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Digital Health Interventions for the Prevention of Cardiovascular Disease: A Systematic Review and Meta-Analysis

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Abstract

Objective—To assess the potential benefit of digital health interventions (DHI) on cardiovascular disease outcomes (CVD events, all-cause mortality, hospitalizations) and risk factors compared to non-DHI interventions.

Patients and Methods—We conducted a systematic search of PubMed, MEDLINE, EMBASE, Web of Science, OVID, CINHAL, ERIC, PsychInfo, Cochrane, and CENTRAL from January 1, 1990 and January 21, 2014. Included studies examined any element of DHI (telemedicine, webbased strategies, email, mobile phones, mobile applications, text messaging, and monitoring sensors) and CVD outcomes or risk factors. Two reviewers independently evaluated study quality utilizing a modified version of the Cochrane Collaboration risk assessment tool. Authors extracted CVD outcomes and risk factors for CVD such as weight, BMI, blood pressure, and lipids from 51 full-text articles that met validity and inclusion criteria.

Results—DHI significantly reduced CVD outcomes (RR=0.61, (95% CI, 0.45–0.83), P=.002; $I^2=22\%$). Concomitant reductions in weight (-3.35 lbs, (95% CI, -6.08 lbs, -1.01 lbs); P=.006; $I^2=96\%$) and BMI (-0.59 kg/m², (95% CI, -1.15 kg/m², -0.03 kg/m²); P=.04; $I^2=94\%$) but not blood pressure (+4.95 mmHg, (95% CI, -4.5 mmHg, 14.4 mmHg); P=.30; $I^2=100\%$) were found in these DHI trials compared to usual care. Framingham 10 year risk percentages were also significantly improved (-1.24%; 95% CI -1.73%, -0.76%; n=6; P<0.001; $I^2=94\%$). Results were

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limited by heterogeneity not fully explained by study population (primary or secondary prevention) or DHI modality.

Conclusions—Overall, these aggregations of data provide evidence that DHI can reduce CVD outcomes and have a positive impact on risk factors for CVD.

Keywords

cardiovascular disease; outcomes; digital health; mobile health; prevention; weight loss; MACE

Introduction

Cardiovascular disease (CVD) is the primary cause for morbidity and mortality, and is associated with markedly rising health care costs in the United States ¹. Approximately one in three deaths can be attributed to CVD ^{1,2}, and over 90% of CVD morbidity and mortality to preventable risk factors ³. According to 2012 statistics, poor diet, smoking, and lack of physical activity continue to account for an overwhelming majority of CVD and death ⁴ with the cost of CVD to the US approaching \$200 billion per year ¹. What is more, the average hospitalization for acute coronary syndrome (ACS) is estimated to cost roughly \$20,000 with repeat events costing up to two and three times the original amount ⁵. Clearly, better interventions to improve CVD prevention, both primary and secondary, are needed.

Internet and smart phone use has grown exponentially in the past decade, opening up the possibility that these increasingly prevalent technological tools could improve health. Digital health interventions (DHI), including such modalities as telemedicine, web-based strategies, email, mobile phones, mobile applications, text messaging, and monitoring sensors, are the most recent iteration of an effort to shift health care burden outside of the walls of medical institutions, and improve individualized care through positive behavior change theory ⁶. Although prior studies have suggested benefits of DHI in focused areas such as smoking cessation ⁷, behavior patterns ⁸, physical activity ⁹, HbA1c ¹⁰, blood pressure ¹¹, and weight loss ¹², evidence concerning the benefit of DHI on CVD risk factors, let alone CVD outcomes such as CVD events, hospitalizations, and all-cause mortality, is lacking. With nearly 50,000 healthcare related apps now available for download ¹³, and numerous internet-based DHI solutions available, the benefit of DHI on CVD prevention and outcomes, both primary and secondary, merits reexamination.

The purpose of this systematic review and meta-analysis was to inclusively review randomized controlled trials (RCTs) and cohort studies incorporating DHI for the prevention of CVD outcomes (CVD events including myocardial infarction, stroke, revascularization, hospitalizations, and all-cause mortality) and modification of risk factors for CVD such as weight, BMI, blood pressure, cholesterol, glucose, and Framingham Risk Scores (FRS). We aim to establish the potential benefit of DHI on both primary and secondary CVD prevention, and identify future needs in DHI and CVD research.

Methods

Data Sources and Searches

This systematic review was conducted in accordance with PRISMA guidelines ¹⁴. We included all RCTs and observational/cohort studies published between January 1, 1990 and January 21, 2014 that examined any element of DHI (telemedicine, web-based strategies, email, mobile phones, mobile applications, text messaging, and monitoring sensors) and impact on CVD. We intentionally and broadly included any studies of adult patients seeking CVD prevention to present a comprehensive overview of DHI studies analyzing CVD outcomes (CVD events, hospitalizations, or all-cause mortality) and modification of risk factors for CVD such as weight, BMI, blood pressure, cholesterol, glucose, and FRS regardless of type of healthcare provider or healthcare setting. Control interventions included usual care following standard guidelines, and could involve non-DHI intervention (such as paper instructions or telephone calls) or no active intervention beyond usual care. We excluded studies in which the intervention lasted less than a month in order to assess long-term impact and sustainability, studies that did not report any CVD risk factors, redundant studies which were repeated in the literature without new data presented, protocol manuscripts, reviews, studies only including usability or adherence data, pediatric studies, and studies where the intervention involved the healthcare provider, rather than the patient.

Our search strategy was performed with the assistance of a medical librarian, and included the databases PubMed, MEDLINE, EMBASE, Web of Science, OVID, CINAHL, ERIC, PsychInfo, Cochrane, and CENTRAL over the specified dates. We included the search terms mobile health, mobile, mhealth, digital health, eHealth, internet, telemedicine, web, smartphone, cardiovascular, cardiac, prevention, outcomes, mortality, morbidity, event, Framingham, blood pressure, weight, BMI, waist circumference, glucose, lipids, cholesterol, smoking, tobacco, quality of life, emergency department, visits, hospitalizations, rehospitalizations, office visits, phone calls, cost, cost of care, and ROI. This strategy identified 574 relevant abstracts with an additional 14 references identified through bibliography searches and personal contacts (Figure 1). Most articles were in English, and those in Spanish, Polish, and German were translated for review.

Study Selection

Two reviewers (RJW and NMC) assessed each of the identified abstracts. Full text versions of potentially eligible studies, categorized for inclusion by either reviewer, were requested (n=73). The two reviewers worked independently to evaluate the full text reports for study inclusion and disagreements were reconciled by consensus. Agreement on study inclusion was high, with kappa = 0.92.

Data Extraction and Quality Assessment

Extracted data included study participant demographics (age, gender, prior internet use, education level, socioeconomic status, race, comorbidities, and baseline markers of CVD), the DHI they received (frequency, type, and duration), and the control intervention. DHIs were identified as involving telemedicine, web-based strategies, email, mobile phones, mobile applications, SMS text messaging, and monitoring sensors. Control comparisons

were heterogeneous and could include a non-DHI intervention or usual care. CVD outcomes included CVD events including myocardial infarction, stroke, or revascularization, hospitalizations, and all-cause mortality. Risk factors for CVD included weight, BMI, blood pressure, cholesterol, (total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides), glucose, and FRS.

Risk of bias and methodological quality was assessed independently by two authors (RJW and CSC) using a modified version of the Cochrane Collaboration risk assessment tool ¹⁵ (Supplementary Figure 1). To evaluate the quality of non-randomized studies, we assessed blinding of the outcome assessors to arm assignment in relation to the outcomes of CVD outcomes and CVD surrogates, comparability of outcome assessment, and completeness of follow-up. The latter criteria followed a revised Newscastle–Ottawa quality assessment tool for observational studies¹⁶ (Supplementary Figure 1) which emphasized proper definition of the CVD pertinent to the study, legitimate DHI intervention, and reasonable follow up. One study (Nolan, 2012) was considered an observational study as the randomization scheme was compromised due to unintentional cross-over of the participants forcing the authors to report the data in separate, non-randomized cohorts. Finally, a study by Wister et al ¹⁷ allowed separation of studies for primary and secondary prevention.

Data Synthesis and Analysis

When possible, we generated meta-analytic estimates of treatment effect using pooled relative risks and random-effects models. Analyses were performed using RevMan v.5.2 (The Cochrane Collaboration; Oxford, UK). We measured heterogeneity for each outcome across studies using the I² test ¹⁸. When standard deviations were missing for a study, imputation of the mean standard deviation of the group for that particular variable was utilized in no more than two values per variable. Imputation of more than two standard deviations was not required for any analysis.

To explore causes of inconsistency in study findings and subgroup-treatment interactions, we planned subgroup analyses comparing results by patient population (primary prevention versus secondary prevention) and DHI subtype (telemedicine, web-based, email reminders, SMS texting, mobile application, and data monitoring). Random effects methods utilizing Mantel-Haenszel methods for combining results across studies were undertaken as part of the RevMan 5.2 software package ¹⁸. Sensitivity analyses controlling for workplace versus healthcare delivered DHI were performed as were sensitivity analyses removing the two observational, non-randomized studies.

We contacted all authors with a prepopulated form including data for verification and missing data for their completion. Of the original 49 authors contacted, 28 returned correspondence with either verification of reported data, or the addition of missing or incomplete data. There was no impact of the funding source on the design, execution, or analysis of the study.

Results

Fifty-one studies met criteria for full-text review and were included in the systematic review with nine studies providing analyzable CVD outcome data. A summary table of studies reporting CVD outcomes is presented in Table 1. Risk of bias among studies reporting CVD outcomes was predominantly low apart from a consistent lack of participant blinding (Table 2) with a funnel plot included (Supplementary Figure 2).

Thirty-nine studies focused on primary CVD prevention (Supplementary Table 1A) and 13 studies primarily involved secondary CVD prevention (Supplementary Table 1B) (one study fit into both categories separately). The total number of patients included was 23,962, with 13,618 assigned to DHI and 10,344 to control groups. Mean age (SD) for all of the participants in the studies was 54.0 (9.4) years with a majority of the participants being Caucasian and 54% male. Five studies evaluated a solely female population, and two focused only on male participants. Socioeconomic status, geographical information, and prior internet usage were not universally reported. Additionally, the timeframe of a majority of studies was between 6 and 12 months, and most studies were published within the past decade. RCTs were blinded with specific mention of study personnel blinded to allocation and grouping during the study and to data analysis, with the exception of three studies ^{19–21}.

CVD outcomes including myocardial infarction, stroke, revascularization, hospitalizations, and all-cause mortality were abstracted from 9 RCTs (2 primary prevention studies, 2 involving patients with heart failure (HF), and 5 secondary prevention studies). The 1267 participants in the DHI arms had 104 events, and the 996 participants in the usual care arms had 162 combined events. Overall, DHI significantly reduced CVD outcomes (RR=0.61, (95% CI, 0.46–0.80); P<0.001; I²=22%; Figure 2). Subgroup analyses showed no interaction between the primary prevention (no prior CVD diagnosis), secondary prevention (known prior CVD diagnosis), and HF groups (P=.11). When the outcome "hospitalizations" was removed from the combined endpoint there remained a 52% reduction in CVD events/deaths that was not statistically significant (RR=0.48, (95% CI, 0.21–1.11); p=0.09). In addition, DHI was associated with a significant reduction in Framingham 10 year risk percentages in the 6 studies reporting FRS data (-1.24%; 95% CI -1.73%, -0.76%; P<0.001; I²=94%).

The effect of DHI in Primary Prevention Studies

Separate subgroup analyses of primary prevention studies (n=2) were unable to provide statistical evidence of a positive effect on CVD outcomes (RR=1.21, (95% CI, 0.58–2.54); P=.61; I²=15%; Figure 2). Eleven primary prevention studies showed a significant reduction in weight (-3.35 lbs (95% CI –5.22 lbs, -1.48 lbs), P<0.001, I²=96%; Figure 3a), but not BMI (n=15) (mean difference = -0.11 kg/m^2 , (95% CI, -0.30 kg/m^2 , 0.08 kg/m²); P=.26; I²=98%; Figure 3b). When the three workplace intervention studies were removed from the pooled analysis, there was a significant reduction in BMI in primary prevention populations (n=12), (mean difference = -0.29 kg/m^2 , (95% CI, -0.5 kg/m^2 , -0.09 kg/m^2); P=.006; I²=98%). We found a significant reduction in systolic blood pressure (SBP) among primary prevention studies (n=23), (mean difference = -2.12 mmHg, (95% CI, -4.15 mmHg, -0.09 mmHg); P=.04; I²=100%; Supplementary Figure 3) which failed to maintain a statistically

significant reduction when two observational studies were removed in sensitivity analysis (mean difference = -1.31 mmHg, (95% CI, -3.43 mmHg, 0.80 mmHg); P=.22; I²=100%).

There was insufficient evidence to show a positive impact on triglyceride levels (n=7) (mean difference = -9.06 mg/dL, (95% CI, -22.7 mg/dL, 4.6 mg/dL); P=.19; I²=99%); however, we found significant reductions in total cholesterol (n=13) (mean difference = -5.39 mg/dL, (95% CI, -9.80 mg/dL, -0.99 mg/dL); P=.02; I²=98%; Supplementary Figure 4a), LDL cholesterol (n=8) (mean difference = -4.96 mg/dL, (95% CI, -8.54 mg/dL, -1.38 mg/dL); P=.007; I²=95%; Supplementary Figure 4b), and glucose (n=6) (mean difference = -1.38 mg/dL, (95% CI, -2.13 mg/dL, -0.63 mg/dL); P<0.001; I²=81%) in primary prevention populations.

The effect of DHI in Secondary Prevention Studies

Subgroup analyses of secondary prevention studies showed significant impact of DHI on CVD outcomes (RR=0.60, (95% CI, 0.43–0.83); P=.002; I²=0%; Figure 2). Pooled data from four secondary prevention trials demonstrated no improvement in weight (–0.93 lbs (95% CI –7.74 lbs, 5.88 lbs), P=.79, I²=97%; Figure 3a), but did show significant reductions in BMI (n=6) (mean difference = -0.31 kg/m^2 , (95% CI, -0.60 kg/m^2 , -0.03 kg/m^2); P=.03; I²=67%; Figure 3b). We found no improvement in SBP in secondary prevention DHI trials (mean difference = 1.98 mmHg, (95% CI, -1.05 mmHg, 5.01 mmHg); P=.20; I²=94%; Supplementary Figure 3).

Similarly, there was no positive impact on triglyceride levels (n=5) (mean difference = -17.19 mg/dL, (95% CI, -49.45 mg/dL, 15.07 mg/dL); P=.30; I²=99%), total cholesterol (n=6) (mean difference = -1.80 mg/dL, (95% CI, -6.23 mg/dL, 2.64 mg/dL); P=.43; I²=94%; Supplementary Figure 4a), LDL cholesterol (n=5) (mean difference = -10.43 mg/dL, (95% CI, -21.69 mg/dL, 0.83 mg/dL); P=.07; I²=100%; Supplementary Figure 4b), or glucose (n=4) (mean difference = 0.45 mg/dL, (95% CI, -9.68 mg/dL, 10.58 mg/dL); P=. 93; I²=100%) in secondary prevention populations.

The impact of various DHI modalities on risk factors for CVD

When we evaluated individual DHI modalities and their effects on risk factors for CVD, we found significant reductions in weight in studies which incorporated three modalities including web-based (-3.18 lbs (95%CI -5.61 lbs, -0.75 lbs), P=.01; I²=98%; Figure 4A), telemedicine (-2.30 lbs (95%CI -2.47 lbs, -2.14 lbs), P<0.001; I²=0%; Figure 4B), and SMS text (-3.85 lbs (95%CI -5.54 lbs, -2.17 lbs), P<0.001; I²=83%; Figure 4C) with email interventions showing no significant reduction in weight (0.74 lbs (95%CI -1.19 lbs, 2.68 lbs), P=.45; I²=0%; Figure 4D). Web-based modalities also had a beneficial impact on SBP (-2.63 mmHg, 95% CI -5.04 mmHg, -0.23 mmHg; p=0.03 I²=100%). Studies that incorporated data monitoring (n=5) reported no weight outcomes, and showed a significant benefit only in reducing diastolic blood pressure (-3.08 mmHg, 95% CI -4.8 mmHg, -1.36 mmHg; P<0.001; I²=0%).

Discussion

This systematic review and meta-analysis demonstrates that digital health has a beneficial effect on CVD risk factors and outcomes. Applying an inclusive definition of DHI broadly applied to studies ranging from two to 36 months, we found a CVD morbidity and all-cause mortality benefit for secondary CVD prevention and heart failure groups, with primary prevention populations showing benefit with regard to weight loss, BMI, SBP, total cholesterol, and LDL cholesterol. However, there was no clear benefit of DHI in primary prevention populations for CVD outcomes, although a reduction in Framingham risk scores was seen in our pooled analyses. In subgroup analysis by DHI subtype, there was particular benefit seen for web-based, telemedicine, and SMS texting DHI approaches, with insufficient data to support a benefit for email DHI.

As noted previously, prior literature on DHI and CVD-related outcomes has been limited. A recent systematic review of PubMed for mobile health and secondary CVD prevention over the prior ten years identified three studies without any quantitative results ²². Other systematic reviews have shown the efficacy of DHI on certain specific risk factors for CVD. Whittaker et al ⁷ showed improvements in smoking cessation across a wide variety of studies. Furthermore, additional work has shown DHI to positively affect behavior patterns ⁸ and physical activity ⁹. Liang et al ¹⁰ showed reductions of nearly 0.5% in HbA1c in 22 studies evaluating mobile phone program or text messaging tactics on participants with diabetes. Uhlig et al showed a favorable change in blood pressure at six months in 26 separate meta-analysis of 36 weight loss studies found that 71% of the studies reported some form of weight loss, although participant and intervention heterogeneity precluded a summary estimate of weight loss achieved through DHI ¹².

In this systematic review and meta-analysis, we note a nearly 40% relative risk reduction in CVD outcomes with DHI, with particular impact on secondary CVD prevention and in patients with heart failure. This level of risk reduction surpasses other prevalent, guideline-based preventative measures such as statins ²³, aspirin ²⁴, or blood pressure reduction with beta-blockade ²⁵. Furthermore, the absolute risk reduction in events was 6.5% in our pooled analysis and 7.5% in secondary prevention populations. This translates into a number needed to treat of 14 and 16 patients, respectively, also surpassing reported absolute benefits of other guideline-based measures. As DHI use does not directly reduce CVD risk, these observed benefits likely reflect increased adherence to evidence-based preventative therapies such as statins, aspirin, or beta-blockers.

We found significant improvements in the risk factors of weight loss, BMI, blood pressure, and LDL-cholesterol in patients seeking primary prevention of CVD. These improvements in risk factors did not translate into an improvement in CVD outcomes in primary prevention studies, at least partly owing to lower risk populations and lack of long-term follow up. Conversely, we found significant reductions in these events in secondary prevention studies despite a lack of consistent reductions in CVD risk factors in secondary prevention studies. This heterogeneity in results is not readily explained by existing studies,

and should prompt future DHI research focusing on furthering our understanding of the variables determining success of specific DHI in specific populations.

Limitations

In an attempt to be inclusive in assessing the impact of DHI on CVD, we collected data utilizing multiple DHI modalities applied in multiple populations. Therefore, as noted previously heterogeneity in study results was present secondary to variation in study populations, DHI types, comparator groups, and lengths of follow up. Heterogeneity in these analyses was not explained by DHI modality or study design. Despite this heterogeneity, the data demonstrate an overall benefit of DHI for CVD prevention. However, the observed level of heterogeneity precludes definitive conclusions regarding specific DHIs that should be clinically applied to CVD prevention at the present time.

In addition, this analysis was unable to assess behavior change and motivational techniques, either of which could impact the outcomes of trials or be a contributor to DHI efficacy. Research attempting to better assess these issues will be vital in future work. Despite these limitations, the existing studies confirm that technological advances such as DHI can have a positive impact on preventative cardiovascular medicine.

Conclusion

The data synthesized and analyzed in this systematic review show a net benefit of DHI on overall CVD outcomes (CVD events, hospitalizations, and all-cause mortality) compared to usual care. These gains are largely driven by improvements in CVD outcomes among higher risk populations such as patients with HF or those targeting secondary CVD prevention. DHI were also associated with improvement in risk factors for CVD in primary studies, suggesting the potential for positive impact of DHI in a wide variety of participants and settings. Further research is needed to determine the most effective DHI modalities and to better understand the determinants of their success in specific cardiovascular risk populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ACS	Acute Coronary Syndrome
BMI	Body Mass Index
CVD	Cardiovascular Disease
DHI	Digital Health Intervention
FRS	Framingham Risk Score
HF	Heart Failure
RCT	Randomized Controlled Trial
ROI	Return on Investment

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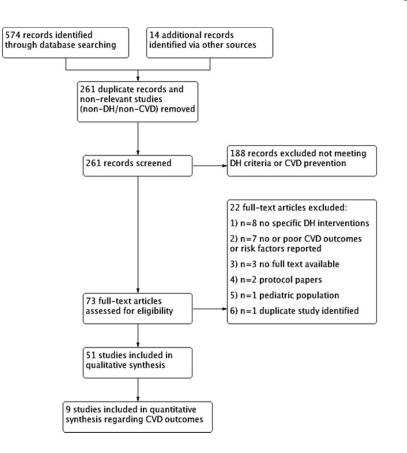


Figure 1. PRISMA schematic for study selection.

	Digital H		Usual			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.2 Primary Preven							
Appel 2011	15	139	15	138	12.8%	0.99 [0.51, 1.95]	
Green 2008	10	520	2	258	3.2%	2.48 [0.55, 11.24]	
Subtotal (95% CI)		659		396	16.0%	1.21 [0.58, 2.54]	
Total events	25		17				
Heterogeneity: Tau ² =				(P = 0.1)	$(28); I^2 =$	15%	
Test for overall effect	Z = 0.51	P = 0.6	1)				
1.1.3 Secondary Prev	ention						
Blasco 2012	3	102	8	101	4.2%	0.37 [0.10, 1.36]	
Frederix 2013	4	40	9	40	5.7%	0.44 [0.15, 1.33]	
Reid 2012	4	115	9	108	5.3%	0.42 [0.13, 1.32]	
Southard 2003	2	53	8	51	3.2%	0.24 [0.05, 1.08]	
Vernooij 2012	32	164	45	166	25.6%	0.72 [0.48, 1.07]	
Subtotal (95% CI)		474		466	44.0%	0.60 [0.43, 0.83]	◆
Total events	45		79				
Heterogeneity: Tau ² =				(P = 0.4)	49); $I^2 = 0$	0%	
Test for overall effect	Z = 3.04	P = 0.0	02)				
1.1.4 Heart Failure							
Dendale 2012	23	80	48	80	26.3%	0.48 [0.32, 0.71]	
Scherr 2009	11	54	18	54	13.7%	0.61 [0.32, 1.17]	
Subtotal (95% CI)		134		134	40.0%	0.51 [0.37, 0.71]	◆
Total events	34		66				
Heterogeneity: Tau ² =				(P = 0.)	$(53); I^2 = 0$	0%	
Test for overall effect	Z = 3.95	P < 0.0	001)				
Total (95% CI)		1267		996	100.0%	0.61 [0.46, 0.80]	•
Total events	104		162				
Heterogeneity: Tau ² =	0.04; Chi ²	= 10.2	3, df = 8	8 (P = 0)	.25); I ² =	22%	0.05 0.2 1 5 20
Test for overall effect	Z = 3.52	P = 0.0	004)				Favours [Digital Health] Favours [Usual Care]
Test for subgroup diff	ferences: Cl	$hi^2 = 4.3$	35. df =	2 (P = 0)	$(0.11), ^2 =$	= 54.0%	ravous (orgital realting ravours (osual care)

Figure 2. CVD Outcomes and DHI.

A	Digit		leb.			~		Maan Difference	Moon Difference
Study or Subgroup	Digit Mean	al Hea SD	lth Total		ual Car SD		Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
1.6.1 Primary Prevent		30	Total	Mean	30	Total	Height	IV, Rahuolii, 35% CI	iv, kandolii, 95% er
Andersen 2013	-0.53	4.3	106	-1.4	7	54	7.2%	0.87 [-1.17, 2.91]	
Appel 2011	-10.1	2.4	139	-1.8	3.8	138		-8.30 [-9.05, -7.55]	-
Bennett 2010	-5.1	7.1	51	0.62	4	50		-5.72 [-7.96, -3.48]	
Bennett 2012	-3	0.8	180	-0.7	0.8	185		-2.30 [-2.46, -2.14]	
Bennett 2013	-2.2		97		10.67	97		-3.30 [-6.28, -0.32]	
Bove 2013	-0.8		120	2.4	22.6	121	4.9%	-3.20 [-8.11, 1.71]	
Dekkers 2011	-7.7	4.7	93	-5.5	3.5	92		-2.20 [-3.39, -1.01]	
Lombard 2010	-0.4	2.6	127	1.8	8.8	123	7.5%	-2.20 [-3.82, -0.58]	_ —
Park 2012	-4.4	3.7	42	1.5	2	37	7.7%	-5.90 [-7.19, -4.61]	I
Senesael 2013	-1.5	12.7	26	-1.1	9.6	26	4.0%	-0.40 [-6.52, 5.72]	
Wong 2013 Subtotal (95% CI)	-2.4	4.4	54 1035	0	4.5	50 973		-2.40 [-4.11, -0.69] -3.35 [-5.22, -1.48]	
Heterogeneity: Tau ² = Test for overall effect:					10 (P <				
1.6.2 Secondary Prev		-		- /					
Blasco 2012	-1.6	4	102	3	4.1	101	7.8%	-4.60 [-5.71, -3.49]	
Reid 2012	12.6	6.2	115	6.8	5.8	108	7.6%	5.80 [4.23, 7.37]	
Southard 2003	-4.4	9.8	53	0.5	6.5	51		-4.90 [-8.08, -1.72]	
Zutz 2007	-3.7		8	-4	9.8	7	2.1%		
Subtotal (95% CI)	5.7		278		3.0	267	23.8%	-0.93 [-7.74, 5.88]	
Heterogeneity: Tau ² =	42.68	$Chi^2 =$	116.7	0. df =	3 (P <	0.0000			
Test for overall effect:				.,			.,		
Total (95% CI)			1313			1240	100.0%	-2.77 [-4.49, -1.05]	
Heterogeneity: $Tau^2 =$	9.59.0	$hi^2 = 4$. df = 1	4 (P <				
Test for overall effect:					40 -	0.0000	.), 1 = 57		-10 -5 0 5 10
Test for subgroup diffe					(P = 0.	50), I ² =	0%		Favours [Digital Health] Favours [Usual Care]
В									
В	ſ	Digital	Health		Usual			Mean Difference	Mean Difference
Study or Subgroup	м		Health SD T				al Weigh		
Study or Subgroup 1.7.1 Primary Preven	M	ean	SD T	otal M	lean	5D Tot		t IV, Random, 95% C	I IV, Random, 95% CI
Study or Subgroup 1.7.1 Primary Preven Bennett 2012	M ition -0	ean	SD T	otal M	lean .	5D Tot	5 9.09	t IV, Random, 95% C	I IV, Random, 95% CI
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013	M ition -0	ean 0.54 0 0.3	SD T 0.14 6.3	otal M 180 -0 197	lean 0.12 0. 0.3 6	5D Tot 13 18 .3 9	5 9.09 7 0.99	t IV, Random, 95% C 6 -0.42 [-0.45, -0.39 6 -0.60 [-2.13, 0.93	I IV, Random, 95% CI
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013 Bove 2013	M ntion -0 -	ean 0.54 0 0.3 0.2	SD T 0.14 6.3 2.2	otal M 180 -0 197 120	0.12 0. 0.3 6 0.5 4	5D Tot 13 18 .3 9 .5 12	5 9.09 7 0.99 1 2.29	t IV, Random, 95% C -0.42 [-0.45, -0.39 -0.60 [-2.13, 0.93 -0.70 [-1.59, 0.19	I IV, Random, 95% CI
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013 Bove 2013 Broekhuizen 2012	M ntion -0 -	ean 0.54 0 0.3 0.2 0.1	SD T 0.14 6.3 2.2 2.8	otal M 180 -(197 120 181	0.12 0. 0.3 6 0.5 4 0 0	SD Tot 13 18 .3 9 .5 12 .6 15	5 9.09 7 0.99 1 2.29 9 5.49	t IV, Random, 95% C -0.42 [-0.45, -0.39 -0.60 [-2.13, 0.93 -0.70 [-1.59, 0.19 -0.10 [-0.52, 0.32	I IV, Random, 95% CI
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013 Bove 2013 Broekhuizen 2012 Claes 2013	M -0 -0 - 0	ean 0.54 0 0.3 0.2 0.1 0.42 0	SD T 0.14 6.3 2.2 2.8 0.42	otal M 180 -(197 120 181 195 (0.12 0. 0.3 6 0.5 4 0 (0).32 0.	5D Tot 13 18 .3 9 .5 12 .6 15 54 10	5 9.09 7 0.99 1 2.29 9 5.49 0 8.59	t IV, Random, 95% C -0.42 [-0.45, -0.39 -0.60 [-2.13, 0.93 -0.70 [-1.59, 0.19 -0.10 [-0.52, 0.32 0.10 [-0.02, 0.22	I IV, Random, 95% CI
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013 Broekhuizen 2013 Claes 2013 Green 2008	M -0 -0 -0 -0 0	ean 0.54 0 0.3 0.2 0.1 0.42 0 0.9	SD T 0.14 6.3 2.2 2.8 0.42 3.6	otal M 180 -(197 120 181 195 (520	0.12 0. 0.3 6 0.5 4 0.32 0. 0.32 0.	SD Tot 13 18 .3 9 .5 12 .6 15 54 10 .4 25	5 9.09 7 0.99 1 2.29 9 5.49 0 8.59 8 1.49	t IV, Random, 95% C -0.42 [-0.45, -0.39 -0.60 [-2.13, 0.93 -0.70 [-1.59, 0.19 -0.10 [-0.52, 0.32 0.10 [-0.02, 0.22 -0.90 [-2.09, 0.29	I IV, Random, 95% Cl
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013 Bove 2013 Broekhuizen 2012 Claes 2013 Green 2008 Hansen 2012	M -0 -0 -0 -0 0	ean 0.54 0 0.3 0.2 0.1 0.42 0 0.9 0.1 0	SD T 0.14 6.3 2.2 2.8 0.42 3.6 0.08 6	otal M 180 -(197 120 181 195 (520 055	lean 2 0.12 0. 0.3 6 0.5 4 0.32 0. 0.32 0. 0 9 0 0.	SD Tot 13 18 .3 9 .5 12 .6 15 54 10 .4 25 08 623	5 9.09 7 0.99 1 2.29 9 5.49 0 8.59 8 1.49 2 9.09	IV, Random, 95% C 6 -0.42 [-0.45, -0.39 6 -0.60 [-2.13, 0.93 6 -0.70 [-1.59, 0.19 6 -0.10 [-0.52, 0.32 6 -0.10 [-0.02, 0.32 6 -0.20, 0.29 6 -0.01 [-0.10, -0.20	I IV, Random, 95% Cl
Study or Subgroup 1.7.1 Primary Preven Bennett 2012 Bennett 2013 Broekhuizen 2013 Claes 2013 Green 2008 Hansen 2012 Jacobs 2011	M -0 -0 - - 0 - - - - -	ean 0.54 0 0.3 0.2 0.1 0.42 0 0.9 0.1 0 0.1 0 0	SD T 0.14 6.3 2.2 2.8 0.42 3.6 0.08 0.4	otal M 180 -0 197 120 181 195 0 520 055 208	lean 2 0.12 0. 0.3 6 0.5 4 0.32 0. 0 9 0 0. -1 0	5D Tot 13 18 3 9 5 12 0.6 15 5 4 10 0.4 25 0 8 623 0.6 10	5 9.09 7 0.99 1 2.29 9 5.49 0 8.59 8 1.49 2 9.09 6 8.59	t IV, Random, 95% C 6 -0.42 [-0.45, -0.39 6 -0.60 [-2.13, 0.93 6 -0.70 [-1.59, 0.19 6 -0.70 [-1.59, 0.19 6 -0.10 [-0.52, 0.32 6 -0.10 [-0.20, 0.22 2 -0.90 [-2.09, 0.29 6 -0.10 [-0.10, -0.10 6 1.00 [0.87, 1.13	I IV, Random, 95% CI
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Figure 3. Figure 3a: Weight and DHI. Figure 3b: BMI and DHI.

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	Digita	I Heal	th	Usu	al Car	e		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	IV, Random, 95% CI
Appel 2011	-10.1	2.4	139	-1.8	3.8	138		-8.30 [-9.05, -7.55]	
Bennett 2010	-5.1	7.1	51	0.62	4	50		-5.72 [-7.96, -3.48]	
Bennett 2012	-3	0.8	180	-0.7	0.8	185	11.8%	-2.30 [-2.46, -2.14]	•
Bennett 2013	-2.2	10.5	97	1.1	10.67	97	10.0%	-3.30 [-6.28, -0.32]	· · · · · · · · · · · · · · · · · · ·
Bove 2013	-0.8	15.7	120	2.4	22.6	121	8.0%	-3.20 [-8.11, 1.71]	
Dekkers 2011	-7.7	4.7	93	-5.5	3.5	92	11.5%	-2.20 [-3.39, -1.01]	·
Park 2012	-4.4	3.74	42	1.5	2	37	11.4%	-5.90 [-7.20, -4.60]	·
Reid 2012	12.6	6.2	115	6.8	5.8	108	11.2%	5.80 [4.23, 7.37]	
Southard 2003	-4.4	9.8	53	0.5	6.5	51	9.8%	-4.90 [-8.08, -1.72]	
Zutz 2007	-3.7	10.1	8	-4	9.8	7	3.9%	0.30 [-9.78, 10.38]	1
Total (95% CI)			898			886	100.0%	-3.18 [-5.61, -0.75]	
Heterogeneity: Tau ² =	13.03.0	hi ² =		df = 9	9 (P < 0				
Test for overall effect:				, 01			x/, 1 = 5	010	-10 -5 0 5 1
		ų.							Favours (digital health) Favours (usual care)
В									
		al Hea			sual Ca			Mean Difference	
Study or Subgroup				Mean				t IV, Random, 95%	
Bennett 2012		0.8	180	-0.7	0.8	3 185	5 99.6	% -2.30 [-2.46, -2.]	14]
Bennett 2013	2.2	10.5	97	1 1	10.67	7 97	7 0 3	% -3.30 [-6.28, -0.3	32]
Dennett LOXD	-2.2	*0.5	51	1.1					
Bove 2013 Total (95% CI) Heterogeneity: Tau ² =	-0.8	15.7 Chi ² =	120 397 0.56, c	2.4 if = 2 (22.6	5 121 403	1 0.1 3 100.0	 -3.20 [-8.11, 1.3] -2.30 [-2.47, -2.3] 	14) + -10 -5 0 5 1
Bove 2013 Total (95% CI) Heterogeneity: Tau ² =	-0.8	15.7 Chi ² =	120 397 0.56, c	2.4 if = 2 (22.6	5 121 403	1 0.1 3 100.0	% -3.20 [-8.11, 1.3	14]
Bove 2013 Total (95% CI) Heterogeneity: Tau ² Test for overall effect	-0.8 = 0.00; 0 :: Z = 27	15.7 Chi ² = .57 (P	120 397 0.56, c < 0.00	2.4 df = 2 (0001)	22.6 P = 0.7	5 121 403 76); I ² =	1 0.1 3 100.0	% -3.20 [-8.11, 1.] % -2.30 [-2.47, -2.]	14] + -10 -5 0 5 1 Favours [experimental] Favours [control]
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C	-0.8 = 0.00; 0 :: Z = 27 Digit	15.7 Chi ² = .57 (P	120 397 0.56, c < 0.00	2.4 df = 2 (0001) Use	22.6 P = 0.7	403 (6); 1 ² =	1 0.1 3 100.0 = 0%	 -3.20 [-8.11, 1.] -2.30 [-2.47, -2.] Mean Difference 	14] + -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² + Test for overall effect C Study or Subgroup	-0.8 = 0.00; 0 :: Z = 27 Digit Mean	15.7 Chi ² = .57 (P al Hea SD	120 397 0.56, c < 0.00	2.4 df = 2 (0001) Use Mean	22.6 P = 0.7 Jal Car SD	403 76); 1 ² = e Total	1 0.1 3 100.0 = 0% Weight	 -3.20 [-8.11, 1.3] -2.30 [-2.47, -2.3] Mean Difference IV, Random, 95% CI 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012	-0.8 = 0.00; (:: Z = 27 Digit <u>Mean</u> -1.6	15.7 Chi ² = .57 (P al Hea <u>SD</u> 4	120 397 0.56, c < 0.00 alth Total 102	2.4 df = 2 (0001) Usu <u>Mean</u> 3	22.6 P = 0.7 ual Can <u>SD</u>	403 76); 1 ² = e Total	1 0.1 3 100.0 = 0% <u>Weight</u> 27.0%	 -3.20 [-8.11, 1.3] -2.30 [-2.47, -2.3] Mean Difference IV, Random, 95% CI -4.60 [-5.71, -3.49] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% Cl
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010	-0.8 = 0.00; (:: Z = 27 Digit <u>Mean</u> -1.6 -0.4	15.7 $Chi^{2} =$ $57 (P)$ $Chi^{2} =$ $Chi^{2} =$ $S7 =$ $Chi^{2} =$ $S7 =$ $Chi^{2} =$ $S7 =$ $S1 =$ $S2 =$ S	120 397 0.56, c < 0.00 dith Total 102 127	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8	22.6 P = 0.7 Jal Car SD 4.1 8.8	403 76); I ² = e Total 101 123	1 0.1 3 100.0 = 0% Weight 27.0% 23.9%	 -3.20 [-8.11, 1.7] -2.30 [-2.47, -2.7] Mean Difference IV, Random, 95% CI -4.60 [-5.71, -3.49] -2.20 [-3.82, -0.58] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV. Random, 95% Cl
Bove 2013 Total (95% CI) Heterogeneity: Tau ² = Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012	-0.8 = 0.00; (:: Z = 27 Digit <u>Mean</u> -1.6 -0.4 -4.4	15.7 $Chi^2 =$	120 397 0.56, c < 0.00 dlth Total 102 127 42	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5	22.6 P = 0.7 Jal Can SD 4.1 8.8 2	403 76); I ² = e Total 101 123 37	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 25.9%	 -3.20 [-8.11, 1.3] -2.30 [-2.47, -2.3] Mean Difference IV, Random, 95% CI -4.60 [-5.71, -3.49] -2.20 [-3.82, -0.58] -5.90 [-7.20, -4.60] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% Cl
Bove 2013 Total (95% CI) Heterogeneity: Tau ² = Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012	-0.8 = 0.00; (:: Z = 27 Digit <u>Mean</u> -1.6 -0.4 -4.4	15.7 $Chi^{2} =$ $57 (P)$ $Chi^{2} =$ $Chi^{2} =$ $S7 =$ $Chi^{2} =$ $S7 =$ $Chi^{2} =$ $S7 =$ $S1 =$ $S2 =$ S	120 397 0.56, c < 0.00 dith Total 102 127	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5	22.6 P = 0.7 Jal Car SD 4.1 8.8	403 76); I ² = e Total 101 123	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 25.9%	 -3.20 [-8.11, 1.7] -2.30 [-2.47, -2.7] Mean Difference IV, Random, 95% CI -4.60 [-5.71, -3.49] -2.20 [-3.82, -0.58] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% Cl
Bove 2013 Total (95% CI) Heterogeneity: Tau ² - Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013	-0.8 = 0.00; (:: Z = 27 Digit <u>Mean</u> -1.6 -0.4 -4.4	15.7 $Chi^2 =$	120 397 0.56, c < 0.00 (th Total 102 127 42 54	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5 0	22.6 P = 0.7 Jal Can SD 4.1 8.8 2	 403 403 76); l² = e Total 101 123 37 50 	1 0.1 3 100.0 = 0% <u>Weight</u> 27.0% 23.9% 25.9% 23.3%	 Mean Difference IV, Random, 95% CI 4.60 [-5.71, -3.49] 5.90 [-7.20, -4.60] 2.40 [-4.11, -0.69] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% Cl
Bove 2013 Total (95% CI) Heterogeneity: Tau ² = Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI)	-0.8 = 0.00; 0 :: Z = 27. Digit <u>Mean</u> -1.6 -0.4 -4.4 -2.4	15.7 $Chi^2 =$	120 397 0.56, c < 0.00 (Ith Total 102 127 42 54 325	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5 0	22.6 P = 0.7 aal Can <u>SD</u> 4.1 8.8 2 4.5	403 76); I ² = e Total 101 123 37 50 311	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0%	 Mean Difference IV, Random, 95% CI 4.60 [-5.71, -3.49] 2.20 [-3.82, -0.58] 5.90 [-7.20, -4.60] 2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% Cl
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a	-0.8 = 0.00; C :: Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C	15.7 $Chi^2 =$	120 397 0.56, c < 0.00 (th Total 102 127 42 54 325 17.14,	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5 0 df = 3	22.6 P = 0.7 aal Can <u>SD</u> 4.1 8.8 2 4.5	403 76); I ² = e Total 101 123 37 50 311	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0%	 Mean Difference IV, Random, 95% CI 4.60 [-5.71, -3.49] 2.20 [-3.82, -0.58] 5.90 [-7.20, -4.60] 2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI
Bove 2013 Total (95% CI) Heterogeneity: Tau ² = Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI)	-0.8 = 0.00; C :: Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C	15.7 $Chi^2 =$	120 397 0.56, c < 0.00 (th Total 102 127 42 54 325 17.14,	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5 0 df = 3	22.6 P = 0.7 aal Can <u>SD</u> 4.1 8.8 2 4.5	403 76); I ² = e Total 101 123 37 50 311	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0%	 Mean Difference IV, Random, 95% CI 4.60 [-5.71, -3.49] 2.20 [-3.82, -0.58] 5.90 [-7.20, -4.60] 2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% Cl
Rove 2013 Total (95% CI) Heterogeneity: Tau ² - Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² -	-0.8 = 0.00; C :: Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C	15.7 $Chi^2 =$	120 397 0.56, c < 0.00 (th Total 102 127 42 54 325 17.14,	2.4 df = 2 (0001) Usu <u>Mean</u> 3 1.8 1.5 0 df = 3	22.6 P = 0.7 aal Can <u>SD</u> 4.1 8.8 2 4.5	403 76); I ² = e Total 101 123 37 50 311	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0%	 Mean Difference IV, Random, 95% CI 4.60 [-5.71, -3.49] 2.20 [-3.82, -0.58] 5.90 [-7.20, -4.60] 2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] 	14] -10 -5 0 5 1 Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect	-0.8 = 0.00; C :: Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C :: Z = 4.4 Digit	15.7 $hi^2 = 57 (P)$ al Hea $\frac{50}{4}$ 4.6 2.6 3.74 4.4 $hi^2 = 8 (P < 1)$ $hi^2 = 8 (P < 1)$	120 397 0.56, c < 0.00 lth Total 102 127 42 54 325 17.14, 0.000 lth	2.4 df = 2 (0001) Usi <u>Mean</u> 3 3 8 1.5 0 0 0 1) df = 3 001) Usi	22.0 P = 0.7 P = 0.7 4.1 8.8 2 4.5 (P = 0.	e Total 101 123 37 50 311 00077); e	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0% 1 ² = 832	Mean Difference IV. Random, 95% CI -4.60 [-5.71, -3.49] -2.20 [-3.82, -0.58] -5.90 [-7.20, -4.60] -2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] Mean Difference	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect	-0.8 = 0.00; C :: Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C :: Z = 4.4 Digit	15.7 $hi^2 = 57 (P)$ al Hea $\frac{50}{4}$ 4.6 2.6 3.74 4.4 $hi^2 = 8 (P < 1)$ $hi^2 = 8 (P < 1)$	120 397 0.56, c < 0.00 lth Total 102 127 42 54 325 17.14, 0.000 lth	2.4 df = 2 (0001) Usi <u>Mean</u> 3 3 8 1.5 0 0 0 1) df = 3 001) Usi	22.0 P = 0.7 P = 0.7 4.1 8.8 2 4.5 (P = 0.	e Total 101 123 37 50 311 00077); e	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0% 1 ² = 832	Mean Difference IV, Random, 95% CI -2.30 [-2.47, -2.: Mean Difference IV, Random, 95% CI -4.60 [-5.71, -3.49] -2.20 [-3.82, -0.58] -5.90 [-7.20, -4.60] -2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17]	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² - Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² = Test for overall effect	-0.8 = 0.00; C :: Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C :: Z = 4.4 Digit	15.7 Thi ² = 57 (P al Hea SD 4 2.6 3.74 4.4 Chi ² = 8 (P < al Hea SD	120 397 0.56, c < 0.00 ith Total 102 127 42 54 325 17.14, 0.000 ith Total	2.4 df = 2 (0001) Usi <u>Mean</u> 3 3 8 1.5 0 0 0 1) df = 3 001) Usi	22.0 P = 0.7 SD 4.1 8.8 2 4.5 (P = 0, (P = 0, sD SD	e Total 101 123 37 50 311 00077); e	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.3% 100.0% ² = 83% Weight	 -3.20 [-8.11, 1.7] -2.30 [-2.47, -2.7] Mean Difference IV, Random, 95% CI -4.60 [-5.71, -3.49] -2.20 [-3.82, -0.58] -5.90 [-7.20, -4.60] -2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] Mean Difference IV, Random, 95% CI 	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect D Study or Subgroup	-0.8 = 0.00; c :: Z = 27 Digit <u>Mean</u> -1.6 -0.4 -4.4 -2.4 = 2.42; C : Z = 4.4 Digit <u>Mean</u> -0.53	15.7 Thi ² = 57 (P al Hea SD 4 2.6 3.74 4.4 Chi ² = 8 (P < al Hea SD	120 397 0.56, c < 0.00 (< 0.00 102 127 42 54 325 17.14, 0.000 Ith Total 102 127 42 54 12.5	2.4 df = 2 (0001) Usi Mean 3 1.8 1.5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	22.0 P = 0.7 SD 4.1 8.8 2 4.5 (P = 0, (P = 0, SD 7	e e Total 101 123 37 50 311 0007); e e Total 54	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 25.9% 23.3% 100.0% ² = 83% Weight 90.0%	 -3.20 [-8.11, 1.7] -2.30 [-2.47, -2.7] Mean Difference IV, Random, 95% CI -4.60 [-5.7], -3.49] -2.20 [-3.82, -0.58] -5.90 [-7.20, -4.60] -2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] Mean Difference IV, Random, 95% CI 	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect D Study or Subgroup Andersen 2013 Senesael 2013	-0.8 = 0.00; c :: Z = 27 Digit <u>Mean</u> -1.6 -0.4 -4.4 -2.4 = 2.42; C : Z = 4.4 Digit <u>Mean</u> -0.53	15.7 chi ² = 5.57 (P al Heas <u>SD</u> 4 2.66 3.74 4.4 (P < bi ² = 8 (P < bi ² = 8 (P < bi ² = 4.3 bi ³ = 4.3	120 397 0.56, c < 0.00 102 127 42 54 325 17.14, 0.000 1th Total 106 26	2.4 df = 2 (0001) Uss Mean -1.4 -1.1	22.0 P = 0.7 SD 4.1 8.8 2 4.5 (P = 0, (P = 0, SD 7	e Total 101 123 37 50 311 00007); e Total 54 26	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 25.9% 23.3% 100.0% 1 ² = 83% Weight 90.0% 10.0%	Mean Difference IV, Random, 95% CI -2.30 [-2.47, -2.: Mean Difference IV, Random, 95% CI -2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] Mean Difference IV, Random, 95% CI 0.87 [-1.17, 2.91] -0.40 [-6.52, 5.72]	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect D Study or Subgroup Andersen 2013 Senesael 2013 Total (95% CI)	-0.8 = 0.00; t: Z = 27 Digit Mean -1.6 -0.4 -0.4 -0.4 -2.4 = 2.42; t Z = 4.4 Digit Mean -0.53 -1.5	15.7 Chi ² = 5.57 (P al Hea <u>5D</u> 4 2.6 3.74 4.4 Chi ² = 88 (P < 8 (P < 4.3 12.7	120 397 397 30.56, c < 0.00 102 127 42 54 325 17.14, 0.000 1th Total 102 127 42 54 325 17.14, 0.000 117 127 42 54 127 42 54 127 127 42 54 127 127 127 127 127 127 127 127	2.4 df = 2 (0001) Usit Mean df = 3 001) Usit Mean -1.4 -1.1	22.0 P = 0.7 4.1 8.8 4.5 (P = 0. (P = 0. 3 4.5 (P = 0. 7 9.6	e Total 00007); e Total 00007); e 80	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.9% 23.9% 23.3% 100.0% 1° = 83% Weight 90.0% 10.0%	Mean Difference IV, Random, 95% CI -2.20 [-2.47, -2.: Mean Difference IV, Random, 95% CI 0.87 [-1.17, 2.9]	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference
Bove 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect C Study or Subgroup Blasco 2012 Lombard 2010 Park 2012 Wong 2013 Total (95% CI) Heterogeneity: Tau ² a Test for overall effect D Study or Subgroup Andersen 2013	-0.8 = 0.00; : Z = 27 Digit Mean -1.6 -0.4 -2.4 = 2.42; C = 4.4 Digit Mean -0.53 -1.5 0.00; C	15.7 $chi^2 =$	120 397 0.56, c < 0.00 102 127 42 54 325 17.14, 0.000 106 106 26 132 0.5, d	2.4 ff = 2 (Mean 3 1.8 1.5 0 Usi Mean -1.4 -1.1 f = 1 (f	22.0 P = 0.7 4.1 8.8 4.5 (P = 0. (P = 0. 3 4.5 (P = 0. 7 9.6	e Total 00007); e Total 00007); e 80	1 0.1 3 100.0 = 0% Weight 27.0% 23.9% 23.9% 23.9% 23.9% 23.3% 100.0% 1° = 83% Weight 90.0% 10.0%	Mean Difference IV, Random, 95% CI -2.30 [-2.47, -2.: Mean Difference IV, Random, 95% CI -2.40 [-4.11, -0.69] -3.85 [-5.54, -2.17] Mean Difference IV, Random, 95% CI 0.87 [-1.17, 2.91] -0.40 [-6.52, 5.72]	14] Favours [experimental] Favours [control] Mean Difference IV, Random, 95% CI -10 -5 0 5 1 Favours [control] Mean Difference Mean Difference Mean Difference

Figure 4.

Figure 4a: Web-based DHI and weight loss: Figure 4b: Telehealth-based DHI and weight loss: Figure 4c: SMS Text-based DHI and weight loss: Figure 4d: Email-based DHI and weight loss:

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Table 1

RCTs reporting CVD outcomes with DHI (n=9)

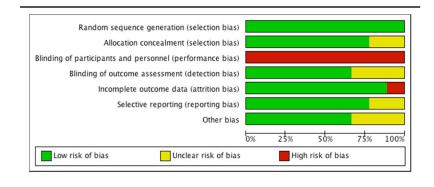
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Study ID	Duration (mo)	Total N	DHI N	Study Population	DHI	Findings
Appel, 2011 ²⁶	24	415	139	Primary Prevention, Hypertension	Web-based	Larger, healthcare site obesity intervention delivered remotely or in person significantly reduced weight (-4.6 kg and -5.1 kg, respectively) vs. controls. No impact on CVD events, rehospitalizations, or all-cause mortality.
Blasco 2012 ²⁷	12	203	102	Secondary Prevention	SMS text, Smart Phone	Healthcare secondary prevention trial showing improved secondary prevention outcomes (repeat CVD events, rehospitalizations, or all-cause mortality; $RR = 1.4$; 95% CI = $1.1-1.7$) with telemonitoring and SMS text.
Dendale, 2012 ²⁸	6	160	80	Secondary Prevention, Heart Failure	Telephone, Data Monitoring	Healthcare-delivered telemonitoring service in HF patients showed significantly reduced all-cause mortality (P=.01) but did not reduce hospitalizations per patient (0.24 vs. 0.42, P=. 06).
Frederix, 2013 ²⁹	4.5	80	40	Secondary Prevention	Email, SMS text, Data Monitoring	Body sensor data-monitoring in CR patients improved exercise capacity (26.88+220.33 ml/min vs. 285.89+385.44 ml/min, P=. 014) and improvements in rehospitalizations.
Green, 2009 ³⁰	12	778	520	Primary Prevention	Telephone, Web-based	Hypertensive patients assigned to usual care vs. a web-based or telephone-based intervention showed those using the web-based platform had a greater percentage of achieving target BP (55% vs. 39% ; 95% CI, 49% – 62% ; P < .001). Increased adverse events in intervention group.
Reid, 2012 ³¹	12	223	115	Secondary Prevention	Web-based	Internet-based data monitoring for physical activity in post-MI patients showed significant improvements in physical activity and QOL compared to usual care. The intervention had a small, non-significant effect on hard CVD outcomes.
Scherr, 2009 ²⁰	6	120	54	Secondary Prevention, Heart Failure	Telephone, SMS text, Data Monitoring	Data monitoring in patients with recent decompensated HF showed a high attrition rate; yet a 50% reduction in CVD endpoints and hospitalizations with a mean improvement in NYHA class by one category in the treatment group.
Southard, 2003 ³²	6	104	53	Secondary Prevention	Web-based	Internet-based secondary prevention tool reduced CVD endpoints (15.7% vs. 4.6%) and provided a significant cost savings. The intervention group had a more robust weight loss $(-3.68$ lbs. vs. 0.47 pounds, $P = 003$), with no other surrogate markers of CVD achieving statistical significance.
Vernooij, 2012 ³³	12	330	164	Secondary Prevention	Web-based	Clinic-based online risk factor improvement tool showed a significant reduction in Framingham scores (–14%; –25% to – 2%) after 12 months in patients randomized to the intervention. No significant reduction in CVD events, death, and hospitalizations in DHI group.

Table 2

Risk of bias for outcomes studies:

Assessment of risk of bias based validity assessment tool used by authors (Supplementary Figure 1) for the nine studies with CVD outcomes analyzed. The x-axis represents the percentage of studies which were found to be of low (green), unclear (yellow), or high (red) risk of bias.



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