Personalized Medicine &Pharmacogenomics: Milestone in Treatment Approach from Traditional to Modern Way

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Abstract

Daily changes in the lifestyle caused so many imbalances in the health condition and using the same medication for all ones is not good. So we approach the modern way in which the treatment is based on the gene studies of a particular person to develop new techniques to treat the diseased condition and prescribed them the best medications that optimized their health perfectly. All the individuals have different gene profiles which makes them venerable and the basis on which we develop these personalized medicines. This genomic portfolio helps in developing the best, safe, and most effective treatment method for a particular person with their unique gene profile. The advancement in personalized medicine can help to detect the diseases at their previous stage with the help of different biomarkers and early detection of genetic events in diseased conditions. By developing this method, there area lot of limitations and challenges that occurred in the way to minimize them different standard measures were also taken to prevent the privacy of individuals. This modern approach provides different applications and benefits in the field of treatment. The detection of various genes is easy through the gene testing help in marking the genes through the biomarkers help to minimize the effect. Nowadays, personalized medicine is mostly preferred by people to treat not only the diseases but also the inherent problem too. Different studies were also performed on a population to get its importance from different scientists, doctors, and pharmacists, and in response that gets good response regarding using such a treatment approach to held. This method not only minimized the side effect of the drug but also guarantee a successful result in treatment.

Keywords Biomarkers, Genomic portfolio, Gene testing, Personalized Medicine, Pharmacogenomic, Venerability

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1. INTRODUCTION

1.1. Personalized Medicine(PM) is a method of treating, diagnosing, and caring for patients with specific ailments. These are the novel techniques for better patient health management and targeted therapies to obtain the greatest outcomes for patient disease treatment. It is not a new concept but a way of caringfor individuals. New technologies such as **Genomics** has been used at a greater level to perform the use of personalized medicines. Personalized medicine is giving the right therapy to the appropriate individual at the appropriate time and in the appropriate amount. Personalized medicine is a relatively new and quickly expanding specialty of

medicine that aims to make therapy as individualized as the disease [1].To determine an individual's susceptibility to disease, new methods of molecular analysis are designed. Generally, personalized medicine consists of two elements i.e. drug, biological, or any other therapeutic entity, and diagnostic test. In today's medicine and healthcare businesses, it's a unique and fascinating topic. It has the potential to change medicine by providing effective and personalized therapy options based on an individual's genetic profile.It not lies only in treatment but also in prevention.

It has a propensity to employ the highest safety margin to monitor therapy with a better response and to provide better patient care[2].In the development of personalized medicines,the adverse outcomes of **trial & error** prescribing methods areno longer dependent**.** For example, the mutation that provides give rise to resistance to certain treatment that provides the clear medical knowledge based upon the treatment ideas that are planned for the individual patient. It is described as "**to provide the right drug with the right dose at the right time to the right patient.**" PM is described as any technology that tries to improve illness prevention, diagnosis, and treatment by identifying the best appropriate care based on a patient's unique features. This is accomplished by the use of diagnostic tools to stratify patients, targeted therapies to target specific biological aspects of a patient's disease, and advanced medicines that are custom-made for each person. PM encompasses both enabling technology and treatment strategies that allow for personalization via disease profiling, patient profiling, and innovative medicines [3].Personalized medicine is promising in improving healthcare while lowering the cost too. For hospital healthcare providers and plan, sponsors, PM represents yet another challenge in uncertain times. Currently, when PM is not effective, the patient may need to change the medications. In media and healthcare, the term "personalized medicines" is frequently used. However, people use the term in a variety of ways, and they aren't necessarily aware that others may interpret it differently. The lack of a single set of uniform dentitions merely adds to the possibility of misinterpretation [4].

1.2 Pharmacogenomics

Pharmacogenomics is a field of genetics that investigates genetic variations in medication responses in people and laboratory animals. It is a broader study of genetic variants in the creation of novel drugs. It is concerned with human genetics and gives a range of medication reactions in different people. Pharmacogenomics aims to uncover gene variants that impact a patient's treatment response and can also reveal disease susceptibility genes that might be used as possible new therapeutic targets.All of this is leading to novel approaches to drug research, personalized pharmaceutical therapy, and illness prevention. Pharmacogenomics also aids in the development of successful pharmacological therapy for a smaller patient group by identifying the same illness phenotype that is characterized by a unique genetic profile. It comprises displaying the advantages for a number of ill person's problems. Pharmacogenomic also presents difficulties in terms of speeding up the procedure when computing the results [5].

Pharmacogenomics can play an important role in identifying responses and non-responds to medication, avoiding adverse effects, and optimizing drug dose. It is the field where the study of genetic variation & drug responses via biomarkers and shows how genes determine individual variability to drug response. Attempt to comprehend how differences in gene expression impact the body's reaction to treatment.Pharmacogenetics and pharmacogenomic studies are both concerned with the genetic information of individual patient drug response variability. Pharmacogenetics researches sequence variation in individual genes is expected to affect medication response, whereas pharmacogenomics researches the total of all gene variations[6].For the appropriate patient, the right medicine at the right dose, as well as its application in the use of cutting-edge technologies to better understand how

drugs work in specific individuals by maximizing drug efficacy while minimizing the side effects. Genes are DNA segments found in every human cell that can affect a person's response to drugs. DNA is a critical component of the body's interactive chemical operating system, guiding the body on how to interact at the cellular level. A single gene can take on a variety of shapes and chemical messengers [7]. It is also because of this interaction that drug activity in the body is affected. Some of the important benefits of Pharmacogenetics are as under:-

- **Better Medication System**
- **Safer Dosing Option**
- **Improvement in Drug Developments**

It is paving the way for the development of successful medication therapeutics in cardiovascular therapeutics for smaller groups of patients based on their genetic profile. In molecular imaging, chemical and biological probes are utilized to discover molecular pathway mechanisms and aid therapeutic decision-making. Clopidogrel medication can have a varying effect on preventing stent thrombosis depending on a patient's genetic variation in CYP2C19, an enzyme that converts Clopidogrel from an inactive to an active state. PCSK9 inhibitors for the treatment of hyperlipidemia are an example of genomic-driven targeted cardiovascular therapies[8].

2. HISTORY

2.1 History of Personalized Medicine

Over the last six decades, it has been evolved that a significant amount of drug response variability is genetically influenced, with age, nutrition, epigenetics, health state, environmental exposure, epigenetic factor, and concurrent therapy all playing major roles. The discovery of highly varied drug responses in the early 1950s led to the formation of pharmacogenetics, a new scientific discipline combining genetics, biochemistry, and pharmacology. Personalized Medicine is considered a traditional approach for understanding and treating the disease based on patient gene profile variation for the selection of drug treatment protocols that minimize the harmful adverse effect to ensure successful results. It is participative, involving the patient in lifestyle choices and active health maintenance to compensate for hereditary predispositions [9].

At the turn of the twenty-first century, the Human Genome Project was completed, and personalized medicine became more concrete. This initiative explored a novel approach by linking people's genetic makeup to their health. The doctors were able to do genetic mapping as a result of this. According to genomic mapping, 99.1% of a person's genetic makeup is identical. The rest is dictated by the differences between the human species. This explains why people react to drugs differently, needing prescription tailoring based on individual variances[10].

Development has been made in recent decades, and in the twentieth century, researchers devised a method known as personalized medications, which is employed in the treatment of patients. At the time of the 21st century, the completion of the Human Genome Project made customized medicine more tangible. This initiative explored a novel approach by linking people's genetic composition to their health. The physicians were able to do genetic mapping as a result of this. According to genomic mapping, 99.1% of a person's genetic makeup is identical. This explains the people's reaction to the medications differently which need prescription based on the individual's characteristics[11].

Personalized medicine can be thought of as a finer-tuned version of established disease diagnosis and treatment methods. Clinicians can use a patient's gene variant profile to help them choose medications or treatment techniques that are less likely to have negative side effects and have better outcomes.PM can also warn clinicians and patients of a person's risk of developing certain diseases before symptoms occur, allowing them to devise a monitoring and prevention strategy. By moving beyond the one-size-fits-all approach to medication,

physicians may now make more effective therapeutic decisions for each patient. The implementation of PM has made significant progress. When all of the infrastructural elements are placed; when we begin to classify and treat the diseases based on their molecular profiles rather than just their most evident indications and symptoms; when insurance companies contribute to various tests and treatments that anticipate the patient's needs rather of reacting to them; when doctors use their knowledge and judgment in conjunction with a network of linked databases to better comprehend and act on the genetic information of the patient.[12]The ambition of Personalized Medicine for the 21stcentury is to offer "the right medicine, at the right amount, at the right time, to the right patient." The available diagnostic methods that allow the best selection of treatment by the products to ensure better patient health is critical to the effective implementation of PM. Manufacturers along with Food and Drug Administration (FDA) organizations have complete control over the items. According to the FDA, The goal of PM is to improve patient health while lowering the risks through more effective treatmentand obeying preventive measures. PM's goal is to divide patients into subpopulations that depend on their response to a therapeutic agent for their particular ailment, rather than to design new drugs for them [13].

2.2 Historical Development of Pharmacogenomics

Pythagoras observed that eating five beans caused a potentially lethal response in some, but not all, people around 510 B.C., and this was the beginning of pharmacogenetics. There have been other milestones since then that have shaped this field of study. Pharmacogenomics has largely been a positive experience. It's also been suggested that pharmacogenetics knowledge is easier for general practitioners to absorb than genetic concepts and that because primary care is the primary area of pharmaceutical prescribing, this could be a stronger motivator for integrating genetic medicine into primary care for an individual.Let's take a look at how pharmacogenomics has evolved [14].

YEAR	SCIENTIST	ACHIEVEMENT
510BC	**Pythagoras**	Investigation of ingesting five beams beans due to In-adequacy of G6PD [15].
1866	**Mendel**	New rules for heredity.
1956	**Carson et. al**	Discovery of G6PD.
1957	**Vogel**	Coined the term **Pharmacogenetics.**
1988	**Many**	Drug transporter discovery and polymorphisms in various phase I and phase II drug-metabolizing enzymes[16].
2000	**Public-private partnership**	The first project on the human genome has been completed [17].
2000	**intl. SN working group**	Human genome sequence completion.

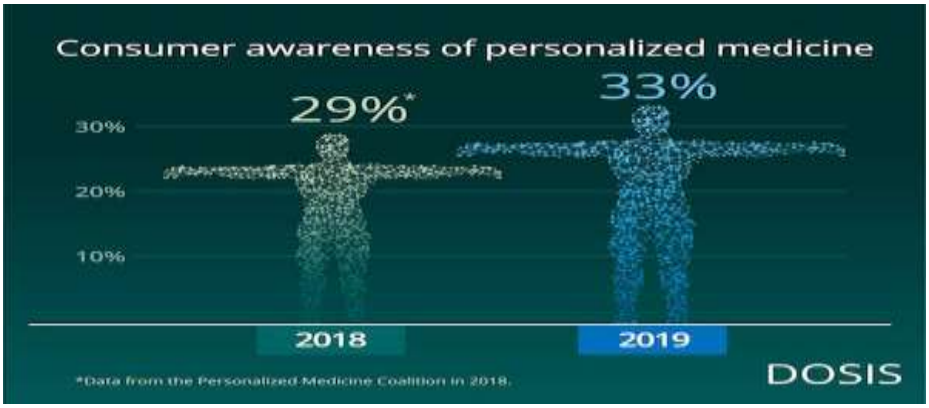
3. SCOPE OF PERSONALIZED MEDICINES

After the development of a new approach which is known as PERSONALIZED MEDICINE. It has been considered vital and various scopes have been specified in different fields.[15]Some of them are discussed below-

- Medical application of genomics
- Advances in molecular diagnostics
- Biochip and microarray technologies
- The influence of PM on medication development.
- The Impact of PMinitiatives on the delivery of health care.
- Creating a scientific foundation for personalized medicine adoption.
- Sequencing programs at the national level.

- The Impact of new personalized medicine concepts based on pharmacogenomics, pharmacogenetics, and pharmacoproteomics[18].
- Coordination of diagnosis and treatment.
- Drug adverse effect prediction and drug safety information.
- Follow-up on the treatment.
- Genome editing and related technologies for therapeutic purposes.
- Personalized medicine's ethical, legal and social challenges.
- Educational strategies and workforce improvement for personalized medicine.
- Information technology strategies for personalized medicine.
- Participant and patient involvement in personalized medicine.
- Personalized medicine using Data science and data analytics.
- Digital health and telemedicine.
- Cost-benefit and economic result for personalized medicine.

4. CONSUMER AWARENESS OF PERSONALISED MEDICINE



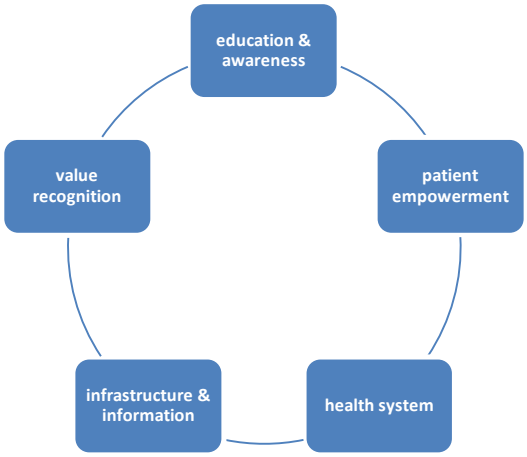
Consumer Awareness is one of the most important parts of any medicine that plays a role to educate people about the importance of personalized medicine to be more used and preferred by the patients. A research study done by DOSIS an AI-powered personalized medicine dosing platform performs a consumer awareness of PM in 2018 among more than 1,000 consumers from the U.S. population to obtain and get a better understanding of the advancement in the PM approaches and general consumers awareness.And in 2019, the report was founded to be raised to 33% from 28% in 2018. So about 4% rise in the consumer awareness program of Personalized Medicine. This shows the good result of the consumer awareness program that more people get the education and idea about the personalized medicine that causes the improvement in the care along with the treatment associated with its practices [19].

5. CHALLENGES OF PERSONALIZED MEDICINE

Personalized Medicine has so many challenges such as - intellectual property rights, payment regulations, patient privacy and confidentiality, data biases and regulatory oversights are just a few of the problems that are faced by PM.For example, genetic data generated by next-generation sequencing necessitates computer-intensive data processing before analysis. Any invention in the medical field, investment, and interest are affected by intellectual property right in personalized medicine[20].

As a result, the US Supreme Court determined in June 2013 that naturally existing genes cannot be copyrighted, but synthetic DNA that is modified or chemically manufactured. In personalized medicine, data biases are equally important. It's critical to make sure that the genes being analyzed originate from a variety of groups. This is done to ensure that the samples do not have the same human biases that we do while making decisions.As the personalized medicine approach is new and has various new implementations, it faced a bunch of challenges in the development area.Ethical, social, and legal challenges are also raised by the Personalized

Medicine Initiative [21]. It will be challenging to develop ways to protect participants' privacy and the confidentiality of their health information. Some of the promising challenges are-



Personalized medicines are young and in the growing stage, it has various hurdles to expanding the technologies as an asset. The initiative of personalized medicine is in the early stage of development and still developing. Cost is the major drawback of personalized medicine. The cost of the personalized medicine itself cost higher [22].

The main drawbacks of pharmacogenomics are the high cost and restricted availability of some tests. Even if there is federal anti-discrimination legislation, privacy concerns remain. These rules make it illegal to discriminate based on genetic information. Although these technologies are difficult to get, the FDA has taken steps to include personalized medicine in its regulatory standards.It takes decades to discover a single molecule in medicine. As a result, patent protection for individualized treatments became more concern, and to take a chance on an individual during clinical trials and testing, they do not always give financial assistance, making it more difficult to integrate tailored medications into our healthcare system.Because genetic testing makes certain volunteers ineligible for certain types of treatment, it's critical to protect the privacy and anonymity of patients who are predisposed to clinical trials[23].

Statistics on Adverse Drug Events

In a survey, there are about 82% of American adults take at least one medicine and about 28% of an adult take five or more medications in daily life [24].

About 700,000 cases of Adverse Drug Events were recorded each year.

Nearly 120,000 patients were needed to be admitted to the hospital for further treatment each year [25].

Every year, about 100,000 people die as a result of adverse drug reactions.

Aside from lung illness, diabetes mellitus, AIDS, pneumonia, accidents, and automobile mortality, adverse drug effects are the fourth greatest cause of death.[26].

New England Journal of Medicine it was mentioned that injuries or death in 1 out of 5 hospitalized patients is caused by Adverse Drug Effect [27].

$3.5 billion is spent annually on additional medical costs owing to Adverse Drug Effects[28].

Adverse Drug Effects are preventable [29].

6. BENEFITS & ADVANTAGES-

By authorizing novel therapy strategies and altering the healthcare system's understanding of medicine. Personalized medicine has the potential to improve medication selection and targeted therapy, minimize side effects, increase patient compliance, shift medicine's focus from reaction to prevention, increase cost-effectiveness, and build patient trust after a product is issued. Patients will have access to a variety of new, specialized medicines that are more effective. Scientists will be able to

construct more efficient clinical trials and develop novel medicinal treatments that target specific genetic flaws.[30]

To address the constraints of conventional medicine, PM is based on the genetic makeup of each patient. It enables healthcare providers to utilize tailored treatments as they shift medicine's focus from reaction to prevention.; forecast disease susceptibility; improve illness diagnosis; predict disease development; customize disease prevention methods; administration of more effective medications; avoid prescription drugs with predictable negative effects;Pharmaceutical clinical trials should take less time, be less expensive, and have a lower failure rate. A**trial and error** process also reduces inefficiencies that raise healthcare expenditures and put patient care at risk [31].

- In ordinary medical care, doctors will be able to use more of their patient's genetic and other molecular information.
- The tendency to predict which medicines will work better for certain patients has been improved [32].
- A greater understanding of the underlying processes that leads to various illnesses.
- A better understanding of how to prevent diagnoses, and cure a wide spectrum of illnesses.
- Better implementation of electronic health records (EHRs) in inpatient care makes medical data more accessible to clinicians and researchers [33].
- Development of new tools for constructing, analyzing, and disseminating large sets of medical data.

It raises the level of patient safety. Many medications have significant side effects that can be fatal. As a result, pharmacogenomics helps patients avoid these dangers by detecting them early on.It also reduces the cost and efficiency of health care.The goal of pharmacogenomics is to determine the most suitable drugs and dosages as rapidly as possible. The extent to which the theoretical advantages can be observed has been extensively addressed in the European Commission reports, scientific literature, and reports from national governments and organizations [34]. We also take into account the findings of four therapeutic case studies. We have categorized the benefits of personalized medicine into the below-mentioned types:-

- Improved treatments for individualized patients.
- Providing benefits to the healthcare systems and society.
- More efficacious development of innovative medicines.
- Improved efficacy: patientsare more likely to receive a drug that provides a clinical benefit, and treatment targeted to those patients who will respond[35].
- Overallsurvival has been improved.
- Reduced adverse events: Personalized Medicine may be targeted at the patients who are less prone to have an adverse reaction, which would reduce safety issues [36].

BIOMARKERS	DRUG NAME	CANCER
HER-2/NEU Receptor	Herceptin (trastuzumab)	Breast cancer
BCR-ABL	Gleevec (imatinib mesylate)	Chronic Myeloid Leukaemia
BRAFV600E	Zelboraf (vemurafenib)	Melanoma
EFGR	Erbuitux	Colon cancer
ALK	Xalkori	Lung cancer

Table- Some Selected Examples of Personalised Medicine Biomarkers in Cancer [37]

Biomarkers are naturally occurring molecules, genes, or characteristics that have a particular physiological & pathological process through which the disease can be easily identified or get indicated. It also predicts aggressive disease recurrence in liver transplant recipients. These biomarkers are very useful

in cancer treatment because they are a good indicator of the cancer cells in the body [38].

7. APPLICATION & PURPOSES-

- Personalized medications are employed in the diagnosis and treatment of ill individuals based on a patient's medical history and give a therapeutic impact. In the treatment of cancer, personalized drugs are critical. In the treatment of cancer patients, nuclear medications or (radioactive substances) are utilized [39].
- Radiation therapy's diagnostic effect is frequently utilized to lead doctors toward a precision/personalized therapeutic effect for patients. With the help of these types of medicines Asthma, chronic obstructive pulmonary disease (COPD), and obstructive pulmonary fibrosis are well treated [40].
- Cancer genomics, or "oncogenomics," is an example of customized medicine in action. To better understand disease pathophysiology and enhance medication development, these strategies are utilized to describe genes linked to cancer. Oncogenomics is one of the genomics' most promising fields, owing to its implications for personalized drug therapy andthe process of drug discovery and development.The patient's pharmacogenomic information is used in the prescription label to enable the doctor to make the best treatment option for the patient [41].

SPECIAL EXAMPLES OF PERSONALISED MEDICINE IN HEALTHCARE 6855

Type of Tests	Disease	Test	Function	Implications for Treatment
Disease Susceptibility test	Breast Cancer	BRCA1	Breast and ovarian cancer are more likely in people who have a detrimental BRCA1 or BRCA2 mutation[42].	Surveillance, risk modification, chemoprevention, prophylactic surgery
Prognostictest	Breast Cancer	Mamma print	Within 5–10 years after the initial occurrence, a test indicates the likelihood of cancer recurrence[43].	Adjust chemotherapy (yes or no)
Companion Diagnostic & effectiveness oriented	Breast Cancer	HER2	Only malignancies with overexpression of HER2 benefit from trastuzumab (Herceptin). Effectiveness [44].	Trastuzumab (yes or no)
Companion diagnostic & safety oriented	Epilepsy and other indications for carbamazepine	HLA-B*1502	Patients with HLA-B*1502 are more prone than others to suffer serious skin responses after using carbamazepine[45].	Carbamazepine (yes or no)
Companion Diagnostic	Warfarin and other coumarin	CYP2C9, VKORC1	The CYP2C9 and VKORC1 genotypes	Warfarin dosage

	derivatives are used to treat atrial fibrillation and other conditions.		derivative influence the optimal maintenance dose for coumadin therapy[46].	
Treatment Response Monitoring tests	Hepatitis C	HCVRNA test	After initiating therapy with pegylated interferon alfa and ribavirin, the test analyses viral RNA levels [47]	Length of treatment

8. RESEARCH METHODOLOGY

Research Methodology is the method based on the survey of healthcare based on the data work collected by the post-facto investigation which includes 3 main phases that are –

- **Phase I - It involves developing a research questionnaire, a hypothetical framework, and a set of hypotheses.**
- **Phase II – Instrument development and data collection via survey.**
- **Phase III – Analysis of obtained data.**

So, in this study, we created a hypothetical framework and hypotheses that were examined in the communication and employed in the questionnaire design. The questionnaires were then validated for validity, utility, reliability, and readability before being given to registered medical practitioners, scientific researchers, and patients.So in this research study, we selected 100 peopleincluding medical practitioners, patients, and medical researchers by checking their backgrounds carefully and then they involved in the process. Then two respondents were also selected from Lucknow and another one from Kanpur by carefully checking of their background also. The questionnaire was mailed to the selected persons and then the data was collected by the respondents by the offline mode so that the respondents meet with the selected person and they can be asked some questions from them from the questionnaire.So after all the data collected by the respondents, we also asked the some question from the respondents that the medical practitioners believe that after working longer training periods they will believe to adopt the PM system in the treatment procedures of the patients. All the data was also collected from all the remaining selected persons but there was no any response was collected from the regulatory bodies and registered pharmacists.We did all of the steps necessary to get the best reaction and data from each one. A total of 92 out of 100 people responded, with 60% being patients, 27% being medical practitioners, and the remaining 13% being medical researchers. Then all the data were analysed by using appropriate analysis techniques for the successful adoption of the Personalized Medicine System.[48]

9. CONCLUSION

By decreasing healthcare expenses, medication development costs, and time, Personalized Medicinehas the ability to enhance better health outcomes. This healthcare revolution will be enabled only by equal participation of patients and consumers in clinical trials, entrepreneurs and innovators developing smart tools and analyzing genetic data, regulators educating consumers and providers and supporting essential policy and regulatory revolutions, and physicians understanding disease at the molecular level. PM has the potential to be beneficial to the healthcare system. With the tailored approach, each individual will obtain their whole genetic information on the day of their birth, which will be entered into an individual medical record. Physicians and doctors would

be able to use this information to develop more efficacious healthcare methods based on patient exposure to various illnesses. By allowing prescribers to select patients for whom treatment is both efficacious and safe, personalized medicine offers the potential to raise the value of currently approved medications with limited market share due to high toxicity or ineffectiveness.Recognizing inter-individual variability in drug response is an important first step in bettering treatment. We've observed several times how combining drug-related diagnostics can increase utilization metrics for new goods while also improving the safety profiles and efficacy of existing chemically based treatments.

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ABBREVIATIONS

PM- Personalized medicine, DNA- deoxyribose nucleic acid, CYP2C19 – Cytochrome P450 2C19, PCSK9 – pro-protein convertase subtilisin/kexin type9, FDA – Food and Drug Administration, G6PD- Glucose- 6- phosphate dehydrogenase, AI - Artificial Intelligence, DOSIS – Dutch Open Source Information System, EHR – Electronic Health Records, U.S – United States, EU- European Union Commission, COPD-Chronic Obstructive Pulmonary Disease, BRCA test - Breast Cancer Gene test, HER2test - Human Epidermal Growth 2 test, VCORC1- Vitamin-k Epoxide Reductase Complex- subunit 1, HCV RNA – Hepatitis C viral load Ribonucleic acid, I.T – Information Technology, BCR-ABL – Bar Code Reader Abnormal Chromosome 22, BRAFV600E – Proto- oncogene (B-raf) or serine/ threonine – protein kinase B-raf, EGFR – Epidermal Growth Factor Receptor, ALK – Anaplastic lymphoma kinase.

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