International Journal of Research in Medical Sciences
Palshikar A et al. Int J Res Med Sci. 2023 May;11(5):1541-1548
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20231037

Original Research Article

A real-world evidence study to evaluate the efficacy of software-driven digital therapeutics on major adverse cardiovascular events, vitals, adherence to medication and lifestyle changes among patients with coronary artery disease or post-coronary interventions

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Received: 18 March 2023
Accepted: 03 April 2023

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ABSTRACT

Background: Coronary artery disease (CAD), a leading cause of cardiovascular disease (CVD) mortality worldwide, is a major health concern in India due to the high rates of the disease. Acute coronary syndrome (ACS) is a prevalent form of CAD that requires prompt treatment. Digital therapeutics (DTx) is an emerging field that employs remote monitoring and behavioural changes to manage diseases, with promising outcomes in ACS and post-percutaneous coronary intervention (PCI) patients. This study evaluates the efficacy of a software-driven DTx intervention in enhancing outcomes for CAD patients.

Methods: This pilot, single-centred, prospective and real-world evidence cohort study aims to evaluate the effectiveness of a software-driven therapeutic intervention (LYFE) in patients with ACS and/or post-PCI. The study enrolled 30 patients over a 3-month follow-up period from October to November 2022. The main outcomes measured were changes in blood pressure, heart rate, medication adherence, the incidence of major adverse cardiovascular events (MACE), all-cause readmission, and lifestyle adherence at 1 and 3 months.

Results: The mean age of the patients was 53.2±12.1 years; 27 (93%) males and 2 (7%) were females. Mean BMI of the patients was 26.3±5.0. The mean difference for systolic blood pressure (SBP) and diastolic blood pressure (DBP) was 7.8±10.9 (p=0.001*), 3.7±5.7 (p=0.002*) respectively with statistically significant reduction, at 3 months. The 25 (83.3%) patients had controlled blood pressure at 3 months. 27 (90%) patients were adherent to the medication and physically active, while 3 (10%) inactive throughout the study period. No CVD death/major bleeding event was reported.

Conclusions: DTx improved medication adherence and blood pressure control in CAD, ACS with post-PCI patients during the study period.

Keywords: ACS, CAD, PCI, DTx, Medication adherence, Blood pressure changes

INTRODUCTION

Coronary artery disease (CAD) is a significant cause of mortality related to CVDs worldwide. Indians have the highest CAD rates, making it a major health concern in the country.[1-3] One of the most common types of CAD is ACS, which encompasses a broad range of conditions, including cardiac arrest, hemodynamic or electrical instability with cardiogenic shock, ST-segment elevation myocardial infarction (STEMI), and other related conditions. The primary treatment for ACS is PCI, which is used to restore blood flow to the affected arteries.[4] The latest guidelines recommend a specific set of

antithrombotic regimes to be followed for better prognosis of ACS patients.[5]

Ensuring adherence to prescribed medication is crucial for effective medical treatment and deriving maximum benefits from it. Patients need to take the recommended medication to manage their condition successfully.[6] A retrospective study has demonstrated that individuals with ACS who maintained a medication adherence rate of at least 90% were less likely to experience MACE than those with an adherence rate of less than 90%.[7]

The adherence to secondary prevention medication after ACS is not up to desired level worldwide.[8] Studies show that low adherence and persistence rates are common among the stroke patients.[9] Post-ACS discharge, reported rate of unplanned readmissions due to cardiovascular issues is 21.4%, and the rate of non-adherence to medication is 37.97%.[10] The adherence rate to post-PCI medications among patients with STEMI is also relatively low (28.4%).[11] Indians are more susceptible to frequent hospitalizations due to complications of CAD, with admission rates being much higher for populations under 40 years old.[3] As a result, there is a pressing need for effective and efficient management strategies to reduce the burden of CAD and its complications.

The field of digital health is expanding and employs technology such as smartphones, wearable devices, and cloud-based platforms to enhance healthcare and wellness. Within this field, DTx is an emerging area that seeks to treat and manage diseases using remote monitoring and promoting positive behavioural changes by utilising approved therapeutic interventions, such as smartphone applications, and has the potential to effectively treat various medical conditions.[12]

Utilizing mHealth tools can enhance medication adherence among people with CVDs.[13] Encouraging results are observed in application of DTx interventions in post-ACS and post-PCI patients with respect to three aspects namely-medication adherence, the correct number of doses and status of cardiac functioning.[14-16]

The present study aims to evaluate the efficacy of the software-driven digital therapeutic intervention on cardiovascular events, vitals, adherence to lifestyle changes and medication among patients with CAD or post-coronary intervention, with the goal of reducing complications and hospitalization.

METHODS

Study design

This is a pilot, single-centred, prospective and real-world evidence cohort study performed with a 3-month follow-up period, to introduce a clinical evidence-based, software-driven therapeutics intervention in patients with CAD and/ post-coronary interventions. A total of 30 patients were enrolled between October to November 2022. This study conducted in compliance with protocol approved by institutional ethics committee (IEC), in applicability to good clinical practice (GCP) guidelines.

Study population and intervention

Patients were included in this study after meeting the eligibility criteria as 1) Patients aged 18 years or older; 2) Patients who have a documented diagnosis of CAD and or who underwent coronary intervention either as an emergency or an elective procedure; 3) Patients willing to comply with the follow-up plan set as per the real world scenario; 4) Patient who has read and signed the informed consent form (ICF); 5) Patients who have basic reading skills (English/Hindi/Marathi)

Intervention

LYFE (by Lupin digital health Pvt Ltd) is a personalised digital heart care program designed by cardiologist that allows patients to monitor and manage heart health. This program consists of Mobile app integrated with connected devices (wireless activity and heart rate tracker, blood pressure monitor, pulse oximeter, glucometer, Smart weighing scale and ECG handheld). Integration of wireless devices allowed patients to measure and monitor their blood pressure, heart rate and physical activity. Patients received reminders on medications, lifestyle modifications and appointments. LYFE program has seven components-1) Comprehensive and proactive monitoring with suite of auto-scheduled lab tests and teleconsultation with the treating cardiologists, 2) Adherence to lifestyle changes and medication through nudges, providing actionable, personalized insights and bite-sized competition 3) Caregiver involvement through training and dedicated caregiver app to get alerts and monitor vitals, 4) Personalized coaching and support from dedicated nutritionists and health coaches to help patient manage disease through diet and exercise plan which is contextual to patient's lifestyle, condition and preference, 5) Education modules on disease for the patient and care giver, 6) Emergency response system to help patient manage any cardiac emergencies. It also includes access to early detection system (symptoms based/auto triggered SOS button on fall detection, erratic heart rate) that alerts doctors and family members and triggers emergency protocol, 7) Access to ambulances equipped to handle cardiac events and pre-determined hospitals based on availability and 1st aid education (Figure 1).

Study outcomes

The major outcomes were to compare mean change in systolic and DBP and heart rate from baseline at 1 month and 3 months, adherence to medication, incidence of MACE, all-cause readmission and adherence to lifestyle modification like exercise and diet at 3 months.

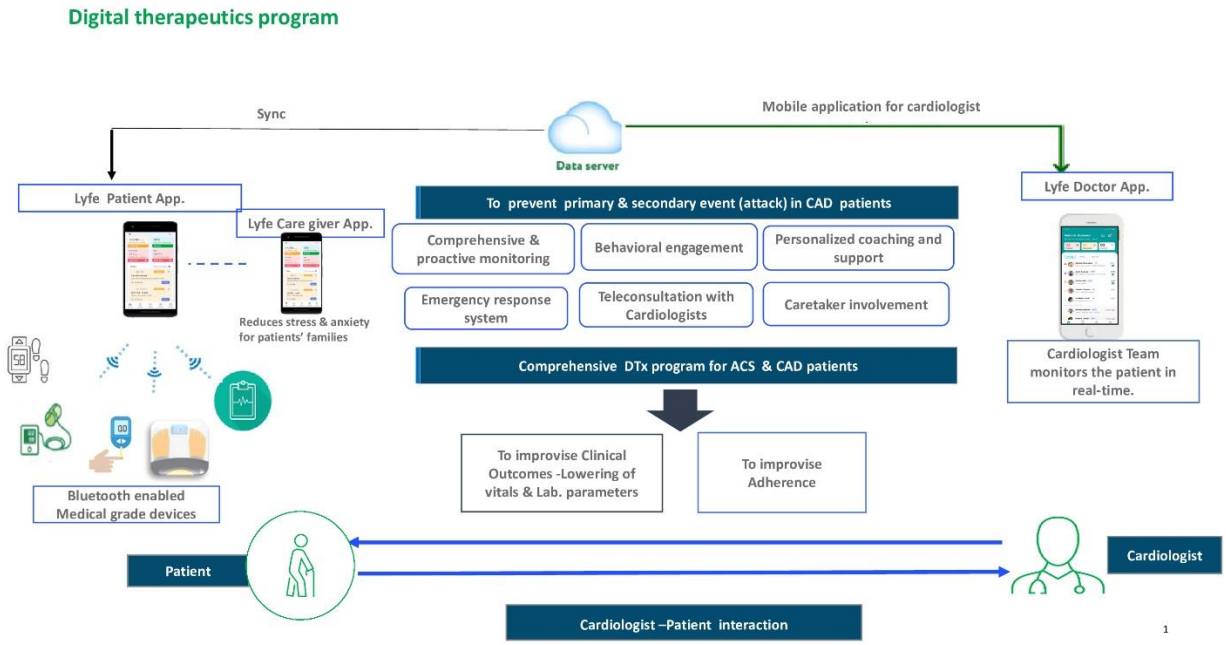

Figure 1: DTx program flowchart for ACS/CAD patients.

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Statistical analysis

Statistical analyses were performed at α=0.05 significance level. Continuous data were presented with mean and standard deviation (SD) and for categorical data the number and percentage of patients within each category were reported. Student pair t-test were used to compare significant change between the baseline and follow up values. P value of less than 0.05 was considered to indicate a statistically significant difference. The statistical analyses were done using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA) and Microsoft corporation (2019), Microsoft excel.

RESULTS

Overview of baseline characteristics

The study enrolled a total of 30 patients for a period of 3 months. Out of 30 patients, 27 (93.3%) were males with a mean age of 53.2±12.1 years. The mean height of the patients was 166.7±7.9 cm and the mean weight was 72.9±13.7 kg, with a mean BMI of 26.3±5.0. Twenty-five (83.3%) of 30 patients did not smoke and 18 (60%) did not consume alcohol. Eighteen (60%) patients preferred a non-vegetarian diet while the remaining 12 (40%) preferred a vegetarian diet. 12 (40%) patients did not have any comorbidities; however, hypertension and type 2 diabetes were present in 9 (30%) and 6 (20%) patients, respectively, while 3 (10%) patients had both conditions. Patients had a mean SBP and DBP of 128.8±20.0 mmHg and 83.8±8.7 mmHg with a mean HR of 81.9±12.1 bpm. Diagnosis revealed the presence of STEMI, NSTEMI, and unstable angina in the study participants (Table 1).

Overall 16 (53.3%) patients suffered single-vessel coronary artery lesions, 6 (20.0%) suffered double-vessel lesions and 3 (10%) suffered triple-vessel lesions. PCI was performed on 22 (73.3%) patients, CABG on 2 (6.7%) and thrombolysis on 1 (3.3%) patient while 3 (16.7%) patients had no interventions and were managed on medications (Table 1).

Compliance and adherence

A total of 27 (90%) of the patients remained active throughout the study period with 23 (76.7%) of the patients responding on track and 4 (13.3%) patients with delayed response. Two (6.7%) patients stopped their journey in between while 1 (3.3%) patient was reported to be inactive (Table 2).

Out of 30 patients, 90% were adherent to medication while the remaining 10% were non-adherents or dropouts (Figure 2).

Clinical outcomes

The mean change in SBP, DBP and HR of the active study participants were analysed from baseline to 1

month and at the conclusion of the 3-month study (Table 3). The mean difference for SBP was 8±17.2 (p=0.018) and for DBP it was 3.7±7.3 (p=0.010) at the end of the 1 month. Furthermore, we found that the improvement continued with the mean difference of 7.8±10.9 (p=0.001) for SBP and 3.7±5.7 (p=0.002) for DBP, at end of the study period.

Table 1: Patients baseline characteristics (n=30).

Characteristics	Values: mean±SD N (%)
Demographics	
Age (years)	53.2±12.1
Weight (kgs)	72.9±13.7
Height (cm)	166.7±7.9
BMI (kg/m^2)	26.3±5.0
Male	28 (93.3)
Female	2 (6.7)
Smoking	
Current smoker	4 (13.3)
Former smoker	1 (3.3)
Never smoker	25 (83.3)
Alcohol	
Current drinker	11 (36.7)
Former drinker	1 (3.3)
Never drinks	18 (60)
Dietary preferences	
Non-vegetarian	18 (60)
Vegetarian	12 (40)
Comorbidities	
Hypertension (HTN)	9 (30)
Type 2 diabetes mellitus	6 (20)
Both (HTN+T2DM)	3 (10)
None	12 (40)
Vitals	
SBP (mm Hg)	128.8±20.0
DBP (mm Hg)	83.8±8.7
HR (bpm)	81.9±12.1
Initial diagnosis	
STEMI	23 (76.7)
NSTEMI	1 (3.3)
Unstable angina	1 (3.3)
Others	5 (16.7)
Coronary artery lesions	
Single vessel	16 (53.3)
Double vessel	6 (20)
Triple vessel	3 (10)
Other	5 (16.7)
Interventions	
PCI	22 (73.3)
CABG	2 (6.7)
Thrombolysis	1 (3.3)
Neither	3 (16.7)

SBP-Systolic blood pressure, DBP-Diastolic blood pressure, HR-Heart rate, bpm-beats per minute.

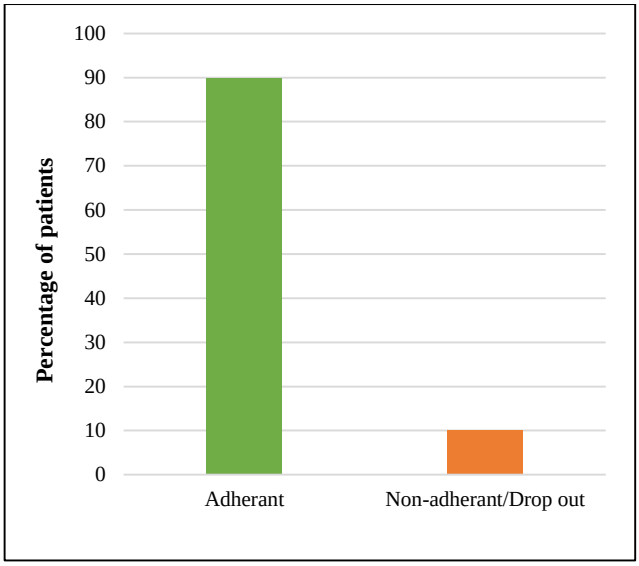

Figure 2: Medication adherence at 3 months.

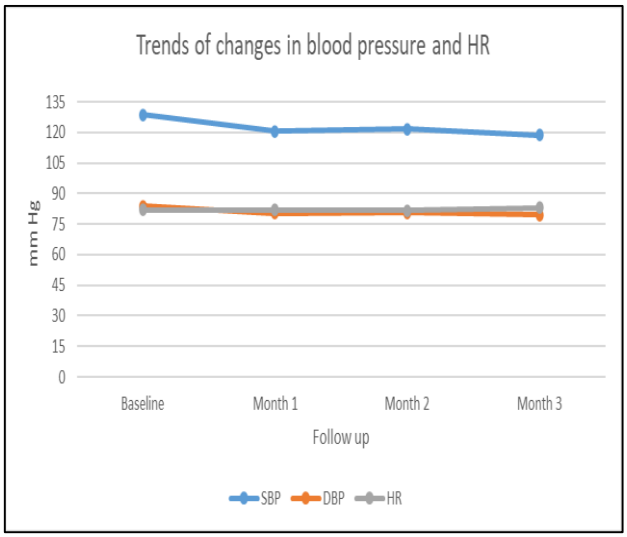

Figure 3: Trends of changes in systolic, DBP and heart rate.

Table 2: Compliance to LYFE (Digital programme) at 3 months (n=30).

Status	Values N (%)
Active	27 (90)
On track	23 (76.7)
Delayed	4 (13.3)
Drop out (Total)	3 (10)
Inactive	1 (3.3)
Journey stopped	2 (6.7)

With regards to cardiovascular events, 1 (3.3%) patient experienced a stroke while no major bleeding events or death were recorded during the study (Table 4).

Table 3: Change in mean SBP, DBP and HR from baseline to 1 month, 2 months and 3 months.

Parameters	N	Value, mean±SD			P value
		Baseline	1st month/ 30 days	Change (Baseline-month 1)	
SBP	29	128.8±20.4	120.7±15.8	8±17.2	0.018*
DBP	29	84.0±8.9	80.3±9.2	3.7±7.3	0.010*
HR	29	82.0±12.3	82.0±9.8	0±10.3	0.971
		Baseline	**3rd month/90 days**	**Change (Baseline-month 3)**	
SBP	27	126.5±18.3	118.7±16.7	7.8±10.9	0.001*
DBP	27	83.2±8.5	79.4±9.9	3.7±5.7	0.002*
HR	27	81.3±12.2	83.1±11.1	-1.8±9.1	0.311

SBP-Systolic blood pressure, DBP-Diastolic blood pressure, HR-Heart rate-bpm, beats per minute. #Paired t-test; *p value is significant if <0.05.

Table 4: Status of cardiac events, blood pressure, and level of activity (n=30).

Clinical outcomes	Values N (%)
Cardiovascular events	
Cardiovascular death	0 (0)
Major bleeding events	0 (0)
Stroke or TIA	1 (3.3)
None	26 (86.7)
Missing/ drop out	3 (10)
Blood pressure status at 3 months	
Under control	25 (83.3)
Beyond range	2 (6.7)
Missing/drop out	3 (10)
Activity level at 3 months	
Active/step count	27 (90)
Non-active	3 (10)

TIA-transient ischaemic attack.

Patients who achieved SBP<140 mm Hg and DBP<90 mm Hg at 3-month follow-up time were considered as patients with blood pressure under control. At the end of the study, 25 (83.3%) patients had controlled blood pressure while 2 (6.7%) patients had it beyond the range (Table 4, Figure 2). Additionally, with respect to activity status, 27 (90%) patients were active and 3 (10%) were inactive throughout the study period (Table 4).

DISCUSSION

The WHO emphasized the significance of following prescribed medication to effectively manage medical conditions and derive maximum benefits from treatment.[1] However, there is a concerning level of non-adherence to secondary prevention, particularly in post-ACS patients, in both developed and underdeveloped countries, increasing the risk of life-threatening events.[17] Forgetfulness has been identified as the most common reason for non-adherence to medication among ACS patients (23.2%). Patients' adherence levels are frequently influenced by five factors namely age, employment status, ACS subtypes, comorbidities count, and the number of prescribed medications per day.[18] Implementing simple strategies that promote adherence and improve treatment outcomes by compliance with medication is crucial to address this issue. Currently, we have implemented a digital health intervention using software to assess its effectiveness in promoting adherence to medication and lifestyle changes, as well as in improving cardiovascular events and vital signs among ACS and post-PCI patients.

Several studies have reported significant success in the application of mobile app-based interventions, majorly in improving cardiac rehabilitation participation, compliance rates and medication adherence among post-ACS patients. A comparative cohort study projected an increase in participation rates from 21% to 63% (p<0.001), following the addition of mobile app-based cardiac rehabilitation (Cardihab).[19] Another study found that using a smartphone app with live health coaching after PCI resulted in high rates of 90-day cardiac rehab enrolment (HR 1.99, 95% CI 1.30-3.06) and 1-month cardiovascular follow-up (HR 1.83, 95% CI 1.43-2.34). The app was also associated with weekly task completion rates of 73.5% (SD 33.9%) at 30 days and 63.5% (SD 40.3%) at 90 days.[20] In a pilot randomized controlled trial conducted on post-discharge patients of ACS or HF, it was found that the group using the app when compared to the control group, had higher rates of completion for cardiac rehab (39% compared to 18%, p=0.03) and medication adherence (75% compared to 50%, p=0.002). Furthermore, the app received an average usability rating of 4.5 out of 5, indicating a high level of satisfaction and compliance with its usability among users.[21] In the present study, the proportion of active participants was found to be high (90%) among all the subjects. Most of these active participants (76.7%) responded on track, while a smaller group (13.3%) experienced a delay in their response.

Various studies have highlighted the positive impact of mobile apps on patient treatment adherence. An observational study by Krackhardt et al reported significant improvement in treatment adherence (96.4%) in comparison to the control group (91.5%) by the addition of an electronic device-based app for patient support.[22] Likewise, in another randomized clinical trial, coronary heart disease (CHD) patients achieved a mean MMAS-8 (Morisky Medication Adherence scale) score of

7.11, in comparison to the standard of the care control group with a score of 6.63 (p<0.008), showing improved medication adherence.[23] Once again, in a prospective observational study, the Smart AF app was found to enhance medication adherence among elderly patients with atrial fibrillation (AF) with statistically significant p values of less than 0.01 at 1 month, 3 months, and 6 months.[24] Our study also supports these findings, as we observed a high rate of medication adherence (90%) among our participants.

The use of digital health interventions has shown promising results in reducing readmissions and improving the prognosis of post-acute myocardial infarction (MI) patients. The MiCORE study reported a 52% reduction rate in hospital readmissions within 30 days post-discharge, by the implementation of smartwatch and mobile application intervention for post-acute MI patients.[25] This finding is consistent with a cardiac rehabilitation program post-MI that involved digital health interventions where significant reductions in rehospitalization (37.9%, p=0.01) and emergency visits (28%, p=0.04) were reported after a 3-month intervention.[26] Coincidentally, the smartphone-based tele clinical care (TCC) intervention reduced the hospital readmissions by 20 (21 readmissions; p=0.02) to the control group (41 readmissions; p=0.02).[21] Poland's managed care in acute MI (MC-AMI) program provides comprehensive care to acute MI patients to improve their prognosis. The 3-month study showed a 45% reduction in MACE rates among participants.[27] In the present study, except for a small number of strokes (3.3%), there were no reports of hospital visits or emergency visits due to any major bleeding events, or fatalities within the study period of 3 months. The MC-AMI program was also evaluated for its impact on all-cause mortality during a one-year follow-up period, and it resulted in a 38% reduction in one-year mortality rates; additionally, the effect persisted even after the completion of the program.[28]

The importance of managing SBP in patients with ACS is well established. A randomized prevention trial by Jorstad et al projected 72% of patients achieving the SBP target at 6 months, and 75% of patients achieving the SBP target at 12 months, in comparison to the control group with 65% at 6 months and 61% at 12 months.[29] Digital health interventions have also shown promising results in reducing SBP among MI patients. One study reported significant reductions in SBP after a 3-month digital intervention, with a mean of -12.6±12.4 mmHg (p=0.001) compared to the control group.[26] Our study showed consistency with Widmer et.al, by showing significant reductions in both SBP and DBP during a study period of 1 month and 3 months (study end).

Number of studies have been conducted to evaluate the effectiveness of mobile health applications in improving activity levels in cardiac patients. A long-term follow-up randomized controlled trial was conducted to assess the impact of a mobile health application over one year on peak oxygen uptake (VO_{2peak}) in cardiac rehab patients.[30] The analysis revealed a significant difference in VO_{2peak} between the intervention and control groups at follow-up (2.2 ml/kg/min, p<0.001). The study also found significant improvements in exercise performance, exercise habits, and self-perceived goal achievement.[30] In another study, an early smartphone-based cardiac rehab program for ACS patients after hospital discharge was examined at the 8-week follow-up.[31] Results showed that the smartphone group had clinically significant improvement in the 6-minute walk test distance (Δ117±76 vs. Δ91±110 m; p=0.02), as well as improved participation and adherence to cardiac rehab.[31] The present study yielded comparable results, as 90% of participants were found to be adherent by the end of the study.

It is important to consider the limitations of this research when interpreting the results. The study aimed to evaluate the practical effectiveness of a software-based digital mobile application without the use of a control group, which may introduce uncertainty into the findings. Furthermore, considering pilot study the small sample size and short duration of the study may restrict the extent to which the outcomes can be analysed more than those applied to a larger population.

The study depicts the integration of a software-driven mobile app led to significant improvements in medication adherence, vital signs regulation and physical activity levels with no reported major cardiac events among patients with CAD and/or ACS post-PCI. It shows consistency with previous research focusing on DTx as a practical and impactful approach to CAD and/or PCI management. Furthermore, the high level of compliance observed among participants suggests that digital technology can play an important role in supporting patient self-management and improving outcomes. However, further research is required to safely establish the clinical relevance of these outcomes and fully explore the circumference of DTx on the CAD management radar.

CONCLUSION

Among the CAD and post-PCI patients, “LYFE” digital therapeutic programme resulted in significantly high medication adherence and achieving blood pressure under control range. Results from initial 90 days are encouraging and promising to achieve sustained results over longer period of time, which may lead to reduced complications and better patient outcomes. By leveraging the power of digital health, the study results suggests that DTx programme will help patients to develop effective and scalable strategies for CAD/ACS post-PCI management in coming days. However, robust evidence by testing it in a larger sample size is needed to apply this approach as a standard medical practice routine.

Funding: The present study received funding support from Lupin Digital Health Limited
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Palshikar A, Gharat CH, Patel K. A real-world evidence study to evaluate the efficacy of software-driven digital therapeutics on major adverse cardiovascular events, vitals, adherence to medication and lifestyle changes among patients with coronary artery disease or post-coronary interventions. Int J Res Med Sci 2023;11:1541-8.