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REVIEW

# Advancing precision medicine in medical education: Integrated, precise and data-driven smart solutions

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## Abstract

Advances in "Precision Medicine" initiative, also known as "Personalized Medicine" is an emerging approach for disease treatment and prevention that has already led to innovative discoveries and has created "smart" applications and solutions tailored to a person's or a group of individuals' genetic profile, lifestyle, and environment interaction. Already many physicians as part of patient care routinely prescribe various molecular/genetic and other tests enabling them to select personalized treatments that improve the chances of survival and reduce exposure to adverse effects. This initiative should provide to medical and healthcare professionals with adequate resources and readily available solutions so that the target to specific treatments and care of the illnesses is achieved while at the same time protecting the privacy and safety of the individual is secured as well as the Electronic Health Records (EHRs) and whatever additional data is necessary within the context of Precision Medicine. This study, through a literature review mostly, and some case study analysis, examine whether personalized medicine is delivered to the patient in an "accurate" and "precise" way, as expected. This requires that Health and Human Services and other stakeholders and agencies collaborate to solicit the right input from patients while at the same time can identify and address any educational, practical, legal, and technical issues and providing smart solutions. The lack of proper medical education and advanced infrastructure are still major barriers to the adoption of Precision Medicine, therefore, the role of medical training in Precision Medicine is also examined and analyzed. Specific examples are discussed in an integrated, precise, and data-driven manner to provide "smart" solutions.

**KEYWORDS**
artificial intelligence, healthcare, medical education, personalized/precision medicine, pharmacogenomics, wise data

## INTRODUCTION

"Precision Medicine" initiative, also known as 'Personalized Medicine' or even 'Stratified Medicine' is a rather recent approach for disease treatment and prevention which has already led to innovative discoveries and treatments and has created "smart" applications and solutions tailored to a person's genetic profile, lifestyle, and environment interaction [1–7]. This approach in healthcare combines knowledge from genomics, transcriptomics, proteomics, proteoforms, metabolomics, big data analytics, population health, and environmental influences [8, 9]. According to the "Precision Medicine Initiative" [10], "Precision Medicine" refers to a person's or a group of individuals' genetic profile, lifestyle, and environment interaction. Former President Barack Obama introduced the national Precision

Medicine Initiative in his State of the Union speech in 2015 and since then there appears to be a preference to the term "precision medicine" instead of "personalized medicine" to describe the use of data and genomics for the treatment of specific groups rather than the individual. In its 2012 report "Towards Precision Medicine," the National Research Council (NRC) clarifies that the approach does not necessarily provide individualized treatments [11, 12]. The term "precision" is taken to mean both "accurate" and "precise" in reference to medical treatments for subpopulations of different genetic profile, disease susceptibility, and response to treatment especially in terms of the right dose and the right time of administration [11, 13]. While acknowledging that there is no universally accepted term, Precision Medicine, Personalized Medicine or even Stratified Medicine are commonly used terms. The European Commission, for example, has selected to use the term Personalized Medicine. This term was selected to be the basis for the International Consortium for Personalized Medicine [14], and it has also been used in the European Council Conclusions on PM for patients (2015/C 421/03) and in the Horizon 2020 work program for SOCIETAL CHALLENGES—Health, demographic change, and well-being. The definition of the term is similar to that provided by the NCR though.

Independently of the specific term used and the progress made so far, many medical doctors and healthcare practitioners are still generally trained the conventional way with a focus on reactive treatment. Ways to improve diagnosis, therapies, and prognosis of diseases toward personalized/precision medicine and stratified or targeted drug/gene therapy are nevertheless explored by many. While in the healthcare industry serious efforts have been made to embrace precision medicine, lack of proper medical education and its delivery including the development of advanced infrastructure are still major barriers to adoption. As mentioned in a report from Personalized Medicine Coalition (PMC) [13], more advanced infrastructure, better education and higher engagement of patients and providers must improve if precision medicine adoption is to increase. This type of transformation requires open and honest collaboration across various stakeholder groups such as leaders, administrators, academics, physicians, researchers, information communication technologists, clinicians, medical personnel, bioethicists, providers, insurers, industry, privacy, and civil liberties advocates, educators, and other experts. At the same time vigilance and preparedness are required to overcome educational, technological, practical, regulatory, and infrastructure obstacles related to new medical practices and processes for clinical adoption to be possible.

Papadopoulou et al. [15] have proposed the concept of "Wise Data" as a solution toward wise decisions which should not necessarily be focused on market imperatives to achieve more efficient medical systems, social cohesion, and improvement of the health of individuals. By combining the recent advances in Bioinformatics and in Healthcare Informatics this study points out ways to improve medical education, management, and practices both at the national and global level. Papadopoulou et al. [16, 17] among others have examined the nature of biomedical and healthcare sciences programs, the curricula, the internships, and practical training needed, the kind of educators, the international guidelines and certifications, and how to shift toward patient-centered medical centers of top-quality medical services.

The motivation of this systematic literature review came from the need to categorize and summarize the previous work that has been done on Precision Medicine and Higher Education and identify the explored and unexplored areas. Our ultimate goal is to help raise awareness on precision medicine and its challenges by focusing on the need to improve medical and biomedical education curricula. We examine alternative smart solutions such as offering well-designed online courses, webinars, conferences but also creating open resources for all stakeholders. Our contribution is to offer inspiration and positive examples for smart and wise solutions and highlight options for actions and solutions.

The overall objective of this study is to address the present-day challenges and to help communicate and disseminate the recent advances in "Precision or Personalized Medicine" as an innovative and highly collaborative approach to clinical care by pointing out how by combining advanced methods and techniques by proper training of students could lead to better health and health care.

Considering the above, this study is mainly a qualitative analysis, and the aims of this review are to make a good collection of articles and other resources which will be made available to any researcher interested in the advances in "Precision Medicine." In addition, we aim to analyze other aspects, such as, the role of Health and Human Services, various medical curricula, type of delivery, and provide examples of best delivery and implementation, to evaluate areas explored and areas of future research. Finally, we aim to showcase, evaluate and align the results with a proposed framework of best practice.

## METHODOLOGY

The methodology of systematic literature review has been used in this study, and it combines literature review, reports on medical education and healthcare as well as various successful case studies examples related to the treatment of cancer, heart disease, lung disease, metabolic diseases, and neurological disorders. A generic literature review was conducted to systematically examine and map the efforts of various stakeholders. It is a comprehensive, critical, and objective analysis of the current knowledge and attempts to identify existing gaps in knowledge. The rationale for the review in the context of existing knowledge is covered in the introduction. The objectives of the study are also stated. The eligibility criteria for both the inclusion and exclusion criteria were decided, and studies were grouped according to their main focus.

### Data collection

This research took place from October 2021 to December, 2022. Five stages were followed: preparation, research questions, and queries, data retrieval, data analysis, data synthesis, and results.

To conduct this review, the PRISMA 2020 statement was used to facilitate the preparation and reporting of the current systematic review [18]. A detailed recording of the available resources has been made. In Figure 1 [18], most of the publications are published articles
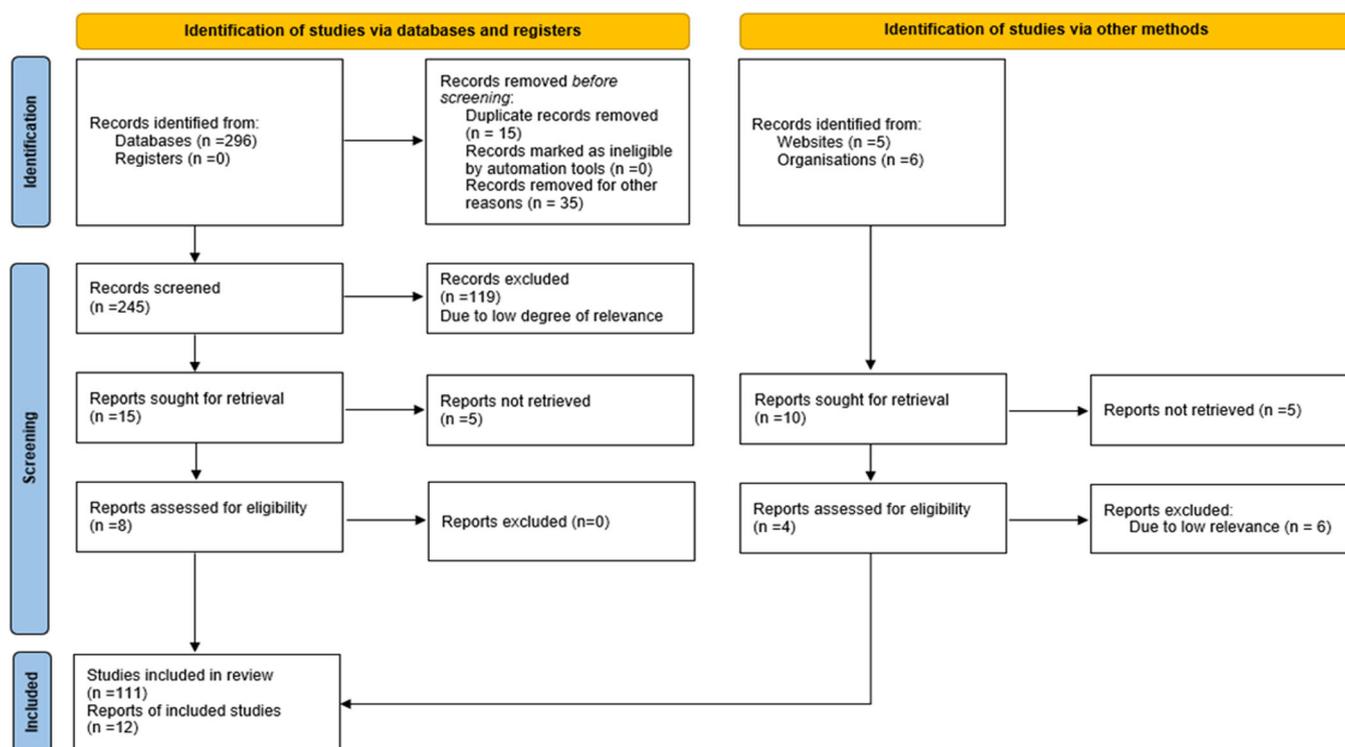
**FIGURE 1** PRISMA 2020 flow diagram for the systematic review which includes searches of databases, registers, and other sources.

and papers. Some reports and mini-reviews were identified. No systematic reviews specific to the topic of research were identified.

The entire research model can be briefly described in Figure 1. PRISMA 2020 flow diagram for new systematic reviews which includes searches of databases, registers, and other sources [18].

## Search terms

The present review has gone through with the help of the search queries that were inserted in search engines. The criterion for the relevance of publications is whether each one includes the following keywords: personalized/precision medicine, healthcare, medical education, artificial intelligence, pharmacogenomics and combination of related phrases. Additional keywords were employed in relation to PM and gene and metabolic disorders, neurological disorders, cancer, gene therapy, CAR T-cell therapy, and PM and AI.

Searched databases: PubMed, Google Scholar, Springer Link, Science Direct, Open Access Publishers, Web of Science, etc. Searched items: Journal articles, conference papers, workshop papers, and technical reports.

## Inclusion/exclusion criteria

The detailed analysis refers to 296 relevant publications that were extracted from online databases. 123 publications are referenced in this study. The following aspects were the inclusion criteria of this

review study: Search applied on full text, to avoid exclusion of papers that didn't include the searched keywords in abstracts or titles or used a different variant of the terms but were relevant for this review. The search was limited to papers written in English. All other languages are excluded. The publication period included all years (2000–2022).

From the 245 papers screened 119 were excluded as the degree of relevance was low. The excluded papers were the result of the two authors working independently to minimize bias and to abide with the eligibility criteria. The few discrepancies were addressed by consensus, taking into the account the agreed selection criteria (see Figure 1 for more details) [18].

The outcome of the search process resulted a total of 296 relevant publications, of which 123 are referenced in this paper.

## Research questions

This study examines the following two main research questions: *a) To what extent the educational programs that exist in biomedical, medical, and healthcare sciences incorporate into their curriculum training in Precision Medicine? b) How medical training can help physicians and biomedical scientists to adopt precise and data-driven smart solutions as key enablers toward this new era of Precision Medicine?* Our study focuses on the state of health and the state of medical education in developed countries mainly, and it proposes a multidimensional framework leading to practical applications which may help bridge gaps that exist in the wise use of genomics and proteomics data,

exposome data and various other ICT applications related to healthcare and personalized medicine which will help the countries to achieve sustainable and healthy societies.

To answer these questions, we must draw valid conclusions from the current literature and examine this in the upcoming years. In addition, it is useful to understand which areas are underexplored where substantial progress has been made, and how to use best practices in the future.

## Data extraction, analysis, quality assessment, and synthesis

During the synthesis phase, extensive analysis mostly qualitative has been done regarding the information gathered from the reviewed reports, papers, and articles. This was necessary for supporting data categorization and data synthesis. The goal was to summarize the main areas of research related to precision medicine delivery using web data. Important findings and conclusions have been included in the results section, supplemented by the references to the included papers. No statistical analysis has been performed in this particular review. Most areas concerned with the synthesis of the studies that were identified, the various perspectives and the trends, and the various stakeholders are presented as well as various recommendations for future work. The results include advances and case studies to help the synthesis and evaluation of best practices. A recommended framework of best practices is proposed as an outcome of the literature review done. Finally, the outcomes of this research are pointed out as well as the impacts and the contribution to the scientific community. Further recommendations for future studies are also presented.

## RESULTS

In relation to the first research question there are studies that point to the following:

From our literature review, it appears that a small amount of teaching time is dedicated to training in precision medicine overall and interdisciplinary patient care more specifically in genomic medicine, including interdisciplinary education by genetic counselors [19–25]. A recent US national survey suggested that students lack insight into the possibility of careers in medical genetics, biomedical informatics, or medical toxicology and many do not consider such training important [26]. The importance of offering meaningful and continuing medical education (CME) offerings and career development has been identified as valuable by educators though. The goal of Precision Medicine is the integration into the curriculum and ensuring every physician is trained in the use of pharmacogenomic data and advanced clinical decision support systems [27–29]. Cecchin et al. [30] in the Editorial "Pharmacogenomics and Personalized Medicine" of a special issue include a good collection of articles on clinical pharmacogenomics, tools, and pharmacogenomics markers

for better drug safety and efficacy plus on genetic variants. Precision medicine holds great promise for improving for example chemotherapy of various cancers and leukemia including anticoagulant therapy for cardiovascular diseases but also using innovative molecular approaches for the sequencing of rare variants and identification of epigenetic features, in identifying genetic determinants concerning drugs in several clinical settings [30–32]. Eventually, physicians need to effectively integrate future advancements into their patients' care as well as educate and guide their students and patients. At this point, precision medicine is not fully realized as there are disparities across various parts of the world in the uptake of precision medicine applications and services as well as on ethical aspects. The attitudes and degree of awareness toward pharmacogenomics and personalized medicine adoption vary substantially among health sciences trainees yet students appear to be proponents of genetics testing and in favor of public endorsement of the concepts of individually tailored medicine [33, 34]. Nevertheless, personalized medicine would fail to achieve its promise if diversity and inclusion are not taken into consideration without engaging underrepresented groups [35–37].

As mentioned by Eden et al. [38] even though medical students support the use of personalized medicine, they do not feel prepared to apply genomics to clinical care. Hyland et al. [24] state that despite the existing enthusiasm genetic and genomic testing is far from becoming a routine. They propose genomic literacy across a range of specialties which could be delivered through courses, workshops and seminars. Haga and Moaddeb [39] identified that 42% of pharmacy schools they examined at least one Pharmacogenomics courses was included as part of the core curriculum, and 8% schools offered a course as an elective. They concluded that less than half of the schools have developed a standalone course.

Similarly, Guy et al. [40] point to the fact that the integration of pharmacogenomics into clinical decisions remains variable and challenging in certain practice settings. Their recommendation is to ensure consistent application across settings, therefore, sufficient education amongst current and future healthcare providers is necessary to further integrate pharmacogenomics into routine clinical practice.

Cheung et al. [41] examined the perception of personalized medicine, pharmacogenomics, and genetic testing among undergraduates in Hong Kong. Despite the higher degree of student awareness on the matter their conclusion is not different it seems from what happens in the majority of countries across the world which calls for the attention to evaluate medical and biomedical curricula and better inform the students on the prospects of Precision Medicine.

A good example implemented towards a hands-on Precision Medicine training program for the Genetics curriculum is the use of a protocol that entails DNA isolation from cadavers and the utilization of exome sequencing to prepare a clinical genetic report of cadavers studied in the anatomy lab. The practical training presented in this study augments the Genetics class but also helps students become aware of the limitations, potential, and complexities of Precision

Medicine [42]. Duong et al. [43] highlight an interesting AI-integrated framework in support of radiology education and provide use case examples informed by their own institution's practice.

Overall, our findings point to the fact that educational programs in biomedical, medical, and healthcare sciences in developed countries are quite diverse in nature. For example, the EU "Eurydice" portal, a good starting point portal, publishes descriptions of national education systems, comparative reports, indicators, and statistics, and updates related to the field of education and there are both public and private, for-profit or non-profit institutions. [44] The US Universities have diverse curricula as well often within the same system for both the public and private Universities [45].

In relation to public awareness of what personalized medicine might be in the US for example, 66% of adults admit they have not read or heard anything about it, and only 13% feel very informed. 17% have heard of genetic counseling, but only 4% have consulted a genetic counselor. On the positive side, 82% reported high interest for more information. Yet, the prevalence of precision medicine treatments and personalized medicines in the market has increased in recent years [13].

As an attempt to clarify further this whole scheme, in Figure 2 we illustrate the various levels of these new initiatives in medicine and their delivery in an integrated manner as there is substantial overlap in the term "precision" and "personalized." Precision medicine certainly applies to the person's genotype, unique Single Nucleotide Polymorphisms (SNPs), phenotype, microbiome, exposome, and lifestyle. When combined with the use of specific biomarkers, diagnostics, and targeted drugs in a predictive and preventive manner and with computational analysis from data provided from the various OMICs data sets, it can lead to personalized medicine in a participatory way. Depending on the health problem the physicians could then use advanced techniques of individualized medicine such as applying CAR-T cell therapy [29] or perhaps even the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPRs), such as CRISPR/Cas9 gene-editing technique [46–48], which can be used to treat human diseases like β-Thalassemia Major using CRISPR-based genome and epigenome editing [49, 50]. At this moment, gene and cell therapy is arguably the most exciting area of biotechnology due to recent progress and possible future treatments.

The next level which combines clinical analytics, big data analytics, data integration, and smart use of the EHRs could lead to personalized healthcare for both the individual patient and also to better future healthcare. Health management, policy-making, and digital health are then connecting all beneficiaries such as the patients, the clinicians, the pharmaceutical industry, the researchers, the administrators, the legislators, and the community. Finally, these efforts lead to system integration from the patient himself to the recruitment for a clinical study to collecting various data, to describing it, to selecting the cure, to analysis and reporting, which then closes the loop as information needs to return to all previous stages and provide knowledge and new smart practices.

There are quite a few benefits related to the use of Precision Medicine as revealed from the literature review [13]. In Figure 3 the main benefits are listed, beginning from a shift of attention from reaction to prevention, to patient-centered care, reduction of the cost that is a common factor for not providing proper treatment, avoiding high-risk procedures, and reducing adverse reactions. The shift is to use cell-based therapies and gene therapies for the specific molecular pathways and to increase patient adherence to treatment.

In relation to the second research question there are studies that point to the following:
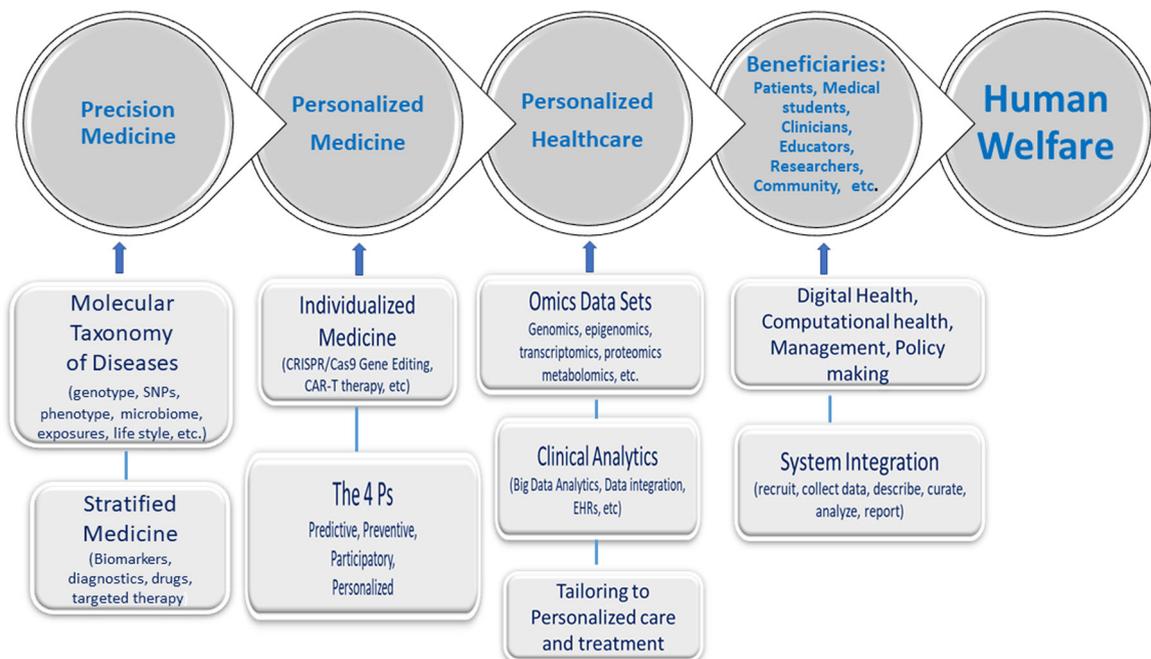


FIGURE 2   Precision Medicine as it relates to Personalized Medicine, Personalized Healthcare and the Beneficiaries.

## Precision Medicine Benefits



- Attention shift from reaction to prevention
- Shift to patient-centered care
- Reduction of cost & high-risk invasive testing procedures
- Shift to cell-based or gene therapy for the molecular pathways of the disease
- Reduction of adverse drug reactions
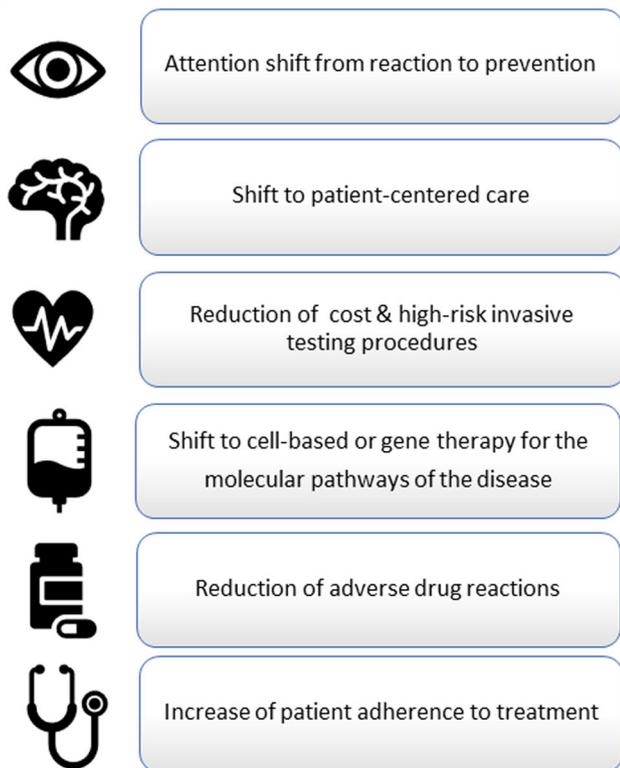- Increase of patient adherence to treatment

**FIGURE 3**    The benefits of Precision Medicine.

The Role of Artificial Intelligence (AI) in Precision Medicine is exceptionally important [51–55]. The healthcare industry already experiences a rapid shift to Precision Medicine requests from physicians and patients and other stakeholders. There are many opportunities to leverage technology to deploy impactful interventions in a precise and efficient manner. As the volume of available data continues to increase at a staggering rate, Artificial Intelligence can serve as the transformational force that drives improvements across the healthcare continuum with various AI-driven tools. AI offers advantages one cannot get through traditional analytics [56–58]. In the following study fundamentals of AI and Big Data are presented in the context of potential applications to data analytics in public health and the medical sciences. Humans will eventually gain unprecedented insights into the diagnosis and possible treatment of diseases as the various AI learning algorithms interact with training data [53].

Twelve technologies on Artificial Intelligence and areas of the healthcare industry have been presented by Partners Healthcare as a projection for the next decade at the World Medical Innovation Forum [59]. Those technologies range from the unification of mind and machine through brain-computer interfaces to the development of imaging and radiology tools, to creating more precise analytics for pathology images, to improving EHRs, to better monitoring of personal and medical devices and smartphones, to advancing cancer treatment and immunotherapy, to containing the risks of antibiotic resistance, the bringing of AI to clinical decision making with AI at the bedside. It is expected that such innovations will revolutionize access to care in both developed and developing regions of the world.

As an example, Johnson et al. [60] in their study provide a guide for clinicians on relevant aspects of AI and machine learning and have identified how cardiovascular medicine could incorporate AI and how these methods could be applied to enable precision cardiology and improve patient outcomes in the future.

Similarly, the studies by Krittanawong et al [61, 62]. present an AI's application in cardiovascular clinical care and discuss its potential role in facilitating precision cardiovascular medicine. The studies by Fitipaldi et al. [63] and Gloyn and Drucker [64] provide an overview of the evidence and barriers to the development and implementation of precision medicine in type 2 diabetes. Rodgers and Collins [65] connect precision medicine to nutrition. Rusek and Krasowska [66] examine noncoding RNA in systemic sclerosis as a valuable tool for translational and personalized medicine. Stankovic et al. [67] present fundamental principles behind machine learning modeling and its current application in Inflammatory Bowel Disease research with the focus on studies that explored genomic and transcriptomic data. Termine et al. [68] explore the use of Big Data through Artificial Intelligence in Neurodegenerative Diseases.

Along the same line of thought, Dorado-Díaz et al. [69] conducted a detailed PubMed search on the evolution of original contributions on AI to the various areas of application in cardiology in the last 5 years. They provide 19 detailed examples from distinct areas of cardiology that, by using AI, diagnostic and therapeutic improvements are possible.

Concerning oncology, Saadeh et al. [70] provide an overview of the components, processes, and resources available to apply precision medicine strategies to drug therapy in cancer medicine. Several resources are reviewed with an emphasis on oncology pharmacy practice that guide treatment options in oncology in relation to somatic mutations and pharmacogenomics. As an example, OncoKB is a precision oncology knowledge base for somatic mutations.

In addition, as mentioned by Arnall et al. [71] clinical pharmacists should integrate Precision Medicine Programs and Systems as part of oncology training and cancer care. Moving from Personalized to Precision Cancer Medicine will require the merging of the genome and transcriptome sequencing and editing technologies if we are to advance the prevention, diagnosis, and treatment of cancers [72–74].

In Table 1 the studies are grouped according to the main focus as it relates to eligibility criteria and searched keywords and phrases.

Overall, in Table 2 the present situation in Higher Education in reference to the required integration of Personalized Medicine into Health Care and Clinical Adoption is shown as a result of the literature review of this study. At the same time the benefits of Precision/Personalized Medicine and the major obstacles for all stakeholders involved are summarized as well as specific solutions are provided. Knowledge and perception of Medical and Pharmacy students towards Pharmacogenomics and Genetics is also presented [6, 8–10, 22, 27–29, 33, 34, 45, 51, 53–55, 59, 67, 74–77, 81–83, 85–107, 112, 113, 121].

**TABLE 1** List of studies in the present review grouped according to the main focus.

| References | Study focus |
| --- | --- |
| [1–17] | Introduction to Precision Medicine (PM) advances, current situation, knowledge gaps |
| [13, 19–26, 36, 38, 40–42, 44, 45, 59, 75–81] | PM and education, curricula, dissemination |
| [21, 25, 28, 30–34, 39, 40, 82–84] | PM and pharmacogenomics, drug development |
| [9, 13] | PM benefits and challenges |
| [8, 9, 15–17, 19, 29, 85, 86] | PM new initiatives and solutions, PM delivery, Big Data Analytics, Next Generation Sequencing |
| [27, 29, 46–50, 55, 63–66, 70–72, 87–101] | PM new treatments and therapies (cancer, gene therapy, CAR T-cell therapy, heart disease, metabolic disorders, neurodegenerative disorders |
| [43, 51–54, 56–58, 60–62, 67–69, 74, 97, 102–104] | PM and Artificial Intelligence (AI), Extended Reality, Deep Learning, Neural Networks |
| [54, 105–111] | PM and Healthcare |
| [35–37, 112, 113] | PM and ethics, legislation, diversity and inclusion |

## DISCUSSION

Precision Medicine or Personalized Medicine is an excellent example of a paradigm shift in the field of medicine and healthcare. There are countries that have already adopted the initiative even though in some there is the preference of one term over the other. For example, in the European Community, the term Personalized Medicine is preferred whereas in the US there is a shift to Precision Medicine term. In Figure 2 one can see how the various terms related to this approach are linked together and there is considerable overlap. For the remaining discussion, it is helpful if one remembers that Personalized Medicine is mostly a practice that manages one's health more holistically where prevention and treatment depend on the genes, lifestyle, and the environment. Precision Medicine on the other hand is perceived as the science of evidence-based medicine which is targeted therapy based on molecular diagnostics. However, both the science and the practice combined result in Precision Healthcare which in turn greatly influences the Healthcare System and all beneficiaries such as patients, physicians, researchers, students and the entire community of various stakeholders.

This review focused on presenting specific present and future applications related to personalized treatment. It also aimed to provide in-depth knowledge mainly to physicians, research scientists, students and decision makers engaged in "Precision Medicine" based on a set of good practices and strategies required in the training of "Precision Medicine" approach and will cover various areas including those related to the education of health professionals. For example, the study examined how data analysts use the developed computational methods to extract insights from next-generation sequencing (NGS), various technology and bioinformatics platforms, and high-throughput screening data [19] but also disseminated the importance of establishing the biological relevance of genomic and proteomic discoveries and related specific gene expression helping to achieve targeted therapy.

In addition, this study touched upon the current legislation and management which would be required for such adoption as it relates to diagnosis, treatment, safety, insurance, and privacy issues. Certain global case studies were selected as examples on how universities, governments, companies, and other stakeholders can effectively or not prepare their faculty, students, countries as a whole, and industries for precision medicine. It appears that new medical education approaches are necessary to keep up with the change, engaging all stakeholders within the health system who must be trained differently focusing on collaborative and multidisciplinary teamwork. Such stakeholders include administrators, educators, medical doctors, nurses, engineers, data analysts, modelers, and the patients. The success of the Precision Medicine approach in our societies will depend mainly on whether such challenges can be addressed through collaborative and shared efforts. So, as it is obvious in Figure 4 from the various data sources -omics, pathology, radiology, other types of imaging, EHRs there should be a flow of information to Data Commons which hosts all incoming data to the platform, from various disparate sources, to be then analyzed with advanced analytics and other tools after Institutional Review Boards (IRB) approvals and then pass into a research environment where aggregated data sets are approved for the user. Upon validation, the promotion of the process passes into a delivery platform where for better treatment algorithms, analytics, and clinical care best practices are shared as well as the impact and products that result. Engage and inform the patient and all stakeholders, secure privacy and safety clarify ethical, legal, and societal issues, and finally, show evidence of regulatory oversight. This last step feeds back to the original steps as there is a need for integration and improvement of efficiency and to close the loop.

It is a fact, that the emerging advances of "Next Generation Sequencing" and the rapid expansion of the Bioinformatics field and computational methods, "Data Mining" and "Machine Learning" will help us improve prognosis, diagnosis, and therapy of diseases but we also need to move from a data management organizational culture to

**TABLE 2**  Bridging education with Precision Medicine (PM) advances: The situation in Higher Education as it relates to major stakeholders.

| Facts-top priorities | Goals | Action |
|---|---|---|
| Students, faculty, clinicians, physicians, insurers, healthcare practitioners etc. are not all yet ready to implement the advances of Precision Medicine (PM) [78, 79] | Integrate PM into the curriculum and ensure every student and physician is trained in the use of medical and pharmacogenomic data and its applications | Mostly in pharmacology and in few medical programs the curricula are to be further modified to include Precision Medicine |
| Small amount of teaching time is dedicated to training in precision medicine overall [21, 80] | Lessen any disparities in access to genomic medicine and genetic counseling<br><br>Raise awareness on Human Health impacts | Need to expand the revision of additional science curricula<br><br>Leverage the best that science education can offer such as offering well-designed on-line courses, webinars, conferences but also create open resources for all stakeholders |
| Integrating Personalized Medicine into Medical Education, Health Care and Clinical Adoption is not yet fully implemented [114, 115] | Reshape health care systems in pursuit of Precision Medicine's benefits for the wellbeing of patients via proper education and training | Training needed at all levels<br><br>Increase resilience by educating all stakeholders<br><br>Improve understanding of health impacts<br><br>Focus on long-term planning and immediate action<br><br>Raise awareness on Human Health impacts and its integration with Precision Medicine |
| High out-of-pocket costs to patients for genetic testing [31, 84, 116] | Lessen any disparities in access to genomic medicine and genetic counseling | Make genetic and genomic services accessible and operational in all clinical settings |
| Primary care workforce may be unprepared to deliver genomic medicine to patients [111, 117] | | Improve service to diverse patient populations<br><br>Enable under-resourced diagnostic centers and clinics to easily transition toward personalized medicine<br><br>Examine the design of health insurance benefits by public and private payers and the type of reimbursement of genetic testing |
| New gene and cell therapies already exist which hold ever more potential to influence modern medicine [109, 118] | Recognize the importance of establishing the biological and drug discoveries in connection to environmental influences and exposures.<br><br>Help withstand global health issues and pandemics | Actions should focus on the impact on Human health and wellbeing due to genetic profile differences and sensitivities, exposures, pandemics, cancer or other genetic disorders and diseases and ensure smooth delivery of information |
| New collaborations and partnerships with governmental (state) and non-state actors are possible [119, 120] | Rethink of the finance and economics in connection to PM so we change the narrative and imagine instead a world of health and prosperity for the generations to come | New ways of communication, synergies and dissemination through proper educational training in PM, health and healthcare |
| Human wellness is not yet ensured [31, 116] | Maximize all efforts toward better health and healthcare, secure human well-being and prosperity | Engage all stakeholders in smart ways to enhance human wellness while at the same time safety, low cost, low side effects and trust are ensured<br><br>Focus on long-term planning and immediate action |
| Lack of longitudinal database registries [110, 111, 114] | Establish longitudinal database registries and train all related stakeholders | Establish biorepositories and registries for underprivileged and marginalized minorities<br><br>Set up clinical studies and population-based research projects serving underserved populations<br><br>Set up appropriate financial support programs |

**TABLE 2** (Continued)

| Facts-top priorities | Goals | Action |
|---|---|---|
| Policies and Regulations [110, 111, 117] | Reexamine policies and regulations related to Health and Healthcare | Upgrade policies and regulations |
| | | Engage and inform the patient and all stakeholders |
| | | Secure privacy and safety |
| | | Clarify ethical, legal and societal issues |
| | | Show evidence of regulatory oversight |
| | | Direct to consumer genetic tests |
| | | Enable cost coverage & reimbursement of diagnostic tests |
| IT and AI for Digital Health [54, 104, 110] | Connect ICTs and AI to Health and Healthcare | Invest on effective health care delivery infrastructure |
| | | Invest on hardware and software |
| | | Invest on advanced data management systems |
| | | Use best practices for health care delivery approaches, processes, and program operations |
| | | Smart use of a computerized decision support system, built seamlessly into the electronic medical record and workflow, could provide a solution |



**Diagnostic Testing-Assessment**

- Genetic and Genomic Biomarkers
- Proteomic Biomarkers
- Metabolomic Biomarkers
- Epigenetic factors
- Proteoforms

**Personalized Treatments**

- Targeted Therapeutics
- Immunotherapies
- Gene and Cell-Based Therapies (ex CAR-T cell therapy
- CRISPR/Cas9 Gene Editing

**IT for Digital Health**

- Invest on effective health care delivery infrastructure
- Invest on hardware and software
- Invest on advanced data management systems
- Use best practices for health care delivery approaches, processes, and program operations
- Revise medical curricula, train educators

**Policies and Regulations**

- Engage and inform the patients and all stakeholders especially educators and medical students
- Secure privacy and safety
- Clarify ethical, legal and societal issues
- Show evidence of regulatory oversight
- Direct to consumer genetic tests
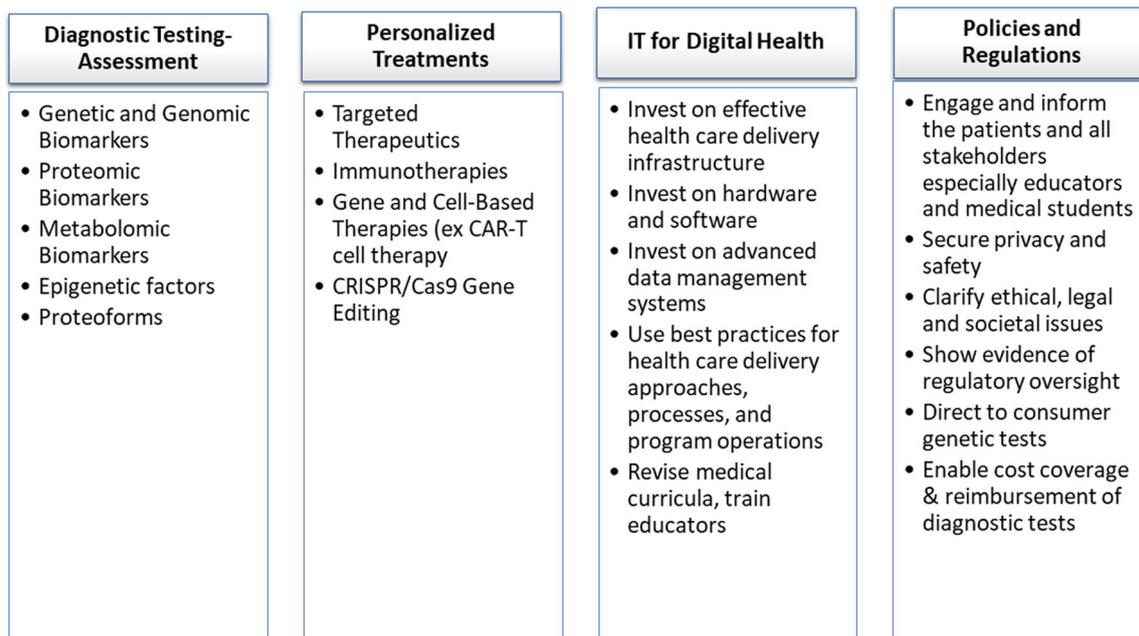- Enable cost coverage & reimbursement of diagnostic tests

**FIGURE 4** Integrating Personalized Medicine into health care and clinical adoption.

a learning organization culture [15]. This perspective requires better collaboration and communication to a wider community of stakeholders capable of integrating into their practices the Precision Medicine approach.

In this study we recognized two main future targets a) ways to improve the biomedical, medical, and healthcare programs and b) ways to help the transformation of the health institutions and services into globally leading healthcare

institutions that are in the position to provide precise and accurate clinical care.

Toward the fruition of those targets, an important contribution and outcome of this study is our proposed framework which gathers the main pillars of Precision Medicine and can be used as a start point in medical educational programs and the specific courses and internships that need to be developed for such training.

At this point, the greatest challenge to integrating personalized medicine into health care is a lack of education with accurate, trusted, and updated information. Freely available educational resources will help increase the level of awareness among patients and healthcare professionals so a number of organizations should continue developing such resources.

In the US mainly, since 2016 Pharmacists have taken a proactive approach to pharmacogenomics and precision medicine education and awareness. Pharmacogenomics and certification programs are common especially in Graduate programs. Such initiatives in pharmacology can serve as good examples of best practice in medical educational programs across the world.

Despite growing acceptance of the concept of patient empowerment, and engagement, responsibility, health orientation, and literacy are still quite low, not yet tailored to individual patient values, characteristics, and circumstances. It would be a great challenge for all stakeholders to effectively encourage this kind of engagement, but to also properly inform the policymakers and other decision-makers so the patients' concerns are alleviated especially when considering the collection of molecular information which may lead to privacy issues, discrimination, job loss, or loss of health insurance coverage.

As a means of employment protection against the misuse of genetic information in relation to health insurance in 2008, US Congress passed the Genetics Information Nondiscrimination Act. Similar acts and regulations are also being developed worldwide such as the EU Charter of Fundamental Rights, Article 21.1 prohibiting discrimination based on genetic features.

Infrastructure and Health Information Management has greatly improved worldwide by adopting Electronic Health Records (EHRs) across various clinical settings. Advances in the digitization of health information as in Electronic Health Records have been examined by a number of researchers as also by Abul-Husn and Kenny [108]. The establishment of EHR-linked population-based biobanks allow translational and implementation research within the context of personalized medicine.

Even though more than 85 percent of physicians in the United States use electronic health records, EHRs are often ill-equipped to process complex molecular information. To help electronic health record developers expand functionality, Health Level Seven (HL7), an organization committed to developing international standards, created the Fast Health Interoperability Resources program [122]. The specific clinical concepts and resources and the list of biomarkers to be included, will help health record developers manage the clinical data more efficiently [122]. It is obvious, early detection and intervention, based on predictive analytics can reduce healthcare costs and improve outcomes for patients, and certainly good electronic health records can also help to improve treatment and care coordination.

## CONCLUSION

It has become clear that the adoption of Precision Medicine requires an integrated approach which combines knowledge from genetic and molecular techniques, bioinformatics, medical informatics and good knowledge of healthcare information systems with various economic, social, political and cultural factors [15]. Bridging Precision Medicine with Medical Education via proper communication can positively contribute to disease and health problems prevention, screening, treatment, patient literacy, Digital Health, and Healthcare [16]. The results of the survey of US public opinion conducted for Personalized Medicine Coalition in 2018 indicate that despite the innovative efforts of researchers, educators, policymakers, and other stakeholders to facilitate the transition to Precision Medicine the American public has concerns related to privacy, security, and cost issues. Most Americans and other people around the world though recognize the value placed in innovative tools and solutions which will quickly identify the right treatment for the right patient but expect education and awareness to improve before the personalized medicines enter the market [13].

This study aimed to point out various integrated, precise, and data-driven smart solutions as key enablers toward this new era of Precision Medicine and biomedical science as supported by new medical education approaches, research, technology, and the development of policies that empower patients, researchers, and providers to work together toward development of this type of individualized care. The lack of proper medical education and advanced infrastructure are still major barriers to the adoption of Precision Medicine thus the role of medical training on Precision Medicine was also examined and analyzed in addition to providing specific application examples which were discussed in an integrated, precise, and data-driven manner to provide 'smart' solutions.

As previously pointed out by Papadopoulou et al. [15] smart data analysis will open new avenues if combined with declines in the cost of generating genomic and proteomic data. New jobs in healthcare systems will be created. Innovative business concepts such as telemedicine, remote sensors, and various mobile health solutions which maintain a reasonable balance between investment and profit would also be needed. High throughput technologies related to DNA sequencing, RNA- sequencing, protein analysis are already recognized of primary importance by scientists. Systems Biology and better health systems develop. What is essential to be done is that this effort needs to be communicated across biomedical sciences and medical schools' curricula.

The wide use of new gene-editing technologies such as CRISPR_Cas9 and CAR-T cell therapies together with initiatives like the Human Proteoform Project (an attempt to map the entire collection of proteins in the human body) proposed by the authors of

Smith et al. [8] are expected to transform the way diseases are treated since proteins are frequent drug targets. Proteoforms result from combinations of genetic polymorphisms, RNA splice variants, and various posttranslational modifications and such projects will greatly improve our understanding of interactions of biological complexes and networks and will accelerate the pace of biomedical research and discovery and to optimal use of health-related information/data for optimized treatment, care, prevention, and research.

Innovation in healthcare and transformation in medicine must be seen as a human-centric process where advanced medical services and processes are utilized and at the same time healthcare providers and citizens are well-informed and are engaged in a participatory and responsible way [123]. The challenges of that kind of adoption remain though, and the use of sophisticated information and communication technologies (ICTs) and the needs are to be considered carefully. In this paper, we have placed emphasis on how smart data and data analytics along with cognitive computing can add value and smart solutions related to Precision Medicine and healthcare. By offering a detailed, comprehensive, and comparative insight into diverse advances in gene and cell technologies and various ICTs and their application across issues and domains within the context of Precision Medicine, this review study contributes positively to the worldwide effort to embrace the best practices of this initiative and to further inform and serve well the medical and healthcare community.

## AUTHOR CONTRIBUTIONS

Paraskevi Papadopoulou conceptualized the review topic, formulated the research questions, performed the literature review search, did the analysis and drafted the article. Miltiadis Lytras assisted in the assessment of the included studies, in the ICT smart solutions needed and in the proposal of the overall framework and future directions. Paraskevi Papadopoulou prepared the manuscript for submission. Both authors contributed to the revision of the article.

## CONFLICTS OF INTEREST STATEMENT

The authors declare no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

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