

ORIGINAL ARTICLE

Clinical Trials and Investigations

A smartphone application to improve adherence to vitamin and mineral supplementation after bariatric surgery

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Abstract

Objective: This trial evaluated a smartphone application's effectiveness in improving adherence to vitamin and mineral supplementation postoperatively.

Methods: This study was a randomized controlled trial comprising 140 patients undergoing bariatric surgery (gastric bypass or sleeve gastrectomy). Participants were randomized 1:1 to the 12-week intervention, using the smartphone application PromMera, or to standard care. The primary end point was adherence to vitamin and mineral supplementation.

Results: Initiation rate and overall adherence to supplementation were high in both groups. Change in objectively measured adherence rate from before the intervention to 1 year post surgery, measured with pharmacy refill data, did not differ between groups for vitamin B₁₂ (−9.6% [SD = 27%] vs. −9.3% [SD = 30%]; $p = 0.48$) or calcium/vitamin D (−12.3% [SD = 29%] vs. −11.5% [SD = 32%]; $p = 0.44$). A modest effect on the secondary end point (subjectively measured adherence, using the Medication Adherence Report Scale-5) was seen immediately after the intervention (intervention group 0.00 [SD = 1.3] vs. control group −1.2 [SD = 3.5]; $p = 0.021$), but this effect did not persist 1 year post surgery. No differences were detected in the prevalence of biochemical deficiencies.

Conclusions: The use of the smartphone application PromMera did not obtain a lasting improvement in adherence to vitamin and mineral supplementation 1 year post bariatric surgery.

INTRODUCTION

Bariatric surgery confers a risk of nutritional deficiencies, and there is a broad consensus on recommending lifelong vitamin and mineral supplementation after surgery [1, 2]. Micronutrient deficiencies may cause long-term complications after bariatric surgery, with substantial impact on health [3, 4]. Nonadherence to chronic medication is a common reason for treatment failure [5], and previous studies have reported suboptimal adherence to vitamin and mineral

supplementation after bariatric surgery [6–17]. Available studies in bariatric surgery have shown divergent results regarding the proportion of patients with poor adherence, ranging from around 20% to 75% [9, 14]. Furthermore, adherence rates appear to gradually decline over time [6, 9]. Known barriers to vitamin and mineral supplementation are forgetfulness, gastrointestinal complaints, and unpleasant smell, taste, or size of supplements, as well as problems with swallowing tablets, the perception that supplements are unnecessary, and financial constraints [6, 12, 13, 17, 18]. Adherence to medication may

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be assessed with different methods, and no method is considered the gold standard [5]. The current state of the art in measurement of adherence is a multimethod approach combining objective measurement with self-reported methods [19].

The field of mobile health (mHealth) interventions to improve adherence to medication is growing [20]. Smartphone applications have the potential to be easily accessible cost-effective interventions to improve adherence. Smartphone applications are effective in improving adherence to pharmacological treatment in a range of medical conditions such as HIV [21], depression [22], and anticoagulation therapy [23], as well as for patients with polypharmacy [24]. However, other studies on smartphone applications have not been able to demonstrate any effect on adherence to medication [25]. Concerning adherence to micronutrient supplementation, previous research with smartphone interventions has shown improved adherence to iron in pregnant women [26, 27]. mHealth interventions for patients undergoing bariatric surgery have been performed regarding preoperative lifestyle changes, postoperative weight loss, physical activity, and recovery at home [28–31], but, to the best of our knowledge, the effect of smartphone applications in improving adherence rates to vitamin and mineral supplementation after bariatric surgery has not been previously studied.

The aim of this study was to investigate whether the use of a smartphone application could improve adherence to vitamin and mineral supplementation after bariatric surgery, as measured objectively with pharmacy claim data. Secondary aims were to assess the effects on subjective adherence rate and micronutrient deficiencies.

METHODS

This was a 1-year randomized controlled trial with a 12-week intervention. The full details of the “PromMera trial” study design have been previously described [32]. The PromMera trial was designed to assess the efficacy of the smartphone application in promoting physical activity (primary end point) and to support intake of vitamins and minerals after bariatric surgery (secondary end point). The part of the study project presented here focuses on evaluating the features of the application designed to facilitate the use of vitamin and mineral supplementation. Patients undergoing bariatric surgery at a county hospital in Sweden were consecutively enrolled in the study at the routine preoperative visit between November 2017 and May 2019.

Study patients

Inclusion criteria were age > 18 and ≤60 years, being accepted for bariatric surgery (gastric bypass or sleeve gastrectomy), the ability to read or understand Swedish, and having access to and the ability to handle a smartphone. Exclusion criteria were any disability preventing daily walking, as this was related to the primary end point in the PromMera trial. Figure 1 shows the study flowchart. Baseline

Study Importance

What is already known?

- The few previous studies on adherence to vitamin and mineral supplementation after bariatric surgery indicate suboptimal adherence rates.
- Smartphone applications are effective in improving adherence to different types of pharmacological treatments. To our knowledge, no previous study has assessed the use of a smartphone application for adherence to vitamin and mineral supplementation after bariatric surgery.

What does this study add?

- Adherence to supplementation was high during the first year following surgery, with no difference between the smartphone intervention group and the control group.
- The smartphone application used in this study did not generally improve adherence to vitamin and mineral supplementation during the first year after bariatric surgery.

How might these results change the direction of research?

- The results suggest that future intervention studies should focus on evaluating the effect of smartphone applications in subgroups of patients struggling with adherence to vitamin and mineral supplementation after bariatric surgery.

characteristics were retrieved from patients' medical charts and the 10-item Beliefs about Medicines Questionnaire-Specific. The Beliefs about Medicines Questionnaire was used to assess participants' attitudes to vitamin and mineral supplementation [33].

Randomization and blinding

Study participants were randomized to the intervention group (smartphone intervention and standard care) or control group (standard care only) in a 1:1 ratio. Women and men were randomized separately in blocks of four and two, respectively, owing to the uneven sex distribution among patients undergoing bariatric surgery in Sweden, where approximately 75% are women [34]. Blinding was not possible because of the nature of the intervention.

Intervention

The intervention group was, in addition to standard care, instructed to use the PromMera application for 12 weeks starting at 6 weeks post

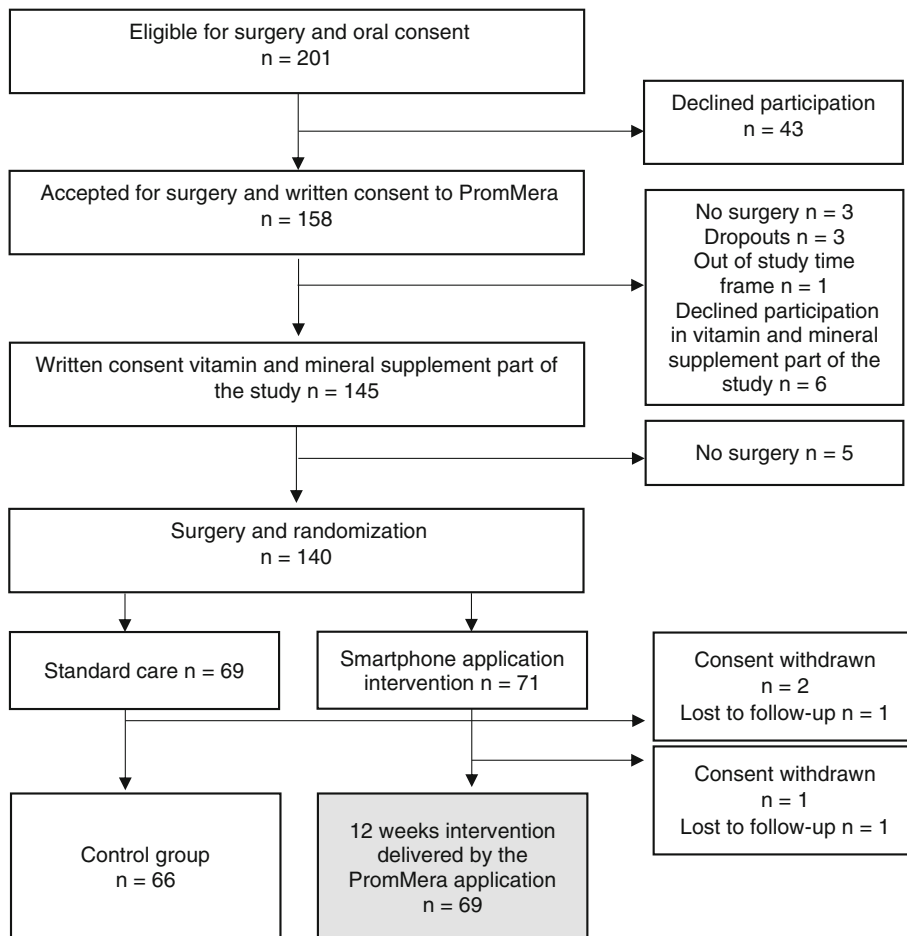


FIGURE 1 PromMera study flowchart

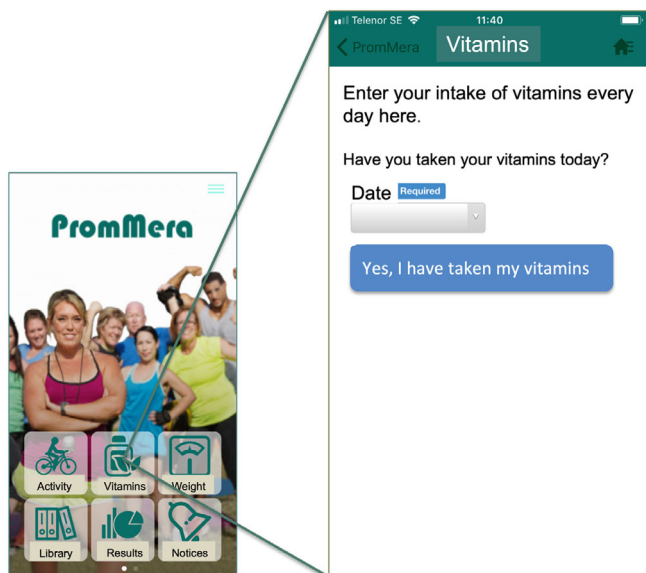


FIGURE 2 The PromMera smartphone application [Color figure can be viewed at wileyonlinelibrary.com]

surgery and to report intake of vitamin and mineral supplements in the application by responding to the following daily question: “Have

you taken your vitamins today?” (Figure 2). A reminder to register intake of supplementation was received every evening. If forgotten, it was possible to report intake from previous days in the application. A summary of the individual’s registered vitamin and mineral use during the past week was received by the participant once a week. Depending on the number of registrations during the week, the application either encouraged participants with low registration rates to find new routines to achieve better adherence or reinforced those reporting a high grade of vitamin and mineral use to keep up the good work. Statistics for the reported use of supplementation, as well as information on current prescriptions, for the entire period were available to the patient in the application. The application provided the user with information about the use of vitamin and mineral supplements and dietary recommendations. This information was available in the app throughout the intervention. It was also sent to the study participants via push notifications according to a predetermined schedule, with more frequent messages during the first weeks of the intervention and less frequent messages toward the end. The intervention strategies within the application were theory based and they comprised different techniques for behavior changes such as recording of use of supplementation (prompt self-monitoring of behavior), encouraging messages and information (action plan), explanatory information on

the risks of nonadherence to supplementation (information on consequences of behavior to the individual), and weekly feedback on vitamin and mineral use (feedback on performance) [35, 36]. The possibility of setting weekly personal goals (goal-setting behavior) was used only for the primary end point, physical activity, because the prescription of supplements was for daily use.

Standard care

Participants in both the control group and in the intervention group received standard care, with preoperative visits including information on vitamin and mineral supplementation given by a dietitian, a surgeon, and a clinical pharmacist. At discharge from the hospital after surgery, all patients received repeated information on supplementation from a surgeon and a dietitian. At postsurgical visits with a dietitian, 6 weeks and 1 year post surgery, follow-up on supplementation was included. Blood samples to detect biochemical deficiencies were taken preoperatively and 1 year post surgery.

Prescribed supplementation

In accordance with local guidelines, all patients received prescriptions for daily oral supplementation with combined calcium/vitamin D (1000 mg/800 IE/d) and vitamin B₁₂ (1 mg/d). Iron (100 mg/d) was prescribed only to menstruating women and patients with preoperative anemia. Additionally, all patients were recommended a daily over-the-counter multivitamin tablet containing folic acid (400 µg/d), thiamine (1.2 mg/d), vitamin A (700 µg/d), vitamin E (8 mg/d), vitamin K (75 µg/d), zinc (7 mg/d), iron (15 mg/d), and copper (900 µg/d). The supplementation was in accordance with the current Nordic guidelines for supplements and follow-up after obesity surgery, except that the current Nordic guidelines recommend 45 to 60 mg/d iron to all patients and higher daily doses of zinc (≥9 mg/d) and copper (2 mg/d) [37]. Supplementation was initiated at discharge from hospital and was prescribed for 1 year by the surgeon who discharged the patients from the hospital. Supplementation regimens were identical after Roux-en-Y gastric bypass and sleeve gastrectomy.

Outcome measures

In the current study, we combined an objective adherence measure with pharmacy refill data with a subjective adherence measure using the Medication Adherence Report Scale-5 (MARS-5) score. The primary outcome was change in adherence rate, assessed with pharmacy refill data, comparing the time period from surgery to start of the intervention (i.e., from surgery to 6 weeks post surgery) with the time period between the end of the intervention and 1 year post surgery (i.e., 18-52 weeks post surgery). The change in adherence was compared between the intervention and the control group.

TABLE 1 Baseline characteristics of participants in the PromMera trial

| | Intervention group (n = 71) | Control group (n = 69) |
|-------------------------------------|-----------------------------|------------------------|
| Age (y) | 42.0 ± 9.8 | 40.9 ± 9.7 |
| Male | 16 (22.5%) | 14 (20.3%) |
| Female | 55 (77.5%) | 55 (79.7%) |
| Weight at surgery (kg) | 116.3 ± 20.3 | 114.2 ± 16.8 |
| BMI at surgery (kg/m ²) | 40.6 ± 5.7 | 40.6 ± 5.6 |
| RYGB | 60 (84.5%) | 53 (76.8%) |
| Sleeve gastrectomy | 11 (15.5%) | 16 (23.2%) |
| Education | | |
| ≤9 years | 7 (10.0%) | 3 (4.4%) |
| 9-12 years | 30 (42.9%) | 37 (54.4%) |
| >12 years | 33 (47.1%) | 28 (41.2%) |
| Hypertension | 19 (26.8%) | 14 (20.3%) |
| Diabetes type 2 | 8 (11.3%) | 6 (8.7%) |
| Cardiovascular disease | 2 (2.8%) | 2 (2.9%) |
| Regular use of medication | 48 (69.6%) | 48 (71.6%) |
| BMQ | | |
| Concerns | 6.8 ± 2.6 (61) | 6.9 ± 2.6 (61) |
| Necessity | 16.9 ± 5.4 (62) | 18.6 ± 4.6 (61) |
| Total | 10.2 ± 5.6 (61) | 11.7 ± 5.8 (61) |

Note: Missing data: Data on education level were missing for two study participants; data on regular medication were missing for four individuals, BMQ necessity was missing for seventeen participants, and BMQ concerns and BMQ total were missing for eighteen individuals. Age, weight, BMI, and BMQ are presented as mean ± SD. All other demographics are presented as n (percentage). Abbreviations: BMQ, 10-item Beliefs about Medicines Questionnaire; RYGB, Roux-en-Y gastric bypass.

Adherence analysis was based on pharmacy refill data from the Swedish Prescribed Drug Register, which is a national register containing all data on prescription refills (dosage, quantity, and date of drug refill) dispensed at pharmacies in Sweden [38]. Adherence rates were calculated for calcium/vitamin D and vitamin B₁₂ as continuous multiple-interval measures of medication availability/gaps (CMA). CMA is defined as the proportion of days covered by a medication during the observation period. A CMA approaching 100% indicates that the patient has purchased medication in accordance with prescription [39, 40]. Adherence calculations were performed using the AdhereR package, RStudio version 1.1.463 (RStudio, PBC, Boston, Massachusetts), CMA version 7 [39].

The study participants were also asked whether they used nonprescribed complete supplementation designed for patients having undergone bariatric surgery, containing all micronutrients recommended, which is an alternative to prescribed supplements.

TABLE 2 Adherence to vitamin B₁₂ and calcium/vitamin D and change in adherence before and after smartphone application intervention in patients after bariatric surgery and in control participants receiving standard care

| | Objectively measured adherence ^a | | | | Subjectively measured adherence ^b | | | |
|--|---|-------------------|------------------------|-------------------|--|------------------|------------------------|------------------|
| | Intervention group (n = 71) | | Control group (n = 69) | | Intervention group (n = 71) | | Control group (n = 69) | |
| | Wk 0-6 (n = 65) | Wk 18-52 (n = 65) | Wk 0-6 (n = 58) | Wk 18-52 (n = 58) | Wk 6 (n = 63) | Wk 6-18 (n = 47) | Wk 6-18 (n = 54) | Wk 6-52 (n = 54) |
| Vitamin B ₁₂ adherence rate (%) | 93.4 (24) | 83.8 (27) | 96.6 (18) | 87.9 (24) | | | | |
| Calcium/vitamin D adherence rate (%) | 91.8 (26) | 79.5 (30) | 94.8 (22) | 83.3 (27) | | | | |
| MARS-5 score at baseline (wk 6) and change from baseline | | | | | 24.2 (1.3) | 0.00 (1.3) | -0.40 (2.0) | 24.3 (1.2) |
| | | | | | | | | -1.2 (3.5) |
| | | | | | | | | -0.9 (2.1) |
| | | | | | | | | 0.021 |
| | | | | | | | | 0.13 |

Note: Data are presented as mean (SD).

Abbreviations: CMA7, continuous multiple-interval measures of medication availability/gaps; MARS-5, Medication Adherence Report Scale-5.

^aAdherence was objectively assessed with pharmacy refill data, from the Swedish Prescribed Drug Register, and CMA7 was used for calculations. The adherence rate was measured from surgery until the start of intervention and from the end of intervention until 1 year post surgery. The change in adherence from before intervention to after intervention was compared between the intervention group and the control group.

^bMARS-5 scores range from 5 to 25, where a higher score indicates higher adherence to vitamin and mineral supplementation. The two p values in part B of the table represent the change from baseline to the end of intervention and the change from baseline to 1 year post surgery, respectively.

Patients using nonprescribed supplements were labeled as missing data for the primary end point because of the lack of pharmacy refill data in the Swedish Prescribed Drug Register.

The study participants completed the five-item MARS-5 at 6 weeks, at 18 weeks, and at 1 year post surgery. The change in score from baseline (week 6) was compared between the intervention group and the control group at the end of the intervention (18 weeks) and at 1 year post surgery. The MARS-5, a widely used tool for self-reported medication adherence, was originally developed for medication in psychiatric disease [41]. The MARS-5 questionnaire consists of five questions on forgetting, changing dosage, stopping, skipping, and taking less medication. The total score ranges from 5 to 25, in which a higher MARS-5 score indicates higher self-reported adherence.

Biochemical data

Prevalence of biochemical deficiencies was compared between the intervention and the control groups. Blood test results were retrieved from medical records before surgery and at the 1-year follow-up. Biochemical deficiencies were defined as levels below the reference range according to the analyzing laboratory (the Department of Laboratory Medicine, County Council of Östergötland, Sweden) for hemoglobin, ferritin, calcium ion, cobalamin, folate, 25-OH vitamin D, parathyroid hormone, and albumin.

Statistical analysis

The primary aim of the PromMera study was to evaluate the effect of the smartphone application on physical activity. A sample size of 140 patients was determined sufficient to evaluate the primary end point. An additional power calculation demonstrated that a total of 110 patients (55 in each group) would provide 80% power to detect a 10% superiority in adherence rate in the intervention group (e.g., 60% vs. 50%) at a 5% significance level, assuming a standard deviation (SD) of 20% in both groups.

Analyses were performed according to intention-to-treat principles. Statistical analyses were performed with SPSS Statistics for Windows, version 25.0. (released 2017; IBM Corp., Armonk, New York). A *t* test was used to compare groups. A one-tailed *t* test was used to compare adherence rates measured with pharmacy refill data and MARS-5. A two-tailed Fisher exact test was used to compare categorical variables. A *p* value <0.05 was considered statistically significant.

The trial was approved by the Swedish Ethical Review Authority (2016/1259-31/4; 2017/1406-32; 2017/2101-32) and registered at www.ClinicalTrials.gov (NCT03480464). Informed consent was obtained from all participants.

RESULTS

In total, 140 patients (71 in the intervention group and 69 in the control group) were randomized and included in the trial (Figure 1). Three

patients withdrew consent, and one patient was lost to follow-up. Patient demographics are given in Table 1. Participants completing the study had a higher mean age compared with those declining participation or prematurely terminating participation: 41.8 (SD = 10.3) years and 36.5 (SD = 9.6) years, respectively ($p = 0.002$). No other statistically significant differences in patient characteristics were found between participants and nonparticipants.

Adherence

Table 2 presents the rates of adherence to vitamin and mineral supplementation at baseline and after the intervention, as well as changes in adherence rates. The number of patients with full data on the primary end point was 65 in the intervention group and 58 in the control group. Four participants (5.8%) in the intervention group and eight participants (12.1%) in the control group used a nonprescribed complete supplement designed for patients who have undergone bariatric surgery and were excluded from analyses because we lacked objective adherence data for them. The mean adherence to vitamin B₁₂ before the intervention was 93.4% in the intervention group and 96.6% in the control group ($p = 0.41$). After the intervention (weeks 18-52), the mean adherence rate for vitamin B₁₂ was 83.8% in the intervention group and 87.9% in the control group ($p = 0.46$). There was no statistically significant difference in change in adherence to vitamin B₁₂ from before the intervention to post intervention between the intervention and control groups (−9.6% vs. −9.3%; $p = 0.48$). The mean adherence rate to calcium/vitamin D before the intervention was 91.8% in the intervention group and 94.8% in the control group ($p = 0.50$). After the intervention, the mean adherence rate for calcium/vitamin D was 79.5% in the intervention group and 83.3% in the control group ($p = 0.47$). There was no significant difference in change in adherence to calcium/vitamin D before and after the intervention between the intervention and control groups (−12.3% vs. −11.5%; $p = 0.44$).

The MARS-5 scores, assessing self-estimated adherence to vitamin and mineral supplementation, at baseline, i.e., 6 weeks post surgery, were 24.2 in the intervention group and 24.3 in the control group ($p = 0.84$). There was a significantly larger decrease in MARS-5 at the end of the intervention in the control group than in the intervention group (control group −1.2 [SD = 3.5] $p = 0.021$ vs. intervention group 0.00 [SD = 1.3]), which indicates lower adherence in the control group. The difference was no longer significant 1 year post surgery, with a decrease in MARS-5 from baseline for the intervention group of −0.4 and for the control group of −0.9 ($p = 0.13$). The proportion of completed MARS-5 questionnaires at baseline was 90% (121/135); at the end of the intervention, it was 75% (101/135), and, at 1 year post surgery, it was 92% (124/135).

Biochemical deficiencies

Table 3 presents the blood test results and prevalence of micronutrient deficiencies preoperatively and 1 year post surgery. The overall

TABLE 3 Laboratory values and prevalence of deficiencies in patients 1 year after bariatric surgery who used a smartphone application and in control participants receiving standard care

| | Before surgery | | | 1 year after surgery | | |
|------------------------------|-----------------------|------------------|---------|-----------------------|------------------|---------|
| | Intervention (n = 70) | Control (n = 66) | p value | Intervention (n = 70) | Control (n = 66) | p value |
| Hemoglobin (g/L) | 140 ± 11 | 139 ± 10 | 0.38 | 134 ± 9 | 133 ± 12 | 0.50 |
| Hemoglobin <ref | 1.4% (1/70) | 0.0% (0/66) | 1.00 | 2.9% (2/69) | 7.9% (5/63) | 0.26 |
| Ferritin ^a (µg/L) | 150 ± 126 | 100 ± 71 | 0.025 | 115 ± 81 | 115 ± 79 | 0.99 |
| Ferritin <ref | 2.5% (1/40) | 10.5% (4/38) | 0.20 | 0.0% (0/66) | 1.7% (1/60) | 0.48 |
| Cobalamin (pmol/L) | 349 ± 139 | 377 ± 128 | 0.28 | 674 ± 270 | 733 ± 346 | 0.28 |
| Cobalamin <ref | 1.8% (1/56) | 0.0% (0/53) | 1.00 | 0.0% (0/66) | 0.0% (0/61) | 0.99 |
| Folate (nmol/L) | 18 ± 10 | 16 ± 10 | 0.23 | 25 ± 11 | 25 ± 13 | 0.90 |
| Folate <ref | 10.7% (6/56) | 15.4% (8/52) | 0.57 | 3.2% (2/63) | 5.0% (3/60) | 0.68 |
| Homocysteine (µmol/L) | 14 ± 11 | 12 ± 4 | 0.39 | 9 ± 3 | 10 ± 3 | 0.46 |
| Homocysteine <ref | 25.0% (10/40) | 21.1% (8/38) | 0.79 | 9.1% (6/66) | 8.3% (5/60) | 1.00 |
| Calcium ion (mmol/L) | 1.25 ± 0.05 | 1.24 ± 0.05 | 0.55 | 1.25 ± 0.04 | 1.24 ± 0.04 | 0.17 |
| Calcium ion <ref | 0.0% (0/25) | 8.0% (2/25) | 0.49 | 0.0% (0/66) | 0.0% (0/60) | 0.99 |
| 25-OH vitamin D (nmol/L) | 62 ± 20 | 62 ± 23 | 0.99 | 77 ± 21 | 76 ± 20 | 0.59 |
| 25-OH vitamin D < ref | 25.5% (12/47) | 29.8% (14/47) | 0.82 | 6.1% (4/66) | 10.0% (6/60) | 0.52 |
| PTH (pmol/L) | 5.3 ± 1.3 | 5.1 ± 1.4 | 0.43 | 5.0 ± 1.8 | 4.5 ± 1.6 | 0.07 |
| PTH < ref | 7.5% (3/40) | 13.2% (5/38) | 0.48 | 13.6% (9/66) | 5.1% (3/59) | 0.13 |
| Albumin (g/L) | 41 ± 4 | 41 ± 3 | 0.43 | 41 ± 3 | 41 ± 3 | 0.68 |
| Albumin <ref | 5.7% (4/70) | 3.0% (2/66) | 0.68 | 1.5% (1/67) | 5.1% (3/59) | 0.34 |

Note: <ref = laboratory value below reference value according to the Department of Laboratory Medicine in County Council of Östergötland. Data given as mean ± SD or percentage (numbers/available samples).

Abbreviation: PTH, parathyroid hormone.

^aOnly ferritin measured together with a normal C-reactive protein is reported in the table.

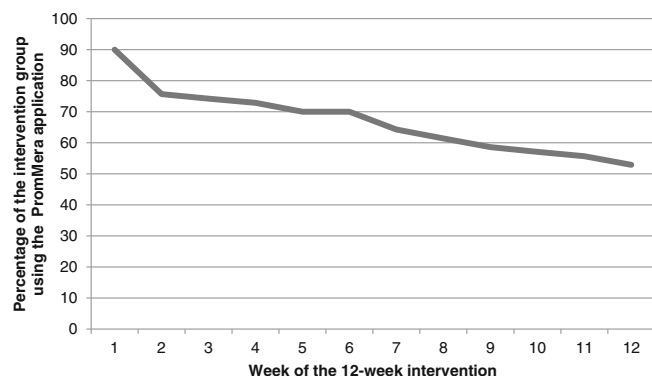


FIGURE 3 Use of the PromMera application during the intervention

rate of deficiencies was low in both the intervention group and the control group, and there was no significant difference in prevalence of biochemical deficiencies between the groups.

Application use

A total of 90% (n = 63/70) of participants in the intervention group used the application at least once. Figure 3 shows the percentage of

participants who used the application from week 1 to week 12. A gradual decline from 90% to just over 50% was observed. A total of 47% (n = 33/70) of the participants used the app ≥80% (≥67/80 d) of the time, and 4.3% (n = 3) used it every day. The overall use in the intervention group was 64% of the days during the 12-week intervention.

DISCUSSION

Patients who were randomized to use of the PromMera smartphone application after bariatric surgery had no improvement in adherence to prescribed vitamin and mineral supplementation, as objectively measured with pharmacy claim data, in comparison with the control group receiving standard care. A modest effect on self-reported adherence was seen immediately after the intervention, but this effect did not persist 1 year after surgery. No differences were detected in the prevalence of biochemical deficiencies.

Both the intervention group and the control group had high initiation rates of vitamin and mineral supplementation in this trial [6]. The high initiation rate in the study cohort may be an effect of repeated information and support from the bariatric multiprofessional team in initiating the vitamin and mineral supplementation. Therefore, this type of standard care appears to provide sufficient support for

initiation of supplementation and could not be improved further with the smartphone application. In a clinical setting with lower initiation rates, it is possible that an app intervention may have been more efficient. Future studies on supplementation after bariatric surgery could preferably target a group of patients who struggle with adherence or specific groups having certain challenges with adherence such as younger patients [6]. Others have reported a low initiation rate of vitamin and mineral supplementation after bariatric surgery [9], and investigating whether use of a smartphone application can improve initiation rates in such clinical settings appears to be important.

Mechanisms affecting adherence to vitamin and mineral supplements after bariatric surgery are complex and multidimensional [5]. Identifying individual barriers is necessary to improve adherence. In a recent study by Smelt et al., the most common reasons for poor adherence or non-persistence were difficulty in remembering to use supplements, gastrointestinal side effects, unpleasant taste or smell, high costs, and the absence of vitamin deficiencies in blood tests [17]. Smartphone applications have the potential to improve adherence when the reason for poor adherence is forgetfulness but cannot be expected to have any effect on patients' avoidance of supplements owing to side effects, unpleasant taste, or financial barriers.

Daily reminders to take medication cannot be expected to have an effect after the end of the intervention; therefore, the intervention might need to be extended. However, if the smartphone application were effective in establishing new habits, one might expect a long-term effect of the 12-week intervention. Several previous research studies using mHealth interventions for micronutrient supplementation have focused on pregnant women [26, 27, 42]. Adherence to micronutrient supplementation during pregnancy is characterized by short-term treatments in highly motivated patients, and such results may not be transferable to other settings of long-term or lifelong micronutrient supplementation such as regimens after bariatric surgery.

In the national context of this study, pharmacy refill databases are objective and reliable measures of adherence [38]. Methodological limitations regarding objective assessment of adherence with pharmacy refill data are the inability to reveal details of daily dispensing and that registration of treatment discontinuation is possibly detected later than the patient actually stopped taking the medication [5].

A modest positive effect on subjectively measured adherence was seen immediately after the end of the intervention, but this effect did not persist 1 year after surgery. However, some caution when interpreting MARS-5 data can be recommended owing to variation in response rate.

A well-known challenge in mHealth interventions is a high attrition rate, and 50% of participants stopped using the PromMera application during the 12-week-long intervention period in this study. That is somewhat higher compared with average for studies with mHealth interventions [43] but in line with results from Heuser et al., who studied an mHealth intervention for home recovery after bariatric surgery [28]. It could be speculated that a higher attrition rate among patients after bariatric surgery may be related to the major life adjustments that the early postoperative phase entails. In a feasibility study,

using an mHealth intervention after bariatric surgery, there was a maintained high registration rate for physical activity throughout a 16-week intervention. However, this intervention incorporated a simple registration of workouts by automatic data transfer from a wrist-worn activity tracker, whereas the PromMera application required manual registration [30]. The PromMera application included personal customizing with goal setting and personalized feedback, and the interventions were based on techniques for behavioral change. The knowledge regarding user-friendliness of applications is rapidly progressing. Future development may include features to further customize the apps and incorporate gamifying features to help maintain interest in the application.

The PromMera application was designed to facilitate adherence to both physical activity and vitamin and mineral supplementation, with the aim of optimizing postoperative outcomes after bariatric surgery. An integrated design was chosen to convey to the patient that several lifestyle changes were needed. It was assumed that it would be beneficial in supporting the establishment of relevant new habits, including taking prescribed vitamins and minerals. However, for the patient needing support only for adherence to vitamin and mineral supplements, it may have been distracting and perceived as burdensome to receive reminders about daily physical activity as well.

Strengths of this trial include the randomized controlled design, a high retention rate to outcome measures, and objectively measured adherence using validated databases. A limitation is the short observation period, which was probably too close to surgery to detect biochemical deficiencies. Being a single-site study limits the generalizability of the results; however, the study population was comparable to all Swedish patients registered in the Scandinavian Obesity Surgery Register as having undergone bariatric surgery in 2018 ($n = 5206$) regarding age, sex distribution, BMI, and educational level. However, our study cohort had a larger proportion of gastric bypass procedures than the total Swedish bariatric population (80.1% vs. 49.3%) [27]. Furthermore, the patient sample represents patients from an entire health care region, including both rural and urban areas. The study population was older than the nonparticipants and drop-outs, which suggests a selection bias because previous research has demonstrated that young age is associated with lower adherence to supplementation [6]. The necessity to have access to a smartphone should not have introduced a risk of selection bias as 90% of adult Swedes were smartphone users, regardless of social status, at the time of the study [44].

CONCLUSION

In this randomized trial, use of the PromMera smartphone application for 12 weeks did not result in a lasting improvement in adherence rates to vitamin and mineral supplementation 1 year post bariatric surgery in comparison with standard care. Smartphone applications for patients who have undergone bariatric surgery may, in future studies, be investigated to specifically target subgroups of patients with poor adherence.○

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CONFLICT OF INTEREST

Torsten Olbers has received reimbursement unrelated to the submitted article from the following: Johnson & Johnson (advisory board, educational activities) and NovoNordisk A/S (advisory board, educational activities), with all reimbursement directed to his institution. The other authors declared no conflict of interest.

CLINICAL TRIAL REGISTRATION

[ClinicalTrials.gov](https://clinicaltrials.gov) identifier NCT03480464.

DATA AVAILABILITY STATEMENT

Data are not yet available data as this is an ongoing study and the primary end point has not yet been published.

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