



A REVIEW ON PRECISION MEDICINE

Dornala Chaitanya Dixit*, Dr M Sri ramachandra, Teppali Jyothi

Associate Professor, Pharmaceutical Analysis, Dr K V Subba Reddy Institute of Pharmacy, Kurnool,
India

Abstract:

Precision medicine is a rapidly evolving field that seeks to customize healthcare, with medical decisions, treatments, practices, and products tailored to the individual patient. Unlike traditional approaches that apply generalized treatments, precision medicine uses genetic, environmental, and lifestyle information to predict more accurately which prevention and treatment strategies for a particular disease will work in which groups of people. This review provides a comprehensive overview of recent advancements and challenges in precision medicine, with a focus on genomics, biomarker discovery, and pharmacogenomics. Key technological developments, including next-generation sequencing and bioinformatics, have enabled the precise mapping of genetic variations associated with diseases, facilitating targeted therapies.

The integration of artificial intelligence and big data analytics is also enhancing our understanding of patient-specific variables, leading to more personalized therapeutic strategies. Additionally, the review explores the implications of precision medicine in major disease areas, such as oncology, cardiology, and infectious diseases, where targeted treatments have shown promising results in improving patient outcomes. However, precision medicine faces significant challenges, including ethical concerns, high costs, regulatory hurdles, and data privacy issues. The need for robust data-sharing infrastructures and interdisciplinary collaboration is critical for advancing precision medicine on a larger scale. Furthermore, disparities in healthcare access and a lack of diversity in genetic research remain obstacles to its equitable implementation. This review highlights the current landscape of precision medicine, emphasizing its potential to transform healthcare by shifting from a reactive to a proactive, patient-centred model. While the field holds immense promise, continued innovation, policy reform, and ethical considerations are essential to overcome current barriers and realize the full potential of precision medicine in routine clinical practice.

Keywords: Precision medicine, Personalized healthcare, Genomics, Biomarkers, Pharmacogenomics, Targeted treatment, Next-generation sequencing (NGS), Data analytics, Artificial intelligence (AI) in medicine, Genetic profiling, Patient-specific therapy, Predictive modelling, Bioinformatics, Healthcare disparities, Ethical and regulatory issues.

1.0 Introduction:

“Precision medicine tailors healthcare to each patient's unique health, integrating fields like genomics and data-driven decision-making” [1]. Precision medicine, now favoured over "personalized medicine," has gained popularity, driven by scientific and political factors [2]. “Precision medicine tailors treatments to subpopulations with shared disease risks or drug responses, replacing "personalized medicine" to avoid misinterpretation. It emphasizes genetic, environmental, social, and behavioural factors, marking a shift from "one-size-fits-all" care [3]. Precision medicine uses decision rules based on patient data to guide treatment, aligning with evidence-based medicine that relies on empirical evidence from randomized controlled trials [1].

1.1 History:

It was further clarified during the classical period when the practice of medicine was differentiated and every doctor became a specialist for one disease, one body part by the adaptation of that ancient "Egyptian medicine" to an individual's health status. This is the first evidence of personalized medicine because doctors realized that dividing the diseases according to human parts of the body can help them in achieving a deeper understanding of illness, and so can attain a better outcome of therapy. Greeks were fascinated by this approach of medicine, and that is why they mention Egyptian medicine constantly in their treatises with admiration.

Ancient Egyptian medicine pioneered personalized care by specializing in specific diseases and body parts, influencing Greek medicine. Hippocratic medicine later adapted this knowledge, removing its magico-religious elements while considering patients' needs and beliefs [4]. Hippocrates advocated treating diseases at their origin with personalized, cause-focused approaches, rejecting superstition in medical practice.. Until the 1950s, medicine relied on standardized approaches using population data. The need for evidence-based methods and predicting drug responses led to the emergence of modern personalized medicine [4].

Precision medicine, rooted in earlier concepts like Sir William Osler's insights, evolved through milestones like the DNA double helix discovery, Sanger sequencing, and the Human Genome Project. However, complex diseases involve multiple genes with limited predictive power, necessitating advanced technologies and approaches [3]. The term "precision medicine" gained prominence in 2015 when President Obama launched the Precision Medicine Initiative. This sparked significant interest and research, as seen in a 1000-fold increase in Google searches. The review highlights key discoveries, ongoing challenges, and insights for future healthcare, including handling epidemics like COVID-19 [4].

1.1.1 Traditional medicine versus precision medicine:

Traditional medicine's "one-size-fits-all" approach led to variable patient responses and side effects. Precision medicine, powered by Big Data and advances in genetics, enables more personalized treatments by analyzing large datasets to identify effective treatments for specific populations [3].

1.2 Scope in medicine:

Precision medicine in cancer tailors treatments based on a patient's genetics, lifestyle, and tumor characteristics. It offers an alternative to standard therapies like chemotherapy and radiation, which are often ineffective for many patients and harmful to healthy tissues. [5]. In precision oncology, doctors sequence tumor genomes to identify mutations and match them with effective therapies. A key example is chronic myeloid leukaemia (CML), where imatinib targets the BCR-ABL fusion protein, offering better outcomes than chemotherapy [5].

CML is driven by the BCR-ABL fusion gene, and imatinib targets this mutation, improving outcomes. Additionally, targeted immunotherapies like CAR T-cell therapy enhance cancer treatment by engineering T cells to target specific cancer antigens [5]. Genetic research has advanced pharmacogenomics, tailoring drug selection and dosing to patients' genetic traits. Guidelines for drug-gene interactions are provided by the CPIC and DPWG [6].

Pharmacogenomics tailors drug selection and dosing based on genetic factors, with validated guidelines for drugs like warfarin and clopidogrel. PGx tests improve treatment efficacy and cost-effectiveness, and pharmacogenomics will play a key role in optimizing therapy in the future [7]. Pharmacogenomics focuses on genetic variations in drug transporters and liver enzymes, integrating this data with electronic healthcare records for efficient access. It offers hope for patients with rare diseases, affecting about one in ten people [8]. Precision medicine offers hope for diagnosing and treating rare diseases, affecting 3.5%–5.9% of the population. Advances in genomic sequencing have enabled significant discoveries in rare diseases and highlighted individual differences in conditions like diabetes [8]. Precision medicine aims to identify the specific cause of hyperglycemia in each diabetic patient and tailor treatment accordingly. For rare diseases, genomic sequencing advances patients directly to precision therapeutics, targeting the root cause with tailored therapies. [8].

Genomic sequencing (GS) as a first-line investigation in rare diseases (RDs) can shorten diagnosis time and address the diagnostic odyssey. The development of tools like Sanger sequencing and PCR has greatly advanced understanding of RDs since Dr. McKusick's 1966 work on Mendelian inheritance [9]. Despite the high cost, whole genome sequencing is expected to become the primary method for diagnosing rare diseases [9].

2.0 Core Concepts:

2.1 Genomics and pharmacogenomics:

Pharmacogenomics (PGx) helps tailor drug treatments based on genetic variations and aids in identifying inherited cancer risks. Genetic testing for cancer syndromes like hereditary breast-ovarian cancer and Lynch syndrome enables early detection and preventive interventions, with ongoing research expanding these strategies [10]. Pharmacogenomics uses genetic data to predict drug response and guide individualized treatment. It builds on pharmacogenetics, focusing on genetic polymorphisms that affect drug efficacy and toxicity. The goal is to reduce adverse effects, improve efficacy, and enable personalized medicine through better drug selection and dosing. [11]. PGx testing identifies genetic polymorphisms and mutations to guide personalized cancer treatment, improving drug efficacy, reducing adverse drug reactions (ADRs), and enhancing patient outcomes (Refer to fig1) [11].



Figure 1: Genomics and pharmacogenomics

2.2 Biomarkers:

Biomarkers are classified into three types: exposure, effect, and susceptibility. In therapeutic development, disease-specific biomarkers, like those in breast cancer (e.g., ER, PR, HER2), enable precision medicine by tailoring treatments to individuals or patient subpopulations, improving efficacy and reducing healthcare costs (Refer to fig2) [12].

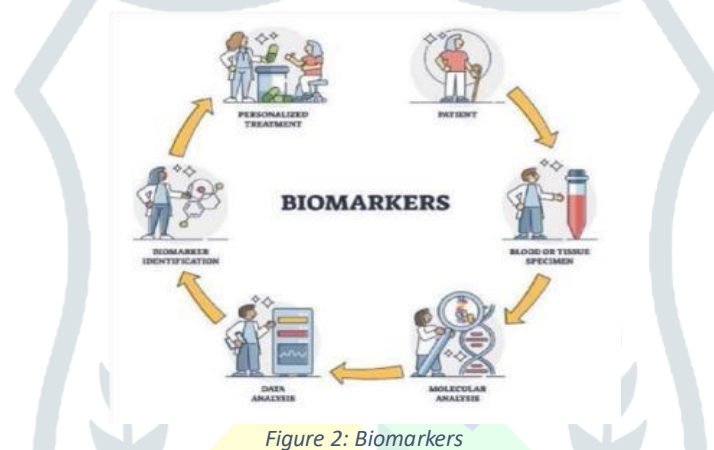


Figure 2: Biomarkers

2.2.1.1 Different types of biomarkers:

There are several different types of biomarkers that can include genetic biomarkers, epigenetic biomarkers, metabolite biomarkers, and protein biomarkers [13].

2.2.1.2 Genetic biomarkers:

Identify mutations or aberrations linked to diseases, guiding treatment decisions, especially in cancer (e.g., oncogenes and proto-oncogenes) [13].

2.2.1.3 Genetic biomarkers for cancer, including:

Oncogenes are mutated or overactive proto-oncogenes that drive uncontrolled cell growth, similar to jammed gas pedals, leading to cancer. Proto-oncogenes are normal genes that regulate cell division. [13].

2.2.1.4 Microsatellite instability (MSI):

A genetic defect increasing cancer risk, found in cancers like colorectal and breast cancer [13].

2.2.1.5 Epigenetic biomarkers:

Measure gene expression changes due to chemical modifications in DNA, aiding in cancer diagnosis and treatment [13].

2.2.1.6 Protein biomarkers:

Proteins produced by diseased cells, useful in cancer detection and monitoring (e.g., PSA, HER2). [13].

2.2.1.7 Metabolite biomarkers:

Small molecules from cellular metabolism, found in bodily fluids, helping detect cancers like lung and pancreatic cancer [13].

2.2.1.8 Transcriptome biomarkers:

Based on differential gene expression, used to understand disease progression, drug efficacy, and patient responses [13].

2.2.1.9 Imaging biomarkers (IB):

Techniques like MRI, PET, CT, and ultrasound to assess tumor size, shape, and progression, aiding treatment customization. AI enhances diagnosis precision. [13].

2.2.2.0 Prognosis:

Predict disease course and survival, guiding therapeutic decisions (e.g., Oncotype DX for breast cancer, Ki-67 for tumor proliferation) [13].

2.2.2.1 Therapy monitoring:

Biomarkers like PET scans, MRIs, and ctDNA track treatment response, guiding therapy decisions. PET/CT and PET/MRI reduce diagnostic variability [13]. Cancer screening: Biomarkers like PSA, CEA, ctDNA (EGFR, KRAS, BRAF), and CA125 help identify cancer risk and monitor treatment response. [13].

2.3 Data Integration:

Data integration in precision medicine faces challenges due to the complexity of medical data, which combine heterogeneous information. Without proper processing and conversion, this data is unusable. A growing gap exists between the generation of omics data and the ability to integrate and interpret it effectively (Refer to fig3) [14].

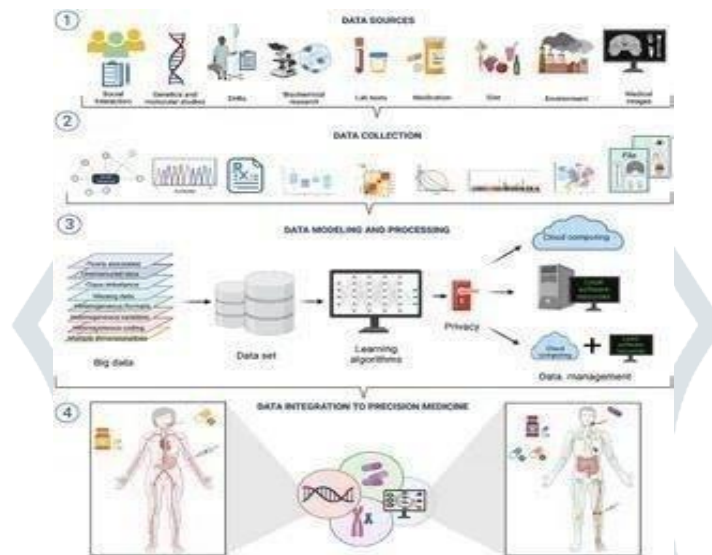


Figure 3: Data Integration

The focus on generating and storing large amounts of data has created a gap in data integration. Healthcare professionals manage vast amounts of patient information, often stored in Electronic Health Records (EHRs), which are digital versions of medical records, covering past, current, and future health conditions [14].

2.3.1 The role Bio-data:

Big data in healthcare is growing through the integration of various data sources, such as EHRs, genomics, and real-time data from IoT devices. It aims to improve service quality, efficiency, reduce costs, and medical errors. Despite challenges in integrating big data and precision medicine, they offer significant benefits in enhancing patient care, resource allocation, and reducing waste in healthcare systems [14]. Big data in healthcare integrates data from various sources like clinical tests, laboratory tests, imaging, and genetics, providing more insightful intelligence compared to traditional single-source observations [14].

2.3.2 Bio Informatics:

Bioinformatics is essential for precision medicine, enabling personalized treatment plans based on individual genetic makeup and health profiles. Although initial costs are high, advancements in technology will make it more affordable and effective for future generations [14]. Bioinformatics in precision medicine involves compiling various omics biomarkers (e.g., SNPs, DNAs, proteins, metabolites) and requires processing raw data, statistical analysis, and data integration. Metabolomics analysis, for instance, uses specialized tools for data mining, integration, and mathematical modeling. Improvements in organizational, technological, and educational aspects are essential for advancing bioinformatics in precision medicine [16].

2.3.3 Artificial Intelligence [AI]:

AI is transforming precision medicine by enhancing personalized care through tailored prevention, diagnosis, and treatment based on genetics, phenotype, epigenetics, and lifestyle. AI leverages multimodal datasets to predict disease characteristics, dose-response, risk, prognosis, treatment response, and patient outcomes [19].

AI is advancing in three key areas: patient care, data analytics, and precision medicine. It is essential for precision medicine, enabling more accurate treatment predictions by analyzing genes, environment, and lifestyle. AI/ML technologies support decision-making by examining big data, scientific knowledge, and providing decision support. Machine learning identifies patterns in data, guiding treatment selection through genomic, proteomic, immune, and morphological profiling. [18].

AI is essential for precision medicine, leveraging big data through highperformance computing, machine learning, and deep learning. It includes technologies like neural networks and natural language processing, enhancing physicians' cognitive capabilities in treatment decisions [17].

3.0 Applications of Precision Medicine

3.1 Oncology:

Precision oncology uses individual tumor characteristics to guide therapy, such as HER2 amplification in breast cancer or EGFR mutations in lung cancer, to predict treatment efficacy. Preclinical models like PDX and PDO help personalize therapy, with advances enabling more patient-derived models for better drug discovery and response prediction, especially for metastatic cancers. [20]. Precision medicine aids cancer prediction through genetic screening and molecular profiling, which can assess tumor sensitivity to treatments like radiation. Technologies such as MR-linac and proton therapy allow for precise targeting, minimizing damage to surrounding tissues [21]. Precision oncology targets somatic mutations, such as driver mutations in oncogenes, to guide cancer treatment. Examples include HER2 testing for trastuzumab in breast cancer, imatinib for chronic myeloid leukemia, erlotinib for lung adenocarcinoma, and pembrolizumab for metastatic melanoma (Refer to fig4) [22].

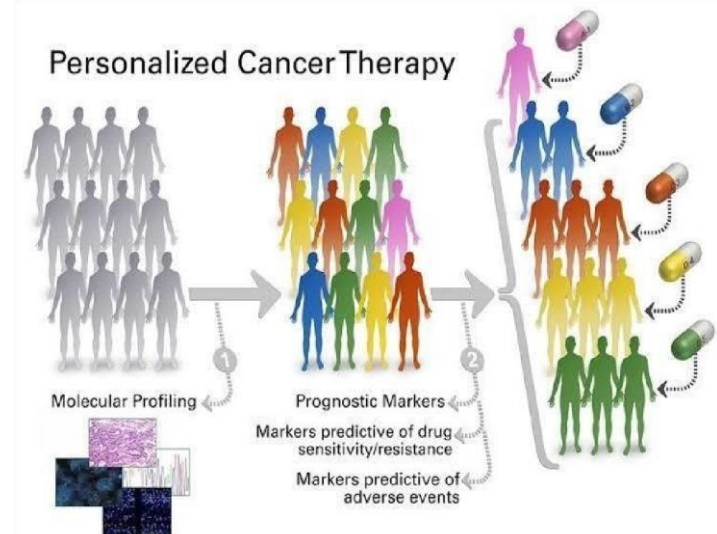


Figure 4: Oncology

3.2 Cardiology:

Precision medicine in cardiovascular disease integrates genetics, lifestyle, and exposures to tailor prevention and treatment. Over the last 50 years, lifestyle modifications (diet, tobacco, exercise) and evidence-based therapies have helped address cardiovascular risk. Nuclear cardiology, using PET and SPECT imaging, has become essential for diagnosing, stratifying risk, and managing heart disease. These technologies provide detailed insights into myocardial perfusion, function, and metabolism, using radiotracers to visualize the heart's structure and Cardiology (Refer to fig5)[23].

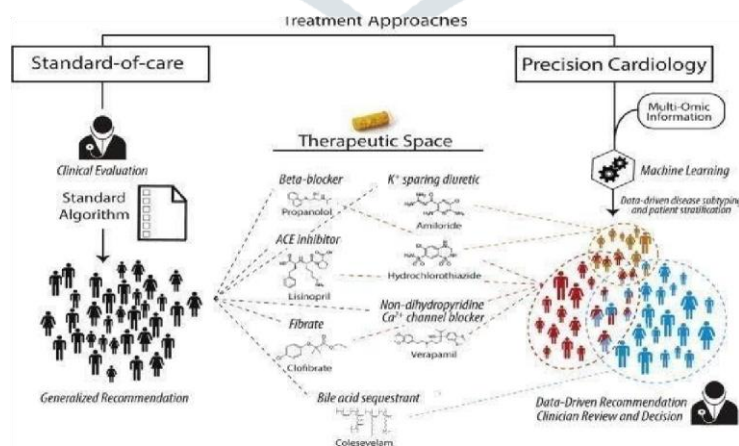


Figure 5: Cardiology

PET is an advanced imaging technique that provides high spatial and temporal resolution, measuring myocardial blood flow and viability through positron-emitting radiotracers. SPECT, another key imaging tool, uses gamma-emitting radiotracers for 3D visualization of the heart, detecting ischemia and infarcted tissue. In cystic fibrosis (CF), caused by CFTR gene mutations, abnormally thick secretions lead to complications like bronchiectasis and pancreatitis. Prior to modern interventions, most CF patients died before age five. [24].

Precision medicine is applied in stroke and cardiovascular disease, including heart failure, atrial fibrillation, and atherosclerosis, which stem from chronic conditions like obesity, diabetes, and hypertension. Cardiovascular professionals encourage healthy lifestyles for primary and secondary prevention to avoid future cardiovascular diagnoses [25].

3.3 Pharmacogenomics:

Pharmacogenomics studies the relationship between genomic variations and drug effects. While pharmacogenetics focuses on the impact of single genes, pharmacogenomics helps guide drug discovery, development, and personalized treatment. It assists doctors in selecting drugs based on patients' genetic profiles, reducing adverse drug reactions (ADRs), and optimizing drug dosages. The Human Genome Project revealed that humans have about 20,500 genes, with 99.5% being identical across individuals [26].

The 0.5% genetic variation among individuals affects traits like eye color, blood type, and disease susceptibility. Structural variations (SV) such as deletions, insertions, and copy number variations (CNV) also play a role. Pharmacogenomic testing enables personalized treatment, optimizing drug therapies and concentrations based on genetic profiles, improving effectiveness and reducing adverse effects. However, challenges remain, including lack of standardized testing, limited education, and ongoing regulatory and ethical concerns [26].

3.4 Rare Diseases:

Historically, rare diseases (RDs) were often considered hopeless, affecting about one in ten people with over 10,000 known conditions. Genomic sequencing (GS) is now a first-line tool for diagnosing RDs, potentially reducing diagnostic delays. Advances like CRISPR have enhanced precision medicine, enabling genetic modifications for disease modeling and patientspecific treatments. In rare diseases, GS can expedite the shift to precision therapeutics, targeting the root cause of conditions. Lessons from precision medicine in rare diseases are also benefiting fields like oncology [27].

4.0 Technological Advances:

4.1 Genomic Sequencing:

New technologies, such as liquid biopsies, are rapidly advancing precision medicine. Liquid biopsies analyze cells, DNA, RNA, proteins, or vesicles from blood to provide insights into tumor biology and metastasis. Advances in DNA sequencing, offering high accuracy at reduced costs, are making personalized treatments based on genetic variations increasingly feasible [29].

Genomic sequencing technologies have advanced significantly, with next-generation sequencing (NGS) now able to rapidly and affordably sequence large numbers of genes. While its clinical utility in precision medicine, especially in oncology, remains debated, NGS allows for treatments tailored to molecular alterations. Initially, Sanger sequencing was the gold standard, but it was expensive and impractical for sequencing multiple targets. Today, NGS can sequence an entire human genome in days for a few thousand dollars, depending on the application (Refer to fig6) [30].

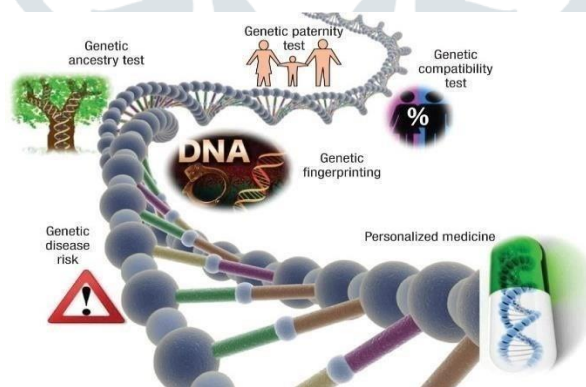


Figure 6: Genomic Sequencing

4.2 CRISPR and Gene Editing:

CRISPR is a powerful gene-editing tool originally part of a bacterial immune response, allowing precise modifications of genes. It has revived interest in gene therapy, which aims to treat diseases like cancer and genetic disorders. CRISPR-Cas9 enables targeted gene modifications using RNA guide sequences, with new high-fidelity versions reducing off-target effects. Gene therapy can be delivered via viral methods (lentivirus, adenovirus) or non-viral methods (lipid-mediated transfection, electroporation). The technology holds promise for more accurate and permanent treatments, though challenges remain in delivery methods and potential side effects [29].

CRISPR-Cas9, derived from bacterial adaptive immunity, enables precise genome editing. In 2012, researchers demonstrated that Cas9 recognizes target sites using a guide RNA (gRNA) and a conserved PAM sequence. This system has been optimized for genome engineering, offering flexibility by allowing the same

gRNA to target various sites. To improve specificity, innovations like Cas9 nickases and truncated gRNAs have been developed, reducing off-target effects by requiring two adjacent nicks or enhancing sensitivity at target sites. Tools like E-CRISP aid in easier target site selection and gRNA construction (Refer to fig7) [32].

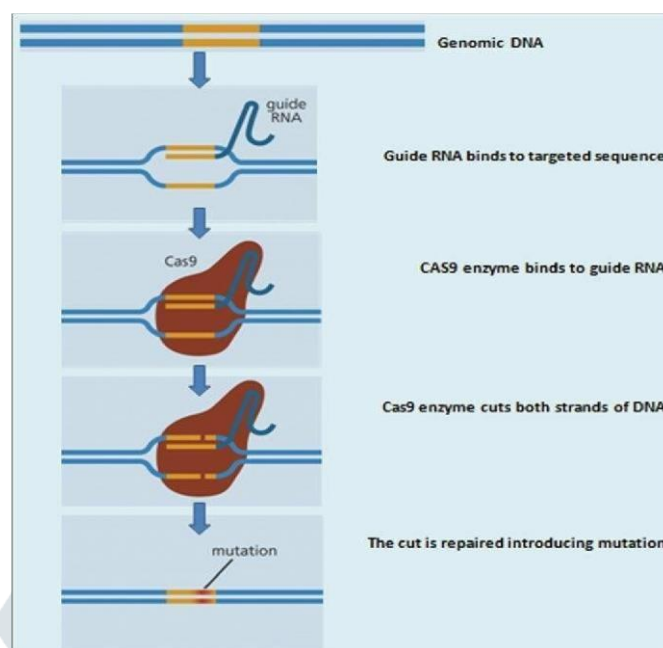


Figure 7: CRISPR and Gene Editing

4.3 Artificial Intelligence (AI):

Artificial Intelligence (AI) is foundational for precision medicine, offering precise and accurate healthcare solutions. Over the last decade, AI has grown significantly, enabling smart product designs, innovative services, and new business models. AI is categorized into artificial narrow intelligence (ANI), artificial general intelligence, and artificial superintelligence, with ANI expected to dominate in the near future. ANI supports physicians by analysing data, identifying correlations, and aiding decision-making. AI and machine learning (ML) enhance drug design by improving understanding of disease pathology, predicting therapeutic targets, and analysing drug efficacy. While promising, AI also raises ethical concerns regarding safety, privacy, and human rights [19]. Data safety and privacy are crucial for AI-driven precision medicine. As data collection and integration grow, trust hinges on robust privacy measures. A secure ecosystem for data storage, management, and sharing is essential, requiring advanced technologies, collaborations, updated regulations, and innovative business models (Refer to fig8) [31].

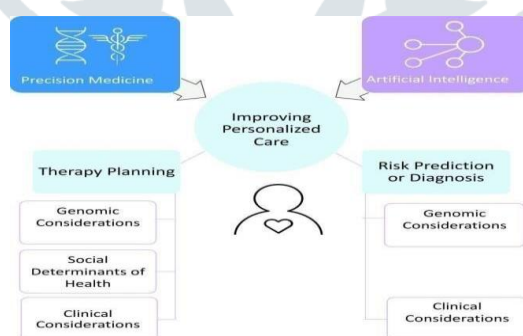


Figure 8: Artificial Intelligence (AI)

5.0 Challenges And Limitations

5.1 Cost and Accessibility:

Precision medicine (PM) enables targeted, cost-effective treatments for patient subpopulations, improving outcomes. However, its cost-effectiveness remains uncertain, necessitating evaluations to guide policy decisions on reimbursement, research, and investment in solidarity-based health systems [33]. Challenges in evaluating the economic efficiency (EE) of precision medicine (PM) include limited real-world evidence on long-term effects, underreporting of unintended outcomes, variable costs across settings, and neglect of patient autonomy and behavior changes. Randomized controlled trials often fail to capture individualized effects, complicating EE assessments [34].

Economic evaluations "identify, measure, value and compare the benefits to the costs of the alternatives being considered" both in terms of cost and outcomes, and combine them in analytical models to determine the cost per

quality-adjusted life year (QALY) gained through a specific intervention compared with a standard of care. Most of the previous systematic reviews incorporated inconclusive evidence relating the cost-effectiveness of PM, mainly due to the poor quality of the studies included. The main points of criticism in this respect had been inadequate sensitivity analyses, poor methodology in most cases, inconsistencies based on lack of clinical evidence and poor quality of data entering into economic models, besides heterogeneity between study designs, models and populations [33].

5.2 Data Privacy and Security:

Healthcare data, including sensitive patient and carer information, must be protected to ensure privacy and trust. Data breaches can lead to personal and professional harm, such as bullying or job loss. Public trust is crucial as they are the primary source of data; without it, precision health systems lose effectiveness. Strict adherence to security, ethical, and regulatory standards is essential for safeguarding healthcare data and enabling the benefits of precision health [35].

Precision health relies on rapidly growing health data, fueled by EHRs, medical imaging, and IoMT devices like wearables. The data lifecycle includes generation, collection, processing, storage, management, analytics, and inference. Data analytics transforms raw data into actionable insights, supporting evidence-based healthcare while safeguarding Protected Health Information (PHI) [36].

5.3 Regulatory Issues:

Regulatory issues in tissue bio resources include the underuse of bio specimens, despite donor expectations for research utility. Adhering to best practices from ISBER, NCI, CTRNet, ISO, and CAP ensures high-quality tissues for biomedical research. While IRB approval is required, human tissues for research lack comprehensive regulatory oversight compared to those used directly in precision medicine (Refer to fig9) [37].

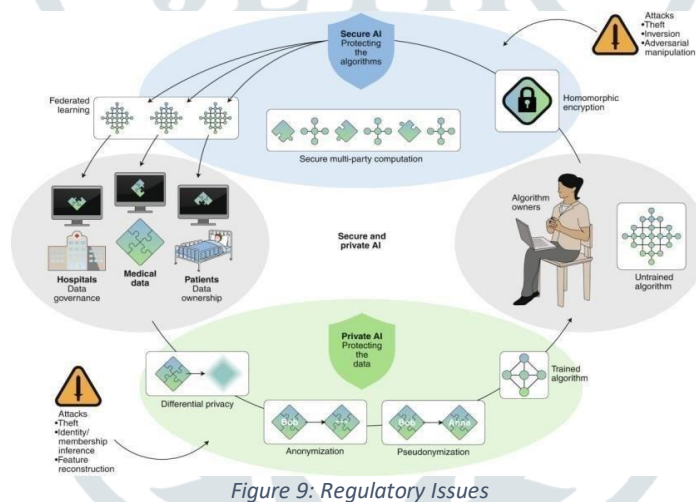


Figure 9: Regulatory Issues

5.4 Equity:

Achieving equity in precision medicine requires scientists and clinicians to oppose misuse of genetic science to propagate biased racial group views. While distinct, precision medicine and eugenics share parallels, emphasizing genetics for societal improvement. The Precision Medicine Initiative must align with the U.S. Constitutional mandate of equal protection under the law [38].

6.0 Ethical and Legal Considerations

6.1 Informed Consent:

Informed consent in precision medicine involves voluntary authorization by a patient or substitute decision-maker. Challenges include future data use, result disclosure, and genetic information considerations. Paediatric consent is case-specific, with minors providing assent and guardians or authorized adults making decisions. A two-step process, such as consenting to genetic screening after initial diagnostic consent, may support informed decision-making [39].

6.2 Genetic Discrimination:

Genetic discrimination is the unfair treatment of individuals or families based on perceived genetic differences from the "normal" human genotype [40]. Genetic discrimination (GD) involves unfair treatment based on genetic differences, impairing human rights, freedoms, and dignity. Similar to other forms of discrimination, GD can lead to exclusion, limited opportunities, and psychological, social, and economic harm. To address this issue, the Genetic Discrimination Observatory (GDO) was established in 2018 to research and develop solutions [41].

For nearly 30 years, concerns about genetic discrimination (GD) have involved medical professionals, advocacy groups, and academia. In 2001, the American College of Medical Genetics and Genomics emphasized strategies to prevent GD. Genetic information can enhance research and diagnoses but may also lead to discrimination, such as unequal treatment based on genetic risks. The Genetic Information and Non-discrimination Act (GINA) protects against workplace and health insurance discrimination but has limitations. Issues of distributive justice arise when access to genetic testing benefits is unequal, requiring fair allocation of resources and burdens [42].

6.3 Patient Privacy:

Healthcare providers must protect patient confidentiality and medical records by implementing best practices for data security, especially with the rise of electronic health information. Providers should secure networks, avoid compromising password security, and use automatic logoffs. Patients should be educated on protecting their privacy and preventing identity theft. Laws like HIPAA and the HITECH Act provide legal frameworks to safeguard patient data. Collaboration between patients and healthcare workers is crucial to prevent data misuse and breaches [43].

7.0 Current and Future Trends

7.1 Personalized Vaccines:

Personalized cancer vaccines, such as sipuleucel-T for prostate cancer and emerging mRNA vaccines for melanoma and pancreatic cancer, show promise but face challenges in improving efficacy and reducing toxicity. These vaccines are customized based on an individual's tumor, genetic makeup, immune response, and health status, aiming for more effective outcomes with fewer adverse reactions compared to conventional vaccines, which typically generate a uniform immune response across individuals [46].

Personalized cancer vaccines start with patient profiling, including genomic analysis, immune response assessment, and biomarker identification. In February 2023, the FDA granted breakthrough designation to a personalized mRNA vaccine combined with a monoclonal antibody targeting PD-1 for treating high-risk stage III/IV melanoma patients, based on the unpublished KEYNOTE-942 phase 2b trial [44].

Hepatocellular carcinoma (HCC) has a poor prognosis, with only 1 in 10 patients surviving five years. A Phase I study from the Kimmel Cancer Centre showed that combining a personalized antitumor vaccine with a PD-1 inhibitor improved survival in HCC patients, offering a potential new treatment approach (Refer to fig10) [45].

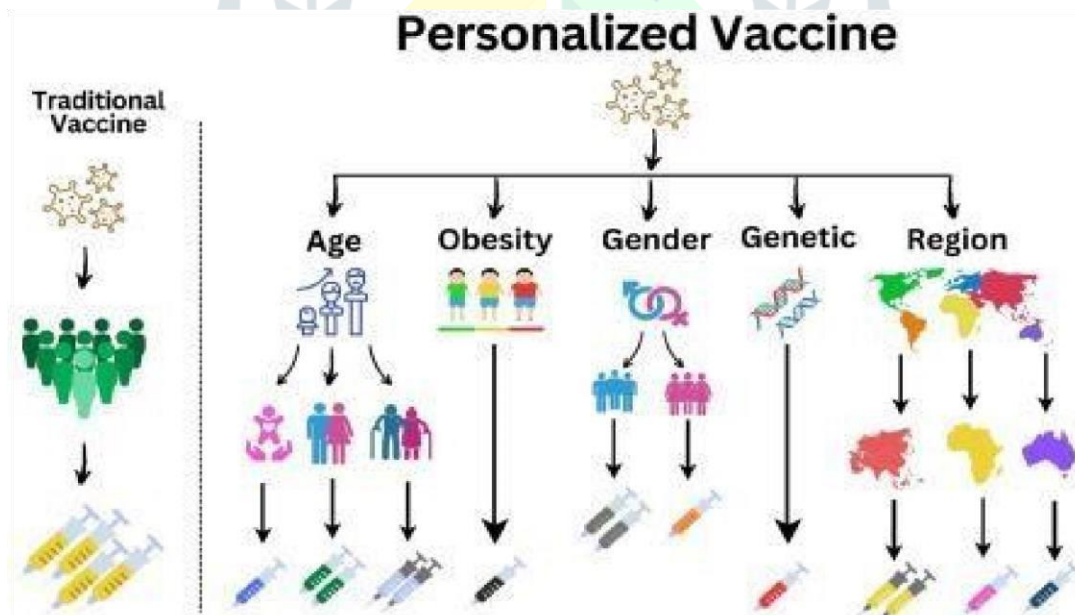


Figure 10: Personalized Vaccines

7.2 Multi-Omics Approach:

Next-generation sequencing (NGS) has revolutionized genomics, epigenomic, and transcriptomic by enabling high-throughput sequencing. However, it generates massive amounts of data (e.g., 200 Gb per whole genome), which can be challenging to interpret and requires significant bioinformatics tools for analysis [48].

Multi-omics integrates clinical and patient-specific omics data (e.g., genomics, metabolomics, and proteomics) to develop personalized therapeutic strategies. It helps identify biomarkers and disease mechanisms for tailored treatments. Despite significant advancements in omics for diseases like cardiovascular disease, challenges remain in effectively combining and leveraging multi-omics data. The goal is to use network medicine to understand disease heterogeneity and guide precision medicine based on individual patient profiles [48].

7.3 Future of Drug Development:

Drug development is becoming increasingly costly and inefficient, but focusing on patient needs rather than just drug details or disease specifics could improve efficiency. Genomics plays a crucial role in personalized medicine by enabling patient stratification based on genomic differences. This requires changes in clinical trial design and drug development business models. While randomized controlled trials remain the gold standard, alternative approaches are being explored to accommodate at-risk populations. Advances in genomics and biomarker testing, alongside evidence-based therapeutics, are driving the industry toward a more efficient and patient-centered drug discovery process (Refer to fig11) [60].

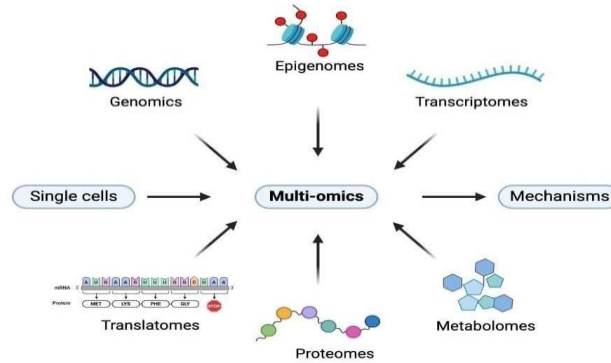


Figure 11: Future of Drug Development

Biomarkers will play a key role in highlighting patient differences, shifting drug discovery from mass-market products to targeted treatments. This shift will create commercial opportunities in target identification, diagnostics, clinical trials, outcomes data, product launch, and market expansion, benefiting drug development [69]. Early trials in molecularly selected patient populations can accelerate proof of concept and improve clinical outcomes, enabling smaller Phase 3 trials and higher success rates. However, biomarker analysis and diagnostic development may increase costs, with some failed drug programs due to incorrect biomarker selection [61].

The pharmaceutical industry's R&D is crucial for discovering new therapies, but the drug development process is lengthy and expensive. Economic estimates related to pharmaceutical innovation, including costs, influence policy decisions, such as healthcare financing reforms and changes in intellectual property laws, which may impact R&D activities [62].

Precision medicine in cancer focuses on sequencing tumors to identify driver mutations and targeting therapies accordingly. Early successes led to collaborations between pharmaceutical companies and academic groups to speed up drug development. However, challenges in using patient-derived xenografts (PDXs) as preclinical models include issues with the tumor microenvironment and the need for immune reconstitution, prompting the development of alternative models [63].

Personalized health monitoring, especially for chronic diseases and aging populations, benefits from deep learning (DL) for accurate, timely predictions. Smart medical gadgets collect patient data (heart rate, blood pressure, blood flow), which is stored in medical repositories. This data is then processed via machine learning, where the collected data acts as testing data to generate predictions [67].

Digital therapeutics (DTx) are evidence-based, software-driven interventions for the prevention and treatment of medical conditions. They focus on modifying patient behavior and remote monitoring to improve health outcomes. DTx is emerging as a promising solution in an era of costly and inefficient drug development, aiming for better and more sustainable health results [65].

Tumor biomarker tests are used to detect or quantify changes in tumor biomarkers for various purposes, including risk stratification, screening, diagnosis, prognosis, predicting therapeutic effectiveness, and follow-up. These tests, often immunologically based, help distinguish between benign and malignant tissues or identify the type of cancer, such as epithelial versus hematopoietic or mesenchymal. Developing and validating these tests requires addressing critical issues, particularly defining their intended use [66].

CRISPR/Cas9 is a powerful gene-editing technology that allows for the correction of genetic errors and the manipulation of genes in cells and organisms. It holds promise for treating genetic diseases through preimplantation genetic modification, but germline modifications, which are permanent, raise ethical concerns, particularly regarding potential non-therapeutic genetic enhancements. The legal boundaries for the use of CRISPR/Cas9, especially for germline editing, are still being debated [68].

7.4 Clinical Trials:

Clinical trials are research studies that assess the safety and efficacy of investigational agents, devices, or biologics in human volunteers. These agents undergo a multi-phase process before receiving approval from regulatory bodies like the USFDA [50].

7.4.1 Clinical trial design:

The shift to precision medicine in cancer treatment has led to changes in clinical trials. Targeted drugs are tested on the patient populations most likely to benefit. For example, basket trials evaluate drugs based on their mechanism of action, rather than the type of cancer they target [49]. Traditional cancer clinical trials include Phase I (safety and activity), Phase II (efficacy and toxicity), Phase III (comparison with standard therapy), and Phase IV (post-marketing surveillance). Advancing a drug to Phase III can cost millions to billions of dollars [51].

7.4.2 Tumour-agnostic/gene-specific basket trials:

Tumor-agnostic/gene-specific basket trials test drugs targeting common gene defects across different cancers, with examples including pembrolizumab for dMMR/MSI-H, larotrectinib/entrectinib for NTRK fusions, and pembrolizumab for TMB-H tumors [51].

7.4.3 Umbrella trials:

Umbrella trials evaluate multiple treatments based on genetic/biomarker subsets within the same cancer type, but face challenges in rare diseases due to small molecular subsets and limited patient enrolment [51].

7.4.4 Platform trials:

Platform trials are master protocols that allow the evaluation of multiple hypotheses and treatments within a single trial, enabling faster and more cost-effective results. However, they are complex to design and implement due to administrative and logistical challenges [51].

7.4.5 Telescope design:

Telescope design combines learning and confirmatory phases (I, II, III) into one trial, allowing simultaneous analysis of both stages, which reduces the drug development timeline and lowers costs (Refer to fig12) [51].

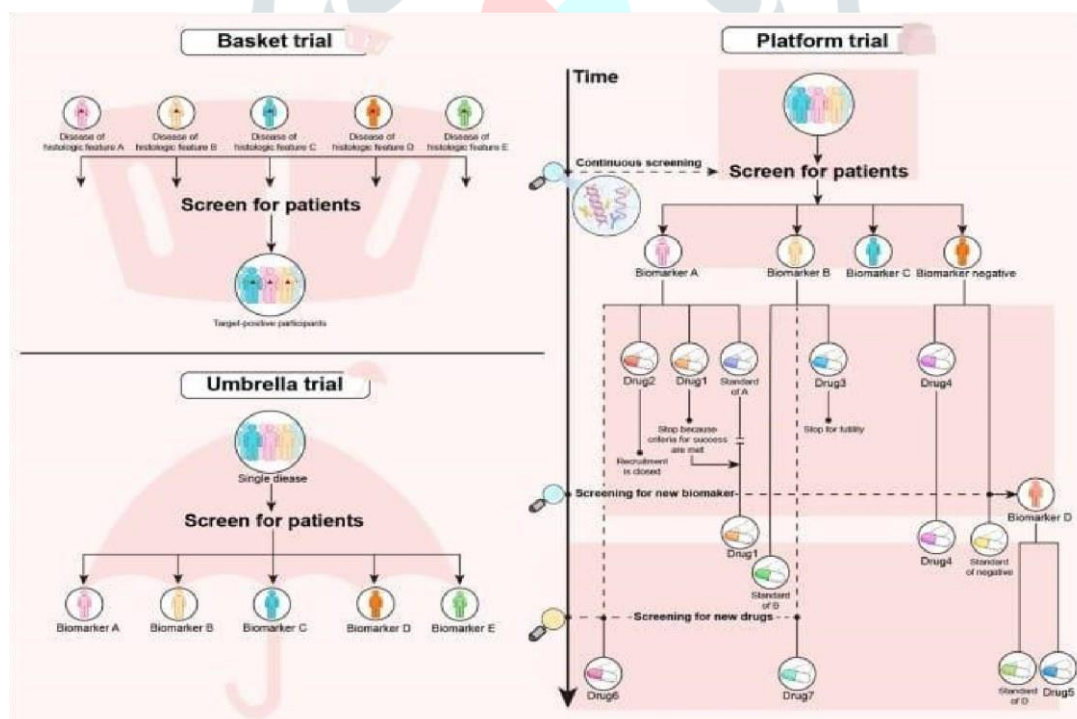


Figure 12: Telescope design

7.4.6 Home-based trials:

Home-based trials use telemedicine to conduct clinical trials remotely, allowing patients, especially those unable to travel, to participate from home. These trials improve patient recruitment, increase enrolment rates, and provide more representative populations for studies [51].

8.0 Global Perspectivess

8.1 Worldwide Implementation:

Over the past two decades, personalized or precision medicine (PM) has advanced significantly with high-throughput genomic technologies. Initially used for research, these technologies now serve as potent diagnostic tools in clinics. Targeted therapies, especially for cancer and rare diseases, have driven a shift from "one-size-

fits-all" to more personalized diagnostics and treatments [54]. In Europe, countries like England, France, Denmark, and Spain adopted national strategies for precision medicine (PM), while countries like Sweden, Germany, and Italy, with regionally organized healthcare, saw healthcare professionals drive bottom-up initiatives to build competence networks and ensure equal access to PM [52].

The German Network for Personalized Medicine (DNPM) was initiated in BadenWürttemberg with regional Centres for Personalized Medicine in university hospitals, focusing on harmonized diagnostics, decision-making, and equal drug access. Similarly, Genomic Medicine Sweden (GMS), launched in 2017, is a bottom-up effort involving a multiprofessional team to implement genomically-based precision medicine in Swedish healthcare (Refer to fig13) [54].

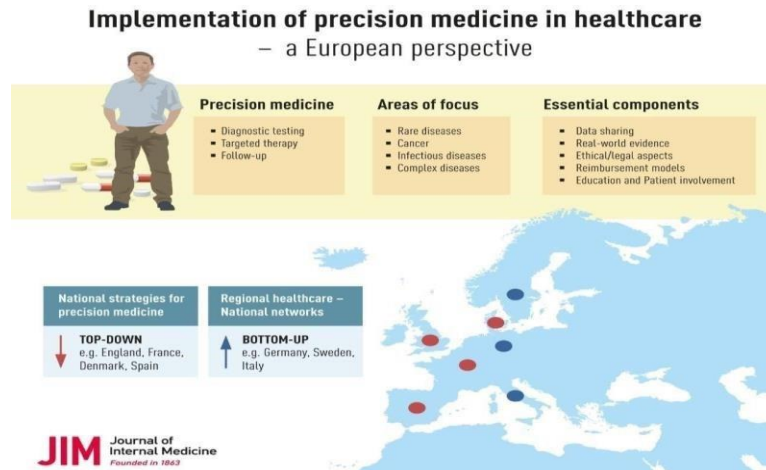


Figure 13: Worldwide Implementation

Genomic Medicine Sweden (GMS) established regional Genomic Medicine Centres in Swedish university hospitals to implement genomic-based diagnostics and spread precision medicine for rare diseases, cancer, and complex conditions. A National Genomic Platform facilitates data storage and sharing nationally and internationally. In Japan, the SCRUM-Japan cancer genome screening project promotes precision cancer screening and treatment through collaboration between research, government, and pharmaceutical agencies [53].

In the USA, clinical laboratories use NGS-based tests, from targeted hotspot panels to comprehensive genome-scale platforms, in CLIA-approved labs. These tests, which may include laboratory-developed tests not FDA-approved, assist in diagnosis, prognosis, and treatment choices. They support FDA-approved drugs, off-label treatments, and targeted therapies in clinical trials for various tumor types [55].

8.2 Collaborative Efforts:

Founded in 2016, the Global Genomic Medicine Collaborative (G2MC) is a U.S.-based, not-for-profit organization aimed at advancing genomic medicine globally. It emerged from a 2014 meeting of genomic leaders and fosters international collaborations in education, policy, pharmacogenomics, and evidence generation. The UK's 100,000 Genome Project, through Genomics England, serves as an example of public-private partnership in genomic medicine, ensuring quality control and collaboration. G2MC works with organizations like GA4GH to support coordinated global efforts in genomic medicine [57].

The STRIPE Initiative is a collaborative effort aimed at advancing pharmacogenomics by standardizing laboratory practices. It brings together diverse stakeholders, including geneticists, clinicians, and bioinformaticians, to foster consensus and drive progress in precision medicine, ensuring a holistic approach to addressing its complex challenges [56]. The "Integrating China in the International Consortium for Personalized Medicine" project, funded by the International Consortium for Personalized Medicine, aims to educate healthcare professionals and empower citizens. It focuses on bridging precision medicine barriers between the EU and China, fostering collaboration for a sustainable healthcare system [59].

The "Integrating China in the International Consortium for Personalized Medicine" (IC2PerMed) aims to develop a shared strategy for precision medicine (PM) research, innovation, and application between the EU and China. The initiative focuses on using Big Data and digital tools to improve sustainability and healthcare quality. IC2PerMed held three workshops to identify priority areas in PM, involving 47 experts (37 from the EU and 10 from China), based on critical factors from the 'ICPerMed Vision for 2030' and policy mapping [58].

9.0 Conclusion:

This review highlights the transformative potential of precision medicine in advancing personalized healthcare. By focusing on the unique characteristics of each patient, including genetic, environmental, and lifestyle factors, precision medicine offers tailored treatment strategies that improve outcomes and minimize adverse effects. However, to fully harness its benefits, it is essential to navigate challenges related to data

integration, ethical considerations, and equitable access. Continued innovation and collaboration across disciplines will be vital in overcoming these obstacles and ensuring that precision medicine becomes an integral part of healthcare, ultimately leading to better patient care and improved public health.

10.0 References

1. Kosorok MR, Laber EB. Precision medicine. *Annu Rev Stat Appl*. 2019 Mar; 6:263-286.
2. König IR, Fuchs O, Hansen G, von Mutius E, Kopp MV. What is precision medicine? *Eur Respir J*. 2017;50(4):1700391.
3. Naithani N, Sinha S, Misra P, Vasudevan B, Sahu R. Precision medicine: Concept and tools. *J Family Med Prim Care*. 2021 Jul 3;10(7):2365-2371.
4. Visvikis-Siest S, Theodoridou D, Kontoe MS, Kumar S, Marschler M. Milestones in personalized medicine: From the ancient time to nowadays—the provocation of COVID-19. *J Pers Med*. 2020 Nov 30;10(4):215.
5. Roberts R. Precision medicine: A new era in cancer therapy. *Cancer Ther*. 2023 Dec 15;12(4):345357.
6. Cecchin E, Stocco G. Pharmacogenomics and personalized medicine. *J Pharmacol Sci*. 2020 Jun 22;144(6):453-460.
7. Getahun KA, Angaw DA, Asres MS, Kahaliw W, Petros Z, Abay SM, Yimer G, Berhane N. The role of pharmacogenomics studies for precision medicine among Ethiopian patients and their clinical implications. *J Pharm Genomics*. 2024 Jul 1;15(7):112-12.
8. Might M, Crouse AB. Why rare disease needs precision medicine and precision medicine needs rare disease. *Rare Dis*. 2022 Feb 15;10(1):1-8.
9. Tesi B, Boileau C, Boycott KM, Canaud G, Caulfield M, Choukair D, Hill S, Spielmann M, Wedell A, Wirta V, Nordgren A, Lindstrand A. Precision medicine in rare diseases: What is next? *J Rare Dis*. 2023 May 21;8(5):123-134.
10. Korngiebel DM, Thummel KE, Burke W. Implementing precision medicine: The ethical challenges. *Genet Med*. 2016 Dec 7;18(12):1233-1239.
11. Williams D, Le Roch KG. In: *Genomic and Precision Medicine*. 3rd ed. 2019.
12. Slikker WS Jr. Biomarkers and their impact on precision medicine. *Toxicol Sci*. 2017 Sep 19;158(1):1-7.
13. Gadade DD, Jha H, Khan F. Unlocking the power of precision medicine: exploring the role of biomarkers in cancer management. *Cancer Manag Res*. 2024 Jan 5; 16:23-31.
14. Badr Y, Abdul Kader L, Shamayleh A. The use of big data in personalized healthcare to reduce inventory waste and optimize patient treatment. *J Pers Health*. 2024 Apr 3;12(4):145-152.
15. Balakrishnan M. Leveraging big data analytics for precision medicine. *J Med Innov*. 2024 Jul 1;18(7):101-108.
16. Azad RK, Shulaev V. Metabolomics technology and bioinformatics for precision medicine. *Trends Biotechnology* 2018 Jan 3;36(1):6-14.
17. Mesko B. The role of artificial intelligence in precision medicine. *J Med Internet Res*. 2017 Sep 20;19(9):e295.
18. Hamamoto R, Suvarna K, Yamada M, Kobayashi K, Shinkai N, Miyake M, et al. Application of Artificial Intelligence Technology in Oncology: Towards the Establishment of Precision Medicine. *Cancers*. 2020 Nov 26;12(12):3532. doi: 10.3390/cancers12123532.
19. Sahu M, Gupta R, Ambasta RK, Kumar P. Artificial intelligence and machine learning in precision medicine: A paradigm shift in big data analysis. *Prog Mol Biol Transl Sci*. 2022; 190:57-100.
20. Letai A, Bhola P, Welm AL. Functional precision oncology: testing tumors with drugs to identify vulnerabilities and novel combinations. *Cancer Cell*. 2022 Jan 10;40(1):26-35. doi: 10.1016/j.ccell.2021.12.004.
21. White-Al Habeeb N, Kulasingam V, Diamandis EP, Yousef GM, Tsongalis GJ, Vermeulen L, Zhu Z, Kamel-Reid S. The use of targeted therapies for precision medicine in oncology. *Clin Chem*. 2016 Dec;62(12):1556-1567. doi: 10.1373/clinchem.2016.261607.
22. Schwartzberg LS, Kim ES, Liu D, Schrag D. Precision oncology: who, how, what, when, and when not? *J Clin Oncol*. 2017 May 1;35(13):1507-1509. doi: 10.1200/JCO.2017.71.7074.
23. Leopold JA, Loscalzo J. Emerging role of precision medicine in cardiovascular disease. *Circ Res*. 2018 Apr 27;122(9):1302–1315. doi: 10.1161/CIRCRESAHA.117.310782.
24. Muacevic A, Adler JR, Ayalew BD, Rodoshi ZN, Patel VK, Alresheq A, Babu HM, Aurangzeb RF, Aurangzeb RI, Mdivnishvili M, Rehman A, Shehryar A, Ahmad. Nuclear cardiology in the era of precision medicine: tailoring treatment to the individual patient. *Cureus*. 2024 Apr 24.

25. Bamba H, Singh G, John J, Inban P, Prajjwal P, Alhussain H, Marsool MD. Precision medicine approaches in cardiology and personalized therapies for improved patient outcomes: a systematic review. *Curr Probl Cardiol.* 2024 May;49(5):102470. doi: 10.1016/j.cpcardiol.2024.102470.
26. Chandra R. The role of pharmacogenomics in precision medicine. *Med Lab Obs.* 2017 Aug 22.
27. Matthew Might 1, Andrew B Crouse 1. Why rare disease needs precision medicine—and precision medicine needs rare disease. *Cell Rep Med.* 2022;3(2):100593. doi: 10.1016/j.xcrm.2022.100593.
28. Tesi B, Boileau C, Boycott KM, Canaud G, Caulfield M, Choukair D, Hill S, Spielmann M, Wedell A, Wirta V, Nordgren A, Lindstrand A. Precision medicine in rare diseases: What is next? *J Intern Med.* 2023 May; 294:397-412. doi: 10.1111/joim.13472.
29. Maggi E, Patterson NE, Montagna C. Technological advances in precision medicine and drug development. *Expert Rev Precis Med Drug Dev.* 2016 May 5;1(3):331-343. doi: 10.1080/23808993.2016.1176527.
30. Morash M, Mitchell H, Beltran H, Elemento O, Pathak JM. The role of next-generation sequencing in precision medicine: A review of outcomes in oncology. *J Pers Med.* 2018 Sep 17;8(3):30. doi:10.3390/jpm8030030.
31. Johnson KB, Wei W-Q, Weeraratne D, Frisse ME, Misulis K, Rhee K, Zhao J, Snowdon JL. Precision Medicine, AI, and the Future of Personalized Health Care. *Clin Transl Sci.* 2020 Oct 12;14(1):86-93. doi: 10.1111/cts.12884.
32. Gaj T, Sirk SJ, Shui S, Liu J. Genome-Editing Technologies: Principles and Applications. *Cold Spring Harb Perspect Biol.* 2016 Dec 8;8(12). doi: 10.1101/cshperspect.a.023754.
33. Kasztura M, Richard A, Bempong N-E, Loncar D, Flahault A. Cost-effectiveness of precision medicine. *Expert Rev Precis Med Drug Dev.* 2019 Nov 15;1(3):331-343. doi:10.1080/23808993.2019.1734973.
34. Gavan J, Yates B, McDade L, et al. Evaluating the value for money of precision medicine from early cycle to market access: a comprehensive review of approaches and challenges. *Value Health.* 2023 Sep 9. doi: 10.1016/j.jval.2023.09.001.
35. Thapa C, Camtepe S. Precision health data: Requirements, challenges and existing techniques for data security and privacy. 2021 Feb 29.
36. Fernández-Alemán JL, Carrión Señor IC, Oliver Lozoya PA, Toval A. Security and privacy in electronic health records: a systematic literature review. *J Biomed Inform.* 2013 Jun;46(3):541-62. doi: 10.1016/j.jbi.2013.02.003.
37. Grizzle WE. Ethical and regulatory issues in the use of human tissues to support precision medicine. *J Health Care Poor Underserved.* 2021 Mar 23;30(4):66-78. doi: 10.1353/hpu.2019.0117.
38. 10.1353/hpu.2019.0117.
39. Matthew DB. Two threats to precision medicine equity. *Ethn Dis.* 2019 Dec 12;29(Suppl 3):42-45.
40. Chen D. Ethical frameworks of informed consent in the age of pediatric precision medicine. *Cambridge Prisms: Precision Medicine.* 2024 May 6.
41. Billings PR, Kohn MA, de Cuevas M, Beckwith J, Alper JS, Natowicz MR. Discrimination as a consequence of genetic testing. *Am J Hum Genet.* 1992 Mar;50(3):476-82.
42. Joly Y, Dalpe G. Genetic discrimination still casts a large shadow in 2022. *Eur J Hum Genet.* 2022 Sep 26;30(9):1320-1322. doi: 10.1038/s41431-022-01194-8.
43. Lee SG, Dotson WD, Ortmann L. Genetic discrimination and misuse of genetic information: areas of possible discrimination, current legislation, and potential limitations. *CDC Blogs.* Published October 3, 2022.
44. Taitsman JK, Grimm CM, Agrawal S. Protecting patient privacy and data security. *JAMA.* Published March 14, 2013.
45. Editorial Precision medicine meets cancer vaccines. *Nat Med.* 2023 Jun 16;29:1287. doi: 10.1038/s41591-023-02073-4.
46. Johns Hopkins Medicine. Personalized vaccine for liver cancer shows promise in clinical trial. Johns Hopkins Medicine. Published April 4, 2024.
47. Kaylor A. Maximizing Personalized Approaches with Precision Vaccinology: Personalized vaccine development tailors' immunization to individual needs, enhancing efficacy, safety, and disease prevention in a patient-centred approach. Published 14 Feb 2024.
48. Ahmed Z. Multi-omics strategies for personalized and predictive medicine: past, current, and future translational opportunities. *Emerging Top Life Sci.* 2022;6(1):61-71. doi:10.1042/ETLS20210068.

49. Wang R-S, Maron BA, Loscalzo J. Multiomics network medicine approaches to precision medicine and therapeutics in cardiovascular diseases. *Arterioscler Thromb Vasc Biol.* 2023;43(4):493-503. doi:10.1161/ATVBAHA.122.318731.
50. Dugger SA, Platt A, Goldstein DB. Drug development in the era of precision medicine. *Nat Rev Drug Discov.* 2017 Dec 8;17(12):810-811. doi:10.1038/nrd.2017.226.
51. Heckman-Stoddard BM, Smith JJ. Precision medicine clinical trials: defining new treatment strategies. *J Clin Oncol.* 2014 May 30;32(15):. doi: 10.1200/JCO.2013. 54.7032.
52. Fountzilas E, Tsimberidou AM, Kurzrock R. Clinical trial design in the era of precision medicine. *Genome Med.* 2022 Aug 31;14(1):84. doi: 10.1186/s13073-022-01023-2.
53. Stenzinger A, Moltzen EK, Winkler E, et al. Implementation of precision medicine in healthcare—A European perspective. *J Intern Med.* 2023 Oct;294(4):437-454. doi: 10.1111/joim.13698.
54. Bando H. The current status and problems confronted in delivering precision medicine in Japan and Europe. *Curr Probl Cancer.*2017 May-Jun;41-3:242-248. doi: 10.1016/j. currproblcancer.2017.02.003.
55. Stenzinger A, Moltzen EK, Winkler E, Molnar-Gabor F, Malek N, Costescu A, Jensen BN, Nowak F, Pinto C, Ottersen OP, Schirmacher P, Nordborg J, Seufferlein T, Fröhling S, Edsjö A, Garcia-Foncillas J, Normanno N, Lundgren B, Friedman M, Bolanos N, Tatton-Brown K, Hill S, Rosenquist R. Implementation of precision medicine in healthcare: A European perspective. *J Intern Med.* 2023 Jul 16.
56. Kohno T. Implementation of ‘clinical sequencing’ in cancer genome medicine in Japan. *Cancer Genomics & Translational Medicine.* 2017 Dec 29.
57. Rogers SL, Jones JS, Brown BG. A collaborative force for precision medicine progress: the STRIPE pharmacogenomics conference series. *Pharmacogenomics J.* 2024 Aug 15;24(8):1-8.
58. Ginsburg GS. A global collaborative to advance genomic medicine. *Am J Hum Genet.* 2019 Mar 7;104(3):407-409.
59. Beccia F, Di Marcantonio M, Causio FA, Schleicher L, Wang L, Cadeddu C, Ricciardi W, Boccia S. Integrating China in the International Consortium for Personalised Medicine: a position paper on innovation and digitalization in Personalized Medicine. *BMC Public Health.* 2024 Feb 14. doi: 10.1186/s12889-02418009-8.
60. Beccia F, Causio FA, Boccia S. Integrating China in the international consortium for personalised medicine: a position paper on healthcare professionals’ education and citizens’ empowerment in personalised medicine. *BMC Med Educ.* 2023 Jun 14. doi: 10.1186/s12909-023-04734-7.
61. Lee VH. Personalized medicine: transforming drug development and healthcare. Nov 12, 2010.
62. Ayers A. Personalized medicine – future impact: Pharma industry perspective. Sep 2010.
63. DiMasi JA, Hansen RW, Grabowski HG. The price of innovation: new estimates of drug development costs. *J Health Econ.* 2003 Mar;22(2):151-85. doi: 10.1016/S01676296(02)00096-2.
64. Bose S, Barroso M, Chheda MG, Salnikow K, Chuang JH, Shen X. A path to translation: How 3D patient tumour avatars enables next generation precision oncology. *Cancer Cell.* 2022 Dec 12;40(12): 14691485.e5. doi: 10.1016/j.ccell.2022.11.015.
65. Damaševicius R, Jagatheesaperumal SK, Kandala NVPS, Hussain S, Alizadehsani R, Gorriz J. Deep learning for personalized health monitoring and prediction: A review on deep learning healthcare, personalized health, telemedicine, and wearable devices. *Health Inf Sci Syst.* 2024 May 9;12(1):12. doi: 10.1186/s13755024-00117-2.
66. Dang A, Arora D, Rane P. Role of digital therapeutics and the changing future of healthcare. *J Health Technol.* 2020 May 31;23(5):121-128.
67. Hayes DF. Biomarker validation and testing. *J Clin Oncol.* 2015 May 5;33(13):1463-4. doi: 10.1200/JCO.2014.59.8922.
68. Kondaka LS, Thenmozhi M, Kohli R. An intensive healthcare monitoring paradigm by using IoT based machine learning strategies. *J Health Technol.* 2021 Jun 16;45(6):11211130. doi: 10.1016/j.jht. 2021.06.003.
68. Redman M, King A, Watson C, King D. What is CRISPR/Cas9? *Science.* 2016 Apr 8.
69. Amir-Aslani A, Mange Matin V. The future of drug discovery and development: shifting emphasis towards personalized medicine. *Drug Discov Today.* 2010 Feb 2;15(3-4):120-6. doi: 10.1016/j.drudis.2009.11.004.