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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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META-ANALYSIS

Efficacy of telemedicine on glycaemic control in patients with type 2 diabetes: A meta-analysis

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Abstract

BACKGROUND

Telemedicine is defined as the delivery of health services *via* remote communication and technology. It is a convenient and cost-effective method of intervention, which has shown to be successful in improving glyceamic control for type 2 diabetes patients. The utility of a successful diabetes intervention is vital to reduce disease complications, hospital admissions and associated economic costs.

AIM

To evaluate the effects of telemedicine interventions on hemoglobin A1c (HbA1c), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), post-prandial glucose (PPG), fasting plasma glucose (FPG), weight, cholesterol, mental and physical quality of life (QoL) in patients with type 2 diabetes. The secondary aim of this study is to determine the effect of the following subgroups on HbA1c post-telemedicine intervention; telemedicine characteristics, patient characteristics and self-care outcomes.

METHODS

PubMed Central, Cochrane Library, Embase and Scopus databases were searched from inception until 18th of June 2020. The quality of the 43 included studies were assessed using the PEDro scale, and the random effects model was used to estimate outcomes and I^2 for heterogeneity testing. The mean difference and standard deviation data were extracted for analysis.

RESULTS

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We found a significant reduction in HbA1c [-0.486%; 95% confidence interval (CI) -0.561 to -0.410, *P* < 0.001], DBP (-0.875 mmHg; 95%CI -1.429 to -0.321, *P* < 0.01), PPG (-1.458 mmol/L; 95%CI -2.648 to -0.268, *P* < 0.01), FPG (-0.577 mmol/L; 95%CI -0.710 to -0.443, *P* < 0.001), weight (-0.243 kg; 95%CI -0.442 to -0.045, *P* < 0.05), BMI (-0.304; 95%CI -0.563 to -0.045, *P* < 0.05), mental QoL (2.210; 95%CI 0.053 to 4.367, *P* < 0.05) and physical QoL (-1.312; 95%CI 0.545 to 2.080, *P* < 0.001) for patients following telemedicine interventions in comparison to control groups. The results of the meta-analysis did not show any significant reductions in SBP and cholesterol in the telemedicine interventions compared to the control groups. The telemedicine characteristic subgroup analysis revealed that clinical treatment models of intervention, as well as those involving telemonitoring, and those provided *via* modes of videoconference or interactive telephone had the greatest effect on HbA1c reduction. In addition, interventions delivered at a less than weekly frequency, as well as those given for a duration of 6 mo, and those lead by allied health resulted in better HbA1c outcomes. Furthermore, interventions with a focus on biomedical parameters, as well as those with an engagement level > 70% and those with a drop-out rate of 10%-19.9% showed greatest HbA1c reduction. The patient characteristics investigation reported that Hispanic patients with T2DM had a greater HbA1c reduction post telemedicine intervention. For self-care outcomes, telemedicine interventions that resulted in higher post-intervention glucose monitoring and self-efficacy were shown to have better HbA1c reduction.

CONCLUSION

The findings indicate that telemedicine is effective for improving HbA1c and thus, glycemic control in patients with type 2 diabetes. In addition, telemedicine interventions were also found to significantly improved other health outcomes as well as QoL scores. The results of the subgroup analysis emphasized that interventions in the form of telemonitoring, *via* a clinical treatment model and with a focus on biomedical parameters, delivered at a less than weekly frequency and 6 mo duration would have the largest effect on HbA1c reduction. This is in addition to being led by allied health, through modes such as video conference and interactive telephone, with an intervention engagement level > 70% and a drop-out rate between 10%-19.9%. Due to the high heterogeneity of included studies and limitations, further studies with a larger sample size is needed to confirm our findings.

Key Words: Telehealth; Telemedicine; Telemonitoring; Behavioural change; Self-management; Diabetes

Core Tip: The findings indicate that telemedicine is effective for improving hemoglobin A1c (HbA1c) and thus, glycemic control in patients with type 2 diabetes. In addition, telemedicine interventions were also found to significantly improve other health outcomes as well as quality of life scores. The results of the subgroup analysis emphasized that interventions in the form of telemonitoring, *via* a clinical treatment model and with a focus on biomedical parameters, delivered at a less than weekly frequency and 6 mo duration would have the largest effect on HbA1c reduction. This is in addition to being led by allied health, through modes such as video conference and interactive telephone, with an intervention engagement level > 70% and a drop-out rate between 10%-19.9%.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder in which the pancreas fails to secrete adequate insulin to maintain glucose homeostasis. Blood glucose levels are normally controlled by a series of anabolic and catabolic hormones, primarily insulin and glucagon, respectively[1]. It is evident that T2DM poses an extensive economic burden and negative consequences to health and healthcare systems. In 2014, an estimated 422 million people suffered from diabetes mellitus[2]. This equates to approximately 1 in 11 adults worldwide, 90% of whom suffer from T2DM[3]. The prevalence has nearly quadrupled since 1980 and current projections suggest that 642 million people will suffer from diabetes by 2040[2]. This is mainly attributed to rapid urbanisation, sedentary lifestyles and poor dietary habits[4]. In 2013, the Global Burden of Disease study found that diabetes was the 9th most common cause for reduced life expectancy. Furthermore, 5 million deaths were attributed to diabetes in 2015, equating to 1 death every 6 s[5]. The estimated global economic burden of diabetes mellitus in 2015 was over 1.2 trillion USD[6].

A longitudinal cohort study that followed 117629 female nurses over 20 years found that participants with T2DM at baseline had a 5-times greater risk of myocardial infarction and cerebrovascular disease when compared to those without diabetes[7]. Additionally, diabetes was the leading cause of blindness in individuals aged 20-74 years in 2011 and it was responsible for 44% of end-stage kidney disease and 60% of non-traumatic lower limb amputations[8]. Diabetes can also cause neuropathy through vascular disruption and direct neuronal injury. This may manifest as peripheral neuropathy affecting the extremities or autonomic neuropathy with organ dysfunction[9,10]. Some studies also suggest that T2DM is associated with a greater risk of depression, vascular dementia and Alzheimer's disease[11,12].

Optimal diabetes management is necessary to slow disease progression, reduce complications and lessen the global healthcare burden[5]. Historically, weight loss and dietary changes have been the primary intervention to decrease visceral adiposity and improve glycaemic control[13,14]. Pharmacological management is also required where lifestyle modifications fail to achieve euglycemia[15]. Glycaemic control is closely monitored using glycosylated hemoglobin A1c (HbA1c) for long-term glycaemic control, *vs* post-prandial glucose (PPG) and fasting plasma glucose (FPG) for short-term control[16]. Regular testing of the eyes, feet, blood pressure, lipids and urinary albumin excretion are also recommended to screen for possible complications[17].

Despite these interventions, 45% of patients with T2DM fail to achieve the target HbA1c[18]. One major barrier to adequate glycaemic control appears to be patient's inability to perform adequate self-care, for example, poor adherence to prescribed medications and lifestyle modifications. A recent meta-analysis found that the adherence rate for anti-diabetic medications varied from 38% to 93%[18]. Qualitative studies suggest that poor adherence can be attributed to forgetfulness, medication side effects and insufficient patient education[19]. Self-care has been defined as the formation of knowledge and awareness needed to survive with the nature of a disease in both a health and social context[20,21]. Self-care behaviours relevant to T2DM that assist the disease management include nutrition, physical activity, blood glucose monitoring, medication adherence, disease knowledge, positive behaviour changes and self-efficacy[21]. Research has shown that self-care behaviours are vital to diabetes self-management and have a direct impact on improving glycaemic control, quality of life (QoL) and decreasing incidence of complications[21,22]. Therefore, healthcare workers should aim to promote self-care behaviours in all T2DM interventions[21].

Other potential barriers to optimal glycaemic control in T2DM include inadequate patient outreach, time constraints and overly cautious prescribing habits[23,24]. These barriers have a profound effect on patient outcomes and healthcare costs. Studies have shown that the average patient cost is approximately 2.5-times higher in diabetes patients with a HbA1c greater than 10% compared to those with a HbA1c within the target range[25]. This is primarily due to a higher number of complications and hospitalisations in diabetics with poor glycaemic control[25]. Therefore, it is clear that effective interventions are required to improve patient outcomes and relieve the healthcare burden associated with T2DM.

In recent years, telehealth, also known as telemedicine, has been recognised as an effective way to deliver health services in rural and regional areas because it can be conducted remotely without compromising patient care[26]. Telehealth refers to the delivery of health services with the use of telecommunications and information technology[27]. It aims to maximise access to health services without any additional expense[28]. Telehealth is a broad term that can be classified as synchronous, asynchronous or remote monitoring. Synchronous telehealth refers to the delivery of health services in real time through smart devices, *e.g.*, videoconferencing, mobile phone or computer. Asynchronous telehealth is when data relating to a patient is collected and reviewed at different points in time. Remote monitoring refers to the continuous evaluation of a patient's clinical status based on specific health readings uploaded by the patient over the phone or online[29].

A review focusing on rural Australians found that telehealth provided better convenience, lower patient costs, improved access to specialist services and reduced hospital admissions[26]. These benefits also apply to patients with reduced mobility and other populations that experience a high degree of isolation[30,31]. Furthermore, telehealth has been shown to improve outcomes in psychiatric patients because it promotes greater self-efficacy and allows patients to maintain existing support networks[32,33]. Service providers also benefit from telehealth due to reduced travel expenses and greater educational opportunities for those working in remote areas[26]. Numerous randomised control trials have been conducted to evaluate the effectiveness of telehealth in patients with T2DM. However, no studies have provided in-depth analysis of the effectiveness of telehealth on health improvement of patients with diabetes[34]. Therefore, this study aimed to utilise a meta-analysis approach to synthesise results from high quality randomised controlled trials, and to comprehensively review literature on the effects of telemedicine interventions on health outcomes for patients with T2DM. The secondary aim is to analyse the effect of telemedicine characteristics, patient characteristics, and self-care outcomes on glycaemic control post-intervention.

MATERIALS AND METHODS

Database search

The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) prior to commencing the database search. Published randomised controlled trials (RCTs) that investigated the effect of telemedicine on T2DM were systematically searched on the following databases; Scopus, PubMed Central, Embase and Cochrane until June 18th 2020. Additional records were identified on Proquest Central (Dissertations and Thesis). The search terms were: Type 2 diabetes* AND Telemedicine OR telehealth OR e-health OR eHealth OR m-health OR mHealth AND HbA1c OR glucose OR insulin OR HOMA OR homeostatic model assessment AND Randomised* OR Randomized* OR RCT.

Inclusion and exclusion criteria

Full-text studies written in English and published between January 1st 1989 and June 18th 2020 were included. The RCTs were required to report at least one primary outcome (HbA1c, insulin or HOMA-IR) and utilise telemedicine intervention in the intervention group(s) to be included. Classic telephone calls were not considered telemedicine. The participants were required to be minimum 18 years of age and have physician diagnosed T2DM or meet the minimum clinical measurements to be diagnosed in the study.

Studies were excluded if the control group contained any component of telemedicine intervention. Studies were excluded if they measured outcomes for less than 24 wk or the data was not separated from individuals with other forms of diabetes, such as Type 1 diabetes. Incomplete post-intervention data and conference abstracts were not included. If the same data set was used in multiple studies, the study with the completed data was included and the other(s) excluded.

Reasonable attempts were made to obtain full-text articles in the cases where it was not available online, including messages to authors on ResearchGate and email. The literature search was performed by De Groot J and Flynn D independently. Any discrepancies in narrowing and excluding studies were resolved in discussion with Robertson D and Sun J.

Selection of studies

Results of the searches were exported into EndNote software and duplicates were removed. Titles of the articles were screened to remove clearly irrelevant or non-RCT studies. Abstracts were read from the remaining list and further studies were excluded based on our criteria. For the remainder of studies, full text was reviewed for the purpose of data extraction, with some further exclusion of papers.

Quality assessment

PEDRO quality assessment was performed for all studies assessed for full text. Studies were excluded if they were scored ≤ 3 out of 10. A conservative approach was utilised, where if a component could not be confirmed, it was rated 0 for that component. The 10 components were randomisation, concealed allocation, group characteristics similar at baseline, subjects blinded, therapists blinded, assessors blinded, key outcome obtained from 85% of participants, intention to treat analysis, between group statistical analysis, and point measures with measures of variability.

Data extraction

Data extraction was completed by Flynn D and Robertson D, whilst De Groot J and Sun J verified all data entries with the full text of the published papers. The following information was collected from each paper; Table 1 study details, information for the PEDRO quality assessment and the primary and secondary outcomes at both pre- and post-intervention. Primary outcomes were HbA1c, HOMA-IR and insulin. Secondary outcomes were FPG, PPG, body mass index (BMI), weight, waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), depression, anxiety, QoL. The data was converted to mean and standard deviation where possible and appropriate. Data was converted from median and range if it was considered to have a normal distribution. The data set was excluded if it was not reported as mean ± SD and it was not appropriate to convert, for example a non-normal distribution. Blood glucose was converted from mg/dL to mmol/L and blood lipids were converted from mg/dL to mmol/L. The short form (SF) health survey is used to measure QoL. Although the survey length can vary, each score is standardised from 0-100, 0 being maximum disability and 100 being no disability. The diabetes treatment satisfaction questionnaire was also included with the same standardisation[35]. Mean difference standard deviation was calculated if not provided by the study using the following equation: $\sigma = \text{sqrt}\ (\sigma_1^2/n_1 + \sigma_2^2/n_2)$. Subgroup information was collected about patient demographics, characteristics about the telemedicine intervention and self-care outcomes.

Subgroups

Descriptive words about the intervention, patient demographic and self-care outcomes were collected from each paper. These were then manually coded into subgroups, as defined in the Supplementary Tables 1-4.

Mode of telemedicine intervention subgroups included Text message, Mobile Application, Interactive Telephone System, Online Server, Website, Videoconference, or Tablet/device. Duration of intervention subgroups included < 6 mo, 6 mo, > 6 mo < 12 mo, or > 12 mo. Focus of intervention subgroups included biomedical parameters, self-management behaviours, or combination of biomedical parameters/self-management behaviours. Model of intervention subgroups included behaviour change, clinical treatment, or behaviour change/treatment combination. Type of telemedicine intervention subgroups included telemonitoring, tele-education, or telemonitoring/tele-education combination. Intervention-lead subgroups included doctor, nurse, multi-disciplinary team, or allied health. Drop-out rate subgroups included 0%-9.9%, 10%-19.9%, or > 20%. Frequency of intervention subgroups included daily, < daily > weekly, weekly, or < weekly. Intervention engagement subgroups included < 70% or > 70%.

The self-care components considered for subgroups were related to: medication adherence, disease knowledge, behaviour change, self-glucose monitoring, hospital visits, self-efficacy, nutrition/diet, and exercise. These were categorised into subgroups based on whether there the telemedicine intervention improved significantly more than the control group in each self-care component. Regarding patient characteristic subgroups; racial group subgroups included Hispanic or Chinese, and comorbid disease subgroups included overweight/obese (BMI ≤ 25) and physician-diagnosed hypertension.

Statistical analysis

The random effects model was used to estimate effect sizes and mean differences in all outcomes and I^2 for heterogeneity testing. Publication bias was analysed using Egger regression analysis that *P* value is more than 0.05 suggesting the publication bias is not significant. Sensitivity analysis was conducted by using removing one study per time and cumulative all studies to identify the results are related to particular study or studies.

Table 1 The characteristics of included studies (require insert reference for each study)

Ref.	Number centres, funding	Participants I/C	Design, location (country/territory)	Mean age intervention (SD)/mean age control (SD) (yr)	Sex (M/F)	Intervention type	Control	Measured outcomes	Key results	PEDro	Notes
Alanzi *et al*[36] 2018	4, none stated	10/10	NB, Saudi Arabia	8 × (18-40), 2 × (41-50)/9 × (18-40), 1 × (41-50)	15/5	Mobile application; Bluetooth transmission of blood glucose, social networking, cognitive behavioral therapy (6 mo)	Usual care	HbA1c	Greater decrease in HbA1c for intervention *vs* control	5	-
Arora *et al*[37] 2014	1, Agile Health LLC and McKesson foundation	64/64	NB, United States	50.5 (10.3)/51 (10.2)	46/82	Twice daily text messages about self-care and medication adherence (6 mo)	Usual care	HbA1c	No significant differences	4	Data converted from median (range)[a]
Bujnowska-Fedak *et al*[38] 2011	Multi-centre, none stated	50/50	NB, Poland	53.1 (25.2)/57.5 (27.4)	51/44	Transmission of blood glucose to computer network *via* glucometer, systems sends text to GP (6 mo)	Usual care with glucometer	HbA1c, FPG, PPG, BMI, SBP, DBP, TC	No significant differences	5	-
Cho *et al*[39] 2017	3, Korean Government	244/240	NB, South Korea	52.9 (9.2)/53.4 (8.7)	307/177	Glucometer and blood pressure measurements sent *via* internet connected device, doctors and nurses send back recommendations (6 mo)	Usual care	HbA1c, FPG, weight, BMI, SBP, DBP, TC, HDL, LDL, TG, WC, PPG, QoL	Greater decrease in HbA1c, PPG and WC for intervention *vs* control	6	-
Crowley *et al*[40] 2016	1, Veterans Affairs	25/25	NB, United States	60 (8.4)/60 (9.2)	48/2	Glucose testing sent *via* telephone voice system daily + fortnightly self-management modules *via* telephone (6 mo)	Usual care	HbA1c, SBP, DBP, Depression	Greater decrease in HbA1c, SBP, DBP for intervention *vs* control	6	-
Dafoulas *et al*[41] 2015	Multicentre, European Community	74/80	SB, Greece	58.28 (0.93)/64.11 (0.6)	68/86	Transmission of blood glucose weekly *via* mobile app + calls from doctors as required (12 mo)	Usual care	HbA1c, QoL	Greater decrease in HbA1c, QoL physical, QoL mental and physical activity for intervention *vs* control	5	-
Dario *et al*[42] 2017	3, European Commission and RENEWING HEALTH project	208/91	NB, Italy	73.05 (5.79)/73.04 (5.28)	168/131	Transmission of glucometer *via* online gateway to doctor	Usual care	HbA1c, QoL, depression, anxiety	No significant differences	5	-
Fortmann *et al*[43] 2017	4, Mckesson foundation and National center for advancing translational sciences grant	63/63	NB, United States	47.8 (9.0)/49.1 (10.6)	32/94	Text messages, up to 3 per day; motivational, educational or call-to-action (6 mo)	Usual care	HbA1c, FPG, TC, HDL, LDL, TG, SBP, DBP, BMI, weight	Greater decrease in HbA1c for intervention *vs* control	6	-
Fountoulakis	2, None stated	54/26	NB, Greece	61.3 (11.4)/63.5 (13.8)	55/25	USB-connected modem	Usual care	HbA1c, BMI	Greater decrease in	5	Separates T1D

et al[44] 2015						compatible with glucometer, data transmitted to computers of Department of Endocrinology			HbA1c for intervention *vs* control		and T2D data. Recruitment '*n*' not provided
Holmen *et al*[45] 2014	2, European Union + 6 others	(1) 51/50, (2) 50/50	NB, Norway	58.6 (11.8)/55.9 (12.2)	(1) 64/37, (2) 55/45	(1) mobile phone based self-management system app (automatic blood glucose transmission, input of diet and exercise info, goal managing). (2) Intervention 1 + telephone behaviour-change counselling from nurse for first 4 mo (12 mo)	Usual care	HbA1c, weight	No significant differences	5	3 arm (2 interventions)
Jeong *et al*[46] 2018	4, Ministry of Health and Welfare, Republic of Korea and Ministry of Trade, Industry, and Energy South Korea	(1) 113/113, (2)112/113	NB, South Korea	53.65 (9.10)/53.16 (9.06)	(1) 64/37, (2) 55/45	(1) telemonitoring: outpatient clinic + tablet unit with auto blood glucose and weight transmission, diet and exercise monitoring with automated feedback texts. (2) telemedicine: intervention 1 + videoconference outpatient clinic (24 wk)	Usual care	HbA1c, FPG, PPG, BMI, body weight, SBP, DBP, HDL, LDL, TG	Greater decrease in FPG for (1) telemonitoring group and (2) telemedicine group *vs* control	6	3 arm (2 interventions)[a]
Kempf *et al*[47] 2017	Multicentre, Boehringer Ingelheim International and University Dusseldorf	102/100	SB, Germany	59 (9)/60 (8)	90/77	Glucometer, weight and pedometer data auto uploaded to online portal + weekly phone calls about lifestyle change and self-management (12 wk, 52 wk follow-up data)	Usual care with self-management guide, scale and step counter	HbA1c, FPG, weight, BMI, SBP, DBP, TC, HDL, LDL, QoL	Greater decease in HbA1c, body weight, BMI, SBP and QoL for intervention *vs* control	8	TG excluded as median (IQR) and skewed
Kim *et al*[48] 2007	1, College of Nursing Catholic University of Korea	30/30	NB, Korea	46.8 (8.8)/47.5 (9.1)	22/29	Self-monitored glucose and medication use was submitted online and weekly recommendations were sent *via* text (6 mo)	Usual care	HbA1c, FPG, PPG	Greater decrease in PPG for intervention *vs* control	5	-
Kim *et al*[49] 2008	1, Korean Government	20/20	NB, Korea	45.5 (9.1)/48.5 (8)	16/18	Medications and self-monitored glucose readings were used to create online medical record + weekly recommendations sent *via* text message (12 mo)	Usual care	HbA1c, FPG, PPG	Greater decrease in HbA1c for intervention *vs* control	5	-
Kim *et al*[50] 2016	1, UB care	110/110	NB, China	52.5 (9.1)/55.6 (10)	88/94	Internet-based self-monitoring of blood glucose + recommendations *via* a website (6 mo)	Usual care	HbA1c, SBP, DBP, TC, TG, HDL, LDL	Greater decrease in HbA1c and FPG for intervention *vs* control	4	-
Kim *et al*[51] 2019	3, HealthConnect Co.	97/94	NB, South Korea	60 (8.4)/56.7 (9.1)	99/73	Smartphone modules for Bluetooth glucometer, diet, exercise *via* activity tracker + clinical decision support (24 wk)	Usual care + Manual glucose logbook	HbA1c, FPG, weight, SBP, DBP, TC, TG, LDL, HDL	Greater decrease in HbA1c for intervention *vs* control	5	[a]
Kleinman *et al*[52] 2017	3, Gather Health LLC	44/46	NB, India	48.8 (9)/48 (9.5)	63/27	Mobile app provided daily reminders for self-management tasks and data + provider	Usual care	HbA1c, FPG, BMI	Greater decrease in HbA1c, greater increase self-reported	7	

						communication and treatment adjustment (6 mo)			medication adherence and BG testing for intervention *vs* control		
Lee *et al*[53] 2020	11, Ministery of Science, Technology and Innovation Malaysia	120/120	SB, Malaysia	56.1 (9.2)/56.3 (8.6)	108/132	Auto transmission of glucometer data *via* online portal with automatic feedback + team encouraged self-management monthly + change to medication if required (12 mo)	Usual care	HbA1c, FPG, SBP, DBP, TC, TG, HDL, LDL, QoL	Greater decrease in HbA1c for intervention *vs* control	7	[a]
Lim *et al*[54] 2016	1, Korea healthcare technology R&D project	50/50	NB, Korea	64.3 (5.2)/65.8 (4.7)	75/25	Bluetooth glucometer and activity monitor, and dietary and exercise transmission to website + tailored feedback to device or mobile (6 mo)	Usual care + self monitored blood glucose	HbA1c, BMI, SBP, DBP, TC, TG, LDL, HDL, WC, FPG, PPG	Greater decrease in HbA1c for intervention *vs* control	5	-
Liou *et al*[55] 2014	6, none stated	54/41	NB, Taiwan	56.6 (7.7)/57 (7.5)	48/47	6 sessions about diet, medication, stress management, goal setting and foot care, including 2 *via* teleconference (6 mo)	Usual care + 1 in-person education session by nurse	HbA1c, BMI, SBP, DBP, TC, TG, LDL, HDL	Greater decrease in HbA1c for intervention *vs* control	5	TG excluded as log-transformed[a]
Luley *et al*[56] 2011	1, none stated	35/35	NB, Germany	59 (9)/58 (7)	34/36	Bluetooth transmission from scales and accelerometer *via* Homebox to server + weekly feedback and progress *via* letters + low calorie diet (6 mo)	Usual care + conventional low fat diet	Weight, BMI, HBA1c, TG, HDL, FPG	Greater decrease in HbA1c weight, BMI and FPG for intervention *vs* control	5	[a]
Nicolucci *et al*[57] 2015	Multi-centre, MSD Italia grant	153/149	NB, Italy	59.1(10.3)/57.8(8.9)	94/92	Bluetooth transmission weight, blood glucose and blood pressure measurements to server *via* internet + remote support and GP feedback	Usual care	HbA1c, weight, SBP, DBP, TC, HDL, LDL, TG, QoL	Greater decrease of HbA1c and increase of mental summary QoL for intervention *vs* control	4	-
Or *et al*[58] 2020	1, Food and Health Bureau	151/148	NB, Hong Kong	63.9 (10.2)/63.7 (9.6)	192/107	Bluetooth glucometer and BP monior + website-based technological surrogate nursing care encouraged self-management *via* tablet with resources (24 wk)	Usual care	HbA1c, SBP, DBP	No significant differences	7	-
Orsama *et al*[59] 2013	1, Finnish funding agency, Technical Research centre Finland & Bayer HealthCare	27/29	NB, Finland	62.3 (6.5)/61.5 (9.1)	26/22	Mobile app transmission of weight, blood glucose, stepcount and blood pressure + automatic feedback with behaviour change focus + website viewing of health record	Usual care	HbA1c, weight, SBP, DBP	Greater decrease in HbA1c and weight for intervention *vs* control	5	Baseline HbA1c up to 2 months were used
Pacaud *et al*[60] 2012	1, Lawson Foundation	(1) 18/21, (2) 29/21	NB, Canada	52.1 (8.8)/56.3 (8.1)	(1) 10/8, (2) 12/17	(1) Webstatic: email consults (12 mo). 1A-male, 1B-female. (2) Web Interactive: online chat and email consults. 2A-male, 2B-female. (12	Usual care + education (face-to-face education,	HbA1c, QoL	No significant differences	5	5 arm (2 interventions and separation by sex). Post-test '*n*

						mo)	group sessions)				'not given[a]
Pressman *et al*[61] 2014	Multi-centre, Samsung	118/107	SB, America	54.8 (9.8)/56.4 (8.7)	122/76	Weekly transmission of blood glucose, blood pressure and weight to case manager *via* device + tailored telephone feedback (6 mo)	Usual care	Weight, BMI, SBP, LDL, HbA1c	No significant differences	6	[a]
Quinn *et al*[62] 2016	Multi-centre, University of Maryland and WellDoc	(1) 37/29, (2) 25/27	NB, United States	47.3 (6.8)/47.4 (7.5)	(1) 32/34, (2) 27/25	Mobile phone coaching App, entering blood glucose, diet, medication info with behavioural, motivation or feedback messages + Web portal (12 mo)	Usual care	HbA1c	Greater decease in HbA1c for intervention *vs* control, no statistical difference for age groups	4	3 arm (separated by age < 55 and > 55)
Ramadas *et al*[63] 2018	3, Monash University	66/62	NB, Malaysia	49.6 (10.7)/51.5 (10.3)	77/51	Web-based nutrition lesson plan and dietary intervention (12 mo)	Usual care	FBG, HbA1c	No significant differences	7	Mean difference provided by study for HbA1c[a]
Rodríguez-Idígoras *et al*[64] 2009	Multi-centre, Roche Diagnostics Spain	161/167	NB, Spain	63.32 (11.13)/64.52 (10.32)	169/159	Transmission of glucometer data *via* mobile + mobile contact by patient or healthcare staff when required + teleconsults (12 mo)	Usual care	HbA1c	Greater decrease in HbA1c for intervention *vs* control	7	-
Shea *et al*[65] 2009	2, Medicare and Medicaid + 6 more	844/821	SB, United States	70.8 (6.5)/ 70.9 (6.8)	616/1049	Home unit with web-enabled computer access to website with education + webcam for videoconferencing + auto uploading glucometer and blood pressure data (5 yr)	Usual care	HbA1c, LDL, SBP, DBP	Greater decrease in HbA1c (years 4-5) and LDL (years 1-4) and SBP (years 1-5) and DBP (years 1-5) for intervention *vs* control	5	Changed from Weinstock 2011, Adjusted mean used
Stone *et al*[66] 2010	Multi-centre, U.S. Air Force	64/73	SB, United States	3 × (< 45), 38 × (45-65), 23 × (> 65)/4 × (< 45), 43 × (45-65), 26 × (> 65)	135/2	Transmission of blood glucose, blood pressure and weight *via* internet-connected device + monthly phone calls: self-management education, medication changes (6 mo)	Monthly phone call	HbA1c, weight, SBP, DBP, TC, HDL, LDL, TG	Greater decrease in HbA1c for intervention *vs* control	7	-
Sun *et al*[67] 2019	1, Science Technology Department Jilin and Jilin University	44/47	NB, China	67.9 (66,71), 68.04 (66, 72) Median (IQR)	37/54	Mobile phone application + Bluetooth glucometer + advice every 2 wk *via* app (6 mo)	Usual care + glucometer + outpatient visits	HbA1c, PPG, FPG, TC, TG, BMI, SBP	Greater decrease in HbA1c and PPG for intervention *vs* control	5	HDL, LDL, BMI, DBP excluded due to median (IQR) and skewed
Tang *et al*[68] 2013	1, Agency for Health Research and Quality	193/189	SB, United States	54 (10.7)/53.5 (10.2)	249/166	Bluetooth glucometer readings + uploaded nutrition, exercise logs, insulin record online + messages with healthcare team and personalised text and video	Usual care	HbA1c, LDL, weight, SBP, DBP	No significant differences at 12 mo, but greater decrease in HbA1c at 6 months of intervention *vs* control	7	-
Vinitha *et al*[69] 2019	5, AstraZeneca Pharma India Ltd	126/122	NB, India	42.4 (8.5)/44.1 (8.9)	168/80	Text messages 3 times weekly: education, lifestyle, medication	Usual care	HbA1c, weight, BMI,	Greater decrease in HbA1c, SBP and FPG	6	TG excluded due to median (IQR)

						(24 mo)		WC, SBP, DBP, FPG, PPG, TC, HDL, LDL, QoL	for intervention *vs* control		and skewed
Wang *et al*[70] 2017	1, Science Technology Department Jilin	106/106	NB, China	52.6 (9.1)/54.7 (10.3)	116/104	Transfer of glucometer data to health centre *via* website + receival of information/advice (6 mo)	Usual care	HbA1c, TC, HDL, LDL	Greater decrease in HbA1c, PPG, FPG and TG for intervention *vs* control	4	FPG, TG, BMI, SBP, DBP, PPG excluded due to median (IQR) and skewed
Wang *et al*[71] 2018	1, National Center for Clinical and Translational Sciences grant	11/6	NB, United States	58.8 (5.9)/49.2 (10.2)	7/10	Smartphone application + Bluetooth scale and glucometer + 12 in-person behaviour-change sessions (6 mo)	Usual care	HbA1c	Greater decrease in HbA1c for intervention *vs* control	5	Paper group intervention not included here
Wayne *et al*[72] 2015	2, Public Health Agency Canada	67/64	NB, Canada	53.1 (10.9)/53.3 (11.9)	28/72	Mobile phone monitoring and health coaching (6 mo)	Health coaching without mobile	HbA1c, weight, WC, BMI, depression, anxiety, QoL	Greater decrease in BMI and greater increase in QoL (Mental SF-12) for intervention *vs* control	5	-
Welch *et al*[73] 2011	1, Baystate Medical Center	25/21	NB, United States	54.4 (10.4)/57.5 (9.5)	31/15	Transmission of comprehensive patient data to clinician *via* internet + 7 in-person visits of 1 h diabetes education (12 mo)	7 in-person visits of 1 h diabetes education	HbA1c, SBP, DBP, BMI	Greater decrease in HbA1c and SBP for intervention *vs* control	4	Depression excluded due to nil measure of variance
Whittemore *et al*[74] 2020	5, none stated	26/21	SB, Mexico	53.9 (9.2)/56.8 (8.3)	16/31	7 weekly self-management group sessions + 6 mo daily text messages about behaviour change + unconnected glucometer (6 mo)	Usual care (waitlist for intervention)	HbA1c, SBP, DBP BMI, depression	No significant differences	7	[a]
Wild *et al*[75] 2016	4, Chief Scientist Office Grant	160/161	SB, United Kingdom	60.5 (9.8)/61.4 (9.8)	214/107	Bluetooth transmission of glucose, blood pressure and weight to website + called when lifestyle and medication changes required (9 mo)	Usual care	HbA1c, SBP, DBP, weight	Greater decrease in HbA1c, SBP and DBP for intervention *vs* control	7	-
Williams *et al*[76] 2012	3, QLD Health, HCF Health and Medical Research Foundation	60/60	NB, Australia	58.4 (8.2)/56.4 (8.3)	76/44	Bluetooth Glucometer + Interactive automated telephone system encouraging self-management behaviours (6 mo)	Usual care	HbA1c, QoL	Greater decrease in HbA1c and improved mental HRQL for intervention *vs* control	5	-
Xu *et al*[77] 2020	1, National Institutes of Health, Veterans Affairs	33/32	NB, United States	54.6 (1.82)/55.34 (1.94)	20/44	Glucose data self reported and collected by automated phone calls/texts, shared with providers with bidirectional communication (12 mo)	Usual care	HbA1c	No significant differences	5	Excluded FPG measures as it was patient-reported
Yip *et al*[78] 2002	1, none stated	41/41	SB, China	55.29 (8.63)/57.54 (8.52)	70/52	4 educational sessions *via* videoconference + telephone	Usual care	HbA1c	No significant differences	5	Additional non-telehealth group

		monitoring (4.5 mo). Outcomes measured at 6 mo)	not included

[a]P < 0.05. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; TC: Total cholesterol; MD: Mean difference; CI: Confidence interval; FPG: Fastening plasma glucose; WC: Waist circumference; PPG: Post-prandial glucose; QoL: Quality of life.

RESULTS

Study selection

We identified 673 total potential studies from the database search, with 1322 additional records identified through other sources. After removing duplicates, 1731 studies remained to be screened by title and abstract. Full-text screening was conducted on the remaining 59 studies, 16 of which were excluded as a result of the study design or data insufficiency. Due to multiple arm trial designs, the final sample for meta-analysis included 43 eligible studies in quantitative synthesis in total (Figure 1).

Study characteristics

The 43 included studies were published between 2002 and 2020, and reported 4365 participants receiving a telemedicine intervention and 4045 participants in the control groups. Participants were recruited from 16 countries including Saudi Arabia, United States, Poland, South Korea, Greece, Italy, Norway, Germany, India, Malaysia, China, Finland, Canada, Spain, Mexico, and Australia. Participants in the intervention group received telemedicine intervention while those in the control group did not. All included studies measured at least one of the required outcome variables, which was consistently HbA1c. The outcomes of SBP, DBP, PPG, FPG, BMI, cholesterol, weight, mental QoL, and physical QoL were also collected from the studies. The demographic characteristics of the participants, intervention and control details, measured outcomes, key results and PEDRO quality assessment of the included studies are summarised and presented in Table 1[36-78].

Primary outcomes and subgroup analysis

Forty-three studies involving 6932 participants measured HbA1c changes in diabetes patients. The pooled effect on HbA1c was -0.486% [95% confidence interval (CI) -0.561 to -0.410, P < 0.001] in the telemedicine group compared with the usual care group, with a significantly high-level of heterogeneity (I^2 = 98.290%, P < 0.001). Our results found that all modes of telemedicine interventions had a significant HbA1c reduction (P < 0.001), six of them with significant heterogeneity (P < 0.001) including text message (-0.591%; 95%CI -0.892 to -0.290, P < 0.001), mobile application (-0.359%; 95%CI -0.502 to -0.215, P < 0.001), interactive telephone (-0.782%; 95%CI -1.172 to -0.391, P < 0.001), internet server/computer network (-0.431%; 95%CI -0.558 to -0.304, P < 0.001), website (-0.539%; 95%CI -0.706 to -0.371, P < 0.001), and device/tablet (-0.278%; 95%CI -0.747

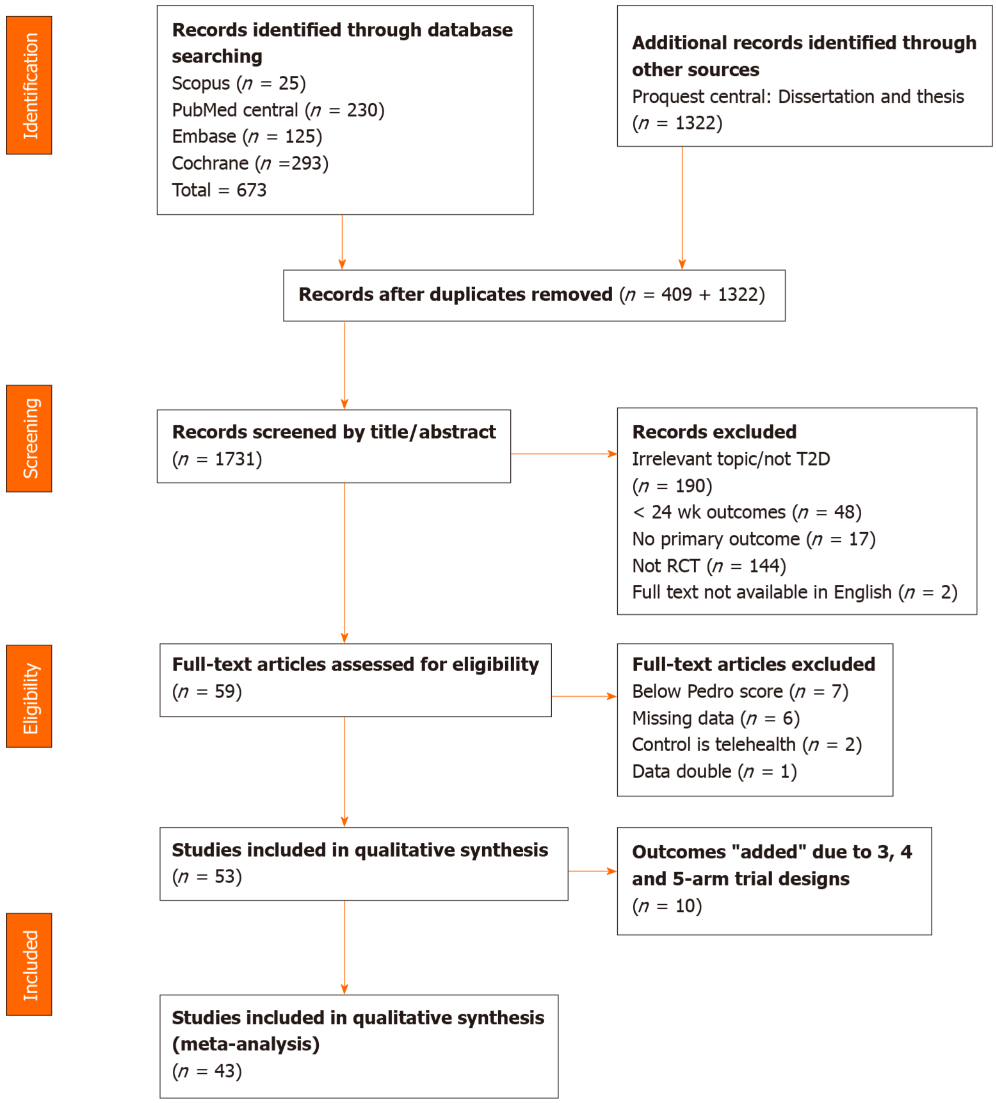


Figure 1 PRISMA flow chart of study selection.

to 0.191, P < 0.001); only videoconference interventions (-0.845%; 95%CI -1.144 to -0.546, P < 0.001) had no significant heterogeneity. A significant HbA1c reduction (P < 0.001) with a significantly high-level of heterogeneity (P < 0.001) was found in all short-term and long-term trials. In addition, interventions of 6 mo duration were observed to have a greater HbA1c reduction (-0.626%; 95%CI -0.766 to -0.486, P < 0.001) compared to trials less than 6 mo, or more than 6 mo. Our results reported that 16 studies had interventions focussed on biomedical parameters only (-0.687%; 95%CI -0.821 to -0.553, P < 0.001) and 24 studies had interventions focussed on both biomedical parameters and self-management behaviours (-0.348%; 95%CI -0.442 to -0.253, P < 0.001) which had a significant HbA1c reduction (P < 0.001) and high level heterogeneity (P < 0.001), compared to 7 studies which had interventions focussed on self-management behaviour only, with no significant HbA1c reduction. Telemonitoring significantly reduced HbA1c (-0.553%; 95%CI -0.662 to -0.445, P < 0.001) and had greater HbA1c reduction compared to those trials using tele-education only (-0.495%; 95%CI -0.683 to -0.307, P < 0.001) and combined telemonitoring and tele-education (-0.391%; 95%CI -0.542 to -0.240, P < 0.001). We also found that those trials with a behaviour change model of intervention (-0.452%; 95%CI -0.575 to -0.329, P < 0.001) and clinical treatment model of intervention (-0.589%; 95%CI -0.725 to -0.453, P < 0.001) reported a significant HbA1c reduction and was associated with heterogeneity (P < 0.001). Six trials conducted a combined behaviour change and treatment model for intervention which also reported a significant HbA1c reduction (-0.401%; 95%CI -0.612 to -0.189, P < 0.001) with heterogeneity (P < 0.001). The telemedicine interventions lead by allied health (-0.939%; 95%CI -1.651 to -0.227, P < 0.01) reported a greater HbA1c reduction compared to those led by doctors (-0.288%; 95%CI -0.512 to -0.064, $P < 0.05$), nurse lead interventions (-0.491%; 95%CI -0.655 to -0.327, $P < 0.001$) and led by a multi-disciplinary team (-0.534%; 95%CI -0.643 to -0.425, $P < 0.001$). Patients who received a weekly intervention (-0.791%; 95%CI -1.167 to -0.416, $P < 0.001$) and less than weekly (-0.835%; 95%CI -1.068 to -0.602, $P < 0.001$) reported a greater HbA1c reduction with high heterogeneity ($P < 0.001$) compared to those patients who received intervention greater than weekly but less than daily (-0.307%; 95%CI -0.462 to -0.152, $P < 0.001$) and daily interventions (-0.439%; 95%CI -0.577 to -0.302, $P < 0.001$). The telemedicine interventions with a drop-out rate of 10-19.9% (-0.645%; 95%CI -0.786 to -0.504, $P < 0.001$) reported a greater HbA1c reduction compared to those with a drop-out rate of 0-9.9% (-0.458%; 95%CI -0.584 to -0.333, $P < 0.001$), or a drop-out rate 20%+ (-0.297%; 95%CI -0.472 to -0.121, $P < 0.001$). The telemedicine interventions with an engagement level > 70% (-0.576%; 95%CI -0.696 to –0.455, $P < 0.001$) a greater HbA1c reduction whilst interventions with engagement levels < 70% did not significantly reduce HbA1c in the analysis.

The self-care outcomes analysis identified that studies with intervention participants with significantly higher self-glucose monitoring (-0.505%; 95%CI -0.923 to -0.087, $P < 0.05$) with high heterogeneity ($P < 0.001$), and significantly higher self-efficacy (-0.810%; 95%CI -1.013 to -0.607, $P < 0.001$) by the end of the intervention showed significant reductions in HbA1c. However, we found that studies where intervention participants had significantly different medication adherence, disease knowledge, hospital visits, nutrition, and behavior change had no effect on HbA1c.

The patient characteristic subgroup analysis revealed that Hispanic participants receiving telemedicine had significantly reduced HbA1c (-0.867%; 95%CI -1.052 to -0.682, $P < 0.001$), which was greater in comparison to the remainder of the studies (-0.464%; 95%CI -0.540 to -0.388, $P < 0.001$). Obese participants receiving telemedicine had high heterogeneity (P < 0.001) but significantly decreased HbA1c (-1.270%; 95%CI -1.971 to -0.568, $P < 0.001$), whilst the hypertensive patients also had decreased HbA1c (-0.100%; 95%CI -0.136 to -0.064, $P < 0.001$). However, the remainder of studies in comparison had a greater reduction in HbA1c (-0.439%; 95%CI -0.516 to -0.361, $P < 0.001$), with high heterogeneity ($P < 0.001$) (Tables 2 and 3).

Secondary outcomes

Our results also found significant reductions in DBP (-0.875 mmHg; 95%CI -1.429 to -0.321, $P < 0.01$), PPG (-1.458 mmol/L; 95%CI -2.648 to -0.268, $P < 0.01$), FPG (-0.577 mmol/L; 95%CI -0.710 to -0.443, $P < 0.001$), weight (-0.243 kg; 95%CI -0.442 to -0.045, $P < 0.05$), BMI (-0.304; 95%CI -0.563 to -0.045, $P < 0.05$), but increase in Mental QoL (2.210; 95%CI 0.053 to 4.367, $P < 0.05$) and Physical QoL (1.312; 95%CI 0.545 to 2.080, $P < 0.001$) for the telemedicine intervention, compared to control. However, twenty-two studies involving 4053 participants were analysed and the pooled effect of SBP was not significant ($P > 0.05$) in the telemonitoring group compared to the control group. Moreover, 15 studies with 2951 participants reported no significant difference in cholesterol change in the intervention group compared to the control group (Figures 2 and 3).

Publication bias

The study by Shea *et al*[65] for SBP and DBP was excluded from the analysis due to its significant publication bias. After removing this study, visual inspection of the funnel plots of SBP and DBP (Supplementary Figure 1) showed a symmetrical distribution of the effect size, and no obvious publication bias was found. Egger's test (Table 2) of SBP (t = 0.937, 95%CI -2.814 to 7.432, $P > 0.05$), DBP (t = 0.896, 95%CI -5.695 to, 2.280, $P > 0.05$), PPG (t = 0.035, 95%CI -9.234 to 8.984, $P > 0.05$), weight (t = 1.225, 95%CI -3.014 to 0.814, $P > 0.05$), mental QoL (t = 1.124, 95%CI -13.969 to 32.978, $P > 0.05$) and physical QoL (t = 0.425, 95%CI -8.626 to 12.046, $P > 0.05$) supported the funnel plot findings indicating that no publication bias was found in the comparison. However, egger's test (Table 2) of HbA1c (t = 2.604, 95%CI -6.389 to -0.815, $P < 0.05$) FPG (t = 2.730, 95%CI -4.501 to -0.524, $P < 0.05$) and BMI (t = 2.963, 95%CI -4.376 to -0.701, $P < 0.05$) indicated significant publication bias in this comparison. Removing any study did not change the overall significant results, suggesting all included studies are contributing to the overall results.

DISCUSSION

This meta-analysis systematically reviewed 43 RCTs examining the effects of

Table 2 Result of all variable analysis of included studies in meta-analysis

Variables	Studies (*n*)	Participant (*n*)	Mean difference			Effect size			Publications Bias
			MD (95%CI)	*Q* test	*I2* (%)	Effect size (95%CI)	*Q* test	*I2* (%)	Egger's *t* (95%CI)
HbA1c	47	6932	-0.486 (-0.561, -0.410)[c]	2689.381	98.290[c]	-1.523 (-1.896, -1.150)[c]	1857.351	97.523[c]	2.604 (-6.389, -0.815)[a]
SBP	22	4053	-0.458 (-1.403, 0.486)	2772.104	99.206[c]	-0.117 (-0.603, 0.370)	1060.208	98.019[c]	0.937 (-2.814, 7.432)
DBP	20	3764	-0.875 (-1.429, -0.321)[b]	683.275	97.219[c]	-0.376 (-0.743, -0.009)[a]	535.388	96.451[c]	0.896 (-5.695, 2.280)
PPG	6	1497	-1.458 (-2.648, -0.268)[b]	437.802	98.858[c]	-1.091 (-1.695, -0.486)[c]	256.915	98.054	0.035 (-9.234, 8.984)
FPG	15	2508	-0.577 (-0.710, -0.443)[c]	163.957	91.461[c]	-1.098 (-1.575, -0.622)[c]	396.579	96.470[c]	2.730 (-4.501, -0.524)[a]
Weight	17	3235	-0.243 (-0.442, -0.045)[a]	120.538	86.726[c]	-0.549 (-0.950, -0.149)[b]	145.580	89.009[c]	1.225 (-3.014, 0.814)
BMI	15	2357	-0.304 (-0.563, -0.045)[a]	120.110	88.344[c]	-0.346 (-0.514, -0.178)[c]	232.373	93.975[c]	2.963 (-4.376, -0.701)[a]
Cholesterol	15	2951	-0.070 (-0.141, 0.002)	492.468	97.157[c]	-0.339 (-0.741, 0.063)[a]	379.019	96.306[c]	1.180 (-7.845, 2.304)
Mental QoL	6	634	2.210 (0.053, 4.367)[a]	842.443	99.406[c]	0.739 (-0.709, 2.186)	736.156	99.185[c]	1.124 (-13.969, 32.978)
Physical QoL	7	1467	1.312 (0.545, 2.080)[c]	210.628	97.151[c]	1.111 (0.432, 1.790)[c]	192.042	96.876[c]	0.425 (-8.626, 12.046)

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.001$. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; TC: Total cholesterol; MD: Mean difference; CI: Confidence interval; FPG: Fastening plasma glucose; PPG: Post-prandial glucose; QoL: Quality of life.

telemedicine on HbA1c, blood pressure, PPG, FPG, weight, BMI, cholesterol, Mental QoL, and Physical QoL in patients with diabetes. Our research reported that telemedicine interventions have a significant effect on lowering HbA1c; -0.486% (95%CI -0.561 to -0.410, $P < 0.001$, $I^2 = 98.290\%$) in comparison to the controls. The improvement of HbA1c control by telemedicine is consistent with previous research[2,79,80]. In addition, our results also report a significance reduction on DBP ($P < 0.01$), PPG ($P < 0.01$), FPG ($P < 0.001$), weight ($P < 0.05$), BMI ($P < 0.05$), Mental QoL ($P < 0.05$), and Physical QoL ($P < 0.001$) in the intervention group. However, our results found no significant effect ($P < 0.05$) on SBP and cholesterol in the intervention group compared to the controls. Although there is significant heterogeneity found in all outcomes, the positive effect of telemedicine is promising. However, the clinical significance of these results must be considered. A 0.875 mmHg reduction in DBP is not very impactful, as normal DBP can range from 80 mmHg or lower[81]. But a PPG reduction of 1.458mmol/L is significant as the upper limit of normal is only 7.8mmol/L[82], which would be a more meaningful change.

Effect of telemedicine characteristics on glycaemic control

In this study, we evaluated the effect of telemedicine intervention characteristics on T2DM in terms of changes to HbA1c. The subgroup analysis showed that interventions provided at a frequency that is less than weekly (-0.835%; 95%CI -1.068 to -0.602, $P < 0.001$, $I^2 = 86.760\%$) provided the greatest reduction in HbA1c. This is an interesting result, with the least frequent intervention revealing the highest glycaemic control. A possible reason for this could be that the participants with less frequent interactions may tend to work towards achieving goals in between each interaction, rather than with a daily or weekly intervention where motivating progress is less experience in each interaction. Patients that received an intervention duration of 6 mo (-0.626%; 95%CI -0.766 to -0.486, $P < 0.001$) also reported a higher HbA1c reduction. A previous study[83] reported similar results suggesting that 6 mo telemedicine intervention significantly improves HbA1c levels in patients with diabetes patients. In

Table 3 HbA1c subgroup analysis for included studies

Subgroups	Studies (*n*)	Participant (*n*)	Mean difference			Effect size		
			Q test	Mean difference (95%CI)	I^2 (%)	*Q* test	Effect size (95%CI)	I^2 (%)
Mode of intervention								
Text message	5	469	55.331	-0.591 (-0.892, -0.290)[c]	92.771[c]	133.957	-1.377 (-2.503, -0.252)[a]	97.014[c]
Mobile app	12	1154	321.220	-0.359 (-0.502, -0.215)[c]	96.576[c]	281.110	-1.308 (-2.009, -0.607)[c]	96.087[c]
Interactive telephone	2	170	9.069	-0.782 (-1.172, -0.391)[c]	88.974b	2.226	-2.600 (-3.243, -1.957)[c]	55.074
Internet server/computer network	7	1288	353.994	-0.431 (-0.558, -0.304)[c]	98.305[c]	332.245	-1.751 (-2.819, -0.684)[c]	98.194[c]
Website	14	1875	843.158	-0.539 (-0.706, -0.371)[c]	98.458[c]	696.131	-1.747 (-2.587, -0.907)[c]	98.133[c]
Video conference	2	164	1.687	-0.845 (-1.144, -0.546)[c]	40.719	25.261	-1.450 (-3.323, 0.424)	96.041[c]
Device or tablet	5	1812	332.123	-0.278 (-0.747, 0.191)[c]	98.796[c]	162.677	-0.905 (-1.725, -0.085)[a]	97.541[c]
Duration of intervention, months								
≤ 6	6	1158	222.519	-0.363 (-0.567, -0.159)[c]	97.753[c]	239.478	-1.290 (-2.186, -0.394)[b]	97.912[c]
6	20	2234	1260.455	-0.626 (-0.766, -0.486)[c]	98.493[c]	740.442	-2.054 (-2.712, -1.396)[c]	97.434[c]
> 6	21	2565	1173.100	-0.380 (-0.507, -0.252)[c]	98.295[c]	674.872	-1.080 (-1.583, -0.578)[c]	97.036[c]
Focus of intervention								
Biomedical parameters	16	2633	1830.624	-0.687 (-0.821, -0.553)[c]	99.181[c]	844.645	-2.406 (-3.174, -1.639)[c]	98.224[c]
Self-management behaviors	7	334	64.189	-0.360 (-0.805, 0.086)	90.653[c]	139.861	-0.740 (-1.753, 0.274)	95.710[c]
Biomedical and self-management	24	3965	687.693	-0.348 (-0.442, -0.253)[c]	96.655[c]	645.659	-1.171 (-1.583, -0.759)[c]	96.438[c]
Telemedicine method								
Telemonitoring	19	3076	1872.902	-0.553 (-0.662, -0.445)[c]	99.039c	1107.777	-2.263 (-2.991, -1.534)[c]	98.375[c]
Tele-education	12	994	125.448	-0.495 (-0.683, -0.307)[c]	91.231c	289.370	-1.068 (-1.767, -0.368)[b]	96.199[c]
Telemonitoring and tele-education	16	2862	501.993	-0.391 (-0.542, -0.240)[c]	97.012c	287.276	-1.002 (-1.415, -0.588)[c]	94.779[c]
Model of intervention								
Behavior change	28	2773	629.401	-0.452 (-0.575, -0.329)[c]	95.710[c]	596.338	-1.041 (-1.426, -0.656)[c]	95.472[c]
Treatment	13	2248	1518.194	-0.589 (-0.725, -0.453)[c]	99.210[c]	710.693	-2.386 (-3.249, -1.522)[c]	98.312[c]
Behavior change and treatment	6	1911	448.804	-0.401 (-0.612, -0.189)[c]	98.886[c]	332.288	-1.934 (-3.070, -0.799)[c]	98.495[c]
Intervention lead								
Doctor	11	987	522.974	-0.288 (-0.512, -0.064)[a]	98.088[c]	391.153	-0.922 (-1.795, -0.048)[a]	97.443[c]
Nurse	15	2747	868.940	-0.491 (-0.655, -0.327)[c]	98.389[c]	474.130	-1.606 (-2.205, -1.006)[c]	97.047[c]
Multi-disciplinary	17	2941	1237.843	-0.534 (-0.643, -0.425)[c]	98.707[c]	852.270	-2.038 (-2.702, -1.375)[c]	98.123[c]
Allied health	4	257	8.094	-0.939 (-1.651, -0.227)[b]	62.935[a]	11.197	-0.600 (-1.137, -0.062)[a]	73.208[b]
Dropout rate								
0%-9.9%	20	2659	779.280	-0.458 (-0.584, -0.333)[c]	97.562[c]	571.285	-1.138 (-1.62, -0.657)[c]	96.674[c]
10%-19.9%	16	2795	709.022	-0.645 (-0.786, -0.504)[c]	97.884[c]	740.889	-2.329 (-3.107, -1.552)[c]	97.975[c]
20% +	10	994	365.413	-0.297 (-0.472, -0.121)[c]	97.537[c]	267.256	-0.902 (-1.632, -0.171)[a]	96.632[c]
Frequency of intervention								
Daily	19	2176	996.897	-0.439 (-0.577, -0.302)[c]	98.194[c]	593.016	-1.408 (-1.959, -0.857)[c]	96.965[c]
< daily to > weekly	10	2005	627.889	-0.307 (-0.462, -0.152)[c]	98.567[c]	602.249	-1.452 (-2.300, -0.605)[c]	98.506[c]
Weekly	7	1095	448.790	-0.791 (-1.167, -0.416)[c]	98.663[c]	353.155	-2.340 (-3.576, -1.105)[c]	98.301[c]
< weekly	5	1162	30.212	-0.835 (-1.068, -0.602)[c]	86.760[c]	131.622	-2.423 (-3.943, -0.902)[b]	96.961[c]
Not mentioned	6	494	33.795	-0.227 (-0.690, 0.237)	85.205[c]	42.744	-0.360 (-1.010, 0.290)	88.302[c]
Rate of use/engagement								

≤ 70%	5	808	406.483	-0.212 (-0.526, 0.102)	99.016[c]	254.620	-1.060 (-2.422, 0.303)	98.429[c]
> 70%	8	1287	150.709	-0.576 (-0.696, -0.455)[c]	95.355[c]	204.974	-2.492 (-3.514, -1.469)[c]	96.585[c]
Not mentioned	34	4837	1782.085	-0.496 (-0.589, -0.403)[c]	98.148[c]	1231.652	-1.361 (-1.771, -0.951)[c]	97.321[c]
Self-care: Medication adherence								
No significant differences	4	557	57.285	-0.268 (-0.459, -0.077)[b]	94.763[c]	39.413	-0.650 (-1.254, -0.047)[a]	92.388[c]
Intervention significantly better	3	541	22.004	-0.265 (-0.677, 0.147)	90.911[c]	60.687	-0.783 (-1.810, 0.245)	96.704[c]
Not mentioned	40	5834	2414.200	-0.522 (-0.605, -0.44)[c]	98.385[c]	1538.553	-1.664 (-2.09, -1.237)[c]	97.465[c]
Self -care: Disease knowledge								
No significant differences	7	685	33.269	-0.025 (-0.169, 0.118)	81.965[c]	39.012	-0.142 (-0.535, 0.252)	84.620[c]
Intervention significantly better	2	197	5.253	-0.590 (-1.401, 0.222)	80.963[a]	42.653	-1.220 (-3.543, 1.102)	97.655[c]
Not mentioned	38	6050	2399.254	-0.530 (-0.611, -0.449)[c]	98.458[c]	1584.253	-1.802 (-2.234, -1.37)[c]	97.655[c]
Self-care: Behavior change								
No significant differences	3	379	0.374	-0.100 (-0.134, -0.065)[c]	0.000	10.944	-0.318 (-0.769, 0.132)	81.726[c]
Intervention significantly better	4	328	94.795	-0.532 (-1.153, 0.090)	96.835[c]	70.276	-1.145 (-2.347, 0.057)	95.731[c]
Not mentioned	40	6225	2477.596	-0.508 (-0.59, -0.427)[c]	98.426[c]	1678.368	-1.656 (-2.079, -1.234)[c]	97.676[c]
Self-care: Glucose monitoring								
No significant differences	1	299	0.000	-0.100 (-0.136, -0.064)[c]	0.000	0.000	-0.634 (-0.866, -0.401)[c]	0.000
Intervention significantly better	3	434	103.754	-0.505 (-0.923, -0.087)[a]	98.072[c]	31.471	-1.795 (-2.897, -0.693)[c]	93.645[c]
Not mentioned	43	6199	2441.038	-0.498 (-0.580, -0.416)[c]	98.279[c]	1807.229	-1.527 (-1.942, -1.113)[c]	97.676[c]
Self-care: Hospital visits needed								
No significant differences	2	339	29.741	-0.440 (-0.744, -0.137)[b]	96.638[c]	0.510	-2.467 (-2.750, -2.184)[c]	0.000
Intervention significantly better	1	246	0.000	0.010 (-0.023, 0.043)	0.000	0.000	0.082 (-0.187, 0.351)	0.000
Not mentioned	44	6347	2341.454	-0.505 (-0.586, -0.424)[c]	98.164[c]	1692.930	-1.519 (-1.906, -1.133)[c]	97.460[c]
Self-care: self-efficacy								
No significant differences	6	1071	90.786	-0.232 (-0.360, -0.105)[c]	94.493[c]	71.592	-0.636 (-1.093, -0.178)[b]	93.016[c]
Intervention significantly better	1	47	0.000	-0.810 (-1.013, -0.607)[c]	0.000	0.000	-2.290 (-3.029, -1.552)[c]	0.000
Not mentioned	40	5814	2311.342	-0.514 (-0.597, -0.430)[c]	98.313[c]	1633.909	-1.638 (-2.077, -1.199)[c]	97.613[c]
Self-care: nutrition								
No significant differences	4	380	42.368	-0.642 (-0.845, -0.440)[c]	92.919[c]	7.474	-2.190 (-2.608, -1.772)[c]	59.861
Not mentioned	43	6552	2567.224	-0.466 (-0.546, -0.387)[c]	98.364[c]	1785.184	-1.457 (-1.853, -1.061)[c]	97.647[c]
Self-care: Exercise								
No significant differences	2	132	7.605	-0.641 (-0.943, -0.338)[c]	86.850[b]	0.209	-2.427 (-2.877, -1.976)[c]	0.000
Not mentioned	45	6800	2636.871	-0.477 (-0.554, -0.400)[c]	98.331c	1824.510	-1.485 (-1.866, -1.104)[c]	97.588[c]
Racial								
Hispanic	2	148	2.118	-0.867 (-1.052, -0.682)[c]	52.782	0.502	-2.791 (-3.245, -2.337)[c]	0.000
Not mentioned	45	6784	2560.239	-0.464 (-0.540, -0.388)[c]	98.281[c]	1804.224	-1.471 (-1.85, -1.092)[c]	97.561[c]
Comorbid disease								
Overweight/obese	4	318	50.425	-1.270 (-1.971, -0.568)[c]	94.051[c]	50.979	-2.034 (-3.280, -0.788)[c]	94.115[c]
Hypertension	1	299	0.000	-0.100 (-0.136, -0.064)[c]	0.000	0.000	-0.634 (-0.866, -0.401)[c]	0.000
Not mentioned	42	6315	2376.371	-0.439 (-0.516, -0.361)[c]	98.275[c]	1787.062	-1.499 (-1.910, -1.087)[c]	97.706[c]

Allied health, diabetes educator, dietician, councillor.

[a]$P < 0.05$.

[b]$P < 0.01$.

$^cP < 0.001$. CI: Confidence interval.

addition, the long-term telemedicine intervention (more than 6 mo) was also found significant for HbA1c improvement, which is consistent with another systematic review[84]. These findings suggested that telemedicine intervention may facilitate HbA1c control for 6 mo or longer.

The impact of telemedicine on HbA1c may be also explained by the different modes of intervention, including text message, mobile app, interactive telephone, internet server, website, video conference and mobile devices[85]. Although all modes of intervention demonstrated significant HbA1c improvement, it is an opportunity to highlight that interactive telephone (-0.782%; 95%CI -1.172 to -0.391, $P < 0.001$) and videoconference (-0.845%; 95%CI -1.144 to -0.546, $P < 0.001$) showed a greater HbA1c reduction than other modes of interventions. A study reported similar results to this, theorising that interactive treatment may facilitate remote healthcare on diabetes management[84]. Our results suggest that all modes of intervention are significant for T2DM telemedicine, but perhaps we should pay more attention to the modes of interactive telephone and videoconferencing. However, due to the number of study limitation for videoconference and interactive phone call interventions, more relevant trials are needed for further confirmation.

In the studies we reviewed, telemonitoring interventions, as well as combined telemonitoring and tele-education interventions significantly reduced HbA1c in T2DM patients. In addition, combined behaviour change and clinical treatment models, as well as either behaviour change or clinical treatment models intervention alone, had significantly improved HbA1c levels. Specifically, clinical treatment models of intervention resulted in the greatest decline in HbA1c. Several published studies evidence the positive effect of diabetes treatment by telemonitoring[83,86-88] and tele-education[83,89]. This may be due to healthy behaviour changes[89-92] in addition to medical treatment[93] resulting in disease improvement during the course of telemedicine interventions.

Similarly, telemedicine interventions that focused on biomedical parameters were most effective at reducing HbA1c, followed by biomedical parameters in addition to self-management behaviour focus. The self-management focus alone did not significantly reduce HbA1c, suggesting that the interventions aimed to achieve specific numeric targets (such as HbA1c level, blood glucose level, kilograms of weight loss) are more effective to achieve glycaemic control.

We also found that telemedicine interventions led by allied health, multi-disciplinary or nurse-led interventions showed a better HbA1c control compared to those led by doctors. Due to the characteristics of diabetes management, patients may require not only medications but also lifestyle guidance[79,90,91]. Interventions lead by nurse, allied health and multi-disciplinary teams may provide a better strategy for long-term diabetes treatment. Interestingly, interventions with drop-out rates between 10%-19.9% revealed the greatest reduction in HbA1c. This could be explained by the notion that interventions with lower drop-out rates might retain participants that can be less compliant to the intervention. This is supported by the result that telemedicine interventions with a higher engagement level (> 70%) have greater HbA1c reduction.

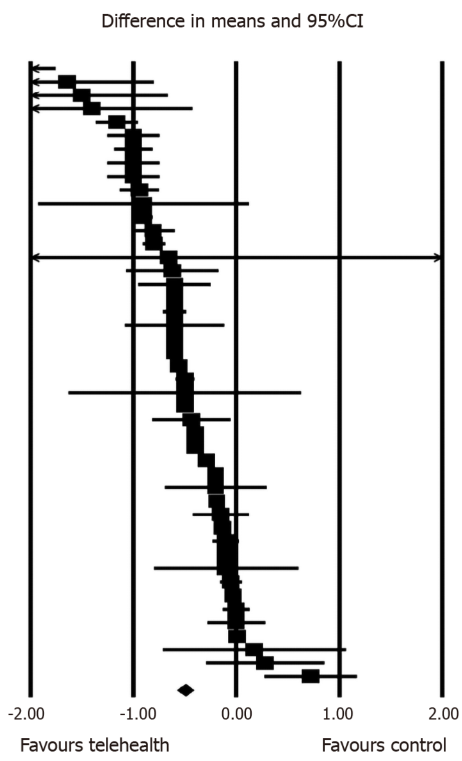
Effect of self-care components on HbA1c

Intervention participants that had significantly higher self-glucose monitoring and significantly higher self-efficacy at the end of the intervention showed significantly higher reductions in HbA1c. These results are consistent with a previous meta-analysis[94]. Furthermore, another meta-analysis highlighted that increased self-glucose monitoring results in a reduction of HbA1c and therefore long-term glycemic control[95]. Higher self-efficacy has also been shown to reduce HbA1c[96]. T2DM patients with better self-care knowledge and perform more self-care behaviors will manage their disease more frequently, improving glycemic control and reducing complications[96]. Thus, it would be beneficial to incorporate self-care education and encouragement in the provision of telemedicine interventions for T2DM.

However, most of the trials did not mention the self-care components of nutrition, behaviour change, hospital visits, disease knowledge and medication adherence. Thus, our result on self-care outcomes should be interpreted cautiously. More research of higher methodological quality and larger number of studies are needed to explore whether telemedicine intervention can facilitate self-care development[94].

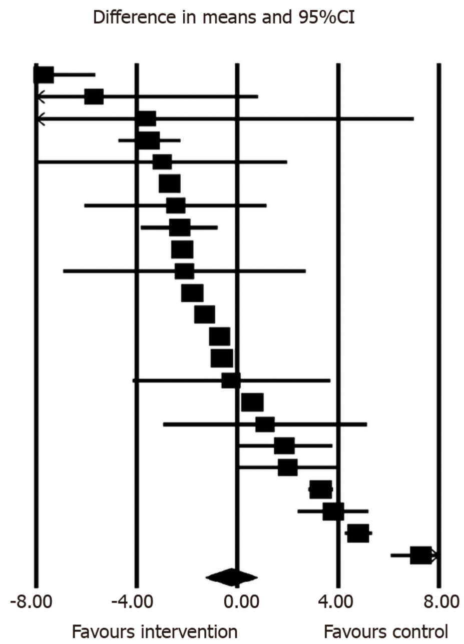
A

Study name	Statistics for each study: Difference in means	Lower limit	Upper limit	*P* value
Kim 2008	-2.020	-2.281	-1.759	0.000
Pacaud 2012 Intervention 1 Male	-1.640	-2.473	-0.807	0.000
Wang 2018	-1.500	-2.329	-0.671	0.000
Quinn 2016 Age >55 years	-1.400	-2.365	-0.435	0.004
Kim 2007	-1.160	-1.362	-0.958	0.000
Crowley 2016	-1.000	-1.249	-0.751	0.000
Fountoulakis 2015	-1.000	-1.179	-0.821	0.000
Luley 2011	-1.000	-1.251	-0.749	0.000
Welch 2011	-1.000	-1.248	-0.752	0.000
Yip 2002	-0.940	-1.123	-0.757	0.000
Quinn 2016 Age <55 years	-0.900	-1.922	0.122	0.084
Stone 2009	-0.900	-0.979	-0.821	0.000
Whittemore 2020	-0.810	-1.013	-0.607	0.000
Fortmann 2017	-0.800	-0.904	-0.696	0.000
Xu 2019	-0.660	-5.987	4.667	0.808
Alanzi 2018	-0.620	-1.067	-0.173	0.007
Kempf 2017	-0.600	-0.948	-0.252	0.001
Kim 2016	-0.600	-0.639	-0.561	0.000
Kleinman 2017	-0.600	-0.708	-0.492	0.000
Liou 2014	-0.600	-1.079	-0.121	0.014
Wild 2016	-0.600	-0.635	-0.565	0.000
Williams 2012	-0.600	-0.674	-0.526	0.000
Dafoulas 2014	-0.560	-0.620	-0.500	0.000
Lim 2016	-0.500	-0.585	-0.415	0.000
Pacaud 2012 Intervention 2 Male	-0.500	-1.621	0.621	0.382
Wang 2017	-0.500	-0.539	-0.461	0.000
Orsama 2013	-0.436	-0.811	-0.061	0.023
Kim 2019	-0.400	-0.428	-0.372	0.000
Vinitha 2019	-0.400	-0.456	-0.344	0.000
Nicolucci 2015	-0.290	-0.319	-0.261	0.000
Cho 2017	-0.200	-0.212	-0.188	0.000
Pressman 2014	-0.200	-0.691	0.291	0.425
Tang 2013	-0.190	-0.225	-0.155	0.000
Jeong 2018 Intervention 2	-0.150	-0.422	0.122	0.279
Rodriguez-Idigoras 2009	-0.130	-0.163	-0.097	0.000
Holmen 2014 Intervention 1	-0.100	-0.223	0.023	0.111
Or 2020	-0.100	-0.136	-0.064	0.000
Ramadas 2018	-0.100	-0.795	0.595	0.778
Wayne 2015	-0.050	-0.152	0.052	0.334
Lee 2019	-0.030	-0.080	0.020	0.240
Holmen 2014 Intervention 2	0.000	-0.126	0.126	1.000
Jeong 2018 Intervention 1	0.000	-0.277	0.277	1.000
Dario 2016	0.010	-0.023	0.043	0.550
Arora 2014	0.175	-0.706	1.056	0.697
Pacaud 2012 Intervention 1 Female	0.280	-0.292	0.852	0.338
Pacaud 2012 Intervention 2 Female	0.720	0.277	1.163	0.001
	-0.497	-0.573	-0.421	0.000



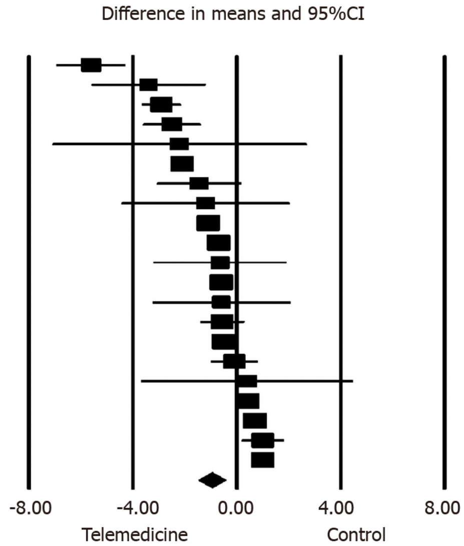
B

Study name	Statistics for each study: Difference in means	Lower limit	Upper limit	*P* value
Crowley 2016	-7.700	-9.733	-5.667	0.000
Liou 2014	-5.700	-12.186	0.786	0.085
Orsama 2013	-3.600	-14.178	6.978	0.505
Stone 2009	-3.500	-4.710	-2.290	0.000
Kempf 2017	-3.000	-7.935	1.935	0.233
Wild 2016	-2.700	-3.085	-2.315	0.000
Jeong 2018 Intervention 1	-2.460	-6.047	1.127	0.179
Lim 2016	-2.300	-3.805	-0.795	0.003
Cho 2017	-2.200	-2.420	-1.980	0.000
Pressman 2014	-2.100	-6.892	2.692	0.390
Tang 2013	-1.800	-2.051	-1.549	0.000
Vinitha 2019	-1.300	-1.690	-0.910	0.000
Lee 2019	-0.710	-1.088	-0.332	0.000
Kim 2019	-0.600	-0.974	-0.226	0.002
Jeong 2018 Intervention 2	-0.240	-4.145	3.665	0.904
Nicolucci 2015	0.600	0.296	0.904	0.000
Welch 2011	1.100	-2.938	5.138	0.593
Whittemore 2020	1.860	-0.008	3.728	0.051
Bujnowska-Fedak 2011	2.000	-0.001	4.001	0.050
Or 2020	3.300	2.842	3.758	0.000
Fortmann 2017	3.800	2.406	5.194	0.000
Kim 2016	4.800	4.266	5.334	0.000
Sun 2019	7.280	6.119	8.441	0.000
	-0.243	-1.268	0.782	0.642



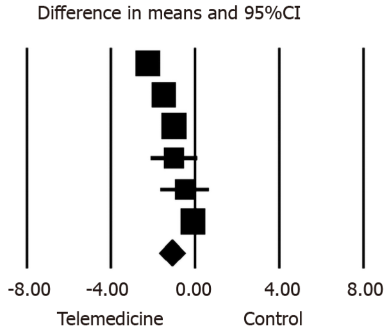
C

Study name	Difference in means	Lower limit	Upper limit	*P* value
Crowley 2016	-5.600	-6.920	-4.280	0.000
Welch 2011	-3.400	-5.590	-1.210	0.002
Stone 2009	-2.900	-3.641	-2.159	0.000
Bujnowska-Fedak 2011	-2.500	-3.595	-1.405	0.000
Orsama 2013	-2.200	-7.081	2.681	0.377
Wild 2016	-2.100	-2.394	-1.806	0.000
Whittemore 2020	-1.450	-3.066	0.166	0.079
Kempf 2017	-1.200	-4.431	2.031	0.467
Cho 2017	-1.100	-1.256	-0.944	0.000
Tang 2013	-0.700	-0.882	-0.518	0.000
Jeong 2018 Intervention 1	-0.640	-3.190	1.910	0.623
Kim 2019	-0.600	-0.884	-0.316	0.000
Jeong 2018 Intervention 2	-0.590	-3.247	2.067	0.663
Lee 2019	-0.560	-1.401	0.281	0.192
Kim 2016	-0.500	-0.850	-0.150	0.005
Lim 2016	-0.100	-0.993	0.793	0.826
Liou 2014	0.400	-3.674	4.474	0.847
Or 2020	0.400	0.144	0.656	0.002
Vinitha 2019	0.700	0.449	0.951	0.000
Fortmann 2017	1.000	0.197	1.803	0.015
Nicolucci 2015	1.000	0.819	1.181	0.000
	-0.960	-1.502	-0.417	0.001



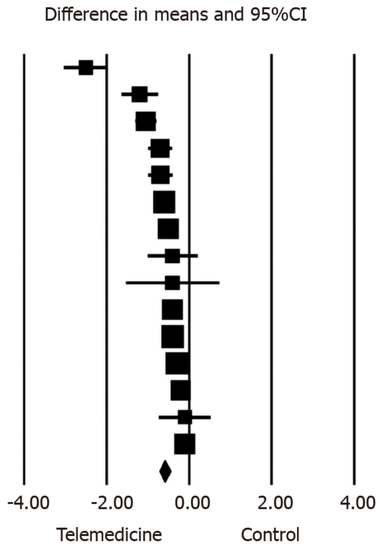
D

Study name	Difference in means	Lower limit	Upper limit	*P* value
Sun 2019	-2.230	-2.501	-1.959	0.000
Lim 2016	-1.500	-1.879	-1.121	0.000
Cho 2017	-1.000	-1.055	-0.945	0.000
Jeong 2018 Intervention 2	-1.000	-2.098	0.098	0.074
Jeong 2018 Intervention 1	-0.500	-1.634	0.634	0.388
Vinitha 2019	-0.100	-0.231	0.031	0.136
	-1.091	-1.695	-0.486	0.000



E

Study name	Difference in means	Lower limit	Upper limit	*P* value
Kim 2008	-2.500	-3.026	-1.974	0.000
Luley 2011	-1.200	-1.642	-0.758	0.000
Fortmann 2017	-1.049	-1.290	-0.808	0.000
Kim 2007	-0.700	-0.981	-0.419	0.000
Kleinman 2017	-0.700	-0.990	-0.410	0.000
Kim 2019	-0.600	-0.660	-0.540	0.000
Lim 2016	-0.500	-0.704	-0.296	0.000
Jeong 2018 Intervention 2	-0.400	-1.001	0.201	0.192
Kempf 2017	-0.400	-1.516	0.716	0.482
Ramadas 2018	-0.400	-0.585	-0.215	0.000
Cho 2017	-0.400	-0.431	-0.368	0.000
Vinitha 2019	-0.300	-0.402	-0.198	0.000
Sun 2019	-0.200	-0.395	-0.005	0.045
Jeong 2018 Intervention 1	-0.100	-0.713	0.513	0.749
Lee 2019	-0.100	-0.277	0.077	0.269
	-0.577	-0.710	-0.443	0.000



F

Study name	Difference in means	Lower limit	Upper limit	*P* value
Luley 2011	-11.500	-13.954	-9.046	0.000
Kempf 2017	-5.100	-6.953	-3.247	0.000
Orsama 2013	-2.500	-4.621	-0.379	0.021
Wayne 2015	-1.670	-3.868	0.528	0.137
Vinitha 2019	-0.700	-1.129	-0.271	0.001
Wild 2016	-0.700	-1.301	-0.099	0.022
Jeong 2018 Intervention 2	-0.430	-1.008	0.148	0.144
Jeong 2018 Intervention 1	-0.410	-0.994	0.174	0.169
Cho 2017	-0.200	-0.400	-0.000	0.050
Kim 2019	-0.200	-0.290	-0.110	0.000
Holmen 2014 Intervention 1	0.000	-2.869	2.869	1.000
Tang 2013	0.010	-0.460	0.480	0.967
Holmen 2014 Intervention 2	0.500	-2.176	3.176	0.714
Nicolucci 2015	0.600	0.141	1.059	0.010
Pressman 2014	0.900	-1.348	3.148	0.433
Fortmann 2017	0.998	-0.174	2.169	0.095
Stone 2009	1.140	-0.092	2.372	0.070
	-0.549	-0.950	-0.149	0.007

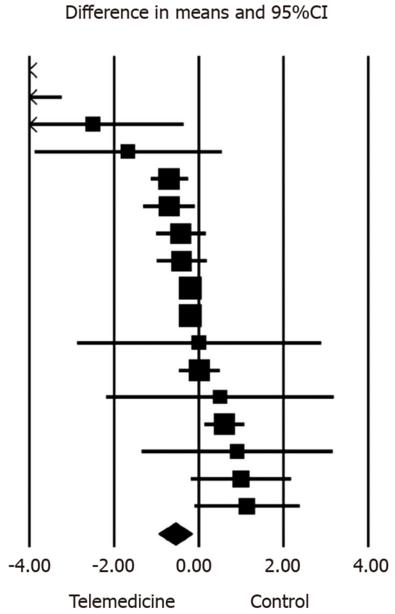


Figure 2 Effects of telehealth intervention on hemoglobin A1c, systolic blood pressure, diastolic blood pressure, post-prandial glucose, fasting plasma glucose, and weight effect size plot. A: Hemoglobin A1c; B: Systolic blood pressure; C: Diastolic blood pressure; D: Post-prandial glucose; E: Fasting plasma glucose; F: Weight. CI: Confidence interval.

Effect of patient characteristics on HbA1c

It is well known that both obesity and T2DM are metabolic diseases that are contributed by an unhealthy lifestyle[97]. In the studies we reviewed, 318 participants were diagnosed with both T2DM and a BMI considered overweight/obese (BMI > 25), which reported a significant HbA1c reduction after telemedicine intervention. There was a similar result for the hypertensive T2DM patients, however there was only 1 study with 299 participants reporting this. There are difficulties determining the number of participants with a BMI > 25 or hypertension in the studies that did not explicitly calculate this. Furthermore, due to the sample size limitation and high heterogeneity, the effectiveness of telemedicine interventions for T2DM and comorbid diseases should be interpreted with caution. Two studies had Hispanic only patients, reporting a total of 318 participants whom had a greater reduction in HbA1c after telemedicine intervention, in comparison to the remainder of studies. Although, the same issue of high heterogeneity and small sample size persists.

Limitations

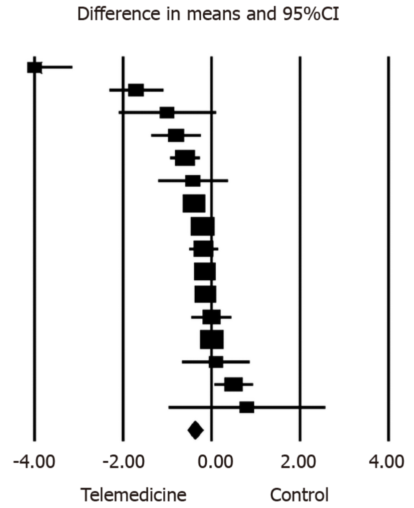
This meta-analysis covered various telemedicine interventions for patients with T2DM. We aimed to perform a comprehensive meta-analysis on the effect of telemedicine intervention in the treatment of T2DM. However, our research has some limitations that must be acknowledged. First, we found high heterogeneity for all outcomes and most of the subgroups. The heterogeneity may be caused by the complexity of telemedicine interventions such as duration, strategies, combinations and telemedicine quality. Second, we found that the effectiveness of self-care outcomes is uncertain due to the study number limitations. More trials with large sample sizes and details on self-care outcomes are needed for further investigation. Lastly, although telemedicine interventions showed a significant improvement in mental and physical QoL, the sample size limitation may cause uncertainty and high heterogeneity. Thus, more trials with large sample sizes are needed for further telemedicine evaluation on mental and physical QoL. Considering these limitations, the results of this meta-analysis should be interpreted with caution.

CONCLUSION

Our findings demonstrated that telemedicine interventions are more effective than the

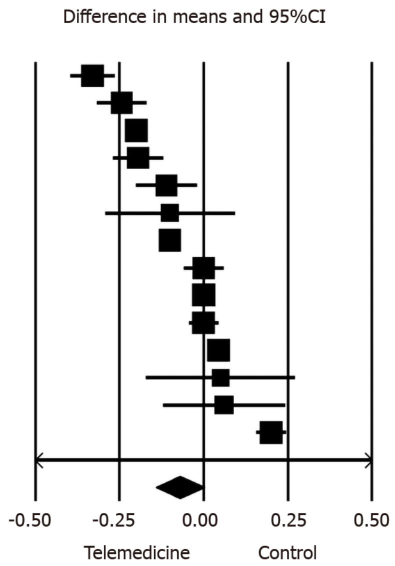
A

Study name	Difference in means	Lower limit	Upper limit	*P* value
Luley 2011	-4.000	-4.840	-3.160	0.000
Kempf 2017	-1.700	-2.298	-1.102	0.000
Liou 2014	-1.000	-2.093	0.093	0.073
Bujnowska-Fedak 2011	-0.800	-1.354	-0.246	0.005
Lim 2016	-0.600	-0.928	-0.272	0.000
Wayne 2015	-0.420	-1.198	0.358	0.290
Vinitha 2019	-0.400	-0.544	-0.256	0.000
Cho 2017	-0.200	-0.255	-0.145	0.000
Pressman 2014	-0.180	-0.501	0.141	0.271
Jeong 2018 Intervention 2	-0.150	-0.363	0.063	0.168
Jeong 2018 Intervention 1	-0.140	-0.361	0.081	0.214
Kleinman 2017	0.000	-0.443	0.443	1.000
Whittemore 2020	0.009	0.004	0.014	0.001
Fountoulakis 2015	0.100	-0.655	0.855	0.795
Fortmann 2017	0.500	0.068	0.932	0.023
Welch 2011	0.800	-0.963	2.563	0.374
	-0.370	-0.535	-0.205	0.000



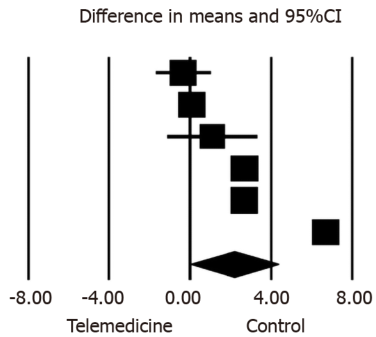
B

Study name	Difference in means	Lower limit	Upper limit	*P* value
Stone 2009	-0.330	-0.395	-0.265	0.000
Lim 2016	-0.243	-0.316	-0.170	0.000
Kim 2019	-0.200	-0.230	-0.170	0.000
Fortmann 2017	-0.194	-0.267	-0.121	0.000
Sun 2019	-0.110	-0.200	-0.020	0.017
Jeong 2018 Intervention 2	-0.100	-0.292	0.092	0.308
Vinitha 2019	-0.100	-0.133	-0.067	0.000
Lee 2019	0.000	-0.057	0.057	1.000
Nicolucci 2015	0.000	-0.030	0.030	1.000
Wang 2017	0.000	-0.043	0.043	1.000
Cho 2017	0.044	0.030	0.058	0.000
Kempf 2017	0.050	-0.170	0.270	0.657
Jeong 2018 Intervention 1	0.060	-0.120	0.240	0.514
Kim 2016	0.200	0.157	0.243	0.000
Liou 2014	11.000	-6.939	28.939	0.229
	-0.070	-0.141	0.002	0.057



C

Study name	Difference in means	Lower limit	Upper limit	*P* value
Wayne 2015	-0.340	-1.696	1.016	0.623
Cho 2017	0.100	-0.060	0.260	0.219
Kempf 2017	1.100	-1.115	3.315	0.330
Nicolucci 2015	2.700	2.389	3.011	0.000
Williams 2012	2.700	2.242	3.158	0.000
Dafoulas 2014	6.704	6.233	7.175	0.000
	2.210	0.053	4.367	0.045



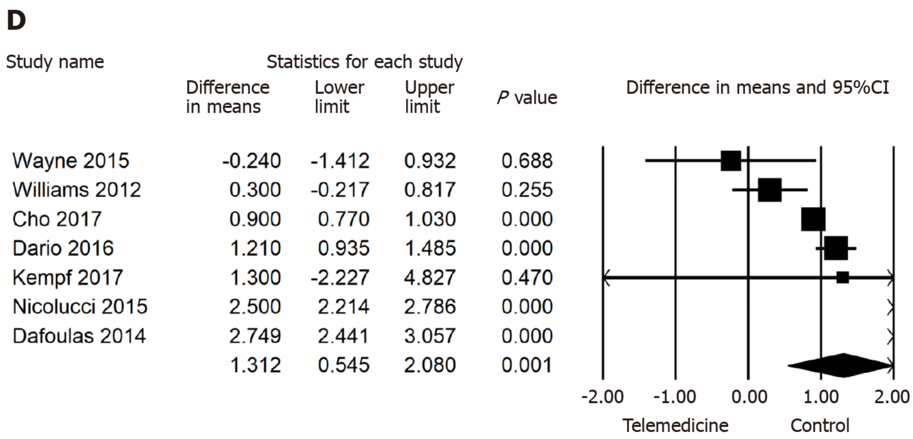


Figure 3 Effects of telehealth intervention on body mass index, cholesterol, mental health and physical health effect size plot. A: Body mass index; B: Cholesterol; C: Mental health; D: Physical health. CI: Confidence interval.

controls for reducing HbA1c in T2DM patients. In addition, the outcomes of DBP, PPG, FPG, weight, BMI, mental QoL and physical QoL improved significantly more in telemedicine interventions when comparing to control. SBP and cholesterol were not significantly different when compared to control. In addition, several components of telehealth characteristics were found to have an effect on glycaemic control through subgroup analysis. The studies that emphasized both behaviour change and treatment models of intervention, as well as interventions delivered *via* modes such as videoconference and interactive telephone had a larger effect on HbA1c reduction. In addition, less than weekly intervention frequency and intervention durations of 6 mo or longer may obtain a better outcome for glucose control. Interventions focused on biomedical parameters, as well as the method of telemonitoring, and those lead by allied health had a better effect on glucose control. Furthermore, interventions with a drop-out rate between 10%-19.9% and engagement levels of > 70% had the greatest HbA1c reduction.

The patient characteristic investigation reported patients with T2DM that were overweight, as well as Hispanic participants showed a greater HbA1c reduction. The current results also suggest that telehealth interventions that improve glucose monitoring and self-efficacy by the end of the study may be important for self-care development and can result in significant HbA1c reduction. Due to the trial limitation, components including nutrition, exercise, behaviour change, medication adherence, and disease knowledge in telehealth interventions have an uncertain effect on HbA1c. Ultimately, due to the characteristics of telehealth interventions and their positive effect of on diabetes management, we recommend the provision of telehealth interventions with emphasis on patient self-care for better management of T2DM, which may enhance long-term glucose control for patients. In addition, future studies should record more details about telehealth methodology and outcomes, especially self-care, for further evaluation.

ARTICLE HIGHLIGHTS

Research background

Telemedicine is defined as the delivery of health services *via* remote communication and technology. It is a convenient and cost-effective method of intervention, which has shown to be successful in improving glyceamic control for type 2 diabetes patients. The utility of a successful diabetes intervention is vital to reduce disease complications, hospital admissions and associated economic costs.

Research motivation

There are numerous randomised control trials that evaluate the effectiveness of telemedicine in patients with diabetes. However, no studies have provided an in-depth analysis of the effectiveness of telemedicine for glycaemic control and other health outcomes for type 2 diabetes patients.

Research objectives

This study aimed to utilise a meta-analysis approach to synthesise results from high quality randomised controlled trials, and to comprehensively review literature on the effects of telemedicine interventions on health outcomes for patients with type 2 diabetes. The secondary aim was to analyse the effect of telemedicine characteristics, patient characteristics, and self-care outcomes on glycaemic control.

Research methods

Fourty-three relevant studies were yielded from PubMed Central, Cochrane Library, Embase and Scopus databases which satisfied quality assessment *via* the PEDro scale. Mean difference and standard deviation was extracted from pre- and post-intervention data regarding all outcomes of interest, and information for subgroup categories was collected. The random effects model was used to estimate outcomes and I^2 was used for heterogeneity testing.

Research results

Telemedicine improves hemoglobin A1c (HbA1c), diastolic blood pressure, post-prandial glucose, fasting plasma glucose, weight, body mass index, mental quality of life and physical quality of life score significantly more than control/non-telemedicine interventions.

Subgroup analysis revealed that telemedicine interventions that involved primarily telemonitoring, used a clinical treatment model, delivered *via* modes such as videoconferencing and interactive telephone, at a rate less frequent than weekly, provided for a duration of 6 mo, led by allied health workers, focussed on biomedical outcomes, had high engagement level and moderate drop out rate were the most effective at reducing HbA1c.

Subgroup analysis about patient characteristics showed that Hispanic patents may benefit more than others in HbA1c reduction. Self-care subgroup analysis demonstrated that telemedicine interventions that significantly improved self-glucose monitoring and self-efficacy more than the control were found to have a higher reduction in HbA1c.

Research conclusions

Telemedicine is a useful and effective intervention for type 2 diabetes patients, which improves glycemic control and numerous other health outcomes significantly better than non-telemedicine interventions/controls. Subgroup analysis demonstrated that optimising the characteristics of telemedicine interventions may have a greater effect at improving health outcomes.

Research perspectives

In a world where telemedicine is more widely used than ever, it is important to ensure that these services are delivered at a high standard and benefit the participating patients. This study emphasises that telemedicine should be utilised as an effective approach to type 2 diabetes intervention.

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