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## Review

# The effects of mobile health interventions on lipid profiles among patients with metabolic syndrome and related disorders: A systematic review and meta-analysis of randomized controlled trials



Maryam Akbari <sup>a</sup>, Kamran B. Lankarani <sup>b</sup>, Ahmad Naghibzadeh-Tahami <sup>c</sup>, Reza Tabrizi <sup>a, d</sup>, Behnam Honarvar <sup>b</sup>, Fariba Kolahdooz <sup>e</sup>, Vahidreza Borhaninejad <sup>f</sup>, Zatollah Asemi <sup>g,\*</sup>

<sup>a</sup> Health Policy Research Center, Institute of Health, Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>b</sup> Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>c</sup> Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

<sup>d</sup> Clinical Neurology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>e</sup> Indigenous and Global Health Research, Department of Medicine, University of Alberta, Edmonton, Canada

<sup>f</sup> Social Determinants of Health Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

<sup>g</sup> Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R, Iran

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## ABSTRACT

**Objective:** The current systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted to summarize the effect of mobile health (m-health) interventions on lipid profiles among patients with metabolic syndrome and related disorders.

**Methods:** Cochrane Library, EMBASE, PubMed, and Web of Science databases were searched to identify the relevant randomized clinical trials published up April 30<sup>th</sup>, 2018. Two reviewers examined study eligibility, extracted data, and assessed risk of bias of included clinical trials, individually. Heterogeneity was measured using I-square ( $I^2$ ) statistic and Cochran's Q test. Data were pooled the standardized mean difference (SMD) effect size by the random-effect model.

**Results:** 18 trials of 1681 citations were identified to be appropriate for the current meta-analysis. Findings random-effects model indicated that m-health interventions significantly decreased total- (SMD  $-0.54$ ; 95% CI,  $-1.05, -0.03$ ) and LDL-cholesterol levels (SMD  $-0.66$ ; 95% CI,  $-1.18, -0.15$ ). M-health interventions had no significant effect on triglycerides (SMD  $-0.14$ ; 95% CI,  $-0.56, 0.28$ ) and HDL-cholesterol levels (SMD  $-0.35$ ; 95% CI,  $-0.81, 0.11$ ).

**Conclusion:** Overall, the current meta-analysis demonstrated that m-health interventions resulted in an improvement in total- and LDL-cholesterol, but did not affect triglycerides and HDL-cholesterol levels.

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## 1. Introduction

Increased total cholesterol and triglycerides, and reduced HDL-cholesterol levels are major risk factors for cardiovascular disease (CVD) and stroke [1]. CVD is the leading cause of morbidity and mortality worldwide [2]. More than 80% of deaths were attributed to CVD and diabetes mellitus in low- and middle-income countries [3]. Metabolic disorders have become a marker of the increasing health inequalities in the worldwide, highlighting the urgent need to implement more effective and cost-effective interventions [4].

Multiple treatments and treatment approaches are documented to decrease of main cardiovascular events. However, interventions that modify lifestyle are among the most effective, are poorly adhered to [5].

New advanced technologies represent a feasible solution for decreasing the complex educational requirement. Existing data have demonstrated the feasibility and high acceptance rate of these technologies especially mobile health (m-health) interventions such as smartphone, mobile phone, short message service (SMS) and mobile application for CVD, diabetes and metabolic syndrome (MetS) care, however their effectiveness in improving lipid profile and glycemic control, or promoting the other aspects of diabetes and CVD management are not fully clarified which might be

\* Corresponding author.

E-mail address: [asemi\\_z@Kaums.ac.ir](mailto:asemi_z@Kaums.ac.ir) (Z. Asemi).

explained by the methodological flaws usually occur in study design [6,7]. In a study by Rossi et al. [8], it was seen that the use of “Diabetes Interactive Diary” (DID) in patients with type 1 diabetes mellitus (T1DM) significantly decreased the risk of moderate/severe hypoglycemia and improved quality of life, but did not affect HbA1c. Moreover, using SMS for 12 weeks in people with type 2 diabetes mellitus (T2DM) significantly decreased total- and LDL-cholesterol, but did not affect other lipid profiles [9]. However, adding mobile application coaching and patient/provider web portals to community primary care than standard diabetes management for 12 months among patients with T2DM did not affect lipid profiles [10]. In addition, educational intervention using the internet and a SMS by cellular phone for 12 months in patients with T2DM maintained glycemic control, but did not influence lipid profiles [11]. Discrepancies in these findings may be due to differences in study design, characteristics of study populations, different technologies used in mobile and duration of the intervention.

We are aware of no systematic review or meta-analyses of randomized controlled trials (RCTs) evaluating the effect of m-health interventions on lipid profiles. Thus, the current meta-analysis was conducted to summarize the available evidence regarding the effect of m-health interventions on lipid profiles among patients with metabolic syndrome and related disorders.

## 2. Methods

### 2.1. Literature search strategy

The online databases were systematically search through PubMed, EMBASE, Web of Science and Cochrane Library databases until April 30<sup>th</sup>, 2018. RCTs that were investigated the effects of m-health interventions/and or solution on lipid profiles identified using the following texts word and MeSH terms: metabolic syndrome (MetS) and related disorders ["diabetes" OR "T1DM" OR "T2DM" OR "overweight" OR "obese" OR "coronary heart disease (CHD)" OR "MetS" OR "hypercholesterolemic"]; intervention ("m-health" OR "mobile health" OR "smartphone" OR "mobile phone" OR "cell phone" OR "Short Message Service (SMS)" OR "mobile application" OR "mobile app" AND "solution" OR "intervention" OR "health promotion" OR "health behavior"); and outcomes ["triglycerides (TG)" OR "total cholesterol (TC)" OR "LDL-cholesterol (LDL-cholesterol)" OR "HDL-cholesterol (HDL-cholesterol)"]. Two reviewers were conducted searches, independently. Reference lists of the included clinical trials and review articles were scanned manually for additional relevant studies. The search strategy of our meta-analysis was limited to English-language publications and there is no restriction to time of publication.

### 2.2. Selection criteria

RCTs were included in our meta-analysis if those met the following inclusion criteria: 1) being a original human randomized clinical trial (with parallel or cross-over design), 2) study participants had metabolic diseases, 3) clinical trials were investigated the administration of m-health interventions and/or solutions on lipid profiles, and 4) sufficient information reported for mean (SD) changes of triglycerides, total-, LDL-, HDL-cholesterol levels at baseline and at the end of intervention in both intervention and control groups. Clinical trial findings in abstracts without full texts, case reports, and those did not achieve the at least required score of quality assessment process were excluded.

### 2.3. Quality assessment

Two reviewers were individually assessed the methodological

quality of included clinical trials (MA and RT) by using the Cochrane Collaboration Risk of Bias tool. The scaling tool includes the following criteria about each risk of bias item: selection bias (random sequence generation and allocation concealment description), performance bias (blinding of participants and personal process), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data or withdrawal of patients addressed), reporting bias (selective reporting), and other source of bias (e.g. bias of study design, study stopped early, extreme baseline imbalance, fraudulent trial). In case of disagreement was resolved by the discussion or approved with third author (ZA).

### 2.4. Data extraction

Two authors (MA and RT) were extracted data from primary selected clinical trials, individually.

Data extracted from each clinical trial using a standardized electronic form of Microsoft Excel 2007 includes the following items: The first author's name, year of publication, sample size (in intervention and control groups), study location, the characteristics of study participant, m-health technology type, duration of intervention, outcome measures (mean (SD) changes for triglycerides, total-, LDL- and HDL-cholesterol at baseline and at the end of intervention in both mhealth intervention and control groups). Any calculation on extracted data such as converting measuring units was performed by the first author (MA). Any disagreement on data extraction was resolved by discussion with the third reviewer (ZA).

### 2.5. Data synthesis and analysis

We were performed our meta-analysis to estimate the treatment effect of m-health interventions on lipid profiles using standardized mean differences (SMDs) and random effects model. For statistical analyses were used Review Manager V.5.3 software (Cochrane Collaboration, Oxford, UK) and STATA version 12.0 (Stata Corp., College Station, TX). Heterogeneity was measured using the Cochran (Q) and I-squared tests ( $I^2$ ) for each outcome across clinical trials. When  $I^2$  exceeded 50% or  $P < 0.05$  were considered as heterogeneity across clinical trials. Subgroup analyses were conducted based on population target (Diabetic vs. non diabetic), duration of study ( $\leq 6$  months vs.  $> 6$  months), total sample size ( $< 100$  vs.  $\geq 100$ ), income country [lower middle income countries (LMICs) vs. higher middle income countries (HICs)], m-health technology type (phone calls vs. Smartphone and/or app vs. SMS) to explore causes of inconsistency in trial results. A sensitivity analyses was conducted to evaluate the reliability of the pooled SMD by using the leave-one-out method. Egger's regression- and Begg's tests were used to detect the probability of publication bias. A P-value less than 0.05 were considered as statistically significant.

## 3. Results

### 3.1. Characteristics of included studies

Forty-four clinical trials met eligible for evaluating with more details by full text review. Based on our inclusion and exclusion criteria, twenty-six studies were excluded due to not an RCT ( $n = 14$ ), no relevant outcome reported ( $n = 5$ ), being study protocol ( $n = 4$ ), and not control group ( $n = 3$ ). Overall, 18 clinical trials were included into our meta-analysis. Fig. 1 shows the process of step by step literature screening and study selection.

Sixteen clinical trials have reported the effects of m-health interventions on triglycerides, seventeen on total-cholesterol, sixteen on LDL-cholesterol, and sixteen on HDL-cholesterol levels. These clinical trials were published between 1998 and 2017. The total

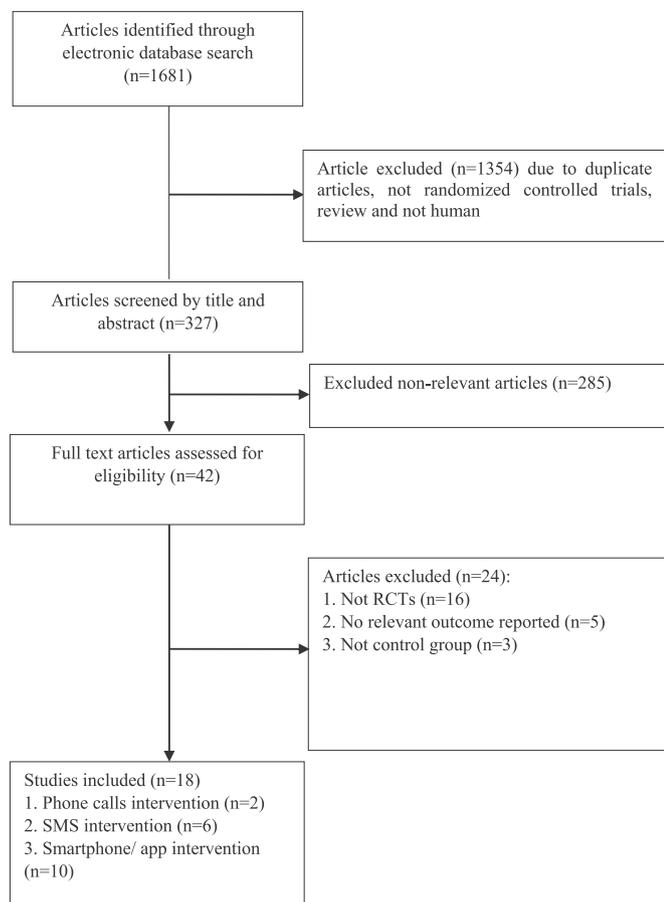


Fig. 1. Flowchart for the selection of eligible studies.

Table 1  
Characteristics of included studies.

Authors (Ref)	Publication year	Sample size (control/ intervention)	Country/population	Duration	M-health technology types	Presented data
Yoon et al. [11]	2008	26/25	Korea/type 2 diabetic patients	12 months	SMS	TG, TC, HDL-C
Hyman et al. [20]	1998	58/65	Texas/hypercholesterolemic	6 month	Phone call	TC
Lim et al. [13]	2016	42/43	Italy/type 2 diabetic patients	6 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Waki et al. [21]	2014	27/27	Japan/type 2 diabetic patients	3 month	Smartphone and/or app	TG, LDL-C, HDL-C
Lim et al. [22]	2011	48/49	Korea/type 2 diabetic patients	6 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Goodarzi et al. [9]	2012	38/43	Iran/type 2 diabetic patients	3 month	SMS	TG, TC, LDL-C, HDL-C
Lombard et al. [23]	2010	54/64	Australia/overweight women	12 month	SMS	TG, TC, LDL-C, HDL-C
Zhou et al. [24]	2016	50/50	China/diabetic patients	3 month	Smartphone and/or app	LDL-C
Karhula(b) et al. [25]	2015	60/155	Finland/type 2 diabetic patients	12 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Karhula(a) et al. [25]	2015	68/168	Finland/heart disease group	12 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Chow et al. [7]	2015	358/352	Australia/coronary Heart Disease	6 month	SMS	TG, TC, HDL-C
Limaye et al. [26]	2016	132/133	India/type 2 diabetes	12 month	SMS	TG, TC, LDL-C, HDL-C
Fukuoka et al. [19]	2015	31/30	California/overweight adults	5 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Silina et al. [27]	2017	60/63	Latvia/overweight and obese subjects	12 month	SMS	TG, TC, LDL-C, HDL-C
Yoo et al. [12]	2009	54/57	Korea/overweight patients with both type 2 diabetes	3 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Rossi et al. [6]	2010	63/67	Italy/type 1 diabetes	6 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Rossi et al. [8]	2013	64/63	Italy/type 1 diabetes	6 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Quinn et al. [10]	2011	56/22	Maryland/type 2 diabetes	12 month	Smartphone and/or app	TG, TC, LDL-C, HDL-C
Dekkers et al. [28]	2011	49/44	Netherlands/overweight	6 month	Phone call	TC

TG, Triglycerides; TC, Total-cholesterol; LDL-C, Low-density lipoprotein-cholesterol; HDL-C, High-density lipoproteins-cholesterol.

number of patients included was 2863 (range from 51 to 710 individuals in each trial), with 1520 (with range: 25–352) assigned to m-health interventions and 1338 (with range: 26–358) to control groups. Duration of m-health interventions was ranged from 6 to 12 months. Ten clinical trials were used Smartphone and/or app as mhealth technology type to control lipid profiles, in ten trials were SMS, and phone call used in two clinical trials as mhealth solutions. Summary table of included trials characteristics is presented in Table 1.

### 3.2. Pooled estimate of the effect of m-health interventions on lipid profiles

Findings random-effects model indicated that m-health interventions significantly decreased total- (SMD  $-0.54$ ; 95% CI,  $-1.05$ ,  $-0.03$ ,  $P = 0.04$ ;  $I^2:97.2\%$ ) and LDL-cholesterol levels (SMD  $-0.66$ ; 95% CI,  $-1.18$ ,  $-0.15$ ,  $P = 0.01$ ;  $I^2:97.1\%$ ). M-health interventions had no significant effect on triglycerides (SMD  $-0.14$ ; 95% CI,  $-0.56$ ,  $0.28$ ,  $P = 0.51$ ;  $I^2:95.8\%$ ) and HDL-cholesterol levels (SMD  $-0.35$ ; 95% CI,  $-0.81$ ,  $0.11$ ,  $P = 0.13$ ;  $I^2:96.4\%$ ) (Table 2 and Fig. 2).

### 3.3. Subgroup and sensitivity analyses

Because of existence heterogeneity, we have evaluated source of potential heterogeneity using subgroup analyses by suspected variables including population target (diabetic vs. non-diabetic patients), duration of study ( $\leq 6$  months vs.  $> 6$  months), total sample size ( $< 100$  vs.  $\geq 100$ ), income country (LMICs vs. HICs), m-health technology type (phone calls, vs. Smartphone and/or app, vs. SMS). Based on the findings of these analyses, the reduction of heterogeneity was found in some of strata of suspected variables (Table 3).

Pooled data from clinical trials using SMS interventions showed greater reduction on serum triglycerides levels compared with the

**Table 2**  
Estimation of the SMD of related indicators with confidence interval 95% between the intervention and placebo groups.

Variable	Number of study	Standardized mean difference	CI 95%	Heterogeneity			
				I-squared (%)	Q	P-value	
Triglycerides	Intervention group (after vs. before)	12	-0.19	-0.35, -0.03	56.6	25.33	0.008
	Placebo group (after vs. before)	12	-0.09	-0.28, 0.11	72.7	40.33	<0.001
Total-cholesterol	Intervention group vs. placebo group	16	-0.14	-0.56, 0.28	95.8	355.06	<0.001
	Intervention group (after vs. before)	14	-0.22	-0.47, 0.03	86.4	96.46	<0.001
LDL-cholesterol	Placebo group (after vs. before)	14	-0.03	-0.23, 0.16	77.7	58.25	<0.001
	Intervention group vs. placebo group	17	-0.54	-1.05, -0.03	97.2	573.44	<0.001
HDL-cholesterol	Intervention group (after vs. before)	12	-0.16	-0.55, 0.24	93.5	168.59	<0.001
	Placebo group (after vs. before)	12	0.00	-0.30, 0.31	89.6	105.36	<0.001
HDL-cholesterol	Intervention group vs. placebo group	16	-0.66	-1.18, -0.15	97.1	519.24	<0.001
	Intervention group (after vs. before)	12	0.13	-0.10, 0.37	80.9	57.58	<0.001
HDL-cholesterol	Placebo group (after vs. before)	12	0.08	-0.01, 0.17	2.2	11.25	0.42
	Intervention group vs. placebo group	16	-0.35	-0.81, 0.11	96.4	417.08	<0.001

Smartphone and/or app interventions (0.12 vs. -0.58 mg/dL, 95% CI: -0.92, -0.23, I<sup>2</sup>: 86.2%) (Table 3).

Total cholesterol levels significantly decreased following m-health interventions in pooled data from clinical trials with <100

participants (-0.36 mg/dL, 95% CI: -0.53, -0.19, I<sup>2</sup>: 0.0%) and with SMS interventions (-1.54 mg/dL, 95% CI: -2.87, -0.20, I<sup>2</sup>: 98.0 %) (Table 3).

Compared with the clinical trials with ≤6 months, m-health interventions with clinical trials >6 months significantly decreased triglycerides levels (-0.17 vs. -1.51 mg/dL, 95% CI: -2.96, -0.07, I<sup>2</sup>: 98.8%). In pooled data from HICs clinical trials, LDL-cholesterol levels significantly decreased compared with the LMICs clinical trials (-1.85 vs. -0.39 mg/dL, 95% CI: -0.73, -0.04, I<sup>2</sup>: 92.4 %). Similar to triglycerides and total cholesterol levels findings, serum LDL-cholesterol levels significantly decreased in pooled data from clinical trials with SMS type (-1.67 mg/dL, 95% CI: -3.21, -0.13, I<sup>2</sup>: 99.0 %) (Table 3).

For HDL-cholesterol levels, clinical trials were shown no significant changes between the intervention and placebo groups by potential suspected variables (Table 3).

Sensitivity analyses were conducted to evaluate the contribution of one by one clinical trial to the overall SMD. After excluding every clinical trial from the meta-analysis for triglycerides, LDL-cholesterol, and HDL-cholesterol, authors found no significant difference between the pre-sensitivity pooled SMD and post-sensitivity pooled SMD, but there was a significant difference between the pre- and post-sensitivity pooled SMD for total-cholesterol after omitting Limaye et al. [27] study (SMD -0.25; 95% CI, -0.57, 0.07) (Table 4).

Fig. 3 indicates the summary of authors' judgments regarding the risk of bias for each included clinical trial.

3.4. Publication bias

According to the results of Egger and Begg tests, there was no evidence of publication bias across included clinical trials for triglycerides (P Egger's test = 0.52, P Begg's test = 0.32), total- (P<sub>Eg</sub> = 0.19, P<sub>Be</sub> = 0.00), LDL- (P<sub>Eg</sub> = 0.16, P<sub>Be</sub> = 0.01), and HDL-cholesterol (P<sub>Eg</sub> = 0.17, P<sub>Be</sub> = 0.41).

4. Discussion

This systematic review and meta-analysis assessed the effect of m-health interventions on lipid profiles in patients with MetS and related disorders. Our findings supported that m-health interventions resulted in an improvement in total- and LDL-cholesterol, but did not affect triglycerides and HDL-cholesterol levels.

New advanced technologies such as m-health interventions aimed at pursuing an acceptable control of risk factors of metabolic disturbances, including dyslipidemia and hyperglycemia. In a study by Goodarzi et al. [9], it was seen that using SMS via mobile phone

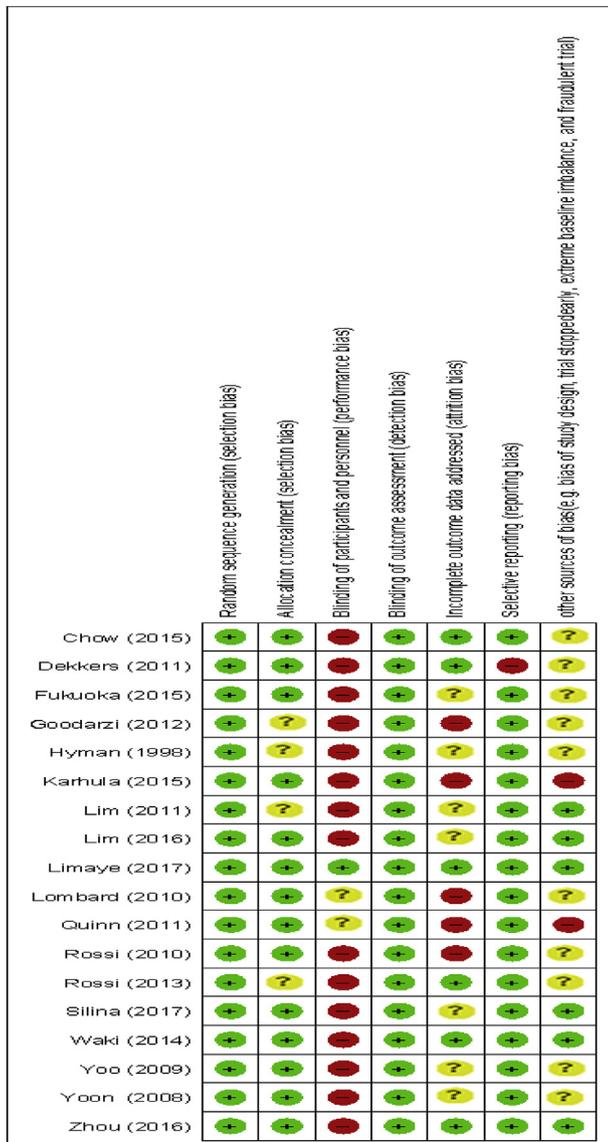


Fig. 2. The methodological quality of included studies (risk of bias).

**Table 3**  
The effects of m-health interventions on lipid profiles based on subgroup analysis.

Variables	Number of SMD included	Subgroups	Pooled OR (random effect)	95% CI	I <sup>2</sup> (%)	Overall I <sup>2</sup> (%)
Triglycerides	Population target	Diabetic	-0.20	-0.70, 0.31	94.5	95.8
		Non-diabetic	-0.02	-0.90, 0.87	97.6	
	Duration of study	>6 months	-0.28	-1.17, 0.62	97.7	
		≤6 months	-0.03	-0.43, 0.36	91.2	
	Total sample size	≥100	-0.12	-0.77, 0.53	97.7	
		<100	-0.15	-0.38, 0.07	36.9	
	Income country	HICs	-0.07	-0.52, 0.39	95.8	
		LMICs	-0.66	-1.55, 0.24	92.0	
	M-health technology type	SMS	-0.58	-0.92, -0.23	86.2	
		Smartphone and/or app Phone calls	0.12 -	-0.56, 0.81 -	96.6 -	
Total-cholesterol	Population target	Diabetic	-0.63	-1.54, 0.29	98.0	97.2
		Non-diabetic	-0.41	-0.93, 0.12	94.8	
	Duration of study	>6 months	-1.07	-2.46, 0.32	98.8	
		≤6 months	-0.17	-0.43, 0.09	82.5	
	Total sample size	≥100	-0.64	-1.43, 0.14	98.4	
		<100	-0.36	-0.53, -0.19	0.0	
	Income country	HICs	-0.23	-0.56, 0.11	93.0	
		LMICs	-2.83	-7.04, 1.38	99.4	
	M-health technology type	SMS	-1.54	-2.87, -0.20	98.0	
		Smartphone and/or app Phone calls	0.03 -0.10	-0.36, 0.42 -0.37, 0.16	89.7 0.0	
LDL-cholesterol	Population target	Diabetic	-0.74	-1.52, 0.05	97.6	97.1
		Non-diabetic	-0.51	-1.18, 0.16	95.8	
	Duration of study	>6 months	-1.51	-2.96, -0.07	98.8	
		≤6 months	-0.17	-0.41, 0.08	78.8	
	Total sample size	≥100	-0.76	-1.50, -0.03	98.2	
		<100	-0.50	-0.94, -0.06	80.7	
	Income country	HICs	-0.39	-0.73, -0.04	92.4	
		LMICs	-1.85	-4.92, 1.22	99.3	
	M-health technology type	SMS	-1.67	-3.21, -0.13	99.0	
		Smartphone and/or app Phone calls	-0.20 -	-0.52, 0.12 -	86.6 -	
HDL-cholesterol	Population target	Diabetic	-0.50	-1.22, 0.21	97.1	96.4
		Non-diabetic	0.00	-0.35, 0.36	85.7	
	Duration of study	>6 months	-0.85	-1.86, 0.16	98.0	
		≤6 months	0.06	-0.15, 0.27	67.3	
	Total sample size	≥100	-0.45	-1.16, 0.26	98.0	
		<100	-0.20	-0.47, 0.08	58.0	
	Income country	HICs	-0.11	-0.32, 0.11	80.6	
		LMICs	-1.94	-6.26, 2.38	99.5	
	M-health technology type	SMS	-0.61	-1.81, 0.58	98.7	
		Smartphone and/or app Phone calls	-0.19 -	-0.42, 0.04 -	72.4 -	

**Table 4**  
The effects of m-health interventions on lipid profiles based on sensitivity analysis.

Variables	Pre-sensitivity analysis			Upper & lower of effect size	Post-sensitivity analysis		
	No. of studies included	Pooled SMD (random effect)	95% CI		Pooled SMD (random effect)	95% CI	Excluded studies
Triglycerides	16	-0.14	-0.56, 0.28	Upper	-0.06	-0.48, 0.36	Karhula (b) et al.
				Lower	-0.12	-0.57, 0.32	Rossi et al.
Total-cholesterol	17	-0.54	-1.05, -0.03	Upper	-0.25	-0.57, 0.07	Limaye et al.
				Lower	-0.63	-1.15, -0.11	Rossi et al.
LDL-cholesterol	16	-0.66	-1.18, -0.15	Upper	-0.35	-0.65, -0.05	Limaye et al.
				Lower	-0.70	-1.25, -0.14	Rossi et al.
HDL-cholesterol	16	-0.35	-0.81, 0.11	Upper	-0.08	-0.28, 0.11	Limaye et al.
				Lower	-0.40	-0.88, 0.07	Rossi et al.

for 3 months by patients with T2DM resulted in a significant decrease in total- and LDL-cholesterol, but did not affect other lipids such as triglycerides and HDL-cholesterol levels. In addition, in people with CHD, using lifestyle-focused text messaging service

compared with usual care led to a modest improvement in LDL-cholesterol levels and greater improvement in other cardiovascular disease risk factors, while did not influence other lipid profiles [7]. Furthermore, diabetic patients receiving care through using

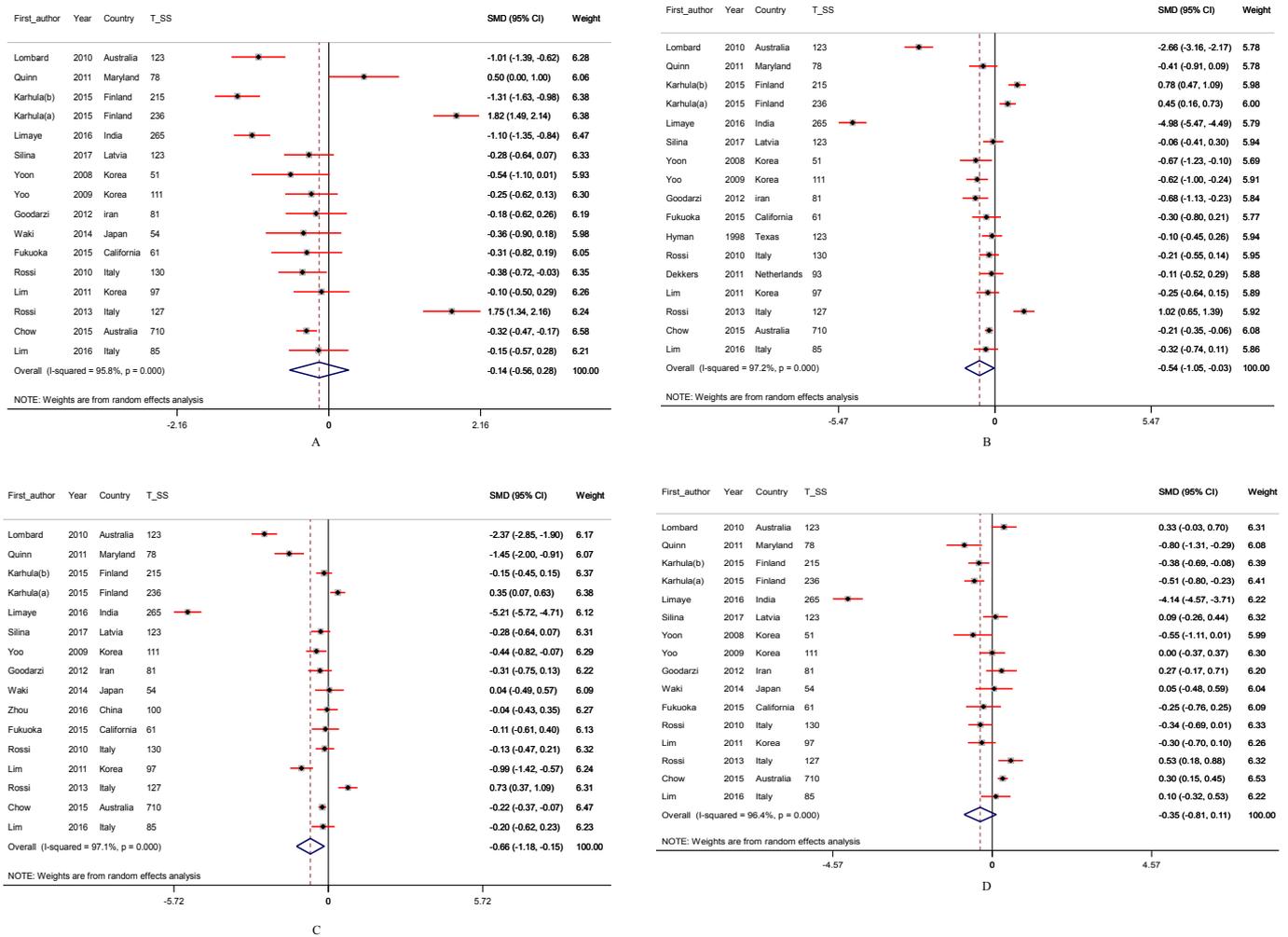


Fig. 3. A-D. Meta-analysis glycemetic control standardized mean differences estimates for (A) fasting glucose, (B) for triglycerides, (C) for total cholesterol, and (D) for LDL-cholesterol in m-health interventions and controlgroups (CI = 95%).

cellular phones and the internet demonstrated a significant improvement in HbA1c, total-, LDL-cholesterol and adiponectin levels [12]. LDL-cholesterol accounts for most of the lipid risk in predicting early CVD [14]. In recent years, using SMS intervention by mobile phone has arisen as a potential means of modifying health behaviors [15]. Previous studies have evaluated the effectiveness of SMS service by mobile phone to change individual health behaviors of smoking, weight loss, and physical activity to improve medical management of diabetic patients [16] or adherence to medication [17]. Moreover, there is very little evidence on the effects of these services on multiple risk factors [15]. Decreasing some risk factors concurrently, rather than targeting single factors, is likely to deliver greater decrease in events [18].

However, using mobile application coaching and patient/provider web portals to community primary care than standard diabetes management for 12 months by patients with T2DM did not affect lipid profiles [10]. In addition, educational intervention through the internet and a SMS by cellular phone for 12 months to people with T2DM maintained glycemetic control, but did not influence lipid profiles [11]. Also, using mobile app and pedometer intervention in people with T2DM did not affect lipid profiles [19]. These discrepancies in studies may be due to differences in study design, characteristics of study populations, different technologies used in mobile and duration of the intervention.

### 5. Conclusions

Overall, the current meta-analysis demonstrated that m-health interventions resulted in an improvement in total- and LDL-cholesterol, but did not affect triglycerides and HDL-cholesterol levels.

### Conflicts of interest

The authors declare no conflict of interest.

### Author contributions

ZA, MA and RT contributed in conception, design, statistical analysis and drafting of the manuscript. KB-L, RT, BH, and FK contributed in conception, data collection and manuscript drafting. The final version was confirmed by all authors for submission.

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