Efficacy of Smartphone-Based Secondary Preventive Strategies in Coronary Artery Disease

Alexandra C Murphy¹²*, Georgina Meehan²*, Anoop N Koshy¹, Phelia Kunniardy², Omar Farouque¹,² and Matias B Yudi¹,²

¹Department of Cardiology, Austin Hospital, Austin Health, Melbourne, VIC, Australia.
²Department of Medicine, The University of Melbourne, Melbourne, VIC, Australia.

ABSTRACT

BACKGROUND: Cardiac rehabilitation programs provide a comprehensive framework for the institution of secondary preventive measures. Smartphone technology can provide a platform for the delivery of such programs and is a promising alternative to hospital-based services. However, there is limited evidence to date supporting this approach. Accordingly, we performed a systematic review and meta-analysis examining smartphone-based secondary prevention programs to traditional cardiac rehabilitation in patients with established coronary artery disease to ascertain the feasibility and effectiveness of these interventions.

METHODS: A systematic search of PubMed, MEDLINE, EMBASE, and the Cochrane Library was conducted. A meta-analysis was performed using a random-effects model with the outcomes of interest being 6-minute walk test (6MWT) distance, systolic blood pressure, low-density lipoprotein (LDL) cholesterol, and body mass index (BMI).

RESULTS: A total of 8 studies with 1120 patients across 5 countries were included in the quantitative analysis. Follow-up ranged from 6 weeks to 12 months. Five studies examined all patients post acute coronary syndrome, 2 studies examined only patients undergoing percutaneous coronary intervention, and 1 study examined all patients with a diagnosis of coronary artery disease, independent of intervention. Exercise capacity, as measured by the 6MWT, was significantly greater in the smartphone group (20.10 meters, 95% confidence interval [CI] 7.44-33.97; P < .001; F = 45.58). There was no significant difference in BMI reduction, systolic blood pressure, or LDL cholesterol levels between groups (P value for all > .05).

CONCLUSION: Publicly available smartphone-based cardiac rehabilitation programs are a convenient and easily disseminated intervention which show merit in exercise promotion in patients with established coronary artery disease. Further research is required to establish the clinical significance of recent findings favoring their use.

KEYWORDS: mHealth, smartphone, cardiac rehabilitation, cardiovascular risk factors, secondary prevention

Introduction

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in the developed world. The rapid rise in CAD burden over recent decades can be attributed to socioeconomic changes, increase in life expectancy, and acquisition of lifestyle-related risk factors.¹ Patients with established CAD are at increased risk of premature death, myocardial infarction, and rehospitalization, and as such, international guidelines advocate for adherence to secondary prevention strategies following diagnosis.²

Cardiac rehabilitation programs provide a comprehensive framework for the institution of secondary preventive measures, such as evidence-based pharmacotherapy, cardiac risk factor optimization, and diet and physical activity recommendations.³ There is extensive literature to date supporting these interventions, with a recent Cochrane review revealing a 13% decrease in all-cause mortality and a 26% decrease in cardiovascular mortality in participants of structured rehabilitation programs.⁴ Despite this, cardiac rehabilitation programs remain generally underutilized, with poor referral and completion rates.⁵⁻⁹ When referred, the commencement of cardiac rehabilitation can be delayed weeks to months post the index event, and can cause a delay in the resumption of work.¹⁰ Furthermore, the opportunity to immediately reinforce the importance of physical activity and lifestyle change is lost. As such, novel models of care have been considered in this population.

Digital health interventions for secondary prevention offer an effective alternative to traditional cardiac rehabilitation and can be implemented immediately.¹¹⁻¹² Early research in this field predominantly focused on telehealth interventions, defined as provision of healthcare via telephone calls, Internet, and videoconferencing,¹³ which although effective, still pose a strain on resource utilization. Smartphone technology is an advance on previous telehealth interventions and can provide an automated platform for a patient-centered program with...
the capacity to incorporate education, motivation, reminders, and support.

Although promising, most of the available evidence in this field is based on pilot and feasibility studies with widely varying treatment lengths and digital intervention types. The exponential growth and availability of smartphone technology may provide a novel tool to optimize secondary prevention of coronary heart disease. This form of digital intervention can be accessed anywhere, at any time, overcoming geographic and resource associated limitations of healthcare delivery and as such has the potential to revolutionize the landscape of secondary prevention. However, the overall value of this approach remains unclear. Accordingly, we have performed a systematic review and meta-analysis comparing the effectiveness of smartphone-based secondary prevention to traditional cardiac rehabilitation programs in the optimization of secondary prevention in patients with CAD.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) Statement was followed (Figure 1) (Table S3). A comprehensive literature search was performed through MEDLINE, EMBASE, PubMed, and the Cochrane Library from establishment to April 2019 using the following search areas: “smartphone,” “rehabilitation,” and “coronary artery disease” (Table S1). Articles were screened based on title and abstract. Full text of the articles meeting the inclusion criteria based on initial screening were then reviewed. Two reviewers (A.C.M. and G.M.) independently extracted the data and resolved conflicts by consensus. Reference lists of reviewed articles were screened to identify further relevant studies.

Studies included were not limited by date, location of study, study design, or publication status. Inclusion criteria were as follows: (1) studies performed in adult patients with established CAD; (2) study design involving a comparison of patients undergoing smartphone-based cardiac rehabilitation against patients undergoing traditional outpatient-based cardiac rehabilitation; (3) studies published in English. In the case of multiple publications involving the same patient cohort, we used the longest available follow-up. A quality assessment of both randomized and nonrandomized controlled trials was performed using the van Tulder scale (Table S2). The van Tulder scale evaluates 11 components, including randomization, allocation.
undergoing percutaneous coronary intervention (PCI),20,26 and
pendent of intervention.19 Compliance with follow-up assess-
iment was quantified using the I statistic. The I statistic pro-
vides an estimate of the amount of variance due to heterogeneity rather than chance and is based on the tradi-
tional measure of variance, the Cochran Q statistic. F = 75% was considered to indicate significant interstudy heterogene-
y.24 As the number of included studies was less than 10, we
did not perform tests to ascertain publication bias.25 We con-
sidered a P value < .05 as statistically significant. Statistical
analyses were performed and Forest plots generated using
comprehensive meta-analysis using the reported study data
(Version 3, Biostat, Englewood, NJ).

Results
A total of 8 studies (7 randomized controlled trials and 1 obser-
vational case-control study) examining 1120 patients were
included in the quantitative analysis.14-20,26 Overall study qual-
ity was deemed high in all eight studies. Follow-up ranged from
6 weeks to 12 months and the indication for cardiac rehabilita-
tion varied. Five studies examined all patients post acute coro-
nary syndrome (ACS),14-18 2 studies examined only patients
undergoing percutaneous coronary intervention (PCI),20,26 and
1 study examined all patients with a diagnosis of CAD, inde-
pendent of intervention.29 Compliance with follow-up assess-
iments varied from 83% to 100% in the smartphone group
compared with 44% to 100% in the control group. Study and
patient characteristics are presented in Table 1. A summary of
the smartphone interventions has been included in Table 2. Due
to significant heterogeneity in outcome reporting, clinical
events such as acute myocardial infarction, unplanned revascu-
larization, stroke, mortality, and recurrent cardiac hospitaliza-
tion were not analyzed.

The results of the meta-analysis of the outcomes of interest
are presented in Figure 2. Exercise capacity, as measured by the
6MWT, was significantly greater in the smartphone group
(20.10 meters, 95% CI 7.44-33.97; P < 0.001; F = 45.58).
There was a numerical reduction in BMI in the smartphone
group seen across studies, but this was not statistically signifi-
cant (–0.53 kg/m2, 95% CI –1.10 to 0.05; P = .07, F = 32.0%).
There was no significant difference in systolic blood pressure
or LDL cholesterol levels between groups (–0.63 mmHg, 95% CI
–3.41 to 2.15; P = .66, F = 0%) and 0.01 mmol/L, 95% CI
–3.41 to 2.15; P = .97, F = 90% respectively). Similarly DBP,
HDL-C, total cholesterol, medication adherence, clinical
events, weight, WC, RHR, smoking status, or glycemic control
were comparable between groups (P value for all > .05) as
assessed on secondary analyses.

Discussion
The purpose of this study was to compare the effectiveness of
smartphone-based interventions to traditional cardiac rehabili-
tation for secondary prevention in patients with CAD. On
review of the literature, smartphone technology appears well
received by patients. The results of the meta-analysis demon-
strate that the application of smartphone-based interventions in
studies ranging from 6 weeks to 12 months has a beneficial
effect on 6MWT capacity. Both smartphone-based and tradi-
tional cardiac rehabilitation had comparable outcomes in the
other measured secondary prevention parameters.

The number of smartphone users today surpasses 3 billion
and is predicted to grow by several hundred million.27
Smartphone users can now access interactive applications from
anywhere at any time. Smartphone users who have undergone
cardiac rehabilitation programs require dedicated multidisciplinary involvement and expend
significant hospital resources. Furthermore, compli-
ance is reliant on patient availability to attend multiple visits
per week which may be impacted by employment and house-
hold commitments.10 Unfortunately, specific compliance with
the smartphone application was not reported in the
included studies, despite discussion comments made of gen-
eral acceptability and usability of the technology. Follow-up
rates were largely similar between groups, except for 2 stud-
ies where follow-up in the smartphone group was roughly
double that of the traditional cardiac rehabilitation group.15,37
Although follow-up assessment cannot be used as a surro-
gate for compliance, there may be a potential improvement in
patient engagement with a smartphone-based platform.
Physical inactivity is independently associated with 12.2% of the global burden of acute myocardial infarction. Accordingly, physical activity is a cornerstone of secondary prevention, with a dose-response relationship existing between 6-MWT and the risk of future cardiovascular events. In this analysis, smartphone-based cardiac rehabilitation was associated with a greater improvement in exercise capacity when compared with traditional programs. Dorje et al have attributed this benefit to the

Table 1. Study and patient characteristics.

|                | BLASCO 2012 | VARNFIELD 2014 | WIDMER 2015 | JOHNSTON 2016 | WIDMER 2017 | MADISON 2019 | FANG 2019 | DORJE 2019 |
|----------------|-------------|----------------|-------------|----------------|-------------|--------------|------------|-------------|
| Smartphone intervention (n) | 102         | 53             | 25          | 86             | 34          | 82           | 33         | 156         |
| Traditional cardiac rehabilitation (n) | 101         | 41             | 19          | 80             | 37          | 80           | 34         | 156         |
| Design          | RCT          | RCT            | Case-Control | RCT            | RCT         | RCT          | RCT        | RCT         |
| Program duration | 12 months   | 6 months       | 3 months    | 6 months       | 3 months    | 3 months     | 6 weeks    | 6 months    |
| Population      | ACS          | ACS            | ACS         | ACS            | ACS         | CAD          | Post PCI   | Post PCI    |
| Follow-up time point | 12 months   | 6 months       | 6 months    | 6 months       | 6 months    | 6 months     | 6 weeks    | 12 months   |
| Follow-up completion (%) |            |                |             |                |             |              |            |             |
| Smartphone CR   | 88          | 77             | 89          | 93             | 92          | 94           | 83         | 100         |
| Traditional CR  | 91          | 43             | 44          | 93             | 85          | 98           | 85         | 100         |
| Age (years)     |             |                |             |                |             |              |            |             |
| Smartphone CR   | 60.6 ± 11.5 | 54.9 ± 9.6     | 60.2 ± 12.1 | 56.8 ± 8.0     | 61.0 ± 13.2 | 62.5 ± 10.7 | 60.2 ± 9.4 | 59.1 ± 9.4  |
| Traditional CR  | 61 ± 12.1   | 56.2 ± 10.1    | 70.4 ± 9.9  | 58.4 ± 8.6     | 61.5 ± 12.2 | 63.6 ± 10.9 | 61.4 ± 10.2 | 61.9 ± 8.7  |
| Male (%)        |             |                |             |                |             |              |            |             |
| Smartphone CR   | 81          | 91             | 76          | 83             | 84          | 78           | 64         | 82          |
| Traditional CR  | 80          | 83             | 89          | 79             | 88          | 85           | 62         | 81          |
| BMI (kg/m²)     |             |                |             |                |             |              |            |             |
| Smartphone CR   | 28.2 ± 5.3  | NR             | 29.2 ± 4.4  | 28.9 ± 5.6     | 29.1 ± 4.6  | NR           | 25.3 ± 3.0 |
| Traditional CR  | 27.7 ± 3.5  | NR             | 30.6 ± 5.6  | 28.4 ± 4.7     | 27.9 ± 3.5  | NR           | 25.4 ± 3.5 |
| Hypertension (%)|             |                |             |                |             |              |            |             |
| Smartphone CR   | NR          | 42             | 95          | 46.5           | 65          | 82           | 46         | NR          |
| Traditional CR  | NR          | 51             | 93          | 47.5           | 61          | 70           | 41         | NR          |
| Diabetes (%)    |             |                |             |                |             |              |            |             |
| Smartphone CR   | NR          | 15             | 27          | 9.3            | 18          | 32           | 27         | NR          |
| Traditional CR  | NR          | 20             | 33          | 16.3           | 18          | 13           | 38         | NR          |
| Hyperlipidemia (%)|           |                |             |                |             |              |            |             |
| Smartphone CR   | NR          | 55             | 68          | 27.9           | 77          | 97           | NR         | NR          |
| Traditional CR  | NR          | 46             | 71          | 16.3           | 88          | 93           | NR         | NR          |
| Smoker (%)      |             |                |             |                |             |              |            |             |
| Smartphone CR   | 77          | 5              | 14          | NR             | 0           | 3            | NR         | 56          |
| Traditional CR  | 74          | 10             | 11          | NR             | 1           | 15           | NR         | 57          |

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; CR, cardiac rehabilitation; NR, not recorded; PCI, percutaneous coronary intervention; RCT, randomized controlled trial.
A meta-analysis by Ettehad et al. indicated that a 10 mmHg reduction in systolic blood pressure is associated with a 20% reduction in major cardiovascular events and a 13% reduction in all-cause mortality. In addition, with every 1 mmol/L decline in LDL cholesterol concentration, there is a 21% reduction in cardiovascular events. As such, close monitoring and aggressive treatment of these parameters are paramount to the optimal management of patients with CAD. Although the pooled analysis in this study did not show a significant advantage of smartphone technology over traditional cardiac rehabilitation in the management of cardiac risk factors, the authors acknowledge the positive results of the large-scale SMART-CR/SP trial by Dorje et al. published in 2019. This was the first randomized controlled trial to show the efficacy of smartphone-based home cardiac rehabilitation in all outcome domains. Although further research is required to support the clinical significance of these findings, this study highlights the potential of smartphone technology as an effective and accessible alternative to traditional rehabilitation programs.

The majority of available evidence in the field of digital health intervention for secondary prevention is based on pilot and feasibility studies with widely varying treatment lengths and intervention types. To our knowledge, this is the first meta-analysis examining only smartphone-based interventions, which is a strength of this study. Furthermore, the assessment of study quality was high which increases the generalizability of our findings. A significant limitation is the intermediate duration of follow-up. In addition, outcome assessments in some studies may be subject to bias due to them being unblinded to the treatment type. As we did not have access to individual study data, we were unable to stratify study outcomes at a specific time period. The variability in patient follow-up may have affected the results of our analysis. As such, the results of this meta-analysis are merely hypothesis generating rather than conclusive. Further studies are required to examine the impact of smartphone-based intervention on clinical events such as acute myocardial infarction, unplanned revascularization, stroke, mortality, and recurrent cardiac hospitalization as these are important measures of success of a secondary prevention program.

**Conclusion**

Publicly available smartphone-based cardiac rehabilitation programs are a convenient and easily disseminated intervention which show merit in exercise promotion in patients with established CAD. Further research is required to establish the clinical significance of recent findings favoring their use. In
particular, larger studies which are adequately powered for clinical endpoints and with longer follow-up are needed to ascertain the effectiveness and sustainability in the long term. In the interim, implementation of these strategies should be considered for the many cardiac patients without access to cardiac rehabilitation and secondary prevention services.

**Author Contributions**

All authors had access to the data and a role in writing the manuscript.

**ORCID iDs**

Alexandra C Murphy https://orcid.org/0000-0002-4248-7537

Georgina Meehan https://orcid.org/0000-0002-1365-7461

**Supplemental Material**

Supplemental material for this article is available online.

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Author/s: 
Murphy, AC; Meehan, G; Koshy, AN; Kunniardy, P; Farouque, O; Yudi, MB

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