IMPERIAL

Acute Remote Medicine Based Assessment of High Risk Atherosclerosis Patients

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy (PhD)

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Statement of Originality

The data present in this thesis are the result of my original work. Where appropriate, the contributions made by other persons have been appropriately acknowledged. No component of the work in the thesis has been submitted for assessment in a higher degree application at this or any other University.

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Dedications

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Thesis Summary

Although there have been significant advancements in medical and interventional therapies, myocardial infarction (MI) remains a major cause of death in the UK. Unplanned readmission rates in the UK are high despite a global trend towards short hospital stays post-MI, sitting at approximately 10% at 30 days post-discharge and even higher at 6 months. The 30-day mortality rate post-ACS in the US is 7.3%, with comparably high rates observed in Europe and the UK. The use of telemedicine technology can provide remote, clinically necessary, diagnostic information, thus eliminating the necessity for patients to visit the hospital. Telemonitoring could improve the management of post-ACS care and reduce the number of unexpected readmissions. Despite these potential benefits, there are considerable barriers to its implementation.

This thesis present four chapters discussing the impact and efficacy of home telemonitoring for cardiac patients post-ACS. I first used a systematic review and meta-analysis to investigate the existing research on the use of telemedicine for patient management post-ACS. Second, I designed and validated a clinical decision support system algorithm for the remote management of patients post-ACS in a nonhospital setting. Third, I conducted a randomised controlled trial (acronym: TELE-ACS) that used a specialised hybrid remote telemonitoring system to monitor patients following their hospital discharge post-ACS. Fourth, I conducted a 6-month cost-benefit analysis of the TELE-ACS protocol and assessed its impact on the health-related quality of life in patients following ACS.

The results demonstrate that a remote monitoring approach in combination with clinical decision algorithm protocol based on patient symptoms, 12-lead ECG data, BP levels, and oxygen saturation levels, significantly decreased the rate of hospital readmissions, emergency

department visits, unplanned coronary revascularisations, and patient-reported symptoms for patients post-ACS. Therefore, the TELE-ACS protocol represents a financially viable approach to reducing readmissions in ACS patients.

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Abbreviations

A&E	Emergency department
ACS	Acute coronary syndrome
AF	Atrial fibrillation
AMI	Acute myocardial infarction
AMU	Acute medicine unit
BMI	Body mass index
BP	Blood pressure
BPA	Best practice answer
CAD	Coronary artery disease
CDSSA	Clinical decision support system algorithm
CI	Confidence interval
CIED	Cardiac implantable electronic device
CKD	Chronic kidney disease
CMOS	High-resolution complementary metal-oxide semiconductor
CV	Cardiovascular
CVD	Cardiovascular disease
DHF	Decompensated heart failure
DM	Diabetes mellitus
ECG	Electrocardiogram
ER	Emergency room
GCP	Good Clinical Practice
GPs	General practitioners
GPS	Global positioning system
GRACE	Registry of Acute Coronary Events
HADS	Hospital Anxiety and Depression Scale
HF	Heart failure
HIC	Health Informatics Collaborative
HR	Heart rate
HRV	HR variability
HTN	Hypertension
ICU	Intensive Care Unit
IHD	Ischemic heart disease
IHF	Ischemic heart failure
ITT	Intention-to-treat

LOS	Length of stay
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
NEWS	National Early Warning Score
NSTEMI	Non-ST elevated myocardial infarction
PCI	Percutaneous coronary intervention
PCP	Primary care physician
PPE	Personal protective equipment
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
PSSS	Perceived Social Support Scale
QTc	QT interval
RCTs	Randomised controlled trials
ROB	Risk of bias
RPM	Remote patient monitoring
RR	Risk ratio
SAQ-7	Seattle Angina Questionnaire-7
STEMI	ST elevated myocardial infarction
TC	Trial Coordinator
TCC	TeleClinical Care
TM	Telemedicine or Telemonitoring
US	Unstable angina

1 Introduction

1.1 Introduction

1.1.1 The Burden of Ischemic Heart Diseases

Ischemic heart disease (IHD) describes heart-related conditions that result from inadequate blood flow due to blockages, either partial or complete, in the arteries that supply blood to the heart. The term “ischemic” pertains to conditions involving the heart that arise when narrowed coronary arteries restrict blood flow and oxygen to the heart muscle (1). IHD is often referred to as coronary artery disease (CAD) or coronary heart disease (CHD), to indicate cardiac issues resulting from the narrowing of coronary vessels that supply the heart. Without appropriate diagnosis and treatment, IHD can lead to critical complications such as heart attacks and may progress to ischemic heart failure (IHF). IHF is a severe cardiovascular (CV) condition characterised by reduced cardiac output due to weakened myocardial contractility. Without appropriate intervention, IHF can cause severe disability or death (2).

In 2019, the World Health Organization (WHO) reported that IHD was the primary cause of mortality globally, accounting for approximately 17.9 million deaths annually. This category, along with CV, respiratory, and newborn disorders, consistently leads global mortality statistics (Figure 1.1). IHD has remained the foremost cause of death since 2000, contributing to 16% (8.9 million) of total global deaths in 2019 alone. In recent decades, mortality rates from IHD in Western nations have markedly declined, due to enhanced primary prevention strategies, advancements in IHD treatment and management, and improved healthcare delivery systems (3). Despite the preventative advancements, a considerable number of adults continue to survive acute myocardial infarctions (AMIs), and many experience ongoing chest pain from stable angina or heart failure (HF). While IHD remains the leading cause of death across various demographic categories, mortality trends globally show a slow yet steady decrease.

However, despite these advancements, CV disease (CVD) still ranks as the leading cause of death worldwide (3).

The prevalence of nonfatal IHD has increased, while IHD-related mortality has declined since 1990 (4). Assessing the global impact of IHD requires calculations of mortality, prevalence, and disability due to IHD among genders, various age groups, and regions worldwide. There is not always a direct relationship between the incidence and prevalence of nonfatal IHD and IHD mortality rates (5, 6). Improved acute and chronic IHD treatment can reduce mortality rates, leading to a higher number of individuals living with chronic IHD conditions (7). However, even with a high risk of IHD, mortality might remain comparably low, potentially decreasing its prevalence. The overall burden of IHD is exacerbated by the symptoms and disabilities that affect individuals who have AMI, HF, or chronic angina pectoris (4).

Despite reductions in IHD mortality and incidence across various global regions, its overall burden continues to rise due to demographic shifts, including population growth and an aging populace (4). Recent studies indicate that the burden of CVD disproportionately affects individuals from lower socioeconomic statuses and with lower education levels. Therefore, enhancing public education about CVD risk factors and early symptoms could alleviate some of the burden associated with IHD. Addressing socioeconomic inequalities might further diminish IHD's impact, according to some researchers (8). Presently, IHD is the primary cause of premature mortality around the world (3, 9). Factors such as development, economic growth, and urbanisation play crucial roles in influencing the prevalence of IHD. Research has demonstrated that regions with lower age-adjusted rates of IHD often correlate with established risk factors such as unhealthy diets, high stress levels, insufficient physical activity, and

smoking. Hence, implementing preventive measures is essential for the effective management of IHD (8).

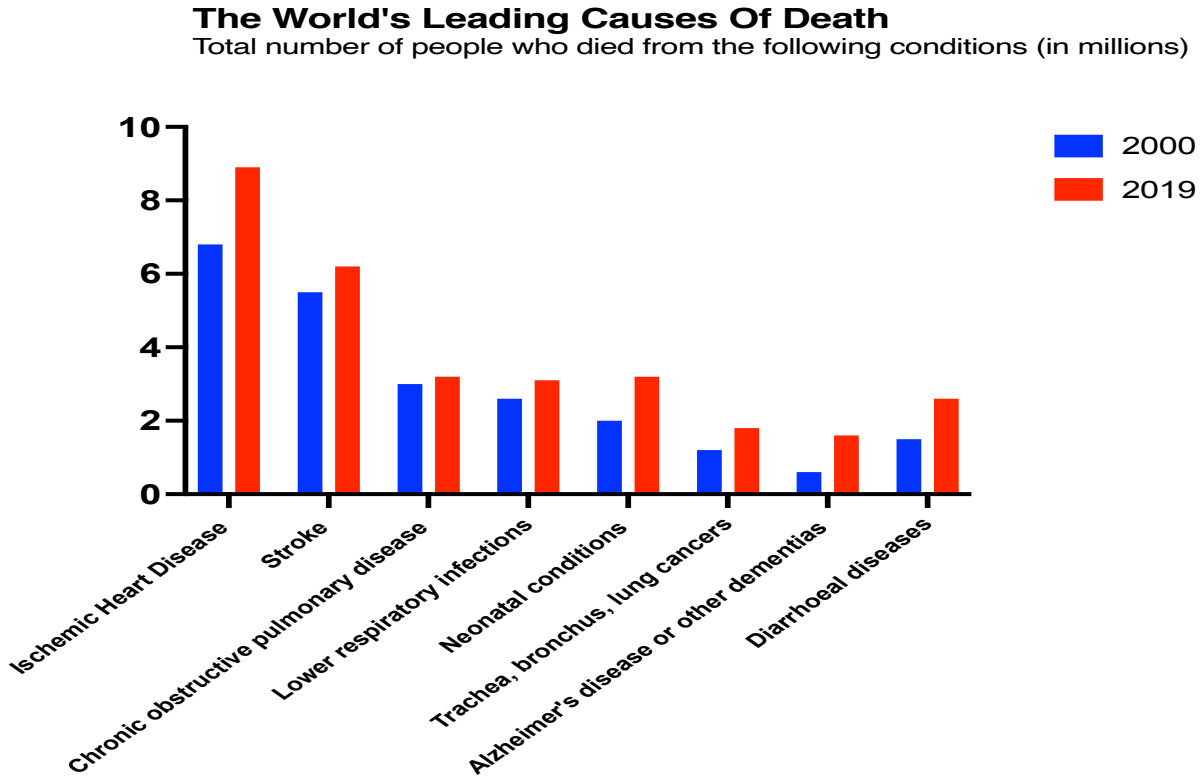


Figure 1.1 Data from the World Health Organization on the primary causes of death globally in 2000 and 2019.

1.1.2 Acute Coronary Syndrome

Acute coronary syndrome (ACS) includes various heart conditions marked by reduced blood flow to the cardiac muscle, such as unstable angina (UA), non-ST elevated myocardial infarction (NSTEMI), and ST elevated myocardial infarction (STEMI). These conditions are primarily caused by the narrowing of coronary arteries by blockages created by blood clots, often associated with atherosclerotic plaque buildup (Figure 1.2) (1). Diagnosing and classifying ACS involves taking a thorough patient history, performing an electrocardiogram (ECG) to identify signs of ischemia, and testing for biochemical markers that indicate myocardial necrosis (10). The terms AMI and UA pectoris are included under the umbrella of

ACS. AMI is characterised by myocardial damage and necrosis due to ischemia, which results in elevated cardiac troponin levels. Conversely, UA pectoris occurs when there is angina without myocardial necrosis or elevated cardiac troponin, reflecting an unstable clinical presentation associated with CAD (1).

Patients presenting with ischemic symptoms should be evaluated for potential ACS. Symptoms indicative of ischemia include discomfort in the upper extremities, jaw, or upper stomach, excessive sweating, nausea, fatigue, and syncope. The principal cause of myocardial necrosis is the mismatch between myocardial oxygen supply and tissue oxygen demand. Myocardial injuries can be categorised as ischemic and non-ischemic. Conditions such as pericarditis, dissecting aortic aneurysm, and mitral valve prolapse are not included in the ACS classification (10). Other ailments, such as musculoskeletal chest pain or discomfort, oesophageal pain, pulmonary embolism, and anxiety or panic attacks, might mimic ACS symptoms. Accurately identifying the underlying cause of these symptoms is essential for guiding the management and treatment strategies (10).

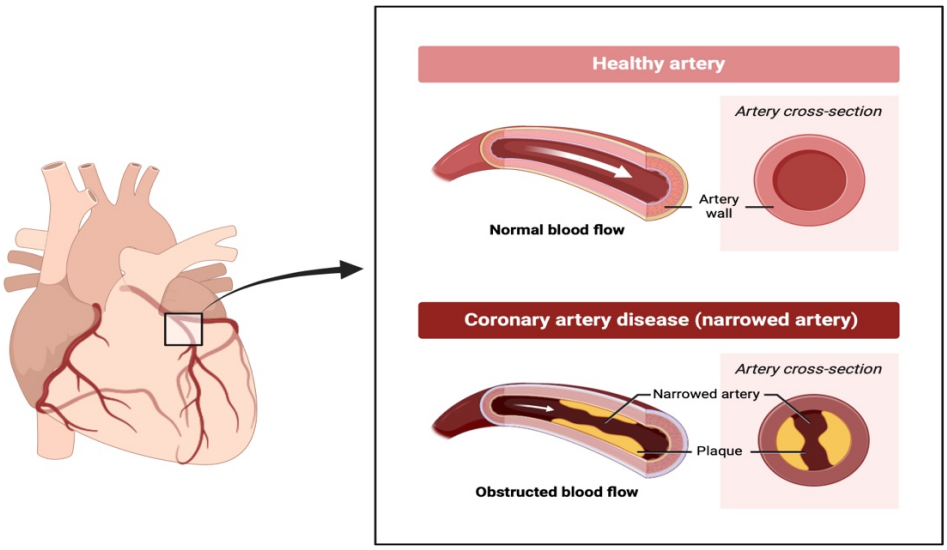


Figure 1.2 ACS is most often caused by atherosclerosis.
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1.1.3 ACS Complications

In the management of ACS, the adoption of contemporary, evidence-based clinical practices, including early revascularisation, antithrombotic treatments, and other preventative strategies, has led to improved outcomes over the past decade (11). However, a Swedish study by Jernberg et al. found that within one year of a myocardial infarction (MI), up to 20% of patients discharged after an ACS episode suffered a subsequent CV event, such as another MI, a cerebrovascular accident, or CV death. This finding is supported by further research from Jernberg et al., which indicated that the risk of recurrent CV events remains high among survivors of an initial MI, with approximately 20% of these individuals experiencing another event within a year. Factors influencing the likelihood of a recurrent event include age, medical history, previous instances of MI, stroke, HF, and whether revascularisation was performed during the initial event (11). The researchers found no significant difference in the impact of common risk factors between stable post-MI patients and those with ongoing MI issues.

Pocock et al. conducted two substantial prospective observational studies involving data from 28 countries and over 23,000 patients who were hospitalised and subsequently discharged after an ACS event. The studies identified 17 independent factors that significantly increased the mortality risk within two years post-discharge. Key predictors of mortality included advanced age, reduced ejection fraction, absence of coronary interventions or thrombolysis, elevated serum creatinine levels, decreased haemoglobin levels, history of heart disease or chronic obstructive pulmonary disease (COPD), use of aldosterone inhibitors or diuretics at discharge, male gender, lower educational attainment, in-hospital cardiac complications, low body mass index (BMI), and ST-segment elevation (12). The mortality rate two years after discharge was 5.5%, an increase from the first-year post-discharge rate of 3.9%.

1.2 ACS in the Context of the COVID-19 Pandemic

1.2.1 COVID-19 and CVD

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly contagious strain of coronavirus, responsible for the swiftly spreading coronavirus-2019 (COVID-19) outbreak. The worldwide dissemination of the illness resulted in significant public concern, and in early March 2020, the WHO announced that COVID-19 had become a global pandemic. The incidence of infection and mortality associated with this illness have been rapidly increasing across the globe. Patients infected with this virus may be either completely asymptomatic or present with a wide variety of symptoms, ranging from mild respiratory issues to severe, potentially fatal dysfunction of the respiratory and CV systems. Death in patients with COVID-19 infection is predominantly caused by failure of the respiratory system (13). However, CV events may also play a role in overall mortality and may even be the major contributing factor in the death of some patients (14).

A study conducted by Dhakal et al. showed that 8-25% of patients diagnosed with COVID-19 had CV conditions. The percentage of cardiovascular issues was much higher in patients who died from the infection. A meta-analysis performed in China that comprised of eight studies and involved a total of 46,248 patients found that hypertension (HTN) was present in approximately 17.7% of patients infected with COVID-19, diabetes mellitus (DM) was present in 8.6% of the patients, and CV disease was present in 5.4% of the patients. A comparison of the pooled odds ratio for HTN, CV disease, and respiratory system disease was made between patients who had severe versus non-severe COVID-19 illness. The results were 2.36 (95% CI: 1.46–3.83), 3.42 (95% CI: 1.88–6.22), and 2.46 (95% CI: 1.76–3.44), respectively (15). The Chinese Center for Disease Control and Prevention conducted a cohort study involving 44,672 patients, which revealed that in comparison to the overall case-fatality rate of 2.3%, patients

with COVID-19 who had concurrent medical illnesses had a higher case-fatality rate. The rates were 10.5% for CV disease, 7.3% for DM, 6.3% for chronic respiratory illness, 6% for high blood pressure, and 5.6% for cancer (16). Results from another study indicated that myocardial injury, defined as an increase in troponin levels above 99% of the upper limit of normal, was sustained by 7-17% of hospitalized patients with COVID-19 (13). According to a study conducted in China, 22% of patients with COVID-19 who were admitted to the intensive care unit (ICU) had a significant increase in the development of myocardial injury in relation to disease severity. This percentage rose to around 59% in patients who died of COVID-19 (17). An estimated 17% of patients with COVID-19 developed cardiac arrhythmias. In comparison to non-ICU patients, the incidence of arrhythmias was significantly higher in patients who were admitted to the ICU (44.4% vs. 6.9% $p = 0.001$) (17-19).

1.2.2 The Burden of COVID-19 on Health Systems

The mortality and morbidity rates associated with COVID-19 continue to rise, putting healthcare systems and providers at risk. Maintaining the safety of healthcare providers is crucial. The burden placed on healthcare systems and providers by the COVID-19 pandemic could result in a rise in health problems, such as insomnia, exhaustion, long hours at work, debilitating fatigue, and risk of transmitting the virus to family members (20). The pandemic has negatively impacted the physical and mental wellbeing of healthcare workers and frontline workers, including paramedics, emergency physicians, nurses, and firefighters (13). Overall, 3.9% of the 3,912,156 patients with COVID-19 globally were healthcare providers (Figure 1.3). Furthermore, 0.5% of the total number of COVID-19-associated deaths (270,426) were healthcare providers (Figure 1.4). Therefore, for every 100 healthcare providers who contracted the disease, one died (21).

Compared to the general population, healthcare workers and patients had similar death and infection rates. Most infections occurred in females; however, most deaths occurred in males. Furthermore, infections were much more prevalent in nurses, while deaths occurred more frequently in doctors (21). Within the data that reported by Bandyopadhyay et al., general practitioners (GPs) had the highest risk of death among physicians, while mental health nursing was the nursing specialty with the highest risk of death. Possible explanations for this are the shortage of personal protective equipment (PPE) in the community and primary care settings, the prioritisation of hospital cases over the cases outside the hospital that possibly went undiagnosed; or the high number of patients seeking GP services. These factors increased viral transmission (21). Additionally, working closely with patients at the community level may put mental health nurses at a higher risk of exposure (22).

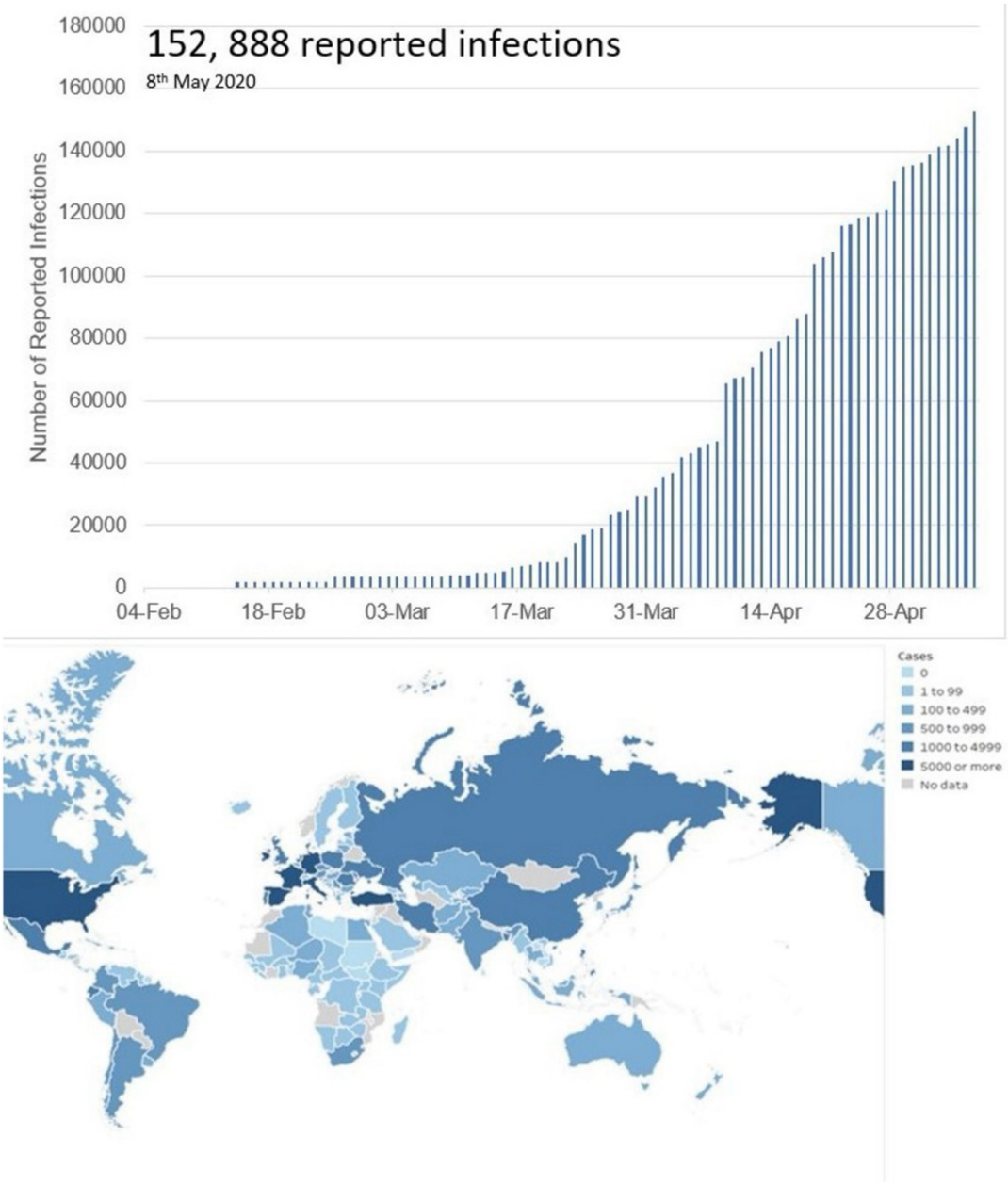


Figure 1.3 Total number of reported COVID-19 infections among healthcare workers globally in early May 2020 (21).

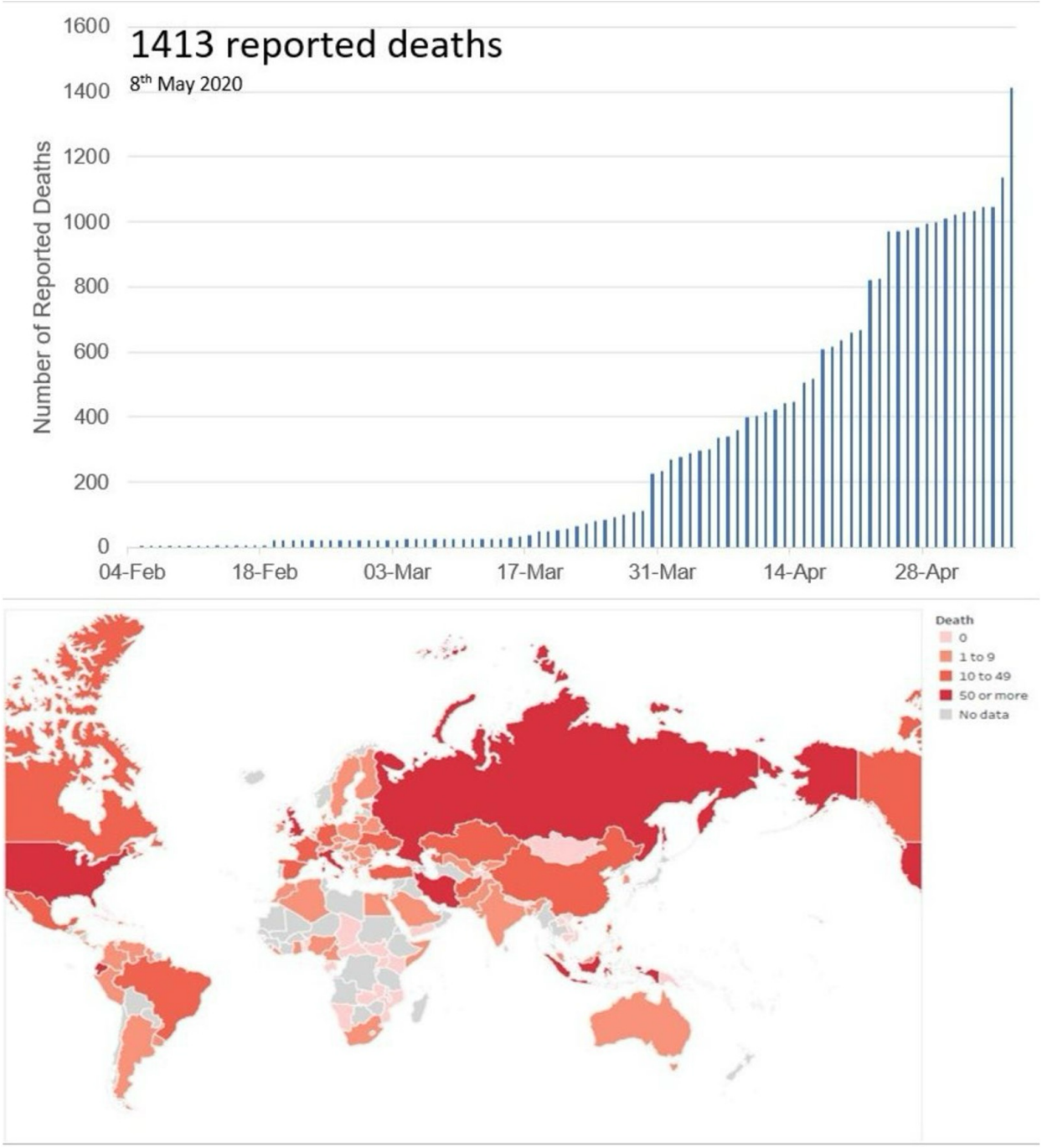


Figure 1.4 Total number of reported COVID-19 deaths among healthcare workers globally in early May 2020 (21).

1.2.3 The Impact of COVID-19 on ACS Management

A variety of presentations, ranging from STEMI to Takotsubo cardiomyopathy, can appear as the first manifestation of a COVID-19 infection (13). Possible causes of myocardial ischaemia and infarction include the rupture of a plaque triggered by a virus-induced stress response or the development of a blood clot due to increased coagulability (15). During the pandemic, patients with STEMI experienced a significant delay in seeking medical help compared to the pre-pandemic period, with an average lag time of 112 minutes versus 60 minutes. This delay was mainly due to patients' fears of contracting or spreading COVID-19 if they were admitted to the hospital and concerns about adding to the healthcare system's burden (23). The pandemic has affected multiple facets of healthcare, including raising the threshold for patients to call emergency medical services, reducing the availability of ambulance services, increasing waiting times in emergency departments (A&E), and causing delays in percutaneous coronary intervention (PCI) due to the additional time required for healthcare workers to put on PPE. It could also have impacted the care delivered to individuals who exhibited a STEMI or other CV emergency (23). The number of people hospitalised for ACS decreased in areas highly exposed to COVID-19 (24).

Patients who have certain risk factors, such as elevated troponin levels or persistent cardiac irregularities on ECG, are recommended to undergo invasive angiography to support revascularisation. This approach is known to diminish complications and enhance outcomes (25). Patients with STEMI who have not undergone medical intervention face a considerably higher risk of death and complications, such as mitral regurgitation and ventricular septal defects. Ideally, the door-to-balloon time should not exceed 60 minutes, and for patients with NSTEMI, angiography should be conducted within 72 hours but preferably earlier (26). During the COVID-19 pandemic, these guidelines remained applicable, with additional measures

taken to assess potential infections and implement safeguards to protect both medical staff and patients. Chest discomfort is a common manifestation seen in COVID-19 cases; however, the symptoms of an actual MI can be clearly identified and distinguished through a comprehensive review of a patient's history. It is crucial to differentiate between type I and type II MI, as serum troponin levels may be elevated in conditions such as arrhythmia, HF, myocarditis, pericarditis, or systemic diseases (type II MI) (25). However, the need for additional diagnostic tests, such as ECG and troponin measurement, along with ensuring the safety of staff and patients, may delay the treatment of critically ill patients.

The global incidence of ACS in emergency situations markedly declined during the COVID-19 pandemic, particularly in the UK (27). Several factors contributed to this trend, such as the perceived heightened risk of hospital visits and a general hesitancy to access medical care to avoid overburdening the healthcare system. The decrease in hospital attendance may result in considerable adverse health outcomes, both immediately and over time. The frequency of out-of-hospital cardiac arrests temporarily doubled during the lockdown period, corresponding with decreased survival rates (Figure 1.5) (28, 29). These developments are likely influenced by the direct impacts of the virus combined with delays in seeking medical help and changes in the provision of healthcare services. Anticipated long-term effects of diminished A&E visits for ACS include an escalation in ischaemic cardiomyopathy, HF, and mortality rates. Should further outbreaks of COVID-19 occur, similar trends in the use of acute cardiac care services are expected.

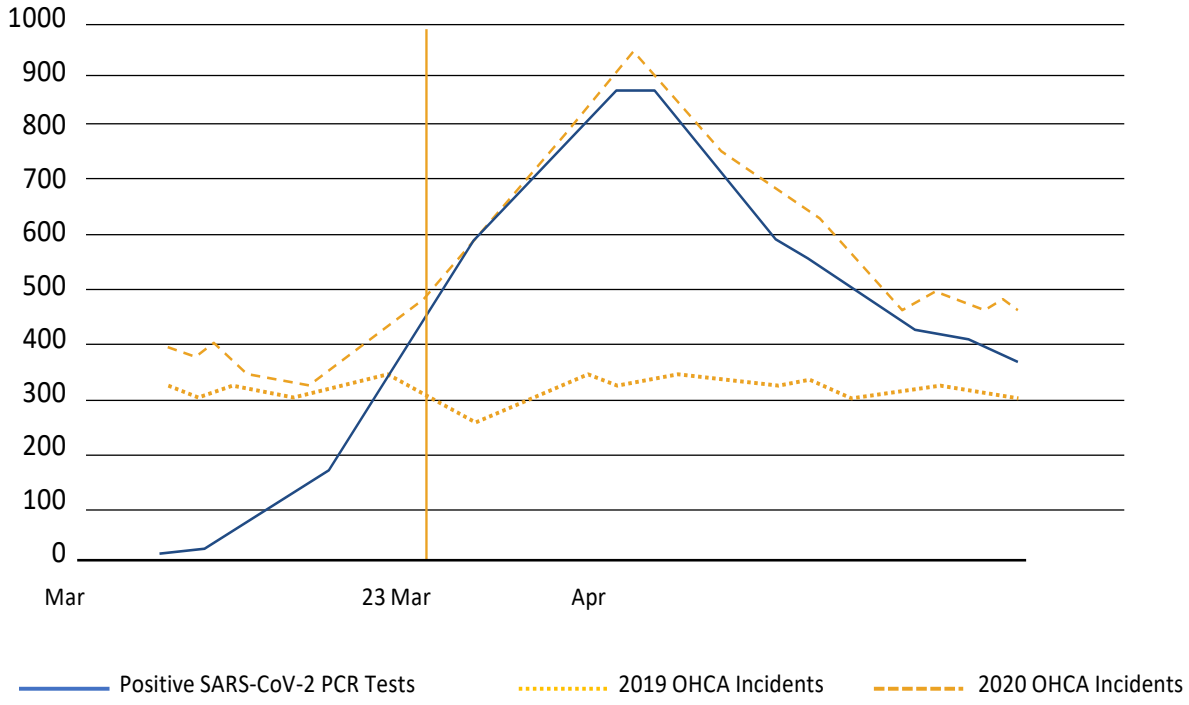


Figure 1.5 The daily occurrence of positive SARS-CoV-2 test results and OHCA incidents in London during March and April of 2019 and 2020, calculated using a 7-day moving average.

1.2.4 Increased Psychological Stress and Anxiety Among Patients During COVID-19

Over 15% of patients that recovered from SARS and MERS infections were later reported to suffer from sleep disorders, frequent traumatic memories, emotional lability, poor concentration, fatigue, and memory problems (30). Kong et al. assessed depression, anxiety, and social support among 144 patients diagnosed with COVID-19 using the Hospital Anxiety and Depression Scale (HADS) and the Perceived Social Support Scale (PSSS). Among the patients, 50 exhibited anxiety symptoms (35%) and 41 exhibited depression symptoms (28%) (31). Although the immune response may result in mental illness due to SARS-CoV-2 infection, the psychological impact of the illness itself, such as social isolation, concerns about infecting others, and stigma, can also contribute to illness (32). Those who survive a life-

threatening medical condition are at risk of prolonged and persistent mental health problems after hospital discharge. The prevalence of depression, stress, and post-traumatic symptoms were approximately 29%, 34%, and 24% after one year, respectively (33).

1.3 The Role of Telemedicine

1.3.1 Telemedicine in Cardiology

According to the American Telemedicine Association, telemedicine and telehealth refer to the use of technologies and services that facilitate the exchange of healthcare and medical information between different locations. This exchange can occur via mobile phones, the Internet, or virtual meetings, with the purpose of supporting or enhance patient care (34). The fields of health care consultations, clinical research, training, and patient monitoring and care have been transformed by telecommunications technology (35). These advancements in healthcare enable remote monitoring and the virtual delivery of clinical care, and are applicable in various settings, including hospitals and homes. The inception of telemedicine occurred in 1967 in Boston, Massachusetts, where a system enabling communication between doctors and patients was established. In 1989, a telemedicine system designed for remote monitoring and diagnosis was first implemented to aid individuals in need of cardiac resuscitation (36). This technology has advanced the remote monitoring of patients suffering from CVDs.

Telemedicine introduced innovative approaches for managing CVDs, significantly enhancing treatment across various cardiology sectors, including HF, CAD, and arrhythmias. It holds a crucial position in delivering efficient CV care to patients (37). Telecardiology, as defined by Brunetti et al., employs telecommunication technologies to facilitate the remote diagnosis and management of heart conditions. Telecardiology applications are categorised into three stages: pre-hospital, in-hospital, and post-hospital. Pre-hospital care involves the use of 12-lead ECG

to identify AMI with ST-segment elevation, which is then communicated to the destination hospital. Telecardiology connects rural and urban hospitals with major centres, improving the availability of echocardiography in ICUs, emergency rooms (ERs), and specialised departments, such as maternity and paediatric units. After hospitalisation, telecardiology supports ongoing care through telephone consultations between GPs and cardiologists, as well as enabling home telenursing for patients with chronic CV conditions and other heart-related issues (37).

Due to the COVID-19 pandemic, numerous non-urgent medical procedures and follow-up appointments with GPs, cardiologists, and other healthcare professionals were postponed or cancelled. This was done to enable more inpatient beds to be allocated to patients with COVID-19 and to protect healthcare workers who face a heightened risk of contracting the virus. Telemedicine and telemonitoring have emerged as viable solutions to enhance healthcare delivery, patient well-being, and outcomes for patients with chronic conditions (38). The home telemonitoring system is designed to link patients from their residences to medical facilities via telecommunication technology and electronic devices, enabling the digital transfer of medical data (39). This approach supports the management of CVDs by facilitating remote healthcare monitoring, thus reducing the need for direct patient examinations. In-person visits are reserved for patients whose diagnostic evaluations necessitate detailed medical examinations. Significant advancements in telemedicine have been achieved, including the deployment of smartwatches capable of detecting irregular heartbeats and medical emergency teams that provide ECG data to A&E for MI evaluations (40). Remote monitoring has been shown to enhance the outcomes and quality of life (QoL) for certain CV patient groups, particularly those with cardiac implantable electronic devices (CIEDs) (41).

1.3.2 Telemedicine in ACS

Telemedicine systems have been implemented in the field of cardiology to aid in diagnosing and treating diseases (42). It has proven to be a valuable resource in managing patients with ACS and has enhanced overall healthcare delivery (43). In cardiology, telemedicine facilitates the remote blood pressure (BP) monitoring (44), the use of pre-hospital ECGs for managing patients with AMIs (45), and arrhythmia observation (46). The pre-hospital transmission of ECG data can reduce the delay between symptom onset and the start of treatment for ACS patients en route to healthcare facilities (47). Telemedicine could significantly benefit individuals with CV conditions and could be an integral part of an extensive strategy to provide high-quality healthcare for those affected by CVDs, particularly MI, which is known to severely impact mortality and morbidity (48). Numerous reviews have highlighted the essential role of telemedicine in healthcare delivery during the COVID-19 pandemic (49). However, the effectiveness of telemedicine in reducing waiting times and mitigating short-term adverse clinical outcomes for STEMI patients undergoing PCI during the COVID-19 pandemic remains unclear (50).

1.3.3 Types of Telemedicine Programs

1.3.3.1 Smart phone-based

Currently, smartphones are highly popular, cost-effective, compact, and portable electronic devices that are widely owned by individuals. Leveraging this evolving technology is appealing due to the potential to track an individual's health without additional expenses (51). Modern smartphone models come with various built-in sensors, such as a high-resolution complementary metal-oxide semiconductor (CMOS) image sensors, global positioning system (GPS) sensors, and microphones (51). The health monitoring capabilities of these devices

support various health-related sensors, enabling the measurement of heart rate, heart rate variability (HRV), respiratory rate, and other health conditions.

1.3.3.2 Phone- and email-based consultations

In 2009, a survey revealed that 97% of UK adults across various age groups and backgrounds used email (52). The adoption of email for medical consultations presents several distinct benefits, including convenience for both patients and healthcare providers due to the ability to send and receive emails on laptops, smartphones, and other mobile devices. Key advantages of telephone consultations include enhanced accessibility, faster communication, potential cost reductions, and the facilitation of regular healthcare services for individuals with chronic conditions. However, for sensitive or intricate matters, patients often prefer face-to-face interactions or telephone consultations as their primary communication method (53, 54).

1.3.3.3 Portable devices and detectors

CVD management can be enhanced through remote patient monitoring (RPM), which has made significant advancements following the introduction of various technologies and services. These innovations enable healthcare professionals to monitor patients both in traditional medical settings and in non-hospital environments. RPM involves the use of multiple home-based medical devices for observing cardiac patients. These devices facilitate ongoing patient surveillance and enable immediate interventions to avert potentially life-threatening situations. They are available to physicians and healthcare teams who engage in comprehensive patient monitoring. The adoption of wearable and non-wearable RPM technologies has improved the efficiency and accessibility of patient care delivery and monitoring. Portable devices and sensors provide data to healthcare teams, enabling them to detect emerging or deteriorating health conditions, which aids in initiating and adjusting treatment plans. These RPM

technologies contribute to enhanced clinical outcomes and, in some instances, can eliminate the need for acute care (55).

Examples of portable devices and detectors:

- BP monitor
- Heart rate monitor
- Electronic stethoscope
- Tele-ECG
- Oximeter
- Body scale
- Smartwatch
- Smartphone
- Mobile cardiac telemetry
- Holter monitors
- Implantable cardioverter defibrillator
- Pacemaker
- Vascular activity monitor
- Portable EKG/ECG monitor

1.3.4 Telemedicine Benefits, Challenges, and Limitations

The utilisation of telemedicine technologies enables the rapid and effective delivery of high-quality health care services and outcomes. Health care expenses can be minimised by reducing unnecessary visits to A&E, mishandling of medications, and hospital admissions (56). One of the most significant advantages of telemedicine is that it enables access to resources and care in rural or underserved areas without incurring higher costs or necessitating extensive travel. It also facilitates the provision of care that is of similar quality or surpasses the quality of traditional methods (56). The COVID-19 pandemic presented numerous challenges to the healthcare system, necessitating adaptations in practices to continue providing safe and

effective care to patients both with and without COVID-19. In response to these rapid changes, many clinical settings adopted telehealth models for both inpatient and outpatient care.

While telehealth offers numerous advantages, it also has certain limitations, including the inability to conduct comprehensive physical examinations and the occurrence of technical difficulties (57). Concerns have been expressed by various critics regarding the potential disruption to continuity of care associated with telehealth, as patients may not receive the thorough background checks and physical assessments typically provided during in-person consultations. Moreover, telemedicine sessions may pose greater risks in terms of privacy and security breaches than traditional face-to-face appointments (58). Healthcare providers utilising telehealth must consistently adhere to regulations to ensure the protection of patient privacy and data security.

Continuous patient monitoring, early identification of potential issues, and improved overall patient communication are some of the benefits associated with the use of RPM protocols (59). However, equity of access to remote monitoring is a major challenge. Factors such as older age, belonging to cultural and ethnic minorities, socioeconomic disadvantage, lack of digital and/or eHealth literacy, and limited access to technology contribute to inequality in accessing remote monitoring (60, 61). In a survey conducted by Engler et al., high cost was found to be the primary reason for patients not using remote monitoring technology (62). Another study by Graves et al. showed that inadequate internet infrastructure is a significant barrier in providing telehealth services in rural areas (63). It is important to address these inequities to prevent health disparities and to ensure that all patients can benefit from the advantages offered by remote monitoring.

1.3.5 Outcomes and Experiences

Telehealth services, once primarily restricted to remote or rural areas, are now being employed to extend the reach of medical services and improve healthcare access. Patients have cited aspects such as convenience, effectiveness, interaction, confidentiality, and comfort as significant when using telemedicine (64). Through telemedicine applications, individuals equipped with mobile phones, tablets, personal computers, and desktop computers can readily communicate with healthcare providers, who can diagnose, monitor, and treat various acute and chronic conditions (65). Despite the proven effectiveness and efficiency of telehealth in enhancing healthcare access and outcomes, certain challenges must be overcome to enable its broader adoption.

1.4 Chapter Summary

This introductory chapter detailed the clinical background of IHD globally, focusing specifically on post-ACS complications, the increased risk of subsequent CV incidents, and the extensive burden these conditions placed on healthcare systems in the COVID-19 era and beyond. I detailed the notable decline in A&E visits for ACS during the pandemic, coupled with a significant rise in out-of-hospital cardiac arrests. This increase was largely attributed to the pandemic's direct impacts, patient hesitancy to seek prompt medical care, and the necessary reconfiguration of healthcare services to manage COVID-19 cases. The chapter ended by expanding on the evidence regarding the role of telemedicine in post-ACS patient care, arguing for the adoption of telehealth technologies to provide vital, remote diagnostic capabilities. This approach could eliminate the need for hospital visits, thereby mitigating the pandemic's impact and enhancing the quality and outcomes of healthcare services through effective remote monitoring.

1.5 Thesis Scope, Aims, and Hypotheses

The principal aims of this thesis are as follows. First, I aimed to employ a systematic review and meta-analysis methodology to thoroughly evaluate the existing research regarding telemedicine's role in managing patients following ACS. The second aim was to design and validate a clinical decision support system algorithm (CDSSA) for remotely managing post-ACS patients in a nonhospital setting. Third, I aimed to use a randomised controlled trial (RCT) format (Telemedicine in High-Risk CV Patients Post-ACS (TELE-ACS)) to utilise a specialised hybrid remote telemonitoring system to monitor patients following their discharge from the hospital after experiencing ACS. Fourth, I aimed to conduct a 6-month cost-benefit analysis of the TELE-ACS protocol and assess its impact on the health-related QoL in patients following ACS over 9 months.

1.5.1 Aims

- To use a systematic review and meta-analysis methodology to rigorously examine the existing evidence regarding the use of telemedicine for managing patients post-ACS. This review will help clarify the effectiveness and applicability of telemedicine in this context.
- To design and validate a CDSSA for the remote management of patients post-ACS in a nonhospital setting. This system is intended to provide real-time, evidence-based guidance to healthcare providers.
- To utilise a bespoke hybrid remote telemonitoring system (TELE-ACS) to monitor patients discharged from the hospital following ACS, employing a RCT format to evaluate its efficacy.
- To conduct a 6-month cost-benefit analysis of the TELE-ACS protocol and assess its impact on the health-related QoL in patients post-ACS.

1.5.2 Hypotheses

- Telemedicine is an effective tool for managing patients post-ACS and leads to comparable or improved outcomes versus standard care methods.
- The use of a CDSSA in the management of post-ACS patients will result in responses that adhere to best practices more closely and improves the safety and accuracy of decision-making.
- A novel telemonitoring system-based algorithm will reduce hospital readmissions for patients post-ACS by using validated technologies coupled with urgent remote consultations with a cardiologist.
- The TELE-ACS protocol provides a cost-effective approach to managing post-ACS patients and represents a financially viable approach to reducing ACS readmissions.

2 The Efficacy of Telemonitoring in the Management of Patients Post-ACS: A Systematic Review and Meta-Analysis of RCTs

2.1 Abstract

2.1.1 Background

Patients who are admitted to hospital due to ACS often experience repeat hospitalisations. Although telemedicine could enhance care for patients post-ACS, there are considerable barriers to its implementation.

2.1.2 Methods

We conducted searches in EMBASE, PubMed, and the Cochrane Library to identify RCTs published between January 2013 and September 2023 that evaluated the use of telemonitoring in assessing post-ACS patients. The risk of bias (ROB) in the included studies was assessed using the Cochrane ROB-2 tool. Our protocol was registered with PROSPERO (CRD42023435472), and the review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Meta-analyses were performed using a random-effects model implemented in RevMan 5.4.1

2.1.3 Results

Six RCTs were identified, comprising 2,964 participants, of which 1,482 received telemonitoring technologies upon hospital discharge and 1,482 received standard care. There were differences in the patient metrics recorded for telemonitoring and the length of follow-ups between the studies. Telemonitoring significantly reduced hospital readmissions compared to standard care (risk ratio (RR) 0.65; 95% confidence interval (CI): 0.47–0.90). Telemonitoring did not significantly affect CV mortality; however, a trend towards mortality reduction was observed (RR 0.62; 95% CI 0.22–1.73). There were no differences in all-cause

mortality (RR 0.98; 95% CI 0.47–2.06) or in the occurrence of major adverse CV events (MACE; RR 0.87; 95% CI 0.47–1.31).

2.1.4 Conclusion

Telemonitoring was associated with a reduction in hospital readmissions for patients post-ACS compared to usual care. Further large scale RCTs are required to elucidate the patient metrics that require monitoring for post-ACS patients.

2.2 Introduction

ACS encompasses a range of conditions associated with myocardial ischemia, such as UA, NSTEMI, and STEMI (66). Over the past decade, advances in early revascularisation, antithrombotic treatments, and additional secondary prevention strategies have significantly enhanced patient outcomes (67). However, up to one in every five patients discharged from the hospital post-ACS after their first MI event experience another CV event (e.g., MI, cerebrovascular accident, or CV death) within one year (68). The health economic implications a second major CV event post-ACS can be significant. Following the first MI, a patient may require a variety of interventions, ranging from medication to major surgery to extensive rehabilitation. The initial ACS event is often associated with a high-cost burden. A second major CV event exacerbates these costs as it indicates a more complicated disease progression, requiring additional or more intensive treatments and further periods of hospitalisation. (67).

Telemedicine, also known as telehealth, represents a crucial progression in the medical field, enabling remote health monitoring and clinical treatment in hospitals, homes, and other environments. The use of telemonitoring could be a valuable method for managing patients with ACS, potentially offering economic advantages (43). The concept is gaining popularity as it provides enhanced continuity of care in the community (69). However, despite telehealth's efficacy and efficiency in improving access to healthcare and outcomes, numerous challenges must be addressed before widespread adoption can be achieved.

This systematic review and meta-analysis investigated and summarised the current available evidence on the use of home telemonitoring for assessing cardiac patients post-ACS. This review aimed to determine whether telemonitoring can provide data to facilitate the effective diagnosis of cardiac patients, eliminating the need for in-hospital assessment.

2.3 Methods

2.3.1 Search strategy and Selection Criteria

This systematic review and meta-analysis was performed according to the PRISMA guidelines (70) and was registered with the PROSPERO international prospective register of systematic reviews (CRD42023435472).

We systematically searched the PubMed, EMBASE, and Cochrane databases for this review. The search process was independently performed by all authors, using the specified keywords and search terms listed in Tables 2.1 and 2.2. We developed a comprehensive search string that aimed to identify RCTs examining the impacts of RPM technologies in the home setting. Ongoing discussion among the authors resulted in the development of two search themes (see Table 2.1): The final search was performed on 12 September 2023 across all databases. Only studies published between January 2013 and September 2023 were included. The PICO framework facilitated the organisation of the pertinent terms employed in the literature exploration; the terms used for each component of the framework are given in Table 2.2.

Table 2.1 Search strings developed for the systematic review

Concepts	Keywords and MeSH terms
#1 RPM and related concepts	("Telemedicine"[MeSH Terms] OR "Telemonitoring"[text word] OR "Remote Patient Monitoring"[text word] OR "Cardiac Telehealth"[text word] OR "Biosensing Techniques"[MeSH Terms] OR "Wearable Device"[text word] OR "Wearable Sensor"[text word] OR "Wireless Monitoring"[text word] OR "Home Healthcare"[text word] OR "Digital Health"[text word] OR "E-Health"[text word] OR "M-Health"[text word] OR "Mobile Health"[text word] OR "Telehealth"[text word] OR "Smartphone-Based Monitoring"[text word] OR "Wireless Sensor"[text word]) AND ("Cardiovascular disease" [MeSH Terms] "Acute Coronary Syndrome"[text word] OR "Post-Acute Coronary Syndrome"[text word] OR "Cardiac Care"[text word] OR "Heart Disease Management"[text word]) NOT ("Self-Monitoring"[text word] OR "Self-Management"[text word])
#2 RCT	("Clinical Trial"[Publication Type] OR "Randomized Controlled Trial" [Publication Type] OR "randomized"[tiab] OR "placebo"[tiab] OR "therapy"[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT ("animals"[MeSH] NOT "humans"[MeSH]).

Table 2.2 PICO framework's representation of the keywords used in PubMed, Cochrane and EMBASE databases Searches.

Strategy	#	Search Terms
Population	#1	Cardiovascular disease, cardiac patients, acute coronary syndrome, myocardial infarction, post-acute coronary syndrome, heart disease management
Intervention	#2	Telehealth, telemonitoring, telemedicine, cardiac telehealth, home monitoring, remote patient monitoring, wearable device, hospital at home, wireless monitoring, home healthcare, digital health, E-health, M-health, mobile health, smartphone-based monitoring, wireless sensor,
Comparison	#3	Usual care, standard care, placebo
Outcome	#4	All-cause and cardiac mortality, number of readmissions, number of A&E visits, patient satisfaction and health-related quality of life
	#5	#1, #2, and #4; #1, #2, #4, and not #3

The Covidence software facilitated the identification and elimination of duplicate entries. The eliminations were corroborated via manual verification. Each author independently evaluated the search results to eliminate out articles deemed not relevant based on their titles and abstracts. The remaining studies underwent thorough examination to determine their eligibility for inclusion.

2.3.2 Inclusion and exclusion criteria

2.3.2.1 Study types

Only RCTs that involved telemonitoring for the management of patients post-ACS were included.

2.3.2.2 Participant types

Humans of any age and gender who were diagnosed with ACS were included. No restrictions were placed on the type of ACS.

2.3.2.3 Intervention types

The intervention of interest was the use of telemonitoring for the management of patients post-ACS.

2.3.2.4 Exclusion criteria

All non-RCTs, studies with only the abstracts available, studies not written in English, and duplicate studies were excluded.

2.3.2.5 Eligibility criteria

The selection process used four key eligibility criteria to identify the articles most pertinent to the research:

- Peer-reviewed clinical studies that explored the application of telemonitoring in home care.
- Scholarly clinical materials that examined the use of telemonitoring for diagnostic purposes.

- Clinical documents or resources focused on the implementation of telemonitoring for diagnosing cardiac patients in a home setting.

2.3.2.6 Review exclusion

The following articles were excluded from inclusion in the review:

- Articles that were not RCT studies.
- RCTs predominantly focused on telemonitoring use for cardiac rehabilitation and medication adherence.
- Studies focused on cardiac rehabilitation and adherence of medication.
- Non-scholarly and non-clinical studies.

2.3.3 Data Collection Processes

All authors used a standardised data extraction form to autonomously gather information from the included publications. Any discrepancies were resolved through deliberation until a consensus was reached. The extracted data encompassed details regarding the study (publication year, authors, research design, geographical location, setting, and telemedicine technology), participants (quantity, group distinctions, gender distribution, and age range), intervention (types of interventions implemented), and controls (comparator categories, such as usual/standard care).

2.3.4 Outcomes

The primary outcomes of interest included all-cause and cardiac mortality, number of readmissions, number of accident and emergency (A&E) visits, and MACE. Secondary outcomes included patient satisfaction and health-related QoL.

2.3.5 ROB

The Cochrane Risk of Bias-2 (ROB-2) tool was used independently by all authors to assess the ROB in the RCTs included in the review (71). Several domains were evaluated for bias: randomisation, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results (71). Each RCT was rated as either "low risk", "some concern", or "high risk" (71).

2.3.6 Statistical Analysis

Data were extracted using a data extraction form and then meta-analysed using the Review Manager (RevMan5.4.1) software. Dichotomous data were analysed using the Mantel–Haenszel test alongside random effects models to generate forest plots and compute the overarching RR and 95% CI for various outcomes, including all-cause and cardiac mortality, number of readmissions, frequency of A&E visits, occurrence of MACE, patient satisfaction, and health-related QoL. Significance was attributed to all Z-test outcomes with p-values < 0.05. An assessment of heterogeneity was conducted via I^2 tests, where values $\geq 75\%$ were categorised as highly heterogeneous and those between 50–75% were regarded as moderately heterogeneous. Statistical analyses were performed using the Review Manager (RevMan version 5.4.1).

2.4 Results

2.4.1 Study Selection

The database searches returned 603 records, and an additional 52 articles were identified by hand-searching the reference lists of relevant literature. Overall, 150 records were removed due being duplicates. The titles and abstracts of the remaining 505 records were screened, and a further 468 were excluded. The remaining 37 articles underwent full text reviews. Six articles met the eligibility criteria and were included in the review. The screening process is summarised in the PRISMA diagram (Figure 2.1).

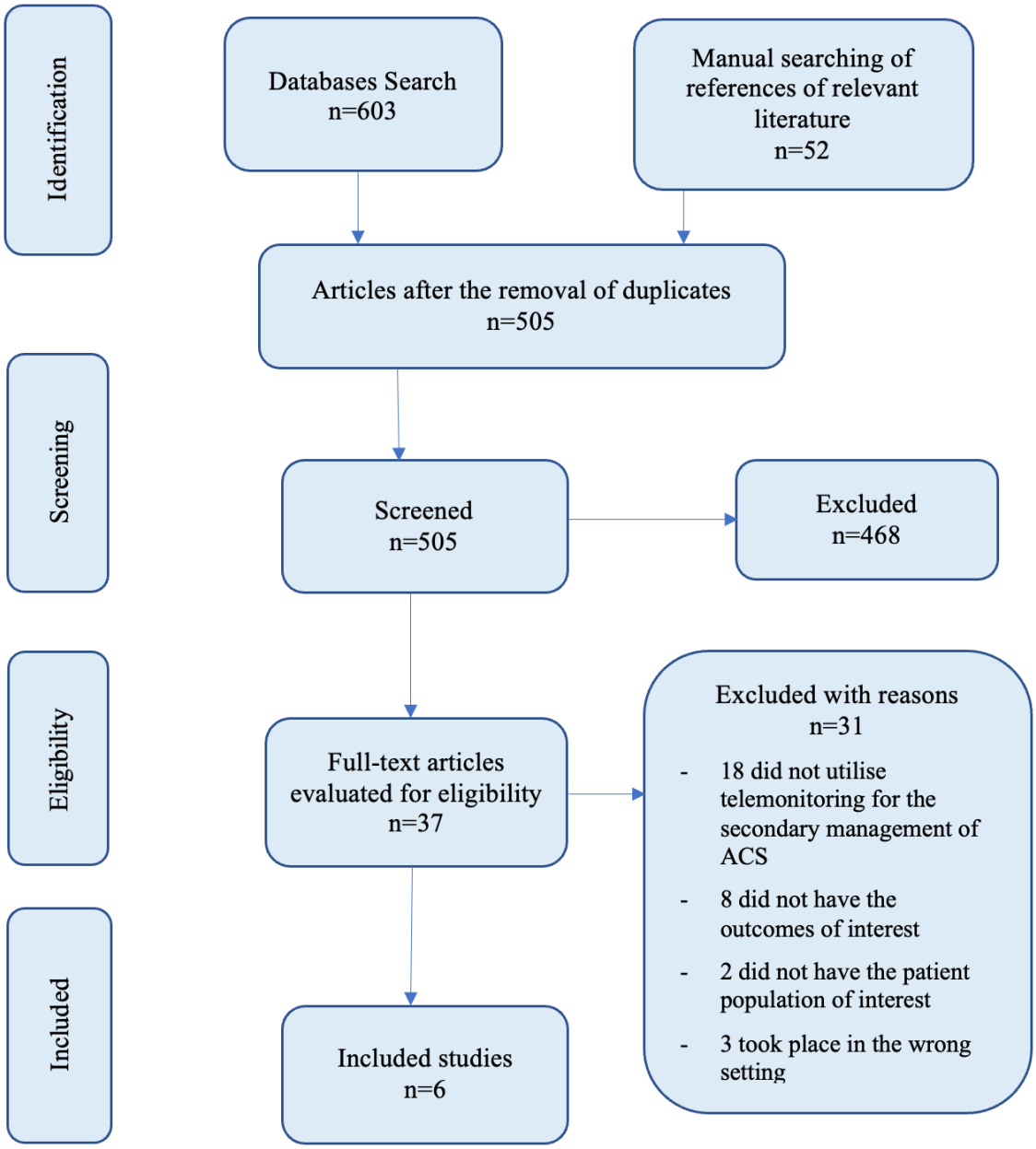


Figure 2.1 PRISMA flow chart detailing the study selection process.

2.4.2 Summary of Included Studies

2.4.2.1 Study characteristics

Six RCTs were included in the systematic review (Table 2.3), which compared the use of telemonitoring interventions to standard care in patients diagnosed with ACS. The RCTs by Garanin et al. and Indraratna et al. also included HF patients, which made up 72% and 22% of the total patient populations, respectively (72, 73). The RCTs were completed between 2015 and 2022.

The RCTs took place across a wide range of locations: 3 took place in Europe, 1 in Australasia, 1 in North America, and 1 in Africa. Follow-up times ranged from 3–18 months. The telemonitoring interventions were used for the full duration of the follow-up time in each study. A variety of telemonitoring methods were utilised, including remote BP and weight monitoring via Bluetooth BP cuffs and weighing scales, and cardiac rhythm monitoring via implantable cardiac monitors.

There was heterogeneity in the primary and secondary outcomes of the 6 RCTs. The most common outcomes measured were readmissions (48, 72-76) and patient satisfaction (48, 73, 75, 76). All outcomes of are summarised in Table 2.6.

2.4.2.2 Patient characteristics

A total of 2,964 patients were included across all the studies. All 6 RCTs evaluated adult populations, with the median age ranging from 55.8–66.27 years. Most patients were males, who comprised 71.6% of the total patient population. Five of the RCTs investigated whether patients had previously had an ACS event, with rates ranging from 4–98.5%. Other relevant baseline and clinical characteristics of the patient population are summarised in Tables 2.4 and 2.5.

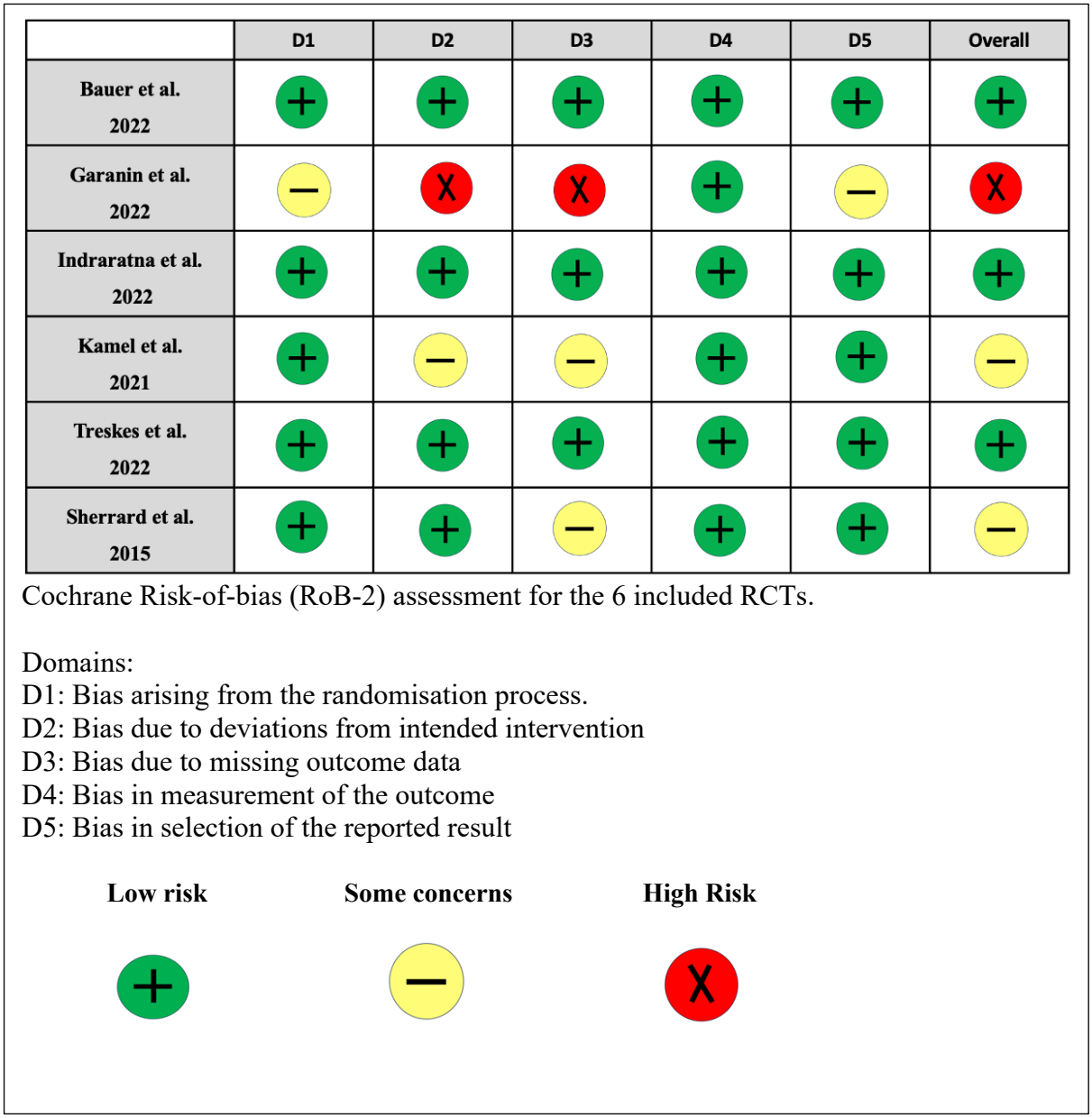


Figure 2.2 Risk of bias among included studies.

The RoB-2 tool revealed that 3 of the 6 RCTs had low ROB, with no concerns of possible bias across any of the 5 domains (Figure 2.2). Two RCTS were deemed to be of some concern, due to potential bias arising from the handling of missing outcome data and a lack of information on the possible deviations from the intended interventions (48, 76). The RCT by Garanin et al. was considered to have a high ROB, due to a lack of information regarding the randomisation process, missing outcome data, and deviations from the intended intervention. As expected,

none of the RCTs were able to blind patients to their allocations due to the nature of telemonitoring interventions.

Table 2.3 Baseline characteristics of the six included studies

Author	Study design	Diagnosis	Study Country & Year	Intervention / Comparators	Telemedicine technology	Follow-up time	Sample size		Outcomes Measures	
							A	B	Primary endpoints	Secondary endpoints
Bauer A et al. (74)	Prospective investigator-initiated, randomised, multicentre, open-label, diagnostic trial	AMI	Germany and Austria 2022	Device data were transmitted daily to the implantable cardiac monitor core lab and were checked daily by a study physician / Conventional follow-up	Implantable cardiac monitors	18 months	201	199	Time to detection of serious arrhythmic events, which included atrial fibrillation 6 min or longer, atrioventricular block class IIb or higher, fast non-sustained ventricular tachycardia.	- Sinus arrest longer than 6 seconds - Cardiovascular death. - MACE - Cerebrovascular events - Unplanned hospitalization - Decompensated heart failure. - Safety
Garanin A et al. (72)	Open randomized prospective study	ACS & HF	Russia 2022	Remote BP and pulse rate which allows measurement to be transmitted via a cellular communication channel to a research center / Standard management	Remote blood pressure (BP) monitoring	3 months	197	195	Hospitalization reasons for ACS or acute decompensated HF.	- BP/HR Monitoring - Adherence to treatment - Cardiovascular Mortality
Indraratna P et al. (73)	Two-center randomized controlled trial	ACS & HF	Australia 2022	The participants assigned to the intervention arm received the TCC app on their smartphone and connected Bluetooth peripheral devices at the time of discharge: a digital sphygmomanometer, a digital weighing scale, and a fitness band / Usual care	Sphygmomanometer Weighing scale Activity monitor	6 months	81	83	- Unplanned readmissions at 30 days - LOS - Physical parameters [BP, Body Weight] - All-cause mortality - MACE	- All-cause readmissions - Cardiac readmissions - Cardiac rehabilitation completion - Medication adherence - Cost-effectiveness - Patient satisfaction
Kamel H et al. (48)	Randomized controlled trial	STEMI patients after primary PCI	Egypt 2021	Monthly videoconferencing teleconsultation using a smartphone application for 3 months starting 1 week after discharge and at least a single F2F clinic visit. In each virtual visit the symptoms of patients, adherence to healthy lifestyle measures, medications, smoking cessation, and cardiac rehabilitation were reviewed / Single F2F clinic visit in the first 3 months after discharge	Videoconferencing teleconsultations	4 months	100	100	MACE – heart failure (HF), non-fatal re-infarction, recurrent anginal pain, re-hospitalization for cardiovascular-related illness, repeat percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and all-cause mortality	- Adherence of Patients to Medications - Cardiac Rehabilitation - Patient Satisfaction

Treskes, R et al. (75)	Single center, nonblinded, feasibility, randomized clinical trial	AMI	Netherlands 2022	Patients were given 4 smartphone-compatible devices (weight scale, BP monitor, rhythm monitor, and step counter). In addition, two in-person outpatient clinic visits were replaced by electronic visits. Four physical outpatient clinic visits were scheduled in the year following the initial event	smartphone-compatible devices (Weight scale, BP monitor, rhythm monitor, and step counter)	12 months	100	100	BP control	- Patient satisfaction - Measurement adherence - All-cause mortality - Hospitalizations for nonfatal adverse cardiac events
Sherrard H et al. (76)	Single-centre randomized control trial	ACS	Canada 2015	Patients received automated telephone calls at one, three, six, nine, and 12 months post discharge. Each call lasted five to eight minutes. Each day, one of two trained cardiac nurses would review the call database and respond to the prompts requiring a call back Usual Care	Interactive voice response (IVR)	12 months	803	805	Increased compliance with medication and decreased adverse event (ER visit, hospitalization, unplanned visit).	- Medication adherence - Decrease in hospitalization, ER visits, and unplanned visits to the PCP - Patient satisfaction

A = Intervention group, B = Control group.

ACS = acute coronary syndrome, AMI = acute myocardial infarction, BP = blood pressure, ER = emergency room, F2F = face-to-face, HF = heart failure, HR = heart rate, LOS = length of stay, MACE = major adverse cardiovascular events, MI = myocardial infarction, PCI = percutaneous coronary intervention, PCP = primary care physician STEMI = ST segment elevation myocardial infarction, TCC = TeleClinical Care.

Table 2.4 Baseline characteristics of the 2,964 patients included in the studies

Baseline Patient Characteristics										
Age, sex and BMI									Intervention Characteristics (Month)	
Author Publication year	Age in Years (Median)		Male (%)		Female (%)		BMI (kg/m^2)		Monitoring duration (Month)	
	A	B	A	B	A	B	A	B	A	B
Bauer et al. (74) 2022	64	65	152/201 (76%)	170/199 (85%)	49/201 (24%)	29/199 (15%)	28·4 (25·5–31·0)	27·2 (24·4–29·9)	18 months	18 months
Garanin et al. (72) 2022	66,2	66,1	103/197 (52%)	100/195 (51%)	94/197 (48%)	95/195 (49%)	28 [24,48-32,22]	28,6 [26-33,45]	3 months	3 months
Indraratna et al. (73) 2022	61.3	61.7	65/81 (80%)	65/83 (78%)	16/81 (20%)	18/83 (22%)	28.5 (4.5)	30.1 (6)	6 months	6 months
Kamel et al. (48) 2021	56.2	55.8	73/100 (73%)	70/100 (70%)	27/100 (27%)	30/100 (30%)	NA	NA	4 months	4 months
Treskes et al. (75) 2022	60.1	59.1	81/100 (81%)	75/100 (75%)	19/100 (19%)	25/100 (25%)	27.1 (24.8-30.1)	27.1 (24.5-30.3)	12 months	12 months
Sherrard et al. (76) 2015	62.3	63.6	577/803 (72%)	591/805 (73%)	226/803(28%)	214/805(27%)	NA	NA	12 months	12 months

Table 2.5 Continued

Baseline Patient Characteristics																
Cardiovascular risk factors No. (%)									Medical History No. (%)							
Author Publication year	HTN		DM		Smoker		Previous ACS		CKD		Stroke		HF Or DHF		AF	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Bauer et al. (74) 2022	139/199 (70%)	147/198 (74%)	60/200 (30%)	59/198 (30%)	64/198 (32%)	62/195 (32%)	27/199 (14%)	35/199 (18%)	21/200 (10%)	22/199 (11%)	8/201 (4%)	12/198 (6%)	13 (6%)	15 (8%)	47 (23%)	11 (6%)
Garanin et al. (72) 2022	NA	NA	38/197 (19%)	43/195 (21,5%)	NA	NA	NA	NA	6/197 (3%)	19/195 (9,5%)	NA	NA	NA	NA	47/197 (23.5%)	53/195 (26,5%)
Indraratna et al. (73) 2022	39/81 (48%)	46/83 (55%)	21/81 (26%)	22/83 (27%)	18/81 (22%)	21/83 (25%)	63/81 (78%)	65/83 (78%)	11/81 (14%)	12/83 (14%)	0	0	18/81 (22%)	18/83 (22%)	16/81 (20%)	20/83 (24%)
Kamel et al. (48) 2021	35/100 (35%)	37/100 (37%)	36/100 (36%)	35/100 (35%)	72/100 (72%)	67/100 (67%)	4/100 (4%)	6/100 (6%)	NA	NA	1/100 (1%)	1/100 (1%)	5/100 (5%)	9/100 (9%)	NA	NA
Treskes et al. (75) 2022	40/100 (40%)	37/100 (37%)	12/100 (12%)	11/100 (11%)	NA	NA	8/100 (8%)	9/100 (9%)	NA	NA	4/100 (4%)	1/100 (1%)	0/100 (0%)	1/100 (1%)	NA	NA
Sherrard et al. (76) 2015	NA	NA	NA	NA	NA	NA	781/803 (97.2%)	793/805 (98.5%)	NA	NA	NA	NA	NA	NA	NA	NA

A = Intervention group, B = Control group

ACS = acute coronary syndrome, AF = atrial fibrillation, BMI = body mass index, CKD = chronic kidney disease, DHF = decompensated heart failure, DM = diabetes mellitus, HF = heart failure, HTN = hypertension, MACE = major adverse cardiovascular events, NA = not available.

Table 2.6 Outcomes of the 6 included studies

Outcomes Measures												
Author Publication year	**All-cause Mortality Rate %**		**Cardiovascular Mortality Rate %**		**Number of Readmissions %**		**Major Adverse Cardiovascular Events (MACE) %**		**A&E Visits**		**Patient Satisfaction**	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**Method of Assessing Satisfaction**	**Key Results**
Bauer et al. (74) 2022	5.00	5.00	4.00	2.00	13	15	12.0	13.0	NA	NA	NA	NA
Garanin et al. (72) 2022	NA	NA	1.52	5.13	4	13	NA	NA	NA	NA	NA	NA
Indraratna et al. (73) 2022	1.23	4.81	1.23	4.81	21	41	2.47	4.82	NA	NA	Patients in the intervention arm filled out a user experience questionnaire which evaluated the TCC program. The questionnaire was designed specifically for this study.	- Average rating for the app: 4.56/5 - 96% of users rated it as *easy* or *very easy* to use
Kamel et al. (48) 2021	NA	NA	1.00	2.00	5	9	11.0	14.0	NA	NA	At 4 months post-discharge, patients completed a survey that assess their satisfaction with the telemonitoring services. The survey was developed by RAND Corporation.	- 61% of patients stated that the telemedicine visits were as good as F2F clinic visits - 87% of patients were satisfied with telemedicine
Treskes et al. (75) 2022	2.00	2.00	1.00	2.00	4	3	NA	NA	NA	NA	Patient satisfaction was measured using the Patient's Satisfaction Questionnaire. Questionnaires were given to patients 1, 6, and 12 months after inclusion.	- Equal outcomes were observed in the Patient's Satisfaction Questionnaire. - Mean (SD) scores for general satisfaction were 82.6 (14.1) in the intervention group and 82.0 (15.1) in the control group ($P = .88$).
Sherrard et al. (76) 2015	NA	NA	NA	NA	13	13	NA	NA	14.7	18.3	Patients were asked a series of three questions to assess their satisfaction with the intervention	- Patient satisfaction with automated calls was high with 85% reporting they would use it again - 90% of patients reported telemonitoring was a good way to follow-up on patients' progress

A = Intervention group, B = Control group, A&E = Accident and Emergency

Three of the six RCTs assessed the rate of MACE, and there was heterogeneity in the components of MACE measured. Bauer et al. defined MACE as a composite of death and major adverse cardiac and cerebrovascular events, including CV death, stroke, systemic arterial thromboembolism, and unplanned hospitalisation for decompensated HF (DHF). Indraratna et al. defined MACE as a composite of all-cause mortality, nonfatal MI, and nonfatal stroke. Kamel et al. defined MACE as a composite of CV mortality, MI, HF hospitalisation, cerebrovascular stroke, and target vessel revascularisation. In all three RCTs, the rate of MACE was lower in the intervention arm compared to the control arm. However, these differences were not statistically significant. The biggest difference was observed in the study by Indraratna et al., with a relative MACE risk of 51% in the intervention arm (2.47% vs 4.82%; RR: 0.51 (0.10–2.72); p = 0.43).

Three RCTs explored the all-cause mortality rate. Only 1 reported a lower mortality rate in the intervention arm compared to the control arm (1.23% vs 4.82%; RR: 0.25 (0.03–2.24); p = 0.22); however, this difference was not statistically significant (72). The other 2 RCTs reported equal mortality rates between the two arms (5% vs 5%; p = 0.58 and 2% vs 2%; p>0.99) (74, 76).

Five RCTs assessed the CV mortality rate. In the study by Bauer et al., the CV mortality rate was higher in the intervention arm than the control arm; however, this difference was not significant (4.00% vs 2.00%, hazard ratio (HR) = 2.76 (0.73–10.42), p = 0.13). In the other RCTs, the CV mortality rate was lower in the intervention arm. None of the studies reported a significant difference in the CV mortality rate between the arms.

All 6 RCTs assessed readmissions at various timepoints. Only the studies by Indraratna et al. and Sherrard et al. explored all-cause readmissions; the other studies focused on readmissions of specific diagnoses. Two RCTs only evaluated HF readmissions (73, 74), 1 evaluated HF or ACS readmissions (72), and 1 evaluated non-fatal cardiac readmissions (75). Five RCTs, regardless of the readmission cause, reported fewer readmissions in the intervention arm compared to the control arm. This difference was only statistically significant in 1 RCT (4 vs 3, OR: 3.40 (1.1–10.8), p = 0.027) (72). Treskes et al. reported more readmissions in the intervention arm compared to the control arm (4 vs 3). However, statistical analyses were not performed, so whether this difference was significant remains unclear. Interestingly, Indraratna et al. found that readmissions were equal between the arms at 30 days, but lower in the intervention arm at 6 months.

Only Sherrard et al. assessed the impact of telemonitoring on A&E visits. The relative risk of A&E visits at 12 months was 77% in the intervention arm compared to the control arm. However, the difference was not statistically significant (14.7% vs 18.3%, RR: 0.77 (0.58–1.03); p = 0.079).

Only Indraratna et al. assessed QoL using the EuroQol- 5 Dimension (EQ-5D), observing significant improvements in both the intervention and control groups. Mean scores were 66.7 (SD = 18) in the intervention arm and 63.1 (SD=21) in the control, with no statistically significant difference between the groups.

Four RCTs investigated patients' satisfaction with the telemonitoring interventions. A variety of questionnaires were used to assess satisfaction at different timepoints. Two RCTs used generic patient satisfaction questionnaires (48, 75) and 2 used questionnaires developed

specifically for their studies (73, 76). Only 1 RCT stated the questionnaire participation rate (73). In general, patients were satisfied with telemonitoring. Treskes et al. found that patients were as satisfied with telemonitoring as they were with standard care (14.1% vs 15.1%; p = 0.88). However, Kamel et al. reported that only 61% of patients found the telemonitoring visits as good as face to face (F2F) visits, despite 87% of patients being satisfied with telemonitoring. Moreover, 34% of patients required help with accessing the telemonitoring visits. The telemonitoring app was well received by patients in Indraratna et al.'s study, with 96% of patients rating it as easy or very easy to use. Similarly, in the study by Sherrard et al., 85–90% of the patients said they would use telemonitoring again and agreed that it was a good way to follow-up on their progress.

2.5 Meta-Analysis Results

2.5.1 CV Mortality Rate

Five studies included in the analysis examined CV mortality rates (48, 72-75), incorporating data from 2,764 patients. The CV mortality rate was 1.01% in the control group compared to 1.51% in the intervention group, with a RR of 0.62 and a 95% CI of 0.22–1.73. The overall effect size revealed no statistically significant difference between the intervention and control groups (z = 0.91; p = 0.36). There was a moderate level of heterogeneity, indicated by an I^2 value of 40% (Figure 2.3).

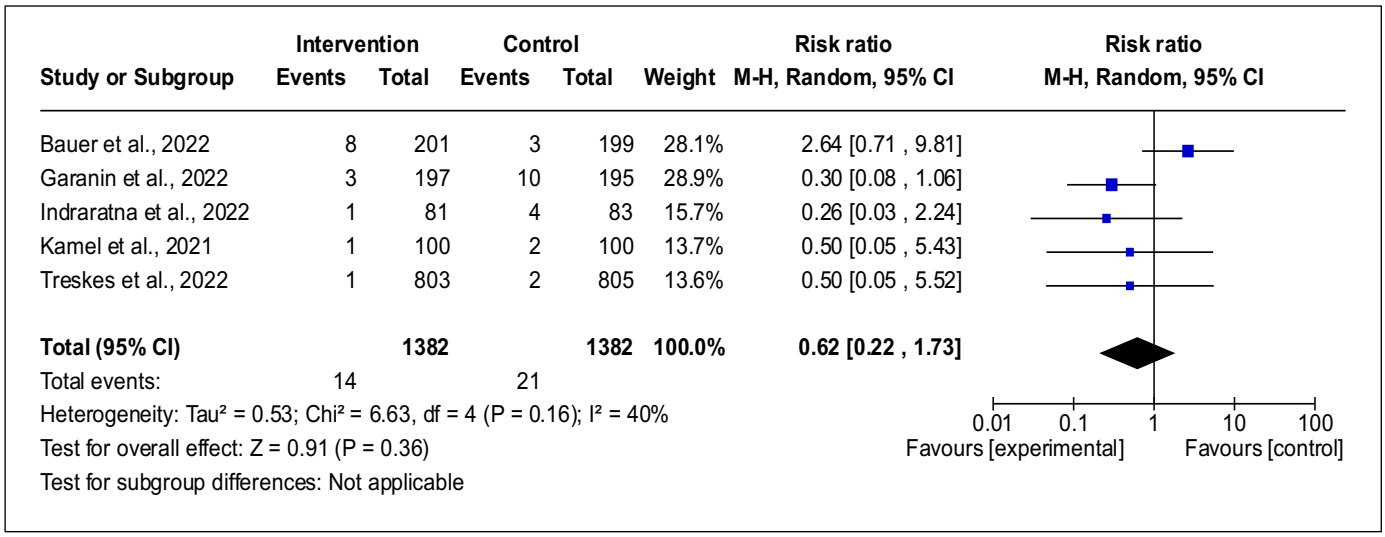


Figure 2.3 A forest plot of CV mortality rates. Weights are from a random effects analysis.

CI = confidence interval.

2.5.2 All-Cause Mortality Rate

Three studies reported the all-cause mortality rate (73-75), providing 764 patients for the meta-analysis. The all-cause mortality rate was 3.92% in the control group and 3.66% in the intervention group, with a RR of 0.98 and a 95% CI of 0.47–2.06. No significant difference was observed in the overall effect size between the intervention and control groups (z = 0.04; p = 0.96). Additionally, heterogeneity was non-existent, as reflected by an I^2 of 0% (Figure 2.4).

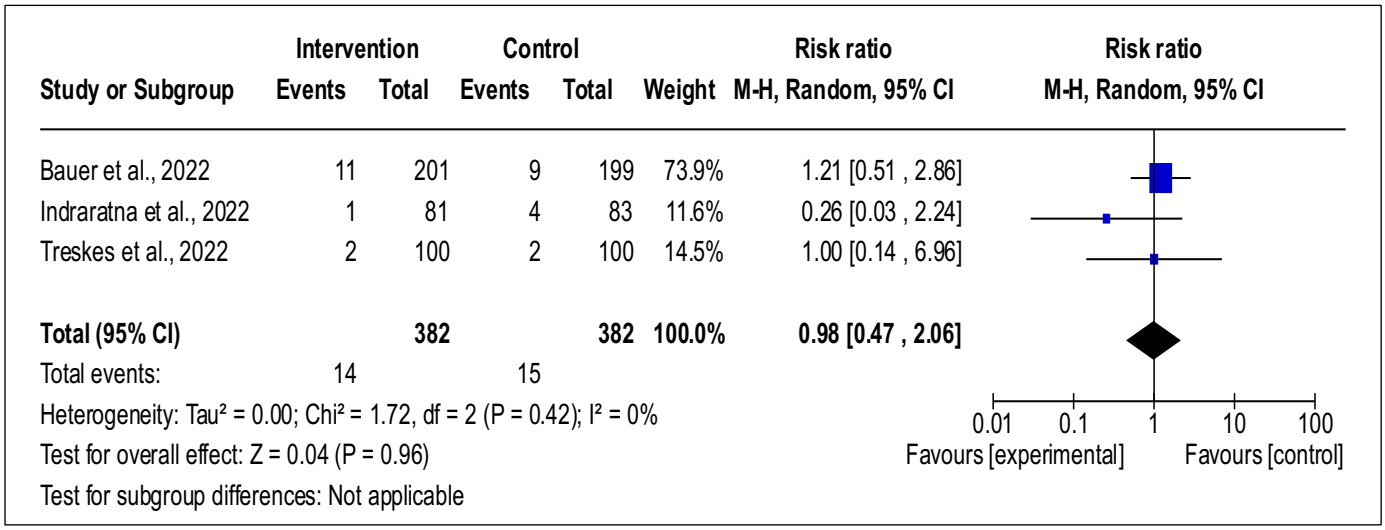


Figure 2.4 A forest plot of all-cause mortality rate. Weights are from a random effects analysis. CI = confidence interval.

2.5.3 Hospital Readmissions

Six studies reported hospital readmissions (48, 72-76), providing data from 2,964 patients for the meta-analysis. The readmission rates were 6.34% and 4.04% in the control and intervention groups, respectively, with a RR of 0.65 and a 95% CI of 0.47–0.90. The overall effect size demonstrated a significant difference between the groups (z = 2.55; p = 0.01). Moreover, the analysis showed low heterogeneity (I^2 = 12%) (Figure 2.5).

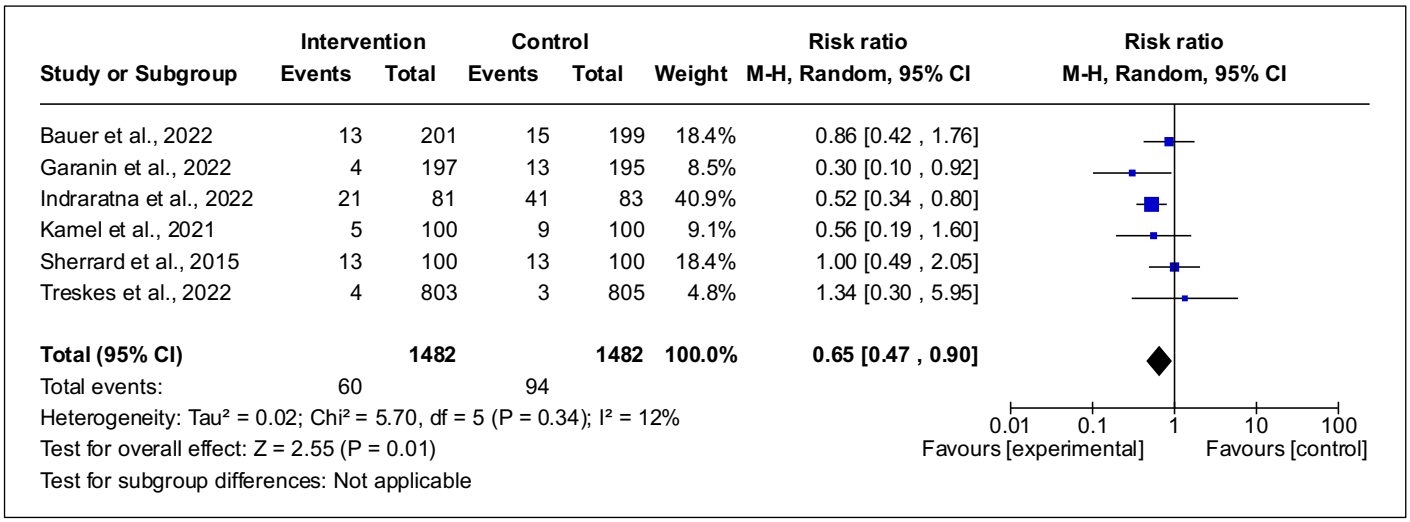


Figure 2.5 A forest plot of hospital readmission. Weights are from a random effects analysis. CI = confidence interval.

2.5.4 MACE

Six studies reported MACE (48, 73, 74), providing data on 2,208 patients for the meta-analysis. The MACE rate was 3.98% in the control group and 3.44% in the intervention group (RR = 0.87; 95% CI 0.47–1.31). The overall effect size indicated no significant difference between the groups (z = 0.67; p = 0.50). Additionally, there was no observed heterogeneity (I^2 = 0%) (Figure 2.6).

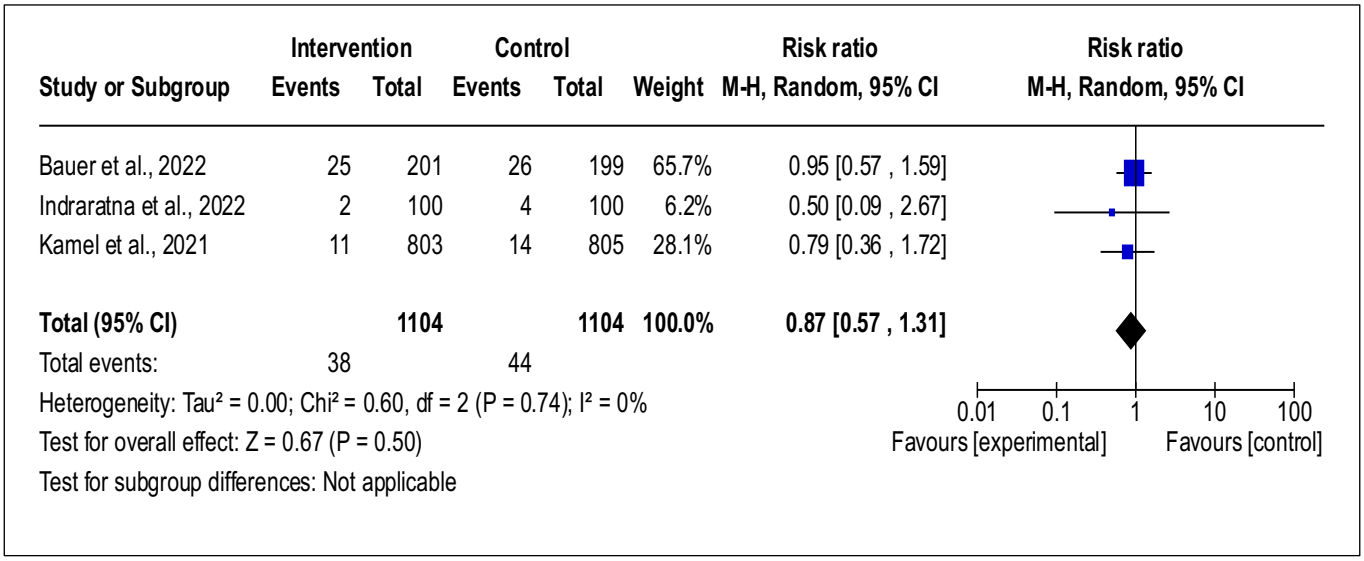


Figure 2.6 A forest plot of MACE. Weights are from a random effects analysis.

CI = confidence interval.

2.6 Discussion

To our knowledge, this is the first systematic review and meta-analysis to evaluate the efficacy of telemonitoring in ACS patients. The outcomes measured in the meta-analysis included MACE, all-cause mortality, CV mortality, and hospital readmissions. We found that telemonitoring significantly reduced the number of non-elective hospital readmissions compared with standard care. However, telemonitoring did not significantly reduce the rate of MACE, all-cause, or CV mortality. The reduction in hospital readmissions might be attributed to the continuous patient engagement and regular communication enabled by telemonitoring, which facilitates early detection and management of health issues. Additionally, the ease of accessing medical advice provides immediate interventions, psychological reassurance, and patient empowerment, which together prevent complications and unnecessary hospital visits.

A trend towards lower event rates of MACE and all-cause and CV mortality was observed with telemonitoring. This, in conjunction with the reduction in readmissions, is plausible, given telemonitoring enables clinicians to identify signs and symptoms early, enabling them to be addressed in a timely manner. Our analysis indicates that telemonitoring is a safe strategy in this patient group and could possibly lead to better outcomes.

Only Indraratna et al.'s telemonitoring intervention favourably impacted the meta-analysis outcomes; however, significance was only reached with the hospital readmissions outcome (48). This intervention involved daily manual measurements of BP, pulse rate, weight, and activity. If readings fell outside a patient-specific range, clinicians were alerted and could escalate accordingly. This suggests that for telemonitoring interventions to be clinically beneficial, they should involve the frequent monitoring of a multiplex of biomarkers. Treskes et al.'s intervention also involved daily manual measurements of BP, steps, weight, and cardiac

rhythm (72). However, this intervention resulted in higher readmissions than usual care and made no difference to the all-cause mortality rate.

In Treskes et al.'s trial, no personalised parameter range was defined: patients were only contacted if systolic or diastolic BP exceeded 139 mm Hg or 89 mm Hg, respectively, or if there were newly diagnosed arrhythmias. Furthermore, the interventions in the two trials were used for different lengths of time, with Indraratna et al. running theirs for 6 months and Treskes et al. for 12 months. Patients are at the highest risk for recurrent CV and other adverse events during the immediate post-ACS period. Therefore, it is reasonable to infer that telemonitoring proves the most efficacious during this period (77). The benefits of telemonitoring might be lost when such interventions are used for longer, which could explain the differences in the outcomes of these trials. There is a need for further larger-scale RCTs to determine the optimal length of time of telemonitoring.

Only one RCT measured A&E visits; therefore, a meta-analysis could not be performed on this outcome. The study demonstrated that telemonitoring reduced the visit rate, though this difference was not significant. To thoroughly investigate the impact of telemonitoring on this outcome, future telemonitoring RCTs should include A&E visits as an outcome measure. We believe that this is an important outcome to assess as it helps to determine the healthcare resource utilisation and patient safety associated with telemonitoring. Telemonitoring interventions could have a similar effect on A&E visits as observed with readmissions, by facilitating the early detection of complications and enabling timely interventions. However, rather than increasing admissions, it is more likely that telemonitoring reduces unnecessary admissions by providing timely medical advice and support, thus preventing minor issues from escalating and reducing the need for hospital visits.

Compliance with telemonitoring interventions is crucial for improving clinical outcomes, particularly if readings must be manually taken and transmitted. Therefore, it is paramount that such interventions are simple and quick to use, and that their benefit is made apparent to patients. Patient satisfaction is important to assess alongside the clinical efficacy of telemonitoring. Four RCTs included in this review assessed satisfaction. Patients were generally satisfied with telemonitoring, with the majority stating that they would use telemonitoring again. Patients were as satisfied with telemonitoring as F2F contact, suggesting that telemonitoring is a feasible alternative to in-person care. Only one RCT reported the response rate to their satisfaction questionnaire. Patients likely favourably engage with telemonitoring because it enables them to contact clinicians from the comfort of their own home, reducing transportation time and costs and the time required off work. However, patients recruited in such trials could be more likely to engage in telemonitoring due to participation bias. Future work should endeavour to assess compliance rates with telemonitoring interventions in addition to satisfaction levels.

As part of the satisfaction questionnaire in an RCT, 34% of patients stated that they required help with setting up the telemonitoring video calls (48). This highlights a crucial drawback of telemonitoring, in that it requires patients to have the necessary equipment (i.e., smartphones and laptops), expertise of use, or access to assistance (usually via family and friends). This issue is likely to be more prevalent amongst the elderly, who are also the group most likely to be diagnosed with ACS (78). Patients who did not have access to these devices were excluded from participating in the RCTs. For instance, in one RCT, 70% of prospective participants did not meet the inclusion criteria because they did not own a smartphone (73).

Future studies could investigate whether there are baseline differences between those included and excluded in these RCTs. Treskes et al. reported that participants in their RCT were approximately four years younger on average than the patients with AMI at the medical centre where the study took place (75). It is unclear whether this difference is due to the nature of the intervention or because younger people are more likely to participate in RCTs (79). Regardless, it is important that telemonitoring interventions are made widely accessible to avoid exacerbating health inequities.

2.7 Limitations

Given the limited data on the impact of these interventions on QoL (only one RCT assessed this outcome), a meta-analysis could not be performed to evaluate this outcome. Therefore, our ability to draw comprehensive conclusions is restricted. The study that did assess this outcome used the EQ-5D to measure QoL improvements, reporting enhancements in both the intervention and control groups. However, the absence of a statistically significant difference between these groups suggests that while telemonitoring interventions may contribute to overall QoL improvements, their distinct effectiveness compared to control measures remains unclear. There is a need for further research in this area to elucidate the specific impacts of interventions on QoL. Therefore, more RCTs should incorporate QoL as a primary outcome to provide a more robust evidence base.

Previous reviews and meta-analyses on this topic have focused on digital health interventions and CV patients as a whole (80, 81). However, there are stark differences in the management of different CVDs and in the types of digital health interventions. Therefore, there is a need for more specificity to draw clinically meaningful conclusions. Our study begins to address this gap in the literature. In January 2023, Saylik et al. conducted a meta-analysis evaluating the efficacy of digital health interventions in patients with ACS, which is the most recent review on this topic (82). They found that digital health interventions were effective at significantly reducing readmissions and all-cause mortality compared to usual care. The reason for these contrasting results is multifold. The authors included non-randomised clinical trials and studies prior to 2013 and evaluated digital health interventions, which is an umbrella term that encompasses telemonitoring interventions (83, 84).

There was notable heterogeneity in the telemonitoring interventions among the included RCTs, from the parameters being monitored to the method and frequency of monitoring. This makes it difficult to draw conclusions regarding the efficacy of telemonitoring. A standardised system of classifying telemonitoring interventions is required, similar to the World Health Organization's classification system for digital health interventions (83). This will aid in identifying and assessing the types of telemonitoring that provide the greatest clinical benefit. This is particularly important as telemonitoring is continuously evolving, with a growing breadth of approaches and technologies.

There was variability in the components of MACE and types of readmissions measured across the RCTs. This lack of consistency is unavoidable in such reviews and, therefore, the meta-analysis results must be considered in this context. Moreover, Bauer et al's RCT is a diagnostic trial, which means conclusions about the impact of implantable cardiac monitoring on clinical outcomes cannot be definitively drawn. The authors estimate that a much larger sample size is required to detect meaningful reductions in clinical outcomes (74).

2.8 Conclusion

This meta-analysis demonstrated that telemonitoring in ACS patients was associated with a significant reduction in non-elective hospital readmissions. Telemonitoring also positively influenced the rate of MACE and all-cause and CV mortality, though this did not reach statistical significance. Telemonitoring was well received by patients, who generally placed such interventions equivalent to face-to-face healthcare. These findings therefore suggest that telemonitoring has the potential to be utilised as an effective adjunct to conventional ACS management. There is a need for further large scale RCTs to assess the parameters that require monitoring in ACS patients, and the optimal method, frequency, and length of monitoring of these parameters required to significantly improve clinical outcomes.

3 Evaluating a Telemedicine-Based Algorithm for the Remote Management of Patients Post-Acute Coronary Syndrome

3.1 Abstract

3.1.2 Background

ACS significantly contributes to the occurrence of hospital readmissions, with non-cardiac chest pain accounting for almost half of readmissions, leading to unnecessary healthcare costs. CDSSAs can potentially enhance outcomes in these patients. We hypothesised that using a novel CDSSA based upon clinical guidelines for the management of patients post-ACS would enhance compliance with optimal medical practices.

3.1.2 Methods

Ten cardiac case scenarios were prepared, each describing a patient recently discharged with a telemedicine package after experiencing ACS. Doctors independently evaluated the scenarios and made management decisions. Following a period of at least 90 days, these same scenarios were reassessed by the same doctors with the aid of the CDSSA. The analysis assessed the difference in management decisions pre- and post-CDSSA. The primary metric was the deviation in points from the best practice answer (BPA).

3.1.3 Results

Thirty-two doctors completed the study. The results suggested a significant difference in outcomes between timepoints. The deviation from the BPA decreased post-CDSSA by an average of 0.2 points. When doctors were divided by speciality and seniority, significant differences were observed between non-cardiology and junior doctors. The deviation from the BPA post-CDSAA decreased by a mean of 0.33 for non-cardiology doctors and 0.36 for junior doctors. However, there was no significant difference between the two sets of measurements for cardiology doctors, consultants, or registrars.

3.1.4 Conclusions

The use of the CDSSA resulted in more aligned responses with best practices, thereby improving the safety and precision of decision-making processes. Junior doctors appeared to benefit most from the CDSSA. Additional research is essential to further explore the advantages of CDSSAs in managing patients remotely post-ACS.

3.2 Introduction

MI is one of the leading causes of mortality in the UK, despite innovative medical and interventional therapies. While lengths of stay in hospital for MI in the UK have decreased in line with global trends, unplanned readmission rates remain high, at 10% at 30 days (85). This is representative of global data, with a recent meta-analysis reporting 30-day readmission rates of between 11–14% and higher rates in the USA (86). These readmissions are for both CV causes, such as further MI, anginal chest pain or HF, as well as non-CV causes, most prominently non-cardiac chest pain, in up to 50% of readmissions, many of which do not require hospital admission (85). The mortality rate for patients 30-days post-discharge for acute MI (AMI) is 7.3%, with little change over time (87). The most current UK data on 30-day mortality among those undergoing coronary intervention for ACS varies between 1.6–43.1%, depending on the presence of ST-segment elevation and shock at presentation (88). Considering the financial implications of unnecessary readmissions post-MI (89), the timely identification and reassurance of patients experiencing non-cardiac chest pain could enhance health service efficiency and reduce patient anxiety. Additionally, the rapid recognition of ACS can accelerate intervention, potentially leading to improved patient outcomes.

During the COVID-19 pandemic, A&E ACS presentations decreased significantly, with a 49% reduction in admissions during the UK lockdown (90). Similarly, there was also a reduction in the number of patients presenting to hospital with potential complications post-ACS, with the risk of short- and long-term complications of ACS rising during this period, in addition to an increased mortality risk (91). While presentation rates are improving, should another viral pandemic occur, demand for emergency cardiac care is expected to follow similar patterns (27).

Therefore, a balance needs to be found between reducing unnecessary hospital readmissions but encouraging appropriate attendance post-ACS. Telemedicine devices that capture heart

rate, BP, oxygen saturation, and ECG data could provide vital clinical patient biometrics without requiring patients to attend hospital or see their local primary care physician (PCP)/GP. There are several methods used to monitor biometrics and clinical symptoms non-invasively in telemonitoring programmes. The most used method is based on a healthcare provider manually reviewing the data. An alternative approach is using CDSSAs (92). Medical algorithms are clinical standards based on evidence-based multidisciplinary best practices. They provide useful prognostic information to healthcare professionals and offer a step-by-step decision tree to optimise patient care.

Our study aimed to develop a CDSSA for managing patients either remotely or when seen in person in a nonhospital setting. One of the first studies that used this CDSSA was the TELE-ACS trial (93), which was a RCT evaluating the effectiveness of using telemedicine devices for home monitoring after hospital discharge in patients who have experienced ACS.

3.3 Methods

This was a cross-sectional questionnaire study that collected quantitative data using an online (Microsoft Forms) questionnaire. The study was conducted at Imperial College Healthcare National Health Service (NHS) Trust, with coverage across three sites (Hammersmith Hospital, Charing Cross Hospital, and St Mary's Hospital). The study population comprised doctors working in cardiology departments or acute medicine units (AMUs). A range of experiences were included, from junior doctors to consultants. Doctors were recruited between 03 November 2021 and 17 May 2022.

Ten novel clinical scenarios were developed based on real-world scenarios of patients being discharged from hospital following an MI that required urgent medical attention via a remote consultation. The patients were given a telemedicine package upon discharge. Each recruited doctor answered a questionnaire on the management approach for each of the clinical scenarios at two separate time points, with or without the use of a CDSSA. The time between answering the questionnaires was at least 3 months to avoid recollection of the original responses. The CDSSA was developed as a supplementary tool, with final management decisions being based on a combination of algorithm-based recommendations and clinical acumen. The doctors were able to make one of four possible management decisions for each scenario: (1) reassurance; (2) arrange an appointment with their PCP/GP (3) visit A&E; and (4) call an ambulance.

3.3.1 Clinical Scenarios

All the scenarios included clinical descriptions, such as the patient's age, primary symptoms, and past medical history. The telemonitoring programme captured heart rate, BP, oxygen saturation and ECG data. The 10 clinical scenarios used are given in Appendix 8.5. Most cases

involved presentations indicative of cardiac-related medical emergencies, including recurrent MI and acute HF; however, a portion of the cases were non-cardiac in nature. The proportion of cardiac and non-cardiac presentations was chosen to represent the real-world distribution of cases. Overall, cases involved complications associated with MI, and 3 cases, which were not connected to the hypothetical patient's previous medical history, were relatively benign.

3.3.2 CDSSA Development

A CDSSA for the management of patients seeking medical attention following an MI who have heart rate, BP, oxygen saturation, and 12-lead ECG data available, was developed using the European Society of Cardiology best practice guidelines (66, 94) and internally validated by a panel of expert cardiologists (Figure 3.1). The assessment categories included these metrics as well as presenting symptoms. Scoring criteria were developed for each assessment category outcome based on whether the category was low (green), medium (orange), or high (red) risk.

The actions recommended based on the scoring assessment were as follows:

- **All green:** Reassure the patient and continue with the scheduled routine, and follow-up as initially arranged.
- **One amber:** Advise the patient to seek non-urgent primary care (PCP/GP).
- **Two ambers:** Advise the patient to attend the nearest A&E, or if not possible, to call emergency services.
- **One red or more than two ambers:** Advise the patient to call emergency services.

Assessment Categories	Scoring Criteria	
Symptoms	Palpitations	Absent
		Present
	Chest Pain	No Symptoms
		New or worsening chest Pain
	Shortness of breath (SOB)	Absent
		New or worsening SOB
	Dizziness	Absent
		Presyncope
		Syncope
Heart Rate	Heart rate 50 to 110 bpm	
	Heart rate 110 -150 bpm	
	Heart rate 35 -50 bpm	
	Heart rate ≥150 bpm	
	Heart rate <35 bpm	
Blood Pressure	SBP 90 – 170 mmHg	
	SBP ≥170 mmHg	
	SBP <90 mmHg	
Saturation (SpO2)	100% - 94%	
	93% - 90%	
	< 89%	
ECG	Normal sinus rhythm (HR: 50 - 100 bpm)	
	New Sinus tachycardia (HR ~120 bpm)	
	New Sinus bradycardia (HR <50 bpm)	
	New Atrial arrhythmia: Atrial flutter & Atrial fibrillation	
	New horizontal or downsloping ST-depression ≥ 0.5 mm in two contiguous leads and/or T inversion > 1 mm in two contiguous leads with prominent R wave or R/S ratio > 1	
	Severe bradycardia (HR <35 bpm) or complete heart block	
	New Left bundle branch block (LBBB)	
	Ventricular tachycardia	
	New ST-elevation at the J-point in two contiguous leads with the cut-point: ≥ 1 mm in all leads other than leads V2–V3 where the following cut-points apply: ≥ 2mm in men ≥ 40 years; ≥ 2.5 mm in men < 40 years, or ≥ 1.5 mm in women regardless of age	

Figure 3.1 Post-MI clinical decision support system algorithm.

ACS = acute coronary syndrome, NSTEMI = non-ST-elevated myocardial infarction), STEMI = ST-elevated myocardial infarction.

3.3.2.1 Primary review of initial algorithm-free responses

The decisions made by the cardiologists in the first step of this experiment were analysed and compared. This analysis enabled any differences that might have occurred in the process of making clinical decisions to be assessed. During the initial assessment, the clinical decisions were made without the assistance of CDSSA. One of 4 possible decisions could be made:

1. Reassure the patient.
2. Advise the patient to call their GP/PCP.
3. Advise admission to the A&E.
4. Advise the patient to call emergency services.

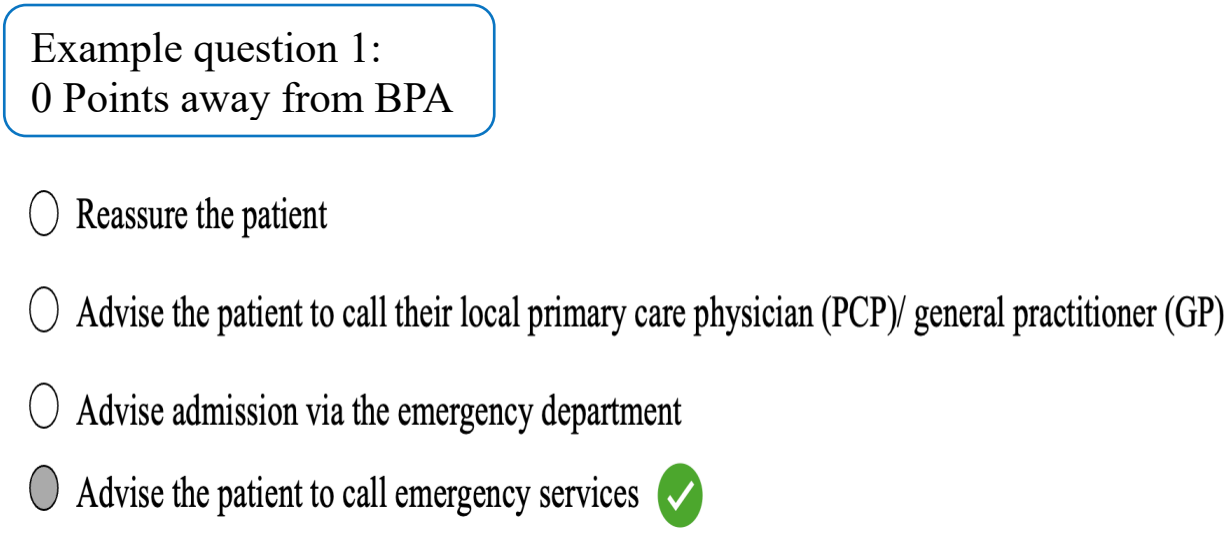
3.3.2.2 Secondary review of algorithm-assisted responses

Approximately 3-4 months later, the next phase was initiated. This time gap was essential to minimise any recency effect influence, as there was a risk that the cardiologists could remember their initial decisions if asked to reevaluate the scenarios too soon, potentially skewing their later judgments. The same cardiac cases were once again reviewed by the same group of cardiologists, who made their management decisions supported by the CDSSA.

3.3.3 BPA

The deviation from the BPA served as the indicator of response accuracy, where fewer deviation points signify a more precise answer. This metric was established by a panel of senior cardiologists at Imperial College NHS Healthcare Trust, who interpreted the European Society of Cardiology guidelines to determine the BPA for each clinical scenario. Figure 3.2

demonstrates the method used to calculate the BPA deviations for each question. For instance, in Question 1, if the respondent chose the fourth option (advise the patient to call emergency services), this aligned perfectly with the BPA, resulting in zero points away from the BPA for this question. Conversely, in Question 2, if the respondent advised hospital admission via the A&E, this deviated from the correct response (advise the patient to call emergency services) by one point. BPA deviations were calculated for all participating physicians across both attempts.



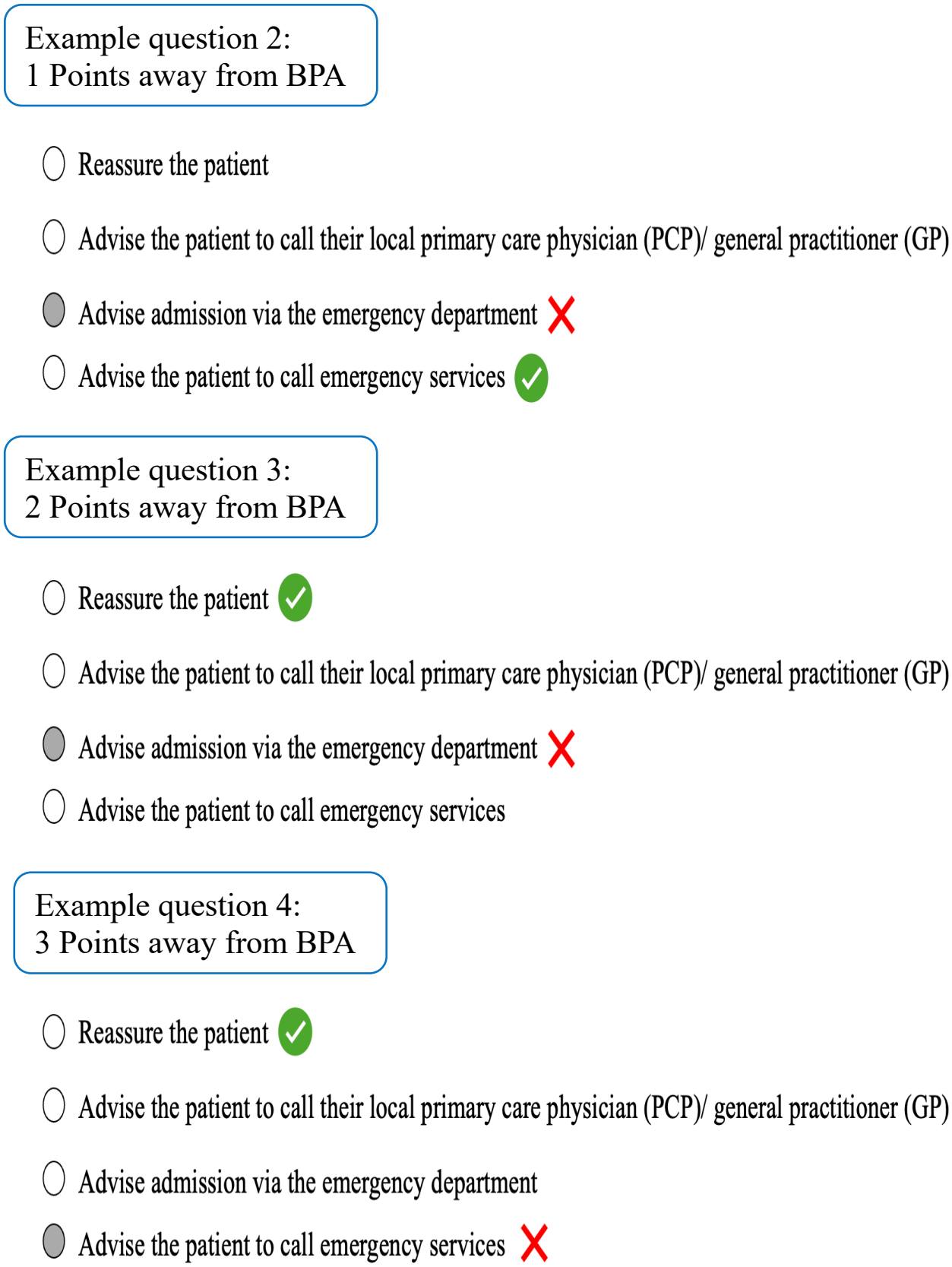


Figure 3.2 How the deviations from the BPA were calculated.

3.3.4 Statistical Analysis

Values for BPA deviations were reported as means and standard deviations for both time points (pre-CDSSA and post-CDSSA). The post-CDSSA score was subtracted from the pre-CDSSA score to calculate the difference between both time points. Linear mixed-effects models were constructed to evaluate the effect of specialities (cardiology versus non-cardiology) and grade of doctor (consultant, registrar, junior doctor) on the difference in BPA deviations. While the unit of analysis was at the question level, there was clustering at the subject level. As a result, respondents were treated as the random effect in the models to account for the variations of the repeated measurements from each respondent. Additionally, due to there being no junior doctor respondents working in cardiology, a multivariable liner mixed-effects model was constructed involving a subgroup of consultant and registrar respondents. Histograms were used to display the spread of scores in the full cohort, and in the speciality and training grade subgroups. RStudio version 1.4.1103 (Boston, MA, USA) with R version 4.1.1 was used for the statistical analyses.

3.4 Results

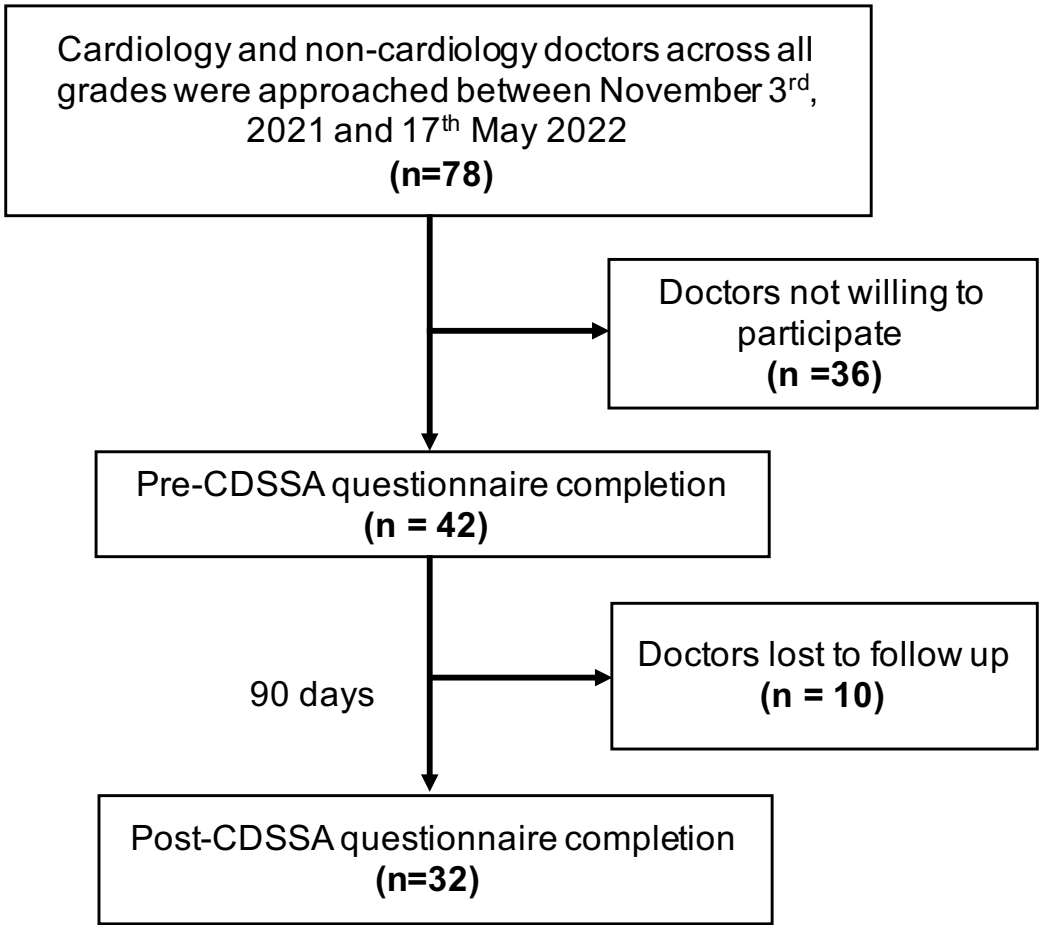


Figure 3.3 Study flowchart.

Table 3.1 Summary of cohort stratified by speciality and grade of doctor

	Consultant	**Registrar**	**Junior doctor**	**TOTAL**
Non-cardiology doctor	2 (11.8%)	3 (17.6%)	12 (70.6%)	17
Cardiology doctor	6 (40%)	9 (60%)	0 (0%)	15
TOTAL	8	12	12	32

Table 3.2 Summary of number of points from BPA pre- and post-CDSS

Subgroup	N doctors	Pre-CDSSA Mean ± SD	Post-CDSSA Mean ± SD	Difference (*) Mean (95% CI)	P-value
All doctors	32	0.62 ± 0.84	0.39 ± 0.62	-0.22 (-0.37, -0.08)	**0.003**
Cardiology	15	0.49 ± 0.63	0.39 ± 0.52	-0.10 (-0.29, 0.09)	0.29
Non-cardiology	17	0.73 ± 0.98	0.40 ± 0.70	-0.33 (-0.56, -0.10)	**0.005**
Consultants	8	0.41 ± 0.65	0.39 ± 0.54	-0.02 (-0.26, 0.21)	0.84
Registrars	12	0.62 ± 0.77	0.40 ± 0.60	-0.22 (-0.48, 0.05)	0.11
Junior doctors	12	0.75 ± 1.00	0.39 ± 0.69	-0.36 (-0.57, -0.14)	**0.001**

(*) Difference expressed as: post-CDSSA minus pre-CDSSA

Thirty-two doctors completed the study (Figure 3.3) (Table 3.1). The analyses compared the outcomes and BPA deviations for the pre- and post-CDSSA decisions. A summary of the results is given in the Table 3.2. For each timepoint, the means and standard deviations of the BPA deviations are reported for each subgroup, along with the differences between timepoints and corresponding CIs. These were calculated as the BPA points post-CDSSA minus the points pre-CDSSA. The significance of the differences is reported.

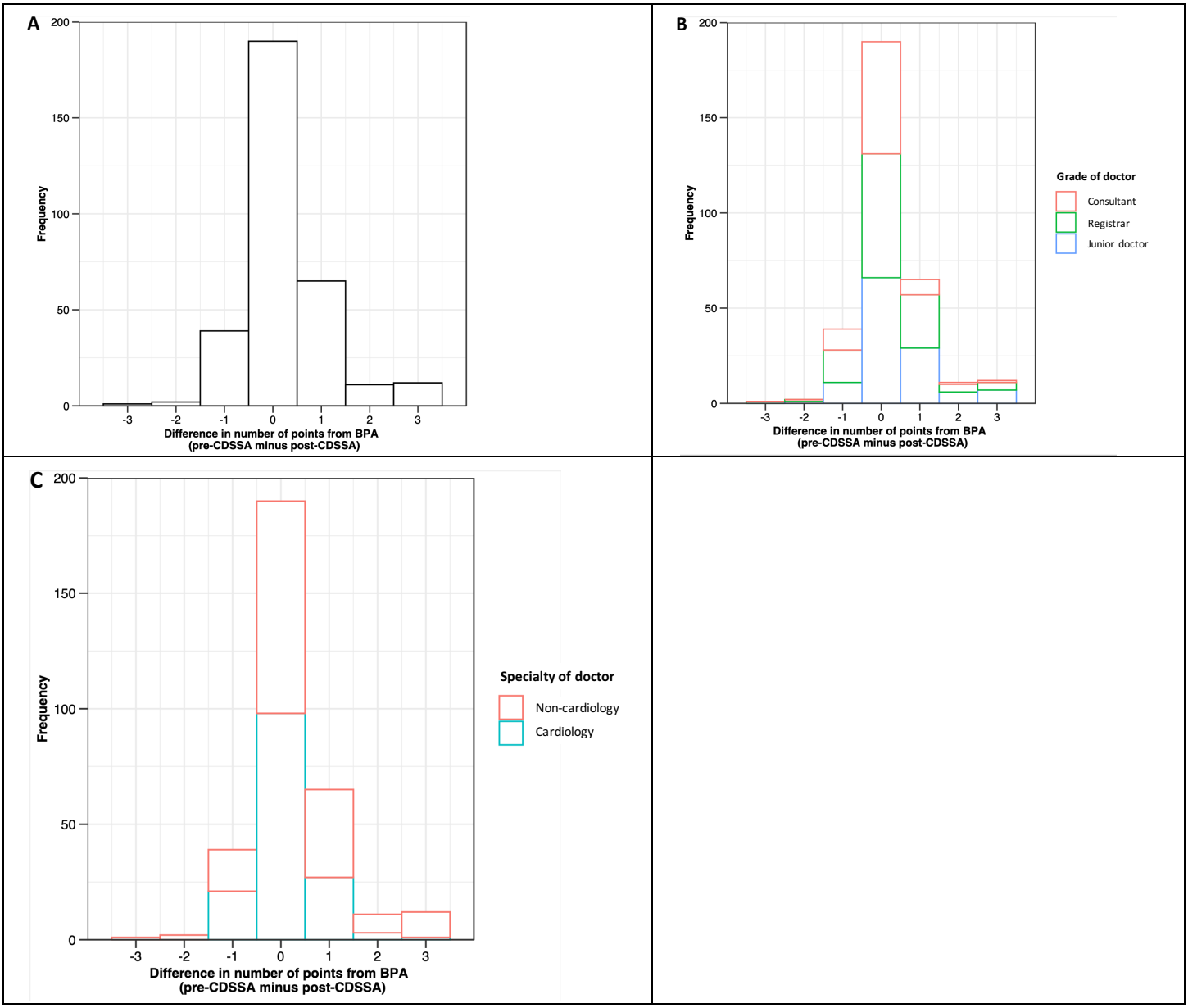


Figure 3.4 Histograms displaying the differences in the BPA deviations following CDSSA implementation.

Following the introduction of the CDSSA, scores were closer to the BPA, with an average improvement of 0.22 points (mean difference = 0.22; 95% CI 0.08–0.37; p = 0.003). This improvement was driven by non-cardiology doctors using the CDSSA (mean difference = 0.36; 95% CI 0.10–0.56; p = 0.005) and by doctor grade, where each level of grade decrease (consultant to registrar to junior doctor) was associated with an average improvement in scores

of 0.16 following CDSSA introduction (fixed effect coefficient: 0.16; 95% CI 0.05–0.27, p = 0.007).

Due to there being no junior doctors in the cardiology cohort, a subgroup analysis of consultant and registrar doctors practicing in either cardiology or medicine was used for the multivariable analysis. Score improvements were significantly driven by doctor grades (fixed effect coefficient 0.13; 95% CI 0.03–0.24, p = 0.05), while no difference in scores was seen based on specialty (fixed effect coefficient 0.07; 95% CI −0.24–0.38; p = 0.66). The two subgroups who exhibited a significant reduction in scores were those with the highest points at the pre-CDSSA timepoint. At the post-CDSSA timepoint, all subgroups demonstrated similar mean values.

3.5 Discussion

The outcomes of this chapter suggest that the CDSSA helped ensure best practice guidelines were followed more extensively and that clinical decision-making was more accurate. Additionally, it was observed that the CDSSA was more advantageous and beneficial to junior doctors compared to senior doctors.

The main objective of conducting this study is to assess the effectiveness of the CDSSA model in ensuring the delivery of optimal management to the majority of patients in hypothetical situations. These hypothetical case scenarios involve a patient who was discharged post-ACS with a telemedicine package and subsequently experienced symptoms such as chest discomfort, acute breathlessness, sustained palpitations, or other cardiovascular issues, and required an urgent medical consultation remotely. If the CDSSA is validated successfully, it could be used for future assessments of telemedicine-based interventions.

Medical algorithms are widely used in the healthcare industry to diagnose and treat various diseases. A medical algorithm refers to a set of rules that represents expert consensus and is designed to help ensure consistent decision-making in healthcare delivery and to guide step-by-step care for patients (95). The National Early Warning Score (NEWS) is one such algorithm that was developed by a multi-professional working group at the Royal College of Physicians of London and is widely used for risk assessment and the early detection of patient deterioration in hospital wards (96). NEWS has been found to be effective at predicting in-hospital mortality by identifying patients who are at an increased risk of developing cardiac arrest, requiring unexpected admission to the ICU, or dying within 24 hours of observation. Results from a comparative study demonstrated that NEWS performed better than 33 other Early Warning Score systems (EWSs) in predicting adverse patient outcomes. The significant

correlation between NEWS and adverse patient outcomes enables healthcare professionals to recognise at-risk patients and intervene promptly, potentially preventing up to 1,800 deaths per year (96, 97). The Global Registry of Acute Coronary Events (GRACE) is another example of a medical algorithm. GRACE is a 6-month post discharge prediction model that was created from an international registry for patients presenting with ACS. This algorithm can be used to stratify the risk of long-term mortality in patients who have suffered an acute coronary event (98).

Medical algorithms are clinical standards, which are derived from evidence-based multidisciplinary best practice guidelines and help healthcare professionals in applying scientific evidence and expert opinion to clinical practice. These tools not only provide useful prognostic information to healthcare professionals but also offer step-by-step decision trees to optimise patient care. In addition, algorithms help identify gaps in knowledge and logical thinking, and thus, are frequently used to train medical professionals, enhancing logical reasoning and critical thinking skills. They can be of particular benefit to inexperienced healthcare professionals who lack confidence in clinical decision-making (99, 100). However, the use of medical algorithms also has a few drawbacks. For instance, algorithms may be rigid and may not cover all possible clinical contingencies, occasionally overlooking important patient factors, such as concurrent medical illnesses, demographics, social history, medical history, and possible drug-drug interactions. They may not incorporate individual differences among patients and may apply only to the majority of patients with a particular condition (99). Therefore, while medical professionals should use these algorithms for assistance during decision-making processes, they should not rely solely on them, as they cannot replace comprehensive evaluation and critical thinking. Medical algorithms are most beneficial when used in conjunction with the expertise of experienced healthcare providers. Employed in this

manner, they can serve as valuable tools for healthcare workers and can help ensure that best practice guidelines are followed (100).

Studies have shown that individuals who are incompetent or less experienced in a particular field often overestimate their abilities. It has been suggested that since these people are less skilled, they perform poorly in a given domain and make wrong choices at a higher rate, as compared to more skilled individuals. Moreover, due to their incompetence, they lack the metacognitive skills to realize that their performance is poor, and instead, end up believing that they are above average. An analysis of 4 studies involving tests of humor, grammar, and logic revealed that participants who scored in the bottom quartile grossly overestimated their test performance and ability (101). In the academic literature, this cognitive bias in which people are so unskilled that they fail to recognize their shortcomings, and rather become overconfident about their abilities, is referred to as the Dunning-Kruger effect. However, it has been hypothesised that people do not start off in a Dunning-Kruger state. In fact, beginners usually start out at a task with being unconfident in their decisions. However, after gaining a little experience, they quickly become overconfident and develop over-inflated perceptions of their abilities. This is known as the "beginner's bubble" of overconfidence (102). This bubble of overconfidence may explain why doctors who have acquired a little experience and improvement in knowledge but are not yet experts in their field may be less likely to make changes to their responses.

Hence, a little learning or experience appears to be dangerous, as it leads to a large degree of overconfidence. However, as the experience continues to grow, individuals pass into a "correction" phase, in which the confidence begins to deflate slowly but the skills continue to

improve (101). Two studies examining the data on financial literacy across the life span provide insight into the pattern of self-confidence and learning curves across the life course. In these studies, it was found that young adults had a marked rise in self-ratings of financial literacy, and self-confidence flattened out among older adults. However, it was observed that in late adulthood, the self-ratings began to rise again. The actual financial knowledge was noted to increase slowly and incrementally throughout adulthood. Hence, the results from these studies indicate that self-ratings of competency show a gradual increase across age groups (102).

The survey results provided insights into the relationship between doctors' competence, confidence, and propensity to alter medical decisions based on the assistance of medical algorithms. Competence was gauged based on a doctor's seniority level, while their baseline confidence was measured based on the number of times they changed their responses between the initial, unaided attempt and the second attempt where they were assisted by a medical algorithm. As shown in Figure 3.5, as doctors gain experience, their critical thinking skills tend to improve, which leads to a temporary decline in confidence levels. Therefore, it was more likely that relatively senior doctors would modify their answers in the second, algorithm-assisted attempt. However, as competence levels further increase, so does confidence, until doctors reach the level of consultant doctors and attain true mastery of their subject.

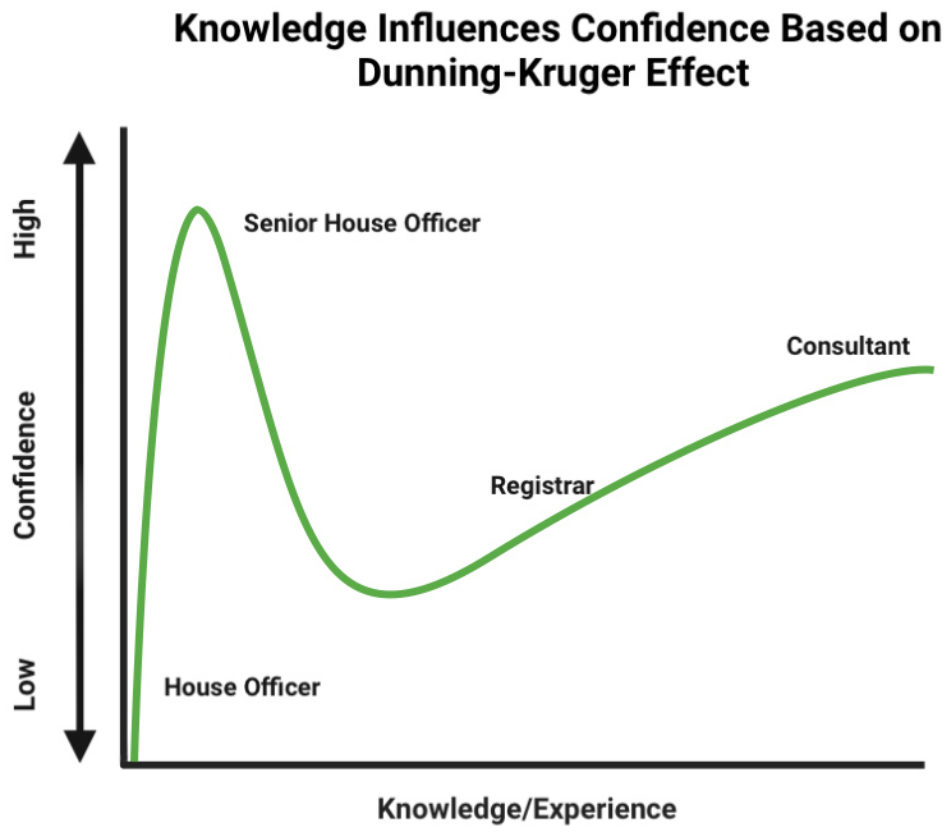


Figure 3.5 A graph illustrating how knowledge influences confidence, based on the foundational studies by Dunning and Kruger, published in the Journal of Personality and Psychology in 1999 (101) and further explored in a 2018 publication (102). The graph includes annotations indicating the likely confidence levels of doctors according to their experience.

The number and significance of factors evaluated by different medical algorithms, such as CDSSAs, may limit their effectiveness. However, our results demonstrate that the use of the CDSSA algorithm was associated with a statistically significant increase in response accuracy. This confirms the ability of medical algorithms to guide medical professionals and ensure that best practice guidelines are followed. Further research on the potential impact of CDSSAs on patient outcomes may yield interesting results. However, these algorithms are only intended to be used as an aid to improve the clinical decision-making process and must always be used in combination with the clinical opinion and expertise of a physician.

While the use of the CDSSA influenced responses, with responses more consistently adhering to established best practices, the structure of the questionnaire means that total number of correct answers does not definitively establish the CDSSA's effectiveness in improving the safety and accuracy of clinical decisions. This is because responses were categorised as "correct" or "incorrect", but not all incorrect answers bear the same level of risk. For instance, if the BPA suggests that a patient should call emergency services, but the physician instead reassures the patient, the potential health risk to the patient is significantly high. Conversely, if the BPA recommends reassurance and the physician advises the patient to see their local PCP/GP, the risk involved is relatively minor. The measure of "degrees away from the BPA" serves as a means of accounting for the various degrees of incorrect responses, enabling more accurate assessments of whether the CDSSA has enhanced decision-making accuracy.

We noted a significant reduction in BPA deviation between the initial, independent attempts and the subsequent, algorithm-supported attempts. This indicates that the CDSSA enhanced the precision of clinical decision-making. Additionally, house officers appeared to benefit most from the use of the CDSSA compared to other doctor groups.

In this study, the extent of modifications made to the initial answers during subsequent attempts served as an indicator of confidence. Specifically, fewer alterations suggested greater initial confidence, while more extensive changes indicated lower initial confidence. Additionally, the experience levels were used as a measure of knowledgeability, with more senior physicians presumed to have greater knowledge. By categorising physicians according to their seniority and examining the degree of answer modifications attributed to each group, the study assessed how much each group depended on the CDSSA. While consultants were expected to have

fewer altered responses compared to their junior counterparts, senior house officers were anticipated to deviate from this pattern due to the Dunning-Kruger effect (101, 102).

Our findings indicated a heightened dependency on the CDSSA among house officers compared to other doctor groups. Regarding answer modifications, consultants made fewer changes than registrars. Intriguingly, despite their intermediate level of experience, senior house officers demonstrated the least reliance on the CDSSA, accounting for the smallest proportion of altered responses relative to their group size. These observations corroborate our initial hypothesis that more experienced doctors would be less inclined to alter their decisions based on algorithmic suggestions. However, senior house officers were an exception, possibly due to the Dunning-Kruger effect (101, 102).

Considering whether CDSSA training would be beneficial for non-doctors, such as specialized nurses, is essential. These nurses play a crucial role in telemedicine clinics, especially if this model is rolled out nationally for post-ACS patients. Although our study involved only doctors, including specialized nurses could provide valuable insights into the broader applicability and benefits of CDSSA. Specialized nurses, given their significant role in patient management (103), could benefit from CDSSA by enhancing their ability to make informed decisions. Involving both doctors and specialized nurses in the study could provide a more diverse perspective on the effectiveness of CDSSA in different healthcare roles, ultimately leading to a more comprehensive understanding of its benefits in telemedicine settings.

3.6 Limitations

Although having a minimum of 90 days between the questionnaire administrations mitigated the recall of initial responses, there is a possibility that doctors could have recalled their initial management choices, potentially diminishing the observed impact of the CDSSA. Nonetheless, the significant findings suggest that this limitation might further underscore the CDSSAs, enhancement of clinical decision-making within this sample. Ideally, extending the interval between the questionnaire administrations to over 12 months would be preferable. However, the shorter interval chosen for this study ensured completion within the established timelines and reduced the likelihood of participant attrition, which could have reduced the statistical power of the findings.

This study had several limitations that future studies should consider. Firstly, the limited sample size of 32 doctors diminishes the reproducibility of the findings and limits the extent to which the results can be generalised. Secondly, nearly 24% of the respondents were lost to follow-up, introducing the risk of attrition bias. This type of bias occurs when the differences between participants who withdraw from the study and those who remain may explain the observed outcomes, rather than the effects of the intervention itself (104). Thirdly, the 10 cardiac scenarios used did not accurately reflect the actual spectrum of clinical encounters and were insufficient to cover the wide variety of situations that doctors typically handle in their practice. However, including more cases in the questionnaire could have led to a decrease in response rates and retention, ultimately reducing the statistical power of the study. Fourth, a potential limitation of our study design is that performing the questionnaire twice could have served as training for participants, leading to improved scores in the second assessment regardless of CDSSA training. To mitigate this, a randomised design with two separate groups, one completing the scenarios with CDSSA training and the other without the CDSSA could

have been used. This approach would help isolate the effect of CDSSA training from any improvements due to familiarity with the scenarios. Lastly, the inability to include doctors from the A&E department due to their lack of available time to participate, means that the findings cannot be extrapolated to the healthcare professionals most likely to meet the specific patient group targeted by this study, namely post-ACS patients who experience cardiac symptoms.

3.7 Conclusions

The COVID-19 pandemic imposed limitations on medical care access. Consequently, developing innovative strategies to handle the increasing population of post-ACS patients was crucial for decreasing morbidity and mortality rates. Enabling the remote management of patients post-ACS discharge through a combination of telemedicine tools and medical algorithms, such as CDSSAs, offers a promising solution. This approach mitigates access barriers to healthcare, helps curb the spread of infectious diseases, and enhances adherence to clinical best practices. Employing the CDSSA led to responses that more closely aligned with best practices, thereby enhancing the precision and safety of clinical decisions. Senior doctors were less inclined to alter their decisions compared to their junior counterparts. Additional research involving more cardiologists and emergency physicians, a larger sample size, varied case scenarios, and extended intervals between assessments is essential to further elucidate the benefits of a telemedicine-based CDSSA.

4 Remote Acute Assessment of Patients with High CV Risk Post-ACS (TELE-ACS): An RCT

This chapter describes the results of the TELE-ACS study on the use of a novel telemonitoring system-based algorithm for patients post-ACS, using well-validated technologies coupled with an urgent remote consultation with a cardiologist. This is the first study of its kind in the UK, highlighting that remote monitoring with a clinical decision algorithm protocol based on patient symptoms can reduce unnecessary hospital readmissions and advise patients to seek emergency care when necessary. The results presented in this chapter have also been published in The Journal of the American College of Cardiology (Alshahrani NS et al., 2024) and are reproduced here under a Creative Commons BY 4.0 license.

4.1 Abstract

4.1.1 Background

Telemedicine initiatives provide remote diagnostic data to support clinical decisions, which can optimise care and decrease unplanned hospital readmissions for patients who are discharged from the hospital post-ACS.

4.1.2 Methods

The TELE-ACS trial is a RCT that investigated the effectiveness of a telemedicine approach compared to standard care for patients who experienced ACS. Eligibility for the study required patients to have at least one CV risk factor along with an ACS event. They were randomised in a 1:1 ratio just before being discharged. The primary endpoint of the study was the incidence of hospital readmissions at the 6-month mark. Secondary endpoints included A&E visits, major adverse CV events, and symptoms reported by the patients. An intention-to-treat (ITT) approach was used for the primary analysis. The trial details were registered on ClinicalTrial.gov (NCT05015634).

4.1.3 Results

From January 2022 to April 2023, 337 patients were randomised and enrolled, with a dropout rate of 3.6%. The mean age of participants was 58.1 years. During the 6-month follow-up, there was a significant decrease in readmission rates (HR 0.24; 95% CI 0.13–0.44; $p < 0.001$) and A&E visits (HR 0.59; 95% CI 0.40–0.89; $p = 0.01$) among those in the telemedicine group. This group also had fewer unscheduled coronary revascularisations, with rates of 3% compared to 9% in the standard therapy group. The incidence of symptoms such as chest pain (9% vs.

24%), breathlessness (21% vs. 39%), and dizziness (6% vs. 18%) were also notably lower in the telemedicine group at 6 months.

4.1.4 Conclusions

The TELE-ACS study demonstrated that a telemedicine-based approach for managing patients post-ACS was associated with decreased rates of hospital readmissions, A&E visits, unplanned coronary revascularisations, and cardiac symptoms reported by the patients.

4.2 Introduction

Globally, approximately 7% of patients with ACS die within a month of being discharged from the hospital (87), and up to 25% are readmitted (105). Almost 50% of these readmissions are due to non-cardiac chest pain (85). The current global recommendations for managing ACS after the acute phase only focus on cardiac rehabilitation and secondary prevention and do not address follow-up or monitoring strategies (106, 107). Consequently, healthcare systems encounter significant difficulties in creating and applying post-discharge care pathways that enhance clinical results and reduce unnecessary healthcare utilisation (108).

Telemedicine systems are diverse and may employ various clinical and wearable technologies (109) in combination with patient-submitted clinical information and interactions that may be human-guided or powered by automated systems and artificial intelligence-driven algorithms (48). In HF management, various protocols have been shown to reduce CV mortality and prevent unplanned hospital admissions (110, 111). Observational studies have indicated that patient-initiated and self-managed remote electrocardiography, when combined with telephone-based clinical consultations, may lead to improved outcomes in patients with ACS (112), This highlights the need for RCTs to verify the potential benefits of such interventions in patients after acute coronary events (113).

The TELE-ACS study (Remote Acute Assessment of Patients with High CV Risk Post-Acute Coronary Syndrome, ClinicalTrials.gov ID: NCT05015634) was designed to investigate the effect of a remote monitoring system initiated by patients on the risk of readmission following ACS. The system incorporates 12-lead ECG, vital signs monitoring, and algorithm-based clinical reviews.

4.3 Methods

4.1.1 Study Design

The study was conducted at the Hammersmith Hospital, part of the Imperial College Healthcare NHS Trust. Patients were recruited from the cardiology clinical areas of Hammersmith Hospital (i.e., the Heart Assessment Centre, Cardiac Day Ward, or A7 Ward). A bespoke hybrid remote telemonitoring system was proposed to assess patients who were discharged from the hospital following AMI, and a RCT format was used to meet the objectives of the study.

4.1.2 Ethical Considerations

The TELE-ACS clinical trial received the necessary ethical approval to be conducted in the UK by the Health Research Authority, Health and Care Research Wales, and Fulham Research Ethics Committee on November 2, 2021, and the ethics number was (21/LO/0651). The ethical approval letter is shown in Supplementary Appendix 8.3. Written consent was obtained for all participants. All studies were conducted based on the good clinical practice guidelines. The trial was registered at ClinicalTrials.gov (ID: NCT05015634; ClinicalTrials.gov: https://classic.clinicaltrials.gov/ct2/show/NCT05015634).

4.2 Subjects

4.2.1 Inclusion Criteria

The inclusion criteria were as follows:

- Patients had to have ACS and be diagnosed with elevated high-sensitivity troponin I who had undergone PCI for non-ST-segment ACS (NSTE-ACS), STEMI, or UA.
- Patients had to have at least one additional CV risk factor.
    - Current or ex-smoker
    - Diagnosed with HTN
    - DM
    - Hypercholesterolemia.
    - Male aged > 50 years.
- Patients or a family member/carer had to have access to a smartphone or smart device.

4.2.2 Exclusion Criteria

The exclusion criteria were as follows:

- Patients who were unable to use the telemedicine equipment, transmit the ECG data via Bluetooth or cellular connectivity, or engage in virtual consultations.
- Patients who had a life expectancy of 9 months or less.

4.3 Screening

Potentially eligible patients were identified by members of the direct care team who alerted the physician members of the research team. The research team and direct care team had access to the electronic medical records of the potentially eligible patients attending the host institution.

An eligibility assessment was conducted by reviewing the medical records against the inclusion and exclusion criteria.

The medical records of the potentially eligible patients were screened by the direct care team and the research team. If all inclusion criteria and no exclusion criteria were met, the participant was given a participant information sheet. If they decided to participate, then they were asked to sign a consent form and were given a copy of both the information sheet and consent form to keep. The consent form and patient information sheet are included in Supplementary Appendix 8.1 and 8.2. Patient notes were not accessed and participants were not approached without prior consent from the patient via the direct care team. Following this, the patient was enrolled and randomly allocated to either the intervention (active) or the control group. An automated eligibility patient screening system for clinical trial eligibility had been developed by the Health Informatics Collaborative team at Imperial College London.

4.4 Randomisation, Allocation, and Blinding

Eligible participants were enrolled and randomised to one of the study arms by the research team. In total, 337 patients were randomised to either the "telemedicine" or "standard care" groups on a 1:1 basis using the IM Inclusion computer randomisation software, owned and developed by Professor Darrel Francis (National Heart and Lung Institute, Imperial College London, UK; https://fbmv-foundbyme.firebaseapp.com) (Figure 4.1). To ensure matching during the randomisation process, participants were stratified according to sex (male or female), age (> 55 or < 55), DM status (DM or no DM), and previous revascularisation (yes or no). Due to the nature of the intervention, participants could not be blinded to their treatment allocation.

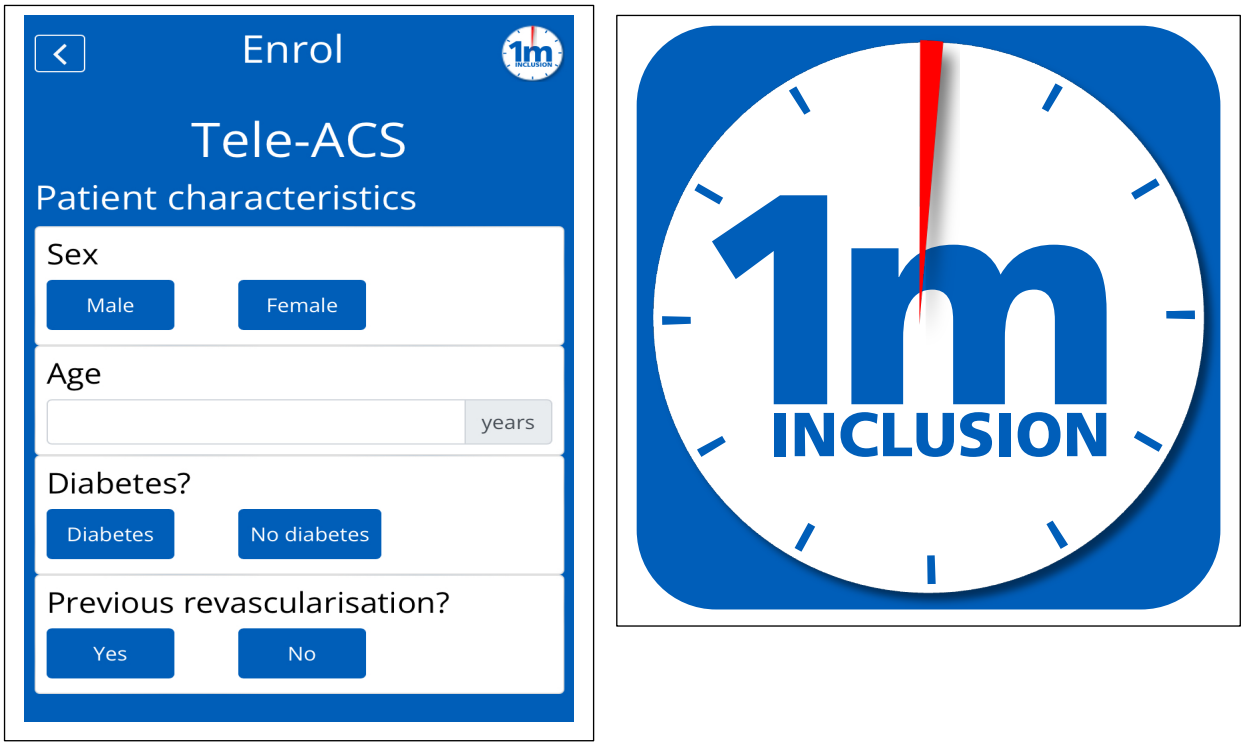


Figure 4.1 The 1M Inclusion randomisation software was used to allocate participants to one of the treatment groups.

4.4 Telemedicine Packages

Participants in the active group selected one of two telemedicine options based on their preference and the availability of devices.

The first telemedicine package option consisted of the following equipment (Figure 4.2):

- SHL Smartheart (SHL Telemedicine, Tel Aviv, Israel), FDA-approved and CE-marked.
- Omron Basic M2 BP Monitor (Omron Corporation, Kyoto, Japan), CE-marked and validated by the British & Irish Hypertension Society.
- Kinetik Wellbeing Finger Pulse Oximeter (Kinetik Wellbeing, Surrey, UK), CE-marked.

The second telemedicine package consisted of the following equipment (Figure 4.3):

- SHL Smartheart (SHL Telemedicine, Tel Aviv, Israel), FDA-approved and CE-marked.
- Current Health (respiration rate, oxygen saturation, pulse rate, body temperature, and mobility and step count), FDA-approved and CE-marked.
- iHealth Feel Wireless BP Monitor, FDA-approved and CE-marked.

4.4.1 SHL Smartheart + BP/Saturation

When the patient developed possible cardiac symptoms, they performed an ECG, took their BP and oxygen saturation readings in accordance with their training, and triggered an alert that was sent to the trial phone (active Monday to Friday from 07:00 to 23:00). The trial coordinator (TC) received this alert and contacted the patient within a few minutes (typically within less than 5 minutes) to collect additional details, the BP and oxygen saturation data, and to review the ECG data that had been uploaded. The TC gathered the patient's historical medical data from trial records and forwarded the ECG data to the trial cardiologist. The TC also provided the BP, oxygen saturation, and primary complaint information to the trial cardiologist via phone. The patient received a phone call from the trial cardiologist, who had access to a high-quality ECG trace and the patient's BP and oxygen saturation levels. This, coupled with the patient's clinical history, enabled them to decide the most appropriate course of further management.

4.4.2 SHL Smartheart + Current Health

When the patient developed possible cardiac symptoms, the patient took an ECG, recorded their BP and oxygen saturation in line with their training, subsequently triggering an alert sent to the trial phone (active Monday through Friday from 07:00 to 23:00). The TC received this this alert and promptly contacted the patient to gather further details, the BP readings, oxygen saturation levels, and to inspect the uploaded ECG. The TC then relayed the patient's historical medical records from the trial documents, sent the ECG, and informed the trial cardiologist of the patient's condition. Following this, the patient was contacted by the cardiologist, who initiated an emergency video consultation via the Current Health platform, an approved web-based platform. With access to a high-quality ECG trace and comprehensive data including BP, respiration rate, oxygen saturation, pulse rate, and body temperature, as well as the patient's clinical history, the trial cardiologist could determine the most suitable plan for further management.

A	B	C
		
SHL Smartheart	Omron Basic M2	Kinetik Wellbeing

Figure 4.2 Telemedicine package 1

Telemedicine package 1, consists of A) a 12-lead ECG belt, B) an automated BP monitor, and C) a pulse oximeter

A	B	C
		
SHL Smartheart	iHealth	Current Health Wearable

Figure 4.3 Telemedicine Package 2

Telemedicine Package 2 consisting of A) a 12-lead ECG belt, B) iHealth Feel Wireless BP Monitor, and C) Current Health Wearable, which enables the continuous capture of oxygen saturation levels, heart rate, respiration, skin temperature, and activity step count.



Figure 4.4 SHL SmartHeart,

4.4.1 Intervention

The participants received adequate training on the two telemedicine packages from a local research fellow before being discharged. This training included instructions on the timing and method for conducting home monitoring, and how to contact the clinical trial team. Additionally, there were follow-up training sessions scheduled to conduct remote ECGs at 2, 4, and 8 weeks after discharge, to ensure the participants were proficient at using the telemonitoring equipment and could provide quality ECG data. The SmartHeart User Manual and ECG Application Workflow is included in Supplementary Appendix 8.4.

Participants were informed that monitoring was available Monday to Friday between 07:00 and 23:00. If the patient experienced chest pain, wakening from sleep, or other significant CV

symptoms during the night, the patient was advised to contact 111 or call an ambulance. Additionally, if a participant did not receive a response from the trial cardiology team within 15 minutes of triggering an ECG, they were instructed to proceed as usual and contact emergency services.

A total of 337 participants were randomised 1:1 to a trial arm using computer randomisation software over 9 months. Participants in the active group were discharged from hospital and equipped with one of the telemedicine packages. When they used the telemedicine package to perform an ECG, the trial team responded to the data when deemed necessary. Participants also received a follow-up call at 3, 6, and 9 months. Participants in the control group received standard clinical care and were followed up via phone at 3, 6, and 9 months.

In the active group, participants' smartphones were paired with the SHL Smartheart device, and participants were instructed to conduct ECGs using the device prior to their discharge (Figure 4.4). The type of telemedicine service received depended on the selected package The services included receiving a phone call or having a trial cardiologist perform an urgent video consultation via the Current Health platform. If participants experienced symptoms such as chest pain, severe shortness of breath, sustained palpitations, or other CV-related issues, they were trained to record their ECG, BP, and oxygen levels. A triggered text message was sent during active hours to the trial mobile phone. Upon receiving the text, the TC would contact the patient for further details. Cardiologists could then review high-quality ECG traces, BP readings, pulse rates, and oxygen levels (if using Smartheart + BP/Saturations), as well as respiratory rate and body temperature (if using Smartheart + Current Health package). This clinical information, coupled with a participant's history and CDSSA guidance (previously described in Chapter 3), helped guide the cardiology team in determining the most appropriate

management plan. The team could choose 1 of 4 possible responses (Figure 4.5). Each use of the telemedicine package was recorded by the cardiologist in the electronic health record and detailed in a study record form, with appropriate follow-ups arranged for specific events (Figure 4.6).

Patients retained the telemonitoring package for the first 6 months following discharge. The follow-up e calls assessed any admissions/presentations to emergency services and the use of the telemedicine package. Patients completed QoL questionnaires (The Short Form Health Survey (36) and The Seattle Angina Questionnaire-7 (SAQ-7)) pre-discharge, then again at 3-, 6- and 9-months post-discharge.

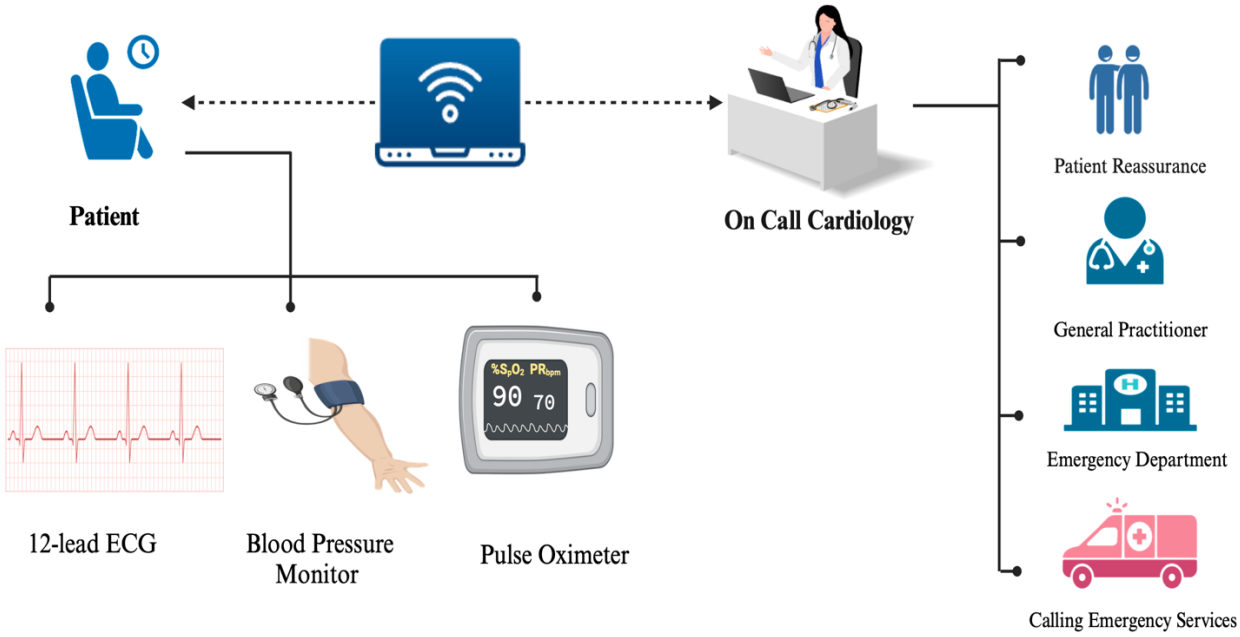


Figure 4.5 Diagram of how the remote telemonitoring system worked.

4.4.2 Usual Care

In the control arm, standard routine clinical care was carried out, with remote follow-up at 3, 6, and 9 months. Participants were advised to contact emergency services if they developed chest pain or other significant CV symptoms.

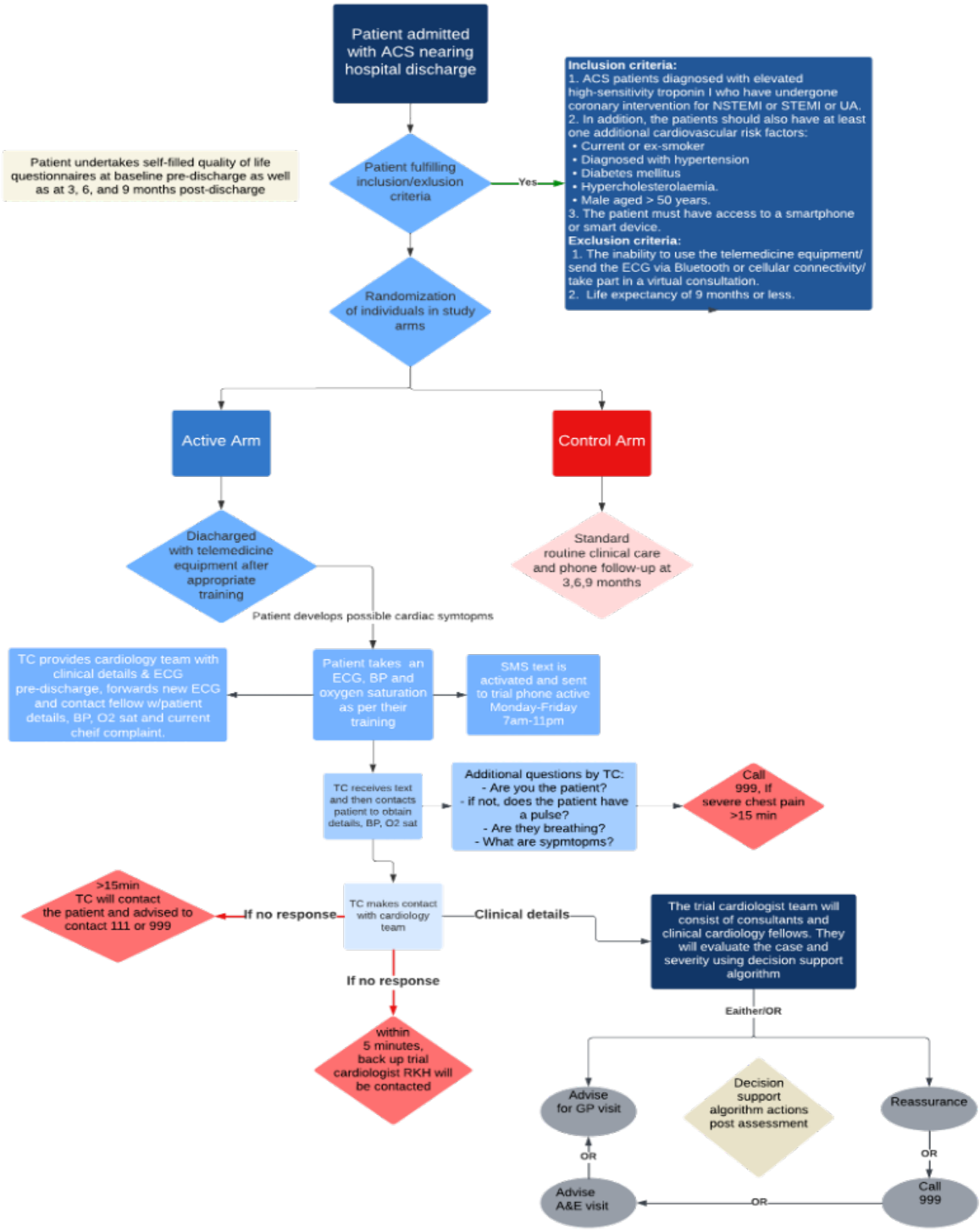


Figure 4.6 Trial workflow diagram.

ACS = acute coronary syndrome; A&E = accident and emergency; BP = blood pressure; ECG = electrocardiogram; HAC = heart assessment centre; hsTnI = high sensitivity troponin I; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; RKH = Ramzi Khamis; TC = trial coordinator

4.5 CDSSA

The CDSSA was developed based on the latest best practice guidelines, specifically the guidelines from the European Society of Cardiology (ESC) for AMI in patients presenting with STEMI and for ACS in patients with NSTEMI. Its purpose was to assist and direct the trial cardiology team. Although this system provided recommendations, the cardiologists retained full authority over final decisions regarding patient management and outcomes (Figure 3.1). A group of senior cardiologists developed this support algorithm based on their expert interpretation of the ESC guidelines for ACS management. The primary goal of the algorithm was to support, not mandate, clinical decision-making. For more detail, please refer to Chapter 3.

4.6 Study Outcome Measures

4.6.1 Primary Outcome

The primary outcome was the difference in the hospital readmission rate (time to readmission) for formal admissions and non-ER visits) after 6 months between the active and control groups.

4.6.2 Secondary Outcomes

There were several secondary outcomes:

- Total length of stay (LOS) at 3, 6, and 9 months.
- All-cause mortality.
- MACE (e.g., MI, stroke, CV death).
- Medical intervention for ACS or HF, including coronary angiography/angioplasty, injectable therapy, or oxygen therapy.
- ER visits not requiring admission or further intervention.
- 9 month readmission rate (with 3 months without intervention) to investigate the learning effect of the intervention.
- Patient-reported QoL outcome measures (weighted to treatment satisfaction domains).

4.7 Safety Measurements

The safety measurements consisted of the measurement of adverse events. Data on all adverse events experienced were recorded.

4.8 Study Closure

The study concluded once 337 patients had been enrolled and monitored for 9 months, after which all necessary data had been collected.

4.9 Demographic and Baseline Variables

Several demographic and baseline characteristics were collected for each participant:

- Patient demographics (including age, gender, ethnicity, and BMI)
- Procedure characteristics
- Risk factors (including smoking status, DM, and family history of CAD)
- History of heart disease
- Other health conditions
- Blood results (including creatinine, eGFR, platelets, cholesterol, and troponin levels)
- Use of cardiac and other drugs
- Pre-discharge observations (including symptoms, heart rate, respiratory rate, BP, and body temperature)

4.10 Sample Size

The sample size was decided based on the number of participants needed to demonstrate a difference between the study groups for the primary outcome (time to first readmission), assumed to be a 'survival' outcome. Local data for the primary outcome over the past 3 years showed a 30% readmission rate at 6 months for any readmission. This rate was assumed in the control group. A two-fold reduction in the risk of a readmission throughout the follow-up period was determined to be a clinically significant improvement. Thus, a HR of 0.5 between the groups was assumed. With a 5% significance level and 80% power, calculations indicated

the need for 153 patients per group (306 in total). To allow for an estimated 10% of patients being censored during the follow-up period (due to death or drop-out), we aimed to recruit 338 participants for the study (Tables 4.1, 4.2 and 4.3).

Table 4.1 The parameters used to determine the number of events required

α (two-tailed)	0.05	Type I error rate
β	0.2	Type II error rate
q_1	0.5	Proportion of subjects that are in Group 1 (Telemedicine package)
q_0	0.5	Proportion of subjects that are in Group 0 (Standard care); 1-q_1
Relative hazard	0.5	Relative hazard (Group 1/Group 0)

The standard normal deviate for $\alpha = Z_\alpha = 1.9600$

The standard normal deviate for $\beta = Z_\beta = 0.8416$

$A = (Z_\alpha+Z_\beta)^2 = 7.8489$

$B = (\log (RH))^2 q_0 q_1 = 0.1201$

Total events needed = A/B = 65

Table 4.2 Sample size calculation

Baseline event rate (BER_0)	0.30 at 6 months	Events/unit time for Group 0
Censor rate	0.05	Censored/unit time (assumed equal for both groups)
Follow-up	6 months	Planned average length of follow-up

Table 4.3 Sample size calculations continued

	N	**Events**	**Cumulative event rate**
Telemedicine package	169	23	0.134
Standard care	169	42	0.250
TOTAL	338	65	0.192

4.11 Confidentiality of Personal Data

To ensure the confidentiality of personal data in our study, pseudonymisation was applied immediately after recruitment. Participants were assigned a unique research study ID, and all data were collected and stored using this ID, whether electronically or physically. Data storage was restricted to university and NHS computers to guarantee encrypted server storage and limited access by authorised staff only. The data collection adhered to the Data Protection Act 2018, General Data Protection Regulation (GDPR), and Data Protection Impact Assessments (DPIA) at Imperial College London and Imperial College NHS Healthcare Trust. All data were generated at the NHS site recruited for this study and recorded in a pseudo-anonymised manner, with the analysis conducted by the research study team at Imperial College London. The analysed data were reported anonymously. Additionally, the SmartHeart Cloud Server, hosted by Amazon Web Services in the USA, stored our data. We signed a non-disclosure agreement with SHL, ensuring they only transferred the data without processing it.

4.12 Data Analysis

4.12.1 Timing of Analyses

A single analysis took place at the completion of the study after all data were collected. No interim analyses were performed.

4.12.2 Analysis Populations

The primary analysis involved analysing the participants in the groups to which they were randomly assigned, regardless of any deviation from the protocol or whether they received the allocated intervention. In other words, they were analysed on an ITT basis. The primary

outcome population included all participants who remained in the study for 2 days or more. Patients who completed less than 2 days of follow-up were excluded.

As the secondary outcomes only related to a portion of the follow-up period (4–6 months), analyses of these outcomes only included participants who remained in the study for the whole period. Participants who dropped out, withdrew, or died were excluded from the analyses of data from that period.

4.12.3 Subgroups

The analysis was performed for all patients combined, with no subgroup analyses performed.

4.11.4 Missing Data

Only observed data were analysed. Missing data were assumed to be missing at Random. No imputation procedures were employed to deal with missing data.

4.13 Summary of Study Data

4.13.1 Subject Disposition

A summary of the number of subjects that reached the various stages of the study is summarised, as are reasons for non-participation and withdrawal. A CONSORT diagram was produced (Figure 4.7), which illustrates the flow of patients throughout the study.

4.13.2 Descriptive Analysis Methods

Continuous variables will be summarised using the number of (non-missing) datapoints, mean and standard deviation if found to follow a normal distribution. Continuous variables not found to be normally distributed will be summarised by the number of datapoints, median and inter-quartile range. Categorical variables will be summarised by the frequency and percentage (based on the non-missing sample size) of values in each category.

4.13.3 Demographic and Baseline Variables

A summary of the demographic and baseline variables is given in Section 4.9. Each measures is summarised descriptively for the two study arms separately. No formal hypothesis tests were be used to compare the two groups for these measures.

4.14. Efficacy Analyses

4.14.1 Primary Efficacy Analysis

The primary study endpoint was the time to first readmission within the first 6 months of follow-up. This was analysed as a survival-type outcome. Patients who did not experience a readmission were censored at the point at which they exited the study or after 6-months, whichever was later. This outcome is summarised for each group based on the estimated percentage of patients free from readmission at 6 months, along with CIs. These estimates were calculated using Kaplan-Meier methods.

A Cox regression was used to compare the time to first readmission. The difference between groups was expressed as a HR and corresponding CI. This was calculated as the HR of

readmission in the active group relative to the HR in the control group. A Kaplan-Meier plot was generated to display the results graphically. The primary analysis was performed using the primary analysis dataset, as outlined in Section 4.12.

4.14.1 Secondary Efficacy Analyses

The first secondary outcome (time to first A&E admission) was analysed using equivalent methods to the primary outcome and the equivalent dataset. Binary secondary outcomes were analysed using a two-sample test of proportions. Percentage differences were calculated as the active group minus the control group, and expressed with the corresponding CI.

All continuous outcomes had positively skewed distributions. Therefore, groups were compared using the Mann-Whitney test. Additional outcomes were related to assistance calls. As this data was relevant to the active group only, it was analysed descriptively.

4.14.3 Safety Analyses

The main safety outcome was the occurrence of adverse events. The number of adverse events is reported descriptively, as outlined in Section 4.13.2.

4.14.3 Technical Details

The data analyses were performed using the statistical software package Stata (version 15.1). Programs recording the details of all data manipulations and analyses were produced and will be kept, so that the analyses can be externally inspected and, if necessary, re-run.

4.15 Results

4.15.1 Patients

A total of 372 patients recruited from a large tertiary heart attack centre in London were assessed study inclusion (Figure 4.7), and 337 were randomly assigned to a group from January 6, 2022, to April 3, 2023. Participants were placed into two groups: 169 were allocated to the telemedicine/active group and 168 received standard care. Participants had an average age of 58.1 years, with males making up 86.1% of the study population.

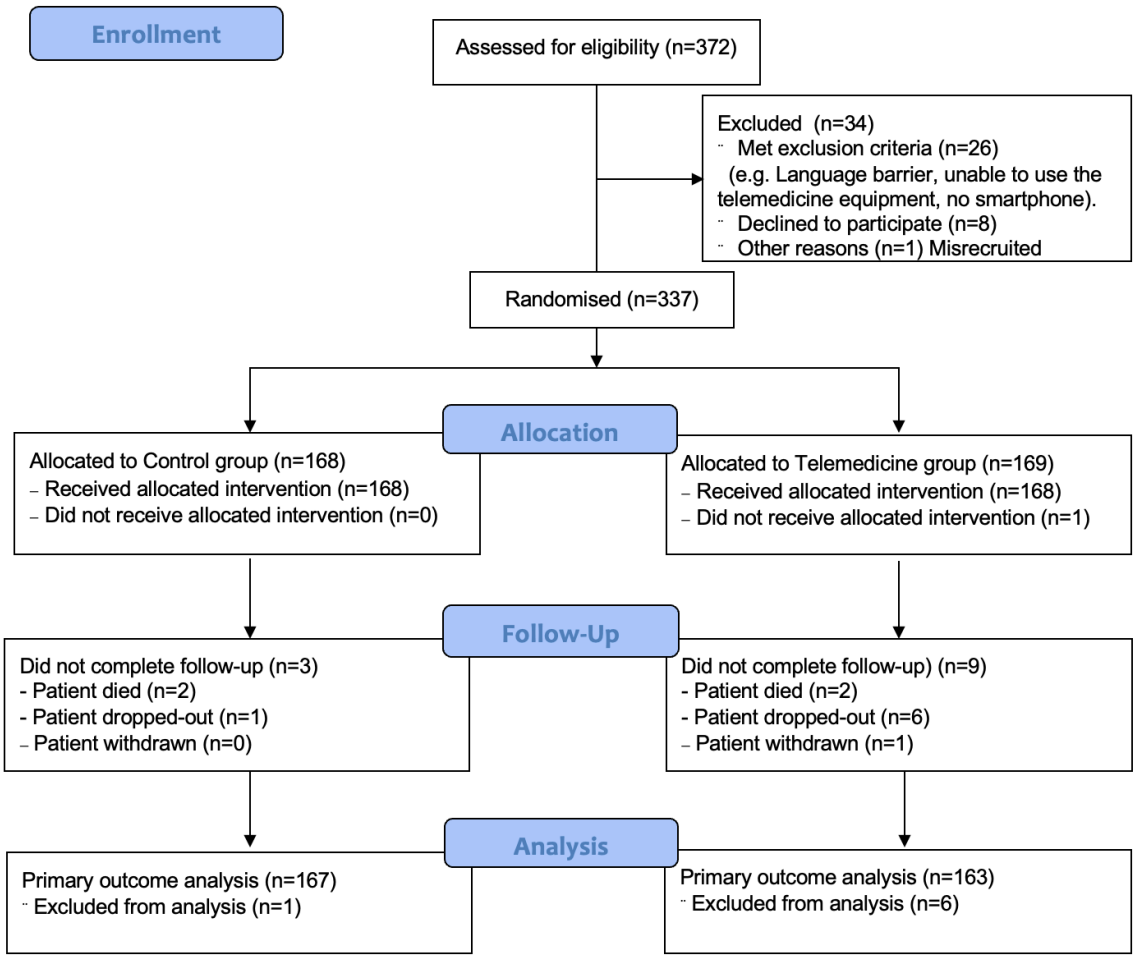


Figure 4.7 CONSORT diagram outlining the flow of participants through the trial, from the assessment of eligibility to the analysis stage.

4.15.2 Number of Patients in Analyses

In total, 337 participants were recruited into the study: 169 in the active group and 168 in the control group. Some participants dropped-out or died during the follow-up period. Only observed data from participants in the study at any point was included in the analysed. Thus, depending on the timepoint of the data collection, different numbers of participants were included in the analysis. A summary of the number of participants analysed for each different type of outcome is shown in Table 4.4.

Table 4.4 Number of patients in different analyses

Variable type	Variable	Category	Control [N=168] n	Active [N=169] n
Baseline	In analysis	Included	168	169
factors		Excluded	0	0
Death	In analysis	Included	167	162
outcome		Excluded	1	7
	Exclusion reason	Drop out	1	6
		Patient withdrawn	0	1
1 – 3 months	In analysis	Included	166	162
outcomes		Excluded	2	7
	Exclusion reason	Drop out	1	6
		Patient withdrawn	0	1
		Death by 3m	1	0
4 – 6 months	In analysis	Included	165	160
outcomes		Excluded	3	9
	Exclusion reason	Drop out	1	6
		Patient withdrawn	0	1
		Death by 6m	2	2
Outcomes	In analysis	Included	165	160
over first		Excluded	3	9
6 months				

	Exclusion reason	Drop out	1	6
		Patient withdrawn	0	1
		Death by 9m	2	2
6 – 9 months	In analysis	Included	165	160
outcomes		Excluded	3	9
	Exclusion reason	Drop out	1	6
		Patient withdrawn	0	1
		Death	2	2
Survival	In analysis	Included	167	163
analyses		Excluded	1	6
	Exclusion reason	Drop out	1	6

4.15.3 Demographic and Baseline Factors

The demographic and baseline factors for both groups were summarised. Categorical variables were expressed as the number and percentage of participants in each category. Continuous variables were expressed as means and standard deviations if they were normally distributed or as medians and inter-quartile ranges otherwise. Participant demographics were examined first, and these are summarised in Table 4.5. Diagnoses and summaries of the procedures undergone are summarised in Table 4.6. The risk factors are reported in Table 4.7. Table 4.8 provides data on participants' history of heart disease. Information on other health conditions is reported in Table 4.9. Blood analysis parameters are summarised in Table 4.10. The medication taken by participants is summarised in Table 4.11. Patients were measured pre-discharge, and a summary of the observations made is shown in Table 4.12.

Table 4.5 Demographics

Variable	Category	Control [N=168]		Active [N=169]	
		n	Summary	n	Summary
Age	-	168	58.6 ± 9.7	169	57.6 ± 8.7
Gender	Female	168	22 (13%)	169	25 (15%)
	Male		146 (87%)		144 (85%)
Ethnicity	White British/Irish	168	58 (35%)	169	62 (37%)
	White Other		20 (12%)		16 (9%)
	Asian		61 (36%)		59 (35%)
	Black		16 (10%)		20 (12%)
	Mixed / Other		13 (8%)		12 (7%)
Height (m)	-	168	172.7 ± 7.6	169	172.1 ± 8.3
Weight (kg)	-	168	84.0 ± 14.2	169	81.4 ± 14.9
BMI (kg/m^2)	-	168	28.1 ± 4.0	169	27.4 ± 4.4

Summary statistics are: mean ± standard deviation, or number (percentage)

Table 4.6 Diagnosis and procedure summaries

Variable	Category	Control [N=168]		Active [N=169]	
		n	Number (%)	n	Number (%)
Indication	STEMI	168	113 (67%)	169	118 (70%)
	NSTEMI		53 (32%)		49 (29%)
	Unstable angina		2 (1%)		2 (1%)
PCI TO (*)	RCA proximal	168	34 (20%)	169	35 (21%)
	RCA mid		23 (14%)		14 (8%)
	RCA distal		16 (10%)		16 (9%)
	Posterior descending		1 (1%)		6 (4%)
	Posterolateral		2 (1%)		3 (2%)
	Left main		3 (2%)		1 (1%)
	LAD proximal		56 (33%)		69 (41%)
	LAD mid		32 (19%)		12 (7%)
	LAD apical		2 (1%)		2 (1%)
	First diagonal		8 (5%)		6 (4%)
	Second diagonal		1 (1%)		2 (1%)
	Proximal circumflex		19 (11%)		20 (12%)
	Intermediate		11 (7%)		21 (12%)
	Obtuse marginal		10 (6%)		14 (8%)
	Distal circumflex		3 (2%)		3 (2%)
	Left posterolateral		0 (0%)		0 (0%)
	Left posterior		0 (0%)		0 (0%)

Type of PCI (*)	Balloon angioplasty	168	161 (96%)	169	160 (95%)
	Angioplasty stent		163 (97%)		166 (98%)
	Laser angioplasty		0 (0%)		1 (1%)
	Rotat atherectomy		0 (0%)		0 (0%)
	CTO		1 (1%)		2 (1%)
	Shockwave		3 (2%)		2 (1%)
Number stents	0	168	1 (1%)	169	1 (1%)
	1		94 (56%)		90 (53%)
	2		57 (34%)		63 (37%)
	3		13 (8%)		11 (7%)
	4		1 (1%)		2 (1%)
	5		2 (1%)		2 (1%)
Number of	1	169	133 (79%)	169	136 (80%)
vessels	2		31 (18%)		23 (14%)
	3		4 (2%)		10 (6%)
Bystander	Any disease	167	86 (52%)	167	70 (42%)
disease (*)	LMC vessel		11 (7%)		7 (4%)
	LAD vessel		42 (25%)		46 (27%)
	LCX vessel		42 (25%)		33 (20%)
	RCA vessel		36 (22%)		28 (17%)
Further PCI	No	168	149 (88%)	169	156 (92%)
pre-discharge	Yes		20 (12%)		13 (8%)
Further PCI	No	168	109 (65%)	169	111 (66%)
planned	Yes		59 (35%)		58 (34%)

(*) Patients can answer in more than one category. Percentage values may not add up to 100%

Table 4.7 Risk factors

Risk factors	Control [N=168]		Active [N=169]	
	n	Number (%)	n	Number (%)
Smoker or Ex-smoker	168	96 (57%)	169	100 (59%)
Diabetes	168	49 (29%)	169	46 (27%)
Male, aged 50+	168	123 (73%)	169	116 (69%)
Cerebrovascular disease	168	19 (11%)	169	9 (5%)
Chronic kidney disease	168	18 (11%)	169	15 (9%)
Previous revascularisation	168	43 (26%)	169	29 (17%)
Family history CAD	168	70 (42%)	169	66 (39%)
Other risk factors	168	125 (74%)	169	125 (74%)

Table 4.8 Heart disease variables

Variable	Control [N=168]		Active [N=169]	
	n	Number (%)	n	Number (%)
History of angina	168	164 (98%)	169	162 (96%)
Arrhythmia	168	5 (3%)	169	6 (4%)
Previous MI	168	27 (16%)	169	31 (18%)
Previous PCI	168	28 (17%)	169	26 (15%)
Previous CABG	168	7 (4%)	169	4 (2%)
Out of hospital cardiac arrest	168	5 (3%)	169	10 (6%)
Cardiac transplant	168	0 (0%)	169	0 (0%)
Valvular heart disease	168	1 (1%)	169	1 (1%)
Valvular surgery	168	0 (0%)	169	0 (0%)
Cardiac device	168	3 (2%)	169	1 (1%)

Table 4.9 Other Health Conditions

Condition	Control [N=168]		Active [N=169]	
	n	Number (%)	n	Number (%)
Chronic pulmonary disease	168	23 (14%)	169	23 (14%)
Thromboembolic disease	168	7 (4%)	169	5 (3%)
Asthma	168	11 (7%)	169	16 (9%)
Liver disease	168	9 (5%)	169	7 (4%)
Chronic neurological disorder	168	19 (11%)	169	7 (4%)
Malignant neoplasm	168	3 (2%)	169	0 (0%)
Haematological disease	168	11 (7%)	169	11 (7%)
AIDS / HIV	168	1 (1%)	169	5 (3%)
Rheumatological disorder	168	4 (2%)	169	4 (2%)
Dementia	168	0 (0%)	169	1 (1%)

Table 4.10 Blood Results

Variable	Control [N=168]		Active [N=169]	
	n	Summary	n	Summary
Creatinine (µmol/L)	168	76 [69, 86]	169	76 [68, 87]
eGFR (mL/min/1.73 m²)	168	>90 [80, >90]	169	>90 [80, >90]
Haemoglobin (g/L)	168	139 ± 19	169	139 ± 15
Platelets (x10^9/L)	168	244 ± 79	169	248 ± 76
WBC (x10^9/L)	168	9.6 ± 2.5	169	9.5 ± 2.8
HbA1c (mmol/mol)	168	41 [38, 47]	169	41 [37, 46]
Total cholesterol (mmol/L)	168	4.9 ± 1.7	169	4.7 ± 1.5
LDL cholesterol (mmol/L)	168	3.2 ± 1.5	169	3.1 ± 1.2
HDL cholesterol (mmol/L)	168	1.1 ± 0.3	169	1.1 ± 0.3
Triglycerides (mmol/L)	168	1.4 [1.0, 2.0]	169	1.4 [1.0, 2.3]
Troponin – admission (ng/L)	168	225 [52, 3448]	169	251 [34, 2418]
Troponin – peak (ng/L)	168	33997 [9422, 86653]	169	27833 [8945, 73261]
Troponin – discharge (ng/L)	168	12187 [4368, 25905]	169	12108 [4199, 56950]

Summary statistics are: mean ± standard deviation, or median [inter-quartile range]

Table 4.11 Cardiac & Other drugs

Medication	Control [N=168]		Active [N=169]	
	n	Number (%)	n	Number (%)
Anticoagulants	168	12 (7%)	169	6 (4%)
Antiplatelets & DAPT	168	168 (100%)	167	166 (99%)
ACE inhibitors	166	132 (80%)	168	132 (79%)
ARBs	168	15 (9%)	169	19 (11%)
ARNIs	161	0 (0%)	168	3 (2%)
Beta blockers	166	152 (92%)	166	151 (91%)
Combined alpha/beta blockers	167	0 (0%)	164	0 (0%)
Calcium channel blockers	167	20 (12%)	167	28 (17%)
Cholesterol lowing meds	168	164 (98%)	169	166 (98%)
Digitalis preparations	164	1 (1%)	166	0 (0%)
Diuretics	168	20 (12%)	166	14 (8%)
Vasodilators	166	59 (36%)	168	47 (28%)
Diabetes medication	168	19 (11%)	169	25 (15%)

Summary statistics are: mean ± standard deviation, or median [inter-quartile range]

Table 4.12 Pre-discharge observations

Variable	Control [N=168]		Active [N=169]	
	n	Summary	n	Summary
Chest pain	168	2 (1%)	169	0 (0%)
Palpitations	168	1 (1%)	169	0 (0%)
Shortness of breath	168	4 (2%)	169	4 (2%)
Dizziness	168	4 (2%)	169	3 (2%)
Heart rate (bpm)	168	69.1 ± 10.3	169	70.9 ± 11.2
Respiratory rate (breaths per minute)	168	17.4 ± 1.2	169	17.4 ± 1.3
Systolic blood pressure (mmHg)	168	114.2 ± 16.3	169	114.7 ± 15.4
Diastolic blood pressure (mmHg)	168	71.3 ± 11.5	169	71.6 ± 11.2
Saturations (% on air)	168	97 [96, 98]	169	98 [97, 99]
Body temperature (°C)	168	36.6 ± 0.4	169	36.6 ± 0.3

Summary statistics are: mean ± standard deviation, median [inter-quartile range] or number (percentage)

4.15.4 Outcome Variables

The next analyses focused on the outcome variables. Initially, the data from the call logs was examined. This data was only relevant for the active group. Data were collected from both in-hours and out-of-hours calls. Data from in-hours calls is summarised in Table 4.13. There were 108 calls in total from 162 participants who completed full or partial follow-ups. The first part of the table gives the data measured at the participant level (one observation per patient in the analysis), while the second part is the call level data (one observation per call).

Table 4.13 In-hours calls

Variable	Category	Patient level analysis [N =162]	
		n	Summary
Number of calls	0 calls	162	94 (58%)
	1 call		41 (25%)
	2 calls		19 (12%)
	3 calls		4 (2%)
	4 calls		3 (2%)
	5 calls		1 (1%)
Number of calls	-	162	0.7 ± 1.0
Variable	Category	Call level analysis [N =108]	
		n	Summary
Call decision	Reassurance	108	59 (55%)
	Reassurance + PCP/GP		29 (27%)
	Advised visit A&E		15 (14%)
	Advised call 999		5 (5%)
Follow-up (*)	Decided not visit A&E	20	6 (30%)
	A&E and discharged		13 (65%)
	A&E and admitted hospital		1 (5%)

Summary statistics are: mean ± standard deviation, or number (percentage)

(*) Figures for those advised to visit A&E or call 999 only.

Overall, 42% of all participants made one or more in-hours call, and 58% did not make any calls. Only 8 participants (5%) made 3 or more calls during the 6-month period. On average, there were 0.7 in-hours calls made per participant. For most calls (82%), the call decision was either reassurance or reassurance plus guidance to visit their PCP/GP. In 14% of calls, the patient was advised to visit A&E, and in 5% of calls, they were advised to call emergency services. When they were advised to visit A&E or to call emergency services, 70% of participants visited the hospital, with 30% deciding not to visit. However, participants were only admitted in 5% of instances. Equivalent data on the out-of-hours calls is reported in Table 4.14. In total, 61 out-of-hours calls were made by 162 participants who partially or fully completed the follow-up period.

Table 4.14 Out-hours calls

Variable	Category	Patient level analysis [N =162]	
		n	Summary
Number of calls	0 calls	162	111 (69%)
	1 call		43 (27%)
	2 calls		7 (4%)
	3 calls		0 (0%)
	4 calls		1 (1%)
Number of calls	-	162	0.4 ± 0.6
Variable	Category	Call level analysis [N =61]	
		n	Summary
Call decision	Call 111 or 999	61	61 (100%)

Summary statistics are: mean ± standard deviation, or number (percentage)

Only 31% of the participants made one or more out-of-hours calls. The majority only made one call. Only one participant made 3 or more calls. The mean number of calls was 0.4 per participant. All decisions were to call emergency services. The remaining analyses related to outcomes measured in both study groups

Table 4.15 details the readmission outcomes. The outcomes are summarised by the number and percentage of responses in each category for each of the two arms. The percentage differences in the binary outcomes between the groups is also reported, along with a corresponding CIs. The final column gives the p-values, indicating the significance of the group differences.

Overall, 29% of the control group experienced one or more readmissions over the first 6-months of follow-up. The equivalent figure was 7% in the active group, a highly significant difference. Therefore, a 22% reduction in the number of readmissions was observed in the active group (95% CI 14–30%).

Readmissions within the first 30 days were significantly lower in the active group, with only 1% readmitted within this period, compared to 16% in the control group. There were also significantly fewer readmissions first 3 months post-discharge, with 16% fewer participants being readmitted in the active group. Readmission during the 3–6-month period was also significantly lower in the active group, with 7% fewer participants readmitted compared to the control group. However, readmission rates did not vary significantly during the 1–3 or 6-9-month period.

Results for the time to first readmission are summarised in Table 4.18, with analyses performed using the 6- and 9-month follow-up data. The Kaplan-Meier estimate of the proportion without readmission is given for both the 6- and 9-month timepoints. The HR for the risk of an admission at any time during follow up in the active group relative to the control group is also reported.

Table 4.15 Readmissions

Variable	Category	Control		Active		Group difference	
		n	Number (%)	n	Number (%)	% (95% CI) (+)	P-value
Readmission	No	165	118 (72%)	160	149 (93%)	-22% (-30%, -14%)	**<0.001**
(any during 6-months)	Yes		47 (28%)		11 (7%)		
Number readmissions	0	165	118 (72%)	160	149 (93%)	-	**<0.001**
over 6-months	1		39 (24%)		8 (5%)		
	2		7 (4%)		1 (1%)		
	3		1 (1%)		2 (1%)		
Readmission within 30 days	No	166	139 (84%)	162	160 (99%)	-15% (-21%, -9%)	**<0.001**
	Yes		27 (16%)		2 (1%)		
Readmission 1 – 3 months	No	166	153 (92%)	162	152 (94%)	-2% (-7%, 4%)	0.56
	Yes		13 (8%)		10 (6%)		
Readmission 0 – 3 months	No	166	128 (77%)	162	151 (93%)	-16% (-24%, -9%)	**<0.001**
	Yes		38 (23%)		11 (7%)		
Readmission 3 – 6 months	No	165	150 (91%)	160	156 (97%)	-7% (-12%, -2%)	**0.01**
	Yes		165 (9%)		4 (3%)		
Readmission 6 – 9 months	No	165	157 (95%)	160	152 (95%)	0% (-5%, 5%)	0.95
	Yes		8 (5%)		8 (5%)		
Cardiovascular readmission	No	165	127 (77%)	160	152 (95%)	-18% (-25%, -11%)	**<0.001**
	Yes		38 (23%)		8 (5%)		
Non-cardiovascular	No	165	151 (92%)	160	154 (96%)	-5% (-10%, 0%)	0.08
readmission	Yes		14 (8%)		6 (4%)		

(+) Percentage differences expressed as outcome for Active group minus outcome for Control group

When only the first 6 months of follow-up were included in the analysis, the time to first readmission was significantly shorter in the control group. The risk of a readmission at any time was four times lower in the active group than the control group. A graphical illustration of the time to first readmission is shown in Figure 4.8.

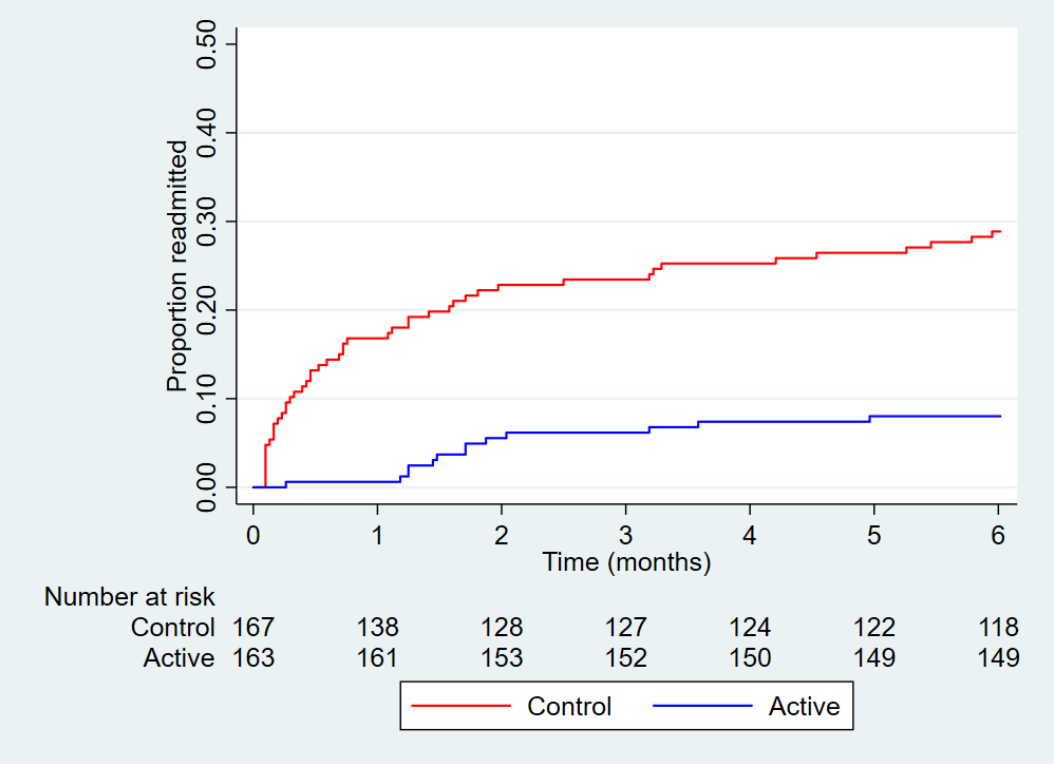


Figure 4.8 Kaplan-Meier graph of the time to first readmission during the 6-month follow-up period.

Further analysis was performed using data from 9 months of follow-ups. Again, a significantly lower risk of readmission was seen in the active group. The effect size was less over the 9-month period, with a HR of 0.35 (compared to 0.24 over 6 months). This was due to the slightly higher readmission rate in the active group over the 6–9-month period. A graphical illustration of the time to readmission over the entire follow-up period is shown in Figure 4.9.

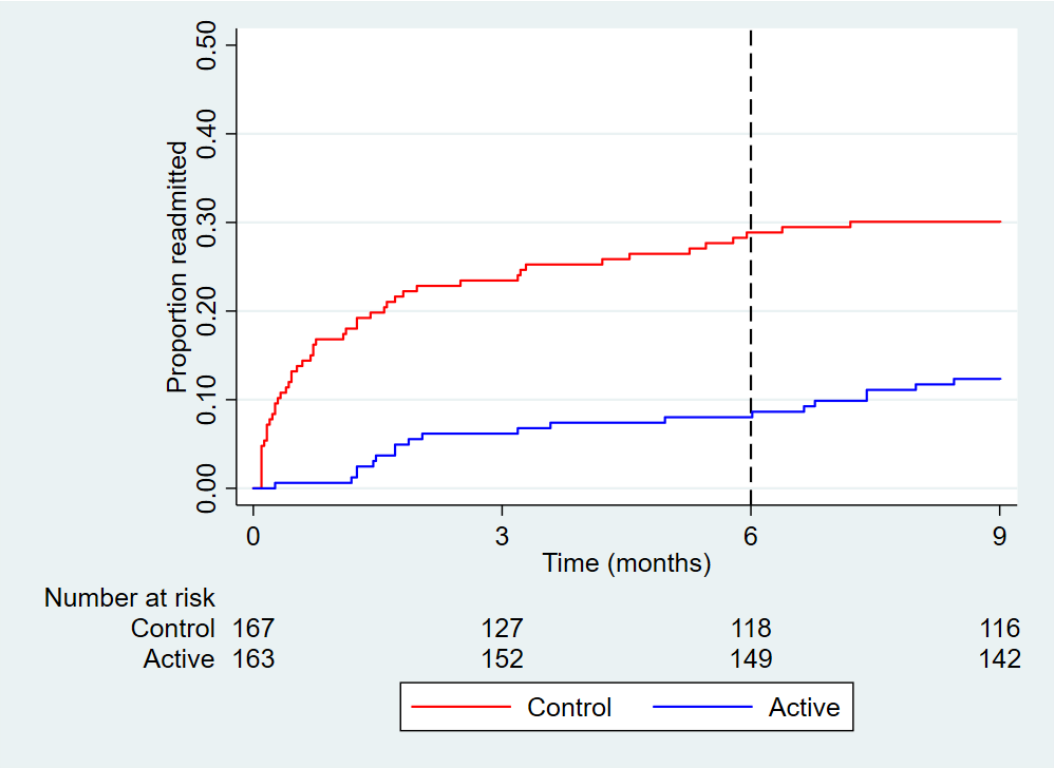


Figure 4.9 Kaplan-Meier graph of the time to first readmission during the 9-month follow-up period.

CV readmissions were significantly less common in the active group, with only 5% of this group undergoing this type of readmission in the 6-month follow-up period compared to 23% in the control group. Non-CV readmission was also lower in the active group; however, but this difference was not statistically significant.

Data on the LOS of the two study groups is summarised in Table 4.16. Categorical variables are expressed as the number and percentage of responses in each category. As most participants experienced no inpatient stay, the mean LOS was, as the median values were all 0. The mean difference in LOS and 95% CI are also presented.

Table 4.16 Length of stay

Variable	Category	Control		Active		Group difference	
		n	Summary (*)	n	Summary (*)	Mean (95% CI) (+)	P-value
Length of stay 1-3 months	0 days	166	130 (71%)	162	153 (94%)		
(categorical)	1 – 4 days		26 (29%)		7 (4%)		
	5 – 9 days		7 (4%)		1 (1%)		
	10+ days		3 (2%)		1 (1%)		
Length of stay 1-3 months	-	166	0.8 ± 2.1	162	0.3 ± 21.4	-0.5 (-0.9, -0.2)	**<0.001**
Length of stay 3-6 months	0 days	165	148 (90%)	160	155 (97%)		
(categorical)	1 – 4 days		12 (7%)		3 (2%)		
	5 – 9 days		2 (1%)		0 (0%)		
	10+ days		3 (2%)		2 (1%)		
Length of stay 3-6 months	-	165	0.7 ± 3.9	160	0.3 ± 2.0	-0.4 (-1.1, 0.3)	**0.01**
Total length of stay over	0 days	165	118 (72%)	160	149 (93%)		
6-months follow-up	1 – 4 days		32 (19%)		5 (3%)		
(categorical)	5 – 9 days		8 (9%)		3 (2%)		
	10+ days		7 (4%)		3 (2%)		
Total length of stay (6m fu)	-	166	1.5 ± 4.4		0.5 ± 2.5	-0.9 (-1.7, -0.2)	**<0.001**
Length of stay 6-9 months	0 days	165	157 (70%)	160	151 (94%)		
(categorical)	1 – 4 days		5 (3%)		4 (3%)		
	5 – 9 days		2 (1%)		1 (1%)		
	10+ days		1 (1%)		4 (3%)		
Length of stay 6-9 months	-	165	0.3 ± 2.5	160	0.7 ± 4.6	0.4 (-0.4, 1.2)	0.74

Summary statistics are: mean ± standard deviation, or number (percentage)
(+) Mean differences expressed as outcome for Active group minus outcome for Control group.

Table 4.17 A&E visits and Other outcomes

Variable	Category	Control		Active		Group difference	
		n	Summary (*)	n	Summary (*)	Difference (95% CI) (+)	P-value
Death (any cause)	No	167	165 (99%)	162	160 (99%)	0% (-2%, 2%)	0.98
(categorical)	Yes		2 (1%)		2 (1%)		
Coronary angiography /	No	165	150 (91%)	160	156 (97%)	-7% (-12%, -2%)	**0.01**
angioplasty	Yes		15 (9%)		4 (3%)		
Any A&E visits over	No	165	104 (63%)	160	120 (75%)	-12% (-22%, -2%)	**0.02**
6-months	Yes		61 (37%)		40 (25%)		
Total A&E visits over 6m	0 visits	165	104 (63%)	160	120 (75%)	-	
(categorical)	1 visit		35 (21%)		35 (22%)		
	2 visits		17 (10%)		2 (1%)		
	3+ visits		9 (5%)		3 (2%)		
Total A&E visits over 6m	-	165	0.6 ± 1.0	160	0.3 ± 0.6	-0.3 (-0.5, -0.1)	**0.005**
A&E visits within 30 days	No	166	136 (82%)	162	148 (91%)	-9% (-12%, -2%)	**0.01**
	Yes		30 (18%)		14 (9%)		
A&E visits 1 – 3 months	No	166	147 (89%)	162	141 (75%)	2% (-6%, 9%)	0.67
	Yes		19 (11%)		21 (13%)		
A&E visits 0 – 3 months	No	166	123 (74%)	162	128 (79%)	-5% (-14%, 4%)	0.29
	Yes		43 (26%)		34 (21%)		
A&E visits 4 – 6 months	No	165	139 (63%)	160	152 (95%)	-11% (-17%, -4%)	**0.002**
	Yes		26 (16%)		8 (5%)		
A&E visits 6 – 9 months	No	165	139 (84%)	160	141 (88%)	-4% (-11%, 4%)	0.31
	Yes		26 (16%)		19 (12%)		

(*) Summary statistics are: mean ± standard deviation, or number (percentage)
(+) Figures are either percentage difference or mean difference. Expressed as outcome for Active group minus outcome for Control group

The results suggested a statistically significant difference in the LOS between the two groups, during the 1–3 month and 3–6-month periods, as well as the total LOS. In all instances, the LOS was shorter in the active group. The total mean LOS over the first 6-months was 1.5 days in the control group and 0.5 days in the active group. Only 4% of active participants stayed in hospital more for 5+ days, compared to 13% in the control group. There was no difference between groups in terms of LOS during the 6–9-month period. Table 4.17 provides the results for death, coronary angioplasty, and A&E visit outcomes.

No significant difference in death was observed between the groups, with only 1% of participants dying in both groups. However, the percentage of participants requiring a coronary angiography/angioplasty was significantly lower in the active group, with 7% fewer participants needing this compared to the control group. Overall, 37% of the control group had one or more A&E visit over the first 6-months of follow-up, significantly higher than in the active group, where only 25% visited during this period. Additionally, 15% of the control group made 2 or more visits, compared to only 3% of the active group. The mean number of A&E visits during this period was 0.6 in the control group, significantly higher than the mean of 0.3 in the active group.

There were no significant differences between groups in terms of A&E visits during the 1–3 month or 0–3-month periods. However, significant differences were observed for visits within the first 30 days and during the 4–6-month period. In the active group, 9% fewer participants visited A&E within the first 30 days, and 11% fewer visited between 4–6 months. A&E visits during the 6–9-month period did not significantly differ between groups. The time to first readmission results are shown in Table 4.18. Using the first 6-months of follow-up only, the time to first readmission was significantly shorter in the control group. The Kaplan-Meier

estimates indicated that 63% of participants were free from readmission at 6-months in the control group versus 76% in the active group (Figure 4.10).

Table 4.18 Time to event outcomes

Variable	Control		Active		Group difference	
	n	% Event (*) (95% CI)	n	% Event (*) (95% CI)	Hazard Ratio (95% CI) (+)	P-value
6-month follow-up						
Time to readmission	167	29% (23%, 36%)	163	8% (5%, 13%)	0.24 (0.13, 0.44)	**<0.001**
Time to A&E visit	167	37% (30%, 45%)	163	24% (18%, 31%)	0.59 (0.40, 0.89)	**0.01**
9-month follow-up						
Time to readmission	167	30% (24%, 38%)	163	12% (8%, 18%)	0.35 (0.21, 0.59)	**<0.001**
Time to A&E visit	167	44% (37%, 52%)	163	32% (26%, 40%)	0.66 (0.46, 0.94)	**0.02**
Time to MI	167	22% (17%, 29%)	163	7% (4%, 12%)	0.27 (0.14, 0.53)	**<0.001**
Time to Stroke	167	5% (2%, 9%)	163	2% (0%, 6%)	0.38 (0.10, 1.42)	0.15

(+) Hazard ratio expressed as risk of event at any time during follow-up in Active group relative to risk for Control group.
(*) Kaplan-Meier estimate of percentage of patient free from outcome event at the final follow-up point (either 6 or 9 months)

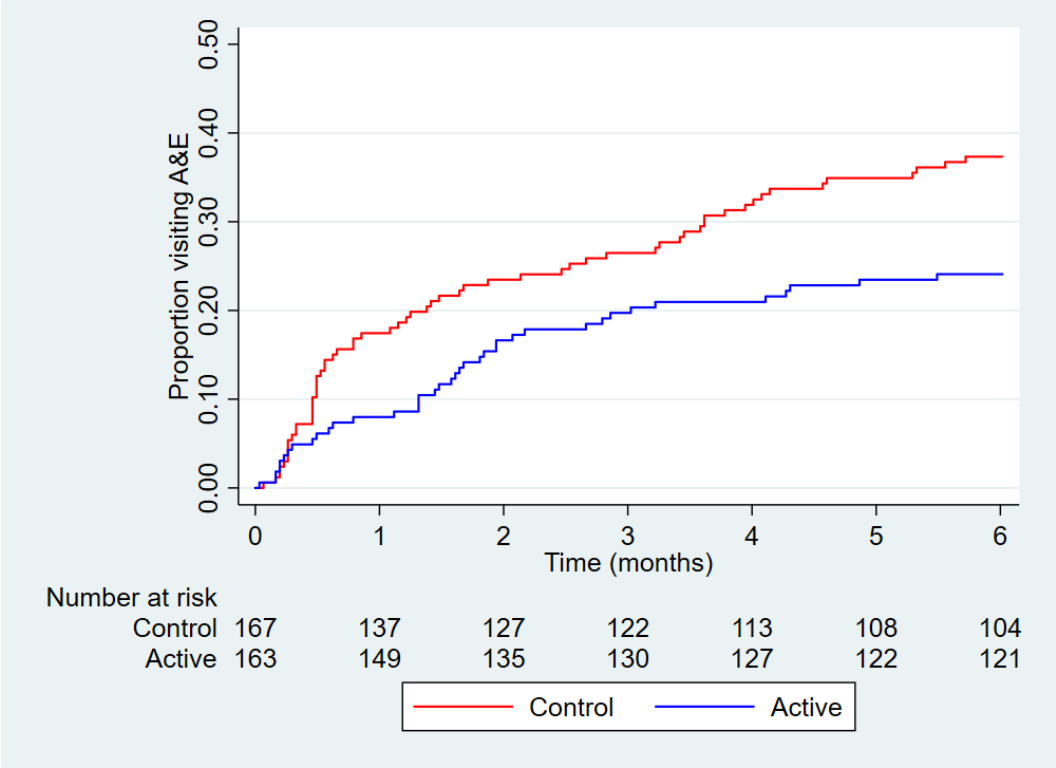


Figure 4.10 Kaplan-Meier graph of the time to first A&E admission during the 6-month follow-up period.

A similar analysis was performed using the full 9-month follow-up period. Again, a significantly longer time to A&E admission was seen in the active group. The results are illustrated graphically in Figure 4.11.

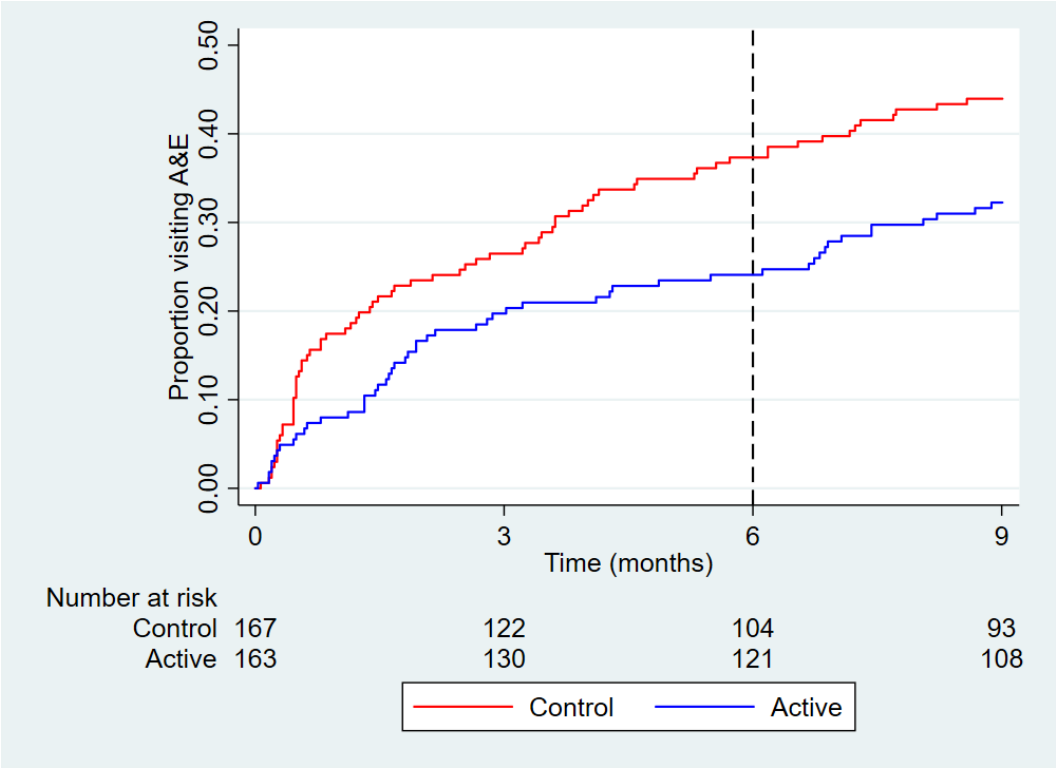


Figure 4.11 Kaplan-Meier graph of the time to first A&E admission over the 9-month follow-up period.

The results for adverse outcomes and MACE are shown in Tables 4.19, and 4.21 and Figures 4.12 and 4.13. MI and revascularisation were significantly less common in the active group. MI occurred in 22% of the control group, but only 7% of the active group. HF was also lower in the active group; however, this difference was not significant. MACE was significantly less common in the active group, with 17% fewer patients experiencing this outcome than in the control group.

Data on PCP/GP visits and symptoms at both the 3 and 6-month timepoints are summarised in Table 4.20. The medians and inter-quartile ranges of PCP/GP visits are reported, along with the median difference between groups. The number and percentage of patients with symptoms are reported in each group, along with the percentage differences between groups. The analyses

indicated that there were no significant differences between the groups in terms of the number of PCP/GP visits in the 1–3-month, 4–6-month, and 6–9-month periods.

The occurrence of chest pain, shortness of breath, and dizziness at both 3 and 6 months was significantly lower in the active group than in the control group. At both timepoints, around 15% fewer participants experienced these symptoms in the active group. There was no significant difference in the occurrence of palpitations between groups at either timepoint, and this symptom was relatively rare.

There was no significant difference between the groups in terms of chest pain, shortness of breath, and palpitations at the 9 month follow-up. There was a slight difference in the occurrence of dizziness between groups; however, this result was of borderline statistical significance. In the active group, 7% fewer participants experienced dizziness in than in the control group.

Table 4.19 Adverse outcomes and MACE

Variable	Category	Control		Active		Group difference	
		n	Summary (*)	n	Summary (*)	Difference (95% CI) (+)	P-value
Myocardial infarction	No	167	130 (78%)	162	152 (93%)	-15% (-23%, -8%)	**<0.001**
	Yes		37 (22%)		11 (7%)		
Stroke	No	167	159 (95%)	162	159 (98%)	-3% (-7%, 1%)	0.14
	Yes		8 (5%)		3 (2%)		
Revascularisation	No	167	151 (90%)	162	156 (96%)	-6% (-11%, -1%)	**0.03**
	Yes		16 (10%)		6 (4%)		
CVD death	No	167	165 (5%)	162	162 (100%)	-1% (-3%, 0%)	0.16
	Yes		2 (1%)		0 (0%)		

(*) Summary statistics are: mean ± standard deviation, or number (percentage)
(+) Figures are either percentage difference or mean difference. Expressed as outcome for Active group minus outcome for Control group.

Table 4.20 visits and symptoms

Variable	Control		Active		Group difference	
	n	Summary (*)	n	Summary (*)	Difference (95% CI) (+)	P-value
Number GP visits 1-3 months	166	2 [1, 3]	162	2 [1, 2]	0 (-1, 0)	0.10
Number GP visits 4-6 months	165	2 [1, 3]	160	2 [1, 3]	0 (-1, 0)	0.20
Number GP visits 6-9 months	165	2 [0, 3]	160	1 [0, 2]	0 (0, 0)	0.38
3-month symptoms						
Chest pain	166	37 (22%)	162	12 (7%)	-15% (-22%, -7%)	**<0.001**
Shortness of breath	166	58 (35%)	162	33 (20%)	-15% (-24%, -5%)	**0.003**
Palpitations	166	9 (5%)	162	4 (2%)	-3% (-7%, 1%)	0.17
Dizziness	166	37 (22%)	162	15 (9%)	-13% (-21%, -5%)	**0.001**
6-month symptoms						
Chest pain	165	39 (24%)	160	15 (9%)	-14% (-22%, -6%)	**0.001**
Shortness of breath	165	64 (39%)	160	34 (21%)	-18% (-27%, -8%)	**0.001**
Palpitations	165	7 (4%)	160	2 (1%)	-3% (-7%, 1%)	0.10
Dizziness	165	30 (18%)	160	9 (6%)	-13% (-19%, -6%)	**<0.001**
9-month symptoms						
Chest pain	165	28 (17%)	160	22 (14%)	-3% (-11%, 5%)	0.42
Shortness of breath	165	50 (30%)	160	49 (30%)	0% (-10%, 10%)	0.95
Palpitations	165	13 (8%)	160	7 (4%)	-3% (-9%, 2%)	0.19
Dizziness	165	25 (15%)	160	13 (8%)	-7% (-14%, 0%)	0.05

(*) Summary statistics are: median [inter-quartile range] or number (percentage)
(+) Figures are either percentage difference or median difference. Expressed as outcome for Active group minus outcome for Control group

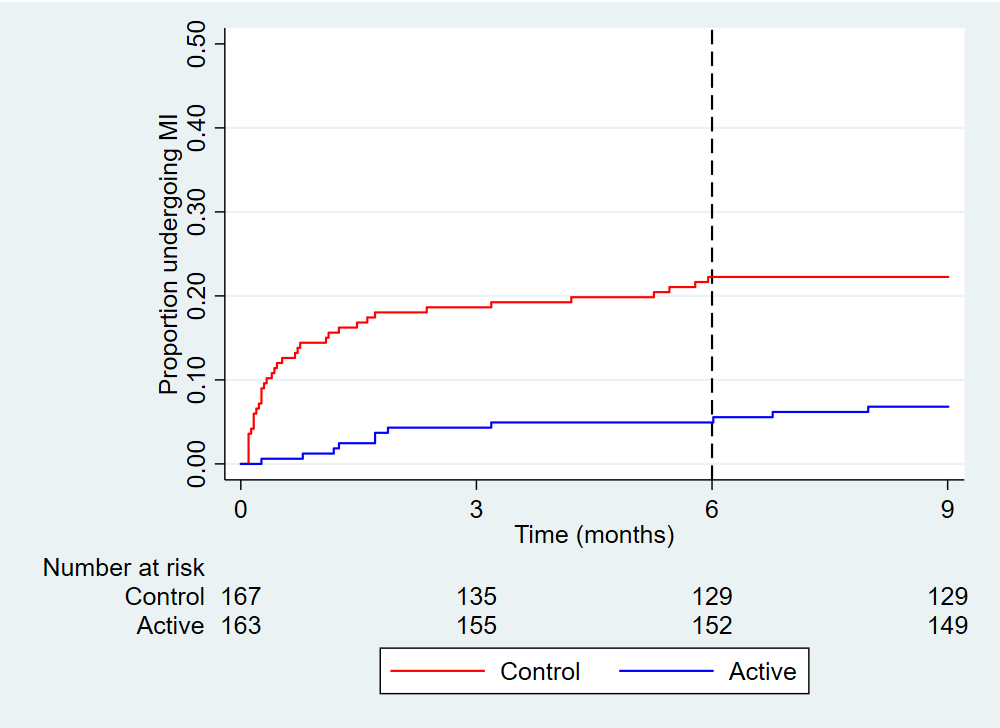


Figure 4.12 Time to myocardial infarction within the 9 months of follow-up. From Alshahrani et al., 2024. CC BY 4.0

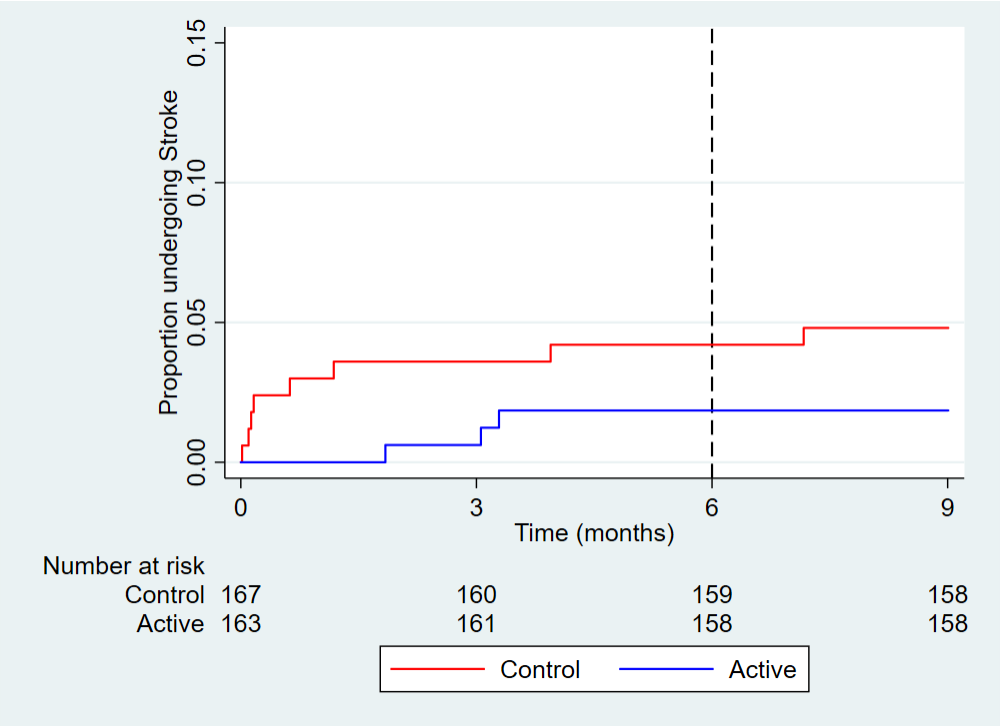


Figure 4.13 Time to stroke within the 9 month follow-up period. From Alshahrani et al., 2024. CC BY

Although the study was not designed to perform powerful comparisons of subgroups, Table 4.22 includes an analysis of the patient subgroups by age, sex, smoking status, and DM presence.

Table 4.21 Summary of the major outcomes at 6 and 9

Outcomes/Variable	**Control**		**Active**		**Group difference**	
	N	Events (95% CI) [(#)]	N	Events (95% CI) [(#)]	Hazard Ratio (95% CI) [(+)]	P-value
Primary outcome 6-month follow-up						
Time to readmission	167	29% (23%, 36%)	165	8% (5%, 13%)	0.24 (0.13, 0.44)	**<0.001**
Secondary outcomes						
Total length of stay	**Control**		**Active**		**Group difference**	
	N	Mean ± SD	N	Mean ± SD	Mean difference [(+)]	P-value
LOS 0-3 months	166	0.8 ± 2.1	162	0.3 ± 1.4	-0.5	**<0.001**
LOS 0-6 months	165	1.5 ± 4.4	160	0.5 ± 2.5	-0.9	**<0.001**
LOS 0-9 months	165	1.8 ± 5.2	160	1.2 ± 5.6	-0.6	**<0.001**
Time to event 6-month follow-up	**Control**		**Active**		**Group difference**	
	N	Events (95% CI) [(#)]	N	Events (95% CI) [(#)]	Hazard Ratio (95% CI) [(+)]	P-value
A&E visit	167	37% (30%, 45%)	163	24% (18%, 31%)	0.59 (0.40, 0.89)	**0.01**
All-cause Mortality	167	1.2% (0.3%, 4.7%)	163	1.2% (0.3%, 4.9%)	1.03 (0.15, 7.31)	0.98
Myocardial infarction	167	22% (17%, 29%)	163	7% (4%, 12%)	0.27 (0.14, 0.53)	**<0.001**
Stroke	167	5% (2%, 9%)	163	2% (1%, 6%)	0.38 (0.10, 1.42)	0.15
Coronary angiography /angioplasty	**Control**		**Active**		**Group difference**	
	N	n (%)	N	n (%)	% Difference (95% CI) [(+)]	P-value
6 months	165	15 (9%)	160	4 (3%)	-7% (-12%, -2%)	**0.01**
9 months	165	16 (10%)	160	4 (3%)	-6% (-11%, -1%)	**0.03**
9-month follow-up	**Control**		**Active**		**Group difference**	
	N	Events [(#)] (95% CI)	N	Events [(#)] (95% CI)	Hazard Ratio (95% CI) [(+)]	P-value
Time to readmission	167	30% (24%, 38%)	163	12% (8%, 18%)	0.35 (0.21, 0.59)	**<0.001**
Time to A&E visit	167	44% (37%, 52%)	163	32% (26%, 40%)	0.66 (0.46, 0.94)	**0.02**

(#) Kaplan-Meier estimate of percentage of patients with event at the last follow-up point

(+) Expressed as outcome for Active group minus outcome for Control group.

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Table 4.22 Time to readmission within 6-month follow-up – Patient subgroups

Subgroup	**Control**		**Active**		**Group difference**	
	n	6m readmission (*) (95% CI)	n	6m readmission (*) (95% CI)	Hazard Ratio (95% CI) (+)	P-value
Males	145	28% (21%, 36%)	139	7% (4%, 13%)	0.23 (0.11, 0.45)	**<0.001**
Females	22	36% (20%, 60%)	24	13% (4%, 34%)	0.30 (0.08, 1.13)	0.08
Age < 50	24	21% (9%, 43%)	27	4% (1%, 24%)	0.17 (0.02, 1.41)	0.10
Age 50+	143	30% (23%, 39%)	136	9% (5%, 15%)	0.25 (0.13, 0.48)	**<0.001**
Never smoked	72	41% (30%, 53%)	66	9% (4%, 19%)	0.18 (0.07, 0.43)	**<0.001**
Curr/Ex smok.	95	20% (13%, 30%)	89	7% (4%, 15%)	0.33 (0.14, 0.80)	**0.01**
No diabetes	118	23% (16%, 32%)	120	7% (3%, 13%)	0.18 (0.07, 0.43)	**<0.001**
Diabetes	49	43% (30%, 58%)	43	12% (5%, 26%)	0.33 (0.14, 0.80)	**0.01**

(+) Hazard ratio expressed as risk of event at any time during follow-up in Active group relative to risk for Control group. (*) Kaplan-Meier estimate of percentage of patient free from outcome event at 6 months.

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Although the intervention was only administered during the initial 6 months of follow-up, we analysed the outcomes during the subsequent 6–9-month period without intervention (Table 4.23). The significant differences in outcomes between the two study groups disappeared during this period, including number of hospital admissions, ER visits, and LOS in hospital. However, the initial effect between 0–6 months was large enough to leave a legacy effect, as shown the Kaplan-Meier graphs (Figures 4.9, 4.11, 4.12, and 4.13).

Table 4.23 6 months to 9 months outcomes

Variable	**Category**	**Control [165]**		**Active [160]**		**Group difference**	
		N	%	N	%	% difference (95% CI) (+)	P-value
Readmission 6 – 9 months	No	157	95%	152	95%	0% (-5%, 5%)	0.95
	Yes	8	5%	8	5%		
A&E visits 6 – 9 months	No	139	84%	141	88%	-4% (-11%, 4%)	0.31
	Yes	26	16%	19	12%		
		Control		**Active**		**Group difference**	
		N	Summary (*)	N	Summary (*)	Mean difference (+)	P-value
Length of stay 6-9 months	-	165	0.3 ± 2.5	160	0.7 ± 4.6	0.4	0.74
Length of stay 6-9 months (categorical)	0 days	165	157 (70%)	160	151 (94%)	-	
	1 – 4 days		5 (3%)		4 (3%)	-	
	5 – 9 days		2 (1%)		1 (1%)	-	
	10+ days		1 (1%)		4 (3%)	-	

(+) Differences expressed as outcome for Active group minus outcome for Control group

(*) Summary statistics are mean ± standard deviation, or number (percentage)

A&E, Accident and emergency

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4.16 Discussion

This RCT focused on patients undergoing treatment for ACS. The RPM service provided post-discharge over a 6-month period was linked to a decreased risk of unplanned hospital admissions compared to standard care. The impact of the remote monitoring approach was significant, with a HR of 0.24 for event-free survival in the group who received active monitoring. Notably, the benefits of the active intervention persisted beyond the initial 6-month intervention period, with a reduced HR of 0.35 for unplanned hospitalisations observed at 9 months.

Participants who received the remote monitoring protocol intervention (as shown in Figure 4.9,) had a decreased frequency of ER visits at both the 6- and 9-month follow-ups. The duration of hospital stays for these participants was notably shorter than for those receiving standard care. This effect was observed early and was maintained at the 3, 6, and 9-month marks. The sustained impact of the intervention on re-admissions, ER visits, and overall hospital stay duration persisted up to 9 months, even though the remote monitoring protocol was discontinued at 6 months. Between 6–9 months, a "catch up" effect was observed, whereby no significant differences in these outcomes were evident. However, the substantial effects of the intervention during the initial 6 months were enough to maintain its benefits until the 9-month follow-up period, as evident in the Kaplan-Meier graphs (Figures 4.9 and 4.11).

Participants in the remote monitoring group experienced fewer significant adverse CV events, primarily MI, with a lower rate of revascularisation observed in this group. This suggested a potential advantage for the active arm, with fewer MIs occurring despite reduced revascularisation. The decrease in revascularisation might have been influenced by the reduced incidence of MIs, though this analysis did not establish causality. Several potential

explanations could account for these findings. One plausible factor was the modification of behaviour due to the high level of support and direct access to the study team provided to participants in the active group. Educating the patients in the telemedicine arm on symptom recognition and the general interaction with the study team at multiple contact points (2, 4, 8 weeks post-discharge and when they developed possible cardiac symptoms) may have influenced their behaviours. These factors might have led to potentially increased compliance with the technology, improved engagement with the study team, the NHS, and the healthcare system in general, along with consideration of psychological factors, which may also have contributed to better outcomes. The Hawthorne effect could have played a significant role, where participants in the active group may have altered their behaviour simply because they were under close observation. Nevertheless, there is no direct evidence supporting this hypothesis, and other studies on remote monitoring have considered different factors and suggested alternative explanations (114-116).

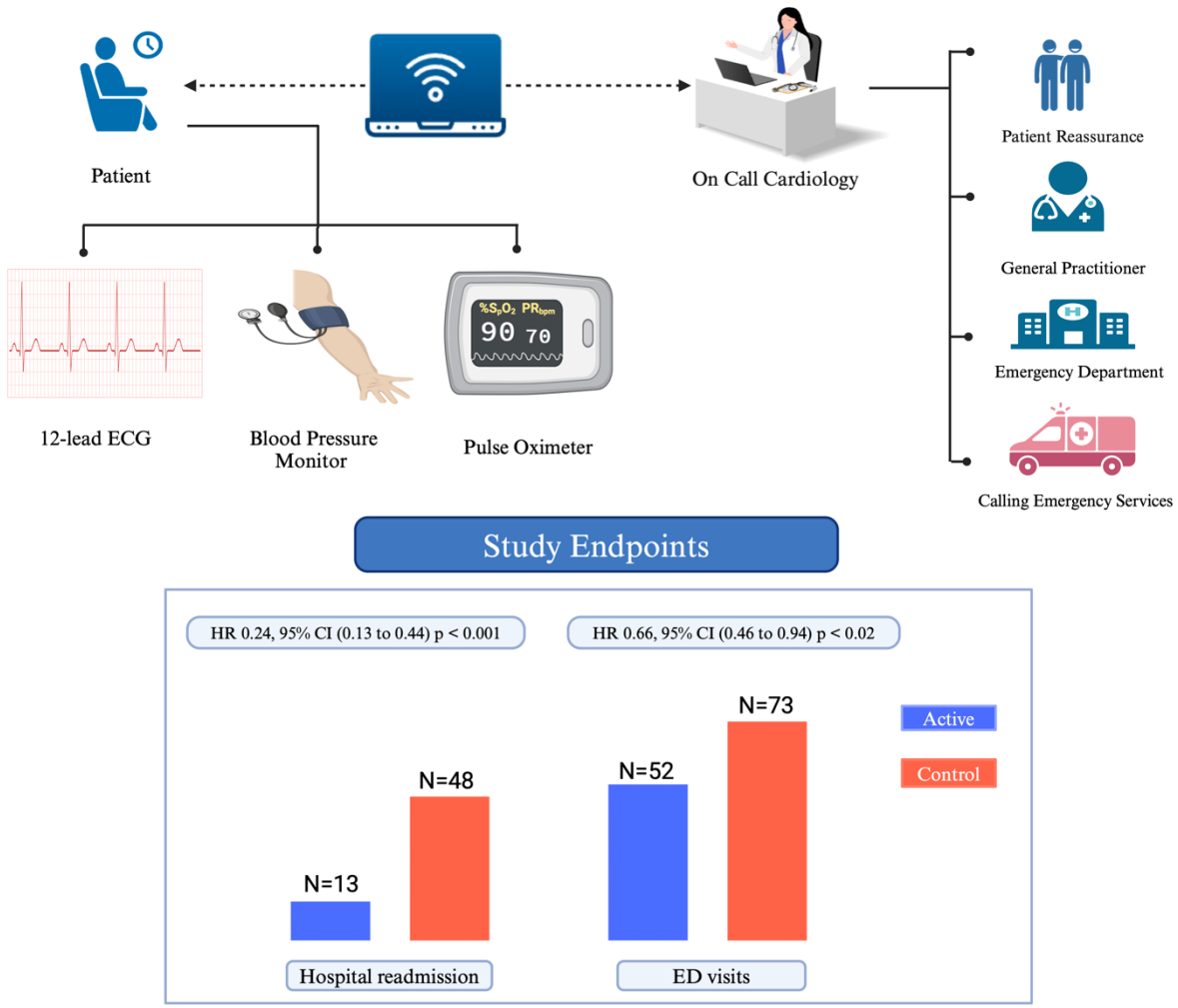


Figure 4.14 Study summary figure.

The upper section of the diagram illustrates the implementation of the TELE-ACS remote monitoring protocol in the active group of the study. The lower section displays bar graphs representing the primary and secondary outcomes of the study. On the left side of the panel, the frequency of hospital readmissions within 6 months was markedly reduced in the active group compared to the control group. On the right side, within 9 months the number of A&E visits was significantly higher in the control group. Remote monitoring concluded after 6 months for participants in the active group. The active arm is shown in blue, while the control arm is shown in red. The confidence interval (CI), hazards ratio (HR), and the number of participants (N) are shown.

Some participants in the active treatment group might have experienced undetected infarcts at home, potentially leading to the underreporting of symptoms. However, the data on objective symptoms and mortality do not support this assumption. The inclusion of a home-administered high-sensitivity troponin test would have strengthened the study, if such a test been accessible and feasible to use. As this technology becomes more globally available, affordable, and user-friendly, it should be considered for use in subsequent research.

The early detection and diagnosis of cardiac symptoms, coupled with prompt treatment, are crucial elements of any telehealth protocol and have been demonstrated to enhance patient safety (117, 118). However, previous research on HF has highlighted the need for these protocols to be comprehensive enough to mitigate unnecessary hospital readmissions and minimise the need for F2F evaluations (119, 120). Our research employed a novel approach that integrated a clinical decision-making algorithm (Table 4.4), with both objective data gathered remotely and subjective data from remote consultations conducted by a clinician to make definitive treatment decisions (95, 121, 122). The use of this strategy, which included a 12-lead ECG (123) at participants' homes, oxygen level and BP monitoring, and telemedicine consultations with a cardiologist, proved effective in reducing hospital admissions in this population.

The diverse range of devices used in telemedicine are rarely evaluated through RCTS, and are generally used as a comprehensive tool for several CV conditions, with most related studies being observational (45). Along with a handful of randomised studies that employed different technologies (112), our study demonstrated a decrease in readmissions for ACS. Furthermore, in the current study, participants with access to remote monitoring experienced significantly fewer symptoms during the intervention at the 3- and 6-month marks; however, no differences

were observed at 9 months. This suggests an impact on the perception of symptoms, particularly when participants are aware that they have access to immediate assessments using appropriate technology and support from the cardiac team. Other research has similarly documented the benefits of remote monitoring for patients with CVDs (124). This discrepancy could partly be explained by the educational material given to the study group on how to use remote monitoring tools. It is also possible that educating the participants about symptoms during their training resulted in a decreased frequency of symptom reporting in the active group, which may have increased the risk that some events were missed.

The role of patient education in managing symptoms following ACS is crucial, influencing both clinical and psychological outcomes. Our study effectively reduced unnecessary readmissions and emergency visits by guiding participants on when urgent care was essential. This proactive approach optimised healthcare resource utilisation and enhanced participant autonomy in managing their health. Furthermore, the personalised care and remote monitoring provided by our team extended beyond clinical support, serving as a crucial source of psychological reassurance. The training and interactions with the study team, documented through numerous correspondences, highlighted the significant emotional relief the participants experienced. These interactions were pivotal in aiding their recovery, facilitating the return to normal activities, and improving their overall QoL post-ACS. These findings advocate for the integration of comprehensive patient education into post-ACS care strategies to improve both clinical and psychological outcomes.

Our protocol offers a readily implementable solution for sufficiently resourced healthcare systems to facilitate “hospital at home” service models. This protocol is particularly well-suited for systems experiencing inpatient capacity constraints, as well as remote regions with

restricted access to F2F cardiology services (125). In scenarios where hospital admissions could pose a risk, such as during the COVID-19 pandemic, a proven system such as ours could be crucial for preventing unnecessary readmissions (49, 126, 127).

The Home Telemonitoring in Patients After Myocardial Infarction (HELP ME) trial is currently underway and is aimed at examining the role of ECG telemonitoring in decreasing the rate of hospital readmissions and A&E visits at 90 days (128). Another ongoing clinical trial, Quality Improvements in Post-Myocardial Infarction Management Using Home-Based Remote Monitoring System (QIBO), seeks to determine whether home-based remote monitoring of ECG and blood pressure will lead to a decline in the frequency of heart failure readmissions at 17 weeks. It will be very intriguing to learn the highly awaited outcomes of these ongoing clinical trials (129).

4.17 Study Limitations

Our study has several limitations, one of which is that we recruited mostly men. From January 2022 to April 2023, we observed a total of 517 patients who presented at the heart attack centre via the ACS pathway. The demographic composition was skewed towards a male majority, with 82% being male (424 patients) and 18% being female (93 patients). The demographics of these patients were mirrored in our study sample. Out of the total, 372 were evaluated for eligibility, culminating in the randomisation of 337 participants. While this gender distribution may not accurately represent the global population of patients with ACS, it does reflect the patient base of our centre.

There was a possibility of recall bias among participants due to the retrospective collection of some symptom data. Technological constraints and infrastructure needs posed further challenges. The American Heart Association's recent publication, "Telehealth in the Management of Cardiovascular Disease Scientific Statement" (117) indicated a trend towards remote patient care. However, this shift revealed systemic inequities and shortcomings within the telehealth system (130). Other concerns include data security and privacy, regulatory hurdles, reimbursement issues, and patient acceptance and participation (131). Our intervention was limited to participants who owned smartphones, meaning it is unclear whether similar outcomes could be achieved for patients without smartphones if they were provided one.

Another possible limitation is the high level of support available to participants in the active group during the study, including access to dedicated team members from 7:00 to 23:00 on weekdays and guaranteed cardiology responses within 15 minutes. Such intensive support might be challenging to replicate in non-trial settings without significant investment and training. Additionally, other factors not covered in this study could affect readmission rates,

including the management of outpatient comorbidities, socioeconomic issues, and disparities within healthcare systems. Future studies could adopt a pragmatic, “real-world” approach, involving a multi-centre, international evaluation of diverse patient populations across various health systems to assess the real-world impact of the telemonitoring protocol more accurately.

4.18 Future Work

To further investigate the lower MI and stroke rates in the telemedicine arm, future studies could focus on collecting detailed behavioural data from participants, such as physical activity levels, dietary habits, medication adherence, and psychological well-being. Analysing whether patients in the telemedicine arm attended A&E more frequently and had more troponin tests could determine if MIs were diagnosed more often due to increased healthcare engagement. Additionally, exploring the impact of patient education on symptom recognition and healthcare-seeking behaviour could be valuable. Conducting qualitative studies to understand patients' perspectives on remote monitoring and their behaviour changes could provide deeper insights.

Furthermore, research could investigate if higher stroke rates are linked to patients undergoing more coronary interventions. While the findings suggest a potential benefit of remote monitoring in reducing adverse CV events, further research is needed to fully understand the underlying mechanisms. Investigating behavioural changes, healthcare engagement, and the potential Hawthorne effect will be crucial for establishing causality and optimising remote monitoring interventions. Moreover, including a sham arm in future studies aims to provide a clearer understanding of the true impact of remote monitoring on patient outcomes, distinguishing between actual effects and placebo effects. However, implementing such a design might be challenging due to the nature of the intervention.

4.19 Conclusion

The TELE-ACS protocol could lead to a notable reduction in readmissions for ACS, potentially easing the load on an already overburdened global healthcare system. To implement this effectively, ongoing innovations in telemedicine technology and software development must be enhanced. Furthermore, policy guidelines should be implemented regarding the integration of telemedicine into clinical care pathways, as recently implemented by the UK National Health Service (132).

4.20 Paper published from this chapter:

Alshahrani NS, Hartley A, Howard J, Hajhosseiny R, Khawaja S, Seligman H, Akbari T, Alharbi BA, Bassett P, Al-Lamee R, Francis D, Kaura A, Kelshiker MA, Peters NS, Khamis R. Randomized Trial of Remote Assessment of Patients After an Acute Coronary Syndrome. J Am Coll Cardiol. 2024 Jun 11;83(23):2250-2259. doi: 10.1016/j.jacc.2024.03.398. Epub 2024 Apr 6. PMID: 38588928.

5 Six-Month Cost-Benefit and QoL Analysis of a Novel Post-ACS Remote Monitoring Protocol

5.1 Abstract

5.1.1 Background

Patients discharged from the hospital after ACS often face a higher risk of unplanned readmissions. Many of these readmissions could be prevented, subsequently reducing unnecessary financial burdens. The TELE-ACS trial aimed to evaluate the effectiveness of a novel telemonitoring protocol, in reducing these readmissions. Our objective was to conduct a 6-month cost-benefit analysis (CBA) of this protocol, considering the perspective of the NHS and the enhancements in patient-reported QoL outcomes.

5.1.2 Methods

Data extracted from the TELE-ACS trial was used with ethical approval. The costs of the intervention encompassed the expenses required to execute the protocol within the group of patients receiving the intervention. The benefits, on the other hand, pertained to the amount of money that was saved as a result of a decrease in the occurrence of adverse events in the intervention arm of the study over the 6-month period. These events included consultations with primary care physicians, visits to the A&E without subsequent hospitalisation, and non-elective all-cause readmissions to the hospital. Participants in both study groups completed self-report QoL questionnaires (SAQ-7 and SF-36) at baseline pre-discharge and again at 3, 6 and 9 months post discharge.

5.1.3 Results

The total study included 337 patients (N=169 in the intervention group and N=168 in the control group) over a 6-month period. After excluding 9 patients who did not complete one month of follow-up, the readmission rate was significantly lower in the intervention group. The

total costs for all events equated to £173,418 for the intervention group compared to £475,713 for the control group, resulting in a net benefit of £277,394 after deducting the £24,901 cost for protocol implementation. The results indicated no statistically significant differences between groups for any of the SF-36 scores, or for SAQ-7 at 3, 6 and 9 months timepoint.

5.1.4 Conclusion

The use of the TELE-ACS protocol over a 6-month period resulted in cost savings of £277,394 for the NHS. Therefore, this intervention is a financially feasible strategy for reducing readmissions among patients with ACS.

5.2 Introduction

5.2.1 Readmissions in Patients with ACS

There are three categories of ACS: STEMI, NSTEMI, and UA. ACS can lead to permanent cardiac muscle damage due to inadequate oxygenation, which can severely impair heart function and increase the risk of arrhythmias (133). Swift restoration of blood flow is therefore critical, as timely treatment significantly improves patient outcomes (133). In England alone, there were 93,251 hospital admissions for ACS during 2022–2023 (134). Significant progress in ACS management in recent decades has resulted in increased survival rates among patients hospitalised for ACS (135). The National Institute for Health and Care Excellence (NICE) reported a decline in in-hospital mortality for ACS from 20% in 1984 to 5% in 2014 in the UK (135). However, individuals discharged after an ACS episode face a heightened risk of unplanned readmissions. The NHS records indicate that readmission rates for patients with ACS sit around 9% within 30 days and 18.8% within 6 months (85, 136), indicating a growing population vulnerable to readmission. Research suggests that approximately 27–30% of these readmissions are preventable (137, 138), imposing undue burdens on patients, families, and healthcare systems. Readmissions are associated with adverse patient outcomes and an increased 1-year mortality (139). They also impose additional financial strains on already stretched healthcare systems, diverting resources from essential patient care (89). The Hospital Readmissions Reduction Program in the USA enforces financial penalties on hospitals that have 30-day MI readmission rates that surpass the national average, as elevated rates are viewed as indicative of inadequate care (140). It is crucial to reduce preventable readmissions to enhance patient outcomes and alleviate healthcare costs.

5.2.2 Telemonitoring as a Strategy to Minimise Readmissions

Telemonitoring is an innovative strategy for reducing unnecessary readmissions among patients with ACS. During the COVID-19 pandemic, telemonitoring programmes were widely adopted to monitor patient health remotely and provide healthcare services (141). Monitoring patients post-discharge enables healthcare providers to promptly detect and address emerging symptoms and signs, thereby pre-empting deterioration and the need for hospitalisation. Furthermore, telemonitoring facilitates expedited care for individuals requiring urgent attention, leading to improved outcomes. Therefore, these interventions have the potential to reduce healthcare system costs by preventing unnecessary readmissions while ensuring patient safety remains uncompromised.

Telemonitoring has been extensively examined as a method for managing HF. A systematic review of 38 RCTs revealed a significant decrease in both all-cause mortality and readmissions associated with telemonitoring interventions in patients with HF (142). However, there is considerably less data available regarding the effectiveness of telemonitoring in patients with ACS, with only a few completed RCTs to date. An RCT was recently conducted to assess the effectiveness of TeleClinical Care intervention in patients with ACS. This intervention involved the remote monitoring of physical parameters, including pulse rate, blood pressure, and weight, in ACS patients. Results from this trial showed that the use of this intervention was associated with a significant decrease in the readmission rate at 6 months (143).

5.2.3 TELE-ACS Trial

A recently concluded RCT, known as the TELE-ACS trial, was conducted under the sponsorship of Imperial College London (93). This investigator-initiated trial, conducted at a single centre, aimed to evaluate the effectiveness of a novel telemonitoring protocol (the TELE-

ACS protocol) in reducing readmissions within 6 months (93). A total of 337 patients hospitalised with ACS were randomly assigned upon discharge to either the control group, who received standard post-ACS care, or the active group, who received the TELE-ACS protocol in addition to standard care.

5.2.4 Cost-Benefit Analysis

To qualify for integration into the NHS, novel interventions such as the TELE-ACS protocol must undergo a stringent technological evaluation by NICE (144). This evaluation entails a thorough examination the evidence pertaining to the intervention's efficacy in terms of both clinical outcomes and costs (144). Should the intervention be determined as both clinically effective and cost-efficient, and subsequently endorsed by NICE for NHS implementation, the NHS is obligated by law to allocate funds for the intervention's provision to its patients (144).

A CBA is a form of economic evaluation used to assess the economic feasibility of an intervention (145). Within a CBA framework, the costs and benefits of an intervention are systematically compared in terms of monetary value (145). CBAs can help determine whether a proposed healthcare intervention is worth pursuing based on whether the benefits outweigh the costs, and if so, by how much (145).

5.2.5 Patient-Reported QoL

QoL is significantly impaired for patients with CVD due to the many physical symptoms they experience, such as fatigue, difficulty breathing, or chest discomfort, which impact their mental, emotional, and social health (146). QoL is a crucial aspect of patient-centred treatment. Measures of both general and disease-specific QoL should be included in the shared decision-making process before cardiac procedures and during the recovery period (147).

5.2.6 Aim and Hypothesis

This study aimed to conduct a 6-month CBA and assess the QoL implications of implementing the TELE-ACS protocol from the standpoint of the NHS. This protocol was used in the recently concluded TELE-ACS trial. The analysis focused on the direct financial implications for the NHS. The hypothesis posited that the protocol would result in overall benefits for the NHS, both in terms of cost savings and enhancements in patient-reported QoL outcomes.

5.4 Methodology

5.4.1 TELE-ACS Study Details

Details about the inclusion and exclusion criteria for the TELE-ACS trial are detailed in the main trial paper (93). Briefly, the TELE-ACS protocol, which was exclusively applied in the randomised intervention arm, incorporates a telemonitoring kit used in conjunction with a validated CDSSA (as shown in Figure 3.1). This kit includes an FDA-approved 12-lead SmartHeart ECG device, a pulse oximeter, and a blood pressure cuff. For more detail, please refer to Chapter 4.

5.4.2 CBA

The study involved a cost-benefit analysis of the intervention over a period of 6 months. The costs of the intervention encompassed the expenses required to execute the protocol within the group of patients receiving the intervention. The benefits, on the other hand, pertained to the amount of money that was saved as a result of a decrease in the occurrence of adverse events in the intervention arm of the study over the 6-month period. These events included consultations with primary care physicians, cardiac visits to the A&E without subsequent hospitalisation, and non-elective all-cause readmissions to the hospital. The study assessed the number of events occurring in the intervention arm relative to those in the control arm, as well as the financial savings resulting from the reduced incidence of events in the intervention arm.

5.4.3 Readmissions, A&E Visits, and GP consultations

During the 3 and 6-month follow-up assessments, participants were asked about any occurrences subsequent to their study enrolment, including the frequency and locations of such events. The electronic medical records of all participants were searched to obtain additional

information regarding these events. However, access to the medical records of participants who sought medical attention outside of Imperial College Healthcare NHS Trust was not feasible. Therefore, these individuals were subsequently contacted via telephone to gather further details regarding these events.

The costs associated with readmissions and A&E visits were derived from the PLICS, which assesses the overall expenses accrued by NHS trusts for patient care, tailored to the specific services used by each participant. PLICS cost data was only accessible for participants who had visited an Imperial Trust hospital before October 2023. For those who visited other hospitals, A&E costs were estimated using the average PLICS cost from available data. Similarly, costs for readmissions were estimated based on the national average for a readmission within the same healthcare resource group (HRG), according to the National Schedule of NHS Costs for the fiscal year 2022/2022 (148). HRGs categorise healthcare activities that typically require comparable resources (149). The average cost of a GP consultation was sourced from the 2022 edition of the Unit Costs of Health and Social Care Manual (150).

5.4.4 TELE-ACS Protocol Costs

Each unit of equipment was expected to have a functional lifespan of two years, during which it could serve up to four patients. There was an assumption that the equipment would not need replacement sooner. To determine staff expenses, the typical hourly wage for a cardiology registrar was used, based on the amount of time they spent engaging with participants. The recruitment period for the trial was not included in this calculation. The average time required for training, contacting, and consulting each participant was calculated.

5.4.5 QoL

Participants in both study groups completed self-report QoL questionnaires (SAQ-7 and SF-36) at baseline pre-discharge. Additionally, the participants were discharged with a package that contained 3 copies of the questionnaire to be completed at 3-, 6-, and 9-months post-discharge. A prepaid envelope was provided in which to return the completed questionnaires, along with details of where to return them. Improvements in patient-reported QoL outcome measures (weighted to treatment satisfaction domains) at 3-, 6- and 9-months post-discharge versus baseline measures were analysed.

5.4.6 Sensitivity Analysis

A sensitivity analysis evaluating both the best-case and worst-case scenarios was conducted to assess the stability of the CBA. The analysis focused on altering A&E costs, as these represented the largest share of estimated expenses and carried the greatest uncertainty. For the first 6 months, the least and most expensive A&E costs were determined using data from the PLICS and were then assigned to any A&E visits that lacked specific PLICS cost data. In the best-case scenario, the highest A&E costs were applied, as the control group had more A&E visits without PLICS costs compared to the active group. This adjustment led to an increased overall benefit and net gain. In contrast, the lowest A&E costs were used in the worst-case scenario to assess potential lower benefits. All other variables in the analysis remained unchanged.

5.4.7 Nationwide Extrapolation

In order to determine how beneficial the protocol would be for NHS England on an annual basis, the results obtained from the CBA analysis were extended to encompass the national

disease burden. The Hospital Admitted Patient Care Activity 2022-2023 report was utilised to approximate the yearly count of patients diagnosed with ACS in England. The readmission rate was assumed to be 10% (151). The per-patient net benefit gained from implementing the protocol was then extrapolated to this patient population.

5.4.8 Statistical Analysis

The study recorded participant costs incurred based on healthcare utilisation (hospital readmissions, A&E attendances and GP appointments). Only cardiac-related hospital costs were considered. Hospital costs which were non-cardiac-related were omitted from the analysis. A detailed breakdown of hospitals costs was available for participants who attended an Imperial College Healthcare hospital. However, some participants attended different hospitals, where this detailed information was unavailable. For these patients, the cost of a hospital readmission and A&E attendance was based on the mean values for patients where detailed data was available.

Cost data was compared between groups using an unpaired t-test. To allow for the skewed distribution of the cost data, CIs for the differences between groups were quantified using a non-parametric bootstrap approach. This was performed with 1000 bootstrap iterations. Patients who completed less than 1 month of follow-up, due to either withdrawal or death were omitted from the cost analysis.

An additional set of analyses compared the number of occurrences of different types of healthcare use between groups. Due to the distribution of these outcomes, a negative binomial regression was used to calculate the ratio of occurrences between groups and the corresponding CI. The outcome variables were component scores from the SF-36 and SAQ-7 questionnaires.

All were measured on a continuous scale. Outcome data at 3, 6 and 9 months were analysed separately. All analyses were performed using Analysis of Covariance (ANCOVA). The score at follow-up was the outcome variable, with the equivalent score at baseline included as a covariate.

5.4.9 Ethical Approval

In compliance with ethical approval, data from the TELE-ACS trial was used (Appendix 8.3).

5.5 Results

5.5.1 Study Population

A total of 337 participants (active arm = 169 vs control arm = 168) were included in this analysis. These participants were recruited between January 2022 and April 2023. Tables 4.6, 4.7 and 4.8 summarise participants' baseline and clinical characteristics, procedural characteristics, and other conditions at baseline (152). Overall, 290 participants (86%) were male, and the mean age was 58.1 years. Baseline statistics were balanced between the two arms, and most participants were receiving optimal medical therapy. There were no significant differences between the participants across both arms (152).

5.5.2 Number of Immediate Remote Consultations

During the initial 6 months, there were 108 immediate remote consultations recorded. Overall, 42% of participants initiated at least one in-hours call. Eight participants (5%) made three or more calls within this 6-month period (Table 5.1). On average, there were 0.7 calls per patient made during in-hours.

Table 5.1 Study in-hours calls logged and call decisions.

Category	Summary
Number of patients (N = 163)	0.7 ± 1.0
0 calls	95 (58%)
1 call	41 (25%)
2 calls	19 (12%)
3 calls	4 (2%)
4 calls	3 (2%)
5 calls	1 (1%)
Call decision (N = 108)	
Reassurance	59 (55%)
Reassurance + GP	29 (27%)
Advised visit A&E	15 (14%)
Advised call 999	5 (5%)
Follow-up (N = 20)	
Decided not visit A&E	6 (30%)
A&E and discharged	13 (65%)
A&E and admitted hospital	1 (5%)

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5.5.3 Outcome of Immediate Remote Consultations

Following each consultation, cardiologists determined the appropriate subsequent actions for the participants. These decisions were made considering the participants' medical histories and readings and assisted by the CDSSA. Table 5.1 and Figure 5.1 summarise the outcomes of all consultations over the initial 6 months. For most calls (82%), the advice given was either to provide reassurance or to offer reassurance along with recommending the participant consult their PCP/GP. In 14% of cases, participants were recommended to visit the nearest A&E, while in 5% of cases, they were advised to call emergency services (999). In instances where the advice was to visit A&E or call emergency services, participants visited a hospital in 70% of cases. However, of those, only 5% were admitted.

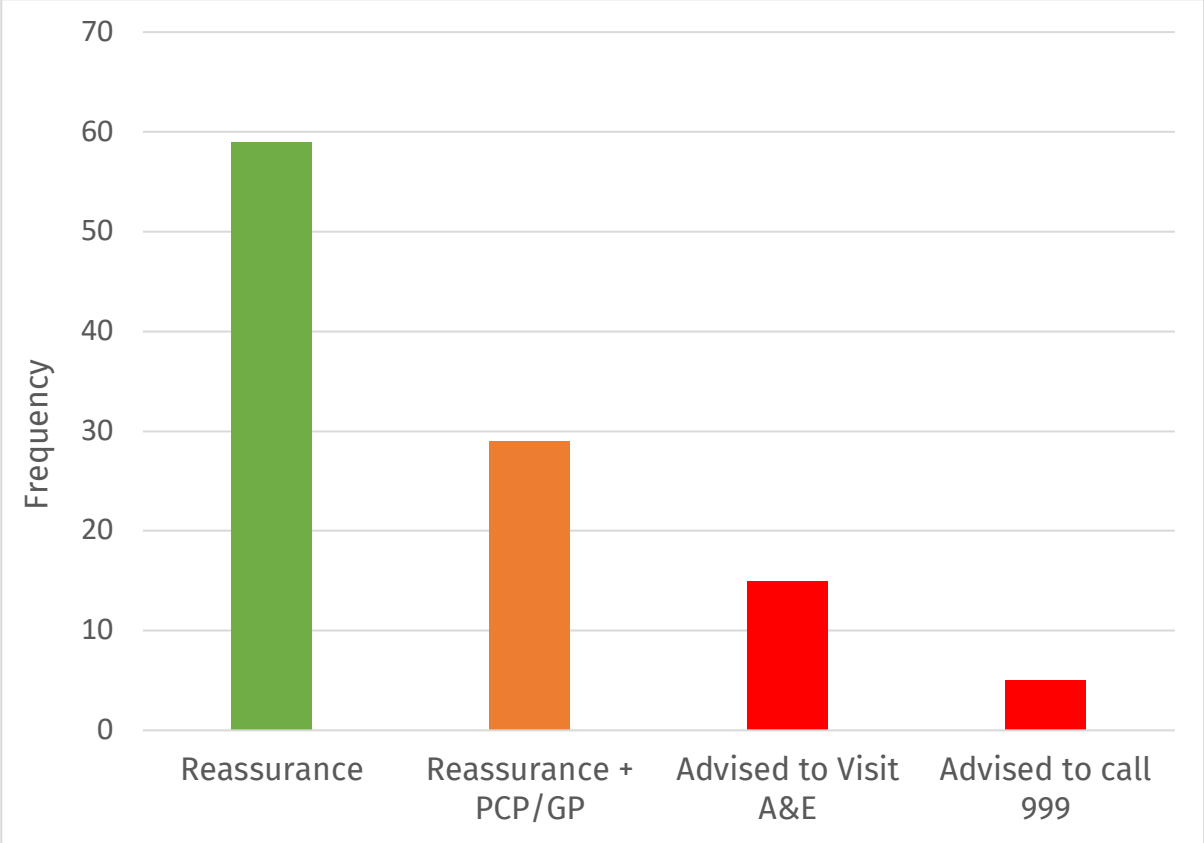


Figure 5.1 The remote consultation outcomes during the first 6 months of follow up.

5.5.4 Assumed Costs

The hospital costs for most participants were known. However, estimated costs were used for those without detailed information. A summary of the assumed costs is shown in Table 5.2. The table also shows the fixed costs used for GP visits and the costs of the intervention.

Table 5.2 Summary of costs

Category	Cost	Cost assumed
Healthcare costs	A&E attendances (*)	£250
	Readmissions (*)	£7,230
	GP visits	£42
Study costs	Equipment costs (+)	£104
(Intervention group only)	Fixed costs	£43
	Patient consultations	£7

(*) Standard costs assumed only for patients with no detailed cost information. Figures based on mean value from patients with detailed information
(+) Figure based on total equipment cost of £415, with equipment to be used by 4 patients each

5.5.5 Group Comparisons

A total of 337 subjects were randomised to either trial arm: 169 to the active group and 168 to the control group. Participants who completed less than 1 month of follow-up were excluded from the cost analysis. Two participants were excluded from the control arm, and 7 from the active arm. The costs of the study were analysed, with the analysis results summarised in Table 5.3. The figures are the mean and standard deviation costs for each study arm. All values are given in 2023 Great British Pounds. The mean differences in costs per participant between the groups are reported, along with corresponding CIs.

Table 5.3 Cost analysis (per patient)

Cost	**Control [N=166] Mean ± SD**	**Active [N=162] Mean ± SD**	**Mean difference (95% CI) (+)**
A&E attendances	163 ± 279	75 ± 162	-88 (-138, -42)
Readmissions	2525 ± 9436	837 ± 4672	-1688 (-3312, -65)
GP visits	177 ± 101	158 ± 101	-18 (-41, 2)
Total healthcare costs	2866 ± 9505	1070 ± 4696	-1795 (-3430, -160)
Equipment costs (*)	0 ± 0	104 ± 0	-
Fixed costs	0 ± 0	43 ± 0	-
Patient consultations	0 ± 0	7 ± 9	-
Toal intervention costs	0 ± 0	154 ± 9	-
Overall cost	2866 ± 9505	1224 ± 4698	-1642 (-4030, -437)

(*) Total cost divided by number of patients in Active group
(+) Differences expressed as costs for Active group minus cost for Control group

The analysis indicated significantly reduced A&E costs in the active group, with costs being lower by a mean of £88 per participant. The cost of readmission was also significantly different between the groups, as the CIs for the group difference did not cross zero. The cost of readmissions was, on average, £1688 less per participant in the active group

GP visit costs were not significantly different between groups, as the CI for the group differences crossed zero. However, a trend toward lower costs was observed in the active group, with costs being £18 less per participant on average. There was a statistically significant difference in the total healthcare costs between the groups, with the CI for the group difference not crossing zero. The total healthcare costs were £1795 less per participant in the active group. The costs of the intervention were, on average, £154 per participant.

When the cost of the intervention and healthcare were factored together, the overall costs of the study were quantified. There was a statistically significantly difference in the overall costs

between groups, with the CI not crossing zero. Lower costs were seen in the active group, with a mean difference between the groups of £162 per participant. The costs were also expressed as the total for each study group, and at the participant level. This information is summarised in Table 5.4. The total healthcare costs were approximately £300k lower in the active group compared to the control group. After factoring in the cost of the interval, the cost difference was £277k.

Table 5.4 Cost analysis (total costs for each group)

Cost	**Control [N=166]**	**Active [N=162]**	**Difference (+)**
A&E attendances	£27,053	£12,200	-£14,853
Readmissions	£419,218	£135,556	-£283,662
GP visits	£27,053	£12,200	-£14,853
Total healthcare costs	£475,713	£173,418	-£302,295
Total intervention costs	£0	£24,901	£24,901
Overall cost	£475,713	£198,319	-£277,394

(+) Differences expressed as costs for Active group minus cost for Control group

The final analyses summarised the healthcare use between the two groups. The mean and standard deviation for the number of occurrences of each type of service are shown for each group. The ratio between the groups is also shown with the corresponding CI. This was calculated as utilisation in the active group relative to utilisation in the control group.

Table 5.5 Healthcare utilisation over 6-months

Outcome	Control [N=166] Mean ± SD	Active [N=162] Mean ± SD	Ratio (95% CI) (+)
Number A&E attendances	0.36 ± 0.62	0.12 ± 0.45	0.33 (0.19, 0.58)
Number Readmissions	0.61 ± 0.98	0.29 ± 0.62	0.47 (0.31, 0.71)
Number GP visits	4.2 ± 2.4	3.8 ± 2.4	0.89 (0.78, 1.02)

(+) Ratio calculated as number of occurrences for Active group relative to number of occurrences for Control group

The data suggests that the number of A&E visits was 3 times lower in the active group than the control group. The number of readmissions in the active group was 50% lower than in the control group. While the number of GP appointments did not vary significantly between groups, there was a trend towards fewer visits in the active arm.

5.5.6 Nationwide Extrapolation

The CBA revealed that, in the intervention arm, on average £1,712.30 were saved per patient over a period of 6 months. This figure was then multiplied with the approximate number of patients diagnosed with ACS in England during 2022-2023, which was determined to be 163,000 (151). Hence, it was found that if the TELE-ACS protocol was implemented in each of these patients for a 6-month duration, NHS England would have accrued a total annual net benefit of £279,106,309.

5.5.7 QoL Data from the TELE-ACS Trial

The analyses compared the QoL outcomes between the groups at each of the follow-up timepoints. The 3-month results are summarised in Table 5.6, the 6-month results in Table 5.7, and the 9-month results in Table 5.8. The number of participants with valid data for each outcome at both the baseline and follow-up timepoint, as well as the mean and standard

deviation values are included. The mean outcome difference in is also shown, expressed as outcome in the active group minus outcome in the control group. The mean differences are presented along with their corresponding CIs. P-values indicate the significance of the differences between the two groups.

At 3 months, slight improvements in several domains were observed in the active group compared to the control group; however, the active intervention did not significantly impact on QoL outcomes as measured by the SF36 and SAQ-7 (Table 5.6). The 6-month outcomes continue to show slight improvements in the active group across the domains again, but no significant differences across all QoL measures (Table 5.7). These results indicate that the intervention did not produce significant improvements in participant-reported outcomes by this midpoint. By 9 months, the means of several outcomes (role physical, role emotional, and pain) showed large differences between the active and control groups, suggesting a possible delayed benefit of the active interventions (Table 5.8). However, these differences did not reach statistical significance, possibly due to the sample size or variability within the data.

Table 5.6 Quality of Life outcomes at 3 months

Outcome	Group	n	Baseline Mean ± SD	3 months Mean ± SD	Difference Mean (95% CI)	P-value
SF36 physical function	Control	90	54.3 ± 30.6	68.9 ± 27.2	0	0.78
	Active	90	57.2 ± 28.0	67.5 ± 29.8	-1.2 (-9.6, 7.2)	
SF36 role physical	Control	90	46.7 ± 44.2	52.5 ± 44.2	0	0.49
	Active	90	51.7 ± 45.3	57.5 ± 44.9	4.6 (-8.5, 17.7)	
SF36 role emotional	Control	90	67.0 ± 42.3	60.0 ± 43.9	0	0.60
	Active	90	62.2 ± 42.8	63.7 ± 44.3	3.4 (-9.6, 16.4)	
SF36 energy / vitality	Control	90	50.6 ± 20.0	51.2 ± 20.5	0	0.39
	Active	90	52.1 ± 20.1	53.9 ± 20.0	2.7 (-3.4, 8.7)	
SF36 mental health	Control	90	69.2 ± 19.1	67.8 ± 21.6	0	0.68
	Active	90	68.0 ± 21.4	69.1 ± 20.5	1.3 (-4.9, 7.5)	
SF36 social functioning	Control	90	60.3 ± 30.0	65.1 ± 28.5	0	0.38
	Active	90	63.2 ± 28.4	68.6 ± 24.8	3.5 (-4.4, 11.4)	
SF36 pain	Control	90	58.2 ± 28.5	72.1 ± 24.7	0	0.28
	Active	90	59.9 ± 29.3	76.1 ± 25.6	4.1 (-3.3, 11.5)	
SF36 general health	Control	90	50.2 ± 18.9	52.5 ± 23.3	0	0.82
	Active	90	52.6 ± 19.8	55.3 ± 21.3	2.7 (-3.8, 9.3)	
SAQ-7	Control	90	54.6 ± 16.7	70.4 ± 18.8	0	0.93
	Active	90	55.3 ± 19.9	70.8 ± 21.9	0.3 (-5.7, 6.3)	

Table 5.7 Quality of Life outcomes at 6 months

Outcome	Group	n	Baseline Mean ± SD	6 months Mean ± SD	Difference Mean (95% CI)	P-value
SF36 physical function	Control	69	54.4 ± 30.4	70.6 ± 29.4	0	0.61
	Active	69	56.8 ± 27.5	73.0 ± 27.6	2.5 (-7.2, 12.1)	
SF36 role physical	Control	69	47.8 ± 43.5	63.0 ± 44.5	0	0.74
	Active	69	53.3 ± 45.2	65.9 ± 42.2	2.4 (-12.2, 17.1)	
SF36 role emotional	Control	69	69.6 ± 40.7	71.0 ± 43.1	0	0.84
	Active	69	56.0 ± 43.3	70.0 ± 43.2	-1.5 (-16.3, 13.3)	
SF36 energy / vitality	Control	69	50.4 ± 18.7	52.3 ± 20.9	0	0.30
	Active	69	51.8 ± 20.1	56.0 ± 20.8	3.7 (-3.4, 10.7)	
SF36 mental health	Control	69	69.2 ± 18.6	71.2 ± 21.7	0	0.87
	Active	69	66.5 ± 21.1	72.1 ± 21.6	0.6 (-6.7, 7.9)	
SF36 social functioning	Control	69	61.2 ± 30.2	72.1 ± 27.8	0	0.45
	Active	69	61.1 ± 30.3	75.4 ± 24.7	3.4 (-5.5, 12.2)	
SF36 pain	Control	69	58.1 ± 27.8	75.9 ± 28.0	0	0.77
	Active	69	60.2 ± 30.3	77.3 ± 25.4	1.3 (-7.7, 10.4)	
SF36 general health	Control	69	50.8 ± 19.4	56.5 ± 23.3	0	0.91
	Active	69	53.5 ± 18.1	57.3 ± 21.4	0.4 (-7.1, 7.9)	
SAQ-7	Control	69	54.9 ± 16.6	72.9 ± 20.9	0	0.63
	Active	69	55.9 ± 21.1	74.7 ± 20.6	1.7 (-5.3, 8.7)	

Table 5.8 Quality of Life outcomes at 9 months

Outcome	Group	n	Baseline Mean ± SD	9 months Mean ± SD	Difference Mean (95% CI)	P-value
SF36 physical function	Control	65	55.8 ± 30.6	69.5 ± 32.8	0	0.27
	Active	65	57.4 ± 27.4	75.5 ± 26.1	5.8 (-4.4, 16.0)	
SF36 role physical	Control	65	50.8 ± 43.1	59.2 ± 45.4	0	0.11
	Active	65	53.5 ± 45.5	71.2 ± 39.8	12.0 (-2.9, 26.9)	
SF36 role emotional	Control	65	70.3 ± 40.5	66.2 ± 43.9	0	0.08
	Active	65	56.4 ± 43.7	79.0 ± 38.9	13.0 (-1.7, 27.6)	
SF36 energy / vitality	Control	65	51.5 ± 17.9	53.3 ± 25.7	0	0.42
	Active	65	51.9 ± 20.3	56.3 ± 17.2	3.1 (-4.5, 10.6)	
SF36 mental health	Control	65	69.5 ± 17.8	69.4 ± 23.3	0	0.14
	Active	65	67.2 ± 21.3	74.7 ± 16.7	5.3 (-1.8, 12.4)	
SF36 social functioning	Control	65	62.9 ± 30.0	72.3 ± 31.8	0	0.17
	Active	65	62.7 ± 31.1	78.8 ± 20.5	6.5 (-2.8, 15.9)	
SF36 pain	Control	65	59.0 ± 27.8	75.3 ± 27.0	0	0.11
	Active	65	59.3 ± 30.6	82.4 ± 23.5	7.1 (-1.7, 15.8)	
SF36 general health	Control	65	51.4 ± 19.5	52.8 ± 26.5	0	0.11
	Active	65	53.5 ± 18.1	59.5 ± 19.7	6.6 (-1.5, 14.7)	
SAQ-7	Control	65	55.5 ± 16.7	72.4 ± 20.3	0	0.18
	Active	65	56.7 ± 21.4	77.0 ± 18.4	4.6 (-2.1, 11.3)	

5.6 Discussion

In this chapter, I conducted a 6-month CBA of the TELE-ACS protocol used in the recently concluded TELE-ACS trial. The analysis adopted the perspective of the NHS and focused exclusively on direct financial costs. As anticipated, the protocol resulted in a net benefit of £277,394.00, primarily due to a significant decrease in readmissions, demonstrating its economic viability for improving system efficiencies. A statistically significant difference in overall costs was observed between the two groups after factoring in the cost of the intervention. Moreover, there was large average cost difference between the two groups. With an estimated annual saving of around £279 million, this strategy offers substantial financial benefits to NHS England, which is timely as the NHS anticipates necessary budget efficiencies for the fiscal year 2024–2025 (153).

Health economic analysis helps determine the cost-effectiveness of a program or intervention and is an important part of the process of developing public health guidance. NICE considers an intervention to be cost-effective if its benefits exceed its costs and it generates a net health benefit for patients (154). However, this criterion alone does not guarantee that an intervention or protocol is truly beneficial for patients. For instance, an intervention may be economically beneficial but may have significant adverse effects in the long run. Therefore, in order to determine if the implementation of a protocol is in a patient's best interests, it is crucial to evaluate not only its economic impact but also its safety and long-term effects on patients' health. This can be done by investigating the impact of the intervention on certain factors, such as morbidity, mortality, and QoL. These factors were the secondary outcomes of the TELE-ACS trial. It is important to assess whether the protocol prevents adverse medical events from occurring or simply delays them beyond 6 months. If the protocol only postpones these events, it means that any savings made in the 6-month period would later be cancelled out.

Additionally, it must be determined whether the protocol negatively impacts health outcomes by limiting patients' access to medical services that are clinically indicated. The TELE-ACS trial resulted in a significant reduction in hospital readmission, A&E visits, unplanned coronary revascularisation, and patient-reported symptoms, thereby addressing these areas of uncertainty.

A 6-month CBA was conducted to fully capture all associated costs and benefits of the TELE-ACS protocol. Typically, the first 6 months of post-ACS hospitalisation are associated with a higher rate of readmissions, many of which are preventable, compared to the first 9 months (155, 156). It is anticipated that the protocol would achieve greater financial gains within this initial 6 month period than if extended to 9 months. With the discontinuation of the protocol after 6 months, there is a possibility that readmission rates could return to their original levels; however, this would be influenced by the lasting effects of the protocol and patient behaviour after its cessation. Therefore, monitoring patients for 9 months provides insights into the long-term financial viability of the intervention post-removal. Analysing the outcomes of CBAs across different durations will aid in determining the most effective duration for protocol application.

A pilot RCT was conducted in 2019-2020 to evaluate the safety, efficacy, and cost-effectiveness of a smartphone app, TeleClinical Care (TCC), in patients who were discharged after being hospitalised for either HF or ACS. A CBA conducted during this trial revealed that the costs of the TCC intervention would be the same as the standard care provided to patients only once the intervention was used in 237 patients (73). The TCC intervention required more staff and closer monitoring, as patients submitted their readings on a daily basis. Hence, in comparison to the TELE-ACS protocol, the TCC intervention was associated with a higher

cost burden. However, it is difficult to compare these findings to ours, as the trial was conducted in Australia and used a different study protocol and methodology. Thus, it would be more beneficial to study the CBAs from more similar trials, like QIBO and HELP ME, to draw direct comparisons with the TELE-ACS protocol (128, 129). A systemic review of cost-related articles on telemedicine interventions published in 2002 found that 36% of the articles reported telemedicine interventions to be cost-saving in comparison to traditional clinic care (157). According to a more recent umbrella review, 7 out of 18 (39%) peer-reviewed systematic reviews published between January 2014 and February 2019 concluded that telemedicine interventions were cost-effective compared to usual care (156). The authors of these studies emphasised the need for a cautious interpretation of these results, as there was a huge diversity in the types of telehealth interventions, study protocols and methodologies, financial evaluations, and medical financing examined in these reviews. To accurately interpret the results of our CBA, more RCTs and corresponding CBAs are needed to evaluate the cost-effectiveness of telemedicine interventions in patients with ACS.

A CBA is a systematic process used to assess an intervention or program by analysing its expected costs and benefits over a long period of time. A key strength of a CBA is that it is flexible rather than standardised, and can be tailored to focus on the costs and benefits that are deemed most relevant to a project. In this research, a targeted analysis was performed to determine the direct financial effects of the protocol on the NHS. This approach was chosen to accurately calculate the cost savings that the protocol might offer to the NHS. However, it may have been possible to select a broader approach utilising a societal perspective, involving indirect financial effects. These indirect impacts may have included costs incurred secondary to absenteeism, transportation, and caregiver expenses. Moreover, non-financial aspects, including QoL, morbidity, and mortality, could also have been incorporated. The patient's

"willingness to pay" could also be used as a method for valuing benefits in a CBA (158). In short, if the CBA were extended to include these dimensions, the overall benefit of the protocol could potentially be much higher.

While the flexibility of CBAs have benefits, it may also prove to be a disadvantage. This is because the flexibility of a CBA may potentially result in biased outcomes, as analysis may include or exclude certain costs or benefits to achieve their desired result. Thus, it is important that the results of such analyses are transparent and external perspectives are used to validate their accuracy. Additionally, it may be challenging to draw direct comparisons between the results of CBAs associated with different interventions if the analyses use varying perspectives and different types of costs and benefits. For instance, one intervention may incorrectly appear to be more cost-effective than another intervention if its CBA accounts for QoL gains while the CBA for the other intervention does not. This is one of the reasons why NICE recommends the use of cost-utility analyses (CUAs) (159). CUAs describe the costs of different interventions using a standardised denominator: quality-adjusted life year (QALY) gained. This enables direct comparisons of the cost-effectiveness of different interventions. Additionally, CUAs enable the comprehensive assessment of the efficacy of interventions in terms of health outcomes. Determining the cost-effectiveness of interventions is simplified using CUAs, as interventions that lie under NICE's "willingness-to-pay" threshold of £20,000–30,000 per QALY are deemed advantageous to patients in terms of the costs and benefits (160). This makes these interventions more likely to be recommended for implementation within the NHS by NICE (159).

Although the TELE-ACS study demonstrated that a telemedicine-based approach for managing patients post-ACS reduced hospital readmissions, A&E visits, unplanned coronary

revascularisations, and PCP/GP visits, there were no statistically significant differences between the groups in terms of patient-reported QoL outcomes at 3-, 6- and 9-months post-discharge compared to baseline. However, by 9 months, a slight increase in several domains (role physical, role emotional, and pain) was observed in the active group, despite the cessation of the intervention protocol at 6 months. This could suggest a lasting effect of the intervention implemented during the first 6 months.

The £24,901 cost for our protocol implementation reflects the specific conditions and resources utilised in our study. However, the actual costs associated with the practical application of RPM program within the NHS are likely to be higher due to several additional expenses involved in the planning and implementation of the protocol. For instance, virtual ward systems integrate technology and remote monitoring to provide hospital-level care to patients at home. These systems require the establishment of necessary technology infrastructure and ongoing technical support (161). Cybersecurity lapses can compromise sensitive patient data and result in violations of patient privacy laws (162, 163). Therefore, it is important to select a secure and reliable technology platform that integrates with the clinical and technical workflows, and also adheres to the data protection regulations (161).

Successful implementation of a remote monitoring program also requires clinical leadership and governance by a registered consultant practitioner, as well as close collaboration among healthcare professionals. Clinical staff must be adequately trained in the use of remote monitoring tools and technology, and should possess the skills and knowledge necessary to deliver high-quality, compassionate care to patients. In addition, standard operating procedures should be established to provide continuous support to patients 24 hours a day in order to ensure patient safety and engagement (161).

Healthcare providers have expressed concerns regarding the financial aspects of RPM protocols throughout different studies (59). The costs associated with remote digital devices, technology infrastructure establishment, and clinical staff training may indeed lead to higher initial expenses and financial burden (164). However, these investments are crucial for achieving the desired patient outcomes and ensuring the sustainability of an RPM protocol. Moreover, it is important to note that RPM may lead to overall cost benefits for the NHS by identifying potential issues early and reducing the number of hospital readmissions as well as outpatient clinic visits (59, 165, 166). Addressing these additional elements is essential for the successful implementation and scalability of remote monitoring for cardiac patients within the NHS. Although these added costs might increase the initial outlay, they are crucial for achieving desired outcomes and ensuring the program's sustainability. Despite these increased costs, the substantial net benefit observed in our study suggests that the intervention could still offer significant economic advantages. Future studies should aim to quantify these additional costs more precisely and explore their impact on the net benefit to provide a comprehensive CBA tailored to the NHS context.

5.7 Limitations

CBAs significantly depend on the accuracy of the data used. Given the restricted access to some electronic patient records, reliance was placed on participants' memory of events, which could be prone to recall bias. This is particularly problematic for participants who completed their 3-month follow-up more than a year prior, as a longer recall period can lead to greater inaccuracies (158). Moreover, we had to approximate the costs for 64% of readmissions and 88% of visits to the A&E department. The presence of recall bias and the potential for estimation errors could lead to an overestimation or underestimation of the true findings of the CBA.

It was assumed that the costs associated with planned outpatient follow-ups were the same for both groups, and thus were excluded from this analysis. However, participants in the active group might have been less motivated to keep their outpatient appointments, believing the protocol provided a sufficient "safety net". Any compulsory rescheduling of missed appointments would generate extra costs. This could mean that the reported net benefit was potentially overestimated. However, similar scenarios might also affect the control group, which experienced higher readmission rates, potentially leading to more missed appointments and the need for more comprehensive follow-ups. The costs related to ambulance use and calls to emergency services were not accounted due to unavailable data. Including these costs might have shown a greater net benefit for the active group.

Another limitation of the study is that several outcomes (role physical, role emotional, and pain) at 9 months did not reach statistical significance, despite showing larger mean differences in between the groups. This may be attributed to the sample size or variability within the data, which could limit the power to detect significant effects. Furthermore, an assumption that the

active group mirrors the demographic of individuals with ACS across England, in both characteristics and event rates, was made for the national extrapolation. The active group, recruited from London, displayed a variety of baseline and clinical characteristics, suggesting that it is likely representative of diverse English regions. Implementing the protocol on a national scale might reduce equipment costs due to economies of scale. However, this possible cost reduction may be mitigated by the fact that equipment prices for this trial were secured at a negotiated rate.

5.8 Future Work

Conducting a more comprehensive CBA would offer a more realistic assessment of the costs and savings associated with the protocol, thereby enhancing the CBA's precision. Since variations in readmission rates occur at 3, 6, and 9 months, a 9-month evaluation could determine when the protocol yields the most cost benefits. Furthermore, the protocol might offer greater economic advantages for patients at higher risk of readmission due to factors such as prior coronary procedures and DM (167, 168). Categorising patients based on these risk factors for detailed analysis is one possible future approach. Additionally, conducting CUAs at 3 and 6 months would facilitate comparisons with other interventions and determine whether they align with the cost-effectiveness standards established by NICE.

5.9 Conclusion

The recently concluded TELE-ACS trial monitored 162 patients over 6 months and demonstrated that a novel telemonitoring protocol resulted in a net benefit of £277,394.00 for the NHS. This suggests that the intervention is an economically feasible option for reducing readmissions of patients with ACS within 6-months post-discharge. However, a comprehensive assessment of the protocol's safety and long-term effects is essential to validate its widespread implementation.

6 Discussion and Future Work

6.1 Summary of Thesis Aims

This thesis had four main objectives which are summarised as follows:

- The first aim was to use a systematic review and meta-analysis to rigorously examine the existing evidence on the use of telemedicine for managing patients post-ACS.
- The second aim was to design and validate a CDSSA for the remote management of patients post-ACS in a nonhospital setting.
- The third aim was to use a bespoke hybrid remote telemonitoring system (TELE-ACS) to monitor patients discharged from the hospital following ACS, employing a randomised controlled trial format to evaluate the system's efficacy.
- The fourth aim was to conduct a 6-month CBA of the TELE-ACS protocol and assess its impact on the health-related QoL in patients post-ACS.

6.2 Summary of the Main Findings

6.2.1 Chapter 2

Chapter 2 is titled “The Efficacy of Telemonitoring in the Management of Patients Post-ACS: A Systematic Review and Meta-Analysis of RCTs”. The main findings are as follows:

- Telemonitoring for patients post-ACS significantly reduced the number of non-elective hospital readmissions compared with standard care. However, there are several obstacles to overcome before telemonitoring can be widely implemented.
- Telemonitoring is a safe strategy for patient post-ACS and could possibly lead to better outcomes.
- Compliance with telemonitoring interventions is essential for improving clinical outcomes and depends on an intervention being simple and quick. Additionally, intervention benefits must be made apparent to patients.
- The limited data from a single RCT using the EQ-5D showed improvements in self-reported QoL for both the active and control groups. The lack of significant differences highlights the need for more research to determine the specific effectiveness of these interventions.
- The meta-analysis demonstrated that telemonitoring significantly reduced the number of non-elective hospital readmissions compared with standard care. However, telemonitoring did not significantly reduce the rate of MACE or all-cause and CV mortality.
- There were differences in the metrics recorded for telemonitoring and length of follow-up between the studies, which makes it difficult to draw conclusions on the efficacy of telemonitoring as a whole.
- Additional large-scale RCTs are needed to clarify the metrics that need to be monitored for patients post-ACS.

6.2.2 Chapter 3

Chapter 3 is titled “Evaluating a Telemedicine-Based Algorithm for the Remote Management of Patients Post-ACS”. The main findings are as follows:

- The CDSSA, developed by a panel of senior cardiologists based on their interpretation of the European Society of Cardiology guidelines for managing ACS, is designed to aid, rather than mandate, clinical decisions.
- Ten cardiac cases were prepared, each describing a scenario in which a patient is discharged post-ACS with a telemedicine package and subsequently experiences symptoms such as chest discomfort, acute breathlessness, sustained palpitations, or other CV issues, and requires urgent remote medical consultation. The study evaluated management decisions before and after the use of the CDSSA. The primary metric for the analysis was the deviation in points from the BPA.
- Thirty-two doctors completed the study. Doctors independently evaluated the scenarios and made management decisions. Following a period of at least 90 days, these same scenarios were reassessed by the same doctors with the aid of the CDSSA.
- The results suggested a significant difference in outcomes between timepoints. The number of points away from the BPA decreased post-CDSSA, by an average of 0.2 points.
- The number of points away from the BPA post-CDSAA decreased by a mean of 0.33 for non-cardiology doctors and 0.36 for junior doctors.
- Junior doctors appeared to benefit most from the CDSSA.
- The use of the CDSSA resulted in responses being more aligned with best practices, thereby improving the safety and precision of decision-making processes.

6.2.3 Chapter 4

Chapter 4 is titled “Remote Assessment of Patients with High CV Risk Post-ACS (TELE-ACS): An ACT”. The main findings are as follows:

- A total of 337 participants were enrolled in the study, with 169 enrolled in the active group and 168 patients to the control group. Overall, the mean age of both groups was 58.12 years, and 14% of the participants were female.
- The participants made a total of 169 calls, 64% of them were made during the active trial hours. The most reported symptom was chest pain/discomfort, followed by shortness of breath, palpitations, and general weakness. Of the 108 calls made during the active hours, 54.6% resulted in participants receiving reassurance. 26.9% were advised to visit their GP, 13.9% told to visit A&E, and 4.62% were recommended to call emergency services.
- By the 6-month follow-up, 13 participants in the active arm were readmitted to hospital versus 48 in the control arm. Thus, the time to readmission (primary endpoint) was reduced with the telemonitoring strategy, as were visits to A&E and MIs. Stroke occurrence was lower in the active arm; however, no difference all-cause death was seen between the groups.
- Participants in the telemedicine group had fewer unplanned coronary revascularisations than those in the control group (3% vs 9%) and were less likely to report chest pain (9% vs 24%), breathlessness (21% vs 39%), and dizziness (6% vs 18%).
- Although telemonitoring in the active study arm ceased at 6 months. the initial effect between 0–6 months was large enough to leave a legacy effect up to 9 months.
- At the 9-month follow-up, hospital readmissions remained lower in the active group compared to the control group (HR 0.35; 95% CI 0.21–0.59). Emergency department visits were also lower (HR 0.66; 95% CI 0.46–0.94), as was the rate of invasive

coronary angiography and/or angioplasty (4% vs 10%; p = 0.03). However, there were no longer any differences in symptoms between the two groups.

- This study demonstrated that remote monitoring using a clinical decision algorithm protocol based on patient symptoms as well as 12 lead ECG, BP, and oxygen levels, results in a significant reduction in hospital readmissions, ER visits, unplanned coronary revascularisations, and patient-reported symptoms for patients post-ACS.

6.2.4 Chapter 5

Chapter 5 is titled “Six-months Cost-Benefit and QoL Analysis of a Novel post-ACS Remote Monitoring Protocol”. The main findings are as follows:

- Data extracted from the TELE-ACS trial was used in accordance with ethical approval.
- Costs were defined as the expenses associated with implementing the protocol within the active group.
- Benefits were defined as the monetary savings resulting from decreased readmissions, A&E visits, and GP consultations within the active group.
- Significantly reduced A&E costs were observed in the active group.
- The cost of readmissions was found significantly differ between the groups, being on average, £1688 less per patient lower in the active group.
- The total healthcare costs were approximately £300k lower in the active group. After factoring in the cost of the intervention, the cost difference was £277k.
- The number of A&E visits was 3 times lower in the active group than the control group, and the number of readmissions in the active group was half that of the control group. However, the number of GP appointments did not vary significantly between groups, although there was a trend towards fewer visits in the active group.
- There were no statistically significant differences between the groups in terms of patient-reported QoL outcomes at 3-, 6-, and 9-months post-discharge compared to baseline. However, by 9 months, a slight increase in several domains (role physical, role emotional, and pain) was observed in the active group.

6.3 Discussion

The TELE-ACS trial demonstrated that remote monitoring using a clinical decision algorithm protocol based on patient symptoms in combination with 12 lead ECG, BP, and oxygen levels for 6 months results in a significant reduction in hospital readmissions, A&E visits, unplanned coronary revascularisations and patient-reported symptoms. The TELE-ACS protocol yielded a net benefit of £277,394.00 over 6 months. Therefore, this intervention represents a financially viable approach to reducing readmissions in patients with ACS.

My PhD dissertation began with a review of the existing literature, enabling me to explore the knowledge and research gaps related to the use of telemedicine for managing patients following ACS. Evidence regarding the effectiveness of telemonitoring for patients following ACS was significantly limited compared to the other strategies used for monitoring cardiac patients, such as those with HF. To the best of our knowledge, no previous strategies in the UK had used well-validated technologies for monitoring patients post-ACS by capturing heart rate, BP, oxygen saturation and ECG data, combined with urgent remote consultations with a cardiologist. Only two previous studies in Europe have involved implantable cardiac monitors for the detection of serious arrhythmic events, which were monitored daily by study physicians, or the use of smartphone technology for BP regulation. There is a need to develop strategies to identify the critical parameters that require monitoring in patients with ACS. Furthermore, it is essential to establish the most effective methods, frequency, and duration of monitoring of these parameters to substantially improve clinical outcomes and identify the obstacles and challenges associated with implementing such monitoring.

My findings from the TELE-ACS trial suggested that a telemonitoring system-based algorithm could significantly reduce hospital readmissions for patients post-ACS. This method proved to

be reliable, quick, and usable. It equipped and empowered high-risk patients with ACS to seek urgent medical help upon experiencing symptoms and to make informed decisions about when to present to emergency services. This approach has potential applications in other common CVDs. The scope of this study extends beyond achieving its primary and secondary outcomes and the financial savings, delving deeper into the impact of this approach on the psychological well-being of patients immediately after hospital discharge. This telemedicine initiative alleviatesd physical health burdens and supported psychological recovery. This is particularly crucial for patients recovering from a heart attack, as they require additional support during the first few months post-discharge. The results are highly encouraging and have the potential to alleviate some of the current pressure on the NHS, as hundreds of thousands of individuals await urgent heart tests, treatments, and check-ups. Enhanced by significant advancements in remote health services, telemedicine may free up significant amounts of time and space in hospitals while maintaining patient safety and improving outcomes.

The RPM service provided post-discharge was associated with a reduced risk of non-elective readmissions to the hospital compared to standard care. Thirteen participants (8%) in the active arm were readmitted to hospital within 6 months versus 48 in the control arm (HR 0.24; 95% CI 0.13–0.44; $p < 0.001$). This outcome was similar to the findings of Indraratna et al. (2022), who observed a significant decrease in unplanned hospital readmissions after 6 months of follow up when using remote BP and heart rate monitoring (21 in the intervention group versus 41 in the control group; $p = 0.02$). This included reductions in cardiac-related readmissions (11 versus 25; $p = 0.03$). Similarly, Garanin et al. (2022) monitored patients with ACS and HF using a combination of sphygmomanometers, weighing scales and activity monitors. Four patients in the monitored group were hospitalised due to DHF or an ACS episode, within 30 days. In contrast 13 patients in the control group were hospitalised for the same reasons ($p =$

0.027; odds ratio =3.4; 95% CI 1.1–10.8). Our findings are unique as our research demonstrated that directly transmitting crucial data and information to the cardiology team, combined with immediate remote consultations with cardiologists, evidently enhanced the quality of care. This approach led to fewer hospital admissions, shorter average hospital stays, fewer patient-reported symptoms, and reduced visits to A&Es, all while maintaining patient safety.

6.4 Limitations

In the systematic review and meta-analysis there was notable heterogeneity in the telemonitoring interventions across the RCTs, from the parameters being monitored to the method and frequency of monitoring. Consequently, the overall effectiveness of telemonitoring cannot be determined. Additionally, there was a lack of consistency in the measurements of MACE and readmission types between the included RCTs. This lack of consistency is unavoidable in such reviews and, therefore, the results have to be considered in this context. As only one RCT assessed QoL and the impact of the interventions on QoL, a meta-analysis could not be performed to evaluate this outcome.

Regarding the CDSSA study, reproducibility and generalisability were both limited by the small sample size of 32 doctors. Furthermore, nearly one-quarter of the participants were lost during the follow-up, potentially opening the study up to attrition bias. This bias occurs when there are differences between the individuals who choose to quit a study and those who stay, and it is possible that these differences, rather than the intervention itself, are responsible for any effects found. Additionally, we were unable to recruit any doctors working in A&E departments because they lacked the necessary free time to complete the surveys.

In the TELE-ACS trial, we recruited mostly men. Our population could have been significantly skewed in comparison to a general ACS population globally; however, it reflected our centre's population. Because data for some of the symptoms were collected retrospectively, there was a possibility of recall bias among patients. Additionally, there were challenges associated with infrastructure requirements, technological barriers, regulation, reimbursement, patient engagement and acceptability, and data security and privacy. In addition, participants were only eligible for the intervention if they had a smartphone or smart device. Furthermore, the

high level of support given to the active group may be challenging to replicate outside a trial setting, requiring significant investment and training.

In the CBA and QoL analysis, costs had to be estimated for some of the readmissions and A&E visits. Therefore, the real CBA outcome could be overestimated or underestimated depending on the amount of recall bias and estimating error. In the QoL analysis, despite larger differences in the means between the active and control groups, the study did not approach statistical significance in several domains after 9 months. (e.g., role physical, role emotional, and pain). This could be due to insufficient power to detect a meaningful effect due to the small sample size or data variability.

6.5 Future Work

Further studies need to establish the feasibility of implementing such interventions in different healthcare systems using system-based CBAs, as well as uncover the causal relationship between remote monitoring and readmission rate reductions. If implementation is found to be infeasible, additional research involving a larger sample size will be necessary to evaluate the longer-term clinical and health economic outcomes.

6.6 Conclusion

The findings of this thesis suggest that remote monitoring with a clinical decision algorithm protocol based on patient symptoms, in combination with 12 lead ECG, BP, and oxygen levels, results in a significant reduction in hospital readmissions, ER visits, unplanned coronary revascularisations and patient-reported symptoms for patients following ACS. Therefore, the TELE-ACS protocol represents a financially viable approach to reducing readmissions in patients post-ACS.

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7 Supplementary Appendix

8.1 Patient information sheet – summary

Imperial College Healthcare NHS Trust | Imperial College London | Research Governance and Integrity Team

SUMMARY PATIENT INFORMATION SHEET:

TELE-ACS: randomised controlled trial investigating the use of a remote monitoring system for post-Acute coronary syndrome (ACS) patients, as assessed by well-validated technologies coupled with an urgent remote consultation with a cardiologist and clinical decision algorithms.

"A study using a remote monitoring system to assess patients who are discharged from hospital following an acute myocardial infarction when they experience chest discomfort, acute breathlessness, sustained palpitations or other cardiovascular symptoms and requires attention".

Thank you for showing an interest in this study. The first page of this information sheet sets out a brief summary. The rest of the document provides more detail. You can ask us for more information at any point -- you are not obliged to participate and can withdraw at any time.

What will the study involve?

As applicable, you might discharge from hospital with the telemedicine package post-PCI procedure. The research and clinical team will use a remote monitoring digital ECG, blood pressure (BP), and oxygen saturation readings for assessment when you develop possible cardiovascular symptoms. You are going to take a 12-lead ECG, BP, and pulse oximetry when required/advised, which might take less than 10 minutes to perform. This information will inform the trial cardiology team on the most appropriate course of further management; this is completely painless and poses no harm. **The table below tells you about the criteria if to take part:**

You must meet these criteria:	**You must not have:**
- Post-PCI procedure; able to give informed consent. - You have had a Myocardial Infarction (heart attack); and your most recent blood test indicated a high level of a substance called troponin (which indicates you have had a cardiac event); and you have had a non-surgical procedure to place a stent (s) in narrowed blood vessels in your heart - Fit to be discharged and have a smartphone.	- Inability to use/engage with the technology. - Life expectancy of 9 months or less.

Condition Studied	**Study Length**	**Number of**
Post-ACS	9 months	You will be provided with a 12-lead ECG device (Smartheart) + BP cuff + pulse oximetry for personal use at home for 6 months, applied when needed for readings as specified later. - You will be also asked to fill out a questionnaire pre-discharge and at 3, 6 and 9 months post-discharge. - You will receive scheduled phone calls as a follow-up at 3, 6 and 9 months. - There will be follow up training calls to perform a remote ECG post-discharge.

- Other than maximise convenience to you by being in the comfort of your home, there are no direct benefits to you beyond knowing you are helping with research.
- The study has no risk of harm, and the device is safe.
- We will protect the confidentiality of your data at all times.

This study has indemnity and insurance coverage from Imperial College London. Your data will be treated in full confidentiality, details of which are outlined in the participant info sheet. Thank you.

Study contact details: nasser.alshahrani@nhs.net Signed: Dr Ramzi Khamis 01/12/2021

8.2 Patient consent form

Imperial College Healthcare NHS Trust | Imperial College London | Joint Research Compliance Office

CONSENT FORM

Study Title: TELEMEDICINE IN HIGH-RISK CARDIOVASCULAR PATIENTS POST-ACS (TELE-ACS)
Principle Investigator: Dr Ramzi Khamis

Please initial the box against each statement that you agree with

1. I confirm that I have read and understood the patient information sheet (PIS V3 1st November 2021) for the above study and have had the opportunity to ask questions.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that sections of my medical notes and information collected during the study may be looked at by responsible individuals from regulatory authorities; from the NHS Trust and Imperial College London where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4. I give / do not give (delete as applicable) consent for information collected about me to be used to support other research in the future, including those outside of the European Economic Area (EEA).	
5. I understand that If I lose capacity to consent during the study, I will be withdrawn. Identifiable data already collected with consent would be retained and used in the study. No further data would be collected, or any other research procedures carried out on or in relation to my participation.	
6. I understand that my GP will be informed of my participation in this study. The research team and the direct care team will review all the results/findings including the incidental findings. These findings will be documented and will be reported your GP and the clinical care team.	
7. I agree to take part in the above study.	
8. I am happy to be contacted with a lay summary of the main findings of the study.	
9. I give / do not give (delete as applicable) consent to being contacted to potentially taking part in other research studies.	

Name of Patient	Date	Signature
Name of person taking consent	Date	Signature

When completed, 1 for patient; 1 for researcher site file (original); 1 to be kept with hospital notes

Patient Identification Number:	

Consent form V1
11th August 2021
IRAS Project ID: **291565**

8.3 Health Research Authority Research Ethics Committee Approval

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

Dr Ramzi Khamis
Imperial College London, Hammersmith Campus
Vascular Sciences, 5th floor ICTEM Building
London
W12 0NN

02 November 2021

Dear Dr Khamis

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Remote Acute Assessment of Patients with High Cardiovascular Risk Post-Acute Coronary Syndrome.**
IRAS project ID:	**291565**
Protocol number:	**21HH7034**
REC reference:	**21/LO/0651**
Sponsor	**Imperial College London**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

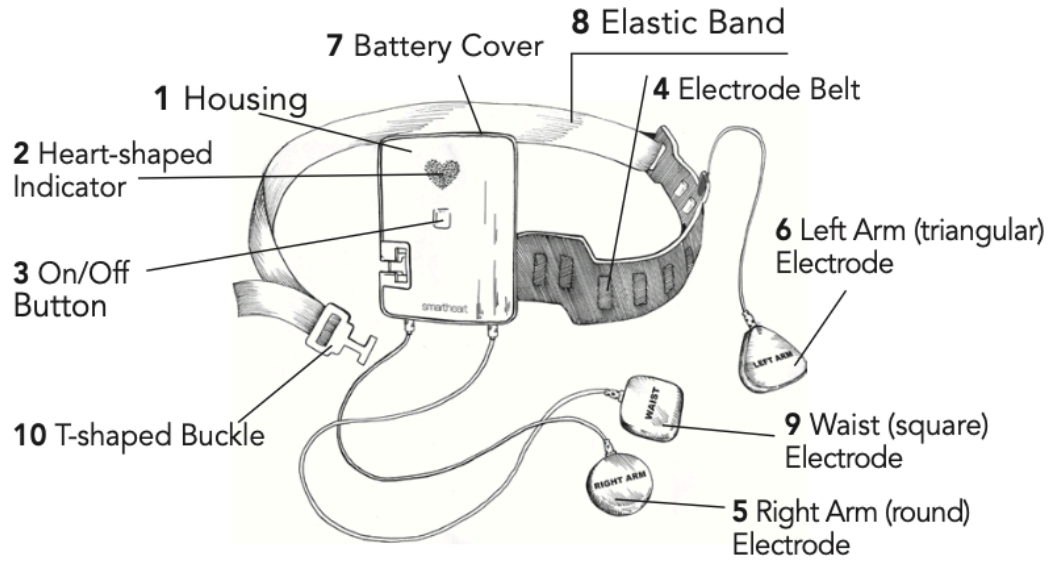
8.4 Patient support instructions - SHL Smartheart





SmartHeart®

The following diagram shows the Smartheart components from the front:



Smartheart Components – Front

1 Housing: Contains the electronics and batteries.

2 Heart-shaped Indicator: Located on the front of the housing, is continuously illuminated when the device is on.

3 On/Off Button: Activates and deactivates the Smartheart device.

4 Electrode Belt: Contains electrodes and is attached to the housing.

5 Right Arm (round) Electrode: A round electrode that is attached to the bottom of the housing by a wire.

6 Left Arm (triangular) Electrode: A triangular electrode, attached directly to the electrode belt by a wire.

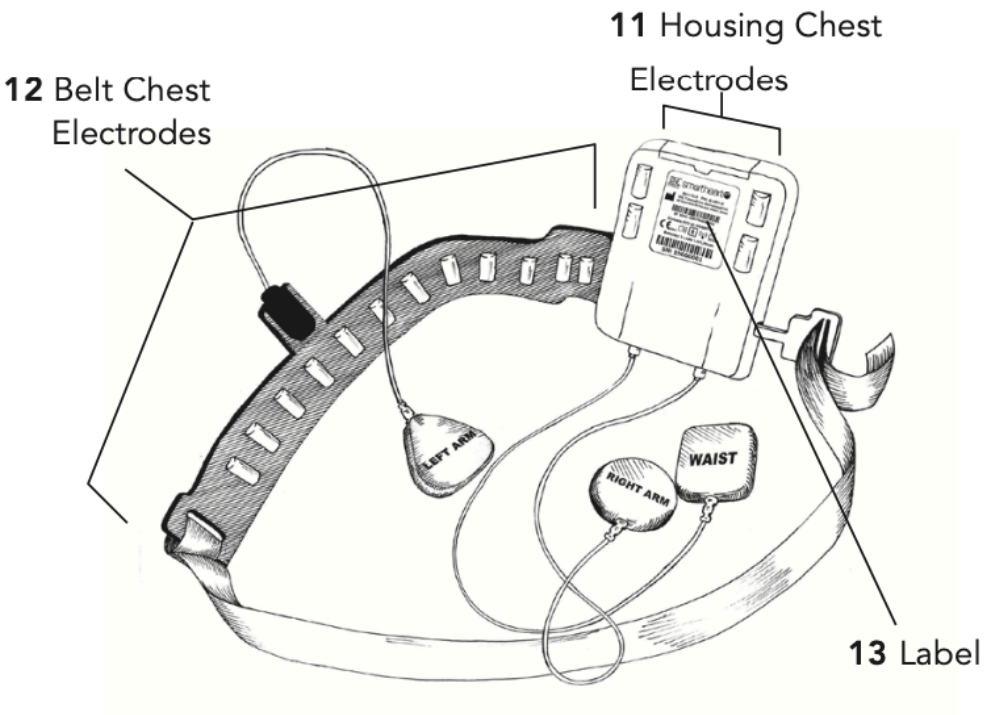
7 Battery Cover: Holds two lithium AAA batteries and is located on the top of the housing.

8 Elastic Band: Elastic extension of the electrode belt with T-shaped buckle attached.

9 Waist (square) Electrode: A square electrode that is attached to the bottom of the housing by a wire.

10 T-shaped Buckle: Used to adjust the length of the elastic band and claps onto the housing.

The following diagram shows the Smartheart components from the back:

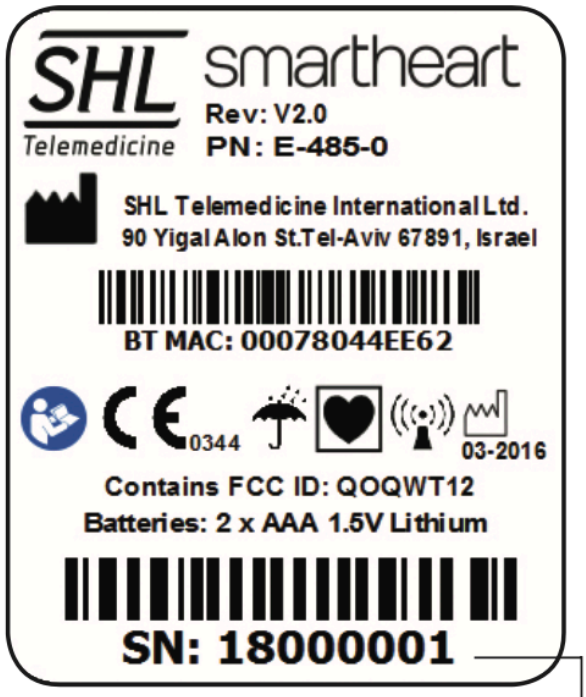


Smartheart Components – Back

11 Housing Chest Electrodes: Four electrodes located on the back of the housing.

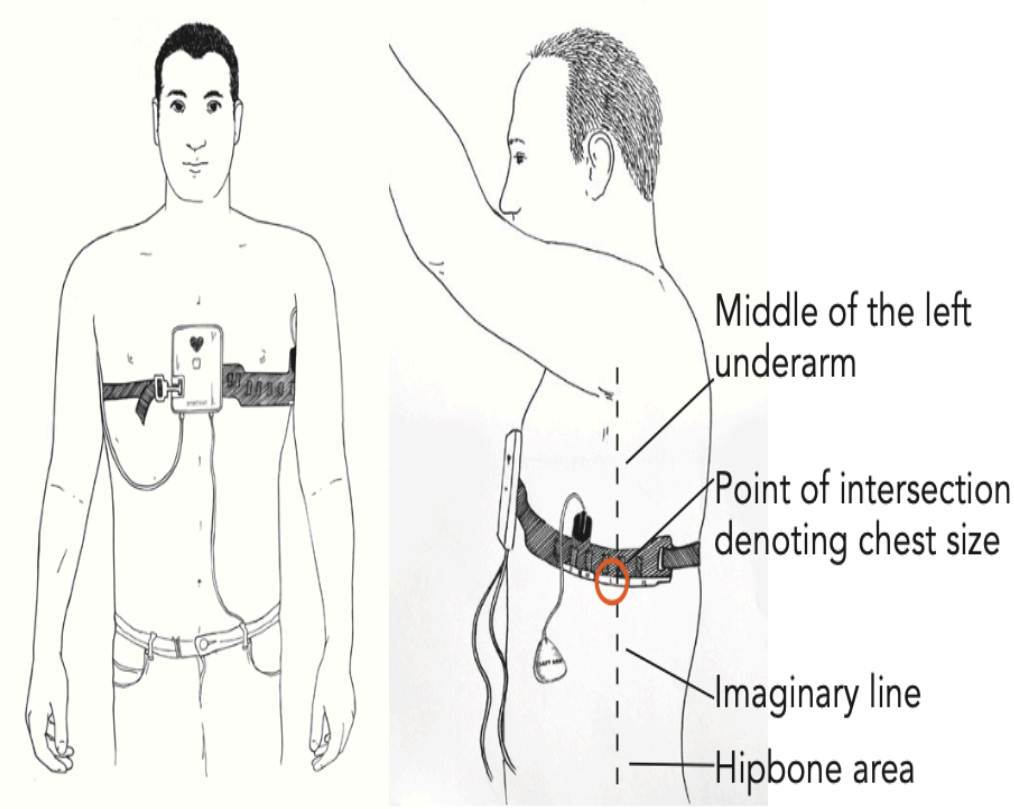
12 Belt Chest Electrodes: The twelve electrodes located on the inner side of the belt.

13 Label: Specifies Product Information including serial number of the Smartheart device.

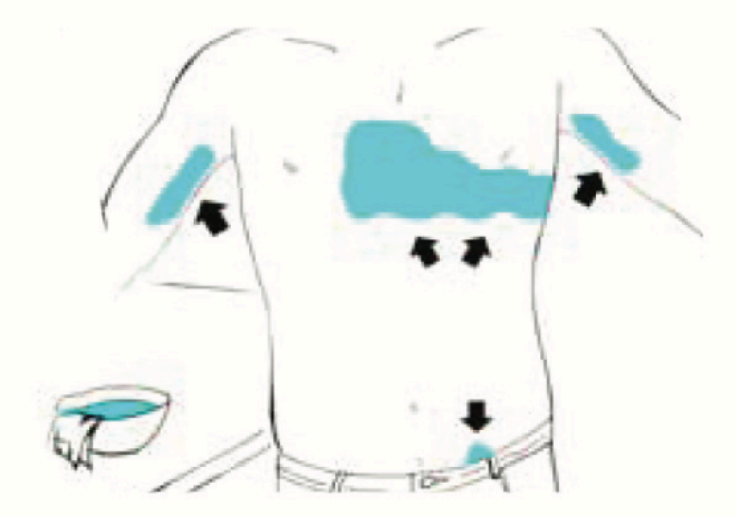


PIN Code/Serial Number

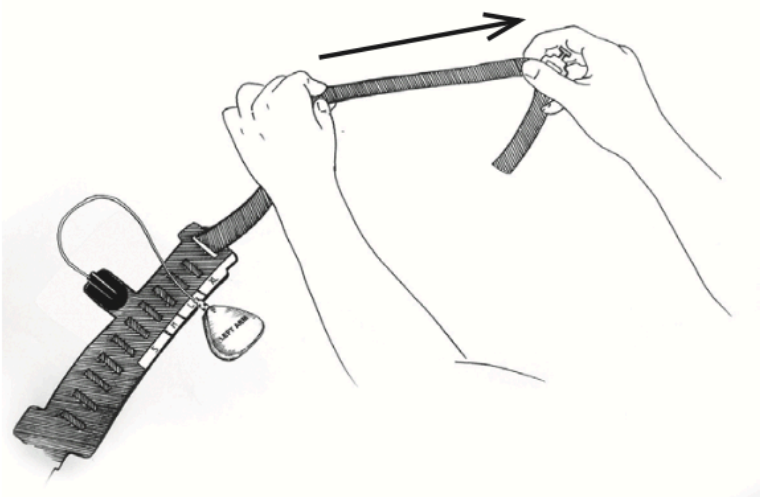
Draw an imaginary line between the middle of the left underarm and the left hipbone to identify the size segment letter that intersects with that line.



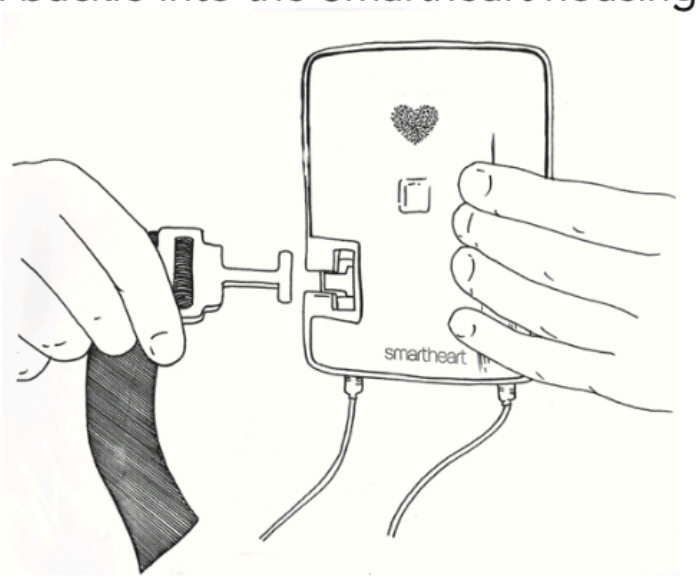
Moisten with water body parts that need to come in contact with the electrodes (left & right arm inner parts, waist and chest).



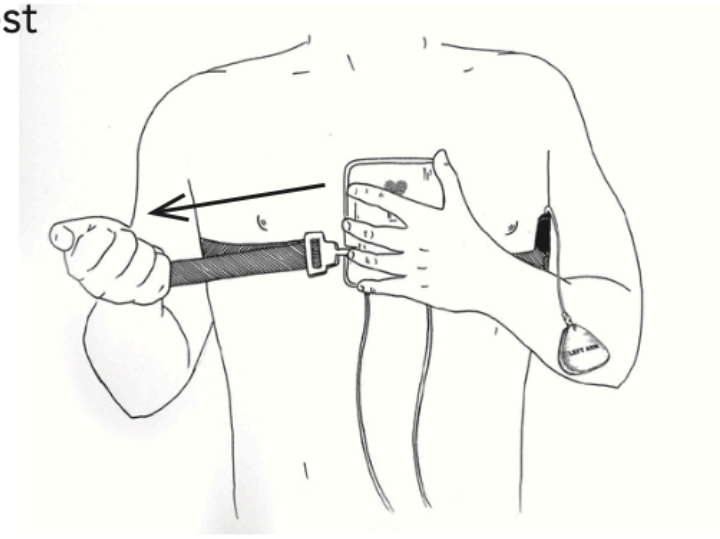
To facilitate attaching the device to your body, slide the T-shaped buckle in the direction of the arrow to the end of the elastic band.



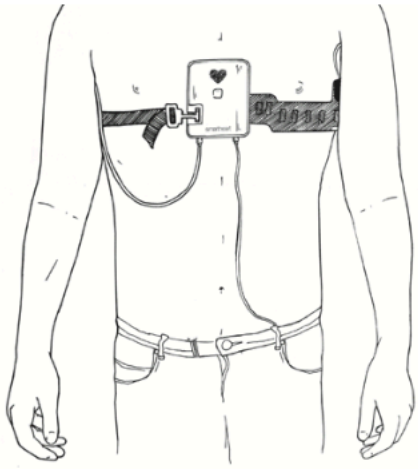
Place the chest electrodes, (on the back of the Smartheart housing), against the center of your chest, wrap the electrode belt around your chest and snap the T-shaped buckle into the Smartheart housing.



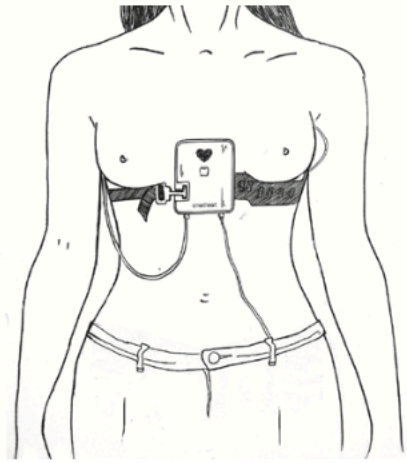
Once the buckle has been clasped, tighten the elastic band until it is tight enough to hold the housing in place. Verify that the position of the housing is in the center of your chest



Position the belt:
Male: Approximately one centimeter (1/2 inches) under the nipples.



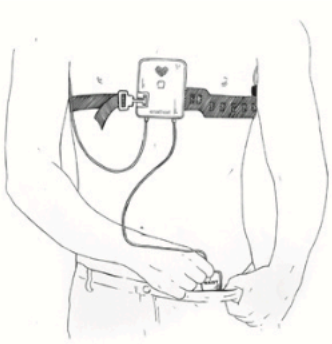
Female: Immediately under the breasts, as high as possible.



! NOTE: Make sure that:

- The heart shaped indicator is On and positioned in the middle of the chest.
- The electrodes on the back of the housing are positioned firmly against your chest.
- The electrode belt is lying flat against your body and is not twisted.

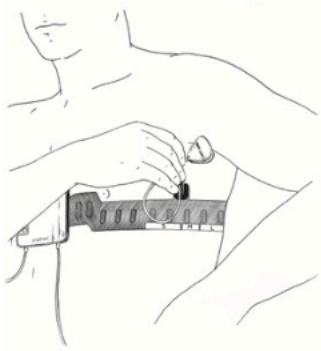
Position the waist (square) electrode at the belt line underneath your lower garment and against your bare skin, halfway between your navel and left hip. Either side of the waist electrode can be placed against the skin.



Raise your right arm, place the Right arm (Round) electrode in your armpit, under your exposed right underarm against the skin, and lower your arm to hold the electrode.



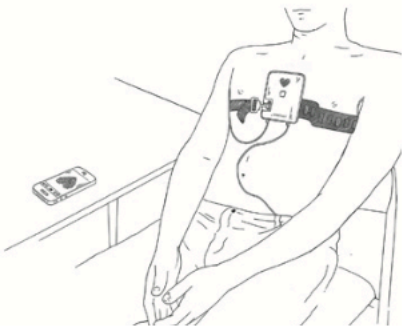
Raise your left arm, place the Left arm (triangular) electrode, that is attached directly to the electrode belt, in your armpit, under your exposed left underarm against the skin, and lower your arm to hold the electrode."



⚠ CAUTION:

Verify that the Left arm (triangular) electrode wire does not caught accidentally between the electrode belt and your chest.

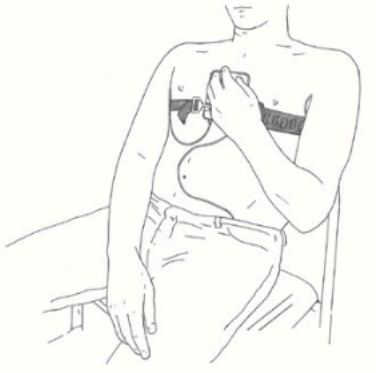
1 ECG is preformed while sitting down, leaning slightly, placing both hands between the thighs and holding lightly against their sides. Make sure that there is contact between the inner arms and the electrodes on the outside of the belt.



2 The ECG data recording and transmission is controlled via the Bluetooth-enabled communication device.

NOTE: While performing the ECG, you should sit completely still and lean back slightly. No vigorous muscle exertion or tension is required. During the recording and transmission, the heart-shaped indicator blinks. Transmission is activated from the Bluetooth-enabled communication device.

NOTE: If the housing chest electrodes are not in complete contact during the recording, use your left hand to press the housing flat against your skin.



REPLACING THE BATTERIES

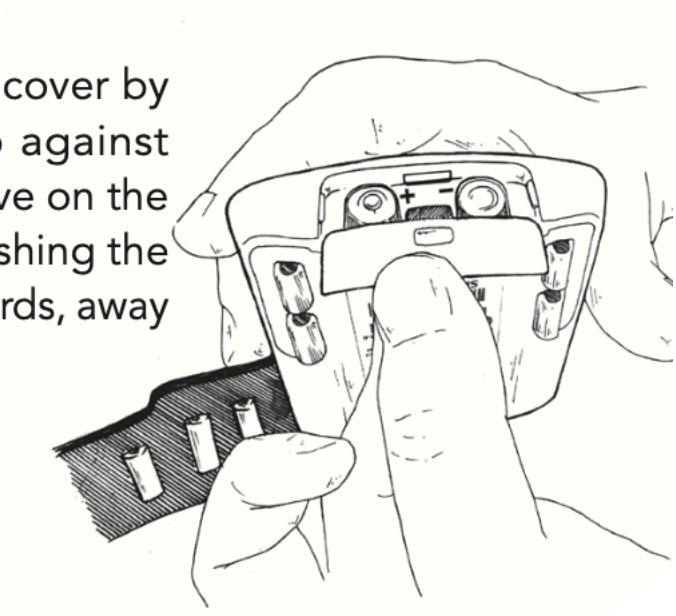
The Smartheart comes with two AAA lithium (1.5V) batteries.

NOTE: Only lithium batteries should be used. In case of an emergency, alkaline batteries can be used, but only if they are fully charged. Alkaline batteries are sufficient for small number of ECGs.

The Smartheart will indicate a low battery. After pressing the On/Off button to turn the device on, low battery is indicated by the heart-shaped indicator blinking three times and then turning off.

The battery cover is located at the top of the Smartheart housing.

1 Remove the battery cover by placing your thumb against the submerged groove on the battery cover and pushing the door down and outwards, away from the device.



2 Remove the old batteries and place the new batteries in the recess, according to the + and - markings engraved in the housing.

The + marking on the housing indicates that the + side of the battery should be facing upwards.

3 Place the battery cover halfway over the batteries, and push and slide the battery cover into the housing until it clicks.

NOTE: Verify that the batteries are operating properly by pressing the On/Off button and making sure that the heart-shaped indicator lights up.
If this indicator does not light up, remove the batteries and repeat the procedure above.

For assistance, you may contact us at:
support@smartheartpro.com.
Old or used batteries should never be disposed of by burning.

ECG Application Workflow

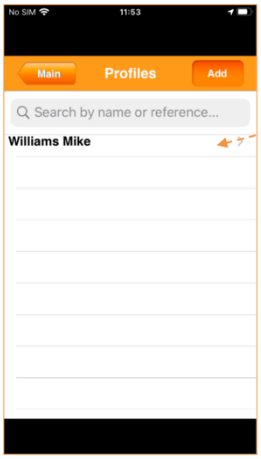
smartheart Main Menu



Application main menu

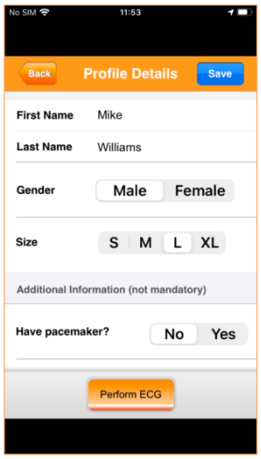
- Click on "Perform ECG" to acquire a new ECG

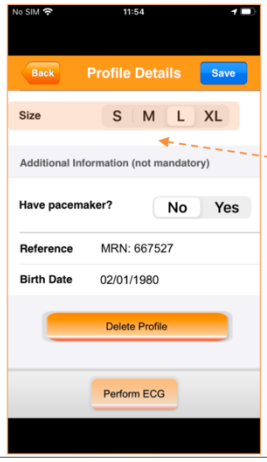
smartheart Patient / Order selection



- Patient name or defined user

smartheart Patient Information

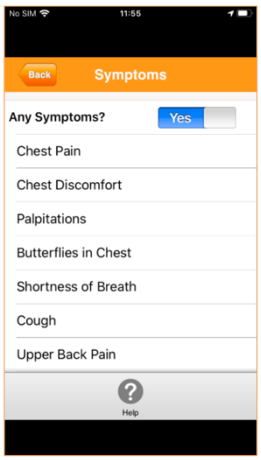


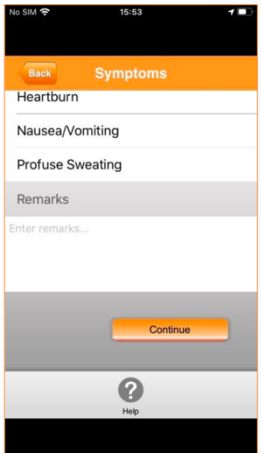


Patient information screen

- Field to be filled out when setting up the patient (according to Research discretion / decision)
- The "Size" field for the electrode belt should be set
- Click on "Perform ECG"

smartheart Symptoms

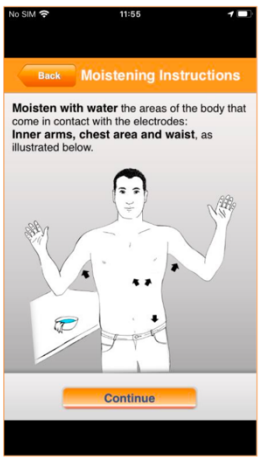




Symptoms

- The patient may report symptoms.
- Symptoms selected here will be reported back in the ECG report.
- Select any patient reported symptoms and click Continue

smartheart ECG Preparation



Guidance screen
reminding the patient to moisten chest

➢ click "Continue"

smartheart ECG Preparation

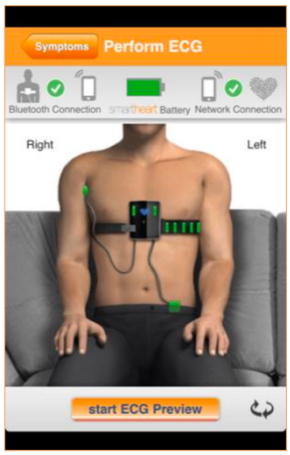


Guidance screen
Reminding the patient to keep a sitting position and Smartheart device placement

- Attach SmartHeart® to the chest
- Turn on SmartHeart device

➢ click "Continue"

smartheart ECG Preparation



Status Screen



- Bluetooth status – turns green when SmartHeart is On and connected to the tablet

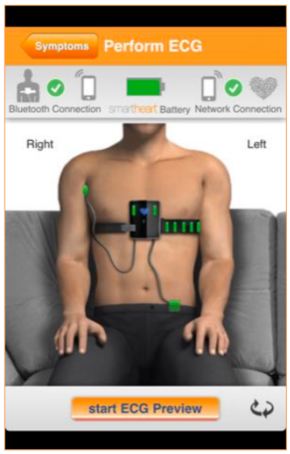


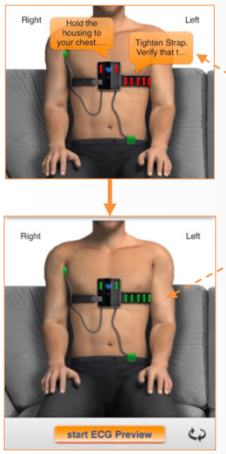
- SmartHeart Battery Status – confirms SmartHeart battery level. SmartHeart uses standard replaceable AAA Lithium batteries.



- Internet Connectivity Status – Confirms Tablet internet connectivity and connection to Smartheart servers.

smartheart ECG Preparation



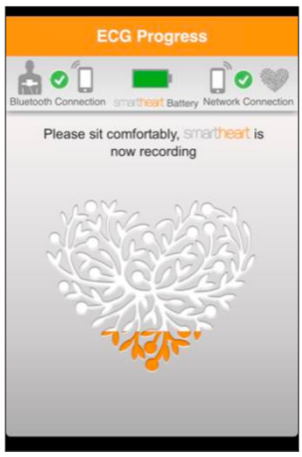


Electrodes status
a real time display of the ECG electrodes placement

- On screen guidance helps the provider attach the device correctly and ensure electrode connectivity
- When electrodes are placed correctly on the patient's chest, all electrodes will show up green

➢ Ensure all electrodes are Green and click "start ECG Preview"

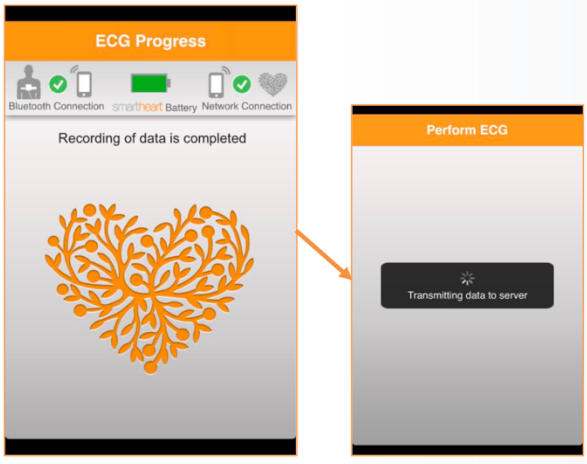
smartheart ECG Acquisition



ECG Acquisition

- ECG is acquired
- Patient will be asked to remain calm and relaxed keeping the same position
- The ECG acquisition process takes about 30 seconds

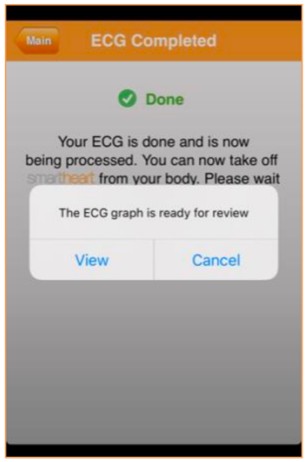
smartheart ECG Acquisition



ECG Completed

- ECG is completed and being sent to the servers

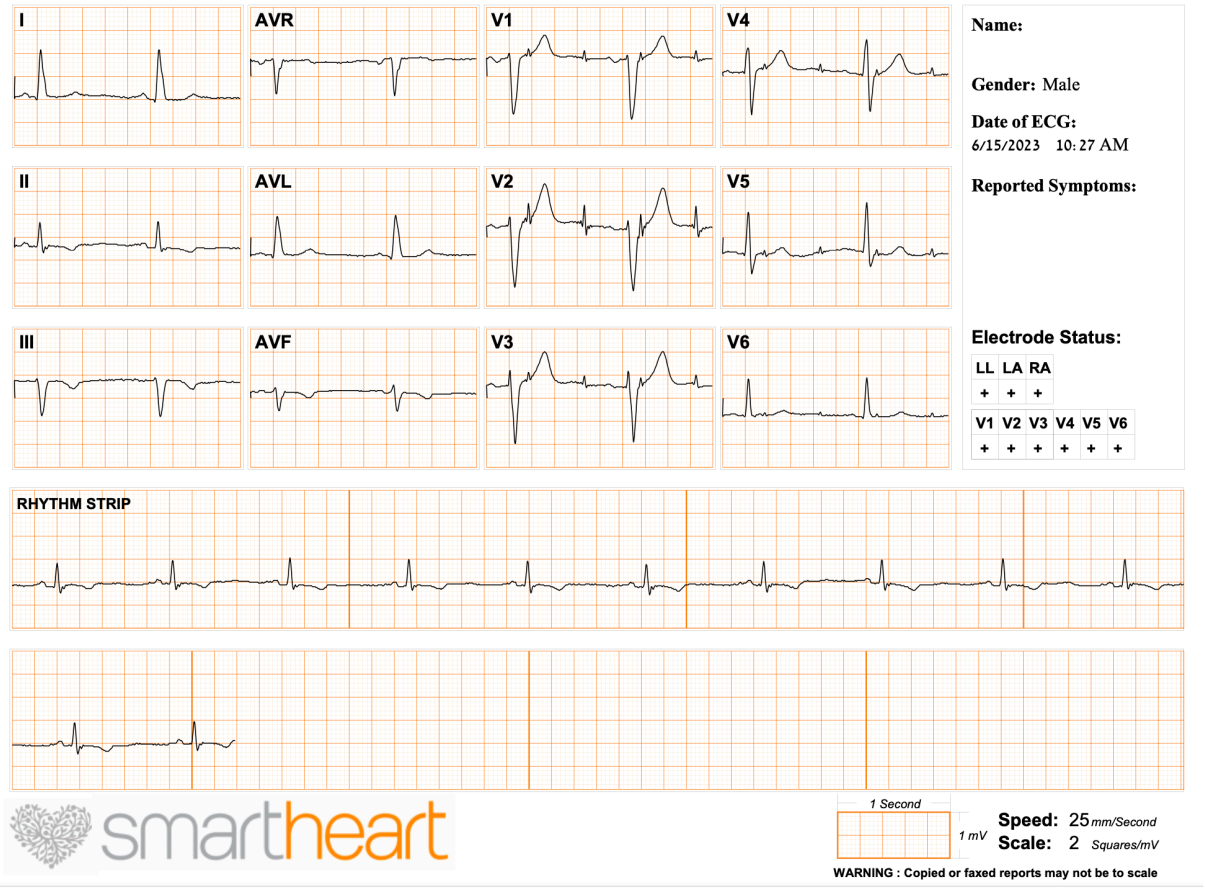
smartheart Process Completion

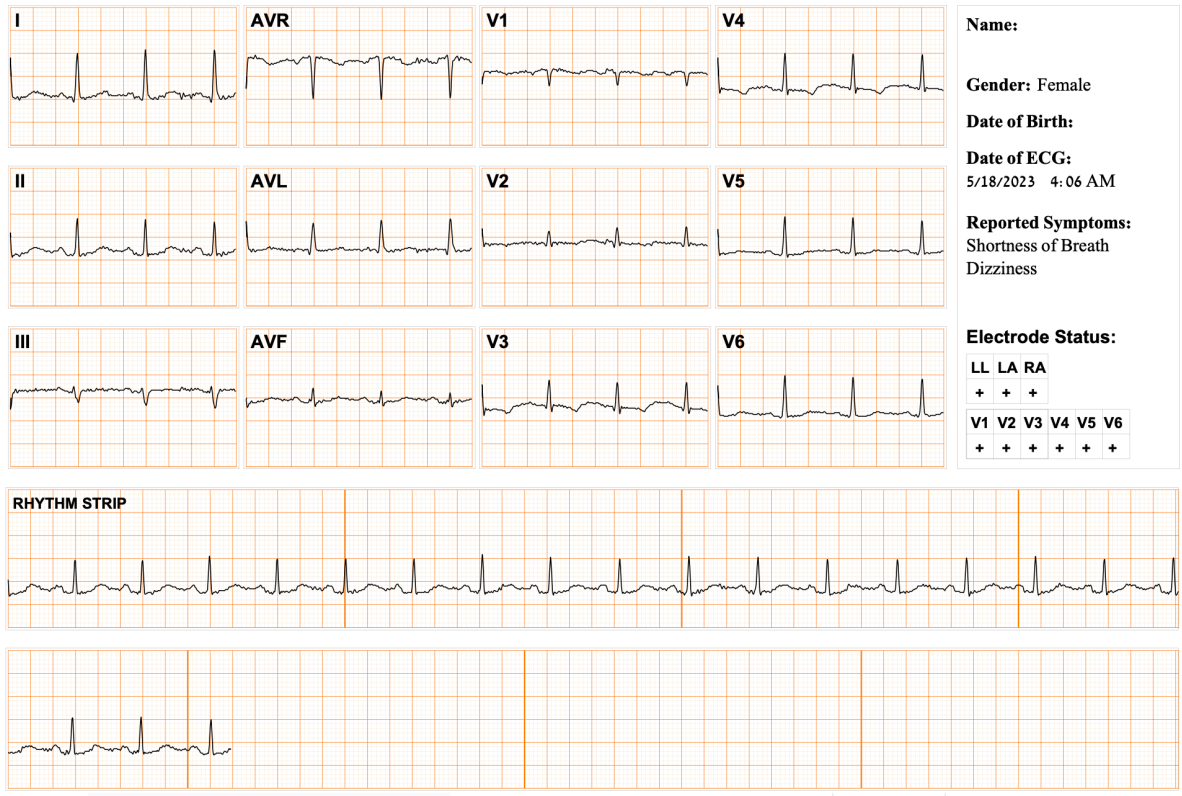


ECG Completed

- Within a few seconds after ECG is completed, it will be available in the application.
- In parallel the ECG PDF report is sent to predefined research email.

Examples of ECGs Generated by SMARTHEART™





Name:

Gender: Female

Date of Birth:

Date of ECG:
5/18/2023 4:06 AM

Reported Symptoms:
Shortness of Breath
Dizziness

Electrode Status:

LL	LA	RA
+	+	+

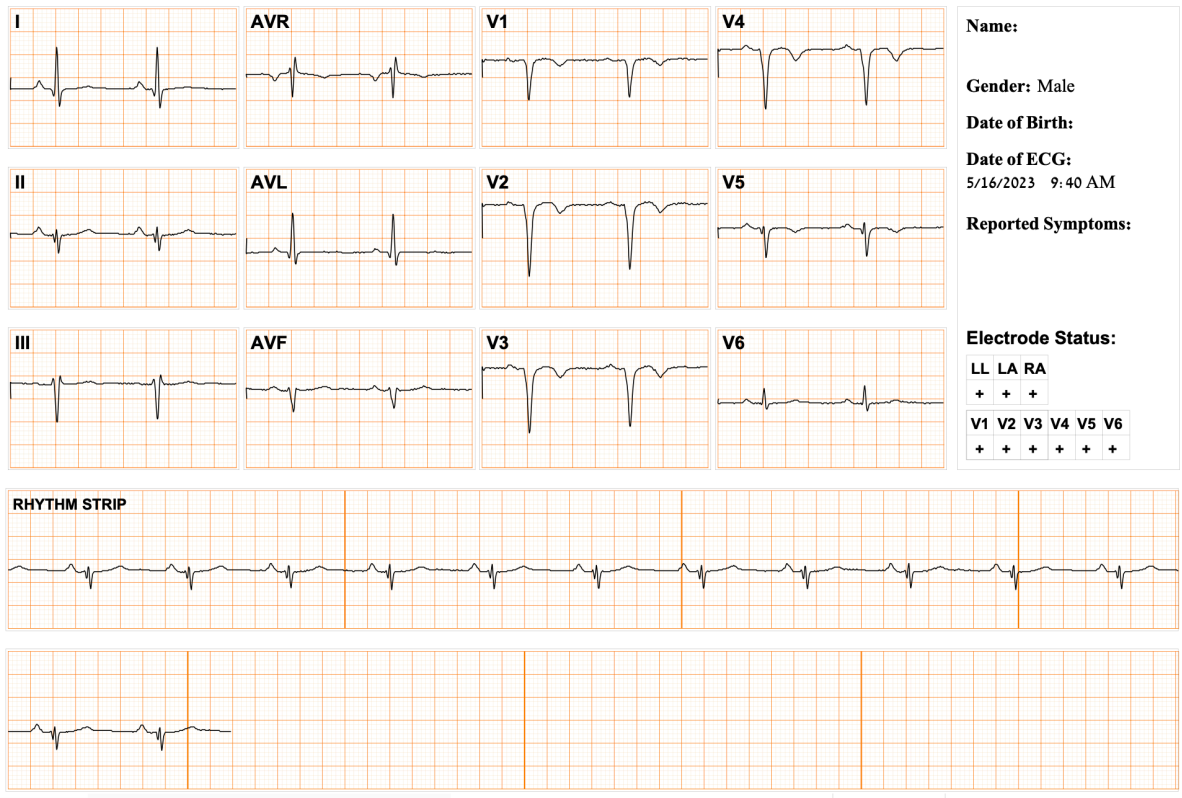
V1	V2	V3	V4	V5	V6
+	+	+	+	+	+

smartheart

1 Second
1 mV

Speed: 25 *mm/Second*
Scale: 2 *Squares/mV*

WARNING : Copied or faxed reports may not be to scale



Name:

Gender: Male

Date of Birth:

Date of ECG:
5/16/2023 9:40 AM

Reported Symptoms:

Electrode Status:

LL	LA	RA
+	+	+

V1	V2	V3	V4	V5	V6
+	+	+	+	+	+

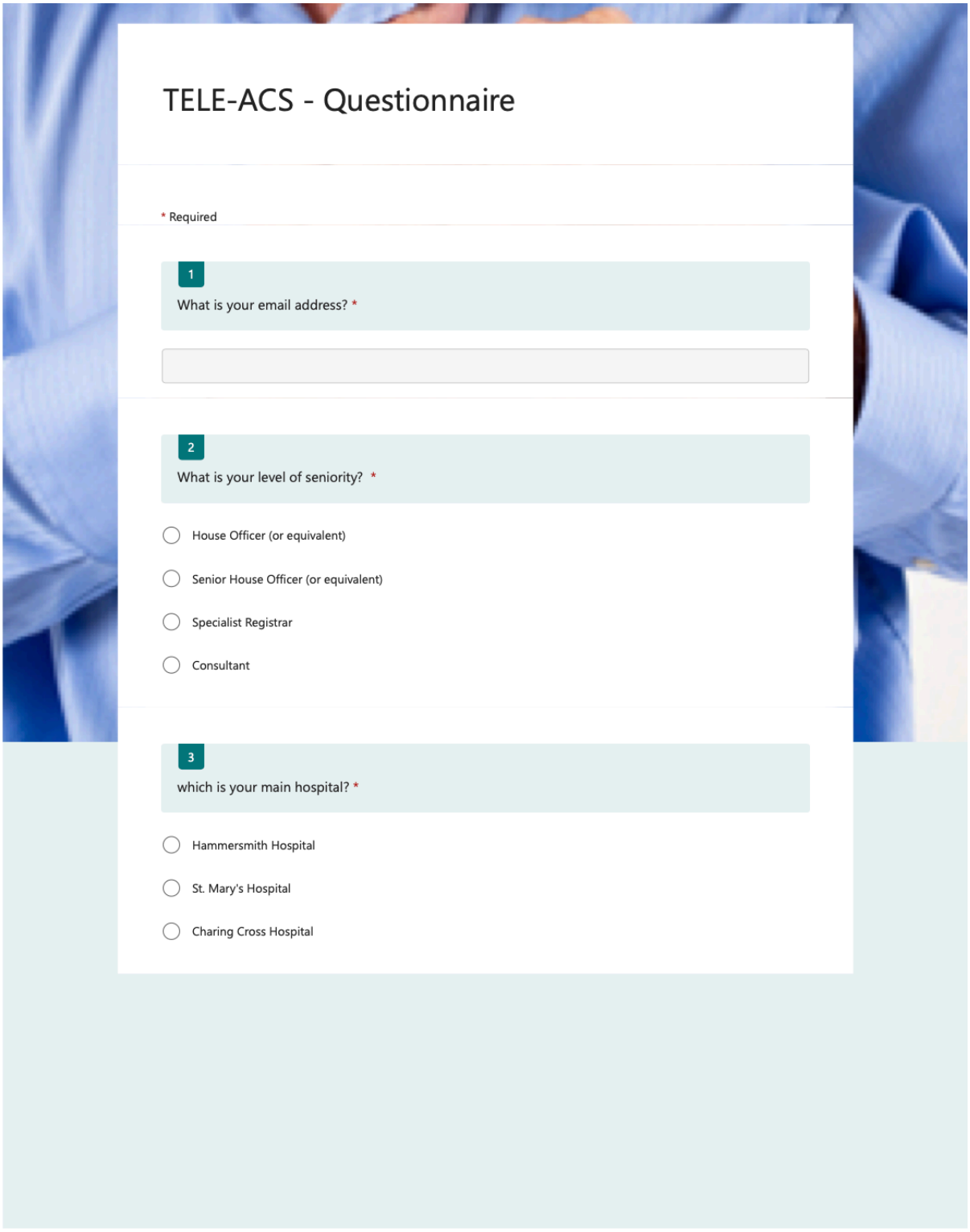
smartheart

1 Second
1 mV

Speed: 25 *mm/Second*
Scale: 2 *Squares/mV*

WARNING : Copied or faxed reports may not be to scale

8.5 Cardiac Scenarios



TELE-ACS - Questionnaire

* Required

1

What is your email address? *

2

What is your level of seniority? *

- House Officer (or equivalent)
- Senior House Officer (or equivalent)
- Specialist Registrar
- Consultant

3

which is your main hospital? *

- Hammersmith Hospital
- St. Mary's Hospital
- Charing Cross Hospital

4

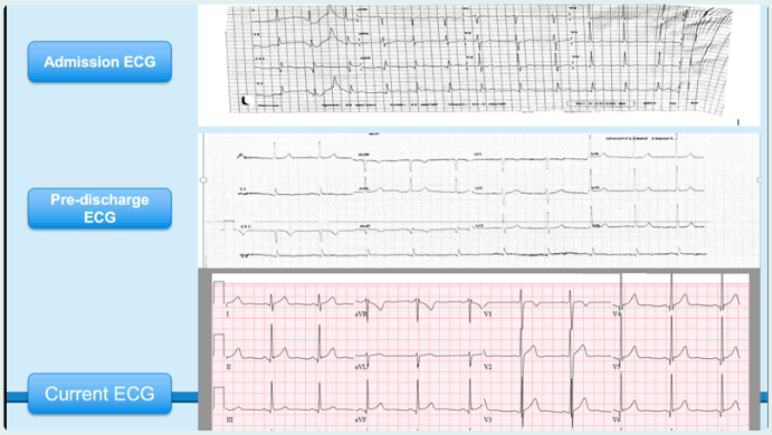
A 48-year-old male has a history of hypertension and a cardiac arrest at the age of 10 after being electrocuted. This gentleman was admitted into the hospital at the Heart Assessment Centre after being brought in by an ambulance. He presented with chest pain accompanied by vomiting after playing 30 minutes of basketball. He went home, from where his wife telephoned for an ambulance. Upon attending, the patient reported to the ambulance crew central chest pain radiating to his left jaw and shoulder, and the pain was accompanied by sweating. He was given 300 mg Aspirin, GTN spray and 10 mg Morphine.

Upon admission, the electrocardiogram showed ST elevation in the inferior leads, suggestive of an Inferior ST Elevation Myocardial Infarction. Left ventricular function was preserved on bedside handheld echocardiogram. He underwent PPCI to the RCA. He was taken back to the catheterisation laboratory 2 days later for staged PCI to the LAD which was also found to be severely stenosed. Both procedures went well with satisfactory results and there is no further revascularisation planned.

Prior to his discharge, there were no further episodes of chest pain, and no new ischaemic changes on his ECG. Pre-discharge his observations revealed: BP= 113/74 mmHg, P= 67 bpm, SpO2= 95% on air, and ECG below.

The patient was discharged from hospital with the telemedicine package (SHL smartheart, Omron Basic M2 blood pressure monitor, and Kinetik Wellbeing Finger Pulse Oximeter). After a couple of days, he now experiences chest discomfort, shortness of breath, and feeling sick. The patient contacts the on-call cardiology team, and he was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 128/78 mmHg, P= 72 bpm, SpO2= 93% on air and ECG below.
*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

5

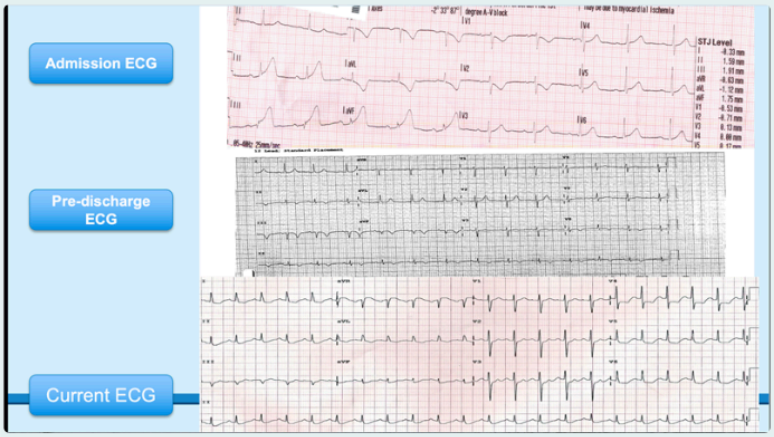
A 72-year-old female presented with 2 day history of worsening chest pain. There was inferior ST-elevation on her ECG (below). There are no known cardiac risk factors. She was given aspirin 300mg, GTN 400 s/l, morphine IV 5mg. PMH: Oesophageal cancer - chemo + radiotherapy. She underwent successful PPCI to an occluded RCA with 3 drug-eluting stents. There was bystander severe distal LCx and moderate-severe mid-LAD disease in small calibre vessel that was for medical management. Her LV function was moderately impaired. She was admitted to CCU for 3 days and was discharged well on optimal medical therapy.

Pre-discharge her observations revealed: BP= 127/75 mmHg, P= 69 bpm, SpO2= 96% on air, and ECG below.

The patient was discharged from hospital with the telemedicine package. A few days later, she now experiences chest pain that gets worse over several minutes associated with palpitations. The patient contacts the on-call cardiology team, and she was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 148/95 mmHg, P= 138 bpm, SpO2= 90% on air and ECG below:

*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

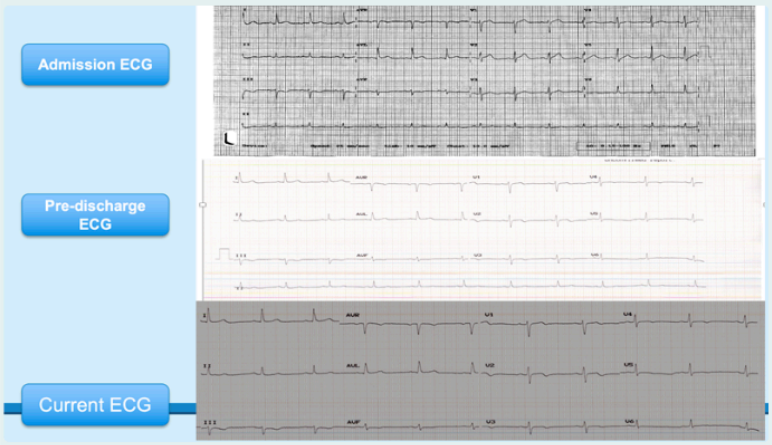
6

A 43-year-old male went to the gym, for the first time in a while. He developed sudden onset severe left sided chest pain at around 16:30, initially 8-9/10 in severity. On going home, his family reported that he looked agitated/ grey/ clammy. However, there was no shortness of breath/ palpitations/ syncope. He called 999 but was informed that there was a long wait, so his family took him to A&E. There was ST-elevation noted on serial ECGs and he underwent urgent PPCI to LAD. The procedure went well with satisfactory results and there is no further revascularisation planned. There was no significant bystander disease that required intervention. He was admitted for 3 days in total.

Pre-discharge his observations were: BP= 112/72 mmHg, P= 71 bpm , SpO2= 96% on air, and ECG below.

The patient was discharged from hospital with the telemedicine package. 2 weeks later he experiences a shortness of breath for a few minutes. The patient contacts the on-call cardiology team, and he was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 136/91 mmHg, P= 68 bpm, SpO2= 98% on air and ECG below: *

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

7

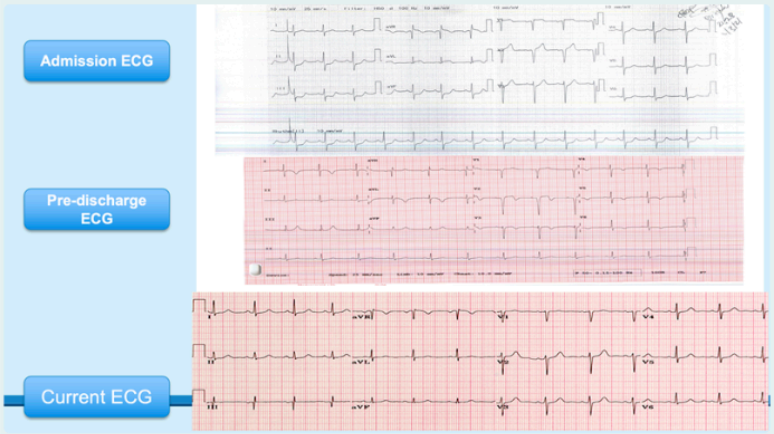
A 28-year-old male at 03:30 pm while he was walking developed chest pain. It was felt as pressure. He had never had any chest pain before. It lasted for 10-20 minutes. At 06:00 pm he had another episode of chest pain which was more intense and lasted for 15 minutes. He took a bus and to hospital. Had chest pain while he was sitting in A&E. There was a mild cough recently but no fever. Has been feeling well otherwise. ECG showed Inferior ST depression and high sensitivity troponin I of 89. He was loaded with clopidogrel 300 mg and aspirin 300mg, as well as Fondaparinux 2.5 mg and given GTN spray. He underwent PCI to LAD with thromboaspiration. On OCT the stent expansion was 80%, so was post-dilated with 3.75 and 4 mm non-compliant balloons. He was haemodynamically stable on discharge, with no report of further chest pain. He was discharged after 48 hours.

Pre-discharge his observations revealed: BP= 118/83 mmHg, P= 71 bpm, SpO2= 99% on air, and ECG below:

The patient was discharged from hospital with the telemedicine package. After 1 month, he feels weakness, dizziness, and feeling sick, and shortness of breath for a few hours. The patient contacts the on-call cardiology team, and he was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 115/81 mmHg, P= 96 bpm, SpO2= 97% on air and ECG below.

*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

8

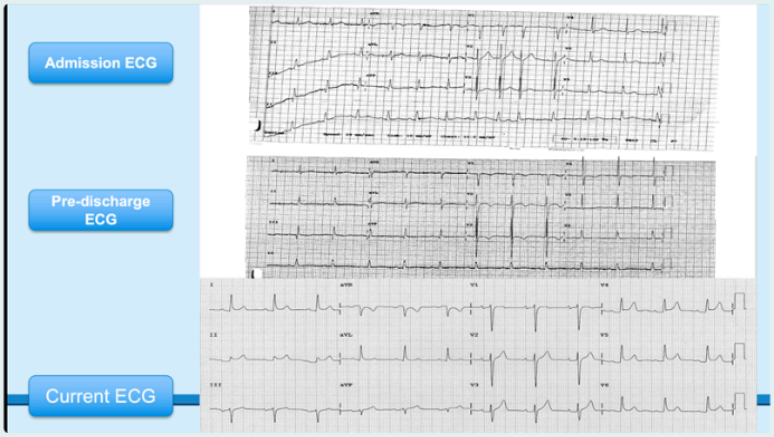
A 76-year-old female was admitted with sudden onset chest pain at 1:55 am. The pain was central and radiated to both arms, shoulders, back and neck, waking her from sleep. It felt different to her previous angina pain. There was associated dizziness and sweatiness. She had her own GTN which helped the pain, but it then came back again. Saturations were low (90%) with LAS. She had 300mg Aspirin and GTN with LAS which helped the pain.
PMH: CKD, chronic anaemia, total knee replacements (2013 and 2015). CABG 2017 (SVG to LAD, LIMA-D1). In 2018 she underwent PCI to LCx, complicated by LMS dissection leading to stenting LMS.

The ECG on admission is shown below. Coronary Angiography showed occlusion of RCA, and she underwent urgent PPCI. She was admitted to CCU a few days, prior to an uneventful discharge. There were no plans for further revascularisation.

Pre-discharge her observations revealed: BP= 125/75 mmHg, P= 68 bpm, SpO2= 99% on air, and ECG below.

The patient was discharged from hospital with the telemedicine package. Within a few days, she experienced chest pain, SOB, palpitations, and has a history of recent flu-like illness. The patient contacts the on-call cardiology team, and she was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 150/104 mmHg, P= 74 bpm, SpO2= 89% on air and ECG below.
*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

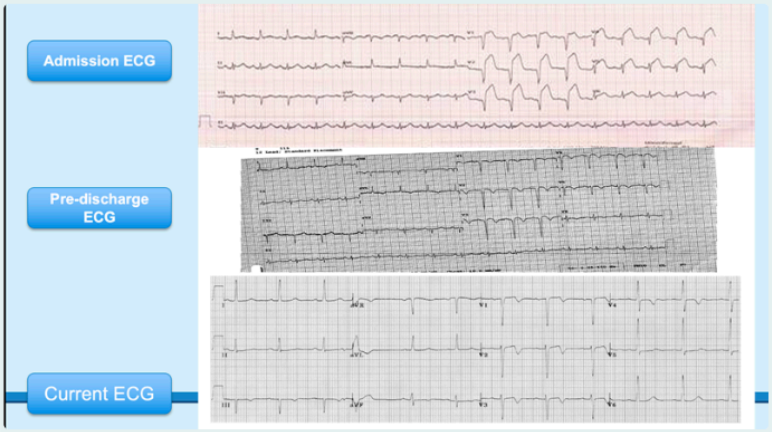
9

A 54-year-old female went for a walk of less than a mile and came back with shortness of breath and central chest pain. There was no associated sweating or palpitations. There was nausea, but no vomiting. The pain was sharp and lasted for quite a while. She self-presented to A&E. Her systolic BP was >200mmHg. She took paracetamol when she came to A&E but the pain was persistent. The ECG is shown below. She underwent urgent PCI for anterior STEMI. She was admitted to CCU for 3 days, prior to an uneventful discharge. She was discharged well on optimal medical therapy

Pre-discharge her observations were: BP= 118/81 mmHg, P= 86 bpm, SpO2= 99% on air, and ECG below:

The patient was discharged from hospital with the telemedicine package. 3 weeks later, she now experiences chest discomfort rather than pain, and feels stressed. The patient contacts the on-call cardiology team, and she was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 123/96 mmHg, P= 72 bpm, SpO2= 98% on air and ECG below:
*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

10

A 65-year-old gentleman was admitted to the Heart Attack Centre as a Primary Angioplasty call from Chelsea and Westminster Hospital ED, where he presented with intermittent episodes of central chest pain at rest. Past Medical History included Diabetes Mellitus type 2, hypertension, hypercholesterolemia, primary hypogonadism, osteoporosis and glaucoma.

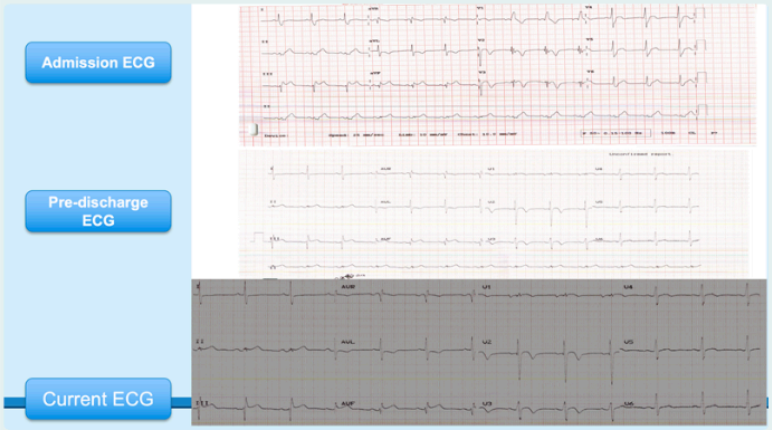
Upon admission to hospital, the initial ECG and troponin were suggestive of an Inferior ST Elevation Myocardial Infarction (below), therefore he was rushed to the catheterisation for revascularization. In the first instance, he proceeded to have percutaneous coronary intervention to the Right Coronary Artery (RCA). During this procedure, the LAD was found to be very heavily calcified as well. A discussion was held with him with regards to the management of bystander disease (surgery vs angioplasty) following which, this gentleman decided in favour of angioplasty. Staged PCI to RCA and LAD was performed on the same day.

Prior to his discharge, we optimised his cardioprotective medication and referred him for cardiac rehabilitation in the community. His observations revealed: BP= 122/75 mmHg, P= 71 bpm, SpO2= 99% on air, and ECG below.

The patient was discharged from hospital with the telemedicine package. He now experiences chest pain, shortness of breath, nausea, dizziness, and fatigue. The patient contacts the on-call cardiology team, and he was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 110/76 mmHg, P= 73 bpm, SpO2= 88% on air and ECG below.

*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

11

A 47-year-old female went to sleep and then 10-15min later awoke with sharp left-sided and central chest pain of 10/10 severity, which radiated to both arms and neck. There was associated vomiting, sweatiness and shortness of breath. There was no syncope, but she felt as if she would pass out. She chewed 300mg aspirin at home. There was ongoing pain in hospital.

In view of her presentation and ECG findings suggestive of myocardial infarction (below), this lady was rushed to the catheterisation laboratory for revascularisation, where she proceeded to have PPCI to the LCx. There was no bystander disease. She was haemodynamically stable on discharge, with no report of further chest pain.

Pre-discharge her observations revealed: BP= 134/92 mmHg, P= 81 bpm, SpO2= 99% on air, and ECG below.

The patient was discharged from hospital with the telemedicine package. 2 weeks later, she currently feels sudden chest pain, and shortness of breath for a few hours. The patient contacts the on-call cardiology team, and she was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 151/104 mmHg, P= 122 bpm, SpO2= 93% on air and ECG below.
*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

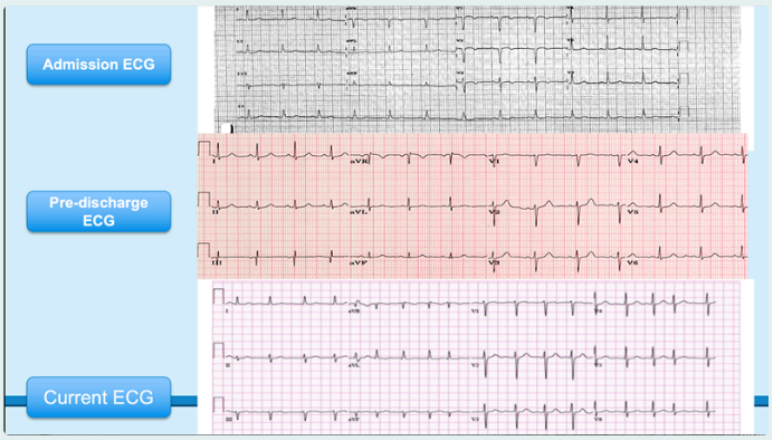
12

A 62-year-old male patient was admitted to HAC via LAS with sudden onset chest pain on gentle exertion. He felt the chest pain was similar to that experienced prior to his CABG. ECG findings demonstrated inferior ST sagging and V-4 TWI- dynamic changes (below) when compared with LAS findings. PMHx: Coronary Artery Bypass Grafts x 3 (LIMA-LAD, SVG-Intermediate, SVG-PDA) last month. He underwent urgent PCI to the native RCA, and was admitted to CCU for 3 days. His LV function was moderately impaired.

Pre-discharge his observations were: BP= 125/86 mmHg, P= 89 bpm, SpO2= 99% on air, and ECG below:

The patient was discharged from hospital with the telemedicine package. He now experiences mild headache, heartburn, weakness, and dizziness. The patient contacts the on-call cardiology team, and he was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 115/74 mmHg, P= 93 bpm, SpO2= 94% on air and ECG below. *

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.

13

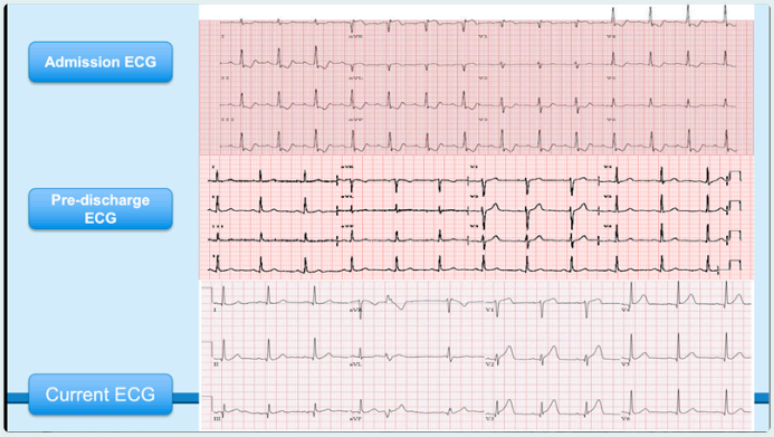
A 54-year-old male patient presents with chest pain that awoke him from sleep. The patient describes the pain as mid-sternal tight and squeezing in nature, associated with shortness of breath, nausea, diaphoresis and pressure in the epigastric region. The admission ECG (below) showed ST depression in the inferolateral leads. He underwent emergency coronary angiography, followed by PCI to the LCx. The patient was admitted to the CCU for 48 hours. There was diffuse bystander disease, for medical management in the first instance. There were no further episodes of chest pain,and no new ischaemic changes on his ECG.

Pre-discharge his observations revealed: BP= 112/75 mmHg, P= 72 bpm, SpO2= 99% on air, and ECG below:

The patient was discharged from hospital with the telemedicine package. 10 days later, he now experiences chest discomfort, general weakness, and palpitations. The patient contacts the on-call cardiology team, and he was able to acquire a 12-lead ECG, a blood pressure reading and an oxygen saturation reading using the telemedicine package. BP= 132/96 mmHg, P= 76 bpm, SpO2= 91% on air and ECG below:

*

Which is the most appropriate option out of the following?



- ◯ Reassure the patient
- ◯ Advise the patient to call the general practitioner (GP)
- ◯ Advise admission via the emergency department
- ◯ Advise the patient to call 999.