

REVOLUTIONIZING HEALTHCARE INTEGRATING GENOMICS TO TRANSFORM PRECISION MEDICINE

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1. Introduction

1.1. Genomics and Precision Medicine:

Precision medicine, commonly referred to as personalized medicine, is one of the most effective methods for treating illnesses for which a workable medication or cure is not yet available. The study of an organism's entire genome is known as genomic science, which incorporates concepts from genetics. Genomic techniques include recombinant DNA, DNA sequencing techniques, and bioinformatics to sequence, assemble, and study genome structure and function. It considers all of an organism's genetic composition, as opposed to only as opposed to "classical genetics," which only takes into account one gene or one gene product at a time. Moreover, genomics focuses on interactions other than those between loci and alleles within the genome, such as epistasis, pleiotropy, and heterosis (Figure 1). Since Fred Sanger's groundbreaking work and more recent next-generation sequencing technology made full DNA sequences for whole organisms available, genomic science has profited from this (Bentley et al., 2008; Wishart, 2016).

In the 1970s and 1980s, Fred Sanger's group developed techniques for genome mapping, sequencing, data storage, and bioinformatics assessments. The human genome project, a very successful global cooperation that saw the publishing of the whole human genome sequence in 2003, was made possible by the work completed in the 1980s. The speed, volume, and affordability of genome sequencing have all significantly improved as a result of the development of next-generation sequence technology. Additionally, hundreds of life-science databases and projects are now able to help scientific study because to advancements in bioinformatics. These databases include well-organized and stored data that is easy to search, compare, and assess (Bentley et al., 2008; Gauthier et al., 2019).

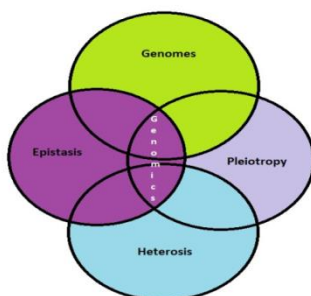


Figure 1. Genomics studies the genomes of whole organisms and other intragenomic interactions (Bentley et al., 2008)

Precision medicine, often known as precision health, represents an innovative strategy for comprehending health and illness through individual patient data. This data encompasses medical diagnoses, clinical characteristics (such as disease severity and functional limitations), biological examinations.

The term "precision medicine" has changed over time, therefore its origins are not totally recognized (Phillips, 2020). But Blood transfusions were revolutionized by the early 1900s discovery of blood types, which made it possible to match donor and recipient blood types and avoided complications resulting from incompatible donor and recipient blood (Dance, 2016; Giangrande et al., 2000; R. J. N. Hodson, 2016). One of the earliest medical specialties to use precision medicine to human disease treatment was transfusion medicine. Since then, the field of precision medicine has evolved to include state-of-the-art techniques for therapy, intervention, and diagnosis that are revolutionizing medical practice. Gene therapy is one example of how precision medicine therapies are improving patient quality of life and prolonging life for many deadly diseases. Before the age of two, spinal muscular atrophy (SMA) type I was invariably fatal in neonates. The fact that children with SMA type I treated with gene therapy are living longer and needing far less invasive respiratory assistance has transformed the lives of these patients and their families (Singh & Gupta, 2020). Precision medicine is gaining a lot of support from government agencies, therapeutic financing companies research funding companies and laypeople, which includes politicians and private donors, due to its current success and future promise.

1.2.Genetics, genomics, and precision medicine

The study of genetics and genomics has advanced exponentially since the discovery of DNA by Friedrich Miescher in 1869, and the first characterizations of genetic material by Watson, Crick, and Franklin in 1953 (Dahm, 2008; Watson & Crick, 1953). It has also advanced since the identification of specific genetic mutations for diseases like cystic fibrosis and color vision in the late 1980s, and today we have an incredible understanding of the genetic basis of health and disease. Genes and their roles in inheritance were studied, and the fields of genetics and genomics were born out of the investigation of an individual's genome and the interactions between that genome and the outside world. The precision medicine revolution was significantly aided by these investigations as well. Consequently, the majority of precision medicine's initial focus has been on genetics and genomics. As Grainger (2016) points out, genetics and genomics account for the majority of the precision medicine data that is now available (Grainger et al., 2016). These days, a genome may be read for about US\$1000 in less than a day (R. J. N. Hodson, 2016). After more than ten years and an estimated US\$3 billion in expenses, the first genome was sequenced in 2001. It's also feasible now that the cost and turnaround time for genetic testing have drastically decreased.

1.3.The “omics” revolution

But the area of precision medicine is quickly expanding to incorporate information not just from genetics and genomes (Peck 2018). Advances in techniques have made it possible to include data from a wide range of other omics sources, including microbiome studies (also known as "microbiomics"), protein ("proteomics"), radiology ("radiomics"), metabolism ("metabolomics"), pharmacology ("pharmacomics"), and others. For this reason, merging data from many domains is often called "multi-omics (Peck & toxicology, 2018)."

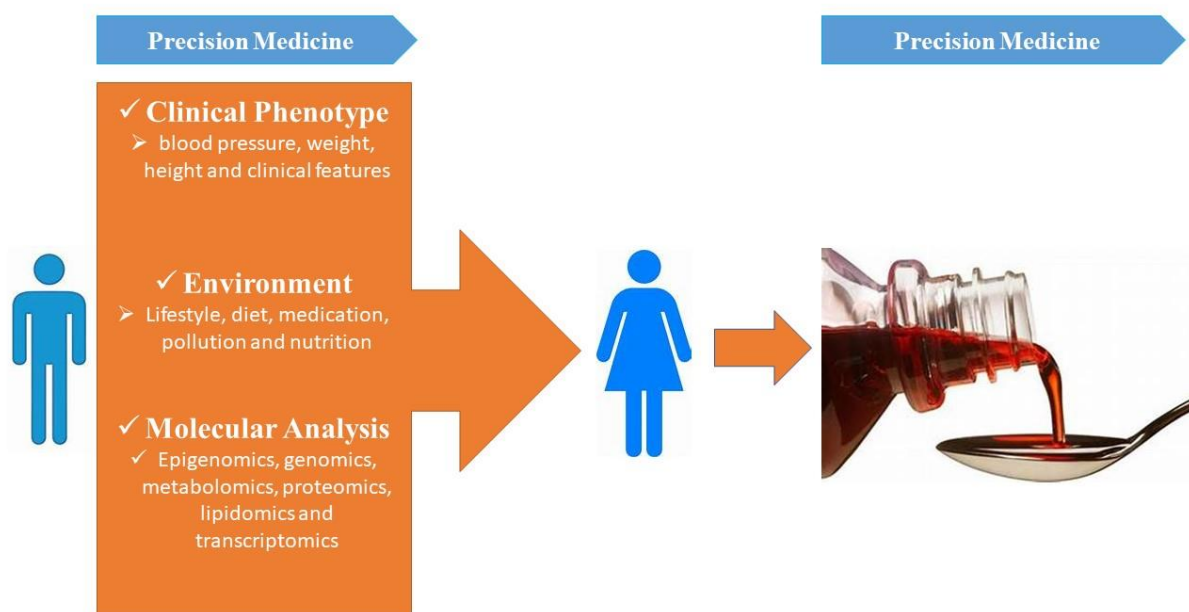


Figure 2. An ambitious challenge for medicine is to guarantee targeted care paths, starting with more tailored strategies. A multilevel approach to treating patients is required to accomplish this goal. The multi-omics approach (transcriptomic, metabolomic, genomic, proteomic, and epigenomics) offers a greater understanding of patient situations at the molecular level, from the underlying causes of diseases to the functional effects. The study of the “exposome,” which is defined as the sum of all exposures a person has during their life and the effects those exposures have on their health (Wild CP.), should incorporate this information. The major issue of environmental exposure quantification in molecular epidemiology is to “exposome” the genome. 2005; (Cancer Epidemiol Biomarkers Prev). Doctors can develop a personalised therapy that is catered to the specific patient by studying the clinical characteristics of the patient (Wild & Prevention, 2005).

1.4. Evolution of health care: the need for transformation

At the beginning of twenty century, the growing fields of medical changed their thought due to experimental work. The germ theory's creation, which blamed microbes for many then-common ailments, was particularly influential. But until a few decades later, when the establishment of academic medical centres made it possible for a scientific-based strategy and the first significant revolution of medical practise, the therapeutic occupation did not easily integrate science into practice. Medicine has been significantly impacted by science. The advantages of the reductionist approach, which condenses the idea of pathogenesis to the fewest feasible causative components, are illustrated by the developing molecular understanding of human diseases. There are advance techniques available for disease treatment due to modern research. However, our healthcare system also demonstrates the drawbacks of the reductionist scientific approach, with complicated chronic illnesses accounting for the majority of health care costs. We have created a strategy that prioritizes urgent care over preventing chronic illnesses (Danchin, 2022).

As we've observed, the learning of basic living processes is strongly tied to development and, more specifically, to the very beginning of life, which is the starting point of evolution. Along with the things, genes, and proteins related to life, we have

talked about the universal metabolic, information-transfer, and compartmentalization processes. Also alluded to are the abstract functions necessary for life. For these abstract processes to be included in physics and chemistry, we require a comparable, real-world framework. This hypothetical situation updates and gathers previous concepts (Danchin, 2022).

According to Berwick, Whittington, and Nolan (2008) Blumenthal and, Buntin, Jain (2010), Better treatment, improved health, and cost savings are the three goals that health information technology, or health IT, is meant to help achieve. Electronic health records, or EHRs, have not gained widespread adoption despite the potential advantages of health information technology (Berwick et al., 2008) . Only 8% of hospitals and 13% of doctors practicing in ambulatory settings in 2008 have at least a basic HER in place. Many are worried about a "digital divide" in health IT access among underprivileged and rural populations since, according to Mostashari, Tripathi, and Kendall (2009), EHR adoption rates have historically been lower in small practices and critical access hospitals (CAHs) (Mostashari et al., 2009).

The HITECH Act of 2009 encouraged the use of health IT by providing financial incentives and technical help for HER adoption and meaningful use (MU) as well as the exchange of health information (Blumenthal 2010). The Secretary of Health and Human Services gave the Office of the National Coordinator (ONC) \$2 billion under HITECH and authorized ONC to launch a health IT initiative at the Regional Extension Center (REC). In order to increase the standard and effectiveness of the healthcare delivery system, the \$720 million REC program was created to offer support and advice on best practices to accelerate the deployment of HER technology and maximize its usage. The primary objective of the REC program was to help at least 100,000 providers overcome the organizational and technological challenges they faced in order to maximize the use of health IT. As per Maxson et al. (2010), the principal responsibilities of the implementation were requirements analysis, product selection, and support for project management about the HER system's deployment. In small, underfunded medical practices in particular, significant outreach could be required in addition to ongoing technical support, practice coaching, and practice facilitation. various practices have various needs, particularly when it comes to employing health information technology for quality improvement, as demonstrated by two previous extension projects that promoted the use of HER in ambulatory care (Blumenthal, 2010; Maxson et al., 2010; Mostashari et al., 2009).

Practices that had already implemented EHRs were also eligible for REC help with optimization, since many practices lack the resources to manage the business and practice adjustments required to enhance care through health IT (Crabtree et al. 2011, p. Practice coaching attempts to "train the trainer" and assist practices and CAHs in increasing their capacity for learning and change management, hence reducing disruption to and fatigue from practices (Crabtree et al., 2011). Engage in coaching and facilitating activities, according to Nagykalai, Mould, and Aspy (2008) assist practitioners in increasing patient care and implementing evidence-based recommendations (Mold et al., 2008).

Table 1. The traditional medical record compared with the prospective approach

Traditional Medical Evaluation and Record	Prospective Evaluation and Record
• Chief Complaint • History of illness • Past Medical History • Family History • Medical History • Physical Exam • Diagnostic Test • Assessment and Plan	• Health Profile Summary • Current Health Status • Health Risk Analysis (Genetic, <u>Environmantal</u> and Lifestyle) • Disease Susceptibilities • 1 year Health plan • 5 year Health plan

Traditional Medical Evaluation and Record	Prospective Evaluation and Record
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• Family History	
• Medical History	• Disease Susceptibilities
• Physical Exam	• Disease Susceptibilities
• Diagnostic Test	• 5 year Health plan
• Assessment and Plan	• 1-year Health plan

1.5.Genomics unveiling the blueprint of life

Nearly two decades ago, the first map of the human genome was published by scientists, and it was heralded as a breakthrough. But it was lacking because only 8% of human DNA had been sequenced. All of an organism's genetic material is collectively referred to as its genome. The majority of the human genome is shared by all people, although some of the DNA differs from person to person. In order to better

understand the differences that might be the cause of diseases, scientists would benefit from building a full human genome. Between 1990 and 2003, an international partnership, In 2003, the genetic sequence from the Human Genome Project that contained data from the euchromatin region of the human genome—where the DNA encodes for protein and the chromosome is dense with genes—became publicly available.

Mineral matter and living stuff have traditionally been seen as distinct from one another. Stones were immovable, In contrast to mobile life, which was linked to some sort of cyclical development and decay, much like the cycles of day and night (Burge, 1898) permanent life was sluggish to weather. Fast silver serves as a demonstration of the mobility of gases and liquids, which exist in the region between these two states. Living beings fall between solids and gasses, comprising all four "elements," in accordance with a cosmogony similar to that of Anaximenes, which is based on the reciprocal modification of the elements (Earth, Water, Air, and Fire) (Guthrie, 1978). Thus life has always been understood to have a source of animation that demonstrated it was more than simply a simple form of stuff. The theory that life originated from the combination of the four elements in specific proportions based on local forms was held by early physicists and atomists. Lavoisier, who was executed by guillotine, was among those who coined the term "biology," but Lamarck ignored his contributions in favor of concentrating on the inner fire. Schwann, Schleiden, and Virchow to look for the atom of life, which they found in the cell. The atom of life, which was discovered in the cell, attracted the attention of Schwann, Schleiden, and Virchow as a result of the rebirth of atomism. Partitioning must thus be the very earliest, most essential, and universal process of life. To be more precise, there are two basic methods in which living things have evolved to deal with compartmentalization: either they have adapted to live as single cells with a more or less complicated envelope, or they have replicated membranes and skins in more complex animals. The advancement of chemistry allowed for the understanding that the inner fire that gave organisms life—and even made some of them warm—was caused. Lamarck (1809) spoke of an active force that propelled life's evolution. Lavoisier (1789) had noted that respiration produced a specified amount of air fixe (our carbon dioxide) and required air vital (oxygen). Studies and experiments with microbes and plants, particularly those involving fermentation, have shown that a second process, metabolism, is essential for the formation of life. Without metabolism, no living thing could exist. It was possible to see dormancy, an intermediate stage present in seeds and spores, but germination was necessary to show that life had begun. But life is not all there is. In actuality, qualities are passed on from parents to offspring of living organisms, at least those that have perpetuated their species (Burkhardt Jr, 2013). Additionally, the person develops into an adult form from some kind of egg or cell as though a function of the adult has already been carried out in one of the parent. Many explanations have been offered for this fact, but it was not until recently—with the emergence of the concept of information and the model of the genetic program that goes along with it—that it became clear that what is passed down through the generations is not a preformed organism but rather a sequence of operations that allow the organism to be constructed. For information transfer to be effective, it must be well structured. It has frequently been observed that these processes are so difficult to reconcile with one another that physicist Freeman Dyson (1988) even claimed that life began twice! Because molecular biology solely takes into account information transfer involving molecules, it is understandable why metabolism and compartmentalization are major issues that all models of life should address yet are frequently ignored by molecular

biology (Dyson, 1988). In summary, moving forward, we will consider living organisms to be analogous to a computer powered by metabolic processes that can understand and execute a genetic program (which may be inherited from previous generations). The genetic code is contained, at least in part, in the genome. The cell may be compared to a Turing machine, and Archaea, Bacteria, and Eukarya are comparable to different operating systems (Danchin, 2004–2005). Since Turing computers, by nature, cannot create other Turing machines, we need to find additional principles in order to expand the metaphor. If such a machine were to reproduce itself, according to John von Neumann's 1966 idea, there would be an internal picture of the equipment that was likewise connected (Danchin, 2008).

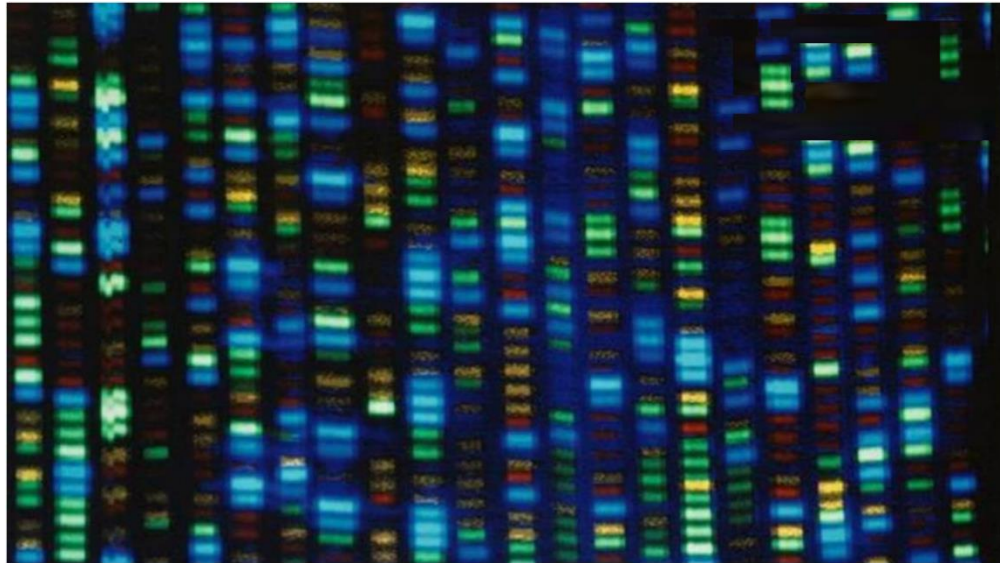


Figure 3. Human life genetic blue print (Andrade et al., 2003)

The Telomere-2-Telomere (T2T) project, which used novel DNA sequencing techniques and computational analysis to finish reading 8% of the genome, is responsible for producing the fully sequenced genome.

The many colours in the new pangenome reference illustrate the numerous directions a sequence could go in: The colour yellow represents a repetition variant, the colour pink an inversion variant, the colours green and blue a deletion variant, and the colour light blue an insertion.

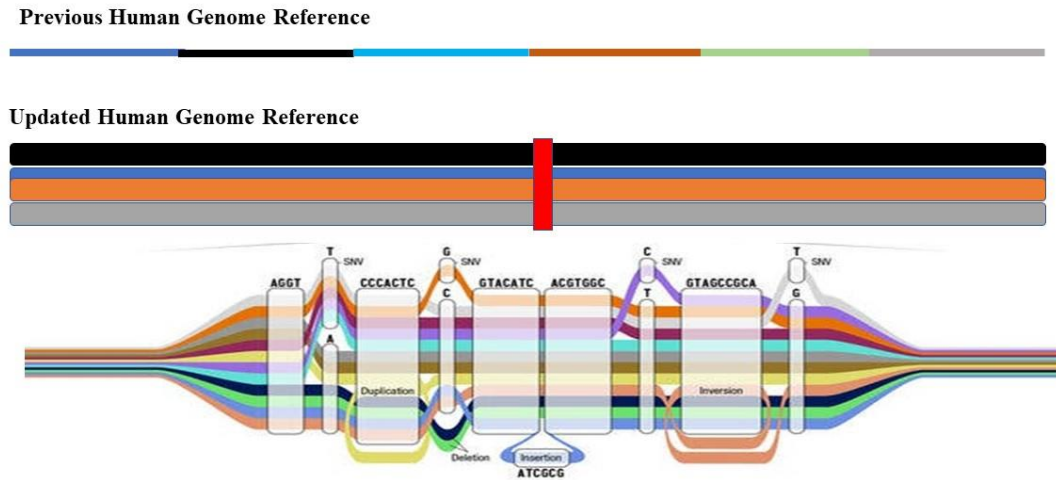


Figure 4. The new pangenome reference shows many possible routes for a sequence to take, represented by the different colors (Liao et al., 2023)

Pink is an inversion variant, green and blue are deletion variants, light blue is an insertion variant, and yellow is a duplication variant.

1.6. Precision medicine tailoring treatments to individual genomes

The twenty-first century medical field will be significantly impacted by the genome project, both in terms of diagnosis and treatment. Finding the genes that predispose people to disease will likely be the most crucial aspect of DNA diagnostics. Nevertheless, some of these conditions, including neurological, cardiovascular, and autoimmune disorders, are polygenic, indicating that two or more genes play a role in their development. Human genetic mapping will enable the identification of specific predisposing genes, and DNA diagnostics will provide the examination of these genes in a broad population. Twenty years from now, we may be able to take a baby's DNA and test fifty or more genes for allelic variations that might predispose the kid to a host of common illnesses [notice that he made this statement in 1992]. For every broken gene, there will be a therapy strategy that works around the gene's limitations. As a result, the approach to medical practice will change from being reactive to preventative. Thanks to preventative medicine, the majority of individuals ought should be able to live normal, disease-free lives without experiencing mental impairment. comprises over 20,000 coding sequences. is optimistic despite this: "I believe we'll see a shift from reactive to proactive treatment." P4 medicine is very participatory, preventive, and individualized. Individual genomes will be standard for medical records in 10 years or so, and we will be able to make inferences [about an individual's health] when paired with phenotypic data. Then, in ways we have never done before, we may begin to create personalized health care programs. We will get substantial and fundamentally new insights into predictive medicine when we compare patient data with individual genotype phenotype correlations in 10 years, when we have billions of data points on each patient. Medical research will evolve into a data-driven science (Wishart, 2016).

1.7. Personal genomics

Genetic testing are offered to certain groups by a multitude of governments and health agencies. These examinations include heel-prick testing for young children and tests for couples who are very likely to have children who have serious genetic diseases. It is the responsibility of medical professionals and public health officials to choose appropriate groups for the testing, get access to the tests, and interpret the results.

However, companies began to commercially sell genetic tests to individuals directly approximately 10 years ago. People can learn about their risk factors for a number of complicated diseases, such as diabetes, cancer, and even neurodegenerative disorders like Parkinson's disease, with these tests, which are usually based on a genetic analysis of a saliva sample mailed to the patient. For a number of reasons, these firms have come under fire; one of the main ones being that people believe they are offering medical advice by sharing information that is relevant to health. In the fine print on their websites, all of the firms state that using the information to make medical decisions is not advised. This is probably partly because of this, as well as the firms' encouragement to avoid lawsuits. However, this is not true. The following instances are provided in the Nuffield Report: 23 and find out whether you have Tay-Sachs, cystic fibrosis, or breast cancer as inheritable indicators. Find out which diseases, such as type 2 diabetes and Parkinson's disease, you are more likely to develop genetically. Predictability is frequently poor, and variations in an individual's risk level above or below the population's are negligible and have little bearing on health. However, people can mistakenly think that their degree of risk is higher or more definite than it actually is because it could be so difficult to explain and understand risk projections. Another indication of inaccuracy is the large variation in the test providers' results. Some consumers have seen fairly startling differences in the risk assessments provided after sending samples to numerous firms. Third, there is a lack of utility: even in cases where the risk assessment is reliable and correct, possible modes of action are nearly never accessible. Thus, the best counsel that can be offered to the concerned person is usually useless and scarcely "empowering": keep up a good diet, live a healthy lifestyle, refrain from smoking and binge drinking, etc (Singh & Gupta, 2020).

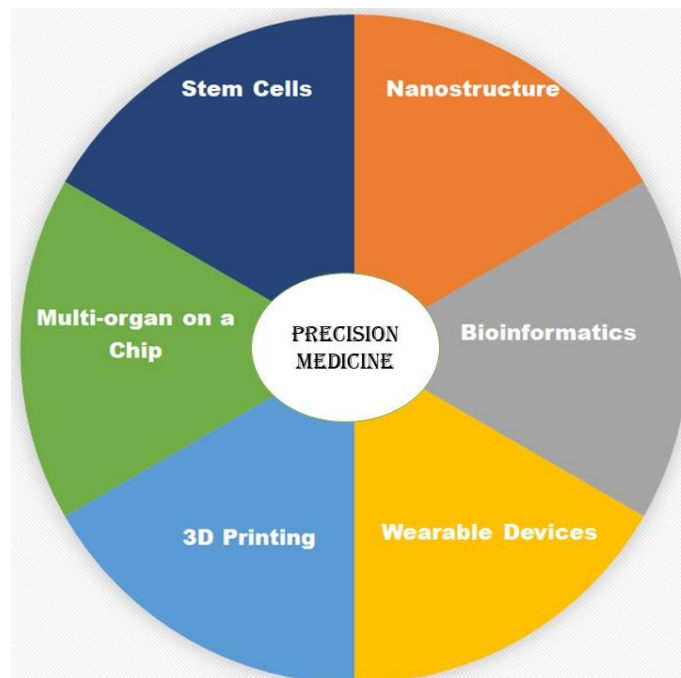


Figure 5. Biomaterials engineering, cell engineering, organs-on-chips, customized implants, and personalized devices, as well as genomics-based methods, enable precision medicine (Moysidou et al., 2021).

1.8. Genomics technologies: Empowering precision medicine

One such industry that gains from AI is healthcare. Medical professionals have always had oversight over this area. The potential for individualized care has increased due

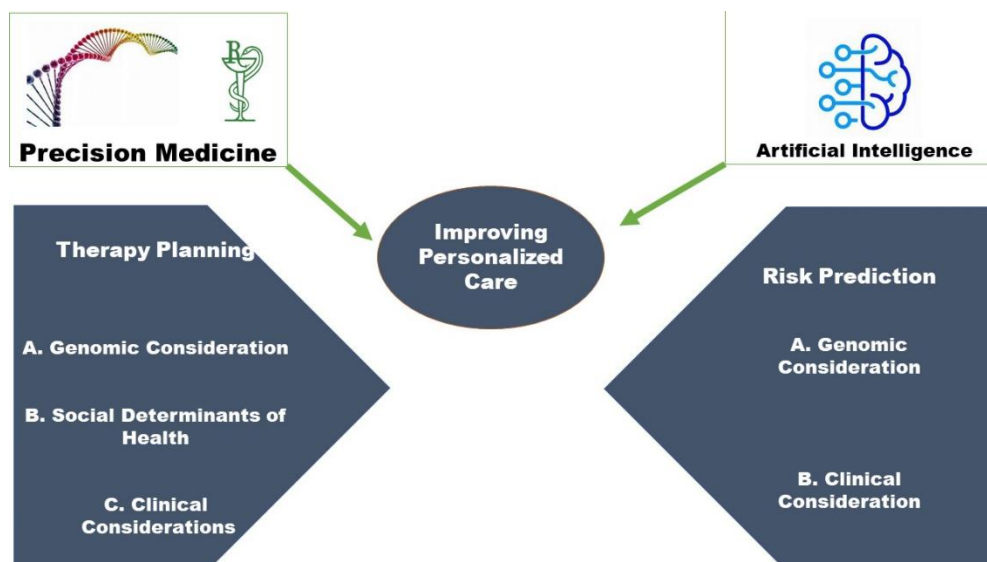


Figure 7. Dimensions of AI and precision medicine's interaction (Johnson, Wei, Weeraratne, Frisse, Misulis, Rhee, Zhao, Snowden, et al., 2021).

Five factors have an impact on the goal of individualised treatment, including the planning of therapy using clinical, genomic, social and behavioral, as well as genetic or other factors, risk prediction or diagnosis.

1.9. Integrating genomics to into clinical practice

The particular disease susceptibilities and treatment reactions of each person depend on their own genetic makeup. This idea serves as the foundation for the emerging field of genomic medicine. In this field, pre-symptomatic health risks are identified and managed, existing disorders are more easily diagnosed, prognostic predictions are improved, and treatment options are guided by the knowledge gained from studying an individual's genomic variants. Rapid developments in DNA sequencing and bioinformatics have made it possible to use genomic medicine in clinical settings.

Genomic data is being used more frequently in therapeutic treatment. Genomic information is durable, and since we know more now than ever before, it can be applied over the course of a patient's life. As a result, Clinicians and patients must embrace genetics for healthcare to improve and recognize when the information might be helpful. Clinicians without a background in genetics frequently claim they are ill-equipped to treat patients using genomic data (Mikat-Stevens et al., 2015).

1.10. Storage of Genomic Data

The ability of modern HER systems to store and process genetic data in clinical practise will be put to the test. Current HER systems cannot handle the potential volume of a complete genetic sequence, as opposed to a small number of genotypes. The auxiliary genetic system is one remedy for this issue (Starren et al., 2013). An auxiliary genomic system can provide federated storage choices, much like an image archiving system that are suited for the diversity and volume of genetic data and conclusions. Extensible Markup Language (XML) files comprising recognized variations as part of a custom panel, star alleles for results of pharmacogenetic testing, and other data from several laboratories may be sent to an institution for the same patient. or even files that contain enhanced sequencing data in Variant Call Format

(VCF). To enable quick retrieval of these data, which range in size from bytes to gigabytes, specific indexing techniques must be used. These data may be utilized to give synthesis deeper perspectives into the outcomes of genomic tests and the ancillary data using an auxiliary genomic system that carries out specific processing and is connected to the HER. At three eMERGE facilities, a genomic auxiliary system has been developed and put to use. At Northwestern University, a prototype auxiliary genomic system for pharmacogenomic testing and reporting was built. The Mayo Clinic also followed similar procedures to create a genomic data warehouse. A distributed system was developed by Partners HealthCare to manage genetic testing for certain objectives (Horton et al., 2017).

1.11. Genomic data analysis: extracting insights for precision medicine

Precision medicine begins with data mining. High-throughput screening biotechnologies generate the data by exploring all facets of complex biological systems in an attempt to discover new information. The extraction of relevant data still presents a significant challenge, despite the discipline's integration of several scientific fields, including medicine, biology, biochemistry, computer science, mathematics, physics, and engineering. This is because the underlying problems we are attempting to address are complex, and the volume, heterogeneity, and many temporal and geographical aspects of the data make it difficult to extract relevant information. Because of this, a significant obstacle facing precision medicine in the future is determining how to transform enormous amounts of data into fresh knowledge that can be specifically applied to each individual (Starren et al., 2013).

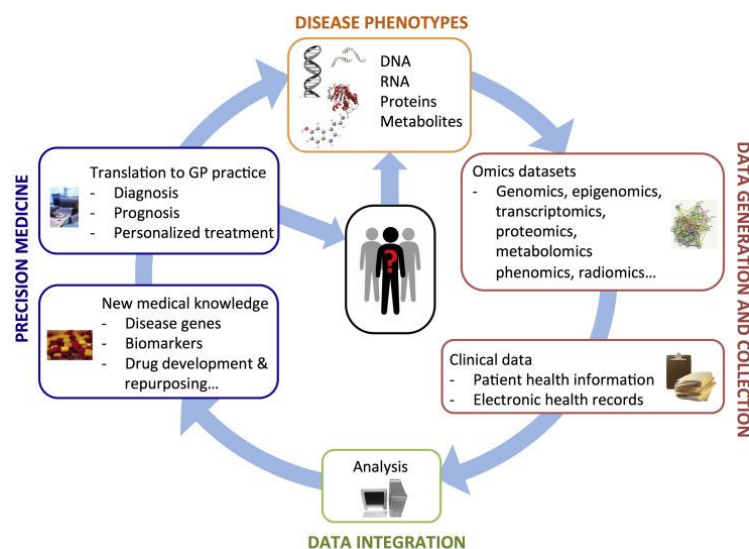


Figure 8. The generation and collection of omics data, which includes information about DNA (genomics), mRNA (expression and coexpression), proteins (proteomics), metabolites (metabolomics), among many other things, can reveal the underlying molecular mechanisms of a person's disease state (disease phenotypes) (Hedayat & Valeri, 2020).

It is possible to provide individualized therapies and treatments based on each person's particular biology. A paradigm shift towards a new medical model called "Precision Medicine" has recently occurred in the healthcare industry as an enhancement of personalised medicine. The new clinical system model focuses on a patient's genes, microbiota, environment, family history, and lifestyle to select accurate diagnostic and therapeutic approaches for each patient.

1.12. Ethical considerations in genomics and precision medicine

The existing public health paradigm of post-diagnostic management is unsustainable despite the best efforts of medical professionals to treat human ailments like cancer or chronic diseases. The majority of clinical units already struggle to provide the best treatment possible to treat patients who have recently been diagnosed.

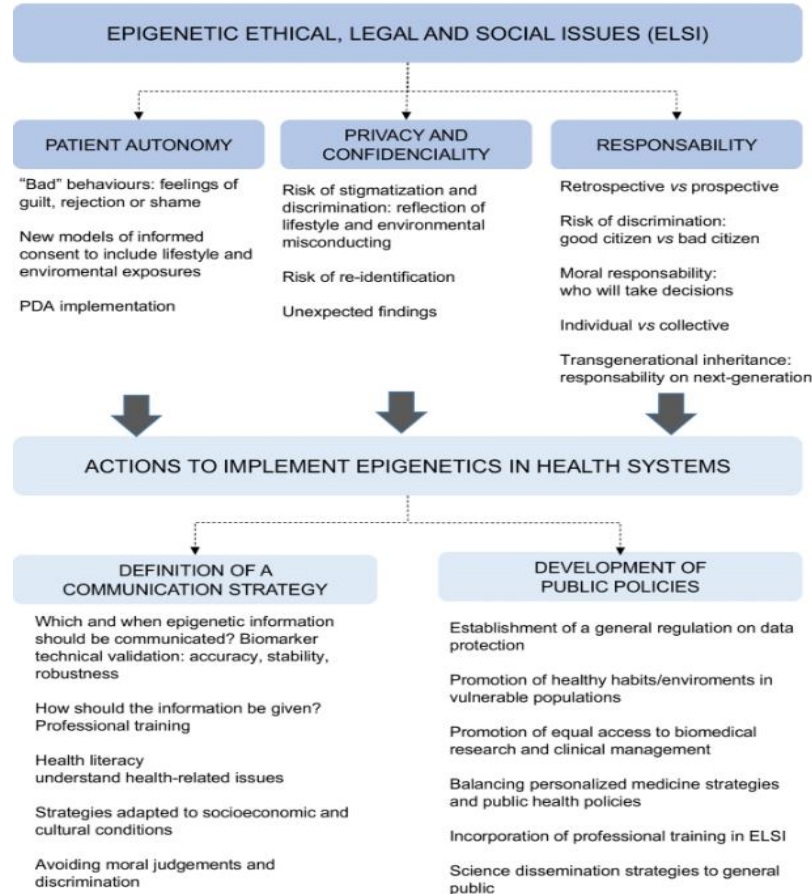


Figure 9. Epigenetic-based biomarkers' usage in the treatment of human illnesses is fraught with ethical, legal, and social problems (ELSI) (Santaló & Berdasco, 2022).

Nine programming areas, including PM, have been highlighted by the World Economic Forum's Center for the Fourth Industrial Revolution. The National Academies of Sciences, Engineering, and Medicine (2018) reports that over 40 nations have contributed to PM projects. For instance, the All of US program, launched by the National Institutes of Health (NIH) in the US, intends to register one million individuals to contribute genetic samples and data for scientific purposes. According to Cyranoski (2016), the China Precision Medicine Initiative will receive \$9.2 billion USD in funding over a 15-year period (Cyranoski, 2016).

Precision medicine (PM) is now being studied in the multiethnic setting of Singapore through the SG10k program and the SingHealth Duke-NUS Institute of PReCiSion Medicine (PRISM) (J. C. Wu et al., 2019). This work will be extended beginning in 2021 as part of the National Precision Medicine project. Because Asian genomes are underrepresented in global databases (Bentley et al., 2008), this effort will contribute to increasing genetic diversity and may lead to the development of more specialized treatment techniques appropriate for Asian populations. According to Popejoy and Fullerton (2016), just 14% of the 2511 genome-wide association studies that have

been carried out as of 2016 included people of Asian ancestry. UN projections for 2019 indicate, however, that 60% of the the globe (Popejoy & Fullerton, 2016). While "personalised medicine" was first used by the Human Genome Project, the phrase "precision medicine" has gained traction over time. The term "personalised medicine" was changed to address concerns that it did not adequately describe the novel approaches driven by genome data and that it could lead to unrealistic expectations for personalised treatments and drugs instead of focusing on developing therapies for disease subtypes largely identified by genomics. Still, in certain systems (like those in the European Union), the phrase "personalised medicine" is used. In contrast, some programs refer to the same idea generally under either label. According to Erikainen and Chan (2019), these phrases reflect overlapping future visions of healthcare and medicine that are influenced by data-intensive biomedical research in different ways. Some authors claim that varied language indicates a preference for distinct goals, values, and conceptual frameworks. Through thorough understanding of the social, cultural, and ethical ramifications of these terms, researchers and decision-makers may build reliable connections with participants that are built on open dialogue and transparency. If the general public and study participants have access to science-related materials that will support the formation of critical understandings, they will be able to engage with significant topics more effectively. The "deficit model," which views public communications as a one-way flow of information from scientists to the general public, should not, however, be automatically adopted by researchers. This is because ethical norms have a complex role in both policy-making and scientific communication (Erikainen et al., 2019).

1.13. Challenges and opportunities in the integration of genomic

From \$100 million in 2001 to \$1,000 in 2014, the price of sequencing has decreased thanks to the introduction of NGS. The medical community now has greater access to sequencing for diagnostic support because to the lower cost. Sequencing has an advantage over other methods for characterizing nucleic acids, such as PCR and microarrays, in that it can produce a wide range of data kinds. For DNA, RNA, and bisulfite sequencing, conventional NGS platforms like the Illumina HiSeq sequencer are frequently utilized. These platforms' short reads have alternatives thanks to recent developments in sequencing techniques. Combining patient genome, transcriptome, and DNA methylome analyses can help with prognostic classifications and diagnosis.

One of the trickiest computational issues to date is short read alignment (SRA), which is essential to the modern bioinformatics pipeline in the study of genomics (Lightbody et al., 2019). Read alignment, which is essentially a string matching issue, is quite complex due to the substantial amount of raw genomic data. The vastness of the human genome is demonstrated by the fact that short read lengths often span between 100 and 300 characters (Sboner, 2011). According to McVicar et al. (2016), a search frequently encompasses the whole reference genome for every read, leading to billions of searches. Many-core processing (McVicar et al., 2016) pre-alignment filters, they have all been used in previous attempts to boost read alignment throughput. Short read alignment's computational difficulties. They states that downstream analysis and experimental design are now seen to be the main areas of concern in computing, as opposed to fifteen years ago when the main bottlenecks were associated with gene sequencing.

1.14. Alignment challenges

Muir et al. (2018) state that the prevailing alignment paradigm, paired sequence alignment, compromises speed and power in order to generate flawless exhaustive alignments via global or local alignment. While both alignments are correct, quadratic complexity—a phenomenon in which processing time grows exponentially as data input rises linearly—means that pragmatic short read alignment cannot be used to map sequences to large reference genomes (Muir & Vander Heiden, 2018).

Banerjee et al. (2021) state that between 50% and 70% of the total time is usually needed to compute the edit distance during short read alignment. To more clearly show this, have a look at the 51 edit distance calls per read of the SRA algorithm SNAP. Considerable investigation into index techniques has contributed to reducing the quantity of candidate sites requiring computation. This has led to the development of many alignment algorithms to pre-filter alignment candidate sites before performing Levenshtein distance computations, in an effort to reduce the search space (Banerjee et al., 2021).

Defining stakeholder roles at any or all phases of policy or guideline creation is essential for accurately evaluating and understanding the policy-making process. There is no one-size-fits-all, ideal method for doing this. A number of frameworks, some of which expressly target important stakeholder consultation, have been established in a number of sectors to help with the planning, development, and analysis of policy.

1.15. Case studies: success stories in genomics driven precision medicine

Conversational chatbots to scale genetic counseling (GC) services, digital delivery of complete genetic services, and digital genomics decision support systems are three use cases that demonstrate the immense potential of these converging technologies. The use cases presented here highlight state-of-the-art technological innovations created to address clinical needs and challenges that occur throughout the genomics continuum of care. These include digital decision aids, chatbots, and digital portals, as well as pre- and post-test counseling and the full service delivery of genomics.

Offering patient-centered choice support for genetic testing is one of the primary responsibilities of genomic counseling, and decision support tools help to do this. One of the main strategic aims and objectives of the next ten years for many pharmaceutical companies, biotech companies, university medical institutions, and the National Institutes of Health is personalized medicine, or more recently, precision medicine (Khoury et al., 2012).

Human genetics has benefited greatly from pharmacogenetic and pharmacogenomics research. The promise of translational research to move genetic linkages from "bench to bedside" for several drugs and drug-related features has been realized (detailed in this article). It is obvious that pharmacogenomics has advanced with astounding efficacy in the GWAS era, when thousands of genetic links for hundreds of phenotypes are discovered.

1.16. Future Directions: Advancements and Genomics in Healthcare

The cost of genome sequencing has dropped dramatically, and the number of firms offering genetic diagnostics has sharply increased, which has hastened the development of personalized medicine. Direct-to-consumer companies, according to

Khan and Mittelman (2018), are quickly providing people with access to genomics, which is changing how doctors and patients see genetic testing. The genetic testing industry is expected to reach \$22 billion globally by 2024 (<https://www.gminsights.com/pressrelease/genetic-testing-market>). Future developments in genomic technology are predicted to have a big influence on the field of genetic testing (Khan & Mittelman, 2018). There are more and more pilot studies using whole-genome sequencing (WGS), even though panels or exomes are still used in the majority of clinical sequencing today. It might allow for the comprehensive examination of all genomic variations. 100,000 individuals with rare diseases or cancer and their families have had their genomes sequenced by Genomics England and the National Health Service (NHS) England, demonstrating the effective large-scale deployment of WGS in direct healthcare. Fast WGS has been demonstrated to reduce morbidity and hospitalization expenses for critically unwell babies admitted as inpatients in the US. These are but a handful of the issues that still need to be resolved, including cost, clinical interpretation, and data storage in health systems, despite the fact that there is much more to learn about the therapeutic potential of WGS in clinical settings. The cost of a number of long-read sequencing methods is currently declining (e.g., PacBio, 10X Genomics), and these methods promise to help us better understand the structure and order of genomic rearrangement—a structure that is challenging to detect with next-generation technology. The diagnostic yield for genetic illnesses may rise if these technologies are able to make a successful transition into the therapeutic market. There will be more technical advancements as the scientific community strives to build expansive, open-access databases of population-scale variations, multiethnic reference genomes, and expanding clinical genetic databases (S. J. Aronson & H. L. J. N. Rehm, 2015). We still anticipate difficulties with genetic testing's interpretation, comprehension, and communication, despite the fact that it is becoming increasingly accurate and dependable. It is possible that genetics will lead to the discovery of new medical pathways, such as the ability to predict lifetime risk for particular diseases. However, predicting the genomic profiles of complex illnesses is more difficult and likely less beneficial therapeutically because these diseases may have multiple underlying genetic and environmental factors (Manolio et al., 2009). However, advances from very large GWASs have made polygenic risk scores (PRSs) increasingly accurate, incorporating a large number of genetic variants into a single test for prediction. Recent studies (Khera et al., 2018) have shown that PRSs can predict several complex diseases, like coronary artery disease and breast cancer, with an accuracy comparable to testing for those diseases' u. It is expected that these assessments will become more accurate as GWASs advance. PRSs not only provide information about lifestyle and family history, but they may also be used to identify high-risk persons in the general population for a variety of ailments. Even though it's unclear how effectively PRSs would function in real therapeutic settings, there are a number of obstacles to overcome before these results may be used to clinical therapy. Many clinical trials are currently being conducted to determine how PRSs affect the treatment of some complicated conditions, including as breast cancer (<https://clinicaltrials.gov/ct2/show/NCT03688204>). However, mounting data indicates that PRS might not be very effective at dispersing throughout communities (Martin & Wang, 2019). European folks fare better than other ethnicities in the early PRS applications. European populations do better than other groups in early PRS applications in terms of prediction accuracy (Martin & Wang, 2019). The existing health inequalities may worsen as a result of this discrimination. The development of predictive analytics for complex illnesses that offers fair clinical value for all populations is necessary to advance personalized medicine in an ethical manner.

Because they can store enormous volumes of genetic data and effectively incorporate pertinent genomic information into clinical treatment, electronic health records will play a more significant role in the adoption of personalized medicine. However, the IT and healthcare infrastructure required for the broad adoption of EHRs is lacking in many developing nations. Patients with the least access to genomics and customized medicine are those who receive treatment in small and rural hospitals that have not yet implemented electronic health records. This division makes it more difficult to apply customized therapy and ensure that a diverse range of ethnicities are represented in genetic research. Through mobile enrollment and education centers, AoURP is relentlessly working to interact with poor communities in order to enhance health for all various groups. The Genomic Medicine Alliance is an international consortium of educational establishments that facilitates cooperation and management of genomic research initiatives in both developed and developing nations. The fact that transnational, coordinated efforts are required to supplement the existing one-off, local implementation efforts of personalised medicine is becoming more and more evident, given the goal of clinical care having a global effect on personalized medicine. The International 100K Cohort Consortium (IHCC) was established in 2018 with the goal of combining genetic data from global, substantial, unselected population cohorts. This consortium is an alliance between the Global Alliance for Genomics and Health (GA4GH), which seeks to promote and facilitate data sharing in genomic research, and the Global Genomic Medicine Collaborative (G2MC), which seeks to develop and share best practices for the application of global genomic medicine. These projects offer broadly applicable frameworks to comprehend the viability of effectively integrating complicated genomic data into health systems. Powerful information engines with great promise to help patients have been created during the past few decades by fundamental discoveries uncovering the genetic pathways of illness. It is predicted that the enormous expenditures incurred over the next ten years to incorporate this state-of-the-art information into standard clinical care would revolutionize medicine as it exists now. Patients' and physicians' interactions with healthcare data may alter as the usage of EHRs in healthcare delivery grows. The future of individualized therapy will be made possible by new paradigms for integrating genetic data with other biological data, artificial intelligence, and robotics in health systems.

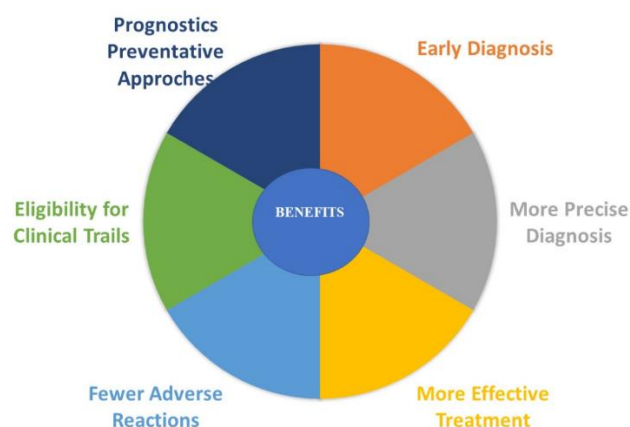


Figure 10. The advantages of genetic medicine are illustrated in this pie chart, which also includes prognostic/preventative methods, early diagnosis, more accurate diagnosis, more effective treatments, less side responses, and eligibility for clinical trials.

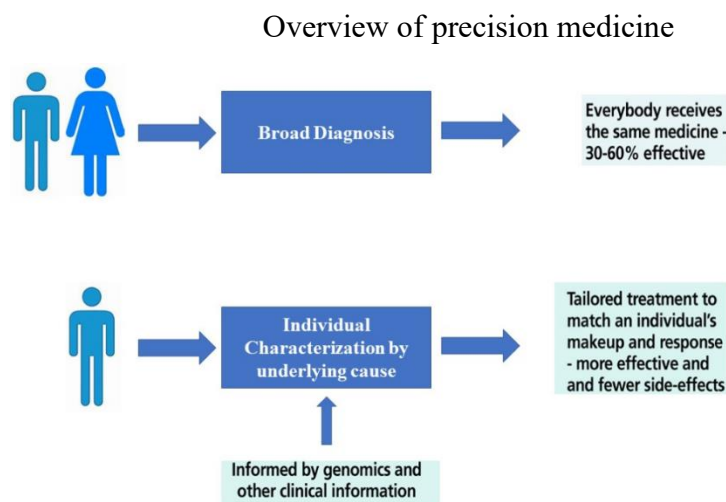


Figure 11. How individual treatments can be tailored by precision medicine to be more efficient and have fewer negative effects.

It is essential that equitable access to genetic research promotes advancements in diagnostic discoveries, translational research, and the creation of novel precision therapies for all in order to enhance the health of future generations. This is especially important for cancer as well as unusual and genetic disorders as well as increasingly common diseases.

Scientific Ethics Declaration

The authors say that they are responsible for the scientific, moral, and legal aspects of this chapter, which is published in Current Studies in Health and Life Sciences 2023.

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