EMBRACING SOCIETY 5.0 WITH HUMANITY

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Society 5.0 is a concept presented by the Japanese as a core concept of their economic system. They believed that technology should not surpass the intelligent of men. As such, in society 5.0 the Japanese government would like to ensure that all technological things are designed to be a human-centered design. In fact, their ministry of education in 2018 has also been readily prepared the future generation through a change in their education system. For example, the minister explains that in Japan, or many parts of the world, university entrance are divided into two main concentrations, which are science and social science. The minister thought of changing the system, as society 5.0 is about creating a technology that is human centered. For instance, they gave an example on designer babies. If, people from hard science learn about philosophy, ethics, and humanities, they won't face such ethical concern when developing a product. This is what is being envision by the Japanese government for their younger generation. Collaboration between science and social science is necessary to build a better environment for our future children. Another example is the companies in Japan, such as Hitachi and Fujitsu has already been implementing this 5.0 by designing product that relied fully on technology but puts human at its center (Hitachi, 2017).

Likewise, it is currently a hot topic in Indonesia. Indonesia as a country with the 4th largest population in the world has not been implemented this concept. Our country is still on the industry 4.0. Yet, with the rising interest in AI, Blockchain, NFT, number of unicorn start-up. and all recent technological changes, our country are ready to compete with any other countries in Southeast Asia. Society 5.0 is coming, and we need to embrace it. To prepare with the society 5.0, It is not only the technological side. It is necessary for us to have a strong principle at hearts that based on our belief system. We, as an Indonesian have known to be religious that most of us believed in God. We also commonly practice our religion and tend to be kind to people because we know God would love our good deeds. I personally think that this will help us to move forward and live together with advanced technology.

Technology begets a very important leap in human's life journey. It is important to keep valued of the benefit but it's more important to look out for the human itself. As its purpose is smarter than us, to help us, it will be very ideal if we embrace the technology using our ability to be kind.

Malang, 21 Maret 2022

Diah Karmiyati

Daftar Isi

Early Detection Services Development for The Indonesian Ethnic Group Specified in The Community Era 5.0

Sri Lestari Utami[106]

Introduction

Various websites that offer DNA testing to predict potential risks and prevent disease early on have been launched. This DNA examination is based on the presence of variants as DNA that is specific and unique to a person. This DNA variant is about 0.5% of the identical 99.5% that a person has when compared to other people. This DNA plays a role in the inheritance of traits from parents to their children, so that variants will be related to several conditions. These conditions can be related to certain health conditions, traits, and ancestral groups.

There are websites that only offer ancestry checks, like 23andme.com and ancestry.com. However, some of them are also used for other purposes, such as paternity tests, disease risk assessments (such as cancer, Alzheimer's, and others), and genetic diseases. Some of them can even be used to examine genetic talent for the type of wine that tends to be liked. There are also websites that offer multiple checks, which are classified because they are basically the same. Several classifications of examinations are available, such as health checks, pharmacy, nutrigenetics, sports, skin other than ancestors. These websites include: pursuit.unimelb.edu.au; genomicdiagnostic.com.au; 24genetics.com; circledna.com. There is already a similar website in Indonesia, which is named dnaku.id. At dnaku.id, it serves DNA testing related to exercise, diet, health, skin, cancer markers, drug and vascular responses [1]–[6]

Degenerative diseases are diseases that can be detected early based on DNA variants. Among these diseases are hypertension, type 2 diabetes mellitus (T2DM), coronary heart disease, stroke, and osteoporosis. The presence of this DNA variant is a genetic polymorphism. For several years, researchers have studied the relationship between various variations in the human genome and

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certain characteristic phenotypes. The results suggest that the mechanism of this inherited genetic susceptibility condition is defined as the presence of mutations or polymorphisms of one or more genes that influence the phenotype. Analysis of variation in this case is a very popular method, the aim of which is to link certain allele variants with characteristic phenotypes, especially in polygenic (multifactorial and complex) diseases. The interaction between genes and the environment causes multifactorial disease. Phenotypes such as susceptibility to disease, response to drugs, vaccines, chemicals, and pathogens can be affected by polymorphisms or variations in DNA sequences. The frequency of polymorphisms is 1%, which occurs more frequently than mutations. Single nucleotide polymorphism (SNP/SNIP) is the most common type of polymorphism. These SNPs occur when a single base of DNA is changed and occur more frequently in human genetics. Markers in various studies often use a single nucleotide polymorphism [7], [8]

The high prevalence of non-communicable diseases in Indonesia is expected to reduce the proportion of the population aged 50 years and over. As a result, this disease causes the dominant mortality or mortality rate in Indonesia. This indicates a change in disease patterns that are dominated by non-communicable diseases such as diabetes mellitus, heart disease, dyslipidemia, obesity, kidney disease, lung disease, and malignancy. This change in pattern can be caused by changes in the environment, technology, or lifestyle. The 2014 Sample Registration System shows the ten most common diseases. Complications of high blood pressure (hypertension) and diabetes mellitus were included in the percentages of 5.3% and 6.7%, respectively.[9], [10] Among several risk factors for T2DM and hypertension, ethnicity is one of them. This can be seen in the diabetes risk questionnaire launched by the American Diabetes Association on its website, which shows one of the questions is about ethnicity or the various studies on primary hypertension and T2DM that show it. [11]

The country of Indonesia is located in Southeast Asia, with an ethnicity classified as Asian. The Indonesian nation is classified from a different point of view. It will be divided into various kinds of ethnic groups. In the classification based on the "New Classification" in the 2010 census data, there will be more than 1,000 ethnic groups. The ethnic groups that rank fifth largest are Javanese, Sundanese, Batak, other Sulawesi ethnicities, and Madura, with a percentage of 40.22, 15.5, 3.58, 3.22, and 3.03. Meanwhile, if we look at the high-resolution analysis of haplotype diversity, there are differences between East

and West Indonesia. The population history of Indonesia is complex as it is a genetic mix of early Austronesian expansion with the genetic contribution of the Filipino population. Genetic mixing with the local population will form Eastern Indonesia. But Western Indonesians are much more complex because of interactions with Mainland Asians and Austronesian settlers, as well as genetic contacts with South Asians and isolated local groups. [12]–[14]

The results of research on gene polymorphisms in Indonesia may show the same or different results in different ethnic group. The study of IL-6-174 G/C gene polymorphisms showed that the C/C genotype was found in all respondents, postmenopausal women with osteoporosis in the Balinese tribe. Meanwhile, there was a significant difference in the IL-6-572G/C gene polymorphism.[15] Another population study in Jakarta showed that 96 respondents (96%) had the GG genotype, 4 respondents (4%) had the GC genotype, and none had the CC genotype. These results showed that there was no significant relationship between the IL-6-G174C gene polymorphism and postmenopausal women. The population of Jakarta is dominated by the Betawi, or Sundanese [16].

The existence of the above explanation causes the writer to be interested in expressing the idea of the need for "Development of Specific Degenerative Disease Early Detection Services for Indonesian Ethnic People in the Era of Society 5.0". This is due to the development of technological advances that use the internet for everything, as well as "big data" gene polymorphisms for the Indonesian ethnic group in the era of Society 5.0. Research shows that although ethnicity is the same, different ethnic groups will have different gene variations. This specific genetic polymorphism can be used to design biomarkers for early detection, especially for degenerative diseases that are multifactorial. Very early knowledge of the health risks of chronic diseases with high rates of mortality and morbidity would be very useful. Preventive measures can be taken by regulating environmental factors such as lifestyle so that genetic factors are not expressed. Although, in the end, someone with sick parents will get sick too, it is hoped that this disease does not appear at a young age or its severity can be reduced. While the examination at dnaku.id. does not cover all degenerative diseases and has very complicated methods, with the existence of "affordable internet signals and big data", it is hoped that the preparation of "biomarkers" with detection technology that is much simpler, flexible, inexpensive, and can be done anywhere will be carried out.

Discussion

Shifting disease trends as a burden in Indonesia

There are five diseases whose prevalence in Indonesia is included in the top 10 non-communicable diseases, namely hypertension, type 2 diabetes mellitus (T2DM), coronary heart disease, stroke, and osteoporosis. This is based on a shift in global trends in causes of death according to the 2018 Institute for Health Metrics and Evaluation (IHME) Report in the 2017 Global Burden of Disease Study, especially in non-communicable diseases from infectious diseases. Among the non-communicable diseases are ischemic heart disease and stroke, in addition to other diseases. The report stated that there was a shift in the ranking of ischemic heart disease and stroke in comparison between 1990 and 2017.

The ranking of ischemic heart disease rose from rank 4 to rank 1. Stroke also experienced the same thing, from rank 5 to rank 3. The report also shows a picture of global mortality from cardiovascular disease in 2007–2017, which experienced an increase in the death rate. This applies to all ages and both genders. The death rate increased approximately from 217 people in 2007 to 232 people in 2017, with one death per 100,000 population. Therefore, the biggest cause of death from various types of non-communicable diseases is cardiovascular disease. This is indicated by the percentage value of 43.3%, or 17.8 million deaths in 2017.

This causes non-communicable diseases to be the largest cause of death globally in 2017, which is 73.4%, or 41.1 million deaths. This figure has increased compared to 2007; it was 33.5 million. [17], [18] As a result, ischemic heart disease and stroke are predicted to be the main causes of premature death in 2040. These two non-communicable diseases are still consistently ranked 1st and 2nd in 2014 when compared to 2016. Meanwhile, diabetes will increase its rank from 15th to 7th in 2040. Other non-communicable diseases will also increase in rank, while most communicable, maternal, neonatal, and nutritional diseases are likely to decline, except for lower respiratory tract infections, which will remain in rank. [17]

Non-communicable diseases in particular also drive the burden of disability because they cause 80% of disability in 2017. Several diseases, such as T2DM and fatty liver, will cause increased disability in metabolic conditions worldwide at various stages of development. One of the leading causes of disability globally for all ages in non-communicable diseases is diabetes. Other causes are

mainly low back pain and headache disorders, which include migraines. When compared between 1990 and 2017, diabetes has increased in rank as the leading cause of global disability. It was ranked 9th in 1990 and 4th in 2017. This report also shows that there are differences in the main causes of premature death and disability among countries classified as socio-economical. The Demographic Index (SDI) ranges from low to very high. Diseases found in countries with low SDI are infectious, maternal, neonatal, and nutritional diseases. Meanwhile, non-communicable diseases are found in countries with high SDI. Ranks 1-4 will be occupied by ischemic heart disease, low back pain, stroke, and lung cancer. The socio-demographic measurement index covering three different aspects of development is referred to as the SDI. These aspects of development are income, education, and fertility. [17]

Between 1990 and 2017, there was a change in the main risk factors for premature death and disability. Malnourished children, premature pregnancy or early birth, and low birth weight for pregnancy were the main risk factors in 1990. Meanwhile, the risk factors in 2017 were high blood pressure, smoking, and high blood sugar. The ranking of these three risk factors differs between women and men. Smoking, high systolic blood pressure, and high fasting plasma glucose were ranked 1, 2, and 3 in males. These three levels in a row in women are high systolic blood pressure, high fasting plasma glucose, and high Body Mass Index (BMI) values. The predictions of these three risk factor rankings in 2040 are that they will have high BMI, high blood pressure, and high blood sugar. The potential number of lives that could be saved if exposure to these risk factors were reduced was around 81 million, 79 million, and 60 million, respectively. [17].

The same thing also happened in Indonesia, namely the shift in disease conditions from infectious to non-communicable. This is in line with demographic changes for the population aged 65+, which is predicted to triple from 2015 to 2045. Although the productive age (14-64 years) is still around for more than 60% of the total population during 2015–2045. There is a change in Indonesia's population from around 266 million (in 2015) to 300 million (2045). Population dynamics changes (age distribution, mortality, fertility, life expectancy, urbanization, and dietary changes) have led to rapid epidemiological changes from communicable to non-communicable diseases over the last 25 years.

This non-communicable disease contributed to 70% of overall deaths in 2017, compared to 39.81% in 1990, making it the burden of disease for that year. Of the 10 root causes of death in Indonesia in 2017, six of them were non-communicable diseases. There was an increase in the incidence of stroke in just 10 years (2007–2017), i.e., 29.2%, so stroke was the leading cause of death during that time. Almost the same value (29%) also occurred in ischemic heart disease as the second cause of death. Diabetes is the disease with the most significant increase because there was an increase of three ranks in 2017 from the sixth rank in 2007. This diabetes disease ranks below ischemic heart disease. There is an increase in the percentage of incidence up to 50.1%. High systolic blood pressure, dietary risk, high fasting plasma glucose levels, smoking, and child and maternal malnutrition are the 5 risk factors that contribute to Disability Adjusted Life Years (DALYs), starting from the largest. [19]

Strategi terbaik penatalaksaan penyakit degeneratif sebagai penyakit kronik

The best strategy for controlling major chronic diseases should focus on monitoring and preventing the progression of chronic diseases at an early stage. This is because chronic disease has two main characteristics: once a person is exposed to a chronic disease, it will remain for almost all of their lives without ever fully recovering, and complications of chronic disease may cause high rates of death and disability. New diagnostic tools need to be developed in this regard, which are based on various molecular biomarkers to observe the physiological state of people in the early stages of chromic disease symptoms so that they can be prevented by diet or therapeutics. Health maintenance management means scientific, behavioral, social, or environmental interventions that will lead to positive changes in people's healthy living habits and lifestyles. This is a successful prevention method and will systematically control major chronic diseases. The focus on fighting chronic diseases in the future will lead to prevention, so the confrontational strategy against chronic disease is a combination of prevention, health promotion, and therapeutic approaches. [20].

This is in line with various strategies for controlling non-communicable diseases and their risk factors in the 2018 Consolidated Report on Indonesia's Health Sector Review, namely: [19]

1. Improving unhealthy lifestyles such as poor diet, lack of physical activity, and smoking, which are major risk factors for noncommunicable diseases, in order to strengthen the Germas or Healthy Living Community Movement.Changes in behavior to a healthy lifestyle are carried out by supporting increased adoption of various physical activities, creating a healthy environment, promoting education about healthy living, developing early detection of risk factors for non-communicable diseases, as well as providing nutritious and healthy food. The Germas movement is carried out by the government, communities, and the public sector.
2. Improving early detection in noncommunicable disease preventionCommunity awareness regarding non-communicable diseases needs to be increased because of the high mortality rate and the possibility of an unproductive population. Various efforts should be made to strengthen the early detection of this disease, which will support the early management of risk factors such as obesity, diabetes, and hypertension. This in turn will reduce the burden of non-communicable diseases. Therefore, early detection capability and capacity should strengthen the level of primary health care through increased routine screening programmes. Primary healthcare facilities supported by BPJS are implementing Minimum Service Standards (MSS), a family-based health approach (PISPK), and a chronic disease management program (Prolanis). These three programs will support early detection of non-communicable diseases.
3. Improving regulations to promote healthy living. Regulations are needed to increase the role of industry in producing nutritious and healthy foods, improve food labeling, and increase consumer awareness. Incentives for the public sector should be created to support these efforts. Limitation of consumption and marketing of minimum food and products that pose health risks (high in salt, sugar, and fat) that can be implemented by implementing measurable targeted taxation.
4. Implementation of health-oriented development. Prevention efforts for non-communicable diseases require the role of various sectors. Supporting infrastructure, provision of nutritious food, and a healthy environment will enable healthy behaviors and lifestyles. This effort will also be supported by other sectors. Health issues should be the main discussion point in policy development for other sectors (health-oriented development).

5. Increased noncommunicable disease surveillance. Data collection systems for non-communicable diseases need to be developed to facilitate a better understanding of the epidemiology of non-communicable diseases in various provinces and districts/cities in Indonesia. Valid data will allow for adequate development of policy development responses to prevent non-communicable diseases.

Strengthening early detection to prevent non-communicable diseases is one of the strategies to control non-communicable diseases and their risk factors in the Bapenas Health Sector Report in 2018. One way is to increase routine screening programs that support early management of risk factors such as obesity, diabetes, and hypertension in order to reduce the burden of non-communicable diseases.

To achieve this goal, the authors formed a study group whose specific objectives were to focus on the design, confirmation, and validation of early detection biomarkers based on specific genetic polymorphisms from genetic maps formed from four non-communicable diseases which, according to Riskesdas in 2018, were included in the top 10 and are a series of cardiovascular diseases, namely hypertension, type 2 diabetes mellitus (T2DM), coronary heart disease, stroke, and osteoporosis. According to Riskesdas (2018), the prevalence of diabetes mellitus in Indonesia is 8.5% based on an examination of blood sugar levels in the population aged 15 years. Hypertension with a prevalence of 8.36% based on a doctor's diagnosis or taking antihypertensive drugs in the population aged 18 years, while the risk based on measurement results is up to 34.11%. The prevalence of stroke is up to 10.9% based on a doctor's diagnosis in the population aged 15 years. [21]

Early detection biomarkers based on genetic polymorphisms of degenerative diseases

The term polymorphism in this case is important to clarify as the presence of two or more gene variants on the same allele. Thus, at least the common variant must have a frequency equal to or higher than 1% of the population, otherwise the variation is considered a mutation. These changes in normal sequences may involve multiple bases, as in the case of minisatellites or variable number of tandem repeats (VNTRs), which vary in size between 15–70 tandem base pairs. Another polymorphism is microsatellite, also known as short tandem repeats (STR), which is characterized by variations in the

number of nucleotides (2–6 base pairs). Recently, single nucleotide variations, known as SNPs, have been analyzed. [7]

There are at least 3.1 million SNPs, or 1 SNP per kilobase (kb) of DNA sequences in the human genome (Frazer et al., 2007). [22] It is important to know whether a polymorphism is functional or not if you want to understand the basic mechanism of a polymorphism associated with a particular phenotype or the resulting behavior, namely to see whether it changes the function of a gene or a set of genes. The function of the associated polymorphism in most cases is uncertain and must be suspected or extrapolated as an effect of the gene containing this polymorphism. In rare cases, polymorphisms may be variations of non-synonymized coding regions that alter the genes that produce protein structures. Most of the potential polymorphisms as regulatory polymorphisms are located in the coding region, including:

1. Promoters in the upstream, downstream, and intron regions that may influence transcription [23]
2. Introns and untranslated regions (UTR) that are transcribed as RNA may affect transcription, RNA splicing, stability, or translation [24]
3. Intergenic areas' unknown functions [25]

Single nucleotide polymorphisms in individuals may have minimal functional impact, but perhaps due to linkage disequilibrium, the sequence of polymorphisms forming a haplotype will be associated with functional or functional gene expression outcomes. [26] Zajickova and Zofkova (2003) mention four possible mechanisms by which the frequency of polymorphisms may affect the phenotype, namely: [27]

1. a misalignment of links to other traits that results in mutations at nearby loci
2. an effect on the stability of mRNA
3. an effect on the rate of gene transcription (the amount of mRNA) and
4. modifying the resulting amino acid sequence

Conclusion

Many studies have been conducted around the world on gene polymorphisms in hypertension, type 2 diabetes, coronary heart disease, and stroke as a degenerative disease. This research has been carried out for a long time, so the design of biomarkers based on the principle of DNA variation has long been used as an early detection

method for degenerative diseases. Changes in the trend of non-communicable diseases such as degenerative diseases, the main cause of death that occurs in the world, also occur in Indonesia as a developing country.

Degenerative diseases such as diabetes, ischemic heart disease, and stroke are increasing in rank, displacing infectious diseases due to changes in environmental factors such as lifestyle. Indonesia, as a country with the fourth largest population in the world, has thousands of tribes and is a country with many isolated islands, will have a variety of gene polymorphisms. This strongly supports the development of biomarkers for early detection of degenerative diseases that are specific to the Indonesian people based on gene polymorphisms or DNA variations. This biomarker must be cheap, affordable, accessible, and easy to use for the Indonesian people. The use of this biomarker early, for example during growth, will be able to regulate environmental factors that are suitable for future health. For example, healthy lifestyle arrangements can be made during the growth period for people who are detected at high risk of suffering from degenerative diseases. This arrangement is expected to reduce mortality and morbidity if the risk of disease is known early. This does not mean that people who are not at risk do not need to adjust their lifestyle to a healthy pattern. This is because genetic factors influence a small number of disease risk factors, while the majority are environmental factors such as lifestyle.

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