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Narrative Review of Precision Medicine in Diabetes

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ABSTRACT

Precision medicine represents a transformative approach to diabetes prevention and management, emphasizing individualized strategies based on genetic, genomic, epigenetic, environmental, and physiological factors. This narrative review synthesizes current literature on precision medicine applications in type 1 and type 2 diabetes, highlighting patient stratification, multi-omic integration, pharmacogenomics, biomarker-guided diagnostics, and the utilization of digital health and real-world data. Evidence indicates that tailoring therapeutic interventions according to patient-specific characteristics can improve glycemic control, optimize drug efficacy, and reduce adverse drug reactions. In type 1 diabetes, precision approaches facilitate early detection, beta-cell preservation, and individualized immunomodulatory strategies, whereas in type 2 diabetes, multidimensional analyses and pharmacogenomics enhance phenotypic classification and treatment personalization. Despite promising advances, barriers remain, including heterogeneity in disease phenotypes, limited access to comprehensive datasets, inequities in health technology adoption, ethical and privacy concerns, and insufficient clinical implementation of pharmacogenomic insights. Future research should prioritize longitudinal cohort studies, standardized methodologies, integration of high-dimensional multi-omic datasets, and equitable deployment of digital health solutions. By addressing these gaps, precision medicine has the potential to enhance individualized care, improve clinical outcomes, and transform the management of diabetes across diverse populations.

Keywords: Precision medicine**,** Diabetes subtypes**,** Pharmacogenomics**,** Biomarkers and Digital health.

INTRODUCTION

Diabetes, a major global health problem, is expected to affect close to 600 million people by 2045. Precision medicine offers a paradigm shift in its prevention and management [1]. The term refers to a medical model emphasizing the prevention and treatment of disease based on characteristics specific to individual patients. Such traits may be genetic, genomic, environmental, or physiological. In fact, multiple definitions of precision medicine exist in the scientific literature, consistent with its evolving meaning [2]. Because precision medicine is the sum of a number of still-abiguous elements, the term should be preferred over personalized medicine, a fully-established concept in which the individual is generally the unit of investigation, intervention, and monitoring. Precision medicine has entered the diabetes research portfolio mainly for two reasons: the high heterogeneity of the disease and the large-scale availability of relevant data [2]. Diabetes is a multitriggered disorder characterized by differences in pathogenetic mechanisms, manifestation, natural course, intervention response, and complications [3]. Many epidemiological studies have demonstrated that multiple patients respond differently to the same antidiabetic compound. Both phenotypic and endotypic classifications currently cover an increasing number of diabetes forms called subtypes or endotypes, associated with specific pathogenetic mechanisms and different provisional and long-term intervention options[2]. These data could justify preventive measures that may delay, hinder, or even, in mono- or oligogenically trigger cases, fully inhibit diabetes onset [1].

Conceptual Foundations of Precision Medicine in Diabetes

Precise medicine for diabetes encompasses a framework on four fundamental building blocks: [1] targeted patient stratification classifies individuals into different subclasses underpinning differential risk for complications, treatment responses, or rates of disease progression; [2] extensive integration of omics data addresses patient heterogeneity to redefine existing substrate classes and creates an opportunity for improved stratification; [3] interoperability of foundational components in advanced analytics and informatics optimizes the clinical value derived from patient data necessary for the creation of real-world evidence, the transition from clinical research to routine practice, and generosity and speed of broader dissemination; and [4] a comprehensive set of translational pathways spanning clinical care, early detection, and therapy ties together the preventive, therapeutic, and predictive components of the advance, thereby enriching the specification of the prospect of precision medicine for diabetes[4]. Equitable opportunities to employ precision medicine for diabetes arise from the opportunity to manage the extremes of risk outside the insulin-treated population early-onset and late-onset types of diabetes before age 19 and 60, respectively 2 and provide for earlier intervention, be it in individuals destined for type 1 diabetes or glucocorticoid-induced type 2 diabetes [1].

Genetic, Epigenetic, and Molecular Determinants of Diabetes Subtypes

Classification of diabetes based on clinical attributes, age at onset, and metabolic dysfunctions has long served as the foundation for its diagnosis and management [4]. Specifically one widely adopted clinical taxonomy proposed in 1998 by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, has enabled timely initiation of disease-specific interventions. Nevertheless, emerging evidence underscores the extensive complexity that underlie diabetes and calls for an even deeper understanding of this condition [3]. Following the recognition that diabetes is not only a disorder of glucose homeostasis and skeletal system but also a multisystem disease marked by diverse etiology with significant interindividual variation, contemporary definitions suggested that diabetes is "a metabolic disorder or group of disorders of glucose homeostasis" [3]. The shift in understanding the pathophysiological basis of diabetes has further matured the concept of precision medicine in the field. Moreover, both well-established classification systems and new conceptual frameworks are needed to take full advantage of these innovative sciences to develop and apply tailored strategies to prevent and treat diabetes and its comorbidities in a timely manner [4].

Pharmacogenomics and Therapeutic Personalization

Pharmacogenomics is the study of the influence of genetic variants on the metabolism, efficacy, and safety of drugs. Individual genetic variations affect the pharmacokinetics and pharmacodynamics of drugs, modifying desired therapeutic effects and inducing adverse drug reactions (ADRs) [2]. Adverse drug reactions prolong hospital stays, contribute to costly medical expenses, and increase morbidity and mortality. Precise administration of the correct dosage of the appropriate therapy is of utmost importance in the management of diabetes [5]. Precision medicine is the application of omics technologies, data analysis, and artificial intelligence to subgroup diabetes for risk stratification and personalized management [5]. A pharmacy-medicine connection pharmacogenomics was established early in the development of precision medicine. Progress in pharmacogenomics has been rapid. In 1997, the U.S. Food and Drug Administration listed the first drug, warfarin, with pharmacogenomic information. Since then, several drugs have been introduced, and the list continues to grow while the supporting evidence becomes more robust [5]. Establishing precision pharmacogenomic treatments in the management of diabetes is considered important. The European pharmaco-genomics initiative PharmGKB provides drug–gene interactions to improve patient safety and efficacy and enhance precision pharmacogenomics therapy [3].The pharmacogenomics of diabetes drugs is reviewed [2]. Table 1 lists diabetes drugs and drug classes with pertinent pharmacogenomic information aiming to improve efficacy or safety. SGLT2 inhibitors (e.g., dapagliflozin, empagliflozin, canagliflozin) and GLP-1 receptor agonists (e.g., liraglutide, semaglutide, dulaglutide) were reported to exhibit pharmacogenomic influences on concentrations and clinical outcomes. Metformin remains the most widely prescribed antidiabetic medicine worldwide. Furthermore, CYP2C9 gene variants have been reported to influence drug response [4]. Even with drug gene connections existing among several diabetes medications, pharmacogenomic information has yet to enter practical clinical operation [4]. The limited number of studies, validation data, and single population evaluation restrict implementation. The ongoing activities at the University of California–San Diego, écoles Polytechnique fédérale de Lausanne, and Basel University aim to widen the spectrum of pharmacogenomic treatment regimens in diabetes[5].

Biomarkers and Diagnostic Stratification in Diabetes

Biomarkers associated with diabetes fall broadly into predictive (indicating future onset), diagnostic (determining current presence), and prognostic (enabling outcome forecasting) categories. Biomarkers often comprise multiple elements, as seen in panels or consideration within algorithms [4]. Use of multi-biomarker panels has increased in recent years, with limited real-world experimentation supporting their utility [5]. Diabetes biomarker types encompass genetic, metabolic, proteomic, and imaging data; these classes collaboratively facilitate risk stratification and refinement of subtype classification. Information on the integration of multi-biometric panels into clinical workflows highlights analytic validity, clinical validity, and clinical utility as core quality dimensions for meaningful adoption in routine practice [6].

Digital Health and Real-World Data in Precision Medicine

Digital health is progressively impacting the precision medicine concept. Wearable technology permits activity monitoring (e.g., step counters or heart-rate monitors) and blood-pressure measurement, to mention but few examples [5]. Remote auto-glucose monitoring can submit blood glucose levels and alert patients via mobile technology. Using Artificial Intelligence in that data permits predicting with precision the status of diabetes evolution, whether one may develop type 2 diabetes, the status of metabolism (even sub-class classes), the strategy to adopt (lifestyle, drugs, and so on), adverse events, and even billing-related conditions[4]. Hospital Electronic Health Record data are gigantic, making patient stratification by sub-groups possible [3]. Transmission with a clear understanding of data engineering also enables life-long follow-up in innovative trials or registries [2]. Various Health Authorities provide recommendations to improve precision medicine, providing data governance Transfer Guidelines, Bioss/authorship recommendation, quality rating, consistency, and cadence in order to transmit meaningful real-world data [2].

Precision Medicine in Type 1 Diabetes

Type 1 Diabetes (T1D) is characterized by the autoimmune destruction of beta cells, leading to absolute insulin deficiency and multiple complications. T1D is not a single entity; evidence from longitudinal studies indicates different forms of T1D with distinct clinical courses [1]. Precision medicine offers the possibility to exploit this heterogeneity to generate tailored interventions. Longitudinal studies of individuals who have developed T1D show different clinical courses characterized by the dynamics of C-peptide secretion over the first years of the disease [4]. Longitudinal studies of individuals who have developed T1D show different clinical courses characterized by the dynamics of C-peptide secretion over the first years of the disease. The knowledge of the disease trajectory allows the stratification of individuals into different clinical stages: (1) Stage 0, people at risk of T1D, (2) Stage 1, people with clinical T1D diagnosed at the pre-symptomatic stage, and (3) Stage 2, individuals with overt T1D [6]. They also offer a viable route to C-peptide preservation, an essential end-point for maintaining normoglycaemia for the longest period possible. The additional possibility of immunomodulation or cell-based therapies (involving beta-cell replacement or the restoration of a normal beta-cell function) offers a more complete protection against multiple co-morbidity and life-long insulin dependency [6]. More accurate diabetes risk scores may help with pre-emptive information. Continuous glucose monitors combined with smartphones allow real-time data collection: advanced algorithms process both static and dynamic data to individualize insulin delivery[4]. Heterogeneity also arises from the longevity of endogenous insulin secretion (C-peptide-positive versus C-peptide-negative). C-peptide status highly influences preventive strategies aimed at insulating beta cells, and closed-loop delivery systems need to be adapted accordingly. Progress toward precision medicine is occurring worldwide [2].

Precision Medicine in Type 2 Diabetes

Diabetes is a global health concern due to its increasing prevalence and comorbid conditions. Because diabetes is a heterogeneous disease with diverse pathophysiological mechanisms, it is challenging to provide precise treatment. Earlier patient-centered diabetes treatment strategies focused on glycaemic control and involved pharmacological treatments such as metformin, glucagon-like peptide-1 receptor agonists, and sodium-glucose cotransporter-2 inhibitors [3]. However, glycaemic control is insufficient for effective prevention of complications such as retinopathy and cardiovascular disease. Consequently, the concept of precision medicine has emerged, whereby phenotypes (or endotypes) are determined and treatment is tailored accordingly [2]. There are two main precision medicine approaches for diabetes: (1) multidimensional analysis to identify subgroups based on clinical, laboratory, and concomitant diseases and (2) pharmacogenomics for drug response prediction based on individual genetic and epigenetic variations [1]. To summarise, precision medicine in diabetes comprises multidimensional analyses to identify different phenotypes and pharmacogenomics to maximise the effectiveness of drugs [2].

Barriers, Ethical Considerations, and Health Equity

The movement towards precision medicine offers new approaches for diabetes management. However, limitations of the data currently used in diabetes precision medicine demand cautious optimism, as many implementation challenges remain [3]. These include the intricacies of diabetes phenotype and endotype definitions in a broad and heterogeneous population, limited access to expansive phenotype data, minimal knowledge of gene–lifestyle interactions, and the multi-disciplinary expertise required to analyze data across diverse domains. These issues are further compounded by widespread inequities in precision health access and implementation [1]. Cost of generative AI presents similar challenges for diabetes precision medicine. Constraints surrounding patient anonymization, data storage and transfer security, demonstration of valid generalization across decentralized platforms, and content ownership during model training and fine-tuning require clear remediation to reduce the extent of both intentional and unintentional patient harm. A "Digital Health Equity" framework could help ensure that data generated through health and consumer devices reach populations in need of enhanced access to health and well-being supports [7]. Alongside the scaling of regional oversight mechanisms, community ownership of data-hub frameworks with transparency protocols detailing access entry points, aggregated data reconfiguration processes, and settings for user anonymity should also be encouraged. Stellar initiatives emerging within the digital health infrastructure seek to bolster privacy protection, algorithm accountability [5], and filtering against detrimental expression through both peer-to-peer platforms and federated data learning avenues. Standardization of existing electronic health record data and the concise development of regulatory standards, workflow consultative services, and open-source algorithms arrayed within community and institutional repositories can further strengthen collaboration towards equitable applied access [6].

Future Directions and Research Priorities

Rapid technological and scientific advances offer unprecedented opportunities for precision medicine in diabetes [1]. Efforts to stratify patients and to target interventions accordingly advance the paradigm of personalized medicine, which seeks to tailor approaches based on individual characteristics [7]. However, despite mobilizing considerable investment and scholarly enthusiasm, the diabetes community remains far from authentic precision medicine, "the use of data of multiple types to define the best prevention or therapy for any individual" [3]. As a step toward this objective, a systematic narrative literature review is warranted to synthesize contemporary knowledge. The systematic review identifies mechanisms that contribute to the heterogeneous diabetes phenotype, stratification according to clinical features, multi-omic integration of high-dimensional datasets, epidemiological and translational frameworks that link clinical data with mechanisms of disease, and discussion of proprietary algorithms [7]. Mapped to these themes, a central priority for the community is to advance knowledge of how diabetes by epidemic subtype, including type 1 diabetes and type 2 diabetes, links to prevention, therapeutic selection, and anticipated clinical course[5-13]. Criteria to further expand the evidence base, in turn enabling richer exploration of the clinical implications of diabetes heterogeneity, form another of the systematic review's outputs. Priorities involve improved standardization of methodologies and terminologies across multidisciplinary domains, collaborative collection and sharing of data to establish clinically relevant datasets, development of integrated high-dimensional data-analytic frameworks for linking heterogeneous data to heterogeneous disease, and direct implementations that allow patients and clinicians to access the practical benefits of the emerging knowledge. Implementation relies on complementary frameworks for building knowledge of population-wide variations and their implications across the diabetes spectrum [14-16]. Opportunities for collaborative networks, randomized controlled trials, and cohorts that leverage routine collection of detailed population-wide data and immutably recorded biospecimen material can stimulate discussions around target questions and decisions, availability of funding, degree of multi-omic integration, and whether to initiate a population-wide longitudinal study of diabetes in childhood, for example. Some consensus-driven opportunities for coordinated work among established and emerging researchers are thus left open to further consideration [5].

CONCLUSION

Precision medicine offers a paradigm shift in diabetes management by enabling interventions tailored to individual biological and environmental characteristics. Through patient stratification, multi-omic integration, pharmacogenomic-guided therapy, and digital health monitoring, precision approaches improve glycemic control, optimize drug efficacy, and support early detection and prevention strategies. In type 1 diabetes, precision medicine facilitates preservation of beta-cell function and individualized immunomodulatory strategies, while in type 2 diabetes, it enhances phenotypic classification and treatment personalization. However, significant challenges remain, including the need for standardized methodologies, equitable access to technology and data, ethical considerations surrounding privacy and consent, and the translation of research findings into clinical practice. Future directions should focus on large-scale, longitudinal studies, high-dimensional data integration, real-world implementation frameworks, and multi-disciplinary collaboration. Addressing these challenges will allow precision medicine to realize its potential, improving clinical outcomes and enabling truly individualized diabetes care for diverse populations worldwide.

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