficiency and effectiveness of care pathway management. In Africa, for example, use of Xpert® technologies in TB control actually led to an increase in the number of interventions deployed (due to the improvement rates in diagnostic accuracy) when running Xpert®, especially when compared to the resource-constrained centralized laboratory requirements for the smear technique. By quickly and accurately diagnosing TB patients, timely treatment can be initiated. A decrease in community spread and in drug resistance due to incorrect diagnosis can also be witnessed. As per Cepheid, the availability of point-of-care testing, including using advanced technologies like automated nucleic acid amplification, enables governments and payers to convert infection control on burdening topics like TB into a smoother endemic reality.



Use case

The role of diagnostics in better managing the liver disease patient journeys[29, 36, 37, 38, 39, 40, 41]

The liver, located in the upper right quadrant of the body and below the diaphragm, is responsible for several functions including detoxification of metabolites, synthesizing proteins, and producing digestive enzymes. Its deterioration over time due to risk factors such as viral hepatitis, metabolic dysfunction, cirrhosis, fatty liver, and more is a classic example of the need to intervene earlier, through appropriate diagnosis, so as to better manage later complications like cancer. Globally, 1.5 billion people suffer from chronic liver disease, leading to two million annual deaths. What's more, chronic liver disease is of particular importance to the Asia Pacific given its high prevalence - 72% of liver cancer deaths are found in this region, and it is known as a "silent killer" due to late diagnosis.

Typically, the first tell-tale sign is inflammation due to infection, known as Viral Hepatitis. Symptoms may include fever, fatigue, pain, metabolic dysfunction, and even jaundice. The most common types of viral hepatitis are Hepatitis A, B, and C, which are not distinguishable by symptoms and, thus, require proper diagnostic technique. Transmission can be as simple as contact with infected individuals, leading to, likely, hundreds of millions of carriers (many unbeknownst) around the world. Particularly of the B and C variety, Viral Hepatitis necessitates rapid interventions like direct-acting antiviral agents.

Worse yet, however, is the progression of Viral Hepatitis in the liver into full-fledged cancer, known as Hepatocellular Carcinoma (HCC). HCC accounts for 90% of liver cancers globally, the sixth most common type of cancer. Over 750,000 people are diagnosed with HCC annually and most often, unfortunately, in the late stages of the disease; nearly 50% of cases are in China alone, due to the country's high prevalence of Viral Hepatitis B and C. Obesity and alcohol abuse are major contributing factors, which are of rising relevance to governments in the Asia Pacific.

This is where the story shows the potential, yet undervalue, of diagnostics. The testing technologies are already widely available – from HBV and HCV screening (e.g. HBsAg, anti-HBs, anti-HCV serology tests), to diagnosis, treatment decision-making and monitoring, to more advanced procedures such as ultrasound imaging or, increasingly, AFP and PIVKA-II surveillance tests as a biomarker to catch the oncogenesis progression much earlier and as a more precise means to determine tumor stage. Indeed, biomarker diagnostic technologies are seen as the future for convenient, inexpensive, non-invasive, and repeatable identification of liver diseases.

Despite the promise, more than half of HCC cases are diagnosed in the later stages of the disease, when the five-year survival rate is less than 10%. Studies show that in the Asia Pacific, closer to 80% of HCC cases are diagnosed in such a stage. Fortunately, discussions are underway to evolve how biomarkers and other diagnostic technologies are adopted in the region to improve early detection. Upon the incorporation by the European Association for the Study of the Liver (EASL) in 2019 of Hepatitis B and C screening as standard of care for primary HCC prevention, the Japanese Society of Hepatology (JSH), with its expert panel on HCC, updated their clinical practice manual in 2021 to include the PIVKA-II biomarker screening approach in its fourth edition revision. In essence, the three prongs of effective liver disease progression management, through greater access to diagnostic technologies, can be summarized as: tackling the risk factors (through HBV/HCV management), earlier identification of those patients with chronic issues, and, ultimately, the surveillance therein in order to pick up early-stage HCC that could potentially benefit from curative therapy.

High degree of unmet needs across the Liver Disease Continuum

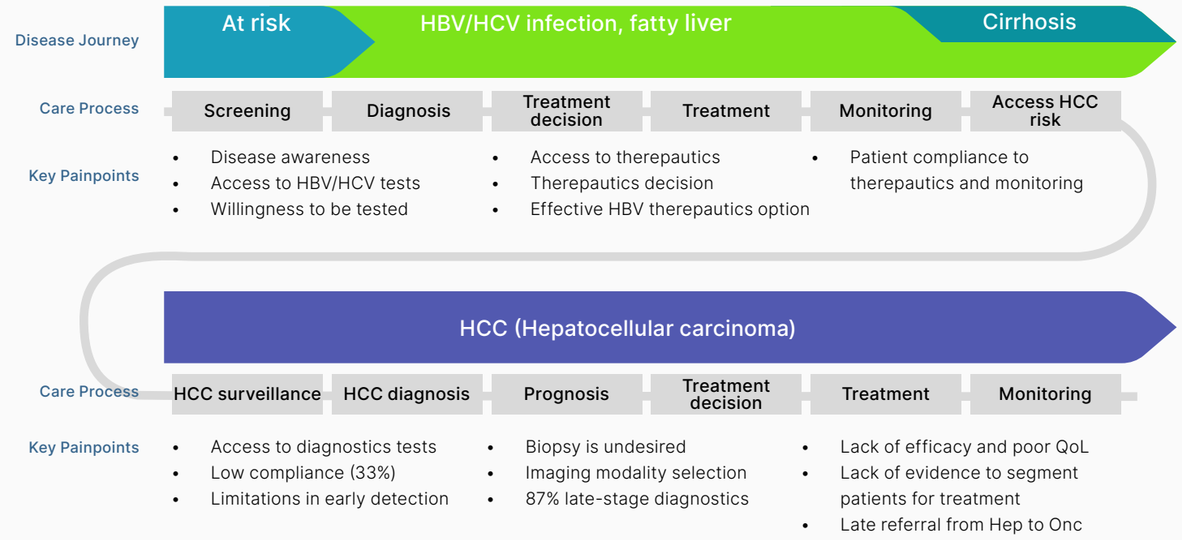


Figure 15
Articulation of the liver disease patient journey, from initial virus through to cancer, and the various challenges along the pathway as a result of the undervalued role of diagnostic technologies.

HCC mortality rates have shown to decrease by as much as 37% through earlier and more advanced diagnostics while survival rates jumped to over 50%, as compared to 27% using more limited protocols. Through screening, surveillance, and other preventative testings, patients that are identified early were able to benefit from curative care with prolonged survival. We hope to see more markets in the Asia Pacific consider the value delivered through these liver diagnostic innovations.

Use case

Precision diagnostics at population scale to address the era of CVD intervention[29, 42, 43, 44, 45, 46]

Cardiovascular Disease (CVD) affects one in every five people, with survival rates lower than certain types of cancer. Especially given the rise of our ageing societies, the direct and indirect costs of CVD to governments and payers is in the billions of dollars. Timely diagnosis, treatment, and effective monitoring are critical; yet, missed diagnoses, re-hospitalizations, inefficient use of healthcare resources, and poor patient experiences remain common in the CVD pathway.

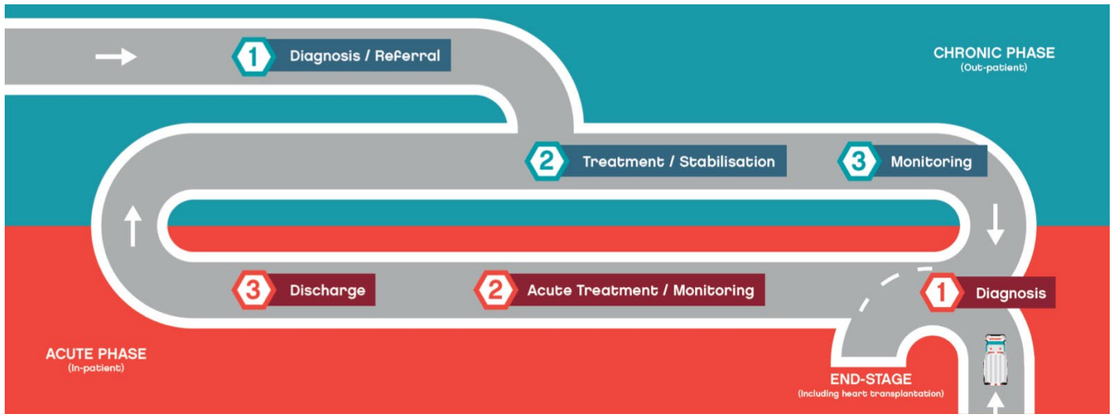


Figure 16
CVD is a diagnostic challenge, given the variety of symptoms involved as well as the chronic and acute nature of the pathway. Greater access to and value recognition of testing is needed.

Among the 18.6 million CVD deaths each year, 58% occur in the Asia Pacific, a region which features a stroke-induced mortality rate that is higher compared with the West. According to recent studies, more prolific screening, including proactively amongst asymptomatic population cohorts, reduces the risk of CVD events by nearly 10% and shows gains in healthy life expectancy of up 27 years. APACMed member Abbott has taken on the challenge of driving greater value for CVD diagnostics in the region, with its High-Sensitive Troponin-I blood test that can be added to conventional testing methods by healthcare practitioners in order to more accurately predict CVD risk, even among healthy individuals. The idea being improved triage of those who most need help.

According to studies tied to Abbott's diagnostic technologies in the Asia Pacific, individuals in the top tier of CVD health risk (as per levels of Troponin-I distribution) demonstrated a 160% increase in mortality, including a 92% risk for an initial cardiac event (e.g. a heart attack) with a resulting life expectancy of only 5-15 years. Clearly, the value for governments and payers in the region lies in increased access and affordability of such diagnostic technologies, as recognition of more appropriately addressing the rising tide of CVD patient management ahead.

How does CVD stack up across the Asia Pacific?

CHINA

There are approximately 290 million people living with CVD in China, the leading cause of death. China has the highest incidence of stroke across the Asia Pacific too, a major cause of hospitalizations over the past decade. CVD is estimated to contribute to more than USD 20 billion in direct and indirect healthcare expenditures, a main cause of poverty especially in the rural regions.

HONG KONG

CVD is the third leading cause of death in Hong Kong, an incidence rate particularly on the rise amongst the younger population. Approximately 30% of people aged 45-54 are considered to be at medium or high risk for developing CVD in the next decade, an 11% increase amongst males. The total direct and indirect CVD expenditures are USD 4.6 billion, with modifiable risk factors (e.g. cholesterol, smoking, obesity) accounting for 65% of the costs.

TAIWAN

CVD accounts for one-in-five deaths in Taiwan, claiming the life of someone every 14 minutes. The rate of heart attacks increased by 30% for males and females under the age of 50, with the most common risk factor being the increase in dyslipidemia (abnormal blood lipid levels). In Taiwan, the average medical costs associated with a heart attack in the first year is nearly USD 10,000.

KOREA

While CVD is the second leading cause of death in Korea (just after cancer), the country has the lowest rate of ischemic heart disease in the Asia Pacific. That said, an estimated 101 per 1,000 Koreans live with atherosclerotic CVD, a total disease burden to the tune of USD 7.2 billion.

SINGAPORE

Every day, 17 Singaporeans die from CVD. CVD is on the rise, with the number of strokes and heart attacks increasing by 40% and 63%, respectively, over the last decade. CVD is now the largest contributor to Singapore's combined early death and disability, accounting for 14.2% of DALYs. In other terms, this figure represents USD 8.1 billion in direct and indirect healthcare expenditures.

AUSTRALIA

CVD is the leading cause of death in Australia, or nearly 30% of total. More than 1,000 Australians experience a stroke every week, 40% of whom will die within 12 months and 50% of survivors becoming dependent on caregivers. CVD accounts for 10.4% of total healthcare expenditures, projected to remain the most expensive disease group at more than USD 14.2 billion over the coming period.

Use case

From wrong diagnoses to 90% accuracy in the Multiple Myeloma pathway[29, 32]

Personalized medicine is the connected cousin of personalized diagnostics, tailoring the treatment pathway by reducing side effects and improving outcomes based on understanding the genetic makeup of individual patients. Diagnostic technologies, then, are the foundation for personalized medicine through the initial identification of abnormal disease conditions using biomarkers, especially when considering the determination of instability in cancer tumors. Cancer prevention, in the form of earlier and even curative intervention, provides value to health systems through more streamlined treatment protocols. Government and payer management of cancer going forward will rely on a population stratification approach, enabled by the power of diagnostic technologies and data.

Breast Cancer

12% of women in the U.S. will be diagnosed with breast cancer over the course of their lifetime - with over **250,000 new cases** diagnosed in 2017. Diagnostic tests utilize varying technologies to identify which of the major subtypes of breast cancer a patient has and enables doctors to design **optimal treatment strategies** for each individual patient leadning to **improved outcomes.**[2]

Metastatic Colorectal Cancer

Routine testing of patients with metastatic colorectal cancer for the KRAS mutation before initiating treatment with epidermal growth-factor receptor (EGFR) inhibitors would save patients from having to undergo ineffective therapy - and result in **$604 million** in annual health care **cost savings.**[3]

Stroke

If genetic testing were performed for every patient before starting treatment with Warfarin, a commonly prescribed anticoagulant, it is estimated that **17,000 strokes could be prevented** while avoiding 85,000 serious bleeding events annually - **saving over 1 billion** in healthcare spending.[4]

Metastatic Melanoma

Metastatic Melanoma is an aggressive cancer with a 5-year survival rate of 15-20%. Advanced genetic testing led to the discovery that 40% of patients have a mutation in the BRAF gene and 20% have a mutation in the NRAS gene. **Targeted treatment** of those specific genetic alterations has shown **high response rates** and impressive survival benefits over conventional chemotherapies.[5]

Lung Cancer

Multiple studies have demonstrated that the majority (60 - 70%) of lung cancers possess genetic biomarkers that could be treated with targeted therapies. Patients matched to **targeted therapies** based on molecular diagnostic testing had **better survival** than those who were not matched.[6,7]

HIV / AIDS

Abacavir is medication used to treat HIV/AIDS. While well-tolerated in most patients, it can cause serious hypersensitivity reactions in others. A strong link was discovered between hypersensitivity to Abacavir and a rare form of the HLA-B gene. Using **genetic tests** to screen patients for this HLA-B gene allows doctors to use a personalized medicine approach, selecting the **safest treatment** for each patient.[8]

Diagnostic Test in Use: From Risk Assessment to Therapy Selection and Beyond

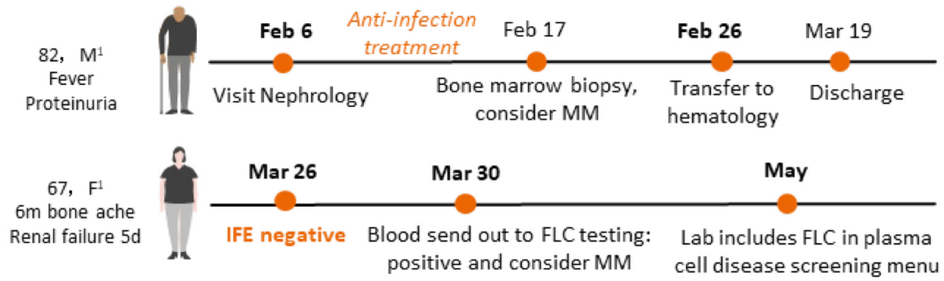
Cancer diagnostics provide vital insights into patient health at every stage of cancer care, including:

- **RISK ASSESSMENT:** Diagnostic tests can be used to search for biomarkers that indicate an elevated risk of developing the corresponding cancer.
- **SCREENING:** Screening tests are used to look for a cancer when a person does not have symptoms and are normally applied to patients in the general population or patients at high risk of a certain cancer to identify the disease as early as possible.
- **DIAGNOSIS:** Tests for diagnosis are used to obtain a definitive diagnosis and determine the type of cancer.
- **STAGING & PROGNOSIS:** Staging or prognostic tests are used to assess the severity of the cancer and/or the risk of recurrence.
- **THERAPY SELECTION:** Many diagnostic tests can indicate which treatments and therapies may work most effectively or rule out those that are unlikely to work, for each patient.
- **MONITORING:** Monitoring tests can tell a patient and their doctor whether a treatment is working or provide information about the likelihood of recurrence.

Figure 17
Outline of the role of diagnostic technologies in improving the cancer patient pathway,as well as specific examples of the value that these technologies deliver to health systems.

For Siemens Healthineers, APACMed member, bringing precision cancer diagnostics to enable precision medicine includes a focus on the Multiple Myeloma (MM) pathway. MM is the second most prevalent form of blood cancer, yet its symptoms (proteinuria, anemia, bone ache) are non-specific and often lead to wrong or delayed diagnoses. Such delays lead to delayed cancer treatment, and many unnecessary tests and procedures. Even when MM is suspected, traditional tests for MM have only moderate sensitivity, require laborious sample collection and manual processes, or are invasive bone marrow biopsies.

In a study undertaken in China, Siemens Healthineers found that 52% of MM cases at the PLA General Hospital were misdiagnosed as kidney disease, and a further 20% misdiagnosed as CVD. Working hand-in-hand with the healthcare practitioners, Siemens Healthineers introduced the serum Free Light Chain (sFLC) assay to the hospital for MM screening and diagnosis. sFLC are now recommended in clinical guidelines for the diagnosis, prognosis, and monitoring of MM, and are available on automated analyzers like the Siemens Healthineers BNII nephelometer. In other words, MM screening is now possible using only a patient's blood sample, with results in 30 minutes.



90%
Diagnosis accuracy

7-20 days
Time saving[2]

3X
Screening coverage increase[3]

Figure 18
"MM does not usually have specific clinical symptoms and its misdiagnosis rate in China is very high," said Professor Li Yan, PLA General Hospital Lab Director. "FLC testing is a more advanced tool with improved accuracy, providing great value to the health system. It is important for us to find these patients early and correctly."

Use case

Non-invasive prenatal testing and next generation sequencing[47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66]

Prenatal screening is a routine medical service for a pregnant woman to evaluate personal risk of fetal aneuploidy. These aneuploidies include but are not limited to: trisomy 21 (Down syndrome), trisomy 18 (Edward syndrome), and trisomy 13 (Patau syndrome). In recent years, maternal plasma cell-free DNA (cfDNA)-based testing, or Non-Invasive Prenatal testing (NIPT), for detection of these trisomy syndromes has become available. Historically, prenatal screening has primarily been conducted using the First-trimester Combined Test (FCT), which combines measurement of Fetal Nuchal Translucency (NT), serum free-β human Chorionic Gonadotropin (free β-hCG), and Pregnancy Associated Plasma Protein A (PAPP-A), taking into account maternal age and previous history of aneuploidy in order to generate a risk score. The confirmation of the diagnosis requires the extraction of tissue of fetal origin for genetic testing, which could only be obtained by invasive techniques such as amniocentesis (amniotic fluid samples containing fetal cells, mostly of epithelial origin) or chorionic villus sampling (placental samples containing mesodermal connective tissue and trophoblastic cells of the placenta). Such techniques bear a risk of complications and even miscarriage for the pregnant woman.

NIPT through the analysis of cfDNA is a major technological advancement in testing for chromosomal anomalies. DNA from the fetus is found circulating in maternal blood from intact fetal cells or after the breakdown of cells (mostly placental) as cfDNA. Only 10-15% of cfDNA circulating in maternal blood is fetal in origin, but this fetal fraction can now be detected and measured. In NIPT, cfDNA is analyzed via Next Generation Sequencing (NGS) to detect quantitative differences in the number of DNA fragments of different chromosomes, so as to distinguish fetal aneuploidies from unaffected pregnancies.

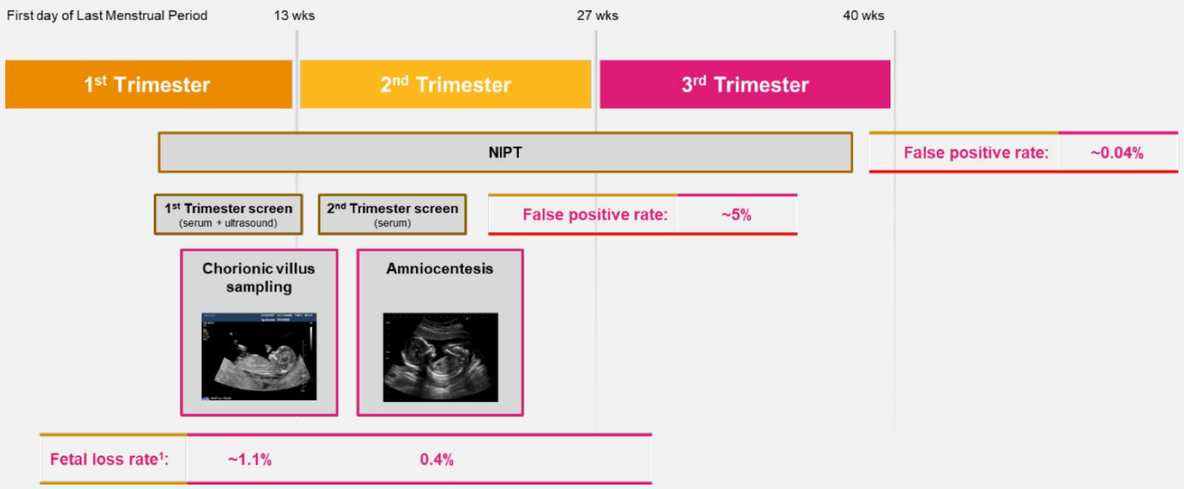


Figure 19
Evolving the paradigm of prenatal screening and diagnostic testing, NIPT reduces the false positive rate for trisomy syndromes as compared to the more traditional (and invasive) protocols.

The clinical benefits of NIPT over conventional screening, namely marked improvement in sensitivity and specificity, has been demonstrated across numerous studies, which result in reduced need for invasive testing, optimized resource allocation, and overall enhanced quality of care and informed pregnancies. Thus, NIPT offer an opportunity to increase the performance of prenatal screening programs for governments and payers in the Asia Pacific.

APACMed member Illumina is actively driving global NIPT adoption. Healthcare authorities in several markets around the world have already started to implement NIPT as a first-line screening, and others are currently evaluating the impact of shifting from existing conventional prenatal screening programs to alternative pathways that use NIPT as a first-line screening or as a second-line screening after FCT. While many professional societies are recommending NIPT, payers in the Asia Pacific have yet to consider NIPT for public funding. This is despite the compelling evidence published over the past decade on the clinical and economic utility of NIPT.

There needs to be more discussion amongst stakeholders in the region about the value story for adoption of prenatal screening and NGS technologies. Particularly when considering the benefits for expectant parents and medical practitioners who are better informed with this technology, allowing for more effective preparation for the needs ahead.

06

Recommended Path Forward

We hope the message is clear – while there is much cause for celebration about the efforts thus far in bringing diagnostic technologies to the fore in the Asia Pacific, more work is still needed in order to appropriately value and unlock access to these solutions for lasting impact. Using the WHO EDL and Lancet Commission as a guiderail, there is a window of opportunity for government and payer leaders in the region to leverage the momentum ahead.

The following are the specific recommendations being made by APACMed, accordingly:

1 Use the COVID-19 crisis as an opportunity to improve healthcare surveillance, thereby laying the foundation for more properly assessing the measurable role of diagnostic technologies. Consider not only the government/payer view, but also wider healthcare ecosystem sentiments and particularly pertaining to those vulnerable cohorts.

(Note: We provide a literary review of available diagnostic technology value frameworks in the Appendix, based on a similar study undertaken in Latin America).

2 Conduct analyses to determine how your market stacks up against WHO and Lancet Commission specifications, including associated clinical protocols. Seek to start identifying those higher quality, effective, and efficient diagnostic solutions which are delivering disproportionately better outcomes, treatments, integrated care, and value for resource allocation.

3 Continue the drive toward approval harmonization, at the sub-regional, Asia Pacific, and international level. This should include aims to improve elements such as review speed, recognition and reliance, as well as data sharing stipulations for adoption of diagnostic technologies. The effort should ideally be undertaken in consultative fashion by working hand-in-hand with the industry.

4 Align resourcing ambitions of UHC (1.0 or 2.0) to the critical role of diagnostic solutions, including from the perspective an upskilled healthcare workforce to enable a new standard of care. Building more integrate networks will provide better patient access to care (from testing to treatment), connect decentralized or community-based models with centralized resources, and continue harnessing of the digitalization trend.

5 Particularly for Archetype 1 markets, most critical is to tackle the historic under prioritization of screening and diagnostics by standing up more robust, fit-for-purpose strategies, national programs, value assessment frameworks, and reimbursement schemes. In addition, we ask to support the calls for the establishment of a coordinated global alliance for diagnostic value discussions, which would span across public and private sectors, of all market archetypes, and embracing a creative variety of stakeholder inputs.

6 For Archetype 2 markets, seek to ensure the evolution process is transparent in terms of investment, coverage, and value-based schemes therein. Specify an evaluation pathway for diagnostic technologies that would more appropriately recognize their value being delivered to healthcare systems, and subsequent suitable reimbursement coding practice improvements which can help to achieve the vision.

We reiterate that the call-to-action is for public + private sector co-creation. The market archetypes and use case illustrations are enlightening from the perspective of demonstrating the art of the possible. Now it's time to collaborate on activating the concepts together. We are here to help, for the collective ambition of providing diagnostic technologies to our populations in need.

07

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The Asia Pacific Medical Technology Association (APACMed) represents manufacturers and suppliers of medical equipment, devices and in vitro diagnostics, industry associations, and other key stakeholders associated with the medical technology industry in the Asia Pacific region. APACMed's mission is to improve the standards of care for patients through innovative collaborations among stakeholders to jointly shape the future of healthcare in Asia-Pacific. In 2020, APACMed established a Digital Health Committee to support its members in addressing regional challenges in digital health.

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08

Appendix (Value Frameworks for Diagnostic Technologies Catalogue)[20]

Framework	Country	Year	Developers	Source	Original VF	Broad spectrum of diagnostic technologies	Specific diagnostic technology
Medical Services Advisory Committee (MSAC)[33]	Australia	2005	HTA agency	Web	✓	✓	
National Framework for Reviewing Codependent Technologies[34]	Australia	2013	HTA agency	Manual searching	✓		Codependent technologies (companion test)
National Institute for Health and Care Excellence. Diagnostic Assessment Programme (NICE DAP)[5]	United Kingdom	2010	HTA agency	PubMed		✓	
Evaluation of Genomic Applications in Practice and Prevention (EGAPP)[35]	United States	2004	Government office	Web	✓		Genetic test
Institut National déxcellence en santé et en services sociaux (INESS)[36]	Canada (Québec)	Not available	HTA agency	Web	✓	✓	
Institute for Quality and Efficiency in Health Care (IQWIG)[37]	Germany	2017	HTA agency	Web		✓	
The Advanced Medical Technology Association (AdvaMed)[38]	United States	2017	Technology producers and consultants	Web	✓	✓	
Value of Diagnostic Information (VODI)[7]	Europe	2018	Technology producers and consultants	Manual searching	✓	✓	
Frueh and Quinn[39]	United States	2014	Independent researchers	PubMed	✓		Molecular test
Palmetto MOLDX[40]	United States	2011	Technology producers and consultants	Manual searching	✓		Molecular test
Bojke, Soares et al[23]	United Kindgom	2018	Independent researchers	PubMed	✓	✓	
Impact assessment framework (IAF)[24]	International	2010	Academic group	PubMed	✓		Tuberculosis diagnostic test
Companion test Assessment Tool (CAT)[25]	International	2015	Independent researchers	Web	✓		Companion test
Lee et al[2]	International	2010	Technology producers and researchers	PubMed	✓	✓	
EUnetHTA[27]	Europe	2008	HTA agency	Web		✓	
Blancquaert Evaluation Framework [26]	Canada	2006	Independent researchers	Manual searching	✓		Genetic test
Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC)[29]	United States	2003	Government office	Manual searching	✓		Genetic test
Genetic testing Evidence Tracking Tool (GEET Evaluation Tool)[31]	International	2009	Scientific associations	Manual searching	✓		Genetic test
EuroGentest Evaluation Model[28]	International	2010	Scientific associations	Manual searching	✓		Genetic test
The United Kingdom Genetic Testing Network (UKGTN)[32]	United Kingdom	2002	HTA agency	Manual searching	✓		Genetic test

VF indicates value framework; HTA, health technology assessment.

continued on next page

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