

# RESEARCH ARTICLE

# **One Medicine for All**

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## ABSTRACT

Innovation in pharmaceutical science has become a particular concern for individual health. For a long time, the practice of "One-Size-Fits-All" medication has been common in healthcare services worldwide, making analytical methods crucial to drug analysis in biological matrices. Suitable methods for determining drug levels in biological matrices aim to prevent medication dosage errors. Every person's condition is different, and their diseases vary, caused by genetics, environment, and lifestyle. Personalized medicine is often described as "the right patient, the right drug, at the right dose, at the right time." This study used a qualitative literature review method, where sources or literature in national and international journals were searched through online media. The analysis results explain that the role of the biological environment is more significant than others in vector-borne diseases, and the role of the genetic nucleus is more significant than others in hereditary diseases. Due to the numerous ecological interactions, we can often change the spread of disease by changing certain aspects of human interaction with their environment without direct intervention in the cause of the disease. The implementation of the science from "Bench to bedside" and "From clinic to community" assumes the provision of long-distance healthcare services by healthcare professionals using information technology, where the implementation of telemedicine (Systematic Review) in healthcare services is crucial, considering some of the problems that arise from manual services. One of the technical implementations of telemedicine is to optimize personalized medicine, which also involves implementing pharmacogenetics approaches in hospitals.

## **KEYWORDS**

Pharmacogenomics, Pharmacological Approach, Personalized Medicine.

## **ARTICLE INFORMATION**

ACCEPTED: 02 May 2023

PUBLISHED: 12 May 2023

DOI: 10.32996/jmhs.2023.4.3.1

#### 1. Introduction

The development of Pharmaceutical Care from rational medication to appropriate medication has made it a part of pharmacy science that includes pharmacogenetics, social science, and patient behaviour, which need to be studied more deeply. Quality of life is also a therapeutic outcome goal of pharmaceutical care activities (Kardela, Bellatasie, Rahmidasari, Wahyuni, & Wahyuni, 2023). However, not all of this knowledge is used to select the appropriate medication. The emergence of resistance to treatment, recurrence of disease, and unwanted effects become the basis for the interest in developing this science. Not all reactions are positive, but many unwanted reactions from drug use still occur, resulting in the onset of disease, abnormal body function, and even death (Aprilia, 2020).

Variations in genes, proteins, and metabolic functions can cause certain diseases, disease progression, and even the body's response to drugs (Riana et al., 2023). Drugs are assumed to be effective for all patients with appropriate indications. In reality, some patients will experience different responses. These responses can be in the form of ineffective drugs or adverse drug reactions (ADRs). Many drug responses do not match the initial diagnosis, including adverse drug reactions, which are unwanted side effects or harmful responses of a drug when given for prophylactic, diagnostic, and therapeutic purposes (Elhassan, 2015). Many factors can influence ADR occurrence, including polypharmacy, disease severity, age, and type of prescribed medication (Islamiyah, 2021). The use of prescribed drugs is currently one of the determinants of health quality. It, therefore, requires special attention, mainly

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to ensure that the pattern of drug consumption is appropriate and rational, which is part of Drug Related Problems in implementing pharmacy services (Muhsinah et al., 2023). Global ADR reports show that ADR cases have increased yearly from 1957 to 2018. Some cases include 24.7% of patients with joint pain in Central Java requiring lifelong NSAID treatment, but reports have shown that 24% of long-term NSAID use results in peptic ulcers. Additionally, 45% of antipyretic analgesic use causes Stevens-Johnson syndrome, which can be fatal (Aragibinafika & Topik, 2023). These cases demonstrate that ADRs occur significantly with drugs frequently used by the community, hence the need for closer drug use monitoring to prevent ADRs.

Referring to the above description, pharmacogenomics has begun to be applied in hospitals, especially in Indonesia, where pharmacogenomics is believed to be one of the fields of science that can explain the differences in individual responses to drugs due to differences in their genetic makeup (Maramis, 2022). In this case, a pharmacogenomic approach is believed to help reduce the risk of side effects and optimize drug effectiveness, thus making treatment more precise. However, a drug's effect is influenced by genetic variations and many factors, such as physiological changes, pathological conditions, and other effects. These factors need to be considered by clinicians in therapy.

In recent years, pharmacogenomics has become a focus of pharmacology development because it studies the contribution of genetic factors to drug response variations. This aims to study drug therapy safety, prescribing, and use (Sry Devi Sutami, Suci Oktaria Ananda Caniago, Suci Ramadani, & Suryani, 2022). One effort can be made to create personalized medicine with a pharmacological approach. Personalized medicine is a management system in the medical world based on genetic information from patients, which is used to determine what treatment is suitable for the patient's disease. This is because not all treatments can be effective for everyone with the same illness. Personalized medicine is expected to avoid side effects such as an individual's allergic reactions to a particular type of drug or the usual dose given. Personalized medicine generally involves using two medical products, namely diagnostic tools and therapeutic products, to improve patient treatment success.

Personalized medicine aims to facilitate clinical decision-making by distinguishing patients likely to benefit from a given treatment from those who may experience side effects without benefiting from the treatment. The term personalized medicine is often described as the right patient receiving the right drug at the correct dose at the right time. More broadly, personalized medicine is defined as the customization of medical therapy based on individual characteristics, patient needs, and treatment preferences throughout all stages of care, including prevention, diagnosis, treatment, and monitoring or follow-up.

## 2. Research Method

This study used a qualitative literature study method (Adlini, Dinda, Yulinda, Chotimah, & Merliyana, 2022). The sources or literature search included national and international journals via online media such as science direct, Wiley, google scholar, sinta, PubMed, and several other sites using the keywords "Personalized Medicine" and "Pharmacological Approaches." After searching, the obtained results were selected based on the data that met the needs of this research. In the article selection process, inclusion and exclusion criteria were determined to obtain articles relevant to the research topic. Study screening was performed using titles and abstracts. Any study deemed relevant was identified and included in this study after a full-text identification process.

## 3. Results and Discussion

## 3.1 Personalized Medicine, the Future Treatment Model

In the modern era, new frameworks and technologies are needed to provide a new approach to complex disorders and serve as a roadmap to personalized medicine, providing much better care at a far lower cost. Personalized medicine sorts patients based on each individual's unique characteristics, both from a genetic aspect and the differences in specific genetic characteristics that can differentiate individuals who will respond better or worse to specific therapeutic approaches.

In this regard, it is known that "Precision medicine," one of the most similar to personalized medicine, has been established by the National Academy of Sciences (NAS) as the use of genomics, epigenomics, exposure, and other data to define individual disease patterns, which potentially leads to better-individualized treatments. Stratification means grouping patients with specific diseases into subgroups based on specific characteristics, which respond more often to certain drugs or have a lower risk of side effects in response to specific treatments.

Limitations of personalized medicine include the availability of genetic tests, cost, insurance coverage, ethical issues, scientific advances, and clinical usefulness evidence. Education may bridge the growing knowledge gap between scientists and practitioners. Genomic information and pharmacogenetic testing have improved our understanding of gastrointestinal disease treatment in general, such as inflammatory bowel disease (IBD), peptic ulcer disease, and colon cancer. However, training at every level should integrate new treatment concepts and options. Medical education should prepare doctors, the general public, trainees, and other health personnel to fulfil the promise of personalized medicine, which provides the correct dose of the right drug to the right patient at the right time.

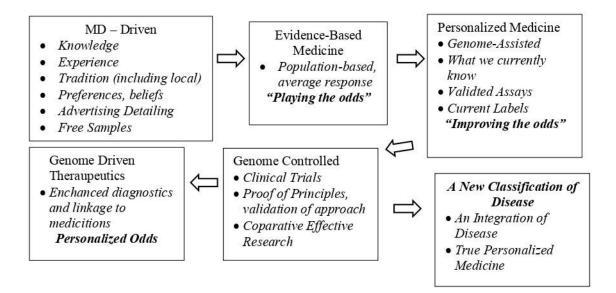
Domain	20 <sup>th</sup> Century	21 <sup>th</sup> Century	
Overarching Goal	Treatment of Disease	Prevention of Disease	
Enabling Technology	Microscope, Culture Techniques, Blopsies	NGS, bioakers, co puters	
Disease Model	Germ Theory	Complex risk, variant response to stress	
Paradim Shifting Force	Flexer Report of 1910	Economics	
Education Focus	Disease Diagnosis and Classification	Normal Responses, Assessment of variants.	
Scientific Focus	Determine Assosiations	Determine Mechanisms	
Scientific Approach	Koch Postulate, Global Statistics	Modelling and Simulation, Performance Characteristics	
Disease Classification	Tissue pathology, syndromes	Genetic and environmental risk, surrogate end points	
Disease time frame	Static, cross sectional	Dynamic, longitudinal	
Physician Focus	Overall organ dysfunction	Activity and trajectory of dysfunction systems	
Assessment	Disease Classification	Outcome Prediction	
Treatment	Trial And Error	Targeted, optimized	
Success measures	Population Based	Individual Based	
Utility of the paradig	Infectious diseases, mendelian genetics, single anget disorders, cancer detection	Inflammatory disease, complex genetics, functional disorders, cancer control.	

Table 1. Differences in Treatment Patterns between the 20th and 21st Century

Abbreviation: NGS, next-generation sequencing.

The above table shows the difference in drug management practices between different eras and highlights the need for hospitals to have various innovative programs for personalized medicine. Pharmacogenomics is a field of study investigating the genetic influence on inter-individual variability in drug response, which has gained much attention for its potential genomic application in individualized treatment. This relatively new field combines pharmacology and genomics to develop effective and safe treatments and dosages tailored to a person's genetic makeup (Vanie, Rizkifani, & Untari, 2019). Many pharmaceutical companies are starting to use pharmacogenomic knowledge to develop and market drugs for people with specific genetic profiles.

Pharmacogenomic studies in pharmacy play a role in understanding a person's response or each individual's response to a drug, as each individual's genes differ. One example of the genetic influence on drug response is based on research showing the SLCO1B1 c.463C>A gene polymorphism with a frequency of 30% for C and 70% for A. These genetic variations between individuals are thought to cause variations in rifampicin response among newly diagnosed pulmonary tuberculosis patients, resulting in differences in clinical outcomes, such as sputum conversion. Genetic variability can occur at the pharmacokinetic and pharmacodynamic levels, even involving the immune system's function. Polymorphism is the variability that occurs in individual populations of  $\geq 1\%$ . (Untari, Rizkifani, Yuswar, & Robiyanto, 2023).



## Figure 1. Scheme for Determining Personalized Medicine Classification

The Food and Drug Administration (FDA) has issued recommendations for pharmacogenomic-based therapies. Based on the list of drugs available in Indonesia, pharmacogenomic approaches can be applied to several drugs with potential side effects.

Medicine	Gen	Alel/Fenotip	Side Effects
Allopurinol	HLA-B	*58:01 Allele Positive	Sindrom Steven Johnson/toxic necrotizing epidermolysis
Azathiaporine	TPMT dan NUDT15	Intermediate atau Poor Metabolizer	Toxicity of bone marrow, gastrointestinal intolerance
Capecitabine	DPYD	Poor Metabolizer	Gastrointestinal and hematological toxicity
Carbamazepine	HLA-A HLA-B	HLA-A: *31:01 alel positif HLA-B: *15:02 alel positif	Mild rash maculopapular exanthema (MPE), hypersensitivity syndrome (HSS), Stevens- Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN); SJS/TEN.
Celocoxib	CYP2D9	Poor Metabolizer	Gastroduodenal bleeding
Citalopram	CYP2D19	Poor Metabolizer	Nausea, vomiting, drowsiness.
Clozapine	CYP2D6	Poor Metabolizer	Hiperglikrmia
Codeine	CYP2D9	Ultra-Rapid Metabolizer	Dizziness or mild headache, nausea, vomiting, dry mouth, itching, blurred vision
Efavirenz	CYP2D9	Poor Metabolizer	Hepatotostik
Fluorouracil	DPYD	Intermediate atau Poor Metabolizer	Hepatotostik
Gefitinib	CYP2D9	Poor Metabolizer	Hepatotostik
Irinotecan	UGT1A1	*28/*28 (Poor Metabolizer)	Diare, Neurtropeni
Isoniazid	NAT	Poor Metabolizer	Hepatotostik
Lapatinib	HLA-DRB1	*07:01 alel positif	Hepatotostik

	HLA-DQA1	*02:01 alel positif	
Metoclopramide	CYP2D6	Poor Metabolizer	Acute Distonic reaction (Extrapyramidal Syndrome)
Nilotinib	UGT1A1	*28/*28 (Poor Metabolizer)	Hiperbilirubinemia
Oxcarbazepine	HLA-B	*15:02 alel positif	DRESS, SSJ
Pazopanib	HLA-B UGT1A1	HLA-B:*57:01 alel positif UGT1A1: *28/*28 (Poor Metabolizer)	Hepatotostik
Propafenone	CYP2D6	Poor Metabolizer	Side effects on the central nervous system
Simvastatin	SLCO1B1	521 TC or 521 CC (Intermediate atau poor function transporters)	Miopati
Sulfamethoxazole and Trimethoprim	NAT	Poor Metabolizer	Hepatotoxicity Hypersensitivity reactions
Sulfasalazine	NAT	Poor Metabolizer	Reaksi Hipersensitivitas
Tolterodine	CYP2D6	Poor Metabolizer	Prolongation of QT interval
Tramadol	CYP2D6	Ultra Rapid Metabolizer	Nausea, vomiting, and respiratory depression.
Warfarin	CYP2D9 and VKORC1- 1639G>A	CYP2D9 and Intermediate or Poor Metabolizer	Bleeding

Case Report; Used together with inhibitor CYP3A4 (Eksperimental, 2022)

## 3.2 Optimizing personalized medicine in Personal Therapy Services

Pharmacogenomics studies how an individual's genetic heritage affects the body's response to drugs. The term comes from the words pharmacology and genomics, thus the intersection of drugs and genetics. Pharmacogenomics holds the consistency that drugs may one day be made specifically for individuals and tailored to each person's genetic makeup. Environment, diet, age, lifestyle, and health status can all affect an individual's drug response. However, understanding a person's genetic makeup is vital to making personalized drugs with greater efficacy and safety.

How a person responds to drugs in positive and negative reactions is a complex trait influenced by many different genes. Scientists need to know all the genes involved in drug response to develop genetic tests that predict a person's response to a particular drug. At one point, scientists discovered that human genes looked at minor variations (or changes) in nucleotide content (DNA base). Everything changed: genetic testing to predict drug response is now possible. Pharmacogenomics combines traditional pharmacy science, such as biochemistry, with annotated knowledge of genes, proteins, and single nucleotide polymorphisms.

Today, health problems have become the main focus of society's life. Of course, the environment and lifestyle cause various diseases in individuals. For example, the role of the social environment is more significant than the others in mental stress, the role of the physical environment is more significant than the others in sunburn, the role of the biological environment is more significant than the others in vector-borne diseases, and the role of the genetic nucleus is greater than the others in hereditary diseases (Ryskalestari, 2023). Because of the many ecological interactions, we often can change the spread of disease by changing certain aspects of human interaction with their environment without direct intervention in the cause of the disease (Triastuti et al., 2023).

Meanwhile, environmental interaction factors such as biological, chemical, and social factors play an essential role in the occurrence of diseases. Individual behavior and lifestyle are the underlying causes of diseases, such as dietary components, smoking, and

physical inactivity. Recently, many sudden deaths have been caused by previously unknown diseases, such as lung cancer, heart disease, or kidney-related diseases. Usually, these certain diseases are caused by irregular lifestyle and eating habits in the living environment and surrounding areas. Riskesdas data in 2021 states that lifestyle, smoking, and dietary patterns are the main contributors to coronary heart disease (CHD), with 50% of CHD patients potentially experiencing sudden cardiac death.

Cardiovascular diseases such as heart disease, cancer, stroke, and kidney failure continue to increase yearly and rank as the highest cause of death in Indonesia, especially at productive ages. Riskesdas data shows that the prevalence of cardiovascular diseases such as hypertension has increased from 25.8% (2013) to 34.1% (2018), stroke from 12.1 per thousand (2013) to 10.9 per thousand (2018), coronary heart disease remains at 1.5% (2013-2018), and chronic kidney disease from 0.2% (2013) to 0.38% (2018). When viewed from the place of residence, urban residents suffer more from heart disease, with a prevalence of 1.6%, compared to rural residents, who only have a prevalence of 1.3%. Riskesdas 2018 data also reported that the prevalence of heart disease based on doctor's diagnosis in Indonesia reached 1.5%, with the highest prevalence in North Kalimantan Province at 2.2%, Yogyakarta at 2%, and Gorontalo at 2%. This shows that lifestyle indeed affects a person's health.

Eating fast food has become a trend in society, even though this habit can lead to certain diseases that ultimately harm the community. Therefore, the various health problems bring different treatments for each individual. Hence, the right solution can be done through personal therapy. Personal therapy is a wide-ranging cognitive-behavioral approach to the multi-problems experienced by patients. One of these personal therapies can be done through telemedicine services for patients.

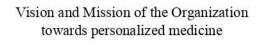
As one of the digital transformation programs, telemedicine services will help support the era of personalized medicine, as it serves as a digital platform for interacting with patients and providing personalized recommendations. Telemedicine services can reach all communities in the country, and it is also an effort to equalize access to healthcare services.

Implementing the "Bench to bedside" and "From clinic to community" science assumes the provision of remote healthcare services by healthcare professionals using information and communication technology. This includes exchanging diagnostic information, treatment, prevention of diseases and injuries, research and evaluation, and continuous education for healthcare providers to improve the health of individuals and the community. Initially, this program was started during the Covid-19 pandemic, when patients found telemedicine helpful and more suitable for healthcare services than before. Patients felt that telemedicine reduced the cost of treatment and eliminated the need for travel. Patients felt that telemedicine was essential during the Covid-19 pandemic, which could support the sustainability of telemedicine usage in the post-Covid-19 era.

In 2017, the Indonesian Ministry of Health launched the Telemedicine Indonesia (TEMENIN) application. TEMENIN provides teleradiology, tele-EKG, tele-USG, and teleconsultation services, which have connected 39 primary and 115 secondary hospitals and community health centers. TEMENIN is the implementation of telemedicine in Indonesia. During the COVID-19 pandemic, the Minister of Health issued Circular Letter No. HK.02.01/MENKES/303/2020 on the Provision of Health Services through the Utilization of Information and Communication Technology in Preventing the Spread of Coronavirus Disease 2019 (COVID-19), which guides health services using telemedicine as a method for preventing the spread of COVID-19. Considering the importance of information and communication technology today and its potential for development and use, the factors that influence the implementation of telemedicine (systematic review) are as follows as a manifestation of the pharmacogenomic approach to personalized medicine

Factors affecting the implementation of Telemedicine (Systematic Review)





Implementation of pharmacogenetic approach in hospitals.

Implementation of telemedicine (Systematic Review) in healthcare services is highly necessary due to several problems that arise regarding manual services. This is also because of changes in regulations from the government that encourage the use of technology-based services, which also affects changes in the organization's vision and mission. One of the technical implementations of telemedicine (Systematic Review) is to optimize personalized medicine and to apply it; it also involves the implementation of pharmacogenomic approaches in hospitals.

#### 4. Discussion

Health is a fundamental need for everyone. However, health often becomes the downstream (impact) of various problems experienced by individuals and their surrounding environment. Nevertheless, health is the initial capital for developing individual potential in life. Improving patients' quality of life is the ultimate goal of the treatment. This is closely related to the success of therapy.

L. Bloom's classical theory states that 4 factors influence the degree of health successively: lifestyle, environment (social, economic, political, cultural), health services, and genetic factors (heritage). These four determinants interact with each other and affect an individual's health status.

Referring to the description above, some drugs that have been identified as having potential side effects with pharmacogenomic approaches, it is better for the hospital system to be actively involved in the development of services, one of which is health digitalization, where three essential things are arranged, namely health technology transformation, data integration and development of digital health applications, and the development of healthy ecosystems, including the development of personalized medicine.

For a long time, "one-size-fits-all" medicine has been standard in healthcare services worldwide. For instance, if patient X has high cholesterol, they are given simvastatin, and the same medicine is prescribed to patient Y who has the same condition. However, patients with the same disease diagnosis can respond differently to a particular medicine. Medicine A may be effective for patient X but not for patient Y, and in some cases, unwanted side effects may occur. Therefore, in recent years, the concept of "personalized medicine" has been developed based on studying the patient's genotype so that they receive the appropriate therapy or medicine for their illness.

Personalized medicine is increasingly used in cancer treatment, where the patient races against time, and treatment must be as effective as possible. In personalized treatment, the patient visits the doctor, and genetic testing is carried out. The doctor can determine the suitable treatment by conducting genetic testing, so the response to the medicine will be more effective. This can reduce costs, and treatment will be safer and more efficient. Therefore, the foundation of personalized medicine lies in biomarkers developed based on genetic variations.

#### 5. Conclusion

Patient safety is the goal of every service provided by hospitals to patients. One effort for patient safety is to ensure that every medication given can be used correctly, with the correct dosage and timing of use. At each medication delivery, the pharmacist provides information about the medication to the patient or their family. This follows the legal basis of the Ministry of Health Regulation Number 72 of 2016 concerning Pharmaceutical Service Standards in Hospitals and the mandate of hospital accreditation, which is patient safety.

Over time, sometimes patients or their families still need further information regarding the use of medications, such as the presence of side effects, co-administration with food or other drugs, or forgetting how to use them. They quickly return to the hospital to ask for or clarify the necessary information regarding the medication. This problem is the starting point for the pharmacy installation to think of easy means for the community to access information or ask questions about medication use.

The digital era allows information exchange to occur quickly, easily, and on a large scale. Social media is an alternative means of realizing the one-size-fits-all drug idea to approaching personalized medicine through pharmacogenetic services towards personalized medicine. One-size-fits-all drugs sort patients based on their unique characteristics, both from a genetic aspect and specific genetic characteristic differences that can differentiate individuals who respond better or less well to specific therapeutic approaches. Knowing the genetic variations associated with certain gastrointestinal disorders may affect disease screening, medication selection, and recurrence surveys.

#### Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

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