Innovation Ecosystems for Precision Medicine Implementation

Hoyt Gong
University of Pennsylvania

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Abstract
Leaders in policy, business and healthcare, while receptive to the potential of precision medicine applications, often struggle with finding a consistent and standardized approach for both evaluating their health system's current readiness for the practical implementation and integration of precision medicine and elucidating the capabilities for future growth. This paper discusses the necessary functions of business producers, resource funders, and regulatory governors to incentivize, establish, and build a continuously growing economic marketplace for precision medicine technologies. Under the broader faculty of precision medicine implementation, the innovation ecosystem refers to the various forms of novel developments in precision medicine and include new products, firms, technology, business models, behavioral changes and policies. Four foundational areas and their corresponding capabilities are studied in the paper: (1) Innovation Governance, (2) Innovation Financing, (3) Community and Partnerships and (4) Workforce and Infrastructure. The potential for international and national-level frameworks informed by this paper and early pilot projects aim to support the development of standards and guidelines that will inform precision medicine policies and regulations.

Keywords
precision medicine, innovation ecosystems, implementation, governance, financing, partnerships

Disciplines
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INNOVATION ECOSYSTEMS FOR PRECISION MEDICINE IMPLEMENTATION

By

Hoyt Gong

An Undergraduate Thesis submitted in partial fulfillment of the requirements for the

WHARTON RESEARCH SCHOLARS

Faculty Advisor:

Stephen M. Sammut

Lecturer, Management Department; Senior Fellow, Health Care Management Department,

THE WHARTON SCHOOL, UNIVERSITY OF PENNSYLVANIA

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Abstract

Leaders in policy, business and healthcare, while receptive to the potential of precision medicine applications, often struggle with finding a consistent and standardized approach for both evaluating their health system’s current readiness for the practical implementation and integration of precision medicine and elucidating the capabilities for future growth. This paper discusses the necessary functions of business producers, resource funders, and regulatory governors to incentivize, establish, and build a continuously growing economic marketplace for precision medicine technologies. Under the broader faculty of precision medicine implementation, the innovation ecosystem refers to the various forms of novel developments in precision medicine and include new products, firms, technology, business models, behavioral changes and policies. Four foundational areas and their corresponding capabilities are studied in the paper: (1) Innovation Governance, (2) Innovation Financing, (3) Community and Partnerships and (4) Workforce and Infrastructure. The potential for international and national-level frameworks informed by this paper and early pilot projects aim to support the development of standards and guidelines that will inform precision medicine policies and regulations.
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Introduction

Leaders in policy, business and healthcare, while receptive to the potential of precision medicine applications, often struggle with finding a consistent and standardized approach for both evaluating their health system’s current readiness for the practical implementation and integration of precision medicine and elucidating the capabilities for future growth. Stakeholders in emerging economies, in particular, shared that they would value a guidance document that includes examples and access to partner communities as they think about how to strategically grow the precision medicine capabilities of their healthcare ecosystems.

Aligned with this need, the Precision Medicine Readiness Principles were developed: a thought leadership project that will begin with developing a living document from which policymakers and others looking to advance precision medicine in their countries can find benchmarks for readiness. Precision medicine offers a more personalized and targeted approach to preventing and addressing disease through screening, diagnosing and treating patients by considering their genetic and biological make-up, surrounding environmental factors and lifestyle behaviors.

The Readiness Principles is developed as a roadmap that identifies precision medicine capabilities across five categories of criteria for progress. Informed by a National Academy of Medicine Discussion Paper (Dzau et al., 2016) and a multi-stakeholder workshop held on the sidelines of the 2019 World Health Assembly, the roadmap will provide a set of exemplary capabilities by which to evaluate a country’s health ecosystem, inform policy and investment, and guide sustainable health ecosystem development.
The above figure illustrates the five core topics of the Precision Medicine Readiness Principles as informed by the National Academy of Medicine Discussion paper and the World Economic Forum’s previous work. Notably the Precision Medicine Readiness Principles require enabling foundational elements and assumes that some supportive infrastructure and health systems are in place. These include a minimum level of physical health infrastructure (e.g. basic sanitation and electricity supply), workforce sophistication (e.g. reading literacy), and country governance (e.g. law-making public bodies).

By identifying best practices and strategic opportunities for precision medicine adoption in a healthcare ecosystem, this living document serves as a gauge from which policy-makers and others looking to advance precision medicine in their countries can (1) find maturity assessment benchmarks for readiness and (2) identify potential steps forward to implementation. These benchmarks are illustrated in the form of “capabilities,” defined as the working set of key elements employed to drive development of precision medicine approaches within healthcare ecosystems. These capabilities, categorized by the five core topics of the Readiness Principles...
illustrated in Figure 1, are neither an exhaustive list nor mandatory criteria; further research and innovation in precision medicine implementation is encouraged. Gaps and barriers uncovered during research will be addressed later in the paper.

This paper is one in a series of five on the Precision Medicine Readiness Principles and addresses the **Innovation Ecosystem** topic. Hence, the capabilities described in this work build on the context provided by the foundational elements of the framework and remain specific to the Innovation Ecosystem topic defined in the following section.

**Innovation Ecosystem Framework**

**Defining the Innovation Ecosystem**

The innovation ecosystem topic aims to address the processes that enable the creation and expansion of a precision medicine marketplace. Specifically, the paper discusses the necessary functions of business producers, resource funders, and regulatory governors to incentivize, establish, and build a continuously growing economic marketplace for precision medicine technologies. The guiding research question for this vertical can be described as “what are the capabilities that build and sustain a precision medicine marketplace?” Under the broader faculty of precision medicine implementation, the innovation ecosystem refers to the various forms of novel developments in precision medicine and include new products, firms, technology, business models, behavioral changes and policies. Such forms of precision medicine “innovation” manifest differently in a global context; innovation may range from the preferential introduction of incremental, marginal improvements in process to significant technological adoption or novel product development. Hence while this paper provides capabilities that may serve as a preparatory model for the implementation of a precision medicine innovation ecosystem, it
discludes specific, prescriptive guidelines as programmes almost always require modifications and adaptations to fit local contexts.

Framework Structure and Components

Figure 2: Innovation Ecosystem Framework

The study of the defined Innovation Ecosystem topic has been developed through desk research, the development of a resource guide, and individual consultations with ~40 key professionals across international health systems representing 10+ stakeholder types. This research pointed to four foundational areas: (1) Innovation Governance, (2) Innovation Financing, (3) Community and Partnerships and (4) Workforce and Infrastructure. For the purposes of this paper, these areas and their corresponding capabilities are defined in the components below.

**Innovation governance** refers to public legislation and regulatory considerations in the provision of precision medicine. These include mandates set forth by ministries of health, market review processes and policy-driven initiatives enabled by the country’s governing system.
**Innovation financing** refers to the funding mix to both set up and regularly reimburse precision medicine programmes. This may range from standalone public or private financiers, public-private funding partnerships and specific financing mechanisms for precision medicine.

**Community and partnerships** refer to the methods in which multi-stakeholder collaboration emerges in an innovation ecosystem. In the precision medicine context, this area explores the changing role of various stakeholders and the ecosystem conditions to enable innovation.

**Workforce and infrastructure** describes the broader health system, human capital and economic considerations necessary in supporting a precision medicine marketplace. Such foundational elements are particular to power the discovery and economic sustainability of precision medicine innovations.

The following section of this paper will explore each of these four areas and their attendant capabilities. The discussion of each area will reflect how capabilities mature as health ecosystems engage more precision medicine approaches overall and is supported by illustrative ongoing case studies.
Innovation Governance

Initial Implementation Roadmap from National Strategic Plan

The national strategy consists of both (1) the aspirational metrics of the Ministry of Health (or equivalent government decision-making agencies) to incorporate precision medicine approaches into care and (2) the outlined steps and partnerships to achieve such targets within a timeframe. Top-down policy entrepreneurship from key government leaders catalyzes the early activity of the precision medicine innovation ecosystem, barring specific cases in which precision medicine approaches are first adopted at the private health provider level. Even in this latter scenario, performance evaluation of such private activity may provide compelling cases for national precision medicine programmes (Moreno and Joly, 2015). As of 2019, over 36 formal national or international strategies for precision medicine have been developed and are captured in figure 3 below.

Figure 3: 36+ Formal National or International Precision Medicine Strategies (Manolio, 2015).
The readiness of a national strategic plan will heavily rest on the government’s prioritization of precision medicine in its health system. In LMICs, the Ministry of Health (or equivalent agencies) may likely have existing strategic programmes for other disease areas, likely infectious or neglected tropical diseases, given other national health priorities. If precision medicine is part of the national strategy, however, initial use cases may be prioritized based on (1) disease burden, (2) its applicability to population health surveillance and (3) a shift to preventative care, particularly for non-communicable disease. In more developed economies, there is greater opportunity to implement complementary initiatives given the increased resourcing and an established foundation. As markets develop, the national strategy may include a broader range of use cases beyond oncology - a common early use case of precision medicine - into other disease areas such as cardiology or rare disease. Greater private sector participation is also observed alongside maturing markets, further discussed in the Innovation Financing section.

**Case Study - Nigeria’s CCP by their Ministry of Health Formalizing Support of Precision Medicine implementation:** In 2015, the Nigeria Ministry of Health announced its new cancer control plan (CCP) that lends formalized support for precision medicine implementation country-wide. Supported by the Clinton Health Access Initiative, the American Cancer Society, and the US National Cancer Institute, the CCP established updated guidelines for cancer management from the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology, which is now taught in Nigeria’s medical training curriculums. The CCP outlines measures to support the Nigerian government’s screening programme with the goal to screen half the eligible Nigerian population by 2022. Over the long term, the Ministry of Health aims to incorporate routine screening of eligible cancers into existing clinical programs.
**Case Study - US NIH All of Us Initiative:** In 2018, the National Institutes of Health (NIH) launched the All of Us initiative (formerly known as the Precision Medicine Initiative Cohort Program) with the objective to collect genomic and health data on a longitudinal basis from one million volunteers in the United States. The initiative acts as a consortium with 100+ programme partners that include data and research centers (DRCs), biobanks, patient participant centers, health care provider organisations and community engagement partnerships. Specific steps exist through the data collection process (consent forms, survey modules, partner protocols) and particular attention is placed on strategic enrollment of demographics underrepresented in biomedical research.

**Open Science Principles**

Contrasted with the more proprietary, innovation ownership models based on trade secrecy and competition, open science, as defined by the Organisation for Economic Co-operation and Development (OECD, 2015), is a movement enabled by information and communication technologies towards transparent data sharing, rapid knowledge dissemination and broad research accessibility. Emerging policy applications of open science have particular relevance in the field of precision medicine by: (1) changing how genomics-related research is conducted and disseminated, and (2) reducing the otherwise high costs and uncertainty of precision medicine if actors were to invest resources in genomics research and development (R&D) as standalone initiatives (Joly, 2011). Importantly, the access to higher volume data as a result of open science principles improves both the granularity of stratified care delivery and the significance of clinical
research discoveries backed by a more robust genomic knowledge base (Global Alliance for Genomics and Global Health, 2014).

Open science for precision medicine research may manifest in various initiatives - e.g. international multi-stakeholder genome research consortia, centrally accessible databases for research and clinical use, or collaborative efforts that avoid duplicate work. In moving towards implementation, various open science guiding principles described by the international GO FAIR initiative (Wilkinson et al., 2016) aim to enable researchers to find, access, interoperate and reuse each other’s research objects. They are described in figure 4 below. Readiness benchmarks for innovation can be found in (1) the extent to which countries follow these principles, (2) the agreed upon standards for exchanging genomic, phenotypic, and clinical data attributes, (3) the recognition of participant consent and privacy, and (4) the balance such open science principles are implemented alongside proper IP ownership regulations.

Figure 4: GO FAIR Open Science Principles (Wilkinson et al., 2016)

While countries are found at various positions on the spectrum of readiness posited above for open science, early collaboration policies for large-scale research groups and involvement in international human genomics initiatives may accelerate the formation of the country’s precision
medicine innovation ecosystem. In low- and middle- income countries (LMICs), policymakers have greater opportunity to design early opt-in incentives into open science and set precedent for national, centralized biorepositories for interoperability and collective contribution. Such leapfrogging avoids the emergence of the potentially scattered, ad hoc siloed genomic programs more common in existing precision medicine programmes. In this latter environment, often in developed countries, policymakers may note inefficiencies with current access restrictions to scientific and research data (e.g. siloed research groups/health systems, data sharing restriction across country borders), which limit the potential for holistic precision medicine R&D advancement for all involved participants. In such cases, the Roadmap for Open Science by the Government of Canada (Nemer, 2020) outlines the steps that should be taken to make federal science open to all, while respecting privacy, security, ethical considerations and appropriate intellectual property protection.

Case study - Estonian Genome Center of the University of Tartu (EGCUT) Biobank: Estonia’s biobank initiative, the EGCUT Biobank, has been funded by the Estonian government since 2000 and includes a collection of health and genetics data from 5% of the Estonia adult population. The EGCUT actively collaborates with many universities, research institutions and consortia given its membership in various international networks such as BBMRI (Biobanking and Biomolecular Resources Research Infrastructure), BBMRI-ERIC (European Research Infrastructure Consortium) and the Public Population Project in Genomics (P3G). The EGCUT maintains a data sharing policy in which collaborators accessing EGCUT resources must send any scientific results obtained from the research project using EGCUT data or samples back to EGCUT for addition in the Estonian Biobank.
Genomics IP Policy and Benefit Sharing

The core question to be addressed by policymakers for genomics IP can be summarized as, “do current national patent regimes promote R&D and innovation in precision medicine while also benefiting the collective interest of public health?” While IP incentives are critical reward measures for precision medicine innovators, policymakers must assess the strength of this pull incentive relative to the benefits of open innovation principles that aim to collectively advance precision medicine in the long term (Hetu and Joly, 2019).

While this paper does not discuss the global controversy surrounding gene patenting, it benchmarks readiness to the transparency in which IP policies for precision medicine innovations are articulated. These defined rulings provide awareness of the risks and rewards associated with an innovation for both technology producers when conducting freedom to operate searches and public-sector organisations considering to open their databases to commercial parties.

Importantly, standard incentive effects of IP rights may be limited or non-existent for innovations addressing health problems mainly affecting LMICs due to (1) its small and uncertain market demand and (2) the lack of capabilities to innovate new precision medicine patents in-house using any data from international open science projects. There is a need for other governance responsibilities, financial mechanisms and multi-stakeholder partnership models to fill the IP incentive gap (Guebert and Bubela, 2014). IP gaps are also observed for LMICs participating in international open genome projects - while data is contributed by and accessible to all involved countries, wealthier nations are more likely to patent innovations from such projects. The MalariaGEN case study illustrates an early use of benefit sharing models to close this gap in its international open science initiative. Under such models, the IP owner
(usually innovators in higher resourced settings) can (1) provide differential access or pricing for innovations used by LMICs or (2) arrange country-specific socially responsible licensing via negotiations with respective government agencies. This, however, does not address how LMIC populations are often not well represented in large genomic data sets. More work on equitable collaboration models is encouraged, particularly for genomics IP and locally relevant data, and is further discussed in the Workforce and Infrastructure section.

### Case Study - Malaria Genomic Epidemiology Network’s (MalariaGEN) GWAS Data

**Release Policy:** MalariaGEN is an international open science project to identify the specific genetic underpinnings of malaria funded by the Grand Challenges in Global Health Initiative through the Gates Foundation and Wellcome Trust. 39 countries currently participate in the MalariaGEN research consortium, sharing and integrating data types (including genetic data) across collaborators. Under its online data release policy, the website states that “the owner of the IP agrees to license it on a reasonable basis for use in the developing world and on a preferential basis to the countries whose citizens are the subject of the database.” This acts as an advantageous patent licensing policy for LMICs that can more equitably benefit from participating in MGEN’s open data project.

Adapted HTA Review Processes for Precision Medicine Technologies

Novel precision medicine technologies may not fit traditional evaluation and market approval processes for biotechnologies. The inclusion of precision medicine in clinical practice has been recognized to “impact each stage of the Health Technology Assessment (HTA) process, from scoping and modelling through to decision-making and review.” (Love-Koh, J., et al. 2018). For instance, companion diagnostics (CDx) and pharmacogenomic tests (PGx) may not fit into
traditional assessment models given their indirect effect on patient outcomes if the resulting information gain from the CDx/PGx changes the course of care. While conventional HTA aims to evaluate the social, economic, organisational and ethical issues of a health intervention, its systematic evaluation varies country to country and often does not cover novel scenarios posed by precision medicine technologies.

Refinements to various components of HTA are encouraged to adapt to the influx of precision medicine algorithms, digital health applications, and 'omics'-based tests. This may manifest in various forms through the approval process and may include, but are not limited to, faster regulatory review timelines, clear pricing standards and relevant medical feedback. However, HTA bodies may struggle to keep pace in creating robust frameworks to formally evaluate precision medicines or may attempt some level of ad hoc review processes on such technologies. Ad hoc reviews, however depend on the ability to determine clear endpoints for precision medicine innovations (e.g. targeted therapies may have direct clinical endpoints whereas companion diagnostics often incur more variable patient pathways) and are discouraged due to its high variability.

To date, only few HTA bodies internationally have accommodated specific considerations or appropriate traditional evaluation methods for precision medicine - e.g. the Diagnostic Assessment Programme at the National Institute for Health and Care Excellence (NICE) in England, the Health Interventions and Technology Assessment Program (HITAP) in Thailand, and the HTA Access Point in Australia). Australia’s entry point for CDx is illustrated as a case study below. Further discussion on the conduct of enabling studies where the necessary data is collected to run HTA models is linked in the “Reimbursement Conditions and Coverage Models” section under Innovation Financing.
Case Study - Australia HTA Access Point for Co-dependent Diagnostic Technologies: The Australian Government Department of Health established a “single entry point,” the HTA Access Point (HTAAP) that assists specific applicants for HTA and reimbursement if they are uncertain about the funding program for which their technology may be eligible, or where their technology may need to be assessed by more than one expert advisory committee. This later case is particularly relevant for designated “co-dependent technologies” such as targeted therapies that require companion diagnostic technology, in which HTAAP will work with the applicant to form a tailored assessment methodology for the eligible technology in hopes that assessment timelines may be reduced.

Innovation Financing

Public Funding and Fiscal Space Utilization

Public funding for precision medicine programmes will depend on the fiscal space, defined as the budgetary allocation for a targeted investment area, available from the Ministry of Finance or respective treasury agency. While constrained by limited resources, especially relative to private funding, public spend can either fully establish or partially underwrite early innovation programmes via some initial mix of grant-based and/or loan financing. These government investments often take the form of milestone-based tranche payments or upfront disbursements but will depend on the project arrangement (Atun, 2017).

While national precision medicine programmes may be ultimately financed by a variety of public and private funding sources, readiness criteria for public funding is defined by (1) the fiscal space allocation to precision medicine from existing budgets or new funding channels (e.g. DAH), and (2) the diversity and investment partners of the funded project portfolio. The former
is based on the ability of a government’s budgetary leadership to audit the return on investment (ROI) of potential precision medicine efforts, measuring the national priority level and understanding of the value from precision medicine. As the innovation ecosystem matures, a greater evidence base of early precision medicine initiatives provides proven traction for further public funding. Similarly self-perpetuating, the latter benchmark highlights the widening types of projects available for funding and the growing co-financing involvement from private innovators as the precision medicine market matures. This funding shift from top-down public spend to greater private investment activity is commonly observed as the innovation ecosystem supports further translation of R&D (although many genomic research initiatives will remain funded by public grants).

While low income countries may not have available fiscal space for precision medicine due to the focus on other national health priorities (e.g. infectious disease or NTDs), public funding remains crucial to the early stages of the innovation ecosystem. In such scenarios where precision medicine remains a national investment interest, precision medicine programmes may be incorporated into related health initiatives of national focus with already ongoing fiscal space spend (e.g. infectious disease surveillance or genomic studies of rare disease prevalent in the LMIC). For emerging and more developed economies able to consider greater public investment, fiscal space remains particularly important to de-risk crowding out effects from the reliance on private aid. Creating fiscal space expansions, often driven by macro-economic growth, budget reprioritization and efficiency improvements, enables the long term financial sustainability of precision medicine approaches (World Health Organization, 2016). The government of Thailand case study below demonstrates the effective use of public funding for precision medicine approaches as an economically growing middle income country, first within highly relevant
disease areas affecting the country (Stevens-Johnson syndrome, SJS, and toxic epidermal necrolysis, TEN) in 2004, now into larger scale 5-year genome catalogue initiatives (2019).

Case study - Public financing of the Genomics Thailand Initiative and PGx studies: In early 2019, the Thai government approved a USD$150 million five-year initiative to catalog the genomes of 50,000 citizens. This project, termed the Genomics Thailand Initiative, aims to expand the understanding of southeast Asia’s underrepresented genomic composition and advance Thailand’s genomics capabilities in personalized diagnostics, drug selection and treatment across various disease areas. Thailand has been engaged with precision medicine research as early as 2004 through the Thai PGx Project for SJS/TEN screening with investments from the Thailand Center for Excellence in Life Sciences (TCELS), a unit under the broader Thai Ministry of Science and Technology. This most recent Genomics Thailand Initiative falls under the broader faculty of the Thailand 4.0 government campaign to close the middle-income country gap towards an innovation-driven economy starting with a competitive genomic medicine industry.

Private Sector Financial Backing

In tandem with public fiscal space, private funding provides the funding scale and expertise to support the precision medicine innovation ecosystem. These private sector financiers range in funding size and involvement - some examples may include development aid agencies, global health philanthropies, biopharmaceutical companies, technology manufacturers, impact investing groups, among various other NGO and corporate investors (Brookings Institute, 2017). The expansion of the precision medicine marketplace is often observed with greater public-private co-financing partnerships and private sector activity standalone.
Readiness benchmarks for private sector financing activity can be viewed as the extent to which private stakeholders are able to participate and fund projects in the innovation ecosystem. Policymakers are encouraged to conduct a stakeholder analysis of relevant private actors in order to map potential collaboration opportunities and current funding gaps in the precision medicine marketplace. Private funders for precision medicine can be broadly categorized into (1) innovation producers, (2) investors, (3) aid donors and (4) service providers. Importantly, the mix of stakeholders shifts depending on the maturity of the innovation ecosystem. For instance, countries at early stages of private financing activity primarily observe aid donors in the form of disease-specific funds and ODA/DAH groups (e.g. foundations, family offices, high net worth individuals). As the marketplace develops, producers - ranging from biopharmaceutical to diagnostic/sequencing companies - and investors - including private equity and venture capital (PEVC) groups - actively deploy financial and in-kind advisory/expertise resources for precision medicine projects. Such stakeholders enter as the innovation ecosystem grows to provide lower-risk operating environments and tenable investment exit opportunities. At advanced stages of readiness, service providers such as private provider systems are able to self-finance precision medicine approaches within their clinical practices.

Private financing of precision medicine technologies in a resource-limited country context remains scarce (Chang et al., 2019). Attention from development assistance for health (DAH) groups and global innovative financing mechanisms (IFIs) including the Global Fund, GAVI, and UNITAID, have historically focused on infectious diseases such as HIV/AIDS, Tuberculosis, and Malaria. As such, non-communicable diseases (NCDs) such as cancers and cardiovascular disease - areas in which precision medicine approaches are currently most applicable - remain underfunded through traditional global health DAH and IFI channels (Allen, 2015). This remains
a notable gap that is further highlighted in the DAH financing disease area breakdown in figure 5 below.

![Development Assistance for Health by Channel of Assistance, 1990-2018. (Allen, 2015).]

Case Study - Series A Financing of 54Gene by Adjuvant Capital: Founded in 2019, 54Gene is an African genomics research, services and development company aimed to include under-represented African genomic data in health research and drug development. In April 2020, U.S.- and Nigeria-based genomics company 54Gene announced a USD$15 million series A financing round led by Adjuvant capital, a global health-focused investment fund for life science technologies backed by the Bill & Melinda Gates Foundation, Novartis and the International Finance Corporation. 54Gene has taken a predominantly private financing approach to grow its capabilities and positioning in the wider precision medicine marketplace, with a total of $21.5M raised VC funding catalyzed by initial participation in accelerators (Y Combinator and Google Developers Launchpad).
Case study - Private equity financing of largest precision medicine provider in Morocco

by Alta Semper: Frontier markets private equity firm, Alta Semper, has invested in Morocco’s largest oncology, radiology and diagnostics services platform, Oncologie Diagnostic du Maroc (“ODM”). The provider owns and operates five facilities for oncology treatments alongside its array of various imaging and genomic diagnostic services available. In addition to financial capital, Alta Semper aims to help ODM’s expansion strategy by providing operating expertise across North and Sub-Saharan Africa alongside access to its existing healthcare holdings in Morocco.

Case Study - UBS $500m Oncology Impact Fund: Swiss multinational bank UBS Group raised ~$500 million from high net worth individuals (HNWIs) for investment by MPM, a healthcare venture capital firm with oncology expertise. The fund serves as an impact investment initiative that invests in early-stage cancer treatments and, in turn, manages the royalties and performance fees from successful drug sales of such investments for impact key performance indicators (KPIs). The UBS Optimus Foundation will manage any such generated capital from initial early stage oncology investments and specifically direct this flow to (1) academic grants to promising oncology-related research and (2) health access initiatives in developing countries. This combination of HNWI impact investors (scale) and VC expertise (domain knowledge and experience) presents a potential replicable financing model for private-driven impact investing in precision medicine technologies.
Blended Finance and The Diagonal Approach

Any patient population stratification method or targeted approach to care delivery is unproductive without accompanied actionable decision-making steps (“effectors”). Countries may lack such foundational effectors such as having sufficient targeted therapy drug supply or proper technical knowledge to interpret genomic risk profiles. Further progress in general health systems strengthening remains critical alongside precision medicine specific investments, and is further discussed in the “Foundational Health Systems Strengthening” section of the Workforce and Infrastructure topic. Aligned with literature on universal health coverage, the diagonal approach to finance health system strengthening “overcomes the barriers between vertical (disease-specific) and horizontal (systemic) approaches by making full use of potential synergies between disease programs and health functions.” (Atun et al., 2012). Instead of financing precision medicine technologies specific to each disease, this cross-cutting framework emphasizes (1) early financing of precision medicine approaches spanning multiple disease areas (2) and reinforcing foundational health and economic effectors critical to any precision medicine intervention.

Blended finance serves as one such “diagonal approach” linking macroeconomic development and specific investment in precision medicine programmes. Specifically, it uses various risk-adjusting financing structures to mobilize private capital alongside development and philanthropic funding towards economic development objectives in emerging markets. An overview is illustrated in figure 6 below. Blended finance approaches often converge in their ability to attract private investment on public-driven development initiatives that incentivize overall economic growth. Such development initiatives can strengthen the precision medicine innovation ecosystem in which infrastructure growth enables further job creation, knowledge
transfer and improved overall health outcomes. The Blended Finance Toolkit from the joint ReDesigning Development Finance Initiative (RDFI) of the World Economic Forum and the OECD (2015) provides more specific recommendations for adopting this investment approach in emerging and frontier markets. Further detail on overall health system strengthening and economic development is discussed in the Workforce and Infrastructure topic.

Case Study - Chile and Pfizer Center for Excellence in Precision Medicine (CEPM): The Chilean Economic Development Agency (CORFO) has provided co-financing of USD$7 million, over a period of four years since 2015, to create the Santiago-headquartered Center of Excellence in Precision Medicine (CEPM). A result of a joint effort between the Chilean government and pharmaceutical company Pfizer, CEPM was formed to promote Chile as a hub for research, development and innovation in Latin America. CORFO acts under the Chilean government mandate towards promoting economic growth and has done so through various initiatives, including its programme to create international ‘Centers of Excellence.’ CEPM acts as one such international program partnership, bolstering Chile’s objective to diversify from a commodity-driven to knowledge-based economy attracting global R&D research. CEPM has focused its initial efforts on non-small cell lung cancer (NSCLC) next-generation sequencing through its technology partner, Thermo Fisher, that invested $3 million in the collaborative project. NSCLC has a high incidence in the region (~2000 cases annually) and its treatment is currently associated with a companion diagnostic to identify eligible patients for medication based on an ALK gene mutation. Since its inception, CEPM has published 140+ articles and improved its technology transfer ecosystem, all while simultaneously strengthening its regional economy through job creation and knowledge transfer from Pfizer’s R&D best practices and collaborations with its other R&D centers globally.
Reimbursement Conditions and Coverage Models

The effective financing of precision medicine innovations is closely tied to its coverage and reimbursement, which remains one of the largest hurdles of successful implementation and marketplace growth (Precision Medicine Coalition, 2015). Clear coverage and reimbursement standards of precision medicine technologies enable innovators and adopters to recognize its financial payoff and cost of use, respectively. Policymakers must formalize (1) the purchasing stakeholder(s) responsible for reimbursement, (2) the circumstances and conditions on which and how precision medicine interventions are covered, and (3) the review process for reimbursement decisions based on health technology assessments (HTA). As regulators and payors increasingly look towards real-world evidence (RWE) assessments for coverage decisions, additional emphasis is placed on evidence generation in which formalized processes for data collection and
indicators for performance review emerge. This discussion is closely linked to the “Adapted HTA Review Processes for Precision Medicine Technologies” section under Innovation Governance.

Measuring coverage and reimbursement readiness for precision medicine can be benchmarked by (1) the shift away from out-of-pocket payment models towards accessibility and coverage within available insurance schemes, and (2) sustainable contracts between health providers and respective public or private payors on key coverage conditions and treatment value (Carbonneil and Lee-Robin, 2009). Further readiness metrics on the progression towards value-based care is discussed in the following section “Experimenting with Value-based Care Instruments.” (1) The first metric contrasts the interim coverage programmes adopted by countries, often patient out-of-pocket or direct fee-for-service payment models, that may not support patient accessibility nor aligned incentives on when precision medicine approaches are applicable. These challenges are magnified in under-insured patient populations, where the payment burden of poorly covered techniques on both the provider and patient disincentivizes the use of precision medicine technologies. While coverage models and payor systems greatly vary across countries, insurance models that replace out-of-pocket expenditure supports the equitable growth of an emerging marketplace for precision medicine (Lewis et al., 2015). As alignment with this readiness metric matures, the country may observe greater coverage of various precision medicine approaches, such as population level screening for certain diseases. (2) The latter metric gauges the extent of favorable adoption conditions and payor-provider incentive alignment. Importantly, an important coverage decision dilemma arises in which (1) providers will not adopt novel precision medicine technologies not financially covered by purchasers, and (2) payors are unwilling to cover innovations due to their uncertain value-add relative to reimbursement costs. Various value-
based reimbursement contracts and alternative payment models (APM) have emerged as potential solutions - one such case study below from genomics tool producer, Illumina, and private insurer, Harvard Pilgrim Health Care highlights an APM in which producers share financial risk with the insurer to cover precision medicine technologies under a fees-at-risk model.

**Case Study - Illumina and Harvard Pilgrim Value-Based Contract for Non-invasive Prenatal Genetic Testing:** In February 2018, US-based private payor Harvard Pilgrim Health Care entered into its first next-generation sequencing (NGS) contract with the genomics tool producer, Illumina, to broaden the eligibility of noninvasive genetic testing to younger women, under the age of 35, with average risk pregnancies to screen for prenatal genetic abnormalities. While Harvard Pilgrim already anticipated the cost of this test to be offset by reduced expenditures on other screening modalities, Illumina agreed to further de-risk the investment by covering any potential increased costs. The collaboration also includes a two-year study on Harvard Pilgrim’s patient population to explore the clinical outcomes relative to total costs of this expanded genetic testing intervention, grounding an experiment of clinical value add to real-world evidence that demonstrates further proof-of-concept for precision medicine technologies.

Experimentation with Value-Based Care Instruments
Ongoing global conversations from clinicians and policymakers alike continue to focus on the value of care, driven by the growing attention to measure outcomes relative to healthcare costs. This shift away from traditional payment models to approaches that highlight value-add is particularly relevant for precision medicine innovations proposed to deliver compelling ROI to patients, health systems and society. Under value-based care approaches, reimbursement is
closely linked to the potential cost-effective outcomes derived from the use of a precision medicine intervention (Miller, 2009).

While countries vary widely in their progress toward value-based health care, a range of experimental value-based approaches for precision medicine has emerged in the past decade. Two particular common approaches have been (1) evidence-based modeling studies and (2) managed entry agreements (MEAs) (Brügger, 2014). (1) On the former, modeling studies aim to demonstrate the proven cost effectiveness of an intervention through pharmacoeconomic metrics (e.g. ICER, QALYs). These studies, most optimally run in partnership with a payor stakeholder involved in model design and critique, utilize real-world evidence to form the compelling return on investment of a precision medicine intervention. (2) MEAs consist of a wide class of innovative reimbursement approaches, such as performance-based risk-sharing agreements (PBRSAs) or coverage with evidence development (CED) practices (Klemp et al., 2011). Payors internationally are exploring these novel technology coverage approaches for early patient access while managing financial and performance uncertainty - a potential path forward to reimburse precision medicine technologies that may not fall under traditional coverage paradigms (Garrison, 2013).

While readiness can be observed based on the country’s experimentation with performance-based approaches such as the ones discussed, this capability remains a gap in many countries, irrespective of income level, due to a lack of data on the value-add of precision medicine and the unaffordable prices of some technologies. It is the hope that such experimental techniques discussed above are a step forward, but more work is encouraged around evidence-based value-based care and pricing.
Community and Partnerships

Diverse Range of Partnership and Delivery Models

Precision medicine innovation has been largely achieved through a variety of multi-stakeholder partnerships (Chataway et al., 2012). Novel opportunities for collaboration across payor, provider, corporate, academia, and other actors have emerged as end-to-end solutions across the precision medicine value chain are unfeasible. An increasing diversity of stakeholders continue to become involved with precision medicine - most recently (1) providers are increasingly piloting genetic testing programmes with genomic sequencing companies alongside annual patient check-up exams; (2) employers are offering genetic testing in newly designed cost-effective health benefit packages. A further sampling of such partnership models from 2015-2016 is illustrated below in figure 7.

Figure 7: Partnership Models for Precision Medicine 2015-2016 (Rock Health, 2016).
The above observations on partnership models and composition are limited to western and northern perspectives; it is not well understood if similar models may translate in LMIC settings due to a lack of data. A known challenge, however, is the lack of well structured public private partnerships (PPPs) in the area of precision medicine for LMICs (Gardner et al., 2007). In Latin America, for instance, various small startups with no solid scientific bases offer precision medicine services while several academic initiatives working on such research endeavors have not applied their discoveries to the clinic. Growth of the innovation ecosystem at early stages of precision medicine readiness may often begin with a top-down policy approach (see “Initial Implementation Roadmap from National Strategic Plan” section under Innovation Governance). However, sustainable precision medicine initiatives must at some point engage industry where then it can be supported through private funds. Government funding is not expected to last forever and can greatly benefit from the scale and expertise provided by various public and private stakeholder organisations. Based on the specific precision medicine use case, these partners may provide financial sponsorship, technology provision and/or in-kind fieldwork expertise. Further detail on this public-private development is explored in the Innovation Financing topic.

**Case Study - Precision Medicine Scotland Innovation Center (PMS-IC) Precision Medicine Ecosystem:** The PMS-IC has been Scotland’s national initiative towards creating the Scottish Precision Medicine Ecosystem (PME) to enable broader academic, industrial and NHS participation throughout the country. Built from investment funding totaling ~£12M through 2016 from the Scottish Funding Council and other various donors, PMS-IC acts as an industry/academic consortium consisting of various partners from the NHS health Boards,
Scottish Universities and industrial genomics partners. PMS-IC coordinates various existing precision medicine academic research and business development initiatives throughout Scotland, providing (1) an environment to facilitate innovation through academic/industry partnerships and (2) a path to commercial market entry for large genomic service providers and small and medium-sized enterprises (SMEs) alike.

University-Industry Collaboration

Part of the innovation policy mix aims to expand the R&D and clinical translation productivity for precision medicine initiatives. Illustrative policy instruments may include grant proposal requests providing project prototyping, testing, and technical assistance ultimately to support commercialization, or advocating for academic consortia models that expand collaboration networks perhaps with industry partners in formal PPP programmes. These services may also be formally associated with technology transfer offices (TTOs) at academic institutions when applicable. Irrespective of the policy instrument, there is a need for universities to foster internal environments that support and motivate participation in the innovation ecosystem (Denee et al., 2012).

Readiness indicators can be measured by (1) the extent to which translation research lags or acts parallel to basic science, and (2) the volume and quality of university-industry collaborations for research translation. On the former, a common challenge experienced by academic institutions globally is the lack of translational initiatives relative to basic research progress. These clinical implementation projects may fall short of conventional grant funding, deemed to not fit standard criteria. Instead, a greater shift is encouraged towards developing industry-minded researchers open to entrepreneurship and clinical institutions open to implementation science. On the latter
benchmark, robust university-industry collaborations drive innovative joint R&D and alignment with the technology pull principle. Under such models, universities may develop genomic tools, tests or practices more based on industry and community needs instead of remaining in academic siloes (Cirera and Maloney, 2017).

Initial steps in closing academic innovation gaps between LMICs and more developed countries may center on building infrastructure and R&D capabilities. Limitations in available clinical settings and academic research institutions with genomics-based infrastructure, in addition to funding gaps, will likely constrain the number of studies, scale of research initiatives and translation necessary for precision medicine initiatives. The H3Africa consortium serves as one notable hallmark addressing this gap through capacity building and is described further in the case study below. This case study, described further below, highlights how LMICs have particular opportunity to develop south-south collaborations and leapfrog multi-institutional partnerships prior to the emergence of bureaucratic red-tape or fragmentation barriers to partnership models present in more developed countries. As the innovation ecosystem matures, more publicly available funding (e.g. competitive research grants), coupled with the growth of supporting infrastructure, enable universities to develop precision medicine R&D initiatives and commercialization programs, either in formal university TTOs, or one-off project spinoffs into commercial ventures. Further discussion is available in the “Workforce and Infrastructure” topic.

### Case study - Human Hereditary and Health in Africa (H3Africa) Consortium:

The H3Africa Initiative is a partnership between NIH, the African Society of Human Genetics, the African Academy of Sciences, and the Wellcome Trust formed in 2010 to facilitate modern research approaches into diseases on the African continent with the goal of improving the health of African populations. Led by African scientists, the H3Africa consortium currently
consists of 51 research projects across 30 African countries to study both population-based genomics of NCDs (e.g. heart and renal disease) and infectious disease (e.g. tuberculosis). In addition to research coordination and funding, the programme also develops the infrastructure, resources, training and ethical guidelines to support a sustainable African research enterprise. The consortium has trained ~500 health staff on precision medicine approaches through 50+ workshops. More statistics can be found on the H3Africa website.

Entrepreneurship, Research and Innovation Hubs

The emergence of precision medicine R&D activity may often arise in co-located geographic areas, often as part of existing biotechnology clusters or standalone research and innovation hubs (Delgado et al., 2010). Such regions serve a key role in the innovation ecosystem as (1) a collaborative knowledge-generating environment linked closely to entrepreneurial activity, and (2) connected ecosystem that bridges burgeoning projects with financial and in-kind resources to achieve market access and scale. Policy instruments aim to support these frontier technology developments through levied programmes such as tax incentives for R&D, market access support, and grant provisions or loan guarantees with accompanying firm-level capacity building and advisory programs. Other formal innovation policy initiatives may support independent entrepreneurial development programmes such as incubators and/or accelerators.

Specific to precision medicine, these innovation environments foster the expansion of novel partnership models as discussed in the earlier “Partnership and Delivery Models” section. Especially noticeable in cluster environments where many active stakeholders co-locate, cross-collaboration among pharmaceutical and biotechnology companies, tool producers, academic research and provider systems may naturally precipitate. Readiness can be observed by the
existing productivity of such innovation centers and the fit of precision medicine initiatives within the region’s portfolio of ongoing R&D activities.

The extent to which precision medicine initiatives are available in such clusters varies globally. In LMICs, technology absorption may govern the precision medicine innovation ecosystem. Conditions may be early to warrant investing in large-scale innovation hubs as compared to addressing present infrastructure and human capital gaps towards local innovation. These various barriers are further addressed in the Workforce and Infrastructure topic. As countries address these challenges, support for early innovation ecosystems may emerge as complementary factors such as the growth of SMEs, availability of financing, and industry activity gradually develops.

**Case Study - Genomics Institute of Singapore (GIS) within the Biopolis Research Cluster:**

GIS, started in 2000 within the larger Biopolis research hub for biomedical sciences. Biopolis itself acts as Singapore’s research cluster hosting myriad public and private biotechnology research organisations, but also as an incubator and accelerator providing co-innovation spaces, life sciences facilities with diverse equipment and proximity benefits promoting idea exchange and joint projects. Over the decades, the Biopolis cluster and GIS have initiated various genomics-based projects in conjunction with neighbouring research institutions and industry partnerships with various co-located large pharmaceutical companies that have established offices within the cluster (e.g. Novartis, P&G, GSK).
Figure 8: Comparison of Cluster Initiatives by Level of Economic Development (Nallari and Griffith, 2013)

Workforce and Infrastructure

Learning Health Care System

The Learning Health Care System concept was developed as a means of averting the traditional model of health innovation: intervention development, then efficacy and effectiveness studies, followed by health technology implementation (Chambers, Feero and Khoury, 2016). The learning healthcare system instead aims to provide more efficient and lower cost means of healthcare delivery improvement via a method that gathers knowledge from many care delivery...
experiences across diverse medical practices and is engineered to promote continuous improvement. Here, health systems have the opportunity to sidestep various existing complexities, data interpretation challenges, and other quality barriers in an ongoing system improvement model that (1) captures data at the clinical encounter across participating sites and (2) using those data to inform ongoing clinical and community practice.

In practice, this often manifests as a system linked by a common EHR and shared databases, in which near real-time findings of precision medicine initiatives can be applied in clinical practice. Implementation science supports this system by providing evidence-based strategies (e.g. system-change interventions, training, supervision, quality monitoring tools) for the purpose of integrating genomics and other precision medicine interventions into system practice (Pritchard et al., 2017). The learning health care system concept is particularly beneficial for LMICs given that the ability to learn is less constrained by available fiscal space - notably the combination of learning health systems with open innovation may enable early stratified care delivery in disease areas traditionally requiring higher investment.

**Case study - American Society of Clinical Oncology (ASCO) CancerlinQ Database:** The only non-profit, physician-led big data analytics platform for oncology in the United States, the CancerlinQ platform formalizes the learning health care system across its member network, spanning 100+ oncology practices, by aggregating the ~1.5 million patient records from contributing member EHRs into the de-identified CancerlinQ database. CancerlinQ then acts as both an academic and research database in which participating physicians can utilize the data to inform clinical decisions and conduct further research. The CancerlinQ network consists of providers across the cancer care continuum (large institutions, community practices, safety net hospitals, and academic medical centers) and enables members to both (1)
utilize insights from one of the largest, oncology database for targeted care delivery and (2) contribute to this larger pool of knowledge with data from their local EHR system.

Foundational Health Systems Strengthening

The discussion of precision medicine innovation cannot occur without broader consideration of the country’s overall health systems development. It must be restated that many precision medicine approaches are unproductive without accompanied actionable decision-making steps (“effectors”). These effectors enable the follow-through of precision approaches and can be illustrated through foundational health system factors such as having sufficient targeted therapy drug supply or providers with proper technical education to interpret genomic risk profiles. Further progress in general health systems strengthening is necessary for the productive utilization of precision medicine tools, such as diagnostics and sequencers, that provide actionable information for personalized patient treatment.

Readiness for precision medicine innovation may greatly vary across the country’s entire range of health systems and is often linked to the available resources present. Maturity of this capability aligns with the progress towards Sustainable Development Goal 3: Good Health and Well-Being from the United Nations. The UN has defined 28 indicators as metrics for the 13 targets of SDG3, many of which are critical for precision medicine innovation. Notably, some of these indicators include “health worker density,” “coverage of essential health services,” “development assistance to medical research & basic healthcare” and “availability of essential medicines.”

Early adoption of precision medicine innovations may manifest as a result of health system strengthening and fundamental population health use cases (often termed “precision public
health”). These activities may include family health history considerations, cascade screening techniques, and national health surveillance programmes in the form of patient registries. There is a need for governments to support locally relevant initiatives - e.g. understanding population-relevant genomic data - that present early steps for precision medicine alongside complementary health systems growth and resourcing. Financing health systems strengthening for precision medicine is further discussed in the “Blended Finance and The Diagonal Approach” section under the Innovation Financing topic. It is only as health systems mature, thereby establishing the foundational “effectors,” that further technology- or resource-dependent precision medicine use cases emerge in standard of care.

**Case study - Genome India Project (GIP):** In early 2020, the Indian Department of Biotechnology (DBT) launched the Genome India Project (GIP) with the goal to build an “indian reference genome” through sequencing 10,000 citizens across India. With a Rs 238 crore budget (USD$325,000), the DBT centrally coordinates between the Centre for Brain Research at Bengaluru-based Indian Institute of Science and 20 institutions that each collect patient samples and conduct its own research. In clinical settings, DBT has further started to establish diagnostic laboratories for genetic testing (subsequently added to coordinated biobanking efforts) and training programs for personnel to set up more such laboratories. Through GIP, the DBT aims to unearth India’s genetic diversity across its various sub-populations while searching for novel genomic biomarkers predictive of key priority diseases for clinical application.
Economic Development

The innovation policy mix aims to establish the systems stability for the potential entry of precision medicine approaches within the country. These foundational instruments reinforce the management, organisational and production capabilities of an economy and strengthen the complementary public goods and services necessary to an innovation ecosystem. While this section focuses on foundational economic development more applicable to LMIC settings, persistent market failures of precision medicine in higher-income countries also warrants novel policy considerations.

One approach to benchmarking readiness is via progression on existing indices (e.g. ease of doing business index, corruption perceptions index) that measure broader socio-political and business environment. This may complement specific economic development considerations for precision medicine: (1) capacity building, (2) highly qualified personnel (HQP) and (3) south-south collaborations. The first metric pertains to the investment in innovation infrastructure - e.g. biobank facilities, laboratories, research equipment - and advisory services - e.g. knowledge transfer groups, precision medicine policy boards governing its ethic, legal, and social implications (ELSI). On the second, there remains a shortage of HQP trained in precision medicine techniques and the use of genomic technologies. Workforce training - e.g. researchers, engineers, policymakers and entrepreneurs alike - remains one of the largest gaps in LMICs. Human resource development plans are highly encouraged policies towards precision medicine adoption; Health Education England (HEE) is a strong case study of how their National Health Service accommodated precision medicine techniques via reskilling their primary health care. Lastly, as the majority of precision medicine partnerships are with developed countries,
promoting south-south collaborations (e.g. H3Africa) has strong potential to foster locally-relevant and equitable developments in precision medicine.

LMICs have a unique opportunity to build advanced initiatives from the start, leveraging best practices and lessons learned from other countries implementing precision medicine. Proactive policy development in key areas such as genomic data sharing or workforce training strategies are highly relevant, and should be considered in tandem with economic growth for maximum impact (as opposed to retroactively delaying precision medicine policy development).

**Case Study - Structural Genomics Consortium (SGC)**: A charitable open science public–private partnership started in 2003 with the core mandate to determine 3D structures of human proteins and parasite proteins that are of biomedical importance (e.g. potential drug targets). Recognized as one of the earliest and largest pioneers of open science, the SGC releases structural genomics data into the public domain through the Protein Data Bank annually. The pre-competitive principles adopted by the SGC translates into other key open science conditions imposed on its researchers and collaborators via a trust agreement that prohibits the patenting of research outputs using SGC data, and stipulates fast dissemination and pre-publication sharing of its structural and chemical biology outputs. The current collaborators to SGC include 17 organizations and includes pharmaceutical companies, governments, academic institutions and NGOs.

Absorptive Capacity

Incremental innovation remains the most prevalent form of precision medicine development; radical or transformational advances in genomic technology are isolated and the majority of
advancements are characterized by a growing maturity of health systems care delivery and the
growth of R&D innovation projects. As such, the absorptive capacity of a country’s innovation
ecosystem - their ability to transfer and adapt precision medicine technologies for use in a local
context - acts as a growth indicator. Global cooperation and net import/export activity aims to
support innovation in low- and high-resourced countries alike (Cirera and Maloney, 2017).

Incipient precision medicine innovation ecosystems may be far from the technological frontier.
Given the characterization as net importers of innovation, LMICs can prioritize building
absorptive capacity for novel precision medicine approaches. Many of the steps to address this
gap are similar to those posited for overall economic development (building innovation
infrastructure, knowledge transfer groups, formalized ESLI/innovation review bodies). By
prioritizing absorptive capacity, LMICs are able to both capture benefits of net innovation
imports of precision medicine technology while building internal country capacity in knowledge
transfer, skill development and genomics education training. In tandem with building
foundational elements of economic activity, strengthening the absorptive capacity of firms acts
to establish the incipient precision medicine innovation ecosystem in LMICs.

More developed countries may present a shift in its innovation ecosystem from absorption- to
production-driven. When technological infrastructure and higher research quality are more
available alongside corresponding literate personnel, countries can begin to shift roles from a
primary net importer of innovation to also an export participant. In investing further in R&D
capabilities and other innovation areas described in this paper, such countries observe growing
partnership models, financing capabilities and governance frameworks that enable growing
sophistication of innovation inputs.
Case study - Israel Precision Medicine Partnership (IPMP): As a joint initiative created by (1) the Planning and Budgeting Committee (VATAT) intermediary between the Israeli Government and high education institutions, (2) Digital Israel and (3) the Israeli Science Foundation, the IPMP acts as a grant-making framework to promote the growth of Precision Medicine in Israel. With an overall budget of 210M NIS (USD$ 62M), IPMP funds many domestic research and long-term infrastructure initiatives with high potential for expanding the country’s use of precision medicine approaches. Beyond acting as a large funding source for various innovation projects, IPMP acts on core principles of biomedical networking, data sharing, and multidisciplinary research to promote a culture of access and collaboration (e.g. local researchers and clinicians in universities, hospitals and healthcare organizations) in its ecosystem.
Gaps and Future Research Areas

Numerous opportunities for future research on relevant capabilities of the precision medicine innovation ecosystem remain, given various implementation gaps (Sammut, 2020). By way of capturing insights from this white paper, the following are offered:

- **Incentivizing private financing activity** - Market incentive gaps in precision medicine pose high investment risks for private sector actors. Current reliance on public funding and philanthropy dollars may be insufficient in LMICs and new cross-cutting “diagonal approach” financing models are encouraged to catalyze private investment activity.

- **Expanding beyond IP policy** - Clear IP policy acts as a market incentive for innovators, but may be insufficient in LMICs alone. There is a need for novel pull incentives from government and financiers alike to fill the IP incentive gap. Benefit sharing and socially responsible licensing approaches may also help close the IP equity gap in international genomic project participation.

- **Value Based Care Partnership Models** - Further incentive alignment is encouraged between payor, provider, and producer stakeholders to form appropriate performance based contracts and evidence-based modeling studies that share risk and recognize value of precision medicine.

- **Measuring and Pricing Innovation** - Gaps in monitoring and evaluation forms a lack of data on precision medicine value-add, and existing value-oriented pricing models may have connotations of unaffordability, particularly in less resourced health systems.

- **Translating novel operating and behavioral models into LMICs** - Novel operating models and behavioral innovations such as open science initiatives and the learning
health care system concept are currently limited to developed countries. There is further room to translate such initiatives into LMICs.

- **Workforce and Infrastructure gaps** - Precision medicine adoption in LMICs requires foundational health system capabilities and qualified personnel that may currently be limited. Further resourcing is needed to address this challenge and will require innovative financing and partnership solutions.

- **Innovation Monitoring and Surveillance** - There is opportunity to establish innovation surveillance and measurement entities for the ongoing landscape analysis of the evolution and diffusion of precision medicine. As the precision medicine innovation ecosystem evolves, regular monitoring generates the evidence base and case studies for further adoption and implementation.

- **Strengthening South-South Collaborations** - Further research is needed on the potential of regional innovation hubs and large scale collaborations in LMICs (e.g. H3Africa) to cover large precision medicine catchment areas prior to achieving the critical mass enabling individual health system adoption of precision medicine.

- **Establishing Optimal Partnership Structures** - Clear groundwork into the assets and liabilities of various collaboration models between North-South countries. Further work is encouraged to establish optimal alliance structures between laboratories, funding agencies, and other respective stakeholders.

- **Understanding the Precision Medicine Theory of Change** - Research is encouraged to understand how thought leadership consensus is built for novel precision medicine innovations, and how it is subsequently promulgated across professionals throughout the health system and wider country for adoption.
Conclusion

Using the readiness frameworks to balance the promise and opportunities of precision medicine with the real-world practicalities of implementing such initiatives provides a path forward for countries. Leapfrogging is possible. The potential for international and national-level frameworks informed by this white paper and early pilot projects can support the development of standards and guidelines that will inform policies and regulations. It is the hope of the author that such work supports the evaluation of precision medicine innovation ecosystems in partner Ministries of Health.
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