

PRECISION BIOSIMILAR THERAPY IN TYPE 2 DIABETES: AN AI-GLYCEMIC DATA INTEGRATION APPROACH

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Abstract

Integrating patient-specific glycemic data with artificial intelligence (AI) models provides a modern approach to guiding biosimilar selection in type 2 diabetes treatment. The framework begins with the collection of patient-level data, including HbA1c values, fasting and postprandial glucose fluctuations, body mass index, age, comorbidities, renal and hepatic function, as well as prior treatment history and response patterns. These multidimensional datasets serve as critical inputs for the AI-driven system. Within the processing layer, machine learning algorithms analyze glycemic variability in conjunction with clinical parameters to create predictive models that forecast insulin responsiveness, safety profiles, and risk of adverse outcomes such as hypoglycemia. This computational step also enables a comparative assessment of available biosimilar insulins, evaluating their efficacy, safety, immunogenicity, and cost-effectiveness in the context of the individual patient profile. The decision-support layer translates these predictions into actionable recommendations, offering clinicians a personalized biosimilar insulin selection and optimized dosing strategy. This AI-driven guidance ensures that the therapy aligns closely with the patient's metabolic needs while minimizing risks and maximizing therapeutic benefit. Finally, the outcome layer emphasizes the clinical advantages of this integration: improved glycemic control, reduced adverse drug events, enhanced adherence, and lower overall treatment costs. Importantly, by aligning biosimilar selection with individualized patient profiles, this approach not only supports precision medicine in diabetes management but also enhances accessibility to affordable therapies without compromising safety or efficacy.

Precision Biosimilar Therapy in Type 2 Diabetes:
An AI-Glycemic Data Integration Approach

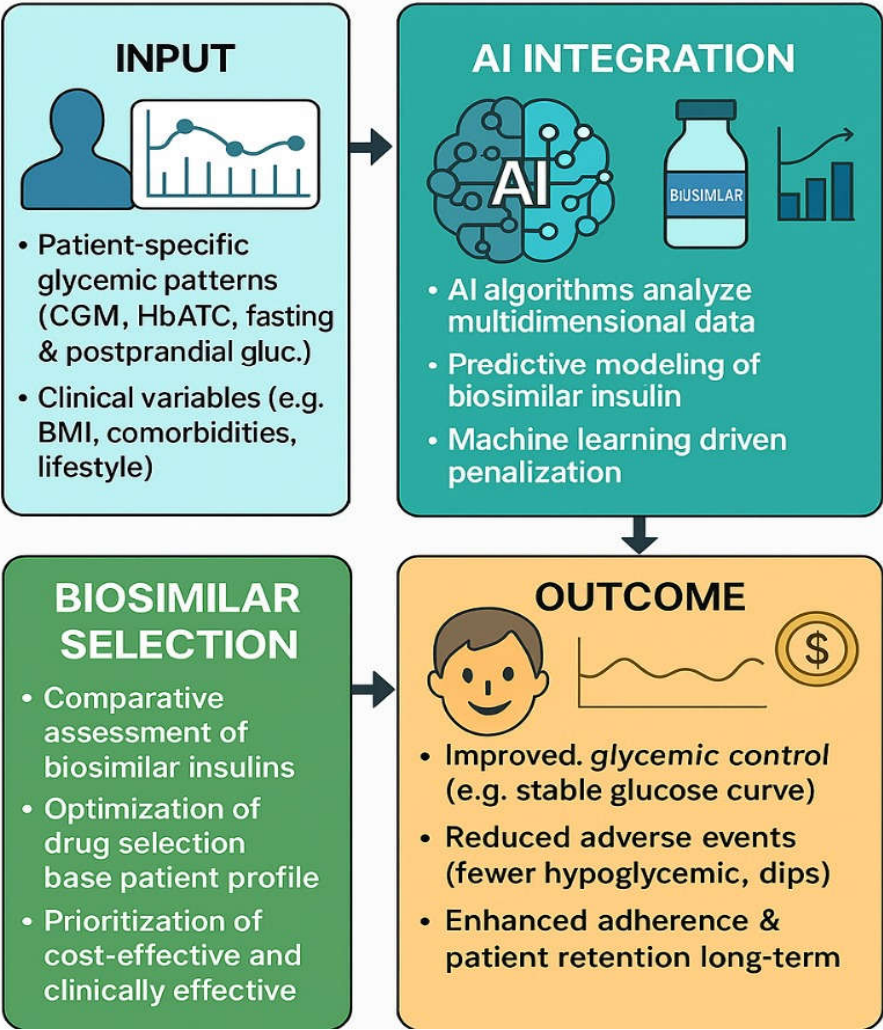


Fig: Graphical abstract

Keywords; Diabetes, Biosimilar, Insulin, Artificial intelligence, Clinical Decision Support

Introduction:

Type 2 diabetes has become a significant global public health issue, largely due to rapid urbanization, unhealthy diets, sedentary lifestyles, and an aging population. The condition reduces functional capacity and living standard, leading to serious health issues and premature demise, particularly in individuals under 60.[1] This increases medical expenses for patients and the healthcare system. People who are overweight or have high blood sugar are at greater risk, and those with higher BMI are especially vulnerable to type 2 diabetes.[2] The economic burden of diabetes is significant, as the costs of care are more than three times higher than average and can be nearly ten times greater when complications occur.[3] Despite advancements in treatment, achieving preferred control of blood glucose, blood pressure, and other key health targets remains a challenge. The rise in diabetes is mainly due to a lack of awareness and not health promotion efforts. The International Diabetes Federation found that about 10.5% of people worldwide had diabetes in 2021. This number is expected to grow to 11.3% by 2030 and 12.2% by 2040.[4] These figures highlight the need for better education and health programs to address this important issue.[5] People with type 2 diabetes are more likely to develop problems with organs such as the kidneys, eyes, and nerves. These complications increase medical costs and reduce living standards.[6] Studies also show that type 2 diabetes can raise the risk of early death by about 15% and shorten life expectancy by up to 20 years.[7]

Insulin remains a key tool in the treatment of type 2 diabetes, especially when patients can't reach blood sugar goals with oral medications alone. Over the past few years, insulin therapy has evolved with new formulations and alternatives to help improve effectiveness, convenience, and affordability.[8] Biosimilar insulins are biologic medications that closely match original brand products in safety and effectiveness while often costing significantly less. As of 2025, the U.S. market includes three approved biosimilars: two long-acting insulin glargine products (Semglee [insulin glargine-yfgn] and Rezvoglar [insulin glargine-aglr]) and one rapid-acting insulin Aspart biosimilar (Merilog).[9] Merilog, approved in 2025, offers a more affordable rapid-acting insulin alternative and has been shown to match the originator (Novolog) in safety and glucose-lowering efficacy.[10] Semglee was the first FDA-designated interchangeable biosimilar insulin, meaning pharmacists can substitute it without needing specific physician approval in many states.

Importantly, biosimilars like Semglee deliver equivalent glucose control to their reference products at prices often 15-35% lower, helping reduce long-term treatment costs.[9]

Table no1: Comparison Between Different Biosimilars.

Type	Structure Modification	Example Biosimilars	Reference Product	Role in T2DM
Insulin Glargine	Gly→Asn (A21), +2 Arg (B-chain C-terminus)	Basaglar, Semglee	Lantus	Long-acting basal insulin
Insulin Lispro	B28 Pro→Lys, B29 Lys→Pro	Lispro Sanofi	Humalog	Rapid-acting, mealtime
Insulin Aspart	B28 Pro→Asp	Aspart Sanofi (developing)	NovoRapid	Rapid-acting, mealtime
Human Insulin (Regular, NPH)	Native insulin sequence	Insugen, Wosulin	Humulin, Novolin	Short-acting & intermediate
GLP-1 Agonists (future)	Modified GLP-1 peptide (resists DPP-4)	Liraglutide, Dulaglutide biosimilars	Victoza, Trulicity	Increases insulin, reduces glucagon, weight loss

Biologic drugs are different from traditional medicines because they are derived from living cells and often utilize recombinant DNA technology. The first biopharmaceutical approved for medical use was recombinant human insulin (Humulin®, produced by Eli Lilly and Company in Indianapolis) [11] in 1982. Since then, advancements in biotechnology have led to the approval of many biologic products, including peptide hormones, growth factors, interferons, interleukins, and monoclonal antibodies, in various regions around the world.[12] Biopharmaceuticals represent one of the fastest-growing segments of the pharmaceutical industry. By 2017, it was projected that they would account for about 20% of global drug spending, growing more rapidly than traditional medicines.[13] Due to the impending patent expirations of many first-generation

biopharmaceuticals, there is significant interest in the production and commercialization of similar biologic products, commonly referred to as “Biosimilars.” A biosimilar product is defined as being highly similar to an already approved biologic product. The new versions of insulin will be submitted for approval using the existing 505(b)(2) regulatory pathway. This pathway is designated for instances where the reference product was previously approved under section 505(b)(1) of the Food, Drug, and Cosmetic Act (FDCA).[14]

Similar biologic products and biosimilars are frequently misclassified as generics, leading to confusion in the pharmaceutical market. The term "generic" specifically refers to medications that are chemically identical replicas of non-biologic drugs, such as traditional small-molecule medications. These generics can be produced with relative ease by replicating the active pharmaceutical ingredient (API) of the reference drug and fulfilling established bioequivalence criteria, which assess whether the generic performs in the same manner as the original.[15] Biologics are complex molecules made from living cells. They have detailed structures and complicated manufacturing processes. Biosimilars are similar products but are not identical to their reference biologics due to natural variations in biological systems. To create biosimilars, manufacturers must replicate the active ingredients and show through clinical studies that the biosimilar has a similar safety and effectiveness to the original product. This complicated process makes it clear that biosimilars are different from generic drugs, and they should not be confused with each other.[16]

Managing type 2 diabetes (T2D) is not a one-size-fits-all approach. Personalized medicine, also referred to as precision or individualized medicine, seeks to customize treatment according to each person’s clinical characteristics, genetic profile, and lifestyle. This strategy recognizes the significant differences in how individuals develop diabetes, react to medications, and experience related complications.[17] Improved treatment response: Many conventional therapies work on average, but nearly half of T2D patients fail to reach blood sugar targets despite adherence. Personalized markers like age, BMI, ethnicity, or genetic variants can help predict who benefits most from which drug.[18] Reduced adverse effects: Genetics can influence how a patient metabolizes drugs like metformin, sulfonylureas, and thiazolidinediones. Pharmacogenomics helps identify patients with variations, such as reduced-function OCT1 for metformin or specific KCNJ11/ABCC8 alleles affecting sulfonylurea response, allowing safer and more effective

dosing.[19] Savings and efficiency: Tailored treatments can reduce hospitalizations, unscheduled visits, and complications, yielding cost savings and a better quality of life.[20] Personalized medicine for type 2 diabetes (T2D) focuses on customized treatments instead of one-size-fits-all methods. This means doctors consider a person's genetics, health markers, behavior, and digital health data. The goal is to make medications work better, reduce side effects, help patients stick to their treatment plans, and decrease long-term healthcare costs. As the price of genetic testing goes down and digital monitoring becomes more common, using these tools in regular diabetes care is becoming easier and more effective.[20]

Personalizing Type 1 and Type 2 Diabetes

Type 1 Diabetes is an autoimmune condition in which the body's immune system demolishes insulin-producing beta cells. While insulin replacement remains the cornerstone of treatment, personalization is increasingly achieved through technology and lifestyle adjustments. For example, continuous glucose monitoring (CGM), insulin pumps, and hybrid closed-loop "artificial pancreas" systems allow individualized insulin dosing based on real-time glucose data and patient activity. These technologies improve glycemic control, reduce hypoglycemia, and enhance quality of life.[21] In addition, research into immunotherapies (e.g., teplizumab) offers the potential to delay or prevent T1D onset in genetically at-risk individuals, further personalizing treatment at the disease-prevention stage.[22] T2D is more heterogeneous than T1D, involving both insulin resistance and beta-cell dysfunction. Treatment personalization focuses on pharmacogenomics, biomarkers, and patient characteristics such as BMI, age, ethnicity, comorbidities, and cardiovascular risk. For example, metformin remains the first-line therapy, but some individuals respond poorly due to genetic variants in transporters like OCT1. Sulfonylureas are more effective in patients with preserved beta-cell function, while GLP-1 receptor agonists and SGLT2 inhibitors are prioritized for patients with obesity or cardiovascular/renal disease.[23] Lifestyle interventions are also highly personalized nutrition plans, exercise programs, and digital health tools (e.g., wearables, telehealth coaching) that are tailored to individual preferences and cultural contexts to improve adherence. Increasingly, real-world data and artificial intelligence are being used to predict who benefits most from specific therapies, supporting precision T2D care.[24]

Artificial intelligence (AI) is swiftly changing the healthcare landscape by facilitating quicker, more accurate, and personalized decision-making. AI involves computer systems that can analyze complex medical data, recognize patterns, and support clinicians in diagnosis, treatment planning, and patient management. Its applications include diagnostics, predictive analytics, drug discovery, and improving operational efficiency within healthcare systems.[25] AI-powered tools have shown remarkable ability in detecting diseases from imaging and clinical data. For instance, deep learning algorithms can analyze radiology scans, retina scans, and pathology slides with accuracy comparable to or even exceeding that of human experts. AI systems are already FDA-approved for tasks such as screening diabetic retinopathy and identifying early breast cancer lesions. Early diagnosis enables timely interventions, improving patient outcomes.[26] AI accelerates drug development by analyzing massive biological datasets to identify drug candidates, optimize trial design, and repurpose existing medications. In oncology, AI supports precision medicine by identifying biomarkers and guiding treatment based on tumor genetics. This reduces costs and shortens the timeline for bringing new therapies to patients.[27] AI-driven CDSS assist clinicians by integrating patient data with clinical guidelines and research evidence. These systems provide recommendations on medication dosing, diagnostic testing, and treatment pathways. For example, AI models in intensive care units help in predicting sepsis hours before it develops, allowing life-saving interventions.[28] AI has emerged as a powerful tool in healthcare decision-making, supporting earlier diagnosis, risk prediction, personalized treatment, and more efficient healthcare delivery. As technologies mature, integrating AI with human clinical expertise offers the potential to reshape modern medicine into a more precise, predictive, and patient-centered system.[29]

Types of Biosimilars

- a. Biosimilar Insulins-Examples are Insulin glargine, Insulin lispro. Use in the management of type 1 and type 2 diabetes to regulate blood glucose.[30]
- b. Biosimilar Monoclonal Antibodies (mAbs)-Examples: Trastuzumab (used in HER2+ breast cancer), Rituximab (used in lymphoma, rheumatoid arthritis). Use in the treatment of cancers and autoimmune disorders.[31]
- c. Biosimilar Growth Factors-Filgrastim (stimulates neutrophils), Epoetin alfa (stimulates red blood cell production). Used to prevent/treat chemotherapy-induced neutropenia, manage anemia in chronic kidney disease or cancer.[32]

- d. Biosimilar Hormones-Somatropin (recombinant human growth hormone). Use in growth hormone deficiency, Turner syndrome, and chronic renal insufficiency in children.[33]

Biosimilars in Diabetes Management:

Diabetes mellitus, especially type 2 diabetes (T2D), is a major global health crisis affecting millions, often requiring insulin therapy. Since the discovery of insulin in 1921, formulations have evolved from animal extracts to advanced recombinant human forms and analogs, improving glycemic control and reducing side effects. The increasing prevalence of diabetes and high insulin costs necessitate cost-effective treatment options. Biosimilar insulins have emerged as a key solution, closely replicating approved biological insulins in quality, safety, and efficacy. They play a critical role in enhancing affordability and treatment adherence, alleviating the financial burden of diabetes management for many patients.[34] Biosimilars are not exact replicas of generic small-molecule drugs; they are designed to be highly comparable to reference biologic insulins. Produced using living cells and advanced biotechnology, biosimilars may have slight variations that are rigorously assessed for clinical equivalence. Regulatory agencies like the EMA and FDA require extensive studies covering structure, pharmacokinetics, pharmacodynamics, safety, and immunogenicity to demonstrate bio-similarity.[35] Significance in Diabetes Management improved the Accessibility and Affordability, Comparable Safety and Efficacy, which have shown that biosimilar insulins provide glycemic control equivalent to their reference products, without increased risk of hypoglycemia or adverse immunogenic responses. This ensures that switching from an originator insulin to a biosimilar does not compromise treatment outcomes.[36] Biosimilar insulins represent a crucial advancement in diabetes management, addressing both the clinical and economic challenges of insulin therapy. By ensuring similar efficacy and safety at a lower cost, they hold the potential to expand global access to insulin and improve long-term health outcomes in people living with diabetes. Their growing adoption underscores their importance in making diabetes care more sustainable and equitable worldwide.[37] While biosimilar insulins are generally less expensive than innovator (originator) insulins, the price reduction is often modest compared to generic small-molecule drugs. This is due to the high cost of manufacturing, complex regulatory requirements, and the need for extensive clinical testing. In some markets, the cost difference between biosimilars and branded insulins is insufficient to drive widespread switching, especially in healthcare systems with pre-established procurement contracts.[35]

Interchangeability, the ability to substitute a biosimilar for an innovator insulin without prescriber intervention, remains a key issue. While regulatory agencies such as the U.S. FDA have provided pathways for interchangeability designation, not all biosimilars hold this status. Physicians and patients may hesitate to switch due to concerns about glycemic control, dosing accuracy, and brand familiarity. Furthermore, automatic substitution policies vary between countries, which can limit widespread adoption.[38] Since biosimilars are derived from living cells, slight structural variations may trigger unwanted immune responses. Although clinical trials have shown no significant differences in immunogenicity between biosimilars and originator insulins, theoretical concerns persist. Both healthcare professionals and patients may perceive a higher risk of hypersensitivity or neutralizing antibody formation, which contributes to resistance to switching.[39]

Clinical research and real-world evidence consistently demonstrate that biosimilar insulins exhibit comparable efficacy, safety, and tolerability when compared to their innovator counterparts. A series of randomized controlled trials have revealed no statistically significant differences in key clinical outcomes, including HbA1c levels, fasting plasma glucose, and the duration patients maintain their glucose levels within the target range. These findings suggest that biosimilar insulins can effectively serve as alternatives to original insulin products, offering the potential for broader access to diabetes management without compromising patient care. Comprehensive analyses further support the notion that these biosimilars adhere to the rigorous standards established for biological therapies, ensuring that patients receive robust treatment options.[36]

Additionally, the incidence and severity of hypoglycemic episodes appear to be remarkably similar between patients utilizing biosimilar insulins and those relying on originator insulins. This compelling evidence further underscores the clinical equivalence of these therapeutic options, providing confidence to both healthcare providers and patients in the use of biosimilar insulins as a viable alternative in diabetes management.[35] Clinical monitoring has found no evidence of increased immunogenicity with biosimilars, and rates of anti-insulin antibody development are consistent with reference products.[39] The adoption of biosimilar insulins is influenced by challenges such as pricing strategies, regulatory variations in interchangeability, and persistent concerns about immunogenicity. However, clinical evidence consistently supports their equivalence to innovator insulins in terms of efficacy, safety, and immunogenicity. Wider

acceptance of biosimilars can reduce healthcare costs and expand patient access to insulin therapy, provided that education, transparent communication, and supportive policies are in place.[40]

Mechanism of Action of Biosimilar Insulins:

Biosimilar insulins are biological medicines that are highly similar in structure, efficacy, and safety to their original (reference) insulin products. They are designed to provide the same therapeutic effects at a reduced cost, thus improving accessibility for diabetes patients. In Type 2 Diabetes Mellitus (T2DM), where insulin resistance and progressive β -cell dysfunction cause chronic hyperglycemia, biosimilar insulins act by mimicking the physiological effects of endogenous insulin on target tissues such as the liver, skeletal muscle, and adipose tissue.

1. Binding to the Insulin Receptor:

Biosimilar insulins are designed to replicate the effects of natural insulin by binding to a specific protein called the Insulin Receptor (IR). The IR is a complex structure found within the cell membrane and is classified as a heterotetrameric transmembrane glycoprotein. It consists of two parts outside of the cell, known as α -subunits, which serve the purpose of binding insulin, and two parts that span the membrane, referred to as β -subunits, which possess intrinsic activity to trigger cellular responses. When a biosimilar insulin molecule attaches itself to an α -subunit, it triggers a change in the shape of the receptor. This conformational change is transmitted across the plasma membrane to the β -subunits, which then become activated.[41] The activation leads to a process called autophosphorylation, whereby phosphate groups are added to specific tyrosine residues located within the intracellular portion of the β -subunit. This modification creates acceptable docking sites for downstream signaling proteins, primarily from a group known as the Insulin Receptor Substrate (IRS) family. These downstream proteins play crucial roles in mediating the effects of insulin within the cell, influencing various metabolic processes such as glucose uptake. The subsequent recruitment and phosphorylation of IRS proteins initiate intracellular signaling cascades, particularly the PI3K-Akt pathway, which mediates metabolic effects like glucose uptake and glycogen synthesis, and the MAPK pathway, which regulates mitogenic responses such as cell growth and proliferation. Importantly, biosimilar insulins must demonstrate comparable receptor-binding affinity and signaling activation to their reference insulin products to ensure equivalent efficacy and safety in clinical use.[41]

2. Tissue-Specific Actions of Biosimilar Insulins:

Biosimilar insulins exert their therapeutic effects through actions on key target tissues, skeletal muscle, adipose tissue, and the liver by activating insulin receptor-mediated signaling pathways. In skeletal muscle, which is responsible for the majority of glucose uptake, biosimilar insulins stimulate the PI3K-Akt pathway, promoting translocation of glucose transporter type 4 (GLUT-4) to the plasma membrane, thereby increasing glucose uptake and enhancing glycogen synthesis. In adipose tissue, they facilitate glucose uptake for triglyceride synthesis, activate lipoprotein lipase to promote lipid storage, and inhibit hormone-sensitive lipase, thus reducing lipolysis and free fatty acid release.[42]

In the liver, biosimilar insulins suppress hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis, while simultaneously promoting glycogen synthesis and lipogenesis. Collectively, these tissue-specific actions help reduce hyperglycemia and restore metabolic balance in type 2 diabetes. Since biosimilars are designed to be highly similar in structure and receptor-binding affinity to their reference products, they produce the same tissue-level responses, ensuring equivalent clinical efficacy and safety.[43]

Artificial Intelligence in Diabetes Care

Artificial Intelligence (AI) has emerged as a transformative tool in diabetes care, offering innovative approaches to diagnosis, treatment optimization, and long-term management. AI applications in diabetes primarily focus on predictive modeling, insulin dosing algorithms, and digital twin technologies.

Predictive Models: AI-driven models can forecast blood glucose fluctuations, risk of hypoglycemia, and long-term complications by analyzing clinical, genetic, and lifestyle data. These predictive insights help clinicians personalize therapy and prevent adverse events.

Insulin Dosing Algorithms: Advanced algorithms assist in recommending optimal insulin doses by analyzing continuous glucose monitoring (CGM) data, carbohydrate intake, and physical activity.[41] These systems are crucial for patients using insulin pumps and hybrid closed-loop systems. **Digital Twins:** A digital twin is a virtual replica of a patient that integrates clinical, lifestyle, and sensor data to simulate disease progression and treatment outcomes. In diabetes,

digital twins allow testing of different interventions (e.g., insulin regimens, diet changes) in silico before implementation, thus personalizing therapy.[44]

Various machine learning (ML) approaches have been applied in diabetes management, each offering unique strengths:

- ✓ **Regression Models:** Used to predict blood glucose levels based on dietary intake, insulin dosage, and activity. Linear and logistic regression are common in risk prediction for diabetes onset and complications.
- ✓ **Decision Trees & Random Forests:** Provide interpretable models for clinical decision-making, such as predicting hypoglycemia episodes or stratifying patients by complication risk.
- ✓ **Neural Networks:** Particularly suited for nonlinear and complex datasets, neural networks can learn patterns from CGM data to improve glycemic forecasting.
- ✓ **Deep Learning:** Convolutional Neural Networks (CNNs) and Recurrent Neural Networks (RNNs) are applied in the interpretation of CGM signals, retinopathy detection from retinal images, and long-term glycemic trend prediction.[45]

Limitations of Current AI Models in Diabetes Therapy:

- ✓ AI systems necessitate large, high-quality datasets for effective performance. Variability in glucose measurement accuracy, missing data, and inconsistent logging of lifestyle factors can negatively impact predictive capabilities.
- ✓ Generalizability is a crucial concern in artificial intelligence (AI), as many models are confined to specific populations, reducing their accuracy with diverse groups. Genetic differences, dietary habits, and socioeconomic factors greatly influence individual responses. To enhance effectiveness across communities, AI models must incorporate a broader range of data sources.
- ✓ **Regulatory and Ethical Challenges:** Clinical validation, approval, and post-market surveillance of AI tools are complex. Data privacy, informed consent, and algorithm transparency are ongoing concerns.
- ✓ **User Adoption:** Patients and clinicians may hesitate to rely on AI tools due to a lack of trust, usability challenges, or a limited understanding of how algorithms make decisions.

- ✓ **Cost and Accessibility:** Advanced AI-driven systems, like artificial pancreas devices, remain expensive and are not equally accessible across all healthcare settings, particularly in low-resource countries.[46]

AI is revolutionizing diabetes care through predictive analytics, automated insulin dosing, and digital twin simulations. Machine learning models, ranging from regression to deep learning, are being integrated into CGM analysis, artificial pancreas systems, and complication screening tools. However, challenges related to data quality, generalizability, regulatory approval, and patient trust remain. Overcoming these barriers will be essential for AI to fully realize its potential in achieving personalized, effective, and accessible diabetes management.[47]

Integrating AI Models with Patient-Specific Data for Biosimilar Selection:

1. Concept of Personalized Biosimilar Matching Using AI

The idea of personalized biosimilar matching is to use AI algorithms that analyze individual patient data, such as clinical history, biomarkers, genomic profiles, and treatment response, to recommend the most suitable biosimilar insulin or biologic. This targets not only efficacy but also factors like immunogenicity, safety, and cost. AI can uncover patterns and predictive markers that guide clinicians toward the best individualized biosimilar choice, moving beyond generic substitution toward truly personalized biologic therapy.[48]

2. Frameworks or Models Where AI Integrates Real-World Data for Drug Selection

Although direct real-world examples of AI-driven biosimilar selection are limited, emerging frameworks suggest how this could be implemented.

AI in Biosimilar Development & Pharmacovigilance: AI tools are already being used to analyze process data in biosimilar manufacturing example, predicting glycosylation profiles, ensuring molecular similarity, and enhancing quality control through real-time process monitoring with AI-driven analytics. Additionally, AI supports pharmacovigilance by detecting rare adverse events and mining literature using NLP techniques to extract safety-related signals.[49] **AI-Driven Drug Response Prediction in T2D:** AI systems analyzing real-world clinical data, age, lab results, prescription history, and comorbidities have been developed for predicting drug response in T2D. For instance, transformer-based models achieved high predictive accuracy (ROC-AUC ~0.99) in

classifying drug choices based on patient profiles.[50] Similarly, a 2025 viewpoint highlights AI's growing capability to analyze vast datasets from EHRs and trials to anticipate individual treatment responses, aiding personalized drug selection.[51] Interpretable AI for Treatment Progression: A recent AI framework using interpretable tree-based models trained on observational data suggests optimized treatment step-ups, with better HbA1c reduction compared to standard clinician decisions, showcasing how AI can support clinical pathways.[52]

3. Potential for AI-Based Decision-Support Systems in Clinical Practice

AI-enhanced decision support systems (CDSS) could guide clinicians in selecting the most appropriate biosimilar based on personalized patient profiles. Potential capabilities include:

Combining Multidimensional Data: AI could integrate clinical metrics, immunological markers, prior insulin responses, and cost constraints, producing ranked biosimilar options. **Predictive Safety and Efficacy Modeling:** Using pharmacovigilance data and patient history, AI can estimate the risk of adverse reactions or immunogenicity before biosimilar switching. **Dynamic Learning Systems:** As real-world evidence accumulates, e.g., outcomes following biosimilar switches, AI models could refine recommendations, improving guidance over time. [52,53]

Benefits of AI-Guided Biosimilar Selection:

1. Improved Clinical Outcomes and Glycemic Control

AI-guided systems can enhance glycemic outcomes by offering personalized, accurate insulin dosing that adapts to each patient's real-time needs. For instance, an AI-based insulin decision support system (iNCDSS) demonstrated glycemic control on par with experienced physicians in hospitalized T2D patients, yielding comparable "time in range" (TIR) results and high physician satisfaction.[54] While not specific to biosimilars, such AI algorithms could similarly optimize matching biosimilar insulin to individual needs, maximizing therapeutic efficacy through personalized dosage and monitoring.

2. Cost-Effectiveness in Diabetes Management

The introduction of insulin biosimilars has already resulted in meaningful cost reductions: e.g., the entry of Basaglar (a follow-on insulin glargine) led to quarterly price declines of approximately 3.4% for glargine insulins.[55] More broadly, biosimilars across therapeutic areas are projected to

slash biologic drug expenses by up to \$54 billion between 2017 and 2026.[51] Incorporating AI to optimally match patients with the most suitable and affordable biosimilar could further enhance cost savings, enabling targeted use of lower-cost alternatives while preserving clinical outcomes.[56]

3. Enhanced Patient Adherence and Satisfaction

AI decision support tools can improve clinical workflows and ease the workload of healthcare providers, which ultimately helps patients. For example, the integrated Non-Communicable Diseases Decision Support System (iNCDSS) received a rating of 4.1 out of 5 from physicians for its usability, safety, and efficiency. Additionally, 98.9% of the AI recommendations were put into practice.[54] In the context of biosimilars, AI could recommend equivalent yet less expensive options seamlessly, minimizing treatment complexity and boosting patient confidence and adherence. [56,57]

4. Data-Driven Healthcare Decision-Making

AI excels at synthesizing vast datasets, including clinical records, pharmacologic profiles, and cost information to inform biosimilar selection. One review highlights how AI and IoT technologies can support biosimilar decision-making by analyzing alignment of molecules, optimizing manufacturing, predicting adverse events, and enhancing regulatory evaluation through text mining and Pharmacovigilance.[58] Such capabilities could be adapted for clinical decision support, drawing on patient demographics, history, and biosimilar performance to recommend optimal therapeutic matches.[58]

Table no 2: Advantages of AI guided Biosimilars.

Benefit Category	AI-Guided Biosimilar Selection Advantage
Clinical Outcomes	Personalized matching improves glycemic control and safety (e.g., TIR)
Cost-Effectiveness	Maximizes use of affordable biosimilars; drives down overall medication costs
Patient Adherence & Satisfaction	Streamlined decision-making increases trust, lowers complexity.
Data-Driven Decision-Making	Integrates multiple data streams for optimal, evidence-based recommendations

Challenges and Limitations:

1. Data quality and interoperability issues

AI models are only as good as the data they learn from. In routine diabetes care, key inputs (A1C, CGM traces, insulin doses, comorbidities, hypoglycemia events) often live in fragmented, heterogeneous systems (EHRs, pharmacy claims, device portals). Missingness, inconsistent coding, device calibration differences, and label noise degrade model performance and reproducibility. Health information exchange and adoption of HL7-FHIR can mitigate these problems by standardizing data elements and semantics, but implementation is uneven across healthcare settings and vendors. Even with FHIR, semantic alignment and provenance tracking remain practical hurdles that limit large-scale, multi-center model training and external validation.[59]

Without high-fidelity longitudinal data (including switch dates, dose changes, concurrent therapies, and outcomes such as time-in-range or hypoglycemia), AI cannot reliably infer which biosimilar is best for a given patient or whether an observed change in control truly followed a switch rather than confounding factors. [59,60]

2. Ethical and privacy concerns with patient-specific data

Personalized biosimilar recommendations require integrating sensitive, identifiable health data. That triggers strict legal and ethical duties on privacy, consent, fairness, and transparency. Recent reviews highlight risks of re-identification, secondary use, and bias when AI is embedded in EHR workflows; they call for stronger governance, auditability, and explicit consent pathways. Regulatory scrutiny is increasing, e.g., proposals to modernize HIPAA security safeguards (encryption/MFA) in response to rising ransomware threats; debates over national data infrastructures (e.g., NHS) underscore the difficulty of truly anonymizing health data. Developers of clinical AI and digital therapeutics must also minimize data collection and formalize data-sharing agreements. [61,62,63] If patients or institutions are reluctant to share detailed histories, AI models will skew toward data-rich subgroups, raising equity concerns and limiting the generalizability of recommendations across diverse populations.[61]

3. Regulatory challenges in AI-driven biosimilar recommendations

From a U.S. perspective, whether an AI recommendation engine is regulated depends on the FDA's Clinical Decision Support (CDS) framework and Software-as-a-Medical-Device (SaMD) policies. CDS that allows clinicians to independently review the basis for recommendations may be "non-device," while opaque or autonomous systems typically fall under device regulation, implying design controls, clinical evaluation, and post-market oversight. In the EU, the AI Act (2024) classifies most clinical AI as high-risk, imposing requirements for data governance, transparency, human oversight, and quality management, while interacting with MDR/IVDR and GDPR. For biosimilars specifically, FDA guidance on biosimilar/interchangeable labeling and post-approval changes sets expectations for evidence and communication; automatic substitution still depends on state law and the product's "interchangeability" designation. An AI tool proposing switches must align with these frameworks and avoid implying clinical superiority where none is established. [64,65,66] An AI that ranks biosimilars by "appropriateness" may be viewed as influencing treatment selection; sponsors and health systems should plan for SaMD pathways, rigorous explainability, and careful claims language consistent with bio-similarity (i.e., no clinically meaningful differences vs the reference).[64]

Future Perspectives

Selecting the optimal glucose-lowering therapy for people with Type 2 diabetes (T2D) is increasingly a precision problem: patient heterogeneity (age, comorbidity, renal function, adherence, prior treatment history) and expanding medicine choices (including biosimilars) make individualized recommendations complex. Continuous and point-in-time glycemic data (CGM traces, fingerstick logs, HbA1c trajectories) provide a rich, patient-specific phenotype that, when combined with AI models, can help predict which therapeutic option (including which biosimilar) will achieve better glycemic control, fewer side effects, and higher adherence for that person. Recent reviews document rapid progress in AI for glycemic prediction and decision support, forming the technical foundation for this integration.[67]

1. Integration with digital health platforms and mobile apps

Digital health platforms and smartphone apps are the natural conduit for bringing patient-specific glycemic data into AI workflows. Modern platforms already ingest CGM streams, wearable activity/sleep data, diet logs, medication timing, and patient-reported outcomes; AI layers built on top of these streams can generate individualized risk scores, glycemic forecasts, and candidate treatment options. Trials and platform studies show AI-enhanced digital interventions can improve glycemic outcomes and engagement by delivering personalized coaching and actionable alerts to patients and care teams. Embedding biosimilar-selection logic in these platforms means patients' real-world glucose responses (variability, hypoglycemia risk, time-in-range) can be used to recommend not only drug class but specific products (including biosimilars) predicted to match the patient's physiological profile and tolerability. [68,69] Practical considerations: to be useful clinically, app AI integrations must enforce strong data standards (FHIR/HL7 for EHR interoperability), privacy controls (consent, encryption), and clear UX that differentiates patient-facing suggestions (behavioral tips, adherence nudges) from prescriptive treatment recommendations (which require clinician sign-off and regulatory safeguards). Interoperability with EMRs allows the app-derived AI insights to be visible in the clinician workflow (medication reconciliation, formulary checks), enabling seamless biosimilar substitution where appropriate.[68]

2. Development of real-time AI decision-support tools for clinicians (CDSS)

Real-time decision support systems for clinicians (CDSS) ingest live glycemic feeds and clinically relevant context (renal function, concomitant meds, prior treatment response) and can produce ranked therapeutic choices, dosing adjustments, and safety alerts. Randomized and pragmatic studies of AI-assisted insulin titration and inpatient glycemic CDSS demonstrate effectiveness at improving glucose control and reducing adverse events, suggesting real-time AI can safely move from insulin algorithms toward recommending choice among multiple injectable biologics and biosimilars. When integrated with drug-formulary modules, the CDSS can prioritize biosimilars that are therapeutically equivalent but cost-favorable while flagging patient features that might argue for using the reference product (history of immunogenic reaction, special populations). [70,71] Key implementation points: transparency (explainable AI outputs) and clinician control are essential. Clinicians must see why the model favors a biosimilar for a given patient (e.g., prior rapid time-in-range improvements on similar molecule classes, low predicted immunogenicity risk) so they can make informed prescribing decisions. Embedding confidence metrics and suggested monitoring plans (e.g., anti-drug antibody checks, closer post-switch glucose monitoring) will increase adoption and safety.[70]

3. Expansion toward multi-omics data integration (genomics, proteomics)

Moving beyond glycemic phenotypes, combining genomics, proteomics, metabolomics, and microbiome data with glycemic traces enables mechanistic, precision selection of therapies. Multi-omics can reveal genetic variants affecting drug pharmacokinetics or pharmacodynamics (for example, variants that alter drug metabolism or insulin signaling pathways), proteomic markers of inflammation that predict poorer response to a drug class, or metabolomic signatures associated with hypoglycemia susceptibility. AI methods deep learning, graph neural networks, and integrative generative models, are proving capable of harmonizing these high-dimensional datasets to derive clinically useful subtypes and treatment-response predictors in diabetes. In practice, a clinician could receive a model output that says: “Patient A has omics signature X + CGM pattern Y → predicted superior response to biosimilar formulation B with low immunogenicity risk,” enabling truly personalized biosimilar selection.[72] Barriers remain: omics data availability, cost, regulatory acceptance, and the need for large, diverse cohorts to avoid bias. However, pilot studies

(e.g., pharmaco-multiomics for metformin response) show promise that expanding data modalities materially improve the prediction of individual drug response.[73]

4. Role of AI in pharmacovigilance of biosimilars

Post-marketing safety monitoring is critical for biosimilars because minor manufacturing differences can, in rare cases, affect immunogenicity or efficacy. AI can revolutionize pharmacovigilance by continuously mining heterogeneous real-world data sources EHRs, claims, lab databases, spontaneous adverse event reports, and patient-reported outcomes, to detect subtle safety signals faster than traditional methods. Natural language processing (NLP) can extract adverse event descriptions from clinical notes; causal inference models can separate confounding in observational data; anomaly detection can flag unexpected patterns (e.g., increased neutralizing antibodies after switching). Reviews and pilot deployments document AI's utility and outline implementation challenges (data quality, regulatory validation, explainability) for drug safety monitoring. For biosimilars, this means more rapid, data-driven comparison against reference biologics and earlier identification of subgroups at risk.[74] Operationally, integrating pharmaco-safety AI with clinical CDSS and digital platforms closes the loop: if AI pharmacovigilance flags a potential issue for a specific biosimilar in a patient subgroup, the clinician CDSS and app can surface alternative recommendations and tailored monitoring for affected patients.[75]

Conclusion:

The combination of specific patient glycemic data, artificial intelligence (AI), and biosimilar therapies is changing how we manage Type 2 diabetes. Using continuous glucose monitoring, digital health platforms, and advanced predictive models, doctors can create personalized treatment paths instead of using a “one-size-fits-all” approach. AI tools help doctors choose the right biosimilars while also improving cost-effectiveness, safety, and access to diabetes care. Looking ahead, using various types of biological data, such as genomics, proteomics, and metabolomics, will offer deeper insights into how patients respond to treatments and the different forms of the disease. This will lead to more personalized biosimilar prescriptions. AI systems will also enhance safety monitoring after biosimilars enter the market. In summary, the collaboration between glycemic data and AI in biosimilar selection can redefine diabetes care. This fits with the overall goal of modern healthcare to be patient-centered, data-driven, and accessible worldwide. As digital systems improve and regulations change, the future treatment of Type 2 diabetes will rely on smart systems that provide effective glycemic control and promote sustainable and fair care for everyone.

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