ASM POSITION PAPER ON

PRECISION MEDICINE INITIATIVE IN MALAYSIA

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2020

POSITION PAPER ON PRECISION MEDICINE INITIATIVE IN MALAYSIA

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Realising the need to understand the current landscape and challenges in Malaysia, as well as the feasibility to mainstream precision medicine in revolutionising the present healthcare delivery system the Academy of Sciences Malaysia embarked on a study to address the objectives.

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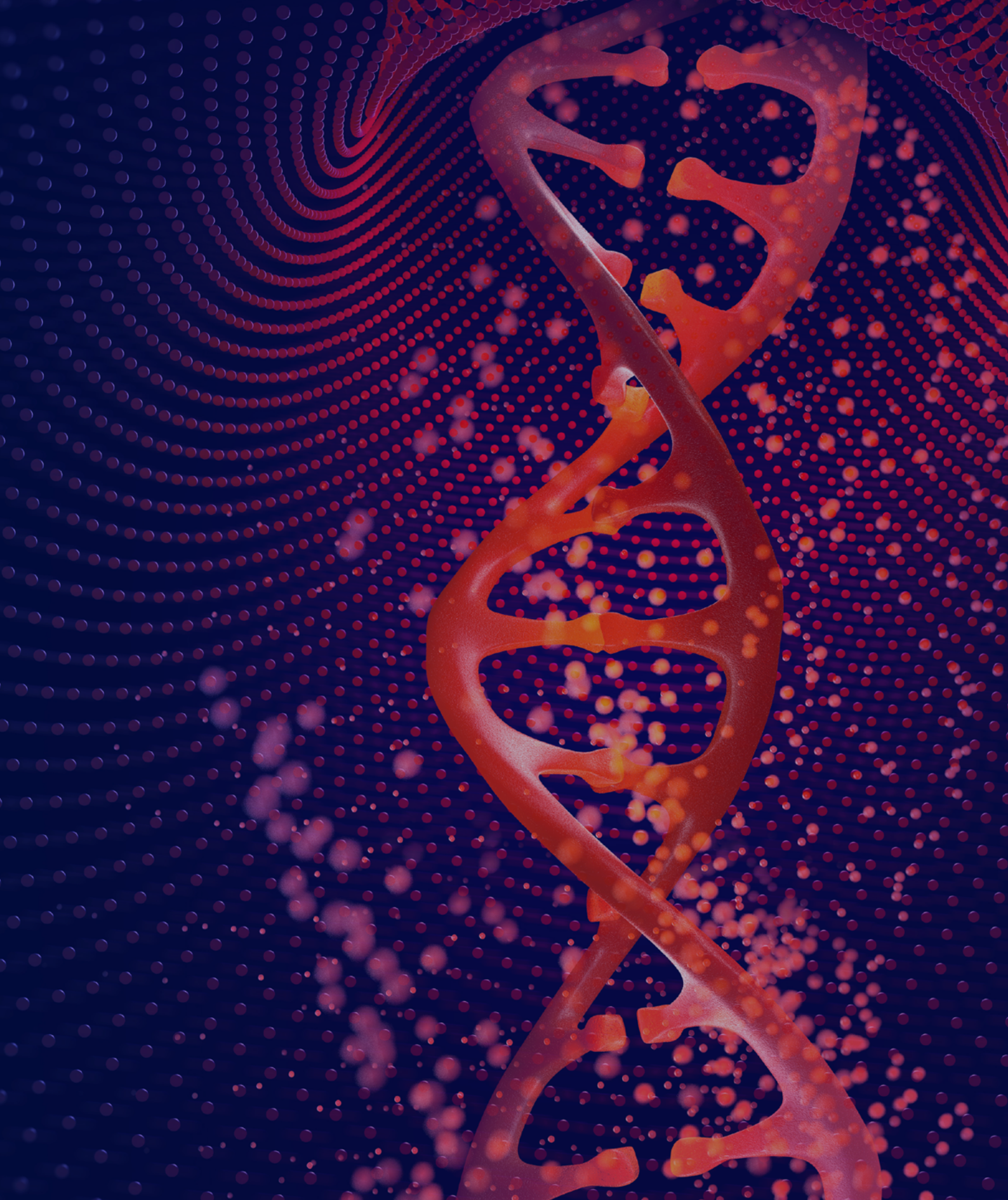
CONTENT



PRECISION MEDICINE: BACKGROUND

Health care has changed over the years. This is further reflected in the steady decline of mortality rates caused by infectious and non-communicable diseases (NCDs) globally. Reduction in such disease burden may be positively attributed to the costs of public health and individual health care. According to World Health Organisation (WHO), the global average life expectancy today is about 70 years. Improved sanitary conditions, advances in science and technology, introduction of preventive medicine (e.g. vaccination campaigns, etc.), new therapies and drugs, better imaging methods, increased public awareness, wider access to healthcare, and promotion of healthy lifestyles have collectively contributed to the prolonged life expectancy.

In line with the longer lifespan enjoyed by today's population, one may note that healthcare providers are allocating more budget for treating chronic diseases, such as cancer, diabetes, cardiovascular diseases, and degenerative diseases. Besides, increasing global population and availability of diagnostic improvements have led to these professionals witnessing more cases of rare diseases, including those rooted in genetic anomalies. Similarly, certain infectious diseases are also re-emerging in the society, namely dengue and tuberculosis, among others. The prevalence of NCDs is rising, while the current health promotion approaches do not seem to be sufficiently effective. Therefore, the clear need to improve early detection of such diseases especially cancers, enhance the outcomes of treatment (e.g. reducing the side-effects), and upgrade relevant preventive approaches cannot be denied.

For many decades, doctors have been treating patients afflicted by the same disease by using identical approach, drugs, and dose. The advances in understanding disease manifestations and pathways involved have thus underlined the transition from traditional reactive medicine based on symptoms, diagnosis, and treatment towards a system that targets a disease pre-symptomatically. The differences between the outcomes of treatments, especially recovery time, survival rate, and adverse effects across individual patients are strongly suggestive of the need to consider genetic variants, which are dissimilar between one another. Concurrently, today's practice of one-size-fits-all is no longer valid for many diseases, wherein healthcare is rapidly moving towards precision medicine (*Figure 1*).

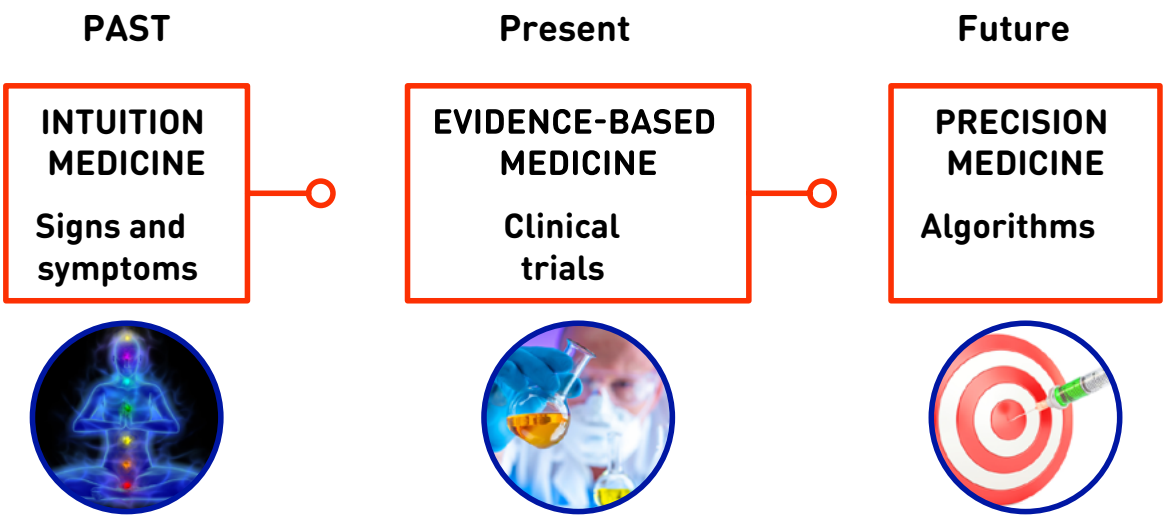


Figure 1: *The Evolution of Medicine (Source: Redrawn from Gamiero et al., 2018)*

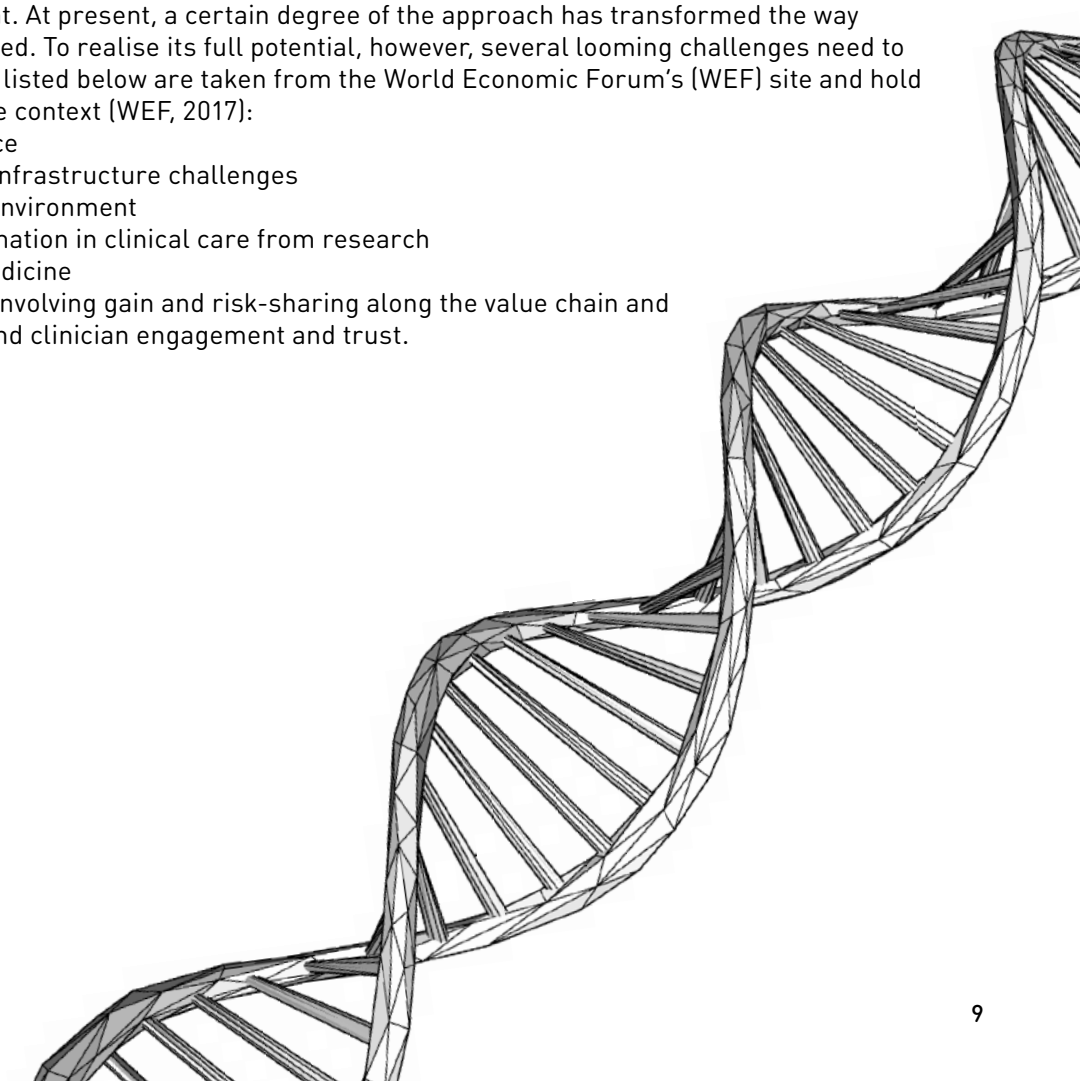
DEFINING PRECISION MEDICINE

In general, Precision Medicine is an emerging but growing approach for accurate disease treatment and prevention strategies. *It is an approach geared towards disease prevention, diagnosis, and treatment; it seeks to maximise effectiveness by considering individual variability in genes and across environments and lifestyles. Furthermore, it strives for redefining the current understanding of disease onset and progression, treatment response, and health outcomes. This can be achieved through the combined analysis of biological, environmental, and behavioural factors that contribute to health and disease. Accordingly, such understanding may lead to more rational disease prevention strategies and accurate diagnoses, better treatment selection, and development of novel therapies* (National Institutes of Health, USA, 2018).

To this end, the future lies in in-depth scrutiny of an individual's personal biological characteristics including the genome profile and by using a diverse range of technologies. Advancements in areas such as genomics, pharmacogenomics, various biomarker panels, medical imaging, bioinformatics, molecular diagnostics, and big data analytics may serve to elevate medicine further to the precision level. Here, the ultimate aim is to achieve an individualised or tailored treatment approach for an individual or a group of individuals (*Figure 2*) for the best possible outcome whilst circumventing any side effects. For example, a patient's cancer biopsy can be fully sequenced at diagnosis and a whole-genome profile is obtained to allow for a more precise diagnosis, identify actionable mutations for targeted therapies, and prognostication.

Moreover, precision medicine is seen to provide high-value healthcare by improving its outcomes while decreasing the cost of treatment. At present, a certain degree of the approach has transformed the way some types of cancers are treated. To realise its full potential, however, several looming challenges need to be resolved first. The obstacles listed below are taken from the World Economic Forum's (WEF) site and hold true in the Malaysian healthcare context (WEF, 2017):

- generating enough evidence
- tackling data sharing and infrastructure challenges
- reshaping the regulatory environment
- adoption of genomic information in clinical care from research
- economics of precision medicine
- creating payment models involving gain and risk-sharing along the value chain and attaining greater patient and clinician engagement and trust.



A 50-YEAR-OLD WOMAN WITH TYPE 2 DIABETES PARTICIPATES IN A PRECISION MEDICINE INITIATIVE

+2 YEARS

- Sample of DNA, health information sent for sequencing & analysis

- Changes diet, medicine dose schedule

- Researchers track glucose levels via chip that sends wireless signals to her wearables, and alert researchers

+5 YEARS

- News on new drug based upon improved molecular understanding

A GLIMPSE OF SUCCESS

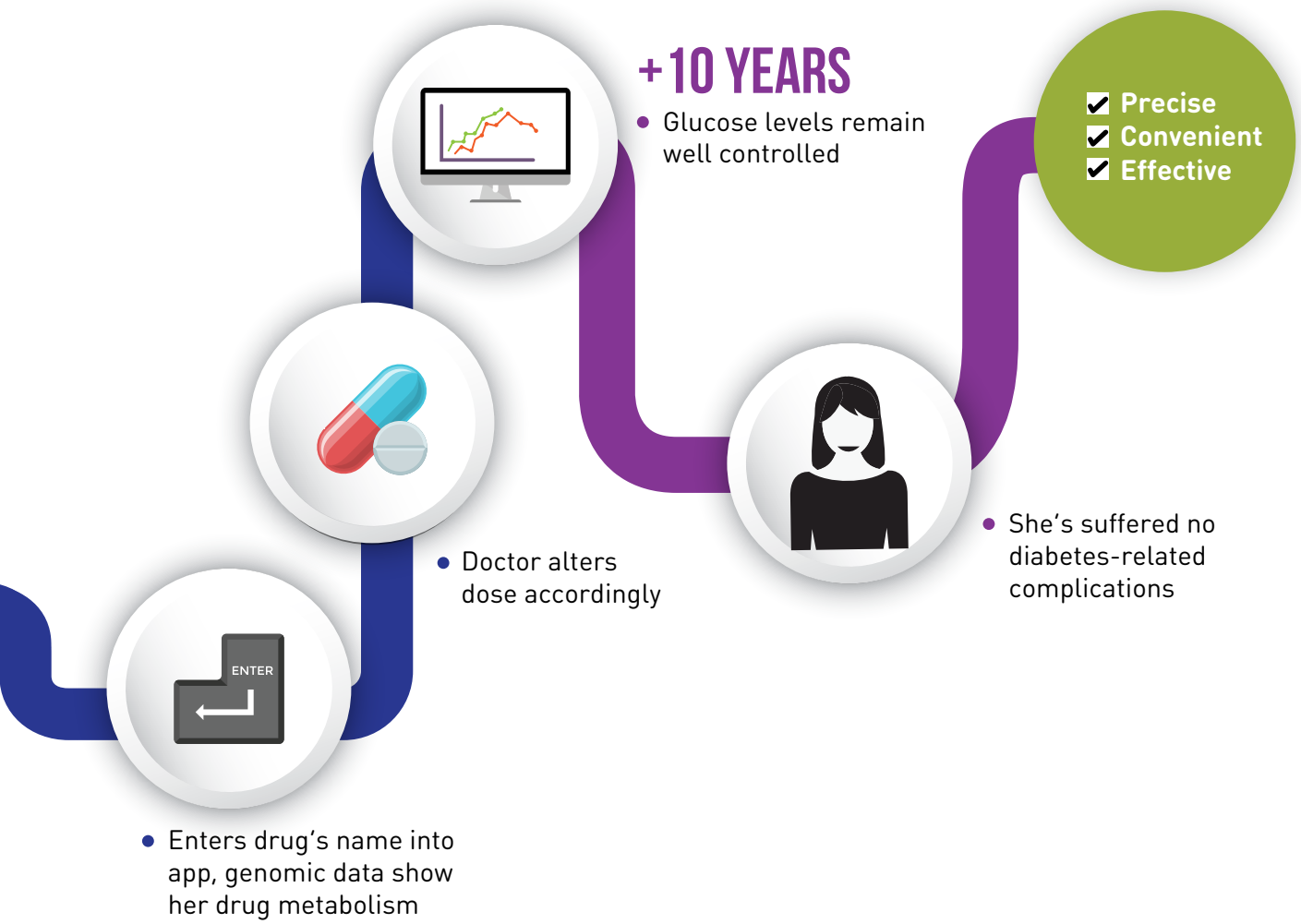


Figure 2: *An illustration of a successful Precision Medicine practice*
Source: *Illustrated from Vision for the Cohort and Precision Medicine Initiative - Dr Francis Collins. 2015.*
YouTube channel: *All of Us Program Workshop https://www.youtube.com/watch?v=0bBYk0MOuDM&t=346s <accessed 21.11.2019>*

THE JOURNEY OF PRECISION MEDICINE IN MALAYSIA

As the country embraces the Fourth Industrial Revolution (IR4.0), the essence and functionality of Healthcare 4.0 should not be overlooked as well. The latter term and its use are particularly inspired by the well-known industrial concept leveraging the elements of personalisation and virtualisation across different industrial domains (i.e. Industry 4.0). In fact, Healthcare 4.0 extends the concept of Industry 4.0 in a scenario wherein patients and healthcare professionals are extensively embedded into the organisation, methodology, and technology. A patient-oriented system underpinned by the concept of data sharing amongst various industry players can thus lead to improved healthcare delivery (CBMS, 2019).

The adoption of precision medicine in Malaysia remains limited and has yet to reach the mainstream status of healthcare in a significantly all-encompassing approach. To date, any initiatives that apply genomics, transcriptomics, methylomics, proteomics, and metabolomics approaches are funded via research grants. Therefore, data generated through these initiatives are currently retained at the institutional level; the absence of a national database that can be harnessed and leveraged upon by Malaysian researchers and clinicians is widely felt.

In 2018, the Ministry of Health Malaysia (MOH) designated six focus areas in embracing Healthcare 4.0 for the future of healthcare in the country:

i. Quality and safety of care
ii. Illness to wellness
iii. Healthcare back to communities, families, and individuals
iv. Inclusive innovations and smart solutions
v. Collaborative partnerships
vi. Public-private integration

Accordingly, MOH has also planned for precision medicine implementation in three phases, which are:

i. Data infrastructure and genomic sequencing
ii. Data analytics and integration
iii. Personalised health and wellness solutions

To expedite the act of mainstreaming the precision medicine initiative, the Task Force has attempted to paint the present landscape based upon pockets of activities carried out across the country. Information gathering was conducted via literature review, personal input from task force members themselves, web searches, and target surveys accordingly. The three main initiatives are as described below, while Figure 3 depicts the players in the ecosystem. Meanwhile, initiatives by other countries are listed in the Appendix (A.2). The survey results obtained show that most research has been done in the area of genomics, whereas services offered are predominantly in molecular diagnostics.

a. UNIVERSITI KEBANGSAAN MALAYSIA - UKM Medical Molecular Biology Institute (UMBI) - The Malaysian Cohort Study

- The study is one of the earliest projects on precision medicine and biobanking in Malaysia. It was approved in 2005 by the Malaysian government to study and determine the roles and interaction of genes, environment, and lifestyle in various diseases through a large-scale population cohort study. The aim is to recruit 100,000 individuals and follow them prospectively in order to capture as much data possible whilst collecting and storing biospecimens for research.
- It was a top-down project approved by the cabinet that ensured sustained funding from 2005–2013. Currently, the project is funded by the Ministry of Higher Education (MOHE).
- The population-based cohort study recruited 106,527 individuals aged between 35–70 years throughout a period of 2007-2012. Participants were engaged for a follow-up every five-year interval. A rich database of information and a Biobank are thus established, both of which have become national resources for research and data.
- UMBI has also embarked on whole-genome sequencing of colorectal cancers, whole-exome sequencing of individuals with hypercholesterolaemia, and genome-wide association study of Type 2 diabetes.

b. UNIVERSITI SAINS MALAYSIA - Malaysian Node of the Human Variome Project (MyHVP) database

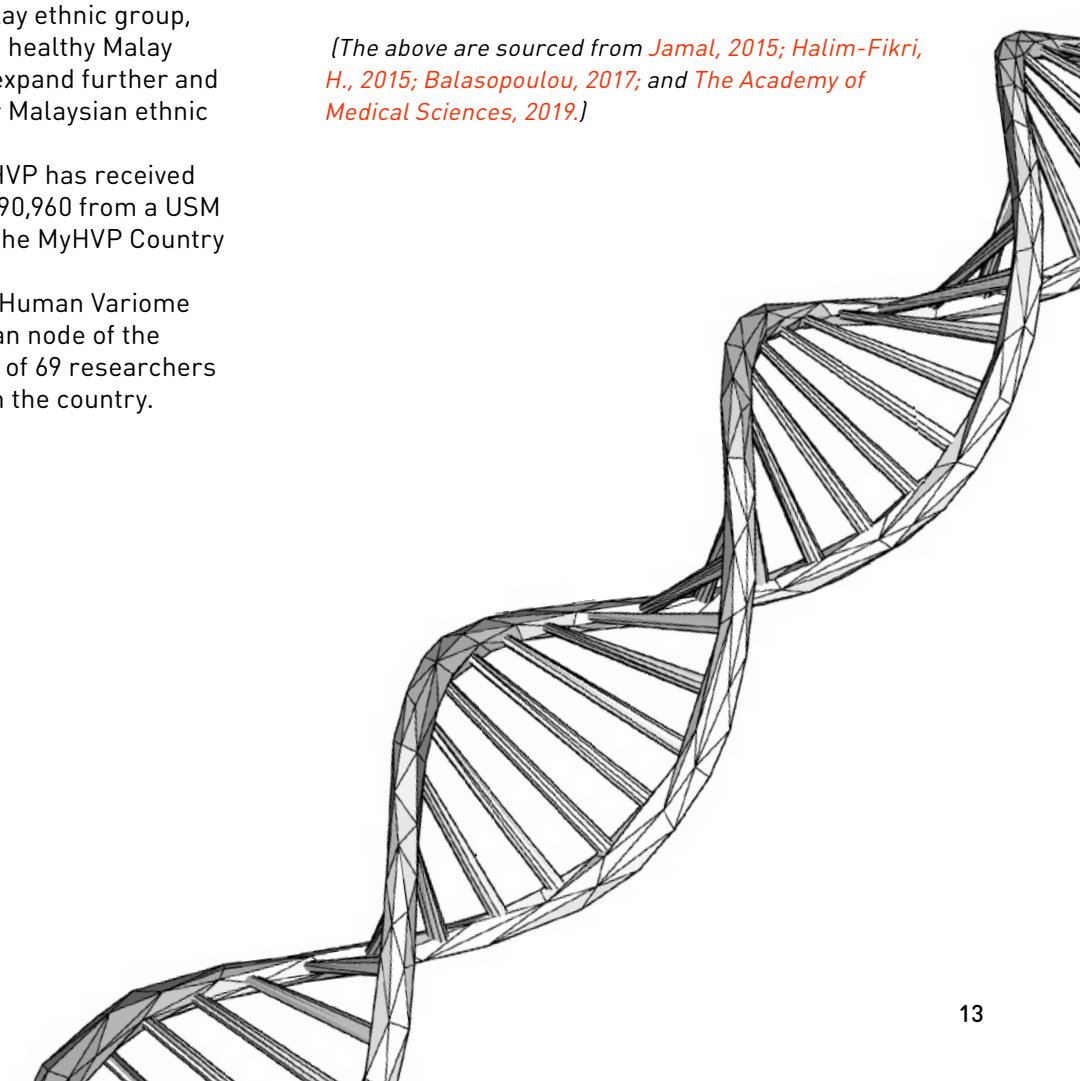
- The goal of the project is to create a genome single nucleotide polymorphism (SNP) database of the major ethnic groups in Malaysia, which will include common diseases such as thalassaemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency, tuberculosis, and Helicobacter pylori infection. Data on the susceptibility of diseases amongst the respective ethnic population will be made available accordingly.
- A specialised database has been developed to store and manage data of genetic variants and the corresponding phenotypes associated with health and diseases encountered by different Malaysian ethnic groups.
- At present, MyHVP database provides information on genetic variations and mutations found in the Malay ethnic group, which is obtained from 103 healthy Malay individuals. It is poised to expand further and detail information on other Malaysian ethnic groups in the near future.
- Since November 2012, MyHVP has received funding amounting to RM790,960 from a USM APEX grant for setting up the MyHVP Country Node.
- Under the umbrella of the Human Variome Project (HVP), the Malaysian node of the international HVP consists of 69 researchers from various institutions in the country.

c. UNIVERSITI MALAYA – GEMS LAB

- GEMS@UM is a public-private partnership between Universiti Malaya and Pathomics Health in Singapore. In particular, the university is tasked with providing space, professional expertise, and access to patients, while Pathomics Health is equipped with funding and precision medicine capability.

- This approach allows the capacity building of scientists, thus also contributing to enhanced research efforts as the partnership enables scientists to access Beijing Genomics Institute and Tempus, a company based in the United States of America (USA). Both parties work with tests for targeted therapy with a high chance of pharma investment; ultimately, this allows patients access to precision medicine via a low- or no-cost route.

(The above are sourced from Jamal, 2015; Halim-Fikri, H., 2015; Balasopoulou, 2017; and The Academy of Medical Sciences, 2019.)



PRECISION MEDICINE IN MALAYSIA – THE PRESENT ECOSYSTEM

Data and registry
- The Malaysian Cohort (UMBI, UKM)
- Malaysian Human Variome Database (USM)
- Thalassemia Registry (IMR, MOH)
- Nasopharyngeal Cancer Database (IMR, MOH)
- Orang Asli Genome (iPROMISE-UiTM)
- Breast Cancer Database [Cancer Research Malaysia (CRM)]

Biobank
- The Malaysian Cohort Biobank (UMBI, UKM) - ~ 120,000 individuals – blood and urine samples
- CRM Malaysian Breast Cancer Cohort (CRM) - ~8,000 Germline DNA blood samples
- UM Oral Cancer Research – 5,299 tumour samples
- UMBI Cancer Biobank - ~3,500 samples and 702 sequenced
- Thalassemia DNA Biobank (IMR) - ~2,000 samples
- CRM Malaysian Breast Cancer Cohort – 1,025 breast tumour samples
- iPROMISE Orang Asli Genome Variation– 110 blood samples – whole genome sequenced

Universities offering Master of Health/Medical Ethics:
- Universiti Malaya (UM)
- Universiti Teknologi MARA (UiTM)

University offering Master of Genetic Counselling:
Universiti Kebangsaan Malaysia (UKM)

University offering Master of Human Genetics and Masters of Pathology (Medical Genetics) :
Universiti Sains Malaysia (USM)

Number of Genetic Counsellors in Malaysia:
5 (certified only 2)

Number of Medical Geneticist:
14

Companies offering direct to consumer genetic testing (based in Malaysia)
- Advanx Health
- DNA Lab
- GenomixLAB
- Easy DNA
- Gnosis Laboratory
- MyDNA Prenetics
- International Biosciences
- Celebre Pro Medic Sdn Bhd

Research institutes and centres with a focus on genomics
- Malaysia Genome Institute (MGI) (MOSTI)
- UKM Medical Molecular Biology Institute (UMBI)
- Institute for Research in Molecular Medicine (INFORMM) (USM)
- Integrative Pharmacogenomics Institute (iPROMISE) (UiTM)
- Human Genome Centre (USM)

Healthcare related entities that offer genome specific services
- Institute of Medical Research (IMR)
- Institute for Research in Molecular Medicine (INFORMM) (USM)
- UKM Medical Molecular Biology Institute (UMBI)
- GEMS@UM
- Cancer Research Malaysia (CRM)
- Malaysian Genomics Resource Centre (MGRC)
- Sengenics
- DNA LAB
- Beacon Hospital
- Subang Jaya Medical Centre
- Gribbles Technology
- Oncode Scientific
- NHK Biosciences Solution
- Neogenix
- BIO3 Scientific Sdn Bhd
- Quantum Diagnostics Sdn Bhd
- TreeCode

**List is non-exhaustive*

Source: *Compiled by ASM @ 2020 based on respective websites, expert engagements, official e-mail communications and Chong (2018)*

Figure 3: *Mapping of efforts and players in the field of precision medicine in Malaysia*

GOVERNANCE & GENETIC DATA CONFIDENTIALITY

The practice of precision medicine in general will result in the acquisition and storage of common personal information and health data, as well as information on the environment, lifestyle, and genetic.

Accordingly, the genetic data of an individual is much more complex than that of biochemical or haematological information such as renal profile or blood count. This is attributable to the uniqueness of one's genome profile, which contains information on genetic variants that confer different risk profiles across individuals. Besides, some of these variants may be of unknown significance at present, but will be known in the future and utilised for further risk profiling, prevention, and screening of certain diseases.

A major concern highlighted regarding personal genetic data is the potential of its exploitation and wrong usage to deprive an individual of health insurance coverage, as well as discriminate against fair employment opportunities should it be made publicly available. Privacy and confidentiality issues are critical in the application of precision medicine; hence, governance of such data needs to be addressed and comprehensively defined.

There are existing laws in Malaysia that can be used to regulate Precision Medicine. However, most of them are rather generic and do not address the use and applicability of genome profiles in a more detailed and specific manner. Certain issues such as genetic discrimination and personnel authorised to order or perform genetic testing are not covered by them. Some examples of the existing laws are:

i. Medical Act 1971 (Act 50) and related medical regulations
ii. Human Tissue Act 1974
iii. Biosafety Act 2007 (Act 678)
iv. DNA Identification Act 2009 (Act 699)
v. The Financial Services Act 2013 (Act 758)
vi. Personal Data Protection Act 2010 (Act 709)

Furthermore, the content of several abovementioned laws is outdated and requires revision, such as the Human Tissue Act 1974.

Meanwhile, there is no existing law present to govern biobanks and genetic databases, including the use of leftover specimens and archived tissues for future analysis. Similarly, Financial Services Act 2013 should address the issue of genetic discrimination, especially in ensuring that insurance providers do not deny coverage for individuals who are in need.

Below are examples of genetic databases and biobanks available, as well as the respective governing laws:

i. Icelandic Health Sector Database – Health Sector Database Bill 1998, Biobank Acts (2000) – dealing with storage of human tissue
ii. UK National Biobank – UK Biobank/Database Human Tissue Act 2004
iii. Estonian Gene Bank – Human Genes Research Act 2000

In the ecosystem of precision medicine, genetic data linked to diagnosis and prognostication will be used as and when necessary and stored in a data centre or data warehouse. Therefore, policies on data security, confidentiality, and access should be put in place, while the databank security should be ascertained to guarantee privacy and confidentiality. Besides, clarification regarding the rights of different parties and individuals (e.g. researchers, industry players, government, law enforcers, or third parties) to access the data is highly necessary. Additionally, databank security is paramount to avoid exploitation and discrimination, especially by health insurance or employers.

Henceforth, all consenting parties should be informed of how their genetic data will be used, stored, and retrieved for future applications or research. Furthermore, their rights to access the data or have theirs removed should be made known to them in detail. The privacy framework that safeguards their personal identifiers (i.e. name and identity card number) and genetic or biological information should also be extensively explained to each participant or patient. Unfortunately, laws governing these procedures are currently not in place within the Malaysian ecosystem.

ETHICS, LEGAL, AND SOCIAL ISSUES

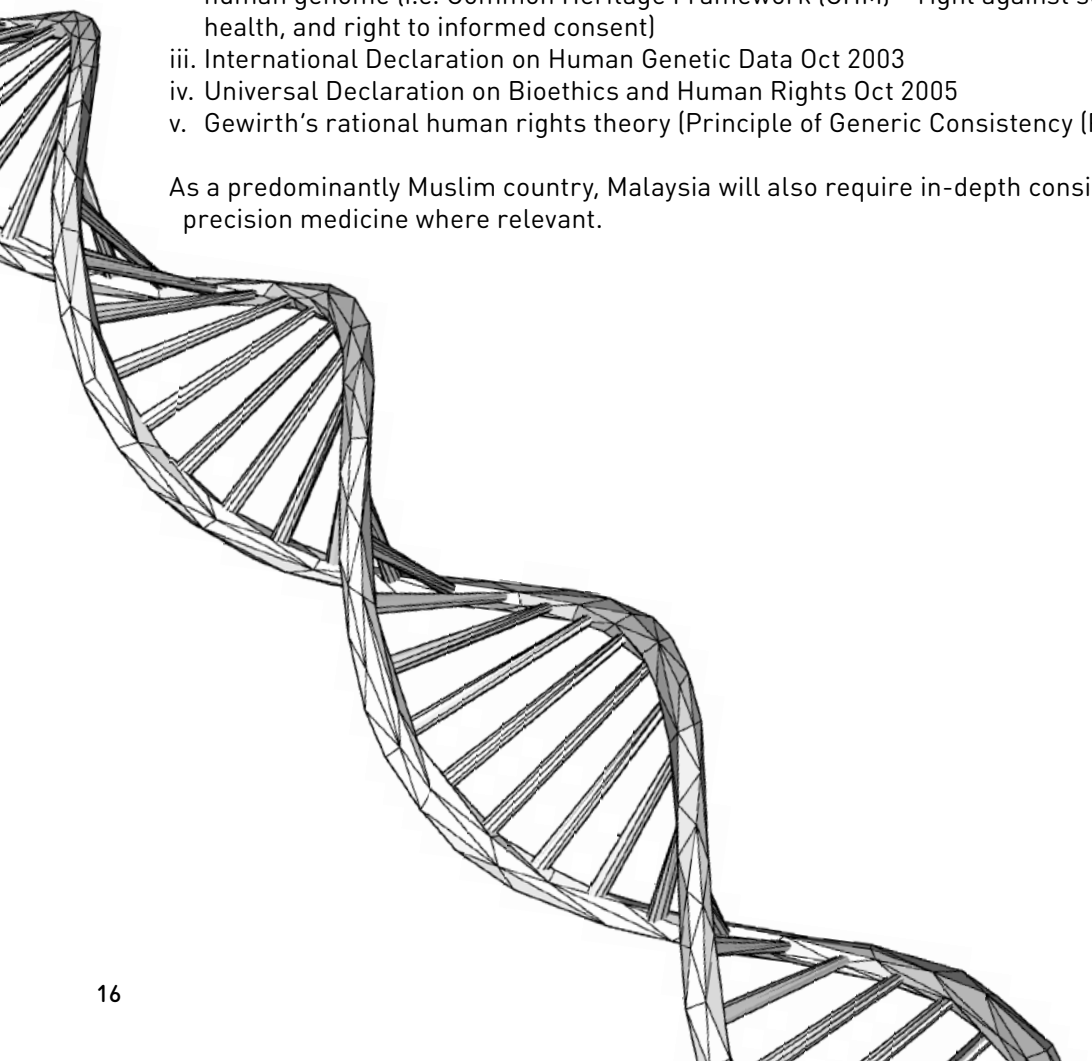
Ethics is a major concern in Precision Medicine, where the big question remains: with the availability of genetic data and information, is Malaysia ready for the upcoming privacy disclosure and other related ethical issues? Besides, can existing laws monitor and coordinate areas such as Precision Medicine, which are dynamically evolving? Are the pertinent laws of Malaysia able to stay abreast with the fast-paced advancement in any related technologies?

This underlines the utmost need for the country to formulate relevant legal framework, policies, and principles in addressing concerns highlighted regarding the use of genetic data and personal insurance. Examples of existing frameworks in other countries include USA-based Genetic Information Non-Discrimination Act (GINA), Code of Medical Ethics of the American Medical Association (AMA), and Australian Insurance Act 1984. Meanwhile, insurance companies also adopt voluntary policies such as voluntary moratorium in the United Kingdom (UK), which will not use genetic information for insurance policies under a certain value following an agreement sanctioned by the court.

For Malaysia to create its own guidelines on medical ethics and laws, the country will need to look at existing international guidelines, codes, and Acts. This will allow data sharing to occur in an equitable manner. Some related international guidelines or codes include:

i. CHM – Convention on Biological Diversity (1992)
ii. Universal Declaration on the Human Genome and Human Rights Nov 1997 – first Instrument on the human genome (i.e. Common Heritage Framework (CHM) – right against self-discrimination, right to health, and right to informed consent)
iii. International Declaration on Human Genetic Data Oct 2003
iv. Universal Declaration on Bioethics and Human Rights Oct 2005
v. Gewirth's rational human rights theory (Principle of Generic Consistency (PGC)

As a predominantly Muslim country, Malaysia will also require in-depth consideration of religious aspects in precision medicine where relevant.



HEALTH ECONOMICS

Improving patient outcomes while factoring in the need to reduce the overall cost and/or risk is the main principle in achieving value-based healthcare. To this end, advancements in next-generation sequencing techniques and other omics-based technologies have enhanced biomarker-driven and targeted therapies. This has also resulted in the precipitous decrement of genome sequencing costs over the last 10 years (Figure 4).

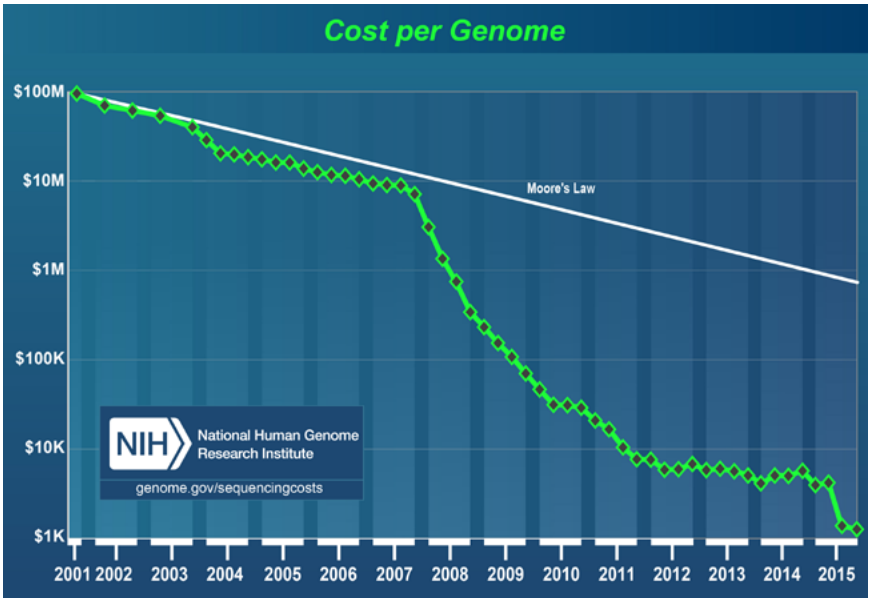


Figure 4: *Cost per genome (NIST, 2015)*

In general, precision medicine promises better outcomes for patients afflicted with certain types of cancer through targeted therapies. Furthermore, the implementation of whole-genome or whole-exome sequencing has resulted in a faster diagnosis of up to 40% for rare diseases (WEF, 2020). Moreover, the identification of pathogenic variants or mutations in respective rare diseases leads to the opportunity for developing or discovering the right treatment, possibly enabling future prenatal or pre-implantation diagnosis. Similarly, targeted sequencing of certain predisposition genes will also allow the identification of those at risk of certain diseases, which include inherited cancers such as familial breast or colorectal cancers.

The challenge, however, is to ensure the affordability, accessibility, and availability of tests that are provided by public and private laboratories alike. For cancers and rare diseases, these test results will also guide the options for targeted therapies, which are expensive and most of which are not in the list of drugs subsidised by the government. Therefore, the element of affordability remains prohibitive in some cases; for example, manufacturing targeted drugs is costly and these drugs are not subsidised (Thong et al., 2019). Furthermore, most of the precision medicine tests carried out in public institutions are limited or performed as part of research projects, hence the limiting accessibility. If they are to be made available at private laboratories, out-of-pocket payments are not reimbursable and insurance companies do not provide coverage for genetic testing. Additionally, European countries such as Holland, among others, have only allowed genetic testing to be done in public laboratories for the purpose of avoiding exploitation and misuse.

In the context of rare diseases, the economic advantage of precision medicine is sufficiently clear. Whole-genome or whole-exome sequencing could provide a definitive answer as opposed to blindly carrying out extensive tests for disease cause identification purposes. For inherited cancers, knowing the genetic mutation status will allow close monitoring and regular screening for an early detection, while an affected individual may opt for preventive surgery. For example, one may undergo mastectomy to prevent breast cancer altogether, rendering it necessary to address the ethical issues surrounding preventive mastectomy.

CASE STUDY

To clearly depict an example of precision medicine in cancer treatment, a case study on the use of trastuzumab in early breast cancer is described as follows.

Case Study: Economic Evaluation of Trastuzumab as adjuvant therapy for early Breast Cancer
(Lee and Kamaruzaman, 2016)

In Malaysia, breast cancer is the most common type recorded in females. Accordingly, this study reported that about 61% of breast cancer cases were detected in stages I and II, while approximately 11% were only identified at the point of late-stage metastatic cancer. Out of the total number, 65% were found to be oestrogen receptor (ER) positive, 57% were progesterone receptor (PR) positive, 28% were human epidermal growth factor receptor 2 (HER2) positive, and 12% were triple-negative. For HER2 positive patients, access to targeted therapy (i.e. trastuzumab) was very limited; only 19% who were eligible could be treated.

In Malaysia, trastuzumab 440mg injection has been approved by the MOH. The base case result considers 100% access to trastuzumab treatment, whereby all HER2 positive patients receive it accordingly as presented in Table 1. The mean discounted cost and Quality-Adjusted Life Years (QALY) per patient receiving chemotherapy + trastuzumab were RM 167,788.81 and 4.099, respectively. For chemotherapy alone, the mean discounted cost and QALY were RM 82,129.71 and 3.074, respectively.

Table 1: Incremental cost-effectiveness ratio (ICER) for the base case

	Total discounted cost per patient	Total discounted Quality-Adjusted Life Years (QALY) per patient	Increment. Cost	Increment. QALY	ICER
ChemoTx + Tras	RM 167,788.81	4.099*	RM 85,659.10	1.025*	**RM 83,544.59**
ChemoTx alone	RM 82,129.71	3.074*			

* QALY values used in the model were up to 5 decimal points. The maximum recommended cost-effectiveness threshold by WHO is 3 GDP per capita.

Local economic evaluation: The base case analysis indicates that 1-year adjuvant trastuzumab treatment generates a deterministic Incremental cost-effectiveness ratio (ICER) of **RM 83,544.59 per QALY gained**. Throughout the patient cohort's lifetime, marginal cost increment of RM 85,659.10 and marginal benefit of 1.025 QALYs per patient are observed when trastuzumab is added to the standard chemotherapy compared to the no-trastuzumab strategy. This result is within the suggested value of cost-effectiveness threshold by WHO, which should be between 1-3 times the value of gross domestic product (GDP) per capita.

Effectiveness: The Overall Survival (OS) significantly favoured trastuzumab-containing regimen over non-trastuzumab control group (HR 0.66; 95% CI: 0.55, 0.77, p<0.00001).

Cost-effectiveness: Systematic review of cost-effectiveness evaluation reported a wide range of ICER/QALY ranging from USD 7,676 to USD 71,491.

In brief, the economics issue here is clear. The targeted treatment is indeed relatively expensive, but it also offers benefits, such as higher cost-effectiveness and better overall survival. Therefore, the next step in the analysis is to conduct a Budget Impact Analysis (BIA), which is normally done to assess the affordability of each health system for the adoption of a new treatment regime in place of conventional treatment. The cost-saving impacts of the new treatment option (i.e. precision medicine approach) versus the conventional treatment can be clearly depicted in BIA.

Besides, insurance companies should be encouraged to include precision medicine-based testing and therapy in their package offerings. The additional costs could be recovered through savings gained as a result of better treatment outcomes, less adverse events, improved preventive approaches for many NCDs and inherited diseases, while participants are also concurrently motivated to take better care of their health. Accordingly, relevant data on the cost-effectiveness of genetic testing and targeted therapies will enable these companies to revise their existing premiums. Similarly, the government will find the information beneficial in planning for a health financing or insurance system that incorporates such aspects.

THE TASK FORCE'S PROPOSAL

The Task Force is proposing key initiatives for precision medicine. The first initiative is to embark on a medium-to-large-scale whole-genome sequencing programme similar to the 100,000 Genomes England project. To date, a limited number of whole-genome sequencing studies have been conducted in Malaysia, which are further small-scaled in nature with regard to the number of genomes. Therefore, the efforts for this goal should be upscaled; it is time for Malaysia to realise that the genetic diversity of its Orang Asli, Orang Asal, and other major ethnic groups such as Malays, Chinese and Indians is a gold mine. The country has such a rich diversity of genomic data in our population, whereby possibly a mere 0.01% is tapped into and characterised.

Furthermore, it is timely for the country to undertake the game-changing initiative on precision medicine for the future health of the nation. This is likely to benefit the patients in many ways: improve treatment responses, avoid adverse effects, provide predictive risk assessment and lifestyle modification, and offer effective preventive strategies. The following information details key areas that will benefit from precision medicine implementation (Box 1):

BOX 1

CANCERS AND OTHER NCDS: Each cancer has its own unique genetic signature. Studies have shown that anti-cancer drugs are effective for an approximate 25% of cases only, whereas 6-8% of patients given the medications will report adverse reactions (Jamal, 2017). Therefore, profiling each tumour will enable the provision of targeted and individualised treatments, whereas the voluminous genome data sourced from our own cancer patients can be implemented for prognostication (i.e. survival prediction) and early detection purposes. Whole-genome sequencing will result in the identification of actionable genetic mutations in up to 45% of cancers, thus leading to better survival. This can be translated into hundreds of millions of Ringgit saved in terms of productive life years gained from longer survival. Accordingly, key NCDs that should be included are diabetes mellitus, cardiovascular diseases, hypercholesterolaemia, stroke, and degenerative diseases.

RARE DISEASES: Rare diseases are not really rare if one is to combine all of them together. It is said that one in seven individuals of a population has a rare disease. In the European Union (EU), it is defined as a condition that affects fewer than 1 in 2000 people (Orphanet, 2020). Unfortunately, many rare diseases have gone undiagnosed as conventional methods are successful for diagnostic purposes. Besides, the cost of a diagnostic work-up for each rare disease may come up to tens of thousands of Ringgit (ask any paediatrician who sees a newborn child with an inborn error of metabolism or a physician faced with a patient with complex clinical manifestations). The use of whole-exome sequencing (currently valued at RM3,000) or whole-genome sequencing (currently valued at RM7,000) may resolve the diagnosis up to 40% of rare diseases.

PATHOGENS: Malaysia is rich in diverse pathogens, especially in the cases of tropical diseases such as dengue, tuberculosis, malaria, filaria, typhoid, and leptospirosis. In particular, certain pathogens are highly problematic in the hospital setting, including Methicillin Resistant Staphylococcus aureus (MRSA), Candida, and Aspergillus, as well as nosocomial pathogens. Meanwhile, others can be linked to cancers such as Hepatitis B (HBV), human papillomavirus (HPV), and H. pylori. Unfortunately, the molecular epidemiology for many of these pathogens are not extensively known locally. Publications of local researchers have shown that they have unique strains, which can be both strategic and rich as a source for research. Additionally, an individual's microbiome can influence precision medicine through their immune response. Molecular characterisation of these pathogens and microbiota together with the respective phenotypic features, including the response and resistance to treatment, will hugely impact future prevention strategies and the development of new diagnostic kits and therapies.

The immediate outcome of a large-scale whole-genome sequencing programme is the formation of a National Genome Database (similar to the National Center for Biotechnology Information or NCBI in the USA), whiwch has emerged as a valuable resource for Big Data research. The biospecimens collected will be stored in a National Biobank or an alternative option, namely a network of smaller biobanks hosted by key institutions. A large genome data bank or repository that is either on-premise or cloud-based will be developed for easy access by local and international researchers alike to facilitate further downstream analysis.

To leverage fully on the genome data (or other omics-based data), phenotype data should also be complete and comprehensive. Therefore, suggestions have been made to achieve this by the implementation of electronic medical record (EMR) system by public and private hospitals both to digitally capture and store the clinical and phenotype data. To this end, MOH has approved a large initiative for nationwide EMR implementation, which in itself is a massive challenge and undertaking. Besides the usual investment for infrastructure, investment in data security should also be guaranteed for secure data transactions in ensuring privacy and confidentiality (i.e. including cybersecurity). Concurrently, these data should be made available for collaborative research purposes, thus underlining the need to address associated issues of data sharing, data transfer, interoperability, cost-recovery, competition, rewards, and incentives.

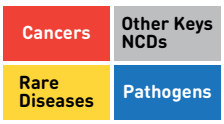
Realising the full promise of precision medicine, the best available care for each individual can thus be provided; for this purpose, researchers and healthcare providers must have access to extensive sets of health and disease-related data linked to each patient. The potential of big data analytics is expansive following the first large-scale whole-genome sequencing programme as part of the Precision Medicine Initiative for Malaysia.

PROPOSED TIMELINE FOR PRECISION MEDICINE TO BE FULLY ADOPTED IN MALAYSIA

YEAR 0

POSITION PAPER

- Buy-in from MOH and other relevant ministries and stakeholders
- Identifying focus areas for pilot studies



YEAR 1-2 (AFTER PAPER IS ADAPTED)

- Governance Framework
- Financial modelling
- Funding for pilot initiatives
- Regulations
- Legislation
- Policies
- Identifying regional centres
- To sequence 10,000 samples

YEAR 3-5

PILOT

- Demonstrate cost-effectiveness
- Demonstrate improvement in health outcomes
- Develop reimbursement models
- Evaluate benefits of precision healthcare
- To sequence 40,000 samples

YEAR 5 ONWARDS

SCALE UP

- Demonstrate cost-effectiveness
- Demonstrate improvement in health outcomes
- Develop reim-bursement models
- Evaluate benefits of precision healthcare
- To sequence 50,000 samples

> YEAR 7

PRECISION MEDICINE AS PRIMARY CHOICE

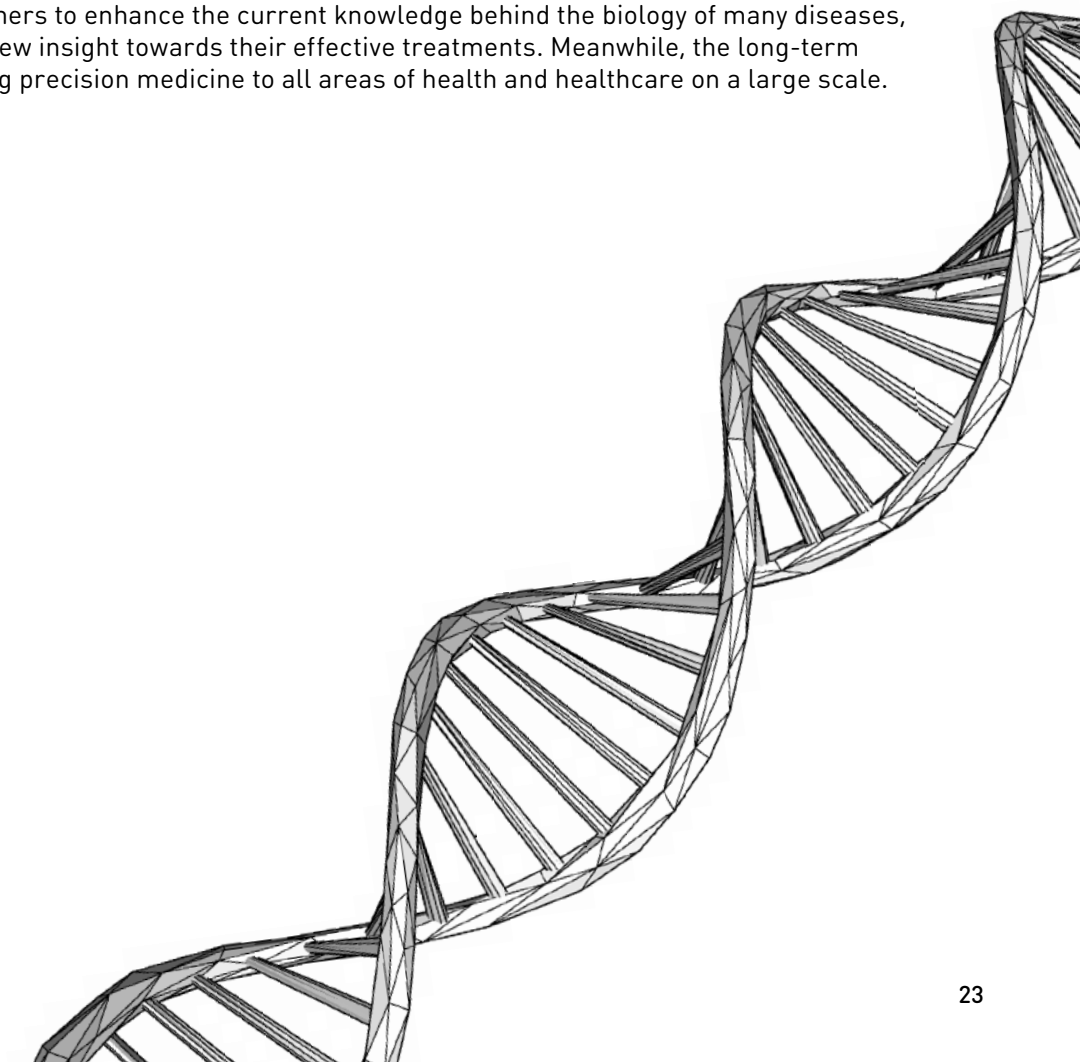
- Unique databases in place
- Fully functional Central biobank
- International partnerships

DISCUSSION

On the global front, high-profile initiatives in precision medicine have been launched in many countries; some examples include the UK's 100,000 Genomes project in 2012 and the USA's Precision Medicine Initiative® (PMI) in 2015. Other country initiatives are listed in Appendix A2. Similarly, technology companies such as Microsoft and Google are also capitalising on the move towards precision medicine, having announced their interest to invest in procurements and infrastructure that advance artificial intelligence (AI), machine learning, bioinformatics, and other next-generation healthcare-related technologies.

Therefore, it is timely for Malaysia to ride with the current disruptive trends in healthcare. Although such efforts have been made in the past, a national-level precision medicine initiative will allow the country to be in the driver's seat of a large-scale genome research programme targeting cancers, NCDs, rare diseases, and infectious diseases. Malaysia can be crowned as the owner of one of the most diverse datasets in the world and assume the golden opportunity of a leadership position in the emerging field of precision medicine. This will undoubtedly render the project an important and valuable card on the table for future participation and collaboration in international research consortiums. In brief, the contributions of new knowledge and healthcare transformation via the Precision Medicine Initiative in Malaysia is unquestionably priceless.

It should be noted that most precision medicine initiatives are equipped with short-term and long-term goals both. The short-term goals involve expanding precision medicine in strategic areas of research and profiling of patients and samples using omics-based technologies. This will accumulate a large volume of data that can be leveraged on by researchers to enhance the current knowledge behind the biology of many diseases, as well as potentially discover new insight towards their effective treatments. Meanwhile, the long-term goals will largely focus on taking precision medicine to all areas of health and healthcare on a large scale.



RECOMMENDATIONS

1. REGULATION AND LEGISLATION

The need to develop a solid and robust legal and regulatory framework cannot be denied; it should include relevant and up-to-date Acts such as the Human Tissue Act and incorporate explicit regulations on data protection, privacy rights, genome testing, consent, access and use of genome data, and non-discrimination, among others. With proper laws and regulations in place, a firm ethical and social framework can be built, which is further strengthened by various codes of conduct.

Accordingly, the development of regulations and legislation should involve multiple stakeholders across various sectors, such as lawyers, bioethicists, geneticists, religious authorities, human rights groups, consumer associations, and relevant non-governmental organisations (NGOs). Obtaining input from all sectors involved can be ensured by carrying out capacity building and awareness programmes for both the public and practitioners.

2. THE BIG DATA INITIATIVE

BOX 2

"Sandbox" is a term commonly used to describe an isolated testing environment for new applications or programs. Similarly, a regulatory sandbox can be defined as "a framework set up by a financial sector regulator to allow small-scale live testing of innovations by private firms in a controlled environment"

Source: https://blog.liquid.com/what-is-a-regulatory-sandbox-and-how-does-it-apply-to-crypto

This national effort should include the establishment of a consortium for Big Data in Precision Medicine. The initiative can be commenced as a pilot effort, whereby the first programme for undertaking is "sandboxing" private-public partnerships by testing out policies through pilot studies.

The ideal model for the Precision Medicine Initiative is as aforementioned: a consortium of research centres with a central coordinating hub running the initiatives. Here, all data should be sent, stored, and managed by the coordinating hub. As practised in Australia (ACOLA, 2018), data centralisation ensures its aggregation and collection by a central intermediary that is responsible for transforming the data. This will ensure the consistency and provide a uniform interface for its users. Besides, the use of a centralised data model can guarantee ease of data access and security management as they are all accessible in one location. Similarly, the data format will be consistent across all due to centralisation, thus improving analyses made in general.

Furthermore, blockchain technologies can be potentially deployed in precision medicine applications. They hold the power to advance the field to the next level, specifically by enabling and incentivising data sharing and collaboration across a consortium of healthcare organisations.

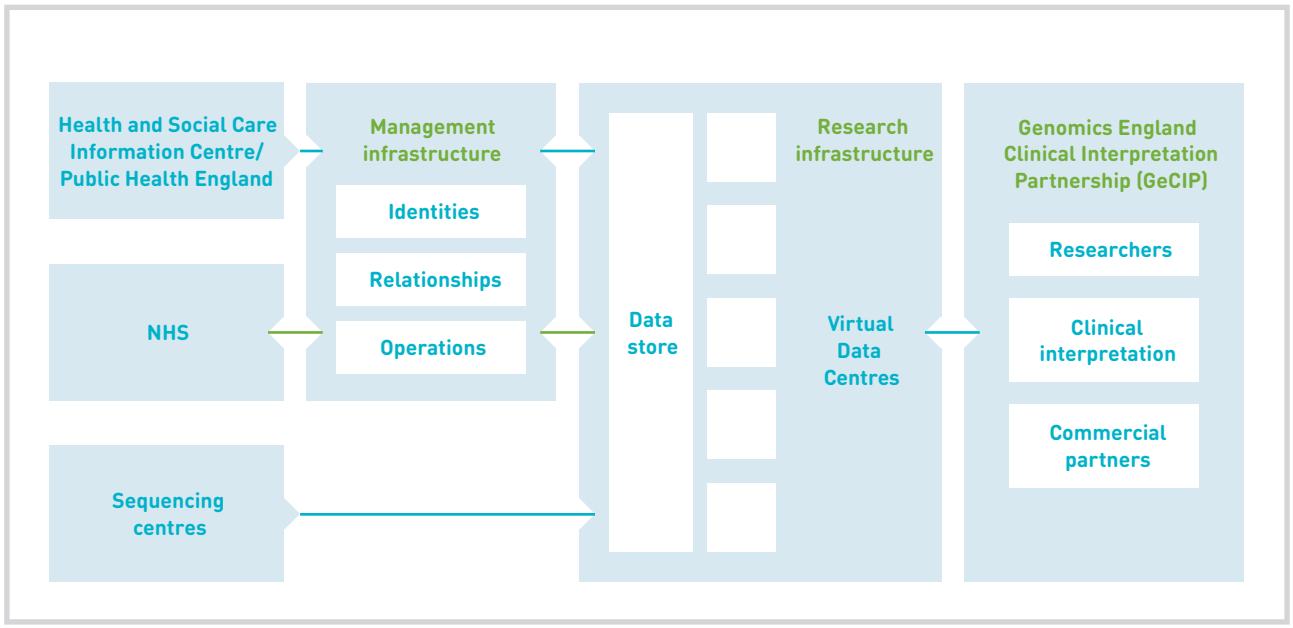


Figure 5: *Informatics Architecture for Genomics England.*
(Source: *The 100,000 Genomes Project Protocol, Genomics England, 2017*)

The diagram (Figure 5) above shows an outline of the informatics architecture adopted in the 100,000 Genomes Project carried out by Genomics England. All clinical, laboratory, and health data flow from the respective National Health Services (NHS) facilities and other organisations into the Genomics England system, where it will be de-identified prior to storage within the research data infrastructure.

Every de-identified sample and its clinical data will be subjected to a unique identification marker as it goes into the Data Centre. It is linked to the patient's identification, whereby the information will pass through the Management Infrastructure to enable re-association of genomic data resulting from the sample. The sample identification will not be made available to researchers in the domain.

3. NATIONAL BIOBANK INITIATIVE

In terms of sample storage and access, the government is urged to follow in the footsteps of countries that have invested significantly in their bio-banking efforts. Examples of such countries include Japan, the USA, and the UK, where all biobanks converge to a central coordinating custodian. Therefore, Malaysia requires a national-level Biobank or a consortium of biobanks. At present, the Malaysian Cohort Biobank is currently the largest in the nation and tasked with storing biospecimens from more than 120,000 individuals.

In contrast, the national-level-funded UK Biobank stores the biospecimens and data sourced from approximately 500,000 individuals, which is now deemed a huge resource for researchers from the public and private sectors both, including pharmaceutical companies. In line with this, clear policies on data transfer and cost recovery have been detailed. Furthermore, the UK government has launched the National Biosample Centre in Milton Keynes in the past few years, where researchers and investigators can store biospecimens at a subsidised cost. This is a clear example of a national-level Biobank that is supported and funded by the governing body.

Alternatively, the All of Us Research Program driven by the National Institutes of Health USA dictates that all biospecimens collected are shipped to the Mayo Medical Laboratories (MML) for the initial unpacking, accessioning, and sorting. At the location, a centralised Biobank can be found, where the biospecimens are processed and stored. Meanwhile, the initial sample processing is performed at the site of collection itself as described in the Biobank Standard Operating Procedures.

4. COLLABORATIVE EFFORTS IN RESEARCH

The importance of undertaking research projects that are both translational and market-driven must be recognised. To this end, the Ministry of Science, Technology and Innovation (MOSTI) has launched the iConnect initiative to bridge the gap across the quadruple helix consisting of the Government, Industry, Academia, and Civil Society. It is highly imperative for the government to provide tax incentives such as tax deductions and exemptions for incentivising the industry for their participation in the initiative.

Therefore, national-level concerted efforts should be planned and undertaken accordingly. The aforementioned initiative is focusing on cancers, other NCDs, rare diseases, and pathogens through the advancement of genomics and other omics-based technologies, which appears to be the best way forward in the immediate future. Despite the availability of numerous references in said areas, research projects and publications derived from them are fragmented, with most of the data being Euro-centric. Additionally, the need for datasets that are representative of the Malaysian population is highly pertinent, which can only be achieved by conducting research at the national scale.

5. IMPROVED ACCESS TO DIAGNOSIS AND TREATMENT

In general, two important measures in the oncology service and rare diseases call for improvements: 1) ensure the access to basic or intermediate care and terminal cases, and 2) ensure the availability and accessibility of all WHO essential medicines as well as pharmaceuticals designated as orphan drugs (Thong et al., 2019).

Furthermore, all new technologies associated with the endeavour should not be of risk to the end-users. Hence, one can anticipate legal, ethical, and safety challenges along the way, with countermeasures being worked on to address them. This includes the production of white papers on Precision Medicine adoption and implementation, as well as surveys, stakeholder engagements, industry consultations, clinical trials and validation, regulatory framework, and proofs of concepts or pilot testing.

6. TALENT MANAGEMENT

Throughout the process, one also needs to look at the talent management and human resource requirements for an effective implementation of the Precision Medicine Initiative. Relevant personnel include clinicians, scientists, medical geneticists, bioethicists, genetic counsellors, bioinformaticians, laboratory managers, and associated support staff (Cutiongco-de la Paz et al. 2018). In addition, medical students may require additional exposure and training in topics related to genetics, genomics, and bioinformatics (McGrath and Ghersi, 2016).

Furthermore, one cannot deny the presence of major gaps in the areas of genetic counselling and bioinformatics, whereby more subject matter experts are sorely necessary. Accordingly, the modules in training designed for these two fields must include the applications of precision medicine. For bioinformatics, in particular, medical professionals (especially doctors and nurses) are required to obtain additional training in either nursing informatics, translational informatics, biomedical informatics, or bioinformatics (Kulikowski, 2012).

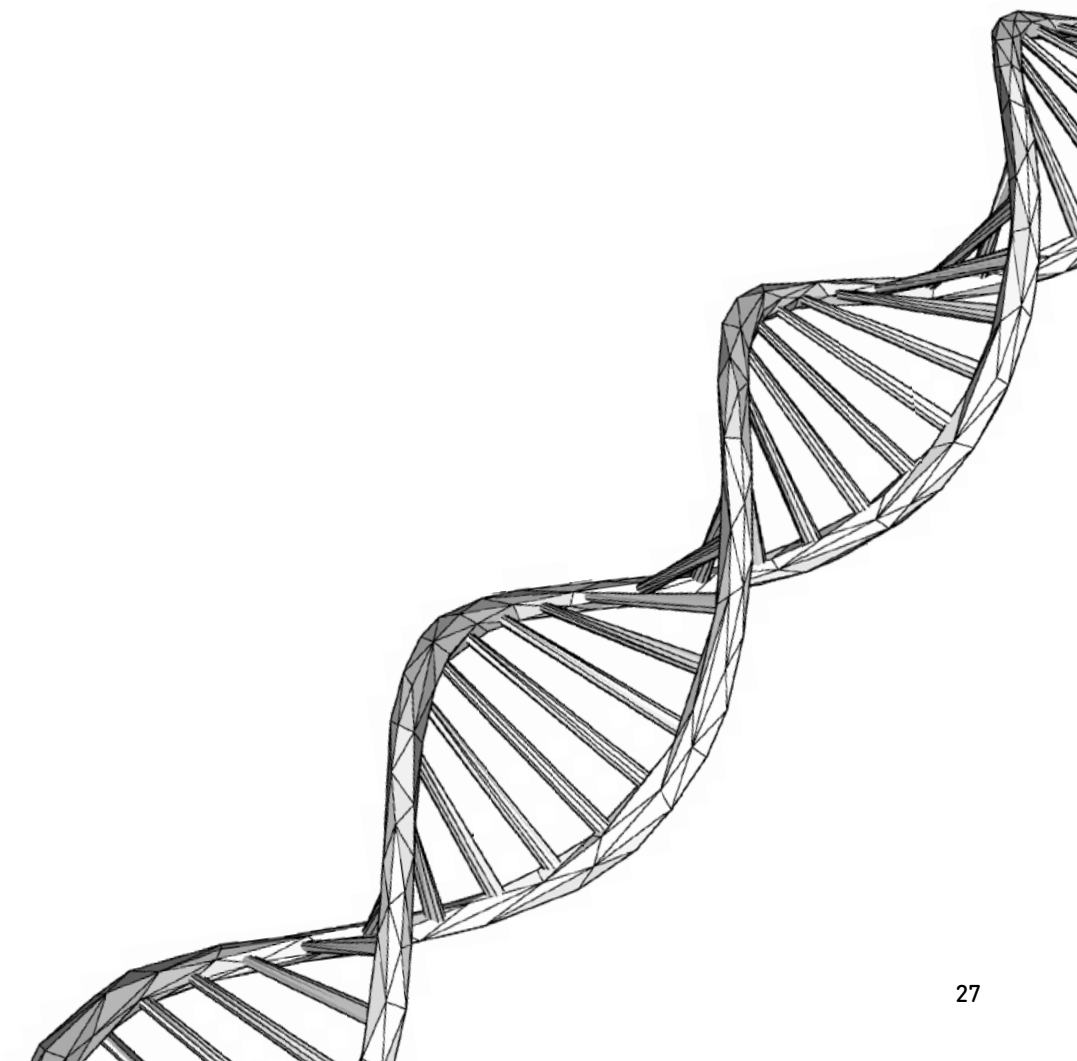
7. LABORATORY ACCREDITATION

All molecular diagnostic laboratories must be ISO 15189-certified (Schneider et al., 2017). Laboratories implementing the standard should strive to:

- Create systems that are as failure resistant as possible, which will identify mistakes before they become a problem and reduce errors by getting things right the first time
- Identify opportunities for improvement at all times
- Involve and empower their staff via involvement in problem-solving and the implementation of relevant solutions.

CONCLUSION

Malaysia needs to push its agenda of precision medicine forward to be continuously highly rated among the healthcare systems globally. Its application will result in better and earlier diagnosis, as well as improved outcomes of treatment. The country is already equipped with an excellent overall infrastructure in terms of laboratories, biobanks, research centres, and institutions. It is also embedded with scientific and technological capabilities required to implement the initiatives and recommendations. On top of this, having a strong precision medicine initiative will further enhance collaborative research efforts with top institutions around the world, especially by leveraging the genomic diversity of its population. Besides, establishment of relevant legislation is required in tandem with addressing and managing any issues of privacy and confidentiality. The future of precision medicine is already here, and Malaysians should not allow our Nation to be left behind. Therefore, the commitment and support by the Prime Minister and the Cabinet are much needed.



REFERENCES

1. Balasopoulou A., et al. (2017), Advancing Global Precision Medicine: An Overview of Genomic Testing and Counseling Services in Malaysia, OMICS A Journal of Integrative Biology, 21 (12) 2017.

2. Bourzac, K. (2016), Power to the patients. Nature: 537, September 2016.

3. Chong, H.Y. et al. (2018), Current landscape of personalised medicine adoption and implementation in Southeast Asia, BMC Medical Genomics, 11:94.

4. Dzau V. et al. (2016), Precision Medicine A Global Action Plan For Impact – Report Of The Wish Precision Medicine Forum 2016.

5. Eva Maria Cutiongco-de la Paz, E.M. et al. (2019), Training in clinical genetics and genetic counselling in Asia. Am J Med Genet. ;1–10.

6. Gameiro, G.R., et al. (2018), Precision Medicine: Changing the way we think about healthcare. Clinics 73:e723.

7. Halim-Fikri, H., et al. (2015), The first Malay database toward the ethnic-specific target molecular variation. BMC Research Notes: 8(176), 2015.

8. Houlding, D. (2019), Opportunities to Advance Precision Medicine with Blockchain-Powered AI. [ebook] The Journal of Precision Medicine. Available at: https://www.thejournalofprecisionmedicine.com/wp-content/uploads/2019/06/jpm219-Houlding.pdf [Accessed 12 Feb. 2020].

9. Jamal, R. (2017), Precision Medicine: Is Malaysia ready? Asia-Pacific Journal of Mol. Medicine: 7(1):1 2017.

10. Jamal, R. et al. (2015), Cohort Profile: The Malaysian Cohort (TMC) project: a prospective study of non-communicable diseases in a multi-ethnic population. International Journal of Epidemiology: 2015, 423–431.

11. Kulikowski C. A et al. (2012), AMIA Board white paper: definition of biomedical informatics and specification of core competencies for graduate education in the discipline. J Am Med Inform Assoc. 19(6):931–8. DOI: 10.1136/amiajnl-2012-001053.

12. Lim, Ka Keat, et al. (2018), Is BRCA Mutation Testing Cost-Effective for Early Stage Breast Cancer Patients Compared to Routine Clinical Surveillance? The Case of an Upper Middle-Income Country in Asia. Applied Health Economics and Health Policy. 16. 10.1007/s40258-018-0384-8.

13. Lee, S. W. and Kamaruzaman, H.F.F. (2016), Health Technology Assessment Section (MaHTAS), Ministry of Health Malaysia. Trastuzumab as an Adjuvant Therapy for Early Breast Cancer and Economic Evaluation.

14. McGrath, S., Ghersi, D. (2016), Building towards precision medicine: empowering medical professionals for the next revolution. BMC Med Genomics 9, 23 DOI:10.1186/s12920-016-0183-8

15. Mukherjee, Shradha (2019), Genomics-Guided Immunotherapy for Precision Medicine in Cancer. Cancer Biotherapy and Radiopharmaceuticals. 34. 10.1089/cbr.2018.2758.

16. National Institute of Health (2018), All of Us Research Program - Operational Protocol.

17. National Institute of Standards and Technology (NIST), US Department of Commerce (2015), Cost per Genome. Available online: https://www.nist.gov/image/costpergenome20154jpg. [Accessed February 2020].

18. Nur Hatin, W and Alwi, Z. (2018), Time to invest in precision medicine. New Straits Times (Malaysia): February 6, 2018 @ 9:01am. Available online: https://www.nst.com.my/opinion/letters/2018/02/332459/time-invest-precision-medicine

19. Orphanet website: About rare disease. Available online: https://www.orpha.net/consor/cgi-bin/Education_AboutRareDiseases.php?lng=EN [Accessed 13 May 2020].

20. Rare Disease Day, What is a Rare Disease? Available online: https://www.rarediseaseday.org/article/what-is-a-rare-disease

21. Schneider, F., Maurer, C., & Friedberg, R. C. (2017), International Organisation for Standardization (ISO) 15189, Annals of laboratory medicine, 37(5), 365–370. DOI:10.3343/alm.2017.37.5.365

22. Scott, A.R. (2016), Read the instructions. Nature: 537, September 2016.

23. Stenehjem, David et al. (2015), Cost-Utility of a Prognostic Test Guiding Adjuvant Chemotherapy Decisions in Early-Stage Non-Small Cell Lung Cancer. The Oncologist. 21. 10.1634/theoncologist.2015-0162.

24. The Academy of Medical Sciences (2019), Improving the development and deployment of diagnostics in Southeast Asia – Workshop Report. 23–24 October 2018, Tagaytay City, Philippines

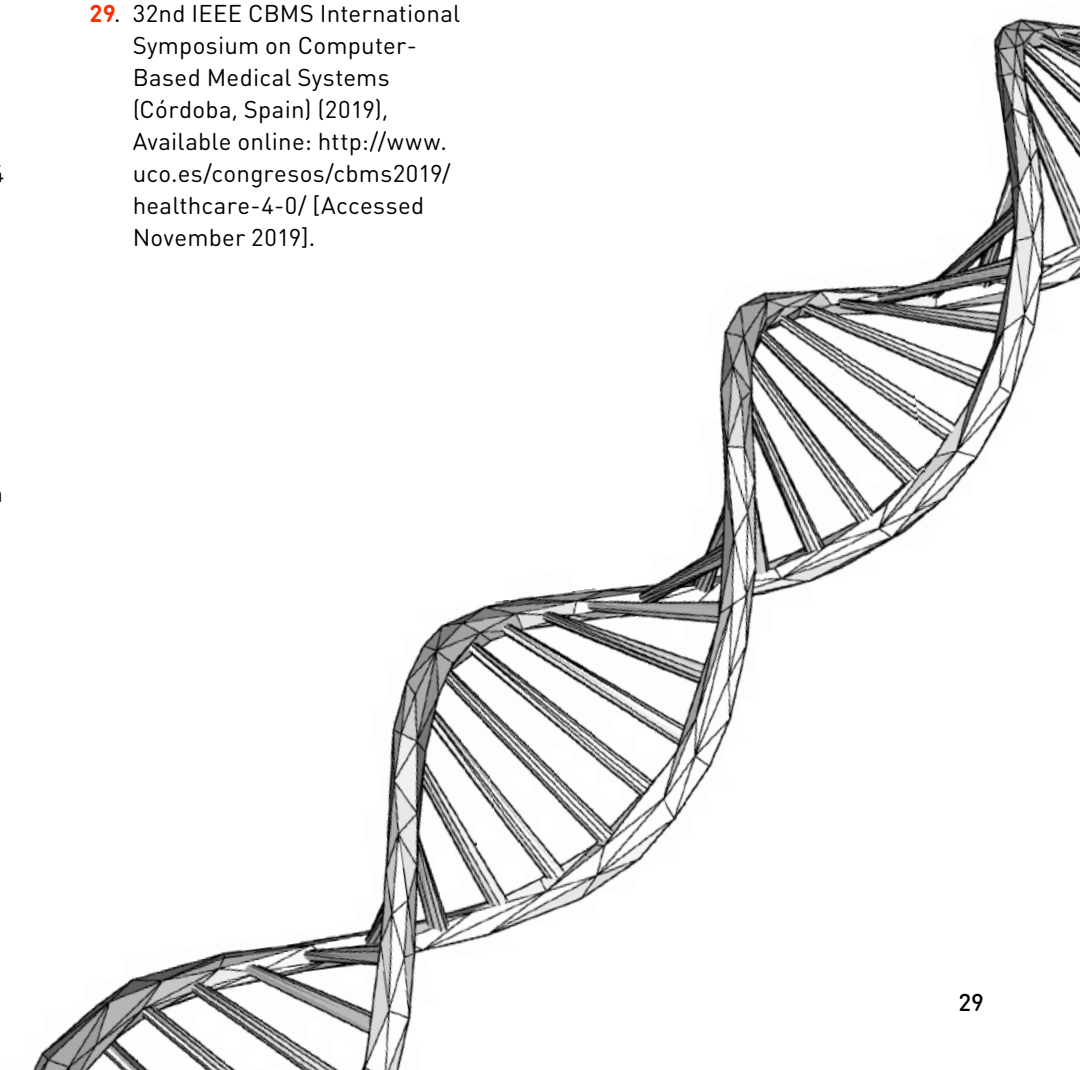
25. Thong M.K. et al. (2019), Whitepaper: Rare Diseases in Malaysia. IDEAS Policy Research Berhad.

26. Williamson, R. et al. (2018), Future of Precision Medicine in Australia. [online] Australian Council of Learned Academies (ACOLA). Available at: https://acola.org/wp-content/uploads/2018/08/future-precision-medicine-australia.pdf [Accessed 2 Jan. 2019].

27. World Economic Forum (WEF) (2017), Shaping the Future of Health and Healthcare Platform. Available online: https://weforum.ent.box.com/v/PrecisionMedicine-2017 [Accessed December 2018].

28. World Economic Forum (WEF) (2020), It takes far too long for a rare disease to be diagnosed. Here's how that can change Available online: https://www.weforum.org/agenda/2020/02/it-takes-far-too-long-for-a-rare-disease-to-be-diagnosed-heres-how-that-can-change/ [Accessed March 2020].

29. 32nd IEEE CBMS International Symposium on Computer-Based Medical Systems (Córdoba, Spain) (2019), Available online: http://www.uco.es/congresos/cbms2019/healthcare-4-0/ [Accessed November 2019].



APPENDICES

A.1: Definition of precision medicine from benchmarked countries/initiatives

SINGAPORE	UK	US	WISH (World Innovation Summit for Health)
A high-value, potentially disruptive technology, one which is a natural fit for a country with strengths in biomedical sciences, data management and storage, analytics, and a technologically advanced healthcare system.	A move away from a 'one-size-fits-all' approach to the treatment and care of patients with a particular condition, to one which uses new approaches to better manage patients' health and target therapies to achieve the best outcomes in the management of a patient's disease or predisposition to the disease.	An approach for disease treatment and prevention that considers the individual variability in genes, environment, and lifestyle for each person.	The tailoring of medical treatment to the individual characteristics of each patient to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment, [allowing] preventative or therapeutic interventions [to] be concentrated on those who will benefit, sparing expense and side effects for those who will not.
(Singapore government definition of Precision Medicine, taken from Business Finland report 2017)	(NHS definition of Personalised Medicine)	(NIH definition of Precision Medicine, 2015)	(United States (US) National Research Council, 2011)

A.2: Initiatives in Other Countries Besides the UK and US

MULTINATIONAL INITIATIVES

Name of project	Goals of specialized programmes
1) Genomic Medicine Alliance	Build collaborative efforts between developed and developing/low-income countries, genotype pharmacogenomically relevant variants in developing nations, develop national/ethnic genetic databases to study genetic disorders that occur in ethnic groups or populations using a data warehouse (or central repository) approach, and engage in public health genomics projects.
2) Genatak	Laboratory network for premarital, prenatal and postnatal detection of recessive diseases and chronic disease risk, genetic counselling and personalized cancer treatment.
3) Global Genomic Medicine Collaborative	The G2MC is a consortium of nations and initiatives aiming to advance genomic medicine; specifically via collaborative programs in sequencing, pharmacogenomics, information technology, education and policy.

(**Source:** *Dzau V., et al. (2016)*)

SINGLE COUNTRY EFFORT

Country	Name of projects	Goals of specialized programmes
1) Australia	**A framework for translating research into public health action**	Develop a national framework for translating genomics discoveries into clinical research and practice, including advice on the results of genomics research and clinical testing.
2) Belgium	**Belgian Medical Genomics Initiative (BeMGI)**	Create a national framework for clinical exome (all expressed genes) sequencing, share variant frequency data, incorporate into international initiatives, and train the next generation of researchers and clinicians.
3) Canada	**Genomics and Personalized Health competition**	Assess the benefits (including economic) of genomic technology to patients and expand the capacity for clinical and translational research in 18 diverse projects.
4) Estonia	**Estonian program for personal medicine**	Sequence the genomes of 5,000 individuals, develop Estonian genotyping array, pilot 50,000 Estonian Biobank members, and link genetic information to EHRs.
5) France	**National Network of Reference & Competence Clinical Centers for Rare Diseases**	Create a national network of molecular genetics laboratories, clinical cancer genetics centers and inter-regional sequencing platforms.
6) India	**Implementation of genomic medicine in India**	Develop infrastructure for genomic medicine implementation, including disease susceptibility assessment across ethnic groups, fetal risk prediction and anomaly diagnosis, and cancer genomics.
7) Israel	**Clalit Health System**	Use genomics in cancer treatment and include anonymized family history data in relatives' EHRs.
8) Japan	**Implementation of genomic medicine project**	Use genomics for optimized diagnosis, treatment and prevention.
9) Korea	**Genome Technology to Business Translation Program**	Use genomics to develop early diagnosis and treatments for personalized medicine and precision medicine.
10) Luxembourg	**Luxembourg Centre for Systems Biomedicine**	A new funding program of the Luxembourg National Research Fund that facilitates the creation of the National Centre of Excellence in Research, a national clinical research centre that aims to identify new methods for the early diagnosis of Parkinson's disease and the stratification of patients in subgroups.

Country	Name of projects	Goals of specialized programmes
11) Qatar	**Qatar Genome Programme**	Establish the Qatari reference genome map from a representative sample of volunteers phenotyped (observe characteristics resulting from the interaction of a genotype with the environment) at the Qatar Biobank for Medical Research, and develop comprehensive gene panels for rare diseases to be used for national neonatal screening to alert couples of possible health risks for their child.
12) Saudi Arabia	**Saudi Human Genome Program**	Identify genetic basis of disease in the Saudi population and implement diagnostic genomic assays involving comprehensive gene panels and clinical exome sequencing.
13) Scotland	**Precision Medicine Ecosystem**	Coordinate precision medicine resources and opportunities across Scotland, collate the findings from individual research projects and improve information sharing to combat diseases.
14) Singapore	**Personalized OMIC Lattice for Advanced Research and Improving Stratification (POLARIS)**	Pilot Transforming Growth Factor Beta-Induced (TGFBI) testing for disease diagnosis and family risk assessment in stromal corneal dystrophies (inherited disorder in the cornea of the eye), then implement a 90-gene screening panel to check for gastrointestinal cancers.
15) Sri Lanka	**Sri Lankan research into Thalassemia**	Use single nucleotide polymorphism (SNP) genotyping to identify carriers of the inherited blood disorder, thalassemia, and find genetic modifiers to make it a more manageable chronic illness.
16) Thailand	**Pharmacogenomics and Personalized Medicine**	Implement the pharmacogenomics card to alert at-risk patients to the top 10 drugs that can cause Stevens-Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN), integrated with a nationwide pharmacovigilance program (an organized campaign to determine a drug's safety).

(**Source:** *Dzau V., et al. (2016)*)

A.3: Possible Collaborating Partners

The following entities have been identified as key stakeholders to move the Precision Medicine Initiative in Malaysia:

i) Ministry of Health
ii) Ministry of Science, Technology and Innovation (MOSTI)
iii) Ministry of Education
iv) Ministry of Women, Family and Community Development
v) Research Institutions
vi) NGOs, i.e. genetic diseases related NGOs
vii) Medical insurance companies
viii) Industry players

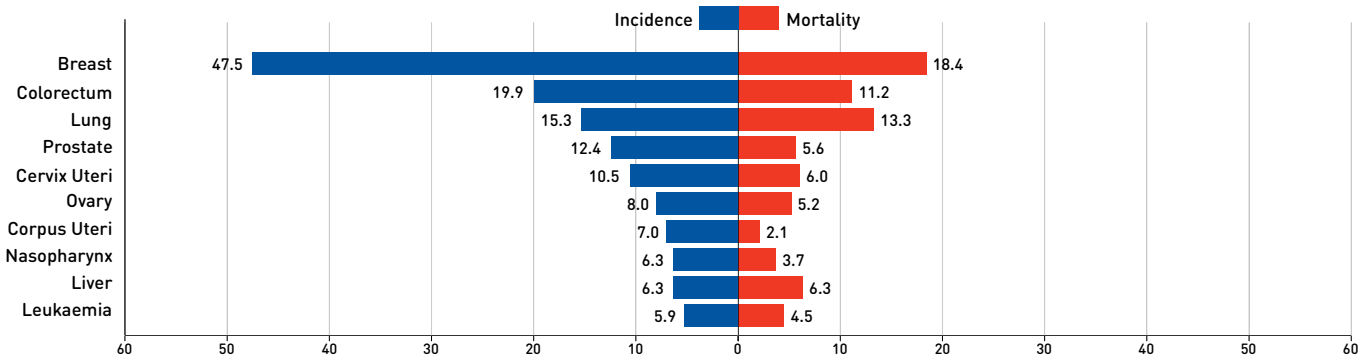
A.4: Disease burden in Malaysia

Cancer Statistics in Malaysia

Summary Statistic 2018			
	Males	**Females**	**Both sexes**
Population	16 526 726	15 515 729	32 042 455
Number of new cancer cases	20 619	23 218	43 837
Age-standardized incidence rate (World)	134.2	147.2	139.9
Risk of developing cancer before the age of 75 years (%)	14.2	14.8	14.5
Number of cancer deaths	13 937	12 458	26 395
Age-standardized mortality rate (World)	92.0	79.8	85.5
Risk of dying from cancer before the age of 75 years (%)	9.4	8.2	8.8
5-year prevalent cases	43 537	62 725	106 262
Top 5 most frequent cancers excluding non-melanoma skin cancer (ranked by cases)	Lung Colorectum Prostate Nasopharynx Liver	Breast Colorectum Cervix Uteri Ovary Lung	Breast Colorectum Lung Nasopharynx Liver

(**Source:** *GLOBOCAN project, Global Cancer Observatory, International Agency for Research on Cancer, WHO 2018 https://gco.iarc.fr/ <accessed 06.01.2020>*)

Age-standardized (World) incidence and mortality rates in 2018, Malaysia, top 10 cancers



(**Source:** *GLOBACAN project, Global Cancer Observatory, International Agency for Research on Cancer, WHO 2018 https://gco.iarc.fr/ <accessed 01.11.2020>*)

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