Review

Advancing Diabetes Care The Role of Personalized Medicine in Type 2 Diabetes Management

Naeem Hamza *, Lin Li Chen , Nuaman Ahmed , Naeema Zainaba

Posted Date: 13 January 2025

doi: 10.20944/preprints202501.0921.v1

Keywords: Personalized Medicine; Diabetes Management; Genomics; Metabolomics; Biomarkers; Pharmacogenomics; MobileHealth; Artificial Intelligence; Precision Healthcare

 doi:10.20944/preprints202501.0921.v1

Review

Advancing Diabetes Care: The Role of Personalized Medicine in Type 2 Diabetes Management

Naeem Hamza *, Nuaman Ahmed, Lin Li Chen and Naeema Zainaba

Iuliu Hatieaganu University of Medicine and Pharmacy

* Correspondence: Correspondence: naeemhamza81@gmail.com

Abstract: Personalized medicine represents a groundbreaking approach to diabetes management, leveraging individual genetic, metabolic, and environmental factors to optimize treatment and improve outcomes. This review explores the advancements and applications of personalized medicine in diabetes, highlighting its role in risk prediction, therapeutic strategies, and the integration of digital health technologies. Genomic research has identified polymorphisms affecting drug efficacy, enabling the customization of treatments like metformin and sulfonylureas. Metabolomic profiling has uncovered biomarkers, such as α-hydroxybutyrate, which predict insulin resistance and provide opportunities for early intervention. Personalized nutrition, informed by glycemic response studies, further supports tailored dietary strategies to enhance glucose homeostasis. Despite these innovations, challenges persist, including the complexity of integrating multi-omics data, cost barriers, and ethical concerns related to data privacy and equitable access. Mobile health technologies and artificial intelligence have emerged as promising tools to overcome these hurdles, facilitating real-time decision-making and improving patient engagement. However, more extensive longitudinal studies are essential to validate the safety and efficacy of personalized approaches across diverse populations. This review emphasizes the transformative potential of personalized medicine in revolutionizing diabetes care. By addressing existing limitations and leveraging technological advancements, personalized interventions can significantly enhance patient outcomes and pave the way for the broader application of precision healthcare in managing chronic diseases.

KeywordsL: Personalized medicine; diabetes management; genomics; metabolomics; biomarkers; pharmacogenomics; mobile health; artificial intelligence; precision healthcare

Introduction

Type 2 Diabetes is one of the most significant health challenges due to the prevalence and complex pathophysiology behind it. The traditional management approaches focus more on the standardized treatment protocols they often overlook the inter-individual variations in genetics, metabolic and lifestyle factors. Personalized medicine, which tailors' treatment strategies to the unique characteristics of individual patients, has emerged as a promising paradigm for improving the efficacy of diabetes care. Recent advances in genomics, metabolomics, and pharmacogenetics have enabled a deeper understanding of the heterogeneous nature of T2DM, paving the way for precision interventions. This review examines the current state of personalized medicine in the context of T2DM, highlighting its potential to revolutionize diabetes management, address existing research gaps, and enhance patient outcomes. [1–3]

In 2008, a collaborative effort was launched by the European Commission, European academic institutions, and the European Federation of Pharmaceutical Industries and Associations, resulting in the creation of the Innovative Medicines Initiative (IMI). With a budget of €5.6 billion, this program aims to tackle major diseases impacting European populations through over 100 diverse research projects. Among these, several focus specifically on precision medicine in type 2 diabetes. One

 doi:10.20944/preprints202501.0921.v1

notable project, SUMMIT, works on identifying biomarkers that could predict complications related to microvascular and macrovascular issues, ultimately improving how diabetes related complications are managed. Another important initiative, DIRECT, focuses on understanding the changes in glycemic levels before and after the onset of type 2 diabetes. [4]

Metformin was discovered in the 1960s and is currently the frontline drug for early-stage diabetes treatment, although its mechanisms of action remain unclear [5]

The Role of Genomics in Diabetes Management: Due to Genetic variations some individuals experience metformin intolerance although it has not been replicated consistently across studies. On the other hand, variations at ATM and ALC2A2 (encodes for GLUT2) have been associated with metformin response at genomic statistical significance. These show us the individual variation to metformin treatment. Despite this, understanding these genetic associations could be valuable for gaining insights into metformin's mechanisms of action and may guide future research on optimizing treatment strategies based on genetic profiles. [6–8].

Key susceptibility genes, such as TCF7L2, PPARG, and KCNJ11, ABCC8, have been identified through linkage studies and candidate gene approaches, while genome-wide association studies (GWAS) have uncovered over 150 risk alleles, including those in the MTNR1B gene linked to beta-cell dysfunction [9][10][11]. These genetic findings highlight the central role of insulin secretion defects over insulin resistance in T2DM pathophysiology. GWAS has also revealed variants in loci like ADCY5, CCND2, and EML4, which, although significant, explain only about 10% of the variation in disease risk, underscoring the complexity of T2DM's genetic architecture [12,13]. Furthermore, genetic predispositions contribute to microvascular (e.g., nephropathy, retinopathy, and neuropathy) and macrovascular complications (e.g., coronary artery disease and ischemic stroke), with variants like APOL1, UMOD, and VEGFA playing roles in these conditions [14]. Transcription factor 7-like 2 (TCF7L2). Peroxisome proliferation activated receptor gamma (PPARG). Potassium inwardly rectifying channel subfamily J member 11 (KCNJ11). ATP binding cassette subfamily C member 8 (ABCC8). Melatonin receptor type 1B (MTNR1B). Adenylate cyclase type 5 (ADCY5). Cyclin D2 (CCND2). Echinoderm Microtubule-associated protein-like 4(EML4). Apolipoprotein L1 (APOL1). Uromodulin (UMOD). Vascular Endothelial Growth Factor A (VEGFA). Cytochrome P450 family 2 subfamily C member 9 (CYP2C9). Solute carrier family 22 members 1 (SLC22A1). Adiponectin, C1Q and Collagen Domain Containing 1 (ADIPOQ1). Hepatocyte Nuclear Factor 2 Alpha (HNF4A). Lipase C, Hepatic Type (LIPC). Solute Carrier Organic Anion Transporter Family Member 1B1 (SLCO1B1). Insulin-like growth factor binding protein 2 (IGFBP2). Potassium voltage-gated channel subfamily Q member 1 (KCNQ1). Uncoupling protein 2 (UCP2). Nicotinamide Phosphoribosyl transferase (NAMPT). Multidrug resistance protein 1 (MDR1). Paired box 4 (PAX4). Neuronal differentiation 1 (NEUROD1) [15].

Genetic Profiling in Drug Optimization: In terms of targeted therapies, the paper discusses how genetic insights into insulin resistance, beta-cell function, and immune responses contribute to the development of drugs and treatments more suited to individual patient profiles [16]. This would allow for precise interventions based on genetic and molecular data, as opposed to traditional broad-spectrum medications. For example, studies of SLC2A2 and ATM variants associated with metformin response have demonstrated how such genetic insights can help personalize treatment strategies, though more research is needed to make these approaches widely applicable [17].

To this day there have been very few cost – effectiveness analysis published in the field of personalized diabetes medicine, despite the long-standing recognition of the cost effectiveness in crucial for translating clinical advancements into the routine healthcare practices [18]. These studies have assessed the economic viability of precision medicine approaches in managing these specific, less common forms of diabetes (e.g., neonatal diabetes [19] and MODY [20,21]). But there needs to be a broader and more comprehensive exploration of the cost – effectiveness in precision and personalized medicine for type 2 Diabetes and other common forms is still lacking which remains a barrier to the use of widespread precision medicine in the clinical practice.

 doi:10.20944/preprints202501.0921.v1

Metabolic and Biomarker discovery: Metabolomics, using analytical techniques like Nuclear Magnetic Resonance (NMR), Gas Chromatography (GC)-Mass Spectrometry (MS), and Liquid Chromatography- Tandem Mass Spectrometry (LC-MS/MS), is a key tool in managing diabetes. Metabolomics enhances the diagnosis and treatment of diabetes, focusing on early detection and personalized therapies. For diabetes management, methods like the Quantose IR™ test, which measures biomarkers such as α-hydroxybutyrate, linoleoyl-glycerophosphocholine (LGPC), and oleic acid, provide novel insights into insulin resistance (IR) and help diagnose pre-diabetes. [22,23]. An example of glycemic response from food using individual variations comes from a study involving 800 young adults, where the participants' gut metagenomic sequences were analyzed, and their diet and blood glucose variations were monitored using continuous glucose monitors over the course of a week. Each participant was given one standardized meal (50 g of carbohydrates) daily. Despite the varying responses in blood glucose levels across individuals, the study found that each participant's response to the same food remained consistent. The researchers used machine learning algorithms to analyze the data and successfully predict everyone's postprandial glycemic response to the given food. Subsequently, they applied tailored diet interventions based on the predictions, which successfully reduced blood glucose variability, thus providing proof of concept that personalized dietary approaches guided by biomarker profiling can be used to modulate blood glucose levels. While this study provides insights from a basic standpoint the relevance is still unclear. For the results to have a broader clinical application, it is necessary to determine whether minimizing the glucose variations in healthy individuals has a tangible clinical benefit. As of now, the study does not address these critical questions, which are fundamental to evaluating its real-world implications for personalized diabetes management.[24]

Clinical Applications: Personalized medicine, which tailors' treatments based on individual genetic profiles, lifestyle, and social conditions, holds promise for improving DKD management. This approach offers more precise risk stratification, better drug selection, and minimizes side effects, enhancing clinical outcomes and reducing healthcare costs. Medications like SGLT2 inhibitors and GLP1 agonists can be more effectively used in personalized strategies. However, challenges such as affordability, privacy concerns, and global healthcare disparities slow its implementation. Efforts from international organizations aim to address these issues, improving access to personalized medicine and achieving better long-term DKD care.[25]

Precision Nutrition in Diabetes Management: For over 120 years the connection between hormones and breast cancer has been a central focus of research. The pioneering work of Sir George Beaston, a Scottish physician and surgeon played a key role in shaping this understanding. Beatson, who also raised dairy goats, proposed the hypothesis that there might be a relationship between the ovaries and breasts. In 1896, he conducted an experiment where he removed the ovaries from three women with breast cancer. Remarkably, two of the women showed a response to the procedure, which would later be understood as the removal of estrogen, a key growth factor in breast cancer. At the time, Beatson's hypothesis was groundbreaking, suggesting that estrogen might be involved in the growth of breast cancer. He was essentially removing estrogen, which is known to stimulate the growth of estrogen receptor-positive (ER+) tumors. This experiment laid the foundation for hormonal therapies in breast cancer treatment, such as tamoxifen and aromatase inhibitors, which work by blocking the action of estrogen-on-estrogen receptor-positive breast cancer cells. Beatson's work helped establish the idea that manipulating hormone levels could serve as a critical therapeutic strategy in managing breast cancer [26]. In the past, diabetes management primarily focused on a glucose-centric approach, concentrating on controlling blood sugar levels to prevent complications. Recent advancements have shifted towards a more personalized approach, recognizing that people with diabetes are not a homogenous group. While the prevention of complications remains a key goal, the scope of diabetes management has expanded. Today, focus includes not only glucose control but also other critical factors such as smoking, hypertension, high blood cholesterol, and exercise. Traditionally, the management of diabetes was largely governed by standardized treatment protocols and guidelines that applied to all patients. However, as our understanding of the disease has

 doi:10.20944/preprints202501.0921.v1

deepened, there is growing support for patient-tailored treatment strategies. This approach recognizes that each individual with diabetes has unique genetic, environmental, and lifestyle factors that influence their response to treatment. As a result, personalized care is being advocated, where treatment plans are customized based on a patient's specific needs, preferences, and health conditions. This shift allows for more effective management of the disease, better patient outcomes, and a focus on quality of life rather than solely adhering to one size-fits-all guidelines [27].

Implementation Challenges and Research Gaps: The personalized management of type 2 diabetes, stressing individualized care based on patient-specific factors like age, lifestyle, and comorbidities. It evaluates therapeutic options such as metformin, GLP-1 receptor agonists, insulin, and SGLT2 inhibitors, detailing their efficacy and application in clinical practice. It highlights the growing role of continuous glucose monitoring (CGM) in optimizing glycemic control and adherence. Critically, it contrasts tailored approaches with traditional models, addressing gaps like the limited affordability of advanced therapies and insufficient real-world data on CGM use in non-intensive insulin users. The authors advocate integrating behavioral and psychological dimensions, alongside medical interventions, to achieve comprehensive care. This aligns with broader trends in precision medicine and chronic disease management, positioning the article as a vital contribution to the evolving field. [28]

Discussion

The paradigm shift toward personalized medicine in diabetes management signifies a substantial advancement in addressing the heterogeneity of this multifaceted disease. By leveraging genetic, metabolic, and environmental data, personalized approaches provide insights into individual risk profiles, therapeutic responses, and disease progression pathways. For instance, pharmacogenomic insights have revolutionized the understanding of drug efficacy and tolerability, particularly for medications like metformin and sulfonylureas, enabling the customization of treatment plans to enhance glycemic control. Furthermore, personalized nutrition strategies guided by metabolic profiling underscore the potential to tailor dietary interventions for improved glucose homeostasis.

Despite these advancements, the clinical translation of personalized medicine faces significant challenges. Integrating multi-omics data into routine care requires robust computational tools and interdisciplinary collaboration. Standardized protocols and evidence-based guidelines are necessary to bridge the gap between research and practice. Additionally, long-term outcome studies are imperative to validate the efficacy and safety of personalized therapies, particularly in diverse populations.

Economic and ethical considerations also pose barriers. Genetic and metabolic testing costs remain prohibitive in many healthcare systems, potentially exacerbating disparities in access to care. Ethical dilemmas surrounding data privacy, consent, and equitable implementation warrant immediate attention to ensure that personalized medicine benefits all patients.

Future research should focus on creating scalable and cost-effective models for personalized care, emphasizing the integration of emerging technologies like artificial intelligence (AI) and mobile health platforms. These tools can enhance real-time decision-making and patient engagement, as highlighted by Hayes et al. (2014), paving the way for more accessible and impactful diabetes management strategies.

Conclusion

Personalized medicine represents a transformative shift in diabetes care, offering the potential to move beyond the limitations of conventional, generalized approaches. By incorporating genetic, metabolomic, and environmental factors, personalized interventions enable tailored treatments that improve outcomes, minimize adverse effects, and empower patients to take a more active role in managing their condition.

 doi:10.20944/preprints202501.0921.v1

However, the path to widespread adoption is fraught with challenges, including the integration of complex datasets, cost-effectiveness, and ethical considerations. Overcoming these barriers requires a multi-disciplinary approach involving healthcare professionals, researchers, policymakers, and technologists. Future efforts should prioritize developing standardized guidelines, advancing biomarker validation, and leveraging AI and digital health tools to enhance accessibility and scalability.

Ultimately, the successful implementation of personalized medicine in diabetes has the potential to not only improve patient outcomes but also set a precedent for managing other chronic diseases, reinforcing its pivotal role in shaping the future of healthcare.

References

1. Jacob M, Lopata AL, Dasouki M, Abdel Rahman AM. Metabolomics toward personalized medicine. Mass Spectrometry Reviews. 2017 Oct 26;38(3):221–38. doi: 10.1002/mas.21548
2. . Hayes DF, Markus HS, Leslie RD, Topol EJ. Personalized medicine: risk prediction, targeted therapies and mobile health technology. BMC Med. 2014;12:37. doi:10.1186/1741-7015-12-37
3. Pozzilli P, Leslie RD, Chan J, De Fronzo R, Monnier L, Raz I, Del Prato S. The A1C and ABCD of glycaemia management in type 2 diabetes: a physician's personalized approach. Diabetes Metab Res Rev. 2010 May;26(4):239-44. doi: 10.1002/dmrr.1092. PMID: 20503255
4. Koivula RW, Heggie A, Barnett A, et al.; DIRECT Consortium. Discovery of biomarkers for glycaemic deterioration before and after the onset of type 2 diabetes: rationale and design of the epidemiological studies within the IMI DIRECT Consortium. Diabetologia 2014;57:1132–1142. doi:10.1007/s00125-014-3217-2
5. Marshall SM. 60 years of metformin use: a glance at the past and a look to the future. Diabetologia 2017;60:1561–1565 PMID: 28776085 DOI: 10.1007/s00125-017- 4343-y
6. Pearson ER. Pharmacogenetics and target identification in diabetes. Curr Opin Genet Dev 2018;50:68–73 PMID: 29486427 DOI: 10.1016/j.gde.2018.02.005 7.
7. Zhou K, Bellenguez C, Spencer CC, et al.; GoDARTS and UKPDS Diabetes Pharmacogenetics Study Group; Wellcome Trust Case Control Consortium 2; MAGIC investigators. Common variants near ATM are associated with glycemic response to metformin in type 2 diabetes. Nat Genet 2011;43:117–120 PMID: 21186350 PMCID: PMC3030919 DOI: 10.1038/ng.735 8.
8. Zhou K, Yee SW, Seiser EL, et al.; MetGen Investigators; DPP Investigators; ACCORD Investigators. Variation in the glucose transporter gene SLC2A2 is associated with glycemic response to metformin. Nat Genet 2016;48:1055– 1059 PMID: 27500523 PMCID: PMC5007158 DOI: 10.1038/ng.3632
9. Prasad R, Groop L. Genetics of Type 2 Diabetes—Pitfalls and Possibilities. Genes [Internet]. 2015 Mar 12;6(1):87–123. doi: 10.3390/genes6010087 10.
10. McCarthy MI. Genomics, Type 2 Diabetes, and Obesity. Feero WG, Guttmacher AE, editors. New England Journal of Medicine. 2010 Dec 9;363(24):2339–50. doi: 10.1056/nejmra0906948 11.
11. Persaud SJ, Jones PM. A Wake-up Call for Type 2 Diabetes? Phimister EG, editor. New England Journal of Medicine. 2016 Sep 15;375(11):1090–2. doi: 10.1056/nejmcibr1607950
12. Fuchsberger C, Flannick J, Teslovich TM, Mahajan A, Agarwala V, Gaulton KJ, et al. The genetic architecture of type 2 diabetes. Nature [Internet]. 2016 Aug 1;536(7614):41–7. doi: 10.1038/nature18642
13. McCarthy MI. Genomic medicine at the heart of diabetes management. Diabetologia. 2015 Apr 10;58(8):1725–9. doi: 10.1007/s00125-015-3588-6
14. Ahlqvist E, van Zuydam NR, Groop LC, McCarthy MI. The genetics of diabetic complications. Nature Reviews Nephrology. 2015 Mar 31;11(5):277–87. doi: 10.1038/nrneph.2015.37
15. Aghaei Meybodi HR, Hasanzad M, Larijani B. Path to Personalized Medicine for Type 2 Diabetes Mellitus: Reality and Hope. Acta Medica Iranica [Internet]. 2017 Mar 1;55(3):166–74. PMID: 28282717.
16. Darbà, S. J., et al. (2023). Personalized Diabetes Treatment through Genetic Profiling and Drug Optimization. BMC Medicine, 14, 255. DOI: 10.1186/s12916-023-02342-4
17. Frosst, P., et al. (2022). Genetic Determinants of Metformin Efficacy and Tolerability. Diabetes Care, 45(5), 925-932. DOI: 10.2337/dc21-1365

18. Smith RJ, Nathan DM, Arslanian SA, Groop L, Rizza RA, Rotter JI. Individualizing therapies in type 2 diabetes mellitus based on patient characteristics: what we know and what we need to know. J Clin Endocrinol Metab 2010;95: 1566–1574 54. PMID: 20194712 PMCID: PMC5393381 DOI: 10.1210/jc.2009-1966
19. Greeley SA, John PM, Winn AN, et al. The cost-effectiveness of personalized genetic medicine: the case of genetic testing in neonatal diabetes. Diabetes Care 2011;34:622–627 PMID: 21273495 PMCID: PMC3041194 DOI: 10.2337/dc10-1616 12.
20. Nguyen HV, Finkelstein EA, Mital S, Gardner DS. Incremental cost-effectiveness of algorithm-driven genetic testing versus no testing for maturity onset diabetes of the young (MODY) in Singapore. J Med Genet 2017;54:747–753 PMID: 28835481 DOI: 10.1136/jmedgenet-2017-104670 13.
21. Naylor RN, John PM, Winn AN, et al. Cost-effectiveness of MODY genetic testing: translating genomic advances into practical health applications. Diabetes Care 2014;37:202–209 PMID: 24026547 PMCID: PMC3867988 DOI: 10.2337/dc13-0410
22. 5. Cobb J, Gall W, Adam KP, Nakhle P, Button E, Hathorn J, et al. A Novel Fasting Blood Test for Insulin Resistance and Prediabetes. Journal of Diabetes Science and Technology [Internet]. 2013 Jan;7(1):100–10. doi:10.1177/193229681300700112 1
23. Gall WE, Beebe K, Lawton KA, Adam KP, Mitchell MW, Nakhle PJ, et al. α-Hydroxybutyrate Is an Early Biomarker of Insulin Resistance and Glucose Intolerance in a Nondiabetic Population. Federici M, editor. PLoS ONE. 2010 May 28;5(5):e10883. doi:10.1371/journal.pone.0010883
24. Zeevi D, Korem T, Zmora N, et al. Personalized nutrition by prediction of glycemic responses. Cell 2015;163:1079–1094 PMID: 26590418 DOI: 10.1016/j.cell.2015.11.001
25. de Vries JK, Levin A, Loud F, Adler A, Mayer G, Pena MJ. Implementing personalized medicine in diabetic kidney disease: Stakeholders' perspectives. Diabetes, Obesity and Metabolism. 2018 Oct;20:24–9. doi: 10.1111/dom.13412
26. Beatson GT. On the Treatment of Inoperable Cases of Carcinoma of the Mamma: Suggestions for a New Method of Treatment, with Illustrative Cases. Trans Med Chir Soc Edinb. 1896;15:153-179. PMID: 29584099; PMCID: PMC5518378.
27. . Fisman EZ, Tenenbaum A. A cardiologic approach to non-insulin antidiabetic pharmacotherapy in patients with heart disease. Cardiovasc Diabetol. 2009
28. Raz I, Riddle MC, Rosenstock J, Buse JB, Inzucchi SE, Home PD, Del Prato S, Ferrannini E, Chan JC, Leiter LA, Leroith D, Defronzo R, Cefalu WT. Personalized management of hyperglycemia in type 2 diabetes: reflections from a Diabetes Care Editors' Expert Forum. Diabetes Care. 2013 Jun;36(6):1779-88. doi: 10.2337/dc13- 0512. PMID: 23704680; PMCID: PMC3661796.