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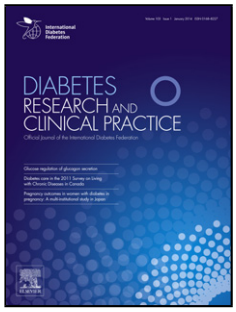

Title: An exploratory trial of basal and prandial insulin initiation and titration for type 2 diabetes in primary care with an adjunct retrospective continuous glucose monitoring: INITIATION STUDY

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TITLE PAGE

An exploratory trial of basal and prandial insulin initiation and titration for type 2 diabetes in primary care with an adjunct retrospective continuous glucose monitoring: INITIATION STUDY

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Structured abstract

Aims: To evaluate basal and prandial insulin initiation and titration in people with type 2 diabetes mellitus (T2DM) in primary care and to explore the feasibility of retrospective-continuous glucose monitoring (r-CGM) in guiding insulin dosing. The new model of care features General Practitioners (GPs) and Practice Nurses (PNs) working in an expanded role, with Credentialed Diabetes Educator-Registered Nurse (CDE-RN) support.

Methods: Insulin-naïve T2DM patients (HbA1c >7.5% (>58mmol/mol) despite maximal oral therapy) from 22 general practices in Victoria, Australia commenced insulin glargine, with glulisine added as required. Each was randomised to receive r-CGM or self-monitoring of blood glucose (SMBG). Glycaemic control (HbA1c) was benchmarked against specialist ambulatory patients referred for insulin initiation.

Results: Ninety-two patients mean age (range) 59 (28-77) years; 40% female; mean (SD) diabetes duration 10.5 (6.1) years) participated. HbA1c decreased from (median(IQR)) 9.9(8.8, 11.2)%; 85(73, 99)mmol/mol to 7.3(6.9, 7.8)%; 56 (52, 62)mmol/mol at 24 weeks ($p<0.0001$). Comparing r-CGM (n=46) with SMBG (n=42), there were no differences in major hypoglycaemia ($p=0.17$) or ΔHbA1c ($p=0.31$). More r-CGM than SMBG participants commenced glulisine (26/48 vs. 7/44; $p<0.001$). Results were comparable to 82 benchmark patients, with similar low rates of major hypoglycaemia (2/89 vs 0/82; $p=0.17$) and less loss to follow up in the INITIATION group (3/92 vs 14/82; $p=0.002$).

Conclusions: Insulin initiation and titration for T2DM patients in primary care was safe and improved HbA1c with low rates of major hypoglycaemia. CDE-RNs were

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effective in a new consultant role. r-CGM use in primary care was feasible and enhanced post-prandial hyperglycaemia recognition.

Key words: type 2 diabetes mellitus, primary care, insulin, retrospective continuous glucose monitoring

Trial registration ACTRN12610000797077

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Introduction

Type 2 diabetes mellitus (T2DM) affects over 1 million Australians and 382 million people world-wide [1]. Good glycaemic control reduces the risk of micro and macrovascular complications in people with T2DM [2]. With progressive islet-cell dysfunction, at 10 years post-diagnosis approximately 50% of patients require exogenous insulin [3].

However, insulin initiation is often delayed [4-6], and up-titration is often suboptimal [7]. Only 17% of insulin-treated people with T2DM achieve target HbA1c levels [8]. There are well-documented reasons for this, including "psychological insulin resistance" (negative perceptions and attitudes that act as barriers to starting insulin) [9] on the part of patients and "clinical inertia" (recognition of a problem but failure to act) on the part of practitioners [10]. However health system factors are also important. In Australia and other countries, people with T2DM are often referred out of primary care to specialist diabetes services for insulin initiation [11, 12]. This can lead to delays in starting insulin, and avoidable periods of hyperglycaemia as cost and limited availability create difficulties accessing endocrinologists and Credentialed Diabetes Educator – Registered Nurse (CDE-RN). In Australia the mean HbA1c level of people with T2DM prior to starting insulin is 9.4% (79mmol/mol) [6] and in the UK is 9.3% (78mmol/mol) [13], well above the recommended targets.

The increasing prevalence of T2DM and limited availability of specialist resources means that this clinical issue must be addressed within primary care [1]. If insulin initiation for people with T2DM was to become part of routine general practice care, this would integrate the patient's diabetes care with care for other common co-morbidities. It could also reduce the more costly use of secondary care [14] and could improve disease control and long-term outcomes.

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For insulin initiation and up-titration to become part of routine general practice care two key issues need to be addressed. The first is to develop a model of care that is feasible, acceptable and sustainable in practice and that makes more efficient use of the members of the diabetes health professional team, including the general practitioner (GP), Practice Nurse (PN), endocrinologist and CDE-RN. The second issue is to develop skills and tools for effective post-initiation blood glucose monitoring (BGM) to help optimise glycaemia levels [6, 8, 15]. One promising and recently available monitoring tool, currently predominantly used in specialist practice, is retrospective continuous glucose monitoring (r-CGM). These devices incorporate a minimally invasive flexible subcutaneous electrode to measure interstitial fluid glucose levels. They are small (size of a 50c piece) and require minimum interaction on the part of the patient. They can be worn for up to a week, following which the data are uploaded to via a USB device to a computer and analysed, giving a graph of each day's glucose pattern and an average trace for the week. Patients need to record their BGL twice daily to calibrate the r-CGM data at upload. A recent meta-analysis in predominantly Type 1 diabetes patients found real-time CGM improved glycaemic control compared with self-monitoring of blood glucose (SMBG) [16]. However evidence on r-CGM in T2DM is lacking.

Our primary aim was to evaluate the impact of a new model of care for insulin initiation in primary care in people with T2DM and inadequate glycaemic control on maximum oral hypoglycaemic agents (OHA). Our secondary aim was to assess the feasibility and acceptability, to both the patient and health professional, of the use of r-CGM in guiding insulin dosing in a primary care patient group, while generating novel preliminary r-CGM data.

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Subjects, materials and methods

The INITIATION study design and protocol is published elsewhere [16]. In brief, this was a large exploratory non-randomised study of a collaborative model of care that we have developed and previously piloted in a small number of practices in accordance with the UK Medical Research Council (MRC) complex development framework [17, 18]. In this model of care the GP and PN (who works in an enhanced role), are mentored by a CDE-RN with endocrinologist support if required. The model of care uses resources and clinical tools introduced to practices (GP and PN) in an educational session and has been described elsewhere [17]. All participating practices in the current study were introduced to the model of care and all participating patients were managed according to the model of care. While this was an exploratory before and after study, we benchmarked our results against data from an ambulatory hospital diabetes services servicing the same geographical area as the majority of the participating practices. Quality-assurance data were collected from consecutive ambulatory non-pregnant adults with T2DM referred by specialist endocrinologists to CDE-RNs for insulin commencement in this benchmark site over the same period as our study. Nested within this primary care study was an exploratory randomised trial of r-CGM. We randomised participating patients to either SMBG alone or SMBG with adjunct r-CGM using an iPro2^{TM} (Medtronic, Northridge CA). Randomisation was undertaken by a researcher independent of the study team using a computerised random number table.

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The study was approved by St Vincent's Health Human Research Ethics Committee and registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12610000797077).

Primary Care Sites

We approached general practices in metropolitan Melbourne and regional Victoria using our University of Melbourne Department of General Practice database of teaching practices, our departmental practice based Research Network, referral network of the study investigators (St Vincent's Hospital, Werribee Mercy Hospital and IDI-Baker) and with the assistance from Medicare Locals. Inclusion criteria for practices were employment of a PN and that the GPs and PNs did not currently routinely initiate insulin as a part of their practice. An invitation letter and a study flyer were mailed to eligible practices. One of the study team members undertook an in-practice briefing visit to practices who had expressed an interest in participating to explain the study in more detail and gain consent.

Consented GPs and PNs at eligible sites attended a 2-hour interactive training session covering the rationale for insulin use; strategies to motivate patients and overcome barriers to insulin initiation; protocols and algorithms for initiation and titration of basal (glargine; Sanofi) and prandial insulin (glulisine; Sanofi) as per study protocol and use of insulin injecting devices (Solostar^{TM}; Sanofi), glucose meters (Freestyle Optium™; Abbott) and r-CGM devices (iPro2^{TM};Medtronic, Northridge CA). The content of the training has been described elsewhere [17].

Patient Screening, Enrolment and Outcome Measures

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Practices undertook an audit of their electronic medical records in the practice to identify potential study patients based on the following inclusion criteria:

- Insulin naïve people with T2DM
- Aged 18-80 years
- HbA1c ≥7.5% (58mmol/mol) performed in the last 6 months
- Treated with maximum tolerated doses of OHA
- OHA doses stable ≥3 months
- Willing to monitor blood glucose ≥twice daily
- Willing to commence insulin

Exclusion criteria were as follows:

- Type 1 Diabetes Mellitus (T1DM)
- Fasting blood glucose <6.0mmol/L
- Major medical or psychiatric illness
- Pregnant or planning pregnancy

Potential patients were sent a letter by their GPs and received a follow-up call by PNs to attend the practice to hear more about the study if interested. Patients who agreed to start insulin and consented to participate were reviewed by the GP who then referred the patient to the PN for a screening visit. At this visit blood was taken for baseline HbA1c levels. A 7-day r-CGM was commenced at this screening visit on all consenting patients.

A week later the patient was reviewed by the PN supported by the study CDE-RN. Eligibility was confirmed based on the HbA1c result and the r-CGM data were

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uploaded (the PN and GP were masked to this baseline trace). A history and examination and patient survey were performed at baseline and 24 weeks. This included the Short Form 36 Health Survey questionnaire version 2 (SF-36 v2) [19] and Audit of Diabetes Dependent Quality of Life (ADDQoL) [20]. At this baseline visit patients were randomised to one of the two monitoring arms of the embedded sub-study (SMBG alone or SMBG + r-CGM). PNs and r-CGM randomised participants completed a user evaluation survey at 24 weeks.

Glycaemia Monitoring

HbA1c assays at baseline, 12 and 24 weeks were performed by a centralised DCCT-aligned laboratory. All participants were provided with a glucose meter (Freestyle Optium™; Abbott) and instructed to perform SMBG testing 2-4 times / day, including a mandatory fasting and at least one two-hour post-prandial measurement. All meters were uploaded at each study visit. Visits were weekly for 4-weeks following initiation of glargine or glulisine, fortnightly for another 4-weeks and monthly thereafter.

In those randomised to SMBG alone, r-CGM 7-day traces were obtained at baseline, 12 and 24 weeks. Health professionals were instructed not to access these traces. For those randomised to the r-CGM arm, traces were performed at baseline and during the week prior to each visit, and these traces were used by GP and PN in clinical management.

Insulin Initiation and Titration Protocol

All enrolled patients commenced glargine, which was titrated against fasting glucose levels every 7-days. OHAs were continued unless modified at the GP's recommendation. After a minimum of 4-weeks following glargine initiation, and if

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fasting glycaemia was in target, at the discretion of the GP a once daily glulisine injection could be initiated prior to the meal with the greatest post-prandial hyperglycaemic excursion. Any ongoing sulphonylurea use was to be withdrawn with glulisine initiation. Insulin dosing schedules are previously described [16]. This was a pragmatic study in the context of ongoing GP clinical practice and GPs had clinical discretion to deviate from insulin protocols on clinical grounds.

Sample size

While this was a large exploratory study, we made a power calculation based on an HbA1c reference value of 8.2% (66mmol/mol) in the INSTIGATE study [5] and assumed no change without intervention. The new model of care was estimated to reduce HbA1c by 0.4% (4mmol/mol) [21]. With a two-sided α=0.05 and 80% power, 102 patients were required to detect an absolute HbA1c reduction before and after implementation of the new model of care. Preliminary research suggested that an average two full-time-equivalent GP practice has 80-100 T2DM patients, with 10% meeting study criteria. A 50% recruitment rate, generating ≈4-5 participants per practice, estimated a need for recruiting 22 general practices. This study will provide novel preliminary data on the effect size of r-CGM in T2DM in primary care.

Statistical Analysis

Stata statistical software package v12 was used. Descriptive statistics were calculated for demographics, glycaemia, quality of life, and satisfaction with r-CGM. Non-parametric tests were used to determine if there was a statistically significant change in HbA1c and to compare time spent below, within and above target glucose ranges on r-CGM.

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For the embedded substudy, baseline characteristics of the SMBG and r-CGM arms were compared using two sample t-tests except for baseline HbA1c, which was compared using a non-parametric (Mann Whitney) test. Secondary analyses utilised two sample t-tests to explore whether there were differences between SMBG and r-CGM groups in the time to glulisine commencement, quality of life and Δ in the percentage time at target (4.0-10.0mmol/L), high (>10.0mmol/L) and low (<4.0mmol/L) glucose levels (as measured by masked r-CGM traces at baseline, 12 and 24 weeks). T-test for proportions was used to determine differences in the proportion of patients commencing glulisine. $P<0.05$ was considered statistically significant.

ΔHbA1c (baseline to 24 weeks) of study vs. benchmark groups were compared using a multivariate regression analysis to adjust for age and baseline HbA1c.

Results

Primary Care Sites

Participating general practices were located in suburban Melbourne (n=21); and regional Victoria (n=1). Sites included private and corporate practices (n=21) and a community health centre (n=1). One practice was a solo GP practice and five were two-GP practices. A median [range] of five [1-9] participants per site were consented. Two CDE-RNs (total 1.0 FTE) provided support to the 22 sites.

Insulin Initiation, Follow Up and Glycaemia

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Between 28 April 2011 and 28 June 2012, 102 of 118 potential participants agreed to commence insulin and participate in the study. Nine subsequently had a screening HbA1c <7.5% (<58mmol/mol) and one withdrew consent prior to insulin initiation, leaving 92 participants. Baseline characteristics of the 92 participants are summarized in **Table 1**. Three participants were lost to follow-up and 89 participants completed the 24-week study (**Figure 1)**. Thirty-three subjects commenced glulisine at mean (SD) 11.8 (5.1) weeks after glargine initiation. The median [IQR] daily insulin dose at 24 weeks was 0.33 [0.24-0.47] IU/Kg body weight at 24 weeks.

Changes in glycaemic parameters for the INITIATION participants are summarized in **Table 2**. Relative to their baseline parameters the reductions in HbA1c and increased CGM time within target glucose range were highly significant for the INITIATION group overall. Thirty-four percent of INITIATION participants achieved HbA1c <7.0% (<53mmol/mol). There was no significant change in glycaemic variability as reflected in the SD of glucose levels between baseline and 24 weeks (Mean [SD] 3.0[0.75] vs. 2.8[0.94]). There were two hypoglycaemic episodes in a single patient where an ambulance was called. In both instances there was no loss of consciousness and the patient self-treated the hypoglycaemia.

INITIATION r-CGM vs. SMBG: Insulin Initiation, Follow-up and Glycaemia

The r-CGM and SMBG sub-groups were similar with respect to age (58.9[11.3] vs. 58.6[10.2]; p=0.88), gender (male 60% vs. 59%; p=0.76) and baseline HbA1c (9.9 (8.8, 10.9) vs. 9.8 (8.7, 11.4)%; (85 (73, 96) vs. 84 (72, 101)mmol/mol; p=0.63). One and two participants were lost to follow-up in the r-CGM and SMBG groups respectively (p=0.48). r-CGM devices performed reliably, with a failure rate of <1%.

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More r-CGM than SMBG subjects commenced glulisine (**Figure 2[a]**). Seventy percent of the glulisine injections were administered prior to the evening meal, 24% with breakfast and 6% with lunch. This pattern did not differ between the two sub-groups (data not shown). The time post-baseline to glulisine commencement Mean [SD] did not differ between groups: r-CGM vs. SMBG 12.3[5.3] vs. 9.8[4.1] weeks; p=0.26). Mean (SD) daily insulin dose in the r-CGM and SMBG sub-groups were 0.34(0.19) vs. 0.46(0.45) IU/Kg respectively, also similar, p=0.33.

At baseline six patients in the r-CGM arm were taking one OHA and at end-study, 16 were (p=0.015), largely due to a decrease in patients taking two OHA medications (33 to 24). The only significant class-reduction occurred with DPP4 inhibitor use (Baseline-SMBG: 16 and r-CGM: 11 vs. End-Study-SMBG: 14 and r-CGM: 7; p=0.036). There were no significant changes in OHA use over the 24 weeks in the SMBG group. There were no differences between the r-CGM and SMBG sub-groups in HbA1c reduction, CGM parameters (**Table 3**), or the proportion achieving HbA1c<7.0% (<53mmol/mol) at 24 weeks (**Figure 2[b]**).

INITIATION Participants: Non-Glycaemic Parameters

Weight increased over the 24 week study in the INITIATION participants (Mean [SD]; 3.1[4.7] Kg; p=0.0001). Changes in the r-CGM and SMBG subgroups (2.9kg vs 3.3kg) were similar (p=0.68). There were no episodes of skin infection related to GCM use.There were no significant changes between baseline and 24 weeks in the SF 36 parameters (data not shown). While the change in ADDQoL between baseline and 24 weeks was not significant in INITIATION participants as a whole (n=67) (+0.063[1.35]; p=0.63) the difference between r-CGM and SMBG sub-groups was

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significant in favor of r-CGM sub-group (+0.40[1.33] vs. -0.31[1.30]; p=0.031). Twelve PNs scored the r-CGM devices at a median (IQR) of 7 (6,7) out of a possible 7 with regard to satisfaction and willingness to continue r-CGM use. Forty-six participants in the r-CGM sub-study arm scored the r-CGM devices on the same parameters, at 6 (6, 7) and 4.5 (4, 6) respectively.

INITIATION vs Benchmark

Eighty-two patients in the benchmark sites were referred for insulin initiation at a specialist centre (Age (range) 60 (25-86) years; 62% male; HbA1c Median (IQR) 9.4 (8.2, 10.8)% ((79 (66, 95)mmol/mol); and Mean (SD) diabetes duration 11.3 (7.1) years). Forty-one were commenced on a basal insulin regimen, 26 on twice daily pre-mixed insulin, nine on basal insulin and one rapid-acting insulin injection or on a basal-bolus regimen. 14 patients were lost to follow-up at 24 weeks including 6 who did not commence insulin, as compared to three in the INITIATION group (p=0.002). Characteristics of patients lost to follow-up were similar in both groups with regard to gender (Male/Female (n) 2/1 vs. 7/7; p=0.60), age (Mean [SD] 50.6[3.5] vs. 54.6[7.5] years; p=0.38) and baseline HbA1c (Median[IQR] 10.8[9, 12.1] vs. 10.5[9.3, 11.9]% (95 [75, 109] vs. 91 [78, 107]mmol/mol); p=0.95). A greater reduction in HbA1c was observed in the INITIATION vs. the Benchmark Group at 12 and 24 weeks. Following adjustment for baseline HbA1c there was a difference at 24 weeks of 0.4% (4mmol/mol) between the groups (p=0.017, 95% CI -0.73 to -0.074%). There were no differences in major hypoglycaemia (2/89 vs 0/82, p=0.17).

Discussion

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Insulin initiation has been perceived as complex by primary care health professionals [22]. The INITIATION study has demonstrated that a model of care whereby a GP and PN team, with appropriate T2DM patient selection and specialist team support, can initiate insulin effectively in a timely, safe and effective manner as shown in highly significant reductions in HbA1c and increased time in CGM target glucose range. The increase in the amount of time below target, although statistically significant, was minor (<30 minutes per day) and of limited clinical significance and comparable to the observation that in healthy people without diabetes CGM records glucose levels of <4.0 mmol/L for approximately 20 minutes each day [23]. Comparison to benchmark insulin initiation suggested that they may achieve comparable glycaemic outcomes to those of specialist diabetes teams. Our model makes more efficient use of the relatively scarce resources of an endocrinologist and CDE-RN for the primary care population with diabetes earlier in the evolution of the disease, in whom diabetes management is less complex and more stringent glycaemic targets may be attained.

The key strength of the INITIATION study is that it has been conducted in a real-world setting. All participating sites had not previously been involved in a clinical trial, nor did they usually initiate insulin in their patients requiring such therapy. Nevertheless the participant attrition rate was low and adherence acceptable, indicating the ready translation of the study protocols into clinical practice. However, this model may not be appropriate for all patients or primary care providers. A PN is essential, but currently only ≈63% of GP practices in Australia employ a PN [24]. Data on the use of r-CGM in T2DM in primary care setting are limited and our study provides pertinent information to guide future research in this area.

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There are limitations to our study. Out of 102 patients recruited, data were only available from 92 patients. Despite being underpowered, we showed significant HbA1c improvement over 24 weeks follow-up. We used an exploratory before and after study design to test the efficacy of the new model of care and to examine the feasibility of embedding r-CGM to guide insulin titration in primary care. All study participants received the new model of care and insulin was initiated and titrated under GP and PN direction. To address this study design limitation, we used specialist benchmarking data as a reflection of current "real-world" management. While a "basal plus" insulin regimen was selected for simplicity and the titration schedule chosen to minimise hypoglycaemia risk, it is recognised that other insulin regimens may better suit some patients. Our convenience sample of practices and patients may not be representative of the wider GP population. A cluster randomised controlled trial to examine the effectiveness of the new model of care is currently underway [17].

Previous studies have evaluated the benefit of CGM technology in diabetes management [25]. Virtually all of the evidence supporting CGM use in patients relates to real-time devices in T1DM patients managed by specialist teams, and have demonstrated improved glycaemia and reduced hypoglycaemia [26, 27]. There is little data available regarding r-CGM in T2DM population and none based in primary care. The r-CGM "wear and forget" devices place fewer demands upon the patient. The INITIATION study is the first to demonstrate the feasibility of r-CGM on a large scale T2DM population in primary care. The devices had a very low failure rate and the technology was rated highly by both patients and health professionals. A greater proportion of r-CGM participants were prescribed rapid acting insulin, which may

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have resulted from greater insights into the glycaemic patterns, particularly those relating to post-prandial excursions. Fewer OHAs were used in combination with insulin, without adversely impacting glycaemia, which may have health economic implications and also reduce regimen complexity for patients. In contrast to previous observations [28], there was no deterioration in quality of life as assessed by ADDQoL in our r-CGM study participants. Our findings regarding recognition of glycaemic patterns, feasibility and quality of life reflect and extend recent observations in a smaller population of T2DM patients already on a basal insulin regimen in specialist care who were provided with real-time continuous glucose monitoring [29].

Compared to a structured 7-point SMGB profile [30], r-CGM is less dependent upon patient adherence and provides greater detail in the management of diabetes, particularly overnight, when finger-prick glucose information is not readily available [31]. We did not observe significant differences in HbA1c or r-CGM parameters between the r-CGM and SMBG only groups, though this sub-study was exploratory and not powered to demonstrate this. A detailed analysis of the glycaemic variability parameters of r-CGM data from both groups will be reported elsewhere.

Each patient was required to perform a minimum of two finger prick glucose readings in a 24-hour period, including one fasting and one other two-hour after a meal. The meal chosen for the post-prandial glucose check was varied. While patients in the SMBG arm only had access to the SMBG readings, those in the r-CGM arm of the study had access to both SMBG and r-CGM data. SMBG readings were required for calibration of the r-CGM sensor trace. Health-care professionals were able to access

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both data from patients assigned to the r-CGM arm of the study to guide the titration of basal insulin and/or the addition and titration of prandial insulin. Experience derived from the review of r-CGM may also have provided the GP and PN with insights into the impact of insulin adjustments upon glycaemia, which they then generalised to participants in the SMBG group [31]. In addition, r-CGM may have served as an effective learning and motivational tool for patients. Potentially some health-care professionals may have accessed r-CGM data (from baseline, 12 and 24 week studies) in SMBG arm participants, despite being instructed otherwise. A larger study with cluster-randomisation would address many of the above limitations.

For the uncomplicated patient with T2DM insulin initiation is most appropriately implemented in primary care [32]. We have demonstrated the efficacy and safety of a collaborative model of care facilitating timely insulin initiation within general practice pathways, with educational resources and insulin initiation protocols being implemented by GP and PN teams supported by a specialist team. A large cluster trial of this model of care incorporating structured SMBG is being conducted to examine its effectiveness and cost-utility. Given that structured SMBG is now the standard of care, a larger follow-on trial comparing structured SMBG with r-CGM is required.

Conflict of interests

We wish to declare the following which may be considered as potential conflicts of interest to this work:

(1) IDB and JF received fellowship support from NHMRC CCRE in Diabetes Science;

(2) Sanofi and Medtronic provided material and financial support for the conduct of this investigator initiated study;

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(3) Abbott and BD provided material support;

(4) JF was supported by NHMRC-PHCRED Career Development Fellowship;

(5) LG received travel support by Sanofi to attend a national conference;

(6) DNO, NC, DL, AJ, JF and JMN had various financial relationships with pharmaceutical industries *outside the submitted work* including consultancies, grants, lectures, educational activities and travel;

(7) All the other authors had no conflict of interests that may be relevant to the work under consideration.

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Table 1: Characteristics of INITIATION study participants at baseline. Values are numbers (percentages) unless stated otherwise

Characteristics at baseline	**N=92**
Age in years Mean (Range)	59 (28-77)
Female	37 (40)
Married/de facto relationship	64 (70)
Unemployed	18 (20)
Highest level of education	
Primary or less	15 (19)
Secondary or trade	46 (55)
Tertiary	22 (26)
Diabetes duration (years) Mean (SD)	10.5 (6.1)
Pre-insulin HbA1c Median (IQR)%; mmol/mol	9.9 (8.8, 11.3); 85 (73, 100)
Complication Status	
Cardiovascular Disease	12 (13.0)

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Proliferative Retinopathy	5 (5.4)
Neuropathy	8 (8.7)
Nephropathy	13 (14.1)
Pre-insulin number of OHA used	
1 Agent	8 (8.7)
2 Agents	59 (64.1)
3 Agents	24 (26.1)
4 Agents	1 (1.1)
Pre-insulin OHA by class	
Metformin	86 (93.5)
Thiazolidenedione	12 (13.0)
Sulphonylurea	73 (79.4)
DPP 4 inhibitor	28 (30.4)
GLP 1 analogue	0 (0)
Acarbose	3 (3.3)

IQR=Interquartile range; SD= standard deviation; OHA=Oral hypoglycaemic agent

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Table 2: Glucose control parameters for INITIATION participants

	Baseline	24 Weeks	P value
HbA1c (Median [IQR]) %; mmol/mol	9.9 [8.8, 11.3]; 85 [73, 100]	7.3 [6.9, 7.8]; 56 [52, 62]	<0.0001
% Time below target* (Median [IQR])	0 [0-0]	2 [0-6]	<0.0001
% Time in target* (Median [IQR])	26.5 [9,49]	71.5 [56.5, 83.5]	<0.0001
% Time above target* (Median [IQR])	71 [50, 91]	26.5 [13, 37]	<0.0001

*% Time based on r-CGM

Table 3: Comparison of r-CGM vs SMBG groups within the INITIATION study (baseline to 24 weeks)

	r-CGM	SMBG	P

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	(N=46)	(N=42)	value
Δ HbA1c Mean (SD)%; mmol/mol	-2.7 (1.8); -30 (20)	-2.4 (1.4); -26 (16)	0.31
Δ % Time below target* Mean (SD)	2.4 (6.6)	4.3 (6.5)	0.18
Δ % Time in target* Mean (SD)	38.2 (31.1)	35.3 (24.3)	0.63
Δ % Time above target* Mean (SD)	-40.6 (31.3)	-39.2 (24.7)	0.82

*% Time based on r-CGM

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Highlights

- The Stepping Up model is GP and Practice Nurse team supported by diabetes educator
- Basal plus insulin in type 2 diabetes in general practice is safe and effective
- Glycaemia improves and hypoglycaemia risk is minimal during 24 weeks follow-up
- r-CGM use in primary care enhance post-prandial hyperglycaemia recognition

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Figure 1: Study Consort flow chart

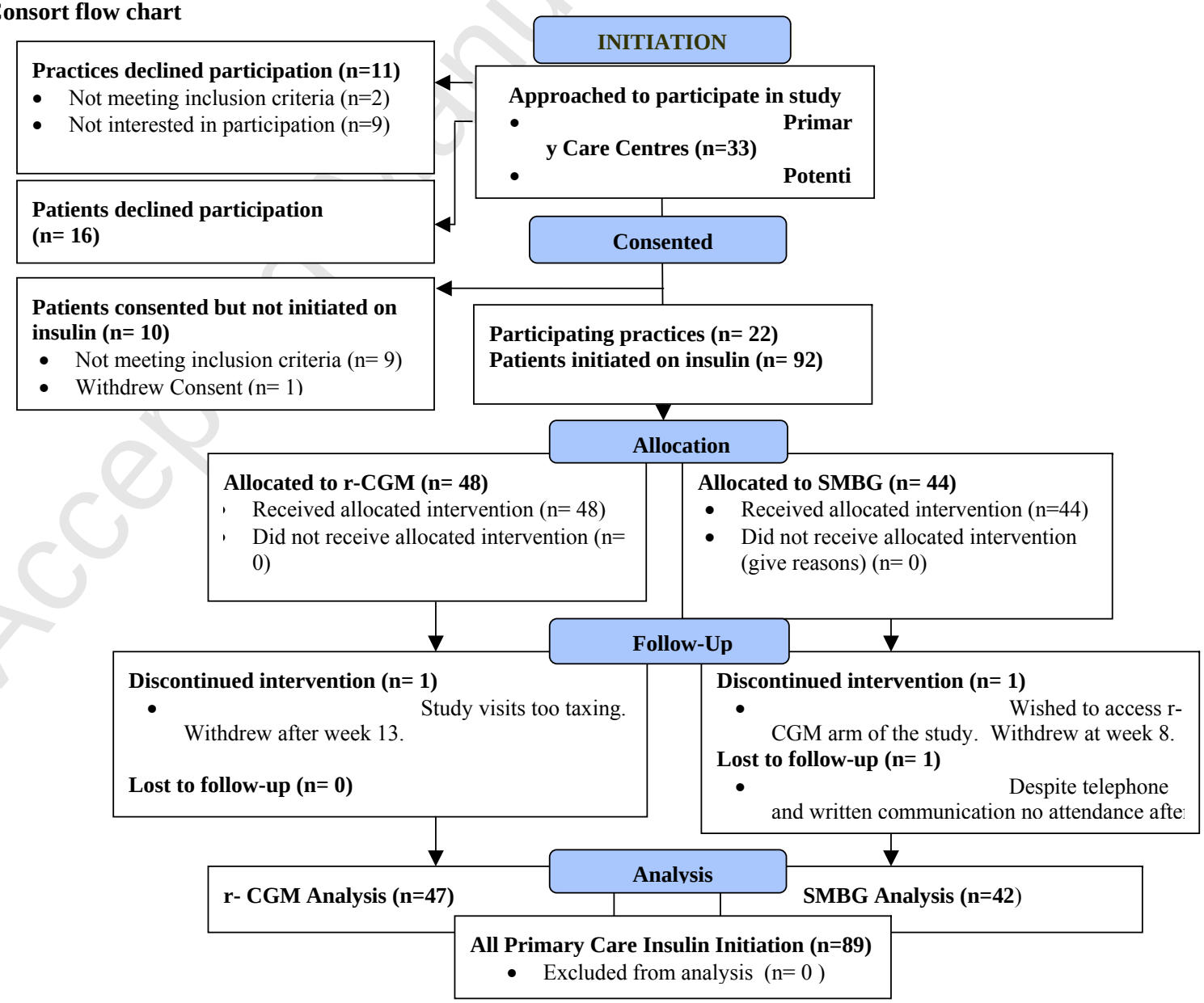
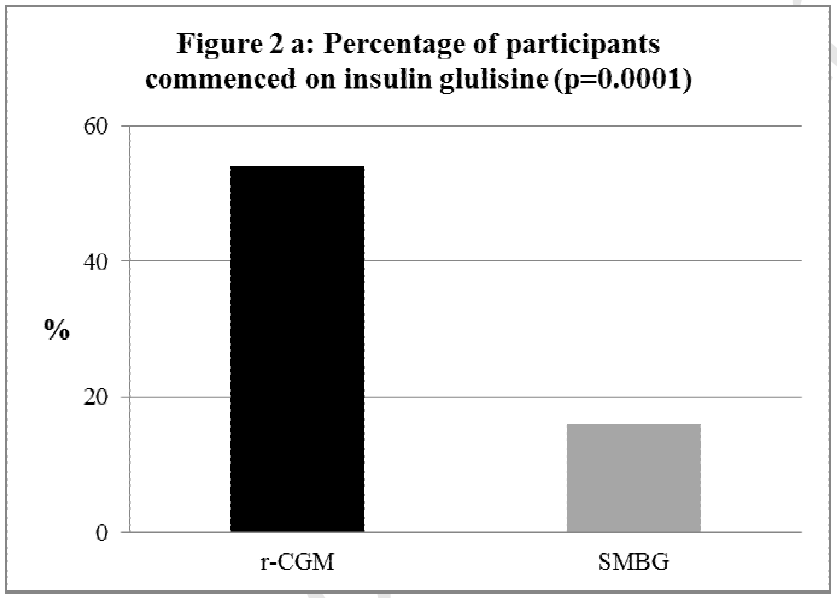
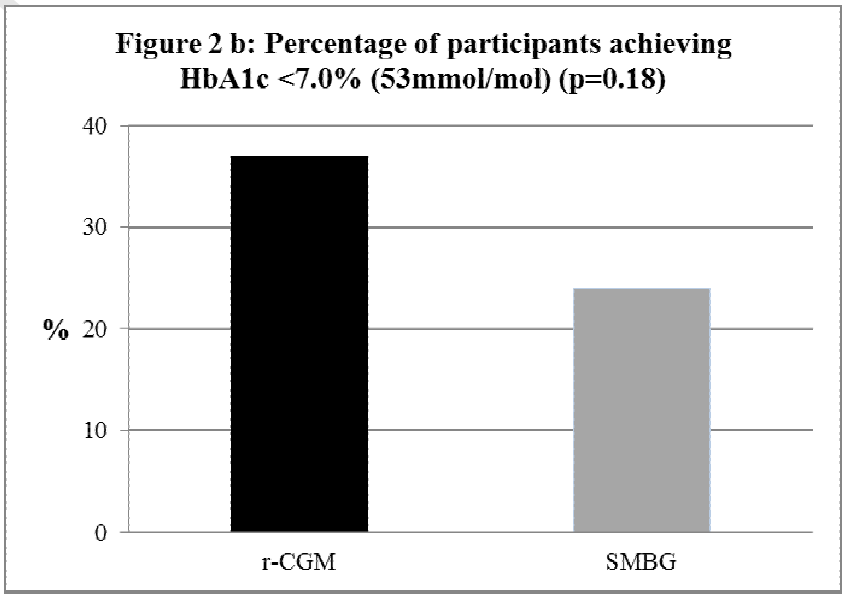


Figure 2: Comparison of r-CGM and SMBG groups at 24 weeks





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