Research Article

A Value-Driven Future Approach to Precision Medicine for Health Sustainability in New Zealand: A Perspective

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The concept of personalized and precision medicine has its origins in the development of pharmacogenomic tools. The primary goal is to predict disease risk proactively, continually monitor human health status, and reduce the costs associated with large clinical trials by tailoring treatments on a personalized level. However, achieving a personalized ecosystem requires further advancements to enable real-time decision-making and accurate predictions of target medicines for the benefit of the community. Theranostic and companion diagnostics are essential tools for imaging diagnosis, drug delivery, and monitoring specific therapeutic responses. Pharmacogenomics and pharmacogenetic testing could hold the potential to determine the response to precisely administered therapeutics and identify adverse reactions. OMICS-based testing, along with sequencing and molecular docking platforms, shows promise in improving prediction capabilities. The reproducible pieces of evidence of precise standards are the pre-requisite to translating precision medicine for their effective use and implementing the policies could help serve the purpose.

Scientific validity, research protocols, methods, and accurate references are crucial for regulating precision medicines.

1. Precision Medicine

Genomic & molecular testing are being used all over the world to predict the disease risks in context to an individual / or a group of population; based on their environmental exposure, epigenetic characteristics, or variation that occurs because of infectious and non-communicable diseases. The application of

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pharmacogenomics introduced the concept of precision and personalized medicine (Vogenberg et al., 2010), which offers several real-life opportunities, including:

- Prevention of disease risks.
- Optimized therapy at individual / or personalized level
- Safer use of drugs to prevent adverse reactions.
- Reduced costs of large clinical trials by treating individuals or groups with similar genomic profiles.

The vision of healthcare driven by precision medicine is to comprehend the biological events of disease prognosis and associated pathogenesis, that enabling the use of targeted treatment modalities for individuals and population groups. This approach will significantly impact the overall healthcare system with decision-making of life -span ranging from reproductive and prenatal life to detailed molecular typing of autopsies at the end of life.

The personalized healthcare ecosystem can be realized by integrating data science, digital health, and precision medicine. Key stakeholders in this ecosystem include patients (participants), providers, clinical laboratories, researchers, and clinicians. The collection of large-scale biological, radiological, and translational bioinformatics datasets from digital-sensing devices and multi-omics information will facilitate real-time research and targeted medicine decisions. Electronic Medical Records (EMR) and robust IT systems will effectively support research and healthcare delivery. Patients, the valued participant of the research projects, are deemed to provide the biospecimens for testing along with the information of family history, environmental exposure (life-style), other medications, epigenetic errors, etc. This data will be shared for further IT processing, linking digital phenotypes with clinical healthcare (Ginsburg & Philips, 2018). Secured data sharing is a valued strategy to integrate high-quality data into healthcare, and should be a priority for the best possible information available for research and patient care.

A managed electronic platform could process EMRs joined with a sequencing platform, providing standardized, comparable, and consistent results. The electronic data storage platform would facilitate reusing the data for further studies and analysis to improve personalized medicines in healthcare. ‘Just-in-time’ information guidelines for clinical actions could help clinicians use the system effectively in following compatible practices.

The analysis of therapeutic efficacy and adverse toxicity effects through genomics and molecular testing will determine the optimized dosing recommended for appropriate clinical use. The clinical uptake can

be varied; for example, the genotyping for major histocompatibility type I allele HLA-B*5701 can detect severe side effects of taking the HIV drug abacavir, while genotype HLA-B*1502 recommends avoiding the antiseizure drug carbamazepine to prevent side effects. Therefore, therapeutic efficacy would be determined by genotyping sequences in some cases (Ginsburg and Philips, 2018).

In Aotearoa (New Zealand), the Te Nohonga Kaitiaki Guidelines have been set for all genomic projects to conduct. The target treatment is selected to understand using a stratified medicine approach in a group population. Regular communications with the community to keep the Whenua/ interested participants informed and engaged to ensuring the integrity of the system at every step of the ongoing project (Genomics Aotearoa).

Oncology and Pediatrics genomic sequencing are being used to find new variation patterns in New Zealand responsible for developing the disease risk. These variations are used to make informed decisions for targeted medicine against that disease. The development of the infrastructure of the scalable National Genomic Centre in Aotearoa is underway. The genomic information and its protection of Maori interests, rights, authorities, etc., are described in the reference (Genomics Aotearoa). Clinical geneticists, genetic pathologists, and counselors work closely on the analytical decision-making and the right communication tools to be established between counselors and patients receiving targeted and personalized treatment. Regulatory guidelines are established to access the clinical genetic data and are not allowed to use for open source. The implementation of genomic health in NZ is currently based on the data profile of the European population. Māori Guidelines and principles are based on specific levels of responsiveness in the genomic projects, organizational structure, and at the system level, as seen in the given reference (Genomics Aotearoa).

2. Theranostics and Companion Diagnostic Testing

The theranostic platform uses an imaging agent for diagnosis, drug delivery, and monitoring the accurate therapeutic response. Iron oxide nanoparticles, quantum dots, carbon nanoparticles, gold nanoparticles, and silica nanoparticles are being used in real imaging to analyze the target drug delivery. Nanoparticles carry small molecules such as proteins, peptides, and nucleic acids to create a comprehensive biomolecular nano-structural therapeutic bearing a higher capacity to target cancers (Xie J et al., 2010). The nanoparticles are designed to recognize the surface markers of tumor cells rather than normal cells, comparable to higher permeability and retention effects. Research to understand the true potential of the

nano drug delivery system is underway, aiming for optimal metabolism and expulsion from the body to meet preclinical and clinical standards (Xie J et al., 2010).

Radiotheranostics are being applied in nuclear medicine for imaging and radiotherapy. Radioactive molecules are attached to gamma/positron emitters for SPE-CT (single positron emission tomography) or PET (positron emission tomography) imaging, as well as beta, alpha, or Auger electron imaging and spectroscopy. For example, radioactive iodine treatment for thyroid cancer, radio-labeled anti-CD-20 antibodies (for Hodgkin's lymphoma), radium-223 for bone metastasis, and fluorodeoxyglucose, which uses the most commonly used isotope fluorine-18 (Aboagye et al., 2023).

Certain medications produce irreversible side effects in some individuals, ending up with costly hospitalization, but some others don't show any adverse reaction using similar medication. The new pharmacogenetics and pharmacogenomics testing can pinpoint the variable response to drugs, including the toxic effects. The genomic profile in individuals predicts the risk for the disease to assess the response of medication in disease prevention. The cytochrome enzymes P450 (CYP450) metabolize the medicines that are attributed to their absorption, distribution, metabolism, and finally excretion. The CYP2D6 enzyme converts codeine into morphine; 5% of the population doesn't metabolize codeine, rendering it ineffective for pain relief. Trastuzumab medication is given in the context of body weight, age, medical history, and blood reactions, mainly prescribed based on dosing guidelines. Overexpression of certain genes, e.g., the HER2 gene, is related to breast and stomach cancer, prompting the use of the target drug trastuzumab. Only HER2+ patients will be treated with trastuzumab. Diagnostics MSK-1 MPACT^{TM} screens 468 genes, and CdX^{TM} screens 324 genes; these oncogenes can identify the number of variables in the diagnosis of certain tumors in patients (Bilkey et al., 2019). Therefore, the therapeutic effects of morphine and trastuzumab are considered under a personalized approach.

The activation of abl-driven protein signaling is inhibited by the BCR-ABL fusion gene. Imatinib, an inhibitor of tyrosine kinase, is the prime example of rational drug design against cancer, blood disorders, and leukemia (Priyadharshini and Teran, 2016).

It is imperative to justify the ethical clarifications and legality in developing precision genetic medicines, including the quality education of healthcare professionals, and inform the public of the implications of companion genetic testing (Vogenberg et al., 2010).

Companion tests predict who is going to benefit from the medicine. Some biomolecular therapies are also to be considered along with companion testing. These are as follows:

a. Genetic therapy using oligonucleotides (anti-sense) for gene silencing of the defective gene.
b. Voretigene neparvovec (Laxturna) is an adeno-associated vector-based one-time gene therapy for the treatment of patients with confirmed biallelic RPE-65 mutation-associated retinal dystrophy, aiming to restore eye function.
c. Gene editing involves modifying the functions of programmable nucleases to alter gene function. CRISPR-Cas9, Zinc Finger Nucleases, and transcription activation-like effector nucleases have been translated into patient care (Bilkey et al., 2019).
d. Mesenchymal Cell Therapy - Chimeric antigen receptor T-cell therapy is used to transform T-cells to fight against cancer cells.
e. Immunological activation of DCs by using autologous tumor lysate can be effective immunotherapy against cancer and may be a better choice than chemotherapy.

Using the commonalities in the biological functional pathways in a specific type of population could help discover that new diagnostics and therapy are considerable approaches to improve the equity base to access precision medicine in healthcare. It can also assist in revealing the associated pathologies to facilitate cancer screening (Bilkey et al., 2019).

3. Population Studies

The potential technologies, such as gene microarray, cell-tissue array, and imaging (micro-CT), are in practice to evaluate the prognosis of cancer. Cancer prediction provides useful information on recurrence, susceptibility, and survivability. Accurate prognosis for tumor type and other risk factors significantly delivers precise molecular and clinical data. Phylogenetic scores obtained through genotyping could help determine the associated genetic links to diseases like diabetes, cancer, and coronary heart disease. Additionally, individual genetic information is an important factor in learning predictive analysis in a large population. It is difficult to align the associated genetic variations more accurately in the context of hereditary characteristics or environmental factors in the population; certainly, it requires more precise and spot-on instruments and methods to discriminate among the many syndromes (Vogenberg et al., 2010).

4. Respiratory Diseases & Personalized Medicine

Chronic lung conditions, e.g., asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, etc., caused by infections, are the common cause of morbidity and mortality across

the globe. These conditions are heterogeneous and always require early diagnosis. The early symptoms are highly non-specific, and confirmation comes later through clinical diagnosis. Proteomics is the best-selected tool to find specific biomarkers involved in cancer. Protein-protein interactions can easily assess whether they respond well to treatment or are non-responders. Diagnosing chronic lung conditions based on one marker is not always sufficient to understand the disease pattern in real-time. It is possible to determine the poor or good prognosis, drug resistance, and other parameters while working on different markers. MALDI Tof MS is used to determine relevant markers in clinical samples, such as serum, BALF, blood, etc. Recently, respiratory proteomics has made progress in providing better information on targeted therapy in the field of lung cancer (Priyadharshini and Teran, 2016).

The heterogeneity of ARDS prevents the identification of phenotypic functions. Sub-phenotypic identifications using OMICS tools and technology could offer further opportunities to develop new diagnostics and personalized treatments in ARDS (Battaglini et al., 2022).

5. Genetic Diagnostics Market

Further exploration of novel research techniques, such as genomes, proteomes, and metabolomes, would assist physicians in attaining a detailed profile of patients' altered genomes, metabolic functions, and other notable characteristics that can monitor the occurred response and outcome of the therapeutic regimen. Companion diagnostics may play a significant role in bridging theranostics and precision medicine (Vogenberg et al., 2010).

Polymorphism occurs in approximately 1.0% of the population and can be utilized to study epidemiology, drug response, and human diseases, including clinical trials. In the era of genomics, it is imperative to establish relevant guidelines regarding the use of the reference genome. DNA variants, defined as single nucleotide polymorphisms, and DNA mutations for the same event, when compared with the reference genome, could contribute to the impact on accuracy in the interpretation and functional state of the acquired disease genome (Karki et al., 2015).

Pharmacogenomics and theranostics are considered to deliver the benefits of standardized molecular analysis for optimized dosing and the selection of the right medication depending upon the altered genes to avoid the occurrence of adverse reactions. Therefore, increasing the drug's effectiveness in the treatment of patients and disease management (Vogenberg et al., 2010).

Presently, commercial products based on companion diagnostics and theranostics are very limited in number (Vogenberg et al., 2010). Genotypic tests for trastuzumab-Herceptin: Trastuzumab, the monoclonal antibodies used in the treatment of gastroesophageal and breast cancer, target the epidermal growth factor in overactive HER2 (ERBB2) genes. Other biosimilar products equivalent to Herceptin are also available, e.g., Kanjini, Trazmera, Ontruzant, Herzuma, and Ogivri. Trastuzumab increases the effectiveness against these cancers with minimal adverse effects, including cardiac toxicity (Vogenberg et al., 2010; Dean et al., 2012). BRCA1/BRCA2 tests are recommended for breast and ovarian cancer (Neff et al., 2017). The germline BRCA1 and BRCA2 mutations are associated with high-grade serious ovarian cancer (HGSOC). Amplichip CYP450 is a genotype test for predicting therapy risk by detecting the activity or reduced activity of the cytochrome P450 enzyme (Dodgen et al., 2013). Genotyping HIV tests detect mutations in protease and reverse transcriptase, the main causes of drug resistance in HIV. These mechanistic enzymes are used for HIV propagation and are important targets for anti-HIV drugs (Shafer RW. 2002).

Pharmacogenomics provide informed drug prescriptions. The VKORC1 genotype (Vitamin K epoxide reductase) encodes the anticoagulant response, allowing physicians to optimize warfarin dosage for greater therapeutic efficacy (Vogenberg et al., 2010; Ginsburg et al., 2018). Pharmacogenetics - DNA fingerprinting is an approach to optimizing treatments with statins linked to the phenotype statin-associated muscle symptoms (SAMS). Genes like SLC01B1, COQ2, HTR7, GATM, etc., are activated to develop myopathy and myalgia when using simvastatin and atorvastatin. Statins are lipid-lowering strategies to prevent cardiovascular diseases. The testing is used to lower the dose of statins, eventually reducing morbidity and mortality in SAMS-linked syndromes (Brunham et al., 2018).

6. Precision Medicine Practice

Oncology Dx genomic assays predict early-stage cancer to provide chemotherapy for high-risk patients (Marchionni et al., 2008). Precision tests based on OMICS could recommend therapy for 1 out of 5 undiagnosed individuals.

Artificial Intelligence and Machine Learning algorithms could help solve the challenges of precision medicine, especially in translational research in healthcare (Sahu et al., 2022). Multidisciplinary expertise with AI and machine learning can also provide predictive algorithms for groups of people who are not identified by clinicians, helping guide the selection of specific groups of patients for early disease treatment. A pilot study on cognitive computing technology (Watson) was configured to support

researchers in analyzing medical literature, patient genomics, chemical, and pharmacological data. Most importantly, the identification of target medicines and appropriate drug positioning to discover novel target drugs can only be achieved by analyzing big data (Chen Y et al., 2016). Personalized treatment eliminates trial errors and inefficiencies that increase the associated cost in population trials, which could undermine patient care.

The Direct-To-Consumer market is projected to grow at 19.5% during the forecast period of 2022-2030. Direct-To-Consumer tests presenting moderate to higher risks in the context of medical testing for healthcare should always demand a comprehensive review by regulations to determine the validity of the tests. According to this report, 65% of individuals are willing to use home genetic tests, but the major concern is sharing data with third-party companies, such as healthcare data processing companies (Business Wire-2022).

Theranostic platforms can be adopted to test several biomarkers using various diagnostics to guide appropriate therapy. They involve medical imaging (MRI), fluorescent markers (organic dye and inorganic quantum dots), spectrophotometry, nuclear imaging agents, DNA sequencing, and deep learning algorithms for accurate analysis (Vogenberg et al., 2010; Ginsburg et al., 2018).

Personal genome analysis qualifies the need for specific anticancer drug effectiveness, even though this is allowed for a small population. Therefore, it does assist in finalizing the exclusion and inclusion of patients for particular drug regimens. Gene CYP2D6 variation increases resistance to the drug Tamoxifen, which is normally broken down by relative enzymes to enhance its efficacy, leaving the drug ineffective for treatment in women with breast cancer. Epidermal genetic information retrieval (EGIR, or Derm Tech) is a non-invasive method for harvesting the stratum corneum of naevi moles, used to detect melanoma by a 17-gene genomic biomarker (Watchman et al., 2011). These tests are often not very expensive.

Most organizations around the world are tirelessly working on high-throughput sequencing not only to study personalized medicine but also to enhance genetic studies. Pharmacy compounding is customizing the unit doses, and fixed doses used in combinations may also be accepted as part of personalized medicine. Computational and mathematical approaches to study the interactions among the drugs and individual biomarkers or enzymes (Molecular docking) are also considered as a personalized approach (Vogenberg et al. 2010).

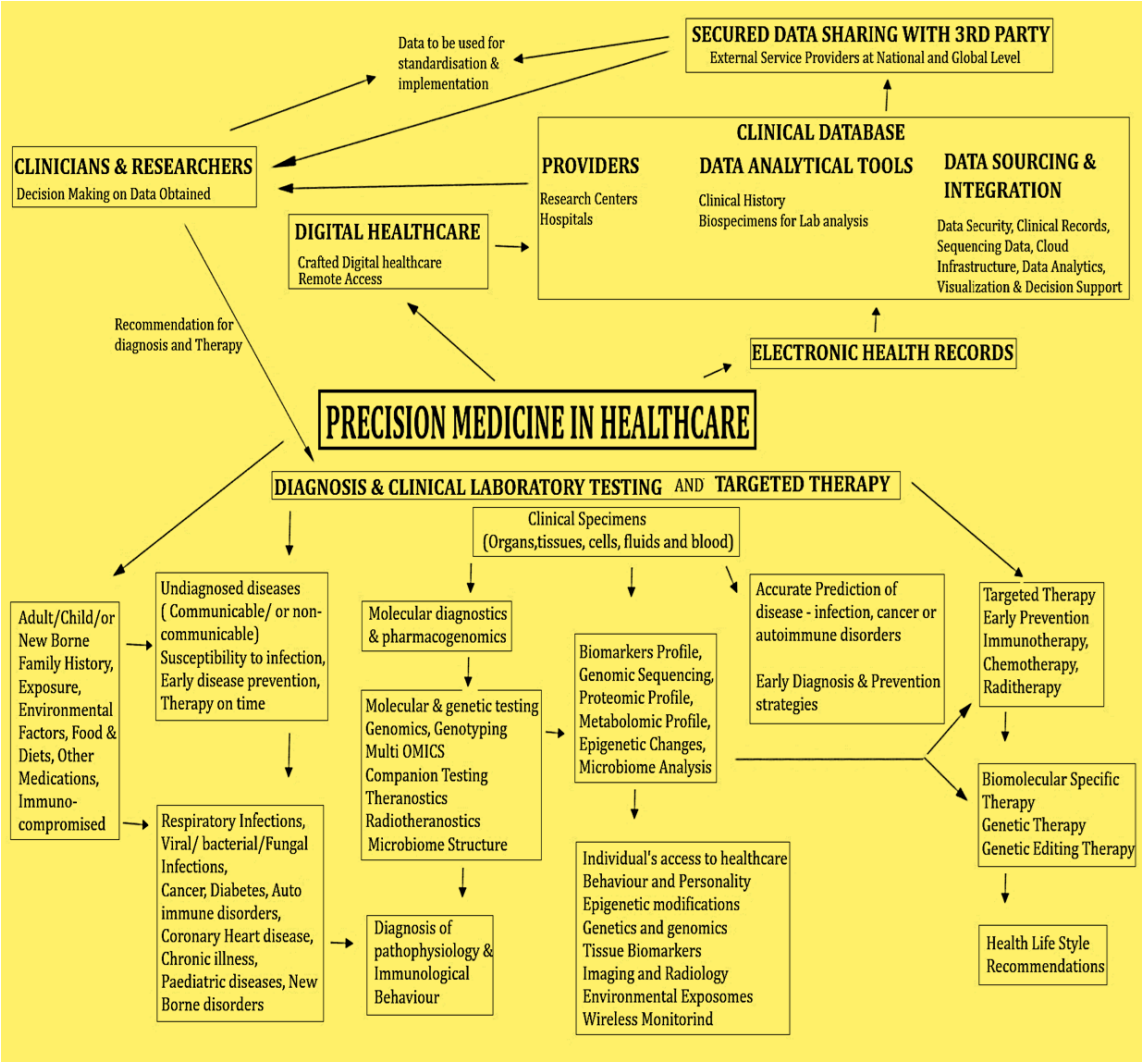

Figure 1. Representation of a model for precision and personalized medicine in healthcare. Recommendations for the diagnosis and specific therapy are provided by Physicians and Clinicians, and all health records are maintained in a clinical database, likely to be securely shared with third-party companies after obtaining consent from patients for further analysis. Artificial intelligence, machine learning, and genetic sequencing data are analyzed and standardized by clinicians and researchers for decision-making.

7. Digital and Tele-Healthcare in Personalized Medicines

The concept of digital healthcare is associated with using novel modalities to employ apps prescribing therapeutic interventions for patients under certain conditions. Clickotine is a smartphone application used to study engagement, efficacy, and safety. Self-reported cessation outcomes were achieved within 7-30 days of abstinence from smoking, resulting in improved health (Lacoveillo et al., 2017).

Telehealth and digital health have become prevalent in real practice during the peak of the COVID-19 pandemic. Personalized medicine healthcare and associated technologies employ advanced analytics. Digital technologies like Artificial Intelligence (AI), Machine Learning (ML), the Internet of Things (IoT), and blockchains are established to manage patients' treatments at the individual level. They have already integrated into business processes in most hospitals. Hospitals, clinics, pharmacies, caregivers, etc., form a complex network to deliver personalized treatment support to patients in need. For more complex and advanced developments, a vast volume of patient, therapeutic, and genomic data is required to provide personalized solutions. Virtual care through digital healthcare provides seamless facilitation to view health records, check prescriptions, and book appointments at any time from home. It is a cost-effective method that saves patients time spent in queues, offers remote access, faster appointments, symptom check-ups, live chat or bot chat, and further consultations to achieve the desired results, increasing the life cycle of patients.

8. Challenges

The implementation of precision medicine remains a challenge, as building evidence-based clinical sequencing requires further research at the national and global levels, with researchers focusing on the same portfolio to optimize the platform. Due to the absence of IT infrastructure and the lack of ability to standardize data analytics and systems precisely, eliminating biased output is challenging. Translational healthcare, digital technologies, and standard policy procedures with common objectives are needed to support the adoption and integration of precision medicine. Reproducible evidence is essential to implement and translate precision medicine into clinical use and policies to serve its purpose (Ginsburg & Philip, 2018).

Unfortunately, a one-size-fits-all approach to medications has been approved based on large clinical trials for traditional medicines. However, integrating personalized medicine into practice will always require an evidence-based gold standard. Therefore, it enforces different rules to understand accurate diagnoses for predicting disease risk, disease prognosis, and the use of target therapeutics. The implementation of policies would clearly define the need for standards in the context of applying therapeutics to avoid unnecessary adverse reactions (Ginsburg & Philip, 2018).

i. **Regulatory Approaches**

A balanced approach should be adopted to fill the current gaps among diagnostics, drug discovery, and economic evaluations of precision medicines. The patient is the consumer and participant in

the research projects; hence, the patient's engagement and trust are important. The participant should be provided with informed consent to ensure their privacy and beneficial outcomes. Participants (consumers - healthy individuals and patients), service providers, third-party service providers, payers, governments, and regulators are the valued stakeholders to be considered in this process, and their successful contribution would certainly improve the quality of life, quality of medical care, efficiency, and efficacy towards clinical care and cost in the coming future (Ginsburg & Philip, 2018).

The determination of regulatory science standards, validated protocols, and research methods, along with the right references, is the urgent requisite to be incorporated into the regulation of personalized medicines in healthcare. Especially in terms of test validity of sequencing methodology platforms, these are the utmost requirements to be implemented into the regulatory system. Therefore, it is still a challenge to fit personalized medicines into standard care.

The larger clinical trials in routine practice are conducted in larger cancer centers and hospitals. However, in the case of personalized treatments, there would be gaps between lab studies and conducting clinical trials by appointing the group population. Therefore, the treatments to be used outside the clinical trials might or might not work precisely (American Cancer Society). To determine the prediction of cancer risk might not be related to the family history or there would be variability in the testing regimen. During cancer treatment, a frequent change in the gene and protein profile might not change the treatment regimen. There will be a concern for the involved cost of regular biomarker testing and treatment against a particular cancer.

Although personalized medicine practice is underway, some issues, alongside regulatory gaps are remained to be improved. These include intellectual property rights, data biases, patient privacy, reimbursement policies (if available for some patients), and confidentiality, which are commonly known challenges (Vogenberg et al., 2010).

ii. **Intellectual property Rights**

Intellectual property rights are always influenced by innovations and investments. It is imperative to patent those gene-related technologies that are likely to produce repeatability and reproducibility confirmation after the initial tests.

iii. **Confidentiality**

Obtaining the patient's consent for gene therapy and providing it to third parties using AI and machine learning for genetic algorithms. Therefore, the "Consent" obtained from patients should be a prominent concern for third-party service providers.

In 2008, the Genetic Information Non-Discrimination Act (GINA) was passed to minimize the patient's highest concern of having their information misused by employers or insurers.

iv. **Differentiation in Data**

The diagnostic data of genomics and next-generation sequencing data for further analysis require an intensive computer processing system, which is the biggest challenge. Interdisciplinary cooperation is needed from all experts in medicine, oncology, computer processing, and AI, etc.

Prediction of disease risks based on genetic data algorithms should be comparable with other human populations (from different geography, race, and environment) to eliminate genetic bias in decision-making.

The human genome roughly has approximately 30,000 errors, which will not easily help attain fidelity in the sequences and can become a hassle in accurate disease prediction. These unexpected variations in the genome producing gaps will remain a question mark in implementing the technology for wider use.

9. New Opportunities

Early screening tests lower the risks for specific types of cancer or autoimmune disorders. Genetic, molecular, and genomic tests are commonly used terms in regular practice by healthcare providers (American Cancer Society).

Cancer diagnosis is carried out by:

- Tumor testing, tumor genetics, biomarker, and subtyping testing.
- Genomic testing, genomic profiling, and genomic sequencing.
- Molecular testing, molecular profiling.
- Somatic testing.
- Next-generation sequencing, etc.

Two types of treatment are most often used in precision medicines: i) Targeted therapy for cancer cells based on a particular marker. ii) Immunotherapy to boost the immune system against the cancer cells.

The most common cancers where precision medicine is being applied are colorectal cancer, breast cancer, lung cancer, leukemia, lymphoma, melanoma, esophageal cancer, stomach cancer, ovarian cancer, and thyroid cancer.

10. Future Prospects

The study of genetic variations, mutations through infections and non-communicable diseases, epigenetic modifications, specifically targeted medicines, development of immunocompromised conditions, etc., are the fields that will take the lead in the foreseeable future. Health information technologies integrating with clinical and healthcare data systems can be intensified by providing incentives through governments. Through digital healthcare exploration, direct-to-consumer testing, and efficient outcomes from digital apps will benefit a larger population, even in remote areas, saving time and extra cost. Participant-centered policies, legislation, and government initiatives could lead to implementing the process. Standardization of precision medicines can be a pre-requisite while working via groundbreaking research initiatives, clinical practice, and medical education, including individual care right from the risk prediction, early treatment, and final recovery.

i. **Role of Pharmacogenetics and Pharmacogenomics in Resolving the Individual Variables**

Quality healthcare management in the community could save millions of dollars by utilizing efficient and effective genetic and molecular testing to control the disease development and therapeutic dosing. Genetic testing is a fairly new technology, not matured enough to deliver the expected results for every type of disease. Apart from genomics, there is a dire need to expand the research on proteomics, metabolomics, and microbiome analysis to calibrate the real status of disease, conferring to eliminating the interfering biases. The other environmental attributes, including climate, diets, individual behavior, etc., should be taken into consideration to prepare prediction maps for the risks involved in disease occurrence.

Using Multi-OMICS Biomarkers could provide more relevant specifications than taking a monogenic biomarker. But there are still gaps in OMICS capacity of data integration, processing, and interpretation. Data standardization & development of central infrastructure for public databases for Multi-OMICS data is yet to be implemented (Menyharta & Gyorffya, 2021).

Healthcare planning for each individual, including comprehensive genomic testing, Multi-OMICS testing implementation, medical precision test model, companion test and therapeutics application model, theranostic and radiotheranostic model, genome database planning (secured storage and sharing of data with the third party), digital healthcare model, etc., are the practical strategies to be integrated into the complex system of precision medicines.

The ultimate goal of precision medicine is early diagnosis of communicable and non-communicable

diseases and their risks, early disease prevention, and treatment with targeted safe drugs with no side effects to increase the healthy life cycle of patients for better patient stratification with an efficient personalized approach.

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References

- Aboagye, E. O., Barwick, T. D., & Haberkorn, U. (2023). Radiotheranostics in oncology: Making precision medicine possible. *CA: A Cancer Journal for Clinicians*, https://doi.org/10.3322/caac.21768
- American Cancer Society. (n.d.). Precision medicine. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/precision-medicine.html
- Battaglini, D., Al-Husinat, L., Normando, A. G., Leme, A. P., Franchini, K., & et al. (2022). Personalized medicine using omics approaches in acute respiratory distress syndrome to identify biological phenotypes. *Respiratory Research*, *23*(318), https://doi.org/10.1186/s12931-022-02233-0
- Bilkey, G. A., Burns, B. L., Coles, E. P., Mahede, T., Baynam, G., & Nowak, K. J. (2019). Optimizing the Precision Medicine for Public Health. *Frontiers in Public Health*, *Sec Epidemiology*, 7, https://doi.org/10.3389/fpubh.2019.00042
- Brunham, L. R., Baker, S., Mammen, A., Mancini, G. B. J., & Rosenson, R. S. (2018). Role of genetics in the prediction of statin-associated muscle symptoms and optimization of statin use and adherence. *Cardiovascular Research*, *114*(8), 1073–1081. https://doi.org/10.1093/cvr/cvy119
- Business Wire. (2022). Direct-To-Consumer (DTC) genetic testing Market Report 2022: Increase in willingness to use direct to consumer genetic testing drives growth. https://www.businesswire.com/news/home/20221221005341/en/Direct-To-Consumer-DTC-Genetic-

Testing-Market-Report-2022-Increase-in-Willingness-to-Use-Direct-to-Consumer-Genetic-Testing-Drives-Growth---ResearchAndMarkets.com

- Chen, Y., Argentinis, E., & Weber, G. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research. *Clinical Therapeutics*, *38*(4), 688-701. https://doi.org/10.1016/j.clinthera.2015.12.001
- Cole, L. (2021). How Digital Tools Will Transform Personalized medicine in 2021 and Beyond? *BiopharmaTrend.com*.
- Dean, L., Kane, M., Pratt, V. M., Scott, S. A., Pirmohamed, M., Esquivel, B., Kattman, B. L., & Malheiro, A. J. (2012). Trastuzumab Therapy and ERBB2 Genotype. In: *Medical Genetics Summaries* [Internet]. Bethesda (MD): National Center for Biotechnology Information (US). https://www.ncbi.nlm.nih.gov/books/NBK558989/
- Dodgen, T. M., Hochfeld, W. E., Fickl, H., Asfaha, S. M., Durandt, C., Rheeder, P., Drogemoller, B. I., Wright, G. E. B., & et al. (2013). Introduction of the AmpliChip CYP450 Test to a South African cohort: a platform comparative prospective cohort study. *BMC Medical Genetics*, *14*(20).
- Genomics Aotearoa. (n.d.). Precision medicine. https://www.genomics-aotearoa.org.nz/education-events/precision-medicine
- Ginsburg, G. S., & Philips, K. A. (2018). Precision Medicine: From Science to Value. *Health Affairs (Millwood)*, *37*(5), 694-701. https://doi.org/10.1377/hlthaff.2017.1624
- Karki, R., Pandya, D., Elston, R. C., & Ferlini, C. (2015). Defining “mutation” and “polymorphism” in the era of personal genomics. *BMC Medical Genomics*, *8*, 37. https://doi.org/10.1186/s12920-015-0115-z
- Lacoviello, B. M., Steinerman, J., Klein, D. B., Silver, T. L., Berger, A. G., Luo, X. S., & Schork, N. J. (2017). Clickotine, A Personalized Smartphone App for Smoking Cessation: Initial Evaluation. *JMIR Mhealth Uhealth*, *5*(4), e56. https://doi.org/10.2196/mhealth.7226
- Marchionni, S., Wilson, R. F., Wolff, A. C., & et al. (2008). Systematic Review: Gene Expression Profiling Assays in Early-Stage Breast Cancer. *Annals of Internal Medicine*. https://doi.org/10.7326/0003-4819-148-5-200803040-00208
- Menyharta, O., & Gyorffya, B. (2021). Multi-omics approaches in cancer research with applications in tumor subtyping, prognosis, and diagnosis. *Computational and Structural Biotechnology Journal*, *19*, 949–960. https://doi.org/10.1016/j.csbj.2021.01.009
- Neff, R. T., Senter, L., & Salani, R. (2017). BRCA mutation in ovarian cancer: testing, implications and treatment considerations. *Therapeutic Advances in Medical Oncology*, *9*(8), 519–531. https://doi.org/10.1177/1758834017714993

- Priyadharshini, V. S., & Teran, L. M. (2016). Personalized Medicine in Respiratory Disease: Role of proteomics. *Advances in Protein Chemistry and Structural Biology*, *102*, 115-146. https://doi.org/10.1016/bs.apcsb.2015.11.008
- Sahu, M., Gupta, R., Ambasta, R. K., & Kumar, P. (2022). Artificial intelligence and machine learning in precision medicine: A paradigm shift in big data analysis. *Progress in Molecular Biology and Translational Science*, *190*(1), 57-100. https://doi.org/10.1016/j.pmbts.2021.12.004
- Shafer, R. W. (2002). Genotypic Testing for Human Immunodeficiency Virus Type 1 Drug Resistance. *Clinical Microbiology Reviews*, *15*(2), 247–277. https://doi.org/10.1128/CMR.15.2.247-277.2002
- Vogenberg, F. R., Barash, C. I., & Pursel, M. (2010). Personalized Medicine, Part I- Evolution and Development into Theranostics. *P&T*, *35*(10), 560-562, 565-567, 576. https://doi.org/10.1016/bs.apcsb.2015.11.008
- Wachsman, W., Morhenn, V., Palmer, T., Walls, L., Hata, T., Zalla, J., Scheinberg, R., Sofen, H., Mraz, S., Gross, K., Rabinovitz, H., Polsky, D., & Chang, S. (2011). Noninvasive genomic detection of melanoma. *British Journal of Dermatology*, *164*(4), 797–806. https://doi.org/10.1111/j.1365-2133.2011.10239.x
- Xie, J., Lee, S., & Xiaoyuan, C. (2010). Nanoparticle-based theranostic agents. *Advanced Drug Delivery Reviews*, *62*(11), 1064-1079. https://doi.org/10.1016/j.addr.2010.07.009

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