IJTI | INTERNATIONAL JOURNAL OF THERAPEUTIC INNOVATION

Case study

Personalized medicine in oncology: advancements, difficulties, and prospects

Divyansh Bansal[1]*, Keshav Kumar[2], Ajay Kumar[3], Ritesh Raj[3], Dhanraj Patidar[3]

[1] Institute of Pharmaceutical Sciences, J. S. University, Shikohabad, Uttar Pradesh, India
[2] Lords International College of Pharmacy, Lords University, Alwar, Rajasthan, India
[3] SAM College of Pharmacy, SAM Global University, Raisen, Madhya Pradesh, India

Corresponding author: Divyansh Bansal, ✉ ajay23kumar3@gmail.com, **Orcid Id**: https://orcid.org/0009-0003-1586-4194

Received - 22-06-2025, **Revised** - 28-07-2025, **Accepted** - 22-08-2025 **(DD-MM-YYYY)**

Refer this article

Divyansh Bansal, Keshav Kumar, Ajay Kumar, Ritesh Raj, Dhanraj Patidar, Personalized medicine in oncology: advancements, difficulties, and prospects. July-August 2025, V3 – I4, Pages - 11 – 21. Doi: https://doi.org/10.55522/ijti.v3i4.0121.

ABSTRACT

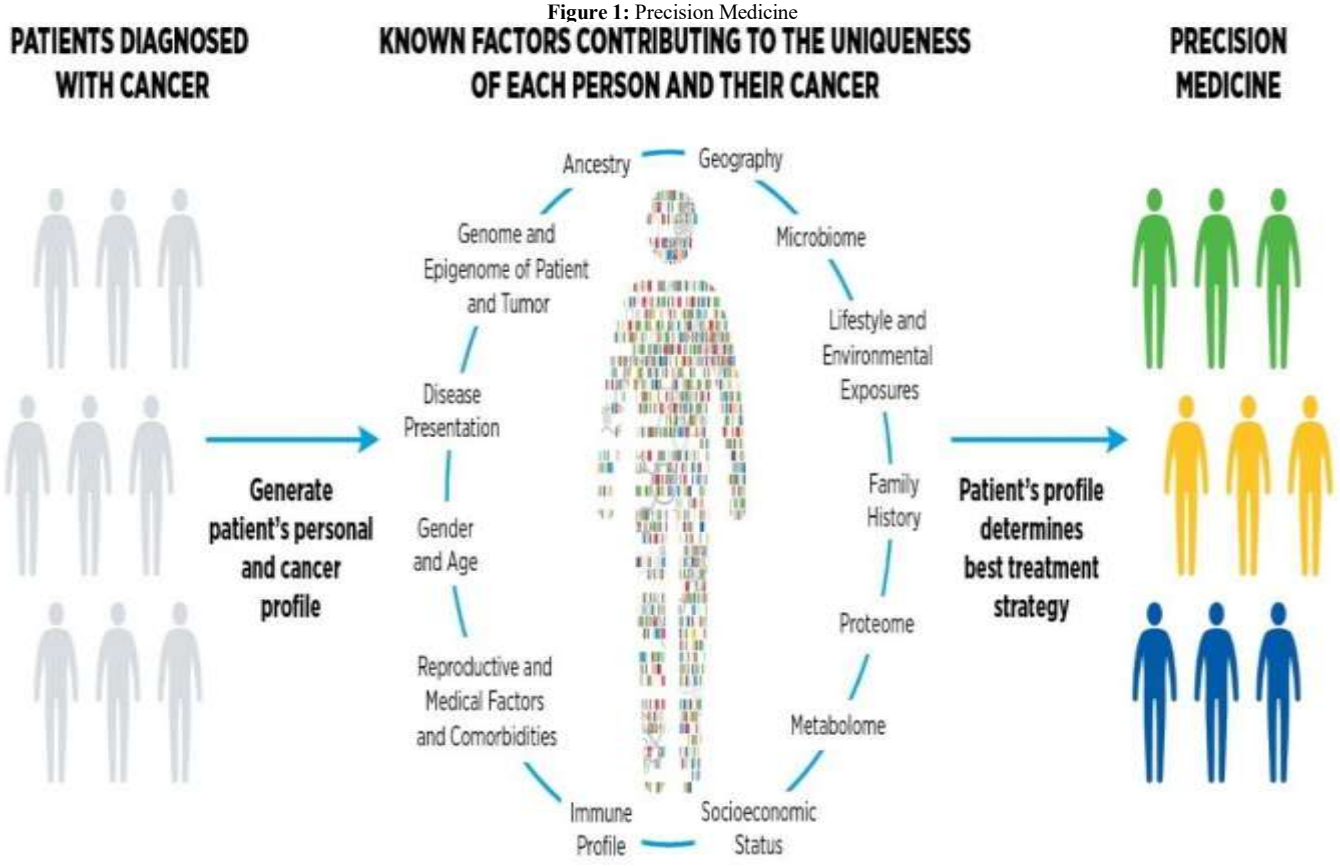
Precision medicine, also called personalized medicine, is broadly defined as treating patients based on characteristics that distinguish them from other individuals with the same disease. The factors that contribute to the uniqueness of a patient and his or her cancer include, but are not limited to, the person's and tumor's genome, epigenome, transcriptome, proteome, microbiome, metabolome, the immune characteristics of the person and of cancer, disease presentation, gender, ancestry, exposures, lifestyle, and comorbidities. Currently, genomics is the predominant factor influencing precision medicine, but as we learn more about the additional factors, such as epigenomics, proteogenomic, metabolomics and tumor immune characteristics, we have begun to integrate this knowledge to further refine the personalized approach to cancer treatment. Although genomic and epigenomic profiling of a patient and of his or her tumor is becoming a routine in the clinic. There is a lot of excitement about the idea of "individualized" medicine. The concept of personalized medicine stems from the idea that since each person has distinct and varied traits at the molecular, physiological, behavioral, and environmental exposure levels, they may require interventions for diseases that are specific to these traits. New technologies like wireless health monitoring devices, imaging procedures, proteomics, and DNA sequencing have shown significant inter-individual diversity in disease processes, which has partially confirmed this idea. This review takes into account the reasons behind personalised medicine, its historical forerunners, the new technologies that are making it possible, some recent experiences, including both successes and failures, methods for screening and implementing personalised medications, and future directions, such as possible approaches to treating people with sterility and fertility problems. We also take into account personalised medicine's present shortcomings. Ultimately, we contend that because biological facts underlie some parts of personalised medicine, personalised medical practices in some contexts are probably inevitable, particularly if pertinent tests and deployment tactics grow more effective and economical. If applied properly, precision medicine could help solve the issues of cancer health inequities and transform the way that cancer is treated.

Keywords: Precision medicine, Personalized medicine, Cancer, Cancer treatment, Genomics.

INTRODUCTION

The general definition of precision medicine, also known as personalised medicine, is the practice of treating patients according to traits that set them apart from other people who have the same illness. A patient's and tumour's genome, epigenome, transcriptome, proteome, microbiome, metabolome, immune characteristics of the individual and of cancer, disease presentation, gender, ancestry, exposures, lifestyle, and comorbidities are some of the factors that create a patient's uniqueness and their cancer, as illustrated in the figure. Precision medicine is primarily influenced by genomics at the moment, but as we gain more insight into other aspects like epigenomics, proteogenomic, metabolomics, and tumour immune characteristics, we are starting to incorporate this knowledge to further improve the individualised approach to cancer treatment. The cost-effectiveness of comprehensive profiling that includes all the other characteristics shown in the figure still needs to be assessed, in addition to ongoing efforts to determine which and to what extent profiling improves outcomes for individuals, even though genomic and epigenomic profiling of a patient and his or her tumour is becoming a standard practice in the clinic [1].

Figure 1: Precision Medicine



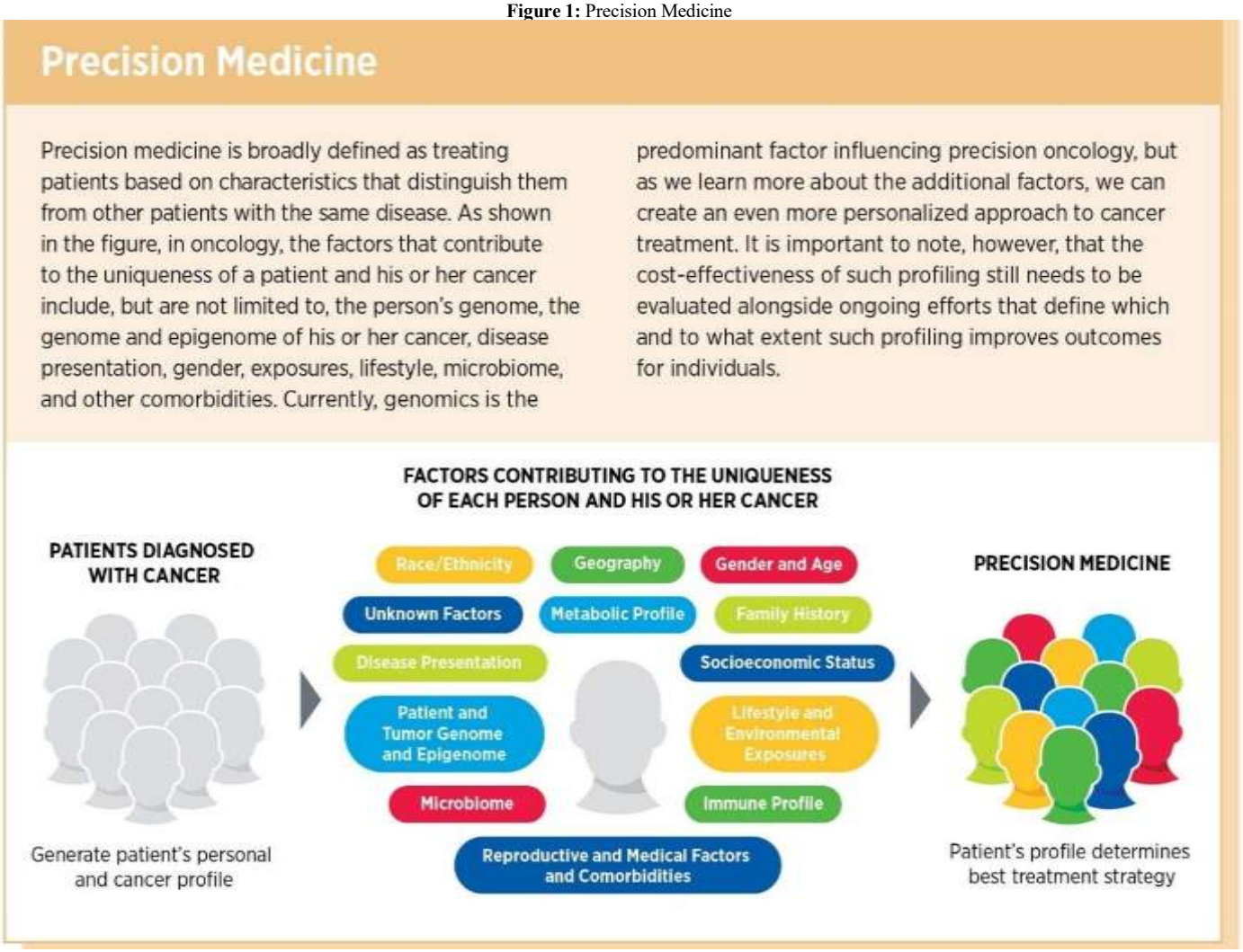
2024 American Association for Cancer Research®. *AACR Cancer Disparities Progress Report 2024*. 2305052-F6.

The use of new, high-throughput, data-intensive biomedical tests, like wireless monitoring devices, imaging protocols, proteomics, and DNA sequencing, has shown the effects of disease processes, as well as the mechanisms and contributing factors, to vary greatly among individuals. This has sparked debate over how much this inter-individual diversity should influence choices on how best to treat, monitor, or prevent a disease in a given person. Since many disease processes are fundamentally heterogeneous, it is now generally accepted that treatment plans for afflicted individuals, as well as potential monitoring or prevention strategies, should be "individualised" to each person's distinct biochemical, physiological, behavioural, and environmental exposure profiles. Personalised medicine has been the subject of numerous high-quality reviews and an increasing number of textbooks created for clinicians and medical students. Some have suggested that there are some significant, albeit frequently subtle, differences between "individualised" and "precision" medicine, even though many people use the terms interchangeably [2].

Personalised medications present several difficulties, particularly when it comes to getting several regulatory bodies to approve them for regular usage. Furthermore, there are numerous problems with the widespread adoption of personalised medications by various health care stakeholders, including doctors, executives, insurance providers, and, eventually, patients. Since many customised or personalised therapies, like autologous CAR-T cell transplant therapies for certain types of cancer and mutation-specific medications like ivacaftor to treat cystic fibrosis, can be very costly, nearly all of these challenges centre on the need to demonstrate that personalised medicine strategies simply outperform traditional medicine strategies. The history and motivations of personalised medicine are examined in this article, along with some background information on the techniques for personalised medicine that have surfaced in recent decades, the obstacles impeding their progress, and what lies ahead. We also look at ways to demonstrate that protocols and strategies in personalised medicine can perform better than those in standard treatment. Crucially, we differentiate between instances and difficulties related to personalised health monitoring, personalised illness prevention, and personalised overt disease treatment [3].

We have come a long way in the last ten years in our understanding and management of the complicated group of diseases known as cancer. We now know that every person's cancer is different, partly due to the biological traits, lifestyle, and environmental exposures of the patient. As a result, the "one size fits all" approach to cancer treatment has given way to precision medicine, which is more individualised. The NCI defines precision medicine, also known as personalised medicine, as a type of medicine that prevents, diagnoses, and treats disease by using knowledge about an individual's genes, proteins, and environment. (see below the figure). If applied properly, precision medicine could help solve the issues of cancer health inequities and transform the way that cancer is treated.

Figure 1: Precision Medicine



Archibald Garrod and Personalised Medicine's Forerunners

The development of personalised medicine is foreshadowed by a lot of western medical history. For the sake of conciseness, we will only discuss a handful of these occurrences that we believe capture the fundamental ideas of personalised medicine. Over a century ago, English physician Archibald Garrod started researching illnesses that would eventually be referred to as "inborn errors of metabolism." Garrod researched several rare disorders, such as alkaptonuria, albinism, cystinuria, and Pentos Uria, that had obvious, outward signs. Among these, his research on alkaptonuria gained some popularity when he noticed that, in comparison to family members without alkaptonuria, some members of families with alkaptonuria displayed measurably outlying values for specific fundamental biochemical assays, such as those from urine. This led him to draw the later-proven conclusion that alkaptonuria was caused by a particular "altered path of metabolism" in those who were afflicted. Additionally, taking into account additional uncommon illnesses such alkaptonuria, because no two members of a species have exactly the same body structure or chemical processes, Garrod contended that "the thought naturally presents itself that these [conditions] are merely extreme examples of variation of chemical behaviour which are probably everywhere present in minor degrees." This more than suggests his opinion that human beings differ greatly, at least in terms of metabolism, and that these variations may contribute to the explanation of overt phenotypic differences between people, including their varied susceptibilities to diseases and the manner in which those diseases manifest [4].

There was a lot of controversy around the new area of genetics at the time Garrod was working. Although Garrod and his contemporaries were unaware of the precise entities we now commonly refer to as genes (i.e., segments of DNA sequence that code for a protein and related regulatory elements), they frequently mentioned "factors" influencing disease that were possessed by specific individuals and were consistent with the modern concept of genes. Discussions based on Mendel's research gave rise to claims regarding the existence of such factors (later, it would be demonstrated that many of the metabolic outliers Garrod saw in individuals with disorders like alkaptonuria were related to deficiencies in genes possessed by individuals with such diseases). Mendel foreshadowed the contemporary field of genetics by observing consistent relationships between the appearance of extremely particular traits in peas only when specific breeding methods were followed. According to William Provine's excellent book, many members of the research community at the time argued about how genes or other factors similar to those Garrod and others were studying could account for the wide range of phenotypic

expression seen in nature. William Bateson and Hugo de Vries were among a group of scholars and researchers known as the "Mendelians" in the historical literature. They concentrated on the distinct characteristics of the elements that were probably in charge of many observable inheritance patterns (like those of focus in Mendel's studies and observations like Garrod's in the context of rare disease). The "Biometricians," led by Karl Pearson, opposed the "Mendelians." Their emphasis on continuous or graded phenotypes, such as height, made them wonder how to reconcile such continuous variation with the overtly discrete (or "either/or") factors and inheritance patterns that the Mendelians and researchers like Garrod were considering [5].

In a series of groundbreaking articles, statistician Ronald Fisher largely settled the Mendelian vs. Biometrician controversy. By proposing that numerous factors (i.e., genes) may contribute in a minor way to a given phenotype, Fisher contended that it was possible to reconcile continuous phenotypic variation with discrete, heritable factors that contribute to this variation. An individual who inherited only one of the 25 genetic variants known to increase height would, on average, be shorter than someone who inherited 10 or 12, and much shorter, relatively speaking, than someone who inherited 22 or 25. This is an example of how the cumulative effect, or sum total, of these factors could produce variation in phenotypes that give the appearance of continuity in the population at large. The use of contemporary high-throughput genetic technologies, such as genotyping chips and DNA sequencing, has validated the idea that there may be numerous genes that contribute to phenotypic expression broadly, some with more pronounced effects and some with less pronounced effects, that interact and collectively contribute to a phenotype in a variety of ways. Because each person has subsets of the literally millions of genetic variants that exist in the human population as a whole, genetic studies have demonstrated that people do vary greatly, which is the basis for a large portion of the current emphasis on personalised medicine. Furthermore, some of these genetic variations might be specific to a person since they may have developed as de novo mutations. Individuals differ greatly in their phenotypes, especially in their susceptibilities to disease and their reactions to therapies, which can be partially explained by these severe genetic variations. It should be noted that while genetic research is the foundation of personalised medicine, it is generally acknowledged that other elements, such as environmental exposures, developmental processes and epigenetic modifications, and behaviours, must also be considered when deciding how best to treat a given patient.

An illustration of the components that must be integrated and evaluated in order to get genuinely personalised treatment. Access to health care is crucial since certain people might not have the financial or geographic means to access technologies and expertise; consequently, interventions may need to be designed with those people in mind. Although somatic alterations to DNA can offer important insights into pathogenic processes, inherited genetic information is essentially only predictive or diagnostic in nature. Imaging and radiography tests, tissue biomarkers (e.g., routine blood-based clinical chemistry panels), and data collected regularly via wireless monitors are all helpful in identifying changes in health status. An intervention's effectiveness can be significantly impacted by environmental exposures and behaviours, which also vary greatly from person to person. As well as markers of a change in health status, epigenetic phenomena should be examined since they alter gene function in response to exposures and developmental or stochastic events [6].

Although this paper focusses more on the necessity of clinical practices that are consistent with personalised medicine than it does on a scientific defence of personalised medicine, it was also prophetic for personalised medicine. More than 60 years ago, Hogben and Sim thought about how clinical practice could examine patients' subtleties to find the right intervention for them. Though their paper will be covered in more detail in the section on "Testing Personalised Medicines," let us just say that the authors felt that a number of items would need to be acquired in order to determine the best course of action for a particular patient in the absence of any prior knowledge of how to treat that patient given his or her characteristics or profile. Therefore, it would be necessary to collect more data about that patient, develop a plan to assess the effectiveness of an intervention selected based on that data, and devise a plan for integrating the findings of the patient-oriented study into future treatment. Even though it seems straightforward in theory, the practical challenges of learning more about a patient and conducting an empirical evaluation of a customised solution can be intimidating.

In high-income nations, the field of oncology has changed over the last 20 years, moving from haematoxylin and eosin (H&E) stains to sophisticated diagnostic tools. PM was created as a result of these developments in fundamental science. It is now understood that malignancies are not always the same, even if they originate from the same tissue and look the same under a microscope. Based only on biomarkers and without regard to the tissue of origin, a number of Oncolytics have received approval in the United States and the European Union. These "targeted" drugs typically have a higher chance of long-term survival, are less toxic, and are far more effective than traditional chemotherapy (Table 1). The metabolism of irinotecan, 5-fluorouracil (5-FU), and underlying autoimmune disorders are the most basic instances of how different hosts are from one another. Immunotherapy's efficacy may even be impacted by the microbiota and antibiotic use. PM has transformed oncology by gaining a deeper understanding of host-related and cancer-related aspects and how they interact, thereby enhancing both the quantity and quality of life [7].

Table 1: Response of Malignancies to TKI (Tyrosine Kinase Inhibitor) and IO (Immuno-Oncology) Compared to Chemotherapy.

Drugs	Cancer type	
Afatinib and erlotinib	Non-small cell lung cancer	The progression-free survival rate for individuals with well-differentiated lung cancer was much greater than that of chemotherapy.
Imatinib	Gastrointestinal stromal tumor	Overall and progression-free survival was much better than when chemotherapy was used.
Cetuximab	Colorectal cancer	Overall and disease progression, colorectal cancer of the RAS wild type has a higher survival rate.
Pembrolizumab	Colorectal and lung cancer	Pembrolizumab outperforms chemotherapy in colorectal and lung cancers with substantial tumour mutation burdens in terms of overall and disease progression-free survival.
Nivolumab and ipilimumab	Renal cell cancer and advanced non-small cell lung cancer	This combination produces better results than traditional chemotherapy for advanced non-small cell lung cancer and renal cell cancer.
Atezolizumab	Triple-negative breast cancer and liver cancer	shows better results than chemotherapy in liver cancer and triple-negative breast cancer with PDL1 expression.

Personalised Medicine's Inception examples

There are numerous instances of interventions that are customised to the unique characteristics of each patient, almost all of which are based on genetic profiles. Before giving some well-known instances, it should be noted that personalised medicine can be used for early disease identification and prevention as well as for the treatment of existing conditions. Because the field of personalised disease diagnosis and prevention has advanced much more recently, we discuss early detection and prevention in the following section and give some historical examples of personalised disease therapies here [8].

The human body uses conventional pharmacotherapies, or medications, to treat illness in two main ways. The body must first react to a drug. The body absorbs the medicine in the first step of this response, which happens in stages. After the medication has been dispersed throughout the body (it may be "bio transformed" or metabolised into beneficial components) it can start to produce effects. Ultimately, any leftover medication or its constituents are eliminated. These procedures are sometimes grouped together under the general term "pharmacokinetics" and are generally known as a drug's "ADME" (Absorption, Distribution, Metabolism, and Excretion). Pharmacokinetic activity is frequently controlled by a distinct set of genes (drug metabolising enzymes, for example), which may contain naturally occurring genetic variants (also known as "polymorphisms") that affect their function and, consequently, how the body reacts to a given drug in the end. Once in the body, a drug's "pharmacodynamic" qualities refer to how it interacts with its target, which is usually a gene or protein that is encoded by a gene, to have an effect. These characteristics include the medication's "affinity" for its target or targets, its "efficacy" (or capacity to modify the target or targets), and its "potency," or the amount of the drug required to cause a certain change in the target. Genetics also affects a drug's pharmacodynamic characteristics.

The pharmacokinetic features of medications that were mediated by genetics were linked to numerous early instances of personalised medicine. This was partly brought about by the biomedical scientific community's comprehension of drug-metabolizing enzymes and how they affect the body's reaction to medications. Weber's book provides a great overview of the pharmacogenetic characteristics of medications and genetic variations in genes that affect therapeutic efficacy and side effects (particularly genetic variations in drug metabolising enzymes). An adverse pharmacological reaction that could be fatal could result from improper dosage of the commonly used blood thinner warfarin. The gene CYP2C9 contributes to the metabolism of warfarin, which targets the specific gene VKORC1. The pharmacologic and pharmacokinetic characteristics of Warfarin vary from person to person due to naturally occurring genetic diversity in the VKORC1 and CYP2C9 genes, which in turn causes variation in how people react to Warfarin. Accordingly, the US Food and Drug Administration has advised that warfarin dosage be tailored to a person's genotype, taking into account the particular genetic variations that person possesses in the VKORC1 and CYP2C9 genes [9].

Primaquine (PQ) is another well-known example of a medication that should only be administered to people who have a particular genetic profile. In regions where malaria is endemic, PQ has been used to treat the disease with varying degrees of efficacy. Nevertheless, military physicians in the past noticed that some of the troops they treated for malaria who received the medication developed jaundice and anaemia before showing signs of what would later be known as "acute haemolytic anaemia (AHA)". Subsequent research revealed that those who developed AHA following PQ injection had G6PD gene variations. In order to determine whether a patient has important variations in the G6PD gene that could deter them from using PQ, current clinical practice with PQ requires that each patient be genotyped.

The medication imatinib is a final, frequently mentioned example of personalised therapy. CML, or chronic myelogenous leukaemia, is treated with imatinib. Imatinib suppresses tyrosine kinase, an enzyme that is elevated when two genomic areas fuse together: the breakpoint cluster region (bcr) and the Abelson proto-oncogene (abl). This fusion event, also known as the "Philadelphia chromosome" or "bcr-abl fusion," occurs in numerous tumours that contribute to the development of CML. Nevertheless, the bcr-abl fusion mutation is not present in the tumours of every person with CML. Imatinib is therefore usually only administered to specific CML patients who have this fusion event [10-12].

Examples of Personalised Medicine in the Present

Drugs like imatinib, PQ, and warfarin that seem to only work or only work without side effects when a patient has a particular genetic profile have sparked a lot of interest in figuring out what genetic variations affect a patient's reaction to various medications and treatments. Personalised disease monitoring (i.e., early detection techniques) and personalised disease preventive strategies have grown out of the desire in developing personalised medications to treat illnesses. A few recent examples of this action are briefly described [13].

The National Cancer Institute's Precision Medicine Initiatives
NCI-MATCH (Molecular Analysis for Therapy Choice)

Launched in 2015, NCI-MATCH is a precision medicine trial that was started in 2015 to see if genetic alterations found in tumours could influence treatment decisions.

The FDA approved dabrafenib and trametinib together to treat any cancer with a genetic mutation in the BRAF gene as a result of the NCI-MATCH experiment (1,109).

Childhood Cancer Data Initiative (CCDI)

Launched in 2019, CCDI aims to:

• Compile information from each child, adolescent, and young adult (AYA) who has been given a paediatric cancer diagnosis, irrespective of the facility where they are treated;

• Develop a national clinical and molecular characterisation strategy that is relevant for all forms of childhood malignancies in order to expedite diagnosis and guide treatment;

• Provide a platform and resources to integrate clinical care and research data to enhance youth cancer prevention, treatment, quality of life, and survivor rates.

Molecular Characterization Initiative (MCI)

• Launched in 2022 as a component of the CCDI, MCI is a nationwide partnership involving the paediatric oncologists, activists, children and AYAs with cancer, researchers, data scientists, and families.

• MCI assists participants and physicians by offering cutting-edge molecular characterisation at the time of diagnosis.

ComboMATCH (Combination Therapy Platform Trial with Molecular Analysis for Therapy Choice)

Launched in 2023, The purpose of the ComboMATCH group of precision medicine cancer clinical studies is to ascertain whether using pharmacological combinations that target particular genetic alterations to treat cancer causes better results (110).

Mutation-Specific Therapies

As is the case with warfarin, PQ, and imatinib, rather than creating a medication and then using observational studies on the people who take it to identify factors that reduce its effectiveness or side effects, efforts are now being made to identify, for example, the genetic profiles that patients possess and then create therapies that specifically target those profiles. Ivacaftor, for instance, was created to treat people with cystic fibrosis (CF) who have extremely precise pathogenic mutations in the CFTR gene. One of the various roles of the CFTR gene is controlled by a "gate-like" structure in the protein that is encoded by the gene. This structure can open and close to regulate the flow of salts into and out of cells. Mucus and other debris accumulate in the lungs when the gate is closed due to a malfunctioning CFTR gene. Disturbances in the CFTR gene are caused by several mutations. For instance, regardless of whether the gate is open or not, certain mutations merely result in the CFTR gene producing nothing. The gate mechanism malfunctions as a result of further mutations. When specific mutations that typically cause the gate to close are present, Ivacaftor is made to open the gate for longer periods of time. Ivacaftor is therefore only helpful for the tiny percentage of CF patients whose CFTR mutations cause this particular gating issue. The number of links between genetic variations and drug efficacy and side effects is increasing. In fact, the US FDA offers a list of approved drug-based interventions that need to be tested to determine whether they are appropriate for a given person: https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm. Other publications, like the report from the Personalised Medicine Coalition (PMC), take into account the real-world effects of authorised personalised medicine procedures [14].

The new class of cancer treatments called immunotherapies is a second example.(25) Immunotherapies come in a variety of forms, but they all aim to prime or activate a person's immune system to combat cancer. One kind of immunotherapy takes advantage of potentially distinct sets of genetic changes that develop in the tumour cells of cancer patients. These changes are called "neo-antigens," and if the host's immune cells correctly identify them, they can frequently trigger an immunological response. In essence, this kind of immunotherapy involves removing T cells and other cells that mediate the patient's immune responses from the patient and altering them to specifically identify and target the neo-antigens discovered in the patient's tumour. These altered cells are subsequently reintroduced into the patient's body to target the tumour cells that are emitting the neo-antigen signals. For two reasons, cytotoxic T cell treatments, like this one, and immunotherapies in general, can be highly patient-specific notwithstanding their noteworthy results. First of all, a patient's neo-antigen profile may be so distinct that cytotoxic T cells designed to identify and combat a particular collection of neo-antigens will not be effective in a patient whose tumour lacks those neo-antigens. Second, although there is a strong push to create "allogeneic" constructs, in which the T cells of one person are altered and inserted into the body of another, using "autologous" constructs alters the patient's own T cells, making them less likely to function as well in another patient [15-20].

Personalizing Early Detection Strategies

A person should be closely watched if they are prone to contracting an illness or if their illness is likely to repeat. In order to establish assertions regarding evidence or indicators of sickness or a pathogenic process, it is presently thought that such monitoring should be performed using "personal thresholds" rather than

"population thresholds." For instance, systolic blood pressure > 140 indicates hypertension, stroke risk, or heart disease, or cholesterol levels > 200 indicate heart disease risk. These population thresholds are based on epidemiologic data and demographic surveys. The legacy values of a measure gathered over time on an individual are used to create personal thresholds, which are used to determine how deviant future values of that measure might be for that individual. A change in health status is indicated by significant departures from historical or average legacy values, regardless of whether those levels exceed a population threshold. For instance, Drescher et al. investigated the usefulness of applying personal thresholds to longitudinal CA125 values obtained on several women, some of whom went on to develop ovarian cancer. The authors discovered that the use of personal thresholds would have detected the existence of ovarian cancer concurrently with, or crucially before, the use of population thresholds in all but one case. The authors also demonstrated that, on average, the use of personal thresholds may have detected ovarian cancer nearly a year earlier than the use of population thresholds. Personal thresholds will probably become the norm rather than the exception in health monitoring protocols as the cost and convenience of monitoring assays and technologies improve (that is, they become affordable and non-intrusive, if not transparent, to an individual user, say through an easily implantable wireless device) [20, 21].

Personalizing Disease Prevention

The use of genetic information to develop personalized disease prevention strategies is now well established in the scientific community, but not yet widely adopted in clinical practice. Numerous outstanding instances demonstrate how the application of genetic data can result in fewer complications from conventional treatment and screening methods as well as a lower risk of disease development. A prime example relates to colorectal cancer, which remains the third leading cause of cancer deaths despite being a highly preventable illness. In 2012 Liao et al. reported compared to individuals whose colorectal tumours contained the wild-type PIK3CA gene, patients receiving postoperative aspirin who had a somatic mutation in the PIK3CA gene had a higher overall survival rate and a lower risk of cancer-specific mortality. In 2015, Nan et al. reported Depending on a person's genotype, aspirin use can have different impacts on their risk of developing colorectal cancer. Those with different genotypes may have a reduced, higher, or no change in their risk of developing colorectal cancer as a result of using aspirin. It would be ideal to restrict the use of aspirin for those persons who are anticipated to experience a side effect based on their genotype, as this medication can have major adverse effects linked to intestinal and cerebral haemorrhage [23].

As another example, in 2018, Jeon et al. reported using broader risk prediction algorithms to decide when to start screening for colorectal cancer. Age and family history are the only variables used in the guidelines at the moment. According to Jeon et al., recommendations for when to begin screening could be altered by 12 years for men and 14 years for women based on information about a person's genetic profile and environmental exposure, particularly the existence of genetic variations linked to colorectal cancer. According to research on the accuracy of pertinent predictions regarding a person's risk for colorectal cancer, the area under the curve (AUC) value for a model that takes into account genetic and environmental factors was 0.62 for women and 0.63 for men. An AUC of 1.0 would indicate a model with perfect predictive accuracy. When only family history data was taken into account, the AUC value was 0.53 for men and 0.54 for women. The significant improvement over models that did not include genetic or environmental information justified their use, even though there is still opportunity for improvement because the AUCs were only ~0.62 for the model that included patient environmental exposure and genetic information [24].

Testing Personalized Medicines

Even though we have maintained that personalised medicine has many historical precedents and legacy insights, primarily in the areas of genetics and rare diseases, it is only recently that the biomedical research and clinical communities have recognised it as a paradigm that should be widely adopted. This implies that not enough time has passed since this acknowledgement for researchers to demonstrate that personalised medicine is effective in a sufficient number of contexts to encourage widespread adoption. This raises concerns about how the general public can evaluate or test the effectiveness of personalised treatment. In the following section, we outline three new approaches to screening personalised medications: N-of-1 clinical trials, intervention-matching trials, and adaptive clinical trials. We contend that while these approaches incorporate aspects of conventional randomised clinical trials (RCTs), they differ greatly from the population-based RCTs that were common in the past [25-27].

N-of-1 Clinical Trials

There is "equipoise" among the many interventions if there is no reason to think that one of them better fits a person's profile (genomic, behavioural, etc.). In this situation, determining which solution could be best for the particular person in issue becomes an empirical question. "N-of-1" or single subject trials are those that concentrate on a single person's reaction to various interventions in order to identify the best intervention. N-of-1 studies frequently take advantage of straightforward crossover designs or even repeated crossover designs, like "ABABAB" designs, in which "A" and "B" stand for distinct interventions, and the sequence "ABABAB" denotes the order in which the patient receives the interventions. Comparing different interventions—for instance, a test intervention and a comparator, or placebo, intervention—is made possible by switching up the interventions and gathering information on how each person responds to them. N-

of-1 trials allow for the use of blinding, multiple endpoints, washout periods, randomisation, and many other design components [29-32].

Serial correlation between the observations and potential carry-over effects from one intervention to another must be taken into account in N-of-1 trials that involve giving an individual various interventions in succession and assessing the results for each. However, these problems can be largely resolved with the right analytical techniques and study design. Because going from one intervention to another may make a person's health worse, crossover-based N-of-1 trials are unfeasible, if not unethical, in situations when a person is experiencing an acute or life-threatening disease. For similar circumstances, consecutive N-of-1 approaches have been suggested, in which metrics are continuously tracked in real time to ascertain if an intervention is effective or harmful. According to Hogen and Sim, N-of-1 trials may be best suited for conducting in real clinical practice when a doctor is faced with equipoise because their focus is on finding the best intervention for a single person rather than on the average response to an intervention in the population as a whole, which is frequently the focus of traditional RCTs [33-35].

Trials of Intervention Matching

The question of how to test the hypothesis that offering interventions to individuals based on these "matches" produces better results than offering those individuals interventions based on some other scheme or strategy emerges if evidence is found that specific features in each patient's profile can be used to identify interventions that might work for each of them. Testing each individual match could necessitate conducting numerous small clinical trials, which could be logistically challenging and require infrastructure and funding to execute. Alternatively, an entire matching technique might be tested against a different approach to intervention delivery (e.g., giving everyone the same intervention). This is basically the driving force behind the "basket" and "umbrella" trials that are currently being used, mostly in cancer contexts. Basket and umbrella trials are used in oncology settings, where a number of patients are enrolled individually, each with the knowledge that they may have distinct characteristics in their profiles that suggest the need for alternative treatments. While umbrella trials exclusively look at one tissue (only lung cancer patients are enrolled), basket trials enrol people regardless of the specific tissue affected by cancer (e.g., lung, breast, and colorectal cancer patients can be enrolled). Tumour profiles are created for each patient, typically via DNA sequencing. The genome of the tumour is examined to determine whether any actionable "driver" perturbations—such as mutations affecting specific genes—are present and are probably causing the tumour to grow. It may be possible to match a class of interventions (i.e., cancer drugs) to the perturbations in the tumour if the mechanisms of action of those interventions are sufficiently understood. For example, if the tumour has a mutation and overexpression of the EGFR gene, it would make sense to use a drug that inhibits the EGFR gene, such as cetuximab. This means that each patient is guided to a specific intervention basket, such as the EGFR inhibitor basket. The trial next aims to test the hypothesis that interventions given to individual patients based on a separate scheme that does not utilise tumour profiling and matching are less effective than interventions given to the various intervention baskets based on the matching system [36, 37].

A case might be made that the matching strategy was problematic rather than that the interventions examined in the trial were flawed if the experiment is unsuccessful (that is, if the matching scheme does not produce better results than something else). If a basket or bucket experiment fails, it would also be incorrect to imply that the idea of personalised medicine is defective because the matching system was flawed. Certain basket trials simply include one basket and no comparison group; instead, they focus on identifying patient profiles that seem to be linked to improved results for the intervention under test. In the medical field, intervention matching methods are probably going to become the norm rather than the exception, particularly with the advent of computing environments like IBM's "Watson" system. Watson is basically a system that has a huge database that has been partially taken from the extensive medical literature. It makes connections between patient data (such genetic profiles, age, sex, etc.) and results (like medication reaction). Statistical techniques have been used to better evaluate the connections between patient profiles and results, strengthening these connections. For instance, Watson has been "taught" to recognise and make connections between anomalies frequently seen in tumours and how such anomalies could be addressed by readily available medications and therapies. As a result, given a patient profile, Watson could determine the optimal course of action based on the state of the research as it is now represented in the literature and Watson's techniques for connecting profiles to results. The application of IBM's Watson system in real-world clinical settings has sparked debates over how to test and implement such a system to complement (rather than replace) doctors' judgements regarding the best course of action for each patient [38, 39].

Adaptive Clinical Trials

Sequential and adaptive clinical trials have been around for decades, but it is much more recent that they have been considered and applied in personalised medicine settings. Basically, one of the main goals of adaptive trials is to reduce the duration of time a patient is receiving what is probably a subpar treatment. Evaluating the effects of each intervention on an individual to determine which is best for that individual (as in a very complex N-of-1 study) may be impractical or even harmful in the context of personalised medicine if there is equipoise between available interventions or between an untested and a conventional intervention for a particular patient. This is due to the possibility that some, if not all, of the interventions will not truly help that person. Given this, it

makes sense to conduct research wherein biomarkers that indicate response or harmful effects are gathered from each trial participant individually, and then those biomarkers are monitored to look for indications that an intervention is not working. The person may switch to a different intervention if there are indications, for example, that the current one is not functioning. Adaptive designs are frequently regarded as more ethical, despite the fact that their real-time evaluation and updating components can make them challenging to implement and that the data they provide may be more difficult to interpret than that of fixed, non-adaptive trials. Furthermore, it is feasible to incorporate adaptive elements into intervention-matching trials, N-of-1 trials, and aggregated N-of-1 trials. Despite the increasing number of publications detailing adaptive trials, Murphy and colleagues' work has drawn a lot of attention because to its emphasis on reducing the duration of a patient's exposure to subpar treatment [40, 41].

Next-Generation and Emerging Strategies in Personalised Medicine

Recent clinical and research endeavours are paving the way for new developments in personalised medicine. In the following, we highlight four of these activities and give a quick synopsis of each. These activities include the development of personalised digital therapeutics, the use of highly customised diagnostic and monitoring protocols to identify disease symptoms, the use of patient-derived cell and organoid "avatars" to determine the best therapies for that patient, and the application of personalised medicine techniques to treat patients with infertility problems [42].

Cellular Avatars Derived from Patients

In order to produce more cell types relevant to a patient's condition without directly biopsying the damaged tissue, it is now possible to harvest cells from individuals and employ pluripotency induction (also known as induced pluripotent stem cell, or "iPSC") techniques on those cells. This enables scientists to create a cellular model of a patient's condition, thereby creating a "disease in a dish." Key molecular diseases that may provide guidance on the optimal course of treatment for a particular patient of interest can be identified by examining these in vitro cellular "avatars." A few other, newly discovered technologies can be added to the use of iPSC technologies in this way to produce even more accurate models of a person's state. For example, In cases when a patient's disease is known to be caused by a mutation, assays based on, for example, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and related constructions can be used to produce isogenic cells, in which some cells contain the mutation in issue and others do not. When these cells are compared, the effects of the mutation can be directly observed while accounting for all pertinent genetic background factors related to the patient's DNA. It is also feasible to use cells taken from an individual to construct "organoids," or partial organs. Given their ability to replicate cell-to-cell interactions and more general tissue function, organoids can shed more light on the molecular diseases linked to a given patient's illness [43].

The usage of patient avatars made from their own cells could be combined with other patient data and action procedures to provide genuinely personalised medical care. Schork and Nazor use patient avatars, among other tools, to explain how various elements of patient diagnosis, intervention selection, and monitoring are integrated and motivated. The ability to support personalised drug screening—actually testing thousands of medications and compounds against a patient's cells (or organoids, potentially altered with CRISPR technologies) to find medications or compounds that specifically address the patient's molecular defects—is a significant feature of the use of cell-based patient avatars in personalised medicine. The drug or substance may be examined for efficacy with the patient using an approved drug "repurposing" protocol if it has been licensed for usage, presumably for a different condition. In cancer contexts, the use of patient-derived cells in personalised drug screening programs has demonstrated some effectiveness because tumour biopsies can produce suitable drug screening material. Whether or not the in vitro models capture pertinent in vivo pathobiology and drug response information that could influence a patient's reaction to a selected medication is the main issue with this technique. Implanting a device into a patient's tumour in vivo and then administering various medications through that device to observe which ones have an impact could be a more straightforward approach for choosing an in vivo experimental cancer intervention [44].

CONCLUSION

Personalized Medicine, or Given that clinically meaningful inter-individual variation has been and will continue to be identified, it is imperative to characterise each patient on multiple levels (e.g., genomic, biochemical, behavioural, etc.) that may provide insight into how they respond to an intervention and then treat them appropriately. Modern biomedical technologies like wireless monitoring devices, proteomics, and DNA sequencing have made it possible to identify this variance, hence highlighting the necessity of some degree of medical personalisation. Future difficulties related to this reality will include improving the effectiveness of how people are classified as well as how personalised medications are developed and tested to demonstrate their value. This is not to suggest that widely effective interventions (such as the classic single agent "block buster" medications) should be disregarded if they are found; rather, it is to suggest that they may be extremely challenging to find in the future. Personalised medicine has a few other problems that might be difficult to resolve in the near future. For instance, the necessity of gathering a lot of data to find the characteristics that discriminate against groups of people who would benefit more from one kind of intervention could raise privacy concerns and raise the possibility that the information about those people could be used for malicious purposes. Thankfully, this

problem does not always occur in healthcare environments. whether present or future, given that it has afflicted numerous other sectors, including as social media, marketing, and finance. Techniques employed in these other sectors may also be applied in healthcare environments. In order to satisfy the needs of every patient, it is also essential to create more effective methods of creating personalised medications (for instance, with regard to cell replacement therapies or mutation-specific medications that only function for a limited percentage of patients). Additionally, while personalised medicine procedures may be more costly at first, paying for them in the future may be challenging. Lastly, improved methods for educating and training medical personnel about personalised medicine must be created and put into practice if different stakeholders are to embrace it.

REFERENCES

1. Aboulkheyr Es, H Montazeri, L Aref, et al, 2018. Personalized Cancer Medicine: An Organoid Approach. Trends in Biotechnology. 36(4), Pages 358–371. Doi: https://doi.org/10.1016/J.TIBTECH.2017.12.005.
2. Adeniji A A., Dulal S, Martin M G, 2021. Personalized Medicine in Oncology in the Developing World: Barriers and Concepts to Improve Status Quo. World Journal of Oncology. 12(2–3), Page 50. Doi: https://doi.org/10.14740/WJON1345.
3. Biankin A V, Piantadosi S, Hollingsworth S J, 2015. Patient-centric trials for therapeutic development in precision oncology. Nature. 526(7573), Pages 361–370. Doi: https://doi.org/10.1038/NATURE15819.
4. Braig Z V, 2022. Personalized medicine: From diagnostic to adaptive. Biomedical Journal. 45(1), Pages 132–142. Doi: https://doi.org/10.1016/j.bj.2019.05.004.
5. Carlsten C, Brauer M, Brinkman F, et al, 2014. Genes, the environment and personalized medicine. EMBO Reports. 15(7), Pages 736–739. Doi: https://doi.org/10.15252/EMBR.201438480.
6. Collins F S, Varmus H, 2015. A New Initiative on Precision Medicine. New England Journal of Medicine. 372(9), Pages 793–795.Doi: https://doi.org/10.1056/NEJMP1500523.
7. Crystal S, Shaw T, Sequist V, et al, 2014. Patient-derived models of acquired resistance can identify effective drug combinations for cancer. Science. 346(6216), Pages 1480–1486. Doi: https://doi.org/10.1126/SCIENCE.1254721.
8. Duan N, Kravitz R L, Schmid C H, 2013. Single-patient (n-of-1) trials: A pragmatic clinical decision methodology for patient-centered comparative effectiveness research. Journal of Clinical Epidemiology. 66(8 SUPPL.8). Doi: https://doi.org/10.1016/J.JCLINEPI.2013.04.006.
9. Farkona S, Diamandis E P, Blasutig I M, 2016. Cancer immunotherapy: The beginning of the end of cancer? BMC Medicine. 14(1). Doi: https://doi.org/10.1186/S12916-016-0623-5.
10. Glasziou P P, 2011. Commentary: The history and place of n-of-1 trials: A commentary on Hogben and Sim. International Journal of Epidemiology. 40(6), Pages 1458–1460. Doi: https://doi.org/10.1093/IJE/DYR031
11. Goetz L H, Schork N J, 2018. Personalized Medicine: Motivation, Challenges and Progress. Fertility and Sterility, 109(6), Pages 952. Doi: https://doi.org/10.1016/J.FERTNSTERT.2018.05.006.
12. Gulland A, 2016. Cystic fibrosis drug is not cost effective, says NICE. BMJ (Online). 353. Doi: https://doi.org/10.1136/BMJ.I3409.
13. Hoeben A, Joosten J, van den Beuken-Van Everdingen, 2021. Personalized medicine: Recent progress in cancer therapy. Cancers. 13(2), Pages 1–3. Doi: https://doi.org/10.3390/CANCERS13020242
14. HOGBEN L, SIM M, 1953. The self-controlled and self-recorded clinical trial for low-grade morbidity. British Journal of Preventive & Social Medicine. 7(4), Pages 163–179. Doi: https://doi.org/10.1136/JECH.7.4.163.
15. Horgan D, Lal J A, 2019. Making the Most of Innovation in Personalised Medicine: An EU Strategy for a Faster Bench to Bedside and Beyond Process. Public Health Genomics. 21(3–4), Pages 101–120. Doi: https://doi.org/10.1159/000497809.
16. Hyman D M, Piha-Paul A, Won H, et al, 2018. HER kinase inhibition in patients with HER2-and HER3-mutant cancers. Nature. 554(7691), Pages 189–194. Doi: https://doi.org/10.1038/NATURE25475.
17. Iacoviello B M, Steinerman J R, Klein D B., et al, 2017. Clickotine, a personalized smartphone app for smoking cessation: Initial evaluation. JMIR MHealth and UHealth. 5(4), Doi: https://doi.org/10.2196/MHEALTH.7226.
18. Jameson J L, Longo D L, 2015. Precision Medicine — Personalized, Problematic, and Promising. New England Journal of Medicine. 372(23), Pages 2229–2234. Doi: https://doi.org/10.1056/NEJMSB1503104.
19. Jonas O, Landry M, Fuller E, et al, 2015. An implantable microdevice to perform high-throughput in vivo drug sensitivity testing in tumors. Science Translational Medicine, 7(284), Pages 284ps10. Doi: https://doi.org/10.1126/SCITRANSLMED.3010564.
20. Jungheim S, Carson R, 2018. Leveraging real-world data to move toward more personalized fertility treatment. Fertility and Sterility. 109(4), Pages 608–609. Doi: https://doi.org/10.1016/J.FERTNSTERT.2018.01.036.
21. Kaner S, Beyer R, Garnett C, et al, 2017. Personalised digital interventions for reducing hazardous and harmful alcohol consumption in community-dwelling populations. Cochrane Database of Systematic Reviews. 2017(9), Doi: https://doi.org/10.1002/14651858.CD011479.PUB2.
22. Klinghoffer R A, Bahrami S B, Hatton B A, et al, 2015. A technology platform to assess multiple cancer agents simultaneously within a patient's tumor. Science Translational Medicine. 7(284), Pages 284ra56. Doi: https://doi.org/10.1126/SCITRANSLMED.AAA7489.
23. Laber E B, Zhao Q, Regh T, et al, 2016. Using pilot data to size a two-arm randomized trial to find a nearly optimal personalized treatment strategy. Statistics in Medicine. 35(8), Pages 1245–1256. Doi: https://doi.org/10.1002/SIM.6783.
24. Lee M, Klein E, 2013. Pharmacogenetics of warfarin: Challenges and opportunities. Journal of Human Genetics. 58(6), Pages 334–338. Doi: https://doi.org/10.1038/JHG.2013.40.

25. Liao X, Lochhead P, Nishihara R, et al, 2012. Aspirin Use, Tumor PIK3CA Mutation, and Colorectal-Cancer Survival. New England Journal of Medicine. 367(17), Pages 1596–1606. Doi: https://doi.org/10.1056/NEJMOA1207756.

26. Lillie O, Patay B, Diamant Jet al, 2011. The n-of-1 clinical trial: The ultimate strategy for individualizing medicine? Personalized Medicine. 8(2), Pages 161–173. Doi: https://doi.org/10.2217/PME.11.7.

27. Luzzatto L, Seneca E, 2014. G6PD deficiency: A classic example of pharmacogenetics with on-going clinical implications. British Journal of Haematology. 164(4), Pages 469–480. Doi: https://doi.org/10.1111/BJH.12665.

28. O'Dwyer E, Druker B J, 2000. Status of bcr-abl tyrosine kinase inhibitors in chronic myelogenous leukemia. Current Opinion in Oncology. 12(6), Pages 594–597. Doi: https://doi.org/10.1097/00001622-200011000-00013.

29. O'Rawe J A, Fang H, Rynearson S, et al, 2013. Integrating precision medicine in the study and clinical treatment of a severely mentally ill person. Peer J. (1), Doi: https://doi.org/10.7717/PEERJ.177.

30. Patel C J, Sivadas A, Tabassum R, et al, 2013. Whole genome sequencing in support of wellness and health maintenance. Genome Medicine. 5(6), Pages Doi: https://doi.org/10.1186/GM462.

31. Patsalias A, Kozovska Z, 2021. Personalized medicine: Stem cells in colorectal cancer treatment. Biomedicine and Pharmacotherapy. Pages 141. Doi: https://doi.org/10.1016/j.biopha.2021.111821.

32. Phillips K A, Douglas M P, Trosman J R, 2017. What Goes Around Comes Around": Lessons Learned from Economic Evaluations of Personalized Medicine Applied to Digital Medicine. Value in Health. 20(1), Pages 47–53. Doi: https://doi.org/10.1016/J.JVAL.2016.08.736.

33. Sayed N, Liu C, Wu J C, 2016. Translation of Human-Induced Pluripotent Stem Cells from Clinical Trial in a Dish to Precision Medicine. Journal of the American College of Cardiology. 67(18), Pages 2161–2176. Doi: https://doi.org/10.1016/J.JACC.2016.01.083.

34. Schork N J, 2013. Genetic parts to a preventive medicine whole. Genome Medicine. 5(6), Doi: https://doi.org/10.1186/GM458.

35. Schork N J, 2015. Personalized medicine: Time for one-person trials. Nature. 520(7549), Pages 609–611. Doi: https://doi.org/10.1038/520609A.

36. Schork N J, Nazor K, 2017. Integrated Genomic Medicine: A Paradigm for Rare Diseases and Beyond. Advances in Genetics. 97, Pages 81–113. Doi: https://doi.org/10.1016/BS.ADGEN.2017.06.001.

37. Shah G L, Majhail N, Khera N, 2018. Value-Based Care in Hematopoietic Cell Transplantation and Cellular Therapy: Challenges and Opportunities. Current Hematologic Malignancy Reports. 13(2), Pages 125–134. Doi: https://doi.org/10.1007/S11899-018-0444-Z.

38. Shi Y, Iorgulescu J B, Valladao S, 2024. Expanding the Reach of Personalized Medicine in Cancer Care: Current Progress and Future Directions of JCO Precision Oncology. JCO Precision Oncology. 8. Doi: 10.1200/PO.24.00068.

39. Simon R, Roychowdhury S, 2013. Implementing personalized cancer genomics in clinical trials. Nature Reviews Drug Discovery. 12(5), Pages 358–369. Doi: https://doi.org/10.1038/NRD3979.

40. Singh D, Dhiman V K, Pandey M, 2024. Personalized medicine: An alternative for cancer treatment. Cancer Treatment and Research Communications. 42, Pages 100860. Doi: https://doi.org/10.1016/J.CTARC.2024.100860.

41. Tabery J, 2011. Commentary: Hogben vs the tyranny of averages. International Journal of Epidemiology. 40(6), Pages 1454–1458. Doi: https://doi.org/10.1093/IJE/DYR027.

42. Tsimberidou A M, Fountzilas E, Nikanjam M, 2020. Review of precision cancer medicine: Evolution of the treatment paradigm. Cancer Treatment Reviews 86. Doi: https://doi.org/10.1016/j.ctrv.2020.102019.

43. Uppada V, Gokara M, Rasineni G K, 2018. Diagnosis and therapy with CRISPR advanced CRISPR based tools for point of care diagnostics and early therapies. Gene. 656, Pages 22–29. Doi: https://doi.org/10.1016/J.GENE.2018.02.066.

44. Wartman L D, 2015. A case of me: clinical cancer sequencing and the future of precision medicine. Molecular Case Studies. 1(1), Pages a000349. Doi: https://doi.org/10.1101/MCS.A000349.