FINAL REPORT
PROJECT TITLE: Long term effectiveness of SMS4BG

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Project Summary:
This report provides a summary of the project taken from the manuscript submitted for publication. The full paper will be made available to NZSSD upon publication.

Background:
The SMS4BG intervention was developed in response to the need for innovative solutions to support self-management in adults with poorly controlled diabetes.[1] SMS4BG arose from a collaboration between the National Institute for Health Innovation and Waitemata District Health Board (DHB), and its development involved a multidisciplinary team of public health and mHealth experts, psychologists, diabetes nurse specialists and a Māori advisory group, with review and input from diabetes specialists and primary care teams.

The programme content covers the 7 key self-management behaviours identified by the Association of American Diabetes Educations: 1) healthy eating, 2) being active, 3) monitoring, 4) taking medication, 5) problem solving, 6) reducing risks, and 7) healthy coping.[2] The programme is tailored by the needs and goals of the individual, and by demographic factors. As well as core motivational and support messages (in Māori, Pacific or non-Māori/Pacific cultural versions), recipients can opt to receive additional modules including; insulin module, young adult module, smoking cessation module, lifestyle behaviour modules (exercise, healthy eating or stress/mood management), and foot care module. Recipients can choose to receive blood glucose monitoring reminders which they can reply to by texting back their result.

A pilot study in 2013 found SMS4BG acceptable, useful, and culturally appropriate.[1] Feedback from this pilot study allowed for further development and refinement of SMS4BG. A two-arm randomised controlled trial (RCT) of the SMS4BG intervention compared to usual care was then undertaken. The trial was funded by the Health Research Council in partnership with Waitemata and Auckland DHBs (through the Research Partnerships for New Zealand Health Delivery initiative) and the Ministry of Health.[3] The aim of the trial was to assess the effectiveness of SMS4BG and inform its implementation as a programme. The trial randomised 366 participants (183 per arm) aged 16 years and over with poorly controlled type 1 or type 2 diabetes (HbA1c≥65mmol/mol) from primary and secondary care services across New Zealand between June 2015 and November 2016. At 9 months follow up, HbA1c was significantly lower in the intervention group compared with the control group (-4.23mmol/mol, 95%CI [-7.30 to -1.15], p=0.01).[4] High levels of satisfaction with SMS4BG were found with intervention participants reporting it to be useful (95%), culturally appropriate (97%), and would recommend the programme to other people with

diabetes (97%).[4] Following completion of the main trial, the first 87 participants (limited due to time and funding constraints) in the control group were offered SMS4BG, of which 64 (74%) accepted.

Research Objectives:
The primary aim of this study funded by a grant from the NZSSD was to determine the long term effectiveness of SMS4BG in adults with poorly controlled diabetes. The specific objective was to assess whether receiving the SMS4BG programme resulted in significant improvements in glycaemic control (HbA1c) at 2 years follow up. These aims and objectives are identical to those in the initial grant application.

Methods:
A follow-up study of the main SMS4BG RCT was carried out using medical records of trial participants. Ethics approval was received through HDEC (14/STH/162). All original trial participants were notified of the follow up study and given the opportunity to opt out.

All participants who consented to take part in the main trial were followed up at 2 years post randomization excluding: (1) those from the control group who received the intervention at the end of the trial, (2) those who had withdrawn their participation, or (3) those who were deceased. Two year HbA1c test results were obtained for each eligible participant from medical records following exactly the same procedures used for data collection of the primary outcome in the main trial with results obtained directly from patient records by clinic/hospital staff.

The primary outcome measure was glycaemic control at 2 years follow up, measured by HbA1c (in mmol/mol, or equivalently in %).

For this study, statistical analyses were performed using SAS version 9.4 (SAS Institute Inc. Cary NC). All statistical tests were two-sided at a 5% significance level. Analyses were performed on the principle of intention to treat, including all randomized participants who provided at least one valid measure on the primary outcome post randomisation. Demographics and baseline characteristics of all participants followed up at 2 years were summarized by treatment group using descriptive statistics. Random effects mixed model was used to evaluate the effect of intervention on HbA1c at 3, 6, 9 and 24 months, adjusting for baseline HbA1c and stratification factors and accounting for repeated measures over time. Adjusted mean differences in HbA1c between two groups were estimated at each visit, by including an interaction term between treatment and month. Missing data on the outcome were taken into account in modelling based on the missing at random assumption. Both 95% confidence interval (CI) and p-value were reported. Model-adjusted estimates on the treatment difference between two groups were reported, together with 95% confidence intervals and p-values.

Results:
Of the 366 randomized participants who consented to take part in the main trial (n=183 per arm), 293 (intervention = 177 and control = 116) were eligible for follow up at 2 years. Of those not eligible, 6 had died, 3 had withdrawn and 64 control group participants were excluded due to receiving the SMS4BG intervention at the end of the

main trial. The final 2 year follow up data collection was completed in March 2019 with 2 year follow up data available for 206 participants (intervention = 127 and control = 79).The loss to follow-up (no 2 year follow up data available or unable to follow up) rate was 28% in the intervention group and 32% in the control group. The baseline characteristics of study participants are presented in Table 1.

Table 1: Baseline characteristics of participants included in 2 year follow up. Values are numbers (percentages) unless stated otherwise

Characteristic	Intervention group N=177	Control group N=116
Gender: Male	89 (50)	68 (59)
Ethnicity		
Māori	35 (20)	29 (25)
Pacific	29 (16)	8 (7)
Asian	8 (5)	7 (6)
New Zealand European	89 (50)	57 (49)
Other	16 (9)	15 (13)
Ethnicity category		
Māori/Pacific	64 (36)	37 (32)
non-Māori/non-Pacific	113 (64)	79 (68)
Diabetes type		
Type 1	63 (36)	39 (34)
Type 2	114 (64)	77 (66)
Location		
High urban	120 (68)	67 (58)
High rural/remote	57 (32)	49 (42)
Smoking status		
Smoker	28 (16)	26 (22)
Non-smoker	149 (84)	90 (78)
Treatment: On insulin	138 (78)	90 (78)
Referral source		
Primary care	71 (40)	47 (41)
Secondary care	101 (57)	68 (59)
Self-referred	5 (3)	1 (1)
Age grouping		
16-24 years	25 (14)	8 (7)
25-49 years	65 (37)	42 (36)
50-64 years	68 (38)	51 (44)
≥65 years	19 (11)	15 (13)
Age (years), mean (SD)	47 (15)	49 (15)
Time since diagnosis (years), mean (SD)	13 (11)	13 (10)

SD – Standard deviation

The baseline characteristics of the 64 control participants excluded from this study did not differ from the remaining control participants on any of the baseline characteristics except for location with a higher proportion of control participants excluded (chose to receive the intervention at the end of the main trial) living in an urban area (p=0.006).

The main treatment effect on the primary outcome is presented in Table 2. The reduction in HbA1c from baseline to 2 year follow-up was significantly greater in the intervention group compared with the control group (mean(standard deviation), -

10.2(17.5) vs. -0.7 (20.0)mmol/mol, adjusted mean difference -9.13, 95%CI [-13.52 to -4.73], p<0.001). (Table 2).

Table 2: Treatment effect on the primary outcome (HbA1c (mmol/mol)). Values are mean (SD) unless stated otherwise.

	Intervention (n=177)	**Control** (n=177)	**Un-adjusted Mean difference (95% CI)** [1]	**P value for difference**	**Adjusted Mean difference (95% CI)**[1]	**P value for difference**
Baseline mean	86.37 (17.83)	83.30 (14.80)				
Change from baseline at 9 months	-8.85 (14.84)	-3.96 (17.02)	-4.97 (-8.35 to -1.58)	0.004	-3.94 (-7.05 to -0.83)	0.013
Change from baseline at 2 years	-10.2 (17.5)	-0.7 (20.0)	-10.18 (-14.94 to -5.3)	<.0001	-9.13 (-13.52 to -4.73)	<.0001

[1] Random effects mixed model without and with adjustment for baseline outcome, diabetes type, ethnicity and region. Both treatment group and visit were included in the model with their interaction term. A random subject effect was added to account for repeated measures on same participant. SD – standard deviation. CI – confidence interval.

A decrease in HbA1c from baseline to 2 year follow-up was observed in 76% of intervention participants compared with 46% of control participants (Chi-square test, p<0.0001). At 2 years 28% of intervention and 14% of control participants HbA1c levels dropped below 65mmol/mol (p=0.02) – the level considered 'poor control' in New Zealand.

Discussion:

This long term follow up study found that the tailored theoretically based SMS diabetes self-management support programme led to not only significant improvements in glycaemic control at 2 years but a larger effect size than was seen at 9 months. This shows that the effects seen post-programme at 9 months were sustained out to 2 years, whereas the improvements in HbA1c initially seen in the control group at 9 months had disappeared at 2 years. It is well recognized that reductions in HbA1c are associated with a decrease in the risk of diabetes complications.[5] A decrease in HbA1c of 1%(11mmol/mol) has been found to result in declines in microvascular complications of 37%, myocardial infarction of 14%, and risk of death by 21%.[5] With a mean reduction in HbA1c of 10.2mmol/mol(0.93%) from baseline, and a statistically significant group difference of 9.13mmol/mol(0.84%) in favour of the intervention, the results seen in this study are clinically relevant in reducing the risk of vascular complications and death. These significant long term results, coupled with a high level of acceptability of SMS4BG reported by the majority of participants[4] support the implementation of SMS4BG to supplement clinical practice.

There are few other long term follow up studies of RCTs of diabetes self-management support programmes[6] and, in particular, none in SMS interventions[7-9] - attesting to the significance of these findings. Although there is some evidence supporting clinically significant changes in HbA1c at long term follow up of in-person diabetes self-management programmes,[10-11] our results showing positive findings from this type of

programme utilising a delivery modality with fewer access barriers than in-person programmes is important.

This follow up study is based on a high quality RCT with an objectively measured primary outcome that is commonly used in diabetes trials, allowing comparison with other programmes. However it is also a pragmatic community-based study design that measures the potential impact in the way the intervention would be delivered if it was implemented on a large scale, with little contact with researchers and alongside usual diabetes care.

We particularly focused on those with poorly controlled diabetes as the group with the greatest need for support and assistance, and where a change in long term control could have the greatest impact. The trial sample included a high proportion of those on insulin and over a third were from rural areas. The sample also has a reasonably high proportion of Māori and other minority ethnicity groups who are at highest risk of diabetes and poor outcomes from the complications of diabetes.

The intervention itself is based on theoretical constructs and techniques that have been shown to be helpful in behaviour change. It builds on our previously successful developments in mHealth for behaviour change, as well as effective diabetes self-management education principles. Importantly, it had high end-user engagement throughout the development process; it was developed with people who have diabetes and clinicians working with these people, as well as a Māori Advisory Group. Feedback from these people was used in the iterative development from conceptualization, pre-testing, pilot testing and through to the final programme that was delivered in the trial. As diabetes is a condition requiring constant ongoing management utilizing a technology which reaches people in their everyday lives could have added benefit over traditional in person programmes delivered away from a patients usual environment.

The main limitation to this follow up study is the exclusion of those in the control group who subsequently received the programme at the end of the main trial. While this was considered a ‘good’ thing to offer the control group participants and was appreciated by those participants, it later interfered with our ability to include all randomized participants in the 2 year follow up analysis. In comparing those control group participants who received the intervention with those who didn’t, the only significant difference is a greater proportion of excluded control participants being from urban areas which could indicate a potential source of bias in these results.

SMS4BG provides a low-cost, scalable solution for increasing the reach of diabetes self-management support. Now that the longer term effect has been established, the case for offering people with diabetes the option of such simple ongoing support is more compelling. Text messaging is simple, cheap, and very acceptable to our population in need. Text messaging is also very accessible – anyone with a mobile phone is able to receive text messages regardless of phone, plan or credit – making it ideal for reaching into population groups without other reliable communication methods. The next steps in research should be to investigate whether large scale implementation of such programmes can have an impact on reducing health inequalities for priority populations.

This study shows that improvements in glycaemic control resulting from a tailored and automated SMS self-management support programme in adults with poorly controlled diabetes are sustained at 2 years. These results provide support for implementation of the programme to supplement current practice.

Project outputs to date:

- A manuscript on the study findings has been prepared. This was first submitted to the BMJ but was not accepted and so has been revised and submitted to Diabetes Care.
- The results of the study have been shared with the Ministry of Health and Waitematā DHB to supplement the business cases currently being considered for implementation of SMS4BG into practice.
- This study has been described in the following conference presentations:
    - Dobson R. Implementation Issues: Feedback from the Sector. MedTech Core Conference. 3rd July 2019, Auckland, New Zealand. (Invited oral presentation)
    - McCool, J. Whittaker, R. Paton, C. Dobson R. Agarwal, S. Assessing the Impact of mHealth in Low Resource Settings. Satellite Session at the 2019 CUGH Conference. 7 March 2019. Chicago, US. (Oral Presentation)
    - Dobson R, Whittaker R, Maddison, R. Taking mHealth from research to practice: Perspectives of health sector end-users. ISRII: International Society for Research on Internet Interventions 10th Scientific Meeting 12-14th February 2019, Auckland (Oral symposium presentation)
    - Dobson R, Whittaker R, Armstrong D, Maddison R, Murphy R, McNamara C, Cutfield R, Khanolkar M, Shepherd M, Jiang Y. mHealth from Research to Implementation: The SMS4BG example. HINZ: Health Informatics New Zealand Conference, 21-23 November 2018, Wellington, New Zealand (Oral presentation)

An abstract will be prepared of the results for submission for presentation at the 2020 NZSSD Annual Scientific Meeting.

References:

1. Dobson R, Carter K, Cutfield R, Hulme A, Hulme R, McNamara C, et al. Diabetes Text-Message Self-Management Support Program (SMS4BG): A Pilot Study. JMIR mHealth uHealth. 2015;3(1):e32
2. Funnell MM, Brown TL, Childs BP, Haas LB, Hosey GM, Jensen B, et al. National standards for diabetes self-management education. Diabetes Care. 2009;32(Supplement 1):S87-S94.
3. Dobson R, Whittaker R, Jiang Y, Shepherd M, Maddison R, Carter K, et al. Text message-based diabetes self-management support (SMS4BG): study protocol for a randomised controlled trial. Trials. 2016;17(1):179
4. Dobson R, Whittaker, R. Jiang, Y. Maddison, R. Shepherd, M. McNamara, C. Cutfield, R. Khanolkar, M. Murphy, R. Effectiveness of text message based, diabetes

self management support programme (SMS4BG): two arm, parallel randomised controlled trial. BMJ 2018;361:k1959.
5. Stratton IM, Adler AI, Neil HAW, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): Prospective observational study. BMJ. 2000;321(7258):405-12.
6. Minet L, Møller S, Vach W, Wagner L, Henriksen JE. Mediating the effect of self-care management intervention in type 2 diabetes: a meta-analysis of 47 randomised controlled trials. Patient education and counseling. 2010 Jul 1;80(1):29-41.
7. Saffari M, Ghanizadeh G, Koenig HG. Health education via mobile text messaging for glycemic control in adults with type 2 diabetes: A systematic review and meta-analysis. Primary care diabetes. 2014;8(4):275-85.
8. Dobson R, Whittaker R, Pfaeffli Dale L, Maddison R. The effectiveness of text message-based self-management interventions for poorly-controlled diabetes: a systematic review. Digital health. 2017 Nov;3:2055207617740315.
9. Hamine S, Gerth-Guyette E, Faulx D, Green BB, Ginsburg AS. Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. Journal of medical Internet research. 2015;17(2):e52.
10. Speight J, Amiel SA, Bradley C, Heller S, Oliver L, Roberts S, Rogers H, Taylor C, Thompson G. Long-term biomedical and psychosocial outcomes following DAFNE (Dose Adjustment For Normal Eating) structured education to promote intensive insulin therapy in adults with sub-optimally controlled Type 1 diabetes. Diabetes research and clinical practice. 2010 Jul 1;89(1):22-9.
11. Ko SH, Song KH, Kim SR, Lee JM, Kim JS, Shin JH, Cho YK, Park YM, Jeong JH, Yoon KH, Cha BY. Long-term effects of a structured intensive diabetes education programme (SIDEP) in patients with Type 2 diabetes mellitus—a 4-year follow-up study. Diabetic medicine. 2007 Jan;24(1):55-62.