

Review of the Effects of
Diabetes Mellitus Group Education with Practitioner-directed Insulin Dosage Adjustments
on Glycaemic Control
at a Public Sector Primary Health Care Clinic in Khayelitsha

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Part A: Protocol

1. Synopsis

Title: Review of the effects of **diabetes group education with practitioner-directed insulin dosage adjustments** on glycaemic control at a public sector primary health care clinic in Khayelitsha.

Background: Glycaemic control in diabetes mellitus is fundamental in reducing morbidity and mortality. Appropriate treatment optimisation and education promoting diabetes self-management are cornerstones in achieving glycaemic control. An intervention focusing on these two aspects of care was held at a clinic in Khayelitsha, a township in Cape Town, between 2013-15. This intervention was designed and run by the clinician of this facility and entailed diabetes group education sessions for adult patients using insulin, and was coupled with the provision of practitioner-directed insulin dosage adjustments based on home blood glucose readings.

This study of audit data aims to evaluate the effect the routine service-improvement intervention had on glycaemic control in the short and medium term. If it is found to have been effective at improving glycaemic control, it could be used to inform the development of local standard operating procedures for the glycaemic monitoring in patients on insulin, and the programme could be implemented at other facilities with the potential of improving diabetes care more broadly across Cape Town, particularly in the poorer areas.

Methods: This is an investigation of audit data, and will use a pre/post design to assess the change in glycaemic control before and after the intervention, both in the short and medium term. It will also assess the effectiveness of the intervention by comparing the outcome in the medium term to a control group: this will be done using a retrospective cohort study design, where the “exposure” is the intervention and the “outcome” is the change in glycaemic control over the study period. It will be an 'as

treated' analysis. Glycaemic control will be assessed using HbA1c (glycated haemoglobin) blood tests, which were done during routine care.

Recruitment for the intervention: The clinicians working at the facility compiled a list of patients on insulin, adding patients seen during clinical consultations. From this list, the clinician running the intervention recruited patients according to glycaemic control (as patients with worse control were considered at highest risk of complications) and presence of diabetic complications (as tight glycaemic control prevents or slows progression of complications). Patients were invited telephonically or by SMS, approximately a week before a new programme was planned.

The control group will be made up of all patients using insulin who attended the same facility during the same time period (and meet all criteria listed below), but differ in terms of not having attended the intervention.

Inclusion criteria:

- Men and women aged between 18 and 70 years at the start of the study period.
- Patients using basal or biphasic insulin.
- Patients attending the same facility throughout the study period.
- The HbA1c blood tests done on the patients need to meet the appropriate time frame criteria (e.g. assessing the change in glycaemic control in the medium term requires two HbA1c blood tests done 3-5 years apart)
- HbA1c result must have been taken while the patient was on insulin therapy for at least 3 months (a folder review is needed to confirm this)

Exclusion criteria:

- Participants recruited to one of the interventions groups, and the last group recruited as there is missing data on their attendance.
- Patients whose folders cannot be found for the folder review, will not be included.

Ethical considerations: This intervention formed part of routine care for diabetic patients at the facility. It was implemented in 2013-2015 and had the aim of improving diabetes patient care. Formal evaluation or research was not intended at that time. However, informal analysis suggests this intervention improves glycaemic control in the short term. A formal assessment on this, as well as the impact of the intervention on glycaemic control in the medium term, will assist in making a decision to implementing this or similar interventions at more sites.

This is fundamentally a routine care folder review audit and informed consent will not be taken from the intervention or control group. It will be conducted by the patient's attending clinician and no identifying information will be divulged outside of this clinician and study supervisor. Measures to protect the confidentiality of study participants will be implemented (all electronic information will be saved in password-protected, encrypted files, and once data collection has been completed, all patient's identifiers will be removed from the data set for data analysis).

No monetary reimbursement was provided for attendance of the intervention.

Benefits: Improved glycaemic control has personal benefits for patients for being at reduced risk of developing diabetic complications; and on a health systems level a reduction in diabetic complications could ultimately lead to significant reduction in health care costs.

No foreseeable physical, psychological, social and economic harms to the participants of the study were identified, nor were any morally controversial ethical issues.

2. Background

The prevalence of diabetes is increasing globally - most rapidly in low- to middle income countries ⁽¹⁾. This is true for South Africa (a high middle-income country with one of the highest income inequalities) ⁽²⁾. Good diabetes management is imperative in preventing disability and premature deaths ⁽³⁾. However, the majority of South African people with diabetes are poorly controlled; in the province of the Western Cape 70% of diabetic patients have a glycated haemoglobin (HbA1c) of more than 8 % (poor control) ⁽⁴⁾.

Poor diabetes control in combination with the increasing prevalence is resulting in high rates of disability and premature mortality in Africa ⁽⁵⁾; the vast majority (79%) of diabetes deaths in Africa are occurring in the less than 60-year age group ⁽⁶⁾. In South Africa the number of diabetes deaths are increasing every year, and in the Western Cape it became the leading natural cause of death in 2017 ⁽⁷⁾.

There is an association between poverty and poorer diabetes control ⁽⁸⁾. Khayelitsha is the largest township in the Western Cape and the poorest area in the City of Cape Town. Its population is growing rapidly and the majority of its residents rely on the public health care sector for their health needs ⁽⁹⁾. It is therefore important to find effective interventions to improve diabetes control in this setting.

An intervention aimed at improving glycaemic control was held at a City of Cape Town administered primary health care facility in Khayelitsha in 2013-15: it entailed weekly group diabetes education in combination with practitioner-directed insulin dosage adjustments based on home glucose readings. This intervention was designed and implemented by one of this facility's health care practitioners as a routine intervention for service improvement (the intention was not to formally evaluate and report the results). Provisional analysis suggests beneficial effects on glycaemic control in the short term. However, a formal assessment on this, as well as the impact of the intervention on glycaemic control in the medium term will assist decision makers on whether this is a worth-while intervention to roll-out at other facilities in this setting.

3. Literature Review

Diabetes significantly contributes to the burden of disease in South Africa, with more than 4.5 million cases estimated in 2019, or 12.8% of the adult population ⁽²⁾. More than 2 million of these cases are undiagnosed ⁽²⁾. The number of cases in the country are increasing rapidly, with South Africa being in the top 10 countries in the world for absolute increase in diabetes prevalence ⁽²⁾. The reasons for this rapid increase include population ageing, rapid urbanisation, and nutritional changes and reduced physical activity associated with obesity ⁽¹⁰⁾.

In the Western Cape approximately half of all known diabetics have an HbA1C of more than 10% (uncontrolled diabetes) ⁽⁴⁾, which puts them at risk of diabetic complications, and therefore disability and premature death. Diabetes is the leading cause of natural deaths in the province ⁽⁷⁾; and when examining the mortality rates for diabetes in the sub-districts of the City of Cape Town, Khayelitsha has very high rates, second only to the sub-district of Mitchell's Plain ⁽¹¹⁾.

Khayelitsha is situated on the outskirts of Cape Town, about 30km from the city centre. It was established in the 1980's, by the apartheid government for black Africans to live. This spatial planning keeps its residents in a poor area far from employment.

Khayelitsha has an estimated population of 442 721 in 2020 ⁽¹²⁾. The majority are black Africans (99%) ⁽¹³⁾, with a significant number of residents being migrants from the Eastern Cape. It has a high unemployment rate, approximately half the households live in informal dwellings ⁽¹³⁾, and many live below the poverty line.

Food insecurity is prevalent in Khayelitsha ⁽¹⁴⁾. This results in the consumption of less diverse traditional foods ⁽¹⁵⁾. The majority of households in Khayelitsha frequently consume highly-processed foods and foods tending to cause obesity, such as “industrially produced bread, processed meat, sugar-sweetened beverages, and sugar” ⁽¹⁵⁾, as these are usually cheap. Furthermore, the high rate of crime and violence means residents are reluctant to use public areas to exercise, leading to reduced physical activity ⁽¹⁶⁾.

For people with diabetes who live in Khayelitsha, these factors (unhealthy diets and lack of physical activity) negatively affect their glycaemic control, and are difficult to change. Poor understanding of diabetes, not prioritising diabetes management and inadequate knowledge around diabetes self-care (including compliance to medication) are other factors that contribute.

Diabetes chronic care in Khayelitsha is mostly provided by clinical medical officers (general practitioners), as well as clinical nurse practitioners at public primary health care facilities. Clinicians with post-graduate training in diabetes is rare.

In South Africa it is not uncommon to encounter patients with very poorly controlled diabetes who have not had adjustments made to their treatment for years ⁽¹⁷⁾. This is likely linked with poor glycaemic control monitoring practices: for example, a folder audit at public primary health facilities in the Western Cape showed that in 2018, 59% of diabetic patients did not have a single HbA1c blood test done in a full year ⁽¹⁸⁾, despite local guidelines recommending 1-4 such blood tests per patient per year ⁽¹⁹⁾. Not testing frequently enough hinders proactive diabetes management, and it is known to be associated with negative effects on glycaemic control ⁽²⁰⁾.

Microvascular complications (these include retinopathy, nephropathy, and neuropathy) are known to reduce quality of life, lead to disability, as well as carry an increased risk of mortality, especially as these complications progress ⁽²¹⁾. Two large scale international studies have shown that improved glycaemic control (as demonstrated by reduction in HbA1c levels) are associated with reduced risk of microvascular complications ⁽²²⁻²⁴⁾. This is the reason guidelines recommend keeping patients' HbA1c at less than 7 or 8 ⁽¹⁹⁾. However, achieving this level of glycaemic control is difficult: it involves both the health care practitioner's medication prescribing and advice, as well as the self-care behaviour of patients.

There is good research-based evidence that people with diabetes ought to receive diabetes self-management education (DSME) ⁽²⁵⁾; with its objective being to "facilitate the knowledge, decision-making, and skills mastery necessary for diabetes self-care" ⁽²⁶⁾. A systematic review, including trials from the United States, Europe, Mexico and Thailand, specifically focussing on group education showed this is effective in improving glycaemic control ⁽²⁷⁾. Group education also appears to have modest beneficial effects in the long term ⁽²⁸⁾.

South African studies, published in 2007 and 2014, assessing the effects of diabetes education on glycaemic control did not demonstrate significant improvements ^(29, 30). Reasons postulated were poor health literacy, poor attendance, no suitable space for group education and lack of prioritisation of the program by facility management. However, another more recent South African study from Khayelitsha, published in 2020, comparing 6 months of "intensified care" to usual care in uncontrolled patients (HbA1c >10) resulted in significant improved

glycaemic control, with an average 1.1% reduction in HbA1c. The intensified care included group education and was thought to be the main reason for the improvement ⁽³¹⁾.

This study of routine audit data will assess an intervention that added weekly practitioner-directed insulin dosage adjustments (based on home blood glucose monitoring) to the group education component (see section "7.2 Intervention" below for a detailed description of the intervention). This is what differentiates this intervention from other diabetes education; and fills the much needed gap in getting diabetic patients on insulin onto the right dosage of medication. It is estimated that 40% of diabetics in the Western Cape use insulin ⁽¹⁸⁾.

4. Problem and Purpose of this Study

Problem: Khayelitsha has a high percentage of people living with uncontrolled diabetes, and the number of people living there with diabetes is increasing. The effect of this is seen with the high mortality rates for diabetes.

Some of the reasons for the poor glycaemic control are:

- Inadequate patient knowledge / understanding about diabetes and its management.
 - Poverty, which contributes to unhealthy diets and lack of physical activity.
 - Poor standard of care as demonstrated by glycaemic control not being monitored frequently enough and medication not being adjusted appropriately.
-
- **Purpose of the review:** If found to be effective at reducing glycaemic control, one could implement and further investigate this type of intervention at other facilities in this setting; one could use lessons learned to improve current group education programmes, and to inform the development of a local standard operating procedure for the glycaemic monitoring in patients on insulin.

5. Hypothesis

Hypothesis:

Patients using insulin who attended **group diabetes education sessions with practitioner-directed insulin dosage adjustments** at their primary health care clinic in Khayelitsha in 2013-15, will be compared to patients on insulin who received usual care at the same facility over the same time period:

It is hypothesised that routine care audit data will show that glycaemic control improved in the short-term; and the intervention had a sustained positive effect on glycaemic control in the medium term when compared to the control group.

Outcome:

- HbA1c reduction on average by 1% in the short term.
- HbA1c reduction was maintained over a 3 year period.
- The intervention group's glycaemic control improved more than the control groups.

6. Aims and Objectives

Aim: to evaluate the effect the intervention had on glycaemic control (based on changes in HbA1c) in the short and medium term using routine care audit data.

Primary Objectives:

1. To evaluate the change in glycaemic control in the intervention group in the short term.
2. To evaluate the change in glycaemic control in the intervention group in the medium term.
3. Assess the effectiveness of the intervention by evaluating the change in glycaemic control in the intervention group and comparing it to a comparison group over a 3-5 year period, using a set time frame.

Secondary Objectives:

1. To evaluate the change in insulin dosage:
 - a. In the intervention group: before and after the intervention
 - b. By comparing the change in insulin dosage in the intervention and control group over the medium term.
2. To assess the number of HbA1cs done annually in the intervention and control group during the study period.

7. Methods

7.1 Study Design

The intervention to be assessed was implemented as a routine care improvement project at a primary health care facility in 2013-2015. Formal evaluation or research was not intended at that time. However, this study now intends to assess its impact on patients' glycaemic control, by using data gathered by a routine care audit.

Evaluating the short term effects of the intervention: this will be done using a pre/post design: comparing glycaemic control before and after the intervention.

Evaluating the medium term effects of the intervention: this will also be done using a pre/post design: comparing glycaemic control before and 3 years after the intervention.

The benefits of the pre/post design is that patients are their own controls. However, a limitation is that changes in glycaemic control may be due to the intervention, but could also reflect other changes (for example changes in clinical care or the natural progression of disease). For this reason a comparative assessment will be carried out.

Assessing the effectiveness of the intervention in the medium term when compared to a control group: this will be done using a retrospective cohort study design, where the "exposure" is in an intervention and the "outcome" is the change in glycaemic control over the study period. The control group will be made up of all patients using insulin attending the same facility during the same time period, who did not attend the intervention. It will be an 'as treated' analysis.

Ideally a randomised control trial is used to assess the effectiveness of such an intervention. However, this intervention was not done under a tightly controlled experimental research setting. This was a health practitioner designed and implemented service improvement project; the study will therefore be using real-world data (audit data), which reflects actual clinical practice but will also impose limitations on the analysis.

7.2 Intervention

The intervention which will be assessed was an 8-week diabetes group education programme held at participants' usual primary health care facility. At the weekly, hour-long education sessions every participant was also advised on the insulin dosage they were meant to use for the next week. These insulin dosage adjustments were made by the health care practitioner, based on the participants average home blood glucose readings from the previous week, according to an insulin titration schedule ([Annexure 1](#)).

The intervention was held at the primary health care clinic in Khayelitsha, called Matthew Goniwe Clinic. This is a City of Cape Town administered clinic offering non-communicable disease care, amongst other services.

The education sessions were held first thing in the morning, at 7h30, which is the clinic's opening time. This time was chosen to allow patients who were employed to attend and then still get to work afterward. Attendance certificates were given to participants who requested these.

The intervention was designed and implemented by one of this clinic's health care practitioners, who started working at the clinic in March 2013. It was implemented as a service improvement project, and was not planned to be a formal research project.

There were a total of 18 groups of patients that attended this intervention, held over a 2-year period (between August 2013 and July 2015). The groups ranged in size from 4 to 11 people (with an average of 8.4) (see table 1).

Table 1: Date and number of participants at the 18 diabetes group education sessions.

Programme	Date of programme start	No. of participants
Group 1	2013/08/07	8
Group 2	2013/09/17	11
Group 3	2013/10/11	14
Group 4	2014/01/20	10
Group 5	2014/01/21	11
Group 6	2014/02/13	10
Group 7	2014/03/17	10
Group 8	2014/03/18	7
Group 9	2014/06/03	11
Group 10	2014/06/20	11
Group 11	2014/07/03	5
Group 12	2014/08/26	4
Group 13	2014/09/11	5
Group 14	2014/10/21	6
Group 15	2015/02/03	6
Group 16	2015/03/04	6
Group 17	2015/04/21	8
Group 18	2015/06/10	?*

* missing data on attendance of group 18.

A total of 141 participants attended this intervention - 86% of whom had good attendance (4 or more sessions attended).

Two participants attended twice (one attended Group 7 and 14, the other attended Group 1 and 10). (see table 2).

Table 2: Attendance: this table shows how many sessions (out of 7) the participants attended in each group

Number of sessions attended (by participant)	No. of participants		Poor versus good attendance	
	Total = 143	%	Total = 143	%
2 sessions	11	8 %	Poor: 14	14 %
3 sessions	9	6 %		
4 sessions	14	10 %	86	86 %
5 sessions	19	13 %		
6 sessions	24	17 %		
7 sessions	66	46 %		

* Participants who attended only the first introductory session are not included.

* Group 18 is excluded due to the missing data on attendance.

Patients were sent SMS's the day before to remind them to attend.

The sessions were held in English. When participants could not understand English:

- For Afrikaans speaking participants: the content was translated into Afrikaans by the health care practitioner.
- For Xhosa speaking participants: a facility nurse, when available, was asked to assist in translating the content. If a nurse was not available, one of the participants was asked to translate.

The programme consisted of 8 sessions with the following topics:

1. Glucose monitors: how and when to use them
2. Diet advice with a focus on carbohydrates
3. What is diabetes and history of insulin
4. Insulin information (including how to inject, storage, duration of action)
5. How to prevent diabetes complications
6. Hypoglycaemia (including symptoms, causes and treatment)
7. Hypertension, dyslipidaemia, smoking
8. What to expect at clinical consultations (including HbA1c blood tests, kidney screening, feet and eye examinations).

At the first session, blood glucose monitors (Accu-Chek Active) were given to every participant – the date and time on every monitor had been set. Participants were instructed how to use these monitors, and how often to test their blood glucose level. A handful of participants already owned a monitor (which they had either been able to buy or had received from another health care facility). Patients were given information on this intervention, and that attendance was voluntary.

Baseline assessments of participants' glycaemic control (HbA1c blood tests at this first session) were not done, as this was not practically feasible due to the situation at the health care facility: the number of patients waiting to be attended to was very high in the morning (the facility had no appointment system so the majority of patients attending for the day arrived in the morning). Therefore there was not enough time for anyone to draw the bloods. (See section "7.7 Outcome measurements" for the limitations of using blood tests that were done during routine care instead of specifically for the intervention.)

At each of the subsequent seven sessions, the participants also received just enough test strips to last for a week of home glucose monitoring:

- Patients using basal insulin once a day (at night) received 7 test strips and were instructed to test their blood glucose levels in the morning before eating.
- Patients on biphasic insulin received 14 test strips and were instructed to test their blood glucose levels twice a day: 30-minutes before breakfast and 30-minutes before supper, to coincide with their insulin injections.

Patients were instructed to write down their blood glucose readings on a monitoring page which had been designed for the programme ([Annexure 2](#)). They were also told to bring this page and their blood glucose monitor to every session.

The glucose test strips used during the programme were available from the health care facility's pharmacy. The monitors were received on request from the representative of the diagnostics company (Roche diagnostics), as was standard practice at all primary health care facilities at the time.

At public sector clinics, patients using insulin are eligible to receive blood glucose testing strips. This is in line with international guidelines that recommend home blood glucose monitoring in patients using insulin ⁽³²⁾. Current evidence does not support the use of home blood glucose monitoring in diabetic patients on only oral diabetic medication ^(33, 34).

From the second session onwards, on arrival, home blood glucose readings were assessed for every patient: the results the participants had written down were verified with the readings saved on the monitors. Insulin dosage adjustments were made based on the average glucose readings for the week, according to the titration schedule. Patients were verbally instructed on these insulin dosage changes, and this was also documented on the monitoring page, which was returned to the participant. This was followed by the group education session.

After the 8 sessions, if further insulin adjustments were needed (if home blood glucose readings had not achieved target values) patients were encouraged to continue to come for weekly insulin adjustments.

The provider documented the following information on the data collection page ([Annexure 3](#)) at every session:

- Attendance
- Average weekly blood glucose readings
- The new recommended insulin dosage for the next week

At the end of the programme, a discharge note ([Annexure 4](#)) with this information was completed and filed in the patients clinical records.

7.3 Recruitment for the intervention

Patients on insulin attending Matthew Goniwe clinic were added to a list to receive a glucose monitor. This list was compiled by doctors, who would collect patients' names and details during clinical consultations.

This list included the patients' latest HbA1c results. Patients with worse diabetes control were prioritised for the intervention, as they were considered at highest risk of complications. The average participants HbA1c was 12.6% (see **table 3** for more information on participants' glycaemic control prior to the intervention). Also, patients with known diabetic complications, in whom tight glycaemic control was needed to prevent or slow progression were also prioritised.

Table 3: Participants most recent HbA1c results, before attending the education sessions (includes HbA1c up to 2 weeks after the start of the intervention)

HbA1c result	No. of participants		%	Glycaemic control
	Total = 143			
< 7.0	0	0	0 %	Good
7.0 - 7.9	3	3	3%	Acceptable
8.0 - 8.9	3	14	10%	Poor
9.0 - 9.9	11			
10.0 - 10.9	13	126	88%	Uncontrolled
11.0 - 11.9	22			
12.0 - 12.9	25			
13.0 - 13.9	25			
14.0 - 14.9	21			
≥ 15.0	20			

* data on group 18 not included due to missing data on attendance.

The HbA1c blood tests were taken during usual clinical visits at Matthew Goniwe clinic. These results were documented on the waiting list and were updated ad hoc; on occasion previously uncontrolled diabetic patients whose glycaemic control had improved prior to the intervention (unknown to the programme organiser) were invited to the education sessions. Also, the HbA1c blood tests were often more than 6 months old as they were not being monitored frequently enough during routine care.

Approximately a week before a new programme was planned, patients were called telephonically to inform them that a glucose monitor was available for them and that they could collect it at the first session of a diabetes education programme. Patients who could not be contacted telephonically were sent an SMS to invite them.

Participation in the programme was voluntary.

7.4 Sampling

Intervention Group - General Inclusion Criteria:

- Men and women aged between 18 and 70 years at the start of the study period.
- Patients who attended 2 or more sessions of the intervention.
- Patients attending the same facility throughout the study period.
- Patients using basal or biphasic insulin.

Evaluating the short and medium term effects of the intervention (pre/post design):

- Patients need to have had an HbA1c **12-months before and up to 2-weeks after the start** of the intervention ("*pre-HbA1c*"), and this HbA1c result must have been taken while the patient was on insulin therapy for at least 3 months.
- **For the short term pre/post design:** Patients need to have had an HbA1c **3 to 15-months after the start** of the intervention ("*post-HbA1c*")
- **For the medium term pre/post design:** Patients need to have had an HbA1c **3 to 5 years after the start** of the intervention ("*3-years-post-HbA1c*")

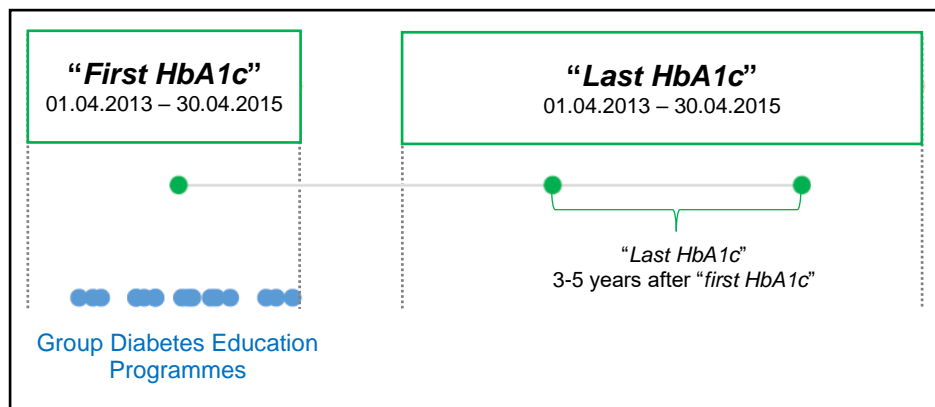
A patient clinic-folder review will be conducted to ensure the "pre-HbA1c" was taken while the patient was on insulin therapy for at least 3 months. During this folder review, a number of data elements will be collected (see section "7.7 Outcome measurements" below).

See section "7.3 Recruitment for the intervention" on how participants were selected for the intervention.

Assessing the effectiveness of the intervention when compared to a comparison group:

- Patients need to have (at least) 2 HbA1c results which are 3-5 years apart, while on insulin therapy for at least 3 months.
 - The “*first HbA1c*” needs to be taken between April 2013 and April 2015, using the earliest result, if there is more than one result in that time period.
 - The “*last HbA1c*” is taken 3-5 years after the first, using the result closest to the 3 year mark, if there is more than one result).

Diagram 1: Time frame of selecting the “first HbA1c” and “last HbA1c”



Intervention group – exclusion criteria:

- Participants who attended the first session only will not be included, but can be included in the comparison group (as-treated analysis).
- Group 18 participants will not be included in the study as attendance is unknown.

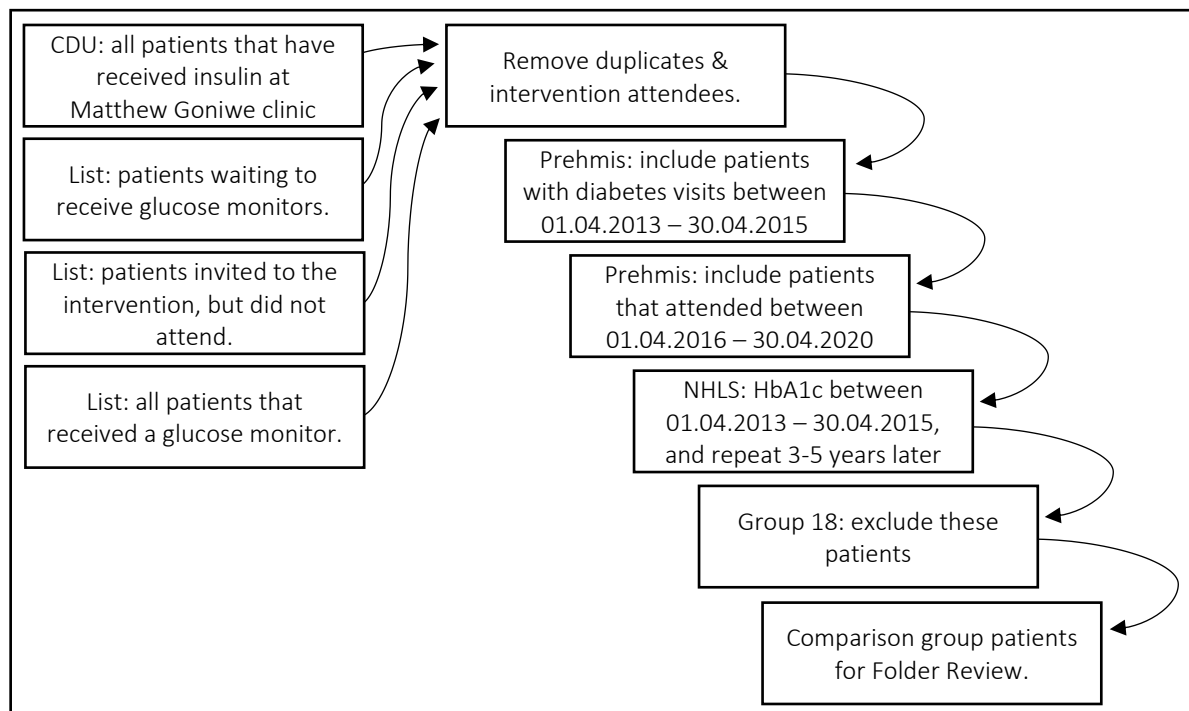
Comparison group sampling:

The comparison patients will have attended the same primary health care clinic as the intervention group, during the same time frame, but differ in terms of not having attended the intervention.

Step 1: Identify all diabetic patients who ever received insulin at Matthew Goniwe clinic, who had an HbA1c done between April 2013 and April 2015, and repeated 3-5 years later – excluding patients who attended the intervention.

1. Matthew Goniwe Clinic patients on insulin will be identified:
 - a. Using pharmaceutical electronic data from the Chronic Dispensary Unit (CDU)
 - i. all patient having ever received insulin from CDU will be identified.
 - b. Using the list of patients waiting to receive glucose monitors (compiled by the clinic doctors)
 - c. Using the list of patients that were invited to the intervention but did not attend.
 - d. Using the list of patients who had received a glucose monitor.
2. This list will be narrowed down by including only those patients that had a recorded diabetes visit at Matthew Goniwe clinic between 01.04.2013 and 30.04.2015 using Prehmis (the City of Cape Town's Patient Record and Health Management Information System).
3. It can be further narrowed down by including only those patients that had a recorded visit between 01.04.2016 – 30.04.2020 using Prehmis.
4. This list will be narrowed down by including only patients that had an HbA1c done between 01.04.2013 and 30.04.2015, and who have a comparison HbA1c 3-5 years later, using NHLS data. HbA1c must have been taken at Matthew Goniwe clinic.
5. Participants of group 18 will be excluded.

Diagram 2: Step 1 of sampling the comparison group



Step 2: To identify patients that had their first HbA1c while on insulin therapy for at least 3 months, a folder review needs to be done.

1. All folders identified in Step 1 will be reviewed
2. The medication at the time of the “first HbA1c” will be reviewed:
 - a. If the patient was on insulin for at least 3 months: they will be included and all necessary data will be collected from the folder (see section “7.6 Outcome measurements” below)
 - b. If the patient is not on insulin at the time of the first HbA1c, but was started on insulin between 01.04.2013 and 30.04.2015, then the next HbA1c that meets the inclusion criteria will be used as the “first HbA1c” (i.e. it must be taken between 01.04.2013 and 30.04.2015, and the patient needs to have been on insulin for 3 months).
 - c. If the patient is not on insulin at the time of the first HbA1c, and does not have another HbA1c between 01.04.2013 and 30.04.2015 while on insulin for at least 3 months, then they will be excluded.
 - d. If the patient is not on insulin during the time period, they will be excluded.
3. Patients’ age at the “first HbA1c” will need to be checked, and only those between the ages of 18-70 years will be included.

Patients’ whose folders cannot be found, will not be included in the study.

Limitations:

- The intervention participants were recruited according to glycaemic control and co-morbidities. This means that they may differ significantly from the control group in that regard: the intervention group may have worse glycaemic control which will dilute the effect of the intervention.
- Patients who remained poorly controlled from the first HbA1c would have been prioritised for the intervention, and patients that improved from the first HbA1c with usual care would have moved down the list of priority. Therefore the recruitment process favours an improved outcome in glycaemic control in the control group.
- HbA1c results are not selected in relation to the intervention, but according to a given time frame. This means the time from the “*first HbA1c*” until the start of the intervention differs, but will have occurred within 2 years of the 3-5 years being assessed.

- This is done because baseline HbA1cs were not done at the start of the intervention, and it is therefore not possible to have the period from “*first HbA1c*” to start of intervention be the same in all participants of the intervention.
- It is done because it ensures the timeframe used to compare intervention and control group is the same.
- Glucose monitor in itself can have beneficial effects on patients’ glycaemic control, and therefore this parameter will be captured during the folder review.
- Patients that attended only one session of the intervention (the introductory session) can be added to the control group: they met the recruitment requirements, making them good candidates to compare with the intervention group. However, a limitation is that they might be different to the patients that attended in some way, as they did not attend.
- For the folder review, data will be collected from clinic folders. It is anticipated that a number of folders might not be found and this could lead to incomplete data.

7.5 Sample Size

Intervention group:

- 141 patients attended the intervention.
- 110 of these patients still attended the same clinic 3 years later.

Some of these participants might be excluded with the criteria documented above.

Comparison group:

The comparison group will contain all patients that meet the inclusion criteria.

The relatively small number may be a limitation to the strength of the study outcome.

7.6 Outcome measurements

The indicator used to assess the outcome of the study is glycaemic control using HbA1c blood results.

These blood tests were done during routine care, and were not taken specifically at the start of this intervention (as a formal assessment of this intervention had not been planned). This is a limitation, as some blood tests are taken fairly long before or after the intervention, which means other factors may have contributed to the change in HbA1c.

The criteria for using an HbA1c blood tests in this study is: patients need to have been on insulin for at least 3 months. This period would have allowed patients to become familiar with insulin injections would ensure that changes in glycaemic control are not solely due to the commencement of insulin.

The HbA1c results will be obtained from the NHLS data base (TrakCare / Disa Lab) using the patients' clinic folder number and/or full name.

Data collection on study participants' baseline characteristics will be done:

From Prehmis (the City of Cape Town's Patient Record and Health Management Information System):

- Gender
- DOB / Age

From folder review:

- Date when diabetes diagnosed
- Date when diabetes treatment started at Matthew Goniwe Clinic
- Date when basal insulin was started, and when biphasic insulin was started
- Insulin dosage at "first", "last", "pre", "post" and "3-years-post" HbA1c
- Date when glucose monitor was given
- Weight and BMI at (or before) "first" HbA1c
- Co-morbidities
- Known diabetic complications (retinopathy, kidney disease (microalbuminuria/nephropathy), peripheral neuropathy, peripheral arterial disease, cardiovascular disease etc.)
- Employment

From records:

- Date the group education sessions were started
- Number of sessions that were attended
- Change in insulin dosage during the intervention

The folder review will be performed at the Matthew Goniwe clinic: COVID-19 safety precautions will be followed at all times (wearing mask, social distancing, sanitizing of hands and surfaces, and maximising ventilation).

7.7 Data management

To ensure accuracy and reliability of the data collected, one person will be responsible for the data collection.

The following recordkeeping and data handling measures will be in place to make sure the patient's identity and data will be kept confidential:

- All electronic information will be saved in password-protected, encrypted files.
- Once the data collection has been completed, all identifiers (e.g. name, date of birth) will be removed from the data set for data analysis. An anonymous unique identifying code will be assigned to each patient. The key to this unique identifying code will be saved in a password-protected, encrypted file.

7.8 Data analysis

The data analysis will be performed using the statistical software Stata. The initial analysis will be a univariate (single variable) analysis, looking at HbA1c results to determine the change in glycaemic control in the intervention group, and comparing this to the comparison group. Later, these results will be assessed in relation to other variables to see how these impacted on glycaemic control (bivariate analyses).

Evaluating the short and medium term effects of the intervention (pre/post design):

Short-term pre/post design:

- Calculate the average change in HbA1c in the short-term.
- *Secondary objective:* calculate the change in insulin dosage.

Medium-term pre/post design:

- Calculate the average change in HbA1c in the short-term.
- Calculate the average change in HbA1c in the medium-term.
- Calculate the difference between the change in HbA1c in the short and medium term.
- *Secondary objective:* calculate the change in insulin dosage in the short and medium term and the difference between the two.

These results will be analysed according to:

- Participants' weight and age
- Participants attendance of the intervention
- Timing of the "pre" and "post" HbA1c blood tests in relation to the intervention
- Duration on insulin prior to the intervention
- Change in glycaemic control in the short term.

Assessing the effectiveness of the intervention when compared to a comparison group:

Baseline characteristics of all subjects will be documented in a table to assess if the intervention and control groups are comparable.

The comparison between intervention and control groups will be an "as treated" analysis.

- Calculate the average change in HbA1c in both groups.
- Assess if the difference between the two groups is significant.
- *Secondary objective*: calculate the average change in insulin dosage in both groups and compare the two.
- *Secondary objective*: assess the number of HbA1cs done annually in the intervention and control group during the study period.

The change in HbA1c in the both groups will be analysed according to:

- Glycaemic control at the start of the study ("first HbA1c")
- Participants' weight and age
- Duration on insulin prior to the intervention
- Possession of glucose monitor

8. Ethics

This intervention was designed for and implemented as part of routine care; formal evaluation thereof was not initially planned. This study will collect and examine routine care audit data to assess the intervention.

Informed consent process

Informed consent will not be taken from the intervention nor the comparison group, as this is fundamentally a folder-review audit.

Risks

Measures to protect the confidentiality of study participants will be implemented (see section “7.7 Data management” above). This study will be conducted by the patient’s attending clinician: no divulging of identifying information will be made outside of this clinician and her supervisor.

Benefits

- If this study shows improved glycaemic control in the intervention arm, it has the potential to motivate for the implementation and further study of this intervention at a greater scale, at more facilities in Cape Town.
- Improved glycaemic control has personal benefits for patients for being at reduced risk of developing diabetic complications; and on a health systems level a reduction in diabetic complications could ultimately lead to significant reduction in health care costs.

Compensation

No monetary reimbursement was provided for attendance of the intervention.

Permissions

Permission from the City of Cape Town will be needed to access the folders for the folder review.

Compliance

This protocol complies with the principles of the Helsinki Declaration of 2013 ⁽³⁵⁾ and the Department of Health’s health research ethics guidelines of 2004 ⁽³⁶⁾.

9. Time Frame

The aim is to complete this study by April 2022. The submission to Human Research Ethics Committee of the University of Cape Town is planned for July 2021. Once ethics approval has been obtained:

- it will take approximately 2 months to do the sampling of the comparison group, to obtain permission from the City of Cape Town, and complete the data collection;
- And a further 2 months for the data analysis and writing up of the findings.

10. Budget

No funding will be received.

11. Outputs

This study will be used to complete a Masters of Public Health mini dissertation, and will be presented to the City Health department (City of Cape Town). It will also be submitted to primary health care journals for potential publication.

12. Conflicts of interest

This study will be performed by the same person who designed and implemented the intervention. This is a limitation due to potential compromised objectivity and bias.

13. References

(1) World Health Organisation. 2016. Global report on diabetes. Available: https://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf?sequence=1 [Accessed 17.04.2021]

(2) International Diabetes Federation. IDF Diabetes Atlas. Ninth edition. 2019. Available: https://www.diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf [Accessed 17.04.2021]

- (3) UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998 Sep 12;352(9131):837-53.
- (4) Western Cape Government Health. Burden of Disease. 2019. Available: https://www.westerncape.gov.za/assets/departments/health/bod_infographic.pdf [Accessed 17.04.2021]
- (5) Mutyambizi C, Pavlova M, Chola L, Hongoro C, Groot W. Cost of diabetes mellitus in Africa: a systematic review of existing literature. *Global Health*. 2018 01 16;14(1):3.
- (6) The Society for Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee. Chapter 1: Epidemiology of type 2 diabetes. In: Amod A, editor. SEMDSA 2017 Guidelines for the Management of Type 2 diabetes mellitus. JEMDSA 2017; 21(1)(Supplement 1): S8-10.
- (7) Statistics South Africa. Mortality and causes of death in South Africa: Findings from death notification. 2017. Available: <https://www.statssa.gov.za/publications/P03093/P030932017.pdf> [Accessed 17.04.2021]
- (8) Berkowitz SA, Meigs JB, DeWalt D, Seligman HK, Barnard LS, Bright OJ, et al. Material need insecurities, control of diabetes mellitus, and use of health care resources: results of the Measuring Economic Insecurity in Diabetes study. *JAMA Intern Med*. 2015 Feb;175(2):257-65
- (9) Statistics South Africa. Use of health facilities and levels of selected health conditions in South Africa: Findings from the General Household Survey, 2011. Available: <http://www.statssa.gov.za/publications/Report-03-00-05/Report-03-00-052011.pdf> [Accessed 17.04.2021]
- (10) Mbanya JC, Ramiaya K. Chapter 19 Diabetes Mellitus. In: Jamison DT, Feachem RG, Makgoba MW, Bos ER, Baingana FK, Hofman KJ, O Rogo KO editors. *Disease and Mortality in Sub-Saharan Africa*. 2nd edition. Washington (DC): The International Bank for Reconstruction and Development / The World Bank, 2006; p. 267-287.
- (11) Groenewald P, Bradshaw D, Daniels J, Zinyakatira N, Matzopoulos R, Bourne D, et al. Local-level mortality surveillance in resource-limited settings: a case study of Cape Town highlights disparities in health. *Bull World Health Organ*. 2010 Jun;88(6):444-51.
- (12) Western Cape Government Health. Circular H 102 / 2020: Population Data. 2020. Available: https://www.westerncape.gov.za/assets/departments/health/h_102_2020_covid-19_population_data.pdf. [Accessed 17.04.2021]
- (13) City of Cape Town. 2011 Census Suburb Khayelitsha. w2013. Available: https://resource.capetown.gov.za/documentcentre/Documents/Maps%20and%20statistics/2011_Census_CT_Suburb_Khayelitsha_Profile.pdf [Accessed 17.04.2021]

- (14) Battersby J. The State of Urban Food Insecurity in Cape Town. Urban Food Security Series; Queen's University and AFSUN: Kingston, ON, Canada; Cape Town, South Africa, 2011. Available: https://www.google.com.tw/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwi29fSS5r3jAhVPG6YKHYED-cQFjAAegQIABAC&url=http%3A%2F%2Fwww.afsun.org%2Fwp-content%2Fuploads%2F2013%2F09%2FAFSUN_11.pdf&usg=AOvVaw3CWbyA289GpcqPCvi3Mlwp [17 April 2021].
- (15) Kroll F, Swart EC, Annan RA, Thow AM, Neves D, Apprey C, et al. Mapping Obesogenic Food Environments in South Africa and Ghana: Correlations and Contradictions. Sustainability [Internet]. MDPI AG; 2019 Jul 18;11(14):3924.
- (16) Smit W, de Lannoy A, Dover RVH, Lambert EV, Levitt N, Watson V. Making unhealthy places: The built environment and non-communicable diseases in Khayelitsha, Cape Town. Health & Place. 2016 May; 39: 196–203.
- (17) The 2012 SEMDSA Guideline for the Management of Type 2 Diabetes. JEMDSA 2012; 17(2)(Supplement1): S1-S95.
- (18) Western Cape Government Health. Annual Performance Plan 2019-2020. Available: https://www.westerncape.gov.za/assets/departments/health/app_2019-2020_19022019.pdf. [Accessed 07.05.2021]
- (19) Knowledge Translation Unit. Practical Approach to Care Kit (PACK). Primary Care Guide for the Adult 2020. Western Cape Edition. Available: <https://knowledgetranslation.co.za/download/8920>. [Accessed 10.05.2021]
- (20) Driskell OJ, Holland D, Waldron JL, Ford C, Scargill JJ, Heald A, et al. Reduced testing frequency for glycated hemoglobin, HbA1c, is associated with deteriorating diabetes control. Diabetes Care. 2014 Oct;37(10):2731-7.
- (21) Cusick M, Meleth AD, Agrón E, Fisher MR, Reed GF, Knatterud GL, et al. Associations of mortality and diabetes complications in patients with type 1 and type 2 diabetes: early treatment diabetic retinopathy study report no. 27. Diabetes Care. 2005 Mar;28(3):617-25.
- (22) United Kingdom Prospective Diabetes Study Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 352: 837–853, 1998
- (23) Stratton IM, Adler AI, Neil HAW, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000 Aug 12; 321(7258): 405–412.
- (24) Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. New Engl J Med 329:977–986, 199

- (25) Chrvala CA, Sherr D, Lipman RD. Diabetes self-management education for adults with type 2 diabetes mellitus: A systematic review of the effect on glycemetic control. *Patient Educ Couns*. 2016 06;99(6):926-43
- (26) American Diabetes Association. 5. Facilitating Behavior Change and Well-being to Improve Health Outcomes: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021 Jan;44(Suppl 1):S53-S72.
- (27) Steinsbekk A, Rygg LØ, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. *BMC Health Serv Res*. 2012 Jul 23;12:213.
- (28) Thongsai S, Youjaiyen M. The long-term impact of education on diabetes for older people: a systematic review. *Glob J Health Sci*. 2013 Jul 28;5(6):30-9.
- (29) van de Sande M, Dippenaar H, Rutten GE. The relationship between patient education and glycaemic control in a South African township. *Prim Care Diabetes*. 2007 Jun;1(2):87-91.
- (30) Mash RJ, Rhode H, Zwarenstein M, Rollnick S, Lombard C, Steyn K, Levitt N. Effectiveness of a group diabetes education programme in under-served communities in South Africa: a pragmatic cluster randomized controlled trial. *Diabet Med*. 2014 Aug;31(8):987-93.
- (31) Allerton J, Mash R. The impact of intensified clinical care on glycaemic control in patients with type 2 diabetes at Khayelitsha Community Health Centre, South Africa: Quasi-experimental study. *Prim Care Diabetes*. 2020 04;14(2):97-103.
- (32) American Diabetes Association. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021 Jan;44(Suppl 1):S73-S84
- (33) Malanda UL, Welschen LM, Riphagen II, Dekker JM, Nijpels G, Bot SD. Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. *Cochrane Database Syst Rev*. 2012;(1):CD005060.
- (34) Farmer AJ, Perera R, Ward A, et al. Meta-analysis of individual patient data in randomised trials of self monitoring of blood glucose in people with non-insulin treated type 2 diabetes. *BMJ*. 2012;344:e486.
- (35) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013 Nov 27;310(20):2191-4.
- (36) Department of Health. Ethics in health research: Principles, structures and processes. Pretoria; 2004. Available: https://www.researchgate.net/profile/Wilbert-Bannenber/publication/242773088_Ethics_in_Health_Research_Principles_Structures_and_Processes/links/5f25658f92851cd302ceada3/Ethics-in-Health-Research-Principles-Structures-and-Processes.pdf [Accessed 07.06.2021]

Annexure 1: Insulin Titration Instructions and Schedule

Insulin Dosage Adjustment - Instructions

Insulin dosage adjustments should be done every 3-7 days, until glycaemic control is achieved. Use average blood glucose levels of at least 3 days; never adjust insulin just on one reading. Instructions on the back of this page.

<p style="text-align: center;">Healthy adult (age 18 – 65 years)</p> <p style="text-align: center;">Goal HbA1C: <7% Goal fasting blood glucose: 4.0 – 7.0</p>	Average Hgt	Dosage adjustment
	> 10	+ 8 units
	8.1 – 10	+ 6 units
	7.1 – 8.0	+ 4 units
	6.1 – 7.1	+2 units
	4.1 – 6.0	No change
	4.0 or less	- 2 units

<p style="text-align: center;">Healthy elderly (age 65 years and older)</p> <p style="text-align: center;">Goal HbA1C: <7% Goal fasting blood glucose: 6.5 - 7.5</p> <p>This includes patients with no (or mild) microvascular disease, good functional status and life expectancy of at least 10-15 years.</p>	Average Hgt	Dosage adjustment
	> 12	+ 8 units
	9.6 – 12	+ 6 units
	8.6 – 9.5	+ 4 units
	7.6 – 8.5	+2 units
	6.5 – 7.5	No change
	Less than 6.5	- 2 units

<p style="text-align: center;">Frail elderly (age 65 years and older)</p> <p style="text-align: center;">Goal HbA1C: 7.6-8.5 Goal fasting blood glucose: 7.5 - 9.0</p> <p>This includes patients with advanced microvascular disease, major co-morbid disease (e.g. IHD), poor functional status and life expectancy of less than 5 years.</p>	Average Hgt	Dosage adjustment
	> 11	+ 6 units
	10 – 11	+ 4 units
	9.1 – 10	+2 units
	7.5 – 9.0	No change
	Less than 7.5	- 2 units

Basal insulin (intermediate acting insulin, e.g. Protophane / Humulin N)

- This insulin is injected once a day: at bed time.
- Patients must monitor their fasting blood glucose levels in the morning (before breakfast).
- Patients must bring their readings to the clinic every 3-7 days.
- The average fasting blood glucose level must be calculated and then the insulin dosage must be adjusted using the appropriate table on the next page (Glycaemic Targets).

Example1: **43 year old** diabetic male. No co morbidities.

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)
11/01	Mon	16u	8.5
12/01	Tue	16u	7.9
13/01	Wed	16u	9.2

- Work out the average fasting blood glucose level: $(8.5 + 7.9 + 9.2) / 3 = 8.5$
- Using the appropriate table on the next page one can see that this patient needs to increase the bedtime insulin dosage by 6 units. He now needs to use 22u of insulin at bedtime.

Biphasic insulin (e.g. Actraphane / Humulin 70/30)

- This insulin is injected 2 times per day: 30 minutes before breakfast and supper.
- Patients must test their fasting blood glucose levels in the morning (before breakfast), and their blood glucose level before supper (i.e. the same time they take their insulin).
- Patients must bring their readings to the clinic every week.
- The average blood glucose levels before breakfast and the average blood glucose level before supper must be calculated.
- The evening insulin dosage is adjusted using the morning blood glucose level and the morning insulin dosage is adjusted using the evening blood glucose level.
- One must be careful with patients who have erratic readings: increasing insulin dosage may result in hypoglycaemia. Instead consider advising the client on diet changes (aim to keep carbohydrate intake the same every day). A referral to the dietician may be indicated.

Example2: **72 year old** female with ischaemic heart disease.

Date	Morning (30 minutes before breakfast)		Evening (30 minutes before supper)	
	Insulin	Blood Sugar	Insulin	Blood Sugar
11/01	20u	7.3	10u	11.5
12/01	20u	8.2	10u	9.5
13/01	20u	8.8	10u	10.7

- Working out the averages:
Morning: $(7.3 + 8.2 + 8.8) / 3 = 8.1$
Evening: $(11.5 + 9.5 + 10.7) / 3 = 10.6$
- Now using the appropriate table on the next page: the patient is injecting the correct amount of insulin in the evening, but needs to inject 4 units more in the morning, i.e.: 24u / 10u bd.

Example3: **54 year old** male. No co morbidities.

Date	Morning (30 minutes before breakfast)		Evening (30 minutes before supper)	
	Insulin	Blood Sugar	Insulin	Blood Sugar
11/01	20u	3.7	10u	22.0
12/01	20u	15.6	10u	5.2
13/01	20u	8.4	10u	14.5

- Blood glucose levels are very erratic. This patient is at risk of a hypoglycaemic episode, especially if the insulin dosage is increased.
- Explain to this patient how to keep his carbohydrate intake the same every day and review his readings again in 1 week.

Annexure 2: Blood glucose Home Monitoring Page

ADJUSTING YOUR BEDTIME INSULIN DOSAGE

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)

Next insulin adjustment date: _____

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)

Next insulin adjustment date: _____

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)

Next insulin adjustment date: _____

Aim:

The aim of these insulin adjustments is for you to have morning blood sugar levels between **4 and 6**



Instructions:

- 1) Inject your insulin every evening at bedtime (8 – 10 pm)
- 2) Test your blood sugar level every morning before breakfast
- 3) Write down your result on this page.
- 4) Bring this page to the clinic every week.

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)

Next insulin adjustment date: _____

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)

Next insulin adjustment date: _____

Date	Day	Bedtime Insulin	Morning Blood Sugar (Before breakfast)

Next insulin adjustment date: _____



Pay attention to the food you eat:

you will notice that the amount you eat and the type of food you eat has a big impact on your blood sugar. Try to follow a healthy diet plan where you eat more or less the same amount of food every day: this will make sure that your blood sugars are more or less the same every morning. Importantly, it is the **carbohydrates** (starch and sugar) you eat that affects you blood sugar.

Low blood sugar:

Blood sugar levels of **less than 4** are too low!

If you have a blood sugar of less than 4: eat or drink something sweet immediately!

Then you need to try and work out why your blood sugar dropped so low. Ask yourself the following questions:

- Did you by mistake inject too much insulin?
- Did you not eat your normal dinner the evening before? Did you eat enough starch yesterday?
- Did you forget your bedtime snack?
- Did you exercise more than usual the day before?

Usually one can find a reason why the blood sugar dropped too low.

WARNING:

Low blood sugars of **less than 3** can result in seizures or coma!

ADJUSTING YOUR MORNING AND EVENING INSULIN DOSAGE

Date	Morning <small>(30 minutes before breakfast)</small>		Evening <small>(30 minutes before supper)</small>	
	Insulin	Blood Sugar	Insulin	Blood Sugar

Next insulin adjustment date: _____

Date	Morning <small>(30 minutes before breakfast)</small>		Evening <small>(30 minutes before supper)</small>	
	Insulin	Blood Sugar	Insulin	Blood Sugar

Next insulin adjustment date: _____

Date	Morning <small>(30 minutes before breakfast)</small>		Evening <small>(30 minutes before supper)</small>	
	Insulin	Blood Sugar	Insulin	Blood Sugar

Next insulin adjustment date: _____

Aim:

The aim of these insulin adjustments is for you to have blood sugar levels between 4.0 and 6.0



Instructions:

- 1) Inject your insulin 30 minutes before breakfast, and 30 minutes before supper every day.
- 2) Also test your blood sugar level 30minutes before breakfast and 30minutes before supper.
- 3) Write down your results on this page.
- 4) Bring this page to the clinic every week.

Date	Morning (30 minutes before breakfast)		Evening (30 minutes before supper)	
	Insulin	Blood Sugar	Insulin	Blood Sugar

Next insulin adjustment date: _____

Date	Morning (30 minutes before breakfast)		Evening (30 minutes before supper)	
	Insulin	Blood Sugar	Insulin	Blood Sugar

Next insulin adjustment date: _____

Date	Morning (30 minutes before breakfast)		Evening (30 minutes before supper)	
	Insulin	Blood Sugar	Insulin	Blood Sugar

Next insulin adjustment date: _____



Pay attention to the food you eat:

you will notice that the amount you eat and the type of food you eat has a big impact on your blood sugar. Try to follow a healthy diet plan where you eat more or less the same amount of food every day: this will make sure that your blood sugars are more or less the same every morning.

Importantly, it is the **carbohydrates** (starch and sugar) you eat that affects you blood sugar.

Low blood sugar:

Blood sugar levels of **less than 4** are too low!

If you have a blood sugar of less than 4: eat or drink something sweet immediately!

Then you need to try and work out why your blood sugar dropped so low. Ask yourself the following questions:

- Did you by mistake inject too much insulin?
- Did you eat less than usual? Did you eat enough starch?
- Did you forget your bedtime snack?
- Did you exercise more than usual?

Usually one can find a reason why the blood sugar dropped too low.

WARNING:

Low blood sugars of **less than 3** can result in seizures or coma!

Annexure 4: Discharge Note for Patient Clinical Records

Self-Monitoring of Blood Glucose with weekly insulin adjustments

Patient name: _____

Folder number: _____

Age: _____

Diabetes since: _____

On insulin since: _____

Using: Basal (intermediate acting) insulin
 Biphasic (pre-mixed) insulin

Initial HbA1c: _____ date _____

Date	Insulin		Average blood glucose	
	AM	PM	AM	PM

Final insulin dosage: _____

Follow-up HbA1c: _____ date _____

Annexure 5: Ethics approval



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



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09 December 2021

HREC REF: 498/2021

A/Prof V Zweigenthal

School of Public Health & Family Medicine
Falmouth Building-FHS
Email: virginai.zweigenthal@uct.ac.za
Student: caroline_neu@yahoo.com

Dear A/Prof Zweigenthal

PROJECT TITLE: REVIEW OF THE EFFECTS OF DIABETES GROUP EDUCATION WITH PRACTITIONER-DIRECTED INSULIN DOSE ADJUSTMENTS ON GLYCAEMIC CONTROL AT A PUBLIC SECTOR PRIMARY HEALTH CARE CLINIC IN KHAYELITSHA-MASTERS CANDIDATE-DR CAROLINE NEUMULLER

Thank you for your response letter, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Kindly note permission is needed from the clinic at which data will be extracted.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020; 06 July 2020 & 01 July 2021.

Approval is granted for one year until the 30 December 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: -Dr Caroline Neumüller will also be involved in this study.

Please quote the HREC REF 498/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

HREC/REF 498/2021sa

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.



HREC/REF 498/2021sa

Annexure 6: Approval for research at the City of Cape Town

Approval for City Health's own staff initiated research

Name: *Caroline Neumüller*

Staff number: *10045240*

Title and MARS number:

Review of the Effects of Diabetes Group Education with Practitioner-directed Insulin Dose Adjustments on Glycaemic Control at a Public Sector Primary Health Care Clinic in Khayelitsha 9495

(Attach summary of research proposal)

Guiding Criteria	Yes/No	Additional Comments
Research topic/title is sound?	yes	
Research has clear aim and objectives?	yes	
Research questions are sound and aligned to the stated objectives?	yes	
Research methodology is sound?	yes	
Research aim and objectives aligned to one or more of the CCT's 11 Priority Objectives?	yes	IDP 2017 – 2022: Excellence in basic service delivery
Research aim and objectives aligned to one or more of the CCT's Strategic Focus Areas?	yes	IDP 2017 – 2022: Caring City (3.1.a Excellence in service delivery), Inclusive City (4.3f: PHC), Well-run City (5.1.d Evidence-led decision-making programme)
Research outputs/deliverables are clearly defined?	yes	
Research demonstrates value for money/resource input?	yes	No CCT resource needed other than assistance in accessing patient folders at 1 clinic and the researcher's time (to be managed within usual leave and time and attendance parameters)
Research poses any potential risks to the CCT?	no	

Approval:

1. Line manager

Signature **Karen Jennings** Digitally signed by Karen Jennings
Name: Date: 2021.12.24
Date: 10:48:26 +02'00'

Comments (e.g. time allocation during work hours and inclusion in WSP)

Training dept. confirmed data collection research activities can be taken as "formal studies" leave (≤ 5 days expected); other time off required during work hours, e.g. supervision, can be accommodated by use of flexitime.

2. Area/Branch Manager Acting Specialised Health Manager

Signature **Natacha Berkowitz** Digitally signed by Natacha Berkowitz
Name: Date: 2021.12.24
Date: 11:05:51 +02'00'

Comments

3. Director City Health

Signature **Soraya Elloker** Digitally signed by Soraya Elloker
Name: Date: 2021.12.24 17:30:00
Date: +02'00'

Comments **Request supported as Acting Director**

Part B: Journal manuscript

Journal manuscript for [Primary Care Diabetes](#)

Title

Review of the Effects of Diabetes Mellitus Group Education with Practitioner-directed Insulin Dosage Adjustments on Glycaemic Control at a Public Sector Primary Health Care Clinic in Khayelitsha

Abstract

Aim: In view of the high burden of poorly controlled diabetes mellitus in South Africa, this study evaluated the effect of diabetes group education sessions, coupled with the provision of practitioner-directed insulin dosage adjustments based on home blood glucose readings, on patients' glycaemic control in the short and medium term.

Methods: Using routine data, glycaemic control was assessed before, after and three years after the intervention. Additionally, patients' change in glycaemic control over a three-year period was compared to a control group.

Results: After the group education sessions and insulin dosage adjustments, the mean HbA1c of 66 intervention patients decreased by 2.03% in the short term, from 12.57% (95%CI [12.05%, 13.09%]) to 10.54% (95%CI [9.96%, 11.11%]), and by a further 0.43% three years after the intervention. However, this change in glycaemic control after three years was not different to that of the control group.

Conclusion: The 2% improvement in HbA1c in the short term is a significant achievement; although this is related to patients' poor initial glycaemic control. The control group's similar improvements over a three-year period is due to the improved clinical care and access to glucose monitors for all patients over the course of the study period at the study facility.

Key words: insulin adjustment; diabetes group education; primary health care; South Africa

Introduction

The number of people living with diabetes mellitus (DM) is increasing globally, particularly in low- to middle-income countries such as South Africa (SA) ^[1]. In 2021 it was estimated that 11.3% of the SA population (4.2 million people) had DM ^[2]. Most people living with DM in SA have poor glycaemic control ^[3], and in 2017, DM became the leading natural cause of death in the province of the Western Cape ^[4].

Poverty is associated with poorer glycaemic control ^[5]. People living in poor areas, such as Khayelitsha (a large township in the Western Cape), rely on the public health care sector for their health needs ^[6]. Therefore, it is important for the public sector to find and implement effective strategies to improve DM care. Improving glycaemic control (lowering HbA1c (glycated haemoglobin)) reduces their risk of morbidity and mortality ^[7].

Patient education, promoting DM self-management and appropriate treatment optimisation form the basis of achieving glycaemic control. In the public health care sector in the Western Cape, DM self-management education is usually provided by health care workers during usual care consultations. A study showed these health care workers had poor practical knowledge on insulin administration ^[8]. Group education has been shown to be effective in improving glycaemic control ^[9, 10], including in a nurse-led African programme ^[11].

As β -cell function reduces over time in type 2 diabetes, it is necessary to appropriately adjust patients' DM treatment to achieve glycaemic control ^[12], which leads to increases in medication dosages. South African guidelines advise a stepwise approach to medication therapy in type 2 diabetic patients ^[13]: starting with oral and lifestyle modifications, and if glycaemic control is not achieved, then insulin is to be initiated and appropriately titrated. However, in SA, it is not uncommon for very poorly controlled patients to not have adjustments made to their treatment for years ^[14].

To address inadequate glycaemic control, a service improvement project was piloted in a Khayelitsha primary health care facility, focussing on diabetic patients using insulin – including both type 1 and type 2 diabetes. The intervention entailed hour-long eight-week DM group education sessions held at participants' usual primary health care facility. In addition, participants received a glucose monitor at the first session and were advised at the subsequent sessions on their insulin dosage for the up-coming week. These insulin dosage adjustments were made by the health care practitioner, based on the participants average

home blood glucose readings from the previous week, according to an insulin titration algorithm.

This study assessed this improvement project through reviewing patients' folders using a quasi-experimental design: a pre-post assessment was used to compare glycaemic control of participants. The change in participants' glycaemic control was also compared to a control group's, a retrospective cohort study design. To assess improved care, changes in patients' insulin dosage was assessed and the annual number of HbA1c tests done per patient were counted.

Methods

Study population

The intervention was implemented at a municipality administered primary health care clinic in Khayelitsha, Cape Town. Those included were adult diabetic patients on insulin. Those prioritised were patients with worse glycaemic control, as they were considered at highest risk of complications; as well as patients with known diabetic complications, in whom tight glycaemic control was needed to slow disease progression.

Between August 2013 and July 2015, 141 clinic patients attended at least two sessions of the intervention, participating in 18 groups (mean participants per group 8.4; range 4 to 11). **Figure 1** describes the sampling and who was excluded, yielding the 78 included for analysis.

To create the control group, 235 patients were identified as having ever been on insulin and attending the facility during the study period. They were identified using the municipality's Patient Record and Health Management Information System (PREHMIS). From **figure 1**, only 93 of these patients met the inclusion criteria for the study.

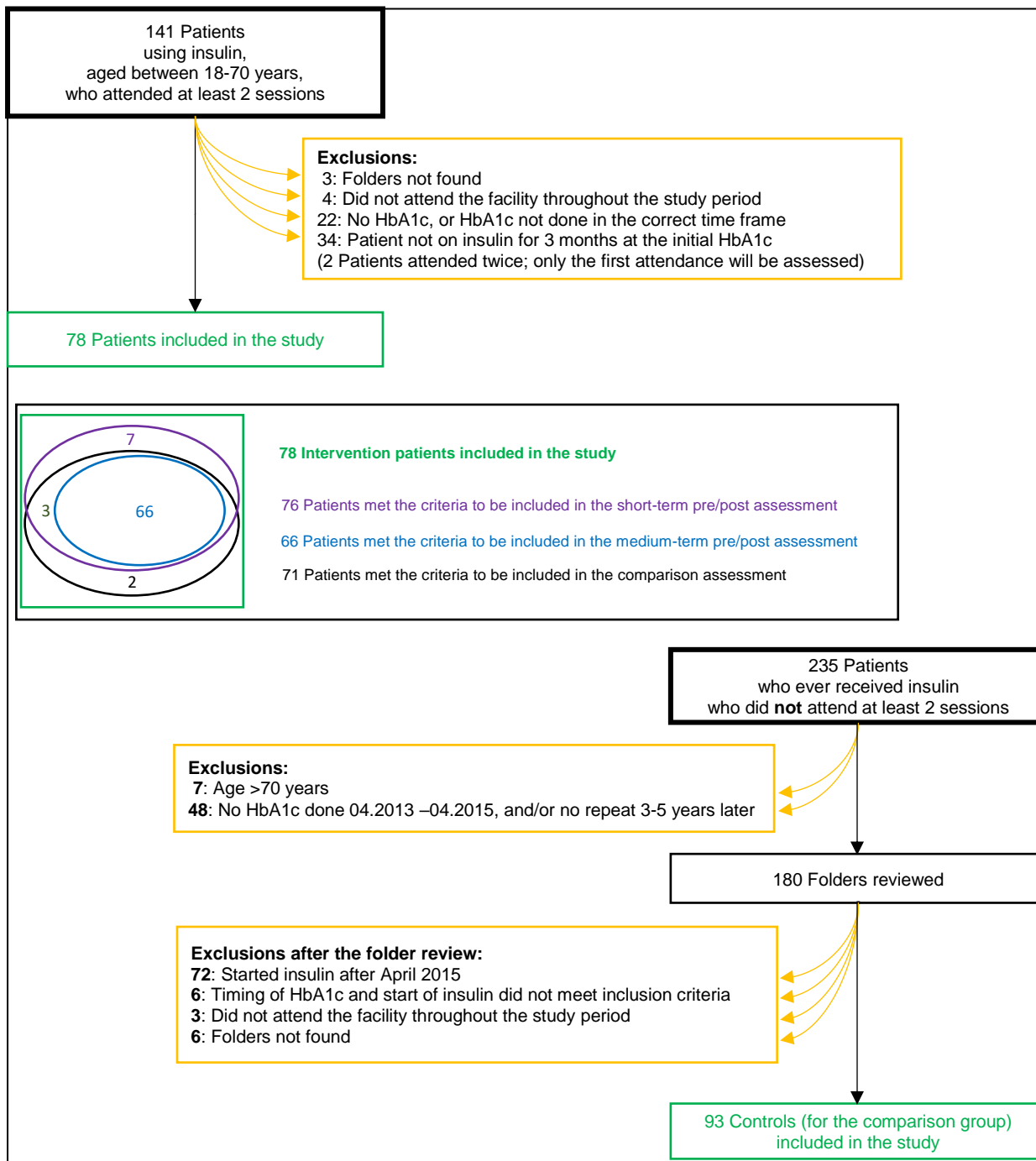


Figure 1: Sampling of intervention study participants and the comparison group

Measurements

Patients' glycaemic control was assessed using HbA1c test results performed at their usual clinic visits. Consequently, the time frame of included HbA1c's needed to be broad to ensure an adequate sample size (see **table 1**). However, the further in time the blood test was done from the intervention, the more likely other factors could contribute to the change in glycaemic control. Additionally, patients needed to be on insulin for at least three months at the time the HbA1c blood test was done.

Table 1: Time frame of included HbA1c blood tests

Name of HbA1c	Time frame of included HbA1c	Assessment design
Pre-HbA1c	HbA1c done 12 months before and up to 2 weeks after the start of the intervention *	Pre-post design: short & medium term assessment
Post-HbA1c	HbA1c done 3 to 15 months after the start of the intervention *	Pre-post design: short-term assessment
3-Years-post-HbA1c	HbA1c done 3 to 5 years after the start of the intervention *	Pre-post design: medium-term assessment
1 st HbA1c	HbA1c done between April 2013 and April 2015 #	Cohort study design
Last HbA1c	HbA1c done 3 to 5 years after the "first HbA1c" #	

* using the result closest to the start of the intervention, if there was more than one result

using the earliest result, if there was more than one result

Data collection, management and analysis

Data collection was performed by the author at the facility in April 2022 and entered directly into an Excel spreadsheet. The data was cleaned and a follow-up visit was done to resolve data queries. All data documents, as well as the key to a unique identifying code (assigned to each patient on the finalised data set, which had all identifiers removed) were saved in password-protected, encrypted files, accessible only to the researcher.

The data was explored using Excel and analysed using Stata 13. Although there appeared to be some outliers in the analyses, all values for variables were included. Descriptive analyses were performed and comparisons, including confidence intervals, were made for the pre-post design. Bivariate analyses were performed using Pearson's correlation for normally distributed data and Spearman's correlation for non-normally distributed data. Multivariate analyses were performed when there were more than one significant variable per analysis, controlling for those variables. P-values of less than 0.05 were considered statistically significant.

To determine if the intervention and control groups were comparable, t-tests for independent samples were performed for numerical data and chi-squared tests for categorical data. The two groups were found to be different (described in the results section). To adjust for this, the two groups were stratified into five subgroups based on initial glycaemic control (HbA1c ranges of 5.0-7.9, 8.0-9.9, 10.0-11.9, 12.0-13.9 and 14.0-18.0). As variances of means did not differ, comparative analyses were run with t-tests by subgroup.

The intervention was implemented in routine care. As this was fundamentally a folder-review audit, informed consent was not taken from study participants. Data management measures were put in place to protect confidentiality. The University of Cape Town's Human Research Ethics Committee granted approval for the study (HREC ref. 498/2021). The City of Cape Town's Health Department approved the folder review audit.

Results

The baseline characteristics of the 78 study participants and 93 control patients are found in **table 2**. The patients included were predominantly female, obese and had poor glycaemic control. Their mean age was 50 years.

Table 2: Baseline characteristics of study participants

	Short-term assessment *	Medium-term assessment *	Comparison #			
			Intervention	Control	P-value	
Number of patients	76	66	71	93		
Mean age (years)	50.6 (48.9-52.2)	50.5 (48.8-52.2)	49.7 (48.0-51.4)	49.8 (48.2-51.4)	0.948	
Mean weight (kg)	87.0 (82.7-91.4)	87.7 (82.9-92.4)	88.4 (83.7-93.1)	87.5 (84.0-91.1)	0.769	
Mean Body Mass Index (BMI) (kg/m ²)	33.9 (32.3-35.5)	34.0 (32.3-35.7)	34.3 (32.6-36.0)	33.7 (32.2-35.1)	0.558	
Median duration since DM diagnosis (years)	7.0 (5.7-8.5)	7.4 (5.7-9.0)	6.7 (5.2-8.3)	4.2 (2.8-5.8)	0.006	
Median duration on insulin (years)	2.4 (2.0-3.2)	2.4 (1.9-3.2)	1.8 (1.3-3.0)	1.0 (0.8-1.3)	0.695	
Median duration from 1 st HbA1c until monitor given (days)	-	-	(n=71) 165 (122-242)	(n=42) ‡ 542 (351-784)	<0.001	
Mean total daily insulin dosage (units)	37.6 (33.1-42.2)	36.6 (31.7-41.5)	33.2 (28.3-38.1)	29.3 (24.7-33.8)	0.249	
Mean HbA1c result (%)	12.61 (12.12-13.20)	12.57 (12.05-13.09)	12.16 (11.66-12.66)	9.75 (9.30-10.20)	<0.001	
Sex – female (%) †	82.9	83.3	84.5	66.7	0.010	
Comorbidities (%)	Hypertension	94.7	95.5	95.8	92.5	0.381
	Dyslipidaemia	11.8	12.1	11.3	18.3	0.216
	Previous stroke	2.6	3.0	2.8	6.5	0.284
	Ischemic heart disease	2.6	3.0	2.8	2.2	0.784
	HIV	9.2	10.6	9.9	15.1	0.153
	Depression	4.0	4.6	4.2	4.3	0.981
Diabetic complications (%)	Any	65.8	65.2	66.2	47.3	0.016
	Retinopathy	32.9	33.3	32.4	16.1	0.014
	Cataracts	6.6	7.6	7.0	4.3	0.445
	Microalbuminuria	34.2	33.3	33.8	24.7	0.203
	Chronic kidney disease	22.4	21.2	21.1	17.2	0.525
	Amputation	1.3	1.5	1.4	1.1	0.847
	Erectile dysfunction	1.3	0.0	0.0	1.1	0.381
	Neuropathy	2.6	1.5	1.4	2.2	0.725
	Peripheral vascular disease	2.6	1.5	1.4	0.0	0.251
	Cardiac autonomic neuropathy	1.3	1.5	1.4	1.1	0.847
Unemployed (%)	55.6 58 unknown	64.3 52 unknown	64.3 57 unknown	56.7 63 unknown	0.632	
Patients known to have died (all-cause) (%) (based on folder review done in April 2022)	5.3	6.1	5.6	4.3	0.695	

Table provides 95% Confidence Intervals in brackets.

* Baseline data taken at the time of the first intervention session

Baseline data taken at the time of the 1st HbA1c date

† PREHMIS data shows that between 2013 – 2016: 67% of diabetic patients attending the clinic were female

‡ 51 of 93 control patients (55%) did not receive a glucose monitor during the study period

Short-term pre-post assessment – change in HbA1c

The mean HbA1c of the 76 intervention participants assessed in the short-term pre-post analysis improved by 2.12%, from 12.61% (95%CI [12.12%, 13.10%]) before the intervention to 10.49% (95% CI [9.96%, 11.02%]) afterwards. The follow-up HbA1c was done after a median duration of 6.1 months from the start of the intervention and the median number of education sessions attended by these participants was 6.5.

Over three quarters (59/76 (78%)) of participants had some improvement in glycaemic control. The number of patients with HbA1c<8% increased significantly from two (2.6%) to ten (7.6%) ($p=0.031$), and the number of patients with HbA1c<10% significantly increased from 11 (14.5%) to 34 (44.7%) ($p=0.007$) after the intervention.

Glycaemic control improved more in patients who were initially poorly controlled ($r=-0.58, p<0.001$). Patients whose HbA1c improved by $\geq 1\%$ ($n=50$) had a mean initial HbA1c of 13.21% (95%CI [12.64%, 13.77%]), compared to 11.45% (95%CI [10.64%, 12.26%]) in the other patients ($n=26$). Glycaemic control also improved more in patients who attended more education sessions ($r_s=-0.3210, p<0.005$); although this correlation was not significant in the multivariate analysis that controlled for initial glycaemic control. However, change in glycaemic control was not significantly associated with BMI, age or duration on insulin prior to the intervention.

To minimise the effect of unmeasured confounders, the time frame for the HbA1c results included was restricted, reducing pre-HbA1c results to within three months of the intervention, and post-HbA1c results to three to six months after the intervention. Only 30 patients met the criteria, and their mean HbA1c improved by 2.41%, from 12.24% (95%CI [11.46%, 13.03%]) to 9.83% (95%CI [9.16%, 10.50%]). This is a larger (but not statistically significant) improvement when compared to the 2.12% improvement of the full analysis.

Short-term pre-post assessment – change in insulin dosage

The mean total daily insulin dosage for participants was almost doubled in the short-term analysis, increasing from 37.6 units (95%CI [33.1, 42.2]) to 70.9 units (95%CI [63.1, 78.7]) per patient. Total daily insulin dosage was increased more in patients who attended more sessions ($r_s=0.5960, p>0.001$), who had higher BMIs ($r=0.4107, p<0.001$) and who were on lower insulin dosages prior to the intervention ($r_s=-0.2701, p=0.018$). Increases in total daily insulin dosage also correlated with shorter duration on insulin in bivariate analysis ($r_s=-0.2758, p=0.016$), but not in the multivariate analysis, controlling for attendance, BMI and initial insulin dosage.

However, change in insulin was not significantly correlated with age and change in HbA1c in the short term.

Medium-term pre-post design – change in HbA1c

Among the 66 intervention participants who met the criteria to be included in the 3-5 year pre-post analysis, the mean HbA1c decreased by 2.03% in the short term, from 12.57% (95%CI [12.05%, 13.09%]) to 10.54% (95%CI [9.96%, 11.11%]). It decreased by a further 0.43% 3-5 years after the intervention, to a mean HbA1c of 10.10% (95%CI [9.58%, 10.63%]). This HbA1c was done after a median duration of 3.2 years from the start of the intervention. Overall the change in HbA1c from the intervention in the short term was maintained over the medium term ($r_s = 0.3922$, $p < 0.001$) (see **figure 2**).

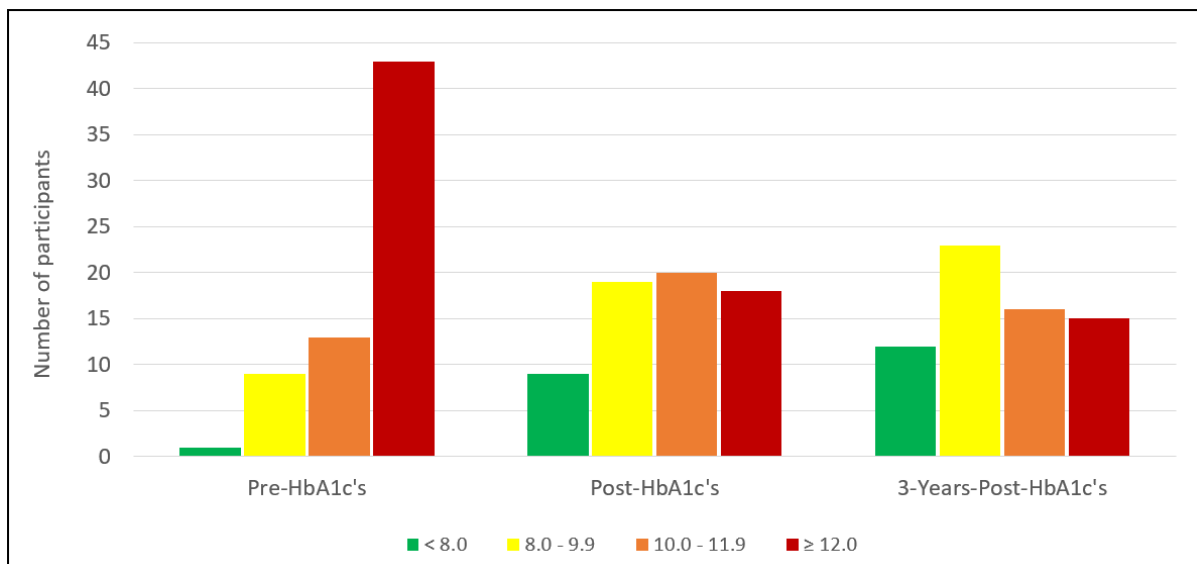


Figure 2: HbA1c results of 66 participants before, after and 3-to-5-years-after the intervention

Among the 66 participants, glycaemic control in the medium term improved more in the initially poorly controlled patients ($r = 0.5668$, $p < 0.001$). Also, patients whose glycaemic control improved were more likely to gain weight ($r = -0.3418$, $p = 0.005$); although controlling for glycaemic control categories prior to the intervention in a multivariate analysis, this correlation was no longer significant. Improvement in HbA1c in the medium-term was not significantly correlated with age, BMI, sex or duration on insulin or number of sessions attended.

Medium-term pre-post design – change in insulin dosage

The mean total daily insulin dosage per patient increased by 34.9 units in the short term, from 36.6 units (95%CI [31.7, 41.5]) to 71.4 units (95%CI [62.7, 80.2]). It increased by just 0.6 units thereafter (in the medium term), to 72.1 units (95%CI [63.6, 80.6]).

The change in total daily insulin dosage overall was maintained over time ($r_s=0.6193$, $p<0.001$); the change in insulin dosage in the short term correlates with the change in the medium term.

The total daily insulin dosage was increased more in patients who had higher BMI ($r_s=0.4851$, $p<0.001$). It was also increased more in patients who were on lower insulin dosages prior to the intervention ($r_s=0.4019$, $p<0.001$), who attended more sessions ($r_s=0.2749$, $p=0.026$) and who were on insulin for a shorter period prior to the intervention ($r=-0.2845$, $p=0.021$). However, only the correlation with BMI was found to be significant in a multivariate analysis when controlling for the other three named variables.

Insulin dosages were also increased more in females compared to males ($t(64)=2.48$, $p=0.016$). However, this is likely due to the small number of males (11 versus 55) and males having significantly lower BMIs than females (28.1kg/m^2 versus 35.1kg/m^2) ($t(63)=3.15$, $p=0.003$). A multivariate analysis confirmed that sex was no longer significantly correlated with increasing insulin dosage when controlling for BMI. Change in total daily insulin dosage in the medium term was not significantly correlated to age, initial HbA1c or change in HbA1c in the short term.

Comparison between intervention and control group

In 2012, only 6.7% (11/164) of all patients had an HbA1c done. This included patients from both the intervention and control groups. This increased to 75.6% in 2013 and continued to increase until 2017, when 92.7% of patients had at least one HbA1c done, and the mean number of tests per patient was 2.0 per annum.

Table 2 demonstrates that the baseline characteristics of the intervention and control groups are significantly different with regards to health and demographic variables, for example the intervention group had a higher proportion of females. The intervention group also had poorer glycaemic control and a higher prevalence of all-diabetic-complications and retinopathy, which relates directly to the selection process – patients with poor glycaemic control and

complications were prioritised for the intervention. Other significant differences relate directly to the intervention: all intervention patients received a glucose monitor compared to 45% of the control group, and the intervention group received their monitors earlier during the study period.

Consequently, the significantly larger reduction in HbA1c between the intervention group (-2.06%) and control group (0.04%) may be due to comparisons made between two significantly different groups.

The pre-post analysis of only intervention patients (described above) demonstrates that patients with higher HbA1c's tended to improve more than patients with lower HbA1c's. This correlation was also found when only analysing the control group ($r = -0.5991$, $p < 0.001$), including controlling for glucose monitor acquisition. Therefore, the larger improvement in the intervention group relates to this group having significantly worse initial glycaemic control.

Stratifying the control and intervention groups into five strata, based on initial HbA1c result ranges, made the groups more comparable. As can be seen in **table 3**, there was no significant difference in change in HbA1c in the control or intervention groups. For most strata, the change in insulin dosage and change in weight were no different in the intervention and control groups. The exceptions were the intervention group's daily insulin dosage increasing more in the 8.0-9.9 sub-group, and their weight increasing more in the 14.0-18.0 subgroup.

Table 3: Changes in HbA1c, insulin and weight of the control and intervention groups by initial HbA1c strata

Variable	HbA1c subgroups		Intervention				Control				p-value	
	First HbA1c	Obs	Mean	Variance	95% CI		Obs	Mean	Variance	95% CI		
Change in HbA1c	5.0-18.0 (All)	71	-2.06	6.75	-2.673	-1.443	93	0.04	5.30	-0.432	0.516	
	5.0-7.9	0	-	-	-	-	20	1.61	3.21	0.772	2.448	-
	8.0-9.9 *	13	0.55	5.14	-0.824	1.916	37	0.54	3.47	-0.078	1.165	0.996
	10.0-11.9	20	-1.30	3.78	-2.205	-0.385	21	-0.52	2.98	-1.309	0.262	0.186
	12.0-13.9 †	22	-2.87	3.73	-3.724	-2.012	11	-2.55	5.03	-4.052	-1.039	0.671
	14.0-18.0	16	-4.01	5.71	-5.286	-2.739	4	-2.35	10.10	-7.406	2.706	0.257
Change in insulin	5.0-18.0 (All)	71	37.52	1559.54	28.174	46.869	93	25.32	1028.05	18.719	31.926	
	5.0-7.9	0	-	-	-	-	20	16.4	406.57	6.963	25.837	-
	8.0-9.9 *	13	46.54	414.44	34.236	58.841	37	27.05	553.39	19.211	34.897	0.011
	10.0-11.9	20	33.85	1635.92	14.920	52.780	21	29.33	2503.33	6.558	52.108	0.753
	12.0-13.9 †	22	32.77	1682.18	14.588	50.958	11	29.27	747.42	10.906	47.639	0.800
	14.0-18.0	16	41.31	2382.23	15.305	67.321	4	22	2378.67	-55.607	99.607	0.488
Change in weight	5.0-18.0 (All)	70	4.46	42.05	2.912	6.005	91	1.51	43.63	0.139	2.890	
	5.0-7.9	0	-	-	-	-	20	-1.34	42.69	-4.393	1.723	-
	8.0-9.9 *	13	-0.39	34.37	-3.935	3.150	36	1.72	31.48	-0.177	3.620	0.256
	10.0-11.9	20	4.06	31.71	1.424	6.696	20	1.13	26.97	-1.300	3.560	0.095
	12.0-13.9 †	22	3.69	38.91	0.921	6.452	11	7.95	66.07	2.485	13.406	0.105
	14.0-18.0	15	10.33	16.46	8.080	12.574	4	-1.88	57.62	-13.954	10.204	0.0004

* HbA1c range 8.0-9.9: the intervention group had significantly worse initial glycaemic control compared to the control group.

† HbA1c range 12.0-13.9: the intervention group had significantly more patients with chronic kidney disease compared to the control group; and the groups are different when looking at the duration from 1st and last test.

Discussion

The majority of households in SA (71.5%) use public sector health facilities [15], particularly those living in low-income densely populated peri-urban settlements. Glycaemic control in diabetic patients attending such facilities is mostly poor. It is in this context that a group-education and insulin dosage adjustment intervention was designed and implemented by a local clinician in 2013-2105. This study sought to determine the effects of this intervention on glycaemic control in the short term, as well review the effect it had after a three-to-five-year period.

The intervention was well attended, with 63% of patients having attended five or more of the eight sessions. Receiving a glucose monitor at the first session, text message reminders the day before sessions, the dispensing of just enough glucose monitoring tests strips to last for one week and the timing of the sessions at 7h30 in the morning, which allowed patients to go to work, contributed to the good attendance. This indicates that the intervention was well accepted and is suitable for the setting. Nonetheless, there were space constraints and language barriers: a small consultation room was used for the group sessions and busy nurses needed to assist with translation.

More females attended the intervention – 85% compared to 67% of all diabetic clinic attenders. The reason for this was not ascertained and may be because males generally have poorer health seeking behaviours [16].

Encouragingly, DM group education coupled with insulin dosage adjustment had a significant beneficial effect on patients' glycaemic control in the short term, particularly for very poorly controlled patients. These effects were maintained over a three-year period. However, when intervention participants were compared to control patients after three years, both groups had similar improvements in glycaemic control. Indeed, the control patients' clinical care also improved over time.

One is unable to assess the impact the group education component had compared to the insulin dosage adjustment component. Their combined effect resulted in a 2% reduction in mean HbA1c. Other SA studies identified looking at these individual components showed a 1.9% reduction mean HbA1c (from a baseline mean of 10.69%) for a hospital based insulin adjustment study [17], and a 1.1% reduction (from a baseline mean of 12.1%) for an intensified clinical care study which included a group education component [18].

Prior to 2013, most diabetic patients at the facility had never had an HbA1c blood test done, despite the national guidelines at that time [19] recommending at least annual HbA1c blood tests in diabetic patients and the facility having had access to this test. DM management without the use of HbA1c blood tests has been shown to be associated with poor glycaemic control [20, 21]. The proportion of diabetic patients in the study population (intervention and control groups) who had an HbA1c test done increased steadily over the study period – from 7.0% & 6.5% in 2012, to 90.1% & 83.9% in 2014. Consequently, most patients' glycaemic control was assessed, allowing appropriate action to be taken to improve patients' control, which benefited all patients attending the facility.

The increase in the number of HbA1c blood tests coincided with the employment of a trained clinician, who championed the importance of this test. Most diabetic patients attending the facility during the study period consulted the clinician, including both intervention and control group patients. In addition, glucose monitors for patients using insulin were introduced for both intervention and control patients over the study period. Home glucose monitoring for patients using insulin was recommended by the national guidelines [19], and has been shown to be an important tool for DM management [26]. Access to these devices required clinic staff to be

proactive to contact the manufacturers for delivery. Almost half (45%) of control patients received blood glucose monitors during the study period.

The study showed significant increases in insulin dosages for poorly controlled patients, in both intervention and control groups. Insulin dosages were increased more in patients who had higher BMIs as they are known to have more insulin resistance [23]. Insulin dosage increases are due to the improved HbA1c monitoring and home glucose monitoring introduced over the study period. This allowed clinicians to make appropriate insulin adjustments.

In the intervention group, the insulin dosage doubled in the short term, suggesting that treatment was insufficiently titrated at prior routine care visits. These high insulin increases were required despite the second education session focussing on diet advice. The aim of teaching about diet early in the intervention was to ensure insulin adjustments were made when patients were following a healthy diet.

Limitations

The intervention was not designed to ascertain its impact. Rather this was a real world study, using routinely collected data [24]. Sampling was not randomised and meant the control group was not comparable. The study was limited by confounders such as the implementation of improved diabetic care implemented over the study period. While it is heartening to find that home monitoring and glycaemic monitoring improved diabetic control, it is unclear how this intervention would fare in settings where these factors were already in place. The study also did not assess the impact the educational component compared to the impact of insulin adjustments. Additionally, the sample sizes for multivariate analyses may have been too small to detect differences when they exist. The acceptability of the intervention was not formally assessed, which may limit future implementation of the program.

Further research

In the years following the intervention, the City of Cape Town introduced a quality improvement DM audit (in 2018), HbA1c blood tests have generally become an accepted part of routine care in practice. Since 2017, glucose monitors were made available to patients from all facilities' pharmacies. Consequently, the standard of DM care has improved. A repeat study of a revised intervention in the current setting, to ascertain if glycaemic control could be further improved, is recommended. This would ideally be a randomised control trial, to avoid some of the limitation of this study, and it could be designed with various treatment arms to be able to differentiate between the impact of the educational component of the intervention versus the

insulin adjustment component. Targeting very poorly controlled diabetic patients would again be advised, as these patients improved the most.

Incentives to enrol in such a study need to be considered as home glucose monitors are more easily available to diabetic patients. Consideration of providing group education sessions at patient's routine health care visits, incorporating telemedicine to regularly adjust patients' insulin dosage [25] and training clinicians on the insulin titration algorithms [25] could be considered.

Conclusion

This study showed that DM group education coupled with practitioner-directed insulin dosage adjustments, at a public primary health facility in a SA low-income setting, lead to significant improvements in patients' glycaemic control, particularly for very poorly controlled diabetic patients. The assessment three years after the intervention showed the improvements were maintained. These findings are noteworthy as most diabetic patients attending public health facilities are poorly controlled and strategies to improve this are needed. These would reduce the number DM complications, improve quality of life of patients.

In the SA context, this study is important due to the high and increasing prevalence of DM. From an economic point of view, interventions, which aim to prevent complications, are recommended as the treatment of complications is very expensive [27]. The focus of the study was on a low-income setting, which is an important to address health inequalities in SA and improve health outcomes for poor communities.

The intervention did not show superior improvement in glycaemic control when compared to a control group. This is due to improvements in clinical care provided at the study facility during the study period, a limitation of a real world study. Further formal research could assess the effectiveness of the intervention in a setting of improved clinical care.

The intervention resulted in a mean 2% improvement in participants' HbA1c and showed success in attendance of the group education sessions. This suggests this type of intervention is acceptable and has the potential of improving DM care at more facilities across Cape Town, and in similar settings globally, particularly in poorer areas.

References

- [1] World Health Organisation. 2016. Global report on diabetes. Available: https://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf?sequence=1 [Accessed 23.10.2022]
- [2] International Diabetes Federation. IDF Diabetes Atlas. Tenth edition. 2021. Available: https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf [Accessed 23.10.2022]
- [3] Western Cape Government Health. Burden of Disease. 2019. Available: https://www.westerncape.gov.za/assets/departments/health/bod_infographic.pdf [Accessed 17.04.2021]
- [4] Statistics South Africa. Mortality and causes of death in South Africa: Findings from death notification. 2017. Available: <https://www.statssa.gov.za/publications/P03093/P030932017.pdf> [Accessed 17.04.2021]
- [5] Berkowitz SA, Meigs JB, DeWalt D, Seligman HK, Barnard LS, Bright OJ, et al. Material need insecurities, control of diabetes mellitus, and use of health care resources: results of the Measuring Economic Insecurity in Diabetes study. *JAMA Intern Med.* 2015 Feb;175(2):257-65. doi: 10.1001/jamainternmed.2014.6888
- [6] Statistics South Africa. Use of health facilities and levels of selected health conditions in South Africa: Findings from the General Household Survey, 2011. Available: <http://www.statssa.gov.za/publications/Report-03-00-05/Report-03-00-052011.pdf> [Accessed 04.10.2022]
- [7] Stratton IM. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 2000 Aug 12;321(7258):405–12. doi: 10.1136/bmj.321.7258.405.
- [8] Parkera N, Coetzee A, Van Wyk L, Conradie M. Practical aspects of insulin administration: what the healthcare provider knows. *JEMDSA* 2022; 27(3) 100-107. DOI: 10.1080/16089677.2022.2057692
- [9] Steinsbekk A, Rygg LØ, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. *BMC Health Serv Res.* 2012 Jul 23;12:213. doi: 10.1186/1472-6963-12-213
- [10] Thongsai S, Youjaiyen M. The long-term impact of education on diabetes for older people: a systematic review. *Glob J Health Sci.* 2013 Jul 28;5(6):30-9. doi: 10.5539/gjhs.v5n6p30

- [11] Hailu FB, Hjortdahl P, Moen A. Nurse-Led Diabetes Self-Management Education Improves Clinical Parameters in Ethiopia. *Frontiers in Public Health*. 2018 Oct 23;6. doi: 10.3389/fpubh.2018.00302.
- [12] Fonseca VA. Defining and characterizing the progression of type 2 diabetes. *Diabetes Care*. 2009 Nov;32 Suppl 2(Suppl 2):S151-6. doi: 10.2337/dc09-S301.
- [13] SA National Department of Health. Standard Treatment Guidelines and Essential Medicines List for South Africa – Primary Health Care level - 2014 Edition
- [14] The 2012 SEMDSA Guideline for the Management of Type 2 Diabetes. *JEMDSA* 2012; 17(2)(Supplement1): S1-S95.
- [15] Statistics South Africa. General Household Survey 2018 (Statistical Release P0318). Available: <http://www.statssa.gov.za/publications/P0318/P03182018.pdf#page=37> [Accessed 06.11.2022]
- [16] SA National Department of Health. The South African National Integrated Men's Health Strategy 2020-2025. Dec 2020
- [17] Kalweit KL, Van Zyl DG, Rheeder P. Titrating insulin in patients with type 2 diabetes using a structured self-monitoring blood glucose regimen. *S Afr Med J*. 2018 Jul 25;108(8):654-659. doi: 10.7196/SAMJ.2018.v108i8.12801.
- [18] Allerton J, Mash R. The impact of intensified clinical care on glycaemic control in patients with type 2 diabetes at Khayelitsha Community Health Centre, South Africa: Quasi-experimental study. *Prim Care Diabetes*. 2020 04;14(2):97-103.
- [19] SA National Department of Health. Standard Treatment Guidelines and Essential Medicines List for South Africa – Primary Health Care level - 2008 Edition
- [20] Camara A, Baldé NM, Sobngwi-Tambekou J, Kengne AP, Diallo MM, Tchatchoua APK, et al. Poor glycaemic control in type 2 diabetes in the South of the Sahara: The issue of limited access to an HbA1c test. *Diabetes Research and Clinical Practice*. 2015 Apr;108(1):187–92. doi: 10.1016/j.diabres.2014.08.025.
- [21] Driskell OJ, Holland D, Waldron JL, Ford C, Scargill JJ, Heald A, et al. Reduced testing frequency for glycated hemoglobin, HbA1c, is associated with deteriorating diabetes control. *Diabetes Care*. 2014 Oct;37(10):2731-7.
- [22] Weinstock R, Aleppo G, Bailey T, Bergenstal R, Fisher W, Greenwood D, et al. The Role of Blood Glucose Monitoring in Diabetes Management. *ADA Clinical Compendia*. 2020 Oct;2020(3):1–32. doi: 10.2337/db2020-31
- [23] Kahn BB, Flier JS. Obesity and insulin resistance. *Journal of Clinical Investigation* [Internet]. 2000 Aug 15;106(4):473–81.

- [24] Gokhale M, Stürmer T, Buse JB. Real-world evidence: the devil is in the detail. *Diabetologia*. 2020 Jul 15;63(9):1694–705.
- [25] Levy N, Moynihan V, Nilo A, Singer K, Bernik LS, Etiebet M-A, et al. The Mobile Insulin Titration Intervention (MITI) for Insulin Adjustment in an Urban, Low-Income Population: Randomized Controlled Trial. *J Med Internet Res*. 2015 Jul; 17(7): e180. doi: 10.2196/jmir.4716
- [26] Chun J, Strong J, Urquhart S. Insulin Initiation and Titration in Patients With Type 2 Diabetes. *Diabetes Spectrum [Internet]*. 2018 Oct 17;32(2):104–11.
- [27] Atun R, Davies JI, Gale EAM, Bärnighausen T, Beran D, Kengne AP, et al. Diabetes in sub-Saharan Africa: from clinical care to health policy. *Lancet Diabetes Endocrinol*. 2017 Aug;5(8):622-667. doi: 10.1016/S2213-8587(17)30181-X.

Part C: Appendices

Appendix A: Acknowledgements

I would like to thank my supervisor Virginia Zweigenthal for her support: guiding me during the course of my dissertation by assisting me with topic selection, recommending articles for literature review, reviewing protocol and manuscript drafts, and advising me on techniques of data analysis.

Appendix B: Data capture instrument

Data collection was performed in April 2022. It was entered directly into an Excel spreadsheet with the following column headings:

Folder number	Number of HbA1c done in 2012
Name	Number of HbA1c done in 2013
Date of birth	Number of HbA1c done in 2014
Date of death	Number of HbA1c done in 2015
Sex	Number of HbA1c done in 2016
Employment	Number of HbA1c done in 2017
Date of 1st education session	Number of HbA1c done in 2018
Number of education sessions attended	Number of HbA1c done in 2019
Pre-HbA1c date	Number of HbA1c done in 2020
Pre-HbA1c result	Date of diabetes diagnosis
Pre-HbA1c AM insulin dosage	Date diabetes treatment started at MG
Pre-HbA1c PM insulin dosage	Date Basal insulin start
Post-HbA1c date	Date Biphasic / BB insulin start
Post-HbA1c result	Date glucose monitor given
Post-HbA1c AM insulin dosage	Co-morbidities
Post-HbA1c PM insulin dosage	Hypertension
3-years-post-HbA1c date	Dyslipidaemia
3-years-post-HbA1c result	HIV
3-years-post-HbA1c AM insulin dosage	IHD
3-years-post-HbA1c PM insulin dosage	Previous CVA
First HbA1c date	Other
First HbA1c result	Known diabetic complications
First HbA1c AM insulin dosage	Retinopathy
First HbA1c PM insulin dosage	Cataracts
First HbA1c weight	Microalbuminuria
First HbA1c height	Chronic kidney disease
Last HbA1c date	Amputation (leg or toe)
Last HbA1c result	Erectile dysfunction
Last HbA1c AM insulin dosage	Congestive Cardiac Failure
Last HbA1c PM insulin dosage	Other
Last HbA1c Weight at	Attended throughout study period

Appendix C: Additional tables and figures

Tables and figures that could not be included in the article for reasons of space limitation.

Table A: Summary of the findings of the pre-post assessments

	Short-term assessment (95% CI)	Medium-term assessment (95% CI)
Number of patients	76	66
Median number of sessions attended	6.5 (6.0-7.0)	6.5 (6.0-7.5)
Mean Pre-HbA1c	12.61 (12.12-13.10)	12.57 (12.1-13.1)
Mean Post-HbA1c	10.49 (9.96-11.02)	10.54 (9.96-11.11)
Mean 3-Years-post-HbA1c	-	10.10 (9.58-10.63)
Median duration from Pre-HbA1c to first session (months)	2.2 (1.8-3.0)	2.1 (1.8-2.9)
Median duration from first session to Post HbA1c (months)	6.1 (5.4-6.7)	6.1 (5.4-6.8)
Median duration from first session to 3-Year-post HbA1c (years)	-	3.15 (3.11-3.24)
Mean total daily insulin dosage at Pre-HbA1c (units)	37.6 (33.1-42.2)	36.58 (31.7-41.5)
Mean total daily insulin dosage at Post-HbA1c (units)	70.88 (63.1-78.7)	71.44 (62.7-80.2)
Mean total daily insulin dosage at 3-Years-post-HbA1c (units)	-	72.08 (63.6-80.6)

Figure A shows the change in HbA1c of 76 intervention participations in the short-term pre-post assessment.

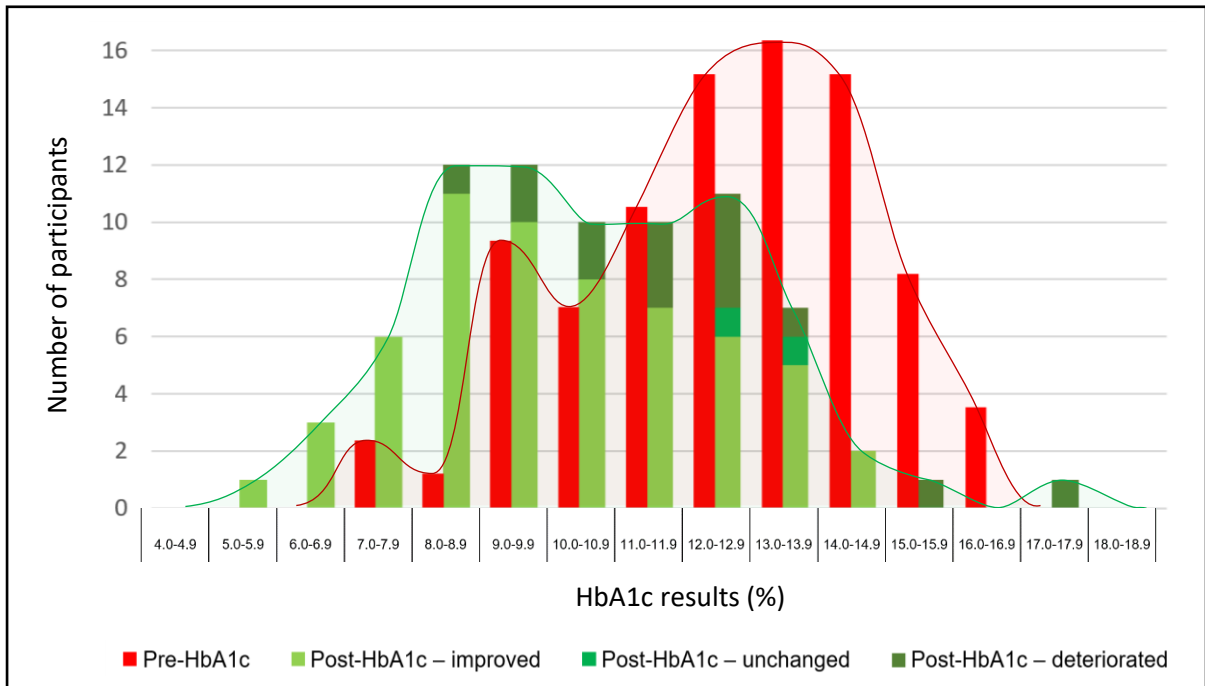


Figure A: Comparing HbA1c results of 76 intervention participants before and after the intervention

Among the 66 participants included in the medium-term pre-post assessment, patients who had the largest improvements in HbA1c with the intervention (in the short term), tended to not improve after the intervention or even deteriorate. Conversely, participants who initially did not improve or deteriorated, tended to improve after the intervention ($r_s = -0.4124$, $p < 0.001$) (see **figure B**).

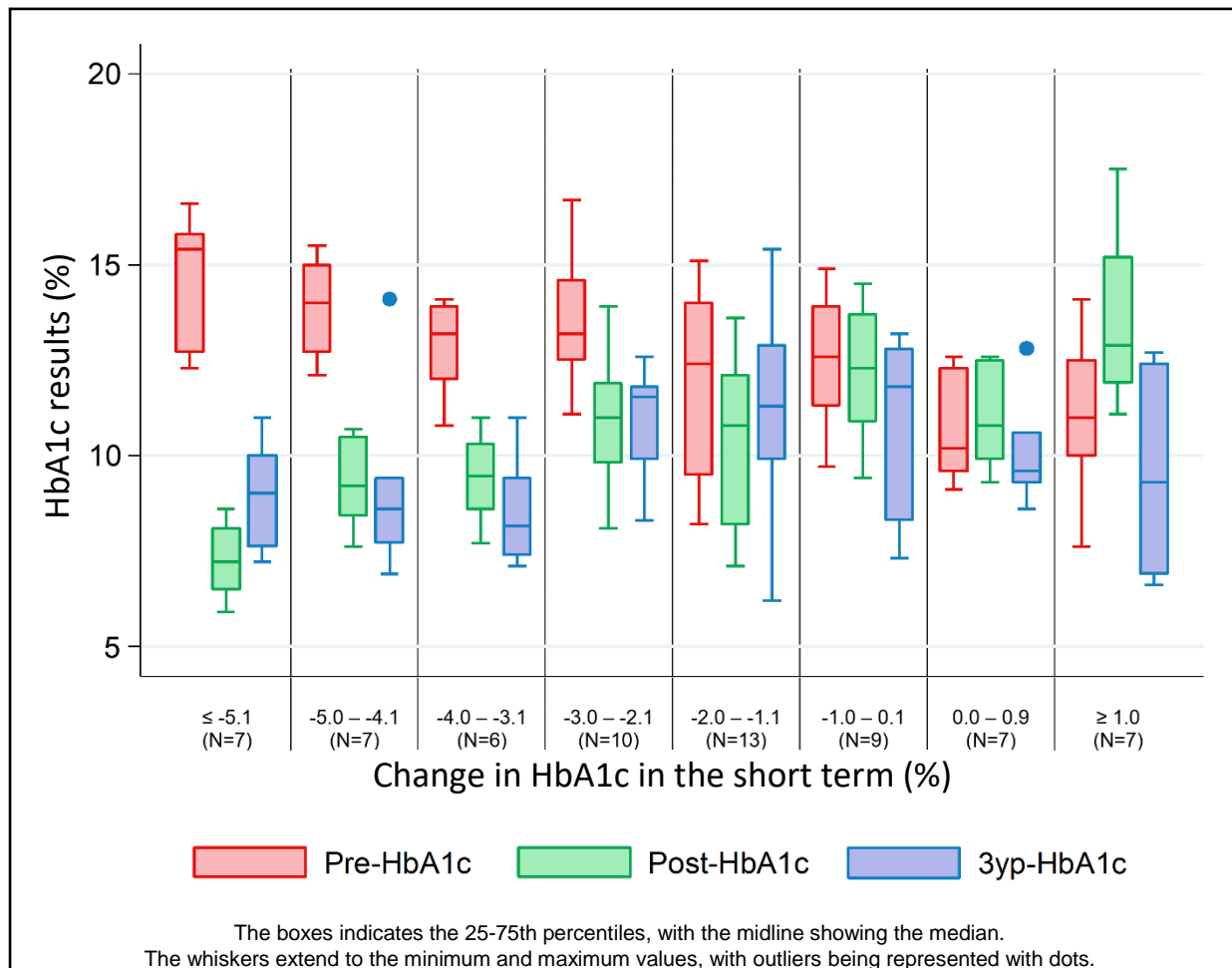


Figure B: Box plot showing HbA1c results before, after and 3-to-5-years-after the intervention, according to the degree of change in HbA1c in the short term

This may indicated that patients, who made changes to their lifestyle during the intervention, contributing to their improved glycaemic control, were not able to maintain these. Patients who did not improve during the intervention perhaps just needed more time; continued care provided during routine visits after the intervention resulted in improvements.

The number of HbA1cs done annually was counted from 2012 to 2020. **Figure C** shows that the number of tests done increased in both intervention and control groups – indicating the standard of routine care improved in both groups.

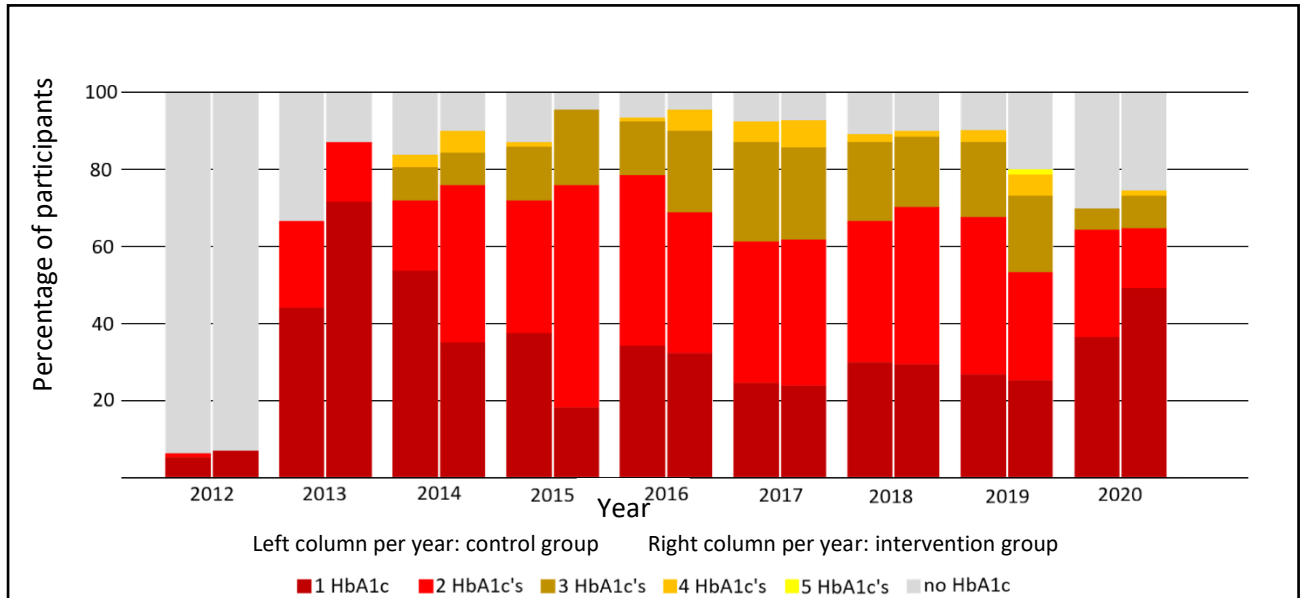


Figure C: Proportion of patients who had HbA1c blood tests done annually - in the control and intervention group - from 2012 to 2020

Appendix D: Author's instructions for the target journal

Pages 65 – 77 contain the Author Information PACK for the *Primary Care Diabetes* Journal.



PRIMARY CARE DIABETES

Primary Care Diabetes is the official journal of [Primary Care Diabetes Europe](#).

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