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Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-045511
Article Type:	Original research
Date Submitted by the Author:	06-Oct-2020
Complete List of Authors:	Hirst, Jennifer; University of Oxford, Nuffield Department of Primary Care Health Sciences; University of Oxford Bobrow, Kirsty; University of Cape Town Farmer, Andrew; University of Oxford, Nuffield Department of Primary Care Health Sciencesd Morgan, Jennie; University of Cape Town Levitt, Naomi; University of Cape Town
Keywords:	DIABETES & ENDOCRINOLOGY, PRIMARY CARE, PUBLIC HEALTH

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Point-of-care HbA_{1c} testing in an urban primary care diabetes clinic in South Africa – a mixed methods feasibility study

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Word count: 4530

Abstract

Introduction

Monitoring and treatment of type 2 diabetes in South Africa usually takes place in primary care using random blood glucose testing to guide treatment decisions. This study explored the feasibility of using point-of-care HbA_{1c} testing in addition to glucose testing in a busy primary care clinic in Cape Town, South Africa.

Subjects: 185 adults aged 19 to 88 years.

Materials and methods

Participants recruited to this mixed methods cohort study received a point-of-care HbA_{1c} test. Doctors were asked to use the point-of-care HbA_{1c} result for clinical decision-making. Qualitative interviews were held with clinical staff.

Results

Point-of-care HbA_{1c} test results were obtained for 165 participants of whom 109 (65%) had poor glycaemic control (>8% HbA_{1c}, 64 mmol/mol). Medical Officers reported using a combination of HbA_{1c} and blood glucose 77% of the time for clinical decision-making. Nurses found the analyser easy to use and doctors valued having the HbA_{1c} result to help with decision-making.

Discussion

This study has found that use of POC HbA_{1c} testing could have potentially averted 30% of patients receiving inappropriate medication or not receiving additional medication when used in routine appointments. Clinicians valued having access to the HbA_{1c} test result to help them make treatment decisions.

Word count:199

Strengths and limitations

Strengths and limitations

- This work demonstrated that POC HbA_{1c} testing can be integrated into patient appointments and used for clinical decision-making.
- It presents a realistic care pathway which can be used in future research or roll-out of POC testing on a wider basis.
- This study did not include any follow-up, so we could not establish whether POC testing had an impact on glycaemic control or long-term health outcomes.
- Paper-based records meant it was difficult to retrieve missing and incomplete data.
- For qualitative data collection, we interviewed clinicians working at the clinic at the time of the study and views may not represent all clinical staff.

Introduction

Diabetes is highly prevalent in South Africa, and is increasing over time.(1-3) An estimated 2.6 million people are living with the condition and there are estimated to be a further 1.2 million who have undiagnosed diabetes.(3) Diabetes is the second most common non-communicable disease in people attending primary care,(4) accounts for 5.7% of all deaths in South Africa, and was the second most common cause of death after tuberculosis overall and leading cause of death in women in 2017.(5) There is a substantial unmet need for diabetes care in the South African population and levels of glycaemic control are suboptimal in studies in the community and primary care.(3) Assessing whether glucose levels, which are directly related to occurrence of disease complications are adequately controlled requires monitoring tests.

Local clinical guidelines recommend random blood glucose testing at every clinic visit. A random glucose above 10 mmol/l is considered uncontrolled glycaemia and indicates the need for a medication review and treatment change.(6) Random blood glucose levels can, however, fluctuate substantially depending on the length of time since the patient last ate and the type of food ingested, meaning they are difficult to interpret and have poor agreement with HbA_{1c}.(6-8) HbA_{1c} testing is recommended at 6-monthly intervals unless there has been a medication change, in which case HbA_{1c} should be re-tested after 3 months.(9, 10).

In primary care settings in South Africa, HbA_{1c} testing is performed in centralised laboratories and consequently, results are not available for immediate or same day review by health care workers. Review takes place at the next patient appointment, which may be up to 6 months later. This limits the use of HbA_{1c} for informing clinical decisions as results are outdated and patients are not able to link their lifestyle behaviours with their HbA_{1c} control.(11)

The emergence of point-of-care (POC) technologies has the potential to improve health care and patient-centred outcomes in diverse settings, including those with limited resources. POC testing may particularly lend itself to diabetes management in low-income settings because equipment maintenance requirements are low, and therefore there are no sample storage or transport requirements, but costs may be a barrier.(12) This is particularly pertinent, as while clinics in South Africa are often located within a small radius of the community they serve which makes patient access easy, clinic visits can be long, resulting in patient dissatisfaction and non-adherence.(13)

There are some reports that POC HbA_{1c} testing may improve HbA_{1c} in South African settings,(14, 15) but this is not supported by randomised trial evidence from other settings.(16) However, it may obviate the need for additional visits to specifically review glycaemic control and medication if this is thought to be indicated by the health provider.

POC HbA_{1c} testing is used as standard practice in tertiary care clinics in Cape Town, particularly in paediatric clinics. A recent South African study followed up 300 diabetes patients in primary care clinics who received POC HbA_{1c} testing for 18 months with the ultimate objective of improving glycaemic control and quality of care. They found that introducing POC HbA_{1c} testing resulted in lower HbA_{1c} and more patients receiving immediate feedback, but it did not change clinical practice.(14) The researchers concluded that there was currently insufficient evidence to support the implementation of POC HbA_{1c} testing in public sector primary care in South Africa. To benefit from the immediate result from a POC test, it is important that results are fed back to patients and clinical decisions take place during the POC appointment(17) to help the patient understand how their behaviour may affect their diabetes control.(11) The work presented here builds on this previous study to understand how a POC

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3 test could be effectively integrated in a primary care appointment and how it may influence patient
4 flow and clinical decision-making.
5

6 The aim of this study was to explore the feasibility and acceptability of implementing and using an
7 HbA_{1c} POC analyser in the routine care of patients with type 2 diabetes at a busy primary care
8 outpatient clinic in Cape Town.
9

10 **Materials and methods**

11 ***Setting***

12
13 This study took place in Gugulethu Community Health Centre, a busy primary care clinic serving a low
14 income community of about 98,000 people with an average headcount of 22,000 per month in the
15 Western Cape, South Africa.
16
17

18 ***Patient population***

19
20 Adults (≥18 years) diagnosed with type 2 diabetes and receiving routine clinic care who were willing
21 and able to provide written informed consent were eligible for the study. We included all possible
22 treatment and monitoring regimens.
23

24 We excluded people who were unable to speak one of the study languages (English, Afrikaans or
25 iXhosa), women who were pregnant or recently pregnant (within 3 months post-partum) by self-
26 report, people with known renal failure (creatinine > 125 µmol/l), those with significant iron deficiency
27 anaemia (Hb < 10g/dl) or known haemoglobinopathy (e.g. sickle cell disease). We also excluded people
28 who did not receive usual care from the clinic.
29
30

31 ***Recruitment and consent***

32
33 Participants were recruited between mid-November 2016 and mid-February 2017 (with a break during
34 the Christmas period). Patients attending their routine scheduled appointments for diabetes care
35 were identified in the waiting room by a trained research assistant and invited to participate in the
36 study. Written and verbal versions of the participant information sheet and informed consent were
37 presented to the participants detailing the exact nature of the study, what it would involve for the
38 participant and the implications and constraints of the protocol. Both documents were available in
39 English, Afrikaans and iXhosa. The participant was allowed as much time as they needed to consider
40 the information, and had the opportunity to question the study investigator, their doctor or nurse, or
41 other independent parties to decide whether they were happy to participate in the study. A copy of
42 the signed informed consent was given to the participant. The original signed form was retained at
43 the study site in the patient folder. Each participant was given a unique and anonymous patient
44 identifying number which was used on the data collection form.
45
46
47

48 ***Embedding the intervention into the clinic workflow***

49
50 We placed an Afinion™ HbA_{1c} assay point-of-care analyser (Abbott, Chicago IL) in the clinic room
51 where nurses admit and register patients for their diabetes clinic visit. Training and support was
52 provided by the manufacturer to nurses who would be responsible for diabetes clinic appointments
53 during the study.
54
55

56 To minimise the potential impact of the analyser on clinic workflow, we obtained finger prick blood
57 sample for the random blood glucose (usual care) and the POC (intervention) at the same time. The
58 POC analyser provided an on screen result within 3 minutes. Both results were recorded in the
59 patient's medical records folder and on the study data collection form.
60

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3 Patients returned to the waiting area where they waited to be seen by a family doctor or nurse
4 practitioner. During this appointment, the HbA_{1c} result, as well as other data collected and recorded
5 by the nurse, were reviewed. Clinicians were asked to base treatment decisions on the POC HbA_{1c}
6 result using local treatment protocols.(9) Any clinical decisions made during the appointment were
7 recorded on the data collection sheet. The clinician was also asked to indicate whether they had used
8 the random blood glucose or HbA_{1c} to base their clinical decision and record the length of time until
9 the patient's next appointment.
10
11

12 **Data collection and analysis**

13 **Quantitative data**

14
15
16 We collected basic demographic data as well as random blood glucose test result, POC HbA_{1c} test
17 result, any clinical decisions made (medication change, advice, combination of advice and treatment
18 change or nothing). We also recorded the time interval until the next appointment, any cartridge or
19 analyser failures, error messages, the temperature in the room where the POC analyser was kept and
20 the gender of people in the waiting area.
21
22

23 **Analysis**

24
25 Results on participants characteristics, current medication use, random blood glucose and HbA_{1c} test
26 results, and all other data collected in the study were tabulated for the full cohort of patients and
27 stratified by diabetes control, defined as controlled (HbA_{1c}≤8%), high HbA_{1c} (HbA_{1c}>8% and ≤10%) and
28 very high HbA_{1c} (HbA_{1c}>10%).
29

30
31 Quantitative data were analysed using Stata version 16SE (StataCorp, Tx). Descriptive results were
32 presented in a table as mean and standard deviation (SD) or percentages. Scatter plots were used to
33 compare random blood glucose with HbA_{1c} in each individual and highlight which participants received
34 a medication change. Numbers above and below the treatment threshold of 8%(64 mmol/mol)
35 correctly diagnosed with random blood glucose were plotted in a 2x2 table to demonstrate how
36 random blood glucose performs in comparison to HbA_{1c} to guide treatment.
37

38 **Qualitative data**

39
40 Data on the usual care process of the participants were collected during the study by observation and
41 by speaking to patients and clinicians to understand patient flow. These included appointment
42 sequence, the number of patients in the waiting area, the number of staff working in the clinic and
43 the number of clinicians usually seen by each patient during a routine visit.
44

45
46 At the end of the study, focus groups were held with doctors and enrolled nurses who were working
47 in the clinic at the time of the study to get their perspectives of having access to a point-of-care HbA_{1c}
48 analyser in the clinic and their confidence in making patient management decisions with the result.
49 Clinicians were provided with an information sheet and informed consent was taken. Structured
50 questions were posed to a group of five doctors who had seen patients who received a POC HbA_{1c} test
51 during the study, and with two nurses who registered patients, operated the POC analyser and
52 recorded the results in the diabetes clinics. Topic guides informed by previous work in this area were
53 used.(11) The doctors were asked open questions about their feelings of having the HbA_{1c} test result
54 in the appointment with the patient, and how this compared with having the random blood glucose
55 result alone in terms of communication with the patient and patient management decisions. Nurses
56 were asked about the patient flow in the clinic and what they felt about patient perception of receiving
57 the test. Interview recordings were transcribed and checked. Initial transcripts were coded in NVivo.
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59
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3 A thematic analysis approach was applied to the open-ended responses. Once coded, Microsoft Excel
4 was used to group responses. The codes were grouped into themes and themes were then compared
5 back to the data to ensure that it had been sufficiently captured. The results are presented to highlight
6 the main analytical findings, and quotations are provided to substantiate the findings for each
7 theme.(18, 19)
8
9

10 ***Ethics and permissions***

11 Ethical approvals were received by University of Oxford in September 2016 (OxTREC reference 42-16)
12 and University of Cape Town in October 2016 (UCT HREC reference 637/2016). All participants
13 provided written informed consent. All the requirements of the Helsinki Declaration of 2008 were
14 fulfilled.
15
16

17 ***Patient and public involvement***

18 No patient involved
19
20
21
22

23 **Results**

24 ***Workflow and processes***

25 In Gugulethu Community Health Centre routine diabetes care is provided through diabetes-specific
26 clinics (diabetes chronic care club) which are run two mornings a week. The morning is divided into
27 three clinic sessions and, on average, 90 patients with type 2 diabetes will be seen over a
28 morning.
29
30
31

32 The patient flow is as follows: on arrival at the health centre, patients are given their clinic folder in the
33 waiting area before measurement and recording of vital signs by a clinic nurse in a staging room. This
34 included measurement of weight, blood pressure, urine dipstick, and a random finger-prick blood
35 glucose measured. The results are written into the patient record in their clinic folder. Thereafter,
36 patients are seen either by Medical Officers and interns for clinical review. This includes a previous
37 HbA_{1c} if the results are in the file or was requested at the previous visit and subsequent medication
38 adjustment, and a new prescription is completed if deemed necessary. An HbA_{1c} test may be
39 requested by the Medical Officer, which requires them to have a venous blood sample drawn in
40 another part of the clinic. The results will be available at the patient's next scheduled appointment
41 (routinely once per month but may be up to 6 months' time).
42
43
44

45 Patients may spend as much as 3 hours in the clinic on one occasion depending on waiting times to
46 receive care or medications. All care, laboratory tests, and treatment are provided free-of-charge.
47

48 ***Quantitative results***

49 One hundred and eighty-five participants were recruited to the study over 13 days between 21st
50 November 2016 and 10th February 2017. There were 18 missing forms, so completed data collection
51 forms were received for 168 participants. Three participants did not receive their HbA_{1c} result due to
52 analytical errors, leaving 165 participants with both an HbA_{1c} and blood glucose test result. The flow
53 chart for participant recruitment is shown in Figure 1.
54
55

56 Mean \pm standard deviation (SD) age of recruited participants was 56.2 \pm 12.6 years with a range of 19
57 to 88 years. Sex was recorded for 43 participants, of whom 28 (65%) were female. The mean \pm SD
58 (range) random blood glucose was 11.31 \pm 5.12 mmol/l (3.3 to 31 mmol/l) and mean \pm SD (range) HbA_{1c}
59 was 9.5 \pm 2.56% (80 \pm 28 mmol/mol) (range 5.4% to 18.5%, 36 to 179mmol/mol). Poor glycaemic control
60

(defined as $>8\%$, 64mmol/mol HbA_{1c} (20)) was recorded in 109 (65%) of the recruited participants, and 65 (39%) had an HbA_{1c} above 10% (86mmol/mol). Current medication use was recorded for 111 (66%) of the participants, over half of whom (58%) were taking metformin alone. Characteristics of included participants are shown in Table 1 for the full cohort and stratified by whether participants had controlled HbA_{1c} ($\text{HbA}_{1c}\leq 8\%$, 64mmol/mol), high HbA_{1c} ($\text{HbA}_{1c} >8\%$, 64mmol/mol and $\leq 10\%$, 86mmol/mol) or very high HbA_{1c} ($\text{HbA}_{1c}>10\%$, 86mmol/mol).

The plot of random blood glucose versus HbA_{1c} for the 165 participants in Figure 2 demonstrates the numbers of participants who would have received correct and incorrect assessments or characterisation if only random blood glucose at a threshold of 10mmol/l were used to make treatment decisions. These numbers are presented in Table 2. Overall, 116 people (70%) were correctly diagnosed by the random blood glucose test and would have received appropriate treatment using the random blood glucose alone. Forty-nine (30%), however, were incorrectly identified as needing treatment, and if random blood glucose alone were used, 11 would have been over-treated, and a further 38 would have been undertreated. The random blood glucose test had a sensitivity of 66% and specificity of 79% compared with POC HbA_{1c} testing.

Mean \pm SD clinic temperature across each of the days of data collection was $25 \pm 1.6^\circ\text{C}$ (range 24°C to 32°C). Gender ratio of 80 people in the waiting area over two days was 74% women to 26% men.

Clinical decision-making

Of the 168 participants for whom results had been received, 13 participants (8%) received a medication change alone, 48 participants (29%) received adherence advice alone, 63 participants (37%) received both and 44 participants (26%) received no treatment or advice. Results stratified by diabetes control are presented in Table 1. Clinicians reported that 14% of clinical decisions were made on HbA_{1c} alone, 7% on random blood glucose and 77% on both HbA_{1c} and RBG.

Figure 3 shows clinical decision making by each participant's blood glucose and HbA_{1c} . It shows that 5 participants (3%) who had an HbA_{1c} below 8% (64mmol/mol) and blood glucose above 10mmol/l received a medication change, and 42 participants (25%) with HbA_{1c} above 8% (64mmol/mol) did not receive a medication change, but they may have received advice on medication adherence. There were 8 participants (5%) with HbA_{1c} above 8% (64mmol/mol) who neither received medication adherence advice nor treatment change.

Study limitations

Some participants were uncertain whether they had diabetes. Two participants who were recruited and reported that they did have diabetes were subsequently reported by doctors to not have diabetes, though one of these had a POC HbA_{1c} of 7.7% , which meets to WHO criteria for diabetes.(21)

Information on gender of participants was only captured for the final two weeks of data collection, but broadly reflected the sex ratio of those in the waiting area of the clinic.

There were three cartridge failures: two because HbA_{1c} was too high ($\text{HbA}_{1c}>18\%$, 173mmol/mol) and one because insufficient blood was applied to the cartridge.

Missing records from the 18 participants were sought in the clinic document area where patient folders are stored but could not be located. Discussion with clinic staff revealed that patient folders were frequently misplaced, meaning that sometimes patients have to be seen by clinic staff with a new, blank folder which did not contain their medical history.

Qualitative results

Five doctors participated in the focus group which centred around feelings about having the HbA_{1c} test result in the appointment and the effect this may have on management decisions and patient behaviour. Overall, the doctors found having the HbA_{1c} result in the appointment helpful. They reported that some patients will try to manipulate their blood glucose levels by fasting before their appointments to receive different care in the clinic.

"You don't know what the patient is going to do before they come here. Some people will eat before they come in, others won't eat and take their medication. So you don't know what you are going to get on the fingerprick glucose that they do on the day, so sometimes their fingerprick will be 6 but their HbA_{1c} will be 15 because they haven't eaten before they came in or whatever the case may be. Having had HbA_{1c} at the time has been helpful."

Usually, the doctors only have the HbA_{1c} from the previous appointment which may be 6 months out of date, it is therefore of very little use for making a clinical decision on the day, so the blood glucose levels are prioritised.

"I think it's a very luxury, it's nice to have the value when you are seeing the patient it's a relevant value now and it's not 6 months old so we do it anyway to get the labs, when we see the patients we tick the lab form to get the HbA_{1c}, but to have it on the day we see them is perfect."

Some scenarios where there were discordant results between random blood glucose and HbA_{1c} were discussed:

Interviewer: *"There was one person here with an HbA_{1c} of 12.5 and a random blood glucose of 3.4. So, would you have chosen to change their medication?"*

Doctor 1: *"Obviously not controlled"*

Doctor 2: *"I would have changed the medication; they are clearly not controlled. A lot of the patients, they know they are seeing the doctor, so well, in my experience, the night before they drink lots of water, a litre, or 2 litres of water, in the morning they wouldn't eat, just because they know they are seeing the doctor. As long as their test the next morning is under 5 then they know they are in the clear. And who knows what they do for the previous 6 months before they saw the doctor. So that value is actually is 12 and lets me know what happens for 3 months before."*

Interview with two nurses

Nurses found the analyser easy to use and enjoyed using it.

"I said I'm not interested because this machine is taking long, but the minute I started I am enjoying this much."

The nurses found that they could perform the test in their busy clinics despite only a short time with each patient. They explained that some patients had to wait for the test to finish running so they could record the result before the patient returned to the waiting room:

"It was a good experience, though it was very time consuming because the patient had to wait. We took all the vitals and we then we did the HbA_{1c} lastly, if the doctor came in and take the other patients so this one would have to wait until the machine is finished because it takes time."

They pointed out that it was important to have two of them in the clinic as they could work together to take measurements, do the tests and make sure the patient flow was not disrupted.

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2
3 *"Because, since its 2 of us, one will do the Hb what what and the other will be doing all the vitals. So*
4 *it's not really that difficult"*
5
6
7

8 **Discussion**

9
10 This study has found that use of POC HbA_{1c} testing could have potentially averted 30% of patients
11 receiving inappropriate medication or not receiving additional medication. It provides evidence of the
12 scale of incorrect identification of controlled or uncontrolled diabetes that would result from
13 measurement of random blood glucose alone in a real clinical setting. We have established that
14 random blood glucose has a sensitivity of 66% and specificity of 79% compared to POC HbA_{1c} using a
15 treatment cut-off at HbA_{1c} 8% (64mmol/mol) in this busy diabetes clinic.
16
17

18 The qualitative work found that nurses liked using the analyser and were able to effectively carry out
19 the POC HbA_{1c} testing during routine appointments without holding up clinics. Doctors reviewing the
20 results valued having access to the HbA_{1c} test result to help them make treatment decisions, but the
21 empirical data suggest that they were influenced by blood glucose results in their clinical decision-
22 making.
23

24 *Comparison with the literature*

25
26 Previous studies have explored how point-of-care HbA_{1c} testing can be integrated into primary care
27 consultations in low resource settings in South Africa.(14, 15, 22) One study demonstrated that POC
28 HbA_{1c} testing leads to more patients receiving immediate feedback and resulted in a small statistically
29 significant reduction in HbA_{1c} of 0.44% (4.8mmol/mol) after 12 months of POC testing, but the POC
30 testing group did not receive any additional treatment intensification.(14) Furthermore, this reduction
31 in HbA_{1c} may not be clinically significant. The researchers concluded that their work did not support
32 the implementation of POC HbA_{1c} testing in public sector primary care in South Africa. More recently,
33 a trial combining treatment intensification (frequent appointments, feedback of HbA_{1c} and education)
34 and POC testing found that treatment intensification had an impact on HbA_{1c} levels, but POC testing
35 on its own did not.(22) However, immediate feedback of HbA_{1c} was part of both the intervention and
36 control groups, and there is unlikely to be any added benefit from performing the test on a POC
37 device.(17) A third study which implemented POC testing near Johannesburg,(15) found that,
38 participants who received two HbA_{1c} tests, showed a significant improvement in HbA_{1c}. In that study,
39 HbA_{1c} fell from 9.7% ± 2.4 (83 mmol/mol) at their first POC test to 8.4% ± 2.4 (68 mmol/mol) at the
40 second test, but all participants received POC testing and there was a 38% dropout rate. A qualitative
41 study from 2017 reporting the perceptions of different stakeholders on the implementation of POC
42 testing in rural primary care settings in South Africa, found that there was a need for scale-up of POC
43 testing in rural clinics, but there were some concerns about the reliability of the technologies.(12)
44
45

46 Glycaemic control in our cohort was overall poor, with 65% of people presenting with HbA_{1c}>8%. Poor
47 diabetes control has been reported in other African countries: in Ethiopia 78% of people tested in an
48 outpatients clinic had HbA_{1c}>10%.(23) A chart review in a South African clinic found that 87% of
49 patients had HbA_{1c} above 7%.(24) Other studies have explored how health service organisational
50 factors contribute to patient's dissatisfaction leading to irregular clinic attendance and lying about
51 medication adherence.(13)
52
53

54 Documentation of the analyser recommend a maximum operating temperature of 25°C, yet
55 temperatures in the nurses' treatment room reached 32°C during this study. We do not know whether
56 this may have affected the performance of the analyser but this is something which would need to be
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2
3 considered before roll-out of these technologies, as many clinics do not have temperature control and
4 may reach high temperatures in summer months.(25)
5

6 Our qualitative work demonstrated that clinicians could integrate these tests into their clinical practice
7 to deliver testing and act on results. Other researchers have reported that POC testing can improve
8 disease management and access to healthcare in resource-limited settings.(12)
9

10 Our study found that in many patients, there was little correlation between random blood glucose
11 and HbA_{1c} which is consistent with previous work in South Africa. (6-8) Data from our cohort gave a
12 sensitivity of 66% and specificity of 79% of using random blood glucose compared to HbA_{1c} at an HbA_{1c}
13 treatment cut-off of 8% (64mmol/mol). Another study reported a higher sensitivity of 77% and a lower
14 specificity of 75%(6), but they used HbA_{1c} of 7% (58mmol/mol) as a cut-off for good control.
15

16
17 Costs of these technologies may still be prohibitively high,(14, 26) but as technologies develop and
18 costs come down, there is scope for widespread rollout in rural and low resource settings.
19 Haemoglobinopathies, which are common in some parts of the world, are frequently linked to altered
20 HbA_{1c}. The Afinion analyser used in this study has been shown to perform well in bloods with
21 haemoglobinopathies and does not show any clinically significant biases.(27)
22

23 24 *Strengths and limitations*

25
26 Our study has demonstrated that POC HbA_{1c} testing can be integrated into patient appointments and
27 used for clinical decision-making during the same consultation in a South African primary care setting.
28 Furthermore, it has quantified the degree of incorrect treatment decisions arising from monitoring
29 random blood glucose in a real-world clinical setting.
30

31 Our study did not include any follow-up, so it was not possible to establish whether POC testing had
32 an impact on glycaemic control or whether it changed longer-term health outcomes. It has, however,
33 demonstrated that the POC test can be delivered within the timeframe of existing appointments and
34 clinicians reported that they were comfortable making clinical decisions on the POC test result. It
35 presents a realistic care pathway which can be used in future research or roll-out of POC testing on a
36 wider basis.
37

38
39 Paper-based records meant it was difficult to retrieve missing data and resulted in incomplete data
40 collection. Paper-based patient records are a real limitation of healthcare in this resource-limited
41 setting and the impact missing patient folders has on care has been reported in other studies.(13)
42

43 In the qualitative data collection, we were limited to the clinicians who were working at the clinic
44 whilst the study was ongoing. That means that we only collected views from two nurses and five
45 doctors, whose views may not be representative of all clinical staff.
46

47 48 *Clinical implications and future research*

49 In our study, clinicians clearly recognised the limitations of using blood glucose for making their clinical
50 decisions as they could not be sure whether the patient had eaten before attending the clinic.
51 Although clinicians understood the value of having an HbA_{1c} test result, some clinicians were still
52 heavily influenced by random blood glucose when making clinical decisions evidenced by the
53 quantitative findings. This study has found that there was discordance between what clinicians said in
54 qualitative interviews and how they acted to make treatment decisions. The reasons for this remain
55 unclear, but this may be because HbA_{1c} results which clinicians usually have access to are from the
56 patient's previous appointment which may have been several months ago. This means they may be
57 reluctant to place too much importance on this in their clinical decision making compared with the
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3 blood glucose level from that day in their usual care practices. A future POC HbA_{1c} intervention should
4 provide comprehensive guidance and training to clinicians on decision-making on the test result and
5 consider not giving clinicians access to random blood glucose results.
6

7 *Conclusion*

8
9 This work demonstrates the importance of having an HbA_{1c} test result for clinical assessments in
10 primary care diabetes appointments. It confirms previous reports that a single random blood glucose
11 result should not be relied upon to make valid decisions about diabetes control and suggests that the
12 use of POC HbA_{1c} testing should be considered for diabetes monitoring and management.(6)
13
14
15

16 **Acknowledgements**

17
18 Thank you to Sindiswa Mmango for recruiting all 185 patients to the study and taking informed
19 consent. The clinical staff at Gugulethu Community Health Centre and for conducting the point-of-
20 care tests and completing data collection sheets. Eleanor Hirst for her assistance with data collection.
21 Felicity Nelson from Alere, South Africa for facilitating the loan of the Afinion analyser. The CDIA group
22 at Groote Schuur Hospital for support and advice during the set-up and data collection phases of this
23 study.
24
25

26 **Contribution statement**

27
28 JH designed the work, acquired the funding, collected and analysed the data and wrote the first draft
29 of the manuscript. KB contributed to the design of the study, contributed to the interpretation, revised
30 the manuscript and approved the final version. AF contributed to the design of the study, contributed
31 to the interpretation, revised the manuscript and approved the final version. JM contributed to the
32 data collection, contributed to the interpretation, revised the manuscript and approved the final
33 version. NL contributed to the design of the study, contributed to the interpretation, revised the
34 manuscript and approved the final version.
35
36

37 **Competing interests**

38
39 None declared
40

41 **Funding**

42
43 This work was funded by a Newton Partnership grant awarded to Jennifer Hirst in 2016. JH is funded
44 by the funded by the NIHR Biomedical Research Centre, Oxford. AF is and NIHR Senior Investigator
45 and receives support from the NIHR Oxford Biomedical Research Centre
46
47

48 **Data sharing statement**

49 Data can be requested by emailing the corresponding author.
50
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Tables and Figures

Table 1 – Patient characteristics and management decisions stratified by HbA1c (excluding 18 participants with missing data)

	All patients (N=168)	Controlled HbA1c (≤8%, 64 mmol/mol) (N=56)	Poor control (HbA1c >8% 64 mmol/mol and ≤10%, 86 mmol/mol) (N=44)	Very poor control (HbA1c >10%, 86 mmol/mol) (N=65)
Age (mean±SD)	56.3±12.6	60.6±13.6	55.51±10.5	53.3±12.1
Sex (N, % female) (N=43)	28 (65%)	10 (62%)	9 (64%)	9 (69%)
HbA1c (%) (mean±SD)	9.5±2.6	6.8±0.7	9.1±0.6	12.1±1.6
Random blood glucose (mmol/l) (mean±SD)	11.3±5.1	8.0±2.4	11.2±4.5	14.4±5.5
Treatment recorded	111 (66%)	33 (59%)	30 (68%)	48 (74%)
Diet only	2 (2%)	2 (6%)	0	0
Metformin	64 (58%)	21 (64%)	17 (57%)	26 (54%)
Oral (not specified)	12 (11%)	5 (15%)	4 (13%)	3 (6%)
Glimipiride and metformin	5 (5%)	2 (6%)	0	3 (6%)
Insulin	6 (5%)	0	3 (10%)	3 (6%)
Metformin and insulin	22 (20%)	3 (9%)	6 (20%)	13 (27%)
Medication not recorded	70 (42%)	23 (41%)	14 (32%)	17 (26%)
Clinical decisions				
Medication change	13 (8%)	0	3 (7%)	10 (15%)
Counselling on adherence	48 (29%)	15 (27%)	20 (45%)	11 (17%)
Combination	63 (38%)	6 (11%)	15 (34%)	42 (65%)
None	44 (26%)	35 (63%)	6 (14%)	2 (3%)
Decision based on				
HbA1c result	23 (14%)	6 (11%)	8 (18%)	9 (14%)
RBG result	12 (7%)	3 (5%)	2 (5%)	4 (6%)
Both	130 (77%)	46 (82%)	34 (77%)	50 (77%)

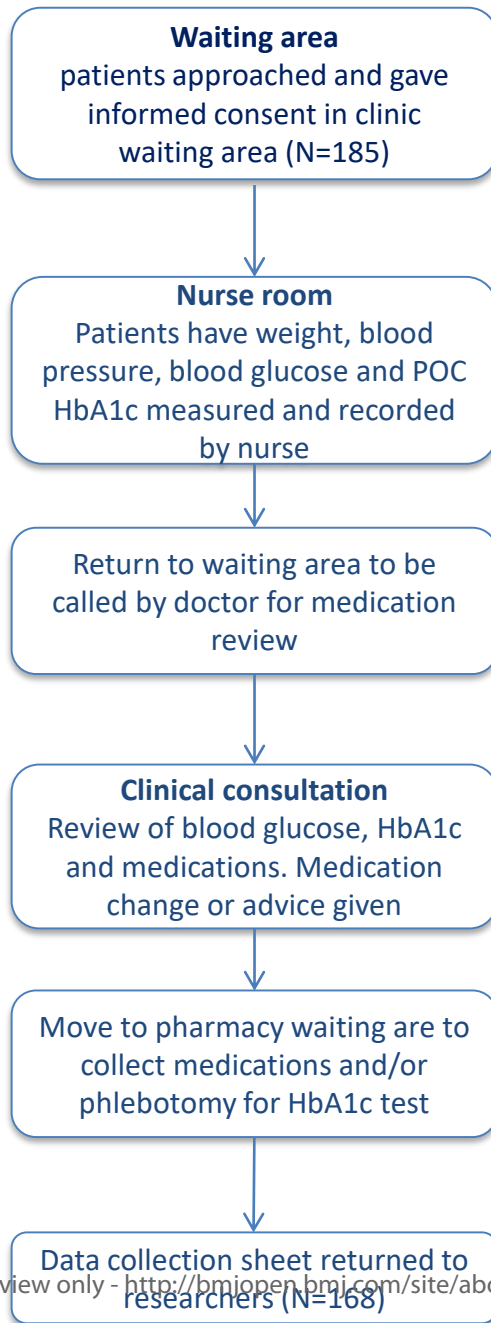
Table 2 – Correct diagnoses between random blood glucose and HbA1c (n=165)

Blood glucose	HbA1c		Total
	≥8% (64 mmol/mol)	<8% (64mmol/mol)	
≥10 mmol/l	75	11	86
<10 mmol/l	38	41	79
Total	113	52	165
	Sensitivity = 0.66		Specificity = 0.79

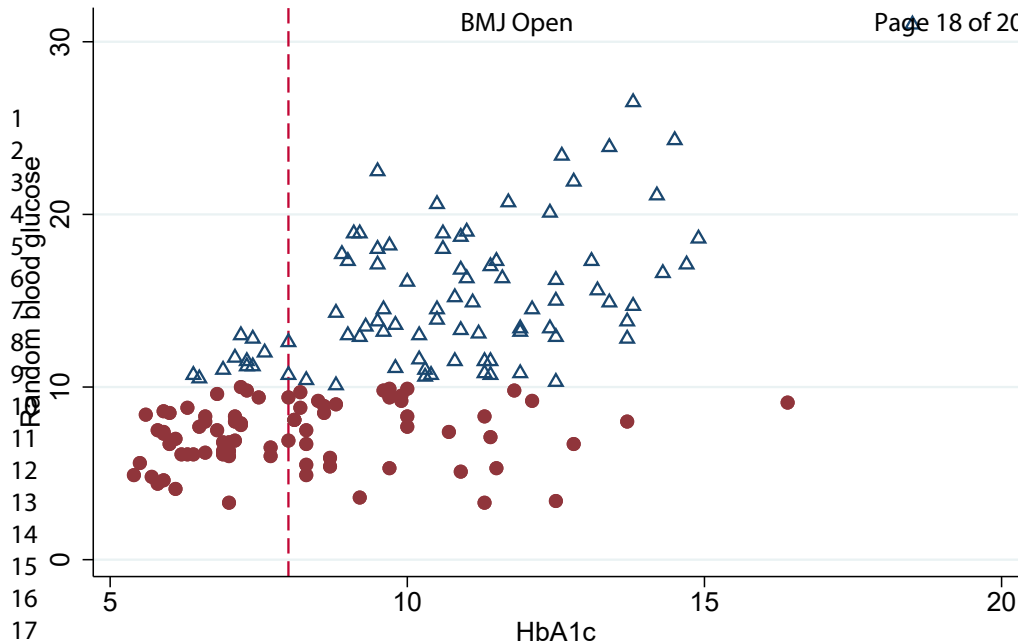
Figure 1 – Patient flow chart

Figure 2 - random blood glucose versus HbA_{1c}, stratified by random blood glucose levels using 10 mmol/l as the treatment decision threshold). Dotted line represents the threshold between controlled and uncontrolled HbA_{1c} (8%, 64 mmol/mol)

Figure 3 - random blood glucose versus HbA_{1c} stratified by clinical decisions or medication change (triangle= no medication change or advice, hollow circle= medication change, solid circle= no medication change)

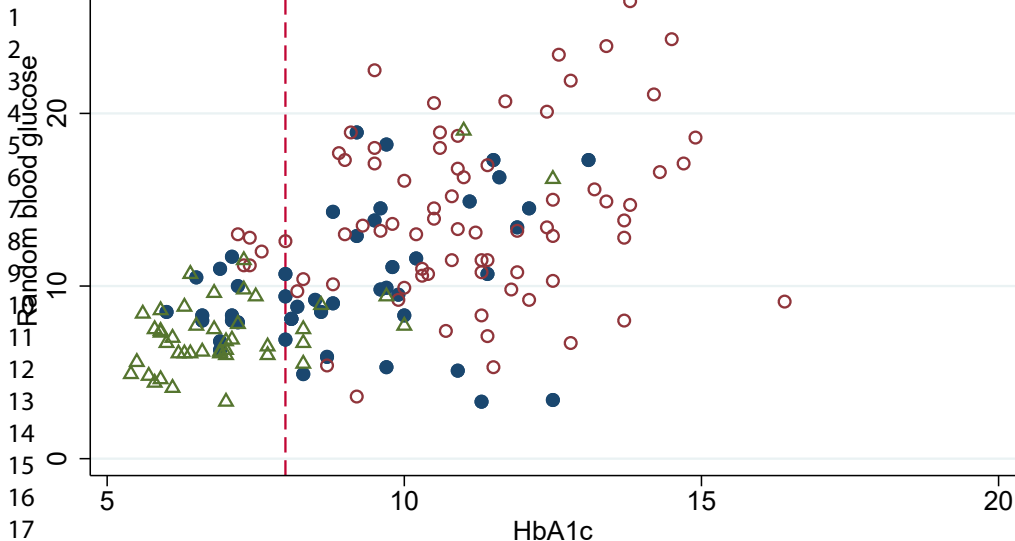


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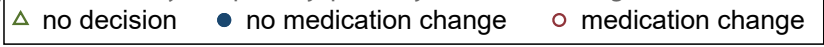


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△ High blood glucose ● Low blood glucose



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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract – page 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found – page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported – page 3
Objectives	3	State specific objectives, including any prespecified hypotheses – page 4
Methods		
Study design	4	Present key elements of study design early in the paper – page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection – page 4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up – page 4-5 (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – page 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group – page 5
Bias	9	Describe any efforts to address potential sources of bias – page 5-6
Study size	10	Explain how the study size was arrived at – page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why – page 5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding – page 5-7 (b) Describe any methods used to examine subgroups and interactions – page 5-7 (c) Explain how missing data were addressed – page 5-7 (d) If applicable, explain how loss to follow-up was addressed – page 5-7 (e) Describe any sensitivity analyses – page 5-7
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed – page 6-7 & Fig 1 (b) Give reasons for non-participation at each stage - na (c) Consider use of a flow diagram – Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders – page 6 (b) Indicate number of participants with missing data for each variable of interest – page 7 (c) Summarise follow-up time (eg, average and total amount) – page 6
Outcome data	15*	Report numbers of outcome events or summary measures over time – page 6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included – page 6-7
		(b) Report category boundaries when continuous variables were categorized n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period – n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses – page 6-7, table 1
Discussion		
Key results	18	Summarise key results with reference to study objectives – page 9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias – page 10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence – page 10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results – page 10-11
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based – page 11

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

Point-of-care HbA1c testing in an urban primary care diabetes clinic in South Africa – a mixed methods feasibility study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-045511.R1
Article Type:	Original research
Date Submitted by the Author:	02-Feb-2021
Complete List of Authors:	Hirst, Jennifer; University of Oxford, Nuffield Department of Primary Care Health Sciences; University of Oxford Bobrow, Kirsten; University of Cape Town Farmer, Andrew; University of Oxford, Nuffield Department of Primary Care Health Sciences Morgan, Jennie; University of Cape Town Levitt, Naomi; University of Cape Town
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Diabetes and endocrinology
Keywords:	DIABETES & ENDOCRINOLOGY, PRIMARY CARE, PUBLIC HEALTH

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Point-of-care HbA_{1c} testing in an urban primary care diabetes clinic in South Africa – a mixed methods feasibility study

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Word count: 4530

Abstract

Introduction

Monitoring and treatment of type 2 diabetes in South Africa usually takes place in primary care using random blood glucose testing to guide treatment decisions. This study explored the feasibility of using point-of-care HbA_{1c} testing in addition to glucose testing in a busy primary care clinic in Cape Town, South Africa.

Subjects: 185 adults aged 19 to 88 years with type 2 diabetes.

Materials and methods

Participants recruited to this mixed methods cohort study received a point-of-care HbA_{1c} test. Doctors were asked to use the point-of-care HbA_{1c} result for clinical decision-making. Qualitative interviews were held with clinical staff.

Results

Point-of-care HbA_{1c} test results were obtained for 165 participants of whom 109 (65%) had poor glycaemic control (>8% HbA_{1c}, 64 mmol/mol). Medical Officers reported using a combination of HbA_{1c} and blood glucose 77% of the time for clinical decision-making. Nurses found the analyser easy to use and doctors valued having the HbA_{1c} result to help with decision-making.

Discussion

Our results suggest that 30% of patients may have received inappropriate medication or not received necessary additional medication if random blood glucose alone had been used in routine appointments. Clinicians valued having access to the HbA_{1c} test result to help them make treatment decisions.

Word count:202

Strengths and limitations

Strengths and limitations

- This work demonstrated that POC HbA_{1c} testing can be integrated into patient appointments and used for clinical decision-making.
- It presents a realistic care pathway which can be used in future research or roll-out of POC testing on a wider basis.
- This study did not include any follow-up, so we could not establish whether POC testing had an impact on glycaemic control or long-term health outcomes.
- Paper-based records meant it was difficult to retrieve missing and incomplete data.
- For qualitative data collection, we interviewed clinicians working at the clinic at the time of the study and views may not represent all clinical staff.

Introduction

Diabetes is highly prevalent in South Africa, and is increasing over time.(1-3) An estimated 2.6 million people are living with the condition and there are estimated to be a further 1.2 million who have undiagnosed diabetes.(3) Diabetes is the second most common non-communicable disease in people attending primary care,(4) accounts for 5.7% of all deaths in South Africa, and was the second most common cause of death after tuberculosis overall and leading cause of death in women in 2017.(5) There is a substantial unmet need for diabetes care in the South African population and levels of glycaemic control are suboptimal in studies in the community and primary care.(3) Assessing whether glucose levels, which are directly related to occurrence of disease complications are adequately controlled requires monitoring tests.

Glycated haemoglobin or haemoglobin A1c (HbA_{1c}) reflects average plasma glucose over the previous eight to 12 weeks(6, 7) and is the preferred test for monitoring glycaemic control and making treatment decisions in people with diabetes.(8) Monitoring of HbA_{1c} in most settings usually requires the patient to have a venous blood sample taken, which is then sent for analysis in a central laboratory. The test result is reported back to the clinician within a few days and the patient will receive the result at a follow-on visit when any necessary adjustments to medication are made.

Local clinical guidelines in South Africa recommend random blood glucose testing at every clinic visit for monitoring diabetes control. A random glucose above 10 mmol/l is considered uncontrolled glycaemia and indicates the need for a medication review and treatment change.(9) Random blood glucose levels can, however, fluctuate substantially depending on the length of time since the patient last ate and the type of food ingested, meaning they are difficult to interpret and have poor agreement with HbA_{1c}.(9-11) HbA_{1c} testing is recommended at 6-monthly intervals unless there has been a medication change, in which case HbA_{1c} should be re-tested after 3 months.(12, 13)

In primary care settings in South Africa, HbA_{1c} testing is performed in centralised laboratories and consequently, results are not available for immediate or same day review by health care workers. Review takes place at the next patient appointment, which may be up to 6 months later. This limits the use of HbA_{1c} for informing clinical decisions as results are outdated and patients are not able to link their lifestyle behaviours with their HbA_{1c} control.(14)

The emergence of point-of-care (POC) technologies has the potential to improve health care and patient-centred outcomes in diverse settings, including those with limited resources. POC testing may particularly lend itself to diabetes management in low-income settings because equipment maintenance requirements are low, and therefore there are no sample storage or transport requirements, but costs may be a barrier.(15) This is particularly pertinent, as while clinics in South Africa are often located within a small radius of the community they serve which makes patient access easy, clinic visits can be long, resulting in patient dissatisfaction and non-adherence.(16)

There are some reports that POC HbA_{1c} testing may improve HbA_{1c} in South African settings,(17, 18) but this is not supported by randomised trial evidence from other settings.(19) However, it may obviate the need for additional visits to specifically review glycaemic control and medication if this is thought to be indicated by the health provider.

POC HbA_{1c} testing is used as standard practice in tertiary care clinics in Cape Town, particularly in paediatric clinics. A recent South African study followed up 300 diabetes patients in primary care clinics who received POC HbA_{1c} testing for 18 months with the ultimate objective of improving glycaemic control and quality of care. They found that introducing POC HbA_{1c} testing resulted in lower HbA_{1c} and more patients receiving immediate feedback, but it did not change clinical practice.(17) The

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2
3 researchers concluded that there was currently insufficient evidence to support the implementation
4 of POC HbA_{1c} testing in public sector primary care in South Africa. To benefit from the immediate result
5 from a POC test, it is important that results are fed back to patients and clinical decisions take place
6 during the POC appointment(20) to help the patient understand how their behaviour may affect their
7 diabetes control.(14) The work presented here builds on this previous study to understand how a POC
8 test could be effectively integrated in a primary care appointment and how it may influence patient
9 flow and clinical decision-making.
10
11

12 The aim of this study was to explore the feasibility and acceptability of implementing and using an
13 HbA_{1c} POC analyser in the routine care of patients with type 2 diabetes at a busy primary care
14 outpatient clinic in Cape Town.
15

16 **Materials and methods**

17 ***Setting***

18
19 This study took place in Gugulethu Community Health Centre, a busy primary care clinic serving a low
20 income community of about 98,000 people with an average headcount of 22,000 per month in the
21 Western Cape, South Africa.
22
23

24 ***Patient population***

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26 Adults (≥18 years) diagnosed with type 2 diabetes and receiving routine clinic care who were willing
27 and able to provide written informed consent were eligible for the study. We included all possible
28 treatment and monitoring regimens. Diabetes diagnosis was based on a measurement of HbA_{1c} with
29 a threshold of ≥6.5%.
30
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32 We excluded people who were unable to speak one of the study languages (English, Afrikaans or
33 iXhosa), women who were pregnant or recently pregnant (within 3 months post-partum) by self-
34 report, people with known renal failure (creatinine > 125 µmol/l), those with significant iron deficiency
35 anaemia (Hb < 10g/dl) or known haemoglobinopathy (e.g. sickle cell disease). We also excluded people
36 who did not receive usual care from the clinic.
37
38

39 ***Recruitment and consent***

40
41 Participants were recruited between mid-November 2016 and mid-February 2017 (with a break during
42 the Christmas period). Patients attending their routine scheduled appointments for diabetes care
43 were identified in the waiting room by a trained research assistant and invited to participate in the
44 study. Written and verbal versions of the participant information sheet and informed consent were
45 presented to the participants detailing the exact nature of the study, what it would involve for the
46 participant and the implications and constraints of the protocol. Both documents were available in
47 English, Afrikaans and iXhosa. The participant was allowed as much time as they needed to consider
48 the information, and had the opportunity to question the study investigator, their doctor or nurse, or
49 other independent parties to decide whether they were happy to participate in the study. A copy of
50 the signed informed consent was given to the participant. The original signed form was retained at
51 the study site in the patient folder. Each participant was given a unique and anonymous patient
52 identifying number which was used on the data collection form.
53
54

55 ***Embedding the intervention into the clinic workflow***

56
57 We placed an Afinion™ HbA_{1c} assay point-of-care analyser (Abbott, Chicago IL) in the clinic room
58 where nurses admit and register patients for their diabetes clinic visit. Training and support was
59
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1
2
3 provided by the manufacturer to nurses who would be responsible for diabetes clinic appointments
4 during the study.
5

6 To minimise the potential impact of the analyser on clinic workflow, we obtained finger prick blood
7 sample for the random blood glucose (usual care) and the POC (intervention) at the same time. The
8 POC analyser provided an on screen result within 3 minutes. Both results were recorded in the
9 patient's medical records folder and on the study data collection form.
10

11 Patients returned to the waiting area where they waited to be seen by a family doctor or nurse
12 practitioner. During this appointment, the HbA_{1c} result, as well as other data collected and recorded
13 by the nurse, were reviewed. Clinicians were asked to base treatment decisions on the POC HbA_{1c}
14 result using local treatment protocols.(13) Any clinical decisions made during the appointment were
15 recorded on the data collection sheet. The clinician was also asked to indicate whether they had used
16 the random blood glucose or HbA_{1c} to base their clinical decision and record the length of time until
17 the patient's next appointment.
18
19

20 **Data collection and analysis**

21 **Quantitative data**

22 We collected basic demographic data as well as random blood glucose test result, POC HbA_{1c} test
23 result, any clinical decisions made (medication change, advice, combination of advice and treatment
24 change or nothing). We also recorded the time interval until the next appointment, any cartridge or
25 analyser failures, error messages, the temperature in the room where the POC analyser was kept and
26 the gender of people in the waiting area.
27
28
29

30 **Analysis**

31 Results on participants characteristics, current medication use, random blood glucose and HbA_{1c} test
32 results, and all other data collected in the study were tabulated for the full cohort of patients and
33 stratified by diabetes control, defined as controlled (HbA_{1c}≤8%), high HbA_{1c} (HbA_{1c}>8% and ≤10%) and
34 very high HbA_{1c} (HbA_{1c}>10%). A threshold of 8% was selected to define uncontrolled diabetes because
35 it is in line with targets in local guidelines for treatment.(13)
36
37
38

39 Quantitative data were analysed using Stata version 16SE (StataCorp, Tx). Descriptive results were
40 presented in a table as mean and standard deviation (SD) or percentages. Scatter plots were used to
41 compare random blood glucose with HbA_{1c} in each individual and highlight which participants received
42 a medication change. Numbers above and below the treatment threshold of 8%(64 mmol/mol)
43 correctly diagnosed with random blood glucose were plotted in a 2x2 table to demonstrate how
44 random blood glucose performs in comparison to HbA_{1c} to guide treatment.
45
46
47

48 **Qualitative data**

49 Data on the usual care process of the participants were collected during the study by observation and
50 by speaking to patients and clinicians to understand patient flow. These included appointment
51 sequence, the number of patients in the waiting area, the number of staff working in the clinic and
52 the number of clinicians usually seen by each patient during a routine visit.
53
54

55 At the end of the study, focus groups were held with doctors and enrolled nurses who were working
56 in the clinic at the time of the study to get their perspectives of having access to a point-of-care HbA_{1c}
57 analyser in the clinic and their confidence in making patient management decisions with the result.
58 Clinicians were provided with an information sheet and informed consent was taken. Structured
59 questions were posed to a group of five doctors who had seen patients who received a POC HbA_{1c} test
60

1
2
3 during the study, and with two nurses who registered patients, operated the POC analyser and
4 recorded the results in the diabetes clinics. Topic guides informed by previous work in this area were
5 used.(14) The doctors were asked open questions about their feelings of having the HbA_{1c} test result
6 in the appointment with the patient, and how this compared with having the random blood glucose
7 result alone in terms of communication with the patient and patient management decisions. Nurses
8 were asked about the patient flow in the clinic and what they felt about patient perception of receiving
9 the test. Interview recordings were transcribed and checked. Initial transcripts were coded in NVivo.
10
11

12 A thematic analysis approach was applied to the open-ended responses. Once coded, Microsoft Excel
13 was used to group responses. The codes were grouped into themes and themes were then compared
14 back to the data to ensure that it had been sufficiently captured. The results are presented to highlight
15 the main analytical findings, and quotations are provided to substantiate the findings for each
16 theme.(21, 22)
17
18

19 ***Ethics and permissions***

20
21 Ethical approvals were received by University of Oxford in September 2016 (OxTREC reference 42-16)
22 and University of Cape Town in October 2016 (UCT HREC reference 637/2016). All participants
23 provided written informed consent. All the requirements of the Helsinki Declaration of 2008 were
24 fulfilled.
25

26 ***Patient and public involvement***

27
28 No patient involved
29
30
31

32 **Results**

33 ***Workflow and processes***

34
35 In Gugulethu Community Health Centre routine diabetes care is provided through diabetes-specific
36 clinics (diabetes chronic care club) which are run two mornings a week. The morning is divided into
37 three clinic sessions and, on average, 90 patients with type 2 diabetes will be seen over a
38 morning.
39
40

41 The patient flow is as follows: on arrival at the health centre, patients are given their clinic folder in the
42 waiting area before measurement and recording of vital signs by a clinic nurse in a staging room. This
43 included measurement of weight, blood pressure, urine dipstick, and a random finger-prick blood
44 glucose measured. The results are written into the patient record in their clinic folder. Thereafter,
45 patients are seen either by Medical Officers and interns for clinical review. This includes a previous
46 HbA_{1c} if the results are in the file or was requested at the previous visit and subsequent medication
47 adjustment, and a new prescription is completed if deemed necessary. An HbA_{1c} test may be
48 requested by the Medical Officer, which requires them to have a venous blood sample drawn in
49 another part of the clinic. The results will be available at the patient's next scheduled appointment
50 (routinely once per month but may be up to 6 months' time).
51
52
53

54 Patients may spend as much as 3 hours in the clinic on one occasion depending on waiting times to
55 receive care or medications. All care, laboratory tests, and treatment are provided free-of-charge.
56

57 ***Quantitative results***

58
59 One hundred and eighty-five participants were recruited to the study over 13 days between 21st
60 November 2016 and 10th February 2017. There were 18 missing forms, so completed data collection

forms were received for 168 participants. Three participants did not receive their HbA_{1c} result due to analytical errors, leaving 165 participants with both an HbA_{1c} and blood glucose test result. The flow chart for participant recruitment is shown in Figure 1.

Mean \pm standard deviation (SD) age of recruited participants was 56.2 \pm 12.6 years with a range of 19 to 88 years. Sex was recorded for 43 participants, of whom 28 (65%) were female. The mean \pm SD (range) random blood glucose was 11.31 \pm 5.12 mmol/l (3.3 to 31 mmol/l) and mean \pm SD (range) HbA_{1c} was 9.5 \pm 2.56% (80 \pm 28 mmol/mol) (range 5.4% to 18.5%, 36 to 179mmol/mol). Poor glycaemic control (defined as >8%, 64mmol/mol HbA_{1c}(23)) was recorded in 109 (65%) of the recruited participants, and 65 (39%) had an HbA_{1c} above 10% (86mmol/mol). Current medication use was recorded for 111 (66%) of the participants, over half of whom (58%) were taking metformin alone. Characteristics of included participants are shown in Table 1 for the full cohort and stratified by whether participants had controlled HbA_{1c} (HbA_{1c} \leq 8%, 64mmol/mol), high HbA_{1c} (HbA_{1c} >8%, 64mmol/mol and \leq 10%, 86mmol/mol) or very high HbA_{1c} (HbA_{1c}>10%, 86mmol/mol).

The plot of random blood glucose versus HbA_{1c} for the 165 participants in Figure 2 demonstrates the numbers of participants who would have received correct and incorrect assessments or characterisation if only random blood glucose at a threshold of 10 mmol/l were used to make treatment decisions. These numbers are presented in Table 2. Overall, 116 people (70%) were correctly diagnosed by the random blood glucose test and would have received appropriate treatment using the random blood glucose alone. Forty-nine (30%), however, were incorrectly identified as needing treatment, and if random blood glucose alone were used, 11 would have been over-treated, and a further 38 would have been undertreated. The random blood glucose test had a sensitivity of 66% and specificity of 79% compared with POC HbA_{1c} testing.

Mean \pm SD clinic temperature across each of the days of data collection was 25 \pm 1.6°C (range 24°C to 32°C). Gender ratio of 80 people in the waiting area over two days was 74% women to 26% men.

Clinical decision-making

Of the 168 participants for whom results had been received, 13 participants (8%) received a medication change alone, 48 participants (29%) received adherence advice alone, 63 participants (37%) received both and 44 participants (26%) received no treatment or advice. Results stratified by diabetes control are presented in Table 1. Clinicians reported that 14% of clinical decisions were made on HbA_{1c} alone, 7% on random blood glucose and 77% on both HbA_{1c} and RBG.

Figure 3 shows clinical decision making by each participant's blood glucose and HbA_{1c}. It shows that 5 participants (3%) who had an HbA_{1c} below 8% (64mmol/mol) and blood glucose above 10mmol/l received a medication change, and 42 participants (25%) with HbA_{1c} above 8% (64mmol/mol) did not receive a medication change, but they may have received advice on medication adherence. There were 8 participants (5%) with HbA_{1c} above 8% (64mmol/mol) who neither received medication adherence advice nor treatment change.

Study limitations

Some participants were uncertain whether they had diabetes. Two participants who were recruited and reported that they did have diabetes were subsequently reported by doctors to not have diabetes, though one of these had a POC HbA_{1c} of 7.7%, which meets to WHO criteria for diabetes.(8)

Information on gender of participants was only captured for the final two weeks of data collection, but broadly reflected the sex ratio of those in the waiting area of the clinic.

1
2
3 There were three cartridge failures: two because HbA_{1c} was too high (HbA_{1c}>18%, 173mmol/mol) and
4 one because insufficient blood was applied to the cartridge.
5

6 Missing records from the 18 participants were sought in the clinic document area where patient
7 folders are stored but could not be located. Discussion with clinic staff revealed that patient folders
8 were frequently misplaced, meaning that sometimes patients have to be seen by clinic staff with a
9 new, blank folder which did not contain their medical history.
10
11
12

13 **Qualitative results**

14
15 Five doctors participated in the focus group which centred around feelings about having the HbA_{1c}
16 test result in the appointment and the effect this may have on management decisions and patient
17 behaviour. Overall, the doctors found having the HbA_{1c} result in the appointment helpful. They
18 reported that some patients will try to manipulate their blood glucose levels by fasting before their
19 appointments to receive different care in the clinic.
20
21

22 *“You don’t know what the patient is going to do before they come here. Some people will eat before*
23 *they come in, others won’t eat and take their medication. So you don’t know what you are going to*
24 *get on the fingerprick glucose that they do on the day, so sometimes their fingerprick will be 6 but their*
25 *HbA_{1c} will be 15 because they haven’t eaten before they came in or whatever the case may be. Having*
26 *had HbA_{1c} at the time has been helpful.”*
27
28

29 Usually, the doctors only have the HbA_{1c} from the previous appointment which may be 6 months out
30 of date, it is therefore of very little use for making a clinical decision on the day, so the blood glucose
31 levels are prioritised.
32

33 *“I think it’s a very luxury, it’s nice to have the value when you are seeing the patient it’s a relevant*
34 *value now and it’s not 6 months old so we do it anyway to get the labs, when we see the patients we*
35 *tick the lab form to get the HbA_{1c}, but to have it on the day we see them is perfect.”*
36
37

38 Some scenarios where there were discordant results between random blood glucose and HbA_{1c} were
39 discussed:
40

41 Interviewer: *“There was one person here with an HbA_{1c} of 12.5 and a random blood glucose of 3.4. So,*
42 *would you have chosen to change their medication?”*
43

44 Doctor 1: *“Obviously not controlled”*
45

46 Doctor 2: *“I would have changed the medication; they are clearly not controlled. A lot of the patients,*
47 *they know they are seeing the doctor, so well, in my experience, the night before they drink lots of*
48 *water, a litre, or 2 litres of water, in the morning they wouldn’t eat, just because they know they are*
49 *seeing the doctor. As long as their test the next morning is under 5 then they know they are in the clear.*
50 *And who knows what they do for the previous 6 months before they saw the doctor. So that value is*
51 *actually is 12 and lets me know what happens for 3 months before.”*
52
53

54 *Interview with two nurses*

55 Nurses found the analyser easy to use and enjoyed using it.
56

57 *“I said I’m not interested because this machine is taking long, but the minute I started I am enjoying*
58 *this much.”*
59
60

1
2
3 The nurses found that they could perform the test in their busy clinics despite only a short time with
4 each patient. They explained that some patients had to wait for the test to finish running so they could
5 record the result before the patient returned to the waiting room:
6

7 *"It was a good experience, though it was very time consuming because the patient had to wait. We*
8 *took all the vitals and we then we did the HbA_{1c} lastly, if the doctor came in and take the other patients*
9 *so this one would have to wait until the machine is finished because it takes time."*
10

11 They pointed out that it was important to have two of them in the clinic as they could work together
12 to take measurements, do the tests and make sure the patient flow was not disrupted.
13

14 *"Because, since its 2 of us, one will do the Hb what what and the other will be doing all the vitals. So*
15 *it's not really that difficult"*
16
17

18 19 20 **Discussion**

21 This study has found that use of POC HbA_{1c} testing could have potentially averted 30% of patients
22 receiving inappropriate medication or not receiving additional medication. It provides evidence of the
23 scale of incorrect identification of controlled or uncontrolled diabetes that would result from
24 measurement of random blood glucose alone in a real clinical setting. We have established that
25 random blood glucose has a sensitivity of 66% and specificity of 79% compared to POC HbA_{1c} using a
26 treatment cut-off at HbA_{1c} 8% (64mmol/mol) in this busy diabetes clinic.
27
28

29 The qualitative work found that nurses liked using the analyser and were able to effectively carry out
30 the POC HbA_{1c} testing during routine appointments without holding up clinics. Doctors reviewing the
31 results valued having access to the HbA_{1c} test result to help them make treatment decisions, but the
32 empirical data suggest that they were influenced by blood glucose results in their clinical decision-
33 making.
34
35

36 *Comparison with the literature*

37
38 Previous studies have explored how point-of-care HbA_{1c} testing can be integrated into primary care
39 consultations in low resource settings in South Africa.(17, 18, 24) One study demonstrated that POC
40 HbA_{1c} testing leads to more patients receiving immediate feedback and resulted in a small statistically
41 significant reduction in HbA_{1c} of 0.44% (4.8mmol/mol) after 12 months of POC testing, but the POC
42 testing group did not receive any additional treatment intensification.(17) Furthermore, this reduction
43 in HbA_{1c} may not be clinically significant. The researchers concluded that their work did not support
44 the implementation of POC HbA_{1c} testing in public sector primary care in South Africa. More recently,
45 a trial combining treatment intensification (frequent appointments, feedback of HbA_{1c} and education)
46 and POC testing found that treatment intensification had an impact on HbA_{1c} levels, but POC testing
47 on its own did not.(24) However, immediate feedback of HbA_{1c} was part of both the intervention and
48 control groups, and there is unlikely to be any added benefit from performing the test on a POC
49 device.(20) A third study which implemented POC testing near Johannesburg,(18) found that,
50 participants who received two HbA_{1c} tests, showed a significant improvement in HbA_{1c}. In that study,
51 HbA_{1c} fell from 9.7% ± 2.4 (83 mmol/mol) at their first POC test to 8.4% ± 2.4 (68 mmol/mol) at the
52 second test, but all participants received POC testing and there was a 38% dropout rate. A qualitative
53 study from 2017 reporting the perceptions of different stakeholders on the implementation of POC
54 testing in rural primary care settings in South Africa, found that there was a need for scale-up of POC
55 testing in rural clinics, but there were some concerns about the reliability of the technologies.(15)
56
57
58
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1
2
3 Glycaemic control in our cohort was overall poor, with 65% of people presenting with HbA_{1c}>8%. Poor
4 diabetes control has been reported in other African countries: in Ethiopia 78% of people tested in an
5 outpatients clinic had HbA_{1c}>10%.⁽²⁵⁾ A chart review in a South African clinic found that 87% of
6 patients had HbA_{1c} above 7%.⁽²⁶⁾ Other studies have explored how health service organisational
7 factors contribute to patient's dissatisfaction leading to irregular clinic attendance and lying about
8 medication adherence.⁽¹⁶⁾
9

10
11 Documentation of the analyser recommend a maximum operating temperature of 25°C, yet
12 temperatures in the nurses' treatment room reached 32°C during this study. We do not know whether
13 this may have affected the performance of the analyser but this is something which would need to be
14 considered before roll-out of these technologies, as many clinics do not have temperature control and
15 may reach high temperatures in summer months.⁽²⁷⁾
16

17
18 Our qualitative work demonstrated that clinicians could integrate these tests into their clinical practice
19 to deliver testing and act on results. Other researchers have reported that POC testing can improve
20 disease management and access to healthcare in resource-limited settings.⁽¹⁵⁾
21

22
23 Our study found that in many patients, there was little correlation between random blood glucose
24 and HbA_{1c} which is consistent with previous work in South Africa. (9-11) Data from our cohort gave a
25 sensitivity of 66% and specificity of 79% of using random blood glucose compared to HbA_{1c} at an HbA_{1c}
26 treatment cut-off of 8% (64mmol/mol). Another study reported a higher sensitivity of 77% and a lower
27 specificity of 75%⁽⁹⁾, but they used HbA_{1c} of 7% (58mmol/mol) as a cut-off for good control.
28

29
30 Costs of these technologies may still be prohibitively high,^(17, 28) but as technologies develop and
31 costs come down, there is scope for widespread rollout in rural and low resource settings.
32 Haemoglobinopathies, which are common in some parts of the world, are frequently linked to altered
33 HbA_{1c}. The Afinion analyser used in this study has been shown to perform well in bloods with
34 haemoglobinopathies and does not show any clinically significant biases.⁽²⁹⁾
35

36 *Strengths and limitations*

37
38 Our study has demonstrated that POC HbA_{1c} testing can be integrated into patient appointments and
39 used for clinical decision-making during the same consultation in a South African primary care setting.
40 Furthermore, it has quantified the degree of incorrect treatment decisions arising from monitoring
41 random blood glucose in a real-world clinical setting.
42

43
44 Our study did not include any follow-up, so it was not possible to establish whether POC testing had
45 an impact on glycaemic control or whether it changed longer-term health outcomes. It has, however,
46 demonstrated that the POC test can be delivered within the timeframe of existing appointments and
47 clinicians reported that they were comfortable making clinical decisions on the POC test result. It
48 presents a realistic care pathway which can be used in future research or roll-out of POC testing on a
49 wider basis.
50

51
52 We did not collect data on frequency of appointments for these participants so we did not know how
53 long since their previous appointment or previous HbA_{1c} test. We did, however, collect information
54 on when the next appointment was scheduled, which allowed us to make a judgement on whether
55 this was congruous participants' random blood glucose and HbA_{1c} test result.
56

57
58 Paper-based records meant it was difficult to retrieve missing data and resulted in incomplete data
59 collection. Paper-based patient records are a real limitation of healthcare in this resource-limited
60 setting and the impact missing patient folders has on care has been reported in other studies.⁽¹⁶⁾

1
2
3 In the qualitative data collection, we were limited to the clinicians who were working at the clinic
4 whilst the study was ongoing. That means that we only collected views from two nurses and five
5 doctors, whose views may not be representative of all clinical staff.
6

7 *Clinical implications and future research*

9 In our study, clinicians clearly recognised the limitations of using blood glucose for making their clinical
10 decisions as they could not be sure whether the patient had eaten before attending the clinic.
11 Although clinicians understood the value of having an HbA_{1c} test result, some clinicians were still
12 heavily influenced by random blood glucose when making clinical decisions evidenced by the
13 quantitative findings. This study has found that there was discordance between what clinicians said in
14 qualitative interviews and how they acted to make treatment decisions. The reasons for this remain
15 unclear, but this may be because HbA_{1c} results which clinicians usually have access to are from the
16 patient's previous appointment which may have been several months ago. This means they may be
17 reluctant to place too much importance on this in their clinical decision making compared with the
18 blood glucose level from that day in their usual care practices. A future POC HbA_{1c} intervention should
19 provide comprehensive guidance and training to clinicians on decision-making on the test result and
20 consider not giving clinicians access to random blood glucose results. For those who are insulin-
21 treated, an alternative to POC HbA_{1c}, where it is unavailable or information about glucose levels are
22 needed, may be structured self-monitoring of blood glucose where there is some proof-of-principle
23 evidence of its use to improve glycaemic control in similar settings.(30) As technologies develop and
24 become cheaper, non-invasive, continuous or flash monitoring could become an option for use in low
25 resource settings.(31)
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29

30 *Conclusion*

32 This work demonstrates the importance of having an HbA_{1c} test result for clinical assessments in
33 primary care diabetes appointments. It confirms previous reports that a single random blood glucose
34 result should not be relied upon to make valid decisions about diabetes control and suggests that the
35 use of POC HbA_{1c} testing should be considered for diabetes monitoring and management.(9)
36
37
38
39

40 **Acknowledgements**

41 Thank you to Sindiswa Mmango for recruiting all 185 patients to the study and taking informed
42 consent. The clinical staff at Gugulethu Community Health Centre and for conducting the point-of-
43 care tests and completing data collection sheets. Eleanor Hirst for her assistance with data collection.
44 Felicity Nelson from Alere, South Africa for facilitating the loan of the Afinion analyser. The CDIA group
45 at Groote Schuur Hospital for support and advice during the set-up and data collection phases of this
46 study.
47
48
49

50 **Contribution statement**

51 JH designed the work, acquired the funding, collected and analysed the data and wrote the first draft
52 of the manuscript. KB contributed to the design of the study, contributed to the interpretation, revised
53 the manuscript and approved the final version. AF contributed to the design of the study, contributed
54 to the interpretation, revised the manuscript and approved the final version. JM contributed to the
55 data collection, contributed to the interpretation, revised the manuscript and approved the final
56 version. NL contributed to the design of the study, contributed to the interpretation, revised the
57 manuscript and approved the final version.
58
59
60

Competing interests

None declared

Funding

This work was funded by a Newton Partnership grant awarded to Jennifer Hirst in 2016. JH is funded by the funded by the NIHR Biomedical Research Centre, Oxford. AF is and NIHR Senior Investigator and receives support from the NIHR Oxford Biomedical Research Centre

Data sharing statement

Data can be requested by emailing the corresponding author.

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Tables and Figures

Table 1 – Patient characteristics and management decisions stratified by HbA1c (excluding 18 participants with missing data)

	All patients (N=168)	Controlled HbA1c ($\leq 8\%$, 64 mmol/mol) (N=56)	Poor control (HbA1c $> 8\%$ 64 mmol/mol and $\leq 10\%$, 86 mmol/mol) (N=44)	Very poor control (HbA1c $> 10\%$, 86 mmol/mol) (N=65)
Age (mean\pmSD)	56.3 \pm 12.6	60.6 \pm 13.6	55.51 \pm 10.5	53.3 \pm 12.1
Sex (N, % female) (N=43)	28 (65%)	10 (62%)	9 (64%)	9 (69%)
HbA1c (%) (mean\pmSD)	9.5 \pm 2.6	6.8 \pm 0.7	9.1 \pm 0.6	12.1 \pm 1.6
Random blood glucose (mmol/l) (mean\pmSD)	11.3 \pm 5.1	8.0 \pm 2.4	11.2 \pm 4.5	14.4 \pm 5.5
Treatment recorded	111 (66%)	33 (59%)	30 (68%)	48 (74%)
Diet only	2 (2%)	2 (6%)	0	0
Metformin	64 (58%)	21 (64%)	17 (57%)	26 (54%)
Oral (not specified)	12 (11%)	5 (15%)	4 (13%)	3 (6%)
Glimipiride and metformin	5 (5%)	2 (6%)	0	3 (6%)
Insulin	6 (5%)	0	3 (10%)	3 (6%)
Metformin and insulin	22 (20%)	3 (9%)	6 (20%)	13 (27%)
Medication not recorded	70 (42%)	23 (41%)	14 (32%)	17 (26%)
Clinical decisions				
Medication change	13 (8%)	0	3 (7%)	10 (15%)
Counselling on adherence	48 (29%)	15 (27%)	20 (45%)	11 (17%)
Combination	63 (38%)	6 (11%)	15 (34%)	42 (65%)
None	44 (26%)	35 (63%)	6 (14%)	2 (3%)
Decision based on				
HbA1c result	23 (14%)	6 (11%)	8 (18%)	9 (14%)
RBG result	12 (7%)	3 (5%)	2 (5%)	4 (6%)
Both	130 (77%)	46 (82%)	34 (77%)	50 (77%)

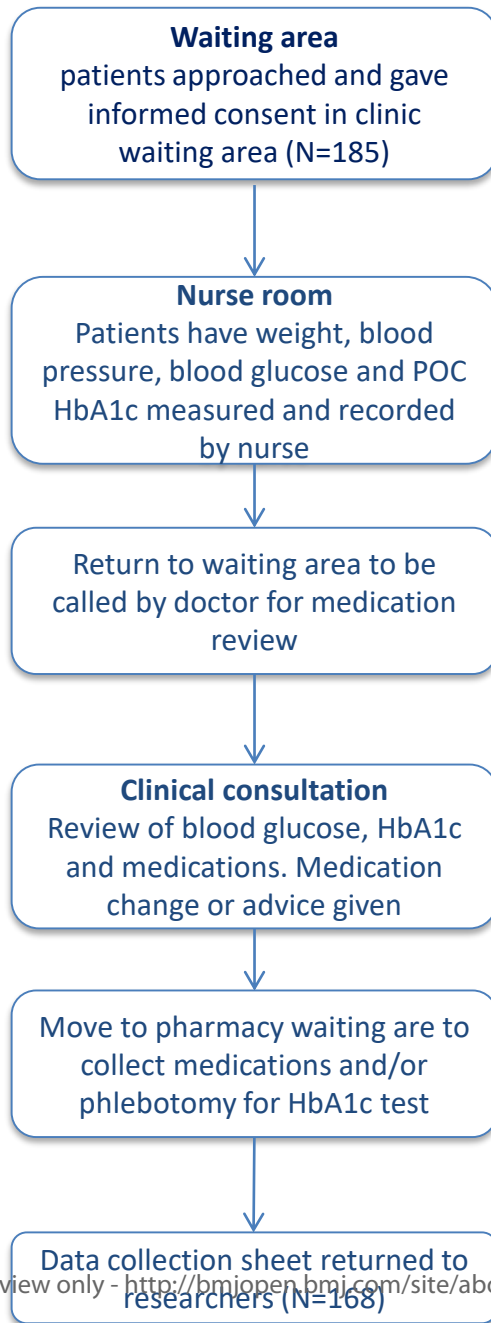
Table 2 – Correct diagnoses between random blood glucose and HbA1c (n=165)

Blood glucose	HbA1c		Total
	≥8% (64 mmol/mol)	<8% (64mmol/mol)	
≥10 mmol/l	75	11	86
<10 mmol/l	38	41	79
Total	113	52	165
	Sensitivity = 0.66		Specificity = 0.79

Figure 1 – Patient flow chart

Figure 2 - random blood glucose versus HbA_{1c}, stratified by random blood glucose levels using 10 mmol/l as the treatment decision threshold). Dotted line represents the threshold between controlled and uncontrolled HbA_{1c} (8%, 64 mmol/mol)

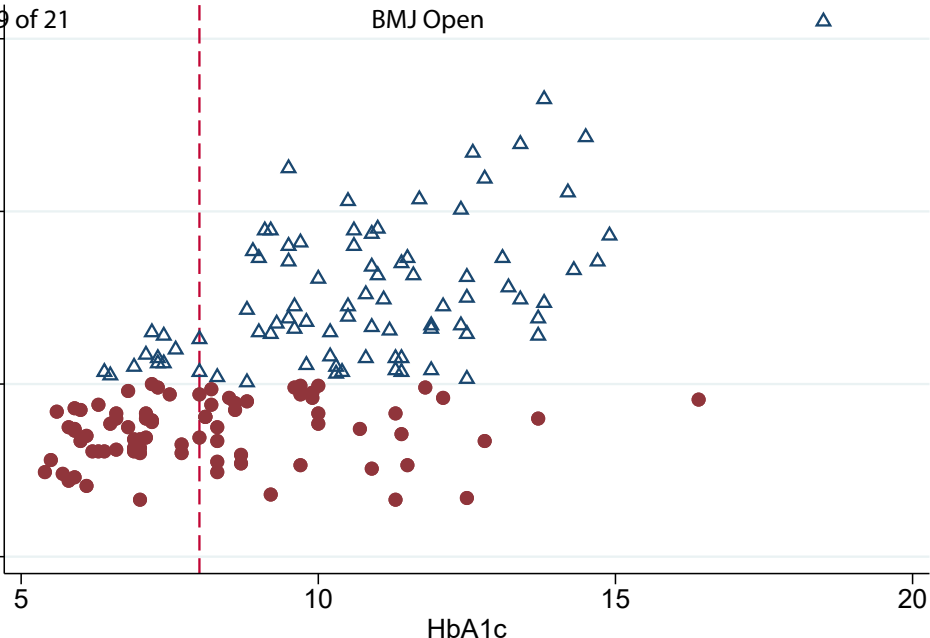
Figure 3 - random blood glucose versus HbA_{1c} stratified by clinical decisions or medication change (triangle= no medication change or advice, hollow circle= medication change, solid circle= no medication change)



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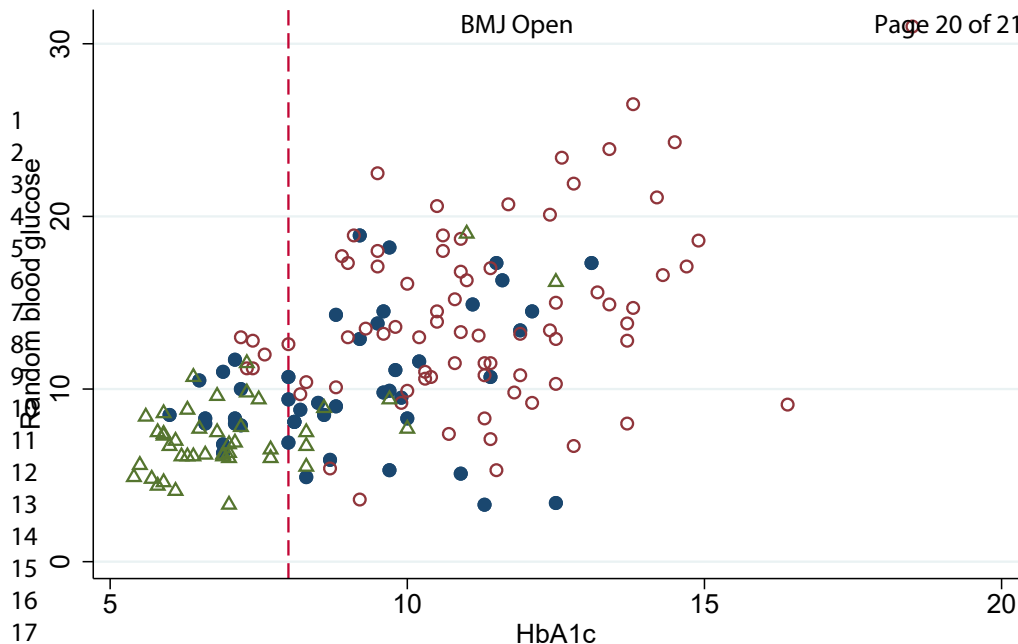
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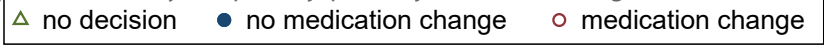


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△ High blood glucose	● Low blood glucose
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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract – page 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found – page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported – page 3
Objectives	3	State specific objectives, including any prespecified hypotheses – page 4
Methods		
Study design	4	Present key elements of study design early in the paper – page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection – page 4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up – page 4-5 (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – page 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group – page 5
Bias	9	Describe any efforts to address potential sources of bias – page 5-6
Study size	10	Explain how the study size was arrived at – page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why – page 5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding – page 5-7 (b) Describe any methods used to examine subgroups and interactions – page 5-7 (c) Explain how missing data were addressed – page 5-7 (d) If applicable, explain how loss to follow-up was addressed – page 5-7 (e) Describe any sensitivity analyses – page 5-7
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed – page 6-7 & Fig 1 (b) Give reasons for non-participation at each stage - na (c) Consider use of a flow diagram – Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders – page 6 (b) Indicate number of participants with missing data for each variable of interest – page 7 (c) Summarise follow-up time (eg, average and total amount) – page 6
Outcome data	15*	Report numbers of outcome events or summary measures over time – page 6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included – page 6-7
		(b) Report category boundaries when continuous variables were categorized n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period – n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses – page 6-7, table 1
Discussion		
Key results	18	Summarise key results with reference to study objectives – page 9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias – page 10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence – page 10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results – page 10-11
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based – page 11

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.