

Review article:

Prospects and Challenges of Precision Medicine in Lower- and Middle-Income Countries: A Brief Overview

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Abstract:

The trend of NCDs in most LMIC countries is slowly but gradually follows that of in the developed countries. There are four significant diseases reported by WHO, which are equally common, such as CVDs, diabetes, cancer, and chronic respiratory disease that causes widespread early death & morbidity. Indeed, it incurs an overwhelming financial burden to most countries in the world. The rise of drug-resistant microbes is another major problem. To overcome this issue, precision medicine (PM) comes into play whereby individual variability in genes, environment, lifestyle, and nutrition of each person is considered for disease treatment & prevention. PM provides a personalized approach, the right treatment to the right people at the right time. Many wealthy countries in the West have started adopting PM though the initial cost is high, ultimately, in the long run, will reduce the healthcare cost by getting rid of the ineffective treatment strategies. However, the PM in LMICs is still at an early stage due to issues such as lack of population-specific data, competency, expertise, and poor financial support.

Keywords: Prospects; Problems; Precision Medicine; Lower- and Middle-Income Countries; Prevalence; Non-Communicable Diseases; Advantages; Adoption; Cost Attainment, or Upsurge; Changeless; Prospects; Oral Health; Nutritional Diseases; Antibiotics; Antimicrobial Resistance; Benefits; Transnational Corporate House.

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1. Introduction

1. A. Definitions Regarding Precision Medicine

US National Library defines PM as “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person”¹. The

same institute Library voices personalized medicine is an older terminology of PM². The Institute for PM defines “PM is a medical approach that proposes to prevent and treat disease based upon a person’s unique genetic makeup and their lifestyle habits”³. After that, PM possesses the strength to diagnose

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precise, explicit predictors of patient outcomes is prompted in tailoring individual clinical care³. US National Cancer Institute defines PM as “a form of medicine that uses information about a person’s genes, proteins, and environment to prevent, diagnose, and treat disease”⁴. In cancer management, PM practices specific evidence about the patient malignant growth to diagnose, in developing strategies for treatment, to assess treatment results and prognosis of the disease. PM evaluates types of cancer cells, as, for breast cancer, whether it is HER2-positive or negative or uses tumor marker investigating tool to attain explicit diagnosis malignancy. Subsequently, PM regularly called personalized medicine⁴. Others scientist describes “personalized medicine refers to an approach to patients that considers their genetic make-up, but with attention to their preferences, beliefs, attitudes, knowledge and social context, whereas PM describes a model for health care delivery that relies heavily on data, analytics, and information”⁵. The PM goes further on genomics and has enormous consequences for both national and international research areas and improvement and implementation of better health care⁵. PM is defined by the National Research Council’s as “the tailoring of medical treatment to the individual characteristics of each patient, classify individuals into subpopulations that differ in their susceptibility, therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not”⁶. The PM was first defined by Clayton Christensen, as furnishing of disease care that can diagnose precisely, and understand the causes of disease. Accordingly, evidenced-based prophetically efficacious treatment strategies were applied to achieve a better outcome. Additionally, Christensen makes clear about the novel terminology, PM, to differentiate from personalized medicine, “because most precisely diagnosed diseases are, in fact, not uniquely personal”⁷.

1. B. A Brief History of PM

The medical doctors, medical professional groups have identified a long back that each patient is unique. Subsequently, medical societies started speaking for many decades that it is documented the prevalence of similar diseases within close relatives and ethnic groups, a range of different drug responses with adverse effects, and various signs and symptoms often observed with the same pathological condition⁸⁻¹¹. Although some notion of personalized medicine exists nearing 60 years, it first appeared

in 1999 in a published manuscript¹²⁻¹⁴. Personalized care ideas and thoughts now are almost in reality because of the development of very highly sensitive newer diagnostic tools^{15, 16}. “Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments, match a blood transfusion to a blood type, cancer cure to our genetic code, the right dose of medicine, as taking our temperature?” President Obama¹⁷. President Obama declared in his 2015 State of the Union address that the PM as a highly resourceful and capable of combatting several unaddressed diseases and improving overall health care^{17, 18}.

1. C. A Few Success Stories of Precision Medicine

Currently, most of the medical treatment strategies are considered on the basis that all patient with the same pathology is almost similar and treatment planning also parallel, although each patient is unique^{19, 20}. Afterward, treatment planning is founded on the “one-size-fits-all” method¹⁹⁻²¹. These treatment strategies of “one-size-fits-all” are often successful for some patients, maybe 50% or more, but not for each patient²²⁻²⁷. Moreover, every human being is born with a unique genetic outline, embossed with data that evidenced their health all over their lives, together with their risk for specific diseases and the power of that individual’s immune system to battle those ailments²⁸. Consequently, denotes the process of rereading the individual patient’s genome to perceive methods to augment individual patients’ health^{29, 30}. Currently, PM in its’ neonatal phase. As scientists yet not able to discover the genetic blueprint of all diseases around the globe. Additionally, there is progress regarding genetic makeup for some diseases yet to develop drug therapy. Furthermore, it has been reported that researches are ongoing and in progress, almost all diseases known to the scientific community. Scientists are very hopeful and confident soon if not the majority, but a big portion of patients will be benefited from these researches related to PM. At the occasion, because of basket trials for breast, lung, or prostate cancer medicine founded on the “genetic mutation of a tumor, rather than the type of tumor”³¹. Basket trials or studies are defined as “test the effect of one drug on a single mutation in a variety of tumor types, at the same time. These studies also have the potential to greatly increase the number of patients who are eligible to receive certain drugs relative to other trial designs.”³². Moreover, these researches open the door and create hope for cancer patients for new medical treatments that, in general, not available

for these cancers considered very difficult to treat³¹. Researchers believe in the next one-decade time PM will progress as much that more than 1 million cancer patients will get the benefits of such development in medical science. Additionally, the scientific community feels that no patient need “suffer through trial-and-error care” because of the availability of information regarding their disease(s)³¹.

1. D. Objectives of the Study

The general objective of the current study is to assess the situation, future possibilities, and utility of PM in LMIC.

2. Materials and Methods

This review has been based on freely available literature from Google, Google Scholar, EBSCO, and PubMed and from the link provided by the Universiti Pertahanan Nasional Malaysia ((UPNM) National Defence University of Malaysia). The terms used were prospects, problems, PM, lower- and middle-income countries, definitions, history, success, prevalence, non-communicable diseases (NCDs), advantages, adoption, cost attainment or upsurge, problems, changeless, prospects, benefits public/people’s health, industries, gain, antibiotics, and antimicrobial resistance. A few manuscripts incorporated required payment to view the full paper but have been provided free of charge by other libraries as part of cooperation with UPNM. This is a narrative review article that will give the effort to describe and deliberate issues related to Prospects and Problems of PM in Lower- and Middle-Income Countries: A Brief Overview, from an academic and point of view, founded on the formerly available document. Furthermore, there has been no effort to develop an accurate database and to use a procedural scheme to nurture a systematic review and meta-analysis.

3. Prevalence of Non-Communicable Diseases in Lower- and Middle-Income Countries

The field of medical care is principally categorized into communicable and NCDs. The possibility and opportunity of PM are enormous, mostly involves NCDs like diabetes mellitus, cancer, Alzheimer’s disease, cardiovascular illnesses, etc.³³. The notion of PM largely assumes more meticulousness in the diagnosis and more accurate and definite prescribing of medicines³³. Internationally, NCDs are the leading cause of death. Most of these deaths due to cardiovascular diseases (CVDs), cancer, chronic respiratory diseases, or diabetes. Additionally, globally, the death rate related NCDs continues to

increase. LMICs suffers much more regarding NCDs than upper-middle and high-income countries. Nearly 75% of global mortality occurs because of NCDs³⁴. The death rate due to NCDs in Malawi is 28%³⁴. Similarly, almost all Sub-Saharan African countries’ death rates due to NCDs are continually increasing^{35,36}. WHO reported that CVDs, diabetes, cancer and chronic respiratory disease – are the most widespread causes of early death and incapability. These four diseases are equally common in both technologically advanced and emerging countries and frequently sufferers are marginalized communities³⁷. There has been a substantial improvement in infectious diseases, infant mortality rate, birth control, family planning, and sanitation in almost all LMICs in the last 60 years. After that, life expectancy has been increased; on the contrary, NCDs increase in a similar rate of developed countries³⁸⁻⁴¹. WHO reported that NCDs caused 63-71% of death around the world. Additionally, it is about 82-85% of deaths in LMICs were due to NCDs. The most upsetting issue is around 40% of these deaths were among the relatively among below the age of 70 years’ population^{42,43}. NCDs deaths are predictable to escalate by 15% internationally between 2010 and 2020⁴⁴.

3A. A Brief Description of Prevalence of Non-Communicable Diseases in Selected Lower- and Middle-Income Countries (Selected Countries) around the Globe

3. A.1. India

The encumbrance of NCDs is mounting excessively among communities of LIMCs. Additionally, NCDs related deaths have augmented the most in the South-East Asia Region (SEAR) from 6.7-8.5 million in the last 12 years. India and Indonesia jointly account for 80% of NCDs related deaths among SEAR countries, and two-thirds (5.8 million) portion NCDs related deaths happen in India alone⁴². It has been reported that NCDs in India reach the level of the epidemic⁴⁵ and has become a major public health issue⁴⁶. Cardiovascular diseases, chronic obstructive pulmonary disease (COPD), cancer, and diabetes mellitus are the four leading causes of NCDs in India^{46,47}. It has also been postulated that these four NCDs will continue to rise in the coming years⁴⁸. It has also been reported that 62% of healthcare disease burden in India is due to these NCDs and a cause for 53% of death⁴⁶. Among these, 53%, a leading cause of deaths were categorized as CVDs (24%), COPD (11%), cancer (6%) and diabetes (2%)⁴⁹.

3. A.2. Brazil

A comparative study regarding NCDs among Shantytown dwellers and general residents of Brazil revealed that hypertension [23.6% (95% CI 20.9–26.4) and 22.9% (21.2–24.6), respectively] and for dyslipidemia [22.7% (19.8–25.5) and 21.5% (19.7–23.4)]. Shantytown peoples had a higher prevalence of diabetes mellitus [10.1% (7.9–12.3)] and overweight/obesity [46.5% (43.1–49.9)], compared to 5.2% (4.2–6.1) and 40.6% (38.5–42.8) of the general inhabitants. Fourteen percent [14.5% (12.1–17.0)] of shantytown inhabitants smoked cigarettes compared to 8.3% (7.1–9.5) of the general populace⁵⁰. Another study reported that NCDs had become a major health issue in Brazil--72% of all deaths were ascribable to NCDs. In Brazil, the principal cause of disease problem is NCDs that include neuropsychiatric diseases were the sole principal contributor. Unprivileged communities of Brazil were the highest sufferers of morbidity and mortality related to NCDs⁵¹. Another study reported that in Brazil, mortality rates in hospitals due to CVDs and diabetic complications were high, especially among poverty-stricken patients. Inadequate, inefficient, and insufficient medical care and control programs in Brazil lead to high mortality among the relatively younger population and loss of productive time⁵².

3. A.3. Mexico

Mexico achieves a lot to decrease morbidity and mortality associated with undernourishment, transmittable infectious diseases such as diarrheal diseases and sanitation, especially among the pediatric population⁵³⁻⁵⁵. Nevertheless, the fifth principal burden of chronic NCDs became the major basis of public health apprehension⁵⁴⁻⁵⁶. Additionally, diabetes mellitus appears as the sole principal cause of disability-adjusted life years and expected to deteriorate in the upcoming day^{57, 58}. Additionally, it has been reported that obvious disparity exists in the management of diabetes, ischemic heart diseases, and cirrhosis in different states of Mexico, which particularly affects poorer communities⁵³. Another global research reported that Mexico (80%) is around a 9% higher mortality rate than the global (71%) rate⁵⁹. Ministry of Health in Mexico declared that an epidemiological emergency due to the enormously high frequency and progress of diabetes⁶⁰ and was projected that 40% of Mexicans existing with diabetes go on undiagnosed, only 50% of the population diagnosed and treated, and only 15% had the diagnosis and control of blood glucose⁶¹.

3. A.4. South Africa

One very recent study reported that NCDs was comparatively high in South Africa, and the most frequent were high blood pressure (17.4%), and stomach ulcers (13.5%)⁶². Another study revealed that chronic NCDs are expanding among older persons in South Africa⁶³. The snowballing load on the healthcare system and budget. Multiple studies have revealed that the prevalence of chronic NCDs was 51.8% in South Africa, and multimorbidity (2-3) was 22.5%. Multivariate logistic regression analysis exhibited that sex, aged population (60-79 years), being non-white, Asian, Black African, poor education level, an affluent community, and the city dwellers area was correlated with NCDs^{44, 64}. There was an enormous development in the management of HIV/AIDS, tuberculosis, reduction of tobacco consumption, fatty acids, salt, and sugar, as well as restriction of promotional activities regarding junk food because of political promise in South Africa⁶⁴. Nevertheless, around 40% of deaths in South Africa are imputable to NCDs, because of scarce resources, infrastructure, and access to healthcare, especially for the marginalized community⁶⁶⁻⁶⁹.

3. A.5. Bosnia and Herzegovina

Bosnia and Herzegovina have an overall trend of the augmented death rate; cancer and CVDs have been increasing due to many unhealthy lifestyles because of war⁷⁰⁻⁷³. WHO reported that in Bosnia and Herzegovina, around 50% of all deaths were due to CVDs and cardiac diseases, identified as the top of the cause morbidity of the country⁷⁴. Another study revealed that nearing 40% were identified as hypertensive and 36% and 45% of men and women, respectively. Overall around 75% of the population were obese [Body Mass Index (BMI) > 25 kg/m²] and 16% and 20% of men and women were overweight (BMI > 30 kg/m²). The mean BMI was 26.5 kg/m² and 27.0 kg/m² among males and females, respectively. Around 40% of the population of the country were smokers⁷³.

4. Advantages of Adoption of Precision Medicine

The medical treatment planning principally reactive throughout history. Currently, communities, including medical doctors, habitually wait till signs and symptoms the disease develops and then plans for treatment. In most diseases, etiology is not understandable, especially chronic diseases like cancer, Alzheimer's and diabetes where genetic and environmental factors are responsible. Thereby, major diseases cause often remain imprecise,

unpredictable, and ineffective. Currently, medical treatment strategies are based on statistical averages. Most of the currently available medicine is effective only in 50% of patients. Accordingly, these drugs are effective for some patients, but not for all. It has been explained as genetic variation exists in the population⁷⁵.

The medical treatment of chronic and life-threatening diseases has sprouting headed for PM for the last few years. After that, the science of PM is progressing towards wider availability for common people. Additionally, PM has begun as a principal method for disease prophylaxis and medical care highly complicated pathologies, utilizing individual distinctions in genes, environment, and lifestyle to cultivate and progress “diagnostics, prognostics, and therapies to target, treat and monitor patients’ conditions”⁷⁶. Moreover, the accomplishment of the Human Genome Project has led to all-embracing progress in research know-hows in genetic and molecular meadows, giving upsurge to the epoch of PM⁷⁷. Presently, cancer management usually involves surgery, chemotherapy, radiotherapy, and immunotherapy. Cancer management depends on types, size, and metastasis. As PM tailored with a genetic make-up individual cancer patient, subsequently, a treatment plan is more accurate and confirmed efficacious against such cancers⁷⁸.

Although in the last two decades, public health has assisted in assimilating genomics into clinical practice and disease prevention⁷⁹. A most important contest of precision public health to understand and utilized all-encompassing information on a large population regarding genomic and environmental factors in improving health care in a specific portion of people⁸⁰. PM methodologies are embedded in the skill to collect comprehensive information of a large population, assimilation different kind data categories, and utilizing better strategies to reveal new understandings about highly complicated chronic pathological conditions⁸¹. After that, there are annoying anxieties exits in the joining of PM and public health⁸⁰. Moreover, it has been reported that PM often focused on the development of new medicines for sick individuals, while not concentrating on the “population-level challenges,” which has further promoted much apprehension among public health scientists⁸². Multiple studies reported that although PM is projected to initiate step-by-step evolutions of specific medication for chronic disabilities caused by NCDs, on the other hand, there are difficulties

in utilizing these newly developed drugs for a large group of the population^{83,84}.

5. Cost Attainment or Upsurge of Treatment by Adoption of Precision Medicine

PM provides “the right treatment to the right patient at the right time”⁸⁵, a model that swings healthcare from the current operating medical care based on “one-size-fits-all”⁸⁶ to a more personalized approach⁸⁷. After that, several rich countries of Europe Union and North America started considering PM as the central theme of the country’s healthcare system despite the high cost of treatment^{5,87-89}. Multiple studies reported that healthcare around the globe progressing in the direction of PM which, ultimately, in the long run, reduce healthcare cost by getting rid of ineffective treatment strategies^{5,90,91}. A research study reported that screening cancer biomarkers among common people were found cost-effective than only high-risk patients⁹²⁻⁹⁵. Genetic testing of breast and ovarian cancer biomarkers among the larger community can prevent 1.91 and 4.88 cases, respectively, every year⁹⁶. The PM offers ample benefits for patients and current stratagems to describe the genetic relations of cancers by utilizing newer equipment and expertise. Nevertheless, a “lack of evidence, data, and a clear strategy on how this will be used to benefit patients across the world, particularly in LMICs”⁹⁷. The high cost of new diagnostics aids and medication for precision medicine often aggravates health disparities. Nevertheless, precision medicine initiates the shifting of the health budget towards higher-priced treatment options than low-priced choices. This shift of the health budget raises the possibility of the sustainability of health service and a massive negative influence on public health, especially LMICs^{84,98,99}.

6. Changeless of Precision Medicine in Lower- and Middle-Income Countries

Currently, most facts banked regarding human genomes are principally from rich countries⁹⁷. Moreover, presently PM in LMICs is principally concentrating on infectious disorders than NCDs. Although NCDs are equally public health threats as communicable diseases in LMICs⁹⁷. Though PM provides enormous benefits for cancer and other patients of chronic NCDs. Yet, Nonetheless, there is not much proof that the obtained information and method of treatment develop will achieve equally effective around the globe, especially in LMICs⁹⁷. As because there is evidence that lot variances exist in molecular findings in cancer genome among patients of

LMICs and rich countries⁹⁷. Another study concluded that PM able to show a new way of treatment options for those diseases previously were not treatable. This further added that the amount of investment made by high-income countries for PM, a similar amount of investment by LMICs in developing PM is impossible¹⁰⁰. One study reported that there five areas of difficulties regarding PM. Reasons Those are **i.** It is hard to ascertain, which analytical tests, equivalent assays, information know-how, and operational systems will reduce expenditures; **ii.** Though specific diagnostic procedures are cheaper, in general, those diagnostic tests remain till now very expensive; **iii.** Misuse of human genome data, especially personal information, to keep confidential and protected, is a complicated issue; **iv.** Moreover, to maintain the quality of healthcare remains problematic issues; and **v.** Additionally, no systems exist that ensure patients' right regarding financial savings for those diagnostic rest required for PM¹⁰¹. Similarly, multiple studies regarding precision medicine concluded that ethical issues regarding data protection and safety^{91,102}. Additionally, it also apprehends to future debate about genetically engineered patients and creation for super-human⁹¹.

7. Prospects of Precision Medicine in Lower- and Middle-Income Countries

Currently, all over the globe, healthcare, especially treatment strategies, are principally dependent on the average efficacy of medicine on the patient^{27, 103, 104}. Effective dose 50 (ED50) is a pharmacological term for the dose or amount of drug that produces a therapeutic response or anticipated effect in 50% of the subjects taking medicine. Whereas, PM denoted as specifically tailored patient care that includes methods of diagnosis, prophylactic measures, screening, and medication separately for each patient grounded on his / her genes, lifestyle, and environment¹⁰⁵. Subsequently, in rich nations increased the accessibility of genetic information regarding diseases and its' pharmacogenomics, and moreover, the costs of data generation reduced, that endorse genomic know-hows in the treating patients¹⁰⁴. However, yet there is ambiguity about the possibility of put on PM methods in LMICs because of the deficiency of population-specific data, competence, expertise, and poor financial support^{104,106}. The PM in Southeast Asia (SEA) remains in the baby stage. Although SEA has 12 sovereign states comprising of 2.2 billion populations and contains both high income and LMICs^{87, 107, 108}.

8. Oral Health and Precision Medicine

Dental caries, chronic periodontitis, orofacial pain, and oral cancer are chronic and repeatedly ruinous diseases. The management of these diseases should replace presently practice reactive strategy to a more dynamic and dedicated method. Precision oral possesses the potential to mitigate the miseries of these long-lasting incapacitating disorders¹⁰⁹⁻¹¹¹. Acuties regarding the human genome and microbiome, their related "transcriptomes, proteomes and metabolomes, and epigenomics and exposomics" have grasped an extraordinary level¹¹². After that, precision oral and dental care is no longer remain as a dream project but currently growing in speed that became a reality in soon¹¹². The primary and principal issue in developing and ensuring PM is the construction of the original cataloging of human ailment⁶. Currently, two major difficulties have been identified regarding precision oral care—disease taxonomies and clinically important information related to genomics, proteomics, or metabolomics were not available¹¹². Although it has been recently reported that biologically-informed disease subtypes and detailed disease taxonomies regarding oral diseases were offered. Nevertheless, dental diseases, especially periodontal diseases and carries, particularly as a specific disease not yet completed¹¹³⁻¹¹⁶. Another study reported similarly that the progress of oral PM presently stands in the investigation and exploration stage. Though significant development achieved in comprehending the pathology of the microbiome for oral diseases, which has promoted for initial struggles in advancement towards the PM. Nonetheless, more research was advocated to interpret the multifaceted relations of these microbial groups in producing oral diseases and health¹¹⁷.

9. Nutritional Diseases and Precision Medicine

It is often blamed that nutrition and diet play a significant role in developing heart diseases, type 2 diabetes mellitus, stroke, and certain cancer¹¹⁸⁻¹²¹. Regardless of the correlation with food habit and development of these NCDs is quite established; nonetheless, traditional mass intervention regarding changing food consumption brings little change in public health status^{122, 123}. Additionally, it has been reported that PM target for nutritional aspect is more productive and with a better health outcome in changing food practice^{124, 125}. There is no consensus definition regarding personalized nutrition. However, PM for nutritional aspect is defined as "an approach that uses the information on individual

characteristics to develop targeted nutritional advice, products, or services¹²³. The principal objective of PM about nutrition is to render the efficacious approach to manage diseases with totally dependent on “the genetics, lifestyle (dietary, exercise and lifestyle choices), metabolic status, gut microbiota and physiological status (nutrient level and disease status)” of any patient without any bad outcome¹²⁶. It has been reported that multiple chronic hereditary metabolic clinical problems can be adequately managed in precision nutritional care¹²⁷⁻¹²⁹. Three most significant areas need to measure in precision nutrition that comprises discrete principles for adequate nutritional “status, biomarker monitoring or techniques for nutrient detection and the applicable therapeutic or intervention methods”¹²⁶. The PM in maintaining diet and nutrition has found effective in the management of end-stage kidney disease and chronic kidney disease. It especially important and essential in regulating a protein-controlled diet in progressive CKD patients¹³⁰. Additionally, the nutritional management of chronic kidney diseases has been reported as an extremely complicated issue¹³¹. A recent study concluded that precision nutrition yet remains in its initial stages¹²⁸ as understanding regarding nutrigenomics and nutrigenetics with specific NCDs remaining in exploring stage such as CVDs^{132, 133}.

10. Antibiotics, Antimicrobial Resistance (AMR), and Precision Medicine

The PM classically denotes medicine for chronic NCDs and effective in patients at a personal or individual level. The PM to address infectious disease is considered as the detailed and accurate information of genetic or phenotypic changeability of invading pathogenic microbes that empowers a meticulous line of attack in the treatment and prevention contagious disease in a specific patient¹³⁴. Currently, the irresistible escalation of super-resistant, multi-drug-resistant strains of pathogens the “super-bugs”¹³⁵ is a serious global public health issue, consequential in seven hundred thousand deaths every year and expected to rise 10 million per year by 2050¹³⁵⁻¹³⁷. It has been reported the “golden era” (1930-1960) of antibiotic development is currently at the end stage, as the scientific community unable to maintain the pace to develop new antimicrobials than the attainment of microbial resistance. Consequently, not many antimicrobials are waiting in the pipeline of the pharmaceutical industry to be marketed soon¹³⁸⁻¹³⁹. After that, physicians, while prescribing resistant

antimicrobials will, promote more resistance and ensures treatment failure¹⁴⁰.

Antimicrobials were the first classes of medicine, for which organized diagnostic tests were performed to forecast the sensitivity of microbes towards invading microbes. Consequently, some scientific community believes antibiotics and infectious diseases were included in the precision healthcare long before. The antibiotic culture sensitivity tests were first introduced in the 1960s for routine hospital care. This test was developed based on culturing the pathogens in a petri dish in the presence of antibiotics and considered as the basis of rational anti-microbial treatment strategy^{141,142}. Throughout the globe, traditional culture sensitivity test consumes nearing two days for rapid-budding microorganisms and several days to weeks for slowly reproducing pathogens for isolation, growth, identification, and finally minimum inhibitory concentration (MIC)^{140, 143}.

Additionally, the old-style diagnostic model for infectious diseases, need to do multiple times and often fail to achieve rock-hard finding, and patients were prescribed antimicrobials based on the assumption¹⁴⁴. Moreover, the currently practiced method of culture and sensitivity test can identify a small fraction of pathogenic microbes readily, although there are more than thousands known pathogens are invalidating humans regularly¹⁴⁵. The advances in genomics are even now started moving forward for the betterment of treatment strategies for infectious diseases and improving the total healthcare system. Genome sequencing and molecular tests can report more sharply, saving critical time for intervention, with specific documentation of attacking microorganisms, along with the sources of microbial contamination, their propagation tactic, and sensitivity patterns towards antimicrobials¹⁴⁴. “Microbial cell-free DNA next-generation sequencing test that identifies and quantifies microbial cell-free DNA in plasma from 1,250 clinically relevant bacteria, DNA viruses, fungi, and eukaryotic parasites”¹⁴⁵. This study also reported that the CLIA (Clinical Laboratory Improvement Amendments) laboratory able to identify the causative pathogens and informed back in majority (85%) of cases to hospital authority by the same day sample receipt of the first 2,000 patient samples tested and with 53.7% of cases had infections with either one or multiple pathogenic microbes¹⁴⁵. After that, whole-genome sequencing-diagnostic tests have the potential to screen antimicrobial-resistant pathogens and their genes disseminating among

humans, animals, foods, and environments^{140,146}. Consequently, it achieves “rapid diagnosis, proper treatment, and better protection,” which ultimately improve overall “patient care and public health”¹⁴⁴.

11. Precision Medicine Benefits May Be Driven Towards Transnational Corporate House Again

World Health Organization promoted essential medicine program started back in 1977¹⁴⁷. “Essential medicines (EM) are those that satisfy the health care needs of most of the population; they should, therefore, be available at all times in adequate amounts and the appropriate dosage forms, and at a price that individuals and the community can afford”¹⁴⁸. The execution of the notion of EM is proposed to be pliable and adjustable to many various healthcare circumstances, precisely which medicines are believed as essential remains a national concern and obligation¹⁴⁷. The following year in 1978 the Alma-Ata assertion during the International Conference on Primary Health Care (PHC) endorses that health is an ultimate human right and the fulfillment of the highest conceivable level of health is the most imperative universal social intent¹⁴⁹. After all these 42 years of struggles of EM and PHC, even in rich countries, marginalized communities and the elderly population are suffering because of the high cost of medicines^{147,150,151}. Additionally, many countries around the planet, especially of LMICs, suffer from poor access to EM and PHC¹⁵²⁻¹⁵⁷. on many occasions, national authorities/governments of LMICs do not much control over medicine prices, maybe because of the adoption of free-market policies¹⁵⁸⁻¹⁶². However, researchers of the Department Health Economics and Health Care Policy, Harvard Medical School, Boston, USA, recommended that the US government should carefully control medicine prices¹⁶³. Subsequently, the question arises precision technology prices can be controlled by the national government exclusively of LMICs and ensure the people healthcare and promote public health^{97,154,164}. Moreover, almost all significant innovations, particularly in healthcare, belong to the transnational corporate house^{155, 165, 166}. As mentioned, “modern businesses, especially the large multinational companies, are the repositories of the most advanced technologies on the planet and the most sophisticated management methods for large-scale delivery of goods and services. There is no solution to the problems of poverty, population, and the environment without the active engagement of the private sector”¹⁶⁷. Subsequently, careful implementation of PM in LMICs with very

innovative policy and planning which will promote public health and ensure peoples’ benefit.

12. Conclusion

The concept of PM with an in-depth understanding of Pharmacogenomics seems to be a revolutionary strategy of health care against the traditional way of population-wide diagnosis and treatment of diseases¹⁶⁸. Conceptually, PM investigates the individual’s diagnosis of diseases on time, prescribe specific medicine, which will be effective and harmless and cost-efficient. It is proven that PM strategy basically depends on the individual genomic profile and specific biomarkers of the diseases. The PM concept also ensures the prediction and prevention of diseases and very efficient in managing severe and rare diseases. However, with all hopes and aspirations, the PM must overcome certain challenges in the process of implementation to achieve the ultimate result of quality health. It is to be mentioned that, the PM concept of healthcare strategy seems to be a great encouragement for the context of LMICs to achieve the overall improvement of healthcare, health, and quality of life. It is understandable that PM success is based on certain technologies such as; information technology (Electronic Medical Record to record a wide range of data), laboratory medicine (to ensure genomic profile and biomarkers), and pharmaceutical industry (to ensure medicine other necessary products). Its success also heavily depends on the coordinated efforts of clinicians and biomedical science experts to explain things and provide management, IT experts to record and manage a wide range of longitudinal clinical, social and behavioral data, data analysts to analyze big data and which will be participative by the patients at large. PM demands that it is a cost-efficient measure of disease diagnosis and treatment, but it seems to need high investment at the beginning and less costly in the long run. But, it is yet to be a matter of great debate about trickle-down benefits in the context of LMICs where there are under quality healthcare, scarcities of scientist and experts, expert to handle the big data and analysis to get precise inference, import-oriented technology, scanty share of GDP on health, high out-of-pocket expenditure, and lack of social and behavioral quality information about individual and collective level. The Proponents of PM should consider the balance of benefits between the transnational companies and the general people for whom the concept has developed. It will also be a big challenge for PM healthcare strategy to transfer

the individual level successes to the population-wide through public health activities that must be accessible, acceptable and affordable to the general people, which is challenging, especially in the context of LMICs.

13. Recommendations

Careful implementation of PM in LMICs with a collaborative, innovative policy & planning, which will promote public health is of utmost importance. Due to the high initial cost, certain measures & initiative can be taken. Among others is to control medicine prices to make it affordable to many people. Active engagement of the private sectors to support and promote PM may ease the burden of LMICs.

14. Key Findings

- Precision medicine is relatively a new concept in LMICs
- Precision medicine can be helpful in treating

NCDs in LMICs

- An innovative and collaborative approach is required for precision medicine implementation
- Precision medicine will help to reduce healthcare cost in the long run

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