Original Article

Can smartphone-based diabetes control apps improve cardiovascular risk among patients with diabetes? A systematic review and meta-analysis

Randa Y. Refin[1*], Fina F. Andika[1], Muhammad F. Abudurrahman[2], Maidar Maidar[3], Amanda Yufika[4], Intan C. Mulya[5], Konstantinos Parperis[6] and Ziad Abdeen[7]

[1]Postgraduate Program of Public Health, Universitas Muhammadiyah Aceh, Banda Aceh, Indonesia; [2]Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia; [3]Faculty of Public Health, Universitas Muhammadiyah Aceh, Banda Aceh, Indonesia; [4]Department of Family Medicine, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia; [5]Department of Obstetrics and Gynecology, Monash University, Victoria, Australia; [6]University of Cyprus Medical School, Nicosia, Cyprus; [7]Al-Quds Nutrition and Health Research Institute, Faculty of Medicine, Al-Quds University, Abu Dies, West Bank, Palestine

*Corresponding author: randayudhistira@gmail.com

Abstract

Despite being the most prevalent complication, cardiovascular risk factors such as blood pressure, weight, and lipid profile have been less considered in digital health studies. The aim of this systematic review and meta-analysis was to gather evidence regarding the impact of digital health applications on cardiovascular risk factors in patients with diabetes. Literature search was conducted following the PRISMA guideline on September 4, 2023, using databases including PubMed, Scilit, Scopus, Embase, and Web of Science, with a pre-planned combination of keywords. Selected studies were original research reporting the influence of smartphone applications on cardiovascular risk factors in diabetic patients. Standardized mean differences (SMD) between the intervention and control groups were analyzed using fixed or random-effects models. Eighteen studies met the criteria, consisting of 1152 patients in the intervention group and 1072 patients in the control group. The results of the meta-analysis showed that the smartphone applications significantly controlled systolic blood pressure (SMD: -5.03 mmHg; 95%CI: -7.018–(-3.041), p<0.001). There was no significance effect on weight, body mass index, total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) and diastolic blood pressure. In the subgroup analysis, triglycerides were lower in the intervention group compared to the control group (SMD: -0.459%; 95%CI: -0.787–(-0.132), p=0.006). Publication bias and the limited number of studies suggest that the evidence from this study is in moderate level. In conclusion, smartphone apps are not only effective in aiding blood sugar control but also in preventing cardiovascular issues in diabetic patients. Further research is still needed to confirm these findings.

Keywords: Cardiovascular, diabetes, hypertension, triglyceride, smartphone

Introduction

The high number of people with diabetes in various parts of the world, which reached 6,059 cases per 100,000 individuals in 2017, has made this disease a global epidemic [1]. Diabetes is a chronic condition that involves dysregulation of blood sugar levels. Cardiovascular disease accounts for the majority of mortality in patients with diabetes. The risk of cardiovascular

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diseases in diabetes patients is 2-fold higher compared to people without diabetes [2]. This is because diabetes causes macro- and microvascular complications. Macrovascular complications can affect coronary arteries and peripheral arteries while microvascular complications can cause retinopathy, nephropathy and neuropathy [3]. Besides diabetes, other independent risk factors for cardiovascular disease are obesity, lipid and cholesterol dysregulation, and hypertension [3]. Unfortunately, these risk factors are also found in conjunction with diabetes, putting patients at double risk of cardiovascular disease.

Diabetics should adopt lifestyle modifications, such as diet and physical exercise that are tailored to the patient's condition to avoid hyperglycemia or, worse, hypoglycemia. In addition, continuous monitoring of blood sugar levels and medication adherence are required. Regular and repeated in-person consultations with the doctor can add to the patient's economic burden, and be a factor in low patient compliance in following the management. Therefore, digital health technology is now being developed as a modality for diabetes management and control, one of which is applications or apps on smartphones. At least 25 smartphone apps have been developed as telemedicine media for people with type 2 diabetes mellitus [4]. The study found a greater reduction in HbA1c in-app users than those who only consulted conventionally [4].

Besides focusing on blood sugar control, diabetes control apps have been developed to monitor complications that develop from the disease, such as cardiovascular disease, diabetic ulcers, and diabetic nephropathy [5-7]. Although cardiovascular is the most common complication in people with diabetes, there are no systematic studies analyzing the effect of digital apps on these disease risk factors. Previous systematic reviews and meta-analyses have focused on blood sugar control efficacy, self-efficacy, self-care activities, and quality of life [4,5,8]. A systematic review measured cardiometabolites as a parameter of digital app efficacy in 2019 but took metabolic syndrome as the research context (not specific to diabetes) [9]. Therefore, this study aims to answer the question, "What is the efficacy of smartphone-based diabetes control apps on cardiovascular risk factors?"

Methods

Study design

This study followed the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA). The protocol had been registered to PROSPERO (CRD42023460368) on October 31, 2023. The process of literature selection, data extraction, and determination of risk of bias was conducted by three individuals each. Differences that arose during the process were resolved through consensus.

Literature search and selection

The literature search was conducted on September 4, 2023, on PubMed, Scilit, Scopus, Embase, and Web of Science databases with the keywords "diabetes" and "smartphone application". Details of the keywords used in each database can be seen in **Table 1**. Additional searches were conducted on relevant previous systematic review articles, reference lists, and connected papers (https://www.connectedpapers.com/).

Inclusion criteria were based on the PICOS (Population, Intervention, Control, and Outcomes) framework, which can be described as follows: Population - patients with type 1 or 2 diabetes; Intervention - smartphone-based diabetes control apps; Control - diabetes patients undergoing conventional consultation; and Outcomes - weight, body mass index (BMI), lipid profile, and blood pressure. Studies were excluded if they were only call- or text-based. In addition, studies conducted on gestational diabetes patients were also excluded. Studies were also restricted to original research (controlled trials with or without randomization) with human subjects and reported in English.

Determination of risk of bias

For randomized controlled studies, the level of risk of bias was determined by Cochrane Risk of Bias 2.0 (RoB 2.0). Meanwhile, for non-randomized controlled studies, the risk of bias was determined by the risk of bias in non-randomized studies - of interventions (ROBINS-I). The

results of this of this analysis were visualized using a web-based application: RobVis (https://mcguinlu.shinyapps.io/robvis/).

Data extraction

Study characteristics, patients, and outcomes were extracted using standardized tables. The extracted outcomes were body weight, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c). All data are presented as mean ± standard deviation (SD). Conversion of median to mean was performed using a web-based calculator (https://www.math.hkbu.edu. hk/~tongt/papers/median2mean.html). Conversion of lipid profiles to mmol/L was performed using the Omni Calculator (https://www.omnicalculator. com/health/cholesterol-units). Correspondence authors of each study were contacted using email in case of incomplete data.

Quantitative analysis

Quantitative analysis was performed using Jamovi version 2.3.21 (https://www.jamovi.org/). Data heterogeneity was assessed based on *p*-Het<0.1 or I^2, with values <25%, 26–50%, and >50% indicating low, moderate, and high levels of heterogeneity, respectively. A random-effects model with a maximum-likelihood counter was applied if I^2>50% or *p*-Het<0.1. Standardized mean difference (SMD) and 95% confidence interval (CI) were used in the meta-analysis. Risk of publication bias analysis using Egger's test and Begg's funnel plot was performed if at least ten studies were included in the meta-analysis. Potential outliers were assessed based on Cook's distance and Q-Q plot.

Subgroup analysis

Subgroup analysis was performed on study groups that recruited patients with cardiovascular risk. Patients were categorized as such if, at baseline, their mean blood levels of total cholesterol, triglycerides, LDL-c, and HDL-c were >5.2 mmol/L; >2.3 mmol/L; >3.4 mmol/L; and <1.2 mmol/L, respectively.

Results

Search and selection of literature results

A search using scientific literature databases identified 5,429 studies, of which duplicate studies were automatically removed using EndNote, leaving 3,207 studies. From these studies, 65 studies were found to have potential for inclusion in both qualitative and quantitative analyses. At the end of the selection process, 12 studies met the criteria. Furthermore, a manual search of the reference list and an AI-assisted search (connected papers) identified 21 potential studies. The overall assessment, however, reduced this number to six studies. This resulted in 18 studies that met the inclusion and exclusion criteria. This process can be seen in the PRISMA flowchart shown in **Figure 1**.

Study characteristics and research subjects

Study characteristics and research subjects can be seen in **Table 1**. Overall, the studies that met the criteria were from 2011 to 2022. Almost all studies were RCTs, except Raghavan *et al*. (2022) who used a non-RCT design. Most of the studies were from China (n=4), followed by the United States (US, n=3). Most patients were aged 50 years and above, totaling 1152 versus 1072 patients (intervention versus control). The male-to-female ratio varied between studies. The duration of the intervention ranged from three to 12 months.

Risk of bias

In randomized studies, the greatest potential bias came from incomplete outcomes due to the high number of patients lost to follow-up. Some studies also did not report clearly, or there were doubts in the randomization procedure. Whereas in non-randomized studies (nRCT), the confounding effect was not fully reported, raising concerns about the study's validity. Overall, most of the studies have low risk, although there are some things require vigilance in data validity. The summaries of risk of bias analysis results are presented in **Figure 2**.

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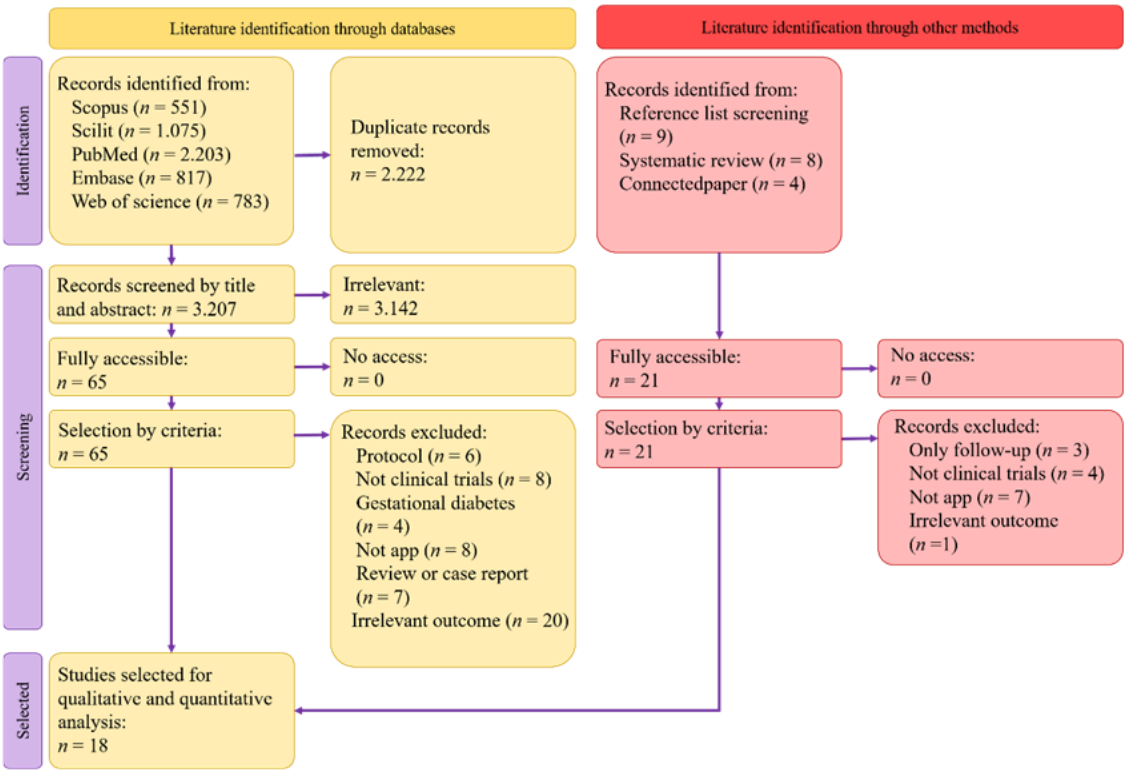

Figure 1. Flowchart of the literature selection process for qualitative and quantitative analysis based on PRISMA guidelines.

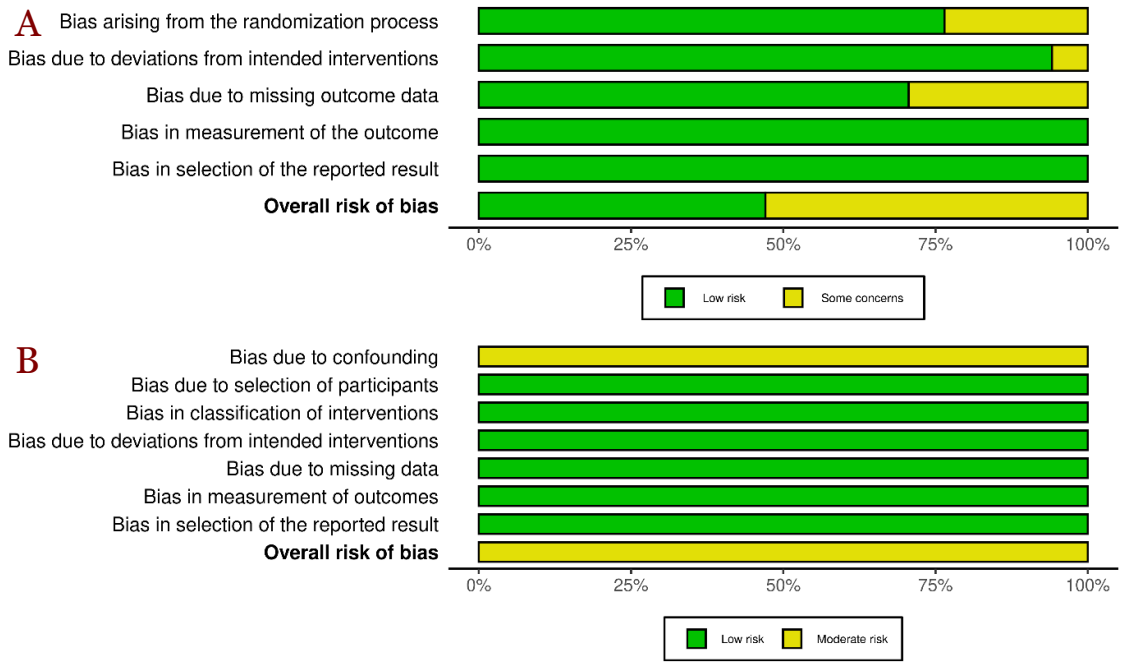

Figure 2. Risk of bias analysis results based on RoB 2.0 for 17 studies (A) and ROBINS-I for 1 study (B).

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Table 1. Study characteristics and research subjects of included clinical trials

Author (year) [Ref]	Country	Subject, n		Age (years)		Male/Female		Intervention detail	
		Intervention	Control	Intervention	Control	Intervention	Control	Application	Duration (months)
Anzaldo-Campos *et al*., (2016) [10]	Mexico	102	100	51.5±11.4	52.5±9.7	39/63	38/62	Brew	10
Baron *et al*., (2017) [11]	United Kingdom	45	36	58.2+13.6	55.8+13.8	31/14	15/21	MTH app	9
Bender *et al*., (2017) [12]	United States	22	23	57.4±9.8	57.7±10	8/14	9/14	PilAm Go4Health	3
Fukuoka *et al*., (2015) [13]	United States	30	31	57.1±9.1	53.4±8.7	7/23	7/24	-	5
Hilmarsdóttir *et al*., (2021) [14]	Sweden	15	15	50.9±11.8	51.5±9.5	6/9	5/10	SidekickHealth	6
Holmen *et al*., (2014) [15]	Norway	51	50	58.6+11.8	55.9+12.2	34/17	30/20	RenewingHealth	4
Huang *et al*., (2019) [16]	Singapore	22	19	49.80±12.31	50.63±10.57	9/13	11/8	Medication app	3
Kim *et al*., (2022) [17]	Korea	32	36	55.18±10.11		16/16	14/22	Doctor Diary	2
Lim *et al*., (2021) [18]	Singapore	72	76	NA	NA	NA	NA	D'LITE	6
McLeod *et al*., (2020) [19]	New Zealand	215	214	NA	NA	NA	NA	BetaMe/Melon	12
Pamungkas *et al*., (2022) [6]	India	30	30	56.2±7.63	54.4±9.2	6/24	20/80	Mobile app	3
Poonprapai *et al*., (2022) [20]	Thailand	78	79	67.36±5.72	67.8±6.18	31/47	32/47	Mobile app	9
Quinn *et al*., (2011) [21]	United States	125	56	53.2±8.4	53.7±8.2	10/12	28/28	Mobile app	12
Raghavan *et al*., (2022) [22]	India	91	82	NA	NA	NA	NA	Diahome	4
Sun *et al*., (2019) [23]	China	44	47	68.15±1.22		19/25	18/29	mHealth app	6
Yang *et al*., (2022) [24]	China	50	50	65.09±6.06	67.34±5.33	18/32	21/29	WeChat	12
Zhang *et al*., (2019) [25]	China	78	78	52±12	55±11	46/32	49/29	Welltang	6
Zhou *et al*., (2016) [26]	China	50	50	53.5±12.4	55±13.1	27/23	30/20	Welltang	3

NA: not reported

Efficacy of smartphone apps on cardiovascular risk factors

The results of the meta-analysis on the effect of diabetes control smartphone apps on body weight, BMI, lipid profile, blood pressure, and HbA1c are presented in **Table 2**. The use of digital health apps did not affect body weight, BMI, and lipid profile (p-total>0.05). However, heterogeneity could be observed in the weight, BMI, and total cholesterol variables (I^2>25%; p-Het<0.1). Reduction in systolic blood pressure values, the effect of using the app was observed to be significant (p-total<0.001; MD: -5.03 mmHg (95%CI: -7.018–(-3.041))) with data tending to be homogeneous (I^2<25%; p-het>0.1). However, statistical significance was not found in the change in diastolic blood pressure. A forest plot of systolic and diastolic blood pressure can be seen in **Figure 3** and **Figure 4**. HbA1c values in the intervention group at the end of the clinical trial were significantly lower (p-total<0.001; MD: -0.539% (95%CI: -0.743–(-0.335))), although the data group had high heterogeneity (I^2>50%; p-Het<0.1). Forest plots for all variables are shown in **Figure 3** and **Figure 4**.

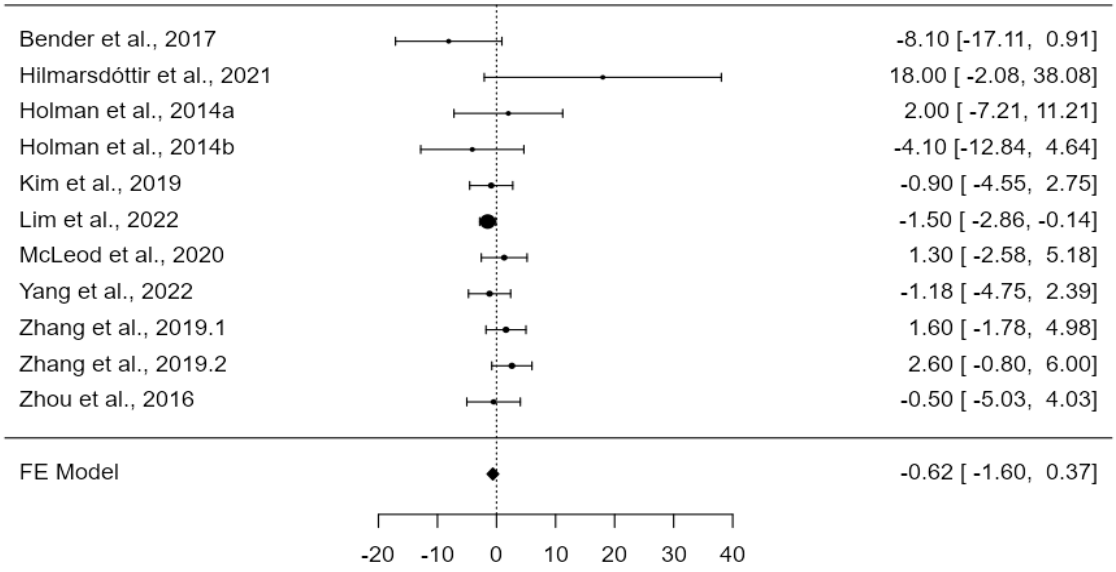

Figure 3. Forest plot for the efficacy of smartphone-based diabetes control apps on cardiovascular risk factors in diabetic patients based on systolic blood pressure.

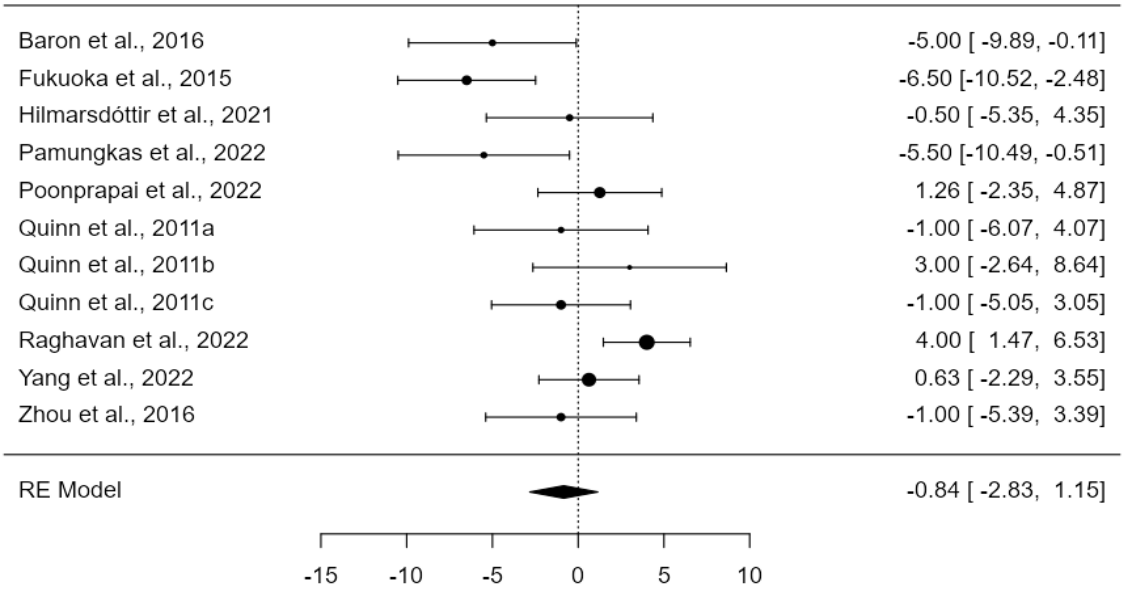

Figure 4. Forest plot for the efficacy of smartphone-based diabetes control apps on cardiovascular risk factors in diabetic patients based on diastolic blood pressure.

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Table 2. Results of a meta-analysis on the effect of smartphone-based diabetes control apps on cardiovascular risk and HbA1c

Variable	Study, n	Subject, n		Model	Mean difference	95% confidence interval	*p*-total	Heterogeneity		Publication bias	
		Intervention	Control					I^2 (%)	*p*-het	*p*-Egger	*p*-Begg
Weight	11	771	766	Fixed	-0.616	-1.61–0.37	0.222	31.69	0.146	0.213	0.879
Body mass index	6	330	320	Random	-0.720	-1.576–0.136	0.099	30.36	0.037	NA	NA
Lipid profile											
Total cholesterol	13	725	750	Random	-0.075	-0.237–0.086	0.361	55.18	0.004	0.939	1.000
LDL-c	14	755	780	Random	-0.067	-0.150–0.016	0.114	0.01	0.066	0.861	0.914
HDL-c	13	711	733	Random	-0.025	-0.060–0.011	0.177	0.20	<0.001	0.090	0.510
Triglyceride	12	703	731	Random	-0.038	-0.242–0.166	0.713	67.58	<0.001	<0.001	0.841
Blood pressure											
Systolic	12	558	588	Random	-5.03	-7.018–(-3.041)	<0.001	18.61	0.168	0.002	0.031
Diastolic	11	514	541	Random	-0.841	-2.828–1.147	0.407	61.93	<0.001	0.053	0.542
HbA1c	18	895	912	Random	-0.539	-0.743–0.335	<0.001	71.71	<0.001	<0.001	0.152

HbA1: glycated hemoglobin; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; MD: mean differences; NA: not applicable

Table 3. Efficacy of smartphone-based diabetes control apps in populations at-risk

Variable	Study, n	Subject, n		Model	Mean difference	95% confidence interval	*p*-total	Heterogeneity	
		Intervention	Control					I^2 (%)	*p*-het
Total cholesterol	4	155	199	Random	-0.107	-0.372–0.159	0.430	28.73	0.147
LDL-c	5	185	229	Random	-0.200	-0.809–0.309	0.521	61.73	0.007
HDL-c	7	476	454	Fixed	-0.022	-0.060–0.017	0.297	0.00	0.900
Triglyceride	5	257	299	Random	-0.459	-0.787–(-0.132)	0.006	0.00	0.078

HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; MD: mean differences

Publication bias

Most of the variables had a symmetrical funnel plot shape (**Figure 3** and **Figure 4**). Only systolic blood pressure formed an unsymmetrical funnel plot with *p*-Begg=0.031. Based on Egger's test, possible publication bias was found for systolic blood pressure and HbA1c variables (*p*-Egger<0.01). Publication bias analysis was not performed on subgroups, due to insufficient number of studies (n<10).

Discussion

Based on the analysis of HbA1c levels, digital health apps were shown to effectively improve blood sugar control in diabetic patients. This is similar to previously reported systematic review and meta-analysis [4,5,8]. As for the efficacy of smartphone-based digital apps on cardiovascular risk, the present study is the first to perform comprehensive pooled estimates. The findings suggest that digital apps can potentially reduce cardiovascular risk in diabetic patients. Indeed, significant results were only obtained in systolic blood pressure and triglycerides. However, it should be noted that, in cardiovascular risk modification, triglycerides are the lipid fraction that changes the fastest compared to other lipid fractions. This is because triglyceride biosynthesis involves very low-density lipoprotein (VLDL) particles, which are highly influenced by diet and physical activity. In terms of blood pressure, changes in arterial stiffness, vascular resistance, and cardiac outcomes are more significantly observed in systolic pressure than diastolic pressure. The consumption of antidiabetic drugs such as metformin, SGLT-2 inhibitors, and GLP-1 receptor agonists also had an impact on reducing systolic blood pressure [2]. A previously published meta-analysis also mentioned that metformin significantly reduced systolic blood pressure, but not diastolic blood pressure [27].

In terms of its pathomechanism, diabetes mellitus causes endothelial dysfunction, which develops into atherosclerosis and other cardiovascular complications [28]. High blood sugar can cause a decrease in blood vessel elasticity, narrowing blood vessels and inhibiting blood flow, thus ultimately increasing the risk of hypertension. Atherosclerotic plaque formation is also caused by dysregulation of oxidative stress in conditions of hyperglycemia or hypoglycemia which facilitates inflammation in the blood vessels and the accumulation of white blood cells in the tunica intima [29]. The presence of triglyceride molecules can be absorbed in a pile of macrophage foam cells that have occupied the intima of arterial vessels [30]. Triglyceride levels are the dominant risk factor for atherosclerosis, even when LDL-c levels are normal [31]. However, it should be noted that hypertension, dyslipidemia, and diabetes mellitus are each independent risk factors for the development of cardiovascular disease.

The use of digital health applications based on smartphones can be a powerful modality in controlling cardiovascular risk factors. Not only that but such digital technology can also be utilized to stratify cardiovascular risk in diabetic patients so that management and rehabilitation can be carried out with precision [32]. Among the applications reported by the studies in this systematic review, only one utilized artificial intelligence. In that study, artificial intelligence technology was used to calculate total carbohydrates based on image capture [33]. This shows the excellent opportunity to develop digital applications for diabetes control and prevention of complications from the disease.

Several factors limit the interpretation of the results in this study. First, there are diverse apps used, including features and operating systems. This study was also unable to show which apps have the best features. Thirdly, no subgroup analysis based on socioeconomic characteristics was conducted due to insufficient studies. Due to the limited number of studies, further studies are needed to prove the efficacy of smartphone-based digital apps in reducing risk factors or preventing cardiovascular complications.

Conclusion

Smartphone-based apps have the potential to be used as a modality to control cardiovascular risk factors in diabetic patients. However, further studies are needed to confirm the effect of these apps, especially on lipid profile indicators. Apps must also be optimized to encourage and guide users to exercise and physical activity. More importantly, researchers need to report

cardiovascular risk parameters when investigating the efficacy of smartphone-based apps. Incorporation of artificial intelligence in such apps can be carried out to increase the utility and ease of use.

Ethics approval

Not applicable.

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Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

All data underlying the results are available as part of the article and no additional source data are required. Supplementary files are available on Figshare (https://doi.org/10.6084/m9.figshare.25537525).

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