Nutr Res Pract. 2023 Dec;17(6):1238-1254
https://doi.org/10.4162/nrp.2023.17.6.1238
pISSN 1976-1457·eISSN 2005-6168

Nutrition Research and Practice

Original Research

Check for updates

The effects of dietary self-monitoring intervention on anthropometric and metabolic changes via a mobile application or paper-based diary: a randomized trial

Taiyue Jin [1*], **Gyumin Kang** [2*], **Sihan Song** [3], **Heejin Lee** [3], **Yang Chen** [3], **Sung-Eun Kim** [4], **Mal-Soon Shin** [5], **Youngja H Park** [6§], **and Jung Eun Lee** [3,7§]

[1]Division of Cancer Prevention, National Cancer Control Institute, National Cancer Center, Goyang 10408, Korea
[2]School of Bio-Medical Science, Korea University, Sejong 30019, Korea
[3]Department of Food and Nutrition, College of Human Ecology, Seoul National University, Seoul 08826, Korea
[4]Department of Food and Nutrition, Sookmyung Women's University, Seoul 04310, Korea
[5]School of Global Sport Studies, Korea University, Sejong 30019, Korea
[6]College of Pharmacy, Korea University, Sejong 30019, Korea
[7]The Research Institute of Human Ecology, Seoul National University, Seoul 08826, Korea

OPEN ACCESS

Received: Feb 27, 2023
Revised: Aug 5, 2023
Accepted: Sep 21, 2023
Published online: Oct 30, 2023

§Corresponding Authors:
Youngja H Park
College of Pharmacy, Korea University, 2511 Sejong-ro, Sejong 30019, Korea.
Tel. +82-44-860-1621
Fax. +82-44-860-1606
Email. yjhwang@korea.ac.kr

Jung Eun Lee
Department of Food and Nutrition, College of Human Ecology, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 08826, Korea.
Tel. +82-2-880-6834
Fax. +82-2-884-0305
Email. jungelee@snu.ac.kr

*Taiyue Jin and Gyumin Kang contributed equally to this work.

ORCID iDs
Taiyue Jin
https://orcid.org/0000-0003-0144-3850
Gyumin Kang
https://orcid.org/0000-0003-3756-0880

ABSTRACT

BACKGROUND/OBJECTIVES: Weight loss via a mobile application (App) or a paper-based diary (Paper) may confer favorable metabolic and anthropometric changes.
SUBJECTS/METHODS: A randomized parallel trial was conducted among 57 adults whose body mass indices (BMIs) were 25 kg/m^2 or greater. Participants randomly assigned to either the App group (n = 30) or the Paper group (n = 27) were advised to record their foods and supplements through App or Paper during the 12-week intervention period. Relative changes of anthropometries and biomarker levels were compared between the 2 intervention groups. Untargeted metabolic profiling was identified to discriminate metabolic profiles.
RESULTS: Out of the 57 participants, 54 participants completed the trial. Changes in body weight and BMI were not significantly different between the 2 groups (P = 0.11). However, body fat and low-density lipoprotein (LDL)-cholesterol levels increased in the App group but decreased in the Paper group, and the difference was statistically significant (P = 0.03 for body fat and 0.02 for LDL-cholesterol). In the metabolomics analysis, decreases in methylglyoxal and (S)-malate in pyruvate metabolism and phosphatidylcholine (lecithin) in linoleic acid metabolism from pre- to post-intervention were observed in the Paper group.
CONCLUSIONS: In the 12-week randomized parallel trial of weight loss through a App or a Paper, we found no significant difference in change in BMI or weight between the App and Paper groups, but improvement in body fatness and LDL-cholesterol levels only in the Paper group under the circumstances with minimal contact by dietitians or health care providers.

Trial Registration: Clinical Research Information Service Identifier: KCT0004226

Keywords: Randomized controlled trial; mobile applications; weight loss; metabolomics

Nutrition Research and Practice

Sihan Song
https://orcid.org/0000-0003-1634-8004
Heejin Lee
https://orcid.org/0000-0002-6811-6726
Yang Chen
https://orcid.org/0000-0002-7796-8322
Sung-Eun Kim
https://orcid.org/0000-0002-1472-2405
Mal-Soon Shin
https://orcid.org/0000-0002-7462-2211
Youngja H Park
https://orcid.org/0000-0003-4348-2217
Jung Eun Lee
https://orcid.org/0000-0003-1141-878X

Trial Registration
Clinical Research Information Service Identifier: KCT0004226

Funding
This research was supported by the Ministry of Science and ICT (MSIT), Korea, under the Information Technology Research Center (ITRC) support program (IITP-2019-2014-1-00720) supervised by the Institute for Information & communications Technology Planning & Evaluation (IITP) and Support Program for Women in Science, Engineering and Technology through the Center for Women In Science, Engineering and Technology (WISET) funded by the Ministry of Science and ICT (No. WISET202003GI01).

Conflict of Interest
The authors declare no potential conflicts of interests.

Author Contributions
Conceptualization: Jin T, Lee JE; Data curation: Jin T, Song S, Lee H, Chen Y, Kim SE, Lee JE; Formal analysis: Jin T, Kang G, Park YH; Investigation: Jin T, Lee JE; Supervision: Park YH, Lee JE; Writing - original draft: Jin T, Lee JE; Writing - review & editing: Jin T, Kang G, Song S, Lee H, Chen Y, Kim SE, Shin MS, Park YH, Lee JE.

INTRODUCTION

The World Health Organization (WHO) reported that about 13.0% of the world's adult population was obese in 2016, and the number of individuals was thrice as many as in 1975 [1]. In Korea, estimates from the Korea National Health and Nutrition Examination Survey reported that the age-standardized prevalence of obesity increased from 26.0% in 1998 to 37.1% in 2021 [2,3]. The WHO addresses that cause of obesity and overweight includes an increase in energy-dense foods high in fat and sugars and an increase in physical inactivity [1]. In conjunction with exercise, change in dietary patterns is a key strategy to prevent and control obesity.

The WHO Global Observatory for eHealth has defined mHealth as "the use of mobile devices—such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and wireless devices—for medical and public health practice" [4]. mHealth has been suggested as a useful tool for dietary modification and obesity management. A systematic review of mHealth has shown that mobile technology interventions could improve dietary habits and physical activity [5]. A recent meta-analysis of 11 randomized trials reported that mHealth-based intervention decreased body weight by 2.45 kg, with the duration of intervention ranging from 1 mon to 1 yr [6]. In a randomized trial, dietary self-monitoring through a mobile application (App) led to an average weight loss of 6.8 kg after a 6-mon intervention [7]. A 3-mon randomized trial also reported an average weight loss of 1.8 kg with dietary self-monitoring through a App, whereas those in control gained 0.3 kg [8]. However, the differences in weight loss between mHealth and traditional self-monitoring tools, such as paper-based diaries (Papers), remain unclear. A randomized trial reported greater weight loss in the device group than in the Paper group (−4.1 kg and −1.3 kg for device and Paper groups, respectively) [9]. However, several randomized trials on weight loss have reported that the effectiveness of Apps and Papers did not significantly differ [10-12]. In another randomized trial, participants were randomly assigned to 3 groups: a App group with weekly group sessions and phone calls, a Paper group with weekly group sessions and phone calls, and a Paper group without any sessions or phone calls. After a 6-mon intervention, weight loss was greater in groups App group or Paper group with sessions and phone calls than in the Paper group without any sessions or phone calls [13]. Further randomized trials are needed to investigate the efficacy of using Apps for weight loss.

Metabolomics is the systematic study of metabolites with molecular < 1,500 Da [14]. Metabolomics has been used to explore markers and pathways related to several phenotypes and diseases. Specifically, untargeted metabolic profiling aims to identify novel metabolic markers related to phenotypes and diseases [15]. Several weight-loss trials have examined metabolic changes. A 1-yr nonsurgical weight loss program was conducted among 91 adults with obesity in Sweden [16]. After the 3-mon low calorie-diet (LCD) phase and the 6-mon weight maintenance-diet (WMD) phase, the mean weight change was −18.5 ± 15.0 kg compared with pre-intervention. Metabolic profiling was performed using serum samples, and a total of 137 metabolites were identified at pre- and post-intervention. Among these, baseline xylitol and changes in branched-chain amino acids (isoleucine, leucine, and valine) and tyrosine were positively correlated with the change in body mass index (BMI). In a Korean randomized trial, 97 adults with obesity were randomly assigned to either the LCD group or the WMD group [17]. Participants in the LCD group were instructed to decrease energy intake by 300 kcal/day for 12 weeks, whereas those in the WMD group maintained a normal diet. During the trial, changes in serum-free fatty acid and acylcarnitine levels from pre- to post-intervention were significantly greater among participants in the LCD group than in the WMD group.

https://doi.org/10.4162/nrp.2023.17.6.1238

In this study, a 2-arm randomized parallel trial was conducted to identify the differences in anthropometries and metabolic profiles between participants using a App vs. a Paper for weight loss.

SUBJECTS AND METHODS

Study participants

Participants were recruited from universities across Seoul, Korea, through posters, online community, and social networking service from July 12 to September 25, 2019. Inclusion criteria were defined as follows: 1) individuals aged 18 to 50 yrs; 2) those who had a BMI ≥ 25 kg/m^2; 3) those who were able to read and write in Korean; and 4) those who owned mobile phones and were willing to adhere to self-monitor diet for weight loss. The following exclusion criteria were applied: 1) participants who had used Apps or Papers for weight-loss purposes within a month; 2) those who were taking any medications; 3) those who had an irregular menstrual period; or 4) those who had a history of diabetes, hypertension, dyslipidemia or thyroid diseases.

When we assumed a 0.8 kg difference (1 kg of SD) between 2 groups, each group required 25 participants to achieve 80% statistical power for the *t*-test. Among the 65 eligible participants (33 men and 32 women), participants who had a BMI < 25 kg/m^2 (n = 1) at baseline; those who were diagnosed with diabetes (n = 1) or dyslipidemia (n = 5) at baseline clinical assessment; and those who withdrew from the intervention (n = 1) were excluded. As a result, a total of 57 participants (30 men and 27 women) enrolled in this study.

All of the study participants completed informed consent before enrollment. This study was approved by the Seoul National University Institutional Review Board (IRB No. 1903/003-013). The trial was finished in December 2019 and was registered at Clinical Research Information Service (cris.nih.go.kr; KCT0004226).

Screening and randomization

Before enrollment, individuals interested in this study were contacted via phone calls and asked for height and weight to calculate BMI. They were also asked for their disease history and medication history. The participants completed a checklist to ensure their eligibility for this study when they visited the study center for the baseline assessment.

Participants were randomly assigned to the App group or the Paper group using a 1:1 allocation in gender-specific strata. The randomization sequence was generated by investigators using PROC PLAN procedure in SAS version 9.4 (SAS Institute, Cary, NC, USA). The investigators and the participants were blinded about the randomization sequence until informed consent was received, and the baseline survey was completed. Participants assigned to odd numbers were allocated to the App group, whereas those assigned to even numbers were allocated to the Paper group.

Intervention

Participants were instructed to record their foods and supplements using the dietary self-monitoring tools. During the 12-week intervention period, participants were instructed to use either a App or a Paper for at least 20 days; 3 days in the first week, including at least one weekend day; any 14 days from the second week to the eleventh week; and 3 days in the last

https://doi.org/10.4162/nrp.2023.17.6.1238

week including at least one weekend day. Age, gender, self-reported physical activity level, baseline height and weight were used to calculate the estimated energy requirement (EER) based on the Institute of Medicine equations [18]. The energy goal was to reduce 500 kcal/day from the EER. Participants were advised to plan their daily diets to meet the energy goal. They were also instructed to maintain daily physical activity during the trial. During the intervention period, we contacted participants once a month to encourage the usage of dietary self-monitoring tools. After the trial, they completed questionnaires about the effectiveness of the dietary self-monitoring tools.

Participants assigned to the App group were instructed to download the "Noom Coach" application (Noom Inc., New York, NY, USA) (https://www.noom.com). After logging into the application, participants were asked to enter their age, gender, current height and weight. The energy goal for each participant was shown in the application. Participants could search for foods and supplements and record the amount they consumed. Portion sizes could be estimated using common unit sizes (e.g., cups and bowls) and standard unit sizes (e.g., gram, milliliter, and kcal). For foods not in the database, participants could create new recipes. After recording their diets, the participants could check the total daily energy they had consumed through the application. Furthermore, we provided instruction leaflets for the "Noom Coach" application and tips for weight loss strategies. Participants were not allowed to use any other dietary self-monitoring applications during the trial.

Participants in the Paper group were given Papers and energy reference books. The energy goal for each participant was noted on the first page of the diary. Date, time, name, and amount of foods and ingredients consumed were recorded on the Paper. Participants were instructed to calculate energy intake roughly using energy reference books. In addition, participants were instructed to use the 2 websites: the Korean Standard Food Composition Table published by the Rural Development Administration and the Food Composition Database published by the Ministry of Food and Drug Safety of Korea, to calculate energy intake. The instruction leaflets for the Papers, 2 website URLs, and weight loss strategy tips were provided. Participants in the Paper group were not allowed to use any mHealth tools during the intervention period. All the Papers were retrieved by the investigators after the intervention.

Anthropometric and metabolic biomarker assessments

Body weight, height, waist circumference, and body composition were measured at pre- and post-intervention. Blood samples at pre- and post-intervention were collected after a 12-h fasting period. Participants were instructed to avoid drinking or taking medicine 2 days before the blood draw. We provided leaflets, including the instructions for the blood draw, and contacted them to remind them again one day before. Moreover, questionnaires to check the fasting condition were carried out. Before the blood draw, blood pressure was monitored twice at a 10-min interval. Serum samples were kept in a deep freezer (−80°C) until the analysis.

Diabetes was diagnosed as a fasting blood glucose ≥ 126 mg/dL according to the American Diabetes Association criteria [19]. Based on the classification of blood cholesterol reported by the National Institutes of Health, participants who met 2 of the following conditions were diagnosed with dyslipidemia: 1) had a total cholesterol ≥ 240 mg/dL; 2) had a triglyceride ≥ 200 mg/dL; 3) had a low-density lipoprotein (LDL)-cholesterol ≥ 130 mg/dL; 4) had a high-density lipoprotein (HDL)-cholesterol < 40 mg/dL [20]. Details in anthropometric and metabolic biomarker assessments were shown in **Supplementary Data 1** and **Supplementary Table 1**.

https://doi.org/10.4162/nrp.2023.17.6.1238

Metabolic profiling

The intervention arms and gender were blinded when performing untargeted metabolic profiling. Details in metabolic profiling using liquid chromatography/mass spectrometry (LC/MS) were shown in **Supplementary Data 1** and **Supplementary Table 1**. The metabolic profiles at pre- and post-intervention were identified to discriminate metabolic changes according to the intervention groups and gender. Manhattan plots, hierarchical cluster analysis, and principal component analysis were performed using xmsPANDA (https://rdrr.io/github/kuppal2/xmsPANDA). xMWAS (https://kuppal.shinyapps.io/xmwas) was used to integrate metabolic profiles with anthropometric and metabolic biomarker assessments at baseline and follow-up [21]. Features with *m/z*, R/T, and metabolic intensity were annotated by Human Metabolome Database to obtain the Kyoto Encyclopedia of Genes and Genomes IDs and compound names [22]. Metabolites were uploaded to MetaboAnalyst 4.0 to match the Homo sapiens library [23]. Candidate metabolic pathways were selected according to pathway impact score, *P*-value, and the number of metabolites detected in the pathway. The pathway impact score represents the centrality of the detected metabolites, whereas the *P*-value represents the perturbation of the pathway [24].

Statistical analysis

The sample size was calculated based on our previous 6-week randomized trial [25]. By assuming the mean ± SD of weight loss difference between the App group and the Paper group is 0.98 ± 1.13 kg, a sample size of 21 per group was required to meet 80% power. Given the possible loss to follow-up, 30 participants per group were recruited.

All the analyses were performed according to the intention-to-treat principle. For the participants who did not complete the intervention period, baseline anthropometric and biomarker data were carried forward to the follow-up. Continuous data were log-transformed or box-cox transformed to improve the normality. Relative changes of anthropometric and metabolic biomarker assessments from baseline to follow-up were calculated based on the following equation: Relative Change (%) = 100 × (follow-up − Baseline)/Baseline. The differences in changes in anthropometries and biomarker levels for normally distributed and skewed data between the App group and the Paper group were analyzed using independent *t*-tests and Wilcoxon Mann-Whitney tests, respectively. In each group, the changes from pre- to post-intervention were analyzed in men and women separately. Changes in metabolic intensity from pre- to post-intervention within each group were analyzed using paired *t*-tests and Wilcoxon signed-rank tests. Log-in history for each group was assessed by the number of record days which was defined as the number of days of recording at least one food on that day. Linear regression was used to evaluate the correlation between the number of record days and weight change within each group. Because 2 participants lost the Papers at the end of the trial, the number of record days per week were calculated among 23 participants in the Paper group. All the analyses were performed using SAS version 9.4 (SAS Institute). The *P*-value < 0.05 in 2-sided tests was defined as significant.

RESULTS

Baseline characteristics

Of the 57 participants enrolled, 54 (94.7%) completed the trial (**Fig. 1**). During the 12-week intervention period, one withdrew in the eleventh week, and the other 2 did not respond. Out of the 54 participants, one failed to visit for blood collection at post-intervention but was

https://doi.org/10.4162/nrp.2023.17.6.1238

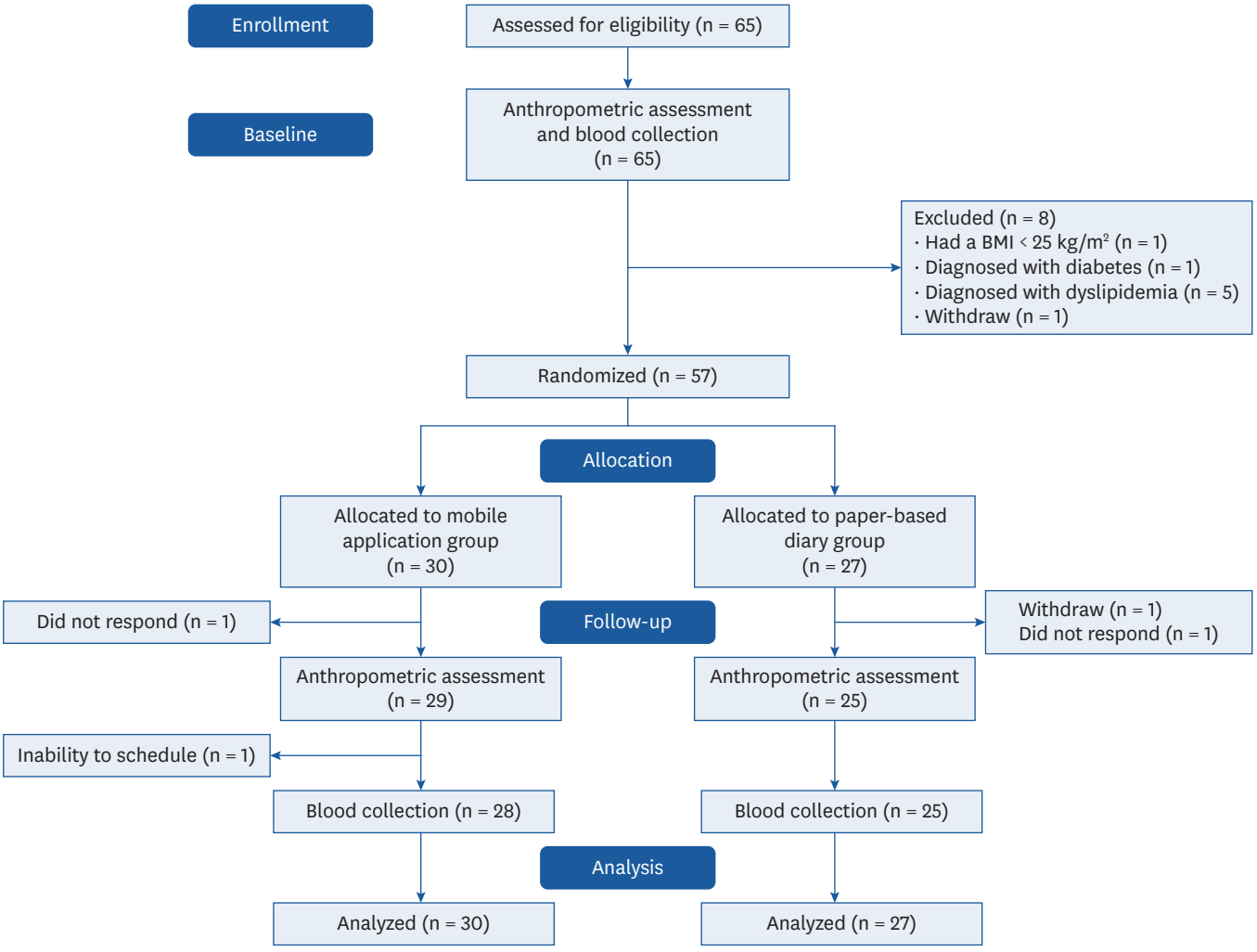

Fig. 1. Flow diagram of the study.
BMI, body mass index.

available for anthropometric assessments. The remaining 53 participants completed both anthropometric and metabolic biomarker assessments at post-intervention. **Table 1** shows the baseline characteristics of the study participants in the App group and the Paper group. The mean age was 25.4 yrs (range from 18 to 37 yrs), and the mean BMI was 27.9 kg/m^2. There were no significant differences in baseline characteristics between the App and Paper groups.

Changes in anthropometric measures

After the 12-week trial, BMI change (mean ± SD) was 0.7 ± 3.0% in the App group and −0.9 ± 3.2% in the Paper group (**Table 2**). However, the BMI change was not significantly different between the 2 groups (P for group difference = 0.11). There was a significant difference in change of body fat mass between the App group and the Paper group (P for group difference = 0.03). Body fat mass increased from pre- to post-intervention among participants in the App group but not in the Paper group. In addition, compared with pre-intervention, waist circumference was significantly decreased at post-intervention in the Paper group (P for difference = 0.04) but not in the App group. When we separated men and women, there were no differences in changes in anthropometric parameters between the 2 groups in either men

https://doi.org/10.4162/nrp.2023.17.6.1238

Table 1. Baseline characteristics of the study participants

Characteristics	All participants (n = 57)	App group (n = 30)	Paper group (n = 27)	*P*-value[1]
Age (yrs)	25.4 ± 4.9	25.0 ± 5.1	25.8 ± 4.7	0.48
Body weight (kg)	80.0 ± 11.2	81.4 ± 12.5	78.5 ± 9.6	0.34
BMI (kg/m^2)	27.9 ± 2.7	28.2 ± 3.1	27.7 ± 2.2	0.66
Gender				0.91
Men	30 (52.6)	16 (53.3)	14 (51.9)	
Women	27 (47.4)	14 (46.7)	13 (48.2)	
Country of origin				0.66
Korea	52 (91.2)	28 (93.3)	24 (88.9)	
China	5 (8.8)	2 (6.7)	3 (11.1)	
Marital status				0.28
Single	48 (84.2)	27 (90.0)	21 (77.8)	
Married	9 (15.8)	3 (10.0)	6 (22.2)	
Smoking status				0.82
Never smoker	51 (89.5)	27 (90.0)	24 (88.9)	
Past smoker	1 (1.7)	1 (3.3)	0 (0)	
Current smoker	5 (8.8)	2 (6.7)	3 (11.1)	
Alcohol consumption				0.82
Never drinker	14 (24.6)	8 (26.7)	6 (22.2)	
Past drinker	3 (5.3)	1 (3.3)	2 (7.4)	
Current drinker	40 (70.2)	21 (70.0)	19 (70.4)	

Mean ± standard deviation for continuous variables and number (%) for categorical variables.
BMI, body mass index; App, mobile application; Paper, paper-based diary.
[1]*P*-value was calculated using independent *t*-tests for continuous variables and Fisher's exact tests for categorical variables.

or women (**Table 3**). Among men, compared with pre-intervention, body fat mass significantly increased at post-intervention in the App group (*P* for difference = 0.05) but not in the Paper group. Among women, there were no significant changes in anthropometric parameters from pre- to post-intervention within either the App or Paper group. When we analyzed the data in the per-protocol analysis, we found similar results (**Supplementary Table 1**).

Table 2. Differences in changes in anthropometrics and metabolic biomarkers between the App group and the Paper group

Characteristics (mean ± SD)	App group (n = 30)				Paper group (n = 27)				*P*-value[3]
	Baseline	12-week	Change (%)[1]	*P*-value[2]	Baseline	12-week	Change (%)[1]	*P*-value[2]	
Anthropometrics									
Body weight (kg)	81.4 ± 12.5	82.1 ± 13.5	0.7 ± 3.0	0.14	78.5 ± 9.6	77.9 ± 10.4	−0.9 ± 3.2	0.18	0.11
BMI (kg/m^2)	28.2 ± 3.1	28.4 ± 3.3	0.7 ± 3.0	0.71	27.7 ± 2.2	27.4 ± 2.4	−0.9 ± 3.2	0.16	0.11
Body fat (kg)	26.2 ± 8.3	27.3 ± 9.0	4.2 ± 10.9	0.03	26.5 ± 6.9	26.0 ± 6.8	−1.6 ± 7.2	0.24	0.03
Lean body mass (kg)	55.2 ± 10.5	54.7 ± 10.3	−0.7 ± 4.0	0.25	52.0 ± 9.1	51.9 ± 9.6	−0.5 ± 2.6	0.52	0.82
Skeletal muscle mass (kg)	30.9 ± 6.4	30.7 ± 6.3	−0.6 ± 4.3	0.34	29.1 ± 5.6	29.0 ± 5.9	−0.4 ± 2.7	0.74	0.83
Waist circumference (cm)	94.5 ± 8.5	93.6 ± 10.1	−1.0 ± 4.3	0.26	93.0 ± 6.9	91.3 ± 6.9	−1.8 ± 4.4	0.04	0.59
Body fat percent (%)	32.2 ± 8.4	33.1 ± 8.3	3.4 ± 9.3	0.06	33.8 ± 7.8	33.5 ± 7.8	−0.8 ± 4.9	0.35	0.06
Metabolic biomarkers									
Fasting glucose (mg/dL)	91.7 ± 6.6	92.7 ± 6.2	1.4 ± 7.0	0.39	93.6 ± 8.8	93.1 ± 7.5	−0.2 ± 5.1	0.64	0.34
Total cholesterol (mg/dL)	168.2 ± 30.8	179.8 ± 32.3	9.6 ± 29.4	0.04	187.6 ± 24.0	187.6 ± 27.2	0.4 ± 11.7	0.74	0.06
Triglyceride (mg/dL)	92.1 ± 33.2	118.8 ± 79.0	31.0 ± 59.6	0.01	99.1 ± 36.5	108.0 ± 42.8	14.3 ± 42.2	0.28	0.23
HDL-cholesterol (mg/dL)	52.6 ± 9.1	53.2 ± 7.5	2.2 ± 11.9	0.65	52.6 ± 8.5	55.3 ± 9.2	5.8 ± 12.2	0.03	0.26
LDL-cholesterol (mg/dL)	97.0 ± 26.8	102.9 ± 26.8	12.5 ± 45.3	0.11	115.2 ± 22.7	110.7 ± 26.8	−3.1 ± 20.6	0.29	0.02
Insulin (μU/mL)	11.0 ± 6.0	12.5 ± 8.0	19.7 ± 43.8	0.20	11.7 ± 8.5	11.2 ± 7.4	11.6 ± 61.8	0.84	0.25
hsCRP (mg/L)	1.1 ± 0.9	1.1 ± 0.8	34.7 ± 135.6	0.86	1.4 ± 1.7	1.2 ± 1.6	−8.4 ± 60.8	0.01	0.27

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hsCRP, high sensitivity C-reactive protein; App, mobile application; Paper, paper-based diary.
[1]Change from baseline to 12 weeks is defined as relative change: Formula = [(Follow-Up Measurement − Baseline Measurement)/Baseline Measurement] × 100.
[2]*P*-value was calculated using paired *t*-test and Wilcoxon signed-rank test, and represented the difference from pre- to post-intervention within the group.
[3]*P*-value was calculated using independent *t*-test and Wilcoxon rank sum test, and represented the difference of the relative change between the App group and the Paper group.

https://doi.org/10.4162/nrp.2023.17.6.1238

Table 3. Differences in changes of anthropometrics between the App group and the Paper group in men and women

Characteristics (mean ± SD)	App group (n = 30)				Paper group (n = 27)				*P*-value[3]
	Baseline	12-week	Change (%)[1]	*P*-value[2]	Baseline	12-week	Change (%)[1]	*P*-value[2]	
Men									
Body weight (kg)	88.3 ± 9.6	89.2 ± 11.0	1.0 ± 2.8	0.14	82.9 ± 8.0	83.1 ± 8.3	0.2 ± 2.0	0.65	0.59
BMI (kg/m^2)	28.6 ± 2.7	28.9 ± 3.1	1.0 ± 2.8	0.14	27.4 ± 2.1	27.5 ± 2.1	0.2 ± 2.0	0.71	0.59
Body fat mass (kg)	25.0 ± 8.5	26.4 ± 9.5	4.9 ± 10.2	0.05	23.3 ± 5.7	23.2 ± 5.6	−0.3 ± 4.8	0.78	0.08
Lean body mass (kg)	63.3 ± 5.5	62.9 ± 5.2	−0.6 ± 2.8	0.36	59.6 ± 4.8	59.9 ± 5.0	0.5 ± 2.2	0.43	0.25
Skeletal muscle mass (kg)	35.9 ± 3.3	35.7 ± 3.2	−0.5 ± 3.3	0.53	33.8 ± 2.9	34.0 ± 3.0	0.7 ± 2.3	0.28	0.28
Body fat percent (%)	27.9 ± 7.3	28.9 ± 7.8	3.8 ± 8.6	0.11	27.9 ± 4.8	27.7 ± 4.6	−0.6 ± 3.7	0.53	0.08
Waist circumference (cm)	96.4 ± 6.4	96.1 ± 8.7	−0.4 ± 3.9	0.49	92.7 ± 5.0	91.8 ± 5.0	−1.0 ± 1.8	0.06	0.56
Women									
Body weight (kg)	73.5 ± 10.9	73.9 ± 11.5	0.4 ± 3.2	0.61	73.9 ± 9.1	72.3 ± 9.6	−2.1 ± 3.9	0.07	0.09
BMI (kg/m^2)	27.7 ± 3.5	27.8 ± 3.6	0.4 ± 3.2	0.99	27.9 ± 2.4	27.4 ± 2.7	−2.1 ± 3.9	0.07	0.09
Body fat mass (kg)	27.6 ± 8.2	28.4 ± 8.6	3.4 ± 12.0	0.34	30.0 ± 6.5	29.1 ± 6.9	−3.0 ± 9.1	0.26	0.27
Lean body mass (kg)	45.9 ± 6.2	45.4 ± 5.4	−0.7 ± 5.1	0.47	43.9 ± 4.0	43.3 ± 4.2	−1.5 ± 2.6	0.06	0.63
Skeletal muscle mass (kg)	25.2 ± 3.8	24.9 ± 3.3	−0.7 ± 5.4	0.50	24.0 ± 2.4	23.6 ± 2.5	−1.5 ± 2.7	0.06	0.61
Body fat percent (%)	37.2 ± 6.9	37.9 ± 6.2	2.9 ± 10.3	0.37	40.2 ± 4.7	39.8 ± 5.1	−1.1 ± 6.1	0.48	0.27
Waist circumference (cm)	92.4 ± 10.1	90.8 ± 11.2	−1.7 ± 4.9	0.22	93.3 ± 8.8	90.8 ± 8.7	−2.6 ± 6.0	0.13	0.56

BMI, body mass index; App, mobile application; Paper, paper-based diary.
[1]Change from baseline to 12 weeks is defined as relative change: Formula = [(Follow-Up Measurement − Baseline Measurement)/Baseline Measurement] × 100.
[2]*P*-value was calculated using paired *t*-test and Wilcoxon signed-rank test, and represented the difference from pre- to post-intervention within the group.
[3]*P*-value was calculated using independent *t*-test and Wilcoxon rank sum test, and represented the difference of the relative change between the App group and the Paper group.

Changes in metabolic biomarker levels

There was a significant difference in change in LDL-cholesterol level between the App group and the Paper group (*P* for group difference = 0.02) (**Table 2**). When compared with pre-intervention, total cholesterol and triglyceride levels were found to be significantly increased at post-intervention in the App group (*P* for difference: 0.04 for total cholesterol and 0.01 for triglyceride levels) but not in the Paper group. In addition, HDL-cholesterol levels increased, and high sensitivity C-reactive protein (hsCRP) decreased significantly from pre- to post-intervention in the Paper group (*P* for difference: 0.03 and 0.01 for HDL-cholesterol and hsCRP, respectively), whereas these parameters did not change significantly in the App group. When we separated men and women, a significant difference in triglyceride change was observed between the App group and the Paper group among women (*P* for group difference = 0.03) but not among men (**Table 4**). When we analyzed the data in the per-protocol analysis, we found similar results (**Supplementary Table 1**).

Changes in metabolic profiles

A total of 9,909 *m/z* features were obtained from the serum samples using LC/MS. The Manhattan plots, heat maps, and PCA score plots are shown in **Fig. 2**. Different clusters between pre- and post-intervention metabolites were shown in the PCA score plots. Among the candidate metabolic pathways, glycerophospholipid metabolism and alpha-linolenic acid metabolism were selected in the App group, whereas pyruvate metabolism and linoleic acid metabolism were in the Paper group (**Fig. 3**).

Among the metabolic pathways selected within the App group, acetylcholine (*m/z*: 146.12 $[M + H]^+$) level decreased significantly from pre- to post-intervention, whereas 1-acyl-sn-glycero-3-phosphocholine (*m/z*: 570.35 $[M + Na]^+$) and alpha-linolenic acid (*m/z*: 317.19 $[M + K]^+$) levels increased at post-intervention (*P* for difference: 0.003 for acetylcholine, 0.01 for 1-acyl-sn-glycero-3-phosphocholine, and 0.04 for alpha-linolenic acid) (**Fig. 4**). Meanwhile, methylglyoxal (*m/z*: 601.27 $[M + H - H_2O]^+$), (S)-malate (*m/z*: 152.06 $[M + NH_4]^+$)

https://doi.org/10.4162/nrp.2023.17.6.1238

Table 4. Differences in changes in metabolic biomarker levels between the App group and the Paper group in men and women

Characteristics (mean ± SD)	App group (n = 30)				Paper group (n = 27)				*P*-value[3]
	Baseline	12-week	Change (%)[1]	*P*-value[2]	Baseline	12-week	Change (%)[1]	*P*-value[2]	
Men									
Fasting glucose (mg/dL)	92.3 ± 6.8	92.8 ± 6.7	0.6 ± 4.0	0.60	96.4 ± 9.2	95.1 ± 7.9	−1.0 ± 6.6	0.46	0.41
Total cholesterol (mg/dL)	165.7 ± 36.1	185.6 ± 35.4	16.3 ± 37.4	0.03	191.8 ± 25.5	194.6 ± 26.5	1.7 ± 7.4	0.49	0.10
Triglyceride (mg/dL)	97.9 ± 32.4	127.4 ± 92.0	31.4 ± 69.2	0.08	99.9 ± 30.3	125.2 ± 49.3	31.1 ± 50.4	0.07	0.71
HDL-cholesterol (mg/dL)	48.9 ± 7.2	51.7 ± 7.3	6.3 ± 8.8	0.01	48.9 ± 6.1	51.9 ± 7.0	6.7 ± 13.4	0.11	0.91
LDL-cholesterol (mg/dL)	97.0 ± 32.2	108.3 ± 30.0	22.6 ± 58.5	0.03	122.7 ± 24.2	117.9 ± 23.4	−3.0 ± 11.7	0.67	0.10
Insulin (μU/mL)	11.4 ± 7.1	13.2 ± 9.8	19.2 ± 37.0	0.12	11.8 ± 8.9	11.1 ± 7.5	13.9 ± 81.3	0.99	0.09
hsCRP (mg/L)	1.1 ± 0.8	1.2 ± 0.9	53.5 ± 167.7	0.49	0.8 ± 0.5	0.6 ± 0.5	−10.0 ± 78.8	0.05	0.09
Women									
Fasting glucose (mg/dL)	91.1 ± 6.5	92.7 ± 5.9	2.2 ± 9.5	0.50	90.5 ± 7.4	91.0 ± 6.6	0.6 ± 2.8	0.52	0.56
Total cholesterol (mg/dL)	171.1 ± 24.3	173.2 ± 28.3	1.9 ± 14.2	0.73	183.2 ± 22.3	180.0 ± 26.8	−1.1 ± 15.2	0.29	0.57
Triglyceride (mg/dL)	85.5 ± 34.0	109.0 ± 62.9	30.6 ± 49.1	0.07	98.2 ± 43.4	89.5 ± 24.7	−3.7 ± 20.9	0.26	0.03
HDL-cholesterol (mg/dL)	56.9 ± 9.3	54.9 ± 7.6	−2.5 ± 13.5	0.33	56.5 ± 9.1	59.1 ± 10.2	4.9 ± 11.2	0.19	0.14
LDL-cholesterol (mg/dL)	96.9 ± 20.0	96.7 ± 22.0	1.1 ± 19.3	0.92	107.1 ± 18.7	103.0 ± 29.1	−3.1 ± 27.7	0.59	0.18
Insulin (μU/mL)	10.5 ± 4.7	11.6 ± 5.4	20.3 ± 52.0	0.39	11.7 ± 8.5	11.4 ± 7.6	9.2 ± 33.2	0.48	0.52
hsCRP (mg/L)	1.3 ± 1.1	1.0 ± 0.6	13.2 ± 87.4	0.25	2.0 ± 2.2	1.9 ± 2.1	−6.5 ± 35.9	0.25	0.81

HDL, high-density lipoprotein; LDL, low-density lipoprotein; hsCRP, high sensitivity C-reactive protein; App, mobile application; Paper, paper-based diary.
[1]Changes from baseline to 12 weeks is defined as relative change: Formula = [(Follow-Up Measurement − Baseline Measurement)/Baseline Measurement] × 100.
[2]*P*-value was calculated using paired *t*-test and Wilcoxon signed-rank test, and represented the difference from pre-to post-intervention within the group.
[3]*P*-value was calculated using independent *t*-test and Wilcoxon rank sum test, and represented the difference of the relative change between the App group and the Paper group.

and phosphatidylcholine (*m/z*: 800.51 $[M + Na]^+$) levels significantly decreased at post-intervention among participants in the Paper group.

Log-in history

Most participants used the tools for at least 20 days. There was no significant difference in log-in days between the App group and the Paper group (*P* for group difference = 0.11) (**Table 5**). However, over the 12-week intervention period, the number of dietary self-monitoring days was significantly higher in the App group than in the Paper group (*P* for group difference < 0.001). When we examined the correlation between the change of body weight from pre- to post-intervention and the number of energy intake self-monitoring days, body weight tended to decrease with increased self-monitoring days in the Paper group (**Fig. 5**).

Table 5. Recording days per week

Characteristics	App group (n = 29)	Paper group (n = 23)	*P*-value[1]
Recording days			0.11
< 20 days	1 (3.5)	4 (16.0)	
≥ 20 days	28 (96.6)	21 (84.0)	
Total recording days	49.1 ± 26.4	27.2 ± 12.3	< 0.01
Recording days per week			
Week 1	5.7 ± 1.4	3.7 ± 1.6	< 0.01
Week 2	3.9 ± 2.8	2.4 ± 1.6	0.11
Week 3	4.1 ± 2.9	1.9 ± 1.7	0.01
Week 4	3.6 ± 3.0	2.0 ± 1.7	0.15
Week 5	3.9 ± 2.6	1.9 ± 1.4	0.01
Week 6	3.5 ± 3.0	2.0 ± 1.5	0.18
Week 7	3.1 ± 2.9	2.0 ± 1.7	0.54
Week 8	3.3 ± 2.8	1.3 ± 1.6	0.02
Week 9	3.1 ± 2.5	1.7 ± 1.2	0.06
Week 10	3.1 ± 2.7	1.7 ± 1.6	0.09
Week 11	3.8 ± 2.4	2.2 ± 1.2	0.03
Week 12	4.1 ± 2.2	2.2 ± 1.3	< 0.01

Values are presented as number (%) or mean ± SD.
App, mobile application; Paper, paper-based diary.
[1]*P*-value was calculated using χ^2 test for categorical variable and independent *t*-test for continuous variable.

https://doi.org/10.4162/nrp.2023.17.6.1238

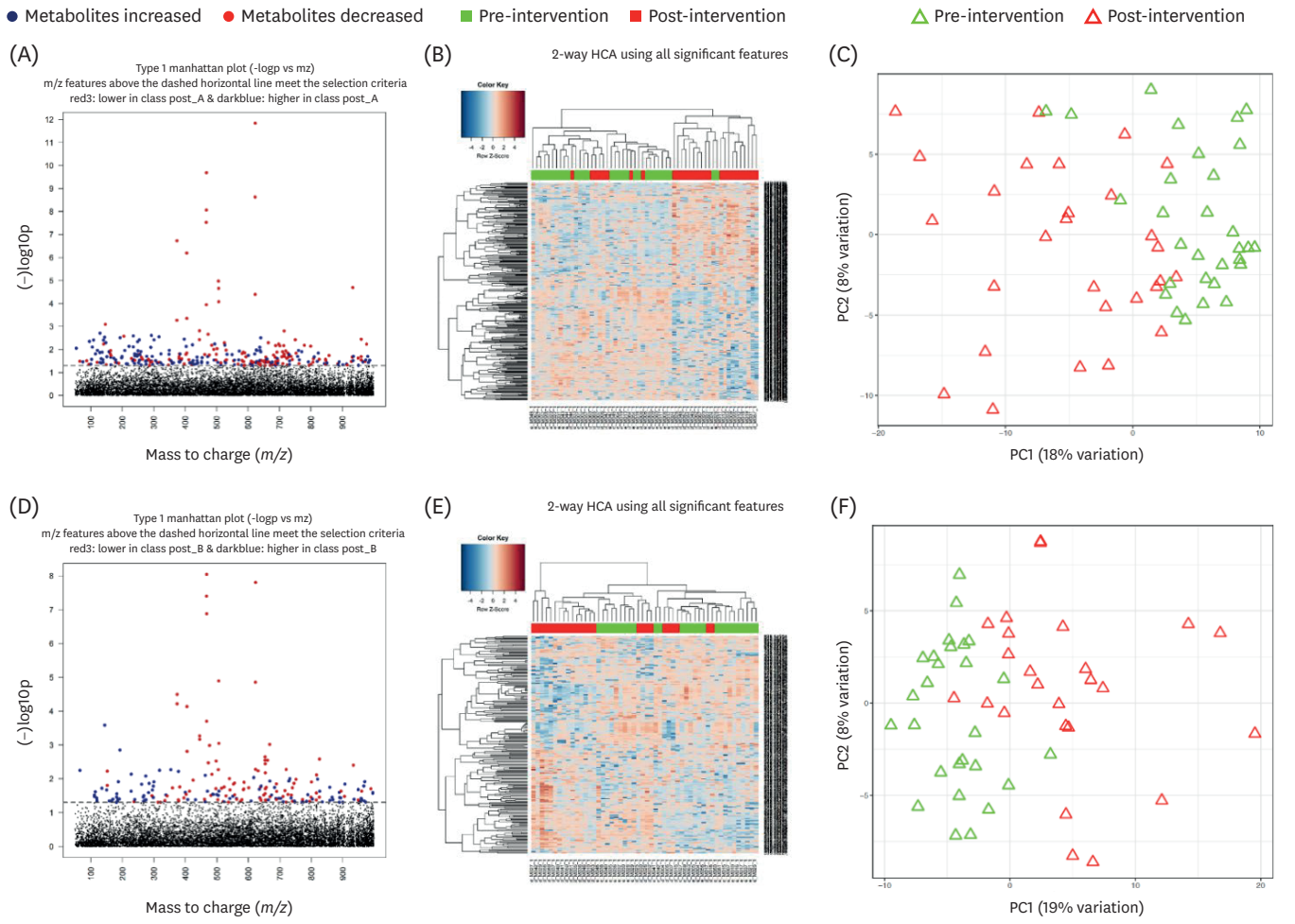

Fig. 2. Manhattan plots, heat maps, and PCA score plots of metabolic profiles within each group. (A-C) Metabolic profiles within the App group. (D-F) Metabolic profiles within the Paper group. (A, D) Manhattan plots including all detected metabolites within the App or Paper group, respectively. The blue dot represents the metabolites significantly increased from pre- to post-intervention, and the red dot represents the metabolites significantly decreased. (B, E) Heat maps include significant metabolites within the App or Paper group, respectively. The green panel represents pre-intervention, and the red panel represents post-intervention. (C, F) PCA score plots within the App or Paper group, respectively. The green triangle represents the metabolite cluster at pre-intervention and the red triangle represents the metabolite cluster at post-intervention.
PCA, principal component analysis; App, mobile application; Paper, paper-based diary.

DISCUSSION

In this 12-week randomized parallel trial of weight loss through a App or a Paper, we found no significant difference in change in BMI or weight between the App and Paper groups. Also, under the circumstances with minimal contact by dietitians or health care providers, we did not find the effect of weight loss by either a App or a paper diary. However, there was a tendency of body fat reduction only in the Paper group, suggesting that writing a food log might encourage participants to eat fewer calories than using a mobile App. LDL-cholesterol also tended to decrease only in the Paper group. When data were analyzed in men and women separately, compared to pre-intervention, triglyceride levels increased at post-intervention in the App group but decreased in the Paper group among women. In the metabolic profiling analysis, compared with pre-intervention, acetylcholine, 1-acyl-sn-glycero-3-phosphocholine, and alpha-linolenic acid levels significantly increased at post-intervention in the App group, whereas methylglyoxal, (S)-malate and phosphatidylcholine

https://doi.org/10.4162/nrp.2023.17.6.1238

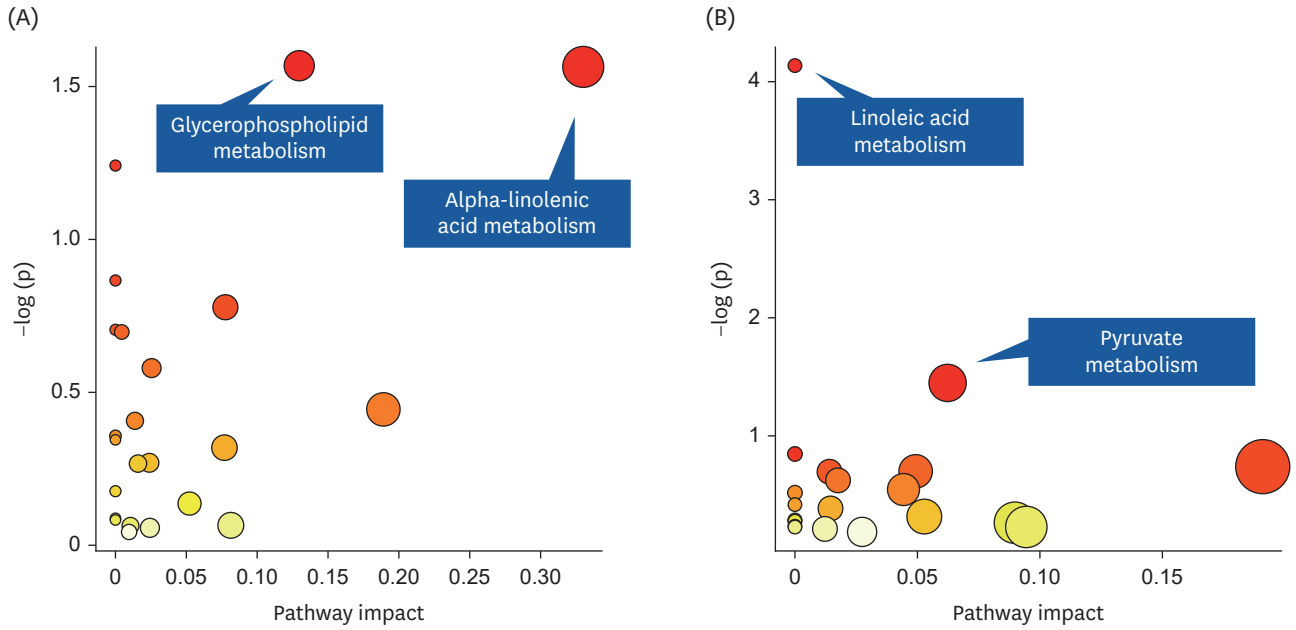

Fig. 3. Metabolic pathway analysis within the App group and the Paper group. (A, B) Pathway impact score plots within the App group and the Paper group, respectively. The size and color of the bubble represent the pathway impact score and *P*-value obtained from metabolic pathway analysis. The annotated pathway represents the selected important metabolic pathway within the App and Paper group.
App, mobile application; Paper, paper-based diary.

levels decreased at post-intervention in the Paper group. Although we did not observe weight change, our study suggests that energy intake self-monitoring for weight loss may confer overall favorable changes in metabolite profiles to a greater extent with the use of a Paper compared to a App.

mHealth has been suggested as a useful tool to facilitate dietary modification and promote healthy behavior. A few intervention studies compared the weight loss effect between Apps and Papers. They suggested that the differences in weight loss were not significant between the 2 tools. A recent US randomized trial involving 276 adults with overweight and obesity compared the weight loss effect of dietary self-monitoring through the MyFitnessPal application (SMART), a Paper with group-based treatments (GROUP), or only a Paper (CONTROL) [10]. Participants in SMART or GROUP received 42 treatment sessions in 18 mon. After an 18-mon intervention, mean body weight changes were −5.5 kg with SMART, −5.9 kg with GROUP, and −6.4 kg with CONTROL. Changes in body weight did not differ across the 3 groups. In another US randomized trial, 57 adults with BMI 25–40 kg/m^2 were randomized into 3 groups; App group, Memo group, and Paper group [12]. Participants allocated in the 3 groups were advised to track their dietary intake for 8 weeks using the "Lost it!" application, the memo function on their App, or a Paper, respectively. In the App group, participants also provided immediate feedback (FB) regarding energy intake. At the end of the trial, participants' body weight significantly decreased by 1.6 kg, 3.0 kg, and 2.0 kg among those in the App, Memo, and Paper group, respectively. However, there was no significant difference in weight loss among the 3 groups. A PDA-based randomized weight loss trial was also conducted among 210 adults with overweight and obesity in the US [26]. Participants were randomly allocated in the PDA group, the PDA + FB group or the Paper group, and were instructed to self-monitor their diets and physical activity for 24 mon. In the PDA group, participants were provided a PDA-based self-monitoring software, whereas those

https://doi.org/10.4162/nrp.2023.17.6.1238

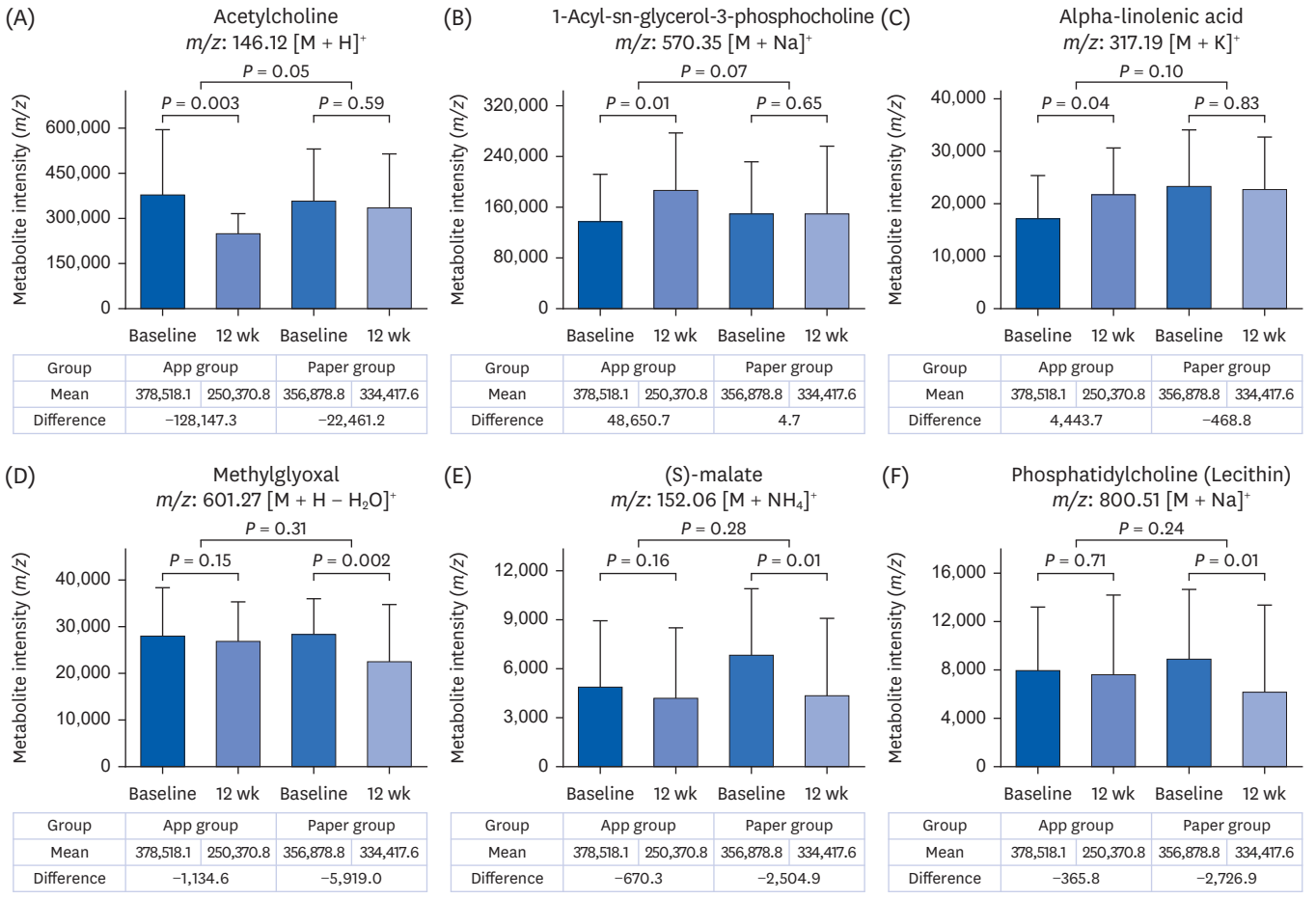

Fig. 4. Differences in changes in metabolite intensity between the App group and the Paper group. The bar graph represents the metabolites significantly changed from pre- to post-intervention within the App and Paper group. The y-axis represents metabolite intensity at pre- and post-intervention within each group. The within-group difference was calculated using pre- and post-intervention metabolite intensity by paired *t*-test and Wilcoxon signed-rank test. The between-group difference was calculated using metabolite intensity difference (post-intervention intensity − pre-intervention intensity) by independent *t*-test and Wilcoxon rank sum test.
App, mobile application; Paper, paper-based diary.

in the PDA + FB group further received FB software through which participants obtained FB on dietary intake. Participants in the Paper group were provided with a standard paper diary and a nutritional reference book. After the intervention period, participants lost their initial body weight by 1.38% in the PDA group, 2.32% in the PDA + FB group, and 1.94% in the Paper group; and the difference in mean weight loss among the 3 groups was not significant. A few intervention trials suggested that neither Apps nor Papers led to significant weight loss. In a US randomized trial, 212 obese adults with different ethnic and socioeconomic backgrounds were grouped into either the App group or the control group [27]. Participants in the App group were encouraged to use the "MyFitnessPal" application and self-monitor their diets according to the application for 6 mon. Meanwhile, participants in the control group were told to choose any activity to produce weight loss. After the 6-mon intervention period, there was no significant reduction in body weight either in the App group or the control group (mean weight change: −0.03 kg for the App group and +0.27 kg for the control group). A meta-analysis of 5 randomized trials reported no greater decrease in BMI among individuals using Apps than those using different tools [6]. In this study, we found no significant difference in changes in BMI or weight between the App group and the Paper group.

https://doi.org/10.4162/nrp.2023.17.6.1238

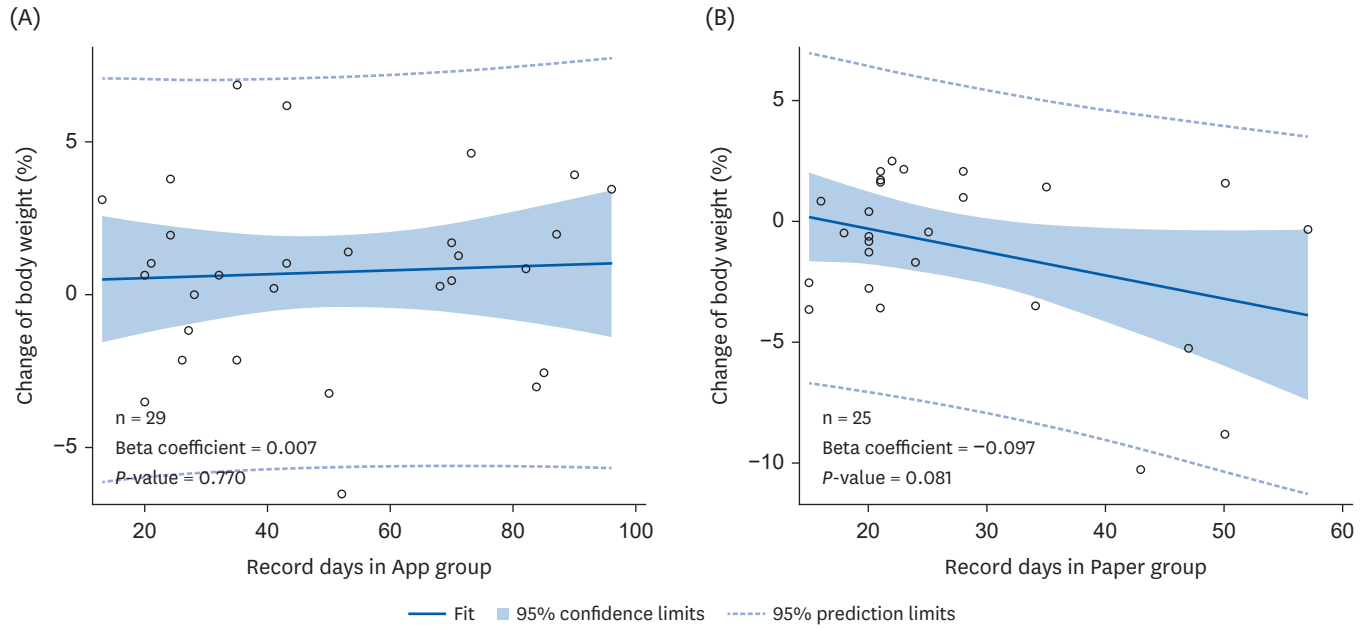

Fig. 5. Change in body weight according to the number of recording days in the App group and the Paper group.
App, mobile application; Paper, paper-based diary.

In this study, the difference in acetylcholine levels was significantly different between the App group and the Paper group, which decreased to a greater extent in the App group than in the Paper group. A recent review reported that the concentration of acetylcholine was higher in obese individuals than in those with normal body weight [28]. As a neurotransmitter, acetylcholine is elevated after a meal and promotes satiety signals in the nucleus accumbens [29]. In addition, participants in the App group had a higher alpha-linolenic acid level at post-intervention compared to pre-intervention. An experimental study suggested that n-3 polyunsaturated fatty acids, particularly docosahexaenoic acid and eicosapentaenoic acid, reduced inflammation and lipogenesis [30]. However, the pro-oxidant effect of alpha-linolenic acid has been reported [31]. Although the reason for the increase in alpha-linolenic acid levels in the App group is unclear, favorable or unfavorable effects of alpha-linolenic acid on oxidation and inflammation warrant further investigation. Participants in the Paper group showed significant decreases in methylglyoxal and (S)-malate levels at post-intervention. Methylglyoxal and (S)-malate were products of glycolysis and decreases in these metabolites may be due to reduced glucose consumption [32,33]. In addition, phosphatidylcholine decreased at post-intervention among participants in the Paper group. As the most abundant phospholipid in the cell membrane, phosphatidylcholine is involved in membrane integrity and fluidity [34]. In the liver, 30% of phosphatidylcholine is synthesized by the phosphatidylethanolamine *N*-methyltransferase (PEMT) pathway [35]. In an *in vivo* study, PEMT knockout ($Pemt^{-/-}$) had significantly lower phosphatidylcholine levels and higher oxygen consumption rates compared with the control group ($Pemt^{+/+}$) [36]. In this study, the decrease in phosphatidylcholine levels may be related to negative energy expenditure among participants in the Paper group.

In this study, no significant changes in BMI or weight loss among participants in the App group or the Paper group were observed. This study minimized aggressive intervention such as in-person education sessions, as it was aimed to examine whether participants could lose their body weight through self-monitoring of energy intake. A meta-analysis suggested that weight loss was significantly greater when participants received frequent in-person contact

https://doi.org/10.4162/nrp.2023.17.6.1238

than those with no in-person contact [37]. A US randomized trial investigated whether App-induced weight loss was modified by the frequency of in-person contacts [38]. A total of 68 obese adults were randomized to receive one of the 4 interventions; intensive counseling plus the App (IC + SP), less intensive counseling plus the App (LIC + SP), intensive counseling only (IC), and the App only (SP). Except for the IC group, all participants were instructed to self-monitor their diets and physical activity for 6 mon. In the IC groups, participants were provided healthy eating and exercise counseling 14 times, whereas the counseling was conducted 7 times in the LIC group over the 6-mon intervention period. At the end of the trial, there was a tendency to lose more weight among participants in the IC + SP and LIC + SP groups compared with the others. However, there was no statistical significance (mean weight change: −5.4 kg for the IC + SP, −3.3 kg for the LIC + SP, −2.5 kg for the IC and −1.8 for the SP, respectively). However, another trial showed that mobile-based intervention alone also showed effective weight loss. A UK randomized trial compared the weight loss effects of the "My Meal Mate" application, a website, and a Paper with no in-person contacts over the trial [39]. Further randomized trials are needed to investigate whether the frequency of in-person contact amplifies the weight loss effect via a App.

There are several strengths in our study. To our knowledge, we first examined the effect of energy intake self-monitoring on changes in anthropometric and biomarker levels and metabolic profiles through a App or Paper. This study had high follow-up and usage rates. Analyzers of metabolic profiles and biomarkers were blinded to intervention arms to avoid detection bias. This study has several limitations. First, as this study is a small pilot study, the findings of this study need to be verified in larger studies. Second, most participants were young adults recruited from the university community; therefore, the generalizability of our findings to children or the older population is limited. Third, the effect of physical activity on weight loss was not assessed during the intervention period. However, participants were instructed to maintain their usual exercise levels and similar physical activity levels persisted in both groups.

In conclusion, in the 12-week intervention study with minimal contact from dietitians or health care providers, we found no significant difference in weight loss between the App group and the Paper group but writing a paper diary showed more favorable changes regarding metabolite profiles. Our study warrants further large and prolonged prospective or intervention studies in view of the effectiveness of the combination of self-monitoring tools and in-person consultation and education.

ACKNOWLEDGMENTS

We would like to thank all participants. We also thank the Noom Coach, Inc. (Seoul, South Korea) for technological assistance.

SUPPLEMENTARY MATERIALS

Supplementary Data 1

Methods of anthropometric and metabolic measurements.

Click here to view

Supplementary Table 1

Differences in changes of anthropometrics and metabolic biomarkers between the App group and the Paper group (per-protocol analysis)

Click here to view

REFERENCES

1. World Health Organization. Obesity and overweight [Internet]. Geneva: World Health Organization; 2021 [cited 2016 April 24]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
2. Korea Centers for Disease Control and Prevention. Korea Health Statistics 1998: Korea National Health and Nutrition Examination Survey (KNHANES I). Cheongju: Korea Centers for Disease Control and Prevention; 2012.
3. Korea Centers for Disease Control and Prevention, Korea Health Statistics 2021: Korea National Health and Nutrition Examination Survey (KNHANES VIII-3). Cheongju: Korea Centers for Disease Control and Prevention; 2022.
4. World Health Organization. Atlas of eHealth country profiles 2015: the use of eHealth in support of universal health coverage based on the findings of the 2015 global survey on eHealth [Internet]. Geneva: World Health Organization; 2020 [cited 2015 April 23] Available from: https://www.who.int/publications/i/item/9789241565219.
5. Free C, Phillips G, Galli L, Watson L, Felix L, Edwards P, Patel V, Haines A. The effectiveness of mobile-health technology-based health behaviour change or disease management interventions for health care consumers: a systematic review. PLoS Med 2013;10:e1001362.
PUBMED | CROSSREF
6. Fakih El Khoury C, Karavetian M, Halfens RJ, Crutzen R, Khoja L, Schols JM. The effects of dietary mobile apps on nutritional outcomes in adults with chronic diseases: a systematic review and meta-analysis. J Acad Nutr Diet 2019;119:626-51.
PUBMED | CROSSREF
7. Turner-McGrievy GM, Wilcox S, Boutté A, Hutto BE, Singletary C, Muth ER, Hoover AW. The dietary intervention to enhance tracking with mobile devices (DIET Mobile) study: a 6-month randomized weight loss trial. Obesity (Silver Spring) 2017;25:1336-42.
PUBMED | CROSSREF
8. Stephens JD, Yager AM, Allen J. Smartphone technology and text messaging for weight loss in young adults: a randomized controlled trial. J Cardiovasc Nurs 2017;32:39-46.
PUBMED | CROSSREF
9. Ross KM, Wing RR. Impact of newer self-monitoring technology and brief phone-based intervention on weight loss: a randomized pilot study. Obesity (Silver Spring) 2016;24:1653-9.
PUBMED | CROSSREF
10. Thomas JG, Bond DS, Raynor HA, Papandonatos GD, Wing RR. Comparison of smartphone-based behavioral obesity treatment with gold standard group treatment and control: a randomized trial. Obesity (Silver Spring) 2019;27:572-80.
PUBMED | CROSSREF
11. Wang J, Cai C, Padhye N, Orlander P, Zare M. A behavioral lifestyle intervention enhanced with multiple-behavior self-monitoring using mobile and connected tools for underserved individuals with type 2 diabetes and comorbid overweight or obesity: pilot comparative effectiveness trial. JMIR Mhealth Uhealth 2018;6:e92.
PUBMED | CROSSREF
12. Wharton CM, Johnston CS, Cunningham BK, Sterner D. Dietary self-monitoring, but not dietary quality, improves with use of smartphone app technology in an 8-week weight loss trial. J Nutr Educ Behav 2014;46:440-4.
PUBMED | CROSSREF
13. Spring B, Pellegrini CA, Pfammatter A, Duncan JM, Pictor A, McFadden HG, Siddique J, Hedeker D. Effects of an abbreviated obesity intervention supported by mobile technology: the ENGAGED randomized clinical trial. Obesity (Silver Spring) 2017;25:1191-8.
PUBMED | CROSSREF

14. Dunn WB, Ellis DI. Metabolomics: current analytical platforms and methodologies. Trends Analyt Chem 2005;24:285-94.
CROSSREF
15. Dunn WB, Erban A, Weber RJ, Creek DJ, Brown M, Breitling R, Hankemeier T, Goodacre R, Neumann S, Kopka J, et al. Mass appeal: metabolite identification in mass spectrometry-focused untargeted metabolomics. Metabolomics 2013;9:44-66.
CROSSREF
16. Geidenstam N, Al-Majdoub M, Ekman M, Spégel P, Ridderstråle M. Metabolite profiling of obese individuals before and after a one year weight loss program. Int J Obes 2017;41:1369-78.
PUBMED | CROSSREF
17. Kang M, Yoo HJ, Kim M, Kim M, Lee JH. Metabolomics identifies increases in the acylcarnitine profiles in the plasma of overweight subjects in response to mild weight loss: a randomized, controlled design study. Lipids Health Dis 2018;17:237.
PUBMED | CROSSREF
18. Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Washington, D.C.: The National Academies Press; 2005.
19. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37 Suppl 1:S81-90.
PUBMED | CROSSREF
20. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-421.
PUBMED | CROSSREF
21. Uppal K, Ma C, Go YM, Jones DP, Wren J. xMWAS: a data-driven integration and differential network analysis tool. Bioinformatics 2018;34:701-2.
PUBMED | CROSSREF
22. Wishart DS, Tzur D, Knox C, Eisner R, Guo AC, Young N, Cheng D, Jewell K, Arndt D, Sawhney S, et al. HMDB: the Human Metabolome Database. Nucleic Acids Res 2007;35:D521-6.
PUBMED | CROSSREF
23. Xia J, Psychogios N, Young N, Wishart DS. MetaboAnalyst: a web server for metabolomic data analysis and interpretation. Nucleic Acids Res 2009;37:W652-60.
PUBMED | CROSSREF
24. Xia J, Wishart DS. MetPA: a web-based metabolomics tool for pathway analysis and visualization. Bioinformatics 2010;26:2342-4.
PUBMED | CROSSREF
25. Ahn JS, Lee H, Kim J, Park H, Kim DW, Lee JE. Use of a smartphone app for weight loss versus a paper-based dietary diary in overweight adults: randomized controlled trial. JMIR Mhealth Uhealth 2020;8:e14013.
PUBMED | CROSSREF
26. Burke LE, Styn MA, Sereika SM, Conroy MB, Ye L, Glanz K, Sevick MA, Ewing LJ. Using mHealth technology to enhance self-monitoring for weight loss: a randomized trial. Am J Prev Med 2012;43:20-6.
PUBMED | CROSSREF
27. Laing BY, Mangione CM, Tseng CH, Leng M, Vaisberg E, Mahida M, Bholat M, Glazier E, Morisky DE, Bell DS. Effectiveness of a smartphone application for weight loss compared with usual care in overweight primary care patients: a randomized, controlled trial. Ann Intern Med 2014;161:S5-12.
PUBMED | CROSSREF
28. Wiss DA, Avena N, Rada P. Sugar addiction: from evolution to revolution. Front Psychiatry 2018;9:545.
PUBMED | CROSSREF
29. Avena NM, Bocarsly ME. Dysregulation of brain reward systems in eating disorders: neurochemical information from animal models of binge eating, bulimia nervosa, and anorexia nervosa. Neuropharmacology 2012;63:87-96.
PUBMED | CROSSREF
30. Pahlavani M, Razafimanjato F, Ramalingam L, Kalupahana NS, Moussa H, Scoggin S, Moustaid-Moussa N. Eicosapentaenoic acid regulates brown adipose tissue metabolism in high-fat-fed mice and in clonal brown adipocytes. J Nutr Biochem 2017;39:101-9.
PUBMED | CROSSREF
31. Serini S, Fasano E, Piccioni E, Cittadini AR, Calviello G. Dietary n-3 polyunsaturated fatty acids and the paradox of their health benefits and potential harmful effects. Chem Res Toxicol 2011;24:2093-105.
PUBMED | CROSSREF

32. Richard JP. Mechanism for the formation of methylglyoxal from triosephosphates. Biochem Soc Trans 1993;21:549-53.
PUBMED | CROSSREF

33. Lu M, Zhou L, Stanley WC, Cabrera ME, Saidel GM, Yu X. Role of the malate-aspartate shuttle on the metabolic response to myocardial ischemia. J Theor Biol 2008;254:466-75.
PUBMED | CROSSREF

34. Hirata F, Axelrod J. Phospholipid methylation and biological signal transmission. Science 1980;209:1082-90.
PUBMED | CROSSREF

35. DeLong CJ, Shen YJ, Thomas MJ, Cui Z. Molecular distinction of phosphatidylcholine synthesis between the CDP-choline pathway and phosphatidylethanolamine methylation pathway. J Biol Chem 1999;274:29683-8.
PUBMED | CROSSREF

36. Jacobs RL, Zhao Y, Koonen DP, Sletten T, Su B, Lingrell S, Cao G, Peake DA, Kuo MS, Proctor SD, et al. Impaired *de novo* choline synthesis explains why phosphatidylethanolamine N-methyltransferase-deficient mice are protected from diet-induced obesity. J Biol Chem 2010;285:22403-13.
PUBMED | CROSSREF

37. Schippers M, Adam PC, Smolenski DJ, Wong HT, de Wit JB. A meta-analysis of overall effects of weight loss interventions delivered via mobile phones and effect size differences according to delivery mode, personal contact, and intervention intensity and duration. Obes Rev 2017;18:450-9.
PUBMED | CROSSREF

38. Allen JK, Stephens J, Dennison Himmelfarb CR, Stewart KJ, Hauck S. Randomized controlled pilot study testing use of smartphone technology for obesity treatment. J Obes 2013;2013:151597.
PUBMED | CROSSREF

39. Carter MC, Burley VJ, Nykjaer C, Cade JE. Adherence to a smartphone application for weight loss compared to website and paper diary: pilot randomized controlled trial. J Med Internet Res 2013;15:e32.
PUBMED | CROSSREF