SMARTPHONE APPLICATIONS FOR THE TREATMENT OF OBESITY IN ADULTS AND ADOLESCENTS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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ABSTRACT

Introduction

Obesity continues to overwhelm health care in the US with 33.1% of adults overweight, and 35.7% of adults obese.[1] Obesity causes the atherometabolic syndrome, which includes the deadly triad of dysglycemia, atherogenic dyslipoproteinemia, and hypertension, and is associated with other health problems such as the development of type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD), atherosclerotic cardiovascular disease, increased risk of certain cancers, degenerative joint disease, sleep apnea, and asthma. Favorable changes in lifestyle remain difficult to achieve, and so clinicians now rely heavily on weight-loss medications and bariatric surgery for the treatment of obesity and its associated health problems. Because of the zeal with which many people use smartphone applications ("apps"), several research groups have attempted to use applications as tools for lifestyle interventions. The applications are used primarily as instruments to decrease caloric consumption and increase physical activity. We conducted a meta-analysis of published studies to determine the strength of current evidence for an effect of smartphone applications on body weight in overweight and obese subjects.

Methods

We performed searches in databases including PubMed, Embase, Web of Science, SCOPUS, and psycINFO. Randomized controlled clinical trials in adolescents or adults that included weight as a primary or secondary outcome and used smartphone

applications in lifestyle interventions were selected for analysis. Only randomized clinical trials (RCTs) that specifically compared subjects randomized to use, or to not use, a smartphone app.

Results

Of 302 published studies on smartphone applications and weight loss, only 12 met our inclusion and exclusion criteria for our meta-analysis. The longest duration to measure weight outcome was 24 months. Taken individually, only 10 of the 12 studies reported statistically significantly more weight loss with versus without a smartphone app, and 2 studies reported significantly *less* weight loss with versus without a smartphone application. Moreover, there was considerable heterogeneity amongst the 12 studies in the smartphone applications they used and how they tested them. Nevertheless, in our meta-analysis combining the 12 studies, we found a statistically significant Hedges' g effect size of -2.260 (95% CI: -3.251 to -1.269, $p<0.001$, $I^2 = 98.591\%$) from the use of smartphone applications as part of a weight loss intervention.

Conclusion

Despite the low number of qualifying studies and their heterogeneity, our meta-analysis suggests that smartphone applications may be useful tools for lifestyle interventions for weight loss. Areas of need include longer-term studies and studies that examine hard clinical endpoints, such as effects on progression to T2DM or atherosclerotic cardiovascular events.

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CHAPTER 1

INTRODUCTION

Chronic positive caloric imbalance causes obesity and presents a risk to health.[2] Body mass index (BMI), calculated as body weight in kilograms divided by the square of the body height in meters, is the most widely used metric to define and classify obesity. In general, a person with a BMI greater than 30 kg/m^2 is defined as obese and a person with a BMI of 25 to 29.9 kg/m^2 is described as overweight.[3] Cutoffs for some racial/ethnic groups have been lowered based on their greater susceptibility to weight-related health problems.[4]

The metabolic syndrome is closely associated with obesity.[5] The syndrome is characterized by increased BMI, hypertension, increased abdominal girth, high plasma concentrations of triglycerides and low concentrations of high-density lipoprotein (HDL), impaired regulation of plasma glucose concentrations, non-alcoholic fatty liver disease (NAFLD), and an increased risk of developing type 2 diabetes mellitus.[5] The metabolic syndrome also increases cardiovascular morbidity and mortality.[6] Importantly, many, if not most, of these health problems reverse with significant weight loss.[7]

The underlying reasons for chronic positive caloric balance and obesity remain poorly understood. Dietary intake and sedentary lifestyle are the proximate causes, but numerous factors contribute to overnutrition and underexertion, such as small but measurable contributions from specific common genetic polymorphisms, food and physical activity environment, lower education level in North America but high socioeconomic status in Asia, commercial food marketing, promotion, and governmental subsidies.[8]

In the US, 33.1% of adults are overweight and 35.7 % of adults obese.[1] Overall, the prevalence of obesity among American women 38.3% is somewhat higher than among American men (34.3%),[9] a pattern that holds throughout most of the world, although some regions report more overweight men than women.[10] Heart disease, stroke, osteoarthritis, non-alcoholic fatty liver disease, type 2 diabetes, and 11 types of cancers have been associated with obesity.[11]

The cost of medical spending on obesity in the US was $\$147 \times 10^9$ in 2008.[12] Estimates indicate that Medicare and Medicaid spending could decrease by 8.5% and 11.8%, respectively, in the absence of obesity.[12]

Favorable changes in lifestyle remain difficult to achieve, and so clinicians now rely heavily on weight- loss medications and bariatric surgery for the treatment of obesity and its associated health problems. The US has undertaken several preventative measures in an attempt to reduce rates of obesity and promote a healthy lifestyle.[13] These efforts include programs and clinical trials that focus on decreasing intake of high-caloric food, increasing physical activity, and improving school health and community health education.[13]

In 2015, 68% of the US adult population owned smartphones.[14] Because of the zeal with which many people use smartphone applications, many commercial ventures have developed applications to assist with lifestyle improvement. With smartphone use becoming increasingly widespread, the general public now has easy access to numerous health and fitness applications focused on weight loss and healthy lifestyles.[15] These applications are designed to encourage users to increase their physical activity, decrease unhealthy or calorically dense food consumption, and increase healthy food intake.[15] It is estimated that 36% of smartphone users have a health application and 60.4% of these people attempted to use it to achieve behavioral health goals.[16] As of 2016, there were 2.2 million health apps in Google Play and 2.2 million health applications were placed in the Apple Store as of early 2017.[17] The global revenue projection for health applications is near $31 billion by 2020.[18] By 2018, it is estimated that more than 50% of the 3.4×10^9 smartphone users will download a health application.[19] It is anticipated that there will be 551 million active smartphone health application users globally in 2020.[18]

The smartphone applications are primarily designed to set up nutritional and physical activity goals. These health applications can be either free or paid applications. It is also important to note that majority of users do not prefer paid applications.[18]

Nutritional goals include monitoring caloric intake, or entering food consumed in a diary, monitoring fruit consumption, and measuring intake of the energy-dense nutritional poor (EDNP) food and beverages. As food diaries are notoriously inaccurate, using the software in smartphone apps to calculate calories based on food portions entered helps to reduce the error. Some of the most popular applications which use these features are: Lose it, Fitbit (which also includes an activity tracker) My Fitness Pal's Calorie Counter, Couch to 5K, Fooducate.[20] Physical activity goals on smartphone applications include monitoring walking and running distances, step counts, amounts of weight lifted, and time spent in various types of exercise. Applications such as Runtastic, Couch to 5K, Fitbit, MapMyRun, RunKeeper provide these features to monitor the physical activity through the built-in accelerometer of the smartphone.[20]

While we have a plethora of smartphone health applications today, the data on their efficacy for weight loss and ability to produce meaningful behavior change is limited. Since the first smartphone was launched only in 1999, there have been only a limited number of well-designed randomized controlled clinical trials evaluating smartphone based applications as weight loss tools.[21] We reviewed existing evidence from well-designed studies testing smartphone health applications for weight loss.

The goal of this study is to perform a meta-analysis of published studies to determine the strength of current evidence for an effect of smartphone health applications on body weight in overweight and obese subjects.

CHAPTER 2
METHODS

Search Strategy

We conducted a systematic search of articles published before March 2017. We searched PubMed (MEDLINE), Embase, Web of Science, SCOPUS and PsycINFO to find relevant articles. We selected articles in which researchers implemented the intervention by the use of smartphone health applications in order to reduce or maintain weight. We used the following search words: smartphone application and their synonyms, weight loss and their synonyms, overweight/obesity and their synonyms and related words. We included articles from the lists of reference articles which met inclusion criteria. Finally, a google scholar search was completed. Two members of the research team performed separate searches for articles to reduce the possibility of missing data.

Study Selection

Inclusion Criteria

1. Randomized controlled clinical trials;
2. Study participants are either adolescents or adults;
3. Weight change is either as a primary outcome or as a secondary outcome;
4. The weight loss intervention should be lifestyle and behavioral modification.
5. Smartphone-based online applications should be one of the interventions in the study.

Exclusion Criteria

Table 1 *Various Search Strategies for Different Databases*	
Database	Search Terms
Pubmed	("mobile application") OR ("mobile applications") OR ("mobile app") OR ("mobile apps") OR ("mobile phone application") OR ("mobile phone applications") OR ("mobile phone app") OR ("mobile phone apps") OR ("smartphone application") OR ("smartphone applications") OR ("smartphone app") OR ("smartphone apps") OR ("health app") OR ("health apps") OR ("health application") OR ("health applications") OR ("tablet application") OR ("tablet applications") OR ("tablet app") OR ("tablet apps") AND ("overweight" OR "obesity" OR "over BMI" OR "over body mass index" OR "high weight" OR "high BMI" OR "high body mass index" OR "abnormal weight" OR "abnormal BMI" OR "abnormal body mass index" OR "morbid obesity" OR "excessive weight" OR "excessive fat") AND ("weight loss" OR "weight reduction" OR "weight losses" OR "lose weight" OR "losing weight" OR "fat loss" OR "body mass reduction" OR "normal BMI" OR "healthy BMI" OR "normal body mass index" OR "healthy body mass index" OR "healthy weight")
Embase	'mobile applications' OR 'mobile application' OR 'mobile app' OR 'mobile apps' OR 'mobile phone application' OR 'mobile phone applications' OR 'mobile phone app' OR 'mobile phone apps' OR 'smartphone application' OR 'smartphone applications' OR 'smartphone app' OR 'smartphone apps' OR 'health app' OR 'health application' OR 'health applications' OR 'health apps' OR 'tablet applications' OR 'tablet application' OR 'tablet app' OR 'tablet apps' AND 'overweight' OR 'obesity' OR 'over BMI' OR 'over body mass index' OR 'high weight' OR 'high BMI' OR 'high body mass index' OR 'abnormal weight' OR 'abnormal BMI' OR 'abnormal body mass index' OR 'morbid obesity' OR 'excessive weight' OR 'excessive fat' AND 'weight loss' OR 'weight reduction' OR 'weight losses' OR 'lose weight' OR 'losing weight' OR 'fat loss' OR 'body mass reduction' OR 'normal BMI' OR 'healthy BMI' OR 'normal body mass index' OR

Table 1 *Various Search Strategies for Different Databases (continued)*

	'healthy body mass index' OR 'healthy weight'
Web of Science	(TI = (mobile applications OR mobile application OR mobile app OR mobile apps OR mobile phone application OR mobile phone applications OR mobile phone app OR mobile phone apps OR smartphone application OR smartphone applications OR smartphone app OR smartphone apps OR health app OR health application OR health applications OR health apps OR tablet applications OR tablet application OR tablet app OR tablet apps)) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years AND (TI = (overweight OR obesity OR over BMI OR over body mass index OR high weight OR high BMI OR high body mass index OR abnormal weight OR abnormal BMI OR abnormal body mass index OR morbid obesity OR excessive weight OR excessive fat)) AND LANGUAGE: (English) ANDDOCUMENT TYPES: (Article) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years AND (TI = (weight loss OR weight reduction OR weight losses OR lose weight OR losing weight OR fat loss OR body mass reduction OR normal BMI OR healthy BMI OR normal body mass index OR healthy body mass index OR healthy weight)) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years
SCOPUS	(TITLE-ABS-KEY ("mobile application" OR "mobile applications" OR "mobile app" OR "mobile apps" OR "mobile phone application" OR "mobile phone applications" OR "mobile phone app" OR "mobile phone apps" OR "smartphone application" OR "smartphone applications" OR "smartphone app" OR "smartphone apps" OR "health app" OR "health

Table 1 *Various Search Strategies for Different Databases (continued)*

	apps" OR "health application" OR "health applications" OR "tablet application" OR "tablet applications" OR "tablet app" OR "tablet apps")) AND (TITLE-ABS-KEY ("overweight" OR "obesity" OR "over BMI" OR "over body mass index" OR "high weight" OR "high BMI" OR "high body mass index" OR "abnormal weight" OR "abnormal BMI" OR "abnormal body mass index" OR "morbid obesity" OR "excessive weight" OR "excessive fat")) AND (TITLE-ABS-KEY ("weight loss" OR "weight reduction" OR "weight losses" OR "lose weight" OR "losing weight" OR "fat loss" OR "body mass reduction" OR "normal BMI" OR "healthy BMI" OR "normal body mass index" OR "healthy body mass index" OR "healthy weight"))
PsycINFO	mobile application OR mobile applications OR mobile app OR mobile apps OR mobile phone application OR mobile phone applications OR mobile phone app OR mobile phone apps OR smartphone application OR smartphone applications OR smartphone app OR smartphone apps OR health app OR health apps OR health application OR health applications OR tablet application OR tablet applications OR tablet app OR tablet apps AND overweight OR obesity OR over BMI OR over body mass index OR high weight OR high BMI OR high body mass index OR abnormal weight OR abnormal BMI OR abnormal body mass index OR morbid obesity OR excessive weight OR excessive fat AND weight loss OR weight reduction OR weight losses OR lose weight OR losing weight OR fat loss OR body mass reduction OR normal BMI OR healthy BMI OR normal body mass index OR healthy body mass index OR healthy weight

1. Studies using devices like PDA (Personal Digital Assistant) for the application intervention;

2. Studies published in a language other than English;

3 Studies using wearable technology such as a pedometer;

4. Studies where the outcomes were variables such as amount of caloric consumption, diet quality or exercise minutes without weight as either the primary or secondary outcome;

5. Studies which used a smartphone application as the intervention in both intervention and control groups but with different features in the applications;

6. Studies using a weight loss drug;

7. Studies which included populations with other conditions or medications that affect body weight/appetite/metabolism.

Data Extraction

We abstracted the general study information (title, author name, publication year), study characteristics (design, primary and secondary outcomes, randomization method), participant characteristics (age, sex, weight, etc.), study intervention types and pre-and post-study weight outcome. We obtained the mean and standard deviation of weight difference and sample size for each study. If the standard deviation was not provided in the study, we calculated it from the standard error of mean or the confidence interval.

Data Analysis

This meta-analysis included the effect size calculation, subgroup analysis, heterogeneity analysis, funnel plot analysis, study quality assessment and risk of bias grading.

Effect size calculation

Effect size described the magnitude of the relationship between two variables.[22] Cohen's d and Hedges' g are standardized measures of effect size.[22] Cohen's d can be measured by the equation given below,

$$Cohen's\ d = \frac{M_1 - M_2}{S_{pooled}},$$

where, $M_1 - M_2$ is the mean weight difference between control and intervention groups and S_{pooled} is pooled standard deviation where,

$$S_{pooled} = \sqrt{\frac{SD_1^2 + SD_2^2}{2}},$$

Here, SD_1 and SD_2 are the standard deviation of the control and intervention groups. Hedges' g can be calculated by equation given below,

$$Hedges'g = \frac{M_1 - M_2}{S^*_{pooled}},$$

where, $M_1 - M_2$ is the mean weight difference between control and intervention groups and S^*_{pooled} is pooled standard deviation where,

$$S^*_{pooled} = \sqrt{\frac{(n_1 - 1)SD_1^2 + (n_2 - 1)SD_2^2}{n_1 + n_2 - 2}},$$

Here, SD_1 and SD_2 are the standard deviation of the control and intervention groups and n_1 and n_2 are the number of participants in those groups respectively.[22] In the effect size calculation Hedges' g will provide a better estimate of effect size especially when the sample size is small.[22] Hedges' g is also called corrected effect size as it reduces the bias compared to Cohen's d.[23] We used Hedges' g to estimate the effect size.

Heterogeneity analysis

Heterogeneity in meta-analysis refers to the variation in the study outcome between studies.[22] Cochran's Q statistic was computed to check for heterogeneity in the meta-analysis and I^2 was calculated to check the magnitude of the heterogeneity.[22] We can use the fixed effects models for homogeneous trials and random effects models for heterogeneous trials.[24] To determine the degree of heterogeneity, Cochrane's Q statistic is computed as [25]

$$Q = \sum_{i=1}^{k} W_i \left(T_i - \overline{T}\right),$$

Here, W_i is weighting factor for i^{th} study assuming the fixed-effects model, T_i is effect size estimate, $\bar{T}$ is mean effect size.[25] Q statistics follows a chi-square distribution with k-1 degree of freedom, where k is number of studies.[25] $p < 0.05$ indicates rejection of the null hypothesis.

In the random effects models, the average intervention effect $\bar{T}$ was computed as,

$$\bar{T} = \frac{\sum_{i=1}^{k} W_i T_i}{\sum_{i=1}^{k} W_i},$$

where T_i is effect size estimate, and W_i is weight assigned to each study.[25] Here, W_i computed as,

$$W_i = \frac{1}{(\sigma_i^2 + \tau_i^2)},$$

where σ_i^2 is the within-study variance and τ_i^2 is between-studies variance (tau-square).[25]

In heterogeneous studies, the random effects model provides more weight to the smaller studies.[24] The I^2 statistic describes the percentage of effect size variation across studies that is due to heterogeneity rather than chance. I^2 = 100% x (Q-df)/Q. I^2 is an instinctive and a simple expression of the inconsistency of studies' results.[24]

According to Cochrane review, a rough guideline to interpret the result of I^2 is as below:

0% to 40%: might not be important;

30% to 60%: may represent moderate heterogeneity;

50% to 90%: may represent substantial heterogeneity;

75% to 100%: considerable heterogeneity.

Funnel plot

The funnel plot is a scatter plot of each of the estimated effects for the trials identified, with the mean weight difference on the horizontal axis, against the Hedges' g on the vertical axis. The vertical axis on the funnel plot is inverted with zero on top. Therefore, studies with less precise estimated effects scatter more widely at the bottom of the plot and the studies with highly precise estimated effects size will gather narrowly at the top of the plot and form the shape of a funnel.[26] A funnel plot was created to check the bias in the meta-analysis. [24]

Subgroup Analysis

We performed subgroup analyses based on time duration of primary weight outcome of the study. These studies ranged from 8-week duration to 24-month duration. These different primary weight outcome durations impact the weight loss in the participants. Therefore, we performed the subgroup analysis to estimate effects for certain differences that exist within all studies.

Study Quality Assessment

The study trials were appraised using the trial appraisal risk of bias criteria from the Cochrane handbook.[24] It included the evaluation of randomization method, allocation concealment, baseline study difference characterization, assessor blinding to study, attrition rate, sample size/power calculation, subject blind to intervention and use of intention to treat analysis.[24,27]

Risk of Bias Grading

Bias is a systematic error or deviation from truth in results or interferences.[24] Here, we will discuss the different type of biases in selected trials. Selection bias is the systematic difference between the baseline characteristics of the groups that are compared.[24] By properly randomized sequence generation and allocation concealment, we can minimize selection bias. Performance bias refers to systematic differences between groups in the care that are provided, or in exposure to factors other than the interventions of interest.[24] Blinding of study participants may reduce the bias. Detection bias is the systematic difference in groups in how outcomes are determined.[24] Binding of outcome assessors may decrease it. Attrition bias refers to the systematic differences between groups in withdrawals from the study.[24] Withdrawals from the study lead to incomplete outcome data. We can decrease attrition bias by conducting an intent to treat analysis. Intent to treat analysis implies that data from all participants who were randomized are analyzed according to their groups of distributions even if they are unable to complete all aspects of the study or withdraw early.[24] Reporting bias is the systematic difference between the reported and unreported findings.[24] It can be minimized by proper reporting of all data outcomes irrespective of their clinical or statistical significance or non-significance. Other sources of bias are defined as a bias not addressed in the previous categories.[24]

Statistical software

Comprehensive Meta-Analysis Software version 3 was used to compute Hedges' g effect size, p-values, t-scores, Q statistics and confidence intervals. A funnel plot was also created using this software. MS Excel was used to aggregate data like location, age, type of intervention from various trials.

CHAPTER 3
RESULTS

General Search Result

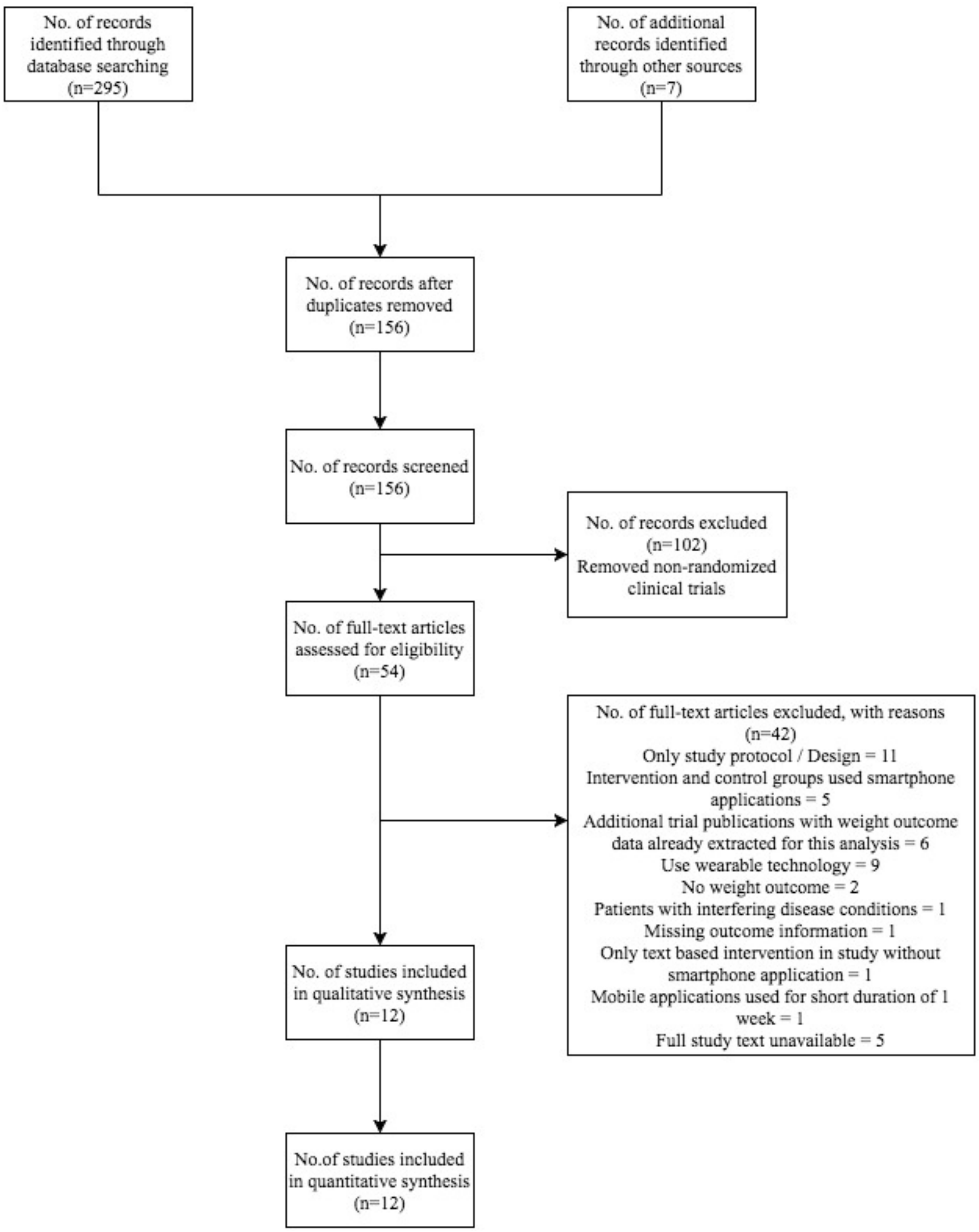

Figure 1 - Flow Chart of Search

Figure 1 shows the flow chart of the process of data search and selection. We searched PubMed, Embase, Scopus, PsycINFO and Web of Science with search strategy described in table 1 and found 295 articles. We included 7 more articles found from review articles. 146 duplicate articles were removed. From the remaining 156 articles, we excluded articles which were not randomized clinical trials. The remaining 54 articles were checked for inclusion-exclusion criteria of this meta-analysis. 42 articles which did not meet the criteria were excluded. The reasons for exclusion are described in Figure 1. The remaining 12 articles were randomized clinical trials with a smartphone application as the intervention with or without e-mail, text messages, websites, social networking applications or face to face counseling in the intervention group of the study.

Study Interventions

Interventions of the studies are shown in Table 2. Study interventions were smartphone application with or without additional interventions. These additional interventions included text messages, email, social networking elements on the application, Facebook or Twitter, use of the website and face to face counseling. The smartphone applications were used to count calories, log food intake, log exercise or set weight loss goals. In several studies, the control group also received various types of interventions which are described in table 2.

Table 2. *Description of Study Interventions*

No.	Author	Experimental group	Application Name	Application function	Control group
1	Laing BY, 2014[28]	Smartphone application + phone call 1 week after starting regarding application use + educational page handout about healthy eating at 3 months	My Fitness Pal	Logging food, exercise, social networking feature that enables users to find friends and share their progress.	Subjects choose any activity to lose the weight + Educational page handout about healthy eating at 3 months
2	Wharton CM, 2014[29]	Smartphone application	Lose it!	Calorie counter	Diet assessment with paper and pencil
3	Glynn LG, 2014[30]	Smartphone application	Accupedo-Pro Pedometer application	Tracking step counts and calories burned, goal setting functionality and goal-achievement feedback. To count steps. Physical activity goal of 10,000 steps and information on the benefits of exercise.	Physical activity goal of walking for 30 minutes per day in addition to their normal activity + information about the benefits of exercise.
4	Carter MC,	Smartphone application + tailored weekly	My Meal Mate (MMM)	Set weight loss goals + self-monitor daily	Food diary accompanied by a calorie-

Table 2. *Description of Study Interventions (continued)*

	2013[31]	text messages.	application	calorie intake + physical activity	counting book.
5	Allen JK, 2013[32]	Smartphone application	Lose It! application	Record food intake, exercise, and weight	Intensive in-person counseling of healthy lifestyle from nutritionist coach weekly for the 1st month and biweekly for the second through sixth month.
6	Godino JG, 2016[33]	Smartphone applications+ text messages + e-mails + website with blog post + technology based communication with health coach (up to 10 brief interactions for 5-15 minutes).	Goal Getter application, Be Healthy application, Trend Setter application	Goal Getter application - set weight goals and review progress. Be Healthy application - two weight challenges per day, Trend Setter application - self-monitor weight, physical activity, and diet daily	Access to health websites different from intervention participants + quarterly newsletters via email with information on health topics relevant to young adults

Table 2. *Description of Study Interventions (continued)*

7	Block G, 2015[34]	Smartphone application + web and email supplemented by automated interactive voice response (IVR) phone calls	Alive-PD application	Log calories, weight, physical activity, social networking	Usual care
8	Naimark JS, 2015[35]	Smartphone application + one face to face meeting with presentation on healthy lifestyle, healthy nutrition and benefits of physical activity	eBalance application	Users log and monitor dietary intake and physical activity	One face to face meeting with presentation on healthy lifestyle, healthy nutrition and benefits of physical activity
9	Haapala I, 2009[36]	Smartphone application	Weight balance application	The program sends a text about weight goals in response to manually entered weight, calorie goals and provides information on healthy nutrition and physical activity	Self-directed dieting
10	Weibin Zhou, 2016[37]	Smartphone application + electronic action plan as pre-visit summaries for physician office visits once a	Welltang mobile application	Provides diabetic education. Manual data entry on self-care. Users can contact the	Usual care and met their primary care physician once a month.

Table 2. *Description of Study Interventions (continued)*

		month + feedback on the blood glucose levels of patients		study team through the application and receive advice if needed.	
11	Turner-McGrievy G, 2011[38]	Smartphone application + Podcast + Twitter	Fat secret calorie counter application	Fat secret calorie counter application - Monitor physical activity and calorie intake, Twitter - Communicate with study counselor and other participants.	Podcast
12	Stephens JD, 2017[39]	Smartphone application + 20-minute face to face counseling on healthy life style+ 30- to- 40-minute face to face counseling on a healthy life style+ text messages from a coach	Lose It! application	Lose It! Application - nutritional and physical activity self-monitoring + social networking	20-minute face to face counseling on a healthy lifestyle by a trained interventionist.

Study Characteristics

7 out of 12 research studies were conducted in the US.[28,29,32-34,38,39] The remaining studies were conducted in the U.K., Ireland, Israel, Finland, China,.[30,31,35-37] The

recruitment methods included flyers, physician referral, advertisements through posters, e-mail, website, Facebook and other social sites to promote recruitment of participants (Table 3).[28-39] 11 studies recruited participants age ≥18 years and 1 study recruited age ≥16-years.[28-39] 10 out of 12 studies enrolled > 50% female participants as is typical of weight loss studies.[28-33,35,36,38,39] The percentage of female participants in the 2 studies which were not predominantly female was 34% and 41%.[34,37] The overall percentage of female participants in all 12 studies was 62 %.[28-39] 9 studies included both overweight and obese participants with BMI > 25 used as lower cut off for inclusion.[28,29,31-34,36,38,39] The remaining 3 studies did not specify BMI cut-offs for the participants.[30,35,37]

4 studies used cash incentives for participants to return for study visits.[28,33,38,39] Laing et al. provided $20 gift card for attending each follow-up visit.[28] JGodino et al. provided incentives of $40 at baseline and $50 at 6 months.[33] Turner-McGrievy et al. provided $20 incentive payment to the participants for completing 3-month and 6-month assessments.[38] Stephen JD et al. provided $25 gift cards for participation.[39] Table 3 shows detailed descriptions of studies included in the meta-analysis.

Table 3. *Study characteristics of Smartphone Application Interventions*

No.	Author	Country	Age	Female (%)	BMI (kg/m^2)	Participant Recruitment Pool	Recruitment Method	Weight change as primary outcome	Incentives Provided
1	Laing BY, 2014[28]	U.S.	≥18 years	73%	≥ 25	All patients who visited two UCLA primary care clinics	Participants were recruited during routine primary care visits with the help of a medical assistant.	Yes	Yes. $20 gift card for attending each follow-up visit.
2	Wharton CM, 2014[29]	U.S.	18-65 years	59%	25-40	Campus community at Arizona State University	Not specified	Yes	No

Table 3. *Study characteristics of Smartphone Application Interventions (continued)*

3	Glynn LG, 2014[30]	Ireland	>16 years	64%	Not specified (Mean BMI = 28.2)	Patients recruited from North Clare Primary Care in the west of Ireland.	Referral by a primary care provider or self-referral in response to the primary care center and community advertisements or mailshots.	No	No
4	Carter MC, 2013[31]	U.K.	18-65 years	77%	≥ 27	Large employers within Leeds, United Kingdom	Advertisements through email, intranet, posters, and newsletters.	No	No
5	Allen JK, 2013[32]	US	21-65 years	83%	28-42	Existing lists of volunteers from prior studies of the study investigators population visiting the hospital and the surrounding neighborhood.	flyers, physician referrals, existing lists of volunteers from prior studies of investigators and self-referrals	Yes	No

Table 3. *Study characteristics of Smartphone Application Interventions (continued)*

6	Godino JG, 2016[33]	US	18-35 years	70%	25-34.9	College students from three universities in San Diego, CA, US.	The combination of print (e.g., newspapers, flyers, posters and magnets) and digital (e.g., emails, electronic bulletins, websites and Facebook) advertisements. In-person recruitment was done at student orientations and health fairs.	Yes	Yes
7	Block G, 2015[34]	US	30-69 years	31%	≥27 (>25 for Asian participants)	Patients with a diagnosis of prediabetes (with either fasting glucose: 5.55-6.94 mmol/L or 100-125 mg/dL; HbA_{1c}: 39-46 mmol/mol or 5.7%-6.4%) in an	Initially identified through an electronic health record query of patients in an ambulatory care health care delivery system, the Palo Alto Medical Foundation (PAMF). Mailed	No	No

Table 3. *Study characteristics of Smartphone Application Interventions (continued)*

						ambulatory care health care delivery system, the Palo Alto Medical Foundation (PAMF).	letters followed by telephone call screening.		
8	Naimark JS, 2015[35]	Israel	≥18 years	84%	Not specified (mean BMI = 25.8)	Employees at large tech companies and other large organizations in south and central Israel	Via e-mail	Yes	No
9	Haapala I, 2009[36]	Finland	25-44 years	77%	26-36	Healthy adult volunteers in general population	Newspaper advertisement and telephone screening.	Yes	No
10	Weibin Zhou, 2016[37]	China	18-74 years	43%	Not specified (mean BMI = 23.04 (experimental group), mean BMI = 23.01(control group))	Patients diagnosed with diabetes mellitus type 2 at Department of Endocrinology at The First Affiliated Hospital, College of Medicine, Zhejiang	Physician referred diabetic patients	No	No

Table 3. *Study characteristics of Smartphone Application Interventions (continued)*

						University			
11	Turner-McGrievy G, 2011[38]	US	18-60 years	75%	25-45	General population in metropolitan Raleigh-Durham, North Carolina, US	Television and email advertisements	Yes	Yes
12	Stephens JD, 2017[39]	US	18-25 years	71%	25-40	Johns Hopkins University campuses employees/students and general population visiting around the campuses	Posters/flyers, Facebook, e-mail advertisement and word of mouth	Yes	Yes.

Overview of weight change outcome measurement

The length of the studies and mean weight difference among the participants before and after the studies are summarized in Table 4. Among the included studies, the shortest duration was 8 weeks long while the longest duration was 24 months to measure the weight as a primary outcome.[29,30,33] 5 studies were less than 6 months in duration and 7 studies were > 6 months in the duration.[28-39] The weight change was calculated as post intervention weight minus pre-intervention weight of all participants. All studies showed negative mean weight change in the experimental groups. The weight change ranged from -0.03 kg to -4.6 kg with a mean change of -2.00 ± 0.42 SEM.[28-39] 8 studies showed negative mean weight change in the control group.[29-35,38] The weight change among the control group ranged from 0.3 kg to -2.9 kg, mean change -0.84 ± 0.30 SEM. [28-39] It is important to note that the control group was not always a true control and may have received a form of intervention as described in table 2.

Statistical Analysis

A meta-analysis is defined as a statistical analysis of results using data obtained from two or more distinct studies.[24] We included results from 12 randomized controlled clinical trials in this analysis.

Individual trial's effect size Hedges' g was calculated using Comprehensive Meta- Analysis Software version 3. The pre-post weight difference in experimental and control group was entered in the software. Hedges' g was selected as effect size statistics as it provides a better estimate of effect size especially when the sample size is small. It

Table 4. *Average Weight Change Following Study Interventions*

Author	Duration of measurement of weight outcome	Experimental Group (kg)				Control Group(kg)			
		Mean Weight Change (kg)	SD	SE	Total No. of Participants	Mean Weight Change (kg)	SD	SE	Total No. of Participants
Laing BY, 2014[28]	6 months	-0.030	4.640	0.453	105	0.270	4.640	0.449	107
Wharton CM, 2014[29]	8 weeks	-1.590	1.980	0.454	19	-2.000	2.110	0.545	15
Glynn LG, 2014[30]	8 weeks	-0.330	1.900	0.283	45	-0.160	2.300	0.343	45
Carter MC, 2013[31]	6 months	-4.600	5.199	0.793	43	-2.900	5.849	0.903	42
Allen JK, 2013[32]	6 months	-1.800	3.700	0.897	17	-2.500	4.100	0.966	18
Godino JG, 2016[33]	24 months	-1.100	19.997	1.407	202	0.300	19.997	1.407	202
Block G, 2015[34]	6 months	-3.260	0.033	0.003	163	-1.260	0.034	0.003	176

Table 4. *Average Weight Change Following Study Interventions (continued)*									
Naimark JS, 2015[35]	6 months	-1.440	0.400	0.048	69	-0.128	0.360	0.066	30
Haapala I, 2009[36]	12 months	-4.500	5.000	0.635	62	-1.100	5.800	0.731	63
Weibin Zhou, 2016[37]	3 months	-0.200	16.877	2.387	50	0.200	17.614	2.491	50
Turner-McGrievy G, 2011[38]	3 months	-2.400	3.400	0.496	47	-2.300	3.000	0.429	49
Stephens JD[39]	3 months	-2.700	21.268	3.820	31	1.500	14.302	2.569	31

Abbreviation – SD –Standard Deviation; SE – Standard Error of Mean; kg - kilogram

was common practice to first calculate fixed-effect model and subsequently switch to random effect model if the heterogeneity was significant. The random effect model corrects for the difference in the observed effect sizes due to sampling error and true variability in population parameter.

Figure 2 shows an effect size of experimental group compared to control group for 12 trials. The corresponding forest plot shows effect sizes and weight of each of the trials. The size of the square on each plot describes the weight assigned to the trial, with a smaller square representing smaller weights and a larger square representing the larger weight. The mean, standard deviation and sample size of each trial was entered and effect size and weight of each study was calculated using Comprehensive Meta-Analysis software version 3. The overall mean effect size, Hedges' g was -2.26 (SE = 0.506, 95% CI: -3.251 to -1.269, $p<0.001$) and it was statistically significant. On average the weight loss in the experimental group was 2.26 SD more than the control group. These results suggest that a smartphone application intervention can produce meaningful weight loss compared to more traditional lifestyle interventions. The standard error shows the confidence in effect size. In this meta-analysis, the effect size is -2.260 plus or minus 0.506.

Cochran's Q statistic was computed to check the homogeneity in the meta-analysis. Table 5 summarizes the test for homogeneity using the random effects model. Q value is 116.77 with $p<0.001$. This result rejects the null hypothesis that the trials are homogenous and accepts the presence of heterogeneity of the trials. I^2 was calculated to check the magnitude of the heterogeneity. With the I^2 value of 98.591, we can confirm the high heterogeneity among the trials.

Tau square is the estimate of between-study variance.[24] In this meta-analysis tau square is 2.846. Square root of tau is the estimated standard deviation of the underlying effect across the study which is 1.687 for this meta-analysis.[24]

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Laing BY	-0.064	0.137	0.019	-0.333	0.204	-0.471	0.638	8.92
Wharton CM	0.197	0.338	0.114	-0.466	0.859	0.582	0.561	8.63
Glynn LG	-0.080	0.209	0.044	-0.490	0.330	-0.382	0.702	8.84
Carter MC	-0.305	0.216	0.047	-0.728	0.119	-1.409	0.159	8.84
Allen JK	0.175	0.331	0.110	-0.474	0.824	0.528	0.597	8.65
Godino JG	-0.041	0.099	0.010	-0.236	0.154	-0.412	0.680	8.95
Block G	-59.960	2.305	5.314	-64.478	-55.441	-26.010	0.000	3.13
Naimark JS	-3.351	0.322	0.104	-3.983	-2.720	-10.401	0.000	8.66
Haapala I	-0.624	0.182	0.033	-0.981	-0.267	-3.425	0.001	8.88
Weibin Zhou	-0.023	0.198	0.039	-0.412	0.366	-0.116	0.908	8.86
Turner-McGrievy G	-0.031	0.203	0.041	-0.428	0.366	-0.153	0.878	8.85
Stephens JD	-0.229	0.252	0.063	-0.722	0.264	-0.909	0.363	8.78
	-2.260	0.506	0.256	-3.251	-1.269	-4.470	0.000	

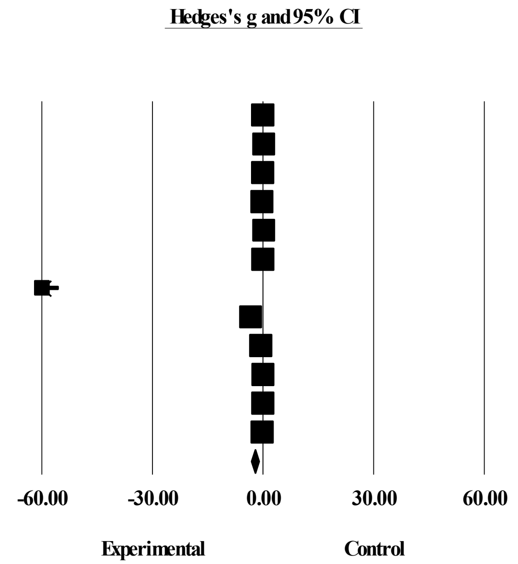

Figure 2. Smartphone Applications and Weight-loss Meta-analysis

Table 5. *Post-Treatment Test for Using Random Effects Model*

No. of trials	Point estimate	Standard Error	Z-value	P-value	Q	Df(Q)	P-value	I-squared	Tau squared	Standard Error	Variance	Tau
12	-2.260	0.506	-4.470	<0.001	780.594	11	<0.001	98.591	2.846	1.610	2.593	1.687

Sub-Group Analysis

Table 6 shows the subgroup analysis. The usual course of lifestyle interventions for weight-loss is that weight is lost quickly in the first 3-6 months, and the point of greatest loss occurs 6 months after beginning treatment; then the weight is typically slowly regained until weight returns to nearly the baseline level over 6-24 months.[40] We selected a duration of 6 months for the subgroup analysis accordingly.

Table 6. *Subgroup Analysis*

Variables	Category	Number of studies	Hedges' g	95 % CI	Heterogeneity			
					Tau^2	Q-value	I^2, %	p-value
Time Duration	≤ 3 months	5	-0.052	-0.251 to 0.147	<0.001	1.085	<0.001	0.897
	>3-6 months	5	-9.884	-13.189 to -6.580	13.344	758.390	99.473	<0.001
	>6 months	2	-0.312	-0.882 to 0.257	0.148	7.893	87.330	0.005

The studies with time duration of ≤ 3 months had effect size of -0.052 (95% CI: -0.251 to 0.147, $I^2 < 0.001\%$, $p = 0.897$), >3-6 months had effect size of -9.884 (95% CI: -13.189 to -6.580, $I^2 = 99.473$, $p < 0.001$) and > 6 months had effect size of -0.312 (95% CI: -0.882 to 0.257, $I^2 = 99.267\%$, $p < 0.005$). We can conclude from this sub group analysis that studies with > 3 to 6-month time duration showed large effect size compared to other time duration groups.

Funnel Plot

Figure-3 shows the funnel plot. As a rule of thumb, the funnel plot test is only conducted to check the bias for the meta-analysis which included more than 10 studies. Studies less than 10 weaken the funnel plot test's power. The funnel plot test was checked with the visual symmetry. Plots without visual symmetry suggest bias.[24]

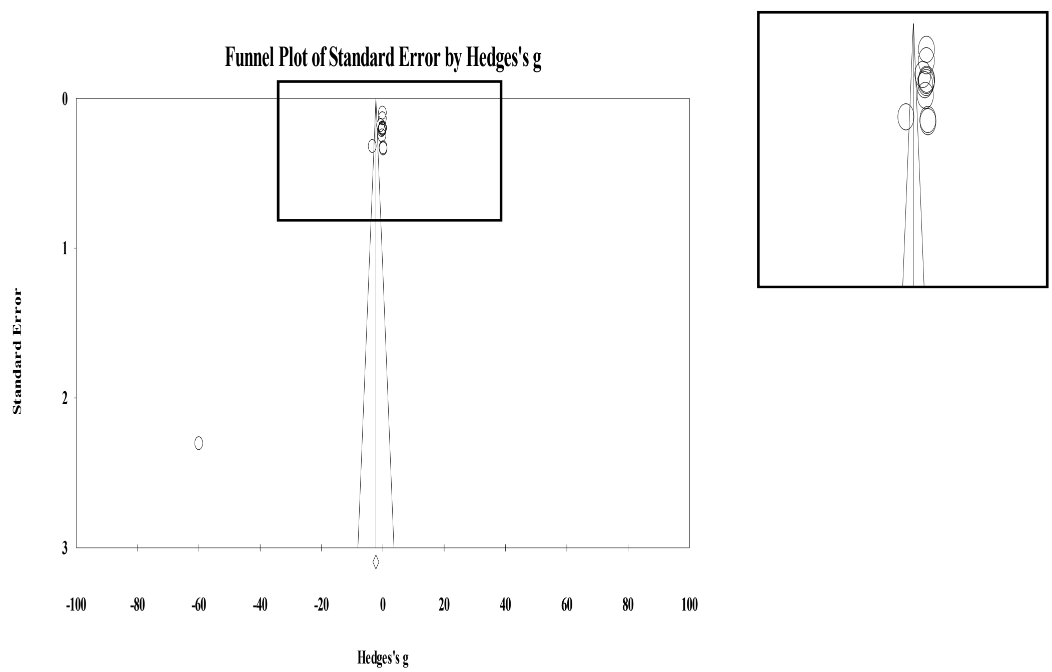

Figure – 3 Funnel plot of meta-analysis

The Egger's test was used to check the asymmetry of the funnel plot with linear regression approach. The null hypothesis for Egger's test is that symmetry exists in funnel plot, the alternative hypothesis suggesting the asymmetry in the funnel plot. The intercept value provides the measure of asymmetry- a larger deviation from zero is indicative of more noticeable asymmetry. The intercept value remains close to zero in the symmetrical funnel plot.[41] In table 7, the Egger's test for this meta-analysis shows the intercept value -12.16595 ($p = 0.01725$). With the p-value <0.05, we can interpret the presence of bias in the study, and the result is statistically significant.

Table 7. *Egger's Regression Test*

Intercept	-12.16595
Standard error	4.26880
95% lower limit (2-tailed)	-21.67742
95% upper limit (2-tailed)	-2.65448
t-value	2.84997
df	10
P-value (1-tailed)	0.00863
P-value (2-tailed)	0.01725

Various factors lead to asymmetry in the funnel plot. The publication bias- the failure to include all relevant trials because they were not published- is the main cause of asymmetry in the funnel plot. It is influenced by various factors like study outcome, study size, and funding resources. Further sources of bias are language bias and citation bias. Language bias is the selection of trials in predominantly available languages like English. Citation bias is the higher citing of studies with positive results compared to those with negative or null results. Other factors like true heterogeneity, poor methodological design of small studies, inadequate analysis and artefactual fraud are also likely to cause asymmetry in the funnel plot.[41]

Missing Data

We encountered various types of missing data like missing trials, missing outcomes and missing individual participants in the meta-analysis.[24] Trials not included in the meta-analysis are either never published or were published in unidentifiable sources. These are most likely to be trials with negative outcomes encountering a publication bias. In addition, the possibility of selective reporting can cause an outcome bias. Incomplete reporting is a possible cause for missing summary data from trials. We excluded trials with missing outcome data or incomplete reporting of weight changes. A factor which significantly increased the validity of this analysis was that 11 out of 12 trials had 'intent to treat analysis' to decrease the bias. The one remaining trial which did not use intention to treat analysis used the completer only analysis.

Quality Assessment of Trials

Quality assessment of trials is summarized in table 8. A total of 9 trials out of 12 trials described the method of randomization.[28,30,31,33-35,37-39] Methods of randomization used were simple, stratified or block randomization with computer software. 4 out of 12 trials stated that allocation was concealed.[28,30,33,34] 8 trials did not conceal the allocation.[29,31,32,35-39] All 12 trials, had no significant differences in baseline characteristics of the experimental and control participants.[28-39]

Sample size and power calculation was adequate in 8 studies.[28,30,33-36,38,39] Due to the nature of intervention- smartphone applications, it was technically impossible to blind the participants. Only one study was able to partially blind the participants for 1 week by asking all participants to carry their smartphone while the application display was not visible to either group.[30] Except for one trial which performed a completers only analysis, all trials performed an intent to treat analysis.[28-39]

Table 8. *Critical Appraisal Quality Rating*

Author	Randomization Method Clear + Appropriate?	Allocation concealment	Difference in baseline Characteristics	Assessors/ Caregiver blind to the study?	Method of Data Collection	Minimal attrition? / The difference between groups?	Attrition Rate	Sample size / power calculation	Subjects blind to intervention?	Intention to treat analysis?
Laing BY, 2014[28]	Yes	Yes	No difference	Partial blinding. Clinicians and clinic staff were blinded to the group assignment. Control group patients were blinded to the name of the	RED Cap TM electronic data capture tools hosted at UCLA. Experimental group completed a survey on their experience using MFP (My Fitness Pal) application. Interview six participants who lost more than 10 pounds. They were asked if they thought MFP helped them lose weight, and if so, how	High attrition (only attrition rate in percentage was provided)	32% in experimental group and 19% in control group (Intent to treat - ITT)	N = 180 to allow 55 % attrition, 80% power	No	Yes

Table 8. *Critical Appraisal Quality Rating (continued)*

				application						
Wharton CM, 2014[29]	Yes	Not described	No difference	No	At the start of the study, participants met with investigators for anthropometric measurements and to complete a short health history, which included questions on health, recent dieting and weight loss, and use of medications and/ or supplements. Customary physical activity data were gathered using a standard physical activity questionnaire.	Experimental 19/19, Control 10/15	0% in experimental and 33.33 % in control group (ITT)	Information not available	No	Yes
Glynn LG, 2014[30]	Yes	Yes	No difference	Yes	At the end of weeks 1, 2, and 8, all participants were contacted via SMS and asked to email their step-count data to the research team using a 'share data' function of the application. The blood pressure was measured by a trained research nurse. The other secondary outcomes were measured at the start and	Experimental 37/45. Control 40/45.	Experimental 17.78 % and Control 11.11 % (ITT	N = 80 to allow 15 % attrition rate, 80% power	No	Yes

Table 8. *Critical Appraisal Quality Rating (continued)*

					end of the study.					
Carter MC, 2013[31]	Yes	No	No difference	Yes (Fieldworkers carrying out measurements on participants were blinded and participants were asked not to discuss about it.)	Eligible participants were invited to attend a baseline enrollment session at the University of Leeds where research assistants measured height, weight, and percentage body fat (BF), and baseline questionnaires self-completed. The surveys were designed to collect information on demographics, technology usage, attitudes toward weight loss, physical activity, eating behavior, and a variety of psychosocial variables	Experimental 40/43, Control 22/43.	Experimental 6.98 % and Control 48.84 % (ITT)	The pilot trial is not statistically powered to detect change in anthropometric measures	No	Yes
Allen JK, 2013[32]	Yes	Not Described	No difference	Not described	Physical activity was evaluated with the Stanford 7-Day Physical Activity Recall. Dietary intake data were collected from 3-day food records and analyzed using the Nutrition Data System for Research (NDSR) software	Experimental 10/17 control 12/18.	Experimental41.18 % and control 33.33 % (ITT)	Not powered to detect statistically significant between-group	No	Yes

Table 8. *Critical Appraisal Quality Rating (continued)*

					version 2012			differences in changes in weight		
Godino JG, 2016[33]	Yes	Yes	No difference	Yes Measurement assessors were blinded to the study intervention.	Primary and secondary outcomes were assessed as a pre-specified exploratory outcome. Additional secondary outcomes were measured through self-report. They include physical activity measured with the Paffenbarger Physical Activity Questionnaire and the Global Physical Activity Questionnaire II	Experimental 185/202 control 196/202.	Experimental 8.42 % and control 2.97 % (ITT)	N = 254 to allow 30% attrition rate, 80% power	No	Yes
Block G, 2015[34]	Yes	Yes	No difference	Yes (The research and clinical staff at PAMF was masked to group assignment)	Enrolled participants completed a brief questionnaire online, which provided information required for randomization.	Experimental 136/163 control 156/176 at 6 months.	Experimental 16.56 % and control 11.36 % (ITT)	N = 314 to allow 15 % attrition rate, 80 % power	No	Yes
Naimark JS,	Yes	Not desc	No diff	Not	Anthropometric measurements of weight and	Experimental	Experimental	N = 60 in experime	No	No

Table 8. *Critical Appraisal Quality Rating (continued)*

2015[35]		ribed	erence	described	waist were obtained by the researcher at the introductory meeting. Participants completed nutrition knowledge, diet quality, and physical activity type and duration questionnaires through the Internet. The experimental participants also completed a satisfaction survey at the end of the study.	56/69 control 29/30 at 6 months.	18.84 % and control 3.33 % (completer only analysis)	ntal group to allow 20 % attrition rate, 80% power		
Haapala I, 2009[36]	Yes	Not described	No difference	Partial blinding (The study nurse was blind to the randomization procedure and general health related data)	Weight, height and waist circumference measurements were performed at each follow-up by two study nurses according to standardized procedures	Experimental 45/62 control 40/63 at 6 months.	Experimental 37.78 % and control 36.51 % (ITT)	N = 156 to allow 30 % attrition rate, 80 % power	No	Yes
Weibin Zhou, 2016[37]	Yes	Not described	No difference	No	All patients completed the diabetes self-care behavior questionnaire and a diabetes knowledge survey. Health and	No	Experimental 0.00 % and	Information not available	No	Yes

Table 8. *Critical Appraisal Quality Rating (continued)*

					medical history were recorded through questionnaires. The study team measured demographic characteristics such as height and weight, waist and hip circumferences, and blood pressure. HbA1c and LDL-C levels were measured in our hospital laboratory		control 0.00 % (ITT)			
Turner-McGrievy G, 2011[38]	Yes	Not described	No difference	No	Dietary intake from 2 days of unannounced 24-hour dietary recalls (1 weekday and 1 weekend day) collected using the Automated Self-administered 24-hour Dietary Recall; physical activity (Paffenbarger Physical Activity Questionnaire); self-efficacy (Weight Efficacy Life-Style Questionnaire [WEL]); and eating behaviors (Eating Behavior Inventory [EBI]). Participants were also asked (on a 1- to 7-point Likert scale) to rate how supported they felt in their	Experimental 44/49 control 42/47 at 6 months.	Experimental - 10.20 % and control - 10.64 % (ITT)	N = 96 to allow 10 % attrition rate, power = 80 %	No	Yes

Table 8. *Critical Appraisal Quality Rating (continued)*

					weight-loss efforts at 6 months.					
Stephens JD,2017[39]	Yes	Not Described	No difference	Not described	Body weight was measured using the Tanita BS-549 scale with the participant in light clothing. Height was measured using a wall stick measurement. Physical activity was evaluated with the Godin Leisure-Time Exercise Questionnaire. Nutrition data were collected using the National Cancer Institute's Automated Self-Administered 24-hour Recall. Self-efficacy for healthy eating and exercise were evaluated with 2 questionnaires.	Experimental 29/31 Control 30/31 at 3 months	Experimental 6.45% and control 3.23 % (ITT)	N = 60 to allow 15 % attrition rate, power = 80 %	No	Yes

Risk of Bias Grading

The risk of bias grading is summarized in Table 9. The risk of bias was graded based on the information given in study quality assessment in table 8. It was graded according to the Cochrane classification as low, high, or unknown risk. From 12 trials, 8 had a low risk of adequate sequence generation selection bias for participant randomization.[28,30,31,33-35,37,38] 4 trials had low selection bias risk for allocation concealment. [28,30,33,34] Because use of smartphone application was the intervention in these trials, it was difficult to blind participants to the intervention. 11 out of 12 trials did not blind the participants from the intervention.[28,29,31-39] Only 1 trial blinded the participants for the initial period of 1 week.[30] 3 trials had a low risk of outcome assessment as they blinded the person who measured the outcome among the participants.[31,33,34] High attrition bias was found in 1 trial; this trial did not use an intent to treat analysis.[35] All trials had a low risk of selection bias due to complete reporting of primary and secondary outcomes results. 1 trial had bias from unequal sample size.[35]

Table 9. *Risk of Bias Adapted from The Cochrane Handbook Trial Appraisal*

Author	Selection Bias		Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias
	Random Sequence Generation	Allocation concealment	Participant Binding	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Another source of bias.
Laing BY, 2014	Low Risk	Low Risk	High Risk	High Risk	Low Risk	Low Risk	Low Risk
Wharton CM, 2014	Unclear Risk	Unclear Risk	High Risk	High Risk	Low Risk	Low Risk	Low Risk
Glynn LG, 2014	Low Risk	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Low Risk
Carter MC, 2013	Low Risk	High Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk
Allen JK, 2013	Unclear Risk	Unclear Risk	High Risk	High Risk	Low Risk	Low Risk	Low Risk
Job G Godino, 2016	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk
Block G, 2015	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk
Jenny Safran Naimark, 2015	Low Risk	Unclear Risk	High Risk	High Risk	High Risk	Low Risk	High Risk
Irja Haapala, 2009	Unclear Risk	Unclear Risk	High Risk	Unclear Risk	Low Risk	Low Risk	Low Risk
Weibin	Low	Unclear	High	High	Low	Low	Low

Table 9. *Risk of Bias Adapted from The Cochrane Handbook Trial Appraisal (continued)*

Zhou, 2016	Risk	Risk	Risk	Risk	Risk	Risk	Risk
Turner-McGrievy G, 2011	Low Risk	Unclear Risk	High Risk	High Risk	Low Risk	Low Risk	Low Risk
Stephens JD, 2017	Unclear Risk	Unclear Risk	High Risk	High Risk	Low Risk	Low Risk	Low Risk

CHAPTER 4

DISCUSSION AND CONCLUSIONS

The purpose of the study is to examine the effect of a smartphone application intervention compared to control. The current meta-analysis incorporating data from 12 randomized clinical trials, described the statistically significant Hedges' g effect size -2.260 (95% CI: -3.251 to -1.269, $p<0.001$, $I^2 = 98.591\%$). This result favored the smartphone application intervention compared to a traditional intervention for weight loss. While this result is encouraging, we need further research about the longer-term weight loss achievable from smartphone applications. The longest trial duration in this analysis was 24 months with only one trial having a long-term weight loss outcome at 24 months.[33] The majority of the trials were 3-6 months' duration with a mean time to measurement of 4.8 months with SE of 0.5. We also need to explore the generalizability and cost-effectiveness of the smartphone application intervention in larger populations of various ethnicities and cultural background.

The systematic review by R. Bacigapulo et al. which included studies published between January 1998 to October 2011 suggested statistically significant weight loss can be achieved from mobile device assisted technologies. Seven articles were included in their meta-analysis. This analysis included trials using wearable technology and studies which used some of the earlier handheld mobile devices without smart features.[42] Another systematic review by KN DiFilippo et al. included four studies in the analysis and the analysis suggested inconsistent weight loss results from a smartphone application intervention. This review included randomized clinical trials, non-randomized trials, and cohort studies in the analysis.[43]

A meta-analysis research conducted by F Liu et el. focused on the only mobile based text message intervention for weight. It showed a statistically significant weight loss effect. The intervention consisted of Short Message Service (SMS) or Multimedia Messaging Service (MMS). A significant weight change of -1.44 kg (95% CI -2.12 to -0.76, I^2 = 59.2%, p=0.003) was seen in comparison to the control group.[44] Another review by GF Mateo et al., had encouraging results on the effect of smartphone apps on weight loss and physical activity. This review included trials with wearable devices in experimental group, and a smartphone application in experimental and control group. The intervention which consisted of a smartphone application with or without a wearable device was associated with significant change in weight of -1.04 kg (95% CI -1.75 to -0.34, I^2 = 41%, p=0.04) when compared to use of smartphone application alone in the control group. The difference in physical activity was observed between the two groups (standardized mean difference 0.40, 95% CI -0.07 to 0.87; I2 = 93%, p=0.09).

This analysis included lower quality evidence from non-randomized trials along with randomized clinical trials. In addition, the control groups did receive a smartphone application intervention which can reduce the magnitude of effect seen. [45]We included only randomized controlled clinical trials in our meta-analysis. Randomized clinical trials used a smartphone application as a weight loss intervention compared to standard coaching methods in control group. Since the control groups were not true controls in any of the 12 trials, the effect size is expected to be smaller than if the controls received no intervention. The main features the smartphone applications used as weight loss interventions in the studies were calorie counting, communication and physical activity tracking.

The smartphone app intervention did not include a wearable device or activity tracker. Our group has previously shown that a smartphone app based lifestyle intervention along with a wearable device produces statistically significant and clinically meaningful weight loss at 3 months.[46] We hypothesize that combined with smartphone app based technology these contemporary devices can be useful weight loss tools.

The biggest strength of our analysis is the inclusion of only randomized controlled trials, decreasing the likelihood of association of weight loss and smartphone application intervention due to confounding and bias. In addition and importantly, 11 out 12 trials performed ITT analysis with only 1 trial conducting a completers only analysis due to high rate of attrition as is typical of lifestyle based weight loss studies.

There are some limitations to our analysis. We conducted the search of trials in locations like PubMed, Web of Science, etc. but we did not search gray literature which could possibly have provided additional detail to this meta-analysis. Gray literature published in print and electric formats at government, academic institutions, business and industry level but not controlled by commercial publishers was not included.[47] We detected the bias in this meta-analysis with asymmetry in the funnel plot. The asymmetry in funnel plot was checked by egger’s test. Finally, publication bias is one of the major factors affecting the overall bias of this analysis.

Another limitation of the meta-analysis is the complex intervention issue. The trials included in the meta-analysis used various combinations of interventions as shown in table 2. This makes it difficult to interpret the exact influence of only the smartphone applications as weight loss intervention. In 5 trials, text messaging was used along with the smartphone application as an intervention among the experimental group.[31,33,36,37,39] A previous review of text messaging based weight loss intervention also showed significant weight loss compared to traditional weight loss methods.[40] This makes findings is difficult to interpret since the weight loss effect could be due to a combination of effects from the smartphone application or text messaging.

Modest weight loss of 5% can produce clinically meaningful health benefits. [48] As shown in Table 5, the mean weight loss achieved varied from -0.030 to -4.6 kg. We have insufficient information to determine if 5 % weight loss was achieved in these trials

Although our results found a large effect size of a smartphone app weight loss intervention in the experimental group compared to the control group, the results should be interpreted with caution due to a small number of trials and possible effects of publication bias.

There is a need for trials of longer duration to determine if weight loss can be sustained beyond the intial 3-6 months. Reports of trials should include details on randomization, allocation concealment, outcome assessor blinding in order to have minimal bias in a subsequent meta-analysis.

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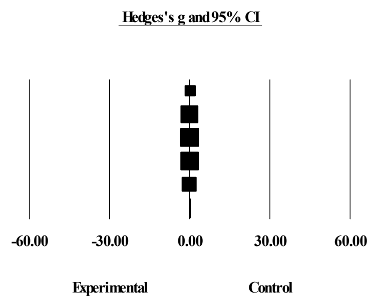
APPENDICES

Appendix A: ≤ 3 months' time duration

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Wharton CM	0.197	0.338	0.114	-0.466	0.859	0.582	0.561	9.00
Glynn LG	-0.080	0.209	0.044	-0.490	0.330	-0.382	0.702	23.54
Weibin Zhou	-0.023	0.198	0.039	-0.412	0.366	-0.116	0.908	26.13
Turner-McGrievy G	-0.031	0.203	0.041	-0.428	0.366	-0.153	0.878	25.08
Stephens JD	-0.229	0.252	0.063	-0.722	0.264	-0.909	0.363	16.25
	-0.052	0.101	0.010	-0.251	0.147	-0.513	0.608	

Statistics for each study

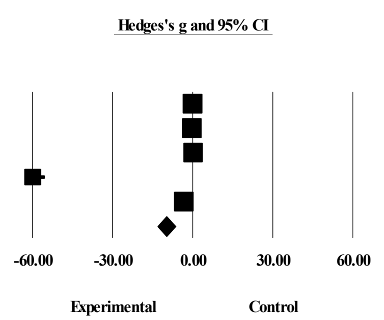


Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
	Effect size and 95% confidence interval						Test of null (2-Tail)		Heterogeneity				Tau-squared			
Fixed	5	-0.052	0.101	0.010	-0.251	0.147	-0.513	0.608	1.085	4	0.897	0.000	0.000	0.037	0.001	0.000
Random	5	-0.052	0.101	0.010	-0.251	0.147	-0.513	0.608								

Appendix B: > 3 to 6 months' time duration

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Laing BY	-0.064	0.137	0.019	-0.333	0.204	-0.471	0.638	21.27
Carter MC	-0.305	0.216	0.047	-0.728	0.119	-1.409	0.159	21.23
Allen JK	0.175	0.331	0.110	-0.474	0.824	0.528	0.597	21.13
Block G	-59.960	2.305	5.314	-64.478	-55.441	-26.010	0.000	15.23
Naimark JS	-3.351	0.322	0.104	-3.983	-2.720	-10.401	0.000	21.14
	-9.884	1.686	2.843	-13.189	-6.580	-5.863	0.000	

Statistics for each study

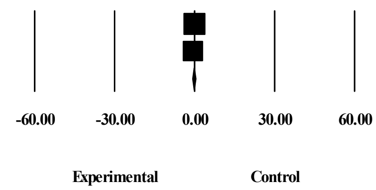


Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
	Effect size and 95% confidence interval						Test of null (2-Tail)		Heterogeneity				Tau-squared			
Fixed	5	-0.554	0.103	0.011	-0.757	-0.352	-5.365	0.000	758.390	4	0.000	99.473	13.344	12.409	153.973	3.653
Random	5	-9.884	1.686	2.843	-13.189	-6.580	-5.863	0.000								

Appendix C: > 6 months’ time duration

Study name	Statistics for each study							
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Godino JG	-0.041	0.099	0.010	-0.236	0.154	-0.412	0.680	53.43
Haapala I	-0.624	0.182	0.033	-0.981	-0.267	-3.425	0.001	46.57
	-0.312	0.291	0.085	-0.882	0.257	-1.074	0.283	

Hedges's g and 95% CI



Model	Effect size and 95% confidence interval						Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	2	-0.175	0.087	0.008	-0.345	-0.004	-2.001	0.045	7.893	1	0.005	87.330	0.148	0.240	0.058	0.385
Random	2	-0.312	0.291	0.085	-0.882	0.257	-1.074	0.283								