Optimising insulin use in people living with type 2 diabetes at primary healthcare facilities: The Tshwane Insulin Project

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Background. In South Africa (SA), glucose control for individuals with type 2 diabetes follows a stepwise approach. According to the guidelines, insulin therapy is started after using two oral agents. However, various challenges may delay the initiation of insulin.
Objectives. To implement a nurse-led, telehealth-assisted programme to address these challenges, aiming to transition patients to insulin safely to achieve better glycaemic control.
Methods. From 2021 to 2023, we conducted a single-arm, unblinded before-and-after study in primary care facilities in Tshwane District, Gauteng Province, SA. Participants were on insulin or two oral agents at maximum doses. Study nurses monitored glycated haemoglobin (HbA1c) results, and participants with HbA1c levels of ≥8% (≥10% during the COVID-19 pandemic) were counselled about insulin use. During an initiation visit, participants received demonstrations and education on using insulin and glucose meters. The participants then tested their glucose levels at home according to a fixed schedule. Over 14 weeks, we implemented monthly clinic visits supplemented by home visits facilitated by community healthcare worker teams. During these visits, glucose results were communicated to the clinic physician via the Vula mobile app, allowing timely adjustments to insulin therapy.
Results. Of the 293 participants, 65% (n=192) were women and 35% (n=101) were men. The mean (standard deviation (SD)) age was 53 (10) years, with a baseline mean (SD) HbA1c level of 12.1% (1.7%). Of those initiated, 169 (58%) were on oral agents and 124 (42%) were on insulin. Biphasic mixed human insulin was prescribed to 185 participants (63%) and intermediate human neutral protamine Hagedorn (NPH) insulin to 108 (37%). Immediately after baseline assessment and during the 14-week study period, 72 participants (23%) were lost to follow-up, and seven were hospitalised during the study period. Glucose values decreased over 14 weeks, with approximately one-third of participants having no insulin adjustments, one-third having one adjustment, and one-third having more than one adjustment. The mean (SD) HbA1c level decreased from 12.1% (1.6%) to 8.8% (1.6%) over the 14 weeks in 240 paired samples (p<0.001). Ten percent of these participants achieved HbA1c levels <7%, and 34% had levels <8%.
Conclusion. The nurse-led, telehealth-supported intervention successfully transitioned participants onto twice-daily mixed insulin or night-time intermediate NPH insulin, resulting in a significant decrease in HbA1c from 12.1% to 8.8%. However, clinics will require additional resources to initiate or intensify insulin therapy in primary care settings.

Keywords: type 2 diabetes, insulin therapy, primary healthcare, Tshwane Insulin Project, implementation study

S Afr Med J 2025;115(6):e2551. https://doi.org/10.7196/SAMJ.2025.v115i6.2551

According to the International Diabetes Federation, 4.2 million adults in South Africa (SA) had diabetes in 2021, with a national prevalence of 11.3%.[1] Diabetes is the leading cause of death among SA women and the second leading cause of death for both men and women.[2] Diabetes can be managed through diet, exercise, medication and regular screening. However, glycaemic control remains suboptimal globally[3,4] and in SA's private and public health sectors.[5-8] Poor glycaemic control has been attributed to failure to initiate and intensify insulin therapy.[9] Approximately 50% of people with type 2 diabetes need insulin injections within 10 years of diagnosis, despite the use of oral glucose-lowering drugs.[10,11]

In SA, management guidelines recommend insulin therapy for individuals with type 2 diabetes who have suboptimal control with maximum doses of oral drugs.[12] However, both healthcare professionals and patients often resist transitioning to insulin, leading to prolonged periods of poor glycaemic control and an increased risk of complications.[13] In Cape Town, a study of primary care centres reported several barriers to insulin initiation, including lack of knowledge and experience among doctors, fear of injections among patients, and systemic issues such as short consultation times, high workload, lack of care continuity and inadequate resources.[14]

To address these challenges, we implemented a translational research programme in SA to increase insulin use in primary care for people with type 2 diabetes who are poorly controlled with oral medication. This initiative was part of the Tshwane Insulin Project (TIP), a 5-year research programme to optimise insulin therapy for individuals with type 2 diabetes in primary care settings.[15] In this article, we report on the outcomes of the TIP, focusing on treatment protocols, frequency of visits and ultimate glycaemic control.

Methods

Study design

A single-arm, unblinded before-and-after design was used for the study.

Setting

The study was conducted across 35 primary care clinics and two community healthcare centres in Tshwane District, northern Gauteng Province, SA (City of Tshwane Metropolitan Municipality). The facility selection criteria included facility manager support, staff willingness, availability of a community health worker (CHW) team linked to the facility, sufficient individuals with type 2 diabetes, and adequate data network coverage.

Study population

Individuals with type 2 diabetes were eligible to participate if they had a glycated haemoglobin (HbA1c) level ≥8% within the past 12 months (increased to ≥10% during COVID-19), were insulin naive or had been on insulin for <3 months, were aged 18 - 70 years, had been on maximum tolerated doses of two oral hypoglycaemic agents for at least 3 months, were compliant if insulin naive, and were willing to commence or change insulin therapy. The participants also needed to be willing to self-monitor their blood glucose.

Participant identification

Fieldworkers identified prospective participants with recent HbA1c tests and traced the results through the National Health Laboratory Service database. They discussed insulin initiation with insulin-naive participants. During clinic visits, nurses and field workers communicated with family physicians and obtained approval for starting night-time or twice-daily insulin. The insulin regimen was based on current treatment and HbA1c results: twice-daily mixed human insulin for HbA1c >12% or postprandial blood glucose levels ≥15 mmol/L on >3 of the past 5 days; and night-time insulin for HbA1c between 8% and 12% with smaller postprandial excursions. Sulphonylureas were discontinued, but metformin was continued according to current guidelines.

Study procedures

Initial visit

The participants received training on insulin use and home glucose monitoring. Those who were already on insulin also had their insulin use and glucose monitoring reviewed. The participants were provided with a glucose meter and strips to test their blood glucose levels twice daily: during fasting and 2 hours after a meal if they were on intermediate human neutral protamine Hagedorn (NPH) insulin, or during fasting and before supper if they were on biphasic mixed human insulin.

Follow-up visits

The COVID-19 pandemic severely affected clinical services, limiting home and clinic visits. Protocols were amended to enrol only participants with an HbA1c level ≥10%, and telephonic visits were introduced without insulin titration. Food vouchers were provided to participants experiencing food insecurity.

Home visits

CHWs conducted weekly home visits to monitor glucose, medication adherence and clinic visit compliance. They checked for hypo- and hyperglycaemia, reinforced education on diet and exercise, inspected injection sites and ensured correct injection techniques. CHWs referred participants to the clinic nurse as needed. Blood glucose data guided insulin titration. The initial home visit focused solely on patient education. Subsequent visits included patient education and insulin titration, co-ordinated via the Vula app in collaboration with the clinic doctor. Post-meal glucose values were evaluated at weeks 10 and 14 to determine whether night-time insulin needed to be switched to twice-daily biphasic insulin.

Telephonic follow-up visits

Owing to COVID-19 restrictions, participants who could not physically contact CHWs were contacted by phone to reinforce insulin and glucose testing compliance. Limited education was provided, and glucose data were collected when possible. Insulin titration occurred at the next clinic visit unless significant hypoglycaemia was identified.

Clinical visits

Monthly clinic visits were scheduled for further insulin titration at weeks 6, 10 and 14, with week 14 being the final visit. The clinic nurse co-ordinated insulin titration via the Vula app. The data collected included weight, height, blood pressure, results of urine analyses, additional information, such as home visits, and any adverse events. Participants with critical signs or blood glucose levels >20 mmol/L were referred to hospitals. Injection site reactions, out-of-study medical visits, hospitalisations and insulin dose adjustments were recorded.

Insulin protocols

Night-time basal insulin protocol

The participants were started on 10 units of intermediate human NPH insulin (protaphane) before bedtime (but not after 22h00), accompanied by a night-time snack.

Titration algorithm for intermediate human NPH insulin

Weekly insulin titration commenced 2 weeks after initiation when possible. The CHW leader (home) or clinic nurse (clinic) communicated the patient's glucose values from the past 5 days to the doctor via the Vula app for insulin titration advice. The maximum dose was set at 20 units of intermediate human NPH insulin. If higher insulin doses were needed, the patient was switched to a twice-daily insulin regimen.

The following titration algorithm was used to adjust the insulin dosage based on the average of the last two morning fasting plasma glucose (FPG) values:

- <4.0 mmol/L: reduce the insulin dose by 2 units and reinforce the night snack
- 4.1 - 7.0 mmol/L: maintain the current insulin dose
- >7.0 mmol/L: increase the insulin dose by 2 units.

Titration algorithm for biphasic mixed human insulin

When indicated, the participants were started on biphasic insulin (actraphane 0.3 units/kg: 2/3 in the morning, 1/3 in the evening). This initiation occurred either after the first week of home glucose monitoring or at week 10 or 14 for those on night-time insulin with high postprandial values.

All participants started on biphasic insulin at times other than baseline and were followed up for at least 4 weeks. Weekly titration began after 2 weeks, following the same protocol used for the night-time insulin group. Premixed insulin was administered twice daily before breakfast and dinner.

The insulin dosage was adjusted according to the titration schedule in Table 1. Titration was based on the blood glucose values from the preceding 3 days.

The first step involved titrating the pre-dinner dose by morning FPG values. Once FPG was controlled, the pre-breakfast dose was titrated according to pre-dinner blood glucose values.

Data management and analysis

The data were analysed in R 4.3.1 (R Foundation for Statistical Computing, Austria, 2023). Descriptive statistics were used to describe the participants' insulin use and glucose values. HbA1c levels before and at the 14-week follow-up were compared using paired *t*-tests. The programme aimed to enrol 300 participants. The level of significance was set at $p<0.05$.

Ethical considerations

The study was approved by the University of Pretoria Faculty of Health Sciences Research Ethics Committee (ref. no. 378/2020), and permission was granted by the Tshwane Research Committee (ref. no. GP_202006_026). The study was conducted following the principles outlined in the Declaration of Helsinki, and all methods adhered to the relevant guidelines and regulations. All participants were informed about the study and provided written informed consent.

Results

Participants were recruited from 2021 to 2023. Of the 314 enrolled participants, 293 remained after 21 participants with no data were excluded. The group comprised 35% men (*n*=101) and 65% women (*n*=192), with a mean (standard deviation (SD)) age of 53 (10) years and a baseline mean (SD) HbA1c level of 12.1% (1.6%). Of the participants, 169 (58%) were initially on oral agents and 124 (42%) were on insulin. Biphasic mixed human insulin was prescribed for 185 patients (63%) and intermediate human NPH insulin for 108 (37%). Of non-insulin users, 57% started on intermediate human NPH insulin, whereas 91% of insulin users started on biphasic mixed human insulin. Baseline HbA1c levels were similar across the groups (Table 2).

The participants were expected to attend three clinic visits over 14 weeks. A fourth visit at week 18 was scheduled for selected participants, such as those who switched from intermediate human NPH insulin to mixed human insulin, within 4 weeks of the week 14 visit. As shown in Table 3, ~70% of the participants attended the required clinic visits.

The percentage of home visits ranged from 57% at week 4 to 21% at week 13, whereas the percentage of telephonic visits ranged from 33% to 49% over the period.

Table 1. Titration algorithm for biphasic mixed human insulin

Lowest glucose value of past 3 days (pre-meal) (mmol/L)	Adjustment of insulin dose (units)
≤3.0 or symptomatic hypoglycaemia	–4
>3.0 - ≤4	–2
>4.0 - ≤7	No change
>7.0 - ≤12	+2
>12.0 - ≤17	+4
>17.0	+6

Blood glucose levels over time

For participants on intermediate NPH insulin, the mean (SD) FPG level decreased significantly from 8.7 (3.7) mmol/L (*n*=52) to 6.7 (1.7) mmol/L (*n*=62) ($p<0.001$). Similarly, in those on biphasic mixed insulin, the mean (SD) FPG level decreased significantly from 9.1 (3.5) mmol/L (*n*=107) to 7.7 (3.0) mmol/L (*n*=137) ($p=0.001$) (Figs 1 and 2).

The mean (SD) post-supper glucose level decreased significantly from 11.2 (2.2) mmol/L (*n*=50) to 9.6 (2.0) mmol/L (*n*=61) ($p<0.001$), while the mean (SD) pre-supper glucose level decreased significantly from 11.5 (3.6) mmol/L (*n*=108) to 9.5 (3.5) mmol/L (*n*=137) ($p<0.001$) (Fig. 3).

Insulin over time

The intermediate NPH insulin dose increased from a mean of 11 to 14 units over 14 weeks. The pre-dinner mixed insulin dose

Table 2. Characteristics of participants by insulin use at the beginning of the study (*N*=293)

		Insulin at start, *n* (%)*		
Variable	*n*	Already on insulin (user) (*n*=124)	Insulin naive (non-user) (*n*=169)	*p*-value†
Insulin	293			<0.001
BMIns		113/124 (91)	72/169 (43)	
IHIns		11/124 (9)	97/169 (57)	
Baseline HbA1c (%), mean (SD)	293	12.21 (1.53)	11.99 (1.77)	0.27
Age (years), mean (SD)	291	52 (10)	54 (10)	0.20
Unknown, *n*		0	2	
Height (cm), mean (SD)	282	164 (7)	164 (8)	0.54
Unknown, *n*		2	9	
Weight (kg), mean (SD)	293	84 (20)	82 (17)	0.32
Serum creatinine (μmol/L), mean (SD)	276	76 (15)	76 (16)	0.87
Unknown, *n*		7	10	
BMI, mean (SD)	282	31 (7)	31 (7)	0.53
Unknown, *n*		2	9	

BMIns = biphasic mixed insulin; IHIns = intermediate human insulin; HbA1c = glycated haemoglobin; SD = standard deviation; BMI = body mass index.
*Except where otherwise indicated.
†Pearson's χ^2 test for proportions, Welch's two-sample test for continuous measurements.

Table 3. Participants' attendance at monthly clinic visits during the follow-up period (*N*=293)

Clinic visit	Attended, *n* (%)	Not attended, *n* (%)
Week 6	225 (77)	68 (23)
Week 10	189 (65)	104 (35)
Week 14	203 (69)	90 (31)
Week 18*	13 (4)	280 (96)

*Supplementary visits were done for participants who switched from intermediate human insulin to biphasic mixed insulin.

increased from 12 units to 14 units, and the pre-breakfast dose increased from 23 units to 25 units. Approximately one-third of the participants had no dose changes, another third had one dose change, and ~17% had two dose changes, with additional modifications occurring less frequently.

Comparison of glucose control levels at baseline and at 14 weeks

There were 240 paired samples, including 38 participants (Table 4). The remaining 65 participants could not be traced for a final HbA1c test. Among those tested, 24 participants (10%) had HbA1c levels <7%, and 77 participants (34%) had levels <8%.

Adverse events

Sixty-four participants (22%) reported hypoglycaemia (blood glucose level <4 mmol/L). Of these episodes, 21 were symptomatic, but none required hospital visits. Fifty-three participants (18%) reported hyperglycaemia (blood glucose level >20 mmol/L). Twenty participants (7%) reported both hypo- and hyperglycaemia during the study period. Seven participants were hospitalised, including two with diabetic ketoacidosis.

Loss to follow-up

Seventy-two participants (23%) were lost to follow-up. After insulin initiation, 21 participants were lost to follow-up and provided no data. Over the 14-week follow-up period, 51 participants were lost to follow-up for reasons such as travelling or relocating to a different province.

Discussion

The TIP recruited 314 people eligible for insulin, of whom 293 contributed data. Of these, 51 participants were lost to follow-up over the 14-week study period. Glucose levels declined significantly over time, and in the 240 pairs available before and after intervention, HbA1c decreased by 3.3% (p<0.001).

The TIP is an intensive intervention that involves identifying participants with suboptimal glucose control, assessing their readiness for insulin, teaching injection techniques and home glucose monitoring, and following up at home or telephonically. Glucose levels were recorded at home and shared with doctors via the Vula app for dose adjustments. Doctors assessed these values at the clinic and made further adjustments if needed. Diabetes education was provided during home and clinic visits. Participants who completed the 14-week follow-up had significantly improved HbA1c levels. This intensive intervention resulted in dose increases for almost half of the patients, showing an agile response to changing HbA1c.

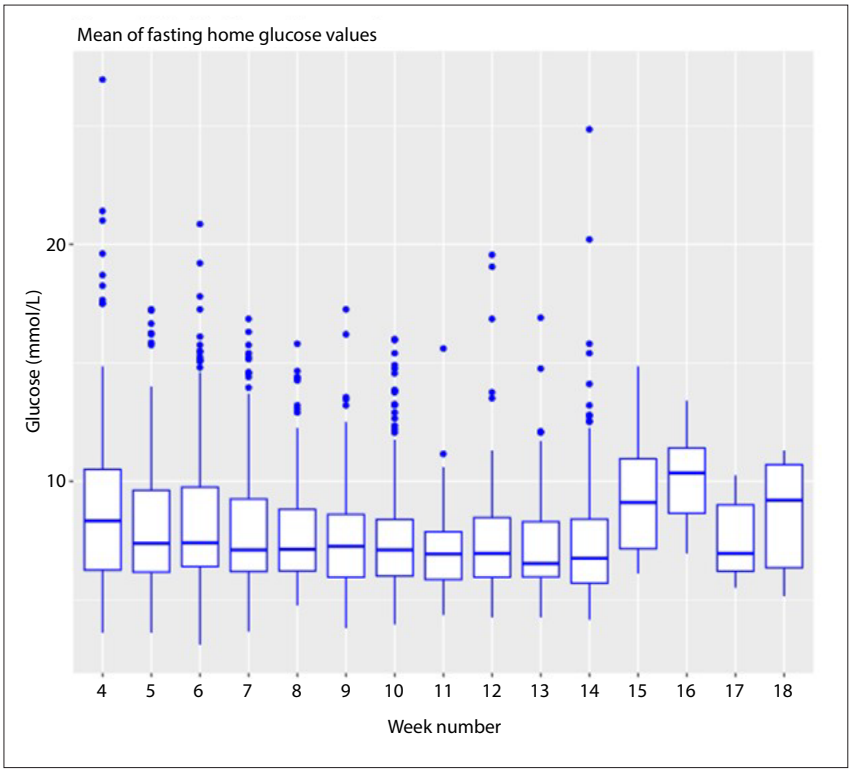

Fig. 1. Fasting blood glucose levels over time (mean of two fasting home glucose values).

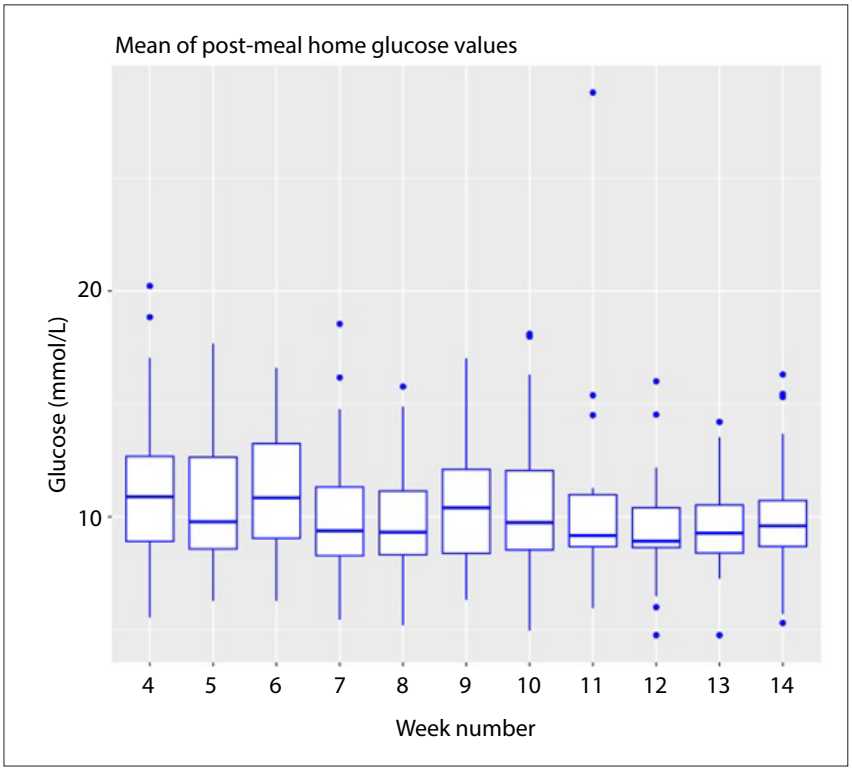

Fig. 2. Post-meal blood glucose levels over time in individuals on night-time intermediate insulin (mean of five post-meal home glucose values).

Many individuals with type 2 diabetes eventually need insulin. Traditionally, insulin was initiated after biguanides and sulphonylureas. However, the American Diabetes Association recommends starting a subcutaneous GLP-1 agonist before insulin.[16] Similarly, >50% of study participants in the

Table 4. Baseline and final HbA1c levels

Variable	*N*	Mean (SD)	*p*-value
Baseline HbA1c (%)	240	12.1 (1.6)	
Final HbA1c (%)	240	8.8 (1.6)	
Difference (%)		3.3 (2.2) (95% CI 3.6 - 3.0)	<0.001

HbA1c = glycated haemoglobin; SD = standard deviation; CI = confidence interval.

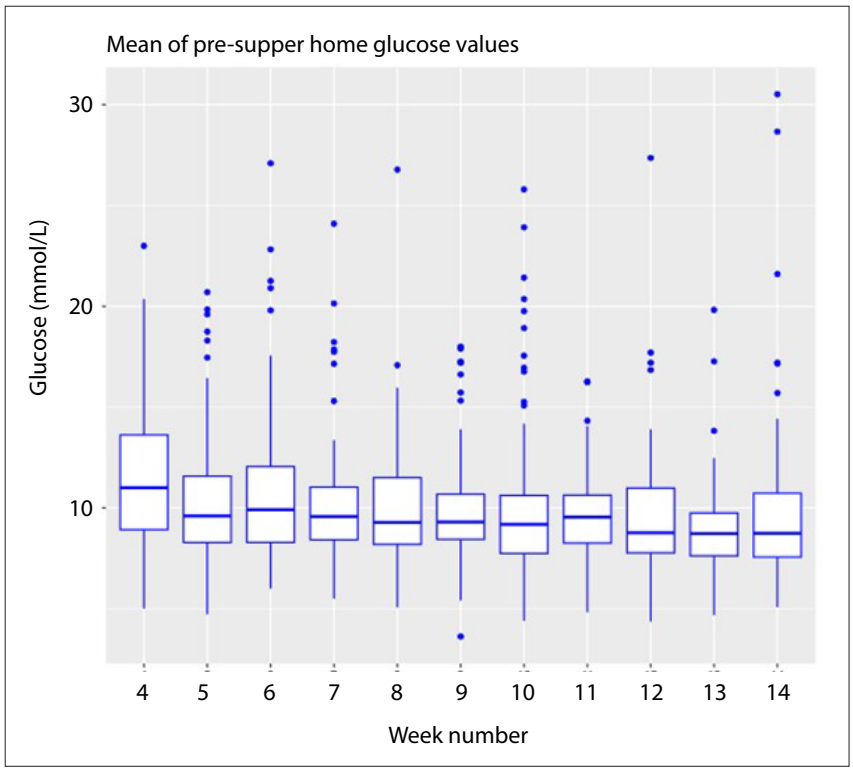

Fig. 3. Pre-supper blood glucose levels over time in individuals on pre-breakfast biphasic insulin (mean of five pre-supper home glucose values).

UK needed insulin to maintain a target FPG level of ≤6.0 mmol/L by year 6.[17] However, transitioning individuals with type 2 diabetes to insulin is often delayed. On average, HbA1c levels remain high at 8% for ~5 years before insulin is initiated, with patients typically waiting >10 years with HbA1c readings >7%.[18] In Tshwane District, an audit of diabetes management at primary care level revealed that most patients on maximum oral medication did not intensify treatment despite failing to meet diabetes control targets.[19]

In 2017, India, a country with a context similar to ours, reviewed its basal and mixed insulin options. They concluded that, based on patient characteristics, any of the four available basal insulins – NPH, glargine (IGlar), detemir (IDet) and degludec (IDeg) – could be used.[20] However, IDeg was noted for its longer action, lower incidence of overall and nocturnal hypoglycaemia, and greater flexibility in administration timing than IGlar and IDet. Premixed analogues administered two or three times daily are generally the preferred intensifying treatment.[21] Newer insulin analogues are costly, however, with analogues being approximately six times more expensive than human insulin.[22] In the USA, insulin prices have now been capped at USD35 per month, with suppliers significantly reducing costs.[23]

The TIP was developed to overcome the challenges in SA primary care clinics, which are often too busy to educate patients on insulin use and home glucose monitoring. Dedicated assistants relieved the burden on clinical staff. The participants received training, home visits from CHWs to ensure correct injection and testing techniques, and comprehensive diabetes education. Individuals in primary care are typically followed up monthly or every 3 months, leading to inconsistent insulin titration. The TIP increased opportunities for insulin titration by measuring glucose levels at home and relaying them to doctors via the Vula app for timely adjustments. Similarly, healthcare providers at clinics used the same structured titration algorithms to adjust intermediate NPH insulin and biphasic mixed insulin.

Innovative patient assistance methods in resource-poor settings are rare. One similar intervention is the mobile insulin titration intervention, which uses basic mobile phone technology for weekly glucose value reporting and titration calls. This intervention demonstrated efficacy, reducing HbA1c levels from 11.4% to 10%.[24]

One limitation of the present study was the absence of a control group, which makes it challenging to attribute improvements solely to the intervention.

A 23% loss to follow-up (n=72) was observed, with 21 participants withdrawing immediately after baseline assessment and 51 discontinuing during the 14-week period. These withdrawals were primarily due to logistic and external factors, such as relocation, work, travel and scheduling difficulties, rather than adverse events. The COVID-19 pandemic may have contributed further to these challenges. While this attrition rate is a limitation, the intervention demonstrated a favourable safety profile with no hospitalisations due to hypoglycaemia. Furthermore, the reasons for attrition do not suggest systemic bias. While the loss to follow-up may affect generalisability, particularly regarding long-term effects, the study provides valuable insights into the intervention's feasibility and short-term efficacy within the observed sample.

Another limitation is the absence of end-of-study weight measurements. Given the short 14-week duration and modest insulin doses, significant weight changes were not anticipated. Furthermore, weight gain with insulin therapy is typically a longer-term effect influenced by dietary and activity patterns, which were not assessed here. Future studies with extended follow-up could explore this further.

SA is currently facing an acute shortage of insulin pen sets, and patients will now have to transition back to vials and syringes, an enormous step backwards in terms of

ease of use and patient satisfaction.[25] The present study highlights that optimising glucose treatment requires more than just access to insulin; it also necessitates comprehensive education for individuals with diabetes and healthcare staff.

Data availability. The datasets generated and analysed during the present study are available from the corresponding author (PNP) on reasonable request. Any restrictions or additional information regarding data access can be discussed with the corresponding author.

Declaration. None.

Acknowledgements. The intervention and improvement in patient care and outcomes would not have been possible without the active collaboration of the Department of Health (Gauteng Province), the City of Tshwane, and all the facility managers, CHWs, nurses and doctors at the various clinics and healthcare centres. We thank Prof. E M Webb for her participation in the project and Dr Cheryl Tosh (University of Pretoria) for editing the manuscript.

Author contributions. All the authors participated in the design and execution of the study. PR performed the data management and statistical analyses. GMM was the nurse manager, and PNP was the project manager. All the authors reviewed and edited the manuscript.

Funding. The programme was funded over a 5-year period by Eli Lilly and Company as part of their Lilly Global Health Partnerships.

Conflicts of interest. None.

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Received 19 August 2024; accepted 16 April 2025.