Improving Adherence to Weight-Loss Medication (Liraglutide 3.0 mg) Using Mobile Phone Text Messaging and Healthcare Professional Support

Ang Li [iD] *[1,2], Michelle Cunich[1,2], Nicholas Fuller[1], Katrina Purcell[3], Allanah Flynn[3], and Ian Caterson[1]*

Background: Adherence to weight-loss medication is suboptimal, leading to poor health outcomes. Short message service (SMS) can potentially improve adherence.

Methods: A total of 3,994 participants with overweight or obesity in Australia receiving Saxenda® (liraglutide 3.0 mg) were enrolled from September 1, 2017, to February 28, 2018, through doctors, pharmacists, or websites and were randomly assigned to receive none, three, or five SMS per week. Participants were additionally offered a face-to-face consultation with a diabetes educator or a call from a dietitian. Medication adherence was measured as whether the total scripts claimed were at least as many as the total claims expected by March 31, 2018, and was modeled adjusting for age, sex, baseline BMI, residential region, enrolment channel, the total number of SMS, and additional patient support.

Results: Participants receiving five SMS (OR, 6.25; 95% CI: 4.28-9.12) had greater adherence than those receiving three SMS (OR, 3.67; 95% CI: 2.67-5.03) or zero SMS per week. The effectiveness of SMS on adherence decreased as participants received more SMS over time. Moreover, the odds of adhering to liraglutide were higher for participants enrolled with pharmacists compared with those enrolled with doctors (OR, 2.28; 95% CI: 1.82-2.86) and for participants who received a face-to-face consultation (OR, 3.10; 95% CI: 1.82-5.29) or a call (OR, 1.31; 95% CI: 1.02-1.68) compared with those who received no extra support.

Conclusions: Integration of SMS into routine clinical practice should consider not only the frequency and content of reminders but also additional patient support to achieve higher and more sustained adherence to medication and health behavior changes.

Study Importance

What is already known?

► One of the major causes of treatment failure is patient noncompliance.

► The use of SMS increases medication adherence and treatment effectiveness for a range of chronic diseases.

What does this study add?

► SMS reminders can improve medication adherence of participants with overweight or obesity prescribed weight-loss medication (liraglutide 3.0 mg), with five SMS per week leading to a better improvement than three SMS per week.

► The effectiveness of SMS reminders on medication adherence decreased as the number of text messages received increased over time.

► Participants who received face-to-face consultations or phone calls had greater medication adherence. Participants who unsubscribed from SMS reminders showed increased adherence with face-to-face consultations.

How might these results change the focus of clinical practice?

► Successful integration of SMS into routine clinical practice needs to consider not only the frequency and content of reminders but also whether, what, and when additional patient support should be provided. Patient support can be particularly useful in cases of stimulus fatigue or withdrawal from digital alerts.

Introduction

Overweight and obesity are a major public health issue worldwide. According to the World Health Organization, more than 1.9 billion adults (39%) aged 18 years and over had overweight, and of those, more than 650 million adults (13%) had obesity in 2016 (1). People

with overweight or obesity have higher rates of mortality and illness than people of normal weight, and high BMI is a risk factor for several chronic conditions, including cardiovascular disease, type 2 diabetes, chronic kidney disease, some musculoskeletal conditions, and some cancers (1). In Australia, the prevalence of overweight and obesity in those aged 15 and over has increased from 57% among adults in 1995-1996 to 67.0% in 2017-2018 (2).

While a range of medical treatments are available to assist with the management of chronic conditions such as overweight and obesity, one of the major causes of treatment failure is patient noncompliance (3). Studies evaluating medication regimens have found that patients took only about half of the prescribed doses and discontinued medication as prescribed over time (4). Low levels of adherence can be a serious problem that may cause therapeutic failure, reduce health-related quality of life, and increase health care costs (5,6).

With the global health and research community working toward improvements in patient adherence, short message service (SMS), along with wide mobile phone ownership among the population, is increasingly used as an intervention to optimize the benefits of medication regimens in the context of limited resources. Among factors associated with poor compliance, forgetfulness, lack of motivation, low health literacy, and misunderstanding of the prescription are common factors reported by patients (7,8). SMS reminders deliver text messages to patients with chronic diseases that enable continuous monitoring, behavioral changes, and personalized interventions at low cost without time or geographical constraints (9).

Numerous studies have shown that the use of SMS increases medication adherence and treatment effectiveness in a range of chronic diseases, including asthma, diabetes, cardiovascular disease, HIV infection, and liver transplantation (10,11). However, the efficacy of SMS interventions can be dependent on the specific content of text messages (11), the frequency (9), the interactivity (12) and the specific chronic disease evaluated. The use of text messages has also emerged as an intervention option to promote healthy behaviors for weight loss and maintenance. The literature evaluating the effectiveness of SMS for weight loss has so far focused on dietary habits and physical activity only (13). One study in the United States revealed that participants who received daily messages related to behavioral and dietary strategies for weight control lost significantly more weight than the comparison group for a sample of men and women with overweight (14). Another study also suggested that a clinically significant effect was observed among participants receiving promotion and prevention text messages (15).

To our knowledge, no studies have evaluated the efficacy of text messages in promoting adherence for weight-loss medications. While patients who received active antiobesity drugs were significantly more likely to achieve a clinically significant amount of weight loss (16), adherence to weight-loss medications was reported to be poor in a general population (17). For example, in a US study using a large sample of health maintenance organization users, the average adherence duration of orlistat, a gastrointestinal lipase inhibitor, and sibutramine, a centrally acting monoamine reuptake inhibitor, was only 2.1 months and 2.9 months, respectively (17). Studies have suggested that better adherence to diabetes medication and weight-loss programs was associated with improved clinical outcomes, such as glycemia control and healthy behaviors (18,19), which highlights the need for the development of effective tools to promote medication or program adherence for adults with overweight or obesity.

Other factors such as poor practitioner-patient relationship and lack of social support are also commonly reported barriers to achieving good adherence to medication (7,8). In a study that investigated a weight-reduction intervention that involved dietary change, behavioral modification, and physical activity, participants who failed to achieve a clinically significant weight loss were more likely to report a lack of personal motivation and insufficient results for their efforts as the main barriers (20). Other studies have indicated that the level of engagement on the topic of obesity between health care professionals (HCPs) and patients is often suboptimal, which can have an adverse effect on the management of obesity (21). Therefore, text messaging that reminds patients about medication instructions and encourages behavioral changes may need to be implemented along with strategies that provide HCP patient support and establish a partnership with patients to achieve better adherence.

According to the World Health Organization, there are five dimensions to adherence to medication regimes: social/economic factors, provider-patient/health care system factors, condition-related factors, therapy-related factors, and patient-related factors (22). This suggests that improvements in adherence involves not only preventing forgetfulness and increasing motivation (patient-related factors) but also having social support and receiving communication on the benefits, instructions, and side effects of medication (social and provider-patient factors). The current study contributes to the literature on digital interventions for medication adherence by exploring the effectiveness of SMS reminders in combination with HCP patient support. The findings have implications for the potential usefulness of electronic-based adherence-promoting strategies and patient support from health care providers that may be used to assist patients with adherence to therapy or medication prescription and, ultimately, improve patient health outcomes and quality of life.

The aim of the current study was to examine the effectiveness of SMS reminders, with and without additional patient support, on the weight-loss medication adherence of patients with overweight or obesity prescribed Saxenda (liraglutide) in Australia from September 1, 2017, to March 31, 2018. Patient-level data were drawn from a structured commercial program provided by Novo Nordisk for patients receiving liraglutide injection 3.0 mg. The patient support program offered weekly emails and SaxendaCare® website access for all participants and face-to-face consultation and phone support for some participants. All participants enrolled in the program were randomized to receive zero, three, or five SMS per week. With consents obtained from participants, deidentified data were reviewed for the evaluation of the effectiveness of SMS reminders, in conjunction with a structured patient support program, in overcoming poor weight-loss medication adherence in the community.

Methods

The study sample comprised participants who enrolled in the SaxendaCare Patient Support Program (PSP) between September 1, 2017, and February 28, 2018 (prescription claims followed until March 31, 2018). SaxendaCare is a free PSP offered by Novo Nordisk and provided to patients who have been prescribed Saxenda, a Therapeutic Goods Administration approved prescription injectable weight-loss medicine. The injectable prescription medicine

assists adults with overweight (BMI ≥ 27) with weight-related co-morbidities or obesity (BMI ≥ 30) to lose weight and maintain weight loss. All patients who had been prescribed liraglutide by their doctors were invited to enroll in the PSP program through the prescribing doctor (general practitioner, endocrinologist, or other specialist), the Saxenda network pharmacists, or the SaxendaCare patient website. Around 60% to 70% of the patients participated in the PSP.

The process of patient enrollment in the PSP is presented in Figure 1. During the period from September 1, 2017, to February 28, 2018, 3,994 participants enrolled in the PSP, of which 1,604 registered via doctors, 1,739 registered via pharmacists, and 651 registered via website. Participants were observed, on average, for 15.54 weeks, with a median of 16.14 weeks and a range from 4.43 weeks to 29.43 weeks. All participants enrolled in the PSP were offered free NovoFine needles, were sent weekly support emails, and had access to the SaxendaCare website.

Additionally, participants who enrolled with prescribing doctors were offered an outbound call from an accredited dietitian or a face-to-face consultation with HCPs (Saxenda credentialed diabetes educators), and participants who enrolled with Saxenda network pharmacists were offered an outbound call from an accredited dietitian. Of those who enrolled with a doctor, 86 participants received a face-to-face consultation and 284 received an outbound call; of those who enrolled with pharmacists, 297 received an outbound call.

Participants who registered into the PSP, regardless of their enrollment channel (prescribing doctors, the Saxenda network pharmacists, or the SaxendaCare patient website) were randomized to receive zero, three, or five SMS per week by random sequence generation using the customer relationship management system (SalesForce). Participants were concealed from group allocation during enrollment, and HCPs and researchers were blinded to group allocation
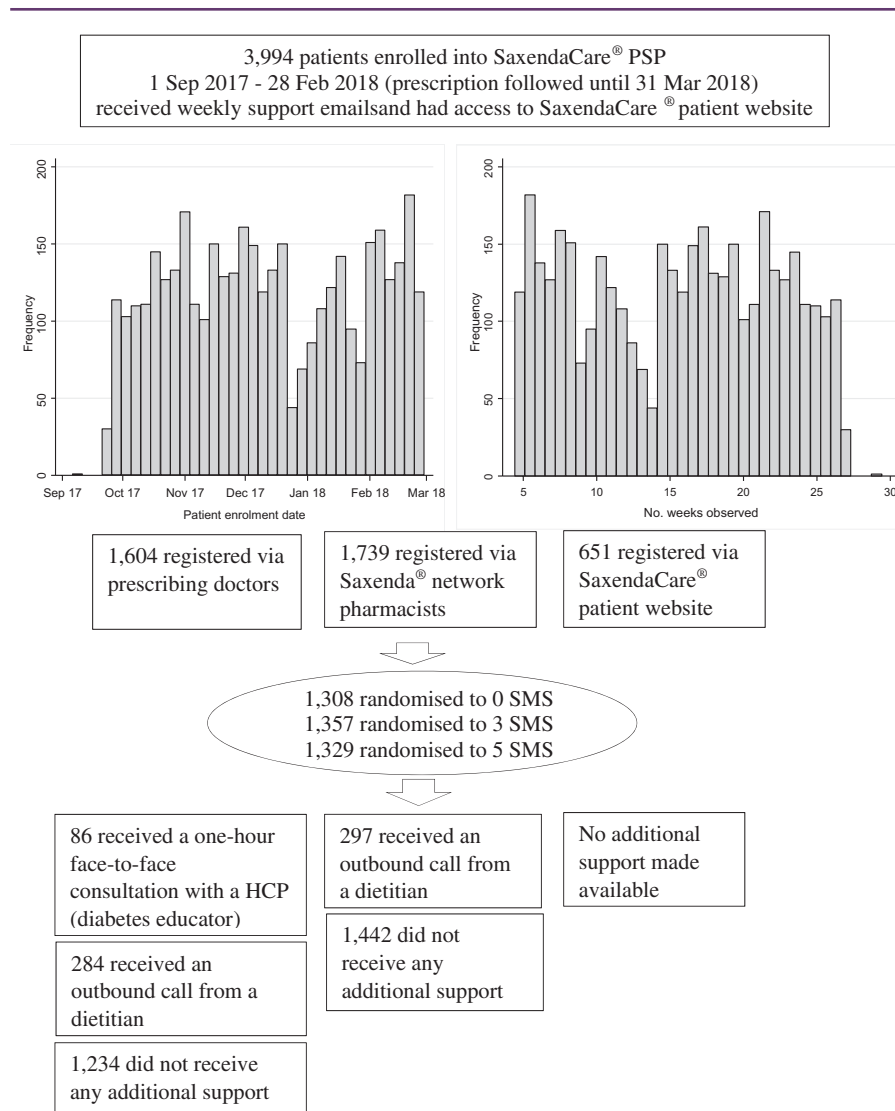

Figure 1 Study flowchart.

after randomization. Among the 3,994 participants, 1,308 (32.75%) received zero SMS per week, 1,357 (33.98%) received three SMS per week, and 1,329 (33.27%) received five SMS per week. Information on age, sex, BMI at enrollment (weight/height^2), and residential state or territory in Australia was collected for all participants enrolled in the SaxendaCare PSP once the participants had given permission. Age was not available for participants who registered through the SaxendaCare patient website, and thus an indicator of missing age was included.

For all patients enrolled in the PSP between September 1, 2017, and February 28, 2018, across the three SMS groups (i.e., zero, three, or five SMS per week), the total number of Saxenda scripts claimed and the total number of months they were observed for the study were recorded between September 1, 2017, and March 31, 2018. Refills typically occurred once a month. Medication adherence was determined by quantifying the total number of scripts claimed relative to the total number of periods under observation; it was defined as a binary variable that took the value of one if at least one script was claimed every 1 or 2 months and zero otherwise, that is, at least $n = 1$ total claims for n total months recorded (n total claims expected) at the end of the study.

The current study used a sample of participants who were routinely enrolled in the PSP (free NovoFine needles, weekly support emails, access to the SaxendaCare website, and an additional outbound call from an accredited dietitian and/or a face-to-face consultation with HCPs), in conjunction with a SMS intervention, when prescribed liraglutide. At enrollment into the program, consents were sought and signed by participants for the use of information, including medication and support services by a commissioned third party for the purposes of program improvement. In line with consents given at time of enrollment, deidentified and aggregated data were collected and reviewed.

The text messages were developed by a team of medical and health professionals experienced in treating patients with overweight or obesity based on theoretically driven and empirically supported evidence (10,23-39). The topics were organized into six sections, including medicine, motivation, nutrition, activeness, coping strategies, and weight management. The text messages contained a mix of educational and motivational content and incorporated self-determination theory and cognitive behavior therapy (28,29,40). The text messages were personalized with the person's name inserted and different greetings according to the time and day the SMS was sent, and they had unique content each time to ensure the medium was kept fresh and supportive to the patient receiving the message. The messages were composed in a preset list and sent out automatically via SalesForce. Table 1 presents the cumulative number of SMS sent to participants in the three and five SMS groups, weekly topics, the number of participants receiving each individual topic, sample messages, and corresponding references at each week.

Another novel aspect of the SMS program is the variety in the day and time of each message and corresponding content to keep participants engaged. The day and time at which each SMS was sent are shown in Table 1. Each message was sent after a set time elapsed post enrollment, providing patients with specific messages based on their enrollment date and weight-management journey. For example, week 10, Monday at 11 AM, "Good morning <first name>, we're going to look at ways to stay on track this week. First up: managing

social eating. Reply STOP to opt out"; and week 39, Saturday at 6 PM, "Hi <first name>, have you moved more today? Maintaining lifestyle changes is central for long-term maintenance of weight loss. Reply STOP to opt out." Patients could choose to discontinue SMS reminders at any time, and for these patients, the opt-out status was recorded.

The sample size calculation was based on an α of 0.05, a power of 0.95, and an effect size of Cohen's *d* of 0.32, with medication adherence as the primary outcome. Accounting for 40% of BMI misreported or missing, at least 420 would be required to detect group differences in adherence. Descriptive statistics were presented as the percentage of patients in each age group, sex, BMI class, enrollment channel, and type of support utilized across zero, three, or five SMS groups. Logistic regression analysis was undertaken to assess the effectiveness of SMS reminders and patient support types in improving adherence to liraglutide. The covariates included SMS group, age group, sex, BMI class, place of residence (Australian state or territory), enrollment channel, type of additional patient support received, the total number of SMS received, and opt-out status. Opt-out status was defined as one if the participant did not discontinue the SMS reminders and zero if the participant unsubscribed from the SMS reminders or did not receive any SMS reminders. Given that patients were enrolled through different channels, the heterogeneity in the effectiveness of the SMS intervention on medication adherence was examined by interacting SMS groups with enrollment channels. The impact of the SMS reminders when additional patient support types were in place (a face-to-face HCP consultation, a phone call from a dietitian, or no additional support) was estimated by interacting SMS groups with support types received. Whether the number of SMS received by the participant affected the effectiveness of SMS was also examined with the interaction between SMS groups and the number of SMS. The level of significance was specified at the 5% level. All analyses were conducted with Stata version 14.0 (StataCorp LP, College Station, Texas).

Results

The characteristics of patients in this study are summarized in Table 2. Among the SaxendaCare PSP participants, 79.74% were female, 86.92% had obesity, 40.16% registered through prescribing doctors (mostly general practitioners), 43.54% registered through the Saxenda network pharmacists, and 16.30% registered through the SaxendaCare patient website. The mean age of participants was 46.09 years with an SD of 12.53, and the mean BMI was 36.88 with an SD of 7.52. There were no significant differences between SMS groups with respect to demographic and clinical characteristics.

Table 3 presents the results from estimating the effectiveness of SMS on treatment adherence using a logistic regression analysis for a sample of participants who had overweight or obesity at enrollment (BMI ≥ 27). The SMS groups were interacted with enrollment channel and patient support types to examine the variation in the response of participants to the SMS intervention. Odds ratios (OR) and 95% CIs for the SMS group, enrollment channel, and type of patient support are reported.

The results for all participants in Table 3 column 1 show that Saxenda medication adherence was greater for participants who received five SMS (OR, 6.25; 95% CI: 4.28-9.12) and three SMS (OR, 3.67; 95%

TABLE 1 Weekly topics and example messages

Month	Week	No. SMS 3 SMS	No. SMS 5 SMS	No. participants 3 SMS	No. participants 5 SMS	Topic	Day range	Time range	Example SMS	Reference
0	0	1	1	1328	1356	Registration				
1	1	2-4	2-6	1319	1340	Getting started	Three or five days out of Mon, Tue, Wed, Thu, Fri, Sat, Sun	Three or five times out of 08:30, 08:45, 09:00, 09:15, 09:30, 10:00, 10:15, 10:30, 10:45, 11:00, 11:45, 12:00, 12:15, 12:30, 12:45, 13:00, 14:00, 15:00, 16:00, 16:30, 17:00, 17:30, 18:30, 19:00, 19:30, 19:45, 20:00, 20:15	Good morning <<first name>>! Congratulations for starting treatment. The SaxendaCare program will be here to coach you through treatment and beyond. Reply STOP to opt out.	[28,29]
1	2	5-7	7-11	1118	1215	Taking Saxenda			Good morning. It's important to follow your Doctors instructions on increasing your dose of medication & managing potential side effects. Nausea (feeling sick) is most common when starting Saxenda, but decreases over time. Use Saxenda only as directed by your healthcare professional. Reply STOP to opt out	
1	3	8-10	12-16	1056	1163	Understand obesity			You're now in Week 3. While you might be focused on weight loss, it's important to remain hydrated & identify sustainable diet & lifestyle changes. Reply STOP to opt out	[23,28,29]
1	4	11-13	17-21	978	1111	Understand core values			Hi <<first name>>. This week try to hold the reasons why you started Saxenda at the front of your mind. Reply STOP to opt out	[24]
2	5	14-16	22-26	898	980	Manage expectation			Good morning, this week the texts we send will look at expectations – of yourself and your body. Reply STOP to opt out	[28,30,31]
2	6	17-19	27-31	812	891	Weight stigma			Hi <<first name>>, this week we'll message you with ways to combat weight stigma, turning you into an ultimate stigma ninja! Reply STOP to opt out.	[10,31,32]
2	7	20-22	32-36	734	857	Reach out for support			Wow–this is a late text! Happy Monday. This week we're focusing on when to recognise you need to reach out for support. Reply STOP to opt out	[10]
2	8	23-25	37-41	704	785	Small changes			Hi <<first name>>. This week we'll be looking at how you can identify small changes to help you achieve a healthier sustainable weight. Reply STOP to opt out	[31,33]
3	9	26-28	42-46	619	722	Managing thinking			Good morning <<first name>>, welcome to month 3. This week we're going to think about your thinking. Hmmm what? More tomorrow. Reply STOP to opt out	[31]

TABLE 1 (continued).

Month	Week	No. SMS		No. participants		Topic	Day range	Time range	Example SMS	Reference
		3 SMS	5 SMS	3 SMS	5 SMS					
3	10	29-31	47-51	562	626	Coping emotion			Monday, Monday! This week we're looking at effective ways to manage your strong emotions, negative and positive. Reply STOP to opt out	[10,25]
3	11	32-34	52-56	542	596	Stay on track			Good morning <<first name>>, we're going to look at ways to stay on track this week. First up: managing social eating. Reply STOP to opt out	[28,29]
3	12	35-37	57-61	497	536	Navigate setbacks			Hi <<first name>>, this week you'll be working on ways to bolster yourself when you have a slip-up & start afresh. Reply STOP to opt out	[25]
4	13	38-40	62-66	483	515	Encourage assessment			Good morning <<first name>>, you've made it to month 4! This week is about taking stock of all you've achieved so far. Reply STOP to opt out	
4	14	41-43	67-71	427	452	Hunger & satiety			Good evening <<first name>>, this week we'll be looking at ways to manage hunger and fullness (satiety) - staying on track is about steering skillfully between both. Reply STOP to opt out.	[34,35]
4	15	44-46	72-76	374	432	Mindful eating			Hi <<first name>>, this week we're going to s l o w things down and work on bringing ourselves back to the present moment - it's all about eating & enjoying food mindfully. Reply STOP to opt out.	[37]
4	16	47-49	77-81	329	347	Hunger & cravings			Hi <<first name>>, this week you'll be identifying ways to cope with hunger and cravings, to help on your journey of weight management. Reply STOP to opt out	[28,35]
5	17	50-52	82-86	292	321	Sleep & nutrition			Good afternoon! How is your sleep at the moment? This week is all about making sure you're getting enough sleep to maintain good health. Reply STOP to opt out	[26]
5	18	53-55	87-91	241	268	Food needed vs tempted			Hi <<first name>>, we hope this week will be a great week! This week we're taking a helicopter view of your eating: the food your body needs vs. food that pops up & tempts you. Reply STOP to opt out	[28,38]

TABLE 1 (continued).

| | | No. SMS | | No. participants | | | | | | |
Month	Week	3 SMS	5 SMS	3 SMS	5 SMS	Topic	Day range	Time range	Example SMS	Reference
5	19	56-58	2-96	212	218	Controlling portions			Good morning <<first name>>. Two sayings you may have heard: size matters and less is more! This week is all about portion sizes! Reply STOP to opt out	[27], SaxendaCare
5	20	59-61	97-101	185	189	Plate method			Good morning! This week we're looking at the Plate Method - filling a normal plate with 1/2 veggies, 1/4 lean protein and 1/4 healthy carbohydrates. Reply STOP to opt out	[40], SaxendaCare
6	21	62-64	102-106	140	144	Dealing with barriers			Morning <<first name>>. Do you sometimes feel there's something holding your health goals back? You're not alone. This week we're tackling roadblocks. Reply STOP to opt out	[28,31]
6	22	65-67	107-111	93	101	Starting active lifestyle			We've all gotta start somewhere, right? This week: starting your active lifestyle if you haven't already! Reply STOP to opt out	[28,29]
6	23	68-70	112-116	61	64	Stick with activity plan			Good morning <<first name>>, this week is a great week to fit-in exercise. There will never be a perfect time so let's jump in with your plan from yesterday. Reply STOP to opt out	[28,31]
6	24	71-73	117-121	35	22	Overcome barriers			Good afternoon <<first name>>! You're approaching the end of month 6. This week we're going to jump the barriers in your way of maintaining activity. Reply STOP to opt out	[28], SaxendaCare

CI: 2.67-5.03) per week than it was for those who did not receive any SMS, controlling for demographic and clinical characteristics as well as enrollment channels and patient support received. Enrollment channels and additional types of support received were also important factors explaining medication adherence. The odds of adhering to Saxenda medication were much higher for participants who were enrolled with pharmacists compared with those who were enrolled with doctors (OR, 2.28; 95% CI: 1.82-2.86) and for participants who received a face-to-face consultation with an HCP (OR, 3.10; 95% CI: 1.82-5.29) or a phone call from a dietitian (OR, 1.31; 95% CI: 1.02-1.68) compared with those who received no extra support. Note that there was no significant difference in adherence to the medication regimen by demographic and clinical characteristics at the 5% significant level.

Participants in the five SMS group had the greatest adherence, followed by those in the three and zero SMS groups (Table 2, column 2). Among

participants who were enrolled through doctors, those who received five SMS (OR, 6.91; 95% CI: 4.50-10.62) or three SMS (OR, 3.36; 95% CI: 2.30-4.90) per week had better adherence to the medication, and those who had a face-to-face HCP consultation (OR, 3.32; 95% CI: 1.94-5.69) or an outbound call from a dietitian (OR, 1.76; 95% CI: 1.30-2.39) also showed significant improvement in adherence. Similarly, receiving five and three SMS per week significantly increased adherence for participants who registered through pharmacists (OR, 4.44; 95% CI: 2.67-7.52; OR, 3.40; 95% CI: 2.06-5.63) (Table 2, column 3) or patient website (OR, 6.96; 95% CI: 3.81-12.70; OR, 4.77; 95% CI: 2.76-8.24) (Table 2, column 4).

The results for the effectiveness of SMS reminders by the type of patient support utilized (Table 2, columns 5, 6, and 7) also show that participants who received five SMS had greater adherence than those who received three SMS per week. For participants who received support in the form of a 1-hour face-to-face consultation with a HCP

TABLE 2 Participant characteristics

	All participants		0 SMS		3 SMS		5 SMS	
	n = 3,994		*n* = 1,308		*n* = 1,357		*n* = 1,329	
	n	%	*n*	%	*n*	%	*n*	%
Age								
Age ≤29	347	8.69	115	8.79	121	8.92	111	8.35
Age 30-39	676	16.93	227	17.35	218	16.06	231	17.38
Age 40-49	1006	25.19	349	26.68	324	23.88	333	25.06
Age 50-59	813	20.36	250	19.11	289	21.30	274	20.62
Age 60+	496	12.42	152	11.62	175	12.90	169	12.72
Sex								
Female	3185	79.74	1042	79.66	1079	79.51	1064	80.06
Male	809	20.26	266	20.34	278	20.49	265	19.94
BMI								
25<=BMI<30 (overweight)	308	13.08	111	14.59	109	13.56	88	11.15
BMI>=30 (obesity)	2046	86.92	650	85.41	695	86.44	701	88.85
Enrolment								
Doctor registration	1604	40.16	497	38.00	570	42.00	537	40.41
Pharmacy registration	1739	43.54	597	45.64	558	41.12	584	43.94
Website registration	651	16.30	214	16.36	229	16.88	208	15.65
Support service								
HCP consultation	86	2.15	24	1.83	28	2.06	34	2.56
Outbound call	585	14.65	197	15.06	196	14.44	192	14.45
No additional support	882	22.08	267	20.41	299	22.03	316	23.78
State								
ACT Australian Capital Territory	53	1.33	13	0.99	24	1.77	16	1.20
NSW New South Wales	1560	39.06	525	40.14	526	38.76	509	38.30
NT Northern Territory	21	0.53	6	0.46	10	0.74	5	0.38
QLD Queensland	751	18.80	229	17.51	257	18.94	265	19.94
SA South Australia	266	6.66	91	6.96	93	6.85	82	6.17
TAS Tasmania	59	1.48	21	1.61	20	1.47	18	1.35
VIC Victoria	954	23.89	309	23.62	328	24.17	317	23.85
WA Western Australia	330	8.26	114	8.72	99	7.30	117	8.80

TABLE 3 Odds ratio estimates on effectiveness of SMS by enrollment channel and patient support

	All patients	Enrollment channel			Patient support type		
		Doctors	Saxenda network pharmacist	Saxenda patient website	Face-to-face consultation with a HCP	Phone call from a dietitian	No extra support
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
SMS (base: 0 SMS)							
3 SMS	**3.67**	**3.36**	**3.40**	**4.77**	1.12	**2.83**	**3.92**
	(2.67-5.03)	(2.30-4.90)	(2.06-5.63)	(2.76-8.24)	(0.27-4.53)	(1.57-5.11)	(2.81-5.48)
5 SMS	**6.25**	**6.91**	**4.44**	**6.96**	**6.28**	**6.86**	**5.98**
	(4.28-9.12)	(4.50-10.62)	(2.62-7.52)	(3.81-12.70)	(1.77-22.31)	(3.70-12.72)	(4.03-8.86)
Enrollment (base: doctor)							
Saxenda network pharmacist	**2.28**	NA	NA	NA	NA	1.15	**2.79**
	(1.82-2.86)					(0.72-1.84)	(2.16-3.60)
Saxenda patient website	1.42	NA	NA	NA	NA	NA	**1.54**
	(0.96-2.09)						(1.04-2.29)
Patient support (base: no extra support)							
Face-to-face consultation with a HCP	**3.10**	**3.32**	NA	NA	NA	NA	NA
	(1.82-5.29)	(1.94-5.69)					
Phone call from a dietitian	**1.31**	**1.76**	0.74	NA	NA	NA	NA
	(1.02-1.68)	(1.30-2.39)	(0.48-1.13)				
No observations				2,354			

Logit models performed adjusting for age, sex, BMI class, residential states/territories, and total number of SMS received. Odds ratios and 95% CIs reported. Estimates in bold indicate significance at 5% level.
NA, not applicable.

(Table 2, column 5), the odds of adherence was 6.28 (95% CI: 1.77-22.31) times greater for the five SMS group than the odds for the zero SMS group. For those receiving a phone call from a dietitian (Table 2, column 6), adherence to Saxenda medication was greater in five SMS (OR, 6.86; 95% CI: 3.70-12.72) and three SMS (OR, 3.92; 95% CI: 2.81-5.48) groups. When no additional patient support options were received by participants (Table 2, column 7), the medication adherence was significantly improved with five SMS (OR, 5.98; 95% CI: 4.03-8.86) and three SMS (OR, 3.92; 95% CI: 2.81-5.48) per week.

The variation in the effect of SMS reminders on medication adherence across the number of SMS reminders is examined in Figure 2. The adjusted predictions of medication adherence for three and five SMS groups were computed over time as the number of SMS reminders received by the participants increased from 1 to 71 messages for the three SMS group and 1 to 121 for the five SMS group. Figure 2 shows that as the number of SMS reminders increased over time, the medication adherence decreased and the SMS intervention became less effective. The probability of adherence for the three SMS group reduced more sharply than that for the five SMS group.

A series of sensitivity analyses were performed to examine the model specification (Table 4). First, a model including participants with and without BMI was estimated to check the effect of participants with missing BMIs in biasing the results (column 1). Second, medication adherence for participants in the SMS groups who unsubscribed the text messages was measured at the time of discontinuance instead of the end of the study to test the robustness of the time point when adherence was measured (column 2). Third, medication adherence was defined as whether the scripts claimed were at least as many as the refills expected (i.e., months observed) (column 3) and as a percentage of the refills expected that were actually claimed (refills expected/refills claimed) (column 4). These two analyses were used

to check the sensitivity of the adherence measure. Next, models were estimated separately for participants who continued with the text messaging (column 5) and participants who withdrew from the text messaging (column 6). Lastly, the study window was restricted to the first 4 months to allow all participants to be observed for at least 3 months.

The findings in the sensitivity analyses overall remained robust to changes in model specifications. In addition, the SMS intervention showed stronger effectiveness for a sample of subscribers who completed the SMS subscription and no effectiveness for a sample of unsubscribers who withdrew from the SMS reminders. Importantly, for participants who unsubscribed from SMS reminders, having a face-to-face consultation with HCP was significantly associated with an increase in adherence to medication (OR, 3.20; 95% CI: 1.69-6.08).

Discussion

This study examined the effectiveness of a commercial SMS intervention, along with a structured patient support program, in improving medication adherence of participants prescribed the weight-loss medication Saxenda (liraglutide 3.0 mg). The results indicated that SMS reminders improved adherence for weight-loss medication in patients with overweight or obesity, and receiving five SMS per week led to a better improvement in medication adherence than three SMS per week. The majority of previous studies delivered SMS daily, weekly, or tailored to the participants' preference or dosage (11). While some studies have found that daily messages can be considered intrusive compared with weekly messages (9), other studies have found no significant difference between daily and less frequent text messages (41). The current study's investigation on the impact of different frequencies with which SMS were sent complements the
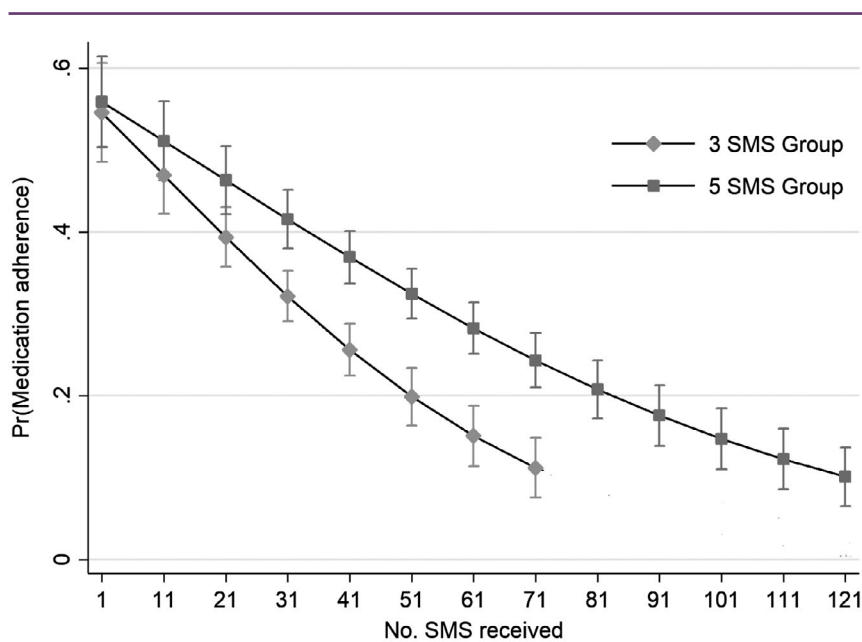

Figure 2 Adjusted prediction on medication adherence across the number of SMS received.

TABLE 4 Sensitivity analyses

	(1) Including participants with or without BMI (OR)	(2) Compliance for unsubscribers measured at withdrawal (OR)	(3) Compliance=1 if no. claims ≥ no. months observed (OR)	(4) Compliance=no. claims/ no. months observed (Coefficient)	(5) Including only subscribers and 0 SMS group (OR)	(6) Including only unsubscribers and 0 SMS group (OR)	(7) Restricting enrollment period September to December 2017 (OR)
SMS (base: 0 SMS)							
3 SMS	**4.61**	**6.84**	**6.49**	**0.21**	**4.69**	**0.63**	1.81
	(3.61-5.89)	(4.86-9.63)	(4.52-9.31)	(0.13-0.27)	(3.32-6.63)	(0.45-0.90)	(0.97-3.34)
5 SMS	**7.27**	**14.91**	**14.16**	**0.29**	**10.04**	0.91	**2.43**
	(5.41-9.75)	(9.86-22.57)	(9.21-21.77)	(0.21-0.37)	(6.29-16.03)	(0.65-1.28)	(1.11-5.31)
Patient support (base: no extra support)							
Face-to-face consultation with an HCP	**2.87**	**4.36**	1.68	**0.19**	**3.38**	**3.20**	0.64
	(1.78-4.61)	(2.49-7.63)	(0.90-3.13)	(0.07-0.31)	(1.74-6.55)	(1.69-6.08)	(0.22-1.89)
Phone call from a dietitian	**1.09**	**1.33**	1.29	**0.07**	**1.41**	1.21	1.35
	(1.02-1.33)	(1.03-1.74)	(0.97-1.73)	(0.01-0.12)	(1.05-1.89)	(0.89-1.66)	(0.96-1.90)
No. observations	3,994	2,354	2,354	2,354	1,671	1,444	1,502

Logit models performed except for linear regression in column 4. Odds ratios (OR)/coefficients and 95% CIs reported. Estimates in bold indicate significance at 5% level.

literature on the influence of reminder frequencies on medication adherence. The study also confirms the use of text messages with a variety of education and motivational content in improving medication adherence and patient engagement (11,42).

In addition, having patient support, in the form of a face-to-face consultation with an HCP or a phone call from a dietitian, was also associated with greater medication adherence, with participants being more responsive to a face-to-face consultation than a phone call. Face-to-face consultations were also associated with a significant increase in adherence for unsubscribers who discontinued the SMS reminders. There are limited studies that examine the use of health providers in assisting with patient education and follow-up (43). The findings in the current study suggest that patients who have social support and engagement with health care providers had better adherence to medication, after controlling for SMS reminders. Thus, patient support might be particularly useful for patients who opt out of SMS reminders or when the effectiveness of SMS reminders wanes. While the association of enrollment channels and patient support types with adherence might partially reflect selection bias of participants, the results concerning these relationships should be taken into consideration when designing measures aimed at achieving better medication adherence for weight loss among participants with overweight or obesity and other chronic diseases.

For patients with chronic diseases, medication adherence tends to decrease over time (4). This study shows that the effectiveness of SMS reminders decreased as the number of SMS reminders received increased over time, and the effectiveness of five SMS seemed to have a slightly slower rate of decline than that of three SMS per week. The attrition might be explained by routine habituation and response fatigue as the result of long duration of frequent reminders (44). At some point, participants might ignore or forget messages and thus reduce their responsiveness to SMS reminders. The positive effects of face-to-face consultations or phone calls, however, suggest HCP patient support can be introduced to compensate for the decreased effectiveness of SMS reminders as patients received more SMS reminders over time. Tapering the frequency of messages or delivering messages when a dose is missed are also alternative strategies to avoid the reduced long-term effects of SMS reminders (44).

The current study has some limitations. First, information on weight-loss outcomes and verification of medication usage was not included in this pilot study. However, the focus of the study was primarily on establishing the usefulness of SMS reminders delivered in varying frequencies per week with and without HCP support for improving weight-loss medication adherence. Second, socioeconomic status has been shown to be related to variations in adherence behavior for weight-loss programs (12) and hence including factors such as education, income, or employment status as covariates would be informative in understanding the heterogeneity in the effectiveness of SMS reminders. Third, the SaxendaCare PSP enrollment channels and patient support types provided by Novo Nordisk were not randomized to individuals. Exogenous measures on these program features would enable the control of the selection of participants into different registration or enrollment methods and support types and thus strengthen the causal interpretation of these program design parameters in increasing medication adherence. Finally, a longer follow-up period would allow the analysis of changes in the efficacy of SMS reminders and quality of life for participants over a longer time period.

This study is consistent with previous studies in other disease areas on the effectiveness of text messaging for medication adherence (10,11).

However, this is the first study to provide empirical evidence on the effectiveness of text messaging and HCP patient support in improving weight-loss medication adherence of participants with overweight or obesity. Being an accessible, scalable, and low-cost intervention, SMS reminders can have a significant impact on adherence to treatment and health outcomes among participants. This study contributes to the literature on the effectiveness of SMS-based interventions by utilizing objective measures of medication adherence and assessing the heterogeneous responses associated with message frequencies, registration channels, and patient support types. The study sheds light on potentially effective and efficient strategies that could be put in place to achieve higher and maintained medication adherence of participants and healthy behavioral changes.

Conclusion

The study evaluated the effectiveness of SMS reminders in conjunction with a structured PSP, such as the SaxendaCare PSP, in overcoming poor weight-loss medication adherence in the community. The results provide evidence on the effectiveness of an SMS messaging intervention for improving medication adherence of participants with overweight or obesity and do support the use of several SMS reminders weekly in conjunction with HCP patient support over time. The incorporation of SMS messaging into routine clinical practice should take into account additional patient support or HCP contact. Patient support can be particularly useful in cases of stimulus fatigue or withdrawal from digital alerts. Participants with chronic disease should be encouraged to take up health care professional support over time to achieve higher and more sustained adherence to medication and health behavior changes.**O**

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