



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Increasing cardiovascular medication adherence

Citation for published version:

Khonsari, S, Chandler, C, Parker, R & Holloway, A 2020, 'Increasing cardiovascular medication adherence: A Medical Research Council complex mHealth intervention mixed-methods feasibility study to inform global practice', *Journal of Advanced Nursing*. <https://doi.org/10.1111/jan.14465>

Digital Object Identifier (DOI):

[10.1111/jan.14465](https://doi.org/10.1111/jan.14465)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Journal of Advanced Nursing

Publisher Rights Statement:

This is the peer reviewed version of the following article: Khonsari, S, Chandler, C, Parker, R, Holloway, A. Increasing cardiovascular medication adherence: A medical research council complex mhealth intervention mixed-methods feasibility study to inform global practice. *J Adv Nurs*. 2020; 00: 1– 15. <https://doi.org/10.1111/jan.14465>, which has been published in final form at <https://onlinelibrary.wiley.com/doi/full/10.1111/jan.14465>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving.

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



1 **ABSTRACT**

2 **Aims** to evaluate a mHealth intervention to increase medication adherence among
3 Iranian coronary heart disease patients.

4 **Design** Quantitative-dominant mixed-methods study

5 **Data Source** Iranian coronary heart disease patients' responses and most recent
6 clinical documents as well as responses from Iranian cardiac nurses who
7 participated in this study.

8 **Methods** The study was conducted between September 2015 and April 2016
9 drawing upon the Medical Research Council's Framework. Phase one comprised of
10 a patients' survey and focus groups with cardiac nurses. The automated short
11 message service reminder was piloted in phase two. We recruited 78 patients and
12 randomised to receive either 12-week daily reminders or usual care. The primary
13 outcome was the effect on medication adherence; secondary outcomes were self-
14 efficacy, ejection fraction, functional capacity, readmission rate and quality of life.

15 **Results** Feasibility was evidenced by high ownership of mobile phones and high
16 interest in receiving reminders. Participants in the intervention group showed
17 significantly higher medication adherence compared to the control group.

18 **Conclusion** The mHealth intervention was well accepted and feasible with early
19 evidence of effectiveness that needs to be confirmed in a fully powered future
20 randomised clinical trial.

21

22 **IMPACT**

23 **Problem?**

- 24 • Poor medication adherence has been identified as a barrier to effective
25 treatment of coronary heart disease.
26 • Acceptability and feasibility of a theory-based mHealth intervention to improve
27 medication adherence for Iranian coronary heart disease patients is not
28 known.

29

30 **Findings?**

- 31 • The mHealth intervention was well-accepted and feasible by Iranian coronary
32 heart disease patients.

- 1 • The mHealth intervention has the potential to increase cardiovascular
2 medication adherence; a definitive Randomised Control Trial is required to
3 confirm the effectiveness.

4

5 **Impact?**

- 6 • Healthcare providers' perceptions and patients' preferences need to be
7 understood when designing interventions.
- 8 • The findings can inform the translation and scale-up of text-messaging to
9 improve medication taking and reduce evidence practice gaps.

10

1 **KEYWORDS**

2 Coronary Heart Disease; Secondary Prevention; Medication Adherence; mHealth;
3 Text Messaging; Nurses; Iran.

4

1. INTRODUCTION

Cardiovascular Disease (CVD) is the main reason for mortality worldwide, accounting for more than 17 million deaths each year (World Health Organisation, 2019). In particular, mortality rates caused by CVD are increasing in low- and middle-income countries (World Health Organisation, 2019). Reducing the prevalence, morbidity and mortality of CVD, as the leading cause of the wider burden of non-communicable disease, is a major world health priority (World Health Organisation, 2019). In Iran, Coronary Heart Disease (CHD) - the most important type of CVD - accounts for nearly 50% of all deaths per year. Approximately 20% of Iranian adults aged 30 years and over in Tehran, the capital city, have symptoms or signs of CHD (Hadaegh, Harati, Ghanbarian, & Azizi, 2009). According to a 10-year population-based cohort study conducted in Iran, the crude CHD incidence rate in men was about twice that in women (11.9 vs. 6.5 per 1000 person-years) (Khalili et al., 2014). Given the high prevalence of and a predicted large rise in CHD over the coming decades, the Ministry of Health and Education of Iran has given priority to research exploring strategies to reduce cardiovascular mortality by 25% in the next 10 years (Mansoori et al., 2018).

1.1 Background

CHD patients could benefit from treatment to reduce the risk of recurrent cardiovascular events and mortality; this is known as secondary prevention that includes Cardiac Rehabilitation (CR), lifestyle changes and pharmacological treatment (Anderson et al., 2016) Research has shown that consistent use of medications and participating in CR can improve risk factors and decrease mortality and hospital readmission (Anderson et al., 2016; Kabboul et al., 2018). Despite the importance of secondary prevention, Medication Adherence (MA) is suboptimal among survivors of cardiovascular events; only a range from 13-60% of patients are fully adherent to anti-platelet, statins, Beta Blockers and the combination of all three (Garavalia, Garavalia, Spertus, & Decker, 2009; Kyanko, Franklin, & Angell, 2013; Rodriguez et al., 2013). According to a systematic review of 76 studies conducted in developing countries including Iran, pooled cardiovascular MA was found to be unsatisfying (only 57.5%) (Bowry, Shrank, Lee, Stedman, & Choudhry, 2011).

1 Poor adherence to medications can be attributed to both intentional (i.e. patient
2 decides not to follow the treatment) and/or non-intentional (i.e. due to uncontrolled
3 barriers such as forgetfulness) reasons(Brown et al., 2016). Almost half of the
4 medication non-adherence is unintentional or due to forgetfulness, complexity of the
5 treatment regimen, problems of accessibility, cost and competing life demands
6 (Brown et al., 2016; Gadkari & McHorney, 2012).

7 There is growing evidence that mHealth interventions are an effective and
8 acceptable means of improving both intentional and non-intentional adherence
9 (Hamine, Gerth-Guyette, Faulx, Green, & Ginsburg, 2015; Thakkar et al., 2016).
10 Mobile phones can deliver interventions via Short Messaging Service (SMS), Smart
11 phone applications (apps), video messaging, “push” notifications, or via mobile
12 websites (Kay, Santos, & Takane, 2011). In a recent systematic review of ten studies
13 of varying designs, 607 patients from five countries were included (Coorey, Neubeck,
14 Mulley, & Redfern, 2018). Interventions targeted hypertension, heart failure, stroke
15 and CR populations. According to the authors, MA, rehospitalisation rate and quality
16 of life were among the factors that were enhanced among mHealth users. The
17 International Telecommunication Union (2018), reported that there were over 87
18 million mobile phone subscriptions (108.2 per 100 inhabitants) in Iran. Iranian main
19 operators communicated more than 40 million SMS each day (Goodarzi,
20 Ebrahimzadeh, Rabi, Saedipoor, & Jafarabadi, 2012), allowing extensive reach,
21 utilisation and potential effectiveness of mHealth solutions. To date and our
22 knowledge, there have been limited studies on the use of mobile phone to improve
23 MA exclusively for patients with CHD in the setting of CR in Iran.

24 **2. THE STUDY**

25 **2.1 Aim**

26 This study aimed to refine and pilot a pre-developed theory-based mHealth
27 intervention (BLINDED FOR PEER REVIEW) using the Medical Research Council
28 (MRC) framework (2018) to improve cardiovascular MA in Iranian adult, male and
29 female CR outpatients. Specifically, the focus of this study was on the preclinical,
30 re/modelling and feasibility phases of the MRC framework.

31

32

1 **2.2 Design**

2 In accordance with the MRC framework (2018), the multi-stage mixed-methods study
3 consisted of the first two consecutive phases of development and feasibility of the
4 intervention in preparation for a full Randomised Controlled Trial (RCT) (Registration
5 number: ISRCTN10549665). A text-messaging mHealth intervention had been
6 developed and piloted previously among ACS patients in Malaysia that showed
7 significant improvements in MA and heart functional status (BLINDED FOR PEER
8 REVIEW). This time we tested the same intervention for Iranian CHD patients after
9 undertaking the stages mapped in the MRC framework to ensure the intervention
10 would be appropriate to the Iranian context. In the first phase, the theoretical basis of
11 the intervention was refined; in the modelling phase, exploring Iranian nurses' and
12 patients' views allowed an understanding of required modifications to the
13 intervention. In the second phase, the feasibility of the intervention was tested.

14 **2.2.1 Phase 1: Intervention (re)Modelling**

15 *The theoretical basis of the intervention*

16 We identified and reviewed the relevant theoretical literature, Behaviour Change
17 Techniques (BCTs) and published evidence base concerning cardiovascular
18 medication non-adherence. The electronic databases CINAHL (Cumulative Index of
19 Nursing and Allied Health Literature), Cochrane, Campbell Collaboration, Medline,
20 Embase, GlobalHealth and PsycINFO to June 2017 were searched using the
21 following keywords: Cardiovascular diseases/ or heart diseases/ or coronary disease
22 AND text messaging/ or reminder systems/ or telephone or mobile applications AND
23 patient compliance/ or MA. The research team identified key findings regarding
24 mHealth interventions and information deemed suitable to the study setting.

25 Iterative decisions about search strategy, data extraction and analysis were
26 discussed in meetings attended by all authors and documented in a study log. Based
27 on the study focus, the following were set as the inclusion criteria:

- 28 -Review or trial mHealth as the main study focus;
- 29 -Study utilised mHealth by adults (>18 years) of both gender;
- 30 -Published in English language;

31 Duplicates were removed and articles were excluded if they exhibited one or more of
32 the following characteristics:

- 1 -The patient was not the study target population (i.e., provider-focused);
- 2 -Described a study protocol;
- 3 -Involved children and/or people younger than 18 as the target population;
- 4 -Used mHealth for acute conditions;
- 5 -Used mHealth for assessment, monitoring or measurement;
- 6 -Proposed or developed a model or device.

7 Publications were initially screened for potential inclusion based on the review of title
8 and abstract by two independent reviewers (BLINDED FOR PEER REVIEW).
9 Information including objectives, types of mHealth intervention used, setting, study
10 sample characteristics, outcomes measured, and results reported were extracted
11 using Microsoft Excel. Usability, feasibility, and acceptability of the applied mHealth
12 intervention, the theoretical basis and the effect on patient's outcome (ie.
13 cardiovascular medication adherence), and any disease-specific clinical outcomes of
14 the intervention were reviewed. A descriptive review of the studies was performed
15 and the findings from these research studies summarised, with emphasis on results
16 reported in trials. Methodological quality was assessed for all full text manuscripts
17 included in the review. Selected studies were evaluated for their quality using the
18 Consolidated Standards of Reporting Trials (CONSORT) guidelines for Randomised
19 Controlled Trials. Any disagreement in interpretation of data and inclusion of studies
20 between reviewers was resolved by consensus (BLINDED FOR PEER REVIEW).

21 *Patients' Perception Survey*

22 A self-completion survey conducted among a convenience sample of male and
23 female CHD (i.e. Myocardial Infarction, angina or revascularisation) patients, aged
24 18 and over presented at CR clinic in a hospital affiliated to Tehran University of
25 Medical Sciences (TUMS). Specifically, the survey aimed at identifying:

- 26 - the pattern of ownership, utilisation of mobile phones in Iranian CHD patients
27 (Objective 1); and
- 28 - a preferable design for the study intervention based on CHD patients'
29 opinions in Iran (Objective 2).

30 Given that the CR clinic at the study setting had on average 120 admissions per
31 month for a 24-session exercise programme, then the required sample size was
32 n=92 with a 95% confidence level, 5% margin of error. Estimating a 70%

1 participation rate, 132 eligible CHD patients attending the CR program were asked to
2 participate over a period of three weeks in September 2015. Of 132 subjects, 123
3 (93.18%) consented and agreed to complete the questionnaire. All patients
4 completed sociodemographic information along with the survey questionnaire, self-
5 reported MA and Health-Related Quality of Life (HRQoL) during a face-to-face visit.

6 *Survey Instruments*

7 Electronic Supplementary Material adapted for use from a similar study (Shet et al.,
8 2010) and consisting of 21 items that covered two main domains of enquiry (1) what
9 is the pattern of ownership and use of mobile phones among CHD patients and; (2)
10 what might a patient-preferred design for a mobile phone-based intervention to
11 influence MA look like was utilised.

12 The Persian-version of the Morisky Self-Reported MA Scale (MMAS-8) was used
13 after receiving a signed license contract and copyright agreement from the owner. It
14 is one of the most reliable and widely used scales to determine adherence to
15 cardiovascular medications. The internal consistency of the MMAS-8 (Cronbach's
16 alpha reliability) is 0.83 with good concurrent and predictive validity. This measure
17 has been also found to positively correlate with pharmacy fills rates ($\geq 75\%$; $r=0.46$;
18 $P<0.001$) (Morisky, Ang, Krousel-Wood, & Ward, 2008). The instrument measures
19 non-adherence to medications for reasons such as forgetfulness, carelessness,
20 feeling better, or feeling worse (AlGhurair, Hughes, Simpson, & Guirguis, 2012).

21 HRQoL was evaluated using the validated Persian translation of the Short Form
22 Health Survey Version 2.0 (SF-12v2). The SF-12v2 is a multi-purpose Short Form
23 (SF) generic measure of health status that uses a Likert scale format with high
24 internal consistency, test-retest reliability, construct validity, and criterion validity
25 (Fleishman, Selim, & Kazis, 2010; Ware et al., 2009). The reliability of the Iranian
26 version of SF-12v2 for both physical and mental summary measures exceeded the
27 0.70 level for Cronbach's alpha indicating satisfactory results (0.87 and 0.82,
28 respectively) (Montazeri et al., 2011). We used the standard four-week recall period
29 version in this study.

30 *Focus Groups*

31 Principal Nurse Supervisors/ Matrons in three hospitals affiliated to TUMS were
32 gatekeepers of the study. They were asked to verbally invite cardiac nurses from CR

1 clinics, provide a brief explanation of the study and arrange a date and venue for the
2 Focus Group Discussions (FGDs). A purposive sample of 23 male and female nurse
3 staff with at least six months clinical experience were recruited. The FGDs were
4 conducted and facilitated by (BLINDED FOR PEER REVIEW) on three different days
5 in November 2015, as part of her PhD studies (which contained qualitative methods
6 training), mentored by (BLINDED FOR PEER REVIEW), a professor in nursing and
7 an experienced qualitative researcher. Before the start of the FGDs, (BLINDED FOR
8 PEER REVIEW) explained the study and the ground rules and importance of
9 maintaining confidentiality. Then she asked all participants to sign the consent forms.
10 The FGDs were conducted in the native language of participants, which was typically
11 Farsi. An interview guide was developed to structure FGDs. Interview questions
12 were pilot tested with colleagues at TUMS to assess timing and ensure validity. All
13 responses were open-ended and the discussions were flexible allowing pursuit of
14 issues raised by the participants that were not in the original FGDs' protocol. FGDs
15 specific objectives were to explore:

- 16 - Iranian cardiac nurses' perspectives about the potential effect of a mHealth
17 intervention among Iranian CHD patients (Objective 3); and
- 18 - Potential barriers and facilitators to implementation of the mHealth
19 intervention through which such interventions may affect cardiovascular MA in the
20 Iranian context (Objective 4).

21 Specifically, participants were asked to reflect on (1) their experience with applying
22 mHealth (2) positive and negative aspects of mHealth (3) challenges of using
23 mHealth for patients and healthcare providers (4) strategies for best implementing a
24 mHealth-based intervention to improve cardiovascular MA. All FGDs were audio-
25 recorded with permission from participants and transcribed verbatim after each
26 session. The average FGD time was fifty minutes. As a validity check, the researcher
27 asked participants to verify a verbal summary of the key points (Krueger, 2014).

28 A thematic coding and categorising were used to interpret the data adapted from
29 approaches to qualitative content analysis discussed by Graneheim and Lundman
30 (2004). Following steps have been taken:

31 The transcript was read and brief notes were taken in the margin when interesting or
32 relevant information was found. After that, the notes made in the margins were

1 reviewed and the different types of information were listed. The next step was to
2 read the list and categorise each item in order to establish a framework of thematic
3 ideas. It was then identified whether or not the categories could be linked in any way
4 and they were listed as major or minor themes. At this stage, the various major and
5 minor categories were compared and contrasted. Finally, all of the categories were
6 reviewed and it was ascertained whether some categories can be merged or if some
7 need to then be sub-categorised. All original transcripts were reviewed and all steps
8 were taken several times to ensure that all the information that needs to be
9 categorised has been so.

10 (BLINDED FOR PEER REVIEW) identified themes that emerged from the data. Data
11 coding was discussed with (BLINDED FOR PEER REVIEW) and (BLINDED FOR
12 PEER REVIEW), allowing comparison of data interpretation and subsequent coding
13 refinement. The results were compared and discussed with other authors to reach
14 agreement.

15 **2.2.2 Phase 2: Feasibility Study**

16 The second phase was conducted between February and April 2016 and included a
17 12-week feasibility RCT (pre-test, post-test parallel group design) to:

- 18 - evaluate the effect of a 12-week mHealth intervention on the primary
19 outcome: MA of Iranian male and female CHD patients participating in CR
20 (Objective 5);
- 21 - evaluate the effect of a 12-week mHealth intervention on the secondary
22 outcomes: MA Self-Efficacy (MASE); cardiac Ejection Fraction (EF); cardiac
23 Functional Capacity (FC); CHD-related readmission/mortality rate and HR-
24 QOL of Iranian male and female CHD patients participating in CR (Objective
25 6);
- 26 - explore the association between socio-demographic factors of the subjects
27 and MA in both intervention and control groups (Objective 7);
- 28 - explore the perception of participants in the intervention group towards the
29 received mHealth intervention at the end of the study (Objective 8); and
- 30 - identify the recruitment and retention rate and inform the sample size required
31 for a future definitive RCT (Objective 9).

32

1 *Sample and Setting*

2 According to Lancaster et al. (2004) for sample size estimation in a feasibility study,
3 a general rule of thumb is to take 30 patients or greater to estimate a parameter. The
4 gatekeepers provided a brief explanation of the study to the CHD patients who were
5 newly admitted to the CR clinic of the same hospital in which the survey and one of
6 the FGDs were conducted. (BLINDED FOR PEER REVIEW) recruited the patients
7 (n=78) who agreed to take part in the study and gained their written consent.

8 *Random Allocation*

9 Block randomisation was used with a block size of four. The blocks were chosen
10 using the random number list generated in Microsoft Excel. Allocation was concealed
11 using a sealed non-transparent envelope. (BLINDED FOR PEER REVIEW)
12 generated the random allocation sequence, enrolled participants at the CR clinic,
13 and assigned participants to interventions.

14 *Control*

15 The control group were not exposed to the study intervention. For the purposes of
16 this study, usual care was defined as the CR care that was currently provided for
17 CHD patients 4 to 6 weeks after discharge from hospitals in Iran that involved 24-
18 sessions of supervised exercise training in combination with educational and
19 psychological support.

20 *Intervention*

21 The intervention group received automated timely medication reminders for 12
22 weeks based on a predefined template every morning (This pattern was defined
23 according to the phase I study findings). The 12 weeks of the intervention was
24 selected as it takes approximately 10 weeks (based on daily repetition) for
25 participants to adopt new behaviours (eg. medication taking) (Gardner, Lally, &
26 Wardle, 2012).

27 A detailed description of the study intervention is presented elsewhere (BLINDED
28 FOR PEER REVIEW). In short, the software consisted of various parts that were
29 responsible for gathering and managing the information related to the patients and
30 their medications, storing data, scheduling, sending text messages and recording

1 delivery reports automatically. Table 1 presents some examples of the text
2 messages based on the principles of the study theoretical frameworks.

3 *Blinding*

4 Due to the nature of the intervention, it was impossible to blind either the participants
5 or the researcher to the study group assignment.

6 *Data Collection*

7 Demographic information were collected at baseline. All participants were assessed
8 face-to-face by (BLINDED FOR PEER REVIEW) in the study site two times: at
9 baseline (pre-test: T1) and at the endpoint of the study (post-test, after 12 weeks:
10 T2). At each point in time, all study outcomes were recorded. At the endpoint of the
11 study, patients who received the intervention were asked to complete a survey on
12 their satisfaction with the intervention. Feasibility were assessed by records of
13 recruitment and participation, reasons for drop-out, and web-analytics to determine
14 text messages' delivery.

15 *Measurement Instruments*

16 The primary outcome of interest was the proportion of participants adhering to a
17 complete cardiac medication regimen at 12 weeks measured using the MMAS-8.
18 Secondary outcomes were:

- 19 - MASE using the 26-item and patient-derived scale (Ogedegbe, Mancuso,
20 Allegrante, & Charlson, 2003);
- 21 - FC using the New York Heart Association (NYHA) classification, LVEF (based
22 on the exercise test and echocardiography reports by cardiologists who were
23 unaware of the study group assignment);
- 24 - CHD-related readmission/mortality rate (based on the most recent patients'
25 documents)
- 26 - HRQoL (using two SF-12v2 questionnaires, one pre-test, one post-test
27 completed by all participants); and
- 28 - patients' perception about the applied intervention using a self-administered
29 survey adopted from the previous study (BLINDED FOR PEER REVIEW).

30

31

1 *Ethical considerations*

2 Ethical approval obtained from the Research Ethics Committee of the University of
3 Edinburgh and the Hospitals in which the study took place (Ethics Approval Code:
4 NURS006 and 92-04-28-28802-145738, respectively).

5 *Data Analysis*

6 All data were analysed using the computer program Statistical Packages for Social
7 Sciences (SPSS) version 21. The significance level in this study was $\alpha=0.05$. The
8 primary outcome from the MMAS-8 provided categorical data including high
9 adherence (score of 8), medium adherence (score of 6 to <8) and low adherence
10 (scores of <6). All secondary outcomes results were provided in categorical data
11 including FC (Class I: no symptoms, II: mild symptoms, III: marked limitation and IV:
12 severe limitations), as well as death and hospital readmission rates except the
13 scores of perceived MASE, EF, and HRQoL. Exploratory statistical analysis was
14 performed to generate preliminary data and assess within and between-group
15 differences in primary and secondary outcomes. All statistical tests upon which each
16 p-value is based have been provided in a footnote to Table 4. Statistical tests were
17 chosen based on the type of variable (e.g. categorical or continuous) and on whether
18 the comparison groups were paired or independent. In particular, for the primary
19 outcome analysis, a Chi-squared test was performed. The outcome of patients' MA
20 level (low, medium and high) was cross-tabulated against the study groups
21 (intervention and control). Since two categories had low number of counts (2 and 3),
22 we confirmed the primary outcome result by merging the medium and low adherence
23 categories into a single category called non-adherence, and then applying a Fisher's
24 Exact test. The Relative Risk (RR) with 95% confidence interval was also calculated
25 based on the risk of non-adherence ("low/medium" adherence) at 12 weeks. The
26 absolute difference in the percentages of patients with non-adherence at 12 weeks
27 was also calculated (with 95% CI calculated using the exact method in Altman et al.
28 2013).

29 The Multiple Logistic Regression was used to assess any association between
30 socio-demographic variables (ie. age, sex, education, marital status, employment,
31 living arrangement, monthly income, family size, diagnosis, diagnosis time, co-
32 morbid, hospital stay) and medication adherence.

1 *Credibility/rigour*

2 There were crucial steps undertaken to ensure the scientific rigour of this study:

3 (1) the controlled study design with participants randomly allocated to both study
4 groups;

5 (2) carefully re-designed and tailored the mHealth intervention to the Iranian context
6 through undertaking the stages mapped in the MRC framework and understanding
7 nurses' perceptions and CHD patients' preferences;

8 (3) applying a reliable and validated quantitative measures for primary and
9 secondary outcomes assessment at baseline and endpoint of the study.

10 (4) issues of trustworthiness for qualitative phase of the study were carefully followed
11 by criteria mentioned by Graneheim and Lundman (2004). To achieve credibility, the
12 participants were selected to have different years of experience, age, and education
13 level. To address dependability and transferability, the authors provided a clear
14 description of the context, participants, data collection and process of analysis and
15 findings followed by some suggestions on how our findings may be transferred to
16 other contexts.

17 **3. RESULTS**

18 **3.1 Phase 1 – Intervention (re)Modelling**

19 *3.1.1 The theoretical basis of the intervention*

20 The theoretical basis of the study intervention was based on the principles of self-
21 efficacy within the Social Cognitive Theory (SCT) (Bandura, 2012). Bandura's SCT is
22 one of the most relevant theoretical perspectives used in MA reasoning. SCT was
23 chosen because it concerns perceived self-efficacy and individual goals that
24 influence the attainment of a new behaviour (eg. taking medications) or the changing
25 of an existing behaviour (eg. medication non-adherence) over time (Bandura, 2012).
26 The intervention also benefited from the application of the principles of the WHO
27 Adherence Model (2003) in which both intra- and interpersonal factors have been
28 identified as important dimensions that influence MA. According to this model, the
29 mHealth intervention was designed to improve cardiovascular MA through
30 addressing the most common barriers to adherence such as patient-related factors

1 (eg. forgetfulness and low self-efficacy in taking medications) and healthcare
2 system-related factors (eg. lack of patient-provider interaction).

3 The Dixon and Johnston's Health Behaviour Change Competency Framework
4 (HBCC) maps each BCT to one or more of three identified routes to behaviour
5 change, namely: Motivation development to promote skills that help that motivation
6 to be transformed into Action; and Prompted or cued routes to behaviour (MAP)
7 (Dixon & Johnston, 2010). The mHealth intervention targeted the third route of the
8 MAP (i.e. the prompted or cued route) that supports behaviour (i.e. medication
9 taking) without the need for the constant cognitive attempt required by the other
10 routes.

11 *3.1.2 Patients' Perception Survey*

12 The results of the Iranian CHD patients' survey confirmed the acceptability of using
13 mHealth interventions using text messaging to improve MA for this group of
14 patients. Mobile phone ownership (n=118/123) and the use of text messages
15 (n=84/123) were relatively high among the respondents of the survey. This finding
16 indicated that using automated medication reminders delivered by text messaging
17 might be the most acceptable mHealth intervention in this particular context. Table 2
18 summarises the remodelling of the intervention based on the findings from both
19 patients' survey and nurses' FGDs following the stages of the MRC framework.

20 *3.1.3 Qualitative Focus Groups*

21 The mean and Standard Deviation (SD) of nurse participants' age was 36.64 (6.69)
22 years, predominantly female (19/23, 82.6%), with an average of 12.06 (SD: 6.51)
23 years' work experience.

24 The data from the FGDs confirmed that Iranian cardiac nurses perceived the
25 mHealth intervention useful for patients who are at risk of medication non-adherence
26 mostly due to unintentional reasons (e.g. forgetfulness and carelessness) during the
27 early phase of discharge from hospital. These illustrative quotes support this
28 assertion:

29 *"It can really work especially for those patients who are forgetful. Some of them*
30 *are so busy; but this intervention sends them reminders so that they'll*
31 *remember...now, it's time for taking medications"* (Participant 10, FG 2).

1 *“The most high risk time is when patients discharge from the hospital. I*
2 *mean...when they are at home and they may forget when and how to take their*
3 *drugs”* (Participant 11, FG 2).

4 Post-discharge follow-up and interaction between patients and healthcare providers
5 play an important role in the statements expressed by all the FGDs; for example, one
6 of the more experienced nurses identified that there is no interaction and follow-up
7 with patients after hospital discharge:

8 *“Unfortunately, most of our patients are missed after going home and are no*
9 *longer in contact with us. That is because our hospitals are inefficient regarding*
10 *patients’ post-discharge follow-up and I can say this kind of intervention is absolutely*
11 *one of the essentials”* (Participant 3, FG 1).

12 During the nurses’ discussions, a key issue identified was the lack of electronic
13 health system to provide a connection between hospital and home. The example
14 below demonstrates that patient-provider connection after inpatient stay can be
15 established through a remote follow-up using mHealth interventions.

16 *“There is no interconnected electronic health system or mHealth in our*
17 *hospitals. How we can provide follow-up for our discharged patients? You*
18 *know...just a few of them may call me if they have questions about their health care*
19 *needs and medications. Patients really need this kind of intervention as a means of*
20 *follow-up and support from their healthcare providers.”* (Participant 9, FG 2).

21 The nurses also expressed their opinions and recommendations about the
22 refinement of the study mHealth intervention. The majority of participants suggested
23 surveying patients and conducting a pilot study to have a better understanding of
24 feasibility and acceptability of the intervention. They also provided suggestions about
25 following-up with patients using other mediums along with text messages as well as
26 pragmatic considerations in developing text message reminders (e.g. less frequent
27 text messages to prevent patients’ dependency and fatigue over time). More
28 information can be found in Table 2.

29 **3.2 Phase 2: Feasibility Study**

30 The final mHealth intervention was piloted after refinement as shown in Table 2.
31 During the recruitment period (February 2016), of 98 CR patients admitted to the
32 outpatient CR clinic, 78 (76.4%) eligible patients consented to participate in the study
33 and were randomly assigned to control (n=39) and intervention groups (n=39).
34 Figure 1 presents the flow diagram of the study based on the CONSORT guideline
35 (Schultz, 2010).

1 Characteristics of all 78 participants are shown in Table 3. All variables were similar
2 between study groups.

3 According to the findings from the second phase, the mHealth intervention improved
4 the primary outcome of the study with a highly significant difference in self-reported
5 MA levels between the control and intervention groups, $\chi^2 (2) = 23.4$; $P < 0.001$. The
6 RR indicated that it was 2.19 times more likely for the control group to be less
7 adherent to their medications than the intervention group (RR = 2.19; 95% CI 1.5 -
8 3.19). The absolute difference between the proportions of non-adherence was
9 estimated to be 51% (95% CI 35% to 64%).

10 Among secondary outcomes, the mHealth intervention was significantly associated
11 with improved MASE scores (U=505; P=0.035) and cardiac FC ($\chi^2 (1) = 9.7$,
12 P=0.002) compared with control group.

13 All secondary outcomes except FC improved significantly in the intervention group at
14 the end of the study. However, these outcomes showed significant negative changes
15 in the control group over time. Table 4 illustrates the baseline and follow-up data
16 obtained from Phase 2 of the study. The study of the association between
17 participants' characteristics and MA indicated that socio-demographic data had no
18 statistically significant relationship with MA.

19 *Findings to Inform Future Definitive Large-scale RCT*

20 In this study, the results showed the majority of the participants (n=28/39, 71.8%) in
21 the intervention group who received SMS reminders to take their cardiovascular
22 medications perceived the mHealth intervention positively. The recruitment approach
23 via CR clinic seemed to work well and indicated feasibility of recruitment. No
24 financial incentives were offered to the patients. The overall attrition rate was only
25 3.8% (n=3/78) with the reason for loss to follow-up readmission for surgery. No
26 harms, unintended consequences or effects were reported. The results of the feasibility
27 trial helped to inform the sample size needed for a future definitive RCT. A sample
28 size of 130 patients per group (260 in total) is required to have 90% power to detect
29 a realistic true difference of 20% or greater for the between-group percentage of
30 patients with high adherence to their medication in a future study, assuming a (two-
31 sided) 5% significance level.

32

1 4. DISCUSSION

2 The results showed positive feedback for the acceptability and feasibility of mHealth
3 intervention to improve cardiocascular MA in an Iranian CR setting. Exploratory
4 analysis also revealed a significant improvement in the primary and secondary
5 outcomes of the study. The findings of patients' perception survey indicated that
6 there is a high ownership of mobile phones and utilisation of SMS among Iranian
7 CHD patients and the mHealth intervention perceived helpful by this group of
8 patients in taking cardiovascular medications. The survey results also confirmed the
9 importance of obtaining patients' preferences (shared decision making) about the
10 timing, frequency and content of text message intervention before they were
11 implemented. This is consistent with the findings from a systematic review which
12 identified that mHealth interventions must be flexible as well as culturally and socially
13 appropriate to the wishes and needs of the patients (Gandapur et al., 2016).

14 In addition to the patients' survey results, the intervention was informed by qualitative
15 findings in which cardiac nurse professionals expressed potential effects of the
16 mHealth interventions, its associated challenges in the context of Iran and pragmatic
17 suggestions to enhance the intervention design. This study revealed that Iranian
18 cardiac nurses were open to the introduction of the mHealth intervention to improve
19 cardiovascular MA and provided suggestions for optimising the design and
20 evaluation of the study intervention. In fact, nurses believed that the use of mHealth
21 intervention would be necessary as it has the potential to improve medication taking
22 and patients' link to healthcare providers after discharge. The results are in line with
23 the findings of a previous study, in which Iranian healthcare professionals have
24 emphasised the necessity of applying eHealth (i.e. an overarching term that includes
25 mHealth and teleHealth) in practice (Ayatollahi, Sarabi, & Langarizadeh, 2015).

26 During the second phase the remodelled intervention was piloted among Iranian
27 CHD patients to evaluate the acceptability and feasibility in practice. It also provided
28 the opportunity to determine sample size, the potential effect (effect size),
29 recruitment and attrition rate. Patients in this study had inadequate MA before the
30 intervention. The mHealth intervention used in this study improved all primary and
31 secondary outcomes at the end of the study. These findings are in line with the work
32 of other researchers that examined the effect of SMS reminders on MA in a variety of

1 medical conditions including asthma (Strandbygaard, Thomsen, & Backer, 2010),
2 cardiovascular (Fang & Li, 2016; Pfaeffli Dale et al., 2015), diabetic , stroke (Arora,
3 Peters, Burner, Lam, & Menchine, 2014; Kamal et al., 2015) and hypertensive
4 patients (Bobrow et al., 2016).

5 **4.1 Implications**

6 Nonadherence to cardiac medications may result in increased morbidity and
7 mortality, thus mHealth interventions may enhance adherence and health outcomes.
8 This study has established feasibility and high satisfaction with a text messaging
9 intervention among patients with CHD. Text message reminders improved
10 adherence in cardiovascular medications, which are critical in preventing progression
11 of the negative outcomes, and the disease-related complications during the
12 vulnerable time following a cardiac event.

13 In developing countries including Iran, the health care resources are concentrated in
14 urban areas and health system performance is constrained by limited infrastructure,
15 inequality and shortages of healthcare providers (Chavehpour, Rashidian,
16 Woldemichael, & Takian, 2019; Seddighi & Mousavi, 2019). However, according to
17 the present study findings, automated text-messaging as a type of mHealth
18 intervention has the potential to help by removing physical barriers to care and
19 service delivery and by improving poor patient-provider communication. This could
20 also help nurses, as the primary providers of healthcare, to achieve the Sustainable
21 Development Goals (SDGs) and support dimensions of Universal Health Coverage
22 (UHC). Unlike complicated interventions and time-consuming face-to-face
23 approaches, SMS reminders are transmitted automatically to patients beyond a
24 specific location with limited efforts from health care professionals. Although there is
25 a potential for low-cost scalability and reproducibility of mHealth, evidence for the
26 effectiveness of mHealth use in improving health-related quality measures, such as
27 disability-adjusted life-years remains limited, especially for the developing world.

28 Finally, economic outcomes are considerable. The effectiveness of mHealth
29 interventions to improve secondary prevention of cardiovascular disease has
30 important implications from financial perspective, as well. This is particularly of
31 importance when considering that medication nonadherence was found to be the
32 leading cause of CHD-related rehospitalisations in Iran, increasing the economic

1 burden of this disease (Heydarpour, Saeidi, Ezzati, Soroush, & Komasi, 2015).
2 Improved cardiovascular health outcomes and eliminated health care expenses for
3 both patients and health system, could justify mHealth solutions. Further research is
4 needed to economically evaluate the mHealth interventions, their costs, and their
5 intended clinical outcomes and potential adverse effects.

6 **4.2 Limitations**

7 There are some limitations to the present study that should also be noted. Because
8 the sample size was small and only included CHD patients who presented at an
9 outpatient CR clinic, they might not represent the wider Iranian CHD population. In
10 addition, the intervention was refined and tailored to the Iranian settings which may
11 limit the generalisability of the study findings to wider country settings. However,
12 linking the components of the intervention to the theory or conceptual framework
13 may be an effective way to address the generalisability issue of the study findings
14 and provide a sound theoretical basis for further studies in other country settings.

15 Another study limitation is the patients' self-completion bias, although the self-report
16 questionnaire is simple, cost-efficient and the most common method of data
17 collection (Basu, Garg, Sharma, & Singh, 2019; Jimmy & Jose, 2011). It may be
18 affected by recall bias and socially desirable responding (Basu et al., 2019; Berben
19 et al., 2011); however, a comparison of other studies demonstrated that there was
20 an association between a patient's self-report of medication intake and blood drug
21 levels (Grover, Oberoi, Rehan, Gupta, & Yadav, 2019; Ho, Bryson, & Rumsfeld,
22 2009). According to the literature, there is no "gold standard" to measure MA
23 behaviour (Basu et al., 2019; Jimmy & Jose, 2011). Direct methods such as the
24 detection of a metabolite or marker in patients' blood are often impractical, costly and
25 invasive (Stewart, Mc Namara, & George, 2014). Moreover, to the researcher's
26 knowledge, electronic monitoring devices for medication taking were not available in
27 Iran during the study time. There was no electronic pharmacy claim data in this
28 country to monitor the prescription refill or measuring adherence using Medication
29 Possession Ratio (MPR) and Proportion of Days Covered (PDC). Pill counts may not
30 be a reliable method because patients can appear adherent by changing
31 medications between bottles or throwing them out before a follow-up visit (Basu et
32 al., 2019; Jimmy & Jose, 2011). To address the issue of subjectivity of self-reporting,

1 we used results of electrocardiograms, stress tests and echocardiograms of the
2 patients to assess the NYHA, FC and LVEF.

3 Our results may also have been subject to the bias inherent in the application of the
4 randomisation, intervention and data collection by the same researcher. Careful
5 efforts were made to prevent any influence on the data collection and analysis during
6 or after the trial. All stages of the study had a clear plan and supervised by two
7 professors and one doctor in nursing who had expertise both in the field of
8 quantitative and qualitative research methods. Having several meetings with all
9 authors and statistician helped to minimise the bias that the pre-assumptions might
10 cause.

11 **5. CONCLUSIONS**

12 Qualitative and quantitative data collected in this study suggested that the mHealth
13 intervention had the desired effect on cardiovascular MA among Iranian CHD
14 patients. The study findings also confirmed that the recruitment and data collection
15 strategies used were feasible for implementation in a larger RCT. According to the
16 MRC framework, the next step will be to assess the intervention cost-effectiveness
17 and to validate the present study results by conducting a definitive RCT. As the
18 major contribution to global practice, the findings inform the translation and scale-up
19 of the text-messaging technology to improve CHD patients' self-efficacy in
20 medication taking and reduce evidence practice gaps.

1 **References**

- 2 ALGhurair, S. A., Hughes, C. A., Simpson, S. H., & Guirguis, L. M. (2012). A
3 systematic review of patient self-reported barriers of adherence to
4 antihypertensive medications using the World Health Organization
5 Multidimensional Adherence Model. *The Journal of Clinical Hypertension*,
6 14(12), 877-886. doi:10.1111/j.1751-7176.2012.00699.x
- 7 Altman, D., Machin, D., Bryant, T., & Gardner, M. (2013). *Statistics with confidence:*
8 *confidence intervals and statistical guidelines*: John Wiley & Sons.
- 9 Anderson, L., Oldridge, N., Thompson, D. R., Zwisler, A.-D., Rees, K., Martin, N., &
10 Taylor, R. S. (2016). Exercise-based cardiac rehabilitation for coronary heart
11 disease: Cochrane systematic review and meta-analysis. *Journal of the*
12 *American College of Cardiology*, 67(1), 1-12. doi:10.1016/j.jacc.2015.10.044
- 13 Arora, S., Peters, A. L., Burner, E., Lam, C. N., & Menchine, M. (2014). Trial to
14 Examine Text Message–Based mHealth in Emergency Department Patients
15 With Diabetes (TEXT-MED): A Randomized Controlled Trial. *Annals of*
16 *Emergency Medicine*, 63(6), 745-754.e746.
17 doi:10.1016/j.annemergmed.2013.10.012
- 18 Ayatollahi, H., Sarabi, F. Z. P., & Langarizadeh, M. (2015). Clinicians' knowledge
19 and perception of telemedicine technology. *Perspectives in health information*
20 *management*, 12(Fall), 1c.
- 21 Bandura, A. (2012). On the functional properties of perceived self-efficacy revisited.
22 *Journal of Management*, 38(1), 9-44. doi:10.1177/0149206311410606
- 23 Basu, S., Garg, S., Sharma, N., & Singh, M. M. (2019). Improving the assessment of
24 medication adherence: Challenges and considerations with a focus on low-
25 resource settings. *Ci ji yi xue za zhi = Tzu-chi medical journal*, 31(2), 73-80.
26 doi:10.4103/tcmj.tcmj_177_18
- 27 Berben, L., Bogert, L., Leventhal, M. E., Fridlund, B., Jaarsma, T., Norekvål, T. M., . . .
28 . De Geest, S. (2011). Which interventions are used by health care
29 professionals to enhance medication adherence in cardiovascular patients? A
30 survey of current clinical practice. *European Journal of Cardiovascular*
31 *Nursing*, 10(1), 14-21. doi:10.1016/j.ejcnurse.2010.10.004
- 32 Bobrow, K., Farmer, A. J., Springer, D., Shanyinde, M., Yu, L.-M., Brennan, T., . . .
33 Tarassenko, L. (2016). Mobile phone text messages to support treatment
34 adherence in adults with high blood pressure (SMS-Text Adherence Support
35 [StAR]) a single-blind, randomized trial. *Circulation*, 133(6), 592-600.
36 doi:10.1161/CIRCULATIONAHA.115.017530
- 37 Bowry, A. D. K., Shrank, W. H., Lee, J. L., Stedman, M., & Choudhry, N. K. (2011). A
38 systematic review of adherence to cardiovascular medications in resource-
39 limited settings. *Journal of general internal medicine*, 26(12), 1479-1491.
40 doi:10.1007/s11606-011-1825-3

- 1 Brown, M. T., Bussell, J., Dutta, S., Davis, K., Strong, S., & Mathew, S. (2016).
2 Medication adherence: truth and consequences. *The American journal of the*
3 *medical sciences*, 351(4), 387-399. doi:10.1016/j.amjms.2016.01.010
- 4 Chavehpour, Y., Rashidian, A., Woldemichael, A., & Takian, A. (2019). Inequality in
5 geographical distribution of hospitals and hospital beds in densely populated
6 metropolitan cities of Iran. *BMC health services research*, 19(1), 614.
7 doi:10.1186/s12913-019-4443-0
- 8 Coorey, G. M., Neubeck, L., Mulley, J., & Redfern, J. (2018). Effectiveness,
9 acceptability and usefulness of mobile applications for cardiovascular disease
10 self-management: Systematic review with meta-synthesis of quantitative and
11 qualitative data. *European journal of preventive cardiology*, 25(5), 505-521.
12 doi:10.1177/2047487317750913
- 13 Dixon, D., & Johnston, M. (2010). Health Behaviour Change Competency
14 Framework: Competences to deliver interventions to change lifestyle
15 behaviours that affect health Retrieved from
16 [http://www.healthscotland.com/uploads/documents/4877-](http://www.healthscotland.com/uploads/documents/4877-Health_behaviour_change_competency_framework.pdf)
17 [Health behaviour change competency framework.pdf](http://www.healthscotland.com/uploads/documents/4877-Health_behaviour_change_competency_framework.pdf)
- 18 Fang, R., & Li, X. (2016). Electronic messaging support service programs improve
19 adherence to lipid-lowering therapy among outpatients with coronary artery
20 disease: an exploratory randomised control study. *Journal of Clinical Nursing*,
21 25(5/6), 664-671. doi:10.1111/jocn.12988
- 22 Fleishman, J. A., Selim, A. J., & Kazis, L. E. (2010). Deriving SF-12v2 physical and
23 mental health summary scores: a comparison of different scoring algorithms.
24 *Quality of Life Research*, 19(2), 231-241.
- 25 Gadkari, A. S., & McHorney, C. A. (2012). Unintentional non-adherence to chronic
26 prescription medications: How unintentional is it really? *BMC health services*
27 *research*, 12(1), 98. doi:10.1186/1472-6963-12-98
- 28 Gandapur, Y., Kianoush, S., Kelli, H. M., Misra, S., Urrea, B., Blaha, M. J., . . .
29 Martin, S. S. (2016). The role of mHealth for improving medication adherence
30 in patients with cardiovascular disease: a systematic review. *European Heart*
31 *Journal-Quality of Care and Clinical Outcomes*, 2(4), 237-244.
32 doi:10.1093/ehjqcco/qcw018
- 33 Garavalia, L., Garavalia, B., Spertus, J. A., & Decker, C. (2009). Exploring patients'
34 reasons for discontinuance of heart medications. *The Journal of*
35 *cardiovascular nursing*, 24(5), 371-379. doi:10.1097/JCN.0b013e3181ae7b2a
- 36 Gardner, B., Lally, P., & Wardle, J. (2012). Making health habitual: the psychology of
37 'habit-formation'and general practice. *British Journal of General Practice*,
38 62(605), 664-666. doi:10.3399/bjgp12X659466
- 39 Goodarzi, M., Ebrahimzadeh, I., Rabi, A., Saedipoor, B., & Jafarabadi, M. A. (2012).
40 Impact of distance education via mobile phone text messaging on knowledge,
41 attitude, practice and self efficacy of patients with type 2 diabetes mellitus in

- 1 Iran. *Journal of Diabetes & Metabolic Disorders*, 11(10). doi:10.1186/2251-
2 6581-11-10
- 3 Graneheim, U. H., & Lundman, B. (2004). Qualitative content analysis in nursing
4 research: concepts, procedures and measures to achieve trustworthiness.
5 *Nurse education today*, 24(2), 105-112. doi:10.1016/j.nedt.2003.10.001
- 6 Grover, A., Oberoi, M., Rehan, H., Gupta, L. K., & Yadav, M. (2019). Self-reported
7 Morisky 8 item medication adherence scale to statins concords with pill count
8 method and correlates with serum lipid profile parameters and Serum
9 HMGCoA Reductase levels. *medRxiv*, 19006148. doi:10.1101/19006148
- 10 Hadaegh, F., Harati, H., Ghanbarian, A., & Azizi, F. (2009). Prevalence of coronary
11 heart disease among Tehran adults: Tehran Lipid and Glucose Study. *Eastern
12 Mediterranean Health Journal*, 15(1), 157-166.
- 13 Hamine, S., Gerth-Guyette, E., Faulx, D., Green, B. B., & Ginsburg, A. S. (2015).
14 Impact of mHealth chronic disease management on treatment adherence and
15 patient outcomes: a systematic review. *Journal of medical Internet research*,
16 17(2), e52. doi:10.2196/jmir.3951
- 17 Heydarpour, B., Saeidi, M., Ezzati, P., Soroush, A., & Komasi, S. (2015).
18 Sociodemographic predictors in failure to complete outpatient cardiac
19 rehabilitation. *Annals of rehabilitation medicine*, 39(6), 863-871.
20 doi:10.5535/arm.2015.39.6.863
- 21 Ho, P. M., Bryson, C. L., & Rumsfeld, J. S. (2009). Medication Adherence; Its
22 Importance in Cardiovascular Outcomes. *Circulation*, 119(23), 3028-3035.
23 doi:10.1161/CIRCULATIONAHA.108.768986
- 24 International Telecommunication Union. (2018). Key Information and
25 communications technology (ICT) indicators for developed and developing
26 countries and the world. Retrieved from [https://www.itu.int/en/ITU-
27 D/Statistics/Pages/stat/default.aspx](https://www.itu.int/en/ITU-D/Statistics/Pages/stat/default.aspx)
- 28 Jimmy, B., & Jose, J. (2011). Patient medication adherence: measures in daily
29 practice. *Oman medical journal*, 26(3), 155-159. doi:10.5001/omj.2011.38
- 30 Kabboul, N., Tomlinson, G., Francis, T., Grace, S., Chaves, G., Rac, V., . . . Krahn,
31 M. (2018). Comparative effectiveness of the core components of cardiac
32 rehabilitation on mortality and morbidity: a systematic review and network
33 meta-analysis. *Journal of clinical medicine*, 7(12), 514.
34 doi:10.3390/jcm7120514
- 35 Kamal, A. K., Shaikh, Q., Pasha, O., Azam, I., Islam, M., Memon, A. A., . . . Khoja, S.
36 (2015). A randomized controlled behavioral intervention trial to improve
37 medication adherence in adult stroke patients with prescription tailored Short
38 Messaging Service (SMS)-SMS4Stroke study. *BMC Neurology*, 15(1), 212.
39 doi:10.1186/s12883-015-0471-5
- 40 Kay, M., Santos, J., & Takane, M. (2011). mHealth: New horizons for health through
41 mobile technologies. *World Health Organization*, 64(7), 66-71.

- 1 Khalili, D., Sheikholeslami, F. H., Bakhtiyari, M., Azizi, F., Momenan, A. A., &
2 Hadaegh, F. (2014). The incidence of coronary heart disease and the
3 population attributable fraction of its risk factors in Tehran: a 10-year
4 population-based cohort study. *PloS one*, *9*(8), e105804.
5 doi:10.1371/journal.pone.0105804
- 6 Khonsari, S., Subramanian, P., Chinna, K., Latif, L. A., Ling, L. W., & Gholami, O.
7 (2015). Effect of a reminder system using an automated short message
8 service on medication adherence following acute coronary syndrome.
9 *European Journal of Cardiovascular Nursing*, *14*(2), 170-179.
10 doi:10.1177/1474515114521910
- 11 Krueger, R. A. (2014). *Focus groups: A practical guide for applied research* (5th ed.).
12 Thousand Oaks, CA: Sage Publications.
- 13 Kyanko, K. A., Franklin, R. H., & Angell, S. Y. (2013). Adherence to chronic disease
14 medications among New York City Medicaid participants. *Journal of Urban*
15 *Health*, *90*(2), 323-328.
- 16 Lancaster, G. A., Dodd, S., & Williamson, P. R. (2004). Design and analysis of pilot
17 studies: recommendations for good practice. *Journal of evaluation in clinical*
18 *practice*, *10*(2), 307-312. doi:10.1111/j..2002.384.doc.x
- 19 Mansoori, P., Majdzadeh, R., Abdi, Z., Rudan, I., Chan, K. Y., The Iranian CHNRI
20 Health Research Priority Setting Group, . . . Zare, M. (2018). Setting research
21 priorities to achieve long-term health targets in Iran. *Journal of global health*,
22 *8*(2), 020702-020702. doi:10.7189/jogh.08.020702
- 23 Montazeri, A., Vahdaninia, M., Mousavi, S. J., Asadi-Lari, M., Omidvari, S., &
24 Tavousi, M. (2011). The 12-item medical outcomes study short form health
25 survey version 2.0 (SF-12v2): a population-based validation study from
26 Tehran, Iran. *Health and quality of life outcomes*, *9*(1), 12. doi:10.1186/1477-
27 7525-9-12
- 28 Morisky, D. E., Ang, A., Krousel-Wood, M., & Ward, H. J. (2008). Predictive validity
29 of a medication adherence measure in an outpatient setting. *The Journal of*
30 *Clinical Hypertension*, *10*(5), 348-354. doi:10.1111/j.1751-7176.2008.07572.x
- 31 Ogedegbe, G., Mancuso, C. A., Allegrante, J. P., & Charlson, M. E. (2003).
32 Development and evaluation of a medication adherence self-efficacy scale in
33 hypertensive African-American patients. *Journal of clinical epidemiology*,
34 *56*(6), 520-529. doi:10.1016/S0895-4356(03)00053-2
- 35 Pfaeffli Dale, L., Whittaker, R., Jiang, Y., Stewart, R., Rolleston, A., & Maddison, R.
36 (2015). Text Message and Internet Support for Coronary Heart Disease Self-
37 Management: Results From the Text4Heart Randomized Controlled Trial.
38 *Journal of medical Internet research*, *17*(10), e237. doi:10.2196/jmir.4944
- 39 Rodriguez, F., Cannon, C. P., Steg, P. G., Kumbhani, D. J., Goto, S., Smith, S. C., . .
40 . Hoffman, E. (2013). Predictors of long-term adherence to evidence-based
41 cardiovascular disease medications in outpatients with stable

- 1 atherothrombotic disease: findings from the REACH Registry. *Clinical*
2 *cardiology*, 36(12), 721-727. doi:10.1002/clc.22217
- 3 Schultz, K. (2010). CONSORT statement: updated guidelines for reporting parallel
4 group randomised trials. *BMC med*, 8, 18-27. doi:10.1186/1745-6215-11-32
- 5 Seddighi, H., & Mousavi, M.-T. (2019). Status of Health, Education and Income
6 Inequality in Iran. *Journal of Community Health Research*, 8(3), 186-193.
7 doi:10.18502/jchr.v8i3.1561
- 8 Shet, A., Arumugam, K., Rodrigues, R., Rajagopalan, N., Shubha, K., Raj, T., . . . De
9 Costa, A. (2010). Designing a Mobile Phone-Based Intervention to Promote
10 Adherence to Antiretroviral Therapy in South India. *AIDS and Behavior*, 14(3),
11 716-720. doi:10.1007/s10461-009-9658-3
- 12 Skivington, K., Matthews, L., Craig, P., Simpson, S., & Moore, L. (2018). Developing
13 and evaluating complex interventions: updating Medical Research Council
14 guidance to take account of new methodological and theoretical approaches.
15 *The Lancet*, 392, S2. doi:10.1016/S0140-6736(18)32865-4
- 16 Stewart, K., Mc Namara, K. P., & George, J. (2014). Challenges in measuring
17 medication adherence: experiences from a controlled trial. *International*
18 *journal of clinical pharmacy*, 36(1), 15-19. doi:10.1007/s11096-013-9877-6
- 19 Strandbygaard, U., Thomsen, S. F., & Backer, V. (2010). A daily SMS reminder
20 increases adherence to asthma treatment: A three-month follow-up study.
21 *Respiratory Medicine*, 104(2), 166-171. doi:10.1016/j.rmed.2009.10.003
- 22 Thakkar, J., Kurup, R., Laba, T.-L., Santo, K., Thiagalingam, A., Rodgers, A., . . .
23 Chow, C. K. (2016). Mobile Telephone Text Messaging for Medication
24 Adherence in Chronic Disease: A Meta-analysis. *JAMA Internal Medicine*,
25 176(3), 340-349. doi:10.1001/jamainternmed.2015.7667
- 26 Ware, J. E., Kosinski, M., Turner-Bowker, D. M., Sundaram, M., Gandek, B., &
27 Maruish, M. E. (2009). *User's Manual for the SF-12v2 Health Survey* (2nd
28 Ed.): QualityMetric, Incorporated.
- 29 World Health Organisation. (2003). *Adherence to long-term therapies: evidence for*
30 *action*. Geneva: World Health Organisation.
- 31 World Health Organisation. (2019). Health statistics 2019: monitoring world health for
32 the sustainable development goals. Retrieved from
33 [https://www.who.int/gho/publications/world_health_statistics/2019/EN_WHS_](https://www.who.int/gho/publications/world_health_statistics/2019/EN_WHS_2019_TOC.pdf?ua=1)
34 [2019_TOC.pdf?ua=1](https://www.who.int/gho/publications/world_health_statistics/2019/EN_WHS_2019_TOC.pdf?ua=1)

35