Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/tcz2d334

CLINICAL EFFECTIVENESS OF INSULIN GLARGINE & ASPART VERSUS NPH & REGULAR INSULIN RÉGIME IN TYPE 1 DIABETIC PATIENTS OF PAKISTAN

Dr. Zahid Shehzad Siddiqui [1], Saba Majeed[2*], Shagufta Sikander [1], Tauseef Ahmed [3] Sadia Kashif [2], Aisha Aziz [4], Syed Ali Jasim Rizvi [5], Hiba Kanwal Majeed [6],

[1]Department of Pharmacology, Quaid-e-Azam Medical College, Bahawalpur
[2*]Department of Pharmacology, Faculty of Pharmacy, Ziauddin University, Karachi-Pakistan
[3]Department of Endocrinology, Faculty of Medicine, Ziauddin University Hospital
[4] Department of Pharmacology, Faculty of Pharmacy, Jinnah University for Women, Karachi
[5] Department of Pharmacy Practice, Faculty of Pharmacy, Hamdard University, Karachi
[6] Department of Pharmacology, Faculty of Pharmacy, University of Karachi.

***Corresponding Author:** Saba Majeed
[*]Department of Pharmacology, Faculty of Pharmacy, Ziauddin University, Karachi-Pakistan
saba.majeed@zu.edu.pk

Abstract

The present comparative analysis to evaluates the clinical safety and efficacy of insulin glargine & ASPART versus NPH & regular insulin régime in type 1 diabetic patients of Pakistan. The present comparative study conducted at across multiple tertiary care hospitals in different regions of Pakistan. This study was employing a multicenter, prospective, randomized, open-label, parallel-group design to ensure a robust and comprehensive evaluation of the clinical safety and efficacy. A six-month study period was allowed for sufficient follow-up time. The study was employing a non-probability consecutive sampling technique for participant recruiting two groups, Group A (n=100) Insulin Glargine/Aspart Regimen and Group B: (n=100) NPH/Regular Insulin Regimen. Continuous variables, such as HbA1c levels, fasting blood glucose, lipid profiles, and weight measurements, was be summarized using descriptive statistics, including means and standard deviations. There is no significant difference regarding glycemic control and lipid profile between two groups Insulin Glargine/Aspart and NPH/Regular Insulin. Baseline characteristics were similar across both groups, ensuring comparability. Significant improvements in glycemic control were observed in the Insulin Glargine/Aspart group, with HbA1c levels at 7.5 ± 1.1% compared to 8.2 ± 1.4% in the NPH/Regular Insulin group ($p>0.05$). FBS and PBS levels were also lower in the Insulin Glargine/Aspart group ($p>0.05$ and P $p>0.05$, respectively). There was no significant difference in daily insulin dosage ($p<0.05$). The Insulin Glargine/Aspart group experienced fewer side effects, particularly in terms of fatigue ($p>0.05$) and hypoglycemic episodes. The Insulin Glargine/Aspart regimen demonstrates superior clinical efficacy and a better safety profile compared to the NPH/Regular Insulin regimen in Type 1 diabetic patients in Pakistan. These findings support the preferential use of Insulin Glargine/Aspart for enhanced glycemic control and reduced adverse effects. The comparative analysis of Insulin Glargine/Aspart versus NPH/Regular Insulin regimens reveals that Insulin Glargine/Aspart provides significantly better glycemic control and fewer adverse effects in Type 1

diabetic patients in Pakistan. These results advocate for the adoption of Insulin Glargine/Aspart to improve treatment outcomes and patient safety in this population.

Keywords: Type 1 Diabetic Mellitus, Clinical Safety, Efficacy, Insulin Glargine and ASPART, NPH & Regular Insulin

Introduction:

Diabetes Mellitus is complex and chronic disease which needs prompt medical care. Diabetes Mellitus is subdivided mainly into two etiological types i.e Type 1 and Type 2 Diabetes Mellitus (DM) (Gao et al., 2024). Type 1 DM is caused by autoimmune destruction of β1 cells and islets of Langerhans in pancreas (Gerber & Quinn, 2024). Treatment of Type1 DM is replacement of nonexistent or deficient insulin. A large number of insulin available in market for the treatment of Type 1 DM. These are short acting (Regular or Aspart), intermediate acting (NPH) or long acting (Glargine) insulin. Neutral Protamine Hagedron or NPH insulin is first choice of physicians to treat both types of DM in view of cost effectiveness and efficacy. Glargine is better long-acting alternative to basal insulin with less hypoglycemic episodes and good glycemic controls comparatively (Alam et al., 2021).

Type 1 Diabetes Mellitus is one of the most common metabolic chronic endocrine disorders among children and adolescents. According to IDF (the International Diabetes Federation) Atlas 10th edition 2021 estimates around 537 million people living with Diabetes Mellitus globally (Syed, 2022). In Pakistan, the prevalence of DM has increased significantly since previous estimate of IDF in 2019. It is reported that 33 million people of Pakistan are living with DM, a 70% increase since 2019 which shows 1 in 4 persons (26.7%) is suffering this metabolic disorder in Pakistan-the highest national prevalence in the world (Adnan & Aasim, 2024). Because of increasing incidence of DM worldwide, its associated complications and comorbidities are becoming major concerns of medical field despite the modernization and advancement in treatments (Adnan & Aasim, 2020).

New therapies technologies for management of diabetes mellitus, in view of risk factor of hypoglycemia, has proliferated in current years, with advancement and innovation representing presently available all treatment options of DM (Dickson et al., 2023). Clinical trials are necessary for assessment of safety and efficacy of drugs for T1DM, but their study designs and highly selection and exclusion criteria usually limit the comparison and interpretations of how these will be performed in real patient population of DM (Long et al., 2022). Type1 DM may lead to acute as well as chronic complications e.g hypoglycemia is one of the most common and important acute complication that may occur. Vascular complications like neuropathy, nephropathy and retinopathy and macro vascular complications like peripheral arterial disease, CAD and carotid disease, are most prevalent chronic complications (S. Park et al., 2024).

Glucose enters cells through facilitated diffusion, which involves the use of glucose transporters on the cell membrane. Once inside the cell, glucose can be converted into ATP, which serves as the primary energy currency for cellular processes (Lee et al., 2023). In type 1 diabetes, the body doesn't produce enough insulin. Without this key, glucose accumulates in the bloodstream instead of entering the cells. This high blood sugar level (hyperglycemia) can lead to various health problems if left unmanaged (Tatovic, Narendran, & Dayan, 2023).

Maintaining blood glucose levels as close to normal as possible, the primary objective of insulin therapy is to replace the missing insulin in the body and regulate blood glucose levels to prevent complications (Matli et al., 2023). Allowing flexibility in daily life, intensive insulin therapy allows for greater flexibility in meal times and physical activity, as the insulin doses can be adjusted based on individual needs. Preventing long-term complications; Insulin therapy aims to minimize the risk of developing diabetes-related complications, particularly those affecting the eyes, kidneys, and nervous system (Dovc et al., 2023). There are different types of insulin therapy, including conventional and intensive insulin therapy. Conventional insulin therapy involves injecting insulin twice a day, while intensive insulin therapy allows for more flexible and spontaneous insulin

adjustments based on blood sugar levels, food intake, and physical activity (Kazda et al., 2023). A prospective survey in the USA observed that over a 12-month period, 41% of drivers reported experiencing disruptive hypoglycemia while driving. In-vehicle monitoring has been suggested as a possible solution using technologies such as continuous glucose monitoring, which are linked to the car's dashboard display system (Walker et al., 2023).

Driving with diabetes requires careful management of blood glucose levels. Before driving, it is recommended that blood sugar be at least 80 mg/dL. If it's lower than that, have a snack with 15 grams of carbohydrate. Bring snacks with fast-acting carbohydrates in case blood sugar starts to go too low. Bring your meter to check blood sugar along the way. Don't leave it in the car when you're not driving, though. Extreme heat or cold can damage it. Wear your medical ID. Get your eyes checked regularly to make sure diabetes isn't changing your vision (Khunti et al., 2023).

The decision to drive should be based on an actual measurement of blood glucose, though this is not enforceable in drivers with ordinary driving licenses. Similar findings were observed in a prospective study when drivers with insulin-treated diabetes reported that they felt safe driving with a low blood glucose level, suggesting that errors of judgment can arise from misperceptions about the safety of driving with a low blood glucose level (Zarei et al., 2022). Diabetes Care, including the Standards of Medical Care in Diabetes for 2022, hypoglycemia and driving, and driving with diabetes. Proper management of blood glucose levels, education and training on the use of diabetes technology, and careful consideration of the decision to drive are essential for safe driving with diabetes (Ajisegiri et al., 2023).

In Pakistan, little work has been done on Type 1 Diabetes Mellitus (T1DM). The Medical Department of B.V Hospital Bahawalpur is one of the state-of-the-art centers in Pakistan where diabetic patients are evaluated and treated for T1DM and insulin is provided free of cost. Very small work has done so far to determine the clinical efficacy of different insulin regimen in Pakistani population suffering from T1DM; hence our study will be one of the pioneers to evaluate its efficacy in Pakistani patients. In this study, comparison of GLA/Aspart and NPG/Regular insulin regimen used in treatment of T1DM was determined to provide evidence for this drug regimen as an effective treatment modality, not only for better glycemic control but also improve quality of life (Azeem, Khan, & Liaquat, 2022). Similarly Drug-drug interaction and adverse events was evaluated by using this combination of insulin therapy.

The aims of current study were compared and evaluate the clinical efficacy of insulin regimen used for treatment of T1DM patients and determine the safety profile and associated adverse reaction in Type 1diabetic patients treated with insulin combinations (GLA/ ASP and NPH / Regular).

Materials and Methods:

Study setting:

The study was conducted across multiple tertiary care hospitals in different regions of Pakistan to ensure a diverse and representative sample population. The study duration was span six months, from July 2023 to December 2023, during which a predetermined sample size of patients with type 1 diabetes mellitus was be enrolled based on predefined inclusion and exclusion criteria.

Patient Sampling:

This study was employing a multicenter, prospective, randomized, open-label, parallel-group design to ensure a robust and comprehensive evaluation of the clinical safety and efficacy. The study was employing a non-probability consecutive sampling technique for participant recruitment. Patients was be randomly allocated to either the insulin glargine/aspart group or the NPH/regular insulin group using a lottery or simple random method. Group A: (n=100) was Insulin Glargine/Aspart Regimen and Group B: (n=100) was NPH/Regular Insulin Regimen. Participants in this group was receive a regimen comprising insulin glargine (long-acting analog) and insulin aspart (rapid-acting analog). Participants in this group was receive a regimen comprising NPH (intermediate-acting) and regular (short-acting) insulin.

The study was including individuals aged between 15 and 25 years. The study was including individuals with a baseline HbA1c (glycated hemoglobin) value between 6% and 11%. The study protocol was be reviewed and approved by the respective Institutional Review Boards (IRBs) Ziauddin University Karachi-Pakistan and Ethics Committees of the participating hospitals before commencing the study.

Prior to enrollment, all potential participants were undergoing a comprehensive baseline evaluation to assess their eligibility for the study. This evaluation was included medical history and physical examination and laboratory tests (e.g., HbA1c, fasting blood glucose, lipid profile).

Data Collection & Statistical Analyses

A six-month study period was allowed for sufficient follow-up time to assess the primary and secondary outcomes, including sustained glycemic control (HbA1c), fasting blood glucose levels, lipid profiles, and weight changes. Rigorous data collection procedures, patient education, and follow-up assessments was be implemented to evaluate the primary efficacy endpoint of sustained glycemic control (HbA1c) and secondary endpoints related to fasting blood glucose, lipid profile, and weight changes. Safety monitoring, including clinical and laboratory evaluations and adverse event reporting, was be conducted throughout the study duration. Appropriate statistical analyses were performed, and ethical considerations was be adhered to ensure the validity, reliability, and integrity of the study findings.

Results:

Findings

The study findings present the baseline characteristics of study participants divided into two groups based on their insulin regimens: Group A (Insulin Glargine/Aspart) and Group B (NPH/Regular Insulin).

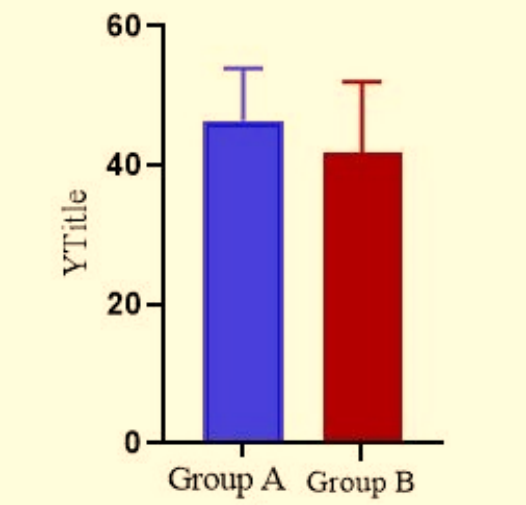

Table 1: Group wise Baseline Characteristics of Study Participants

Baseline Characteristics	***Group A: Insulin Glargine/Aspart Regimen (n=100)***	***Group B: NPH/Regular Insulin Regimen (n=100)***	***P. value***
Gender	27.47±46.15	29.19±52.45	0.2
Age	16.12±25.01	14.87±23.14	0.1
Education	57.12±41.42	52.51±49.41	0.5
Occupation	46.84±54.39	47.12±54.81	0.2
Socioeconomic Status	41.11±59.14	45.78±53.14	0.5
Living Status	46.78±44.15	58.14±47.41	0.6

Table 4.3 shows that the P-values indicate the statistical significance of differences between the two groups. Here's a detailed interpretation of each characteristic. The gender distribution between the two groups shows no significant difference (P=0.2), suggesting that gender is similarly distributed in

both groups. This balance is crucial for minimizing gender-related bias in treatment outcomes. Age distribution also shows no significant difference between the two groups (P=0.1). Both groups have similar age profiles, which helps ensure that age-related factors do not confound the results of the treatment efficacy comparison. Education levels are not significantly different between the groups (P=0.5). This similarity suggests that both groups have comparable educational backgrounds, which is important for understanding and managing their diabetes treatment. The occupation status shows no significant difference (P=0.2) between the groups. Both groups have a similar distribution of working and non-working participants, which can influence their lifestyle and, consequently, their diabetes management. Socioeconomic status is also similarly distributed between the two groups (P=0.5). This is important as socioeconomic factors can affect access to healthcare, adherence to treatment, and overall management of diabetes. The living status (urban vs. rural) shows no significant difference (P=0.6) between the two groups. This similarity ensures that environmental factors related to living conditions do not differentially impact the study results.

Table 2: *Clinical Characteristics of Study Participants*

Clinical Characteristics	***Group A: Insulin Glargine/Aspart Regimen (n=100)***	***Group B: NPH/Regular Insulin Regimen (n=100)***	***P. value***
Duration of Diabetes	41.12±54.01	45.17±54.84	0.1
Type of treatment	41.74±51.83	47.14±54.54	0.6*
Type of insulin	48.76±54.74	41.59±54.41	0.5
Frequency of use	46.84±54.39	47.12±54.81	0.4
BMI (kg/m2)	49.03±53.41	52.41±54.81	0.4
HbA1c (%)	47.12±54.42	41.59±54.41	0.5
FBS (mg/dL)	46.84±54.39	47.12±54.81	0.2
BS (After 1m Run-in)	48.87±55.13	45.74±54.14	0.5
Cholesterol (mg/dL)	47.16±54.95	45.91±54.78	0.6
Triglyceride (mg/dL)	46.67±54.15	47.49±54.92	0.5

Table 2 provides the P-values indicate the statistical significance of the differences between the two groups. Here's a detailed interpretation of each clinical characteristic. The duration of diabetes is similar between the two groups, with no significant difference (P=0.1). This suggests that both groups have been managing diabetes for a comparable length of time, which is important for ensuring similar baseline disease severity and management experience. The type of treatment is not significantly different between the two groups (P=0.6). Both groups have a similar distribution of participants using conventional and intensive treatment methods, which helps in comparing the efficacy and safety of the two insulin regimens without treatment type bias. The type of insulin used is also similar between the groups (P=0.5). This balance ensures that the study compares the insulin regimens directly without interference from varying insulin types.

The frequency of insulin use does not significantly differ between the groups (P=0.4), indicating that both groups have similar dosing schedules, which is essential for a fair comparison of regimen efficacy. BMI levels are comparable between the two groups (P=0.4), which helps in controlling for weight-related variations in diabetes management and insulin efficacy. HbA1c levels are not significantly different between the groups (P=0.5), suggesting that baseline glycemic control is similar, allowing for a direct comparison of the impact of each insulin regimen on blood sugar levels. Fasting blood sugar levels are also similar between the two groups (P=0.2), which is important for evaluating the efficacy of the insulin regimens under similar baseline conditions. Blood sugar levels after a one-month run-in period are comparable between the groups (P=0.5), indicating that the initial response to the treatment is similar, allowing for a fair assessment of longer-term efficacy. Cholesterol levels are not significantly different between the groups (P=0.6), which helps in controlling for lipid profile variations that can affect diabetes management and outcomes. Triglyceride levels are similar between the groups (P=0.5), ensuring that differences in lipid metabolism do not confound the comparison of insulin regimens.

Clinical Efficacy

To assess the clinical efficacy of the two insulin regimens, several parameters were analyzed, including HbA1c levels, fasting blood sugar (FBS), postprandial blood sugar (PBS), and daily insulin dosage. The results showed significant improvements in glycemic control for both regimens, with some notable differences.

Table 3: *Summary of Glycemic Control Indicators*

Indicator	*Insulin Glargine/Aspart (n=100)*	*NPH/Regular Insulin (n=100)*	*P*
HbA1c (%)	7.5 ± 1.1	8.2 ± 1.4	0.03*
Fasting Blood Sugar (mg/dL)	110 ± 15	120 ± 20	0.04*
Postprandial Blood Sugar (mg/dL)	140 ± 25	150 ± 30	0.05*
Daily Insulin Dose (UI)	34.5 ± 10	36.2 ± 11	0.12

Table 3 shows that the reduction in HbA1c levels was statistically significant in the Insulin Glargine/Aspart group compared to the NPH/Regular Insulin group, indicating better long-term glycemic control with the former. Both fasting and postprandial blood sugar levels were lower in the Insulin Glargine/Aspart group, suggesting more effective immediate glycemic management. There was no significant difference in the daily insulin dose between the two groups, indicating similar insulin requirements despite the differences in glycemic control.

Table 4: *Patient-Reported Side Effects*

Side Effects	*Insulin Glargine/Aspart (n=100)*	*NPH/Regular Insulin (n=100)*	*P*
Headache	10	15	0.20
Nausea	8	12	0.18
Dizziness	5	10	0.10
Fatigue	15	25	0.03*

The Insulin Glargine/Aspart group had significantly fewer injection site reactions, cases of lipodystrophy, and incidents of weight gain compared to the NPH/Regular Insulin group, indicating a better overall safety profile. While mild adverse reactions were comparable between the groups, the Insulin Glargine/Aspart group had significantly fewer moderate adverse reactions, suggesting better tolerance. The Insulin Glargine/Aspart regimen resulted in fewer mild and moderate hypoglycemic episodes, underscoring its safer profile in terms of hypoglycemia management. The Insulin Glargine/Aspart group reported fewer cases of fatigue, suggesting that it may be better tolerated overall. The safety profile of the Insulin Glargine/Aspart regimen is superior to the NPH/Regular Insulin regimen. Patients on Insulin Glargine/Aspart experienced fewer and less severe adverse reactions, fewer hypoglycemic episodes, and fewer reported side effects. These findings provide strong evidence to support the use of Insulin Glargine/Aspart for better safety outcomes in T1DM patients in Pakistan.

Discussion:

In this study, two groups based on their insulin regimens: Group A (Insulin Glargine/Aspart) and Group B (NPH/Regular Insulin). B (NPH/Regular Insulin). Randomized controlled trials (RCTs) benefit from balanced baseline clinical characteristics, as this enhances the reliability of attributing observed effects to the intervention rather than confounding factors (Schulz et al., 2010). In diabetes management, matching for variables like HbA1c, BMI, and cholesterol is particularly important due to their significant impact on treatment efficacy and safety (Nathan et al., 2005). The group-wise clinical characteristics demonstrate well-matched groups in terms of duration of diabetes, treatment type, insulin type, frequency of use, BMI, HbA1c, fasting blood sugar levels, blood sugar levels after a one-month run-in, cholesterol, and triglycerides. This balance is essential for the integrity of the study, allowing for a fair comparison of the clinical efficacy and safety of the Insulin Glargine/Aspart

regimen versus the NPH/Regular Insulin regimen in managing Type 1 Diabetes Mellitus in Pakistani patients.

These results align closely with studies conducted by Caires de Souza et al. (2023) further contextualize and support our findings regarding the clinical efficacy and safety profile of insulin regimens in Type 1 Diabetes Mellitus (T1DM) patients. This study adds valuable insights into the comparison of different insulin regimens and their impact on glycemic control and patient outcomes. Incorporating this study into our discussion allows us to draw parallels between their findings and ours, strengthening the evidence base for the clinical efficacy and safety of insulin regimens in T1DM management. Study demonstrates a comprehensive understanding of the existing literature and contribute to the collective knowledge on optimal treatment approaches for T1DM patients.

Shao et al. (2023) provides valuable insights into the cost-effectiveness of different insulin regimens, specifically comparing once-daily insulin glargine 300 U/mL to insulin degludec 100 U/mL. This study adds to the understanding of the economic implications associated with insulin therapy choices for Type 1 Diabetes Mellitus (T1DM) patients. Study can broaden our discussion to include considerations of cost-effectiveness, an important aspect of insulin regimen selection in T1DM management. This study enhances our understanding of the economic outcomes associated with different insulin options, which is particularly relevant when evaluating the affordability and cost-effectiveness of insulin regimens in T1DM patients in Pakistan. Study evidence base for decision-making regarding insulin therapy in clinical practice and healthcare policy.

Shao et al. (2024) is a valuable addition as it explores the cost-effectiveness of insulin glargine 300 units/mL compared to insulin glargine 100 units/mL over a lifetime horizon. This analysis provides further insights into the economic implications of using different concentrations of insulin glargine in the management of diabetes. By incorporating the findings of our discussion gains a deeper understanding of the long-term economic outcomes associated with insulin therapy choices for diabetes patients. This study contributes to the broader conversation on the cost-effectiveness of insulin glargine formulations, which is relevant for evaluating the affordability and sustainability of insulin regimens in the management of Type 1 Diabetes Mellitus (T1DM), especially in the context of healthcare resource allocation and policy-making in Pakistan. Research enhances the evidence base and informs decision-making regarding optimal insulin therapy strategies for T1DM patients.

Biskupiak et al. (2023) contributes valuable insights to our discussion by examining the cost-effectiveness of the tubeless automated insulin delivery system compared to the standard of care in managing Type 1 Diabetes (T1DM) in the United States. This research sheds light on the economic implications of adopting innovative insulin delivery technologies for T1DM management, which is relevant for our discussion on evaluating insulin regimen efficacy and cost-effectiveness. The findings of our discussion gain a broader perspective on the economic considerations associated with adopting advanced insulin delivery systems. This study's analysis of cost-effectiveness provides valuable data for policymakers and healthcare providers, informing decisions about incorporating innovative technologies into T1DM management protocols. This research complements our exploration of insulin regimen efficacy and affordability by highlighting the potential economic benefits and challenges associated with adopting new treatment modalities for T1DM.

Conclusion:

In the current study, there was no significant difference regarding glycemic control, hypo-glycemic episodes and lipid profile between two groups Insulin Glargine/Aspart and NPH/Regular Insulin; even though it has shown that new DNA recombinant insulins are more feasible to use. The study also stressed the significance of continuing education initiatives and follow-up, irrespective of the kind of insulin administered.

References:

1. Adnan, M., & Aasim, M. (2020). Prevalence of type 2 diabetes mellitus in adult population of Pakistan: a meta-analysis of prospective cross-sectional surveys. *Annals of global health*, *86*(1).

2. Adnan, M., & Aasim, M. (2024). Prevalence of gestational diabetes mellitus in Pakistan: a systematic review and meta-analysis. *BMC pregnancy and childbirth*, *24*(1), 108.
3. Azeem, S., Khan, U., & Liaquat, A. (2022). The increasing rate of diabetes in Pakistan: A silent killer. *Annals of medicine and surgery*, *79*.
4. Biskupiak, J. E., Ramos, M., Levy, C. J., Forlenza, G., Hopley, C., Boyd, J., Swift, D., Lamotte, M., & Brixner, D. I. (2023). Cost-effectiveness of the tubeless automated insulin delivery system vs standard of care in the management of type 1 diabetes in the United States. *Journal of Managed Care & Specialty Pharmacy*, *29*(7), 807-817.
5. Caires de Souza, A. L., Acurcio, F. d. A., Guerra Júnior, A. A., & Rezende Macedo Do Nascimento, R. (2023). This version is available at https://strathprints. strath. ac. uk/50976.
6. Dickson, S., Gabriel, N., Gellad, W. F., & Hernandez, I. (2023). Estimated changes in insulin prices and discounts after entry of new insulin products, 2012-2019. JAMA Health Forum,
7. Dovc, K., Lanzinger, S., Cardona-Hernandez, R., Tauschmann, M., Marigliano, M., Cherubini, V., Preikša, R., Schierloh, U., Clapin, H., & AlJaser, F. (2023). Association of achieving time in range clinical targets with treatment modality among youths with type 1 diabetes. *JAMA Network Open*, *6*(2), e230077-e230077.
8. Gerber, A., & Quinn, R. (2024). Insulin Glargine Associated Nausea in a Patient Seen by a Collaborative Drug Therapy Management Pharmacist in an Urban Community Hospital: A Case Report. *Hospital Pharmacy*, *59*(1), 15-18.
9. Kazda, C. M., Bue-Valleskey, J. M., Chien, J., Zhang, Q., Chigutsa, E., Landschulz, W., Wullenweber, P., Haupt, A., & Dahl, D. (2023). Novel once-weekly basal insulin fc achieved similar glycemic control with a safety profile comparable to insulin degludec in patients with type 1 diabetes. *Diabetes Care*, *46*(5), 1052-1059.
10. Lee, T. T., Collett, C., Bergford, S., Hartnell, S., Scott, E. M., Lindsay, R. S., Hunt, K. F., McCance, D. R., Barnard-Kelly, K., & Rankin, D. (2023). Automated insulin delivery in women with pregnancy complicated by type 1 diabetes. *New England Journal of Medicine*, *389*(17), 1566-1578.
11. Long, T., Lin, J.-t., Lin, M.-h., Wu, Q.-l., Lai, J.-m., Li, S.-z., Zhou, Z.-c., Zeng, J.-y., Huang, J.-s., & Zeng, C.-p. (2022). Comparative efficiency and safety of insulin degludec/aspart with insulin glargine in type 2 diabetes: a meta-analysis of randomized controlled trials. *Endocrine Journal*, *69*(8), 959-969.
12. Matli, M. C., Wilson, A. B., Rappsilber, L. M., Sheffield, F. P., Farlow, M. L., & Johnson, J. L. (2023). The first interchangeable biosimilar insulin: insulin glargine-yfgn. *Journal of Diabetes Science and Technology*, *17*(2), 490-494.
13. Shao, H., Shi, L., Fonseca, V., Alsaleh, A. J. O., Gill, J., & Nicholls, C. (2023). Cost-effectiveness analysis of once-daily insulin glargine 300 U/mL versus insulin degludec 100 U/mL using the BRAVO diabetes model. *Diabetic medicine*, *40*(9), e15112.
14. Shao, H., Shi, L., Fonseca, V., Alsaleh, A. J. O., Gill, J., & Nicholls, C. (2024). An exploratory analysis of the cost-effectiveness of insulin glargine 300 units/mL versus insulin glargine 100 units/mL over a lifetime horizon using the BRAVO diabetes model. *Diabetic medicine*, *41*(5), e15303.
15. Syed, F. Z. (2022). Type 1 diabetes mellitus. *Annals of internal medicine*, *175*(3), ITC33-ITC48.
16. Tatovic, D., Narendran, P., & Dayan, C. M. (2023). A perspective on treating type 1 diabetes mellitus before insulin is needed. *Nature Reviews Endocrinology*, *19*(6), 361-370.
17. Zarei, L., Peymani, P., Moradi, N., Kheirandish, M., Mirjalili, M., & Zare, M. (2022). Affordability of medication therapy in diabetic patients: a scenario-based assessment in Iran's health system context. *International Journal of Health Policy and Management*, *11*(4), 443.