



## Effectiveness of Remotely Delivered Interventions to Simultaneously Optimize Management of Hypertension, Hyperglycemia and Dyslipidemia in People With Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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**Background:** Remotely delivered interventions may be more efficient in controlling multiple risk factors in people with diabetes.

**Purpose:** To pool evidence from randomized controlled trials testing remote management interventions to simultaneously control blood pressure, blood glucose and lipids.

**Data Sources:** PubMed/Medline, EMBASE, CINAHL and the Cochrane library were systematically searched for randomized controlled trials (RCTs) until 20<sup>th</sup> June 2021.

**Study Selection:** Included RCTs were those that reported participant data on blood pressure, blood glucose, and lipid outcomes in response to a remotely delivered intervention.

**Data Extraction:** Three authors extracted data using a predefined template. Primary outcomes were glycated hemoglobin (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), systolic and diastolic blood pressure (SBP & DBP). Risk of bias was assessed using the Cochrane collaboration RoB-2 tool. Meta-analyses are reported as standardized mean difference (SMD) with 95% confidence intervals (95%Cl).

**Data Synthesis:** Twenty-seven RCTs reporting on 9100 participants (4581 intervention and 4519 usual care) were included. Components of the remote management interventions tested were identified as patient education, risk factor monitoring,

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coaching on monitoring, consultations, and pharmacological management. Comparator groups were typically face-to-face usual patient care. Remote management significantly reduced HbA1c (SMD -0.25, 95%CI -0.33 to -0.17, p<0.001), TC (SMD -0.17, 95%CI -0.29 to -0.04, p<0.0001), LDL-c (SMD -0.11, 95%CI -0.19 to -0.03, p=0.006), SBP (SMD -0.11, 95%CI -0.18 to -0.04, p=0.001) and DBP (SMD -0.09, 95%CI -0.16 to -0.02, p=0.02), with low to moderate heterogeneity (I<sup>2</sup>= 0 to 75). Twelve trials had high risk of bias, 12 had some risk and three were at low risk of bias.

Limitations: Heterogeneity and potential publication bias may limit applicability of findings.

**Conclusions:** Remote management significantly improves control of modifiable risk factors.

**Systematic Review Registration:** [https://www.crd.york.ac.uk/prospero/display\_record.php?RecordID=258433], identifier PROSPERO (CRD42021258433).

Keywords: blood pressure, cholesterol, lipids, systematic review, telehealth

#### INTRODUCTION

Adults diagnosed with diabetes are at high risk of major adverse events such as myocardial infarction, stroke, end stage renal failure, foot ulceration, amputation and death (1, 2). The risk of these complications can be reduced by control of blood glucose, blood pressure and lipids (3–7). Optimal control of these risk factors is infrequently achieved in routine practice, representing a missed opportunity to prevent major adverse events (6, 8). This may be due to limited access to specialists, lack of cohesive healthcare delivery and ineffective patient education (9, 10).

The medical management of people with diabetes usually involves frequent face-to-face appointments with multiple specialists (11). This can contribute to confusion about how intensively risk factors should be controlled and who is responsible for managing these risk factors (12). It also disadvantages patients in rural and remote settings who may not be able to access specialist medical services easily (13).

Remotely delivered risk factor management programs have been proposed as a more efficient way to control multiple risk factors (14–18). Risk factor monitoring, healthcare consultations, medication prescription and behavioral support can occur remotely to facilitate optimizing blood glucose, blood pressure and lipids (17–19). No previous meta-analysis or overviews have evaluated the benefit of simultaneous remote management of all these risk factors (17, 18, 20). Evidence on the effectiveness of interventions that simultaneously control multiple modifiable risk factors is needed to inform how most efficiently to deliver preventive management. This systematic review and meta-analysis aimed to pool evidence from randomized controlled trials (RCTs) testing the effectiveness of remote risk factor management programs for people with diabetes in simultaneously controlling blood glucose, blood pressure, and lipids.

#### METHODS

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-

Analyses (PRISMA) guidelines (21), and is registered with PROSPERO (CRD42021258433).

#### **Data Sources and Searches**

The PubMed/Medline, EMBASE, CINAHL and Cochrane library databases were searched independently by three authors (MF, LS AD) for English language articles of RCTs published from 1<sup>st</sup> January 2000 to 20<sup>th</sup> June 2021. This date restriction was applied due to the relative recent introduction of remotely-delivered healthcare and in order to provide a contemporary assessment of intervention strategies. The search combined three term groups; 1) 'controlled trial' (e.g. randomized, clinical trial), 2) 'remote' (e.g. telehealth), and 3) 'disease and treatment' (e.g. diabetes, dyslipidemia). The full search string is shown in **Supplementary Text 1**. Reference and citation lists of eligible articles were also manually searched.

#### **Study Selection**

Eligible articles were published RCTs that evaluated the effect of remote medical management interventions in comparison to usual care. The population of interest were adults  $\geq$ 18 years old with either type 1 or type 2 diabetes mellitus irrespective of disease duration or history of cardiovascular disease. The interventions were remotely delivered healthcare (e.g. internet or phone-based monitoring or telehealth consultations) aimed at optimizing glycemic control, systolic blood pressure (SBP) and/ or diastolic blood pressure (DBP) and total cholesterol (TC) and/ or low-density lipoprotein cholesterol (LDL-c). The control group received usual medical management without remotely delivered healthcare. Each RCT identified was screened by at least two authors (MF, LS, AD, BC). Trials that did not aim to control all three risk factors or failed to report them were excluded.

#### **Data Extraction and Quality Assessment**

The primary outcome was the impact of the remotely delivered interventions on: 1) hemoglobin A1c (HbA1c %), 2) TC and LDL-c (mmol/L), and 3) SBP and DBP (mmHg) compared to the control groups. Secondary outcomes included incidence of adverse events including hypoglycemia, postural hypotension,

hospital admission, death, limb-related events including leg revascularization or lower limb amputation, other medication related side-effects, major adverse cardiovascular events (MACE), development of micro-vascular complications including progression of retinopathy, neuropathy (including incident foot ulceration), or nephropathy, and all-cause mortality. Other secondary outcomes were health-related quality of life and cost-benefit analyses.

A standardized data extraction form was developed to extract the following data from each study: title, authors, year published, country of publication, number of participants, participant characteristics, intervention setting, type, frequency and duration of remote and usual care intervention(s), primary and secondary outcomes, study limitations and whether intention-totreat or per-protocol analyses. Two authors independently extracted data, which were checked by a third author (MF, LS, AD, BC). Where studies reported multiple follow-up data, the longest follow-up duration was used. Where there were more than one intervention arm, all intervention groups were included. Meta-analyses included the number of participants completing the trial rather than numbers initially randomized as outcome data were only available for this group. Study authors were contacted for all potentially eligible studies to obtain additional and missing data.

Methodological quality was assessed independently by three authors (AD, LS and BC) using the Cochrane collaborations revised risk-of-bias tool for randomized trials (RoB 2) (22). Following independent evaluation, discussions were held between assessors to arrive at a consensus score. Where this was not possible, a final consensus on the overall risk of bias was made by an independent fourth assessor (MF). In relation to the tool, five outcomes were possible for each criterion which were 'yes', 'probably yes', 'no information', 'probably no', or 'no' (22). Studies were rated as low risk of bias if all domains were judged to be at low risk of bias, high risk of bias if any domain was judged to be at high risk of bias, or 'some concerns' of bias if any domain was judged to have some concerns but no domain had a high risk of bias (22).

## **Data Synthesis and Analysis**

Numerical data were reported as mean and standard deviation (SD) and categorical data as number and percentage (%). Metaanalysis were performed for any primary or secondary outcome with data extractable from a minimum of three studies. The meta-analyses were conducted using the inverse-variance method for continuous outcomes and the Mantel-Haenszel statistical method for dichotomous outcomes with random effect models anticipating substantial heterogeneity (23). The results were reported as standardized mean difference (SMD) (24) or risk ratio (RR) and 95% CI for dichotomous outcomes (23). All statistical tests were two-sided and a p value <0.05 was considered significant. Heterogeneity was assessed using I<sup>2</sup> statistic values (interpreted as 0 to 49%: low, 50 to 74%: moderate and 75 to 100%: high) (25). Several sensitivity and subgroup analyses were carried out including leave-one-out (LOO) sensitivity analyses and analysis excluding studies with high risk of bias. Several sub-group analyses were also carried out (see Supplementary Text 2). Five distinct aspects of the remote management programs tested were defined to clarify which aspects of the interventions were most important in improving outcome in subgroup meta-analysis. Subgroup meta-analysis was also planned to evaluate whether remote management was more effective in studies that only included a higher risk population at entry who were at greater risk of MACE. Higher-risk was defined as: a documented history of cardiovascular disease, a diabetes duration of greater than 10 years, HbA1c of >10.0% and/or LDL of >2.0 mmol/L and/or SBP of >130 mmHg and/or a DBP of >80 mmHg or a previous history of diabetes related complications at entry. Publication bias was assessed by funnel plots comparing the summary estimate of each study and its precision (1/standard error) (26). All analyses were conducted with Review Manager (RevMan) version 5.4. (The Cochrane Collaboration, 2020).

## RESULTS

Of 2458 unique articles identified, 46 were assessed for full-text eligibility and 27 RCTs were included (**Figure 1**) (27–53). Most full-text screened studies that were excluded did not target or report on the impact of the remotely-delivered intervention on all key risk factors of interest (**Supplementary Table 1**). Of 33 contacted authors from potentially eligible studies, four replied with the request for additional data (32, 37, 39, 44).

## **Study and Participant Characteristics**

The included studies had a total of 9153 participants randomized and reported outcomes on 4581 participants randomized to an intervention group and 4519 to usual care. Sample sizes of individual trials ranged from 36 to 1665 (Table 1) and follow-up durations ranged from 3 to 60 months. Supplementary Table 2 reports the inclusion and exclusion criteria of each trial and the total number of participants screened and excluded. Six RCTs included people with type 1 diabetes (27, 29, 31, 33, 38, 46) and all others exclusively included participants with type 2 diabetes. Several studies excluded participants with severe complications such as foot ulcers, progressive nephropathy or retinopathy. Three studies recruited participants deemed to be at high risk of diabetes complications based on entry criteria (35, 41, 51). Participant medications at baseline and follow-up are shown in Supplementary Table 3, and baseline risk factors are shown in Supplementary Table 4, and study outcome measures, additional supports and methods of risk factor monitoring are shown in Supplementary Table 5.

# Description of the Types of Interventions Tested

A detailed description of the types of interventions is given in **Supplementary Table 5**, with **Supplementary Table 6** providing a summary overview of the key elements of the intervention provided in each trial used in the meta-analyses. Twenty out of



the twenty-seven RCTs provided remote patient education without any in-person education (28-31, 35-37, 39-43, 45-50, 52, 53), nineteen RCTs provided remote risk factor monitoring (29, 31-34, 36-39, 41-47, 51-53), twenty-two RCTs provided remote coaching regarding risk factors without the use of inperson coaching (27-37, 39, 41, 43-44, 46-49, 51-53), twelve provided remote consultation without any in-person consultation (31, 35, 36, 40-47, 49) and fourteen provided remote pharmacological advice or reminders to the patient or treating team (28, 30, 34, 37-38, 41-44, 46-48, 50, 51) (see **Supplementary Text 3** for further info).

## **Description of Control Groups**

In most studies, the control group received usual care (**Supplementary Table 5**). This typically consisted of regular primary care physician management of participant risk factors based on guideline recommendations. Ten RCTs failed to provide a definition of usual care (27, 30, 35, 37, 39, 44, 47, 50, 52, 53). One RCT delivered non-health related text-messages to the control group (35). One RCT provided the control arm with the same blood glucose monitoring system as their intervention group, but the data was not transmitted to an online portal for further intervention (38).

TABLE 1   Characteristics	of study participants in included	randomized controlled trials (n=27).
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TOTAL COH	ORT							INTI	ERVE	NTION	GROUP			CON	TROL	GROUP	
Study	Country	Study setting	Design	Number randomized	Attrition	Follow- up duration	Population description	Type of remote intervention tested	Ν	Age	Females	Diabetes duration	Control group description	N	Age	Females	Diabetes duration
Aytekin Kanadli (27)	Turkey	Hospital	Two-arm RCT	91	3/91	3- months	People with diabetes attending an endocrinology unit	Telephone-based education and monitoring	44	NR	27 (61.4%)	NR	Routine treatment and care	44	NR	29 (65.9%)	NR
Blackberry (28)	Australia	Primary care/ community	Stratified cluster RCT	473	22/473	18- months	Patients with poorly controlled type 2 diabetes	Practice nurse led telephone coaching	236	63.6 (10.4)	109 (46.0%)	10 [5-15]	Usual general practice care	237	61.9 (10.5)	95 (40.0%)	9 [5-13]
Bond (29)	USA	Hospital	Two-arm RCT	62	NR	6- months	People ≥60 years with diabetes	Web-based education and monitoring program	31	66.2 (5.7)	13 (41.9%)	16.1 (10.5)	Standard diabetes care	31	68.2 (6.2)	15 (48.4%)	17.8 (11.7)
Crowley (30)	USA	Primary care/ community	Two-arm parallel group RCT	359	29/359	12- months	African American patients with type 2 diabetes	Nurse- administered telephone intervention	182	56.0 (12.0)	126 (69.0%)	NR	Usual care	177	57.0 (12.0)	133 (75.0%)	NR
Davis (31)	USA	Primary care/ community	Non- blinded, two-arm, parallel- group single-site BCT	165	NR	12- months	People ≥35 years with uncontrolled diabetes	Education through videoconferencing	85	59.9 (9.4)	62 (72.9%)	8.5 (6.6)	Usual care	80	59.2 (9.3)	61 (76.3%)	10.3 (8.1)
de Vasconcelos (40)	Brazil	Primary care/ community	Parallel group RCT	36	5/36	6- months	Patients with type 2 diabetes	Health tele- coaching programme <i>via</i> telephone	18	60.9 (NR)	14 (58.3%)	10 (8.5)	Usual care	18	59.6 (NR)	10 (41.7%)	8.67 (6.4)
Eakin (32)	Australia	Primary care/ community	Non- blinded, two-arm, parallel- group, pragmatic RCT	302	53/302	24- months	People with type 2 diabetes and physically inactive or overweight	Telephone-based weight and activity intervention	151	57.7 (8.1)	67 (44.4%)	4.0 [2.0-7.0]	Usual care & mailed results	151	58.3 (9.0)	65 (43.0%)	5.0 [2.0-10.0]
Harno (33)	Finland	Mixed primary care & hospital	Two-arm, parallel- group, multi-center RCT	175	NR	12- months	People with diabetes	E-health app and diabetes management system and text messaging	101	NR	NR	NR	Usual care	74	NR	NR	NR

(Continued)

Remote Risk Factor Management in Diabetes

TOTAL COH	IORT							INT	ERVE	NTION	GROUP			CON		GROUP	
Study	Country	Study setting	Design	Number randomized	Attrition	Follow- up duration	Population description	Type of remote intervention tested	Ν	Age	Females	Diabetes duration	Control group description	N	Age	Females	Diabetes duration
Holbrook (34)	Canada	Primary care/ community	Two-arm, pragmatic RCT	511	66/511	6- months	People with type 2 diabetes	Web-based diabetes risk factor tracker & education	253	61.0 (13.1)	130 (51.4%)	8.7 (9.0)	Usual care	258	60.5 (11.9)	122 (47.3%)	10.0 (10.7)
Huo (35)	China	Hospital	Single- blinded, parallel- group multi- center, RCT	502	34/502	6- months	People diagnosed with type 2 diabetes and CHD within the prior 3 years	Text-messaging behavior support	251	59.5 (9.4)	43 (17.1%)	NR	Standard care only	251	59.5 (9.1)	45 (17.9%)	NR
Kempf (36)	Germany	Mixed primary care & hospital	Single- blinded, two-arm, parallel- group, single- center RCT	202	69/202	12- months	Type 2 diabetes with poor control (HbA1c >7.5%), BMI >27 kg/m <sup>2</sup> , and two oral medications	Web-portal and remote monitoring and telephone calls	102	NR	48 (47.0%)	NR	Standard care and limited home-based monitoring	100	NR	41 (41.0%)	NR
Krein (37)	USA	Primary care/ community	Two-arm, multi-site RCT	246	30/246	18- months	Patients with poorly controlled type 2 diabetes	Nurse practitioner-led telephone-based case management	123	61 (10.0)	2 (2.0%)	11 (10.0)	Usual care	123	61 (11.0)	6 (5.0%)	11 (9.0)
Leichter (38)	USA	Primary care/ community	Non- blinded, two-arm, parallel- group, single- center RCT	98	28/98	12- months	People with diabetes	Computer based monitoring and phone-based consultations	49	45.5 (11.8)	24 (49.0%)	NR	In-clinic consultations	49	50.9 (11.7)	19 (38.8%)	NR
Lim (39)	Singapore	Mixed primary care & hospital	1:1 parallel group multi- center RCT	204	9/204	6- months	Asian patients with type 2 diabetes	Smartphone application and remote coaching	99	50.8 (10.0)	39 (37.1%)	4.2 (3.6)	Usual care	105	51.6 (9.4)	33 (33.3%)	5.2 (4.5)
Liou (40)	Taiwan	Primary care/ community	Two-arm, multi-center RCT	95	NR	6- months	People with type 2 diabetes and HbA1c >7% for >1 year	Internet-based education program and video conferencing education program	54	56.6 (7.7)	26 (48.1%)	NR	Usual care	41	57.0 (7.5)	21 (51.2%)	NR

(Continued)

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TOTAL COH	IORT							INT	ERVE	NTION	GROUP			CON	ITROL	GROUP	
Study	Country	Study setting	Design	Number randomized	Attrition	Follow- up duration	Population description	Type of remote intervention tested	Ν	Age	Females	Diabetes duration	Control group description	Ν	Age	Females	Diabetes duration
Nicolucci (41)	Italy	Primary care/ community	Non- blinded, two-arm, Parallel- group, multi-center RCT	302	53/302	12- months	People >45 years with type 2 diabetes and HbA1c between 7.5 and 10%, and SBP >130mmHq	Monitoring and education program delivered <i>via</i> telephone	153	59.1 (10.3)	59 (38.6%)	8.3 (6.2)	Usual practice	149	57.8 (8.9)	57 (38.3%)	8.7 (6.2)
Odnoletkova (42)	Belgium	Primary care/ community	Non- blinded, two-arm, parallel- group RCT	574	88/574	18- months	People with type 2 diabetes receiving anti- diabetic therapy	Nurse-led telephone coaching and pre-made education material	287	63.8 (8.7)	114 (39.7%)	NR	Usual care	287	62.4 (8.9)	107 (37.3%)	NR
Quinn (43)*	USA	Primary care/ community	Multi-Arm cluster RCT	213	50/213	12- months	Patients aged 18 to 64 with type 2 diabetes	Mobile and web- based self- management patient coaching system and provider decision support <i>via</i> telenhone	23 <sup>‡</sup> 22 <sup>§</sup> 62	52.8 (8.0) 53.7 (8.2) 52.0 (8.0)	11 (47.8%) 12 (54.5%) 31 (50.0%)	7.7 (5.6) 6.8 (4.9) 8.2 (5.3)	Usual care	56	53.2 (8.4)	28 (50%)	9.0 (7.0)
Ramallo- Farina (44)	Spain	Primary care/ community	Open-label multi-center cluster RCT	1123	NR	24- months	Patients with type 2 diabetes	Web-based platform and mobile text	537	55.9 (7.0)	253 (47.1%)	8.4 (6.8)	Usual care	586	55.2 (7.3)	300 (51.2%)	8.6 (6.8)
Shahid (45)	Pakistan	Hospital	Two-arm parallel group RCT	440	NR	4- months	Patients with type 2 diabetes living	Telephone coaching delivered by	220	49.0 (8.8)	85 (38.6%)	NR	Usual care	220	49.21 (7.92)	85 (38.6%)	NR
Shea (46)	USA	Primary care/ community	Non- blinded, parallel- group, two- arm, multi- center RCT	1665	872/ 1665	60- months	People with diabetes aged over 55 years in medically underserved areas	Case management via remote education and home telemedicine unit for	844	70.8 (6.5)	536 (63.5%)	11.2 (9.6)	Usual care	821	70.9 (6.8)	510 (62.1%)	11.0 (9.2)
Tang (47)	USA	Primary care/ community	Parallel group RCT	415	36/415	12- months	Patients with uncontrolled type 2 diabetes	Online diabetes management system	202	54.0 (10.7)	83 (41.1%)	NR	Usual care	213	53.5 (10.2)	83 (39.0%)	NR
Varney (48)*	Australia	Hospital	Non- blinded,	94	23/94	12- months	People with type 2	Telephone coaching	47	59 (10.5)	13 (27.7%)	12.6 (8.4)	Usual care	47	64 (8.7)	17 (36.2%)	13.1 (8.6)

TABLE 1 | Continued

(Continued)

Remote Risk Factor Management in Diabetes

TOTAL COP	HORT							INTI	ERVE	NTION	GROUP			CON	ITROL	GROUP	
Study	Country	Study setting	Design	Number randomized	Attrition	Follow- up duration	Population description	Type of remote intervention tested	Ν	Age	Females	Diabetes duration	Control group description	N	Age	Females	Diabetes duration
			parallel- group, single- center BCT				diabetes and HbA1c > 7%										
Vinitha (50)	India	Hospital	Double blinded (investigator & outcome assessor), parallel- group, Multi-center RCT	248	30/248	24- months	Newly diagnosed people with type 2 diabetes with (HbA1c) > 6.5%, who were treatment naïve	Text-messaging behavior support	126	42.4 (8.5)	40 (31.7%)	NR	Standard care	122	44.1 (8.9)	40 (32.8%)	NR
Wild (51)	UK	Primary care/ community	Single blinded, parallel- group, multi-center	321	12/321	9- months	People with type 2 diabetes and HbA1c >7.5%	Telemonitoring & support <i>via</i> web- portal	160	60.5 (9.8)	54 (33.8%)	7.4 (5.7)	Usual care	161	61.4 (9.8)	53 (32.9%)	7.4 (5.8)
Yoo (52) <sup>†</sup>	South Korea	Mixed primary care & hospital	Open-label multi-site RCT	123	12/123	3- months	Overweight patients with type 2 diabetes and hypertension	Online data monitoring system and physician feedback <i>via</i> text- message	62	57.0 (9.1)	27 (47.4%)	6.0 (5.4)	Usual care	61	59.4 (8.4)	19 (35.2%)	7.2 (6.0)
Zhou (53) <sup>†</sup>	China	Hospital	Two-arm parallel group RCT	114	6/114	3- months	Patients with type 2 diabetes	Diabetes telemedicine system and data monitoring and feedback <i>via</i> internet, text or telephone	57	NR	NR	NR	Usual care	57	NR	NR	NR

Data are presented as n (%), mean (standard deviation SD), or median [interquartile range] unless otherwise specified. BMI; body mass index, CHD; coronary heart disease; NR; not reported, HbA1c; glycated hemoglobin, RCT; randomized controlled trial\* Where the SD was not reported and instead the 95% confidence intervals (Cls) were reported, these were converted to SD using the equation  $SD = \sqrt{N} \times (upper limit 95\% Cl)/3.92$ . Where only the standard error (SE) was reported, this was converted to SD by using the formula:  $SD = SE \times \sqrt{N}$ . <sup>†</sup>Reported baseline characteristics for a subset of the randomised cohort only (those who completed the trial). Ramello-Farina et al. (44) had several intervention groups and only the patient intervention group were included. Quinn et al. (2011) had three intervention groups: <sup>‡</sup>intervention groups a: online coaching only, <sup>§</sup>group b: coaching and primary care providers portal, and || group c:

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coach PCP portal with decision-support.

## **Risk of Bias of Included Studies**

Overall, 12 trials were deemed to be at high risk (27, 29, 33, 36, 38, 40–42, 45, 49, 51, 53), 12 trials had some concerns regarding their risk of bias (30–32, 35, 37, 39, 43, 46–48, 50, 52) and three were at low risk of bias (**Supplementary Table 7**) (28, 34, 44). Problems identified with high-risk studies included lack of detail on the appropriateness of analyses (27, 29), lack of allocation concealment (45, 51), differences in baseline risk factors (HbA1c) between the intervention and control groups (33), missing outcome data (36, 41, 42, 49) and differences in how data were collected between the intervention and control groups for the primary outcome (38, 40, 53).

### **Primary Outcome Measures**

**Supplementary Table 8** reports on the main risk factor outcomes based on last known follow-up included in the meta-analysis.

#### Impact of Remote Intervention on HbA1c

A meta-analysis of all 27 RCTs incorporating 3579 participants in the intervention group and 3726 participants in the control group found that remote risk factor management significantly reduced HbA1c compared to usual care (SMD -0.25, 95% CI -0.33 to -0.17, Z=6.17, p=<0.001; **Figure 2A**) with a moderate degree of heterogeneity (I<sup>2</sup>= 60%). The funnel plot was asymmetrical (**Supplementary Results, Figure 1.1**). LOO sensitivity analyses suggested removal of any individual RCT did not affect the significance of the finding (**Supplementary Results, Table 2.1**). Exclusion of studies with high risk of bias did not change the significance of the outcome (**Supplementary Results, Figure 3.1**). Subgroup analyses focused on remote intervention type or a high-risk population did not change the significance of the outcome (**Table 2** and **Supplementary Results, Figures 4.1-4.5 and 5.1**).

#### Impact of Remote Intervention on Blood Lipids

A meta-analysis of 18 RCTs incorporating 2208 participants in the intervention group and 2343 participants in the control group found that remote risk factor management significantly reduced TC compared to usual care (SMD -0.17, 95% CI -0.29 to -0.04, Z=2.64, p=0.008) with a moderate degree of heterogeneity  $(I^2 = 72\%)$  (Figure 2B). The funnel plot was asymmetrical (Supplementary Results, Figures 1.2). LOO sensitivity analyses suggested removal of one study reduced the heterogeneity and effect size substantially (46) (Supplementary **Results, Figures 2.2**). Exclusion of studies with high risk of bias changed the significance of the outcome (SMD -0.20, 95% CI -0.40 to 0.00, Z=1.91, p=0.06) with a high degree of heterogeneity  $(I^2 = 81\%)$  and the funnel plot was symmetrical (Supplementary Results, Figures 3.3, 3.4). Subgroup analyses of remote interventions showed only the coaching of risk factor modification significantly reduced TC compared to usual care (Table 2 and Supplementary Results, Figures 4.6-4.10). There were insufficient studies to undertake subgroup analysis of a high-risk population.

A meta-analysis of 25 RCTs incorporating 3399 participants in the intervention group and 3549 participants in the control group found that remote risk factor management significantly reduced LDL-c compared to usual care (SMD -0.11, 95% CI -0.19 to -0.03, Z=2.78, p=0.006) with a moderate degree of heterogeneity  $(I^2 = 56\%)$  (Figure 2C). The funnel plot was asymmetrical (Supplementary Results, Figures 1.3). LOO sensitivity analyses suggested removal of any individual RCT did not affect the significance of the main finding (Supplementary Results, Table 2.3). Exclusion of studies with high risk of bias did not change the significance of the outcome (Supplementary Results, Figure 3.5). Subgroup analyses suggested that patient education, consultation and pharmacological management but not coaching of risk factor modification significantly reduced LDL-c compared to usual care (Table 2 and Supplementary Results, Figures 4.11-4.15). Subgroup analysis also suggested that the interventions did not significantly reduce LDL-c in the high-risk population (Supplementary Results, Figure 5.2).

#### Impact of Interventions on Blood Pressure

A meta-analysis of all 27 RCTs incorporating 3580 participants in the intervention group and 3726 participants in the control group found that remote risk factor management significantly reduced SBP compared to usual care (SMD -0.11, 95% CI -0.18 to -0.04, Z=3.25, p=0.001) with a low degree of heterogeneity ( $I^2$ = 44%) (Figure 3A). The funnel plot was asymmetrical (Supplementary Results, Figure 1.4). LOO sensitivity analyses suggested removal of any individual RCT did not affect the significance of the main finding (Supplementary Results, Table 2.4). Exclusion of studies with high risk of bias changed the significance of the outcome (SMD -0.09, 95% CI -0.18 to 0.00, Z=1.96, p=0.05) with a moderate degree of heterogeneity ( $I^2$ = 56%) and the funnel plot was asymmetrical (Supplementary Results, Figures 3.7, 3.8). Subgroup analyses focused on remote intervention type did not change the significance of the outcome (Table 2 and Supplementary Results, Figures 4.16-4.20). Subgroup analysis suggested that the interventions did not significantly reduce SBP in the high-risk population (Supplementary Results, Figure 5.3).

A meta-analysis of all 27 RCTs incorporating 3180 participants in the intervention group and 3328 participants in the control group found that remote risk factor management significantly reduced DBP compared to usual care (SMD -0.09, 95% CI -0.16 to -0.02, Z=2.38, p=0.02) with a low degree of heterogeneity ( $I^2 = 44\%$ ) (Figure 3B). The funnel plot was asymmetrical (Supplementary Results, Figure 1.5). LOO sensitivity analyses suggested removal of any individual RCT did not affect the significance of the main finding (Supplementary Results, Table 2.5). Exclusion of studies with high risk of bias did not change the significance of the outcome (Supplementary Results, Figure 3.9). Subgroup analyses suggested that monitoring of risk factors, coaching of risk factor modification and pharmacological management but not patient education and consultation significantly reduced DBP compared to usual care (Table 2 and Supplementary Results,

Studg or subgroup         Mean         SU         Iotal         Weight         IV, Random, 95% Cl         IV, Random, 95% Cl           Aytekin Kanadili 2016         7.5         0.7         44         7.9         1.5         44         2.4%         -0.34 (-0.76, 0.08)           Blackberry 2013         7.9         1.2         221         7.9         1.4         219         4.9%         -0.03 (-0.76, 0.08)           Crowley 2013         7.8         1.3         166         7.9         1.2         221         7.9         1.4         219         4.9%         -0.08 (-0.29, 0.14)           Davis 2010         8.2         3.7         85         8.5         2.7         80         3.4%         -0.012 (-0.43, 0.18)           Eakin 2014         7.4         1.3         118         7.3         1.6         131         4.1%         -0.04 (-0.38, 0.11)           Haix 2014         7.4         1.3         118         7.3         1.6         121         4.9%         -0.36 (-0.64, -0.17)           Haix 2019         0.7         1.3         2.4         7.3         1.6         2.21         4.9%         -0.36 (-0.64, -0.17)           Hubrook 2009         6.8         1.2         2.24         7.3	
Prytemi Rearrow       Cols       Cols <thcols< th=""> <thcols< th="">       Cols       Cols<!--</td--><td></td></thcols<></thcols<>	
Bond 2007         6.4         1.2         31         7.1         1         31         1.8%         -0.63 [-1.14, -0.12]           Crowley 2013         7.8         1.3         166         7.9         1.3         164         4.5%         -0.08 [-0.29, 0.14]           Davis 2010         2.8         2.7         7.8         1.3         166         7.9         1.3         164         4.5%         -0.08 [-0.29, 0.14]           de Vasconcelos 2018         7.2         1.2         16         7.3         1.7         15         1.1%         -0.07 [-0.77, 0.64]           Eakin 2014         7.4         1.3         118         7.5         1.6         221         4.8%         -0.03 [-0.66, -0.06]           Eakin 2014         7.4         1.3         1.3         1.7         7.4         3.4%         -0.03 [-0.64, -0.17]           Hubrook 2006         6.8         1.2         2.4         7.3         1.6         2.21         4.9%         -0.03 [-0.64, -0.17]           Hubrook 2006         6.8         1.2         2.1%         5.6         3.0%         -0.03 [-0.24, -0.17]           Kempf 2017         7.6         1.2         7.7         8.2         1.3         3.0%         0.05 [-0.22, 0.32]	
Crowley 2013         7.8         1.3         166         7.9         1.3         164         4.5%         -0.08 [-0.29, 0.14]           Davis 2010         8.2         3.7         85         8.5         2.7         80         3.4%         -0.08 [-0.29, 0.14]           Davis 2010         8.2         3.7         85         8.5         2.7         80         3.4%         -0.07 [-0.77, 0.64]           Eakin 2014         7.4         1.3         118         7.5         1.6         131         4.1%         -0.014 [-0.39, 0.11]           Hamo 2006         7.3         1.1         10         7.3         1.7         7.4         3.4%         -0.36 [-0.66, -0.06]           Holbrook 2009         6.8         1.2         2.24         7.3         1.6         2.31         4.9%         -0.35 [-0.54, -0.17]           Hou 2019         0.7         1.3         2.44         7.2         1.5         2.34         6.0%         -0.36 [-0.84, -0.17]           Kemp 2017         7.6         1.2         7.2         1.5         2.34         6.0%         -0.48 [-0.83, -0.13]           Krein 2004         9.3         2.1         106         9.2         2         1.03         8.8%         -0.38 [	
Davis 2010         8.2         3.7         85         8.8         2.7         80         3.4%         -0.12 [-0.43, 0.18]           de Vasconcelos 2018         7.2         1.2         1.6         7.3         1.7         15         1.1%         -0.07 [-0.77, 0.64]           Eakin 2014         7.4         1.3         118         7.3         1.6         131         4.1%         -0.014 [-0.39, 0.11]           Hamo 2006         7.3         1.1         101         7.4         3.4%         -0.36 [-0.66, -0.06]           Hubtrook 2009         6.8         1.2         224         7.3         1.6         221         4.9%         -0.36 [-0.54, -0.17]           Huu 2019         0.7         1.2         224         7.3         1.6         221         4.9%         -0.36 [-0.54, -0.17]           Kempf 2017         7.6         1.2         7.8         2.1         56         3.0%         -0.48 [-0.83, -0.13]           Krein 2004         9.3         2.1         106         9.2         2         103         3.8%         -0.05 [-0.22, 0.32]           Leichter 2013         7.4         1.1         3.7         1.2         37         2.0%         -0.38 [-0.66, -0.09]           Lim 2021	
De vasculterius 2016       7.2       1.2       1.6       7.3       1.7       7.4       0.07       7.0.57       0.05       0.07       0.57       0.05       0.07       0.57       0.05       0.07       0.57       0.05       0.05       0.07       0.05       0.05       0.07       0.05       0.0	
Hamo 2006         7.3         1.1         101         7.3         1.7         74         3.4%         -0.36 [-0.66, -0.06]           Holbrook 2009         6.8         1.2         224         7.3         1.6         221         4.9%         -0.36 [-0.66, -0.06]           Huo 2019         0.7         1.5         2.2         1.5         2.4         5.0%         -0.36 [-0.64, -0.17]           Kemp 2017         7.6         1.2         2.7         8.2         1.3         56         3.0%         -0.04 [-0.83, -0.13]           Krein 2004         9.3         2.1         106         9.2         2         103         3.8%         -0.05 [-0.22, 0.32]           Leichter 2013         7.4         1.1         31         7.1         1.2         37         2.0%         0.26 [-0.21, 0.73]           Lim 2021         6.7         1         94         7.1         1.1         101         3.6%         -0.03 [-0.66, -0.09]           Liou 2014         7.6         1.1         54         8.1         3.41         2.4%         -0.42 [-0.83, -0.13]           Odnoletkova 2016         6.9         1         240         7         1.1         246         5.0%         -0.03 [-0.65, -0.13]	
Holbrook 2009         6.8         1.2         224         7.3         1.6         221         4.9%         -0.35 [-0.54, -0.17]           Huu 2019         0.7         1.3         2.4         7.2         1.5         234         5.0%         -0.36 [-0.54, -0.17]           Kempf 2017         7.6         1.2         77         8.2         1.3         56         3.0%         -0.48 [-0.83, -0.13]           Krein 2004         9.3         2.1         106         9.2         2         103         3.8%         0.05 [-0.22, 0.32]           Leichter 2013         7.4         1.11         3         7.1         1.2         37         2.0%         0.26 [-0.21, 0.73]           Lim 2021         6.7         1         9.4         7.1         1.1         36%         -0.38 [-0.66, -0.09]           Liou 2014         7.6         1.1         54         8.1         1.3         41         2.4%         -0.42 [-0.83, -0.13]           Odnoletkova 2016         6.9         1         240         7         1.1         24%         -0.38 [-0.63, -0.13]           Quinn 2011a         7.7         1         23         8.5         1.8         19         1.3%         -0.55 [-1.17, 0.07] <td></td>	
Huo 2019         0.7         1.3         234         7.2         1.5         234         5.0%         -0.30 [-0.4%, -0.17]           Kempf 2017         7.6         1.2         7         8.2         1.3         56         3.0%         -0.43 [-0.83, 0.13]           Krein 2004         9.3         2.1         106         9.2         2         103         3.8%         0.05 [-0.22, 0.32]           Leichter 2013         7.4         1.1         3         7.1         1.2         37         2.0%         0.26 [-0.21, 0.73]           Lim 2021         6.7         1         94         7.1         1.1         101         3.6%         -0.38 [-0.66, -0.09]           Liou 2014         7.6         1.1         54         8.1         1.3         41         2.4%         -0.42 [-0.83, -0.13]           Nicolucci 2015         7.4         114         7.3         1.1         155         -0.38 [-0.66, -0.09]           Quinn 2011a         7.7         1         240         7         1.1         154         -0.38 [-0.63, -0.13]           Quinn 2011b         7.9         1.4         2.3         8.5         1.8         19         1.3%         -0.55 [-1.17, 0.07]	
Netling 2017         1.5         1.2         1.7         6.2         1.3         5.05         3.054         7.048 [70.87, 051, 051]           Krein 2004         9.3         2.1         1.06         9.2         2.1         1.03         3.8%         0.05 [-0.22, 0.32]           Leichter 2013         7.4         1.1         1.3         7.7         1.2         37         2.0%         0.26 [-0.21, 0.73]           Lim 2021         6.7         1         94         7.1         1.1         1.01         3.6%         -0.38 [-0.66, -0.09]           Liou 2014         7.6         1.1         54         8.1         1.3         41         2.4%         -0.04 [-0.83, -0.01]           Nicolucci 2015         7.4         1         1.4         7.3         1.1         1.5         4.0%         -0.38 [-0.63, -0.13]           Odnoletkova 2016         6.9         1         2.40         7         1.1         2.46         5.0%         -0.09 [-0.27, 0.08]           Quinn 2011a         7.7         1         2.3         8.5         1.8         19         1.3%         -0.37 [-0.09, 0.25]	
Leichter 2013         7.4         1.1         33         7.1         1.2         37         2.0%         0.26 [-0.21, 0.73]           Lim 2021         6.7         1         94         7.1         1.1         101         3.6%         -0.38 [-0.66, -0.09]           Liou 2014         7.6         1.1         54         8.1         3.41         2.4%         -0.42 [-0.83, -0.01]           Nicolucci 2015         7.4         1         114         7.3         1.1         135         4.0%         -0.38 [-0.63, -0.13]           Odnoletkova 2016         6.9         1         240         7         1.1         246         5.0%         -0.09 [-0.27, 0.08]           Quinn 2011a         7.7         1         23         8.5         1.8         19         1.3%         -0.37 [-0.99, 0.25]	
Lim 2021         6.7         1         94         7.1         1.1         101         3.8%         -0.38 [-0.66, -0.09]           Liou 2014         7.6         1.1         54         8.1         1.3         41         2.4%         -0.42 [-0.83, -0.01]           Nicolucci 2015         7.4         1         114         7.3         1.1         135         4.0%         -0.38 [-0.63, -0.13]           Odnoletkova 2016         6.9         1         240         7         1.1         246         5.0%         -0.09 [-0.27, 0.08]           Quinn 2011a         7.7         1         23         8.5         1.8         19         1.3%         -0.55 [-1.17, 0.07]           Quinn 2011b         7.9         1.4         22         8.5         1.8         19         1.3%         -0.37 [-0.99, 0.25]	
Liou 2014         7.6         1.1         54         8.1         1.3         41         2.4%         -0.42 [0.83, -0.01]           Nicolucci 2015         7.4         1         14         7.8         1.1         35         4.0%         -0.38 [-0.63, -0.13]           Odnoletkova 2016         6.9         1         240         7         1.1         246         5.0%         -0.09 [-0.27, 0.08]           Quinn 2011a         7.7         1         23         8.5         1.8         19         1.3%         -0.35 [-1.17, 0.07]           Quinn 2011b         7.9         1.4         22         8.5         1.8         19         1.3%         -0.37 [-0.99, 0.25]	
Quinn 2011b         7.9         1.4         22         8.5         1.8         19         1.3%         -0.38         (-0.38)         (-0.38         (-0.38)         (-0.38         (-0.38) <t< td=""><td></td></t<>	
Quinn 2011a         7.7         1         23         8.5         1.8         19         1.3%         -0.55         [-1.17, 0.07]           Quinn 2011b         7.9         1.4         22         8.5         1.8         19         1.3%         -0.37         [-0.99, 0.25]	
Quinn 2011b 7.9 1.4 22 8.5 1.8 19 1.3% -0.37 [-0.99, 0.25]	
Quinn 2011c 7.9 1.7 62 8.5 1.8 19 1.8% -0.34 [-0.86, 0.17]	
Ramano-rama 2020 7.3 1.4 575 7.3 1.4 471 5.6% 0.00 [-0.14, 0.14]	
Shea 2009 7.1 1.2 330 7.3 1.5 463 5.5% -0.14 [-0.29, -0.00]	
Tang 2013 8.1 1.7 186 8.3 1.8 193 4.7% -0.11 [-0.32, 0.09]	
Varmey 2014 8.2 1.1 35 8.4 1.1 35 2.1% -0.18 [-0.55, 0.29]	
Wild 2016 7.9 1.4 146 8.4 1.3 139 4.3% -0.37 [-0.60, -0.13]	
Yoo 2009 7.1 0.8 57 7.5 1 54 2.7% -0.55 [-0.93, -0.17]	
Zhou 2014 6.8 1.2 53 7.5 1.6 55 2.6% -0.56 [-0.95, -0.18]	
Total (95% Cl) 3579 3726 100.0% -0.25 [-0.33, -0.17]	
Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 70.70, df = 28 (P < 0.0001); l <sup>2</sup> = 60%	
Favours [experimental] Favours [control]	
Experimental Control Std. Mean Difference Std. Mean Difference	
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% Cl IV, Random, 95% Cl	
Aytekin Kanadli 2016 4.94 1.59 44 5.93 1.46 44 4.1% -0.64 [-1.07, -0.21]	
Biackberry 2013 4.2 0.95 221 4.28 1.05 219 6.9% -0.08 [-0.27, 0.11]	
de Vasconcelos 2018 4.56 1.17 16 4.49 1.13 15 2.2% 0.06 [-0.65, 0.76]	
Harno 2006 4.74 1.11 101 5.03 1.03 74 5.5% -0.27 [-0.57, 0.03]	
Kempf 2017 4.97 1.06 77 4.89 1.16 56 5.0% 0.07 [-0.27, 0.42]	
Linu 2014 4.64 1.01 54 4.95 0.95 41 4.3% -0.31 [-0.72, 0.10]	
Nicolucci 2015 4.76 1.03 114 4.63 0.91 135 6.2% 0.13 [-0.12, 0.38]	
Odnoletkova 2016 4.19 0.88 241 4.4 1.27 246 7.1% -0.19 [-0.37, -0.01]	
Quinn 2011a 3.91 0.86 23 4.34 1.03 19 2.7% 0.044 [-1.06, 0.17]	
Quinn 2011c 4.5 1.09 62 4.34 1.03 19 3.4% 0.15 [-0.37, 0.66]	
Ramallo-Farina 2020 4.79 1.03 375 4.72 0.97 471 7.5% 0.07 [-0.07, 0.21]	
Shea 2009 4.14 0.92 330 4.72 1.08 463 7.4% -0.57 [-0.71, -0.43]	
Valida 2019 4.6 1.1 112 4.7 1 106 6.0% -0.09 [-0.36, 0.17]	
Wild 2016 4.1 0.9 146 4.3 1.2 139 6.4% -0.19 [-0.42, 0.04]	
Yoo 2009 4.1 0.7 57 4.5 0.8 54 4.7% 0.53 [.0.91, 0.15]	
Zhou 2014 4.91 1 55 4.7 0.64 55 4.7% 0.23 (*0.15, 0.60)	
Total (95% CI) 2208 2343 100.0% -0.17 [-0.29, -0.04]	
Heterogeneity: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 66.96, df = 19 (P < 0.00001); l <sup>2</sup> = 72%	1
Favours [experimental] Favours [control]	
Experimental Control Std. Mean Difference Std. Mean Difference	
Experimental Control Std. Mean Difference Std. Mean Difference Std. Mean Difference Difference Study or Subgroup Mean SD Total Weight IV, Random, 95% CI IV, Random,	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.032 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.11         2.40         -0.05 [-0.32 n 1.4]         -0.05 [-0.32 n 1.4]	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         4.8%         -0.25 [-0.23, 0.00]         -0.25 [-0.23, 0.00]         -0.25 [-0.23, 0.00]         -0.25 [-0.23, 0.01]         -0.25 [-0.23, 0.	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         6.5         2.67         1.64         8.0         3.5%         -0.22 [-0.52, 0.09]           Davis 2010         2.32         1.61         85         2.67         1.61         80         3.5%         -0.22 [-0.52, 0.09]	
Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         166         2.67         1.61         80         3.5%         -0.22 [-0.43, 0.00]           Davis 2010         2.32         1.61         85         2.67         1.61         80         3.5%         -0.22 [-0.47, 0.09]           de Vasconcelos 2018         2.53         0.39         16         2.6         0.79         15         1.1%         -0.08 [-0.78, 0.63]	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.12         2.60         A2 [19         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         166         2.67         1.57         164         4.8%         -0.02 [-0.32, 0.04]           Davis 2010         2.32         1.61         85         2.67         1.61         80         3.5%         -0.02 [-0.52, 0.09]           de Vasconcelos 2018         2.51         0.93         16         2.6         0.79         15         1.1%         -0.08 [-0.78, 0.63]           Eakin 2014         2.35         0.88         118         2.16         0.81         131         4.3%         -0.22 [-0.50, 0.01]	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI <td< td=""><td></td></td<>	
Study or Subgroup         Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         1.66         2.67         1.61         80         0.95 [-0.23, 0.14]           Davis 2010         2.32         1.64         85         2.67         1.64         8.9         -0.22 [-0.52, 0.09]           de Vasconcelos 2018         2.53         0.93         16         2.6         0.79         15         1.1%         -0.08 [-0.78, 0.63]           Eakin 2014         2.35         0.88         118         2.16         0.86         74         3.6%         -0.29 [-0.59, 0.01]           Horbrook 2009         2.43         0.78         2.21         5.4%         -0.02 [-0.32, 0.04]         -           Huo 2019         2.5         0.7         234         2.5         0.8         231         5.5%         0.00 [-0.18, 0.18]	
Experimental         Control         Std. Mean Difference         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.21         0.26         2.49         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         166         2.67         1.57         164         4.8%         -0.02 [-0.23, 0.14]           Davis 2010         2.32         1.61         80         3.5%         -0.22 [-0.3, 0.47]	
Study or Subgroup         Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.1         2.66         0.84         -1.95         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.02 [-0.78, 0.63]           Davis 2010         2.32         1.61         85         2.67         1.51         1.1%         -0.08 [-0.78, 0.63]           Hamo 2006         2.52         0.88         118         2.16         0.81         131         4.3%         -0.22 [-0.59, 0.01]           Hamo 2006         2.52         0.88         118         2.16         0.81         2.34         6.74         3.6%         -0.24 [-0.59, 0.01]           Hamo 2006         2.52         0.8         118         2.16         0.81         2.34         5.5%         0.00 [-0.	
Study or Subgroup         Experimental         Control         Std. Mean Difference         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-074, 0.10]         VI, Random, 95% CI         VI, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-074, 0.10]           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.02 [-0.43, -0.01]           Davis 2010         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.22 [-0.52, 0.09]           de Vasconcelos 2018         2.35         0.93         16         2.6         7.4         3.6%         -0.22 [-0.50, 0.01]           Hamo 2006         2.52         0.8         118         2.16         0.81         131         4.3%         -0.22 [-0.50, 0.01]           Hamo 2006         2.52         0.8         101         2.76         0.86         7.4         3.6%         -0.02 [-0.50, 0.01]           Holtrook 2009         2.43         0.78         2.25	
Study or Subgroup         Experimental Mean         Control         Std. Mean Difference         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Davis 2010         2.32         1.64         1.66         2.67         1.64         4.8%         -0.22 [-0.23, 0.14]           Davis 2010         2.32         1.64         1.66         2.67         1.61         80         3.5%         -0.22 [-0.52, 0.09]           Eakin 2014         2.35         0.83         16         2.6         0.81         131         4.3%         0.22 [-0.30, 0.47]           Harro 2006         2.52         0.8         110         2.76         0.663         -0.24 [-0.58, 0.03]         -0.24 [-0.59, 0.01]           Holbrook 2009         2.43         0.78         0.81         -0.24 [-0.59, 0.01]         -0.26 [-0.59, 0.01]         -0.26 [-0.59, 0.01]           Holbrook 2009         2.43         0.78         2.24         5.5%         0.00 [-0.18, 0.18]         -0.26 [-0.59, 0.	
Study or Subgroup         Experimental         Control         Std. Mean Difference         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.12         2.68         0.42         1.9         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         166         2.67         1.67         164         4.8%         -0.02 [-0.43, -0.00]           Davis 2010         2.35         0.88         118         2.16         0.81         131         4.3%         -0.22 [-0.52, 0.09]           Harro 2006         2.53         0.88         118         2.16         0.81         131         4.3%         -0.22 [-0.50, 0.01]           Habro 2016         2.55         0.8         118         2.16         0.81         2.21         0.43, 0.01]           Harro 2006         2.43         0.78         2.42         2.5         0.81 <td></td>	
Experimental         Control         Std. Mean Difference         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95%, CI         VI, Random, 95%, CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.12         2.66         0.84         2.19         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         166         2.67         1.57         164         4.8%         -0.02 [-0.78, 0.63]           Davis 2010         2.35         0.93         16         2.6         0.79         15         1.1%         -0.08 [-0.78, 0.63]           Hamo 2006         2.52         0.8         118         2.16         0.81         131         4.3%         -0.22 [-0.59, 0.01]           Hamo 2006         2.43         0.78         2.42         2.5         0.8         2.34         5.5%         0.00 [-0.18, 0.18]           Huo 2019         2.5         0.77         2.45         0.83 </td <td></td>	
Study or Subgroup         Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-074, 0.10]         VI, Random, 95% CI         VI, Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-074, 0.10]         VI, Random, 95% CI           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.02 [-0.43, -0.00]           Davis 2010         2.32         1.64         166         2.67         1.57         1.64         4.8%         -0.22 [-0.52, 0.09]           de Vasconcelos 2018         2.55         0.93         16         2.6         0.78         1.57         -0.08 [-0.27, 0.42]           Hamo 2006         2.52         0.8         118         2.16         0.81         131         4.3%         -0.22 [-0.52, 0.09]	
Experimental         Control         Std. Mean Difference         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VR. Random, 95% CI         VR. Random, 95% CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.21         0.87         2.41         0.56         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         165         2.67         1.61         80         3.5%         -0.22 [-0.3, 0.47]           Davis 2010         2.32         1.61         85         2.67         1.61         80         3.5%         -0.22 [-0.3, 0.47]           Harro 2006         2.52         0.81         1.276         0.66         74         3.6%         -0.28 [-0.59, 0.01]           Huo 2016         2.55         0.7         2.4         2.5         0.81         2.24         2.5%         0.00 [-0.18, 0.18, 0.18]           Krein 2004         2.74         0.85         1.03         1.03         4.007 <td< td=""><td></td></td<>	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95%, CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Biackberry 2013         2.22         0.87         2.12         2.66         0.84         -1.95         0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.61         65         2.67         1.57         164         4.8%         -0.022 [-0.52, 0.09]           Davis 2010         2.32         1.61         65         2.67         1.61         80         3.5%         -0.22 [-0.52, 0.09]           de Vasconcelos 2018         2.51         0.83         118         2.16         0.81         131         4.3%         -0.22 [-0.52, 0.09]           Harro 2006         2.43         0.78         2.24         2.54         0.81         2.21         0.59, 0.01]           Huo 2019         2.5         0.7         2.45         0.83         2.24         0.56         0.01         3.35	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95%, CI         VI, Random, 95%, CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.02 [-0.43, -0.00]           Davis 2010         2.32         1.61         1.65         2.67         1.57         1.64         4.8%         -0.02 [-0.63, 0.17]           Hamo 2006         2.35         0.88         118         2.16         0.81         131         4.3%         -0.22 [-0.50, 0.01]           Hamo 2006         2.52         0.8         148         2.41         0.84%         -0.01 [-0.30, 0.05]           Huaro 2019         2.5         0.7         2.34         2.5         0.8         2.04         0.01 [-0.16, 0	
Study or Subgroup         Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-074, 0.10]         VI, Random, 95%; CI           Aytekin Kanadii 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-074, 0.10]         VI, Random, 95%; CI           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.02 [-0.43, -0.01]           Davis 2010         2.32         1.64         1.66         2.67         1.57         1.1%         -0.02 [-0.67, 0.63]           Ge Vasconcelos 2018         2.55         0.83         116         2.76         0.86         74         3.6%         -0.22 [-0.50, 0.01]           Hamo 2006         2.52         0.8         118         2.16         0.81         131         4.3%         -0.22 [-0.30, 0.47]           Hubrook 2009         2.43         0.78         2.24         5.5%         0.00 [-0.18, 0.18]         -0.24 [-0.27, 0.42]           Kempf 2017         3.03         1.16         7.255         0.78         2.39 <td< td=""><td></td></td<>	
Study or Subgroup         Experimental         Control         Std. Mean         Difference         V, Random, 95%, Cl         V, Random, 95%, Cl           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         V, Random, 95%, Cl           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         V, Random, 95%, Cl           Biackberry 2013         2.22         0.87         2.12         2.68         0.44         1.68         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         1.66         2.67         1.61         80         3.5%         -0.02 [-0.3, 0.47]           Davis 2010         2.35         0.88         118         2.16         0.81         131         4.3%         -0.22 [-0.3, 0.47]           Harro 2006         2.55         0.81         12.76         0.66         74         3.6%         -0.29 [-0.30, 0.7]           Huo 2019         2.5         0.7         2.4         2.5         0.83         56         3.1%         0.07 [-0.27, 0.42]           Krein 2004         2.74         0.85         106         2.82	
Experimental         Control         Std. Mean Difference         Std. Mean Difference           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95%, CI           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]         VI, Random, 95%, CI           Biackberry 2013         2.22         0.87         2.12         2.60         0.84         2.19         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.61         65         2.67         1.61         80         3.5%         -0.02 [-0.52, 0.09]           Davis 2010         2.32         1.61         85         2.67         1.61         80         3.5%         -0.02 [-0.52, 0.09]           Harro 2006         2.15         0.93         1.6         7.4         5.6         7.4         3.6%         -0.22 [-0.52, 0.09]           Huo 2019         2.5         0.7         2.4         2.5         0.81         2.21         0.40%         -0.29 [-0.3, 0.47]           Huo 2019         2.5         0.7         2.4         2.5         0.82         2.45 </td <td></td>	
Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Mean         SD         Total         Weight         V, Random, 95%, Cl         V, Random, 95%, Cl           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Blackberry 2013         2.22         0.87         221         2.26         0.84         219         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.02 [-0.43, .0.00]           Davis 2010         2.32         1.61         1.65         2.67         1.57         1.64         4.8%         -0.02 [-0.62, 0.09]           Harro 2006         2.35         0.38         118         2.16         0.81         1.31         4.3%         -0.22 [-0.52, 0.09]           Harro 2006         2.43         0.78         2.24         2.54         0.81         1.31         4.3%         -0.22 [-0.52, 0.09]	
Study or Subgroup         Experimental         Control         Std. Mean Difference         VK. Random, 95%, Cl         VK. Random, 95%, Cl           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 (-0.74, 0.10)           Blackberry 2013         2.22         0.87         221         2.26         0.84         2.19         5.4%         -0.03 (-0.3, 0.14)           Crowley 2013         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.22 (-0.43, -0.00)           Davis 2010         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.22 (-0.43, -0.00)           Davis 2010         2.32         1.61         1.65         2.67         1.51         1.80         -0.22 (-0.52, 0.09)           Harro 2006         2.52         0.88         118         2.16         0.81         1.31         4.3%         -0.22 (-0.52, 0.09)           Harro 2006         2.52         0.8         1.18         2.16         0.81         2.21         5.4%         -0.01 (-0.32, 0.05)           Hubrook 2009         2.43         0.78         2.24         5.5%         -0.01 (-0.38, 0.07)	
Study or Subgroup         Experimental         Control         Std. Mean         Difference         V, Random, 95%, Cl         V, Random, 95%, Cl         V, Random, 95%, Cl           Aytekin Kanadil 2016         2.98         0.92         44         3.29         1         44         2.4%         -0.32 [-0.74, 0.10]           Blackberry 2013         2.22         0.87         2.12         2.68         0.84         2.19         5.4%         -0.05 [-0.23, 0.14]           Crowley 2013         2.32         1.64         1.66         2.67         1.57         1.64         4.8%         -0.22 [-0.3, 0.47]           Davis 2010         2.32         1.61         85         2.67         1.61         80         3.5%         -0.22 [-0.3, 0.47]           Harro 2006         2.53         0.88         118         2.16         0.81         1.31         4.3%         -0.22 [-0.3, 0.47]           Huo 2016         2.55         0.81         1.276         0.86         74         3.6%         -0.29 [-0.30, 0.7]         -0.47           Huo 2016         2.57         0.7         2.4         2.5         0.83         56         3.1%         0.07 [-0.27, 0.42]         -0.29 [-0.30, 0.7]           Krein 2014         2.7         0.45	

FIGURE 2 | (A) Forest plot showing the effect of remote risk factor management on HbA1c, (B) Forest plot showing the effect of remote management on total cholesterol, (C) Forest plot showing the effect of remote risk factor management on LDL-cholesterol.

Risk		SUBGROUP ANAL	LYSIS OF REMOTE INTE	RVENTION TYPES		SUBGROUP ANALYSIS
	PATIENT EDUCATION	MONITORING OF RISK FACTORS	COACHING REGARDING RISK FACTOR MODIFICATION	CONSULTATION	PHARMACOLOGICAL MANGEMENT	LATION AT ENTRY
HbA1c	(SMD -0.26, 95% Cl -0.35 to -0.17), Z=5.51, p<0.0001 (l²= 59%)	(SMD -0.27, 95% Cl -0.37 to -0.17), Z=5.32, p<0.0001 (I <sup>2</sup> = 67%)	(SMD -0.24, 95% Cl -0.32 to -0.16), Z=5.98, p<0.0001 (I <sup>2</sup> = 49%)	(SMD -0.19, 95% Cl -0.29 to -0.10), Z=3.96, p=0.0001 (l²=29%)	(SMD -0.14, 95% Cl -0.23 to -0.06), Z=3.36, p = 0.0008 (l²=48%)	(SMD -0.39, 95% Cl -0.53 to -0.25), Z=5.52, p <0.0001 (l <sup>2</sup> = 0%)
тс	SMD -0.14, 95% Cl -0.29 to -0.01), Z=1.89, p=0.06 (I²=71%)	NA	(SMD -0.18, 95% Cl -0.34 to -0.02), Z=2.23 p=0.03 (l²= 72%)	(SMD -0.15, 95% Cl -0.35 to 0.05), Z=1.48, p=0.14) (I²= 75%)	(SMD -0.13, 95% Cl -0.31 to 0.06), Z=1.35, p=0.18 (I²= 84%)	NA
LDL-c	(SMD -0.09, 95% Cl -0.19 to -0.00), Z=2.01, p=0.04 (I²=58%)	NA	(SMD -0.06, 95% Cl -0.13 to 0.00), Z=1.853, p=0.06 (P=30%)	(SMD -0.10, 95% CI -0.18 to -0.02), Z=2.54, p=0.01 (I²=8%)	(SMD -0.19, 95% Cl -0.17 to -0.01), Z=2.26, p=0.02 (l²=37%)	(SMD 0.02, 95% Cl -0.12 to 0.15), Z=0.23, p=0.82 (P=0%)
SBP	(SMD -0.10, 95% Cl -0.18 to -0.01), Z=2.19, p=0.3 (I²=53%)	(SMD -0.12, 95% Cl -0.19 to -0.04), Z=2.97, p=0.003 (l <sup>2</sup> =13%)	(SMD -0.09, 95% Cl -0.17 to -0.02), Z=2.41, p=0.02 (l²=46%)	(SMD -0.10, 95% Cl -0.18 to -0.03), Z=2.60, p=0.009 (l²=7%)	(SMD -0.13, 95% Cl -0.21 to -0.04), Z=2.97, p=0.003) (I <sup>2</sup> =48%)	(SMD 0.08, 95% CI -0.05 to 0.22), Z=1.19, p=0.24 (I²=0%)
DBP	(SMD -0.07, 95% Cl -0.17 to 0.03), Z=1.41 p=0.16 (I²=48%)	(SMD -0.14, 95% Cl -0.26 to -0.02), Z=2.32, p=0.02 (l <sup>2</sup> =60%)	(SMD -0.13, 95% Cl -0.20 to -0.05), Z=3.26, p=0.001 (l <sup>2</sup> =36%)	(SMD -0.07, 95% Cl -0.19 to 0.04), Z=1.23, p=0.22 (I²=52%)	(SMD -0.12, 95% Cl -0.18 to -0.06), Z=3.80, p=0.0001 (l²= 4%)	NA

Five distinct aspects of the remote management programs tested were defined in an attempt to clarify which aspects of the interventions were most important in improving outcome: 1) patient education, 2) monitoring of risk factors, 3) coaching to improve risk factor control, 4) health care professional telehealth consultation and 5) pharmacological management. We only included remote risk factor monitoring RCTs in a meta-analysis where either blood pressures, blood glucose or blood lipids were remotely monitored. Sub-group meta-analyses (MA) were performed for any primary outcome with data available from a minimum of three studies per remote intervention component. If the component of the intervention was not delivered remotely, this study was excluded from meta-analysis. HbA1c =glycated hemoglobin A1c, TC = total cholesterol, LDL-c = low density lipoprotein cholesterol, SBP= systolic blood pressure, DBP= diastolic blood pressure, SMD= standardized mean difference, 95% Cl= 95% confidence interval and l²= measure of statistical heterogeneity. Subgroup meta-analysis was also planned to evaluate whether remote management was more effective in studies which only included a higher risk population defined as; a documented history of cardiovascular disease, a diabetes duration of greater than 10 years, HbA1c of > 10.0% (54) and/or LDL of >2.0 mmol/L (55) and/or systolic blood pressure of > 30 mmHg and/or a diastolic blood pressure of sequences of sequences analysis outcome was statistically significant, and the red squares indicate where it was not and the yellow squares indicate where meta-analysis was not possible. The full results are reported in **Supplementary Results**.

**Figures 4.21-4.25**). There were insufficient studies to undertake subgroup analysis of a high-risk population.

#### Secondary Outcome Measures

Supplementary Tables 9 and 10 report the secondary outcome data. One study reported on major adverse cardiovascular events (51), but none of the studies reported on limb revascularization or amputation, or progression of microvascular disease or worsening of existing comorbidities. One study reported that the cost of the intervention was more than the control due to telemonitoring service costs and additional nurse phone consultations (51). None of the studies undertook a costbenefit analysis. Quality of life data were reported in seven RCTs (28, 34-36, 41, 50, 51), but could not be combined in meta-analysis due to heterogeneity of instruments used. Two studies reported significant improvements in quality of life in the remote management group at follow-up compared to baseline (36, 41). Fifteen RCTs reported on adverse outcomes (28, 30, 32, 34-39, 41, 42, 46, 48, 51, 53). Four RCTs reported on medication related side effects including hypoglycemia and postural hypotension (32, 39, 51, 53). Mortality during follow-up was reported in 17 RCTs (27-32, 34, 35, 37, 39, 41-43, 46-48, 51).

A meta-analysis including 15 RCTs incorporated 2979 participants in the intervention group and 2955 participants in

the control group found that remote risk factor management had no effect on overall adverse outcomes (RR = 0.88, 95% CI 0.70 to 1.09, Chi<sup>2</sup> = 12.85, p=0.24) with a low degree of heterogeneity (I<sup>2</sup>= 7%) (**Supplementary Results, Figure 6.1**). The funnel plot was asymmetrical (**Supplementary data, Figure 7.1**). Additional meta-analyses of individual adverse events including mortality, hypoglycemic episodes and hospital admission showed no significant difference between groups (**Supplementary Results, Figures 6.2-6.4**).

## DISCUSSION

This meta-analysis suggested that remote management significantly improved control of the five modifiable risk factors for diabetes-related major adverse events. Small reductions in HbA1c and TC and modest reductions in LDL-c, SBP and DBP were found. The main findings were robust in sensitivity analyses but clarity on which components of the remote management were most effective was limited because all interventions included a composite of different intervention types. Remote risk factor management had no effect on the rate of adverse outcomes including mortality, hypoglycemic episodes and hospital admissions.

Aytekin Kanadii 2016         126         13         44         130         15         44         2.0%         -0.28 [-0.70, 0.14]           Blackberry 2013         133         14         221         136         16         219         5.3%         -0.20 [-0.39, -0.01]           Bond 2007         128         13         11         10         11         10         11         -0.20 [-0.76, 0.24]           Crowley 2013         138         24         166         133         17         164         4.7%         -0.26 [-0.76, 0.24]           Davis 2010         128         37         85         131         44         10         0.11         -0.26 [-0.39, 0.20]           Eakin 2014         133         16         118         15         131         4.0%         -0.26 [-0.39, 0.22]           Eakin 2014         133         16         118         131         14         20         -0.39         -0.21           Harmo 2006         133         12         138         120         137         13         24         0.02 [-0.39, 0.21]           Holbrook 2009         131         16         274         132         18         241         5.3%         0.01 [-0.20, 0.34]
Biackberry 2013         133         14         221         136         16         219         5.3%         -0.26 [0.39, -0.01]           Bond 2007         128         13         131         10         10         15         -0.26 [0.76, 0.24]           Crowley 2013         138         24         166         133         17         164         4.7%         0.24 [0.02, 0.46]           Davis 2010         128         37         85         131         34         80         3.2%         -0.06 [0.39, 0.22]           de Vasconcelos 2018         128         14         141         15         0.8%         -0.75 [1.48, 0.02]           Eakin 2014         133         16         118         131         15         131         4.0%         0.07 [1.48, 0.02]           Hamo 2006         135         12         11         137         2.07         4.32%         -0.09 [0.39, 0.21]           Hubrook 2009         131         16         124         125         16         2.24         0.03 [0.42, -0.05]           Huc 2019         135         19         2.34         15.4%         0.16 [0.02, 0.34]
Bond 2007         128         13         31         11         10         31         1.5%         -0.26 [0.7, 0.24]           Crowley 2013         138         24         166         133         17         164         4.7%         0.24 [0.02, 0.46]           Davis 2010         128         37         85         131         34         80         3.2%         -0.08 [-0.39, 0.22]           de Vasconcelos 2018         126         14         16         141         24         15         0.8%         -0.75 [-1.48, -0.02]           Eakin 2014         133         16         118         131         15         134         40%         0.32 [-0.12, 0.38]           Hamo 2006         135         22         101         137         20         74         3.2%         -0.09 [-0.39, 0.21]           Hub 2019         135         19         234         132         18         234         5.4%         0.16 [-0.02, 0.34]           Krein 2004         146         24         105         133         16         33         16         37         17%         0.02 [-0.5, 0.56]           Lim 2021         131         12         94         135         13         101         3.5%<
Crowley 2013         138         24         166         133         17         164         4,7%         0.24 [0.02, 0.46]           Davis 2010         128         37         85         131         34         80         3.2%         -0.08 [0.39, 0.22]           de Vasconcelos 2018         126         14         16         141         24         15         0.8%         -0.75 [-1.48, -0.02]           Eakin 2014         133         16         118         131         14         0.4         0.03 [0.23]           Hamo 2006         131         16         137         20         74         3.2%         -0.09 [0.39, 0.21]           Hub 2019         135         19         234         54         0.49         0.13 [0.12, 0.36]           Krein 2004         146         24         135         18         224         5.3%         -0.02 [0.15, 0.54]           Leichter 2013         135         16         37         1.7%         0.02 [0.15, 0.54]           Liou 2014         130         13         16         37         1.7%         0.12 [0.35, 0.59]           Linu 2014         130         13         16         13         135         14         2.1%         0.04 [0
Davis 2010         128         37         85         131         34         80         3.2%         -0.08 [0.39, 0.22]           de Vasconcelos 2018         126         14         16         141         24         15         0.8%         -0.75 [-1.48, 0.02]           Eakin 2014         133         16         118         131         15         131         4.0%         0.17 [-1.48, 0.02]           Hamo 2006         135         22         101         137         20         74         3.2%         -0.09 [-0.39, 0.21]           Holbrook 2009         131         16         224         135         18         221         5.3%         -0.23 [-0.42, -0.05]           Huo 2019         135         19         234         132         18         234         5.4%         0.21 [-0.5, 0.41]           Kempl 2017         136         17         7.7%         0.20 [-0.5, 0.54]
de Vasconcelos 2018       126       14       16       141       24       15       0.8%       -0.75 [-1.48, -0.02]         Eakin 2014       133       16       118       131       15       131       4.0%       -0.23 [-0.42, 0.05]         Harmo 2006       135       22       101       137       20       74       3.2%       -0.09 [-0.39, 0.21]         Holbrook 2009       131       16       224       135       18       221       5.3%       -0.23 [-0.42, 0.05]         Huo 2019       135       19       234       132       18       234       5.4%       0.16 [-0.02, 0.34]         Kempf 2017       136       17       77       133       12       56       2.7%       0.02 [-0.15, 0.54]         Leichter 2013       135       16       33       133       16       37       1.7%       0.12 [-0.35, 0.59]         Linu 2014       130       13       54       132       14       12       14       12       14       14         Voldelevoldevoldevolde       136       13       101       3.5%       -0.32 [-0.60, -0.04]
Eakin 2014         133         16         118         131         15         131         4.0%         0.031         (0.13         (0.12, 0.38)           Hamo 2006         135         22         101         137         20         74         3.2%         0.096         (0.39, 0.21)           Holbrook 2009         131         16         224         135         18         221         5.3%         -0.026         (0.39, 0.21)           Huo 2019         135         19         234         132         18         214         5.3%         -0.026         (0.39, 0.21)           Kempl 2017         136         17         77         133         12         56         2.7%         0.20         [0.45, 0.36]           Leichter 2013         135         16         31         133         16         37         1.7%         0.12         [0.35, 0.59]           Linz 0214         130         13         5         13         101         3.5%         -0.32         [0.60, 0.04]           Liou 2014         130         13         15         14         2.1%         -0.14<[-0.55, 0.26]
Halbro 2006     135     22     101     137     20     74     3.2%     -0.09 [0.39, 0.21]       Holbrook 2009     131     16     224     135     18     224     5.3%     -0.23 [0.42, 0.05]       Huo 2019     135     19     234     132     18     224     5.4%     0.16 [0.02, 0.34]       Kempf 2017     136     17     77     133     12     56     2.7%     0.20 [0.15, 0.54]       Krein 2004     146     24     106     144     22     103     3.7%     0.09 [-0.18, 0.36]       Leichter 2013     135     16     33     133     16     37     1.7%     0.12 [0.35, 0.59]       Lim 2021     131     12     94     135     101     3.5%     -0.32 [0.60, 0.04]       Liou 2014     130     13     54     132     15     41     2.1%     -0.24 [0.25, 0.25]       Ordnoletkova 2016     126     144     130     12     246     5.5%     -0.14 [-0.55, 0.26]       Quinn 2011a     134     25     23     133     20     19     1.1%     0.04 [-0.66, 0.667]       Quinn 2011c     128     19     1.4%     -0.26 [-0.77, 0.26]
Hua 2019     131     10     2.24     133     10     2.24     5.37     0.25     0.42     0.53       Hua 2019     135     19     2.24     132     18     0.16     [-0.02, 0.34]       Kenpl 2017     136     17     77     133     12     66     2.7%     0.02     [-0.15, 0.54]       Krein 2004     146     24     106     144     22     103     3.7%     0.09     [-0.18, 0.36]       Leichber 2013     135     16     33     133     16     37     1.7%     0.09     [-0.18, 0.36]       Lin 2021     131     12     94     135     13     101     3.5%     -0.32     [-0.60, -0.04]       Liou 2014     130     13     54     12     135     4.0%     -0.02     [-0.55, 0.26]       Ordnoletowa 2016     128     14     130     15     2.46     5.5%     -0.04     [-0.32, 0.04]       Quinn 2011a     134     25     23     133     20     19     1.1%     0.04     [-0.56, 0.65]       Quinn 2011b     134     16     22     133     20     19     1.4%     -0.26     [-0.77, 0.26]
Kempf 2017         138         17         77         133         12         56         2.7%         0.20 [-0.15, 0.54]           Krein 2004         146         24         106         144         22         103         3.7%         0.00 [-0.15, 0.54]           Leichter 2013         135         16         31         33         16         37         1.7%         0.12 [-0.55, 0.59]           Linz 2021         131         12         94         135         13         101         3.5%         -0.32 [-0.60, -0.04]           Linz 2014         130         13         45         132         141         -0.14 [-0.55, 0.26]
Krein 2004         146         24         106         144         22         103         3.7%         0.09 [-0.18, 0.36]           Leichter 2013         135         16         33         133         16         37         1.7%         0.12 [-0.35, 0.59]           Lim 2021         131         12         94         135         101         3.5%         0.32 [-0.60, 0.04]           Liou 2014         130         13         54         132         15         41         2.1%         -0.14 [-0.55, 0.26]           Nicolucci 2015         136         10         114         136         12         154         4.0%         0.00 [-0.25, 0.25]           Odnoletkova 2016         128         14         130         12         246         5.5%         0.14 [-0.56, 0.65]           Quinn 2011a         134         16         22         133         20         19         1.1%         0.04 [-0.56, 0.67]           Quinn 2011c         128         19         2         139         19         1.4%         -0.26 [-0.77, 0.26]
Leichter 2013         135         16         33         133         16         37         17%         0.12 [-0.35, 0.59]           Lim 2021         131         12         94         135         101         3.5%         -0.12 [-0.35, 0.59]           Lim 2021         131         12         94         135         101         3.5%         -0.12 [-0.55, 0.26]           Liou 2014         130         13         4         122         135         4.0%         0.00 [-0.25, 0.26]           Nicolucci 2015         136         10         114         136         12         125         4.0%         0.00 [-0.25, 0.26]           OdmieltKova 2016         128         14         2.1%         -0.14 [-0.56, 0.65]
Lim 2021         131         12         94         135         13         101         3.5%         -0.32 [-0.60, -0.04]           Liou 2014         130         13         54         132         15         41         2.1%         -0.14 [-0.55, 0.26]           Nicolucci 2015         136         10         135         24         2.1%         -0.04 [-0.55, 0.26]           Odnoletkova 2016         128         14         241         130         15         246         5.5%         -0.14 [-0.32, 0.04]           Quinn 2011a         134         16         22         133         20         19         1.1%         0.05 [-0.56, 0.67]           Quinn 2011c         128         16         21         13         20         19         1.1%         0.05 [-0.57, 0.26]
Liou 2014         130         13         54         132         15         41         2.1%         -0.14 [-0.55, 0.26]           Nicolucci 2015         136         10         114         136         12         135         4.0%         0.00 [-0.25, 0.26]           Odnoletkova 2016         128         14         214         130         15         246         5.5%         -0.14 [-0.32, 0.04]           Quinn 2011a         134         16         22         133         20         19         1.1%         0.06 [-0.56, 0.67]           Quinn 2011c         128         19         2         13         20         19         1.4%         -0.26 [-0.77, 0.26]
Nicolucci 2015         136         10         114         136         12         135         4.0%         0.00 [-0.25, 0.25]           Odnoletkova 2016         128         14         130         15         246         5.5%         -0.14 [-0.32, 0.04]           Quinn 2011a         134         25         23         133         20         19         1.1%         0.04 [-0.56, 0.65]           Quinn 2011b         134         16         22         133         20         19         1.1%         0.04 [-0.76, 0.65]           Quinn 2011c         128         19         62         133         20         19         1.4%         -0.26 [-0.77, 0.26]
Odnoletkova 2016         128         14         241         130         15         246         5.5%         -0.14 [-0.32, 0.04]           Quinn 2011a         134         25         23         133         20         19         1.1%         0.04 [-0.56, 0.65]           Quinn 2011b         134         16         22         133         20         19         1.1%         0.05 [-0.56, 0.67]           Quinn 2011c         128         19         62         133         20         19         1.4%         -0.26 [-0.77, 0.26]
Guinn 2011a         134         25         23         133         20         19         1.1%         0.04 [-0.56, 0.65]           Guinn 2011b         134         16         22         133         20         19         1.1%         0.05 [-0.56, 0.67]           Guinn 2011c         128         19         62         133         20         19         1.4%         -0.26 [-0.77, 0.26]
Quinn 2011b         134         16         22         133         20         19         1.1%         0.05 [-0.56, 0.67]           Quinn 2011c         128         19         62         133         20         19         1.4%         -0.26 [-0.77, 0.26]
Quinn 2011c 128 19 62 133 20 19 1.4% -0.26 [-0.77, 0.26]
Ramallo-Fanna 2020 128 16 375 130 17 471 6.6% -0.12[-0.26,0.02]
Shar 2019 132 20 320 120 0 220 3.37 *0.23 [0.42, -0.05]
Tano 2013 120 11 186 121 12 193 5.0% -0.09[0.29.011]
Varies 2014 132 14 35 138 14 36 17% -0.42 [0.89,0.05]
Vinitha 2019 124 8 112 128 12 106 3.7% -0.39[-0.66, -0.12]
Wild 2016 131 12 146 134 11 139 4.3% -0.26 [-0.49, -0.03]
Yoo 2009 133 16 57 134 14 54 2.4% -0.07 [-0.44, 0.31]
Zhou 2014 125 12 53 129 12 55 2.3% -0.33 [-0.71, 0.05]
Total (95% Cl) 3580 3726 100.0% -0.11 [-0.18, -0.04]
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 50.35, df = 28 (P = 0.006); l <sup>2</sup> = 44%
Test for overall effect: Z = 3.25 (P = 0.001) Favours [experimental] Favours [control]
R
Experimental Control Std. Mean Difference Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI iV, Random, 95% CI
Aytekin Kanadli 2016 82 10 44 82 9 44 2.3% 0.00 [-0.42, 0.42]
Blackberry 2013 76 9 221 77 11 219 5.9% -0.10 [-0.29, 0.09]
Bond 2007 70 7 31 73 7 31 1.7% -0.42 [-0.93, 0.08]
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.3, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 [-1.29, 0.15]
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 [-1.29, 0.15]           Eakin 2014         79         9         118         79         9         131         4.5%         0.00 [-0.25, 0.25]
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 [-1.29, 0.15]           Eakin 2014         79         9         131         4.5%         0.00 [-0.25, 0.25]
Bond 2007         70         7         31         73         7         31         17%         -0.42 [0.33, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [0.36, 0.26]           de Vasconcelos 2018         16         76         9         15         0.9%         -0.57 [-1.29, 0.15]           Eakin 2014         79         9         118         79         9         131         4.5%         0.00 [-0.25, 0.25]           Hamo 2006         79         11         10         82         137         74         3.6%         -0.02 [-0.55, 0.05]           Holtrook 2009         74         10         224         75         11         221         5 %         -0.09 [-0.28, 0.09]
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         6         76         9         15         0.9%         -0.57 [-1.29, 0.15]           Eakin 2014         79         9         118         79         9         131         4.5%         0.00 [-0.25, 0.25]           Harmo 2006         79         11         101         82         13         74         3.6%         -0.025 [-0.55, 0.05]           Holbrook 2009         74         10         224         75         11         221         5.9%         -0.09 [-0.28, 0.09]           Kempf 2017         80         10         77         79         9         56         3.0%         -0.01 [-0.24, 0.45]
Bond 2007         70         70         71         71         73         7         31         17.%         -0.042         0.93,0.081           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         -0.06,0.261           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57         -1.29,0.151           Eakin 2014         79         9         118         79         9         131         4.5%         0.00         -0.25,0.251           Harmo 2006         79         11         10         82         13         74         3.6%         -0.02         -0.25,0.251           Holbrook 2009         74         10         224         75         11         21         5.9%         -0.02         -0.28,0.091
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 [-1.20, 0.15]           Eakin 2014         79         9         118         79         9         131         4.5%         0.00 [-0.25, 0.25]           Harmo 2006         79         11         101         82         13         74         3.6%         -0.025 [-0.56, 0.05]           Holbrook 2009         74         10         224         75         11         221         5.9%         -0.09 [-0.28, 0.09]           Krein 2004         83         12         106         83         11         103         4.1%         0.00 [-0.27, 0.27]           Leichter 2013         79         73         77         37         19%         0.28 [-0.19, 0.75]           Linx 2021         79         8         94         84         101         3.8%         -0.02 [-0.21, 0.33]
Bond 2007         70         7         31         73         7         31         17%         -0.42         0.03, 0.08           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 </td
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 [-1.20, 0.15]           Eakin 2014         79         9         18         79         9         131         4.5%         0.00 [-0.25, 0.25]           Harmo 2006         79         11         101         82         13         74         3.6%         -0.25 [-0.55, 0.05]           Krein 2004         83         12         10         77         79         9         56         3.0%         0.10 [-0.24, 0.45]           Krein 2004         83         12         106         83         11         103         4.1%         0.00 [-0.27, 0.27]           Leichter 2013         79         7         33         77         7         19         0.28 [-0.19, 0.75]           Liou 2014         80         11         54         78         9         1.28         0.29 [-0.19, 0.75]           Liou 2014
Bond 2007         70         7         31         73         7         31         17%         -0.42         0.93         0.08           Davis 2010         70         20         85         71         20         80         3.5%         -0.05
Bond 2007         70         7         31         73         7         31         17%         -0.42 [0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [0.36, 0.26]           de Vasconcelos 2018         71         8         6         76         9         15         0.9%         -0.57 [-1.29, 0.15]           Eakin 2014         79         9         118         79         9         131         4.5%         -0.05 [-0.26, 0.25]           Hamo 2006         79         11         10         82         17         4.5%         0.00 [-0.25, 0.25]           Holbrook 2009         74         10         224         75         11         221         5.9%         -0.09 [-0.28, 0.09]           Krein 2004         83         12         106         83         11         103         4.1%         0.00 [-0.27, 0.27]           Lim 2021         79         8         94         84         81         101         3.8%         -0.62 [-0.91, -0.33]           Liou 2014         80         11         54         78         9         41         2.4%         0.19 [-0.21, 0.60]           Nicolucci
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 [-1.20, 0.15]           Eakin 2014         79         9         18         79         9         13         4.5%         0.00 [-0.25, 0.25]           Harno 2006         79         11         101         82         13         74         3.6%         -0.25 [-0.56, 0.05]           Hobrook 2009         74         10         224         75         11         221         5.9%         -0.08 [-0.28, 0.09]           Kempl 2017         80         10         77         79         9         56         3.0%         0.10 [-0.24, 0.45]
Bond 2007         70         7         31         73         7         31         17%         -0.42         0.93         0.08           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         -0.05         0.30         0.80           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         -0.05         0.26         0.25
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [-0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         16         76         9         131         4.5%         0.00 [-0.25, 0.25]           Hamo 2006         79         11         10         82         15         0.9%         -0.05 [-0.36, 0.26]           Hamo 2006         79         11         10         82         15         0.9%         -0.05 [-0.25, 0.25]           Hamo 2006         79         11         10         82         17         4.36%         0.00 [-0.27, 0.27]           Krein 2004         83         12         106         83         11         103         4.1%         0.00 [-0.27, 0.27]           Lichter 2013         79         7         33         77         7         37         19%         0.28 [-0.19, 0.73]           Liou 2014         80         11         54         78         9         41         2.4%         0.19 [-0.21, 0.60]           Nicoloucci 2015         80 <td< td=""></td<>
Bond 2007         70         7         31         73         7         31         17%         -0.42         0.93         0.08           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         0.03         0.08           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57         1.29         0.15           Hamo 2006         79         11         11         82         17         75         11         21         5.9%         -0.05         1.25         0.05           Holtrook 2009         74         10         224         75         11         221         5.9%         -0.02         1.055         0.05           Krein 2004         83         12         106         83         11         103         4.1%         0.00         1.02.70         2.27         1.03         1.03         1.03         1.03         1.03         1.03         1.03         1.03         1.04         1.03         1.04         1.04         1.03         1.03         1.03         1.03         0.01         0.02         0.02         0.02         1.03
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [0.33, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [-0.36, 0.26]           de Vasconcelos 2018         71         8         6         76         9         131         4.5%         0.00 [-0.25, 0.25]           Hamo 2006         79         11         10         82         74         3.6%         -0.02 [-0.55, 0.05]           Hamo 2006         74         10         224         75         11         221         5.9%         -0.09 [-0.28, 0.09]           Krein 2004         83         12         106         83         11         103         4.1%         0.00 [-0.27, 0.27]           Lichter 2013         79         7         33         77         7         37         19%         0.28 [-0.19, 0.75]           Lico 2014         80         11         54         78         9         41         2.4%         0.09 [-0.21, 0.60]           Nicolucci 2015         80         7         114         79         7         35         4.5%         0.01 [-0.21, 0.60]           Odnoletko
Bond 2007         70         7         31         73         7         31         17%         -0.42         0.93         0.08           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         -0.05         0.28         0.28         0.28         0.25         -0.05         0.26         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.25         0.05         0.00
Bond 2007         70         7         31         73         7         31         17%         -0.42         0.33         0.08           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         -0.05         0.33         0.08           de Vasconcelos 2018         71         8         6         76         9         15         0.9%         -0.57         1.29         0.15           Hamo 2006         79         11         10         82         74         3.6%         -0.025         0.55         0.65           Hamo 2006         74         10         224         75         11         21         5.9%         -0.025         0.55         0.65           Holbrook 2009         74         10         224         75         11         21         5.9%         -0.025         0.25         0.55         0.65           Krein 2004         83         12         106         83         11         103         4.1%         0.001         0.27         0.25         0.55         0.65           Lim 2021         79         8         9         41         2.4%         0.001         0.2
Bond 2007         70         7         31         73         7         31         1.7%         -0.42 [0.93, 0.08]           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 [0.36, 0.26]           de Vasconcelos 2018         71         8         6         76         9         15         0.9%         -0.05 [-1.20, 0.15]           Eakin 2014         79         9         118         79         9         131         4.5%         -0.05 [-0.55, 0.05]           Hamo 2006         79         11         101         82         75         11         221         5.9%         -0.09 [-0.28, 0.09]           Kemir 2017         80         10         77         79         9         56         3.0%         -0.10 [-0.24, 0.45]           Linc 2014         79         7         33         77         7         37         19%         0.28 [-0.19, 0.75]           Linu 2014         80         11         54         78         9         41         2.4%         0.19 [-0.21, 0.60]           Nicolucci 2015         80         71         17         9         13         19         1.2%         0.25 [-0.36, 0.86]
Bond 2007         70         7         31         73         7         31         17%         -0.42 (0.93, 0.08)           Davis 2010         70         20         85         71         20         80         3.5%         -0.05 (-0.36, 0.26)           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57 (-1.29, 0.15)           Eakin 2014         79         9         118         79         9         131         4.5%         0.00 (-0.25, 0.25)           Hamo 2006         74         10         224         75         11         221         5.9%         -0.02 (-0.25, 0.25)           Hobrook 2009         74         10         224         75         11         221         5.9%         -0.02 (-0.28, 0.09)           Krein 2004         83         12         106         83         11         103         4.1%         0.00 (-0.27, 0.27)           Lim 2021         79         8         9         41         2.4%         0.19 (-0.21, 0.60)
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Bond 2007         70         7         31         73         7         31         1.7%         -0.42         0.93         0.05           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         6.36         0.26           de Vasconcelos 2018         71         8         16         76         9         15         0.9%         -0.57         1.29         0.15           Eakin 2014         79         9         118         79         9         131         4.5%         0.00         1-0.25         0.25           Hame 2006         79         11         10         82         17         73         37         73         7         7         14         74         3.5%         -0.25         -0.55         0.05           Holbrook 2009         74         10         224         75         11         221         5.9%         -0.06         10-24         0.45         -0.55         0.05         -0.62         0.09
Bond 2007         70         7         31         73         7         31         1.7%         -0.42         0.43         0.05           Davis 2010         70         20         85         71         20         80         3.5%         -0.05         0.36.026           de Vasconcelos 2018         71         8         67         9         15         0.9%         -0.57         1.28         0.15           Eakin 2014         79         9         118         74         3.6%         -0.25         0.55         0.05           Hame 2006         79         11         10         224         75         11         221         5.9%         -0.09         10.24.045           Krein 2004         83         12         106         83         11         103         4.1%         0.00         10.24.045           Lim 2021         79         8         9         41         2.4%         0.019.021.021         -0.01         -0.01           Dicoluci 2015         80         77         137         1.9%         0.28 [-0.19.0.75]         -0.01         -0.01           Uim 2014         80         11         54         79         135         4.5%
Bond 2007 70 7 31 73 7 31 1.7% -0.42 [0.93,0.08] Davis 2010 70 20 85 71 20 80 3.5% -0.05 [0.36,0.26] de Vasconcelos 2018 71 8 16 76 9 15 0.9% -0.57 [-1.29,0.15] Eakin 2014 79 9 118 79 9 131 4.5% 0.00 [-0.25, 0.25] Hamo 2006 79 11 101 82 13 74 3.6% -0.25 [-0.55, 0.05] Holbrook 2009 74 10 224 75 11 221 5.9% -0.09 [-0.28, 0.09] Kempf 2017 80 10 77 79 9 56 3.0% 0.10 [-0.24, 0.45] Krein 2004 83 12 106 83 11 103 4.1% 0.00 [-0.27, 0.27] Leichter 2013 79 7 33 77 7 37 1.9% 0.28 [-0.19, 0.75] Lim 2021 79 8 9 44 84 81 101 3.8% -0.62 [-0.1, 0.33] Liou 2014 80 11 54 78 9 41 2.4% 0.19 [-0.21, 0.60] Nicolucci 2015 80 7 114 79 7 135 4.5% 0.14 [-0.11, 0.39] Odmoletkova 2016 75 9 224 76 11 9.246 6.1% -0.11 [-0.29, 0.07] Quinn 2011a 82 11 23 79 13 19 1.2% 0.028 [-0.33] Quinn 2011b 78 9 22 79 13 19 1.2% 0.028 [-0.33] Quinn 2011b 78 9 22 79 13 19 1.2% 0.028 [-0.0, 0.63] Quinn 2011b 78 9 22 79 13 19 1.2% 0.028 [-0.0, 0.63] Quinn 2011b 78 9 22 79 13 19 1.2% 0.028 [-0.0, 0.63] Quinn 2011b 78 9 35 80 9 36 1.9% -0.03 [-0.33, 0.05] Tang 2013 72 9 156 73 8 193 5.5% 0.12 [-0.33, 0.05] Varney 2014 77 9 35 80 9 36 1.9% -0.32 [-0.33] 0.00 [-0.7, 0.27] Wid 2016 76 9 146 78 9 139 4.8% -0.22 [-0.45, 0.01] Yoo 2009 80 9 57 62 8 54 2.7% -0.23 [-0.45, 0.01] Yon 2014 77 8 53 75 7 55 2.6% 0.26 [-0.11, 0.64] Total (95% C1) 3180 3328 100.0% -0.09 [-0.61, 0.02] Heterogeneity: Tau <sup>3</sup> = 0.01; Chi <sup>3</sup> = 46.29, df = 26 (P = 0.008); l <sup>3</sup> = 44%
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The generalizability of the findings of this meta-analysis need to consider the populations studied. These were mainly people with diabetes without a history of major adverse events but with poor risk factor control at entry (56–59). The findings may not be generalizable to populations where risk factors are already well controlled or those with a past history of diabetesrelated major adverse events (60). It is also likely that the not all populations are able to engage with remote delivery of healthcare (61, 62). While some RCTs provided participants with mobile phones, computers or internet services or training (43, 44, 51, 52), most did not. There appears to be a separation between those who have access to, and the ability to understand diverse technological resources, and those who do not ('the digital divide') (62). For many vulnerable populations such as older persons and those from low socioeconomic, very remote and low educational backgrounds and those with physical disability and/or visual or hearing impairment, remote interventions may not be suitable or readily available. Therefore, factors such as access to the internet of things and electronic devices, user friendliness and ease of navigation of medical technology are important considerations when designing remote interventions. For some populations and certainly for some aspects of medical management, in-person models of care such as home visits are essential and therefore entirely remotely delivered models of care are unsuitable (55). Subgroup analyses suggested that multiple components of the interventions contributed to the value of the remote management. This included patient education, monitoring of risk factors, coaching, remote consultations and pharmacological management for HbA1c and SBP. The components of patient education for TC and DBP, risk factor coaching for LDL-c, remote consultation for TC and DBP and pharmacological management for TC appeared to be less effective. Conclusions on this are however limited due to the integrated nature of all the interventions studied.

There were several limitations to this meta-analysis. First, an individual-level data analysis was not possible and thus it was not possible to analyse the effect of differing population characteristics and intervention types in detail. The interventions tested were heterogeneous and included multiple components. We sought to examine which components were more effective but since all interventions include more than one component, this analysis was incomplete. An intention to treat analysis was not possible due to loss to follow-up. Most funnel plots suggested a risk of publication bias and thus the effect of the interventions may have been overestimated. Due to lack of consistent data, we could not perform pooled analyses of planned secondary outcomes including quality of life, cost-effectiveness, micro-vascular outcomes, limb events or MACE. A cost-benefit analysis of using remote intervention compared to standard care remains an important area of future research. Lastly, the adherence to treatments were not reported in most studies and therefore we could not evaluate the impact of adherence on outcome. There were several strengths to our study including carefully planned analyses, the inclusion of RCTs which reported on all three risk factors of interest, extensive evaluation of risk of bias and the reporting of sensitivity and subgroup analyses to evaluate relationships between subgroups and individual studies and pooled outcomes.

## CONCLUSION

This meta-analysis suggests that remotely managing modifiable risk factors significantly lowers HbA1c, total cholesterol, LDLcholesterol, and systolic and diastolic blood pressure in people with diabetes. Patient coaching on risk factor management and the provision of pharmacological management were identified as the most effective interventions at improving risk factor control. Further research is needed to rigorously clarify the most effective components of remote management.

#### REFERENCES

- Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. *Clin J Am Soc Nephrol* (2017) 12:2032–45. doi: 10.2215/CJN.11491116
- Singh N, Armstrong DG, Lipsky BA. Preventing Foot Ulcers in Patients With Diabetes. JAMA (2005) 293:217–28. doi: 10.1001/jama.293.2.217
- Bonaca MP, Nault P, Giugliano RP, Keech AC, Pineda AL, Kanevsky E, et al. Low-Density Lipoprotein Cholesterol Lowering With Evolocumab and Outcomes in Patients With Peripheral Artery Disease: Insights From the FOURIER Trial (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk). *Circulation* (2018) 137:338–50. doi: 10.1161/CIRCULATIONAHA.117.032235

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**. Further inquiries can be directed to the corresponding author.

## **AUTHOR CONTRIBUTIONS**

MF conceived the research topic, conducted the search strategy, extracted the data, analyzed the data, and wrote the manuscript. LS extracted the data, cleaned the data, and reviewed the manuscript. AD conceived the research topic, conducted the search strategy, extracted the data, cleaned the data, and reviewed the manuscript. BC extracted the data, cleaned the data, and reviewed the manuscript. JG conceived the research topic, supervised the other authors in writing the manuscript, and reviewed the manuscript. JG is the guarantor of this work, and as such had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to the article and approved the submitted version.

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#### SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fendo.2022. 848695/full#supplementary-material

- Heart Protection Study Collaborative Group. Randomized Trial of the Effects of Cholesterol-Lowering With Simvastatin on Peripheral Vascular and Other Major Vascular Outcomes in 20,536 People With Peripheral Arterial Disease and Other High-Risk Conditions. J Vasc Surg (2007) 45:645–54. doi: 10.1016/j.jvs.2006.12.054
- Anand SS, Caron F, Eikelboom JW, Bosch J, Dyal L, Aboyans V, et al. Major Adverse Limb Events and Mortality in Patients With Peripheral Artery Disease: The COMPASS Trial. J Am Coll Cardiol (2018) 71:2306–15. doi: 10.1016/j.jacc.2018.03.008
- Golledge J, Ward NC, Watts GF. Lipid Management in People With Peripheral Artery Disease. Curr Opin Lipidol (2019) 30:470–6. doi: 10.1097/ MOL.000000000000638
- 7. Fernando ME, Seneviratne RM, Tan YM, Lazzarini PA, Sangla KS, Cunningham M, et al. Intensive Versus Conventional Glycaemic Control

for Treating Diabetic Foot Ulcers. Cochrane Database Syst Rev (2016) 1: CD010764. doi: 10.1002/14651858.CD010764.pub2

- Thomas Manapurathe D, Moxon JV, Krishna SM, Rowbotham S, Quigley F, Jenkins J, et al. Cohort Study Examining the Association Between Blood Pressure and Cardiovascular Events in Patients With Peripheral Artery Disease. J Am Heart Assoc (2019) 8:e010748. doi: 10.1161/JAHA.118.010748
- Coppola A, Sasso L, Bagnasco A, Giustina A, Gazzaruso C. The Role of Patient Education in the Prevention and Management of Type 2 Diabetes: An Overview. *Endocrine* (2016) 53:18–27. doi: 10.1007/s12020-015-0775-7
- Toledo FG, Triola A, Ruppert K, Siminerio LM. Telemedicine Consultations: An Alternative Model to Increase Access to Diabetes Specialist Care in Underserved Rural Communities. *JMIR Res Protoc* (2012) 1:e14. doi: 10.2196/resprot.2235
- McGill M, Blonde L, Chan JCN, Khunti K, Lavalle FJ, Bailey CJ, et al. The Interdisciplinary Team in Type 2 Diabetes Management: Challenges and Best Practice Solutions From Real-World Scenarios. J Clin Transl Endocrinol (2016) 7:21–7. doi: 10.1016/j.jcte.2016.12.001
- Espinoza P, Varela CA, Vargas IE, Ortega G, Silva PA, Boehmer KB, et al. The Burden of Treatment in People Living With Type 2 Diabetes: A Qualitative Study of Patients and Their Primary Care Clinicians. *PloS One* (2020) 15: e0241485. doi: 10.1371/journal.pone.0241485
- Song HJ, Dennis S, Levesque J-F, Harris MF. What Matters to People With Chronic Conditions When Accessing Care in Australian General Practice? A Qualitative Study of Patient, Carer, and Provider Perspectives. *BMC Fam Pract* (2019) 20:1–13. doi: 10.1186/s12875-019-0973-0
- Golledge J, Fernando M, Lazzarini P, Najafi B, Armstrong DG. The Potential Role of Sensors, Wearables and Telehealth in the Remote Management of Diabetes-Related Foot Disease. *Sensors* (2020) 20:4527. doi: 10.3390/ s20164527
- Drovandi A, Wong S, Seng L, Crowley B, Alahakoon C, Banwait J, et al. Remotely Delivered Monitoring and Management of Diabetes-Related Foot Disease: An Overview of Systematic Reviews. J Diabetes Sci Technol (2021) 19:19322968211012456. doi: 10.1177/19322968211012456
- Su D, Zhou J, Kelley MS, Michaud TL, Siahpush M, Kim J, et al. Does Telemedicine Improve Treatment Outcomes for Diabetes? A Meta-Analysis of Results From 55 Randomized Controlled Trials. *Diabetes Res Clin Pract* (2016) 116:136–48. doi: 10.1016/j.diabres.2016.04.019
- Timpel P, Oswald S, Schwarz PEH, Harst L. Mapping the Evidence on the Effectiveness of Telemedicine Interventions in Diabetes, Dyslipidemia, and Hypertension: An Umbrella Review of Systematic Reviews and Meta-Analyses. J Med Internet Res (2020) 22:e16791. doi: 10.2196/16791
- Wu C, Wu Z, Yang L, Zhu W, Zhang M, Zhu Q, et al. Evaluation of the Clinical Outcomes of Telehealth for Managing Diabetes: A PRISMA-Compliant Meta-Analysis. *Medicine* (2018) 97:e12962. doi: 10.1097/ MD.000000000012962
- Najafi B, Reeves ND, Armstrong DG. Leveraging Smart Technologies to Improve the Management of Diabetic Foot Ulcers and Extend Ulcer-Free Days in Remission. *Diabetes Metab Res Rev* (2020) 36(Suppl 1):e3239. doi: 10.1002/dmrr.3239
- Marcolino MS, Maia JX, Alkmim MB, Boersma E, Ribeiro AL. Telemedicine Application in the Care of Diabetes Patients: Systematic Review and Meta-Analysis. *PloS One* (2013) 8:e79246. doi: 10.1371/journal.pone.0079246
- Moher D, Liberati A, Tetzlaff J, Altman DG. Prisma Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PloS Med* (2009) 6:e1000097. doi: 10.1371/journal.pmed.1000097
- Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB
   A Revised Tool for Assessing Risk of Bias in Randomised Trials. *BMJ* (2019) 366:14898. doi: 10.1136/bmj.14898
- Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. Cochrane Handbook for Systematic Reviews of Interventions Version 6.2 (Updated February 2021) (2021) (Accessed 5th July 2021).
- 24. Takeshima N, Sozu T, Tajika A, Ogawa Y, Hayasaka Y, Furukawa TA. Which is More Generalizable, Powerful and Interpretable in Meta-Analyses, Mean Difference or Standardized Mean Difference? *BMC Med Res Methodol* (2014) 14(1):30. doi: 10.1186/1471-2288-14-30
- Higgins JP, Thompson SG. Quantifying Heterogeneity in a Meta-Analysis. Stat Med (2002) 21(11):1539–58. doi: 10.1002/sim.1186

- Sterne JA, Gavaghan D, Egger M. Publication and Related Bias in Meta-Analysis: Power of Statistical Tests and Prevalence in the Literature. J Clin Epidemiol (2000) 53(11):1119–29. doi: 10.1016/S0895-4356(00)00242-0
- Aytekin Kanadli K, Ovayolu N, Ovayolu O. Does Telephone Follow-Up and Education Affect Self-Care and Metabolic Control in Diabetic Patients? *Holist Nurs Pract* (2016) 30(2):70–7. doi: 10.1097/HNP.00000000000137
- 28. Blackberry ID, Furler JS, Best JD, Chondros P, Vale M, Walker C, et al. Effectiveness of General Practice Based, Practice Nurse Led Telephone Coaching on Glycaemic Control of Type 2 Diabetes: The Patient Engagement and Coaching for Health (PEACH) Pragmatic Cluster Randomised Controlled Trial. *BMJ* (2013) 347:f5272. doi: 10.1136/bmj.f5272
- Bond GE, Burr R, Wolf FM, Price M, McCurry SM, Teri L. The Effects of a Web-Based Intervention on the Physical Outcomes Associated With Diabetes Among Adults Age 60 and Older: A Randomized Trial. *Diabetes Technol Ther* (2007) 9(1):52–9. doi: 10.1089/dia.2006.0057
- 30. Crowley MJ, Powers BJ, Olsen MK, Grubber JM, Koropchak C, Rose CM, et al. The Cholesterol, Hypertension, and Glucose Education (CHANGE) Study: Results From a Randomized Controlled Trial in African Americans With Diabetes. Am Heart J (2013) 166(1):179–86. doi: 10.1016/ j.ahj.2013.04.004
- Davis RM, Hitch AD, Salaam MM, Herman WH, Zimmer-Galler IE, Mayer-Davis EJ. TeleHealth Improves Diabetes Self-Management in an Underserved Community: Diabetes TeleCare. *Diabetes Care* (2010) 33(8):1712–7. doi: 10.2337/dc09-1919
- 32. Eakin EG, Winkler EA, Dunstan DW, Healy GN, Owen N, Marshall AM, et al. Living Well With Diabetes: 24-Month Outcomes From a Randomized Trial of Telephone-Delivered Weight Loss and Physical Activity Intervention to Improve Glycemic Control. *Diabetes Care* (2014) 37(8):2177–85. doi: 10.2337/dc13-2427
- Harno K, Kauppinen-Mäkelin R , Syrjäläinen J. Managing Diabetes Care Using an Integrated Regional E-Health Approach. J Telemed Telecare (2006) 12(Suppl 1):13–5. doi: 10.1258/135763306777978380
- Holbrook A, Thabane L, Keshavjee K, Dolovich L, Bernstein B, Chan D, et al. Individualized Electronic Decision Support and Reminders to Improve Diabetes Care in the Community: COMPETE II Randomized Trial. CMAJ (2009) 181(1-2):37–44. doi: 10.1503/cmaj.081272
- 35. Huo X, Krumholz HM, Bai X, Spatz ES, Ding Q, Horak P, et al. Effects of Mobile Text Messaging on Glycemic Control in Patients With Coronary Heart Disease and Diabetes Mellitus: A Randomized Clinical Trial. *Circ Cardiovasc Qual Outcomes* (2019) 12(9):e005805. doi: 10.1161/ CIRCOUTCOMES.119.005805
- Kempf K, Altpeter B, Berger J, Reub O, Fuchs M, Schneider M, et al. Efficacy of the Telemedical Lifestyle Intervention Program TeLiPro in Advanced Stages of Type 2 Diabetes: A Randomized Controlled Trial. *Diabetes Care* (2017) 40 (7):863–71. doi: 10.2337/dc17-0303
- Krein SL, Klamerus ML, Vijan S, Lee JL, Fitzgerald JT, Pawlow A, et al. Case Management for Patients With Poorly Controlled Diabetes: A Randomized Trial. Am J Med (2004) 116(11):732–9. doi: 10.1016/j.amjmed.2003.11.028
- Leichter SB, Bowman K, Adkins RA, Jelsovsky Z. Impact of Remote Management of Diabetes via Computer: The 360 Study-a Proof-of-Concept Randomized Trial. Diabetes Technol Ther (2013) 15(5):434–8. doi: 10.1089/ dia.2012.0323
- 39. Lim SL, Ong KW, Johal J, Han CY, Yap QV, Chan YH, et al. Effect of a Smartphone App on Weight Change and Metabolic Outcomes in Asian Adults With Type 2 Diabetes: A Randomized Clinical Trial. JAMA Netw Open (2021) 4(6):e2112417–e. doi: 10.1001/jamanetworkopen.2021.12417
- Liou JK, Soon MS, Chen CH, Huang TF, Chen YP, Yeh YP, et al. Shared Care Combined With Telecare Improves Glycemic Control of Diabetic Patients in a Rural Underserved Community. *Telemed J E Health* (2014) 20(2):175–8. doi: 10.1089/tmj.2013.0037
- 41. Nicolucci A, Cercone S, Chiriatti A, Muscas F, Gensini G. A Randomized Trial on Home Telemonitoring for the Management of Metabolic and Cardiovascular Risk in Patients With Type 2 Diabetes. *Diabetes Technol Ther* (2015) 17(8):563–70. doi: 10.1089/dia.2014.0355
- Odnoletkova I, Goderis G, Nobels F, Fieuws S, Aertgeerts B, Annemans L, et al. Optimizing Diabetes Control in People With Type 2 Diabetes Through Nurse-Led Telecoaching. *Diabetes Med* (2016) 33(6):777–85. doi: 10.1111/dme.13092

- Quinn CC, Shardell MD, Terrin ML, Barr EA, Ballew SH, Gruber-Baldini AL. Cluster-Randomized Trial of a Mobile Phone Personalized Behavioral Intervention for Blood Glucose Control. *Diabetes Care* (2011) 34(9):1934– 42. doi: 10.2337/dc11-0366
- 44. Ramallo-Fariña Y, García-Bello MA, García-Pérez L, Boronat M, Wagner AM, Rodríguez-Rodríguez L, et al. Effectiveness of Internet-Based Multicomponent Interventions for Patients and Health Care Professionals to Improve Clinical Outcomes in Type 2 Diabetes Evaluated Through the INDICA Study: Multiarm Cluster Randomized Controlled Trial. *JMIR Mhealth Uhealth* (2020) 8(11):e18922. doi: 10.2196/18922
- Shahid M, Mahar S, Shaikh S, Shaikh Z-U-D. A Randomized Controlled Trial of Mobile Phone Intervention to Improve Diabetes Care in Rural Areas. *Endocr Pract* (2015) 25(3):166–71.
- 46. Shea S, Weinstock RS, Teresi JA, Palmas W, Starren J, Cimino JJ, et al. A Randomized Trial Comparing Telemedicine Case Management With Usual Care in Older, Ethnically Diverse, Medically Underserved Patients With Diabetes Mellitus: 5 Year Results of the IDEATel Study. J Am Med Inform Assoc (2009) 16(4):446–56. doi: 10.1197/jamia.M3157
- 47. Tang PC, Overhage JM, Chan AS, Brown NL, Aghighi B, Entwistle MP, et al. Online Disease Management of Diabetes: Engaging and Motivating Patients Online With Enhanced Resources-Diabetes (EMPOWER-D), a Randomized Controlled Trial. J Am Med Inform Assoc (2013) 20(3):526–34. doi: 10.1136/ amiajnl-2012-001263
- Varney JE, Weiland TJ, Inder WJ, Jelinek GA. Effect of Hospital-Based Telephone Coaching on Glycaemic Control and Adherence to Management Guidelines in Type 2 Diabetes, a Randomised Controlled Trial. *Intern Med J* (2014) 44(9):890–7. doi: 10.1111/imj.12515
- de Vasconcelos HCA, Lira Neto JCG, de Araujo MFM, Carvalho GCN, de Souza Teixeira CR, de Freitas RWJF, et al. Telecoaching Programme for Type 2 Diabetes Control: A Randomised Clinical Trial. *Br J Nurs* (2018) 27 (19):1115–20. doi: 10.12968/bjon.2018.27.19.1115
- 50. Vinitha R, Nanditha A, Snehalatha C, Satheesh K, Susairaj P, Raghavan A, et al. Effectiveness of Mobile Phone Text Messaging in Improving Glycaemic Control Among Persons With Newly Detected Type 2 Diabetes. *Diabetes Res Clin Pract* (2019) 158:107919. doi: 10.1016/j.diabres.2019.107919
- Wild SH, Hanley J, Lewis SC, McKnight JA, McCloughan LB, Padfield PL, et al. Supported Telemonitoring and Glycemic Control in People With Type 2 Diabetes: The Telescot Diabetes Pragmatic Multicenter Randomized Controlled Trial. *PloS Med* (2016) 13(7):e1002098. doi: 10.1371/ journal.pmed.1002098
- Yoo HJ, Park MS, Kim TN, Yang GJ, Cho TG, Hwang SH, et al. A Ubiquitous Chronic Disease Care System Using Cellular Phones and the Internet. *Diabetes Med* (2009) 26(6):628–35. doi: 10.1111/j.1464-5491.2009.02732.x
- Zhou P, Xu L, Liu X, Huang J, Xu W, Chen W. Web-Based Telemedicine for Management of Type 2 Diabetes Through Glucose Uploads: A Randomized Controlled Trial. *Int J Clin Exp Pathol* (2014) 7(12):8848–54.
- 54. Zoungas S, Chalmers J, Ninomiya T, Li Q, Cooper ME, Colagiuri S, et al. Association of HbA1c Levels With Vascular Complications and Death in Patients With Type 2 Diabetes: Evidence of Glycaemic Thresholds. *Diabetologia* (2012) 55:636–43. doi: 10.1007/s00125-011-2404-1

- 55. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). *Eur Heart J* (2020) 41 (1):111–88. doi: 10.1093/eurheartj/ehz455
- Chou R, Dana T, Blazina I, Daeges M, Jeanne TL. Statins for Prevention of Cardiovascular Disease in Adults: Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA* (2016) 316(19):2008–24. doi: 10.1001/jama.2015.15629
- Palmer SC, Tendal B, Mustafa RA, Vandvik PO, Li S, Hao Q, et al. Sodium-Glucose Cotransporter Protein-2 (SGLT-2) Inhibitors and Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists for Type 2 Diabetes: Systematic Review and Network Meta-Analysis of Randomised Controlled Trials. *BMJ* (2021) 372:m4573. doi: 10.1136/bmj.m4573
- Emdin CA, Rahimi K, Neal B, Callender T, Perkovic V, Patel A. Blood Pressure Lowering in Type 2 Diabetes: A Systematic Review and Meta-Analysis. JAMA (2015) 313(6):603–15. doi: 10.1001/jama.2014.18574
- 59. Verma S, Bain SC, Buse JB, Idorn T, Rasmussen S, Orsted DD, et al. Occurence of First and Recurrent Major Adverse Cardiovascular Events With Liraglutide Treatment Among Patients With Type 2 Diabetes and High Risk of Cardiovascular Events: A *Post Hoc* Analysis of a Randomized Clinical Trial. *JAMA Cardiol* (2019) 4(12):1214–20. doi: 10.1001/jamacardio. 2019.3080
- 60. Standards of Medical Care in Diabetes-2017: Summary of Revisions. *Diabetes Care* (2017) 40(Suppl 1):S4–5. doi: 10.2337/dc17-S003
- Lam K, Lu AD, Shi Y, Covinsky KE. Assessing Telemedicine Unreadiness Among Older Adults in the United States During the COVID-19 Pandemic. *JAMA Intern Med* (2020) 180(10):1389–91. doi: 10.1001/jamainternmed. 2020.2671
- Wilson J, Heinsch M, Betts D, Booth D, Kay-Lambkin F. Barriers and Facilitators to the Use of E-Health by Older Adults: A Scoping Review. BMC Public Health (2021) 21(1):1556. doi: 10.1186/s12889-021-11623-w

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