REVIEW ARTICLE

An Updated Overview on Personalized Medicine: The Next-Gen Paradigm

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ABSTRACT

Personalized medicine is a translational approach that utilizes an individual's genetic profile to guide illness prevention, diagnosis, and treatment choices. The human genome project data is being used to enhance personalized treatment. "Personalised" medicine is beneficial over "individualized" medicine as it suggests that future hazards may be predicted based on the individual's genes. The advancement of technology for personalized medicine depends heavily on standardization, integration, and harmonization. The scientific practices at various research sites, the connection between science and healthcare, and the relationship between science, healthcare, and broader society, including the legal and ethical paradigms, the dominant cultural and political ethos, and the expectations of patients and citizens - all need to be in harmony. There are several descriptions of the current existing legislation that regulates genetic screening and genomic medical services in various countries around the world, highlighting discrepancies and specifying areas of law where harmonization may be needed to enable the use of individually tailored medication globally. The promise of personalized medicine can only be fulfilled by placing the individual at the centre of personalized medicine and tailoring care to each patient's unique psychological and social needs in addition to their biological profiles.

Keywords: Translational medicine, Genetics, EEgulation, Efficacy, Healthcare, Patient care

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INTRODUCTION

With the trend of customizing almost everything, from water bottles to other gift items, it's not surprising that medicine is fully taking root in this area as well. As scientific knowledge has grown over the years, there has been a slow but steady shift away from traditional medicine. Traditionally, the way drugs have been made and how medicine has been practiced has been based on finding treatments that work for a whole population. Patients' unique physiologies and psychological make-ups result in varying therapeutic responses, which has led to the development of treatments specifically designed to address these nuances. In this context, the concept of "personalized medicine" (PM) emerged, which entails adapting a patient's care to their specific molecular or genetic make-up and how that contributes to disease development.

Thus, the practice of diagnosing, treating, and preventing sickness in individuals on the basis of insufficient evidence that is extrapolated from population norms is becoming increasingly uncommon. Of late, people have started putting on a lot of faith in "personalized medicine" because they believe it can provide more specific treatment. With more accurate diagnosis, prognosis, and therapies, precision or personalized medicine aims to avoid the "one size fits all" mindset in healthcare.[1–5] One critical aspect driving this change is the emergence of new methods and technologies that tend to provide comprehensive molecular-level biological profiling of people. Much progress has been made in transitioning from disease treatment to patient care.

The terms used interchangeably for personalized medicine are 'precision', 'individualized' and 'stratified' medicine in accordance with the National Research Council. Personalized medicine is often referred to as P4 medicine, i.e., predictive, preventive, personalized and participatory.[6,7] However, there was concern that the term "personalized" could be misconstrued to suggest that therapies and prevention strategies are being established uniquely for each individual;

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in precision medicine, the emphasis is on determining which approaches will be effective for which patients based on their genetic, environmental, and lifestyle characteristics. Therefore, the Council has favored the phrase "precision medicine" over "personalized medicine."

While going for a diagnosis, doctors always take into account the individual's age, gender and familial background, along with co-morbidities, the person's psychosocial, lifestyle, and sometimes familial and financial problems and then customize the therapy based on the patient's specific needs. And yet, in the last 60 years or so, there has been a growing push for medical practice to adopt a more "scientific" approach.[8] Evidential bases for medical practice (EBM) have likely always existed, but how we interpret and use this evidence has evolved through time. EBM is the deliberate, unambiguous, and reasonable use of the most up-to-date evidence in choosing among potential therapies for specific patients.[9] The focus on personalized medicine nowadays is on tailoring medical research to individual patients on the basis of EBM as well as genetics. Figure 1 portrays the elements of personalized medicine.

Thus, the current article provides an overview of personalized medicines' needs, challenges, applications and regulatory perspectives.

Need for Personalized Medicine

There is an ardent need for tailored medicine to improve drug safety and efficacy to substantiate healthcare. Table 1 delineates the vital differences between traditional *vs* personalised medicine. Using genomes and proteomics knowledge about the patient seems to be the best approach to achieve this. However, information of human genome diversity and its relationship to drug pharmacokinetics and pharmacodynamics has created a rare opportunity to use such data to improve healthcare. Also, adverse drug reactions leading to hospital admissions and drug-related morbidity and mortality cost, and morbidity could be reduced by making use of personalized medicine. All aspects of an individual's health and illness, including susceptibility, screening, diagnosis, prognosis, pharmacogenomics, and monitoring, will be improved. This would further also facilitate early detection of changes. Thus, personalized medicine has been sought after as a revolution in improving patient care.

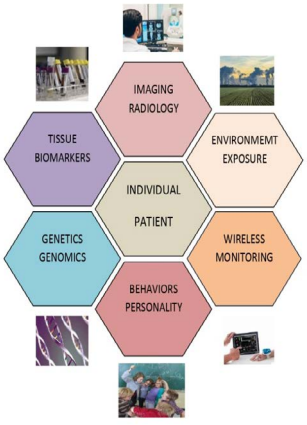

Figure 1: Illustration of elements of personalized medicine

Challenges Associated With Personalised Medicine

The key barriers to integrating precision medicine into standard clinical care are the lack of available tools, knowledge, and research.

Health Data Issues

Health data may come in many forms (including observations, evaluations, and orders) and be collected by a wide variety of people (including doctors, nurses, patients, and robots), all of whom may produce quite diverse outcomes. The open electronic health record (EHR) is a specification for an open-source software platform that may be used to create EHR in a clinical knowledge domain.[14] Table 2 displays the categorization of various data types according to the sorts of clinical and administrative inputs that are required by the open EHR standard. This type of data doesn't include clinical or administrative information; it provides documents about the processes, including error records, access logs, and information on how the system interacts with other systems. Despite the fact that it is not directly connected to the delivery of healthcare, it is the most significant key for data protection, data validity, and data tracking.[15,16]

Information is stored in databases so that it may be retrieved later. A sufficient level of specificity, depth, and context is needed for it to be effectively comprehended and analyzed.

The majority of healthcare data is generated by medical equipment. Like all other calibrated instruments, they can measure physical attributes to a certain degree of precision. To state the obvious, no measurement is without flaw and everyone has a certain margin of error. Also this is equally true when documenting patients' subjective experiences. Knowing the particular source of the data, such as a medical opinion or an individual's summary, in such circumstances may have an impact on how the data are interpreted. When working with people and clinical measurements, the deviation is created not just by random external variables but also because of the individuals' circumstances and responses to arbitrary external and internal influences. So, it's important for researchers to pay close attention to the intra-patient variability in clinical trial measures.

Moreover, the professional's degree of education and experience and the unique qualities of each patient may also account for the majority of this type of variation.

Civil, Legal and Moral Issues

Additionally, personalized medicine presents moral, civil, and legal concerns as well. Privacy and the security of participants' personal and health data must be safeguarded. Participants must be aware of the risks and advantages of participating in research, therefore, informed consent procedures must be robust.

Costs

Precision medicine faces additional challenges due to its high costs. Implementing technologies like DNA sequencing on

Table 1: Differences between traditional and personalised medicine

Traditional medicine	*Personalised medicine*
Traditional Chinese Medicine (TCM), Ayurveda, and other forms of alternative medicine have different tenets and practices from one another. All the same, they have the same rising popularity and track record of patient success.	Clinical, genetic, genomic, and environmental data about an individual are used to influence healthcare decisions in the rapidly developing area of personalized medicine. The goal of customized medicine in health care is to provide each patient with treatment tailored to their needs at every stage of health and illness.
In light of this evidence, the present study team is asking, "Do these traditional systems share characteristics that result in their accomplishments, and how do they vary from mainstream medicine's approaches?" When compared to standard medical care, what unexplained factors allow them to successfully cure previously hopeless cases? Could modern medicine take use of the strengths of other approaches? When compared with traditional medicine, does today's conventional medicine seem more at home in the contemporary world?	Personalized medicine makes use of our growing molecular knowledge of illness to improve preventative healthcare measures while individuals are well and to initiate medication therapy at the earliest stages of the disease. Overarchingly, the purpose of personalized medicine is to tailor medical treatment to each individual in ways never before possible.[11]
The study team identified the essential ideas, philosophical understandings, and holistic viewpoints of three prominent traditional medical systems (TIM, TCM, and Ayurveda) in order to delve into the problems. The group has made an effort to clarify the possibility of shared fundamental principles and commonalities across the systems. The group also considered the potential synergies between traditional and Western medical practices.[10]	Although DNA from many cells is identical, the way that genes in one organ (and the cells they are expressed in) behave varies from that of genes in other organs. Although several tumor forms in cancer may share the same DNA, their gene expression patterns vary. We can study the gene expression profiles of hundreds of genes at once using technologies like gene-expression microarray and can differentiate between a gene expression profile that is linked with cancer and a normal profile.
Cohort-based epidemiological studies, which primarily derive their results at the population level and do not account for an individual's genetic diversity, have guided standard medical therapy for many years.[12]	The genetic make-up and medical history of an individual are taken into consideration by modern customized medicine before a treatment plan is created. Contrary to conventional customized medicine, which bases treatment on a patient's family history, social situation, environment, and lifestyle, this approach does not consider these factors.[13]

a wide scale takes a lot of money. Drugs that aim to correct underlying molecular or genetic causes of disease are also likely to be on the costly side. These precision medicines are also expected to become a problem regarding reimbursement from third-party payers (such as private insurance companies).

Health outcomes, healthcare services, and biomedical research could all benefit from the application of personalized medicine. In order for precision medicine's full potential to be realized, the field must first address infrastructural, equity, and knowledge gap challenges.

Personalized Medicine: Pros and Cons

As already explained, PM refers to practicing gene-based technologies to learn about a patient to unearth the apt therapeutic approach(es) that would be most effective for them.[17,18] Significant scientific advancements in recent years have strengthened the bonds between personalized medicine and preventative medicine. While this method has its advantages in terms of patient care, especially when considering the patient's genetic profile, it still faces obstacles, most of which come from the general public. Certain issues must be tackled for the sake of the protection and equitable treatment of persons.[20,21] The primary goal of personalized medicine is to be precise, rigorous, and able to prevent and treat illness with efficacy and safety.[19] The benefits of personalized medicine are not limited to the treatment of patients; rather, they may also be used to prevent and forecast illness by detecting genetic predispositions, therefore anticipating a possible patient.[19,22] This approach may result in significant

Table 2: Various types of data collection used in personalized medicine

Type of data	*Usage*	*Example*	*Machine*
Observation	For recording information from the patient's world—anything measured by a clinician, a laboratory or by them, or reported by the patient as a symptom, event or concern	Temperature, Blood pressure	Sensors
Evaluation	For recording opinions and summary statements (usually clinical), such as problems, diagnoses, risk assessments, goals, etc., that are generally based on observation evidence	Diagnosis, Adverse drug reaction risk	
Instructions	for recording orders, prescriptions, directives, and any other requested interventions	Laboratory orders	
Actions	for recording actions, which may be due to Instructions, e.g. drug administrations, procedures, etc	Laboratory reports, Surgery reports	Automatic analysis
Administrative	for recording administrative events- e.g. admission, discharge, consent, etc.	Patient ID number, name, gender Date of birth	Based on ID cards
System usage	For system used to store data	Audit trails, messaging logs	

healthcare cost reductions.[23] Other potential benefits of personalised medicine include reduced unwanted side effects, the accurate diagnosis of disease, the use of genomic testing for preventative purposes, and the discovery of previously unknown medical conditions.

Although it has been used in various fields and has been shown to offer many benefits for patient care, risks must not be ignored.[24] These include issues with informed consent, privacy, discrimination based on genetics, and consumer-based genetic testing. There is critical need to address ethical and legal concerns. Research recruitment based on individuals' genotypes also raises some moral concerns. Nonetheless, genetic data collected for one research might serve as a foundation for reuniting study participants in a different study.[25]

Other drawbacks and difficulties are associated with using personalized therapy, like, validity uncertainties of genomic testing, equality challenges, and implementation. There are also concerns raised about financial incentives for private enterprises to promote their services excessively, the probable abuse of genetic information by private corporations, and discrimination based on genomic data.

These descriptions of the pros and downsides of personalized medicine can shed light on the challenges of the practice, which in turn can drive future strategies for healthcare system readiness, reducing errors, and maximizing personalized medicine's benefits. Figure 2 indicates the benefits as well as challenges of personalized medicines.

Applications of Personalised Medicines

Personalised Medicines in Therapy

- *Cystic fibrosis*

One of the most egregious examples of how diagnosis and treatment have improved is cystic fibrosis (CF). Around 70,000 people worldwide are affected with CF, a multisystemic genetic illness that is inherited by an autosomal recessive mechanism and is brought on by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Drugs that can (at least partially) restore CFTR channel function on a molecular basis have been developed and approved.[26]

- *Monogenic Diabetes*

'Monogenic Diabetes,' caused by mutation of a single gene, is another example of a successful implementation of the customised medical process.[27] The majority of instances of Maturity Onset Diabetes of the Young (MODY) are caused by HNF1 and HNF4 mutations (MODY 3 and MODY 1, respectively). MODY types 1 and 3 patients are often identified before age 25 and exhibit no signs of insulin resistance. Sometimes they get an incorrect Type 1 Diabetes diagnosis, which is followed by a lifetime of insulin therapy. On the other hand, these patients might start taking SUs with a correct diagnosis.

Figure 2: Benefits vs challenges of personalized medicine

- *Malignancies*

One of the greatest difficulties in biomedical research is the development and widespread implementation of personalised medicine approaches for detecting and treating cancer at an early stage. The ideal path of cancer patient diagnosis, therapy, and follow-up care may be determined by using tumor genetic profiles and personalized oncology.[28, 29] Hepatocellular carcinoma is just one type of cancer that has long benefitted from molecular characterization's role in the differential diagnosis and treatment of malignancies.[30] Due to the existence of somatic mutations in specific genes like the epidermal growth factor receptor (EGFR) and anaplastic lymphoma receptor tyrosine kinase (ALK), targeted kinase inhibitors, for example, provide individualized therapy.[31-33]

Together with traditional medicines, tailored therapy options made possible by molecular characterization and segmentation into subgroups have also proven effective against breast cancer.[34, 35]

Personalised Medicines In Occupational Health

Personalized medicine projects may reassess vulnerability evaluation methodologies to account for complex workplace-personal connections, which could benefit occupational health. These methods aim to create a "gene-environment" viewpoint that considers employees' vulnerability owing to "omic" traits as well as a scientific understanding of occupational risk variables and knowledge of specific occupational risk situations.[36] "Omic" approach may help in improved detection of the damaging aspects of the xenobiotics since the discovered alterations, including as genomic, epigenomic, proteomic, and metabolomic changes, may be the consequence of the interaction. Occupational vulnerability to benzene hematotoxicity in exposed employees was shown to be influenced by genetic abnormalities implicated in the repair of DNA double-strand breaks and genomic upkeep, including BRCA2, WRN, RAD51, BLM, and TP53.[37, 38]

As a result of using a more individualized approach, it is possible that the interaction between chemicals and organisms will be included at the hazard identification stage of risk assessment. This might also improve the speed and accuracy with which toxicologically relevant data on molecular alterations can be generated, aiding in the discovery of novel dangers by the inclusion of additional pathways in their biological or biochemical contexts in toxicological investigations.[39] In new occupational situations, such as those involving minimal exposure levels, using novel materials, and/or applying complicated mixes, this method may be even more crucial for facilitating appropriate risk assessment.

However, from a pathophysiology standpoint, more information

is needed to understand the extent and frequency of a particular disease in a population, along with the differences that arise due to geographical and racial factors. Thus, as cutting-edge technologies and big data pave the way for PM, they possibly will also lead to advancements in occupational health as well.

Legal Aspects of Personalised Medicines

It is quite challenging for individualized diagnostics and medications to penetrate healthcare systems due to concerns about data security, patient privacy rights, and the use of data for research leading to legal issues.[40] There are several descriptions of the currently existing legislation that regulates genetic screening and genomic medical services in various countries around the world, highlighting discrepancies and specifying areas of law where harmonization may be needed to enable the use of individually tailored medication globally.[41] However, the relevant authorities have established no regulations regarding personalized pharmaceuticals. Pharmacogenetics, pharmacogenomics, and molecular diagnostics, which are all parts of personalized medicine, include much of the relevant topics.[42]

There is currently insufficient oversight from regulatory bodies on the integrity of tests to identify a genotype variation or an SNP from a specific patient.[43] The review and approval process for molecular diagnostic tests, which often utilize complicated multianalyte test formats, will need to evolve when new technologies and medications that function in tandem with companion diagnostics become available. Currently, labels only contain information about known dangers, but information gleaned from pharmacogenomic testing during medication development and from studies of marketed pharmaceuticals might uncover new dangers that should be included in the labeling.[44] On the label, together with risk information derived from extrapolating *in-vitro* pharmacogenomic testing and *in-vivo* drug responsiveness, the appropriate amount should be based on segregated treatment populations according to genotype/phenotype profiles.

FDA and Personalised Medicines: Regulatory Aspects

The FDA is working with researchers, pharmaceutical firms, producers of medical devices and biologics, as well as other stakeholders, in keeping with its fundamental goal of better understanding and preparing for the promise of personalized medicine. Various aspects of product development and usage are addressed by the FDA's continuous efforts to make customized medicine practicable, including:

- Initial stages of development
- Regulatory procedures and guidelines
- Product utilization

No clear stance on pharmacogenetics has been defined till yet by regulatory bodies. There will be new regulatory hurdles to overcome when new medications are provided to specific categories. Pharmacogenetics data is not mandatory by any government agencies. Although pharmacogenetics is not directly included in the European Medicines Evaluation Agency's current recommendations, the usefulness of a "community approach" for clinical trials solves the purpose

Figure 3: ICPerMed Vision 2030

of identifying medication interactions. The Food and Drug Administration has begun to frame guidelines for pharmacogenomics research. *In-vivo* drug metabolism/drug interaction studies" (www.fda.gov/cber/guidelines.htm) from 1999 mention the use of pharmacogenetic data in establishing medication dosage, and the FDA now considers genetic differences to be one of several variables that contribute to drug response. The FDA's scientific advisors have suggested including that same piece of data on the drug's label. Better research on this area is required. It is anticipated that regulatory organizations will work on the rules of customized medication when it spreads worldwide.

Future Perspective

According to the International Consortium for Personalised Medicine (ICPerMed), the growth of the biological, social and economic sciences and technical improvement propel PM forward. Therefore, a necessary condition for its effective execution is a significant investment in research and innovation. Here, the hypothesis outlines how, by 2030, PM will pave the way for the next evolution of healthcare. The goal is to recognize PM as a medical specialty centered on the peculiarities of the person, resulting in enhanced diagnostic, therapeutic, and preventative efficacy, increased economic value, and equal access for all people via five key aspects (Figure 3). ICPerMed envisions the implementation of these key aspects in healthcare within the five main viewpoints by 2030.

CONCLUSIONS

Pharmaceutical therapy is still strongly associated in the public's mind, despite the fact that personalized medicine using a pharmacogenetic approach has the potential to increase medication effectiveness and decrease adverse drug responses. The electronic health record may aid in its improvement, but physicians must also pay close attention to a variety of other issues, particularly those that pertain to patient engagement. Personalized medicine has emerged as a key motivator for R&D and the introduction of novel products in the pharmaceutical sector. Using pharmacogenomics, researchers hope to create more effective and less dangerous treatments.

Author Contributions

Himanshu Sharma: Article writing, editing; Urmi Bhadouria: Figures; Teenu Sharma: Conceptualisation, final compilation, Praveen Kumar: Review of article,; Arindam Chatterjee: Editing

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