Supplemental Material

Supplementary Table 1

A) Primary CVD Prevention (39):
B) Secondary CVD Prevention (13):

Supplementary Figure 1: Validity Assessment Tools:

Supplementary Figure 2: Funnel plot for CVD outcomes among primary and secondary prevention along with heart failure.

Supplementary Figure 3: Systolic Blood Pressure and DHI.

Supplementary Figure 4a: Total-Cholesterol and DHI.

Supplementary Figure 4b: LDL-Cholesterol and DHI.

Table 1A) Primary CVD Prevention (39):

Study ID (Name, Year)	Study Type	Study Length (mo)	Total (N)	Digital Health (N)	Study Population	Digital Health Intervention	Findings
Andersen 2013 [34]	RCT	2.5	160	106	Primary Prevention	Email	Workplace email intervention with high adherence increased exercise capacity (1.45 mL/min/kg (95% CI 0.64-2.27) and reduced BP (4.81 mmHg (95% CI 0.47-9.16), (weight reduction not significant) especially those who started with a low fitness level to begin with.
Appel, 2011 [26]	RCT	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) above controls.
Bennett, 2010 [35]	RCT	3	101	51	Primary Prevention	Web-based	Healthcare delivery of weight loss intervention showed improved weight loss in a dose-dependent fashion (quartile 4 vs. 1: -4.16 kg; 95% CI -1.47, -6.84) over controls.
Bennett, 2012 [36]	RCT	24	365	180	Primary Prevention, Obesity	Telemedicine and web-based	Healthcare delivered weight loss intervention in underserved, primarily black population, showing a significant reduction in weight at 12 months (-1.03 kg 95% CI, −2.03 to −0.03 kg) with no effect on blood pressure.
Bennett, 2013 [37]	RCT	12	194	97	Primary Prevention, Obesity	Telemedicine	Healthcare delivered multi-faceted weight loss intervention in underserved, primarily black population, demonstrating significant weight reduction at 12 months (−1.4 kg; 95%CI, −2.8 to −0.1 kg; P = .04).
Bove, 2013 [38]	RCT	6	241	120	Primary Prevention, Hypertension	Telephone, Web-based	Healthcare-delivered telemedicine hypertension program in primarily underserved, African American women showed no additional improvement with intervention.
Broekhuizen, 2010 [39]	RCT	12	340	181	Primary Prevention	Telephone, Web-based	Healthcare-delivered, web-based lifestyle intervention in familial hyperlipidemia had no benefit over usual care.
Claes, 2013 [40]	RCT	36	314	195	Primary Prevention	Telephone, Web-based	Personalized online and one-to-one coaching with self-employed lawyers in Belgium showing similar reductions in FRS, cholesterol, and blood pressure.
Colkesen, 2011 [41]	Cohort	7	176	176	Primary Prevention	Web-based	Workplace-delivered HRA and prevention program improved 10-yr CVD risk scores after 6 mo by 5% with

							more prominent reductions occurring in higher risk participants.
Dekkers, 2011 [42]	RCT	6	185	93	Primary Prevention	Web-based	Workplace-delivered, internet-based primary prevention program showed non-significant reductions in body weight (-2.1 kg, 95%CI -4.4 to 0.2) and aerobic fitness (2.3 ml/kg/min, 95%CI -0.2 to 4.8).
Frisch, 2009 [43]	Cohort	12	200	200	Primary Prevention, Metabolic Syndrome	Telephone, Smart Phone, Data Monitoring	Transmission of weight data in overweight patients showed improvements in calorie restriction and weight reduction (5.8$\pm$6.1 kg and 4.3$\pm$5.1 kg).
Goessens, 2008 [44]	Cohort	6	50	50	Primary Prevention	Web-based	Nurse-led internet-based risk factor reduction program was scarcely used (1.3 log ins/wk) with a relative reduction in risk factors, but no specific surrogate CVD marker data reported.
Green, 2009 [30]	RCT	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 (56%; 95% CI, 49%-62%; P < .001). Increased adverse events in intervention group.
Hansen, 2012 [45]	RCT	3	12287	6055	Primary Prevention	Web-based, Email	Population health intervention of internet-based lifestyle changes showed poor compliance (22%) and no increase in physical activity (1575; 845-2580 vs. 1560; 840-2520).
Jacobs, 2011 [46]	RCT	6	314	208	Primary Prevention	Telephone, Web-based, Email	A multi-faceted digital health intervention in highly educated participants showed no difference versus usual care in terms of lifestyle behaviors or CVD surrogates
Joo, 2007 [47]	Cohort	3			Primary Prevention	SMS text	Cohort using a population health SMS text intervention showed reductions of weight (1.6 kg; P<0.001), waist circumference (4.3 cm; P<0.001), and BMI (0.6 kg/m^2; P< 0.001), respectively.
Kim, 2013 [48]	Cohort	2	18	18	Primary Prevention	Web-based	Small, cohort, workplace, pilot study to improve physical activity showed significant reductions in Framingham CVD risk (-2.4%), waist circumference (-2.9 cm), diastolic blood pressure (-9.9 mm Hg), and fasting plasma glucose (-16.7 mg/dL).
Kiselev, 2012 [49]	RCT	17.6	199	97	Primary Prevention, Hypertensi	Web-based, Email, SMS text	Healthcare-guided SMS intervention in hypertensive patients had a relatively high withdrawal rate (36%) but showed a 5-fold improvement in adherence to ideal BP

					on		(77%) compared to control group.
Kulick, 2013 [50]	RCT	3	61	32	Primary Prevention	Web-based, Email	Three-month healthcare-delivered internet and email-based intervention showed improvements with both diet scores and lipids with the digital health intervention and high-intensity counseling without apparent differences between the two.
Lieber, 2012 [51]	Cohort	3	972	972	Primary Prevention	Web-based	Population-based, web-based intervention showed an improvement in physical activity in low-moderate risk female participants.
Logan, 2012 [52]	RCT	12	110	55	Primary Prevention, Diabetes/Htn	Telephone, Email, SMS text, Data Monitoring	Diabetic and hypertensive patients provided data monitoring and an automated educational system had significantly reduced SBP from baseline (9.1±15.6 mmHg; P < 0.0001), and compared to telemonitoring alone (7.1±2.3 mmHg; P < 0.005). There was more pronounced depression and antihypertensive effects in the treatment arms.
Lombard, 2010 [53]	RCT	12	250	127	Primary Prevention	SMS text	Young urban women with young children in Australia cluster randomized to support group and SMS texting intervention. Those in the treatment group lost weight (-0.2 kg; -0.90 to 0.49) compared to the control group who gained weight (+0.83 kg; 0.12 to 1.54), however the response rate was only 12%.
Marquez Contreras, 2004 [54]	RCT	6	104	52	Primary Prevention, Hypertension	SMS text	Healthcare intervention on clinics in Spain showed SMS text reminders for hypertension had no significant improvement in medication compliance and attainment of target BP goals over control for 6 months.
McManus, 2010 [19]	RCT*	12	527	263	Primary Prevention, Hypertension	Telephone, Data Monitoring	Unblinded, open-label data monitoring and telemedicine RCT showed significant improvement in antihypertensive effects in both arms of the program (difference between groups 3.7 mm Hg, 0.8-6.6; p=0.013).
McTigue, 2009 [55]	Cohort	12	50	50	Primary Prevention, Obesity	Web-based, Email	Clinic-based, multifaceted cohort study in patients with obesity showed significant reductions in SBP (7.33±11.36 mm Hg) and weight (4.79±8.55 kg) with reasonably high compliance.
Nolan, 2011 [56]	RCT	6	680	415	Primary Prevention	Telephone	Clinical setting with participants at high risk of CVD demonstrating that telephone intervention reduces blood pressure, lipids, and 10 year CVD risk through improvements in physical activity and diet.

Nolan, 2012 [57]	Cohort	4	387	194	Primary Prevention, Hypertension	Web-based, Email	Initially a clinic-based RCT for antihypertensive treatment through an online portal diluted by crossover of patients, essentially rendering a cohort study finding no differences between the two groups; however in those participants who received over 8 messages throughout the trial had substantial benefit in blood pressure, lipids, and 10-yr risk scores.
Park, 2012 [58]	Cohort	3	79	42	Primary Prevention	Web-based, SMS text	Clinic-based observational study in overweight, post-menopausal women compared to a similar cohort had significant reductions in waist circumference (3.0 cm) weight (2 kg), blood pressure (6.5/4.6 mmHg), and LDL-C (-11.3 mg/dL).
Rossi, 2009 [59]	Cohort	3	50	50	Primary Prevention, Diabetes	SMS text, Smart Phone	Smart-Phone application studied in a cohort of overweight participants in Italy showed significant improvements in diet, moderate physical activity, weight (-2.5 kg; -3.2, -1.8), waist circumference (-3.7 cm; -4.6, -2.9), and BMI (-1.0; -0.7, -1.2) kg/m^2 with 82% adherence.
Rossi, 2010 [60]	Cohort	5	140	140	Primary Prevention	Telephone, SMS text, Smart Phone	Clinic-based feasibility study utilizing a smart phone application to assist type 1 diabetics in managing glucose levels and insulin dosing showed reductions in fasting plasma glucose (-6.7%), but not HbA1c, without adverse events.
Senesael, 2013 [61]	RCT	6	57	26	Primary Prevention	Email	Clinic-based study in patients at moderate risk for CVD showed similar reductions in BP in both groups, and no further changes in other surrogate CVD markers after 6 mo.
Sheridan, 2011 [21]	RCT*	3	160	81	Primary Prevention	Web-based	Clinic-based primary prevention intervention using an online decision aid and adherence messages with high retention (96%) reduced CVD risk scores -1.1% (-0.16%, -2%), especially in higher risk subgroups.
Stuckey, 2011 [62]	Cohort	2	24	24	Primary Prevention	Smart Phone, Data Monitoring	Clinic-based data monitoring intervention in overweight patients in underserved communities showed significant reductions in physical activity, diet, BMI, blood pressure, and lipids.
Thiboutot, 2013 [63]	RCT	12	500	282	Primary Prevention	Web-based	Clinic-based trial encouraging patients to discuss certain lifestyle and preventative measures with their PCPs. There were no changes in blood pressure after 12 months, and only slight adjustments in interactions with PCPs.

Verheijden, 2004 [64]	RCT	8	146	73	Primary Prevention	Web-based	Clinically based web intervention in 73 higher-risk Canadian patients demonstrating no difference in weight, blood pressure, or lipids. Very low uptake of the program.
Wakefield, 2011 [65]	RCT	12	302	195	Primary Prevention	Telephone	302 US war veterans with hypertension and diabetes randomized to intensive home reporting system showed no change in HbA1c between groups and only a difference between control and high-intervention groups for blood pressure.
Widmer, 2014 [66]	Cohort	3	508	462	Primary Prevention	Web-based, Smart Phone	Workplace-generated single-cite observational study demonstrating further surrogate Framingham CVD risk reduction (-0.6±0.1%) in a low-risk population of primarily younger females.
Wister, 2007 [17]	RCT	12	296	153	Primary Prevention	Telephone	611 divided into primary and secondary prevention randomized for 12 months demonstrating only a significant change in Framingham 10 year CVD risk.
Wong, 2013 [67]	RCT	12	104	54	Primary Prevention	SMS text	Workplace SMS intervention on reducing the incidence of diabetes in primarily inactive, men showing a reduced risk of disease development (RR = 0.35; 95% CI: 0.10-1.24).

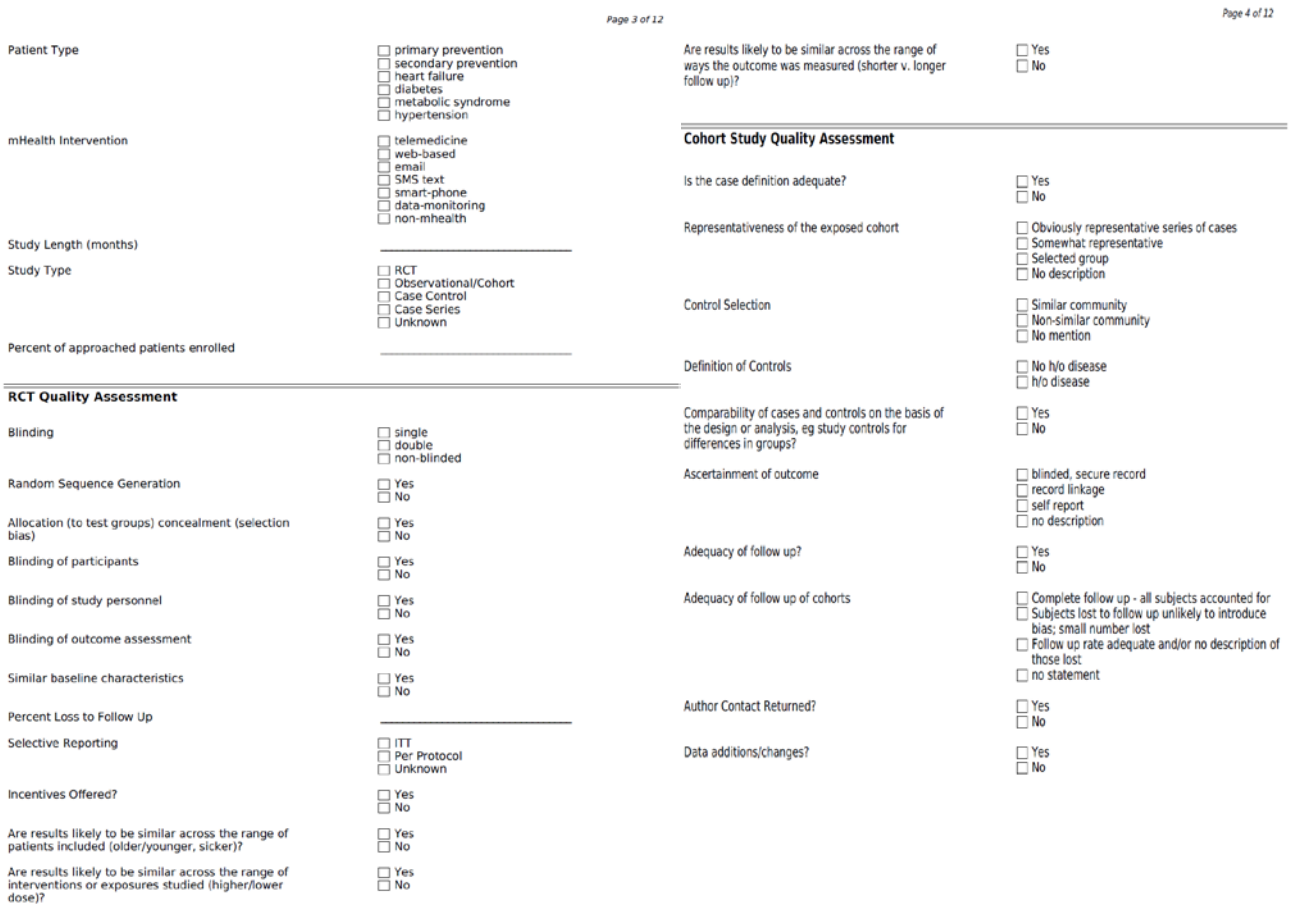
B) Secondary CVD Prevention (13):

Study ID (Name, Year)	Study Type	Study Length (mo)	Total N	Digital Health N	Study Population	Digital Health Intervention	Findings
Blasco 2012 [27]	RCT	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]	RCT	6	160	80	Secondary Prevention, Heart Failure	Telephone, Data Monitoring	Healthcare-delivered telemonitoring service in HF patients showed significantly reduced all-cause mortality (5% vs. 17.5%, P = 0.01) and non-significant improvements in hospitalizations per patient (0.24 vs. 0.42, P = 0.06).
Frederix, 2013 [29]	RCT	4.5	80	40	Secondary Prevention	Email, SMS text, Data Monitoring	Body sensor in CR patients improved exercise capacity (26.88+220.33 ml/min vs. 285.89+385.44 ml/min, P= 0.014) and a non-significant improvements in rehospitalizations.

Korzeniowska-Kubacka, 2011 [68]	Cohort	2	62	32	Secondary Prevention	Telephone, Data Monitoring	Data monitoring in post-MI patients showed no significant difference in aerobic exercise parameters compared to control group with both groups significantly improving above baseline.
Lee, 2013 [69]	RCT	3	60	30	Secondary Prevention	Telephone, Web-based, Data Monitoring	Data monitoring in post-MI patients showed significant improvements in aerobic activity metrics compared to usual care; however no change in resting blood pressure, and no other outcomes or metrics reported.
Maric, 2010 [70]	Cohort	6	20	20	Secondary Prevention, Heart Failure	Web-based	Recently hospitalized HF patients utilized data monitoring through a web portal showing non-significant improvements in QOL, surrogate markers (BNP), and 6MWT.
Reid, 2012 [31]	RCT	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]	RCT*	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]	RCT	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.
Theissing, 2013 [71]	RCT	3	164	58	Secondary Prevention	Web-based	Online, clinic-based intervention in obese patients showed substantial improvements in lifestyle behaviors related to diet, however no significant differences between the group for waist circumference and weight.
Vernooij, 2012 [33]	RCT	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.
Wister, 2007 [17]	RCT	12	296	153	Primary	Telephone	611 divided into primary and secondary prevention

					Prevention		randomized for 12 months demonstrating only a significant change in Framingham 10 year CVD risk.
Zutz, 2007 [72]	RCT	3	15	8	Secondary Prevention	Web-based	Small, hospital-based RCT testing “virtual CR” in patients with a primary indication for such. Although user feedback was positive, there were no significant benefits to the intervention.

Supplementary Figure 1: Validity Assessment Tools:



Patient Type
- ☐ primary prevention
- ☐ secondary prevention
- ☐ heart failure
- ☐ diabetes
- ☐ metabolic syndrome
- ☐ hypertension

mHealth Intervention
- ☐ telemedicine
- ☐ web-based
- ☐ email
- ☐ SMS text
- ☐ smart-phone
- ☐ data-monitoring
- ☐ non-mhealth

Study Length (months) _____

Study Type
- ☐ RCT
- ☐ Observational/Cohort
- ☐ Case Control
- ☐ Case Series
- ☐ Unknown

Percent of approached patients enrolled _____

RCT Quality Assessment

Blinding
- ☐ single
- ☐ double
- ☐ non-blinded

Random Sequence Generation
- ☐ Yes
- ☐ No

Allocation (to test groups) concealment (selection bias)
- ☐ Yes
- ☐ No

Blinding of participants
- ☐ Yes
- ☐ No

Blinding of study personnel
- ☐ Yes
- ☐ No

Blinding of outcome assessment
- ☐ Yes
- ☐ No

Similar baseline characteristics
- ☐ Yes
- ☐ No

Percent Loss to Follow Up _____

Selective Reporting
- ☐ ITT
- ☐ Per Protocol
- ☐ Unknown

Incentives Offered?
- ☐ Yes
- ☐ No

Are results likely to be similar across the range of patients included (older/younger, sicker)?
- ☐ Yes
- ☐ No

Are results likely to be similar across the range of interventions or exposures studied (higher/lower dose)?
- ☐ Yes
- ☐ No

Are results likely to be similar across the range of ways the outcome was measured (shorter v. longer follow up)?
- ☐ Yes
- ☐ No

Cohort Study Quality Assessment

Is the case definition adequate?
- ☐ Yes
- ☐ No

Representativeness of the exposed cohort
- ☐ Obviously representative series of cases
- ☐ Somewhat representative
- ☐ Selected group
- ☐ No description

Control Selection
- ☐ Similar community
- ☐ Non-similar community
- ☐ No mention

Definition of Controls
- ☐ No h/o disease
- ☐ h/o disease

Comparability of cases and controls on the basis of the design or analysis, eg study controls for differences in groups?
- ☐ Yes
- ☐ No

Ascertainment of outcome
- ☐ blinded, secure record
- ☐ record linkage
- ☐ self report
- ☐ no description

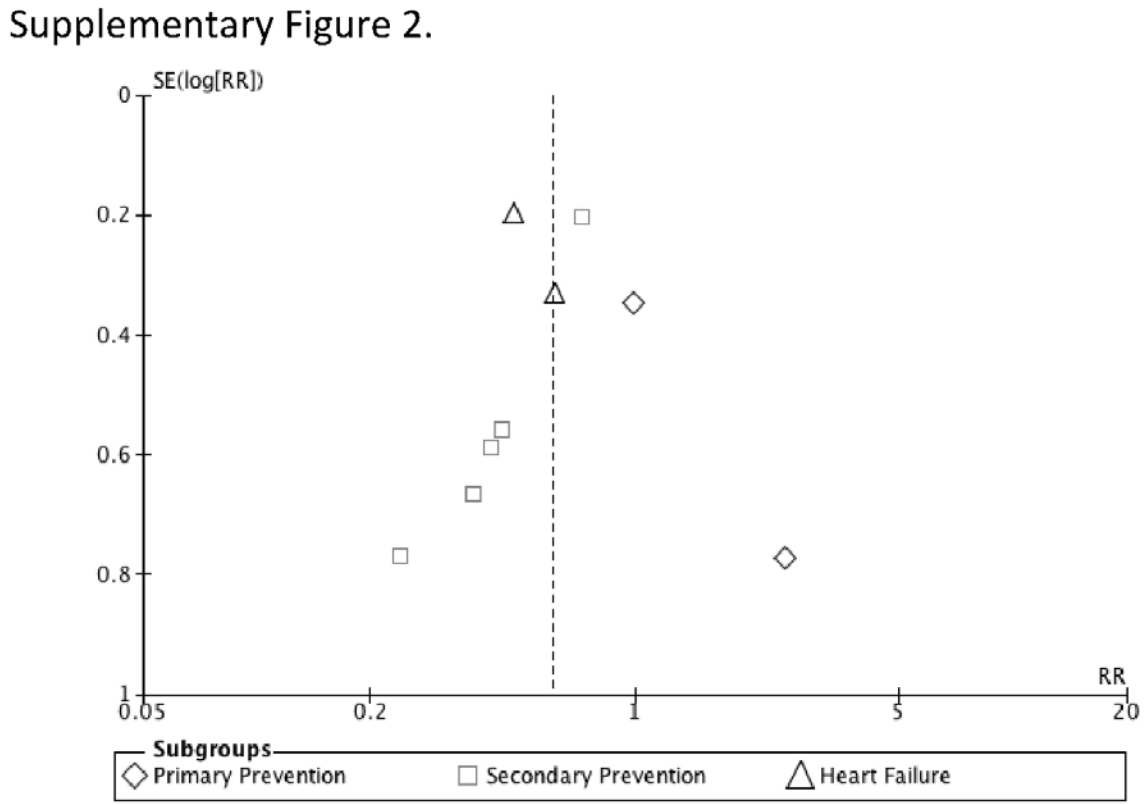
Adequacy of follow up?
- ☐ Yes
- ☐ No

Adequacy of follow up of cohorts
- ☐ Complete follow up - all subjects accounted for
- ☐ Subjects lost to follow up unlikely to introduce bias; small number lost
- ☐ Follow up rate adequate and/or no description of those lost
- ☐ no statement

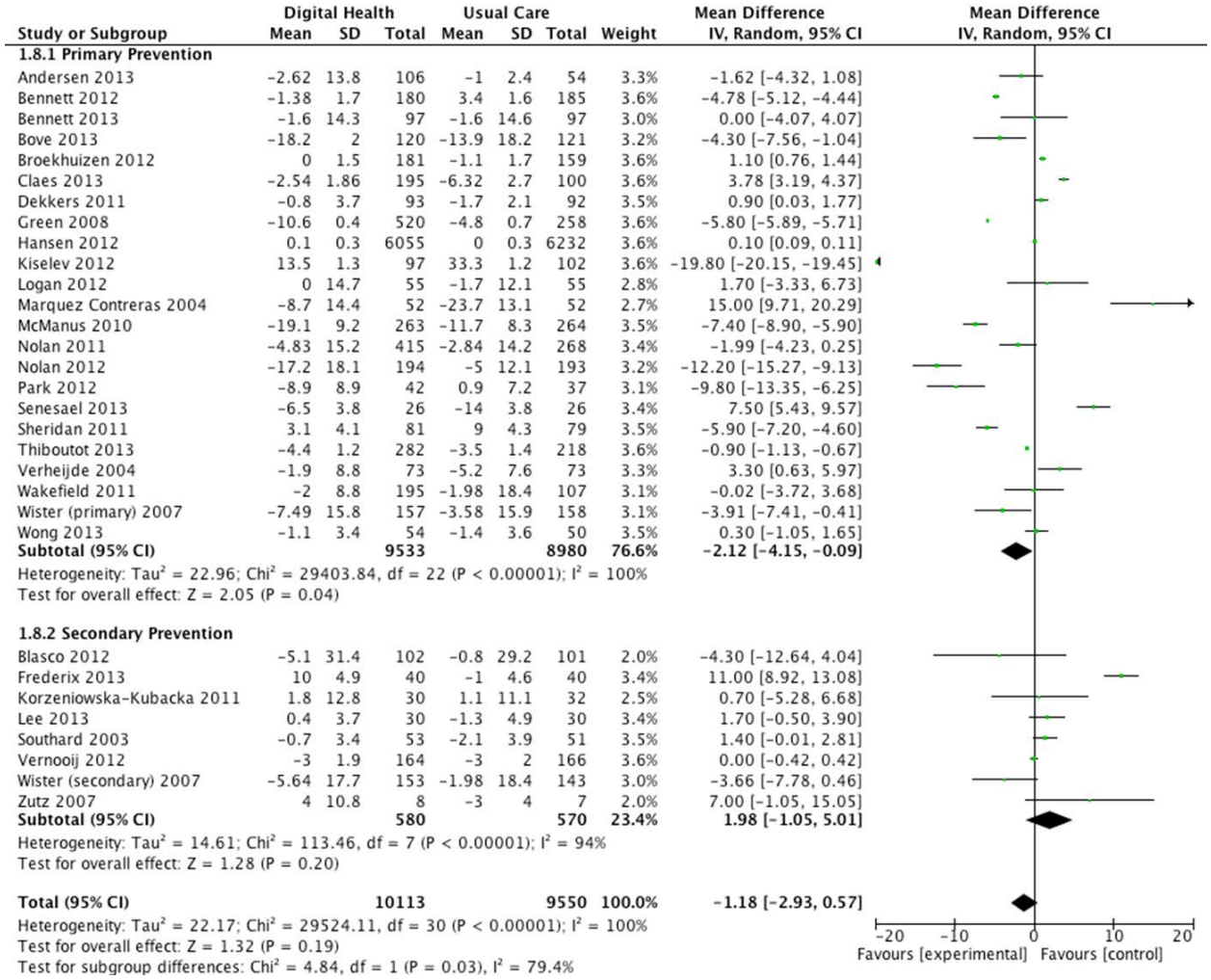
Author Contact Returned?
- ☐ Yes
- ☐ No

Data additions/changes?
- ☐ Yes
- ☐ No

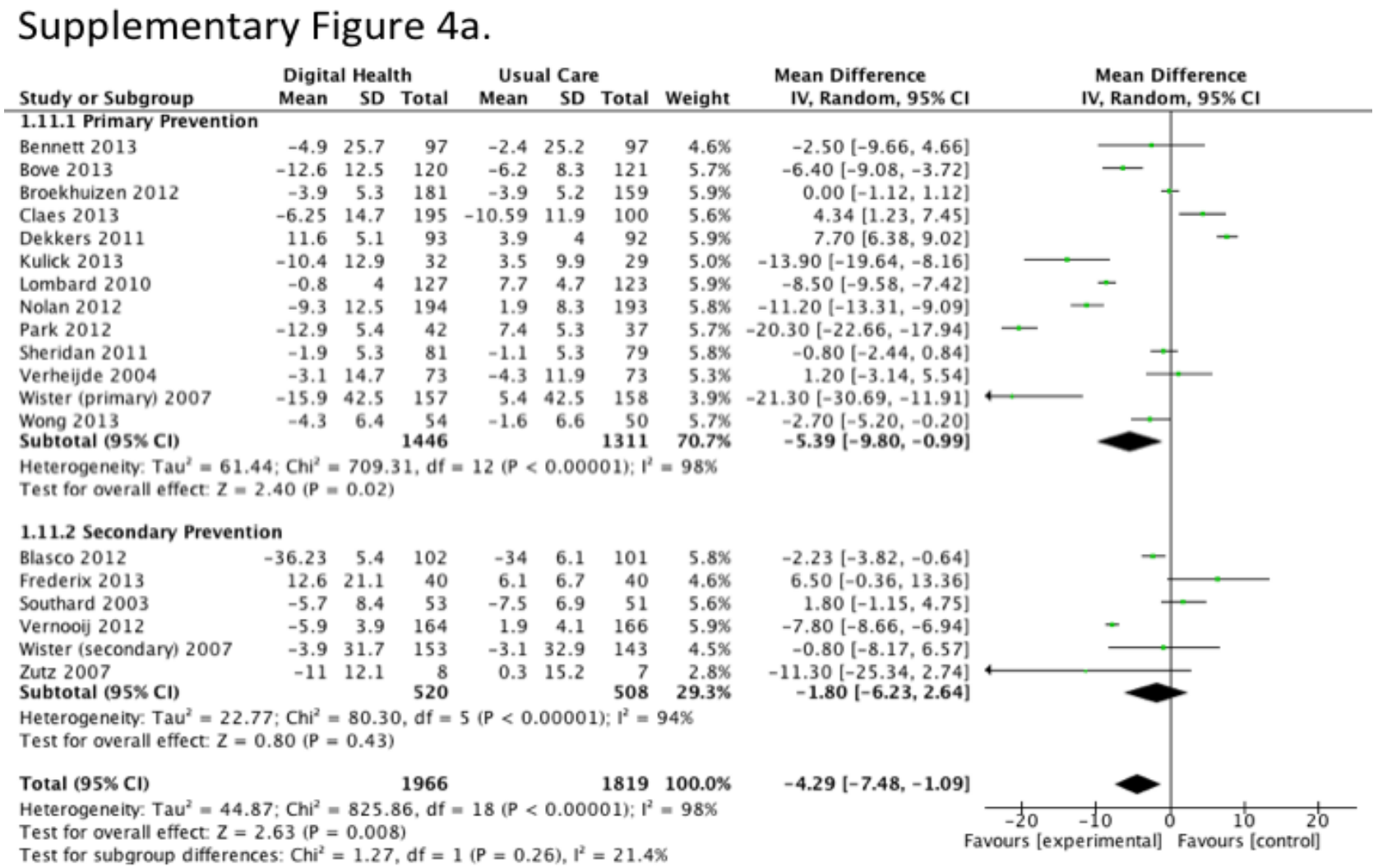
Supplementary Figure 2: Funnel plot for CVD outcomes.



Supplementary Figure 3: Systolic Blood Pressure and DHI.



Supplementary Figure 4a: Total-Cholesterol and DHI.



Supplementary Figure 4b: LDL-Cholesterol and DHI.

Supplementary Figure 4b.