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The Evolution of Personalized Healthcare: Strategies on Public Health through the Philosophy and Practice of Personalized and Precision Medicine (PPM) to Secure the Human Healthcare and Biosafety

Sergey Suchkov[1-5, 7,10*], Hiroyuki Abe[4,6], Masaki Tan[3,4,11], Steven Dooley[8,9], Holland Cheng[12], Elena Antonova[15,16], Philip D. Cotter[13], Alena Borisova[1], Arturo Solis[17] and John Aitken[14]

[1]*The Russian University of Medicine, Moscow, Russia*

[2]*The Russian Academy of Natural Sciences, Moscow, Russia*

[3]*EPMA, Brussels, EU*

[4]*ISPM, Tokyo, Japan*

[5]*PMC, Washington, DC, USA*

[6]*Abe Cancer Clinic, Tokyo, Japan*

[7]*New York Academy of Sciences, USA*

[8]*Medical Faculty Mannheim of the University of Heidelberg, Manheim, Germany*

[9]*University Hospital Mannheim II, Manheim, Germany*

[10]*American Heart Association (AHA), Houston, TX, USA*

[11]*NAKADA Geriatric Health and Welfare Facilities and Kitakami Kiboen Geriatric Health and Welfare Facilities, Miyagi, Japan*

[12]*T College of Biological Sciences, UC Davis, CA, USA*

[13]*ResearchDx and PacificDx, Irvine, CA, USA*

[14]*Otakaro Pathways, Christchurch, New Zealand*

[15]*Filatov's Moscow Clinical Pediatric Hospital, Moscow, Russia*

[16]*Sechenov University, Moscow, Russia*

[17] *Human Photosynthesis Study Center, Aguascalientes, CP 20000, México*

***Corresponding Author**
Sergey Suchkov, the Russian University of Medicine, Moscow, Russia.

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Abstract

The traditional approach to public health has focused on treating existing diseases rather than on prevention and health promotion. With the rise of chronic diseases linked to unhealthy lifestyles, there is a growing need for a shift towards integrated healthcare. In this article, we explore the potential introduction of innovative approaches such as Lifestyle Medicine (LM) and Personalized and Precision Medicine (PPM) into public health, as well as the challenges the traditional healthcare system may face in practice when integrating PPM and LM.

1. Introduction

Throughout history, public health practice and its philosophy have mainly focused on finding and treating existing diseases by classifying various disorders (nosology), rather than focusing on health, genomic variations or so-called pre-illness conditions. Additionally, many chronic conditions (obesity, type

1/2 diabetes, cardiovascular and metabolic disorders) are partly linked to unhealthy lifestyle and harmful habits, including poor nutrition, smoking, and low physical Activity, and high stress levels

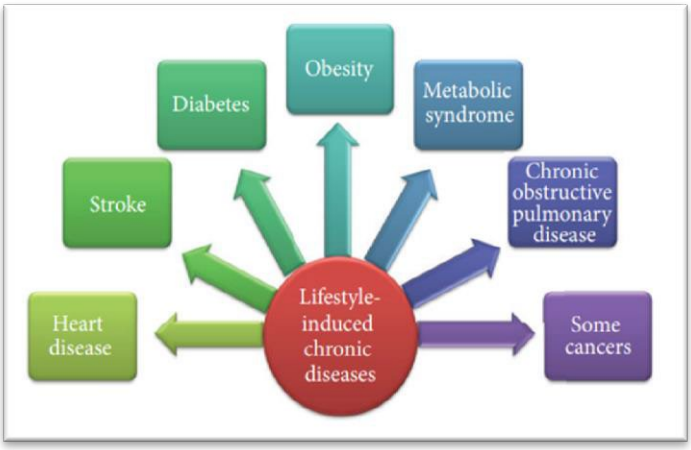


Figure 1: Lifestyle-Induced Chronic Disease

Lifestyle medicine is not a new or alternative medical discipline. lifestyle medicine is considered in the broadest sense as follows: (i) nutrition, as it relates to dietary supplements, medical foods, and functional foods; (ii) physical activity as defined by the entire spectrum of movement, from anaerobic to aerobic, and from mild to vigorous in intensity; (iii) stress management and behavioral modification, as needed, and all the aspects that modulate behavior such as mind-body medicine, psychosocial influences, and social networks; (iv) environmental exposure to contaminants found in air, food, water, and radiation, due to the ubiquitous nature of toxins and their compounding concentration in the environment, leading to the well-recognized increasing toxin burden in physiological systems that relates directly to chronic disease. Personalized lifestyle medicine encompasses a broad array of disciplines in order to effectively prevent and treat disease, including the interface of technological advances with modern medicine discoveries for eventual dissemination into clinical medicine approaches. (Figure. 1).

Over time, chronic illnesses have become more common due to changes in demographics and lifestyle, as well as medical development that have increased survival rates, which, in turn, has led to a rise in an amount of people suffering from chronic disorders. As a result, this cohort of patients requires a greater amount of resources and lifelong costly therapy. In this context, lifestyle medicine is a rapidly growing field that addresses the key aspects of health-related behavior, which are the key causes of chronic conditions, early death, and healthcare costs. Ultimately, lifestyle medicine can ease and improve course of aging and contribute to the goals that have been recognized in geriatric medicine for high quality of life and well-being Eventually, lifestyle medicine (LM) can ease and improve the aging process, and promote targets that have been recognized in geriatric medicine as essential to high quality of life and well-being, resulting in decreasing in disease chronicity, morbidity and disability.

A comprehensive and integrated approach focused on "whole-person health" is becoming a compelling foundation for healthcare providers and systems. This strategy combines a fundamental commitment to prevention with a systematic focus on addressing the underlying and root causes of premature illness, disability, and death [1-12].

In this case, policy formation in the field of personal health protection and promotion is becoming one of the priority tasks of national healthcare systems and the innovative advances in design-driven biotechnology combined with worldwide practice and individual experience have stressed that the main link in the modern healthcare strategy, that might exert reliable control over morbidity, mortality and disabling levels and significantly decrease the cost of treatment for persons-at-risk and for those who had fallen-ill, is Personalized & Precision Medicine (Personalized & Precision Medicine (PPM) (Figure. 2) [13-23,25-27,34-37,42-46,48-56].

PPM as the big change to foresee, to predict and to prevent is rooted in a big and new science that is based on progress in the OMICS portfolio (genomics, proteomics, and metabolomics) and bioinformatics

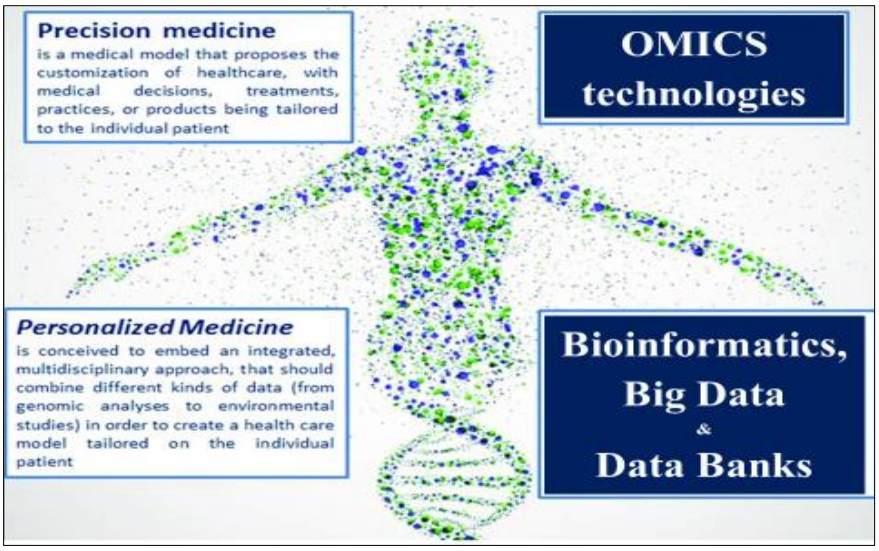


Figure 2: Personalized & Precision Medicine (PPM) Integrated with Bioinformatics and Armed with Data Sets

The medicine of the XXI century being as PPM is able to protect and preserve human health throughout the life. In this regard, an upgraded model of healthcare service, which includes the philosophy, principles and armamentarium of PPM. New ways of organizing those systems based on the different needs of stakeholders' standards are required to meet these challenges. Spanning from the molec-ular understanding of biological phenomena to the implement of computational resources to study the general behavior of living systems, precision medicine is normally conceived to embed an integrated, multidisciplinary approach, that should combine different kinds of data (from genomic analyses to environmental studies) in order to create a health care model tailored on the individual pa-tient. On the other hand, new approaches and techniques have fostered the division of population into many subgroups, which even-tually need different and specific treatments (the so-called stratified medicine), thus paving the way to the decomposition of the universality of human kind, into a myriad of unique variants that will be able to detect individual specificities and therapeutically ad-dress them (Figure. 3A, B).

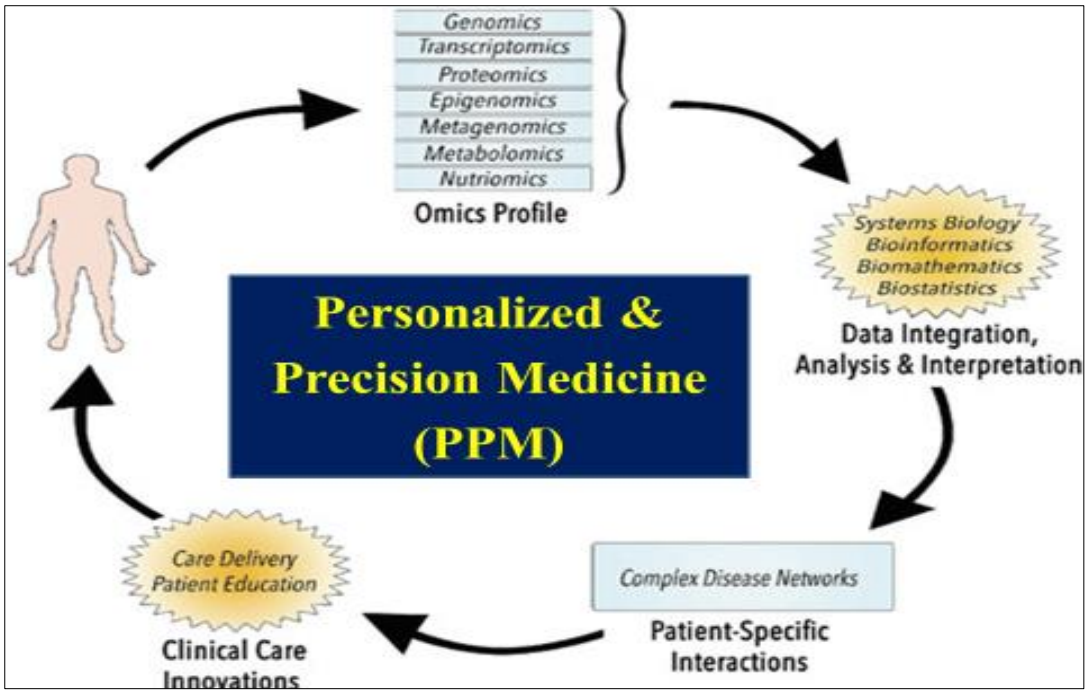


Figure 3A: Role & Impact of OMICS Technologies and Bioinformatics for Personalized & Precision Medicine

Multi-OMICS data are initially collected from patients and/or persons-at-risk and integrated to create their individual molecular profiles. These profiles are then matched to previously defined disease profiles that can guide the selection of treatment. This is achieved either through a match to known biomarkers, omics signatures or network/pathway signatures. The appropriate drug is then selected based on this match, to improve the chance of successful treatment and reduce the probability of side effects.

Bioinformatic analysis of large and complex OMICS datasets has become increasingly useful in modern day biology by providing a great depth of information, with its application to PPM. Data mining of OMICS datasets has enabled the generation of new hypotheses based on differentially regulated biomolecules associated with disease mechanisms, which can be tested for improved diagnostic and therapeutic targeting of chronic diseases. Importantly, integrating multi-OMICS data using a systems bioinformatics approach will advance the understanding of the layered and interactive network of bioregulation that exchanges systemic knowledge to facilitate the development of a comprehensive human body profile.

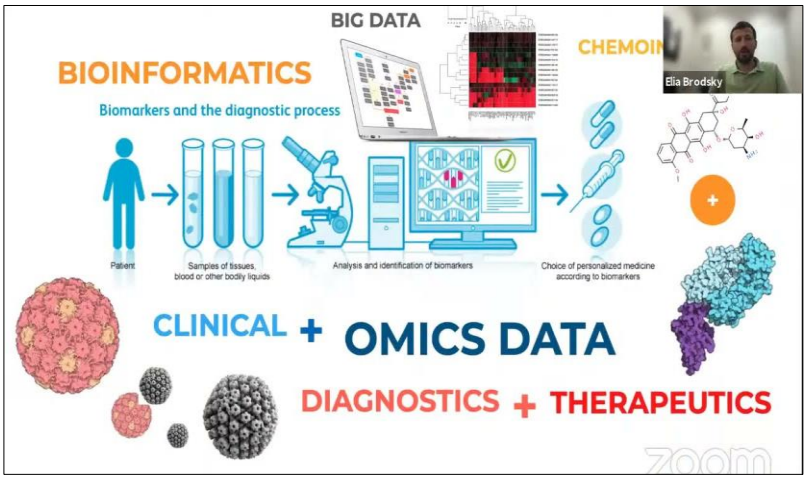


Figure 3B: A Basic Framework of Personalized & Precision Medicine (PPM)

The integration of IT-supported OMICS profiles permits accurate modeling of complex diseases and opens windows of opportunities for innovative clinical applications to subsequently benefit the patient. OMICS data embody a large mixture of signals and errors, where our current ability to identify novel associations comes at the cost of tolerating larger error thresholds in the context of Big Data. Major investments need to be made in the fields of bioinformatics and biostatistics to develop translational analyses of OMICS data and make the best use of high-throughput technologies. Meanwhile, several bottlenecks slow-down the transition from conventional medicine to PPM: generation of cost-effective high-throughput data; hybrid education and multidisciplinary teams; data storage and processing; data integration and interpretation; and individual and global economic relevance. So, there is a strong need for important developments in the analysis of Big Data and forward strategies to accelerate the global transition to PPM.

In which are being introduced into the routine practice to ensure visualizing and detecting of pathology area that was previously unknown to clinicians [57-61]. To achieve the practical implementation of PPM concept into daily clinical practice and healthcare services, it is necessary to develop a fundamentally new approach based upon the pre-early (subclinical), prognostic and predictive recognition of biomarkers long before the disease clinical manifestation. This approach offers a real opportunity to implement preventive and individualized measures that can have a positive influence on population health (Figure. 4).

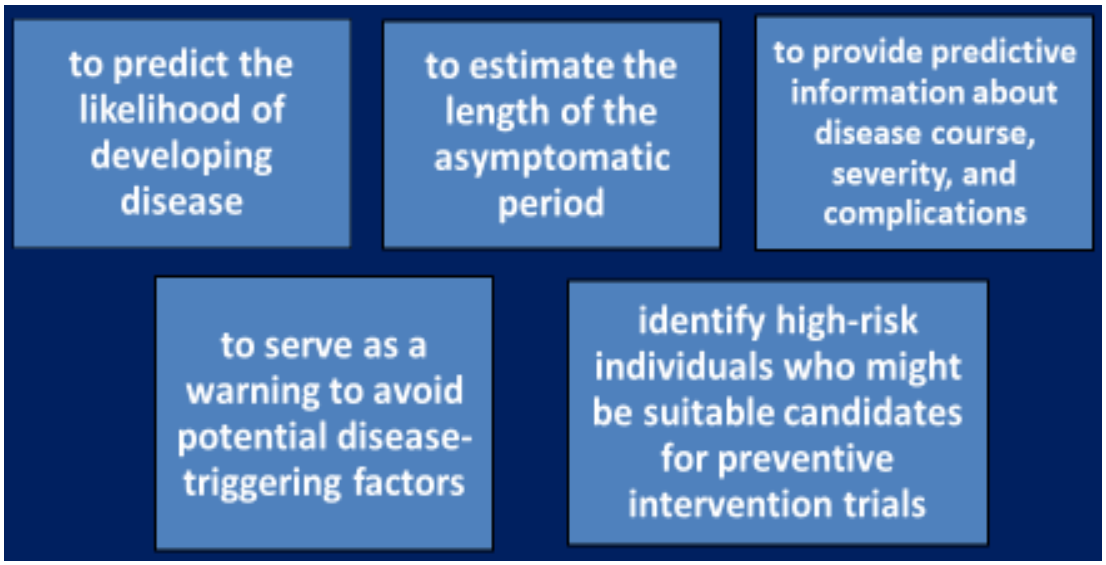


Figure 4: Impacts to be assumed for the Practical Implementation of Predictive Biomarkers into PPM

Predictive biomarkers have emerged as key players in the realm of PPM, revolutionizing disease management and treatment strategies. These biomarkers, derived from various molecular sources such as genes, proteins, and genetic mutations, offer valuable insights into individual treatment responses, enabling tailored therapeutic interventions. A prognostic biomarker is used to estimate the outcome for a patient in the absence of a treatment. A predictive biomarker is used to estimate the benefit for a specific treatment.

A combination of canonical OMICS technologies and integrating interactomics-related one, environmental biomarkers and clinical and dietary data are becoming of great importance to prognose risks of chronic disease progression, possible complications and thus of disabling sin chronic diseases are preceded by a long subclinical (symptom-free) stage or a period of latency [62-64]

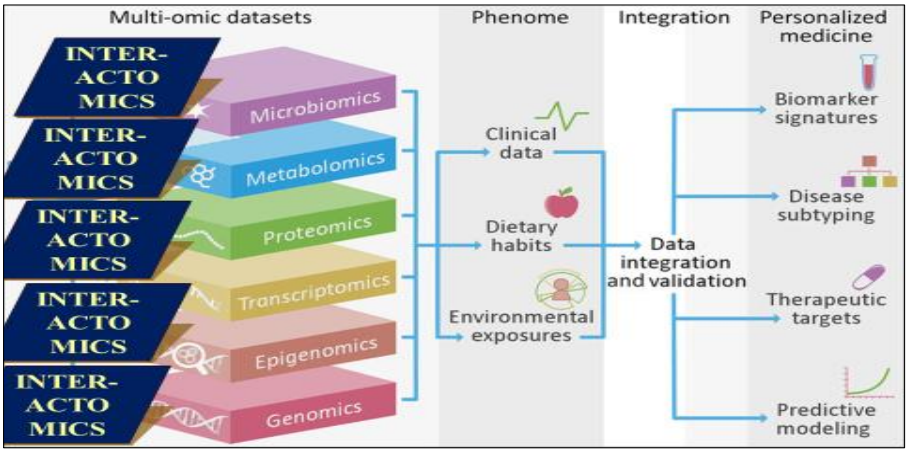


Figure 5A: Multidimensional Understanding of the Disease Biology and Pathogenesis - integration of Multi-OMICS Biological Datasets and Phenotypic Data as Key to the Development of Personalized & Precision Medicine (PPM) in Chronic Diseases

Disease progression and drug response may vary significantly from patient to patient. Fortunately, the rapid development of high-throughput & OMICS technologies has allowed for the identification of potential biomarkers that may aid in the understanding of the heterogeneities in disease development and treatment outcomes. IT-supported and integrated realization of PPM via the discovery and development of biomarkers for disease detection, therapy, and prediction of drug response will involve the integration of technologies which analyze control and disease-relevant samples at the OMICS levels, which will be critical in piecing together targetable mechanisms of action for both drug development and monitoring of therapy in order to fully apply PPM to the clinic.

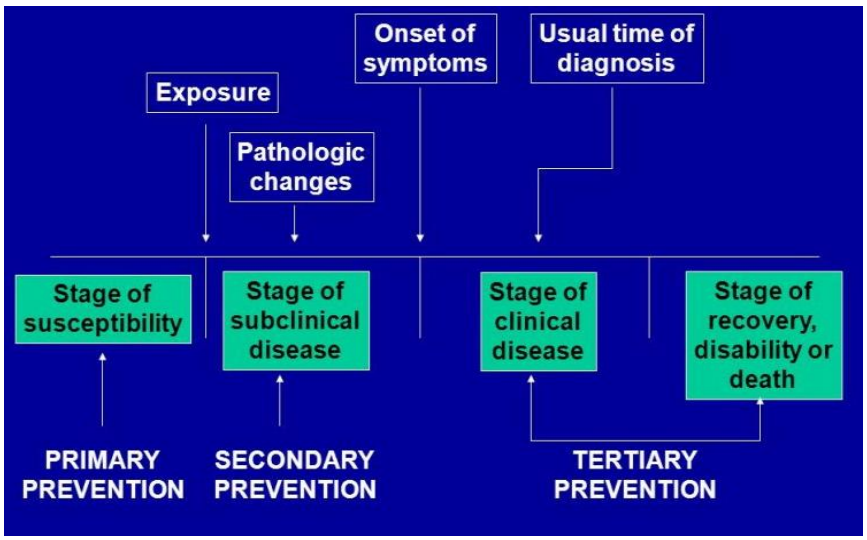


Figure 5B: Natural History of Chronic Multi-Stage Disease – Stages of Disease Continuum

Chronic diseases have a characteristic natural history, although the time frame and specific manifestations of disease may vary from individual to individual and are influenced by preventive and therapeutic measures. The process begins with the appropriate exposure to or accumulation of factors sufficient for the disease process to begin in a susceptible host. After the disease process has been triggered, pathological changes then occur without the individual being aware of them.

This stage of subclinical disease, extending from the time of exposure to onset of disease symptoms, is usually called the incubation period for infectious diseases, and the latency period for chronic diseases. During this stage, disease is said to be asymptomatic (no symptoms).

Although disease is not apparent during the incubation period, some pathologic changes may be detectable with screening methods. Most screening programs attempt to identify the disease process during this phase of its natural history, since preventive intervention at the subclinical (pre-early) stage is likely to be more effective than treatment given after the disease has progressed and become symptomatic. The onset of symptoms marks the transition from subclinical to clinical disease. Most diagnoses are made during the stage of clinical disease. In some people the disease process may never progress to clinically apparent illness. In others, the disease process may result in illness that ranges from mild to severe or fatal. Ultimately, the disease process ends either in recovery, disability or death.

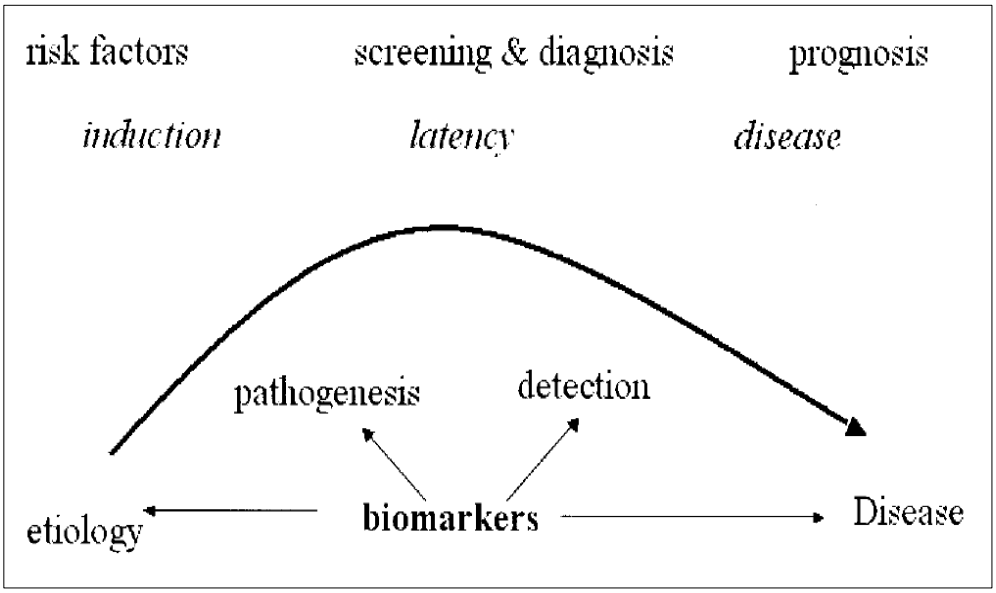


Figure 5C: Disease Pathway and Impact of Disease-Related Biomarkers

Chronic diseases are persistent health conditions that affect our quality of life, increase morbidity and mortality, and are a global challenge. Further, the increasing prevalence of chronic diseases requires the development of new methods for the early detection of these disease-specific biomarkers. The biomarkers have different temporal relationships with the manifestation of disease.

A biomarker is any measurable biological moiety that can be assessed and measured as a potential index of either normal or abnormal pathophysiology or pharmacological responses to some treatment regimen. Every tissue in the body has a distinct biomolecular make-up, which is known as its biomarkers, which possess particular features, viz., the levels or activities (the ability of a gene or protein to carry out a particular body function) of a gene, protein, or other biomolecules. A biomarker refers to some feature that can be objectively quantified by various biochemical samples and evaluates the exposure of an organism to normal or pathological procedures or their response to some drug interventions.

Biomarkers are tools that are used by health professionals to aid in the identification and management of chronic diseases. Biomarkers can be diagnostic, predictive, or prognostic. Several individual or grouped biomarkers have been used successfully in the diagnosis and prediction of certain chronic diseases, however, it is generally accepted that a more sophisticated approach to link and interpret various biomarkers involved in chronic disease is necessary to improve our current procedures.

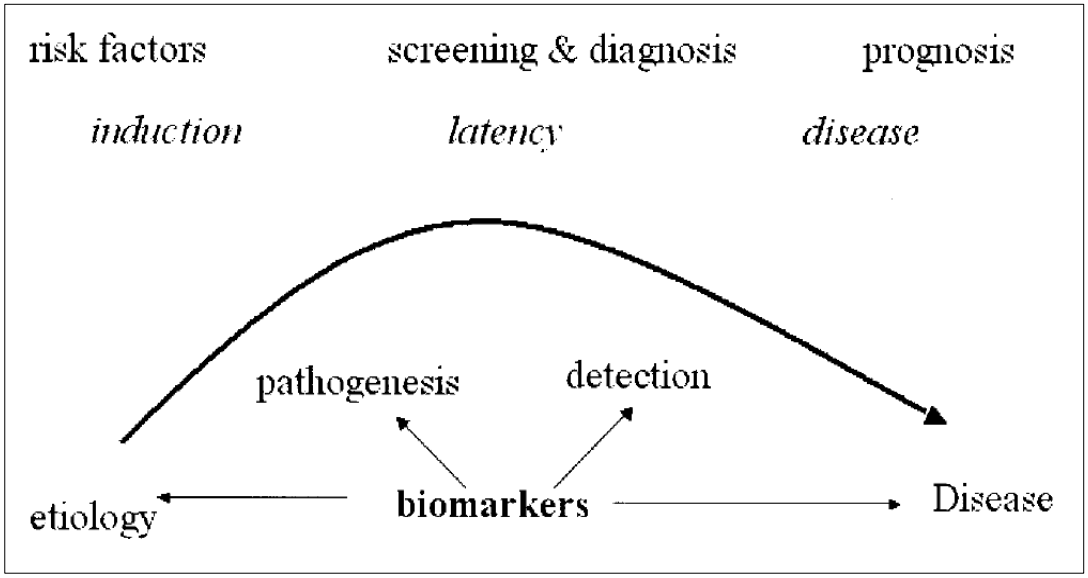


Figure 5D: Natural History of Chronic Multi-Stage Disease – Risk Factors through the Stages of Disease Continuum

Chronic diseases share common risk factors and conditions. Genetic risk factors refer to inherited traits and genetic variations that can increase an individual's susceptibility to specific diseases or health conditions. These factors are determined by a person's genetic makeup and family history. They can include gene mutations or variations that make certain diseases more likely to occur, such as a family history of breast cancer or a genetic predisposition to high cholesterol levels. Behavioral risk factors include lifestyle choices and actions that contribute to the development of chronic diseases. These factors are usually within an individual's control and include behaviors like smoking, unhealthy diet, lack of physical activity, excessive alcohol consumption, and poor sleep habits. Environmental risk factors are external factors in an individual's surroundings that can impact health. These factors include exposure to pollutants, toxins, and hazardous substances and the physical, social, and economic conditions of one's environment. Demographic risk factors are characteristics of an individual's personal and social attributes that influence health outcomes. These factors include age, gender, race, ethnicity, socioeconomic status, education level, and marital status. Demographic risk factors may affect an individual's access to healthcare, exposure to certain environmental conditions, and cultural factors that impact health behaviors and outcomes. Physiological risk factors are aspects of an individual's physical health and bodily functions that can contribute to the development of chronic diseases. Physiological risk factors directly affect the body's functioning and can lead to a higher risk of conditions such as heart disease, diabetes, and stroke.

While some risk factors, such as our age, sex, and our genetic make-up, cannot be changed, many behavioral risk factors can be modified, as well as a number of intermediate biological factors including high blood pressure, being overweight or obese, elevated blood lipids, and pre-diabetes. Societal, economic, and physical conditions influence and shape behaviour and indirectly affect other biological factors. The recognition of these common risk factors and conditions is the conceptual basis for an integrated approach to chronic disease. The leading chronic diseases include cardiovascular diseases, cancers, diabetes, and chronic respiratory diseases. While they are not passed from person to person like infectious diseases, they share many of the same risk factors, explaining why the 'spread of chronic diseases across the globe' has been driven by rapid urbanization and the globalization of unhealthy lifestyles.

An example of a technologies and thus the protocol aimed to demonstrate predictive and subclinical risks as suitable to tumor progression to be monitored, screened and analyzed, is a method of cancer-related genome profiling (named as oncovital screening and monitoring)(Figure. 6A, B).

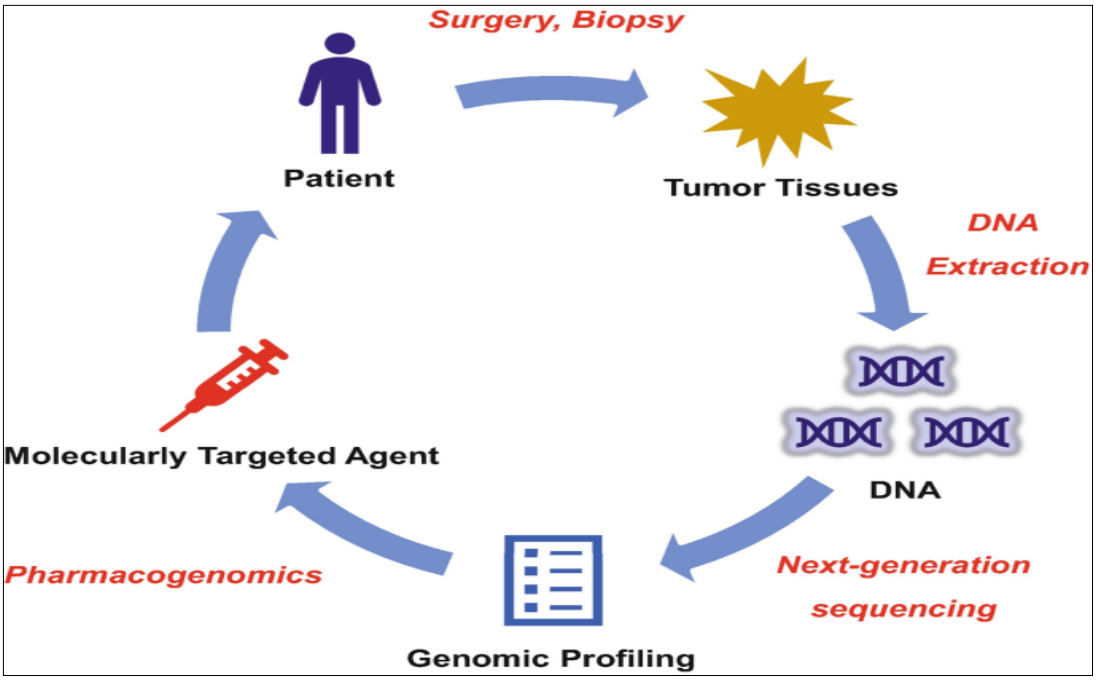


Figure 6A: A Platform for Comprehensive Genomic Profiling in Human Cancers and Targeted Therapy Selection

Because cancer involves the interaction of multiple altered genes and proteins within cancerous cells, as well as within the cells of the surrounding normal tissue, a global approach is needed to capture the status of the 20,000 to 25,000 genes in the human genome.

New technologies are allowing scientists to conduct genome-wide searches and look globally for all of the changes in genes or proteins that contribute to cancer's development and progression. These new approaches are sometimes referred to as genome-wide profiling, or genomic profiling.

Recent innovations in next-generation sequencing (NGS) technologies have enabled comprehensive genomic profiling of human cancers in the clinical setting. The ability to profile has launched a worldwide trend known as PPM, and the fusion of genomic profiling and pharmacogenomics is paving the way for PPM for cancer. The profiling is coupled with information about chemical therapies available to patients with specific genotypes. Comprehensive genomic profiling (CGP) is a next-generation sequencing (NGS) approach that uses a single assay to assess hundreds of genes including relevant cancer biomarkers, as established in guidelines and clinical trials, for therapy guidance. CGP can detect biomarkers at nucleotide-level resolution and typically comprises all major genomic variant classes (single nucleotide variants, indels, copy number variants, fusions, and splice variants). Additionally, CGP can detect genomic signatures such as TMB and MSI (tumor mutational burden and microsatellite instability, respectively), maximizing the ability to find clinically actionable alterations.

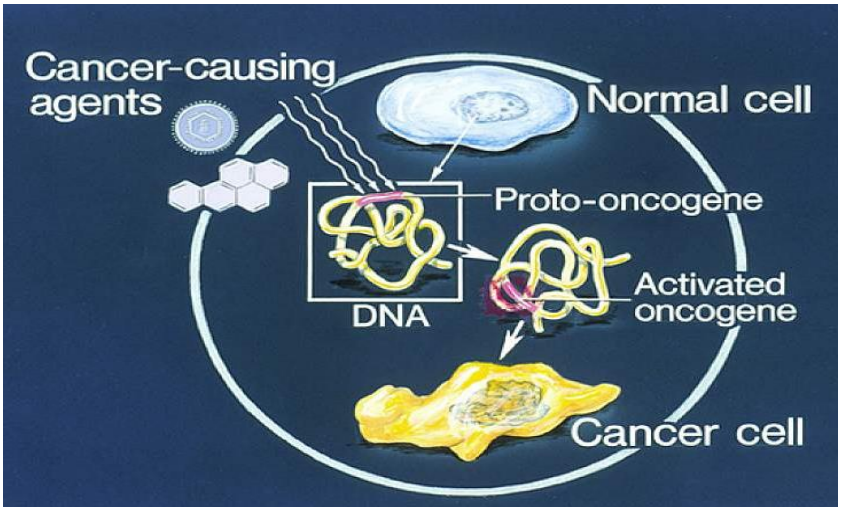


Figure 6B: Genetic Changes Cause Normal Cells to Become Cancerous - Genomic Profiling to Help Prevent and Treat Cancer

The number of druggable tumor-specific molecular aberrations has grown substantially in the past decade, with a significant survival benefit obtained from biomarker matching therapies in several cancer types. Molecular pathology has therefore become fundamental not only to inform on tumor diagnosis and prognosis but also to drive therapeutic decisions in daily practice. The introduction of next-generation sequencing technologies and the rising number of large-scale tumor molecular profiling programs across institutions worldwide have revolutionized the field of precision oncology. As comprehensive genomic analyses become increasingly available in both clinical and research settings, healthcare professionals are faced with the complex tasks of result interpretation and translation.

The implementation of PPM through molecular profiling technologies has increasingly been integrated with standard clinic-pathological evaluations to enhance diagnosis, prognostication, and prediction of clinical outcomes. Although there have been clear successes in the era of molecular characterization, the utility of NGS and other omics-based tests remains unproven on many fronts. A vision for the future of PPM will integrate comprehensive multi-OMICS tumor characterization, dynamic monitoring of liquid biopsy samples, annotation that is automated through advancements in artificial intelligence but guided by experts' clinical input, the enrollment of patients into innovative clinical trials that not only test molecular profile–drug matching but also investigate the utility of different drug-assignment algorithms, and the real-time addition of information from each case to global knowledge bases to enhance precision cancer medicine learning. The path forward in PPM will require not only extension beyond genomics from a technical viewpoint, but also the education and engagement of end-users such as clinicians and patients, the increase of access to genotype–drug matching through adaptive and other innovative clinical trial designs, and the promotion of data sharing to maximize knowledge gain.

The other unique example of subclinical and anticipated risks to be screened and established is Circulating Tumor Dna (Ctdna) And Cells (Ctcs) (Figure. 7A, B).

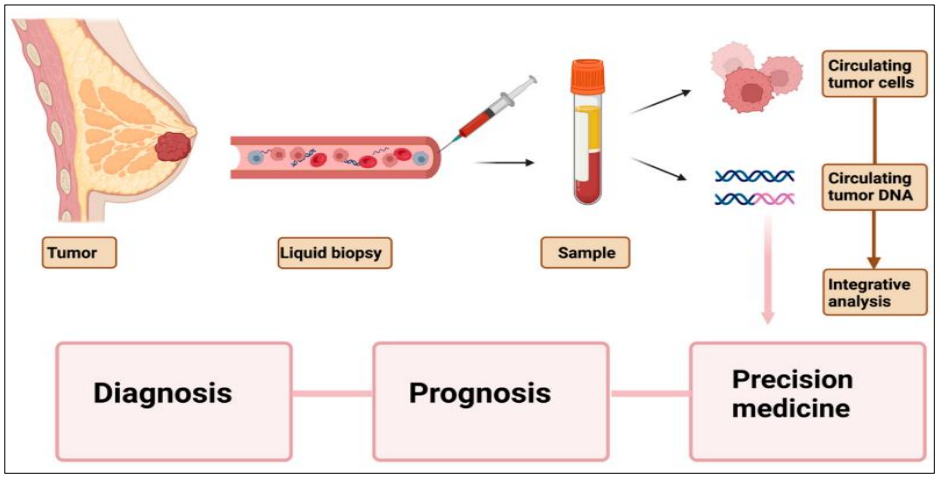


Figure 7A: Peripheral Blood-Based Biopsy for Cancer Diagnosis, Prognosis, and PPM

Circulating blood markers such as CTCs and ctDNA are gaining prominence in cancer diagnosis, therapy monitoring, and development of PPM. However, to bring these liquid biopsy markers into clinical practice, strategies for integrative analyses of these bioanalytes along with existing diagnostic tools need to be developed. Elevated levels of these biomarkers during cancer treatment could potentially serve as indicators of cancer progression and shed light on the mechanisms of metastasis and therapy resistance. Thus, liquid biopsies serve as tools for cancer detection and monitoring through a simple, non-invasive blood draw. These circulating markers have significant prospects for use in assessing patients' prognosis, monitoring response to therapy, and developing PPM.

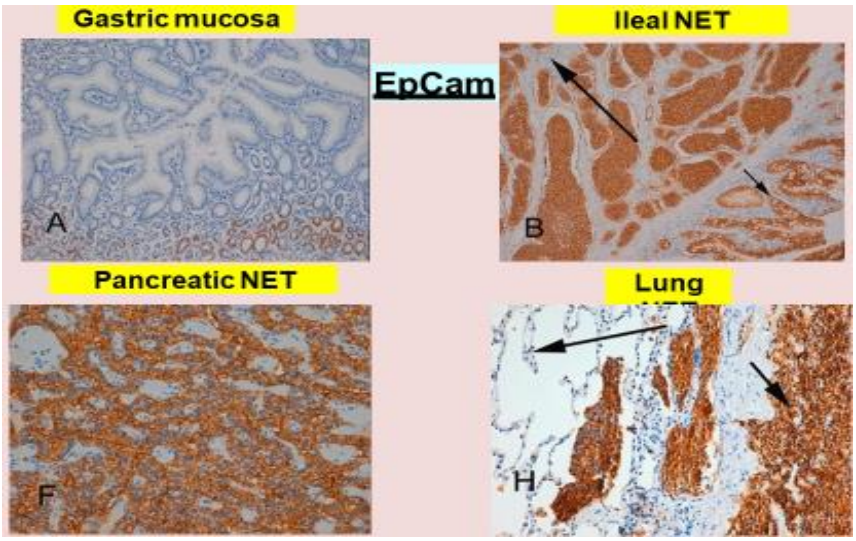


Figure 7B: Circulating Tumor Cells (CTCs)

CTCs as a biomarker of the latest generation would make up a minute fraction of the total number of cells circulating in blood. CTCs are a rare subset of cells found in the blood of patients with solid tumors, which function as a seed for metastases. Cancer cells metastasize through the bloodstream either as single migratory CTCs or as multicellular groupings—CTC clusters. The CTCs preserve primary tumor heterogeneity and mimic tumor properties, and may be considered as clinical biomarker, preclinical model, and therapeutic target. The potential clinical application of CTCs is being a component of liquid biopsy. CTCs are also good candidates for generating preclinical models, especially 3D organoid cultures, which could be applied in drug screening, disease modeling, genome editing, tumor immunity, and organoid biobanks.

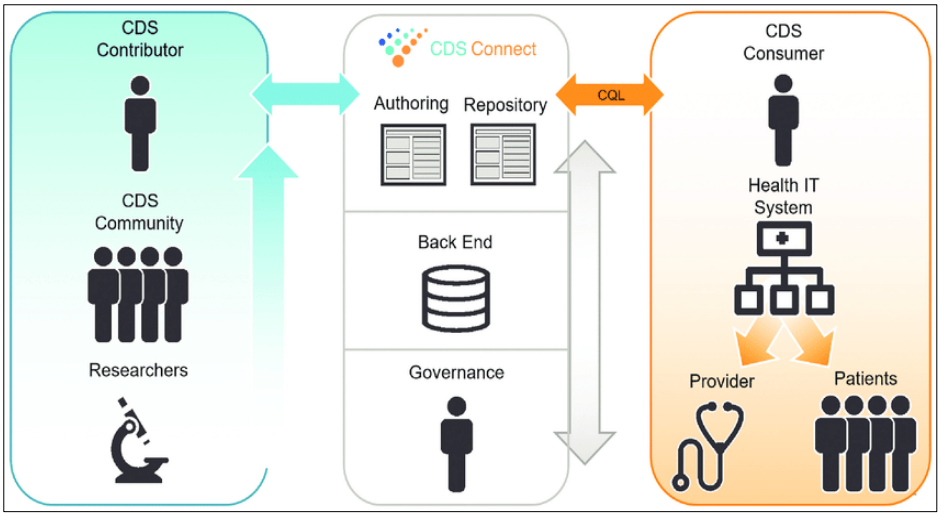
The detection of CTCs is usually dependent on molecular markers, with the epithelial cell adhesion molecule being the most widely used, although molecular markers vary between different types of cancer. Properties associated with epithelial-to-mesenchymal transition and stemness have been identified in CTCs, indicating their increased metastatic capacity. Only a small proportion of CTCs can survive and eventually initiate metastases, suggesting that an interaction and modulation between CTCs and the hostile blood microenvironment is essential for CTC metastasis. Single-cell sequencing of CTCs has been extensively investigated, and has enabled researchers to reveal the genome and transcriptome of CTCs. Herein, we also review the clinical applications of CTCs, especially for monitoring response to cancer treatment and in evaluating prognosis. Hence, CTCs have and will continue to contribute to providing significant insights into metastatic processes and will open new avenues for useful clinical applications. Meanwhile, Cell Search® Method is the only FDA-approved system based on a surface expression of epithelial cell adhesion marker (EpCAM). Studies examining CTCs have the significant potential to detect the fundamental processes of metastases, including the mechanisms involved in extravasation of CTCs from the primary focus of tumor, how CTCs cooperate with blood cells to survive in the circulatory microenvironment, and how CTCs intravasate into the distant metastatic site to initiate new tumors.

Great molecular features of CTCs can greatly promote to recognize targets for anti-metastatic therapies. Only a small percent of CTCs can finally produce metastases. Therefore, research focusing on these highly metastatic CTCs may provide deeper insights into therapeutic targets related to CTCs. CTCs and circulating tumor DNA (ctDNA) are both found in liquid biopsy samples. An exploration of the advantages and disadvantages of each substrate present in the liquid biopsies, and how to better integrate them into clinical practice is needed to achieve more precise diagnoses. Among liquid biopsy methods, CTCs offer significant advantages because isolated CTCs can remain viable, which can optimize CTC-derived explants or three-dimensional organoid cultures used in functional testing or for drug-screening assays. Circulating biomarkers have a large potential in prognosis, therapy monitoring, and PPM for both patients and individuals-at-risk of developing illness (pre-cancer). However, there is an urgent need to advance diagnostic methods in the early stages of cancer when minute liquid biopsy markers are detected.

Advancements in high-throughput technologies has provided new opportunities to understand the pathophysiology of chronic (multi-stage) disease, and these studies have produced large data amounts and information at different molecular levels. The integration of those multi-OMICS data means that thousands of proteins (proteomics), genes (genomics), RNAs (transcriptomics), metabolites (metabolomics) and interactome-based networks (interactomics) can be studied simultaneously, revealing interaction networks between the molecular levels. So, integrated analysis of IT-supported and integrated multi-OMICS data will provide useful insight into the pathogenesis, key therapeutic targets and biomarker discovery [65].

Advancements in multi-OMICS methodologies in combination with bioinformatics and biostatistics have made it possible to

precipitate the discovery and development of specific biomarkers for complex chronic conditions. While there are still many challenges to overcome, current efforts for the discovery and development of disease-related biomarkers will assist in optimal decision-making throughout the course of drug development and improve our understanding of the disease mechanisms. In this context, the use of biomarker-based tests should concider not only increased survival and improved life quality but also enhanced clinical decision support (CDS) & making Which helps to avoid unnecessary therapy and reduce toxicity (Figure. 8A, B).



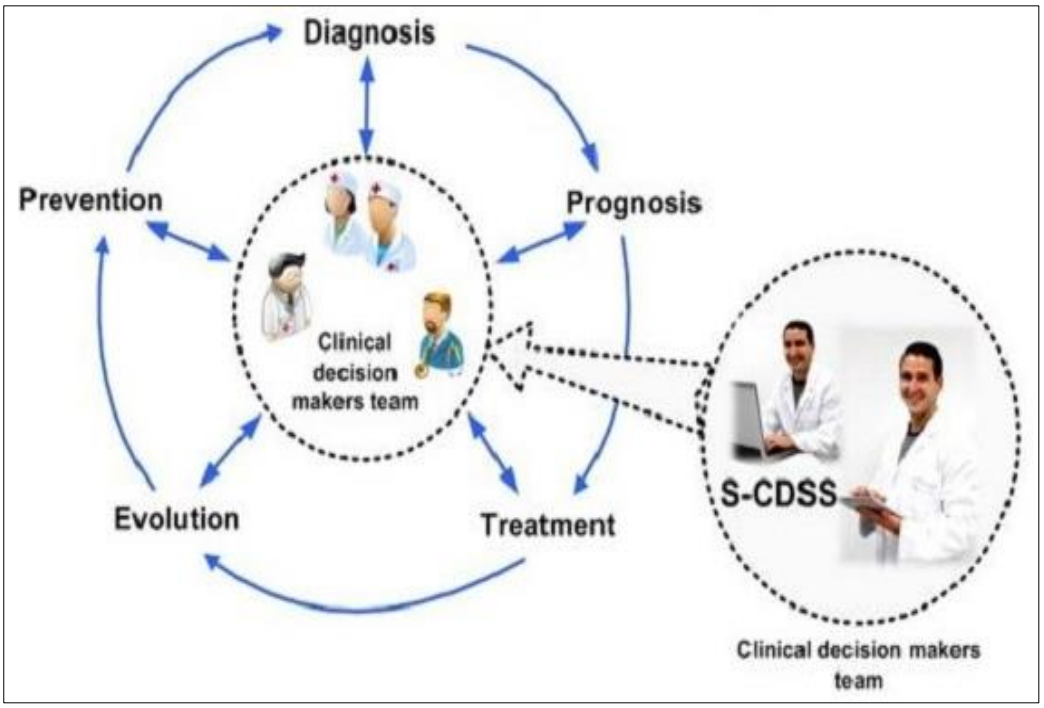


Figure 8A, B: Natural History of Chronic Multi-Stage Disease – Stages of Disease Continuum

Background healthcare systems devote substantial resources to the development of clinical decision support (CDS) largely independently. CDSS are designed to help clinicians with decision-making tasks, such as determining a diagnosis or recommending a treatment for a patient. The process of translating evidence-based practice into useful and effective CDSS may be more efficient and less duplicative if healthcare systems shared knowledge about the translation, including workflow considerations, key assumptions made during the translation process, and technical details. CDSS operates on the principles of data analysis and machine learning. It sifts through vast amounts of patient data to identify patterns and correlations. By providing data-driven insights, it minimizes the chances of oversight or misdiagnosis. Moreover, it streamlines decision-making, saving precious time in critical situations. CDSS also plays a crucial role in preventive healthcare. This proactive approach can prevent the escalation of health issues, reducing the burden on the healthcare system. CDSS is an administrative as well as clinical tool which helps in improving operational efficiency of healthcare practices. It is designed

to assist physicians & other health professionals in clinical decision-making tasks. It is an adaptation of decision support system generally used to aid business management. CDSS deployment helps managing data faster decision-making, and higher workflow efficiency in patient care.

Each decision-maker values the impact of their decision to use PPM on their own budget and well-being, which may not necessarily be optimal for society as a whole.It would be extremely useful and important to create a resource that integrates various data for further treatment and prevention according to the concept of PPM. This is necessary to provide more precision and personalized measures for patients, which will lead to improved treatment outcomes, a reduction in adverse events and more rational use of healthcare resources, including diagnostic, prognostic, preventive and therapeutic (targeted) etc. The CDS structure uses advantage of EHR, data production techniques, clinical databases, domain expert knowledge bases, available technologies and standards to provide decision-making support for healthcare workers. The architecture will work extremely well in distributed EHR environments in which each hospital has its own set of distributed knowledge bases, which is specialized in a specific domain (i.e., oncology), and the model realizes colaboration, integration and interoperability between these knowledge bases. In this context, CDSSs have been hailed for their potential to reduce medical mistakes and increase health care quality and efficiency, as well as been widely promoted for improving clinical outcomes, referring to the practice of medicine based on the best available scientific evidence.

The opportunities of PPM (including diagnostic and theranostics, PPM-guided targeted therapy) are the ways to recommend a kind of protocols being tailored individually and to secure the highest clinical efficacy and minimized adverse effects and reactions whilst being used in preventive or canonical therapeutic modes. Biomarker-based personalized nutrition (compared to drug-driven treatment) can enhance quality of life and longevity by managing chronic conditions, reducing risk factors, and ultimately improving overall wellness. A new approach that could significantly improve the financial sustainability of healthcare systems and enhance treatment outcomes is the personalization of healthcare. It is believed to be more adapted to the emergence of new disease patterns and the growing prevalence of certain chronic illnesses (e.g., cancers), caused by trends like aging and unhealthy behaviors. So, a combination of genomic, phenome- and exposome-related biomarkers is becoming of great importance to be applied in PPM and need to be translated into the routine practice to predict risks of the disease chronification and thus of disabling. Meanwhile, healthcare specialists have identified the main barrier to the PPM implementation as a lack of medical guidelines. Therefore, it is essential to develop best practices and guidelines to support the implementation of precision and preventive medicine. At the same time, public health recommendations for PPM-driven lifestyle modifications, including diet and physical activity, are being widely promoted for disease prevention and treatment. PPM, therefore, refers to a recently developed approach in which an individual's health metrics from point-of-care diagnostics are utilized to create Lifestyle Medicine-oriented preventive, prophylactic, therapeutic, and rehabilitative strategies aimed at improving health outcomes in managing and potentially curing chronic diseases. PPM has drastically changed and is keeping on changing the landscape of healthcare. In reality, PPM is the new revolution in medicine which is dramatically modifying the traditional paradigm in medicine with huge consequences for health care systems. And putting PPM-tools in a public health perspective requires an apprehension of the current and future public health challenges. PPM has fundamentally transformed and is keeping on changing the landscape of healthcare. In fact, PPM is a revolutionary transformation in medicine that significantly shifts the traditional healthcare paradigm, with profound implications for the healthcare system. The implementation of PPM tools within the context of public health requires an understanding of the current and future challenges in this field. Besides, PPM is expected to enable future healthcare professionals to more reliably control morbidity, mortality, and disability rates. It will also significantly reduce costs and improve the effectiveness of treatment for those who have fallen ill, already diseased or persons-at-risk. PPM represents a new paradigm in healthcare management, primarily based on a precise approach to prevention, pre-clinical diagnostics, and the targeted delivery of drugs to tissues with exceptional precision levels.

In this context, the healthcare system model is being refined and transformed, incorporating the philosophy and tools of PPM aimed at detecting the subclinical stage of diseases. PPM focuses on preventive and predictive measures for pathologies, which contribute to the creation of personalized strategies for managing a healthy lifestyle, reducing morbidity rates, and enhancing the working capacity of the population. Achieving the goals based on the values of PPM requires a combination of the latest fundamental research with clinical medicine, accompanied by the implementation and promotion of new next-generation translational applications. It is important to note that there is an opportunity for strategic partnerships between regulatory authorities, the government, and various sectors such as economic, academic, medical, and business.

The PPM based system approach is a definitive method that will significantly impact the global healthcare systems modernization. Our primary challenge is to create robust platforms, both legally and economically, for advanced medical services using cost-effective risk assessment models, followed by personalized preventive treatments focused on the early (preclinical) stages of chronic diseases. This approach will dictate a series of questions and comments that should be utilized in implementing PPM-related resources into daily clinical practice, including (Figure: 9).

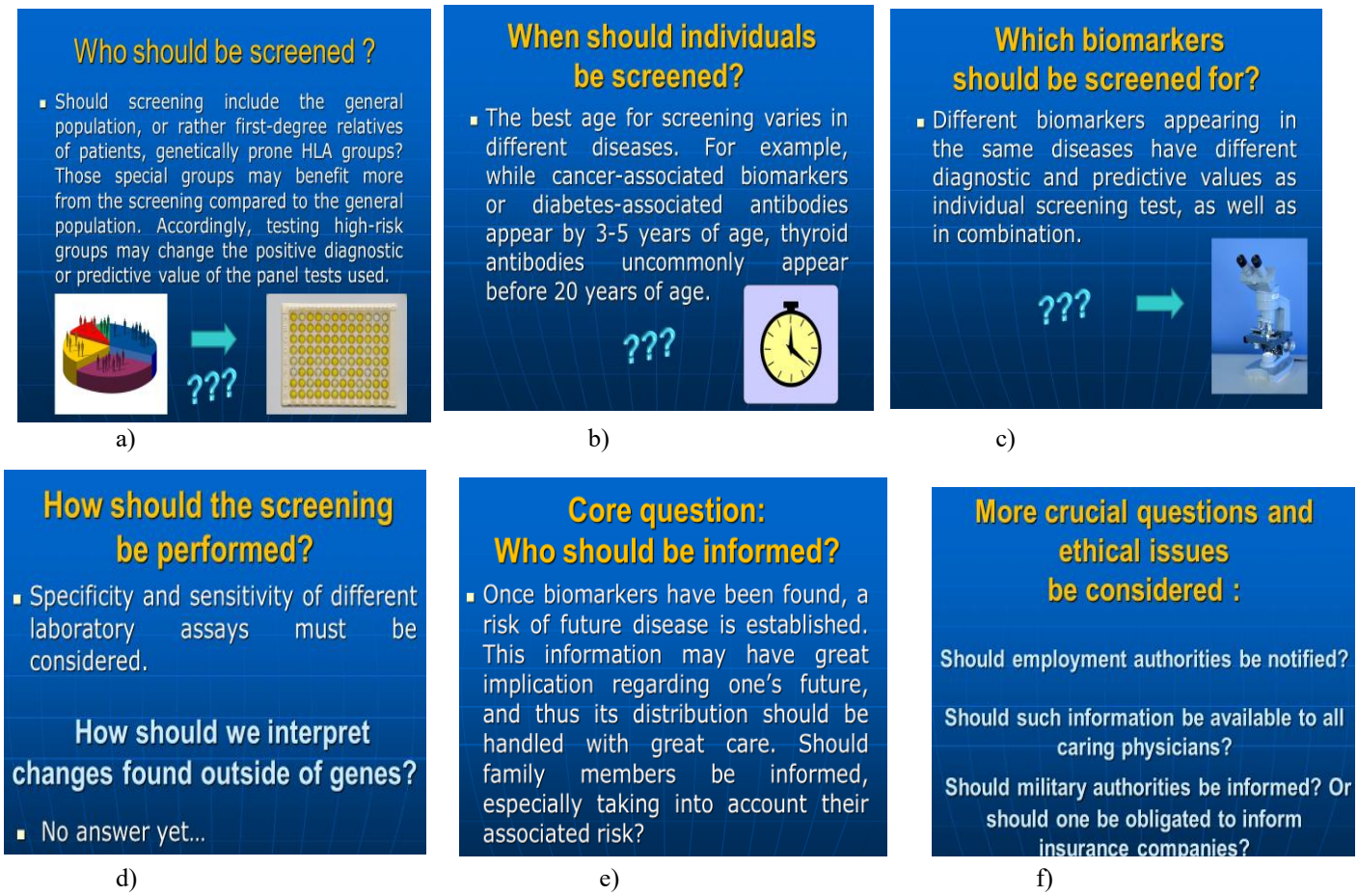


Figure 9: A significant strategy for integrating PPM-related resources into clinical practice for healthcare professionals should include:

a) A broad and unique network of clinicians and hospitals to facilitate the clinical development and advancement of PPM-driven solutions. (ii) Retrospective and prospective access to research-grade clinical biospecimens to support biomarker discovery and validation;

b) Retrospective and prospective access to research-grade clinical biospecimens to support biomarker discovery and validation

c) leading edge integrated technology platforms for biomarker discovery and validation: OMICS-based approaches, immune monitoring and bioinformatics;

d) new diagnostic, theranostic, predictive and prognostic biomarker applications for full clinical applications spectrum in managing chronic conditions;

e) integrated electronic solutions to support decision-making in the clinical healthcare system with conditional reimbursement for innovative targeted drugs and diagnostics based on economic assessment of health and cost benefits in PPM-guided healthcare system;

f) Approval and integration of novel PPM-driven solutions within an enhanced healthcare system.

As you may notice, healthcare systems are facing a multitude of fundamental challenges. The emergence of PPM in practice will depend on the interaction between various stakeholders, whose needs would require new approaches to organizing systems in order to address these challenges. In turn, medicine is undergoing significant changes, shifting from a morphological and phenotypic orientation to a molecular and genotypic one, which emphasizes the necessity of prediction, precision and prognosis, the discussion about the importance of genome-based information and technologies for the healthcare system as a whole, and especially for public health, is still in its early stages. Thus, collaborative work is identified as a key factor in taking action on the social determinants of health (Figure: 10).

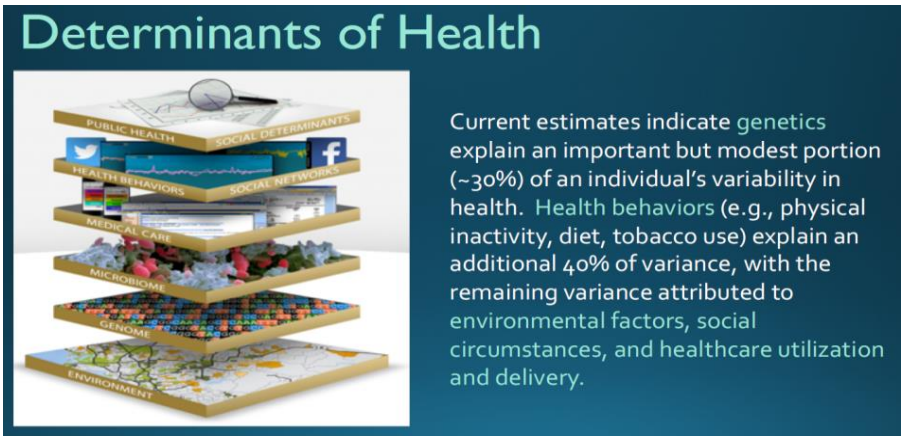


Figure 10: Determinants of Health

Many factors combine together to affect the health of individuals and communities. Whether people are healthy or not, is determined by their circumstances and environment. To a large extent, factors such as where we live, the state of our environment, genetics, our income and education level, and our relationships with friends and family all have considerable impacts on health, whereas the more commonly considered factors such as access and use of health care services often have less of an impact. Because of the devastating health effects of social determinants of health (SDoH), it is important for the primary care provider to assess and monitor these types of stressors. This can be done via surveys, geomapping, or various biomarkers. To date, however, each of these methods is fraught with obstacles. There are currently are no validated "best" SDoH screening tools for use in clinical practice. Nor is geomapping, a perfect solution. Although mapping can collect location specific factors, it does not account for the fact that patients may live in one area, work in another and travel frequently to a third.

Social determinants of health (SDOH) are the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks. The social determinants of health (SDH) are the non-medical factors that influence health outcomes. They are the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies and political systems. The SDH have an important influence on health inequities - the unfair and avoidable differences in health status seen within and between countries. In countries at all levels of income, health and illness follow a social gradient: the lower the socioeconomic position, the worse the health. Because this requires comprehensive actions from stakeholders whose collaboration must be coordinated and precise, decisions need to be made to facilitate understanding and awareness of the social determinants of health and the social gradient. Additionally, it is essential to involve various sectors and professions to address the present time challenges, clinical specialists, PPM presents a significant challenge for clinical practice and medical education. Companies in biotechnology, biopharmaceuticals, and medical insurance are already integrating PPM and PPM-based public health models into their development strategies. Meanwhile, payers are currently skeptical and may justifiably fear the constantly rising costs. However, they will also embrace this new era if they are offered solutions that combine targeted diagnostics, precise treatments, and digital tracking tools. Ultimately, they will pay less for ineffective treatments and over diagnosis and may have fewer specialist consultations and treatments due to targeted preventive measures. With this development strategy, all future healthcare professionals should be trained to provide patient-centered care as part of multidisciplinary teams.

In this sense, all healthcare professionals of the future should be educated to deliver patient-centric care as members of interdisciplinary teams (Figure. 11).

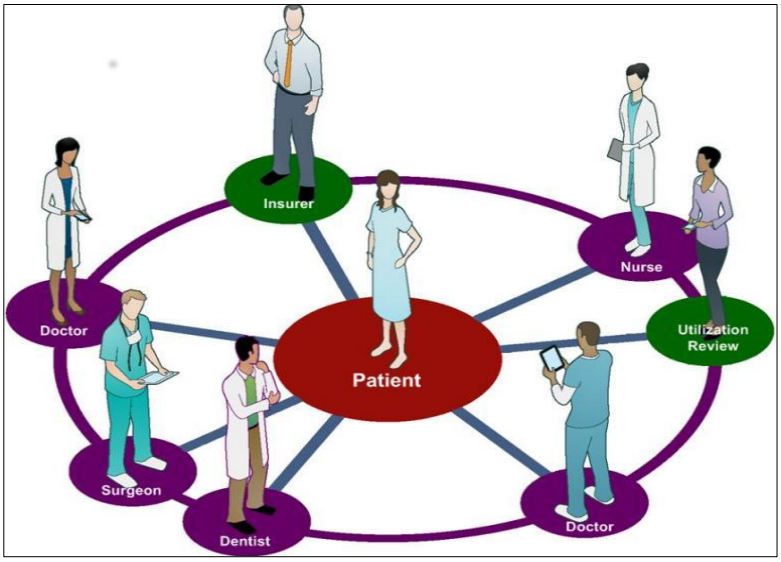


Figure 11: Multidisciplinary Patient-Centered Team Approach in PPM-Guided Communication and Optimal Care

In the domain of healthcare, one facet that has garnered significant recognition and is widely adopted is the interdisciplinary team. Utilizing this approach, healthcare becomes a collaborative exercise that leverages the unique skills of various professionals to provide optimum care to patients. Multidisciplinary patient-centered team approach promotes communication and optimal care. An interdisciplinary team plays a pivotal role in the healthcare sector.

The cumulative expertise and broad perspective that such a team offers are key components in addressing today's complex healthcare challenges. Interdisciplinary teams facilitate comprehensive care by integrating knowledge from various healthcare disciplines. This integrated approach allows the formation of a cohesive and holistic care plan for patients. It enables better communication among healthcare professionals, thereby encouraging consensus on treatment strategies and improving patient outcomes. By ensuring diversity in skill sets, it promotes innovation in healthcare solutions. Interdisciplinary teamwork emphasizes a patient-centered approach, prioritizing the needs and preferences of the patient.

The specific composition of an interdisciplinary team in nursing can be highly flexible, encompassing various healthcare professionals based on the needs and care plans of the patient. Teams may alter over time to seamlessly adapt to the evolving health needs of the patient. Interdisciplinary teams have found widespread application within the healthcare industry. They are often considered synonymous with the best-practice models in areas such as chronic care, geriatric care, palliative care, and rehabilitation. Interdisciplinary teams are also becoming increasingly prevalent in managing mental health conditions effectively.

Emphasizing evidence-based practice, quality improvement approaches and bioinformatics.

PPM and public health require a unified interdisciplinary approach for the effective and safe implementation of new technologies in diagnosis, prediction, prevention, and therapeutic, prophylactic, and rehabilitative methods aimed at complete healing. Thus, PPM-based health policy on the PPM approach could become the primary resource for utilizing PPM therapies within modern healthcare systems, ensuring population well-being and improving public health. Based on our experience, a symbiotic relationship between PPM and public health may exist. This approach is only feasible with data integration across various influence levels and the proper use and interpretation of these unique data sets. Therefore, applying PPM tools in the context of public health requires understanding current and future challenges in this field. The principles of PPM and efforts to address health issues in a timely manner can be applied to public health. However, this will require careful analysis and collaborative efforts to keep population health needs at the forefront of all PPM discussions and investments.

It is important to remember that, regardless of the diagnostic tools used, the final decision regarding a patient will have to be made by the physician. Therefore, closer collaboration between the physician and the patient (or person-at-risk) will replace the classic physician-dominated dialogue with a more effective collaboration between physician and patient. Thus, the current "physician-patient" model should gradually be replaced by a "medical advisor-healthy person-at-risk" model. Biological and medical data from individuals can be analyzed together with environmental data to determine the factors affecting health and well-being.

This mentioned approach should be based on postulates that will transform the fundamental culture and social mentality! Recognizing the need for care focused on prevention and coordination, the concepts of the patient-centered medical home, patient-aligned care teams (PACTs), and the chronic care model were developed [66-67].

These approaches emphasize patient engagement, shared decision making, and team-based care. However, none of these

approaches have outlined a clinical workflow that systematically and proactively operationalizes these models with a risk-based personalized care approach. Personalized health planning offers a clinical workflow that operationalizes all these features.

In this context, personalized goals and objectives are present at every stage of disease onset and progression, leading to the development of a Personalized Health Plan (PHP) that addresses lifestyle, risk modifications and disease management, and later, Personalized Health Management & Wellness Program (PHMaWP) [68-77].

It is important to note that the integration of PPM resources and data-driven health management provides a roadmap for PPM-guided healthcare. This approach confirms the data-driven efficacy, individualized lifestyle coaching for health promotion and presents a comprehensive view of human health through the integration of OMICS-based, digital health, and clinical data.

Among the essential PPM-related resources relevant to managing individualized health programs are:

a) genetic predisposition screening and disease-related debut prognostication;

b) individualized genomic risk screening and quantification (including subclinical and symptom-free stages of disease which cannot be diagnosed and confirmed through the application of canonical diagnostic armamentarium);

c) Human post-therapeutic reactions and their prevention and correction via biomarkers screening including bioindicators of the disease evolution and complications and prognostication of the responses to treatment associated with pre-selecting of the proper therapeutic and surgical manipulations.

Thus, the Health and Wellness Program for Seniors (HWePS) might be considered as a technology-enhanced, multi-level, integrated health equity intervention model HWePS includes four key components: a health literacy intervention based on assessments of individual and community needs; personalized (self-) care management involving nurse coaching and peer support; community initiatives for promoting healthy living and aging; and information and communication technology (ICT) systems [78]. As a multi-level health equity project, HWePS targets individual- and community-level factors that contribute to health disparities in later life. It will provide insights into the effectiveness and implementation of an integrated, multi-level preventive community care model, which, in turn, can help improve the health outcomes of older residents and reduce disparities in underserved urban communities.

In this context, the use of IT-processed OMICS -information in clinical care- could significantly reduce neonatal morbidity and mortality and enhance outcomes for this population. Genetic testing has proven to be both feasible and clinically useful. As such, genetic testing can offer valuable insights into an individual's genes, their products, and chromosomes, making it a vital component of the PPM toolkit. It can demonstrate its relevance to specific clinical outcomes, such as survival or tumor response, by analyzing pre-treatment samples from patients and/or at-risk individuals who have undergone uniform treatment interventions. Various testing platforms are available to accelerate the development of these technologies, including [79-81]:

a) Canonical Diagnostic Testing - to secure a person's choices about health care and disease management;

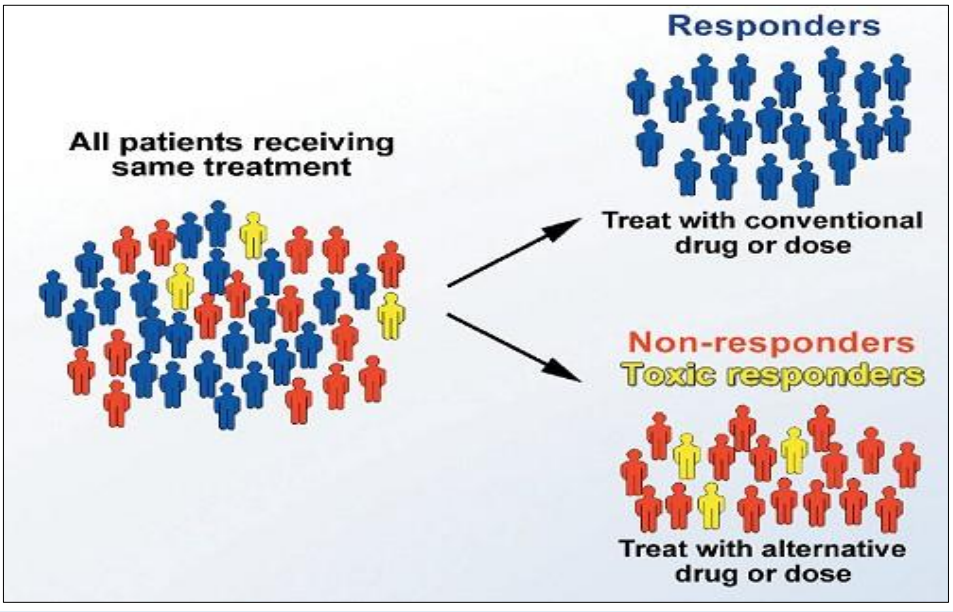
b) Carrier Testing - to detect individuals who carry a single copy of a gene mutation that causes a genetic disorder - this type of testing is offered to individuals who have a family history of a genetic disorder and individuals from certain ethnic groups with a higher risk of specific genetic or pre-cancer conditions;

c) Predictive and Prognostic Testing;

d) Newborn Screening - to identify genetic disorders and other conditions, including monogenic and orphan diseases;

e) Prenatal Testing (NIPT) - to identify genetic or chromosomal changes in a fetus before birth to secure the national biosafety;

f) Pharmacogenomics testing (Figure. 12A,B) - focused on personalizing drug therapy to the most effective and safest dosage for an individual patient, enhancing both clinical efficacy and individualized safety;



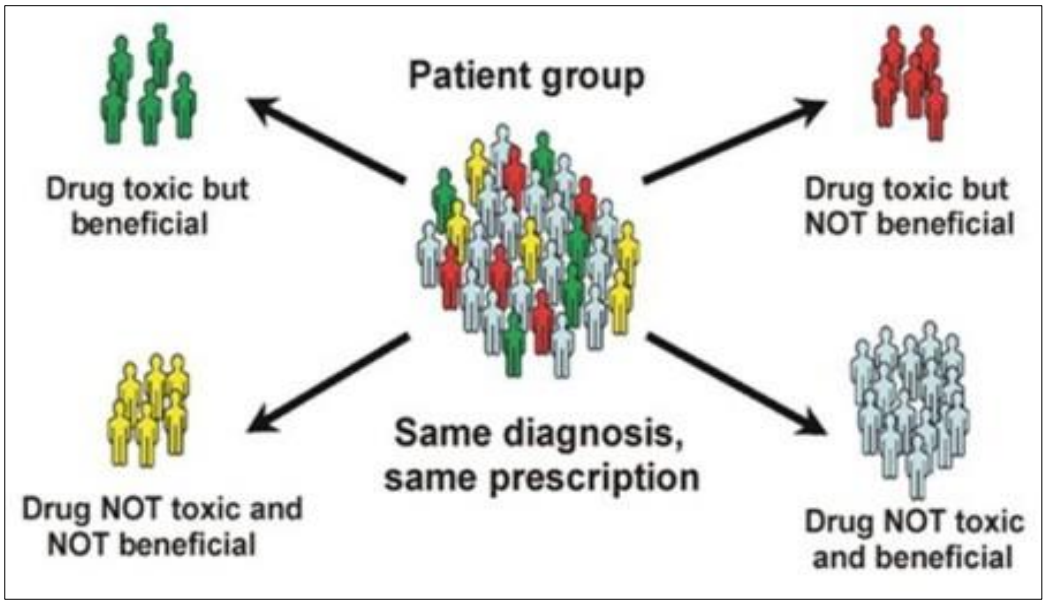


Figure 12A, B: The Alternatives of the Pharmacogenomics-Related Testing

Pharmacogenetic testing provides information about your genes to help your health care provider choose the medicine and dosage that are the "best fit" for you. The tests use a sample of your saliva (spit), blood, or cells swabbed from your cheek. Pharmacogenomics is an important example of the field of PPM, which aims to tailor medical treatment to each person or to a group of people. Pharmacogenomics looks at how your DNA affects the way you respond to drugs. In some cases, your DNA can affect whether you have a bad reaction to a drug or whether a drug helps you or has no effect. Pharmacogenomics can improve your health by helping you know ahead of time whether a drug is likely to benefit you and be safe for you to take. Knowing this information can help your doctor find medicine that will work best for you. Pharmacogenetic testing is a type of PPM, which uses information about your genes, environment, and lifestyle to find out which approaches to disease treatment and prevention will work best for you.most effective and safest dosage for an individual patient, enhancing both clinical efficacy and individualized safety;

g) Nutriogenomic testing - plays an important role not only in treating diseases and illnesses but also in promoting health and wellness through both basic and clinical research; and it is critical for the future of both personalized nutrition and precision healthcare [82-83].

The landscape of genomic testing has significantly with the advent of direct-to-consumer (DTC) genomic testing to secure genetic risk prediction tools for a wide array of common diseases and thus the national health stability [84-86]. DTC testing marketed directly to consumers without the involvement of healthcare providers, is expanding the number of people who can access genetic testing of their DNA. These test sare designed to offer information about an individual's genetic risk for specific medical Conditions.

Such information can help individuals (including those at risk) make informed decisions about their health, lifestyle choices, and facilitate discussions with healthcare providers. DTC tests enable genetic testing without medical oversight, such as without physician referrals and result interpretation. Thus, these approaches allow for free access to genetic profile information, increasing personal freedom, but also introduce the risk of false (positive and negative) or misinterpreted results, along with potential health and psychological consequences. Additionally, low-risk general wellness tests are offered for purposes considered general wellness by the FDA (e.g., tests predicting athletic abilities or assessing a child's potential in specific sports).

The main goal of PPM is to extend healthy life and increase the working-age population, while simultaneously and promptly detecting pathological changes in the body and implementing targeted measures to prevent diseases. Implementing PPM requires significant effort until the current "physician-patient" model is gradually replaced by a new model of "medical advisor-healthy person-at-risk." This underscores the need to develop global scientific, clinical, social, and educational projects in the field of PPM to define the scope of this new domain. To fully harness the unique potential of PPM and PPM-based Public Health, new generations of precise diagnostic, predictive, prognostic, preventive, therapeutic, rehabilitative, and digital products must be aligned with new thinking and practices among all participants in the healthcare system. Consequently, healthcare providers, public policy sectors, and consumer industries will need to develop new and creative models and products. Undoubtedly, future generations will view the 21st century as the era when medicine became preventive and personalized, and its outcomes became predictive and guaranteed.

In this context, it is essential to strengthen the functions of national and local governments, particularly regarding a comprehensive understanding of the root causes of health disparities, participatory governance that engages and empowers

individuals and communities, and adopting new roles in creating conditions where power is shared, and health and well-being are co-produced with citizens and communities. This requires concerted actions by individuals, agencies, and all levels of government that can affect the social determinants of health, fostering whole-system approaches to addressing health inequities.

Since recently developed economical models clearly demonstrate the efficacy of PPM, if introduced as the integrative medical approach into the healthcare services [87, 88].

Current paradigms for PPM-guided healthcare and public health initiatives are being challenged by several macroeconomic trends that will drive the convergence of healthcare and life sciences ecosystems. This paradigm shift will transform translational research and put health sciences firmly on the path toward delivering personalized healthcare. The intelligent use of longitudinal healthcare data and the potential of next-generation gene sequencing as a unifying platform that accelerates drug discoveries and ushers in the biomarker era will push personalized healthcare forward. Many advances have been made possible by the growing power of healthcare information technology. However, although many current systems excel at performing and automating the transactional tasks they were designed for, they are often siloed and proprietary, lacking the ability to integrate, analyze, and visualize data comprehensively across populations and at the individual level. The new healthcare delivery paradigm will require an unprecedented collaborative environment that provides data for an integrated view. This will necessitate investment in context-specific analytics platforms that leverage valuable data to support translational research.

Some observations: individuals under regular monitoring that helps detect pathological shifts at subclinical stages have a higher life expectancy and can remain functional for 8–15 years longer than those receiving traditional treatment. This means society could save more than $20,000–40,000 per person annually. At the community level, annual savings per individual may range from several thousand to several tens of thousands of dollars. In oncology, for example, a 10 percent reduction in cancer incidence could translate into savings of $4.4 trillion for society.

This highlights the need for investments in high-tech OMICS technologies and context-specific analytics platforms to transform transactional data already generated from clinical care and trials into actionable information that accelerates discoveries and their implementation into practice. Today, designing translational applications for PPM is a grand question; tomorrow it will become a clinical decision support issue in the PPM-guided healthcare environment to reward the latter and reimburse for value. In practice, a new buzzword has emerged in the health sciences lexicon: PPM-based public health. Initial efforts toward PPM-based public health are underway, but much work remains to establish a robust evidentiary foundation for its application. PPM and PPM-based Public Health require a transdisciplinary approach to support the safe and effective deployment of new enabling diagnostic and therapeutic technologies, emphasizing not just treatment but cure! Thus, this necessitates novel training, as society is in urgent need of widespread dissemination of new systemic thinking. With the creation of new educational platforms in balanced proportions, rather than a primitive physician, there will emerge a medical artist capable of enriching standard medical practices with creative elements to provide patients with genuine hope for survival and individuals at risk with confidence in disease prevention. This justifies the development of global scientific, clinical, social, and educational projects in the PPM field to define the new branch's content.

The next decade will provide a window of opportunity to establish infrastructures worldwide that will enable scientific advances to be effectively and efficiently translated into evidence-based policies and interventions that improve population health. Policymakers now have the opportunity to protect consumers, monitor the implications of OMICS technologies, IT algorithms, and Big Data-related analytics for health services, and ensure that OMICS-guided diagnostic and therapeutic advances are harnessed to prevent disease and enhance health.

We have a chance to prepare public health professionals, the public, and policymakers for the forthcoming changes. The examples presented illustrate approaches for national, European, and international institutionalization of public health genomics aimed at addressing these challenges.

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