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Recommendation of precision medicine application in Indonesia from multiple perspective: a review

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ABSTRACT

Recently, precision medicine has gained much attention. Precision medicine helps reduce trial-and-error prescribing and minimize adverse drug reactions while improving the drug's effectiveness. Precision medicine is a medical method that seeks to maximize healthcare quality by tailoring the healthcare process to each patient's unique characteristics. In the era of rapid technological growth and data explosion, precision medicine's development has become very promising. Development of techniques for obtaining medical data; significant reductions in the cost of bio sequencing; massive development of computing tools, storage systems, and wireless communication systems; as well as the development of data analysis techniques based on artificial intelligence have all become significant driving forces in the advancement of precision medicine. In this manuscript, we summarized previous studies on precision medicine development. In addition, we discussed the opportunities and potential challenges of precision medicine development, particularly in Indonesia. Despite its promising potential, many challenges remain to be overcome to develop precision medicine. Good regulations for patient data ownership and clinical data-sharing, followed by sufficient data infrastructure and human resource capabilities, are the most critical factors in ensuring success in precision medicine. Moreover, guaranteeing data safety, patient privacy, and genome fairness are other issues that must be addressed.

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1. INTRODUCTION

The rapid development of intelligent medical devices and the frequency increase of routine genomics examinations have created an explosion of health-related big data worldwide. In 2018, health care institutions managed an average of 8.41 petabytes of data, which is a nine-fold increase from 2016 [1]. This large amount of data can provide valuable clinical information if further analysis is carried out. Furthermore, this information helps medical doctors make clinical decisions and better patient outcomes [2].

From the health data perspective, the explosion of data is an essential impetus for the development of precision medicine. The data explosion or "big data bang" in terms of health data can be seen in Figure 1. As precision medicine develops, doctors will be able to evaluate the genetic changes displayed by each patient and plan for personalized treatment. Moreover, precision medicine aids doctors in evaluating how specific treatments affect the entire body and determining the best medication dose to optimize the drug's beneficial effects while minimizing undesired side effects. Many practical problems can be mitigated by precision

medicine development. For example, only 40% of patients benefit from common asthma and diabetes drugs [3]. In addition, 6.5% of UK NHS hospital admissions in 2015 were from adverse drug reactions, accounting for 8,000 beds and costing at least 1 billion pounds sterling [3]. Precision medicine helps shift the medical paradigm from reaction to prevention, minimizes trial-and-error prescription and adverse medical reactions, catalyzes new drug development, and improves patient adherence to their treatment program. The term big data itself was introduced in 1997 in the context of data visualization [4]. Big Data is a terminology used to denote a number of distinct topics: from gathering and combining enormous volumes of data to the vast array of sophisticated digital approaches aimed at revealing patterns related to human phenomena [4].

Since the human genome project's breakthrough in 2003 [5], precision medicine has received approval from many medical organizations and has been used all around the world [6]. In recent years, precision medicine has appeared as a method for interpreting big data and omics functionality and applying them to healthcare delivery [7]. Unlike conventional treatment principles where drug delivery must be “fit to all”, precision medicine considers biological factors such as genetics, coexisting medical conditions, habits, and the environment of each patient in determining the appropriate treatment. Habits and lifestyles are closely related to genetic factors that cause disease formation [8]. Access to data related to a person's lifestyle could determine their disease risk, especially chronic disease. Likewise, the possibility of using lifestyle data can be used to mitigate the impact of biological variants on data-based diseases.

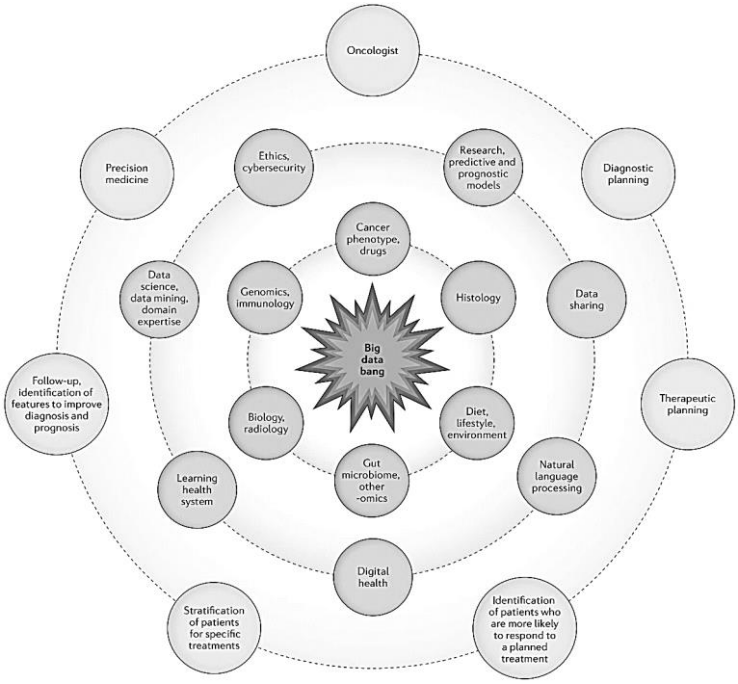


Figure 1. Big data bang in precision medicine development [9]

One of the crucial factors used as the basis for applying precision medicine is the results of the genomic examination. A single individual genomic sequence data can generate up to 200 gigabytes [10]. A prediction by The Global Alliance for genomics and health suggested that by 2025, there will be 100 million genomes sequenced that generate more than 20 million gigabytes of data [11]. With the genomic information of each individual, it will be easier for clinicians to establish a diagnosis and appropriate treatment both in terms of dose and frequency, which could result in medical expenses reduction [12]. In a disease with a high prevalence in a population, the slightest development in the treatment paradigm will significantly impact cost and patient outcomes.

In addition to patient genomic data utilization in the application of precision medicine, in the future, if a new patient comes to the hospital, the symptoms and results of laboratory tests can be compared with millions of other patients with similar diseases and characteristics and then matched to the appropriate treatment. With this method, it is hoped that the success of treatment in other patients with similar individual characteristics can be given or taken into consideration for the new patient. In the end, each patient will receive

a specific treatment according to their own characteristics [13]. This is in accordance with the principle of precision medicine: "Medicine needs to be given to the right patient, with the right drug, and at the right time".

In the recent decade, precision medicine has gained much attention and is being developed rapidly. However, precision medicine has not received enough attention in many developing countries. Let us take the example of Indonesia, the country with the fourth most populous population globally. Although Indonesia has very diverse individual characteristics, not many ongoing studies discuss precision medicine. Indonesian society alone consists of 1,340 ethnic groups [14]. With various types of stature and body shape, Indonesian people have very different human body characteristics. Therefore, it is crucial to develop precision medicine in Indonesia. This prompted the author to conduct a survey of research related to precision medicine and its opportunities in Indonesia.

In this manuscript, we explore the potential of precision medicine development in improving the quality of health in Indonesia. This manuscript consists of four sections. Section 1 contains the introduction. In section 2, we describe the research method used in this manuscript. Then, section 3 presents literature studies about former research in precision medicine. In this section, we also discuss the opportunities for precision medicine development in Indonesia and its current challenges. Further, the strategy for precision medicine implementation in Indonesia is also discussed in section 3. Finally, we conclude the discussion in the last section.

2. RESEARCH METHOD

Our objective in writing this review is to discuss how we can develop and implement precision medicine, particularly in Indonesia. In addition, we summarized difficulties that may occur in the process and intuitively formulated strategies to overcome it. The arguments were derived from recent high-quality meta-analyses, systematic reviews, and selected literature. We extensively searched Scopus, PubMed, and Google Scholar for articles describing precision medicine in this critical narrative review. Furthermore, we also included manuscripts related to factors supporting the development and implementation of precision medicine. These factors include supporting technologies such as big data, genomic sequencing tools, genetic analysis techniques, and even artificial intelligence.

Moreover, we included manuscripts with interest in potential challenges faced in implementing precision medicine. The following keywords were used in the search strategy: precision medicine, omics data, electronic health records, genomic data, medical big data, and artificial intelligence for medicine. The language of the search was limited to English and Indonesian. There were no limitations on the year of publication or study. As a result, 71 published works were gathered. Any research study types were considered in this manuscript. However, unpublished data, submitted manuscripts, and technical notes were excluded.

3. RESULTS AND DISCUSSION

3.1. Literature study

Genomics has a central role in the broad implementation of the precision medicine revolution [15]. Genome-wide association study (GWAS) is an approach used in genomic research to link certain genetic variations to a disease. The ability to generate large amounts of genome sequence data has driven the application of GWAS to many diseases. When genetic markers are identified, they can be exploited to understand how a gene contributes to the development of a disease and can be used in both prevention and treatment strategies [16].

A study by Blatt in 2020 [17] analyzed GWAS data using homomorphic encryption (HE). The HE framework was applied to GWAS with age-related macular degeneration (AMD) patients consisting of 12,461 cases and 14,276 controls, which were then genotyped with 263,941 markers. This study successfully demonstrated an accurate GWAS analysis for a dataset of more than 25,000 individuals. The first stage carried out in this HE is collecting participants' data. Next, each participant encrypts the data and sends it to the data bank. Then the HE clouds computer performs the computation. Finally, the encrypted results are forwarded to the GWAS coordinator for further analysis. These stages can be seen in Figure 2. Such research using GWAS shows that big data has the potential to develop medical science, which, if applied in clinical practice, can improve the quality of health services, especially in the era of precision medicine.

Furthermore, several studies discuss the role of big data in the application of precision medicine. For example, big data analysis was used for precision medicine in lung cancer patients in a research conducted in Spain in 2019 [18]. The data used in this study was patient information originating from electronic medical records. Analysis of medical records was carried out using the natural language processing (NLP) framework. These clinical records are subsequently turned into valuable data, which is then integrated with genomic, imaging, and bibliographic data from sources like PubMed.

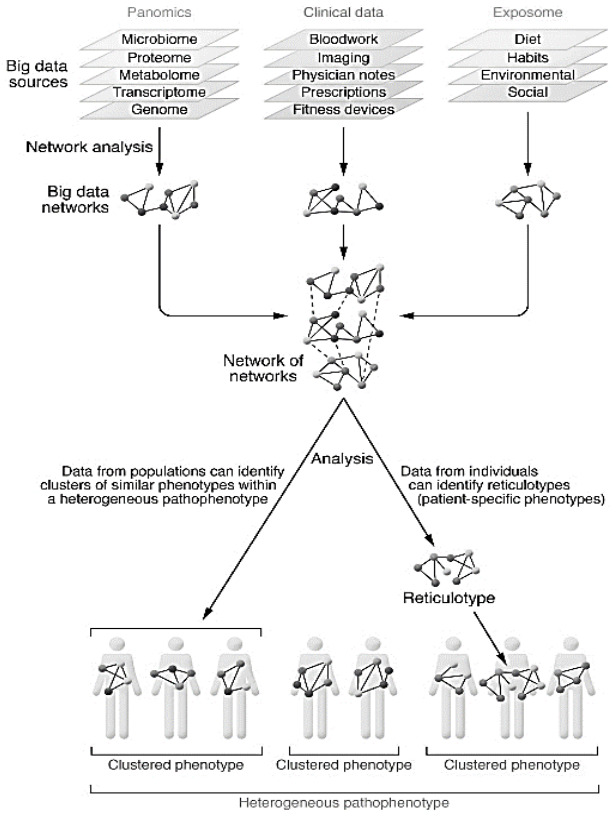


Figure 2. HE GWAS analysis stages [16]

The research method used in [18] is a cohort with 1,000 patients from 2009 to 2018 diagnosed with non-small cell lung cancer (NSCLC). Semantic indexing and information analysis are carried out using big data along with machine learning techniques. Heterogeneous information sources are integrated and analyzed by an interactive user interface. There were 251,730 documents analyzed. As a result, clinicians and policymakers may use this vast amount of data to establish public health interventions and conduct new clinical studies. Furthermore, the interactive system enables practitioners to quickly get personal information about each patient and develop predictive models for long survival, detect patient risks, and minimize overtreatment.

Big data has also been used to analyze cancers triggered by the gut microbiome. Several studies suggest that the gut microbiome can trigger cancer or specific gut microbes [19], [20], [21]. The gut microbiota consists of tens of trillions of microorganisms, including 1,000 different bacteria, fungi, archaea, parasites, and viruses known for more than three million genes [22]. In addition, impaired inflammatory and the immunological interplay between the host and the gut microbiota have been linked to a number of malignancies [23].

The "omics" technology used for microbiome analysis is constantly evolving, although most research is still in its infancy. Manasi *et al*. [24] conducted a study based on this theory in 2018. The study analyzed datasets of rRNA gene sequences in 509 samples of colorectal adenoma and colorectal cancer (CRC) patients. Gene sequence data were processed using a strain-specific method herein termed strain select, UPARSE bioinformatics pipeline (SS-UP) or a closed reference quantitative insights into microbial ecology (QIIME-CR). In addition, machine learning analysis was performed to determine potential microbial biomarkers' consistency and diagnostic capability.

In recent years, large-scale analyzes of the fecal and endothelial (mucosal) microbiome have been applied to patients with cancer to analyze the differences between samples from various populations. Hence, therapeutically relevant microbiome profiles linked to various cancer types can be validated [9], [25]. The data processing process to search for marker microbiota to become a clinically applicable model is visualized in Figure 3. The description of the presence of microbiota in the gut is different for each individual. Hence, this information can be helpful in the application of precision medicine.

In addition to cancer, big data analysis has also been used in cardiovascular disease phenotyping. A 2016 study by Amit *et al*. [26] analyzed the association between genetic and lifestyle risks for coronary disease. This research method uses polygenic scores from deoxyribonucleic acid (DNA) polymorphism sequences.

Genetic risk was quantified in three prospective cohorts. The Cox proportional hazard model, a type of statistical methods, is used to analyze data on DNA sequences and patient lifestyle factors. It is revealed that individuals with a high genetic risk factor who followed three of the four healthy lifestyle criteria (no obesity, regular exercise, no smoking, and a good diet) had a 46 percent lower relative risk of coronary events. Big data has the potential to provide a more precise understanding between precision genomics and phenotyping by improving pathophenotyping categorization, increasing sample size, and attempting analytical strategies that can be leveraged in the application of precision medicine [26]. Figure 4 shows heterogeneity in cardiovascular disease requiring compilation from multiple sources of big data. Precision phenotypes can help to discover patient clusters, whereas looking at reticulotypes can help to refine them more by understanding the molecular (network) causes of distinct patient-specific traits [27].

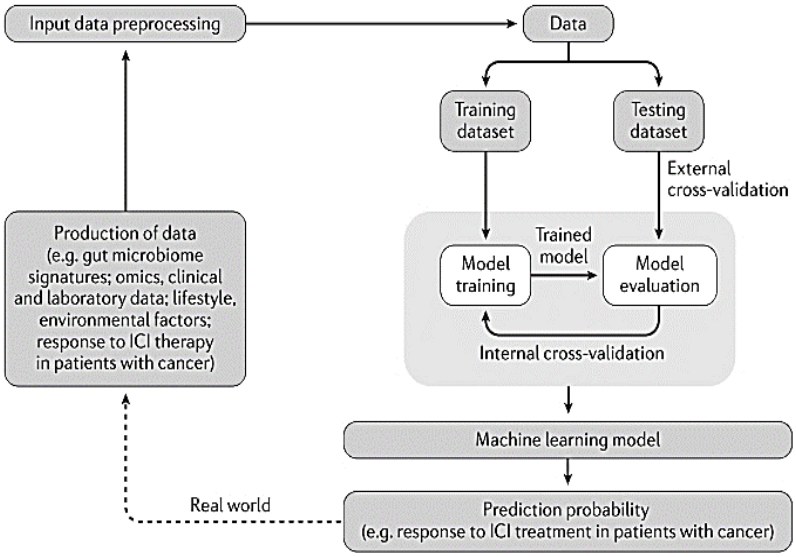


Figure 3. Machine learning workflow representation [9]

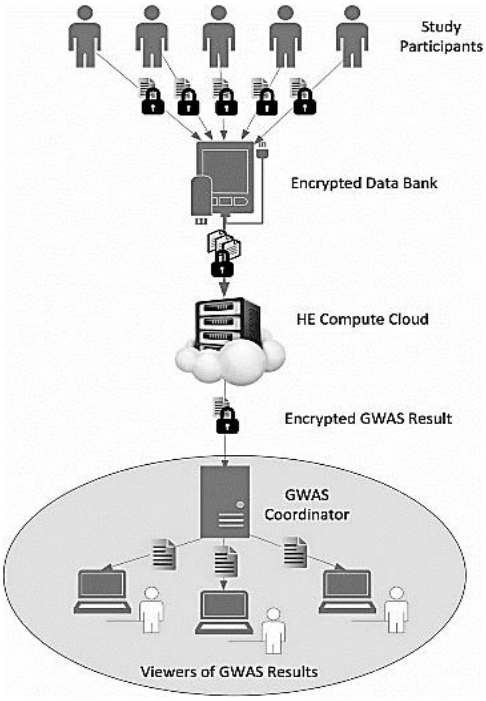


Figure 4. Big data in precision cardiovascular phenotyping [27]

Furthermore, a review by Lieneke [28] introduced the opportunity for big data as the fourth source of information in clinical decision-making in Parkinson's disease (PD) patients, called quadruple decision making. When making a clinical decision, professional expertise, scientific evidence, and patient preference are the primary sources of information. That study revealed that personalized disease prediction employing machine learning approaches combined with a decision support system can fill the gap between evidence-based therapy and each patient's unique features. In addition, A project in 2018 studied the incidence of tuberculosis (TB) using big data analysis and precision medicine/predictive intelligence. The study used public domain data by the world health organization (WHO) to create an accurate predictive model based on key performance indicator (KPI) levels to determine the incidence of TB from 2000 to 2030 using a linear regression algorithm. With the availability of abundant data, it is possible to assess trends that can lead to decision-making in the realm of public health in TB-prone countries such as Indonesia [29].

There are some studies about big data and its potential in precision medicine in Indonesia. For example, [30] analyzes the classifier performance on electrocardiogram (ECG) interpretation for precision medicine using big data and deep learning techniques. Research [31] discussed several efforts devoted to accomplishing precision oncology using big data in Indonesia. Further, study [32] discussed strategies for implementing precision health care in older adults with diabetes in Indonesia. The study concluded that the precision health care strategies for diabetes patients can be broken down into seven phases: doing deductive teaching for a short period of time; assessing the level of self-management and cardiovascular disease risks; arranging a patient brainstorming session to share insights on glycemic targets and specific behavior; generating a list of patients' concerns and prioritizing them; establishing a goal and formulating a plan of action; carrying put follow-up; and keeping track of goal attempts. Moreover, research [32] shows that there are eight components to precision health care in patients with diabetes: personalized genetic or lifestyle factors, self-management, glycemic target and control, interdisciplinary collaborative practice, patient preferences, patient priority-directed care, and evidence-based practice. Even though there are several studies about precision medicine in Indonesia, the number of continuous research and study is still relatively limited and far from enough to develop precision medicine applications.

3.2. Precision medicine opportunities

Based on the case study above, in general, the stages of data analysis in health services include data sources, data cleaning, data analytics, and applications. Big data holds great potential for healthcare providers to systematically use data and analytics to discover previously unknown interesting patterns. In addition, big data can also uncover the inefficiencies of large data stores to build predictive models for best practices that improve healthcare quality and reduce operating costs. Further, big data can be applied in three areas of precision medicine: the realm of basic research, clinical research, and clinical practice as shown in Table 1.

Table 1. Big data applications in precision medicine

Basic research	Clinical research	Clinical practice
Contribute to the identification of molecular targets for new medical therapeutics.	Developing targeted therapies for clinical trials based on medical big data.	Aiding in the diagnosis of patients and the targeting of therapies based on their specific molecular or behavioral profile.
Exploring bio-markers that can be used to identify individuals who will respond more positively to targeted therapies or who will have adverse effects.	Developing new diagnostic techniques or studies for predicting outcomes.	Providing more effective preventive care by more accurately predicting disease onset.

3.2.1. Electronic health records utilization

Electronic medical record systems generate large amounts of data every day. This is a rich source of information that healthcare organizations can use to explore interesting facts and findings that can help improve patient care. Again, each patient is unique and should be treated according to its own characteristic. Therefore, combining big data omics and medical science is at the core of precision medicine. The explosion of electronic data has driven data science's fast and enormous rise in medicine. A learning health system that combines data science, analytics, and precision medicine can perform research in the context of clinical care and simultaneously make greater use of and improve the tools and information available to give improved patient outcomes.

3.2.2. Advancement in technology

One can say that now is the best time to develop precision medicine, and many people would agree. This is because the hardware technology supporting big data has developed rapidly in the last two decades. Among these technologies is the computing power of the hardware. To process extensive data requires a

capable computing device. Luckily, our computing developments follow or even exceed Moore's law which says that computers' capability doubles every 18 months. This corresponds to about 60% annual growth. The graph of the development of computing technology is presented in Figure 5.

Another technology that supports big data is data storage devices. This device used to be very expensive. However, in recent years, data storage costs have been drastically reduced as shown in Figure 6.

The data transmission speed between one device and another is also essential for big data analysis. Luckily, our current bandwidth development and data transmission speed follow Nielsen's law, which states," A high-end user's connection speed grows by 50% per year". So naturally, this impacts the cost of the internet, which becomes much more affordable. The graph of internet bandwidth development can be seen in Figure 7.

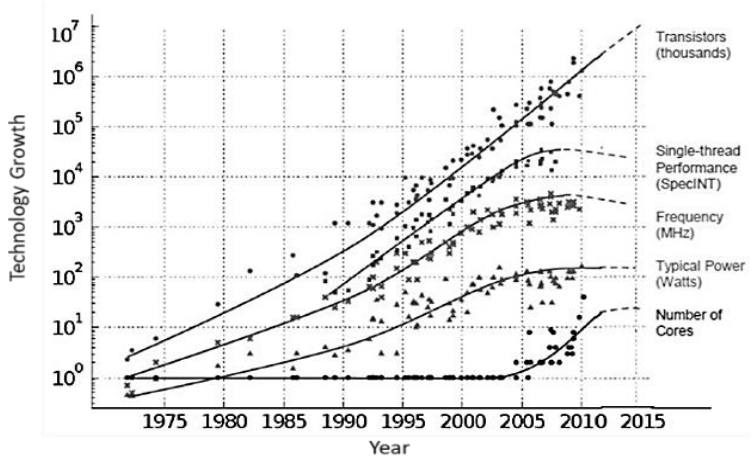


Figure 5. Computation power over the years [33]

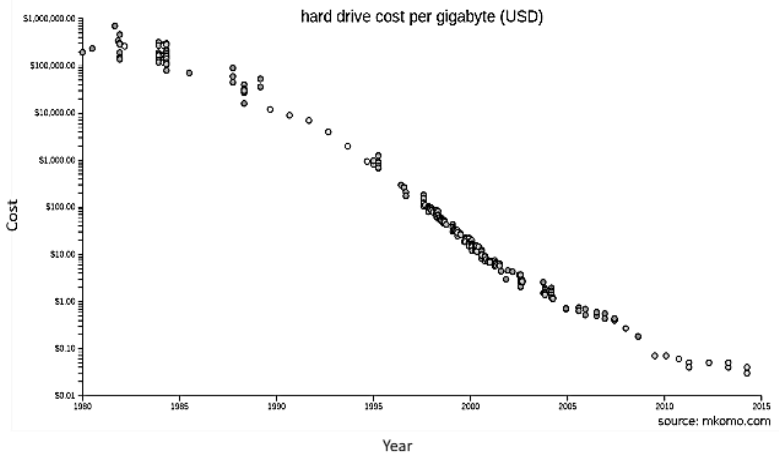


Figure 6. Storage costs over the years [34]

3.2.3. Rapid development of data analysis technique

Data analysis techniques using artificial intelligence have developed rapidly. Since the early development of artificial intelligence in the 1970s, artificial intelligence techniques have experienced ups and downs. However, since the end of the artificial intelligence (AI) winter II era in 1993, AI has experienced rapid improvements as shown in Figure 8. In 1997, AI defeated the world chess grandmaster, Kasparov. Since then, AI has grown so rapidly that today we can enjoy AI technology everywhere, from smart houses to autonomous cars. It is predicted that the rapid development of AI will not stop in the near future. Therefore, this AI growth gives hope to the development of precision medicine using big data.

3.2.4. Citizen participation

Over the last decade, as the internet has been increasingly intertwined with daily life, people have gotten more comfortable revealing personal information online. Previously we felt uncomfortable and insecure about putting our personal information online, even on social media. But, nowadays, we are very comfortable posting our selfies, daily activities, and even putting our credit card information in the payment service. Therefore, this behavior shift can be leveraged for the sake of personalized medicine development. For example, if many patients are willing and consent to share their genomics data, it will contribute to precision medicine research at a significant level [36].

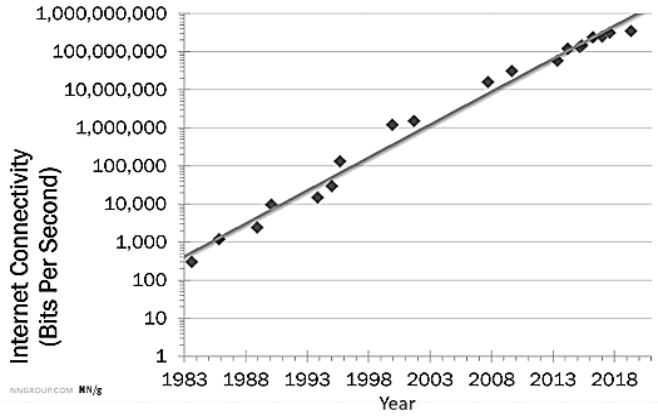


Figure 7. Internet bandwidth over the years [35]

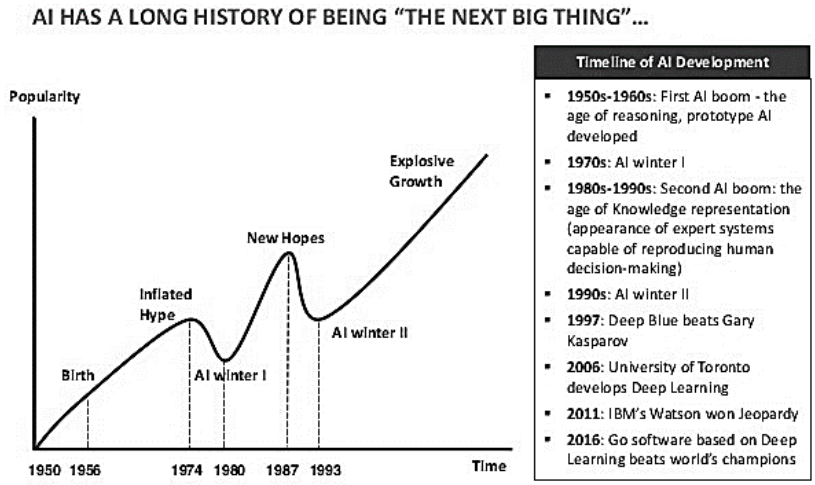


Figure 8. AI growth over the years [37]

3.2.5. Biological data explosion

The explosion of biological data (e.g., RNAs, genes, proteins, and metabolites) is a valuable property for the development of precision medicine. Not only the amount and variation, the heterogeneity of data that can also be collected is also increasing rapidly as shown in Table 2. Furthermore, by using different methods, one data source can produce data that has varying coverage, bias, and noise robustness [38].

3.3. Precision medicine challenges

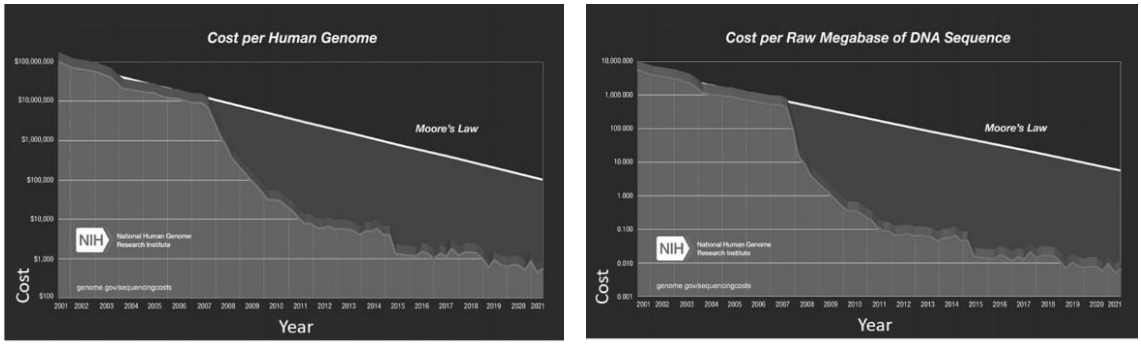
3.3.1. Data analysis cost and complexity

As aforementioned, identifying the genetic basis of a patient's disease is very important in developing precision medicine through whole genome sequencing and analysis. Genome sequencing cost used to be very expensive. However, thanks to the Moore law of computational power, as well as newly developed algorithms and sequencing techniques, the genome sequencing cost has decreased significantly in the last 20 years as

shown in Table 2. Existing human biological data Figure 9(a) and (b). However, why the precision medicine development cannot grow as fast as the sequencing cost reduction? One of the main reasons is the difficulty in interpreting and analyzing the genome data.

Table 2. Existing human biological data

Database type	Database name	Contents	Source
Genomic	NCBI gene [39]	Genomic	NCBI gene [38]
	DGV [40]	More than 8,000,000 structural variation data of the human genome were identified in healthy control samples. Structural variation is defined as genomic alterations involving segments of DNA larger than 50bp.	dgv.tcag.ca
	Ensmbl genome [41]	More than 50,000 genomes data.	ensembl.org
	GOA [42]	More than 80,000 high-quality gene ontology (GO) annotations.	ebi.ac.uk/GOA
Immunological	IMGT/mAb-DB [43]	1,257 data of monoclonal antibodies (IG, mAb), fusion proteins for immune applications (FPIA), composite proteins for clinical applications (CPCA), and related proteins (RPI) of therapeutic interest.	imgt.org
	AbMiner [44]	More than 600 antibodies data and genes encoding the antibodies.	discover.nci.nih.gov/abminer
Metabolomic	Reactome [45]	More than 2,500 human biological pathway and more than 11,000 human proteins including isoforms.	reactome.org
	HMDB [46]	220,945 human metabolite entries.	hmdb.ca
	SugarBindDB [47]	1,266 glycan interactions data.	sugarbind.expasy.org
	UniCarbKB [48]	Data of more than 3,700 glycan structures.	unicarbkb.org
Proteomic	RSCB PDB [49]	56.800 data of human biological 3D macromolecular.	rcsb.org
	IntAct [50]	Contains more than 209,000 human protein interactions.	ebi.ac.uk/intact
	UniProt [51]	Human proteome with more than 70,000 proteins.	uniprot.org
	HPP [52]	19,750 predicted proteins encoded by human genome.	hupo.org
Organelle	OrganelleDB [53]	4,233 organelle proteins, and subcellular structures/complexes of human genes.	mcdb.lsa.umich.edu/organelledb
	MITOMAP [54]	The human mitochondrial database consisted of 54,594 full-length sequences and	mitomap.org
	HmtDB [55]	52,947 genomes of human mitochondria.	hmtdb.uniba.it
Transcriptomic	NCBI GEO [56]	More than 2,000 human gene expression datasets.	ncbi.nlm.nih.gov/geo
	Expression atlas [57]	Localization of gene expression (RNA or protein) data across species and biological conditions.	ebi.ac.uk/gxa
Epigenomic	NCBI epigenomics [58]	More than 5,000 epigenetic modifications data.	ncbi.nlm.nih.gov/epigenomics
	4DGenome [59]	Contains more than 3,000,000 chromatin interactions.	4dgenome.int-med.uiowa.edu



(a) (b)

Figure 9. Cost over the years per (a) human genome and (b) Raw megabase of DNA sequence [60]

A wide range of skills and expertise are required to extract and analyze genome data. Namely, IT professionals, molecular biologists, computational biologists, pathologists, geneticists, genetic counselors, research nurses, and physicians who have a thorough knowledge of diseases and treatment modalities [61].

Therefore, although sequencing data costs and speeds are rapidly decreasing, it's unlikely that analysis complexity will follow suit in the near future.

According to study [61], using sequencing approaches for diagnosis is challenging due to the lack of a complete and high-quality human reference genome. When it comes to quality, clone-based approaches for mapping and sequencing the human reference genome did not provide a fully integrated or assembled sequence that was well distributed across all loci. As a result, sequence collapse inside repeating regions, such as segmental duplications, is a common cause of improper sequence assembly. In other words, we are facing an increasing gap between biomedical big data generation and our ability to analyze and utilize them for precision medicine development. This cost and complexity have become a major issue in precision medicine development, especially in developing countries such as Indonesia.

3.3.2. Data ownership

Any kind of patient data typically being stored in a medical institution. Then, it looks like such data belongs to the institution. However, actually, the data is the property of the patients, and the institution only acts as a data custodian. Therefore, a patient's consent is required to access and use such data outside the clinical use. In addition, there is country law that states that the patient's data should be stored in a designated period and should be destroyed after that period has ended. Many big data techniques, such as deep learning, require thousands to millions of datasets, which require a relatively long time to be collected and processed. Hence, patients' consent to retain and use their data for extensive training and modeling is an absolute requirement. However, it is difficult to obtain patients' consent for such private and personal data in many cases, especially in Indonesia. This results in significant difficulties in developing precision medicine.

3.3.3. Data-sharing regulation

Until now, medical record data in Indonesia is stored in each medical institution. Furthermore, not all medical records are documented in electronic form. This certainly makes it challenging to develop precision medicine in Indonesia. In addition, data harmonization might become another issue. Despite the fact that data harmonization is the basis of illness management, registration, and research programs, it is not implemented in all areas of health care at this time [62]. Therefore, good and strong regulations are needed to regulate data harmonization and data-sharing related to medical records.

3.3.4. Data security

Today, electronic data security still becomes a major concern for many citizens worldwide. Some patients are hesitant to engage in a precision medical plan because they are concerned about their personal information being leaked [63]. However, this concern is not without reason. Since October 2009, 1142 largescale data breaches have been reported by health and business organizations to the United States Department of Health and Human Services. However, among those breaches, only seven cases resulted in fines [64].

Data anonymity is another issue. Although at the time of data collection, the patients do not give any personal information, recent research [65] shows that de-anonymize genetic data and re-identify individual identities are possible. Genotyping microarrays of high-density single nucleotide polymorphism (SNP) from complicated DNA mixtures can be used to de-anonymize genetic data and re-identify individual identities. Finally, a robust security infrastructure is needed to achieve successful big data collection and its utilization for precision medicine development. Therefore, the security of patient personal data can be ensured.

3.3.5. Data infrastructure

Although large medical institutions look modern and have sophisticated equipment, almost all medical institutions in Indonesia do not have the technological infrastructure that is capable of storing and processing very large datasets. Big data research will necessitate a one-of-a-kind environment for storing, handling, combining, curating, and analyzing massive amounts of data. Clinical systems are designed to confine data types like a laboratory, imaging, and pathology test. However, the big data realm necessitates data integration [66]. Therefore, fast, capable, and reliable storage and computing devices are needed to store and process large data. This, of course, requires a relatively high cost. Therefore, it is necessary to make a regulation on who has the right and obligation to store the data, who needs to bear the costs, and what is the protocol for accessing the data. Furthermore, in Indonesia, many remote areas still do not even have access to electricity and the internet. This certainly hinders the development of precision medicine, so it is necessary to solve this problem as fast as possible.

3.3.6. Clinical regulation

Clinical trials and health economic assessments are both important sources of evidence for implementing health interventions [67]. In the principle of evidence-based medicine, achieving the stage of

implementing the development of medical actions requires a relatively long and complicated clinical trial process. The final stage of precision medicine is a new medical action and dosage according to the patient's personal characteristics. Therefore, it is necessary to establish regulations related to clinical trials to implement precision medicine so that the goal of precision medicine to improve the quality of medical services can be achieved. But then, one question arises. Given that this is personalized medicine, is a clinical trial required for each patient? If not, wouldn't the clinical analysis results for precision medicine in one patient be different from other patients?

3.3.7. Technical expertise

Technicians who have special skills in getting data, processing data, and storing data are required in precision medicine development and implementation. Experts such as IT specialists, molecular biologists, computational biologists, pathologists, geneticists, genetic counselors, research nurses, and physicians with a thorough understanding of the disease and treatment options are needed to develop and implement precision medicine. Therefore, extensive and continuous training is required. Furthermore, it will demand sufficient training and educational efforts, along with continuous revisiting and modifying educational programs to reflect the continually growing precision medicine [68].

3.3.8. Genome-based discrimination

In Indonesia's structure of society, several dominant tribes become the majority. Then, the population distribution in Indonesia is also uneven and relatively centralized on the island of Java. Furthermore, the infrastructure development between one and the other region in Indonesia varies. If not taken seriously, these three things have the potential to cause genome-based discrimination in the development of precision medicine.

3.4. Strategy for precision medicine implementation in Indonesia

Precision medicine should guarantee that patients receive the correct therapy at the right dose at the right time, with the least amount of side effects and the most significant amount of efficacy. However, it will alter the way health care is delivered and taught, as well as how medical care is practiced and accounted for. Therefore, it will require simultaneous collaboration among Indonesian medical care stakeholders. In Table 3, we sum up the roles of stakeholders related to health care that will help to ensure the success of precision medicine implementation in Indonesia.

Table 3. Roles of medical care stakeholders to ensuring success of precision medicine in Indonesia

Stakeholders	Roles
Regulator	Fund primary research for precision medicine [69].
	Assuring the quality and accuracy of research dissemination, as well as effective medical practice standards and electronic health record integration [69], [70].
	Provide access to quality and safe care [70].
Research	Conduct relevant pilot trials for data collecting in precision-medicine-focused domains (e.g., genomic projects [71], molecular mechanisms [72]).
	Develop effective clinical decision support tools to convert validated data into knowledge immediately applicable to diagnosis, prognosis, or treatment [73].
Academia	Educate students about pharmacogenomics as well as improve the understanding of disease-related molecular pathways [74].
Medical institution	Facilitate the clinician to apply pharmacogenomic findings to their practice [75].
	Provide multiple systems to be available on the EHR and accessible for clinicians [76].
Pharmaceutical industry	Develop drug discoveries and translate these discoveries into clinically efficacious drugs [77].
Patient group and society	Raise participation in health initiatives.
Other supporting bodies	Assure that the regulatory frameworks necessary to protect patient safety and fairness are in place (e.g., network infrastructure, data security, ethical committee).

4. CONCLUSION

In this era of rapid technological development, the opportunity for the development of precision medicine can be said to have reached its highest point. The development of techniques for obtaining medical data, a significant reduction in the cost of bio sequencing, the development of computing tools, storage systems, and wireless communication systems, as well as the development of data analysis techniques using artificial intelligence have become the main driving forces for the development of precision medicine.

Nevertheless, there are still many challenges that need to be faced in order to develop precision medicine in Indonesia. Starting from the issue of patient data ownership, data-sharing regulation, data security and privacy, data infrastructure, clinical regulation, and human resource capabilities to the potential for genome discrimination. It will demand simultaneous coordination among Indonesian medical care stakeholders.

Moreover, many ethical issues must be addressed in the advancement of precision medicine. For example, will the health insurance system cover the costs of prevention, diagnosis, and proper treatment? How can we equitably distribute precision medicine outcomes to society? Finally, who will have access to it? Many related stakeholders need to collaborate and work together simultaneously to overcome these challenges and actualize precision medicine implementation in Indonesia.

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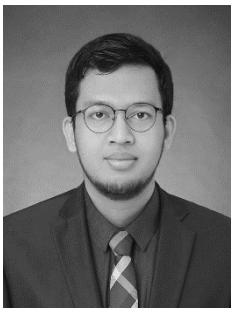

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