ORIGINAL ARTICLE

Mobile health for cardiovascular risk management after cardiac surgery: results of a sub-analysis of The Box 2.0 study

Tommas Evan Biersteker [1], **Mark J. Boogers** [1], **Martin Jan Schalij** [1,*], **Jerry Braun** [2], **Rolf H. H. Groenwold** [3], **Douwe E. Atsma** [1], and **Roderick Willem Treskes** [1]

[1]Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands; [2]Department of Cardiothoracic Surgery, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands; and [3]Department of Clinical Epidemiology and Biomedical Data Sciences, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands

Aims	Lowering low-density lipoprotein (LDL-C) and blood pressure (BP) levels to guideline recommended values reduces the risk of major adverse cardiac events in patients who underwent coronary artery bypass grafting (CABG). To improve cardiovascular risk management, this study evaluated the effects of mobile health (mHealth) on BP and cholesterol levels in patients after standalone CABG.
Methods and results	This study is a *post hoc* analysis of an observational cohort study among 228 adult patients who underwent standalone CABG surgery at a tertiary care hospital in The Netherlands. A total of 117 patients received standard care, and 111 patients underwent an mHealth intervention. This consisted of frequent BP and weight monitoring with regimen adjustment in case of high BP. Primary outcome was difference in systolic BP and LDL-C between baseline and value after three months of follow-up. Mean age in the intervention group was 62.7 years, 98 (88.3%) patients were male. A total of 26 449 mHealth measurements were recorded. At three months, systolic BP decreased by 7.0 mmHg [standard deviation (SD): 15.1] in the intervention group vs. -0.3 mmHg (SD: 17.6; $P < 0.00001$) in controls; body weight decreased by 1.76 kg (SD: 3.23) in the intervention group vs. -0.31 kg (SD: 2.55; $P = 0.002$) in controls. Serum LDL-C was significantly lower in the intervention group vs. controls (median: 1.8 vs. 2.0 mmol/L; $P = 0.0002$).
Conclusion	This study showed an association between home monitoring after CABG and a reduction in systolic BP, body weight, and serum LDL-C. The causality of the association between the observed weight loss and decreased LDL-C in intervention group patients remains to be investigated.
Keywords	Electronic health • eHealth • Mobile health • mHealth • Coronary artery bypass grafting • Controlled BP • Lipid lowering • Coronary artery disease • Tertiary prevention

Introduction

After coronary artery bypass grafting (CABG), patients remain at high risk of adverse events due to coronary artery disease (CAD). All-cause mortality is 6.2% within the first year after isolated CABG, and 30.7% within 10 years.[1,1] Of these deaths, 65% have a cardiac cause, with non ST-elevation myocardial infarction to be the leading cause of death, followed by heart failure.[2,3] Clinical trials have shown that a 5 mmHg reduction of systolic blood pressure (BP) reduces the risk of major cardiovascular events by about 10%.[4] Adequate regulation of serum low-density lipoprotein (LDL-C) levels is also of importance. In a meta-analysis of 49 clinical trials with 312 175 participants, each 1-mmol/L (38.7 mg/dL) reduction in LDL-C was associated with a relative risk of major vascular events of 0.77.[5] Therefore, current European guidelines on cardiovascular disease prevention stress the importance of reducing LDL-C and BP levels in patients who underwent CABG.[6] However, a study in 16 646 patients in

24 European countries found that only a minority of patients achieved adequate control of these risk factors 6 months after CABG or percutaneous coronary intervention (PCI): 48.6% continued smoking, 42.7% had a BP $\geq$140/90 mmHg, and 80.5% had an LDL-C of $\geq$1.8.[7] Moreover, only one-third of all patients with CAD attended cardiac rehabilitation after undergoing CABG or PCI.[7,8]

Interactive mobile health (mHealth) has been shown to be an effective intervention on lifestyle through health education.[9–11] Mobile health is defined as the use of mobile phone and wireless technologies to support the achievement of health objectives.[12] The electronic health (eHealth) working group of the European Society of Cardiology (ESC) now recommends the use of mHealth to support remote clinical care and improve psychosocial health, diet, and smoking cessation, in the primary, secondary, and tertiary prevention of CAD.[6,13,14] However, positive effects of mHealth on cardiovascular risk management has not yet been definitively demonstrated: several randomized controlled trials (RCTs) suggested a beneficial effect of mHealth interventions on patient self-management,[15–20] although other studies found no statistically significant improvement.[21–25] Moreover, no published results are available on the use of mHealth in patients after CABG.

The use of mHealth devices, such as a BP monitor and weight scale, may be beneficial in the outpatient follow-up of patients with a high (residual) CAD risk. In order to improve cardiovascular risk management, the aim of the present study—*The Box 2.0*—is to evaluate the effects of mHealth on BP, body weight, and cholesterol levels in patients after standalone CABG surgery.

Methods

Study design, recruitment, and population

As previously described, *The Box 2.0* was a non-randomized observational cohort study with a prospective intervention group and a historical control group for comparison.[26] This study was conducted at the department of cardiothoracic surgery of the Leiden University Medical Center (LUMC), a tertiary care hospital in The Netherlands, and registered under NCT03690492 (ClinicalTrials.gov) and NL65959.058.18 (ToetsingOnline.nl). The study complied with the Declaration of Helsinki, and was approved by the ethics committee. The current study is a *post hoc* analysis of *The Box 2.0*.

As lack of attainment of lipid target levels following CABG is associated with long-term mortality,[27] frequent lipid level measurements are performed in patients after CABG. However, not all cardiac surgery patients need this form of cardiovascular risk management. In order to improve comparability, solely patients who underwent CABG were selected for the present substudy to ensure comparability regarding BP and lipid level outcomes. As a wide variety of concomitant surgical procedures could be performed, affecting outcomes, patients undergoing concomitant procedures were excluded, as well as those with incomplete BP data at the end of follow-up. We deemed BP data to be complete if there was an available BP measurement at the last outpatient clinic visit. The aim of introducing these selection criteria was to optimize comparability between both study groups. Other exclusion criteria were: pregnancy, incapacitation or mechanical support at the moment of inclusion, ventricular septal rupture, implantation of a ventricular assist device, and emergency cardiac surgery defined as a score 1 or 2 at the Interagency Registry for Mechanically Assisted Circulatory Support scale.

Between December 2017 and September 2018, 365 adult patients who underwent cardiac surgery via sternotomy were consecutively screened and included in the control group, 117 of whom underwent standalone CABG surgery. From September 2018 to November 2020, another 365 patients were consecutively screened and included in the intervention group, 111 of whom underwent standalone CABG surgery. Study results of all 730 patients are described separately.[28] Eligible patients were recruited at the outpatient clinic before surgery, 4 to 6 weeks before surgery, or on the ward during admission, 1 to 5 days before surgery or between 3 days after surgery and 1 day before discharge. Eligible patients were given oral and written study information, and were given at least 24 h to consider participation. All patients were recruited by a nurse practitioner (NP) and signed the informed consent form before discharge. To ensure all eligible patients

were approached with study information and informed consent forms, the study team reviewed the weekly surgery schedule of the thoracic surgery department, and a weekly meeting with this department was held. Discharge from the department of cardiothoracic surgery marked the start of follow-up. The total duration of follow-up was 92 days.

Control group

Control group patients underwent standardized follow-up, defined as two physical outpatient clinic visits; one visit 2 weeks after initial discharge and one visit 3 months after discharge. The 2-week visit consisted of an examination of the sternal wound and, if applicable, the vein harvesting wound, and a 12-lead 10 s electrocardiogram (ECG) was made. At 3 months, another ECG was made, the BP and a laboratory test for cholesterol levels were taken, and a transthoracic echocardiogram was performed. No mHealth was used in these patients.

Intervention group

Intervention group patients received mHealth intervention *The Box*, consisting of an activity tracker, BP monitor, thermometer, and a weight scale (all from Withings, Issy les Moulineaux, France). These devices are shown in *Figure 1*. During the first two weeks of follow-up, patients were requested to take daily measurements with the Withings devices. For the remainder of the 3-month follow-up, measurements were taken three times a week.

Furthermore, the standard first outpatient clinic visit, 2 weeks after discharge, was replaced by an electronic visit (eVisit). This eVisit consisted of an identical patient interview compared to the standard outpatient clinic follow-up and was performed by the same NP, who also checked the sternum wound and, if applicable, also the vein harvesting wound via the webcam. During follow-up, the therapeutic regimen could be revised based on the results of mHealth measurements such as BP as well as on symptoms. The outpatient clinic visit, 3 months after discharge, was identical to the outpatient clinic visit of control group patients, and marked the end of follow-up. Importantly, except for the receiving the mHealth intervention, consisting of this eVisit and scheduled measurements, the follow up of intervention and control groups was equal. A flow chart of patient flow has been published previously.[26]

The NP checked all sent-in data three times per week. An automated alarm was triggered in case of a data irregularity, which made these irregularities stand out from other measurements. In case of an irregularity, the NP contacted the patient within 48 h after the data were received. An overview of data irregularities has been published previously.[26] Based on these irregularities, the NP could amend the medication regime if necessary. Importantly, patients were instructed to contact emergency services if needed, as The Box served to support their convalescence.

Medication

Patients were discharged with either metoprolol or sotalol, unless they were on bisoprolol or other beta-blockers before surgery. As internal cardiothoracic guidelines changed in 2019, we expected significantly more intervention group patients to be discharged with sotalol instead of metoprolol. BP medication was based on daily BP readings during the admission period, and updated until the day of discharge. As the NP could act on data irregularities, BP medication could be amended accordingly during follow-up. This was done in case patients registered three consecutive measurements above either 140 mmHg (systolic BP) or 90 mmHg (diastolic BP), unless a reading was deemed to be incorrect. The NP always discussed medication changes with one supervising cardiologist, who was dedicated to this project.

Cholesterol levels were checked before surgery and medication was either started or amended based on these results. As cholesterol levels were only measured before surgery and after follow-up, not during follow-up, cholesterol medication was only changed in case of potential side-effects.

Connectibility and technical assistance

The Box 2.0 was handed out before discharge from the LUMC; required mobile applications were installed by eHealth-technicians if necessary. A helpdesk was available throughout the duration of each patients' participation in the study, to assist with technical issues. Patients, who did not own a smartphone, were equipped with a loan device free of charge. To warrant the privacy of all study patients, patients were provided with an @hlc.nl email address based on

Figure 1 The box and its contents.

a randomly generated code as the individual's login name, combined with a randomly generated password. The @hlc.nl domain is owned and maintained by the LUMC, its data are stored on LUMC servers. Online data from the mHealth devices were accessed via the Application Programming Interface (API; Withings). The Withings API allowed all device data to be automatically imported in the electronic medical records of the LUMC, via a protected authentication protocol (OAUTH2). Patients were phoned by eHealth-technicians after two weeks of not receiving any mHealth measurement, reminding them of the importance of these measurements.

Study endpoints

The primary endpoints of this study were the systolic and diastolic BP, as well as body weight and serum LDL-C levels at the end of follow-up. Secondary endpoints were total cholesterol, HDL, LDL-C/cholesterol ratio and triglycerides at the end of follow-up, as well as BP control and the percentage of patients with an adequate LDL-C at the end of follow-up. These parameters were all measured at the end of follow-up. BP control was defined as a BP below the threshold of hypertension—<140/<90 mmHg—as it was defined by the ESC guidelines,[29] measured with a manual sphygmomanometer (Welch Allyn 707) at the outpatient clinic. ESC guidelines were also used to define LDL-C adequacy: in patients with a very high cardiovascular risk, the treatment target for LDL-C is <1.8 mmol/L or a reduction of at least 50% from baseline LDL-C.[30]

Statistical analysis

Demographic and baseline characteristics are summarized for all subjects as mean ± standard deviation (SD), median and interquartile range (IQR), or

frequencies for continuous and categorical variables, respectively. Normality was assessed using the Shapiro–Wilk test. Variables with a skewed distribution were compared using a Mann–Whitney U-test. Categorical variables were compared with Fisher exact tests. Blood pressure and cholesterol results were adjusted for age, gender, body mass index, hypertension at baseline, and antihypertensive treatment at baseline, as these were confounding variables, as well as for baseline differences: length of hospital stay, and either systolic BP at baseline for the analyses of systolic BP endpoints, or diastolic BP at baseline for the analyses of diastolic BP endpoints. All analyses were performed with SPSS version 25.0 (released 2017, IBM SPSS Statistics for Windows, IBM Corp, Armonk, NY, USA).

Results

Patient characteristics

A total of 228 patients were enrolled in this substudy; 117 controls and 111 intervention group patients. All baseline characteristics are presented in *Table 1*. In both groups, 98 patients were male (84% of controls and 88% of intervention group patients, respectively; $P = 0.35$). Mean age in the intervention group was 62.7 years vs. 65.3 years for controls ($P = 0.05$) and significantly more controls had a history of hypertension ($n = 74/117$, 63% vs. $n = 51/111$, 46%; $P = 0.01$). Diastolic BP at discharge was higher in intervention patients than in controls (81.2 mmHg vs. 75.6 mmHg; $P = 0.0005$). As expected, significantly more intervention group patients were discharged with sotalol compared to controls ($n = 80/117$, 68% vs. $n = 96/11$, 87%; $P = 0.002$), and as a result less metoprolol was used ($n = 31/117$, 27% vs. $n = 11/111$, 10%; $P = 0.002$). At baseline, serum cholesterol levels did not differ significantly between both groups, nor did the percentage of patients treated with cholesterol lowering medication. Importantly, there were no cases of familial hypercholesterolemia in the study population. None of the patients had a contra-indication for the use of statins.

Protocol adherence

A total of 26 449 mHealth measurements have been recorded by all intervention group patients, on 6295 unique measurement days. Patients registered a median of 222 measurements (IQR: 164–304) on a median of 52 of out 92 days (IQR: 37–84). A summary of all measurement totals is provided in Table A1 of the Appendix. *Figure 2* presents the protocol adherence for all intervention group patients. A total of 16 (14.4%) Box patients registered no measurements for ≥21 consecutive days and were considered non-adherent. Data of all non-adherent patients was used for the analyses; no patients dropped out of the study.

Medication

During follow-up, BP medication was unchanged in 105 (89.7%) control group patients vs. 72 (34.9%) intervention group patients ($P < 0.00001$). This is presented in *Table 2*. In significantly more intervention group patients (26; 23.4%) vs. controls (4; 3.5%; $P < 0.00001$), BP medication was added or the dose was increased. On the other hand, BP medication was removed or the dose was reduced in 11 (10.0%) of all intervention group patients vs. 6 (5.1%) controls ($P = 0.21$).

Cholesterol medication was amended in 4 (3.6%) intervention group patients and 4 (3.4%) controls ($P = 0.96$). Reasons were myalgia ($n = 3$), inadequate initial treatment ($n = 3$), drug interactions ($n = 1$), and dizziness on atorvastatin ($n = 1$). All medication changes are presented in Table A2 of the Appendix.

Endpoint: BP

Results of the BP endpoints are presented in *Table 3*. The primary endpoints, being systolic and diastolic BP at the end of follow-up, were both lower in the intervention group. The systolic BP was significantly lower in intervention patients than in controls (mean: 129.5 mmHg vs.

Table 1 Baseline characteristics

	Control (n = 117)	Intervention (n = 111)	P value
Gender, male (%)	98 (83.8%)	98 (88.3%)	0.347
Age, years (SD)	65.3 (9.9)	62.7 (9.3)	**0.046**
BMI, kg/m^2 (SD)	27.8 (4.1)	26.8 (3.9)	**0.043**
History of smoking (%)	67 (57.3%)	65 (58.6%)	0.894
Hypertension (%)	74 (63.2%)	51 (45.9%)	**0.011**
Hypercholesterolemia (%)	50 (42.7%)	51 (45.9%)	0.690
Diabetes Mellitus (%)	40 (34.2%)	28 (25.2%)	0.150
History of myocardial infarction (%)	46 (39.3%)	57 (51.4%)	0.084
History of PCI (%)	37 (31.6%)	37 (33.3%)	0.888
History of CABG (%)	3 (2.6%)	0 (0.0%)	0.247
History of CVA/TIA (%)	9 (7.7%)	10 (9.0%)	0.812
Peripheral arterial disease (%)	6 (5.1%)	9 (8.1%)	0.430
Urgent operation (%)	49 (41.9%)	43 (38.7%)	0.686
Resternotomy (%)	9 (7.7%)	6 (5.4%)	0.597
Length of hospital stay, days (IQR) [Range]	6 (4–7) [2–24]	6 (6–7.5) [5–16]	**<0.0001**
Readmission (%)	8 (6.8%)	2 (1.8%)	0.103
MACE before initial discharge (%)	5 (4.3%)	4 (3.6%)	1.000
LVEF, % (SD) (wel of niet?)	54.4 (8.8)	54.9 (8.3)	0.640
Systolic BP, mmHg (SD)	139.2 (20.6)	141.0 (18.3)	0.478
Diastolic BP, mmHg (SD)	75.6 (11.3)	81.2 (12.5)	**0.0005**
Use of ≥1 antihypertensive drug (%)	99 (84.6%)	86 (77.5%)	0.168
ACE inhibitor	64 (54.7%)	62 (55.9%)	
Angiotensin receptor blocker	27 (23.1%)	16 (14.4%)	
Calcium antagonist	37 (31.6%)	14 (12.6%)	
Diuretic	27 (23.1%)	12 (10.8%)	
Antiarrhythmics/betablockers			
Amiodarone (%)	2 (1.7%)	3 (2.7%)	0.273
Sotalol (%)	80 (68.4%)	96 (86.5%)	**0.002**
Metoprolol (%)	31 (26.5%)	11 (9.9%)	**0.002**
Bisoprolol (%)	3 (2.6%)	1 (1.0%)	0.340
Total cholesterol, mmol/L (IQR) [Range]	4.6 (3.7–5.5) [2.0–7.5]	4.4 (3.8–5.4) [2.4–8.6]	0.867
LDL, mmol/L (IQR) [Range]	2.9 (2.0–3.6) [1.0–5.6]	2.4 (2.0–3.4) [0.9–6.1]	0.297
HDL, mmol/L (IQR) [Range]	1.1 (0.9–1.3) [0.5–2.4]	1.1 (1.0–1.3) [0.7–2.7]	0.307
Cholesterol ratio (IQR) [Range]	4.2 (3.2–5.2) [1.8–9.0]	3.8 (3.2–4.8) [2.0–9.5]	0.288
Triglycerides, mmol/L (IQR) [Range]	1.5 (1.0–2.2) [0.5–5.6]	1.5 (1.0–2.0) [0.4–5.5]	0.521
Use of cholesterol lowering drug(s) (%)	114 (97.4%)	109 (98.2%)	0.694
Statin	97 (82.9%)	96 (86.5%)	
Ezetimibe	6 (5.1%)	4 (3.6%)	
Statin + ezetimibe	8 (6.8%)	8 (7.2%)	
PCSK9 inhibitor + ezetimibe	3 (2.6%)	1 (1.0%)	

Significant *P* values are highlighted in bold text.
[a]No other antiarrhythmics or betablockers were used in the study population.

137.4 mmHg, respectively; *P* = 0.02). The diastolic BP showed no significant difference, although it was lower in intervention patients than in controls (mean: 76.8 mmHg vs. 77.9 mmHg, respectively; *P* = 0.17). Notably, in the intervention group, both systolic and diastolic BP were significantly lower at the end of follow-up than at baseline: -7.0 (SD: 15.1) and -3.5 (SD: 16.8), respectively. In the control group, systolic and diastolic BP were slightly higher at the end of follow-up than at baseline: 0.3 (SD: 17.6) and 4.7 (SD: 17.3), respectively. When

comparing both study groups, the systolic BP difference was significant (*P* = 0.016) while the diastolic BP difference was not (*P* = 0.30).

For the secondary endpoints, 82% of intervention patients had an adequate BP (*n* = 91/111) vs. 57% of the control group (*n* = 67/117; *P* = 0.0004). Antihypertensive treatment was amended in 39 intervention group patients (35%) vs. 11 controls (9%; *P* < 0.0001). No correlation was found between adherence (measurement days) and systolic or diastolic BP at the end of follow-up (*P* = 0.24).
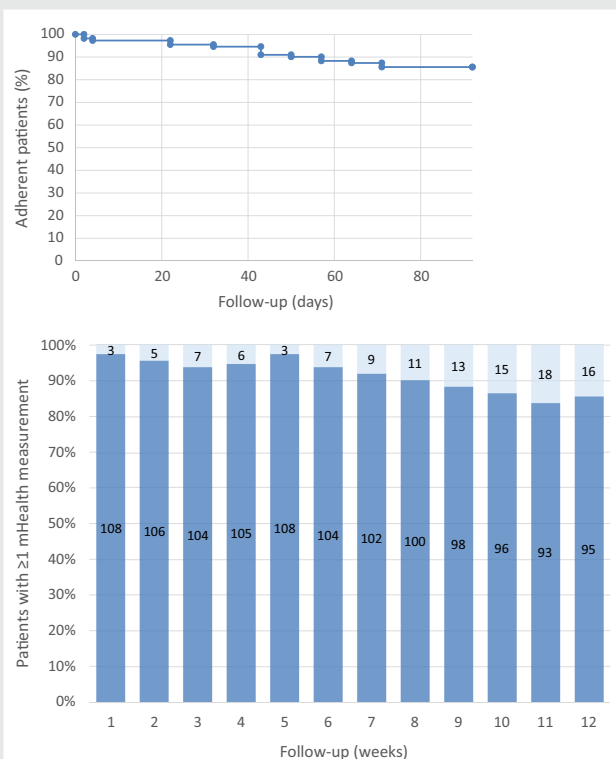
Figure 2 mHealth device use and Kaplan–Meier estimates of non-adherence, defined as ≥21 consecutive days without at least one registered mHealth measurement regarding BP, weight, temperature or ECG. Step count measurements were not included in this analysis.

Table 2 Blood pressure medication regime during follow-up

BP medication during follow-up			P value
BP medication *added*	3 (2.6%)	15 (13.5%)	**<0.00001**
Dose increased	1 (0.9%)	11 (9.9%)	
BP medication *removed*	6 (5.1%)	10 (9.0%)	0.21
Dose reduced	0 (0.0%)	1 (1.0%)	
BP medication *unchanged*	105 (89.7%)	72 (64.9%)	**<0.00001**
Medication *switched,* comparable dose	2 (1.7%)	2 (1.8%)	1

Significant P values are highlighted in bold text.

Table 3 Blood pressure outcomes

	Control (n = 117)	Intervention (n = 111)	P value
Systolic BP, mmHg (SD)	137.4 (19.1)	129.5 (17.2)	**P = 0.02**
Diastolic BP, mmHg (SD)	77.9 (10.5)	76.8 (9.6)	P = 0.17
Adequate BP (%)[a]	67 (57.3%)	91 (82.0%)	**P = 0.0004**
Systolic BP difference from baseline, mmHg (SD)	0.3 (17.6)	-7.0 (15.1)	**P = 0.02**
Diastolic BP difference from baseline, mmHg (SD)	4.7 (17.3)	-3.5 (16.8)	P = 0.30

Significant P values are highlighted in bold text.
[a]Adequate BP is defined as a systolic BP <141 and a diastolic BP <91. These results are adjusted for age, gender, BMI, hypertension at baseline, and antihypertensive treatment at baseline.

Endpoint: body weight and cholesterol levels

Results of the body weight and cholesterol endpoints are presented in *Table 4*. During follow-up, intervention group patients lost an average of 1.76 kg (SD: 3.23), while controls on average gained 0.31 kg (SD: 2.55; P = 0.002). Serum LDL-C levels at the end of follow-up were significantly lower in the intervention group vs. controls (median: 1.8 vs. 2.0, respectively; P = 0.0002).

For the secondary endpoints, 59% of intervention patients had an adequate LDL-C at the end of follow-up (n = 65/111) vs. 38% (n = 44/117; P = 0.002) of all controls. Both groups saw a decrease in serum LDL-C levels compared to baseline, with a 28.0% reduction (IQR: 4.2%–49.6%) in the intervention group vs. a 16.7% reduction (IQR: -6.3%–46.2%) in controls. This was a significantly greater decrease in the intervention group compared to controls (P = 0.04). No correlation was found between adherence (measurement days) and LDL-C at the end of follow-up (P = 0.57).

Discussion

Main findings

This study reports the effects of an mHealth intervention on cardiovascular risk factors, in which patients made 26 449 measurements over the course of 6295 unique measurement days. A significant decrease of systolic and diastolic BP as well as serum LDL-C was observed in the intervention group. As the mHealth intervention caused BP levels to be available throughout the follow-up period, BP medication could be amended whenever needed. As expected, this was done in significantly more intervention group patients

as compared to controls. This is the main explanation for the significant decrease in systolic and diastolic BPs at the end of follow-up. The same cannot be said of the significant decrease in serum cholesterol levels, as these levels were only assessed before and after follow-up. The observed decrease in serum LDL-C levels is, however, hypothesized to be partly related to an educational consequence of the intervention, such as increased patient engagement and empowerment, and partly to the weight loss at the end of follow-up that has been observed in intervention group patients but not in controls. The reason for this significant difference between intervention and control group patients may be related to the frequent confrontation to the intervention group patients' body weight, as they were requested to weigh themselves multiple times per week.

Protocol adherence

Patients were instructed to take mHealth measurements every day for the first 2 weeks after discharge, followed by three times a week after these initial 2 weeks. This should lead to 47 unique measurement days and 235 total measurements. Our intervention group patients measured a median of 222 total measurements (IQR: 164–304) during a median of 52 unique days (IQR: 37–84); 95 (85.6%) intervention group patients remained adherent over the course of 3 months. As is shown in *Figure 2*, however, protocol adherence decreased over time as did the number of patients who logged at least one mHealth measurement per week. Disengagement is a known factor in mHealth,[31] and has been reported before.[32] Consistent feedback may positively impact the patient's

Table 4 Weight and cholesterol outcomes

	Control (n = 117)	Intervention (n = 111)	P value
Weight loss during follow-up, kg (SD)	−0.31 (2.55)	1.76 (3.23)	**0.002**
Total cholesterol, mmol/L (IQR) [Range]	3.7 (3.3–4.4) [2.0–8.1]	3.6 (3.3–4.2) [2.3–6.6]	0.15
LDL, mmol/L (IQR) [Range]	2.0 (1.7–2.7) [1.0–6.0]	1.8 (1.4–2.2) [0.3–4.7]	**0.0002**
HDL, mmol/L (IQR) [Range]	1.1 (0.9–1.3) [0.5–3.7]	1.1 (0.9–1.3) [0.4–2.1]	0.47
Cholesterol ratio (IQR) [Range]	3.4 (2.8–4.1) [0.9–7.8]	3.4 (2.7–4.0) [1.9–7.2]	0.27
Triglycerides, mmol/L (IQR) [Range]	1.4 (1.0–1.9) [0.5–4.7]	1.4 (1.1–2.4) [0.5–5.6]	0.12
Adequate LDL (%)[a]	44 (37.6%)	65 (58.6%)	**0.002**
LDL <1.8 mmol/L (%)	*37 (31.6%)*	*61 (55.0%)*	***0.0003***
LDL decreased by >50% (%)	*20 (17.1%)*	*24 (21.6%)*	*0.41*
LDL difference from baseline, % (IQR) [Range]	-16.7 (46.2–6.3) [-67.3–181.8]	-28.0 (-49.6–-4.2) [-90.7–43.3]	**0.04**
Cholesterol medication amended (%)	4 (3.4%)	4 (3.6%)	0.96

Significant P values are highlighted in bold text.
[a]Adequate LDL is defined as an LDL <1.8 mmol/L or a >50% reduction compared with the previous measurement. These results are adjusted for age, gender, BMI, hypertension at baseline, and antihypertensive treatment at baseline.

engagement. As the LUMC recently developed its own app for Box patients to use, further increasing the engagement is currently being studied.

Comparison with literature

To our best knowledge, no results of other studies have been published regarding the effect of mHealth on BP, body weight, or cholesterol levels in post-cardiac surgery patients. In other populations with an increased cardiovascular risk, mHealth interventions have been found to significantly decrease both systolic and diastolic BPs.[33–35] The differences in systolic BP after an mHealth intervention were found to be -3.9 to -7.5 mmHg, which is in line with the 7.0 mmHg systolic BP reduction of the current study. Importantly, studies have shown that a 3 mmHg reduction in systolic BP can reduce stroke mortality by 8%.[36]

Although we found a significant impact of The Box on BP outcomes, an earlier RCT that evaluated The Box in myocardial infarction patients found no significant difference in these outcomes between Box users and controls.[37] However, The Box became a standard of care in the management of various outpatient groups of the cardiology department of the LUMC due to the appreciation by both patients and care providers.[38] Over these years, The Box has been continuously improved on the patients' side as well as for staff members. Currently, NP's have an easier overview of patients' measurements, and measurement alerts have been introduced. This has improved the detection of data irregularities and, as such, may have led to an improvement in BP treatment during follow-up.

While numerous studies have evaluated mHealth interventions for BP management, very few studies have evaluated mHealth for the management of weight or hyperlipidemia. Studies that have been conducted, often used SMS or phone calls as an intervention and have been mostly unable to show significant benefit. More recent studies have shown the effect of gamification on cardiovascular health outcomes: in 2021, two RCTs were published that demonstrated significant effects on medication adherence,[39] as well as increased physical activity and reduced HbA1c levels.[32] The latter RCT provided patients with a Withings activity tracker and weight scale for the duration of one year, and an app that provided them with points and levels based on patients meeting their weekly goals and measurement frequencies. As is also seen in the current study, adherence was very high at the start of the intervention and then slowly declined. However, the RCT as well as the current study show an indirect educational effect of the mHealth intervention; the selected outcome measures were not influenced by medication changes that could have directly impacted these outcomes. This indirect educational effect is hypothesized to be caused by an increased patient engagement and empowerment; due to taking daily measurements, patients are confronted with their lifestyle and (the management of) their illness on a daily basis. However, modifying cardiovascular risk factors with the use of gamification is a new area and more research is needed to determine the scale of this effect and the psychology behind it.

Strengths and limitations

The main strength of this study is the protocol adherence of the intervention group, with a high mHealth measurement count and a high number of unique measurement days. Although patients were consecutively included and the exclusion criteria were the same for both the intervention and control group, the non-randomized nature and inclusion of a historical control group were a major limitation. Moreover, selection bias may have occurred due to the impact of COVID-19 after March 2020. This is the main reason for some differences at baseline, such as age, history of hypertension, and length of stay. We corrected for these parameters in the statistical analyses.

Another factor to take into consideration is the cost of The Box, which is around €350 ($350) and currently not refunded by the Dutch healthcare system as well as most healthcare systems around the world, making this intervention less accessible to patients. If cardiovascular risk management is the only requirement, these costs can be reduced as in this case, only a BP monitor, activity tracker, and potentially a weight scale would have to be handed out.

Conclusion

This study demonstrated mHealth to be a potentially useful intervention strategy for BP, weight and cholesterol management. However, long-term effects of mHealth on lifestyle and cardiovascular risk management could not yet be assessed and need to be addressed in further research.

Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Appendix 1

Table A1 mHealth measurement totals

	Total	Median	IQR	Range
Blood pressure	6767	45	29–87	1–307
Weight	5939	47	28–84	0–172
Temperature	4482	32	9–76	0–116
Step count days	7975	90	64–92	0–92
ECG's	1289	11	5–14	0–102
Measurement total	26 449	222	164–304	1–561
Unique measurement days	6295	52	37–84	0–92

Table A2 BP medication comparison between controls and intervention group patients at baseline and at the end of follow-up

	Control (n = 117)	Intervention (n = 111)	P value
Baseline			
No BP medication	18 (15.4%)	25 (22.5%)	0.17
1 BP medicine	53 (45.3%)	68 (61.3%)	
2 BP medicines	36 (30.8%)	18 (16.2%)	
3 BP medicines	10 (8.5%)	0 (0.0%)	
ACE inhibitor	64 (54.7%)	62 (55.9%)	
Angiotensin receptor blocker	27 (23.1%)	16 (14.4%)	
Calcium antagonist	37 (31.6%)	14 (12.6%)	
Diuretic	27 (23.1%)	12 (10.8%)	
End of follow-up			
No BP medication	19 (16.2%)	26 (23.4%)	0.19
1 BP medicine	55 (47.0%)	64 (57.7%)	
2 BP medicines	33 (28.2%)	21 (18.9%)	
3 BP medicines	10 (8.5%)	0 (0.0%)	
ACE inhibitor	56 (47.9%)	67 (60.4%)	
Angiotensin receptor blocker	30 (25.6%)	17 (15.3%)	
Calcium antagonist	35 (29.9%)	15 (13.5%)	
Diuretic	27 (23.1%)	10 (9.0%)	

Appendix: medication changes

Effect	Study arm	Cholesterol treatment at discharge	Cholesterol treatment at the end of follow-up	Reason for treatment change
Medication switch	Control 1	Atorvastatin 40 mg once daily	Ezetimib 10 mg once daily	Persistent costo-myalgenous pain during follow-up
Medication switch	Control 2	Atorvastatin 40 mg once daily	Atorvastatin 40 mg + ezetimib 10 mg once daily	During follow-up, a high LDL (4.6 mmol/L) at discharge was noticed
Medication switch	Control 3	Atorvastatin 40 mg once daily	Rosuvastatin 10 mg once daily	Generalized myalgia
Medication switch	Control 4	Simvastatin 40 mg once daily	Atorvastatin 40 mg once daily	Inadequate treatment according to ESC guidelines
Medication switch	Intervention 1	Pravastatin 40 mg once daily	Rosuvastatin 10 mg once daily	Inadequate treatment according to ESC guidelines
Medication switch	Intervention 2	Atorvastatin 40 mg once daily	Rosuvastatin 20 mg once daily	After consultation of a otorhinolaryngologist for dizziness, it was advised to switch from atorvastatin to a different statin
Medication switch	Intervention 3	Atorvastatin 40 mg once daily	Rosuvastatin 20 mg once daily	Generalized myalgia
Medication switch	Intervention 4	Atorvastatin 40 mg once daily	Rosuvastatin 20 mg once daily	Amiodarone was started during follow-up. As a result, atorvastatin was switched as it is known to interactwith amiodarone.

Effect	Study arm	BP treatment at discharge	BP treatment at the end of follow-up	Reason for treatment change
Medication switch, comparable dose	Control 1	Sotalol 3 × 40 mg + perindopril 2 mg	Metoprolol 50 mg + valsartan 2 × 40 mg	A bothersome cough during follow-up
Medication switch, comparable dose	Control 2	Metoprolol 2 × 25 mg + perindopril 2mg	Metoprolol 2 × 25 mg + losartan 25 mg	A bothersome cough during follow-up
Medication switch, comparable dose	Intervention 1	Sotalol 3 × 40 mg + perindopril 2 mg	Sotalol 3 × 40 mg + losartan 50 mg	A bothersome cough during follow-up
Medication switch, comparable dose	Intervention 2	Sotalol 2 × 80 mg + perindopril 4 mg	Sotalol 2 × 80 mg + losartan 50 mg	A bothersome cough during follow-up
BP medication added	Control 1	Sotalol 3 × 80 mg + perindopril 4 mg	Sotalol 3 × 80 mg + perindopril 4 mg + nifedipine 2 × 30 mg	Persistent hypertension during follow-up
BP medication added	Control 2	Metoprolol 2 × 25 mg + perindopril 2 mg	Metoprolol 2 × 25 mg + candesartan 8 mg + hydrochlorothiazide 25 mg	Persistent hypertension during follow-up
BP medication added	Control 3	Metoprolol 50 mg	Metoprolol 25 mg + perindopril 2 mg	Persistent hypertension during follow-up
BP medication added	Intervention 1	Sotalol 2 × 80 mg + perindopril 4mg	Sotalol 2 × 80 mg + perindopril 4 mg + amlodipine 5 mg	Persistent hypertension during follow-up
BP medication added	Intervention 2	Sotalol 2 × 80 mg + lisinopril 10mg	Sotalol 2 × 80 mg + lisinopril 20 mg + amlodipine 10 mg	Persistent hypertension during follow-up
BP medication added	Intervention 3	Metoprolol 25mg	Metoprolol 25 mg + perindopril 2mg	Persistent hypertension during follow-up
BP medication added	Intervention 4	Propranolol 2 × 10 mg + hydrochlorothiazide 25 mg	Propranolol 2 × 10 mg + hydrochlorothiazide 25 mg + perindopril 2 mg	Persistent hypertension during follow-up
BP medication added	Intervention 5	Sotalol 3 × 40 mg	Sotalol 3 × 40 mg + perindopril 2mg	Persistent hypertension during follow-up
BP medication added	Intervention 6	Sotalol 3 × 80 mg + diltiazem 300mg	Sotalol 3 × 80 mg + diltiazem 300 mg + irbesartan 75 mg	Persistent hypertension during follow-up
BP medication added	Intervention 7	Sotalol 2 × 80mg	Sotalol 2 × 80 mg + amlodipine 10 mg	Persistent hypertension during follow-up
BP medication added	Intervention 8	Sotalol 3 × 80 mg + lisinopril 2.5 mg	Sotalol 3 × 80 mg + lisinopril 2 × 10 mg + hydrochlorothiazide 12.5 mg	Persistent hypertension during follow-up
BP medication added	Intervention 9	Sotalol 2 × 80 mg	Sotalol 2 × 80 mg + perindopril 2mg	Persistent hypertension during follow-up
BP medication added	Intervention 10	Sotalol 2 × 80 mg + perindopril 2 mg	Sotalol 2 × 80 mg + amlodipine 5 mg + valsartan 160 mg	Persistent hypertension during follow-up
BP medication added	Intervention 11	Sotalol 2 × 80 mg	Sotalol 2 × 80 mg + perindopril 2 mg	Persistent hypertension during follow-up
BP medication added	Intervention 12	Sotalol 3 × 80 mg	Metoprolol 100 mg + perindopril 4 mg	Persistent hypertension during follow-up
BP medication added	Intervention 13	Sotalol 2 × 80 mg	Sotalol 2 × 80 mg + perindopril 2 mg	Persistent hypertension during follow-up
BP medication added	Intervention 14	Metoprolol 75 mg + hydrochlorothiazide 25 mg	Metoprolol 75 mg + hydrochlorothiazide 25 mg + valsartan 80 mg	Persistent hypertension during follow-up
BP medication added	Intervention 15	Sotalol 2 × 80 mg + perindopril 4 mg	Sotalol 2 × 80 mg + perindopril 8 mg + amlodipine 10 mg	Persistent hypertension during follow-up
Dose increased	Control 1	Sotalol 3 × 40 mg + losartan 25 mg	Sotalol 3 × 40 mg + losartan 50 mg	Persistent hypertension during follow-up
Dose increased	Intervention 1	Sotalol 3 × 80 mg + perindopril 4 mg	Bisoprolol 2.5 mg + perindopril 8 mg	Persistent hypertension during follow-up
Dose increased	Intervention 2	Sotalol 2 × 80 mg + enalapril 10 mg	Sotalol 2 × 80 mg + enalapril 2 × 10 mg	Persistent hypertension during follow-up

Continued

Effect	Study arm	BP treatment at discharge	BP treatment at the end of follow-up	Reason for treatment change
Dose increased	Intervention 3	Sotalol 2 × 80 mg + perindopril 2 mg	Sotalol 2 × 80 mg + perindopril 4 mg	Persistent hypertension during follow-up
Dose increased	Intervention 4	Sotalol 3 × 80 mg + perindopril 1 mg	Sotalol 3 × 80 mg + perindopril 2 mg	Persistent hypertension during follow-up
Dose increased	Intervention 5	Sotalol 2 × 80 mg + enalapril 2.5 mg	Sotalol 2 × 80 mg + enalapril 2 0mg	Persistent hypertension during follow-up
Dose increased	Intervention 6	Sotalol 2 × 80 mg + perindopril 2 mg	Sotalol 2 × 80 mg + perindopril 6 mg	Persistent hypertension during follow-up
Dose increased	Intervention 7	Sotalol 2 × 40 mg + perindopril 6 mg	Metoprolol 12.5 mg + perindopril 8 mg	Persistent hypertension during follow-up
Dose increased	Intervention 8	Sotalol 2 × 80 mg + candesartan 4 mg	Sotalol 2 × 80 mg + candesartan 2 × 4 mg	Persistent hypertension during follow-up
Dose increased	Intervention 9	Sotalol 2 × 40 mg + irbesartan 75 mg	Sotalol 2 × 40 mg + irbesartan 150 mg	Persistent hypertension during follow-up
Dose increased	Intervention 10	Perindopril 4 mg	Perindopril 6 mg	Persistent hypertension during follow-up
Dose increased	Intervention 11	Sotalol 2 × 80 mg + perindopril 2 mg	Sotalol 2 × 80 mg + perindopril 4 mg	Persistent hypertension during follow-up
BP medication removed	Control 1	Sotalol 3 × 40 mg + lisinopril 2 × 5 mg + amlodipine 5 mg	Sotalol 3 × 40 mg + lisinopril 10 mg	Hypotension during follow-up
BP medication removed	Control 2	Metoprolol 25 mg + perindopril 2 mg + diltiazem 200 mg	Diltiazem 200 mg	Hypotension during follow-up
BP medication removed	Control 3	Metoprolol 50 mg + lisinopril 5 mg + nifedipine 30 mg	Lisinopril 5 mg	Hypotension during follow-up
BP medication removed	Control 4	Metoprolol 50 mg + losartan 100 mg + hydrochlorothiazide 25 mg	Losartan 100 mg	Hypotension during follow-up
BP medication removed	Control 5	Metoprolol 25 mg + perindopril 2 mg	None	Hypotension during follow-up
BP medication removed	Control 6	Metoprolol 2 × 25 mg + lisinopril 5 mg + amlodipine 5 mg	None	Hypotension during follow-up
BP medication removed	Intervention 1	Metoprolol 75 mg + losartan 50 mg + hydrochlorothiazide 12.5 mg	None	Hypotension during follow-up
BP medication removed	Intervention 2	Sotalol 2 × 80 mg + perindopril 2 mg	Sotalol 2 × 80 mg	Hypotension during follow-up
BP medication removed	Intervention 3	Sotalol 3 × 80 mg + perindopril 4mg	Sotalol 2 × 80 mg	Hypotension during follow-up
BP medication removed	Intervention 4	Metoprolol 25 mg + enalapril 2 × 20 mg	None	Hypotension during follow-up
BP medication removed	Intervention 5	Sotalol 3 × 80 mg + enalapril 10 mg + amlodipine 5 mg	Sotalol 3 × 80 mg + enalapril 10 mg	Hypotension during follow-up
BP medication removed	Intervention 6	Sotalol 2 × 80 mg + losartan 50 mg + diltiazem 300 mg	Sotalol 2 × 80 mg	Hypotension during follow-up
BP medication removed	Intervention 7	Sotalol 2 × 80 mg + perindopril 2 mg	Sotalol 2 × 80 mg	Hypotension during follow-up
BP medication removed	Intervention 8	Sotalol 3 × 40 mg + amlodipine 5 mg	Sotalol 3 × 40 mg	Hypotension during follow-up
BP medication removed	Intervention 9	Sotalol 2 × 80 mg + hydrochlorothiazide 12.5 mg	Sotalol 2 × 80 mg	Hypotension during follow-up
BP medication removed	Intervention 10	Sotalol 3 × 40 mg + losartan 50 mg	Sotalol 3 × 40 mg	Hypotension during follow-up
Dose decreased	Intervention 1	Metoprolol 150 mg + olmesartan 20 mg + amlodipine 15 mg	Metoprolol 150 mg + olmesartan 20 mg + amlodipine 10 mg	Hypotension during follow-up

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