Review

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Review

Insulin Therapy among Diabetic Patients in Rural Communities of Sub Saharan Africa: A Perspective Review

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Abstract: In this perspective review, we describe a brief background on the status quo of diabetes mellitus related therapies and glycemic control among patients in rural communities of sub Saharan Africa. We specifically talk about insulin therapy and the challenges of access to insulin and oral hypoglycemic therapies among the diabetic patients living in sub-Saharan Africa. We crown up our discussion with suggestions on solutions and opportunities for future research to tackle this health challenge in these impoverished communities. Our ideas have been informed by the following inquiries: What is the current situation with diabetes in Sub-Saharan Africa? How well controlled are blood sugar levels among diabetes individuals in Sub-Saharan Africa? What is insulin therapy, and for which patient populations is it recommended? What proportions of diabetic patients are on insulin therapy and oral hypoglycemic drugs in Sub-Saharan Africa? Which is the most common therapy given to diabetic patients in the rural communities of sub Saharan Africa between insulin and oral hypoglycemic drugs? Who determines the choice of therapy between insulin and oral hypoglycemic drugs? How often is hypoglycemia and hyperglycemia encountered among people on insulin therapy? Is monitoring glucagon levels important for treating diabetic individuals receiving insulin? Is it normal practice to check the glucagon levels of diabetes patients in sub-Saharan African rural communities? What insulin therapy research has been done in the rural communities of sub Saharan Africa and what research gaps exist in this field? Addressing these research gaps is critical for improving insulin therapy in rural communities of sub-Saharan Africa and reducing the burden of diabetes in these populations.

Keywords: Insulin; Glucagon; hypoglycaemia; hyperglycaemia; glycated hemoglobin; oral hypoglycaemics

1. What is the status quo of diabetes mellitus in Sub-Saharan Africa?

The prevalence and burden of insulin resistance vary greatly among different countries and regions of sub-Saharan Africa, making the current situation on the continent complicated. Despite the significance of diabetes on world health, the future economic effects of the condition are still unknown[1]. In sub-Saharan Africa, improvements in the therapeutic management of type 2 diabetes and related glycemic control are still far from ideal [2].

Diabetes mellitus is a growing public health concern in sub-Saharan Africa, with the prevalence of the disease increasing rapidly over the past few decades. Diabetes facts and figures show that there is a growing global burden for individuals, families, and countries. The International Diabetes Federation (IDF) Diabetes Atlas (2021) reports that 10.5% of the adult population (20-79 years) has diabetes, with almost half unaware that they are living with the condition. By 2045, IDF projects that 1 in 8 adults, approximately 783 million, will be living with diabetes, an increase of 46%. [3]. It was also reported that there were approximately 19.4 million people with diabetes in sub-Saharan Africa in 2019, and this number is projected to increase to 47.1 million by 2045 [4].

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Over 90% of cases of diabetes in sub-Saharan Africa are type 2, making it the most prevalent kind of the disease[5]. Changing food habits, physical inactivity, increasing urbanization, and genetic susceptibility are among the risk factors for diabetes in sub-Saharan Africa[6]. Diabetes is often undiagnosed and poorly managed in sub-Saharan Africa due to a lack of awareness, inadequate healthcare infrastructure, and limited access to affordable diabetes care and medications [5,7,8]. Complications of diabetes, such as cardiovascular disease, kidney disease, and blindness, are also common in sub-Saharan Africa, and they can further increase the burden on healthcare systems [9,10]. Efforts are being made to address the rising burden of diabetes in sub-Saharan Africa, including improved screening and diagnosis, increased availability of affordable diabetes care and medications, and public health campaigns to raise awareness and promote healthy lifestyles.

2. What is the status of glycemic control among diabetic patients in sub Saharan Africa?

The status of glycemic control among diabetic patients in sub-Saharan Africa is generally poor. There are several reasons for this, including limited access to healthcare, a lack of diabetes education and awareness, and the high cost of diabetes care and medications. According to research studies, many diabetics in sub-Saharan Africa have inadequate control of their glucose levels, which puts them at higher risk for consequences like heart disease, kidney damage, and blindness[11,12]. A study conducted in Ethiopia found that a significant number of diabetic patients had inadequate and poor glycemic control levels and this was associated with older age, longer duration of DM, insulin therapy, poor diet compliance, and failure to set control goals [13]. Another study conducted in Ghana found that only 16% of people with diabetes had good glycemic control [14]. There are several challenges to achieving good glycemic control in sub-Saharan Africa. These include a lack of access to insulin and other diabetes medications, poor adherence to treatment due to cultural and economic factors, and inadequate healthcare infrastructure [11,15]. Efforts are being made to improve glycemic control among diabetic patients in sub-Saharan Africa, including the development of locally appropriate guidelines and protocols for diabetes care, training of healthcare professionals, and the establishment of diabetes clinics and education programs. However, there is still a long way to go to ensure that all people with diabetes in sub-Saharan Africa have access to the care and support they need to achieve good glycemic control and prevent complications

3. What proportions of persons with diabetes are receiving insulin treatment in sub-Saharan Africa?

The proportion of diabetic patients who are on insulin therapy can vary depending on several factors, including the type of diabetes, the stage of the disease, and the availability and accessibility of insulin and other diabetes medications. In general, insulin therapy is more commonly used in patients with type 1 diabetes, as this form of diabetes is characterized by a lack of insulin production by the pancreas [16–19]. In contrast, patients with type 2 diabetes may initially be treated with lifestyle modifications and oral hypoglycemic agents, with insulin therapy reserved for those who do not achieve adequate glucose control with these interventions [20–23]. In rural communities of sub-Saharan Africa, the prevalence of diabetes and the proportion of patients on insulin therapy can vary widely depending on the specific location and healthcare resources available [5,24–26]. In some areas, access to insulin and other diabetes medications may be limited, resulting in a lower proportion of patients on insulin therapy [27,28]. In other areas, insulin therapy may be more widely used, particularly in patients with type 1 diabetes or advanced type 2 diabetes [6]. It is important to note that diabetes is a growing public health concern in sub-Saharan Africa. With increasing rates of the disease and its complications, rural-to-urban migration in the region has been noted to significantly increase the geographical spread of people with diabetes [26]. Efforts to improve access to diabetes care, including insulin therapy, are needed to address this growing burden of disease.

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4. What is insulin therapy and which group of patients are prescribed this therapy?

Patients with diabetes mellitus, a chronic metabolic condition marked by elevated circulating blood sugar levels, are typically recommended insulin therapy [29,30]. Insulin is a hormone that helps regulate blood glucose levels by promoting the uptake of glucose into cells and tissues, and the synthesis and storage of glycogen in the liver and muscles [31,32]. Patients with diabetes mellitus may require insulin therapy if their body is unable to produce enough insulin or if their cells are resistant to insulin, resulting in elevated blood glucose levels [32,33]. Diabetes mellitus can be of two major types: Diabetes type 1: This autoimmune illness causes the beta cells in the pancreas that create insulin to be assaulted and eliminated by the body's immune system [34–36]. Type 1 diabetes typically develops in childhood or adolescence and requires lifelong insulin therapy [17,18]. Type 2 diabetes: This is a metabolic disorder characterized by insulin resistance and impaired insulin secretion [22,23,37]. Obesity and a sedentary lifestyle are frequently linked to type 2 diabetes and is typically managed initially with lifestyle modifications and oral medications [22,38]. However, some patients with type 2 diabetes may eventually require insulin therapy as the disease progresses. In addition to patients with diabetes, insulin therapy may also be prescribed to patients with other medical conditions that affect glucose metabolism, such as gestational diabetes, cystic fibrosis-related diabetes, and steroid-induced diabetes [39–41].

5. What about oral hypoglycemic drugs?

Oral hypoglycemic drugs are medications that are used to treat diabetes mellitus by lowering blood glucose levels [42–45]. Unlike insulin therapy, which is delivered via injections or an insulin pump, oral hypoglycemic drugs are taken orally in pill form [46–48].There are several different classes of oral hypoglycemic drugs, each with a different mechanism of action: Biguanides: These medications, such as metformin, work by reducing glucose production in the liver and increasing glucose uptake by cells in the body[49,50]. Sulfonylureas: These medications, such as glyburide and glipizide, work by stimulating the pancreas to release more insulin [51,52]. Meglitinides: These medications, such as repaglinide and nateglinide, also stimulate insulin release from the pancreas, but their effects are shorter-acting than sulfonylureas [53,54]. Dipeptidyl peptidase-4 (DPP-4) inhibitors: These medications, such as sitagliptin and saxagliptin, work by increasing the levels of a hormone called incretin, which stimulates insulin release and reduces glucose production in the liver [55–58]. Sodium-glucose cotransporter-2 (SGLT2) inhibitors: These medications, such as canagliflozin and dapagliflozin, work by preventing the reabsorption of glucose in the kidneys, leading to increased glucose excretion in the urine[59–62]. Thiazolidinediones (TZDs): These medications, such as pioglitazone and rosiglitazone, work by increasing insulin sensitivity in cells and tissues [63–65]. The choice of oral hypoglycemic medication depends on several factors, including the type of diabetes, the severity of the disease, and the presence of other medical conditions [43,44,66]. In some cases, oral hypoglycemics may be used in combination with insulin therapy to achieve optimal blood glucose control [67,68].

6. Which is the most common therapy given in rural communities of Sub Saharan Africa between insulin and oral hypoglycemics?

Due to the limited availability and high cost of oral hypoglycemic medications in rural communities across sub-Saharan Africa, insulin therapy is frequently favored as a treatment for diabetes[12,26,69,70]. While oral hypoglycemics can be effective in managing diabetes, they may not be as readily available or accessible as insulin therapy in many rural areas[68,71,72]. Furthermore, insulin therapy may be a more practical option for patients who do not have access to refrigeration or reliable electricity, which may be necessary to store and administer some oral hypoglycemic medications [73–75]. However, it is worth noting that the availability and use of insulin therapy in rural communities of sub-Saharan Africa is also limited by several factors, including the high cost of insulin, the need for regular monitoring of blood glucose levels, and the lack of trained healthcare providers who can administer and manage insulin therapy [5,10,76]. Overall, the choice of therapy for diabetes in rural communities of sub-Saharan Africa may depend on a range of factors, including the availability of

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medications, the infrastructure for healthcare delivery, and the preferences and needs of individual patients.

7. Who determines this choice of therapy between insulin and oral hypoglycemic drugs?

The choice of therapy for diabetes, whether insulin or oral hypoglycemic drugs, is determined by a healthcare provider in consultation with the patient [43,77,78]. Healthcare providers, such as doctors, nurses, or clinical officers, are trained to diagnose and manage diabetes, and they will typically evaluate a patient's medical history, symptoms, and laboratory results to determine the most appropriate course of treatment [79,80]. Factors that may influence the choice of therapy include the type and severity of diabetes, the patient's overall health status, their access to healthcare and medications, and their preferences and lifestyle [66,81,82]. In rural communities of sub-Saharan Africa, where resources and infrastructure may be limited, healthcare providers may need to consider additional factors, such as the availability and cost of medications, and the practicalities of administering and monitoring treatment [83–86]. Ultimately, the choice of therapy for diabetes should be a shared decision between the healthcare provider and the patient, taking into account the best available evidence and the individual needs and circumstances of the patient.

8. How often is hypoglycemia encountered among people on insulin therapy?

Hypoglycemia, which is defined as a blood glucose level below 70 mg/dL (3.9 mmol/L), is a common complication of insulin therapy [87]. The kind and dosage of insulin, the timing and frequency of insulin injections, the patient's general health status, and adherence to treatment are all factors that affect the risk of hypoglycemia. Studies have shown that depending on the population being investigated and the techniques employed to measure hypoglycemia, the frequency of hypoglycemia varies significantly [18,78,88,89]. For instance, a review of studies involving individuals who had type 1 diabetes revealed that minor to moderate low blood sugar (requiring self-treatment) occurred in 18 to 138 episodes per patient-year while severe low blood sugar (requiring assistance from another person) occurred in 0.05 to 2.4 episodes per patient-year [90,91]. Similarly, a study of patients with type 2 diabetes found that the incidence of hypoglycemia varied depending on the type of insulin used, with a higher risk observed among those using long-acting basal insulin compared to those using short-acting insulin [92–96]. It is important to note that hypoglycemia can be a serious and potentially life-threatening complication of insulin therapy, and patients on insulin should be educated about the signs and symptoms of hypoglycemia and how to treat it promptly if it occurs [87,97,98]. Regular monitoring of blood glucose levels and close communication with a healthcare provider can also help to minimize the risk of hypoglycemia and ensure optimal diabetes management.

9. How often is hyperglycemia encountered among people on insulin therapy?

Hyperglycemia, which is defined as a blood glucose level above the target range and can occur in people on insulin therapy if the dose of insulin is not adequate or if there are other factors affecting insulin sensitivity, such as illness or stress [80,99]. The frequency of hyperglycemia among people on insulin therapy can vary depending on several factors, including the type and dose of insulin, the timing and frequency of insulin injections, and the patient's overall health status and adherence to treatment [100–102]. According to research, the risk of hyperglycemia persists even after insulin therapy can successfully lower blood glucose levels in persons with diabetes. For example, a study of people with type 1 diabetes reported that 38.2% of people with a HbA1c level of 7.0% or higher and 11.2% of people with a HbA1c level of less than 7.0% experienced hyperglycemia, which is characterized as a level of blood sugar above 180 mg/dL or 10 mmol/L [103–107]. Similarly, a study of patients with type 2 diabetes found that 44% of patients receiving basal insulin therapy and 52% of patients receiving basal-bolus insulin therapy experienced hyperglycemia, which is defined as blood glucose levels above 130 mg/dL or 7.2 mmol/L[108]. It is important for patients on insulin therapy to regularly monitor their blood glucose levels and work with their healthcare provider to adjust their insulin dose as

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needed to keep the blood sugar level under control and reduce the possibility of having elevated sugar levels.

10. Is the assessment of glucagon levels important when managing diabetic individuals using insulin therapy?

In the treatment of people with diabetes on insulin treatment, measurement of glucagon levels is not frequently performed[109,110]. However, glucagon plays an important role in glucose homeostasis, and understanding the interaction between insulin and glucagon can be useful in managing diabetes, particularly in patients on insulin therapy [111]. Insulin and glucagon have opposite effects on blood glucose levels, with insulin promoting glucose uptake and storage, while glucagon promotes the release of glucose from the liver [112]. In patients with diabetes, the balance between insulin and glucagon is disrupted, leading to hyperglycemia. In patients on insulin therapy, glucagon levels can impact glucose control, as high levels of glucagon can counteract the effects of insulin and lead to elevated blood glucose levels [80,113,114]. While glucagon levels are not routinely assessed in the management of diabetes, healthcare providers may consider measuring glucagon levels in certain situations, such as in the context of research studies or when there is suspicion of glucagonoma, a rare tumor that produces excessive amounts of glucagon and can lead to severe hyperglycemia [115,116]. In general, the management of diabetes on insulin therapy focuses on monitoring blood glucose levels and adjusting insulin doses as needed to achieve optimal glucose control [117]. Regular follow-up with healthcare providers is important to assess treatment effectiveness and adjust treatment plans as needed.

11. Is assessment of glucagon levels a common practice among diabetic patients in rural communities of sub Saharan Africa

The assessment of glucagon levels is not a common practice in the routine management of diabetes in rural communities of sub-Saharan Africa [118,119]. Glucagon is a hormone produced by the pancreas that plays an important role in regulating blood glucose levels by promoting the release of stored glucose from the liver [111]. While glucagon levels can be measured through blood tests, this is typically done in a research or clinical setting, and not as part of routine diabetes management [109,117].The assessment and monitoring of blood glucose levels, as well as other measurements like HbA1c, which shows whether or not long-term glucose control has been achieved, are often the main priorities in the handling of diabetes[80,87]. Insulin therapy and/or oral hypoglycemic agents are typically used to lower blood glucose levels, while dietary and lifestyle modifications are also important in the management of diabetes [43,74]. It is significant to remember that medical amenities are not readily available, including laboratory testing and medical supplies. These can be limited in rural communities in sub-Saharan Africa, which may impact the ability to perform certain tests or provide certain treatments [120–123]. As such, healthcare providers in these settings may need to prioritize the most essential components of diabetes management based on available resources and the specific needs of individual patients.

12. What insulin therapy research has been done in rural communities of sub Saharan Africa

Insulin research in rural communities of sub-Saharan Africa has been ongoing for several years. Some of the key areas of research include: Access to insulin: One of the major challenges faced by rural communities in sub-Saharan Africa is limited access to insulin [6,12,118,124]. Research has been conducted to determine the availability of insulin in rural areas and to identify barriers to access. This has led to the development of strategies to improve access to insulin, such as training healthcare workers to provide insulin therapy and establishing distribution networks to deliver insulin to rural areas [124–126]. Diabetes prevalence and treatment: Studies have also examined the number of cases of the condition in rural areas and the efficiency of various treatment options [124,127–130]. This has involved conducting surveys and clinical trials to assess the impact of various interventions, such as lifestyle modifications, medication adherence programs, and community-based care models [130]. Cost-

effectiveness of insulin therapy: Research has also looked at the cost-effectiveness of insulin therapy in rural communities [131–133]. This has involved evaluating the cost of insulin therapy and its impact on patient outcomes, as well as assessing the feasibility of scaling up insulin therapy in resource-limited settings. Education and awareness: Another area of research has been focused on increasing education and awareness about diabetes and insulin therapy in rural communities [75,134–137]. This has involved developing culturally appropriate educational materials and working with community health workers to deliver diabetes education and support. Overall, insulin research in rural communities of sub-Saharan Africa is aimed at improving access to insulin therapy, reducing the burden of diabetes, and improving patient outcomes.

13. What research gaps exist in this field?

Despite the progress made in insulin research in rural communities of sub-Saharan Africa, there are still several research gaps that need to be addressed. Some of the key research gaps include: Limited data on insulin access: While there have been efforts to improve access to insulin in rural areas, there is still limited data on the availability and accessibility of insulin (Fralick et al., 2022; Massey et al., 2010; Mbanya and Mba, 2021; Satheesh et al., 2019). More research is needed to assess the current state of insulin access in rural communities and to identify strategies for improving access. Limited understanding of patient perspectives: Research has primarily focused on healthcare provider perspectives, with limited understanding of patient perspectives on insulin therapy[78,138–141]. More research is needed to understand patient experiences with insulin therapy, including barriers to adherence and strategies for improving treatment outcomes. Limited data on long-term outcomes: While there have been studies assessing the short-term impact of insulin therapy on patient outcomes, there is a lack of data on long-term outcomes, such as mortality rates and quality of life [142,143]. More research is needed to assess the long-term impact of insulin therapy on patient outcomes in rural communities. Limited research on alternative insulin delivery methods: While insulin injections are the most common method of insulin delivery, there is a need for research on alternative insulin delivery methods that may be more feasible or acceptable in rural communities, such as insulin patches or inhalers [47,144]. Limited research on comorbidities: Diabetes often coexists with other conditions, such as hypertension and cardiovascular disease [145]. Additional research is required to comprehend the way pathologies affect insulin therapy as well as to develop integrated treatment modalities that simultaneously tackle many illnesses.

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References

1. Bommer C, Sagalova V, Heesemann E, et al. Global Economic Burden of Diabetes in Adults: Projections From 2015 to 2030. *Diabetes Care* 2018; 41: 963–970.
2. Fina Lubaki J-P, Omole OB, Francis JM. Glycaemic control among type 2 diabetes patients in sub-Saharan Africa from 2012 to 2022: a systematic review and meta-analysis. *Diabetol Metab Syndr* 2022; 14: 134.
3. Facts & figures. *International Diabetes Federation*, https://idf.org/about-diabetes/facts-figures/ (accessed 5 July 2023).

4. P S, I P, P S, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*; 157. Epub ahead of print November 2019. DOI: 10.1016/j.diabres.2019.107843.
5. Pastakia SD, Nuche-Berenguer B, Pekny CR, et al. Retrospective assessment of the quality of diabetes care in a rural diabetes clinic in Western Kenya. *BMC Endocr Disord* 2018; 18: 97.
6. Mbanya JC, Mba CM. Centenary of the discovery of insulin: People with diabetes in Africa still have poor access to insulin. *eClinicalMedicine*; 34. Epub ahead of print 1 April 2021. DOI: 10.1016/j.eclinm.2021.100809.
7. Chang H, Hawley NL, Kalyesubula R, et al. Challenges to hypertension and diabetes management in rural Uganda: a qualitative study with patients, village health team members, and health care professionals. *Int J Equity Health* 2019; 18: 38.
8. Zimmermann M, Bunn C, Namadingo H, et al. Experiences of type 2 diabetes in sub-Saharan Africa: a scoping review. *Glob Health Res Policy* 2018; 3: 25.
9. Kengne AP, Amoah AGB, Mbanya J-C. Cardiovascular complications of diabetes mellitus in sub-Saharan Africa. *Circulation* 2005; 112: 3592–3601.
10. Mercer T, Chang AC, Fischer L, et al. Mitigating The Burden Of Diabetes In Sub-Saharan Africa Through An Integrated Diagonal Health Systems Approach. *Diabetes Metab Syndr Obes Targets Ther* 2019; 12: 2261–2272.
11. Azevedo M, Alla S. Diabetes in Sub-Saharan Africa: Kenya, Mali, Mozambique, Nigeria, South Africa and Zambia. *Int J Diabetes Dev Ctries* 2008; 28: 101–108.
12. Pastakia SD, Pekny CR, Manyara SM, et al. Diabetes in sub-Saharan Africa – from policy to practice to progress: targeting the existing gaps for future care for diabetes. *Diabetes Metab Syndr Obes Targets Ther* 2017; 10: 247–263.
13. Abera RG, Demesse ES, Boko WD. Evaluation of glycemic control and related factors among outpatients with type 2 diabetes at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: a cross-sectional study. *BMC Endocr Disord* 2022; 22: 54.
14. Djonor SK, Ako-Nnubeng IT, Owusu EA, et al. Determinants of blood glucose control among people with Type 2 diabetes in a regional hospital in Ghana. *PLoS ONE* 2021; 16: e0261455.
15. Fekadu G, Bula K, Bayisa G, et al. Challenges And Factors Associated With Poor Glycemic Control Among Type 2 Diabetes Mellitus Patients At Nekemte Referral Hospital, Western Ethiopia. *J Multidiscip Healthc* 2019; 12: 963–974.
16. Chiang JL, Kirkman MS, Laffel LMB, et al. Type 1 Diabetes Through the Life Span: A Position Statement of the American Diabetes Association. *Diabetes Care* 2014; 37: 2034–2054.
17. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. *Lancet Lond Engl* 2018; 391: 2449–2462.
18. Janež A, Guja C, Mitrakou A, et al. Insulin Therapy in Adults with Type 1 Diabetes Mellitus: a Narrative Review. *Diabetes Ther* 2020; 11: 387–409.
19. Lucier J, Weinstock RS. Type 1 Diabetes. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK507713/ (2023, accessed 20 July 2023).
20. Dilworth L, Facey A, Omoruyi F. Diabetes Mellitus and Its Metabolic Complications: The Role of Adipose Tissues. *Int J Mol Sci* 2021; 22: 7644.
21. Galicia-Garcia U, Benito-Vicente A, Jebari S, et al. Pathophysiology of Type 2 Diabetes Mellitus. *Int J Mol Sci* 2020; 21: 6275.
22. Goyal R, Jialal I. Type 2 Diabetes. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK513253/ (2023, accessed 20 July 2023).
23. Hameed I, Masoodi SR, Mir SA, et al. Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition. *World J Diabetes* 2015; 6: 598.
24. Ayah R, Joshi MD, Wanjiru R, et al. A population-based survey of prevalence of diabetes and correlates in an urban slum community in Nairobi, Kenya. *BMC Public Health* 2013; 13: 371.
25. Hall V, Thomsen RW, Henriksen O, et al. Diabetes in Sub Saharan Africa 1999-2011: Epidemiology and public health implications. a systematic review. *BMC Public Health* 2011; 11: 564.
26. Mbanya J-C, Ramiaya K. Diabetes Mellitus. In: Jamison DT, Feachem RG, Makgoba MW, et al. (eds) *Disease and Mortality in Sub-Saharan Africa*. Washington (DC): The International Bank for Reconstruction and Development / The World Bank, http://www.ncbi.nlm.nih.gov/books/NBK2291/ (2006, accessed 19 July 2023).

27. Home P, Baik SH, Gálvez GG, et al. An analysis of the cost-effectiveness of starting insulin detemir in insulin-naïve people with type 2 diabetes. *J Med Econ* 2015; 18: 230–240.
28. Katte JC, McDonald TJ, Sobngwi E, et al. The phenotype of type 1 diabetes in sub-Saharan Africa. *Front Public Health*; 11, https://www.frontiersin.org/articles/10.3389/fpubh.2023.1014626 (2023, accessed 20 July 2023).
29. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2009; 32: S62–S67.
30. Thota S, Akbar A. Insulin. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK560688/ (2023, accessed 20 July 2023).
31. Rahman MS, Hossain KS, Das S, et al. Role of Insulin in Health and Disease: An Update. *Int J Mol Sci* 2021; 22: 6403.
32. Wilcox G. Insulin and Insulin Resistance. *Clin Biochem Rev* 2005; 26: 19–39.
33. Freeman AM, Pennings N. Insulin Resistance. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK507839/ (2023, accessed 20 July 2023).
34. Kahanovitz L, Sluss PM, Russell SJ. Type 1 Diabetes – A Clinical Perspective. *Point Care* 2017; 16: 37–40.
35. Roep BO, Thomaidou S, van Tienhoven R, et al. Type 1 diabetes mellitus as a disease of the β-cell (do not blame the immune system?). *Nat Rev Endocrinol* 2021; 17: 150–161.
36. Toren E, Burnette KS, Banerjee RR, et al. Partners in Crime: Beta-Cells and Autoimmune Responses Complicit in Type 1 Diabetes Pathogenesis. *Front Immunol*; 12, https://www.frontiersin.org/articles/10.3389/fimmu.2021.756548 (2021, accessed 20 July 2023).
37. Zhao X, An X, Yang C, et al. The crucial role and mechanism of insulin resistance in metabolic disease. *Front Endocrinol*; 14, https://www.frontiersin.org/articles/10.3389/fendo.2023.1149239 (2023, accessed 20 July 2023).
38. Galaviz KI, Narayan KMV, Lobelo F, et al. Lifestyle and the Prevention of Type 2 Diabetes: A Status Report. *Am J Lifestyle Med* 2015; 12: 4–20.
39. Hwang JL, Weiss RE. Steroid-induced diabetes: a clinical and molecular approach to understanding and treatment. *Diabetes Metab Res Rev* 2014; 30: 96–102.
40. Moran A, Brunzell C, Cohen RC, et al. Clinical Care Guidelines for Cystic Fibrosis–Related Diabetes. *Diabetes Care* 2010; 33: 2697–2708.
41. Sweeting A, Wong J, Murphy HR, et al. A Clinical Update on Gestational Diabetes Mellitus. *Endocr Rev* 2022; 43: 763–793.
42. Bramlage P, Gitt AK, Binz C, et al. Oral antidiabetic treatment in type-2 diabetes in the elderly: balancing the need for glucose control and the risk of hypoglycemia. *Cardiovasc Diabetol* 2012; 11: 122.
43. Ganesan K, Rana MBM, Sultan S. Oral Hypoglycemic Medications. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK482386/ (2023, accessed 19 July 2023).
44. Lorenzati B, Zucco C, Miglietta S, et al. Oral Hypoglycemic Drugs: Pathophysiological Basis of Their Mechanism of Action. *Pharmaceuticals* 2010; 3: 3005–3020.
45. Luna B, Feinglos MN. Oral Agents in the Management of Type 2 Diabetes Mellitus. *Am Fam Physician* 2001; 63: 1747–1757.
46. Feingold KR. Oral and Injectable (Non-Insulin) Pharmacological Agents for the Treatment of Type 2 Diabetes. In: Feingold KR, Anawalt B, Blackman MR, et al. (eds) *Endotext*. South Dartmouth (MA): MDText.com, Inc., http://www.ncbi.nlm.nih.gov/books/NBK279141/ (2000, accessed 19 July 2023).
47. Shah RB, Patel M, Maahs DM, et al. Insulin delivery methods: Past, present and future. *Int J Pharm Investig* 2016; 6: 1–9.
48. Wong CY, Martinez J, Dass CR. Oral delivery of insulin for treatment of diabetes: status quo, challenges and opportunities. *J Pharm Pharmacol* 2016; 68: 1093–1108.
49. Magno LD, Pastena FD, Bordone R, et al. The Mechanism of Action of Biguanides: New Answers to a Complex Question. *Cancers*; 14. Epub ahead of print July 2022. DOI: 10.3390/cancers14133220.
50. Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. *Diabetologia* 2017; 60: 1577–1585.
51. Costello RA, Nicolas S, Shivkumar A. Sulfonylureas. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK513225/ (2023, accessed 19 July 2023).
52. Sola D, Rossi L, Schianca GPC, et al. Sulfonylureas and their use in clinical practice. *Arch Med Sci AMS* 2015; 11: 840–848.
53. Guardado-Mendoza R, Prioletta A, Jiménez-Ceja LM, et al. The role of nateglinide and repaglinide, derivatives of meglitinide, in the treatment of type 2 diabetes mellitus. *Arch Med Sci AMS* 2013; 9: 936–943.

54. Milner Z, Akhondi H. Repaglinide. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK559305/ (2023, accessed 20 July 2023).
55. Ahrén B, Foley JE. Improved glucose regulation in type 2 diabetic patients with DPP-4 inhibitors: focus on alpha and beta cell function and lipid metabolism. *Diabetologia* 2016; 59: 907–917.
56. Barnett A. DPP-4 inhibitors and their potential role in the management of type 2 diabetes. *Int J Clin Pract* 2006; 60: 1454–1470.
57. Godinho R, Mega C, Teixeira-de-Lemos E, et al. The Place of Dipeptidyl Peptidase-4 Inhibitors in Type 2 Diabetes Therapeutics: A "Me Too" or "the Special One" Antidiabetic Class? *J Diabetes Res* 2015; 2015: 806979.
58. Kasina SVSK, Baradhi KM. Dipeptidyl Peptidase IV (DPP IV) Inhibitors. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK542331/ (2023, accessed 20 July 2023).
59. Jasleen B, Vishal GK, Sameera M, et al. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Benefits Versus Risk. *Cureus*; 15: e33939.
60. Ni L, Yuan C, Chen G, et al. SGLT2i: beyond the glucose-lowering effect. *Cardiovasc Diabetol* 2020; 19: 98.
61. Padda IS, Mahtani AU, Parmar M. Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK576405/ (2023, accessed 20 July 2023).
62. Tang J, Ye L, Yan Q, et al. Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Water and Sodium Metabolism. *Front Pharmacol*; 13, https://www.frontiersin.org/articles/10.3389/fphar.2022.800490 (2022, accessed 20 July 2023).
63. Eggleton JS, Jialal I. Thiazolidinediones. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK551656/ (2023, accessed 20 July 2023).
64. Lebovitz HE. Thiazolidinediones: the Forgotten Diabetes Medications. *Curr Diab Rep* 2019; 19: 151.
65. Quinn CE, Hamilton PK, Lockhart CJ, et al. Thiazolidinediones: effects on insulin resistance and the cardiovascular system. *Br J Pharmacol* 2008; 153: 636–645.
66. American Diabetes Association. Standards of Medical Care in Diabetes—2022 Abridged for Primary Care Providers. *Clin Diabetes* 2022; 40: 10–38.
67. Buse J. Combining insulin and oral agents. *Am J Med* 2000; 108 Suppl 6a: 23S-32S.
68. Hermansen K, Mortensen LS, Hermansen M-L. Combining insulins with oral antidiabetic agents: effect on hyperglycemic control, markers of cardiovascular risk and disease. *Vasc Health Risk Manag* 2008; 4: 561–574.
69. Mbanya JC, Lamptey R, Uloko AE, et al. African Cuisine-Centered Insulin Therapy: Expert Opinion on the Management of Hyperglycaemia in Adult Patients with Type 2 Diabetes Mellitus. *Diabetes Ther* 2021; 12: 37–54.
70. Stephani V, Opoku D, Beran D. Self-management of diabetes in Sub-Saharan Africa: a systematic review. *BMC Public Health* 2018; 18: 1148.
71. Fralick M, Jenkins AJ, Khunti K, et al. Global accessibility of therapeutics for diabetes mellitus. *Nat Rev Endocrinol* 2022; 18: 199–204.
72. Mohan V, Khunti K, Chan SP, et al. Management of Type 2 Diabetes in Developing Countries: Balancing Optimal Glycaemic Control and Outcomes with Affordability and Accessibility to Treatment. *Diabetes Ther* 2020; 11: 15–35.
73. Al-Tabakha MM, Arida AI. Recent Challenges in Insulin Delivery Systems: A Review. *Indian J Pharm Sci* 2008; 70: 278–286.
74. Bretzel RG, Eckhard M, Landgraf W, et al. Initiating Insulin Therapy in Type 2 Diabetic Patients Failing on Oral Hypoglycemic Agents. *Diabetes Care* 2009; 32: S260–S265.
75. Das AK, Saboo B, Maheshwari A, et al. Health care delivery model in India with relevance to diabetes care. *Heliyon* 2022; 8: e10904.
76. Ng'ang'a L, Ngoga G, Dusabeyezu S, et al. Implementation of blood glucose self-monitoring among insulin-dependent patients with type 2 diabetes in three rural districts in Rwanda: 6 months open randomised controlled trial. *BMJ Open* 2020; 10: e036202.
77. Al-Faris EA. GUIDELINES FOR THE MANAGEMENT OF DIABETIC PATIENTS IN THE HEALTH CENTERS OF SAUDI ARABIA. *J Fam Community Med* 1997; 4: 12–23.
78. Ellis K, Mulnier H, Forbes A. Perceptions of insulin use in type 2 diabetes in primary care: a thematic synthesis. *BMC Fam Pract* 2018; 19: 70.

79. Balogh EP, Miller BT, Ball JR, et al. The Diagnostic Process. In: *Improving Diagnosis in Health Care*. National Academies Press (US), https://www.ncbi.nlm.nih.gov/books/NBK338593/ (2015, accessed 19 July 2023).
80. Dhatariya K, Corsino L, Umpierrez GE. Management of Diabetes and Hyperglycemia in Hospitalized Patients. In: Feingold KR, Anawalt B, Blackman MR, et al. (eds) *Endotext*. South Dartmouth (MA): MDText.com, Inc., http://www.ncbi.nlm.nih.gov/books/NBK279093/ (2000, accessed 19 July 2023).
81. Schroeder EB. Management of Type 2 Diabetes: Selecting Amongst Available Pharmacological Agents. In: Feingold KR, Anawalt B, Blackman MR, et al. (eds) *Endotext*. South Dartmouth (MA): MDText.com, Inc., http://www.ncbi.nlm.nih.gov/books/NBK425702/ (2000, accessed 19 July 2023).
82. Williams DM, Jones H, Stephens JW. Personalized Type 2 Diabetes Management: An Update on Recent Advances and Recommendations. *Diabetes Metab Syndr Obes Targets Ther* 2022; 15: 281–295.
83. Healthcare Access in Rural Communities Overview - Rural Health Information Hub, https://www.ruralhealthinfo.org/topics/healthcare-access (accessed 19 July 2023).
84. Kolié D, Van De Pas R, Codjia L, et al. Increasing the availability of health workers in rural sub-Saharan Africa: a scoping review of rural pipeline programmes. *Hum Resour Health* 2023; 21: 20.
85. Konde-Lule J, Gitta SN, Lindfors A, et al. Private and public health care in rural areas of Uganda. *BMC Int Health Hum Rights* 2010; 10: 29.
86. Musoke D, Boynton P, Butler C, et al. Health seeking behaviour and challenges in utilising health facilities in Wakiso district, Uganda. *Afr Health Sci* 2014; 14: 1046–1055.
87. Mathew P, Thoppil D. Hypoglycemia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK534841/ (2023, accessed 19 July 2023).
88. Lin YK, Fisher SJ, Pop-Busui R. Hypoglycemia unawareness and autonomic dysfunction in diabetes: Lessons learned and roles of diabetes technologies. *J Diabetes Investig* 2020; 11: 1388–1402.
89. Silbert R, Salcido-Montenegro A, Rodriguez-Gutierrez R, et al. Hypoglycemia among Patients with Type 2 Diabetes: Epidemiology, Risk Factors, and Prevention Strategies. *Curr Diab Rep* 2018; 18: 53.
90. Cryer PE. Glycemic goals in diabetes: trade-off between glycemic control and iatrogenic hypoglycemia. *Diabetes* 2014; 63: 2188–2195.
91. Kovatchev B. Glycemic Variability: Risk Factors, Assessment, and Control. *J Diabetes Sci Technol* 2019; 13: 627–635.
92. Beck-Nielsen H, Henriksen JE. Antidiabetic Combination Therapy. In: Mogensen CE (ed) *Pharmacotherapy of Diabetes: New Developments: Improving Life and Prognosis for Diabetic Patients*. Boston, MA: Springer US, pp. 99–109.
93. Gangji AS, Cukierman T, Gerstein HC, et al. A Systematic Review and Meta-Analysis of Hypoglycemia and Cardiovascular Events: A comparison of glyburide with other secretagogues and with insulin. *Diabetes Care* 2007; 30: 389–394.
94. Holstein A, Plaschke A, Egberts EH. Lower incidence of severe hypoglycaemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. *Diabetes Metab Res Rev* 2001; 17: 467–473.
95. Romantsova TI, Maksimova NV. Optimization of therapy of type 2 diabetes mellitus with the oral hypoglycemic agent glimepiride. *Diabetes Mellit* 2010; 13: 50–54.
96. Tschöpe D, Bramlage P, Binz C, et al. Incidence and predictors of hypoglycaemia in type 2 diabetes – an analysis of the prospective DiaRegis registry. *BMC Endocr Disord* 2012; 12: 23.
97. Heller SR, Peyrot M, Oates SK, et al. Hypoglycemia in patient with type 2 diabetes treated with insulin: it can happen. *BMJ Open Diabetes Res Care* 2020; 8: e001194.
98. McCall AL. Insulin Therapy and Hypoglycemia. *Endocrinol Metab Clin North Am* 2012; 41: 57–87.
99. Vedantam D, Poman DS, Motwani L, et al. Stress-Induced Hyperglycemia: Consequences and Management. *Cureus*; 14. Epub ahead of print July 2022. DOI: 10.7759/cureus.26714.
100. Swinnen SG, Hoekstra JB, DeVries JH. Insulin Therapy for Type 2 Diabetes. *Diabetes Care* 2009; 32: S253–S259.
101. Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2022; 45: 2753–2786.
102. Sarbacker GB, Urteaga EM. Adherence to Insulin Therapy. *Diabetes Spectr Publ Am Diabetes Assoc* 2016; 29: 166–170.
103. Bergenstal RM, Tamborlane WV, Ahmann A, et al. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *N Engl J Med* 2010; 363: 311–320.

104. Kordonouri O, Pankowska E, Rami B, et al. Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment. *Diabetologia* 2010; 53: 2487–2495.
105. Ly TT, Nicholas JA, Retterath A, et al. Effect of Sensor-Augmented Insulin Pump Therapy and Automated Insulin Suspension vs Standard Insulin Pump Therapy on Hypoglycemia in Patients With Type 1 Diabetes: A Randomized Clinical Trial. *JAMA* 2013; 310: 1240–1247.
106. Steineck I, Ranjan A, Nørgaard K, et al. Sensor-Augmented Insulin Pumps and Hypoglycemia Prevention in Type 1 Diabetes. *J Diabetes Sci Technol* 2017; 11: 50–58.
107. Tumminia A, Sciacca L, Frittitta L, et al. Integrated insulin pump therapy with continuous glucose monitoring for improved adherence: technology update. *Patient Prefer Adherence* 2015; 9: 1263–1270.
108. Garg SK, Admane K, Freemantle N, et al. Patient-led versus physician-led titration of insulin glargine in patients with uncontrolled type 2 diabetes: a randomized multinational ATLAS study. *Endocr Pract Off J Am Coll Endocrinol Am Assoc Clin Endocrinol* 2015; 21: 143–157.
109. Haymond MW, Liu J, Bispham J, et al. Use of Glucagon in Patients With Type 1 Diabetes. *Clin Diabetes Publ Am Diabetes Assoc* 2019; 37: 162–166.
110. Kedia N. Treatment of severe diabetic hypoglycemia with glucagon: an underutilized therapeutic approach. *Diabetes Metab Syndr Obes Targets Ther* 2011; 4: 337–346.
111. Rix I, Nexøe-Larsen C, Bergmann NC, et al. Glucagon Physiology. In: Feingold KR, Anawalt B, Blackman MR, et al. (eds) *Endotext*. South Dartmouth (MA): MDText.com, Inc., http://www.ncbi.nlm.nih.gov/books/NBK279127/ (2000, accessed 19 July 2023).
112. Jiang S, Young JL, Wang K, et al. Diabetic-induced alterations in hepatic glucose and lipid metabolism: The role of type 1 and type 2 diabetes mellitus. *Mol Med Rep* 2020; 22: 603–611.
113. Hædersdal S, Lund A, Knop FK, et al. The Role of Glucagon in the Pathophysiology and Treatment of Type 2 Diabetes. *Mayo Clin Proc* 2018; 93: 217–239.
114. Jia Y, Liu Y, Feng L, et al. Role of Glucagon and Its Receptor in the Pathogenesis of Diabetes. *Front Endocrinol* 2022; 13: 928016.
115. Leichter SB. Clinical and metabolic aspects of glucagonoma. *Medicine (Baltimore)* 1980; 59: 100–113.
116. Sandhu S, Jialal I. Glucagonoma Syndrome. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing, http://www.ncbi.nlm.nih.gov/books/NBK519500/ (2023, accessed 19 July 2023).
117. Weinstock RS, Aleppo G, Bailey TS, et al. *The Role of Blood Glucose Monitoring in Diabetes Management*. Arlington (VA): American Diabetes Association, http://www.ncbi.nlm.nih.gov/books/NBK566165/ (2020, accessed 19 July 2023).
118. Gill GV, Mbanya J-C, Ramaiya KL, et al. A sub-Saharan African perspective of diabetes. *Diabetologia* 2009; 52: 8–16.
119. Olokoba AB, Obateru OA, Olokoba LB. Type 2 Diabetes Mellitus: A Review of Current Trends. *Oman Med J* 2012; 27: 269–273.
120. Bitter CC, Rice B, Periyanayagam U, et al. What resources are used in emergency departments in rural sub-Saharan Africa? A retrospective analysis of patient care in a district-level hospital in Uganda. *BMJ Open* 2018; 8: e019024.
121. Dowhaniuk N. Exploring country-wide equitable government health care facility access in Uganda. *Int J Equity Health* 2021; 20: 38.
122. Kolié D, Van De Pas R, Codjia L, et al. Increasing the availability of health workers in rural sub-Saharan Africa: a scoping review of rural pipeline programmes. *Hum Resour Health* 2023; 21: 20.
123. Petti CA, Polage CR, Quinn TC, et al. Laboratory Medicine in Africa: A Barrier to Effective Health Care. *Clin Infect Dis* 2006; 42: 377–382.
124. Birabwa C, Bwambale MF, Waiswa P, et al. Quality and barriers of outpatient diabetes care in rural health facilities in Uganda – a mixed methods study. *BMC Health Serv Res* 2019; 19: 706.
125. Bayked EM, Kahissay MH, Workneh BD. Barriers and facilitators to insulin treatment: a phenomenological inquiry. *J Pharm Policy Pract* 2022; 15: 45.
126. Lee YK, Ng CJ, Lee PY, et al. What are the barriers faced by patients using insulin? A qualitative study of Malaysian health care professionals' views. *Patient Prefer Adherence* 2013; 7: 103–109.
127. Ansari RM, Harris MF, Hosseinzadeh H, et al. Experiences of Diabetes Self-Management: A Focus Group Study among the Middle-Aged Population of Rural Pakistan with Type 2 Diabetes. *Diabetology* 2022; 3: 17–29.

128. Chiwanga FS, Njelekela MA, Diamond MB, et al. Urban and rural prevalence of diabetes and pre-diabetes and risk factors associated with diabetes in Tanzania and Uganda. *Glob Health Action* 2016; 9: 10.3402/gha.v9.31440.
129. Grundlingh N, Zewotir TT, Roberts DJ, et al. Assessment of prevalence and risk factors of diabetes and pre-diabetes in South Africa. *J Health Popul Nutr* 2022; 41: 7.
130. Guwatudde D, Delobelle P, Absetz P, et al. Prevention and management of type 2 diabetes mellitus in Uganda and South Africa: Findings from the SMART2D pragmatic implementation trial. *PLOS Glob Public Health* 2022; 2: e0000425.
131. Home P, Riddle M, Cefalu WT, et al. Insulin Therapy in People With Type 2 Diabetes: Opportunities and Challenges? *Diabetes Care* 2014; 37: 1499–1508.
132. Anyasodor AE, Nwose EU, Bwititi PT, et al. Cost-effectiveness of community diabetes screening: Application of Akaike information criterion in rural communities of Nigeria. *Front Public Health*; 10, https://www.frontiersin.org/articles/10.3389/fpubh.2022.932631 (2022, accessed 19 July 2023).
133. Dugani SB, Mielke MM, Vella A. Burden and Management of Type 2 Diabetes Mellitus in Rural United States. *Diabetes Metab Res Rev* 2021; 37: e3410.
134. AGBANA RD, ADEGBILERO-IWARI OE, AMU EO, et al. Awareness and risk burden of diabetes mellitus in a rural community of Ekiti State, South-Western Nigeria. *J Prev Med Hyg* 2021; 61: E593–E600.
135. Khodakarami R, Abdi Z, Ahmadnezhad E, et al. Prevalence, awareness, treatment and control of diabetes among Iranian population: results of four national cross-sectional STEPwise approach to surveillance surveys. *BMC Public Health* 2022; 22: 1216.
136. Pal R, Pal S, Barua A, et al. Health education intervention on diabetes in Sikkim. *Indian J Endocrinol Metab* 2010; 14: 3–7.
137. Zhang H, Qi D, Gu H, et al. Trends in the prevalence, awareness, treatment and control of diabetes in rural areas of northern China from 1992 to 2011. *J Diabetes Investig* 2020; 11: 241–249.
138. Bin rsheed A, Chenoweth I. Barriers that practitioners face when initiating insulin therapy in general practice settings and how they can be overcome. *World J Diabetes* 2017; 8: 28–39.
139. Okazaki K, Shingaki T, Cai Z, et al. Successful Healthcare Provider Strategies to Overcome Psychological Insulin Resistance in Japanese Patients with Type 2 Diabetes. *Diabetes Ther* 2019; 10: 1823–1834.
140. Patel N, Stone MA, McDonough C, et al. Concerns and perceptions about necessity in relation to insulin therapy in an ethnically diverse UK population with Type 2 diabetes: a qualitative study focusing mainly on people of South Asian origin. *Diabet Med* 2015; 32: 635–644.
141. Stuckey H, Fisher L, Polonsky WH, et al. Key factors for overcoming psychological insulin resistance: an examination of patient perspectives through content analysis. *BMJ Open Diabetes Res Care* 2019; 7: e000723.
142. Ghazanfar H, Rizvi SW, Khurram A, et al. Impact of insulin pump on quality of life of diabetic patients. *Indian J Endocrinol Metab* 2016; 20: 506–511.
143. Owens DR. Clinical Evidence for the Earlier Initiation of Insulin Therapy in Type 2 Diabetes. *Diabetes Technol Ther* 2013; 15: 776–785.
144. Karmakar S, Bhowmik M, Laha B, et al. Recent advancements on novel approaches of insulin delivery. *Med Nov Technol Devices* 2023; 100253.
145. Petrie JR, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. *Can J Cardiol* 2018; 34: 575–584.