What is the value of digital tools for cardiovascular patients?

A comprehensive review of evidence for effectiveness and cost-effectiveness for prevention and management

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Aim

The potential of digital health in the prevention and management of cardiovascular disease is increasingly recognised. The aim of this paper is to provide an overview of the current evidence and remaining gaps of digital health tools for cardiovascular patients. For that purpose, the research team reviewed the most important digital health trials from 2000 until the end of 2019.

Executive summary

The number of people with cardiovascular disease is increasing yearly. This leads to continuously increasing workload and costs and hence pressure on healthcare systems in Europe. At the same time, new technologies such as wearables, biosensors, smartphone applications and artificial intelligence are being developed in a fast pace. In the last decade, there is an increased interest in applying these new technologies to advance cardiovascular diagnosis and care with the aim to improve patient outcomes and to reduce the economic pressure on many healthcare systems in Europe.

The use of technology in medicine is called digital health. Digital health is often divided in two main components, namely mHealth and telemedicine. mHealth comprises the use of smartphones, tablets and wearable technologies for health services. Telemedicine on the other hand can be defined as the delivery of remote care.

Digital health has the potential of improving primary prevention of cardiovascular disease by increasing patient empowerment and remote follow-up with smartphone applications, text messaging and internet-based interventions. This report looks at the potential of digital health for the following modifiable risk factors: arterial hypertension, diabetes mellitus (type 2 diabetes), smoking, overweight and obesity, and a sedentary lifestyle.

Key findings in the role of digital health in arterial hypertension:

- Current evidence suggests that telemonitoring could be effective in reducing blood pressure, but more research is needed to confirm the added value of telemonitoring to self-monitoring.
- More research is also required to confirm the cost-effectiveness of this intervention.
- Smartphone applications have much potential in remote monitoring and improving hypertensive patients' medication adherence. However, there is not yet enough evidence to confirm the effectiveness of mHealth applications in hypertension management.

Key findings in the role of digital health in diabetes mellitus (type 2 diabetes):

- Telemonitoring of blood glucose in type 2 diabetes patients seems to improve control of glycaemia, health-related quality of life and HbA1C. More trials are needed to support the implementation of telemonitoring.
- The use of text messaging and smartphone applications could also play a role in the chronic management of type 2 diabetes. Text messaging could increase therapy adherence and improve lifestyle choices. More research and larger trials will be indispensable to confirm the cost-effectiveness in comparison with standard care and telemonitoring.
- Several trials demonstrate that smartphone application can reduce HbA1C. This suggests that smartphone applications will play a role in type 2 diabetes management in the future. More research is needed to confirm this.

Key findings in the role of digital health in smoking cessation:

- Internet-based smoking cessation programmes present very contradictory results. A recent meta-analysis of 2019 suggests that internet-based smoking cessation interventions increased the odds of cessation by 29% in the short term and by 19% in the long term. However, more evidence is needed to implement internet-based intervention in regular care.
- Evidence shows that text messaging is an effective intervention to improve cessation rates and that it could be a standard element of smoking cessation interventions.
- Smartphone applications could be effective; however only four trials on such interventions were published between 2015 and the end of 2019. More evidence is needed.

Key findings in the role of digital health for weight loss:

- Internet-based weight loss interventions have positive effects on diet choices, physical activity and weight.
- Smartphone applications can help to achieve a moderate short-term weight loss. More research is needed to demonstrate long-term results and to assess the cost-effectiveness of these interventions.
- The effectiveness of text-messaging interventions for weight loss remains debatable. Two meta-analyses demonstrated a small effect of text-messaging interventions in short-term weight loss. However, lack of long-term results indicate that further studies

are required. Research is also needed on the cost-effectiveness of text-messaging interventions.

Key findings in the role of digital health for improving physical activity:

- Pedometer- or activity tracker-based interventions are associated with reduced sedentary time among adults in the short term. Larger and longer trials are still needed to evaluate long-term effects and cost-effectiveness of these interventions.
- Smartphone applications for increasing physical activity have positive effects, however the effects are small. More research and larger trials are needed to confirm the long-term maintenance of higher physical activity.
- Text messaging can lead to increased physical activity.
- The effect of online social networks, gamification and incentives has been investigated in multiple small trials. Most of these interventions show modest improvement of physical activity.

Furthermore, digital health has also proved to be effective to deliver remote cardiac rehabilitation in patients with ischemic heart disease. Our key findings regarding telerehabilitation are the following:

- Home-based exercise training or telerehabilitation for ischaemic heart disease patients is an effective way to deliver exercise training in patients who cannot attend centre-based cardiac rehabilitation.
- Home-based exercise training or telerehabilitation for ischaemic heart disease patients is an effective way to deliver exercise training as an add-on to centre-based cardiac rehabilitation to increase long-term effects of cardiac rehabilitation.
- Several trials suggest that telerehabilitation, whether standalone or as add-on, is cost-effective. However, larger studies in different healthcare systems, as well as more cost-effectiveness research are needed.

Review of evidence on digital health for secondary prevention of ischaemic heart disease identified that:

- Lifestyle management of ischaemic heart disease with the help of digital health tools is an effective way to optimise risk factor profiles of patients.

- Telephone counselling, text messaging and smartphone applications are effective, while Internet-based interventions have failed to prove effectiveness up to now.
- Smartphone applications have the potential to provide very accessible pocket-size interventions.

Telemonitoring of heart failure patients is already well studied but some controversy regarding its effectiveness remain. Similarly, most studies show positive effects on exercise capacity and quality of life (QoL) in telerehabilitation of heart failure. However, there is uncertainty with respect to long term outcomes. The key points regarding telemonitoring in heart failure patients are the following:

- Many trials have demonstrated the effectiveness of telemonitoring in reducing rehospitalisation and in improving heart failure patients' quality of life.
- Meta-analyses of these trials demonstrate significant improvement in outcomes from telemonitoring interventions, especially in the short term. However, some large multi-centre trials have failed to demonstrate effectiveness of telemonitoring.
- New randomised multicentre studies are needed to identify which telemonitoring interventions are effective.

The key points regarding telephone follow-up in heart failure patients are the following:

- Telephone counselling can be effective in reducing hospital admission for heart failure but seems most effective in improving patients' health knowledge and self-care skills.
- Cost-effectiveness of a structured telephone counselling approach remains questionable.

The key points regarding smartphone applications and text messaging interventions for heart failure patients are the following:

- There is not yet very strong evidence for the use of smartphones in improving heart failure patients' self-management with long-term outcomes.
- Most trials have very small sample sizes and short follow-up periods.
- The potential of smartphone use in long-term management of heart failure may be considerable. But it needs to be demonstrated through long-term randomised multi-centre trials.

The key points regarding telerehabilitation in heart failure patients are the following:

- There is still a debate whether telerehabilitation is effective in reducing rehospitalisation and mortality in heart failure patients.
- More research in home-based exercise training in heart failure is needed to investigate the long-term effects.

The key points regarding home-hospitalisation in heart failure patients are the following:

- Home-hospitalisation supported by IT technology could potentially reduce the need for hospital beds and improve heart failure patients' outcomes and quality of life.
- Home-hospitalisation research is still in its infancy, awaiting strong proof from randomised controlled trials.
- The necessary technology and organisation can, nevertheless, already be used to help in safely discharging heart failure patients earlier.

Digital health provides many opportunities in the field of cardiac arrhythmia. Smartphones, smartwatches, and bio patches are exciting new technologies for ambulatory monitoring and screening of atrial fibrillation. Nonetheless, more research is still required to confirm the cost-effectiveness of these interventions. Specifically:

- Smartwatches, handheld devices and bio patches show some promising results for long-term monitoring and mass screening; however, more research is needed to confirm their accuracy and cost-effectiveness.
- More research is also needed to investigate the role and implementation of digital health monitoring in current workflows and care pathways.

Key findings regarding prehospital emergency ECG include:

- Prehospital ECGs can be transmitted through telemedicine devices, telephone, smartphones etc.
- Multiple studies demonstrated that prehospital ECG is associated with lower door-to-balloon time and increased survival.

Review of evidence in digital health for anticoagulation treatment in atrial suggest that:

- Digital health technology can increase patients' adherence to treatment.

- No good cost-effectiveness studies are available, but it may be expected that these low-cost interventions will prove to be cost saving.

Multiple trials have reported the effectiveness and cost-effectiveness of remote monitoring of cardiovascular implantable electronic devices (CIEDs) by reducing rehospitalisation, mortality and healthcare costs in combination with high patient and health professional satisfaction. Specifically,

- Most trials and meta-analyses demonstrate that remote monitoring of CIEDs is effective in reducing rehospitalisation, mortality and healthcare costs.
- The use of intrathoracic impedance monitoring with CIEDs, an early warning of impending decompensation in heart failure patients, needs further investigation.
- Patient-reported health status and ICD acceptance did not differ between patients on remote monitoring and patients receiving usual care.
- Studies demonstrate high satisfaction with remote monitoring.
- Patients with a preference for remote monitoring were more likely to be higher educated and in employment.

The key points regarding use of wireless implantable hemodynamic monitoring systems are the following:

- The CHAMPION trial demonstrates a large reduction in hospitalisation after six months follow-up for patients with severe heart failure.
- More research is needed to consistently implement implantable hemodynamic monitors in standard care, but most trials show promising results.

The key points regarding remote monitoring of CIEDs for detection of cardiac arrhythmias are the following:

- Arrhythmias detected by remote monitoring are predictive of adverse events.
- Device-detected atrial fibrillation is associated with an increased risk of ischaemic stroke.
- Changing the OAC administration based on arrythmia detection by CIED is feasible.

The key points regarding implantable loop recorders are the following:

- Implantable loop recorders are effective in the diagnosis of unexplained syncope.

- Implantable loop recorders can play an important role in the diagnosis of paroxysmal atrial fibrillation and life-threatening arrhythmias.

Artificial intelligence could potentially play a big role in electrocardiography (ECG) diagnosis, cardiovascular imaging and risk prediction models.

Co-creation of digital health tools with all relevant stakeholders, including patients and health professionals, is key to overcome common barriers such as lack of personal motivation, low digital literacy, lack of interoperability and increased workload. Furthermore, integration of the electronic medical records is important not to overwhelm physicians with digital health tools and data.

There are already many digital health trials in cardiology. Unfortunately, most of these trials are performed in one centre with a small sample size. Hence more studies are desirable to investigate the long term effects of digital health interventions and the cost-effectiveness thereof.

List of abbreviations

ACS: Acute Coronary syndrome

AF/AFIB: Atrial Fibrillation

AUC: Area under the Curve

BP: Blood pressure

CABG: Coronary artery bypass grafting

CAD: Coronary artery disease

CIED: Cardiovascular implantable electronic devices

CR: Cardiac rehabilitation

CRT: Cardiac resynchronisation therapy

CVD: Cardiovascular disease

EC: Exercise capacity

ECG: Electrocardiography

EMR: Electronic medical record

EU: European Union

FDA: Food and Drug administration

GDPR: General Data Protection Regulation

GPS: Global positioning system

HbA1C: Glycated haemoglobin

HF: Heart failure

HFmrEF: HF mid-range ejection fraction

HFpEF: HF with preserved ejection fraction

HFrEF: Heart failure with reduced ejection

ICBT: Internet delivered Cognitive behavioural therapy

ICD: Implantable cardioverter-defibrillator

ICT: Information and communications technology

IHD: Ischemic heart disease

ILR: Implantable loop recorder

INR: International Normalized Ratio

IVRS: Interactive voice response system

MI: Myocardial infarction

MRI: Magnetic resonance imaging

NHS: National Health Service

OAC: Oral anticoagulation

PCI: Percutaneous coronary intervention

PPG: Photoplethysmography

QoL: Quality of life

RCT: Randomized Controlled trial

RM: Remote monitoring

SMS: Short messaging service

SPECT: Single-photon emission computed tomography

STEMI: ST-elevation myocardial infarction

T2DM: Type 2 diabetes mellitus

VKA: Vitamin K antagonist

Methodology of search

The literature search was performed following the principles of a systematic review. The initial searches were performed in June 2019 and continuously updated until early December 2019. The MEDLINE and EMBASE database were utilised for the search. All MESH terms belonging to 'heart diseases', 'cardiovascular disease' or 'digital health' were reviewed. All published articles from 2000 until the end of December 2019 were included. The main inclusion criteria were articles in English and studies performed in humans. Abstract, conference papers and systematic reviews were excluded. All references (titles plus abstracts) were evaluated by one expert. In addition, the references of recent meta-analyses and the references of all systematic reviews were assessed to ensure completeness of the review. Furthermore, the references were checked for all included papers in the review (snowballing) to complete the list. No quality assessment was applied for the annexes was used to give a full overview of published trials in digital health. Articles were selected for this review text on the basis of study design, sample size and endpoints with preference for multicentre RCTs, studies with large sample size and studies reporting long term clinical outcomes.

Introduction

Cardiovascular disease (CVD) includes all heart and circulatory diseases. CVD has many forms and includes:

- Ischaemic heart disease (IHD), also known as coronary artery disease (CAD). This is caused by atherosclerosis in which fatty plaque deposits cause the coronary artery walls to narrow, resulting in reduced blood flow to the heart. This is the primary cause of heart attacks.
- Chronic stable angina, which is chest pain that occurs when the heart is working hard (stress, exercise) and needs more oxygen. This is often induced by physical exertion and indicates a damaged heart function or narrowing of the coronary arteries.
- Peripheral artery disease in which narrowed arteries reduce blood flow to the limbs, common in diabetics and smokers. This is a major cause of lower-limb amputations.
- Heart rhythm disturbances. Sudden cardiac death is often the first and final appearance of other underlying CVDs and, consequently, is a permanent concern for most patients with CVD. Atrial fibrillation (AF or AFIB) is the most prevalent arrhythmia with irregular heart rate symptoms that may cause stroke, heart failure, palpitations, fatigue, and shortness of breath.
- Heart failure (HF), which occurs when damage to the heart muscle is severe enough to prevent it from functioning properly; rates of morbidity and mortality from severe HF are higher than many cancers. In particular, regular rehospitalisation of HF patients creates a personal and socio-economic burden.
- Valvular heart disease, of which aortic stenosis and mitral valve insufficiency are most common.
- Congenital and inherited heart conditions, often resulting in reduced quality of life (QoL) and increased risk of sudden death.
- A stroke is a medical condition in which poor blood flow to the brain results in cell death. There are two main types of stroke: ischemic, due to lack of blood flow, and haemorrhagic, due to bleeding. Digital health for stroke prevention or management is not in the scope of this review paper.

The prevalence of cardiovascular disease increases yearly (1). More than 85 and 49 million people with CVD are living in Europe and the EU, respectively. In 2015, there were just under 11.3 million new cases of CVD in Europe and 6.1 million in the EU (1). Cardiovascular disease such as HF, AF, and ischaemic cardiomyopathies make up a large portion of the chronic disease burden, carrying an important socio-economic impact (2). CVD is estimated to cost the EU economy €210 billion a year. This amount comprises around 53% (€111 billion) in healthcare costs, 26% (€54 billion) in productivity losses, and 21% (€45 billion) in informal care of people with CVD (1). The cost presents a challenge for the current healthcare budgets in Europe (3). There is an increased need for the care and monitoring of elderly people living at home and of people with chronic diseases (3). The shortage of qualified staff to care for patients with chronic diseases stimulates the search for innovation in healthcare systems (4). The recent technological revolution has created an opportunity to redesign and improve the quality of our current healthcare (5).

Digital health is most frequently defined as the use of information and communication technologies to treat patients, conduct research, educate patients and healthcare professionals, monitor acute but mostly chronic diseases, and to monitor and compare the national public CVD status with other countries (6).

Digital health consists of two main components, namely, mHealth and telemedicine. mHealth can be further divided into the use of a smartphone, tablet, or wearable technology for health services (3). Examples of mHealth interventions are smartphone applications and Internet-based programmes for self-management and lifestyle monitoring. Telemedicine can be defined as the delivery of remote care. It can be divided into two components: telerehabilitation and telemonitoring (3).

Digital health has high potential (6) in facilitating a modern delivery of sustainable and efficient healthcare. Moreover, it can enable a high quality of personalised care and optimal patient satisfaction.

The key to exploiting the clear potential of digital health in delivering safe, effective, sustainable, and satisfactory care will be streamlining the implementation process. One problem that many digital health solutions have had up to now is that these interventions have been mainly technology-driven. Co-creation of innovative applications with health professionals and patients will be essential for the future of digital health. The lack of interoperability with other digital tools, electronic medical records (EMRs), and reimbursement issues are additional hurdles in the large-scale implementation of digital health in healthcare (5).

The following topics will be discussed in this report:

- Digital health in primary prevention of cardiovascular disease
- Digital health in secondary prevention of ischaemic heart disease
- Digital health in heart failure management
- Home-hospitalisation for heart failure
- Digital health in cardiac arrhythmia diagnosis and management
- Digital health for cardiovascular implantable devices
- Big data and artificial intelligence in cardiology
- Considerations for implementing digital health

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Chapter 1: Digital Health in primary prevention

Digital health can play an important role in primary prevention. Internet-based tools and smartphone applications can be used for screening, lifestyle monitoring, self-management, adherence to pharmacotherapy, education, and psychological support (1). An advantage of digital health is the potential to transform prevention into more patient-centred care with content that is customised to patients' individual needs and preferences.

A growing number of patients have wearable devices for activity tracking and, hence, an increased healthy lifestyle awareness. These trackers have high potential; however, relatively little evidence is currently available regarding long-term health effects (2). Most digital health solutions at this moment focus on only one aspect of cardiovascular prevention (most often physical activity). More scientific research is needed on integrated solutions that can monitor the whole spectrum of cardiovascular risk factors (diabetes mellitus, arterial hypertension, smoking, inactivity, obesity, etc).

In this chapter, we will focus on studies from 2015 to 2019 that examine the effectiveness of smartphone and Internet applications in improving selected cardiovascular risk factors: arterial hypertension, diabetes mellitus, smoking, obesity, and sedentary lifestyle., obesity and sedentary lifestyle.

Hypertension

Hypertension, also known as high or raised blood pressure (BP), is a condition in which the blood vessels have persistently raised pressure (3). BP is created by the force of blood pushing against the blood vessel walls (arteries) as it is pumped by the heart. The higher the pressure, the harder the heart has to pump (3). Long-term hypertension can lead to heart damage and even heart failure (HF). Furthermore, high BP is associated with cardiovascular events such as IHD (4-5). European guidelines recommend BP goals of <140/90 mmHg in all patients or even 130/80 mmHg if treatment is well tolerated (6). The first step in hypertension management is a healthy lifestyle. Salt restriction, moderate alcohol consumption, weight reduction, smoking cessation, physical activity, and high consumption of fruits and vegetables have proven to be effective in lowering BP (6).

Nineteen trials and three meta-analyses conducted from 2015 until the end of 2019 looked at BP telemonitoring, and 72% of those studies showed a significant reduction in BP. More research and larger trials are needed to show the effectiveness and cost-effectiveness of these interventions. Details on the research review are provided in Annex 1.

Self-monitoring of BP already plays a big role in diagnosing hypertension and improving BP control. Telemonitoring is a remote interaction between patients and health professionals without the need for face-to-face consultation. It is in addition to self-monitoring. Margolis et al. (7) demonstrated in 2018 that home BP telemonitoring is effective, and the effects are sustained for twelve months after the end of the intervention. An integrated ICT-based system, which included home BP telemonitoring and a smartphone application, was tested by Albini et al. (8) in 2016. After a randomised control trial (RCT) with 690 patients, they concluded that this intervention could be effective in improving hypertension management and lowering clinical inertia (8). The TASMIN-4 trial conducted in 2018 was based on a randomised set of 1182 patients in three different categories: control (394 patients), self-monitoring (395 patients), or telemonitoring and self-monitoring (393 patients) (9). McManus et al. (9) demonstrated that both self-monitoring and telemonitoring resulted in significantly lower BP. The TASMIN-4 trial revealed that self-monitoring is more cost-effective than usual care. There was no clarity whether the addition of telemonitoring further improves the cost-effectiveness (10).

The effectiveness of telemonitoring was confirmed in 2017 in a meta-analysis by Duan et al. (11).

Fourteen trials and one meta-analysis conducted from 2015 until the end of 2019 investigated the effectiveness of smartphone applications in reducing BP. Of these studies, 73% showed that the use of smartphone applications can result in a significant BP reduction. More research and larger trials are necessary to determine which specific features of the smartphone applications are the most (cost-)effective. More details on the research review are described in Annex 1.

Smartphone applications are used in the management of hypertension. However, most corresponding trials have had small sample sizes. In 2016, Kang et al. (12) reported that a smartphone application was effective in improving medication adherence in hypertensive patients, and in 2019, Lee et al. (13) tested a smartphone self-monitoring application and demonstrated that it resulted in significant reductions, compared with usual care.

Eight trials conducted from 2015 until the end of 2019 studied the effectiveness of text messaging in reducing BP. Of these trials, 75% showed that text messaging can lead to a significant reduction in BP. More research with preferably larger trials is required to confirm the observed reduction and to assess the cost-effectiveness of these interventions. More detailed information is provided in Annex 1.

In 2016, Bobrow et al. (14) reported on the effectiveness of weekly short message service (SMS) messages based on an RCT with 1372 patients. They postulated a small reduction in systolic BP control after twelve months.

In conclusion, current evidence suggests that telemonitoring could be effective in reducing BP. However, more research is required to confirm the added value of telemonitoring to self-monitoring alone. Furthermore, smartphone application and text-messaging have high potential for hypertensive patients in remote follow-up of blood pressure and improving medication adherence. However, there is currently insufficient evidence regarding the effectiveness of mHealth applications in hypertension management.

Diabetes mellitus type 2

Type 2 diabetes is a chronic disease that occurs either when the pancreas does not produce sufficient insulin or when the body cannot effectively utilise the insulin it produces. Insulin is one of the hormones that regulate blood sugar. Long-term uncontrolled diabetes can seriously damage many organs, especially the nerves and blood vessels (15).

Type 2 diabetes mellitus (T2DM) is associated with an increased risk of CVD. Therefore, intensive management of T2DM is required to prevent CAD or stroke. Possible additional complications are renal failure, diabetic ulcers, and even amputations (16). The prevalence of T2DM is high and increasing. It is estimated that nearly one out of ten people in Europe has diabetes, implying approximately 60 million people. By 2045, this number is expected to increase to 81 million (22%) (17). HbA1c is often used as an outcome in diabetes trials. Glycated haemoglobin, or HbA1c, is used to monitor the average blood glucose levels of the last three months. This provides a useful longer-term gauge of blood glucose control. Twenty-four trials and seven meta-analyses conducted from 2015 until the end of 2019 investigated the effectiveness of telemonitoring for T2DM patients in reducing HbA1c. Of these studies, 90% indicate that text messaging can lead to a reduction in HbA1c. Nonetheless, more research or larger trials are required to confirm the effectiveness and cost-effectiveness in comparison with standard care and self-monitoring. Further details on the research reviews are provided in Annex 1.

Telemonitoring of diabetes mellitus is the remote monitoring of blood glucose levels by health professionals. Telemonitoring enables continuous monitoring and enables quicker interventions (for example medication change) by health professionals compared to self-monitoring in combination with regular visits to the health professionals.

Telemonitoring of diabetes mellitus patients has been studied in multiple trials. Unfortunately, these are mainly small, single-centre trials. Telemonitoring of blood glucose in TD2M patients seems to improve control of glycaemia, health-related QoL, and HbA1c (18-22). Some trials suggest that telemonitoring of T2DM patients can potentially reduce costs in comparison with usual care (22), but more evidence is needed. A meta-analysis in 2015 concluded that further trials are needed to prove the benefits of telemonitoring in enhancing diabetes management (23).

Fifteen trials and three meta-analyses conducted from 2015 onwards studied the effectiveness of text messaging in reducing HbA1c for T2DM patients. In 66% of these analyses, it was shown that text messaging can lead to a reduction in HbA1c. More research or larger trials will be indispensable to confirm the effectiveness and cost-effectiveness in comparison with standard care. More detailed information on the corresponding research reviews is provided in Annex 1.

Text messaging interventions can also play a potential role in the chronic management of T2DM. The former could increase therapy adherence and improve lifestyle choices. In 2019, Huang et al. (24) and Haider et al. (25) both demonstrated in meta-analyses that text messaging results in declined HbA1c and improved blood glucose control. Moreover, it is considered as a low-cost initiative to motivate T2DM patients to adhere to a healthier lifestyle.

Twenty-three trials and five meta-analyses conducted from 2015 to 2019 explored the effectiveness of smartphone applications for reducing HbA1c in T2DM patients. In 82% of the trials, it was concluded that smartphone applications can result in reduced HbA1c. The five meta-analyses demonstrated that these applications might effectively improve HbA1c control. Nevertheless, more research or larger trials are required to assess and confirm its long term effectiveness and cost-effectiveness in comparison with standard care. More details on the research review can be found in Annex 1.

Smartphone applications can provide T2DM patients with educational content, self-monitoring, and direct communication with health professionals. In 2019, Zhang et al. (26) demonstrated the difficulty in achieving long-term effective glucose improvement solely by using a self-management app. But in combination with interactive management, it can support rapid and sustained glycaemic control. Another trial conducted in 2019 by Yu et al. (27) reported the effectiveness of a smartphone application in reducing HbA1c.

Unfortunately, firm conclusions cannot be drawn in view of the relatively small trial sample size. A meta-analysis by Hou et al. (28) in 2018 claimed a 0.57% reduction in HbA1c for T2DM patients using smartphone applications. This observation indicates that smartphone applications could play a role in T2DM management in the future. Smartphone applications may also play a role in clinical decision-support systems or in the prevention and treatment of T2DM in remote or less-developed areas (29, 30).

Smoking Cessation

Smoking is a major modifiable risk factor for IHD, certain cancers, and multiple other diseases (31). Smoking cessation is a major part of every prevention programme. Current cessation interventions consist of pharmacological treatment and cognitive behaviour therapy. These rely heavily on health professionals initiating the treatment. Digital health could provide opportunities to engage less-motivated and/or remote smokers as well as enable long-term monitoring.

Internet-based interventions are an innovative way to deliver smoking cessation interventions. Sixteen trials and one meta-analysis conducted from 2015 to 2019 studied the effectiveness of Internet-based interventions for effective smoking cessation. Of these trials, 59% revealed that Internet-based interventions can lead to smoking cessation. More research or larger trials are necessary to assess and confirm the effectiveness in comparison with standard care. More details on the related research review are described in Annex 1.

A number of small trials indicated a positive effect of Internet intervention on cessation rates (32, 33). On the other hand, large RCTs with more than 1000 patients suggest that Internet-based interventions have no additional effect on cessation rates in comparison with usual care. Graham et al. (34) demonstrated in 2018 that the use of an Internet-based intervention combined with social networks can enhance all three recommended components of an evidence-based smoking cessation programme (skills training, social support, and pharmacotherapy use). However, no higher cessation rates were observed. In 2016, Neri et al. (35) and Harrington et al. (36) came to the same conclusion. A tailored Internet-based intervention trial in 2017 reported an increase in hard-core smokers' receptivity to smoking cessation information and a decrease in cigarette consumption by only one cigarette per day (37).

A recent meta-analysis report by McCrabb et al. (38) on the effectiveness of an Internet-based smoking cessation intervention claimed that these interventions increased the odds of cessation by 29% in the short term and by 19% in the long term. In conclusion, more evidence is necessary to implement an Internet-based intervention in regular care.

Seventeen trials and three meta-analyses (2015–2019) showed that in 80% of the trials, text messaging can be effective in achieving smoking cessation. However, more research or larger trials are required to assess the long term effectiveness of these interventions. More detailed information is provided in Annex 1.

The use of text messages is an alternative innovative way to increase cessation rates. Multiple trials have demonstrated a positive effect of text messaging as a smoking cessation intervention (39-43). This conclusion was confirmed by an RCT (2017) with 8000 Chinese patients (44) and in two meta-analyses (45, 46). There is sufficient evidence that text messaging is an effective intervention for improving cessation rates. Hence, it could be a standard element of smoking cessation interventions.

Three out of four trials (2015–2019) reported the effectiveness of smartphone applications in achieving smoking cessation. More detailed information on the reviews can be found in Annex 1.

Crane et al. (47) demonstrated in 2019 that a smartphone application could result in higher self-reported three-month continuous smoking cessation. The evidence-based behaviour-change therapies implemented in the full version of the application were:

1) Supporting identity change: users thinking of themselves as non-smokers.
2) Rewarding cessation by praise, virtual prizes, and showing users the amount of money they save each day they are not smoking.
3) Changing routines: advising on ways to avoid smoking cues by changing routine.
4) Advising on medication use: promoting the use of one of the evidence-based smoking cessation medicines (47).

The above conclusion was confirmed in a study by Masaki et al. (48) in 2019. Their application consisted of a smoking cessation diary, messages and educational videos, and counselling chat sessions with an artificial intelligence nurse (48).

Weight loss management

Overweight and obesity are independent predictors for IHD (49). Weight loss interventions are not only important to reduce obesity; these interventions also influence a number of "major" risk factors including hypertension, high cholesterol, and T2DM (50). Weight loss programmes consist of physical activity training and dietary advice.

Internet-based weight loss interventions have been assessed in multiple large trials. Harden et al. (51) demonstrated in 2015 that an Internet-based worksite weight loss programme was able to reduce weight in 22% of the participants. Plaete et al. (52) showed in 2015 that a digital health intervention was able to improve physical activity levels as well as fruit and vegetable intake. Other trials confirmed the positive effects of Internet-based weight loss interventions on diet choices, physical activity, or weight (53-56).

Smartphone applications are another way to deliver weight loss interventions. Twenty-five trials and three meta-analyses conducted from 2015 until the end of 2019 looked at the effectiveness of smartphone applications for weight loss, and 89% of the trials showed that smartphone applications can lead to weight loss. More research or larger trials are needed to confirm the long-term results and to assess the cost-effectiveness of these interventions. Details on the research review are provided in Annex 1.

Goldstein et al. (57) and Muralidharan et al. (58) showed in 2019 that smartphone applications can help to achieve a moderate short-term weight loss. Three other trials demonstrated the positive effects of smartphone applications on weight loss (59-61). The short-term efficacy of smartphone-based interventions was confirmed in two recent meta-analyses (62, 63). However, all of these RCTs had relatively small sample sizes (between 100 and 833 patients).

Kurtzman et al. (64) performed an interesting trial in 2018, testing the combination of social incentives and gamification within digital health devices. Gamification is the use of game-design elements. They demonstrated that using digital health devices to track behaviour led to significant weight loss through 36 weeks, but the gamification interventions were not effective at promoting weight loss when compared to the control group (64).

The effectiveness of text messaging interventions for weight loss remains debatable. Eight trials and two meta-analyses conducted from 2015 until the end of 2019 looked at the effectiveness of text messaging for weight loss, and 75% of the trials showed that text messaging can lead to weight loss. More research or larger trials are needed to confirm the long-term results and to assess the cost-effectiveness of these interventions. Details on the research review are provided in Annex 1.

An RCT conducted by Sidhu et al. (65) concluded that text message intervention was not successful in the maintenance phase of a weight intervention. Two meta-analyses demonstrated a small effect of text messaging interventions in short-term weight loss (66, 67). However, a lack of long-term results indicates that further efficacy studies are required.

Physical activity

A sedentary lifestyle and physical inactivity are important risk factors for IHD (68). Physical activity is, therefore, an important part of primary and secondary prevention programmes. Regular physical activity is associated with beneficial effects on insulin sensitivity, metabolic syndrome, weight, BP, and QoL (69). Current guidelines recommend a minimum of 150 minutes of moderate-intensity aerobic physical activity or at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week (70).

Seventeen trials and two meta-analyses conducted from 2015 until the end of 2019 looked at the effectiveness of pedometers in increasing physical activity, and all of the trials showed that pedometers can lead to increased physical activity. More research or larger trials are needed to confirm the long-term maintenance of higher physical activity. Details on the research reviews are provided in Annex 1.

Pedometers or activity trackers can be used to collect objective data on physical activity, which health professionals can use to give feedback to patients. Macniven et al. (71) demonstrated in 2015 that a pedometer-based programme is effective in reducing occupational sedentary behaviour. In 2016, Finkelstein et al. (72) confirmed that a pedometer-based programme combined with cash incentives was successful in increasing short-term physical activity. A meta-analysis by Qui et al. (73) in 2015 also concluded that step counter-based programmes are associated with reduced sedentary time among adults. Current evidence suggests the possible effectiveness of these interventions; however, more large trials and cost-effectiveness analysis are needed.

Twenty-two trials and four meta-analyses conducted from 2015 until the end of 2019 looked at the effectiveness of smartphone applications in increasing physical activity, and 81% of the trials showed that smartphone applications can lead to increased physical activity. More research or larger trials are needed to confirm the long-term maintenance of higher physical activity. Details on the research reviews are provided in Annex 1.

All recent smartphones have a built-in accelerometer which can be used as an objective measure of physical activity. Multiple studies have researched the effect of smartphone applications in motivating people to move more. Most of these studies are single-centre and have only small sample sizes, so it is difficult to draw a conclusion about their effectiveness. Direito et al. (74) conducted a meta-analysis in 2017 on physical activity promoted by digital health technologies and concluded that they only had small effects in improving physical activity and reducing sedentary time. This conclusion was confirmed by a meta-analysis published in 2019 by Romeo et al. (75).

Fourteen trials conducted from 2015 until the end of 2019 looked at the effectiveness of text messaging on increased physical activity, and 79% of the trials showed that text messaging can lead to increased physical activity. Details on the research reviews are provided in Annex 1.

The effect of online social networks, gamification, and incentives were also investigated in multiple small trials. Most of these interventions show modest improvement in physical activity. Again, more evidence is needed to confirm the effectiveness and to justify implementation in standard care (76-78).

Conclusions

Digital health can have an impact on different cardiovascular risk factors to reduce the risk for a future CVD. Blood pressure telemonitoring could be effective approach for the diagnosis of arterial hypertension and for the follow-up of BP. More research is required to demonstrate the value of adding telemonitoring to self-monitoring alone. There is currently insufficient evidence to confirm the effectiveness of mHealth applications in hypertension management. Telemonitoring of T2DM patients has been studied in multiple small, single-centre trials. Most of these studies show positive effects of telemonitoring on HbA1c. Text messaging interventions can also play a potential role in the chronic management of T2DM. Smartphone applications for T2DM management seem to have high potential however most trials had small sample size and short follow-up. More long-term studies with large sample size are required to confirm the effectiveness of digital health in the management of T2DM. Internet-based interventions are an innovative way to deliver smoking cessation. Numerous studies show contradictory results, so more evidence is necessary to implement an Internet-based intervention in regular care. Multiple trials demonstrate the effectiveness of text messaging for improving cessation rates. Hence, it could be a standard element of smoking cessation interventions. Internet-based weight loss interventions seem to have positive effects on diet choices, physical activity, or weight. Numerous smartphone applications show positive effects on short-term weight loss. However, larger trials are needed to confirm the long-term results and to assess the cost-effectiveness of these interventions. The effectiveness of text messaging interventions for weight loss remains debatable. Pedometer-based and smartphone-based interventions seem an effective method to improve physical activity in primary prevention. The long-term maintenance of the higher physical activity level of both interventions is still uncertain.

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Chapter 2: Digital Health in secondary prevention of ischaemic heart disease (IHD)

Premature CVD mortality is decreasing in most European countries due to better medical care and prevention. However, the reduction in mortality rates has slowed down (1-3). Suspected causes are the rising prevalence of obesity and diabetes, along with an ageing population (3,4).

CVD recurrence rates are also high (up to 5–15% recurrence rate in the first year after myocardial infarction), partially due to insufficient implementation of secondary prevention measures, as shown recently in the EuroAspire audits (1,5). This high prevalence of CVD events leads to an immense economic burden (6).

Secondary prevention consists of two pillars: optimal medical therapy and a healthy lifestyle (7,8). Multiple trials have confirmed the positive effects of aspirin, statins, and BP-lowering agents on recurrent CVD events (9-11). Healthy lifestyle counselling is often incorporated in cardiac rehabilitation (CR). Therefore, current European guidelines recommend CR for all patients with CAD (7,8). CR comprises different core components such as physical activity, risk factor modification, nutritional counselling, and psychosocial wellbeing (7,8). Unfortunately, only a few eligible patients participate in CR mainly due to transport and schedule constraints (12).

Digital health has the potential to overcome these barriers and to improve CR access and uptake. Recent publications have demonstrated that telerehabilitation (delivery of cardiac rehabilitation by digital means) can be as effective as centre-based CR and can improve participation (13-15). This could be important in remote areas or areas with few CR services. Furthermore, it has the potential to empower patients and keep cardiovascular care affordable (7).

Exercise training at home and Telerehabilitation of IHD

The beneficial effects of physical activity on a daily basis in primary and secondary prevention is well established (16,17). Physical activity has positive effects on blood lipid profiles, BP, insulin resistance, inflammation, etc. (7,16-18). Therefore, exercise training is a central part of CR and secondary prevention of IHD. Despite the protective and beneficial effects, participation rates after an IHD event remain low; less than 50% of eligible patients attend CR (12,19). Multiple trials studied the predictors of poor participation in CR; these include distance to the CR centre, lower socio-economic status, older age, and female gender (12,19). Home-based exercise programmes have been studied since the 1980s (20-21), but our focus is on studies from 2000 on.

Thirty-two trials and five meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of home rehabilitation for IHD, and all trials showed that home rehabilitation for IHD could be an effective alternative for centre-based CR. Details on the research review are provided in Annex 2.

Ades et al. (22) demonstrated in 2000 that home-based, trans-telephonically monitored CR had comparable effects on QoL and exercise capacity (EC) as an on-site CR programme. In 2001, a retrospective analysis showed that stable post coronary artery bypass grafting (CABG) patients receiving a detailed exercise prescription to follow at home do as well as those in supervised rehabilitation (23). Arthur et al. (24) confirmed in 2002 that home CR was efficient for low-risk CABG patients. In 2006, Kortke et al. (25) conducted one of the first studies to investigate the cost-effectiveness of trans-telephonic ambulatory rehabilitation in cardiac surgery patients. They concluded that the intervention could reduce total rehabilitation costs by 58% (25). In 2007, Jolly et al. (26) conducted one of the largest RCTs showing that home-based CR programmes for low- to moderate-risk patients do not produce inferior outcomes compared with traditional CR programmes.

Several meta-analyses have reviewed the evidence on home-based CR. They concluded that home-based CR results in short-term improvements in EC and health-related QoL compared to usual care (27-30). A meta-analysis by Buckingham et al. (30) in 2016 concluded that costs of home-based and centre-based CR are equivalent for patients with IHD.

One way to supervise home-based exercise training in secondary prevention of myocardial infarction (MI) is the use of pedometers. In 2010, Furber and his team (31) conducted an RCT with 215 patients and demonstrated that a pedometer-based telephone intervention could be offered as an effective option for patients not attending CR to increase and maintain their physical activity levels after hospitalisation. Sangster et al. (32) tested the same intervention in 2015 with a larger RCT, confirming that this low-contact intervention was feasible to provide CR in underserved rural areas. A recent trial in 2019 using a pedometer feedback intervention in phase III CR demonstrated that pedometer feedback was superior to providing usual physical activity recommendations without follow-up (33).

Thirty-four trials and three meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of telerehabilitation for IHD, and 97% of all trials showed that telerehabilitation for IHD does not have significantly inferior outcomes compared to a centre-based supervised programme. Details on the research review are provided in Annex 2.

More recent approaches use mHealth technology such as smartphones, text messaging, Internet, and virtual reality in telerehabilitation programmes. Dalleck et al. (34) demonstrated that a videoconference-delivered CR programme is feasible for risk factor modification and exercise monitoring. In 2011, Worringham et al. (35) demonstrated that a smartphone, ECG, and GPS-based system for remotely monitoring exercise could be used effectively for remote CR.

A trial called TELEREHAB III by Frederix et al. (36) was published in 2015. They used accelerometer monitoring in combination with text messaging to deliver telerehabilitation as an add-on to standard CR. This RCT showed that a six-month telerehabilitation programme leads to larger improvement in both physical fitness and QoL (36). Frederix et al. (37) demonstrated in 2017 that this intervention induced persistent health benefits and remained cost-effective up to two years after the intervention ended. Maddison et al. (38) performed a randomised controlled telerehabilitation trial in 2019 which comprised a smartphone and chest-worn sensor to monitor and educate patients. They demonstrated that the intervention was an effective and cost-effective delivery model that could improve overall CR utilisation rates by increasing reach and satisfying unique participant preferences (38).

Several meta-analyses reviewed the effect of mHealth-supported telerehabilitation. Huang et al. (39) demonstrated in 2015 that telehealth-delivered CR was not inferior to centre-based CR. Rawstorn et al. (40) and Claes et al. (41) came to the same conclusion in 2016 and 2017, respectively. Rawstorn et al. (40) concluded that telerehabilitation was as effective as traditional CR for improving modifiable cardiovascular risk factors and functional capacity. In 2018, a meta-analysis by Wu et al (42) had a comparable message that the efficacy of hybrid CR (a combination of centre-based CR with telerehabilitation) is similar to that of standard CR, and a 2019 meta-analysis by Su et al. (43) concluded that mHealth CR is effective in engaging patients in an active lifestyle, improving QoL, and reducing rehospitalisation.

Reflecting on the current evidence, the conclusion can be made that home-based exercise training or telerehabilitation for IHD patients is an effective way to deliver exercise training in patients who cannot attend centre-based CR and as an add-on to centre-based CR to increase its long-term effects. Most trials demonstrate comparable results in EC between centre-based CR and telerehabilitation with often a better impact on QoL for the telerehabilitation intervention. Several trials suggest that telerehabilitation as a standalone or as an add-on is cost-effective. However, larger studies in different healthcare systems, as well as more research on cost-effectiveness, are needed.

Lifestyle management in secondary prevention of IHD

Improving physical activity is a major part of secondary prevention programmes and CR but tackling other cardiovascular risk factors is also crucial to prevent recurrent events. Other components of lifestyle management programmes in CR are smoking cessation, stress and mental health management, nutritional counselling, and medication adherence. Participation in CR programmes can often help to improve the risk factor status of IHD patients, and digital health tools may help to maintain the long-term self-management of IHD after CR with an array of personal smartphone-based technologies (44).

In 2002, Vale et al. (45) demonstrated that a telephone coaching intervention is effective for increasing medication adherence. With the sequel RCT of 792 patients in 2003, Vale et al. (46) demonstrated that a telephone coaching intervention is a highly effective strategy to reduce total cholesterol and address other coronary risk factors. Multiple other studies demonstrated that telephone counselling and follow-up are effective options for long-term lifestyle management (47-51). Hansen et al. (52) showed in 2007 that a nurse-led systematic telephone follow-up intervention also could improve the physical dimension of health-related QoL compared with usual care. A large observational trial in 2013 by Nymark et al. (53)

showed that telephone counselling led to a 27% reduction in utilisation and a 22% reduction in-hospital care costs. In 2014, Kotb et al. (54) demonstrated that a telephone support intervention for IHD patients led to reduced feelings of anxiety and depression and improved systolic BP control and the likelihood of stopping smoking.

In 2003, Southard et al. (55) tested an Internet-based case management system. They concluded that it could be used as a cost-effective intervention for patients with CVD. Levine et al. (56) performed a cluster RCT of 15847 patients in 2011 using an Internet-delivered intervention. After two years, only one of seven clinical indicators of cardiovascular risk factor management was improved. This result corresponds to a 2008 study by Holmes-Rovner et al. (57) concluding that coaching post-hospitalisation for acute coronary syndrome (ACS) was modestly effective in accomplishing short-term but not long-term lifestyle behaviour change. Norlund et al. (58) demonstrated in 2018 that an Internet-based cognitive behavioural therapy (iCBT) for a myocardial infarction (MI) population did not result in lower levels of symptoms of depression or anxiety compared with the standard as usual. Possibly, low adherence to the Internet intervention could have influenced the effects of the iCBT.

A meta-analysis by Devi et al. (59) in 2015 concluded that there was not enough evidence for the impact of Internet-based interventions for secondary prevention of IHD on healthcare utilisation and cost-effectiveness to draw conclusions.

The introduction of smartphones and smartphones gave health professionals the opportunity to deliver ‘pocket-size’ secondary prevention programmes. Blasco et al. (60) demonstrated in 2012 that a telemonitoring programme via smartphone messages appears to be useful in improving the risk profile of ACS patients. In 2013, Quilici et al. (61) used motivational smartphone SMS messages to improve the rate of antiplatelet medication intake after stent implantation. Three recent large RCTs using text messaging interventions for lifestyle promotion in secondary prevention of IHD demonstrated significant improvements in risk factor profiles (62-64).

Smartphone applications provide other opportunities in addition to text messaging. In 2014, Forman et al. (65) showed that a smartphone application for CR delivery was safe and agreeable to patients and clinicians. A 2019 RCT by Santo et al. (66) including 163 patients concluded that patients with IHD who used medication reminder apps had better medication adherence compared with usual care. In a study using 176 IHD patients, Johnston et al. (67)

demonstrated in 2016 that a smartphone application can improve patient self-reported drug adherence and may be associated with a trend towards improved cardiovascular lifestyle changes and QoL. In 2018, Coorey et al. (44) investigated the effect of smartphone applications on CVD self-management in a meta-analysis of ten trials. Multiple behaviours and CVD risk factors seemed modifiable in the shorter term with the use of smartphone apps (44).

In 2019, Jin et al. (68) published a meta-analysis of thirty studies investigating telehealth interventions for secondary prevention, showing no significant difference in all-cause mortality but a significant reduction in rehospitalisation in the intervention group. They concluded that telehealth interventions with a range of delivery modes could be offered to patients who cannot attend CR, or as an adjunct to CR for effective secondary prevention.

Conclusions

Home-based exercise training and telerehabilitation can be effective ways to increase physical activity in CAD patients. They can be provided as standalone programmes or as an add-on to centre-based CR to increase the long-term effects of CR. There is some evidence that these interventions can be cost-effective, but more research is needed to confirm that. Important to mention is the fact that most trials have had relatively small sample sizes.

Lifestyle management of IHD with the help of digital health tools is an effective way to optimise the risk factor profile of patients. Telephone counselling, text messaging, and smartphone applications are especially effective, while Internet-based interventions, as yet, have failed to prove effective. Smartphone applications have the potential to provide accessible pocket-size interventions.

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Chapter 3: Digital health in heart failure management

Heart Failure (HF) can be defined as the heart's reduced ability to pump or fill with blood, and therefore, the heart cannot create sufficient cardiac output (1). HF has recently been classified into three subtypes, namely, HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF), and HF with mid-range ejection fraction (HFmrEF), according to the ejection fraction, natriuretic peptide levels, the presence of structural heart disease, and diastolic dysfunction (2).

HF is the leading cause of hospitalisation in Europe (3) and accounts for a large part of the healthcare expenditure. A study conducted in 2012 by a research group at the International Centre for Circulatory Health at Imperial College London estimated the costs related to HF in 24 EU member states in one year to be US$33.14 billion (~ €29 billion) (4,5). The bulk of the costs are driven by frequent, prolonged, and repeat hospitalisations. HF is associated with high rehospitalisation rates; up to 50% of patients are readmitted to the hospital within six months of discharge (6). This has a large impact on QoL and on healthcare budgets across Europe.

Acute HF, or decompensated HF, is often preceded by signs and symptoms such as weight gain, dyspnoea, reduction in physical activity, etc. Remote patient management or monitoring in patients with HF might help to detect early signs and symptoms of cardiac decompensation, thereby enabling a prompt initiation of the appropriate treatment and avoiding hospitalisation (7).

Telemonitoring of HF is one of the most researched and implemented topics within digital health. Multiple studies have demonstrated the feasibility and effectiveness of remote monitoring of HF patients (7,8), but the possibilities for digital health in HF reach much further. For example, biosensors can be used to measure thoracic impedance to predict HF decompensation, and smartphone applications can be used to educate patients and enable self-management.

Telemedicine in HF

Telemonitoring

It is well established that long-term follow-up of HF patients and disease management programmes for self-management enhance survival rates and QoL. Face-to-face disease management programmes are successful but require significant resources and patient efforts (9). Therefore, new technologies are being researched to allow remote disease management programmes which might be more cost-effective than face-to-face programmes.

Sixty-three trials and seven meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of telemonitoring in HF patients, and 63% of the trials showed that it is effective in reducing mortality and healthcare utilisation. All seven meta-analyses concluded that telemonitoring seems to reduce mortality and rehospitalisation. Details on the research review are provided in Annex 3.

Telemonitoring can reduce patient-professional contact and, therefore, make long-term HF care more accessible as well as decrease healthcare costs. Cleland et al. (10) performed one of the first telemonitoring trials for HF in 2005. In an RCT with 426 patients, they demonstrated that home telemonitoring can play a valuable role in the management of selected patients with HF. In 2017, Pinna et al. (11) tested telemonitoring in an RCT of 461 patients. The study showed that telemonitoring of both vital signs and respiration was feasible in patients with HF. Giordano et al. (12) in 2007 and Woodend et al. (13) in 2008 both carried out RCTs with HF patients and demonstrated that a home-based tele-management strategy could reduce hospital readmissions and costs (12) as well as improve functional status and QoL (13).

In 2010, Chaudry et al. (14) included 1653 patients in a multicentre RCT where telemonitoring was performed with a telephone-based interactive voice response system. They reported no significant differences between the telemonitoring group and the usual care group in rehospitalisation, number of days in the hospital, and the number of hospitalisations and deaths. These results from one of the largest telemonitoring trials were surprising, considering that other trials at the time demonstrated the effectiveness of telemonitoring for HF patients. One of the potential reasons is the fact that adherence to the telemonitoring system was low at the end of the study period; in its final week, only 55% of the patients were still using the system at least three times per week (14).

In the same period, three other RCTs found no significant effects (15-17). A 2011 study by Wade (15) demonstrated that an Internet-based telehealth intervention in an elderly HF population did not result in better outcomes than usual care. Boyne et al. (16) performed an RCT in 2012 with 382 patients, and no significant differences were found regarding time to first HF hospitalisation. The authors hypothesised that the 'disappointing results' could be due to a relative underpowering of the intervention group combined with a very well-treated control group (16). However, they revealed in a 2014 sub-analysis that tailored telemonitoring was an effective way to educate patients with HF and to improve their self-care abilities and sense of self-efficacy (18). The third trial in 2011 that failed to show the effectiveness of telemonitoring was the TIM-HF trial (17). This RCT with 710 patients tested a telemedical management system using portable devices for electrocardiogram (ECG), BP, and body weight. They concluded that this strategy was not associated with a reduction in all-cause mortality compared with usual care (17).

In 2012, Dendale et al. (8) demonstrated that a telemonitoring-facilitated collaboration between the general practitioner and HF clinic reduced mortality and number of days lost to hospitalisation, death, or dialysis in HF patients. The TIM-HF 2 trial (7), which included 1,571 patients, was published in 2018 and demonstrated that a structured remote patient management intervention used in a well-defined HF population reduced the number of days lost due to unplanned cardiovascular hospital admissions and all-cause mortality. Moreover, three meta-analyses were published in 2014 (19) and 2018 (9,20) evaluating, respectively, remote monitoring and telemonitoring of HF patients. Nakamura et al. (19) concluded that remote monitoring for HF patients was effective. Yun et al. (9) demonstrated that telemonitoring of HF patients reduced mortality risk, and intensive monitoring with more frequent transmissions of patient data increased its effectiveness. In this recent meta-analysis, thirty-seven RCTs were included.

Pekmezaris et al. (20) also published a meta-analysis on home telemonitoring for HF patients. They concluded that home telemonitoring decreased the odds of all-cause mortality and HF-related mortality at 180 days but not at 365 days. This was also concluded by Frederix et al. (21) in 2019, demonstrating that an initial six-month telemonitoring programme was not associated with reduced all-cause mortality in HF patients at long-term follow-up (after the monitoring period ended) but resulted in a reduction in the number of days lost due to HF readmissions. So, telemonitoring intervention for HF seem only to have a positive effect in a short period after the intervention has ended. This suggest that long-term telemonitoring is needed for HF patients.

In conclusion, many trials have demonstrated the effectiveness of telemonitoring in reducing rehospitalisation and improving QoL for HF patients. In addition, meta-analyses of these trials demonstrate significant improvement in outcomes for the telemonitoring interventions, especially in the short term. However, some large multi-centre trials failed to demonstrate telemonitoring effectiveness. Potential reasons can be patient selection, low adherence to the telemonitoring approach, or less intense intervention in these studies. Therefore, new multi-centre studies are needed to determine how to make telemonitoring effective for all patients and feasible for health professionals.

Telephone follow-up

Telemedicine or remote monitoring was introduced as a potential way to reduce the likelihood of deteriorating cardiac illness or the prospect of hospital readmissions (22). Next to telemonitoring systems, which involve the transmission of information on symptoms and signs, structured telephone support is another option for long-term monitoring (22).

Forty-two trials conducted from 2000 until the end of 2019 looked at the effectiveness of telephone follow-up for HF patients, and 69% of these trials showed that it is effective in reducing mortality or healthcare utilisation. Details on the research review are provided in Annex 3.

Clark et al. (23) demonstrated in 2007 that telephone monitoring is well accepted by elderly HF patients. Furthermore, Smith et al. (24) confirmed the effectiveness of a telephone-supported HF patient approach in 2008. However, they also concluded that organising such an approach was costly and did not lead to reduced healthcare utilisation.

In a 2016 prospective observational study of 1816 patients, Laborde-Casterot et al. (25) showed that multi-disciplinary HF disease management delivered by phone may improve survival. The TEACH-HF, a 2015 RCT with 1033 patients, demonstrated that home follow-up phone calls were associated with significantly fewer hospital readmissions (26). Furthermore, Baker et al. (27) showed in 2011 that progressive, reinforcing telephone education for HF patients was effective in improving knowledge, health behaviours, and HF-related QoL compared to a single education session. A recent trial in 2018 by Grustam et al. (28) demonstrated that nurse telephone support approaches are viable options for chronic HF patient follow-up. They even showed that the nurse telephone support approach was cost-effective in comparison with usual care.

To conclude, trials show that telephone counselling can be an effective option in long-term HF management. Telephone counselling can be effective in reducing HF patient admission but seems most effective in improving patients' knowledge and self-care. A question remains regarding the cost-effectiveness of a structured telephone counselling approach.

Smartphone applications in heart failure

Smartphone applications and text messaging are more recent tools for remote monitoring of HF patients. Text messaging gives health professionals the opportunity to interact with patients in a less intrusive way. Smartphone applications have the potential to enable pocket-size delivery of multidisciplinary HF patient care. Cajita et al. (29) performed a survey in 2017 considering the acceptance of an mHealth application by elderly HF patients. For applications, they underline the importance of co-creation to ensure that the developed mHealth-based interventions will not only address the patient's needs but also be user-friendly for this mainly elderly population.

Most trials using smartphone applications or text messaging for HF patients only assess feasibility or patient and healthcare professional satisfaction. Below, the studies reporting health outcomes are provided.

Scherr and his team showed in 2006 (30) and 2009 (31) that smartphone-based telemonitoring of HF patients has the potential to reduce the frequency and duration of HF hospitalisations. Multiple studies confirmed that smartphone technology is suitable for continuous and secure medical data transmission in HF telemonitoring (32,33). Smartphones can also play a role as an electronic pillbox or be used as an mHealth intervention (smartphone application) for improving medication adherence in HF patients (34). Nundy et al. (35) showed in 2013 that text messaging was associated with a high rate of satisfaction and possible improvements in HF self-management. In 2012, Austin et al. (36) tested a smartphone-based interactive voice response system (IVRS) with daily self-management and clinical monitoring messages. In this single cohort study of sixty patients, they concluded that an IVRS self-management support system can be an effective technology to reduce HF readmissions (36).

In 2017, Dang et al. (37) tested a smartphone intervention in an RCT with sixty-one patients from a minority population. Interestingly, they concluded that the smartphone intervention offered a modality to help reduce ethnic disparity and could lead to improvements in QoL and self-efficacy (37). Athilingam et al. (38) tested the HeartMapp application in 2017 in a small pilot feasibility RCT. HeartMapp was downloaded on the patient’s smartphone, and the patient was trained to use the application features including daily weighing, symptom assessment, responding to tailored alerts, vital sign monitoring using a BioHarness-3 chest strap, HF education, performing a breathing exercise, and walking. They concluded that the results warrant further exploration of the use of HeartMapp to improve HF patient outcomes.

In conclusion, there is not yet strong evidence for the use of smartphones in long-term management of HF for long-term outcomes. Acceptance by patients, however, is good. Most trials have small sample sizes and short follow-up periods. The potential of smartphone use in long-term management of HF seems enormous; however, there is a need for large multi-centre trials to demonstrate the effectiveness and cost-effectiveness for these interventions.

Telerehabilitation in HF

The HF guidelines of the European Society of Cardiology suggest that HF management must be holistic, containing appropriate pharmacological and device therapy, CR, remote monitoring of cardiac implantable electronic devices (CIEDs), and regular follow-up (39). CR is often an underestimated part of long-term HF management.

Taylor et al. (40) demonstrated in a 2019 meta-analysis that exercise-based CR can lead to reductions in the risk of all-cause and HF-specific hospitalisation as well as potential important gains in QoL for people with HF. Like in CR for IHD, there are many possible barriers to participation (41). Telerehabilitation could be a promising solution to overcome some of the barriers and provide guideline-consistent monitoring of physical activity (42).

Thirty-five trials and three meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of home rehabilitation for HF patients, and 91% of the trials showed that home rehabilitation for HF is effective in improving EC and QoL or reducing healthcare utilisation. Details on the research review are provided in Annex 3.

In 2000, Oka et al. (43) researched a home-based (walking) exercise programme for HF patients, monitoring adherence and progress as well as providing individualised feedback by weekly phone calls. They demonstrated that this intervention lowered fatigue and improved emotional function. Gary et al. (44) showed in 2004 that home-based, low-to-moderate-intensity exercise is an effective strategy for improving functional capacity and QoL. Another interesting trial was conducted by Smart et al. (45) in 2005. They used heart rate monitors, exercise diaries, and weekly telephone calls to monitor home-based exercise and concluded that this intervention was feasible for HF patients.

After these first three trials, Evangelista et al. (46) performed an RCT with ninety-nine patients in 2006. They demonstrated the beneficial effects of a low-level, home-based walking programme on weight loss in overweight and obese patients with advanced HF. A home-based walking programme was also investigated in 2007 by Dracup et al. (47) with a cohort of 173 patients with systolic HF. However, they concluded that the intervention did not result in improved clinical outcomes at the one-year follow-up.

An RCT in 2009 demonstrated that a home-based exercise programme was as effective as standard CR and provided a similar improvement in QoL (48). However, a study by Jolly et al. (49) in the same year failed to demonstrate any benefit from the addition of a home-based exercise programme in a community-based HF population. (49). Piotrowicz et al. (50) demonstrated in 2015 that home-based telerehabilitation was safe and effective for HF patients. Furthermore, the telerehabilitation intervention had an effect that was similar to standard care on QoL and was well accepted by the HF patients (51). In 2015, Piotrowicz et al. (52) also tested a home-based Nordic walking exercise programme for HF patients. They included 111 patients with HF, including those with a CIED, and demonstrated that home-based telemonitored Nordic walking was safe and effective (52).

The year 2019 was productive for telerehabilitation trials. Dalal et al. (53) conducted the REACH-HF trial in which home-based telerehabilitation was assessed in an RCT with 216 HFrEF patients. They concluded that a home-based IT-facilitated intervention for HFrEF patients was clinically superior for disease-specific health-related QoL at twelve months and offered an affordable alternative to traditional centre-based programmes to address current low CR uptake rates for HF patients (53). Piotrowicz et al. (42) carried out the TELEREH-HF trial, which has been the largest telerehabilitation study for HF patients yet. In this trial, the effects of a nine-week programme of hybrid telerehabilitation for patients with HF were not associated with an increase in the percentage of days alive and out of the hospital and did not reduce mortality and hospitalisation over a follow-up period of fourteen to twenty-six months in comparison with usual care (42).

The cost-effectiveness of telerehabilitation for HF patients was assessed by Hwang et al. (54) in 2019 in a small RCT (53 patients). HF patient telerehabilitation was found to be less costly and as effective for the healthcare provider as traditional centre-based rehabilitation.

In conclusion, there is still debate on whether telerehabilitation is effective in reducing rehospitalisation and mortality in HF patients. Two trials published in 2019 agree that telerehabilitation for HF patients is effective in increasing QoL, but neither trial found significant differences in rehospitalisation or percentage of days alive. More research in home-based exercise training for HF patients is needed to investigate the long-term effects.

Conclusions

Many trials have studied telemonitoring for HF patients, and many of them show that it is effective in reducing rehospitalisation and in improving QoL. However, some large multi-centre trials have failed to demonstrate the effectiveness of telemonitoring. Therefore, future studies must investigate ways to make telemonitoring effective for patients and feasible for health professionals. Telephone follow-up can be an effective way to reduce healthcare utilisation. The effectiveness of smartphone applications and text messaging for long-term follow-up still needs much research. Current research suggests that it is a feasible and well-accepted intervention to possibly improve HF outcomes. Most studies demonstrate that home-based rehabilitation is effective in improving EC and QoL. However, only a few studies have investigated the long-term outcomes, and these studies show contradictory results. More research is needed to investigate the long-term effects.

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Chapter 4: Home-hospitalisation of heart failure patients

Heart Failure (HF) is associated with a high rate of rehospitalisation in a population with a low life expectancy (five-year life expectancy around 50%) (1-5). Frequent rehospitalisation of HF patients not only leads to increased healthcare costs, but it is also associated with functional decline, confusion, and in-hospital infections. As such, innovative delivery care models for HF patients are researched due to this important socio-economic burden and negative impact on QoL (1-5). Limited research shows that hospital-at-home programmes could reduce hospital admissions and allow patients to stay at home as much as possible.

Hospital-at-home, or home hospitalisation, is the delivery of acute hospital-level care in a home setting. Hospital-at-home comprises only the treatment of an acute HF decompensation at home, which normally takes place in the hospital and should be distinguished from permanent follow-up, telemonitoring, telerehabilitation, and early discharge interventions. During the home hospitalisation intervention, a physician or healthcare professional delivers daily home care during the acute decompensation of HF. Daily home care can consist of diagnostic tests including clinical examination, ECGs, blood samples, and administering HF therapy such as intravenous fluids or medications (6).

At this moment, there is little evidence regarding the effects of the hospital-at-home intervention for HF patients. A previous systematic review and meta-analysis based on six studies concluded that a hospital-at-home care programme foresees possible benefits in reducing acute hospital readmission and costs (6). The quality and quantity of the included studies were modest, which makes it difficult to gather real evidence for this model's efficacy.

However, with the implementation of digital health and the development of new technologies for distant surveillance, hospital-at-home interventions for HF patients (and potentially also for those with other indications in cardiology) may play an important role in reducing HF rehospitalisation and in improving QoL for HF patients in the future. Details on the research review are provided in Annex 4.

Conclusions

Home hospitalisation supported by IT technology could potentially reduce the need for hospital beds and improve HF patients' outcomes and QoL. However, the research is still in its infancy, awaiting strong proof from RCTs. The necessary technology and organisation can be used to help safely discharge HF patients earlier.

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Chapter 5: Digital health in cardiac arrhythmia diagnosis and management

Cardiac arrhythmia is defined as an irregular, very fast or very slow heart rate. Tachycardia is the presence of a fast heart rate (above 100 beats per minute). Bradycardia is a very slow heart rate (below sixty beats per minute). Common symptoms of cardiac arrhythmias are palpitations (sensations of an uncomfortable, irregular heartbeat), chest pain, dizziness, dyspnoea, and syncope.

The most prevalent arrhythmia is atrial fibrillation (AF), especially in elderly people. AF happens when electrical impulses fire off from different places in the top chambers of the heart (the atria) in a disorganised way. These irregular impulses cause the atria to quiver or twitch, which is known as fibrillation. This results in an irregular and often rapid heart rate that can increase the risk of strokes, HF, and other heart-related complications. Therefore, cardiac arrhythmias are associated with substantial morbidity, mortality, and economic costs (1).

Every day, patients visit general practitioners or emergency departments for palpitations, (pre) syncope, or feeling of irregular pulsations (2). Diagnosis of cardiac arrhythmia is, however, difficult because cardiac arrhythmias are often intermittent. Ambulatory ECG monitoring is therefore used to monitor ECG data over an extended period of time. This permits an evaluation of the dynamic and transient differences in the heart rhythm. However, ambulatory Holter monitoring is still limited in duration and can therefore still miss a significant portion of cardiac arrhythmias. The use of smartphone or smartwatch applications and handheld devices could help in long-term monitoring of intermittent cardiac arrhythmias. The advantage of these tools is that patients can monitor their own heart rhythm every time they feel symptoms.

Digital health can also be useful in the treatment of cardiac arrhythmias, especially in AF. Anticoagulation therapy is crucial in preventing strokes in patients with AF. However, making decisions about anticoagulation for individual patients remains a difficult area of clinical practice, balancing the risk of ischaemic stroke against that of major bleeding (3). Digital health can provide education, telemonitoring of adherence, or even allow self-management of anticoagulation therapy.

Telemedicine may also play an important role in cardiac emergencies. Multiple trials have investigated the role of prehospital ECG transmission in the triage of acute coronary syndromes. This comprises e-transmission of ECGs taken by the emergency staff with portable ECG devices and sent to the physician for quicker diagnosis and treatment.

Smartphone for arrhythmia detection

The last five years have seen an explosion of new trials testing smartphone applications for the detection of cardiac arrhythmia, mainly, AF. Most smartphone applications use photoplethysmography (PPG) for the detection of heartbeats. PPG is an optical technique that analyses changes in skin colour and light absorption (4).

Twenty-three trials conducted from 2000 until the end of 2019 looked at the effectiveness of smartphone applications for AF screening, and all trials showed that smartphone applications are effective for AF screening and detection. Details of the research review are provided in Annex 5.

In 2015, Haberman et al. (5) published one of the first trials testing the feasibility and accuracy of cardiac arrhythmia detection with the use of PPG in a smartphone application. They concluded that smartphone ECGs accurately detect baseline intervals, atrial rate, and rhythm and enable screening in diverse populations. In 2013, Harrington et al. (6) tested a smartphone application on an iPhone and found that the application was able to accurately detect and classify an irregular pulse from signals in the patients' fingertips.

Fibricheck is an FDA-approved application for AF detection. Patients place the left index finger over the flashlight and camera, holding the finger horizontally and keeping it in place for one min (4,7). The smartphone camera is used to obtain a PPG measurement to calculate the local arteriole blood volume pulse variation. The pulse rhythm is then identified based on the RR interval (4). PPG signal quality was sufficient for analysis in 93%, and single-lead ECG quality was sufficient in 94% of the participants (8). However, arrhythmia detection with smartphones has still some issues such as artefacts due to patient movement and positional variability (9).

The Apple Heart study (10), published in 2019, was one of the most anticipated trials in the field of digital health. Smartwatches were used to identify AF based on the PPG signal combined with an irregular pulse notification algorithm. When AF was detected by the smartwatch during this study, a telemedicine visit was automatically initiated. After that, an ECG patch was mailed to the participant to be worn for up to seven days to confirm the diagnosis of AF. The researchers of the Apple Heart study demonstrated that this diagnostic approach was feasible for AF screening. However, the effectiveness of this approach in diagnosis was slightly disappointing. AF could be confirmed by the ECG patch in only 34% of the patients who were diagnosed with AF by the smartwatch. This suggests that there is a large number of false-positive results, which can cause unnecessary healthcare costs and anxiety (10). More studies on using smartwatches for mass AF screening and the cost-effectiveness of this approach are needed.

Tison et al. (11) published another trial in 2018 which investigated the detection of AF with a commercially available smartwatch. The smartwatch used in this study also combined a PPG signal with an algorithm based on artificial intelligence. The authors concluded that the smartwatch was able to detect AF but had some loss of sensitivity and specificity in comparison with a standard ECG (11).

These studies show that smartphones and smartwatches could be promising tools for permanent ambulatory monitoring of heart rhythm; however, improvements in accuracy are still needed. The PPG signal-based approach offers the advantage that it can be used without the need for additional devices other than widely available smartphones.

Handheld ECG devices or single-lead ECGs are other tools that can be used for mass screening or for long-term monitoring of intermittent palpitations. A trial of 1001 patients using the AliveCor Kardia monitor (handheld single-lead ECG device) combined with a smartphone application demonstrated the efficacy of this approach for AF screening in patients with a high risk of stroke (12). Another study using the Kardia Mobile device (handheld single-lead ECG device) in combination with a smartphone application demonstrated the capability of handheld ECG devices to screen for and detect AF with high sensitivity and specificity (13).

Hendriks et al. (14) performed a prospective cross-sectional study in 2012 with the Zenicor handheld ECG device. They showed that intermittent short ECG recordings for four weeks were more effective than 24-hour Holter monitoring in detecting AF and paroxysmal supraventricular tachycardia (14). A cohort study in 2015 confirmed that handheld ECG recorders might play a role in mass screening for AF in elderly people (15). Jacobs et al. (16) demonstrated in 2018 that AF screening using a handheld ECG recorder during influenza vaccination is likely to be cost-saving for the Dutch population aged 65 years and over.

In 2016, Chan et al. (17) performed a community screening trial of 13122 patients in Hong Kong. The study team concluded that AF screening using a smartphone-based wireless single-lead ECG was feasible for large cohorts and that it was able to diagnose a significant proportion (0.5–3.0%) of citizens with AF. Early detection of AF can have a significant impact on health outcomes and costs. Lowres et al. (18) demonstrated in 2014 that screening of cardiac arrhythmias in pharmacies using a smartphone application with an automated algorithm is both feasible and cost-effective. Furthermore, mass screening for AF has also been proven to be well accepted by patients (19).

Handheld single-lead ECG devices in combination with smartphones can provide the opportunity to deliver low-cost mass screening for prevalent arrhythmias such as AF.

Lastly, bio patches have been developed to continuously measure ECGs over an extended period. Most of these patches are also capable of monitoring other parameters such as respiratory rate, body position, temperature, and quality of sleep or physical activity (4). In 2013, Rosenberg et al. (20) tested the single-use, non-invasive, waterproof, long-term continuous monitoring Zio® Patch, concluding that it improved clinical accuracy (20). A 2018 RCT with 2,659 patients demonstrated that a self-applied wearable ECG patch resulted in a higher rate of AF diagnosis compared with delayed monitoring (21).

In conclusion, the field of ambulatory monitoring is evolving rapidly, with new tools becoming available for screening and long-term monitoring. Smartwatches, handheld devices, and bio patches show some promising results for long-term monitoring and mass screening. However, more research is still needed to confirm the cost-effectiveness of these interventions. More research is also needed to investigate the role and implementation of digital health screening in current workflow and care pathways.

Prehospital emergency ECG

Prehospital ECGs involve the use of telemedicine to transmit an ECG to the physician before the patient arrives at the hospital. The ECG can be taken at the patient's home or from the ambulance. E-transmission of the ECG accelerates the IHD diagnosis. This can optimise referral to the right centre (centres that are able to perform percutaneous coronary intervention (PCI) and speed up the start of treatment. The European guidelines for managing an ST-segment elevation acute myocardial infarction (STEMI) recommend that all patients presenting with symptoms suggestive of an ACS receive a 12-lead ECG before arriving at the hospital. This prehospital ECG allows them to determine which hospital the patient should be referred to in order to start the right treatment early (22,23).

For patients with MI, the current guidelines recommend timely (<90 min) reperfusion therapy. In research, this is often measured as door-to-balloon time, which is the time between the arrival of a patient with STEMI in the emergency room and the time that a balloon is inflated to revascularise the occluded coronary artery. A shorter door-to-balloon time is associated with better survival. Therefore, a prehospital ECG could help to improve quick and correct referral to the right hospital for revascularisation.

Forty-two trials and one meta-analysis conducted from 2000 until the end of 2019 looked at the effectiveness of prehospital ECGs, and 91% of these trials showed that they are effective in reducing door-to-balloon time and mortality. Details on the research review are provided in Annex 5.

The prehospital ECG can be transmitted through telemedicine devices, telephones, smartphones, etc. Multiple studies have demonstrated that prehospital ECGs are associated with lower door-to-balloon time and increased survival (23-27). Rasmussen et al. (24) demonstrated in 2014 that telemedicine for prehospital triaging and treatment of STEMI was feasible and allowed 89% of patients living up to 95 km from the invasive centre to be treated with primary PCI within 120 min of the emergency medical service call. A cohort study of 288,990 patients in 2014 confirmed that prehospital ECGs led to increased survival in STEMI and non-STEMI patients (25).

Digital Health for anticoagulation treatment in atrial fibrillation

Atrial fibrillation (AF) can lead to blood pooling in the atria, which can cause blood clots to form. These blood clots can migrate to your brain and occlude a brain artery, causing a stroke.

Therefore, adherence to oral anticoagulation (OAC) therapy is important in preventing strokes and systemic thromboembolism in AF (28,29). Non-adherence or failed persistence can result in poor clinical outcomes and increased healthcare costs (30). Education and telemonitoring may help in increasing adherence to OAC therapy. In vitamin K antagonists (VKA) therapy (a type of oral anticoagulation medication), close monitoring of the international normalised ratio (INR) and regular adaptation of medication dosage is important due to the difficult balance of bleeding risk when patients take too much VKA and thromboembolic risk when patients do not take enough VKA.

Eighteen trials and two meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of digital health interventions in reducing bleeding complications, and 85% of these trials showed that digital health interventions are at least as safe as usual care. Details on the research review are provided in Annex 5.

The first telemedicine trials demonstrated in 2001 that telephone-based OAC therapy can be endorsed by primary-care physicians and had a positive impact on patients' satisfaction and knowledge about their antithrombotic therapy (31). Furthermore, Witt et al. (32) demonstrated in 2005 that telephone-based OAC therapy reduced the risk of anticoagulation therapy-related complications compared to usual care. Desteghe et al. (28) in 2018 and Proschaska et al. (33) in 2015 demonstrated that telemonitoring of OAC therapy increases medication adherence. Smartphone applications can be used for education, reminders, and monitoring. Stephan et al. (34) demonstrated in 2018 that a smartphone application can improve disease knowledge and enable a shared decision process. Two meta-analyses published respectively in 2006 and 2011 showed that patient self-management and self-testing of INR is associated with significantly fewer deaths and thromboembolic events (35,36).

In conclusion, the use of digital health technology can help to increase the quality of OAC therapy in patients with AF. No good cost-effectiveness studies are available, but it may be expected that these low-cost interventions will prove to be cost-saving.

Conclusions

Digital health provides many opportunities in the field of cardiac arrhythmia. Smartphones, smartwatches, and bio patches are exciting new technologies for ambulatory monitoring and screening of AF. Multiple studies have already demonstrated promising results; however, more research is still needed to confirm the cost-effectiveness of these interventions.

It is important to always check if the digital health tools are clinically validated before using them in clinical practice. E-transmission of prehospital ECGs could improve the triage of patients presenting with chest pain. This can result in better door-to-balloon times and possibly better survival of ACS. Lastly, digital health could play a vital role in improving adherence to OAC therapy in patients with AF. Most studies show promising results; however, studies with higher sample sizes are needed as well as cost-effectiveness analyses of digital interventions.

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Chapter 6: Digital health for cardiovascular implantable devices

Cardiovascular implantable electronic devices (CIEDs) include pacemakers, implantable cardioverter defibrillators (ICDs), and cardiac resynchronisation therapy (CRT). A pacemaker device is used to generate electrical impulses to regulate the electrical conduction system of the heart in patients with bradycardia or an atrioventricular block. The goal of an ICD is to prevent sudden cardiac death. ICDs keep track of the heart rate, and when an abnormal heart rhythm is detected, the device will deliver an electric shock to restore a normal heart rhythm. A CRT is the insertion of two electrodes in the left and right ventricles of the heart, respectively, to treat HF by coordinating the function of both ventricles. A CRT device is indicated when patients suffer from a low ejection fraction or when the electrical activity of the heart has been compromised.

In 2015, the Heart Rhythm Society recommended that remote monitoring (RM) should be offered to all patients with CIEDs. RM of CIEDs was originally devised to decrease the need for in-hospital follow-up and to increase access, but new research has established that RM is also an efficient method to improve patient outcomes (1-4).

Currently, CIEDs contain multiple sensors and technologies that enable daily monitoring of several important parameters in HF and cardiac arrhythmias (1). Most current CRTs and defibrillator devices can monitor daily physical activity, arrhythmias, and thoracic impedance, which helps in the early detection of HF decompensation. Furthermore, pacemakers and internal loop recorders permit long-term monitoring of cardiac rhythm and can help to detect paroxysmal AF or severe ventricular arrhythmias.

Next to CRT devices, pacemakers, and defibrillators, new wireless implantable hemodynamic monitoring systems are being developed. The CardioMEMS system consists of a miniaturised, wireless monitoring sensor that is implanted in the pulmonary artery (PA) during a minimally invasive procedure to directly measure PA pressure. Increases in PA pressure detected by the CardioMEMS system can predict an HF decompensation. This allows for a more personalised and proactive management to reduce the likelihood of hospitalisation (4).

In conclusion, early detection of cardiac arrhythmias and HF decompensation has the potential to prevent hospitalisations, major adverse cardiovascular events, and even death (1-4).

Remote monitoring of cardiac implantable electronic devices

Eighteen RCTs, twenty-four observational studies, and three meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of RM of CIEDs on reducing healthcare utilisation and mortality, and 80% of these trials showed that it is effective in reducing healthcare utilisation and mortality. Sixteen cost-effective analyses showed that RM of CIEDs is a long-term cost-effective solution. Details on the research review are provided in Annex 6.

The ATTITUDE trial in 2010 (5) and the IN-TIME (6) trial in 2014 were early publications reporting improved survival among patients assigned to remote management of CIEDs. Saxon et al. (5) performed an observational study of 185778 patients with a CIED. The 69556 patients receiving remote follow-up had higher one- and five-year survival rates compared with patients who only received in-hospital device follow-up (50% reduction; $P<0.0001$). The IN-TIME trial (6) was a randomised trial with 664 patients comparing implant-based, multiparameter telemonitoring (333) vs standard care. Hindricks et al. (6) concluded that telemonitoring of CIEDs can significantly improve clinical outcomes for patients with HF (odds ratio 0.63, 95% CI 0.43-0.90).

These early results were confirmed by several other studies. In 2015, Varma et al. (3) observed 269471 consecutive CIED patients, 127706 of whom (47%) used RM. They demonstrated that RM was associated with improved survival, irrespective of device type. Interestingly, a graded relationship with the level of adherence was found, which suggests that intensive use of RM is needed to further improve patient outcomes. The EFFECT study (7) in 2015 was an RCT enrolling 987 consecutive patients with ICDs. De Simone and his team demonstrated that RM reduces death and cardiovascular hospitalisations. The 2013 ECOST trial randomised 433 patients (8) and concluded that long-term RM of ICDs was as safe as standard ambulatory follow-up.

More recent trials by Morgan et al. (9) and Boriani et al. (10) failed to confirm the beneficial effect of RM in two large RCTs. The 2017 REM-HF trial (9) recruited 1650 patients and had a median follow-up time of 2.8 years. This study showed no significant improvements in outcomes for patients followed by RM. Better usual care of CIEDs in England and a lower NYHA classification in this cohort were proposed by Morgan et al. (9) as possible reasons. The MORE-CARE trial in 2017 (10) demonstrated no beneficial effect of RM of CIEDs. In this RCT, 865 patients were enrolled, and the median follow-up time was two years. Even though RM did not improve patient health outcomes in the MORE-CARE trial, it did lead to a non-significant reduction in the use of healthcare resources due to a marked reduction in in-office visits (10).

In 2016, Böhm et al. (11) performed an RCT investigating a telemedicine system to alert fluid status in ICD patients by inaudible text message alerts to the responsible physician. This study did not demonstrate improved outcomes in the telemedicine group, possibly due to low adherence to the treatment protocol by both physicians and patients. In a 2015 study by Lüthje et al. (12) using fluid states, RM also could not demonstrate a significant effect on HF-related hospitalisations, ICD shocks, or mortality (12). The DOT-HF trial (13) in 2011 was an RCT with 335 patients using CIEDs to measure intrathoracic impedance. Patients were alerted with a sound when increases in pulmonary fluid retention were detected. This study showed that an implantable diagnostic tool to measure intrathoracic impedance with an audible patient alert did not improve outcomes and increased HF patients' hospitalisations and outpatient visits (13).

In 2017, Hindricks et al. (14) performed a pooled analysis of three large trials that investigated the role of daily RM of ICDs: IN-TIME (6), TRUST (15), and ECOST (8). The study concluded that daily RM reduced all-cause mortality mainly by preventing HF exacerbations (14). Klersy et al. (16) carried out a meta-analysis of eleven RCTs (5,702 patients) in 2016 to investigate the safety and effects of implantable device telemonitoring. An important conclusion of this meta-analysis was that RM was as safe as standard care and was associated with a marked reduction in planned hospital visits. Furthermore, RM also resulted in lower costs (16).

Guédon-Moreau et al. (17) demonstrated in a 2014 RCT with 310 patients that an RM system for ICDs was cost-saving from the French health insurance perspective. Lorenzoni et al. (18) also demonstrated in a 2014 observational study with 15254 patients that RM of CIEDs was cost-saving. Hummel et al. (19) in 2019 and Capucci et al. (20) in 2017 confirmed the cost-effectiveness in lifelong RM of ICDs. In 2016, Piccini et al. (21) conducted a nationwide cohort study in Italy with 92566 patients who received RM for CIEDs and concluded that RM was associated with a reduction in hospitalisation and healthcare utilisation.

In conclusion, most trials and meta-analyses demonstrate that RM of CIEDs is effective in reducing rehospitalisation, mortality, and healthcare costs. However, the use of intrathoracic impedance monitoring with CIEDs, an early warning of impending decompensation in HF patients, needs further investigation.

Patient and staff experiences of remote monitoring of cardiac implantable electronic devices

Experience and acceptance by healthcare providers and patients using RM for CIEDs are important for implementation in regular care. The REMOTE-CIED trial (1) in 2019 investigated whether remote follow-up had an effect on patient-reported outcomes and acceptance of the ICD. Versteeg et al. (1) concluded that patient-reported health status and ICD acceptance did not differ between patients on RM and those receiving usual care. Petersen et al. (22) reported in 2012 that 95% of the patients were satisfied with the remote follow-up.

A survey study by Timmermans et al. in 2019 (23) demonstrated high satisfaction with RM, but a subgroup preferred in-clinic follow-up. Patients with a preference for RM were more likely to be higher educated ($P = 0.04$) and employed ($P = 0.04$). This suggests that physicians should also include patients' preferences and concerns to tailor device follow-up to individual patients' needs and preferences (23). In 2015, Mairesse et al. (24) demonstrated that physicians regard RM of CIEDs as a clinically useful technology that affords significant benefits for patients and healthcare organisations.

Wireless implantable hemodynamic monitoring systems

Intracardiac pressures are an important predictor for impending pulmonary congestion and could help to predict HF decompensations in time to prevent hospital admissions (25). Three RCTs, thirteen observational and cost-effect studies, and one meta-analysis conducted from 2000 until the end of 2019 looked at the effectiveness of wireless implantable hemodynamic monitoring systems in effectively monitoring HF patients. All of these studies showed promising results. Details on the research review are provided in Annex 6.

In 2002, Magalski et al. (26) published one of the first studies to evaluate the accuracy of an implantable hemodynamic monitor in HF patients. They concluded that the implantable hemodynamic monitor was accurate over time to monitor the patient's hemodynamic condition. The COMPASS-HF trial was one of the first RCTs that investigated the clinical outcomes of implantable hemodynamic monitor-guided care. Bourge et al. (25) concluded in 2008 that the intervention did not significantly reduce all HF-related events compared with the control group.

Later, the CHAMPION trial was conducted using the CardioMEMS Heart Sensor. In 2011, Abraham et al. (27) demonstrated a large reduction in hospitalisation after six months of follow-up for patients with severe HF who were managed with the wireless implantable haemodynamic monitoring system. The monitoring system was able to reduce decompensation leading to hospitalisation compared with standard HF management strategies after a median of 17.6 months of follow-up (28). High pulmonary artery pressure (known as pulmonary hypertension) is when the pressure lung arteries becomes abnormally high. This strains the right side of the heart and could lead to heart failure. Pulmonary artery pressure-guided HF management used in the CHAMPION trial led to a 49% reduction in total HF hospitalisations and a 58% reduction in all-cause thirty-day readmissions (29). Later, several papers confirmed that in populations similar to those of the CHAMPION trial, the CardioMEMS device is cost-effective if the effectiveness is sustained over sufficiently long periods (30-32).

More research is needed to consistently implement implantable hemodynamic monitors in standard care, but most trials show promising results.

Arrhythmia detection with implantable devices

Remote monitoring of CIEDs may help in early detection of cardiac arrhythmias and, in that way, reduce decompensation, risk of stroke, and sudden cardiac death. A 2019 study by Perino et al. (33) showed a high prevalence of device-detected AF after pacemaker implantation (45% AF >6 minutes, 39% >1 hour, 32% >6 hours, 24% >24 hours). In 2006, Cheung et al. (34) demonstrated that AF was detected in 24% of patients without a history of AF within one year after implantation. Ventricular high rate episodes (suggestive of AF) are frequently encountered in RM of pacemakers (35). A meta-analysis by Mahajan et al. (36) in 2018 demonstrated that RM of CIEDs detected subclinical AF in 35% of new CIED implants and that the presence of subclinical AF was associated with elevated stroke risk.

Multiple studies demonstrated that cardiac arrhythmias diagnosed during RM of CIEDs have a significant influence on major health outcomes. In 2017, Van Gelder et al. (37) showed that subclinical AF present for more than 24 hours is associated with an increased risk of ischaemic stroke or systemic embolism. A pooled analysis by Boriani et al. (38) in 2014 confirmed that device-detected AF burden is associated with an increased risk of ischaemic stroke. Lorenzoni et al. (19) showed that RM not only provides a potential to reduce the risk of stroke by early detection of new-onset AF but is also a cost-saving follow-up. A small qualitative study in 2017 showed that RM had a significant positive impact on health-related QoL for pacemaker patients (39).

RM can be used to adapt anticoagulation therapy in paroxysmal AF patients. The ANGELS AF trial in 2012 (40) demonstrated that it was possible to improve OAC use by supplying attending physicians with reports about the patient’s risk factors and AF information from continuous ICD monitoring. Furthermore, Waks et al. (41) showed in 2018 among patients with rare AF episodes and low-to-moderate stroke risk that changing the OAC administration based on arrythmia detection by the pacemaker or the implantable cardiac device is feasible and decreased anticoagulation utilisation by 75%. Mascarenhas (42) demonstrated in 2019 that AF burden assessment by CIEDs allows an individualised disease-guided approach to safely withdraw long-term OAC in patients with high bleeding risk.

Lastly, an RCT by Martin et al (43) in 2015 with 2718 patients showed that RM in ICD can be used for early initiation and interruption of anticoagulation without resulting in a significantly high level of strokes. However, there was also no significant reduction in bleeding complications (43).

In conclusion, arrhythmias detected by RM are predictive of adverse events, but it is unclear if treatment based on the detected abnormalities has a positive influence on outcomes.

Physical activity monitoring with implantable devices

Almost all CIEDs contain a single axis accelerometer to estimate daily physical activity. Palmisano et al. (44) in their 2018 study of 770 patients, showed that lower device-measured physical activity was associated with a higher risk of atrial arrhythmias, hospitalisations, and death. Device-based telerehabilitation should be studied to improve physical activity in patients with CIEDs.

Implantable loop recorder monitoring

Thirty-nine trials and two meta-analyses conducted from 2000 until the end of 2019 looked at the effectiveness of implantable loop recorders (ILRs) in increasing the diagnostic yield in patients with unexplained syncope, and 93% of these trials showed that it is effective in increasing the diagnostic yield. Details on the research review are provided in Annex 6.

ILRs have become increasingly popular for long-term cardiac rhythm monitoring. Multiple studies have demonstrated that ILR can play an important role in the diagnosis of unexplained syncope (45-49). Krahn et al. (46) showed in 2004 that long-term monitoring of patients with unexplained syncope led to the detection of more significant asymptomatic arrhythmias than anticipated. A meta-analysis by Solbiati et al. (50) in 2017 confirmed that in about half of all unexplained syncope subjects implanted with an ILR, the device made a diagnosis possible (50).

Thirty-two trials and one meta-analysis conducted from 2000 until 2019 looked at the effectiveness of ILRs in increasing the diagnosis of paroxysmal AF, and 91% of these trials showed that they are effective. Details on the research review are provided in Annex 6.

ILRs can also help to diagnose paroxysmal AF, and it is well established that Holter monitoring test (electrocardiogram) frequently misses this. A Holter monitor is a small, chest-worn wearable device that records all your heartbeats. Doctors often ask to wear a Holter for monitoring for one to two days. ILRs are implanted in the thorax and will also record all your heartbeats. However, ILRs can be used to monitor your heartbeats for a longer period which can increase the diagnostic yield of paroxysmal cardiac arrythmias.

ILRs provide the opportunity for long-term rhythm monitoring (51). A 2019 study by Diederischsen et al. (52) demonstrated that a considerable burden of previously unknown AF was detected when long-term monitoring was applied in at-risk patients. Two recent RCTs in 2016 and 2017 showed that, compared to usual care, ILR monitoring achieved a more rapid diagnosis of unexplained syncope and atrial tachycardia (53,54). Lastly, Rincoig et al. (55) used in 2019 a Markov model to establish that the use of ILRs is cost-effective for the UK NHS in identifying AF in a high-risk population.

ILRs can play an important role in the diagnosis of unexplained syncope, paroxysmal AF, and life-threatening arrhythmias in patients with recurrent complaints of syncope or palpitations.

Conclusions

Cardiovascular implantable electronic devices are becoming more common in cardiac patients as the indications for device placement continue to expand and the research data supports device placement compared to medical therapy (56). Multiple trials have reported the effectiveness of remote monitoring of CIEDs in reducing rehospitalisation, mortality, and healthcare costs in combination with high satisfaction from patients and health professionals. The use of devices that measure pulmonary artery pressure, such as the CardioMEMS system, seems to be effective. The role of CIEDs in detecting arrhythmias is still unclear. It is well established that device-detected arrhythmias are predictive of adverse events, but it is unclear if treatment based on the detected abnormalities has a positive influence on outcomes. Lastly, it is well established that ILRs should play an important role in the diagnosis of unexplained syncope, paroxysmal AF, and life-threatening arrhythmias in patients with recurrent complaints of syncope or palpitations.

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Chapter 7: Big data and artificial intelligence in cardiology

Big data

An increasing amount of data, including health data, is collected all over the world, and the use of digital health tools will only increase data flows (1). The introduction of electronic medical records (EMRs) has caused exponential growth in data availability in hospitals (2). This data can be collected not only from the EMRs in clinical practice but also from wearable devices, biosensors, genome sequencing, patient-reported outcomes, data about Internet use, and much more (2). This digital revolution is steering medicine away from manual data entry and relatively basic statistical tools to a bottom-up data management that involves real-time data extraction and analysis of various sources (3).

Big data can be defined as large datasets that cannot be analysed, searched, interpreted, or stored using traditional data-processing methods (4). These datasets are mostly processed and analysed by applying artificial intelligence and machine learning algorithms (5), but the most-used definition of big data was introduced by Doug Laney in 2001 and known as the 3V's: volume, variety, and velocity (5,6). Currently, big data is defined as the 4V's after the addition of veracity.

In most big datasets, the volume surpasses one petabyte of data (2). Nowadays, data can be stored in countless variations, can come from multiple sources, and often exist in unstructured formats (5). Structured data are highly organised and, therefore, easy to analyse (e.g. ECG data, age, drug dose, etc.). Unstructured data can be textual or non-textual and can be human- or machine-made (7). Unstructured data for healthcare can potentially give a more comprehensive view of a patient by integrating social and environmental information which possibly correlates with health.

The high speed at which data are generated increases the gap between the volume of data available and our ability to analyse and interpret them in time (5). The risk is that physicians are inundated with data that require a more sophisticated interpretation while being expected to perform more efficiently (5).

Artificial intelligence and machine learning may help to process and analyse big data sets and present them as smaller lumps of understandable information, enabling doctors to provide more efficient, convenient, personalised, and effective care (8). Evidence for the use of big data analytics is increasing. Big data analytics can be used for predictive risk models, pharmacogenomics, ECG diagnosis, and image analysis as well as to facilitate research.

Artificial intelligence

Artificial intelligence is defined by the European Commission as: “Systems that display intelligent behaviour by analysing their environment and taking actions – with some degree of autonomy – to achieve specific goals. Artificial intelligence-based systems can be purely software-based, acting in the virtual world (e.g. voice assistants, image analysis software, search engines, speech and face recognition systems) or artificial intelligence can be embedded in hardware devices (e.g. advanced robots, autonomous cars, drones or Internet of Things applications) (1).”

Artificial intelligence is increasingly integrated into our daily lives in areas such as transportation, computer gaming, and digital voice assistants (e.g. Alexa, Siri) (9). Nowadays, artificial intelligence is also trending in medicine to improve patient care by speeding up processes and achieving greater accuracy, opening the path to providing better healthcare overall (9).

Machine learning is an extension of artificial intelligence and is defined as a system’s ability to autonomously acquire knowledge by extracting patterns from large data sets (10). Machine learning has three important forms: supervised machine learning, unsupervised machine learning, and reinforcement. Supervised learning uses a human-labelled classification of an observation (e.g. ‘Does this ECG represent sinus rhythm or atrial fibrillation?’) to predict the desired and known outcome; it helps in classification and regression problems but requires significant amounts of data and is time-consuming because the data have to be labelled by humans (8). Unsupervised learning focuses on discovering underlying hidden patterns in the dataset without human feedback. Lastly, reinforcement is a hybrid technique with the objective of maximising the algorithms’ accuracy using trial and error (8,10).

The most recent innovation in the field of artificial intelligence is deep learning and neural networks. Deep learning mimics the human brain by using multiple layers of artificial neural networks that can generate automated predictions from the input. Activated neuronal layers continue to pass a value to the next layer of neurons until the final ‘output layer’ of neurons is reached (8). Simply put, deep learning is a more advanced technique within machine learning that requires bigger data and stronger computers, but it can offer automatic improvement and a high accuracy level.

Use of artificial intelligence in cardiology

Imaging

Artificial intelligence can play a role in detection, classification, segmentation, tracking, and even report generation in cardiovascular imaging (11). A 2019 study by Seah et al. (12) of a dataset of 103489 chest radiographs demonstrated that a machine learning algorithm was able to detect and highlight the cardiomegaly and pleural effusions with an area under the curve (AUC) of 0.82.

The deep learning algorithm of Madani et al. (13) in 2018 had an accuracy of 91.7% in comparison with the 79% accuracy of four board-certified echocardiographers in analysing fifteen standard echocardiographic views. (13). Samad and his colleagues (14) demonstrated in 2018 that a deep learning algorithm was able to predict survival with higher accuracy after analysing the echocardiography of multiple cases. Playford et al. (15) showed, also in 2018, that artificial intelligence was able to calculate the aortic valve area without left ventricular outflow tract measurements in evaluating aortic stenosis. Narula et al. (16) used machine learning in 2016 to differentiate hypertrophic cardiomyopathy from normal heart hypertrophy in 2D-echocardiography with an overall sensitivity of 87% and specificity of 82%. In a large retrospective study of 8000 echocardiograms, Zhang et al. (17) demonstrated in 2018 that artificial intelligence was able to classify hypertrophic cardiomyopathy (AUC 0.93), cardiac amyloid (AUC 0.87), and pulmonary hypertension (AUC 0.85) with high accuracy.

Gonzalez et al. (18) demonstrated in 2018 that a neural network is able to calculate Agatson scores from unenhanced chest CT exams without prior segmentation of coronary artery calcifications. Furthermore, it is faster and more accurate in comparison with standard methods.

Tao et al. (19) showed in 2019 that an artificial intelligence tool trained on a dataset of 596 magnetic resonance imaging (MRI) examinations is able to outperform manual segmentation.

In 2017, Dawes et al (20) used cardiac MRI scans and blood tests from 256 heart disease patients. The artificial intelligence tool measured the movement of 30,000 points that are marked on the heart structures in each heartbeat. By combining these data with the patients' eight-year health records, the artificial intelligence tool was able to predict the patients' survival rates for the next five years with an accuracy of 80% as compared to 60% for clinicians. In 2019, Otha et al. (21) evaluated myocardial-delayed enhancement on MRIs with an accuracy of 78.9–82.1%.

In 2017, Nakajima and his team (22) trained an artificial neural network to classify potentially abnormal areas on myocardial perfusion images as true or false. The diagnostic accuracy of the artificial neural network was compared with 364 expert interpretations. The artificial intelligence tool was diagnostically as accurate or more accurate in various clinical settings, including patients with previous MI and coronary revascularisation.

Deep learning has been used to predict obstructive disease from myocardial perfusion SPECT (23). In 2018, Betancur et al. (23) used myocardial perfusion imaging of 1638 patients to train the deep learning tool. This resulted in significantly better diagnoses of coronary obstructive disease.

These studies show the significant potential of artificial intelligence in cardiac imaging analysis.

Electrocardiogram (ECG)

In 2017, Isin et al. (24) used a deep learning algorithm for automated arrhythmia detection on an ECG using an online dataset of over 4000 long-term ECG Holter recordings, including rare conditions. It showed a correct recognition rate of 98.5% and an accuracy of 92% (24). Rapjukar et al. (25) developed a deep learning tool in 2017 from 64000 single-lead ECGs to assess arrhythmia. Single-lead ECGs only use two electrodes and it is often used in smartwatches or handheld ECG devices.

Their results showed that the deep learning tool was non-inferior to six cardiologists. In 2019, Hannun et al. (26) developed in a deep neural network to classify twelve rhythm classes using 91232 single-lead ECGs from 53549 patients who used a single-lead ambulatory ECG monitoring device. It was validated against an independent test dataset annotated by a consensus committee of board-certified practising cardiologists; the deep neural network achieved an AUC of 0.97. Galloway et al. (27) used ECGs and artificial intelligence in 2019 to screen for high levels of potassium.

Risk assessment and risk prediction models

In 2018, Kwon et al. (28) developed a deep learning tool to detect in-hospital death without attempted resuscitation. The tool outperformed standard methods, showing higher sensitivity and lower false alarm rates. In 2017, Motwani et al. (29) evaluated the five-year risk of death in 10,030 suspected coronary heart disease patients. The artificial intelligence tool was superior to traditional clinical judgement and coronary computed tomographic angiography.

In 2019, Alaa et al. (30) showed a better risk prediction as compared to the Framingham score using a model with 473 variables. Interestingly, the tool was also able to detect new possible risk factors such as individual usual walking pace.

Conclusions

Artificial intelligence and big data hold great potential for improving certain healthcare functions, e.g. routine screening and diagnostics, avoiding medical errors and adverse reactions, understanding disease transmission pathways, supporting chronic disease management, and improving patient safety (1). Furthermore, they will allow more personalised healthcare and boost clinical and pharmacological research. However, more attention needs to be paid to the ethical considerations of artificial intelligence and for a balanced regulatory structure to regulate new innovations and protect personal data.

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Chapter 8 Considerations for implementation of Digital Health

This report has demonstrated the potential of digital health interventions in improving health outcomes and saving costs for cardiovascular prevention, detection, and management (1). The facilitators and barriers for the step between digital health research and implementation will be discussed in this chapter. Furthermore, it is important to consider the potential impact of digital health on social inequalities. Low health or digital literacy, the lack of user-friendliness, and doubts over the meaningfulness of information can also create new health inequalities (2).

Patient-related considerations

Important barriers for patients include accessibility, privacy, data security concerns, lack of personal motivation, and low digital literacy (1,3). Access to the Internet in the EU has increased significantly in the last ten years (4). For many people in the EU, using the Internet has become an increasingly important part of their daily lives; 84% of the EU's population are Internet users, with smartphones being the most frequently used device. However, digital literacy is still surprisingly low. Only 57% of the EU's population aged 16–74 had a basic level of digital literacy in 2017 (5). Low digital and health literacy are especially associated with older age and low socio-economic status.

Older people often feel isolated, and the older they get, the more they tend to depend on medical and social care without family support structures (2,6). Being able to use the Internet can be life-transforming and can improve QoL for seniors who possess the know-how to navigate it. Therefore, the introduction of digital health is only beneficial for those who have sufficient digital literacy. Attention is needed so that elderly people with lower digital literacy are not forgotten.

In 2012, Kontos et al. (7) demonstrated that patients with lower levels of education had significantly lower odds of going online to look for a healthcare provider; using email or the Internet to communicate with a doctor; tracking their personal health information online; using a website to help track diet, weight, and physical activity; or downloading health information to a mobile device. Digital health and patient empowerment go hand-in-hand. However, for some patients with a lower educational background, it is hard to master the skills they need to use digital health tools. One important reason is that many digital health solutions are developed for people who already possess a much broader set of 'health skills', including awareness, attention, ambition, and self-discipline, to use new technologies for better health outcomes (2). New technology thus enhances already existing skills, which makes digital health particularly attractive and amenable to the educated—and potentially impenetrable for people with lower education.

Migrants are often a vulnerable population with sometimes little to no access to health services. In addition, poverty, discrimination, and cultural and language barriers are regularly present. There are many differences between ethnic minorities and migrant communities in their technology use, but even if they possess the needed technology for digital health services, several other barriers are present that could turn into inequalities. Language is one of the most important barriers, but many migrants are also not used to the format, style, and 'candidness' of information found on European websites, which may not fit their own cultural or religious values (2).

The previous examples show that it is important to ensure that digital health tools do not lead to increased inequalities in health. Therefore, patients should be involved in creating new digital health tools because of the important role they play in health decisions. The involvement of health professionals and patients in developing new digital tools is called co-creation. However, at this moment, most healthcare innovations are mainly technology-driven. In the future, digital health research and innovation must be driven more by patients' and physicians' needs. Next to co-creation, tailoring interventions to individual levels of health and digital literacy or to specific target groups can improve the adoption of digital health (8,9).

Recommendations for reducing patient-related considerations

1. Increasing access to digital health technology

Governments must invest in an infrastructure where all citizens can have access to affordable healthcare. One of the key initiatives will be co-creation. This means that various categories of end users have a say in the design of digital health tools.

There is also a need for cultural change whereby patients check with their doctors and do not take all information on the Internet at face value. In addition, implementation of video consultations, chatterbots, and similar tools would allow better patient-health professional communication (2). Last but not least, individuals must be better aware of data protection and safety because these could become important inhibitors for patients and even health professionals.

2. Reduce technological pressure

Technology is evolving faster than ever, and the result is that hardware and software are almost outdated from the moment people buy them. Not everybody is able to afford or to use all new technologies. Governments must create frameworks to make all digital health tools accessible for everyone, including to people who only have access to outdated technology. National health authorities and social security administrations could consider offering such patients appropriate digital health tools either as a donation or via financial subsidies that would allow them to purchase everything necessary to manage their conditions more effectively through digital health technology (2).

3. Improve digital literacy

Individuals only feel empowered if they are able to use digital health tools confidently. Since digital literacy comprises a whole set of different literacies, there is a growing need to educate and train individuals in all these elements, especially members in vulnerable and at-risk groups. In addition, there must be more focused information campaigns and training activities directed to the general public since average literacy levels in all categories tend to be low, and digital health literacy is a blurry notion for most people. There is a lack of understanding of what it entails and how it can add value, and there is even less information on common solutions and issues in a cross-border context, combined with concerns over data protection and confidentiality (2).

Physician-related considerations

Digital health allows physicians to diagnose, monitor, and treat patients remotely. Furthermore, digital health could reduce healthcare professionals’ workload by taking over some of the daily tasks. In reality, however, digital health is often added to existing care rather than being streamlined into it, leading to an increased workload (1). This results in the perception that digital health implementation always means a higher workload. Change is difficult in most healthcare organisations because healthcare professionals and, indeed, patients can be resistant to changes in the care they deliver or receive. This resistance can arise from the fear of losing something of value or the fear they will not be able to adapt to the new ways. Therefore, it is important to pay attention to integration in the clinical workflow during the development of digital health tools.

Evidence that a new intervention improves patient health outcomes is also crucial for implementation in medicine. Many physicians only implement new treatments or diagnostic strategies when there is overwhelming evidence that they are better than the current care. Therefore, more research and especially larger RCTs are needed to demonstrate the effectiveness of digital health interventions which will convince physicians of the positive effects. Improved patient health outcomes are also important to persuade governments and healthcare organisations to invest in these digital health strategies (1).

Another important consideration is the fact that current healthcare professionals are not trained to use digital health in patient care. Therefore, current and future healthcare professionals must be educated about the opportunities and the use of digital health.

In most EU countries, there is no reimbursement for digital health, and healthcare professionals are not paid for digital health services (1). Healthcare professionals can be hesitant to use innovative digital health when they are not compensated for these efforts.

Lastly, at this moment, a clear regulatory framework for the use of digital health and artificial intelligence in healthcare is lacking (1). This results in uncertainties such as who is responsible for decisions made by artificial intelligence systems or who is responsible for data leakage when an RM system is hacked.

Technical considerations

Digital health is trending not only in cardiology but in most medical disciplines. The result could be that physicians become overwhelmed by digital tools and data. Interoperability and integration in EMRs are important facilitators for implementation. Another barrier is the fact that technology development is moving much faster than scientific validation is performed. Therefore, digital tools are often only validated when the technology is already outdated.

Digital health tools are used in decision-support systems, patient monitoring, diagnosis, and treatment choices. Therefore, system reliability and trustworthiness are important in persuading physicians to use these tools (1,10,11).

Legal and ethical considerations

In 2014, the European Commission launched a strategic reflection on the use of big data in healthcare (12,13). This resulted in ten policy recommendations formulated to stimulate the EU and national level deployment of big data without compromising people's privacy and safety (12). Only recently (June 2019), the Joint Action supporting the eHealth Network that was created under the Cross-border Patient's Rights Directive 2011/24/EU published a report on policy action for the innovative use of big data in health with a long-term goal to develop a European cross-national exchange format for EMRs (12,14,15). Furthermore, it is the ambition of the 2019-2024 European Commission to develop a legislative European approach to the human and ethical implications of artificial intelligence in the first 100 days of the new European Commission (12).

A legal framework for the use of digital health and artificial intelligence in healthcare is important because they can play a big role in risk prediction, diagnosis, and treatment choices within the field of cardiology. It must be ensured that these tools are of high quality. A legal framework can provide regulatory bodies with the information needed to monitor and assess the quality of digital health tools to make sure that the tools used in European healthcare are safe and compliant with the General Data Protection Regulation (GDPR).

This legal framework is not only necessary to ensure quality control but also to clarify questions about responsibility. For example, should health professionals be fully responsible for decisions suggested or made by artificial intelligence algorithms (16)? This dilemma creates issues such as when an algorithm suggests an intervention that seems banal but is also unhelpful, useless, and expensive or dangerous, should the provider second-guess the recommendation? Obviously, the first thought is 'Yes', but on the other hand, if providers only implement the choices they would have made on their own, we lose all the benefits of the artificial intelligence analysis of big data.

Lastly, a legal framework is also important to ensure privacy and data security. Patients are becoming more aware of the value of their medical data and often only feel comfortable sharing their medical information with their health providers (16,17). A study of Kalkman et al (17) demonstrated that patients reported multiple concerns when asked to share medical data for research projects. Patients were more willing to share data when privacy-protecting measures were present and when the data handling, responsibilities and accountability was transparent (17).

The European Commission has already taken big leaps to establish a legal framework to ensure data security and protection of personal data with the introduction of the GDPR and ePrivacy (18,19).

Legal issues aside, there are also ethical considerations for implementing digital health and artificial intelligence in healthcare. Their potential is evident; however, they may pose a possible threat to patient preference, privacy, and safety.

Conclusions

Co-creation of digital health tools with all relevant stakeholders, including most notably patients and health professionals, is needed to overcome common barriers such as lack of personal motivation, low digital literacy, lack of interoperability, and increased workload. Furthermore, integration in EMRs is important to prevent overwhelming physicians with digital health tools and data. A European legal framework is needed to regulate digital health and artificial intelligence in healthcare to ensure quality and data security. The European Commission aims to create a clear framework which will help to implement digital health in standard practice.

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Chapter 9 Conclusions

The burden of cardiovascular disease (CVD) in the EU and Europe is high. Each year cardiovascular disease causes over 1.8 million deaths in the European Union (36% of all deaths) (1,2). This results in a significant challenge for healthcare systems regarding qualified personnel and infrastructure. For this reason, innovative ways to address these challenges, such as digital health are explored to deliver sufficient and better care to patients at a reasonable cost.

In primary prevention, evidence suggests that digital health can be used in lifestyle management intervention to reduce cardiovascular risk and play an important role in screening of patients with high cardiovascular risk, especially in remote areas and in less developed countries.

In secondary prevention multiple trials suggest that telerehabilitation can be as effective as centre-based CR. However, more trials with larger sample sizes are needed to confirm this. Lifestyle management programmes delivered with digital health could be effective to prevent recurrent heart attacks. Research suggest that text messaging is more effective than internet-based interventions.

The role of digital health in heart failure management remains under discussion especially in telemonitoring. Many trials suggest that telemonitoring is effective in HF, however some large multi-centre trials failed to demonstrate the effectiveness of telemonitoring. Also, more research is needed to prove the effectiveness of telerehabilitation in a HF population. Recent telerehabilitation trials in HF show conflicting results.

Digital health for AF detection is a relatively new field. There is still a need for more multi-centre RCTs, but current evidence suggest that it can be a valuable tool for AF detection and mass screening. It can also be important in improving adherence to OAC treatment.

Remote monitoring of CIEDs is effective in reducing rehospitalisation, mortality and healthcare costs. However, the use of intrathoracic impedance monitoring with CIEDs as an early warning of impending decompensation in heart failure patients, needs further investigation. AF detection by remote monitoring is a predictor for adverse events but it is still unclear if it is effective to adapt OAC treatment on the basis of the CIED-detected arrythmias.

Digital health gives patients and health professionals the chance to transform current healthcare models. However, there is still need for big multi-centre trials to confirm the effectiveness and the cost-effectiveness of these digital interventions in cardiology. Lastly, Digital health has great potential, but it is important not to forget patients with lower digital literacy. Attention to the needs of elderly, disabled and cultural differences between ethnic groups is needed.

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Annex 1: Digital health in primary prevention

List of trials on Digital Health for hypertension in primary prevention

Author	Design	Sample Size	Intervention	Conclusion
Lee et al. 1, 2019	RCT	234 patients	Mobile self-monitoring application	Significant differences were found in the mean change of systolic blood pressure at three months in the monitoring group and the non-monitoring group (−16.0 vs. −5.7, $p = 0.008$)
Vedanthan et al. 2, 2019	Cluster RCT	1460 Hypertensive patients Usual care=491 Paper-based=500 Smartphone=491	Smartphone for health professionals with tailored messages and specific recommendations	Strategy combining tailored behavioural communication and mHealth for community health workers led to improved linkage to care, but no significant SBP reduction.
Marquez-Contreras et al. 3, 2018	RCT (1:1)	154 hypertensive patients	ALERHTA app to promote health education and reminder of appointments	Intervention group had higher drug adherence and improved percentage of hypertensive patient control.

Tobe et al. 4, 2019	Randomized Multicentre double-blind parallel group study	243 patients 125 active intervention 118 passive intervention	-Active intervention: information on the well as advice to get follow-up with if the measured BP was above target -Passive intervention: Only information about healthy lifestyle and behaviour changes.	Despite an overall reduction in BP over the study, there was no difference in the BP change between groups from baseline to final for systolic BP
Chandler et al. 5, 2019	Two-arm small-scale efficacy RCT	56 Hispanic patients 26 intervention 28 control	-Smartphone application, electronic medication tray and Bluetooth blood monitor: SMS reminders, education -Control group: SMS with only education	Significant lower systolic blood pressure after 9 months between the intervention and control group
Augustovski et al. 6, 2018	Cluster RCT	1432 patients Control 689 Intervention 743	Community health worker-led home visits, physician education, and text-messaging	Among low-income patients with uncontrolled hypertension in Argentina, a multicomponent intervention led by community health workers was cost-effective.

Bengtsson et al. 7, 2016	Explorative, longitudinal study	50 patients	Self-management: Motivational messages Reminders Education Feedback	(1) significantly reduced BP over the course of 8 weeks (2) that optimal effects appeared to be achieved after a relatively short period (3) patients benefiting most were those with moderate to high BP at study start.
Senecal et al. 8, 2018	Retrospective Observational study	3330 hypertensive patients	Digital health intervention for desktop and mobile phone with motivational and educational materials assisting in the management of hypertension	A DHI as an adjunct to a workplace health program is associated with greater improvement in blood pressure and BMI at 1 year.
Ciemins et al. 9, 2018	Prospective observational study Matched 1:3 allocation with control	484 patients 353 control 131 intervention	The BP monitor integrates directly with iPhone or Android devices. Nurses or providers monitored the BP database. Patients with out-of-range values were flagged and called	HBPM enabled by smartphone technology is a feasible and affordable method to improve HTN control among patients to improve population health, meet quality measure requirements, and may become a necessity under new value-based payment systems.
Morawski et al. 10, 2018	2-arm, randomized clinical trial	411 patients 202 control 209 intervention	The Medisafe app, which includes reminder alerts, adherence reports, and optional peer support.	Among individuals with poorly controlled hypertension, patients randomized to use a smartphone app had a small improvement in self-reported medication adherence but no change in systolic blood pressure compared with controls.

Varleta et al. 11, 2017	Prospective, multicentre, randomized, controlled study	314 patients 163 intervention 151 control	Text messages contained educational information about healthy diet, salt intake, antihypertensive medication schedule, and the importance of medication intake and adherence, among others.	At 6-month follow-up, text messaging resulted in an increase in reporting antihypertensive drug adherence in this hypertensive Latino population. This approach could become an effective tool to overcome poor medication adherence in the community.
McGrath et al. 12, 2017	Phase II randomized, blinded, controlled trial	134 patients 67 control 67 intervention	Sleepio is a multicomponent online intervention consisting of sleep–hygiene education and cognitive behavioural therapy.	A simple, low-cost, web-delivered sleep intervention is feasible does not result in short-term improvements in blood pressure.
Bobrow et al. 13, 2016	Pragmatic, single-blind, 3-arm, randomized trial	1372 patients 457 information SMS 458 interactive SMS 457 usual care	Personalized SMS text-messages were sent to information-only message and interactive message group participants at weekly intervals, at a time and in a language selected by the participant. Participants allocated to the interactive adherence support received the same messages as the information-only group but could also respond to selected messages using free-to-user "Please-Call-Me" requests.	A small reduction in systolic blood pressure control compared with the usual care at 12 months. There was no evidence that the interactive intervention increased this effect.

Paula et al. 14. 2015	RCT	40 patients 20 control 20 intervention	A pedometer was provided to be used during the 4-week intervention period. During the study, twice a week, text messages (SMS) were sent or phone calls were made to stimulate compliance with the general protocol.	The results of the present study demonstrated that a SMS supported DASH diet combined with walking promotes a clinically relevant reduction in ABPM in patients with type 2 diabetes and hypertension.
McMannus et al. 15, 2018	RCT	1182 patients 394 control 395 self-monitoring 393 telemonitoring	-For those self-monitoring alone, they were asked to record their readings on paper and send them for review to their practice in a reply-paid envelope. -Participants in the telemonitoring group were trained to send readings via a simple free SMS text-based telemonitoring service with web-based data entry back-up.	Self-monitoring, with or without telemonitoring, when used by general practitioners to titrate antihypertensive medication in individuals with poorly controlled blood pressure, leads to significantly lower blood pressure than titration guided by clinic readings.
Monahan et al. 16, 2019	RCT	1182 patients 394 control 395 self-monitoring	-For those self-monitoring alone, they were asked to record their readings on paper and send them for review to their practice in a reply-paid envelope. -Participants in the telemonitoring group were trained to send readings via a	Overall, probabilistic sensitivity analysis suggested that self-monitoring regardless of transmission modality was likely to be cost-effective compared with usual care (89% probability of cost-effectiveness at £20 000/quality-adjusted life year), with high uncertainty as to whether telemonitoring or self-monitoring alone was the most cost-effective option.

		393 telemonitoring	simple free SMS text-based telemonitoring service with web-based data entry back-up.	
Vamadevan et al. 17, 2016	Single cohort study	6016 patients	During intervention, a nurse care coordinator screened, examined, and entered patient parameters into mobile phone–based clinical decision support system to generate a prescription, which was vetted by a physician.	The changes in systolic blood pressure, diastolic blood pressure, and FPG observed at 18 months of follow-up were −14.6 mm Hg (95% CI: −15.3, −13.8), −7.6 mm Hg (CI: −8.0, −7.2), and −50.0 mg/dL (95% CI: −54.6, −45.5), respectively, and were statistically significant even after adjusting for age, sex, and Community Health Centre.
Lee et al. 18, 2016	Single cohort study	213 patients divided for analysis in Low transmission frequency 67 Middle transmission frequency 73 High transmission frequency 73	For participants who went through the consent procedure, a netbook (mini notebook) equipped with the SmartCare application, a video camera, and a medical device (BP and weight scale) were provided for telemonitoring. Based on the accumulated data and CDSS result reports, health managers in the SmartCare centre provided participants with telemonitoring and consultation services according to the prescribed manual.	SBP showed a decrease in the Middle and High Groups over the 6 months, whereas DBP showed a slight decrease in the Low and High Groups. Patients who received the SmartCare services with higher measurement frequency levels at home showed greater effectiveness regarding the provided services compared with those patients with lower levels of BP, weight, and BMI control.

Rubinstein et al. 19, 2016	RCT	637 prehypertensive patients 316 intervention 321 control	Participants were randomly assigned to receive either monthly motivational counselling calls and weekly personalised text messages to their mobile phones about diet quality and physical activity for 12 months	The intervention did not affect change in systolic blood pressure (mean net change -0·37 mm Hg [95% CI -2·15 to 1·40]; p=0·43) or diastolic blood pressure (0·01 mm Hg [-1·29 to 1·32]; p=0·99) compared with usual care.
Dandge et al. 20, 2019	Single cohort study	2456 patients were screened	Non-physician health workers equipped with tablet computers that were linked with point-of-care devices for blood pressure (BP) screened adult individuals for hypertension and diabetes. They connected those individuals with hypertension and diabetes to a study physician via Skype and handed over a printed e-prescription. Medication adherence checks, BP and fasting blood sugar measurements were done once a month and doctor consultations once in three months during follow-up.	After 24 months of intervention, control of BP and blood sugar was achieved in 54.0% and 34·1% of individuals with hypertension and diabetes, respectively. Blood pressure control rate improved by 12% (7.9%-16.0%) in known hypertensive individuals over the intervention period. Blood pressure control rate improved by 12% (7.9%-16.0%) in known hypertensive individuals over the intervention period.
Adams et al. 211, 2018	RCT	64 patients 5 min dose 23 10 min dose 19	A smartphone application (Tension Tamer [TT]) that implements Breathing awareness meditation as a stress management strategy. For 5-,	Mixed modelling results showed a significant time effect for systolic BP (SBP) with a dose-response effect at Months 3 and 6. Adherence declined over time and was lowest in the 15-min dose condition, though SBP reductions were maintained. Generally, adherence was negatively associated with dose as the study progressed.

		15 min dose 22	10-, or 15-min intervals twice daily over 6 months.	
Jung et al. 22, 2017	Quasi-experimental study	64 patients 31 intervention 33 control	It consisted of a four-week, in-class educational phase, community-based eHealth monitoring, and monthly telephone counselling for 24 weeks.	Specifically, the systolic BP among intervention group participants was 133.9 mm Hg at baseline and 122.5 mm Hg after 24 weeks of follow-up. Participants in the intervention group showed greater improvement in self-efficacy, self-care behaviour, and social support than did participants in the control group 24 weeks post-intervention.
Kaplan et al. 23, 2017	Single-arm retrospective observational study	5115 patients	Hello Heart, is a publicly available mHealth technology. The application provides a mobile platform through which patients can record and track self-measured BP recordings over time. Other features include periodic reminders to measure BP, interactive educational modules to improve use knowledge base, and connectivity for wireless BP measurement devices	Of 5115 eligible subjects, 3803 (74%) recorded BP for ≥2 weeks. In the 4-week subgroup, 23% achieved BP reduction of ≥10 mmHg versus 24% in the 22-week subgroup ($p < 0.001$). Among 783 subjects reporting baseline hypertension 57% of the 4-week and 69% of the 22-week subgroups achieved BP normalization (all $p < 0.001$). Higher engagement was associated with greater BP reduction and engagement was higher among those with greater clinical need of BP control.
Milani et al. 24, 2017	Double arm cohort study	556 patients 400 matched controls 156 intervention	Digital-medicine patients completed questionnaires online, were asked to submit at least one blood pressure reading/week and received medication management and lifestyle recommendations via a clinical pharmacist and a health coach. Blood pressure units	At 90 days, 71% of digital-medicine vs 31% of usual-care patients had achieved target blood pressure control. Mean decrease in systolic/diastolic blood pressure was 14/5 mm Hg in digital medicine, vs 4/2 mm Hg in usual care ($P < .001$). Excess sodium consumption decreased from 32% to 8% in the digital-medicine group ($P = .004$).

			were commercially available that transmitted data directly to the electronic medical record.	
Toro-Ramos et al. 25, 2017	Single arm cohort study	50 patients	A mobile application platform with human coaching. The programme included in-app human coaching with bi-weekly phone calls, meal logging, blood pressure tracking and educational material	The HPP yielded overall improvements in weight (-3.04±4.04 kg, P=<0.001), diastolic blood pressure (-5.06±11.89 mm Hg, P=0.004), and hypertension category (-0.48±0.74 mm Hg, P=<0.001). Sustained engagement of 80% resulted in significant reductions in systolic blood pressure (-7.75±12.56, P=<0.001) and weight (-3.73±4.01 kg, P<0.001) for programme completers, contributing to hypertension category change (-0.58±0.64 mm Hg, P<0.001).
Haricharan et al. 26, 2017	Single arm cohort study	41 patients	A short message service (SMS)-based health promotion campaign could improve Deaf people's knowledge of hypertension and healthy living.	SMSs were effective in improving Deaf people's knowledge of hypertension and healthy living. However, SMS-campaigns should be cognizant of Deaf people's unique needs and communication preference and explore how to accommodate these.
Thatthong et al. 27, 2019	RCT	67 patients 35 control 32 intervention	The intervention group received a sodium reduction counselling program in weeks 2 and 6. The intervention group also received sodium reduction key messages from the innovative technology (LINE) on their smartphones twice a week	Although the knowledge score increased in both groups, the innovative nutritional education tool was more effective than the general healthcare counselling program regarding the blood pressure level reduction.
Silveira et al. 28, 2019	Single cohort study	10 family physicians	Computerized clinical decision support systems (CDSS): integrating clinical and laboratory data on a particular patient, from which it performs	In this study, a CDSS developed to assist the management of patients with hypertension was feasible in the context of a primary health care setting in a middle-income country, with good user satisfaction and the potential to improve adherence to evidence-based practices.

		535 patients	cardiovascular risk calculation and provides evidence-based recommendations.	
Kang et al. 29, 2016	Single cohort study	38 patients	A mobile app, based on clinical practice guidelines to help patients with hypertension manage their disease.	This study showed that a mobile app for hypertension management based on CPGs is effective at improving medication adherence.
Albini et al. 30, 2016	RCT	690 patients	An integrated ICT-based Patients Optimal Strategy for Treatment (POST) system including Home BP monitoring teletransmission, a dedicated web-based platform for patients' management by physicians (Misuriamo platform), and a smartphone mobile application (Eurohypertension APP, E-APP), over a follow-up of 6 months.	Office BP control (<;149/90 mmHg) was 40.0% in control group, and 72.3% in POST group at 6-month follow-up. At the same time Home BP control (<;135/85 mmHg average of 6 days) in POST group was 87.5%.
Kim et al. 31, 2016	Subset RCT	95 patients 52 intervention 43 control	A blood pressure monitoring device connected with a mobile phone, reminders for self-monitoring, a Web-based disease management program, and a mobile app for monitoring and education.	Improvements in patient activation were associated with improvements in blood pressure control (beta=0.04, P=.02). This relationship was further strengthened in reducing cigarettes (beta=-0.60, P<.001), alcohol drinking (beta=-0.26, P=.01), and systolic (beta=-0.27, P=.02) and diastolic blood pressure (beta=-0.34, P=.007) at 6 months.

Ghezeljeh et al. 32, 2018	RCT	100 patients 1) 25 education 2) 25 control 3) education + social network 4) education + phone follow-up	1) in centre education 3) smartphone-based social networking (Telegram®): The researcher sent the patients necessary information and advice in the form of key tips using educational images and videos on a weekly basis. The patients were encouraged to keep in touch with the researcher. 4) In centre education + weekly telephone follow-up	Those patients who underwent self-management (SM) education training (with and without follow-up) had statistically significant differences from those in the control group in terms of SM behaviours ($p < .001$). There was no statistically significant difference between different types of follow-up.
Cairns et al. 33, 2018	RCT	91 patients 45 intervention 46 control	Participants typed BP readings into their mobile phone or smartphone. The telemonitoring service sent reminders when BP readings were overdue (dependent on the most recent BP, between 24 and 96 hours since the missing reading), and incorporated an individualized medication reduction schedule	BP was lower in the intervention group, most markedly at 6 weeks: intervention group mean (SD), systolic 121.6 (8.7)/diastolic 80.5 (6.6) mm Hg; control group, systolic 126.6 (11.0)/diastolic 86.0 (9.7) mm Hg; adjusted differences (95% confidence interval), systolic −5.2 (−9.3 to −1.2)/diastolic −5.8 (−9.1 to −2.5) mm Hg. Diastolic BP remained significantly lower in those self-managing to 6 months: adjusted difference −4.5 (−8.1 to −0.8) mm Hg.
Davidson et al. 34, 2015	RCT	38 patients 18 intervention	The Smartphone Medication Adherence Stops Hypertension program was developed using a patient-centred, theory-guided, iterative design process.	Generalized linear mixed modelling revealed statistically significant time-by-treatment interactions ($p < 0.0001$) indicating significant reductions in resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) for the SMASH group vs. the standard care (SC) control group

		20 control	Electronic medication trays provided reminder signals, and Short Message Service messaging reminded subjects to monitor BP with Bluetooth-enabled monitors.	across all time points. At month 6, 94.4% of the SMASH vs. 41.2% of the SC group exhibited controlled BP (p < 0.003).
Anthony et al. 35, 2015	RCT	123 patients 1) 47 EMR only 2) 33 EMR + reminders 3) 43 bidirectional	1) The research assistant showed each subject how to use our EMR and submit BP measurements. 2) + a text message reminder (e.g., 7, 8, or 9 am and pm) to check and record the patient's BP 3) + asking the patient to check and subsequently send a text message response with their current BP	Among 121 patients, those in the bi–directional text messaging group reported the full 14 measurements more often than both the EMR–only group (P < .001) and the EMR + reminders group (P = .038). Also, the EMR + reminders group outperformed the EMR–only group (P < .001).
Ahmed et al. 36, 2016	RCT	428 patients 214 control 214 intervention	Patients attended doctor-led once-weekly 2 –hour educational sessions for one month including: definitions of high BP, symptoms and complications of HTN, BP home monitoring, BP control goals, follow up intervals as well as nutritional and exercise advice. Intensification of medications adherence was done through scheduled	A team-based educational intervention for both staff and patients led to significant improvement in SBP, DBP, MRA and BP control in adult hypertensive patients, primary health care setting

			appointments, SMS messages and phone calls to remind patients of refill due dates.	
Buis et al. 37, 2017	RCT	123 patients 60 intervention 63 control	BPMED is an automated text message system that sends daily medication reminders to users at individually customized times. BPMED also sends two educational messages per week, with content based on HTN management recommendations from the American Heart Association.	BPMED participants consistently showed numerically greater, yet nonsignificant, improvements in measures of medication adherence (mean change 0.9, SD 2.0 vs mean change 0.5, SD 1.5, P=.26), SBP (mean change –12.6, SD 24.0 vs mean change –11.3, SD 25.5 mm Hg, P=.78), and DBP (mean change –4.9, SD 13.1 mm Hg vs mean change –3.3, SD 14.3 mm Hg, P=.54).
Frias et al. 38, 2017	RCT	109 patients 40 4-week intervention 40 12-week intervention 29 usual care	Participants used digital medicines, the wearable sensor patch, and the mobile device app for 4 or 12 weeks. Providers in the DMO arms could review the DMO data via a Web portal.	For patients failing hypertension and diabetes oral therapy, this DMO, which provides dose-by-dose feedback on medication ingestion adherence, can help lower BP, HbA1c, and LDL-C, and promote patient engagement and provider decision making.
Maslakpak et al. 39, 2016	RCT	123 patients 41 SMS	Intervention for the reminder cards group consisted of education in the appropriate usage and ordering of the cards. The patients in the text messaging group were sent 6 messages a week. Both groups	The findings of the present research demonstrated that training and distance-monitoring via SMS and reminder cards promote medication adherence of patients.

		41 reminder cards 41 control	were presented with the same educational content.	
Milani et al. 40, 2017	Single cohort study with 400 matched controls	156 patients	Blood pressure units were commercially available that transmitted data directly to the electronic medical record. Digital-medicine patients completed questionnaires online, were asked to submit at least one blood pressure reading/week and received medication management and lifestyle recommendations via a clinical pharmacist and a health coach.	At 90 days, 71% of digital-medicine vs 31% of usual-care patients had achieved target blood pressure control. Mean decrease in systolic/diastolic blood pressure was 14/5 mm Hg in digital medicine, vs 4/2 mm Hg in usual care ($P < .001$).
Hacking et al. 41, 2016	Mixed methods study	223 patients 109 intervention 114 control	The intervention group received 90 SMSs over a period of 17 weeks. Thereafter, the baseline questionnaire was readministered to both groups to gauge if any improvements in health knowledge had occurred.	No statistically significant changes in overall health knowledge were observed between the control and intervention groups. The intervention group had positive increases in self-reported behaviour changes. These were reaffirmed by the focus groups, which also revealed a strong preference for the SMS campaign and the belief that the SMSs acted as a reminder to change
Hoffmann-Petersen et al. 42, 2017	RCT	356 patients 175 intervention	In the intervention group, antihypertensive treatment was based on TBPM with transmission of the measurements and subsequent	The decrease in daytime ABPM in the intervention group was systolic/diastolic, $-8\pm12/-4\pm7$ mm Hg. This did not differ significantly from the control group's $-8\pm13/-4\pm8$ mm Hg. An

		181 control	communication by telephone or e-mail.	equal number of participants obtained normal daytime ABPM, in the intervention group 17% (31/175) versus control 21% (37/181), P=0.34.
Fishman et al. 43, 2013	RCT	778 patients 1)258 control 2)259 home BP monitoring and secure patient website training 3)261 + pharmacist care management	2) the home BP monitor and MyGroupHealth: a suite of online services so you can e-mail your doctor, refill prescriptions, request appointments, get test results, and look up health information. 3) + pharmacist care management delivered through Web communications	A 1% improvement in number of patients with controlled BP using home BP monitoring and web-based pharmacist care-the e-BP program-costs $16.65 (95% confidence interval: 15.37- 17.94) relative to home BP monitoring and web training alone. Each mm HG reduction in systolic and diastolic BP achieved through the e-BP program costs $65.29 (59.91-70.67) relative to home BP monitoring and web tools only. Life expectancy was increased at an incremental cost of $1850 (1635-2064) and $2220 (1745-2694) per year of life saved for men and women, respectively.
Choi et al. 44, 2014	RCT	49 patients 25 intervention 24 only home BP monitor no intervention	The experimental group received remote video consultation twice a week. The consultation was mainly related to BP monitoring, which included a BP check, drug intake data, and clarification of events that may have affected their BP. Patients received a home BP monitor	There was a statistically significant decrease in systolic blood pressure (F=10.26, p=0.003), but diastolic blood pressure showed no significant difference (F=2.802, p=0.101).
Dealleaume et al., 45, 2015	Single arm cohort study	35778 patients	Patients were given validated home BP monitors and reported monthly average home BP readings by Internet or phone.	The percentage of active participants at or below target BP increased from 34.5% to 53.3% (P < .001) and increased 24.6% to 40.0% (P < .001) for those with diabetes. The mean difference in office BP over 1 year between participants and nonparticipants was -5.4/-2.7 mmHg (P < .001 for systolic BP, P = .01 for diastolic BP) for all participants

			Patients and providers received feedback.	
Okura et al. 46, 2016	Community-based clinical observational study	69 patients	BP was measured at home twice a day (morning and evening) using the oscillometric automatic device. Body weight (BW) and percent body fat (%BF) were measured. Daily walking steps (DWS) were calculated by a pedometer These daily parameters were transmitted through the Internet to a central server computer. Using a personal computer at home, patients were able to know their daily parameters.	They had significantly reduced systolic BP after induction of the telemedicine system. This study showed that the telemedicine system is useful to improve physical parameters, including BP, BW, BMI, and %BF, especially by promoting walking with a pedometer.
Liu et al. 47, 2018	Three-parallel group, double-blind randomized controlled design	128 patients 43 control 42 User-driven 43 Expert-driven	Expert-driven program: the weekly e-mails consisted of predetermined exercise and dietary goals. User-driven e-mail counselling enabled the participants to set their own goals or to select the interventions used to reach their behavioural goal.	Expert-driven groups showed a greater systolic blood pressure decrease than controls at follow-up (expert-driven versus control: −7.5 mmHg, 95% CI= −12.5, −2.6, p=0.01). Systolic blood pressure reduction did not significantly differ between user- and expert-driven.
Mensario et al. 48, 2019	An exploratory randomized controlled trial.	106 patients 51 control	The self-administered online intervention (“Living Better”) is composed of nine modules and presented via a web page aimed at progressively establishing	This study demonstrates that the Internet is a viable alternative for the delivery and dissemination of interventions focused on promoting healthy habits, and a totally self-administered intervention can produce long-term positive results.

		55 intervention	healthy eating habits and increasing the level of physical activity as recommended by the guides. In addition, the web page offered useful tools, such as downloading documents online and videos. Participants accessed the program through a computer (no mobile version was developed).	
Choudhry et al. 49, 2018	Two-arm pragmatic cluster randomized controlled trial	4078 patients 2040 Control 2038 Intervention	Telephone-delivered behavioural interviewing by trained clinical pharmacists, text messaging, pillboxes, and mailed progress reports	A remotely delivered multicomponent behaviourally tailored intervention resulted in an increase in medication adherence but did not change clinical outcomes.
Nolan et al. 50. 2018	Multicentre, 2 parallel group, double-blind, randomized controlled trial	264 patients 131 control 133 intervention	Used multimedia and interactive tools to increase motivation and skill for self-care (exercise, diet, medication adherence, and smoking cessation). Control used self-care education. Both received fully automated weekly emails	At 12 months, e-counselling versus control evoked greater reduction in systolic BP and pulse pressure in the intervention group
Fisher et al. 51, 2019	Single arm cohort study	130 patients	Home monitors are equipped with technology allowing measurements to be transmitted in real-time and automatically uploaded into the EMR. For	A home-based BP control program run by non-physicians can provide efficient, effective and rapid control, suggesting an innovative paradigm for hypertension management.

			those patients whose home BP is elevated, medication adjustments are made by telephone consultation with a patient navigator, following the clinical algorithm as outlined in the software platform.	
Lu et al. 52, 2019	Single arm cohort study	432 patients	Following enrolment, patients received a home telehealth device kit for automatic blood pressure monitoring which enables data transmission between the patient's home and telehealth service centre.	Home telehealth care combined with care management by public health nurses based in public health care centre was feasible and effective for improving blood pressure control among patients with hypertension.
Pan et al.53,2018	RCT (1:1)	110 patients	Received home telemonitoring for blood pressure delivered by a team comprising a GP, a hypertension specialist, a general nurse and an information manager	The intervention group had a greater reduction in BP compared with the control. Similarly, higher proportions of patients with normal BP were achieved in the intervention group. The reduction in SBP for the participants in the intervention group was positively correlated with the utilisation of the app (P<0.05).
Dehmer et al. 54, 2018	Cluster randomized clinical trial	450 hypertensives 222 control 228 intervention	Intervention patients received home BP telemonitors and transmitted BP data to pharmacists who adjusted antihypertensive therapy accordingly.	Home blood pressure monitoring and pharmacist case management to improve hypertension care can be implemented without increasing, and potentially reducing, overall medical care costs.

Margolis et al. 55, 2018	RCT	450 hypertensives 222 control 228 intervention	Intervention patients received home BP telemonitors and transmitted BP data to pharmacists who adjusted antihypertensive therapy accordingly.	This intensive intervention had sustained effects for up to 24 months (12 months after the intervention ended). Long-term maintenance of BP control is likely to require continued monitoring and resumption of the intervention if BP increases.
Bosworth et al, 56, 2018	RCT	429 patients 213 education control 215 Intervention	During 12 monthly phone calls, medication adjustments were made at intervals based on patients' laboratory values, medication interactions, reported and observed medication adverse effects, clinical assessment, patients' report of medication adherence, and disease monitoring.	No differences were seen in systolic blood pressure, diastolic blood pressure, or low-density lipoprotein at 6 or 12 months. Despite increased access to pharmacist resources, we did not observe significant improvements in CVD risk for patients randomized to the intervention compared to education control over 12 months.
Kim et al. 57,2015	RCT	374 patients 1) 124 Home BP monitoring 2) 124 Telemonitoring BP 3) 126 telemonitoring + remote care	1) received typical clinical care using home BP monitoring. In-office physician care at FU appointments every 8 weeks for 24 weeks. 2) patients received remote monitoring of home BP through the LG Smart Care system. In-office physician care at FU appointments every 8 weeks for 24 weeks.	No difference between the three groups was observed in the primary end point (adjusted mean sitting SBP was as follows: group 1: −8.9±15.5 mm Hg, group 2: −11.3±15.9 mm Hg, group 3: −11.6±19.8 mm Hg

			3) remote monitoring of home BP and remote physician care without in-office physician care.	
Edelman et al. 58, 2015	Patient-level randomized controlled trial	377 patients 193 intervention 184 control	Telephonic behavioural self-management intervention	In nine community fee-for-service practices, telephonic nurse case management did not lead to improvement in A1c or SBP. Gains seen in telephonic behavioural self-management interventions in optimal settings may not translate to the wider range of primary care settings.
Farahmand et al. 59, 2019	RCT	56 patients 28 intervention 28 control	The intervention was a 60-minute SCE discharge program with 4 re-educative telephone follow-ups every 2 weeks based on 4 chapters of the designed SCE program and booklet.	SCE discharge program with telephone re-educative follow-ups was effective in reducing mean BP. The use of this program as a discharged plan for older adults with HTN and comparison of readmission rates for a longer period are recommended.
Nishizawa et al. 60, 2016	Single cohort study	341 patients	Each participant was given an automated HBP monitoring device. During the course of this study, lifestyle modification counselling and antihypertensive treatment were performed by one physician	Home BP-guided approach helped achieve a decrease in the participants' HBPs (initial average: 151.3±20.0/86.9±10.2 mm Hg to 120.2±12.1/70.8±10.2 mm Hg) over the 4 years.
Jo et al. 61, 2019	Prospective observational study	7751 patients	Self-blood pressure monitoring for 3 months with automated BP device	Mean BP significantly decreased from 142/88 to 129/80 mm Hg ($P < .001$), and attainment of the target BP increased from 32% to 59% ($P < .001$) after SBPM. The rate of awareness of the BP goal increased from 57% to 81% ($P < .001$).

Lee et al. 62, 2016	RCT	382 patients	Cloud BP system integrated with computerized physician order entry (CPOE)	The proportion of patients with BP control at two, four and six months was significantly greater in the intervention group than in the control group. The average capture rates of blood pressure in the intervention group were also significantly higher than the control group in all three checkpoints.
Yi et al. 63, 2015	RCT	900 patients 450 control 450 intervention	Intervention participants received a home blood pressure monitor and training on use, whereas control participants received usual care.	Self-blood pressure monitoring was not shown to improve control over usual care in this largely minority, urban population. The patient population in this study, which included a high proportion of Hispanics and uninsured persons, is understudied.
Or et al. 64, 2016	RCT	63 patients	Patient-Centred, Computer-Based Self-Monitoring System	The patients in the intervention group had a significant decrease in mean systolic blood pressure from baseline to 1 month ($p < 0.001$) and from baseline to 3 months ($p = 0.043$) compared with the control group. Significant improvements in the mean diastolic blood pressure were seen in the intervention group compared with the control group after 1 month ($p < 0.001$) and after 2 months ($p = 0.028$), but the change was not significant after 3 months
Carrera et al. 65, 2016	Single cohort study	20 participants	Mobile application	Overall, the robustness, usability and efficiency of BP control are very good
Sun et al. 66, 2016	Single cohort study	20 participants	Mobile application	Participants' attitude toward self-reflection and perceived control over that behaviour stayed unchanged in the first two weeks of intervention and then increased significantly in the following two weeks.
Mao et al. 67, 2017	Retrospective analysis	1012 patients	Mobile phone app-based health coaching	Mobile phone app-based health coaching interventions can be an acceptable and effective means to promote weight loss and improve blood pressure management in overweight or obese individuals

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List of meta-analysis on Digital Health for hypertension in primary prevention

Author	Design	Studies included	Intervention	Conclusion
Tucker et al. 1, 2017	Meta-analysis	36 articles	Randomised trials comparing self-monitoring to no self-monitoring in hypertensive patients	Self-monitoring alone is not associated with lower BP or better control, but in conjunction with co-interventions (including systematic medication titration by doctors, pharmacists, or patients; education; or lifestyle counselling) leads to clinically significant BP reduction which persists for at least 12 months.
Duan et al. 2, 2017	Meta-analysis	46 articles	Effectiveness of home blood pressure telemonitoring (HBPT)	Compared with usual care, HBPT improved office systolic blood pressure (BP) and diastolic BP by 3.99 mm Hg (P<0.001) and 1.99 mm Hg (P<0.001. A larger proportion of patients achieved BP normalisation in the intervention group (P<0.001). For HBPT plus additional support (including counselling, education and so on) versus HBPT, the mean changes in systolic and diastolic BP were 2.44 mm Hg (P=0.05) and 1.12 mm Hg (P=0.07).
Fletcher et al. 3, 2015	Meta-analysis	28 articles	Effect of Self-Monitoring of Blood Pressure on Medication Adherence and Lifestyle Factors	Pooled results of 13 studies demonstrated a small but significant overall effect on medication adherence in favour of SMBP interventions. Where SMBP interventions had a significant effect on lifestyle factor change, the effect was unlikely to be clinically significant. Pooled results of 11 studies demonstrate a significant overall effect on diastolic blood pressure in favour of SMBP.
Morrissey et al. 4, 2017	Meta-analysis	26 articles	Effectiveness and content analysis of interventions to enhance medication adherence and blood pressure control in hypertension	The meta-analysis found a modest main effect of adherence interventions on SBP (MD -2.71 mm Hg, 95% CI -4.17 to -1.26) and DBP (MD -1.25 mm Hg, 95% CI -1.72 to -.79).

Alessa et al. 5, 2017	Meta-analysis	21 articles	The effectiveness of apps in lowering blood pressure, as well as their usability and patients' satisfaction with their use.	Most of the studies reported that apps might be effective in lowering blood pressure and are accepted by users. However, these findings should be interpreted with caution, as most of the studies had a high risk of bias.
McLean et al, 6, 2016	Meta-analysis	7 articles	Interactive digital interventions (IDIs) to support patient self-management of hypertension	IDIs lower both SBP and DBP compared to usual care. Results suggest these findings can be applied to a wide range of healthcare systems and populations. However, sustainability and long-term clinical effectiveness of these interventions remain uncertain

1. *Tucker KL, Sheppard JP, Stevens R, et al. "Self-monitoring of Blood Pressure in Hypertension: A Systematic Review and Individual Patient Data Meta-analysis." PLoS Medicine 14, no. 9 (2017): E1002389.*
2. *Duan Y, Xie Z, Dong F, et al. "Effectiveness of Home Blood Pressure Telemonitoring: A Systematic Review and Meta-analysis of Randomised Controlled Studies." Journal of Human Hypertension 31, no. 7 (2017): 427-437.*
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7. *Tucker KL, Sheppard JP, Stevens R, et al. "Self-monitoring of Blood Pressure in Hypertension: A Systematic Review and Individual Patient Data Meta-analysis." PLoS Medicine 14, no. 9 (2017): E1002389.*
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List of trials on Digital Health for TD2M management in primary prevention

Author	Design	Sample Size	Intervention	Conclusion
Fukuoka et al. 1, 2015	Single cohort study	6030 patients	Mobile technology	Opportunistic screening using a two-step approach: diabetes risk profile and HbA1c measurement detected a large percentage of individuals with prediabetes
Nicolucci et al. 2, 2015	RCT	302 patients	Home telehealth	Use of the HT system was associated with better metabolic control and quality of life; a marginally nonsignificant lower resource utilization was also documented
Kim et al. 3, 2015	Survey	90 patients	Smartphone application	This smartphone-based application can be a useful tool leading to positive changes in diabetes related self-care activities and increase user satisfaction
Ramadas et al. 4, 2015	Single cohort study	66 patients	Internet-delivered dietary intervention program (myDIDeA)	The process evaluation of myDIDeA demonstrates its feasibility, and future studies should identify the possibility of extending the use of Internet-based intervention programs to other health behaviours
Pellegrini et al. 5, 2015	Single cohort study	8 patients	Smartphone technology	Sedentary time decreased by 8.1 ± 4.5 %, and light physical activity increased by 7.9 ± 5.5 % over the 1-month period. The results suggest that NEAT! is an acceptable technology to intervene on sedentary time among adults with type 2 diabetes
Welch et al. 6, 2015	Parallel-group RCT	199 patients	Internet-based diabetes management platform	Diabetes dashboard intervention significantly improved diabetes-related outcomes among Latinos with poorly controlled T2D compared with a similar diabetes team condition without access to the diabetes dashboard

Jamal et al. 7, 2015	A cross-sectional survey	304 patients	Online health-related information	Study demonstrates that participants seeking online health-related information are more conscious about their diabetes self-care compared to non-health-related information seekers in some aspects more than the others
Block et al. 8, 2015	RCT	339 patients	Alive-PD, delivered via the Web, Internet, mobile phone, and automated phone calls	Alive-PD improved glycaemic control, body weight, BMI, waist circumference, TG/HDL ratio, and diabetes risk
Lee et al. 9, 2015	RCT	37 patients	Telemonitoring	The results of this study reinforce the need for monitoring as well as educational initiatives for Muslims with diabetes who fast during Ramadan
Waki et al. 10, 2015	Single cohort study	5 patients	Smartphone application	DialBetics with FoodLog was shown to be an effective and convenient tool, its new meal-photo input function helping provide patients with real-time support for diet modification
Bin Abbas et al. 11, 2015	Single cohort study	100 patients	Text messaging	Mobile phone text messaging increased adherence to diabetes therapy and improved the clinical outcome in Saudi patients with type 2 diabetes.
Kumar et al. 12, 2015	RCT	268 patients	Mobile reminders	Mobile reminders during opportunistic screening in primary health care setting improve screening yield of diabetes
Weymann et al. 13, 2015	RCT	561 patients	Web-based interactive health communication applications (IHCAs)	There were no main effects of the intervention on other dimensions of patient empowerment or decision-related outcomes

Nobis et al. 14, 2015	RCT	260 patients	Web-based intervention in reducing depression	A guided, web-based intervention to reduce depression in adults with type 1 and type 2 diabetes is effective in reducing both depressive symptoms and diabetes-specific emotional distress
Rollo et al. 15, 2015	Single cohort study	10 patients	Mobile Phone Image-Based Dietary Assessment Method	These findings demonstrate the performance and feasibility of the NuDAM to assess energy and macronutrient intake in a small sample
Katalenich et al. 16, 2015	RCT	98 patients	Diabetes Remote Monitoring and Management System (DRMS)	An automated system like the DRMS may improve glycaemic control to the same degree as usual clinic care and may significantly improve the social/vocational aspects of quality of life
Capozza et al. 17, 2015	RCT	93 patients	Text message-based personalized behavioural intervention	This study demonstrated a practical approach to implementing and monitoring a mobile health intervention for self-management support across a wide range of independent clinic practices
Wayne et al. 18, 2015	RCT	138 patients	Mobile phone monitoring	Health coaching with and without access to mobile technology appeared to improve glucoregulation and mental health in a lower-SES, T2DM population
Boudreaux et al. 19, 2015	Single cohort study	421 patients	Computerized tobacco SBIRT system	The HERA promoted initial contact with a smoking cessation provider and the faxed referral further promoted treatment initiation, but it did not lead to improved abstinence
Fountoulakis et al. 20, 2015	RCT	70 patients	Telemonitoring on HbA1c and BMI	Telemonitoring can result in reduction of HbA1c and frequency of hypo- and hyperglycaemias. This beneficial effect is slightly attenuated 6 months after terminating telemonitoring
Sepah et al. 21, 2015	Single-arm study	220 patients	Web-based diabetes prevention program	Users of the Prevent program experienced significant reductions in body weight and A1c that are maintained after 2 years

Carallo et al. 22, 2015	RCT	312 patients	Telemedicine	The present study demonstrates that a health care program based on GPs empowerment and taking care plus remote consultation with Consultants is at least as effective as standard outpatient management, in order to improve the control of T2DM
Bartholomew et al. 23, 2015	RCT	100 patients	Cell Phone/Internet Technology	The use of CIT for self-management of hyperglycaemia during pregnancy increased glucose reporting compliance by a small but statistically significant amount compared to the use of the traditional control method
Shahid et al. 24, 2015	RCT	440 patients	Mobile phone intervention	Mobile phone technology in rural areas of Pakistan was helpful in lowering HbA1c levels in intervention group through direct communication with the diabetic patients
Patnaik et al. 25, 2015	RCT	100 patients	Mobile phone intervention	Intervention in the form of intensive lifestyle education and phone calls and SMS significantly decrease their stress score
Greenwood et al. 26, 2015	RCT	90 patients	Telehealth Remote Monitoring	An eHealth model incorporating a complete feedback loop with telehealth remote monitoring and paired glucose testing with asynchronous data analysis significantly improved A(1c) levels compared to usual care
Ronda et al. 27, 2015	Survey	632 patients	Web patient portal	The diabetes patient web portal might be improved significantly by taking into account the patients' experiences and attitudes
Kenealy et al. 28, 2015	RCT	171 patients	Telecare	Telecare led to patients and families taking a more active role in self-management

Given et al. 29, 2015	RCT	50 patients	Telemonitoring	Telemedicine may help meet the growing demand on diabetes services due to increasing numbers of women being diagnosed with GDM
Welch et al. 30, 2015	Single cohort study	30 patients	Remote home monitoring (RHM) device suite comprising a Bluetooth	These findings provide encouraging empirical support for the usability and clinical value of a diabetes telehealth program integrating a user-friendly cellular pillbox and clinical decision support tools that was delivered to an urban poor T2D clinic population
Tildesley et al. 31, 2015	Single cohort study	926 patients	Internet intervention	Initial and prolonged improvement was found in A1C levels for all reporters. The data support that numerous patients can be followed up effectively using the Internet for as long as 30 months
Phillips et al. 32, 2015	Single cohort study	113 patients	Web-based decision support system	A novel decision support program improved A1c with little hypoglycaemia
Celik et al. 33, 2015	A one group pretest-posttest design	221 patients	Mobile communication technologies	This study demonstrated that a short message services-based information and reminder system on insulin injection administration provided to insulin-dependent patients with diabetes by nurses resulted in improved self-administration of insulin and metabolic control
Carral et al. 34, 2015	A prospective, single-centre, interventional study with two parallel groups	104 patients	Web-based telemedicine system	A Web-based telemedicine system can be a useful tool facilitating the management of pregnant diabetes patients, as a complement to conventional outpatient clinic visits
Tildesley et al. 35, 2013	RCT	57 patients	Real-time continuous glucose monitoring (RT-CGM) and an	The use of both IBGMS and RT-CGM significantly improved A1C levels in patients with type 2 diabetes treated with insulin in a randomized trial over a 6-month period

			Internet blood glucose monitoring system (IBGMS)	
Griffith et al. 36, 2016	Single cohort study	17 patients	Shared Decision-Making Approach to Telemedicine	Patients in this feasibility study demonstrated improvement in haemoglobin A1c values, and reported better understanding of diabetes
Mochari-Greenberger et al. 37, 2016	Retrospective analysis	466 patients	Tele-Behavioural Health Intervention	This study documented significant decreases in depression, anxiety, stress, and glucose levels, as well as increased frequency of glucose self-testing, among participants in a diabetes behavioural telehealth program
Shane-McWhorter et al. 38, 2016	Single cohort study	75 patients	Telemonitoring	Telemonitoring projects improve clinical outcomes in patients with diabetes
Chow et al. 39, 2016	Retrospective analysis	191 patients	Blood glucose self-monitoring and internet diabetes management	The inverse correlation between reporting frequency and A1C, as well as the significant difference in A1C only for the frequent testers, suggests that frequent SMBG has an effect on reducing A1C
Roelofsen et al. 40, 2016	Single cohort study	633 patients	Online Platform for T2DM Patients	Platform use was associated with more favourable clinical and psychological characteristics relative to non-use
Ajay et al. 41, 2016	Single cohort study	6797 participants	Mobile phone–based clinical decision support system	A nurse-facilitated, mobile phone–based clinical decision support system-enabled intervention in primary care was associated with improvements in blood pressure and blood glucose control and has the potential to scale-up in resource poor settings

Anzaldo-Campos et al. 42, 2016	RCT	301 patients	Short-Term Mobile Technology	Project Dulce with and without wireless technology substantially improved glycaemic control and diabetes knowledge in high-risk patients with type 2 diabetes in a Mexican family medical unit
Petullo et al. 43, 2016	Retrospective analysis	867 patients	Electronic Messaging	EM use was associated with improved glycaemic control, even after controlling for electronic portal access and other variables, but not with hospitalizations or emergency visits.
Peimani et al. 44, 2016	RCT	150 patients	Mobile Short Message Service (SMS)	Sending short text messages as a method of education in conjunction with conventional diabetes treatment can improve glycaemic control and positively influence other aspects of diabetes self-care
Aguiar et al. 45, 2016	RCT	101 patients	The intervention group received the PULSE Program, which contained print and video resources on weight loss (Self-Help, Exercise and Diet using Internet Technology [SHED-IT] Weight Loss Program)	The PULSE Program improved several Type 2 diabetes mellitus risk factors in men, including weight and glycated haemoglobin
Maxwell et al. 46, 2016	Single cohort study	26 patients	Pharmacist-Led Telehealth Clinic	Six months of CVT clinic attendance significantly improved A1C values and the overall percentage of patients meeting their goal A1C values in this veteran population
Goh et al. 47, 2016	Single cohort study	84 patients	Caloric-monitoring mobile phone app	This study provides insight into the nature and extent of usage of a caloric-monitoring app among patients with type 2 diabetes and managed in primary care
Kim et al. 48, 2016	Single cohort study	29 patients	Patient-Centred, Smartphone-Based	A 12-week application of the PSDCS to patients with inadequately controlled type 2 diabetes resulted in a significant HbA1c reduction with tolerable safety profiles

Bentley et al. 49, 2016	RCT	27 patients	mHealth of portable technology	mHealth device was acceptable and promising for helping individuals with T2DM to reduce their HbA1c and lose weight
Pfammatter et al. 50, 2016	A prospective, parallel cohort design	1925 patients	mHealth Intervention	A text messaging intervention was feasible and showed initial evidence of effectiveness in improving diabetes-related health behaviours, demonstrating the potential to facilitate population-level behaviour change in a low/middle income country
Quinn et al. 51, 2016	RCT	118 patients	Mobile health intervention	The mobile health intervention was as effective at managing Type 2 diabetes in older adults as younger persons
Lim et al. 52, 2016	RCT	100 patients	Individualized health management system employing advanced medical information technology	This u-healthcare service provided effective management for older patients with type 2 diabetes
Crowley et al. 53, 2016	RCT	50 patients	Telemedicine	A comprehensive telemedicine intervention improved outcome among veterans with PPDM despite clinic-based care
Kim et al. 54, 2016	RCT	182 patients	Internet-Based Glucose Management System	The IBGMS was effective in improving blood sugar levels among patients with diabetes
Grady et al. 55, 2016	Single cohort study	40 patients	OneTouch Reveal (OTR) is a cloud-based web application	OTR web application in combination with the OTV meter helped subjects with T1DM and T2DM effectively manage their diabetes and was associated with improved BG control over 12 weeks

Brown et al. 56, 2016	Observational study	24 patients	RN Diabetes Virtual Case Management	This study demonstrates safety and efficacy of RN virtual chronic disease management for an older population of patients with long-standing diabetes
Piette et al. 57, 2016	RCT	72 patients	Mobile Health Support	In this study we found that caregiver feedback increased engagement in m-health and may improve patients' health status relative to standard approaches
Wild et al. 58, 2016	RCT	321 patients	Supported Telemonitoring and Glycaemic Control	Supported telemonitoring resulted in clinically important improvements in control of glycaemia in patients with type 2 diabetes in family practice
Rasmussen et al. 59, 2016	RCT	40 patients	Telemedicine	In the direct comparison of home video consultations vs standard outpatient treatment in type 2 diabetes mellitus, telemedicine was a safe and available option with favourable outcomes after six months treatment
Agboola et al. 60, 2016	RCT	126 patients	Personalized text messaging	Personalized text messaging can be used to improve outcomes in patients with T2DM by employing optimal patient engagement measures
Ferrara et al. 61, 2016	RCT	2280 patients	Diabetes Prevention Program (DPP)-derived lifestyle intervention	A DPP-derived lifestyle intervention modestly reduced postpartum weight retention and increased vigorous-intensity physical activity
Gatwood et al. 62, 2016	RCT	48 patients	Tailoring mobile phone text messages	Tailoring mobile phone text messages is a novel way to address medication nonadherence and health beliefs
Nelson et al. 63, 2016	Pre-post single group	80 patients	SMS	MED had a positive, short-term impact on adherence, which did not translate to improvements in HbA1c

Kardas et al. 64, 2016	RCT	60 patients	COMODITY12 system	Study proved that the COMODITY12 system is well accepted by type 2 diabetes patients taking part in clinical trial, leading to several clinical benefits, and improved quality of life
Sayakhot et al. 65, 2016	RCT	116 patients	Web-based program	The study suggested that both approaches, standard education and standard education plus web-based program, resulted in excellent knowledge scores, but not statistically significant difference between groups
Devkota et al. 66, 2016	Retrospective study	1510 patients	Online Patient Portal	Patients with more active e-mail communication via a patient portal appeared to have the greatest likelihood of HbA1c control
Zhou et al. 67, 2016	RCT	100 patients	Mobile app	Diabetes patients using the Welltang application achieved statistically significant improvements in HbA1c, blood glucose, satisfaction of patients to use of Welltang, diabetes knowledge, and self-care behaviours
Shariful Islam et al. 68, 2016	RCT	236 patients	SMS	There was no significant difference between the groups. Post hoc subgroup analyses suggested that the SMS intervention worked better in women, those with a baseline HbA1c >8%, and those with a shorter duration of diabetes.
Hsu et al. 69, 2016	RCT	40 patients	Cloud-Based Diabetes Management Program	Mobile health technology could be an effective tool in sharing data, enhancing communication, and improving glycaemic control while enabling collaborative decision making in diabetes care
Hansel et al. 70, 2017	RCT	120 patients	Fully Automated Web-Based Program	Among patients with T2DM and abdominal obesity, the use of a fully automated Web-based program resulted in a significant improvement in dietary habits and favourable clinical and laboratory changes

Tutino et al. 71, 2017	Single cohort study	3586 patients	Web-based Joint Asia Diabetes Evaluation (JADE) programme	Integrated care augmented by information technology improved cardiometabolic control, with additional nurse contacts reducing the default rate and enhancing self-care
Dobson et al. 72, 2016	Single cohort study	42 patients	Text messaging	A tailored text message-based intervention is both acceptable and useful in supporting self-management in people with poorly controlled diabetes
Baron et al. 73, 2017	RCT	81 patients	Mobile telehealth	Findings from this study must be interpreted with caution given the small sample size, but they do not support the widespread adoption of MTH to achieve clinically significant changes in HbA1c
Michaelides et al. 74, 2016	Single cohort study	43 patients	Mobile prevention diabetes program	Our findings support the effectiveness of a uniquely mobile prediabetes intervention, producing weight loss comparable to studies with high engagement, with potential for scalable population health management
Kerfoot et al. 75, 2017	RCT	456 patients	Team-based online game	Patients with diabetes who were randomized to an online game delivering DSME demonstrated sustained and meaningful HbA1c improvements
Saslow et al. 76, 2017	RCT	25 patients	Online lifestyle program	Individuals with type 2 diabetes improved their glycaemic control and lost more weight after being randomized to a very low-carbohydrate ketogenic diet and lifestyle online program rather than a conventional, low-fat diabetes diet online program
Rushakoff et al. 77, 2017	Cross-sectional analysis	24079 patients	Virtual glucose management service (vGMS)	Implementation of the vGMS was associated with decreases in hyperglycaemia and hypoglycaemia
Chung et al. 78, 2017	Single cohort study	20,655 patients	Internet secured messages	Patients with diabetes frequently used secure messaging for medical advice in addition to routine visits to care providers

Fortmann et al. 79, 2017	RCT	126 patients	mHealth SMS-Based Intervention	Use of a simple, low-cost text messaging program was found to be highly acceptable in this sample of high-risk, Hispanic individuals with type 2 diabetes and resulted in greater improvement in glycaemic control compared with UC
Sugita et al. 80, 2017	RCT	41 patients	Text messaging	Our results suggested that medication adherence at 6 months after discharge in patients with type 2 diabetes did not significantly change by text messages, which aimed to improve their HL levels
Plotnikoff et al. 81, 2017	RCT	84 patients	Smartphone technology	eCoFit is an innovative lifestyle intervention which integrates smartphone technology, social support, and the outdoor environment to improve aerobic and muscular fitness
Kleinman et al. 82, 2017	RCT	91 patients	mHealth intervention	Participants assigned to m-Health had increased medication adherence and frequency of BG testing compared with usual care participants
Kempf et al. 83, 2017	RCT	202 patients	Telemedical Lifestyle intervention Program	In advanced-stage type 2 diabetes, TeLiPro can improve glycaemic control and may offer new options to avoid pharmacological intensification
Limaye et al. 84, 2017	RCT	265 patients	A virtual assistance-based lifestyle intervention	A virtual assistance-based lifestyle intervention was effective, cost-effective and acceptable in reducing risk factors for diabetes in young employees in the information technology industry, and is potentially scalable
Frias et al. 85, 2017	Cluster RCT	109 patients	Digital Medicines	For patients failing hypertension and diabetes oral therapy, this DMO, which provides dose-by-dose feedback on medication ingestion adherence, can help lower BP, HbA1c, and LDL-C, and promote patient engagement and provider decision making

Davis et al. 86, 2017	Single cohort study	51 patients	Internet based intervention	A practical, customized video intervention may help improve patient self-efficacy, reduce problems with medication use, and improve medication adherence in diabetes patients
Andrews et al. 87, 2017	Single cohort study	18 patients	Telemedicine	Despite competing demands and frustration with the telemonitoring interface, many participants demonstrated intervention engagement and substantial improvement in HbA1c ($1%)
Abaza et al. 88, 2017	RCT	73 patients	Text messaging	SMS education is a feasible and acceptable method for improving glycaemic control and self-management behaviours among Egyptian diabetics
Threatt et al. 89, 2017	Single cohort study	12 patients	Telehealth	Mean A1C can be improved with telehealth DSME/S services in an underserved, free clinic population
Wang et al. 90, 2017	RCT	212 patients	Telemedicine	The Internet-based U-Healthcare system of integrated management in diabetes not only achieved better glycaemic control, effectively improved HbA1c levels and decreased triglyceride levels but also enhanced patients' adherence to the medical team's instructions
Murray et al. 91, 2017	RCT	374 patients	Web based self-management intervention	The HeLP-Diabetes programme is an effective self-management support programme that is implementable in primary care
Newby et al. 92, 2017	RCT	81 patients	Telephone + email	iCBT for depression is an efficacious, accessible treatment option for people with diabetes
Hansen et al. 93, 2017	RCT	165 patients	Video consultations	Video consultations preceded by uploading relevant measurements can lead to clinically and statistically significant improvements in glycaemic control among patients who have not responded to standard regimens

Kassar et al. 94, 2017	Single cohort study	106 patients	Telemedicine in correctional facilities	Improvements in glycaemic, blood pressure, and lipid control for prisoners with diabetes can be achieved with teleconsultations to correctional institutions
Mora et al. 95, 2017	Single cohort study	87 patients	Accu-Chek Connect diabetes management system	Use of the Accu-Chek Connect diabetes management system is associated with increased treatment satisfaction and improved glycaemic control among individuals with insulin-treated diabetes
Van Olmen et al. 96, 2017	RCT	781 patients	Mobile phone intervention	The finding that text messages did not show an additional effect on diabetes control implied that expectations about mHealth should be cautious
Ebert et al. 97, 2017	RCT	261 patients	Internet-based guided self-help treatments	The trial indicates that Internet-based guided self-help treatments for depression in people with diabetes can have sustained effects on depressive symptoms, well-being and emotional distress associated with diabetes
Dario et al. 98, 2017	RCT	243 patients	Telemonitoring	Enhancement of HRQoL should represent the most critical goal of DM healthcare delivery. Effects of TM on HRQoL of diabetic patients should be studied further
Lee et al. 99, 2017	Cluster randomised study	85 patients	Telemonitoring	A reduction of 1.07% in glycated haemoglobin levels was observed in the telemonitoring group compared to 0.24% in the control group ($p < 0.01$)
Kumar et al. 100, 2018	Single cohort study	146 patients	Diabetes Mobile App	This program was associated with a clinically meaningful and significant reduction in A1C and can potentially increase access to effective diabetes self-management education and support for individuals with diabetes

Everett et al. 101, 2018	Single cohort study	55 patients	Smartphone app	The Sweetch mobile intervention program is a safe and effective method of increasing PA and reducing weight and HbA1c in adults with prediabetes
Li et al. 102, 2018	RCT	374 patients	Web based self-management intervention	Facilitated access to HeLP-Diabetes is cost-effective, compared to usual care, under the recommended threshold of £20,000 to £30,000 per QALY by National Institute of Health and Care Excellence
Zanuidin et al. 103, 2018	Single cohort study	29 patients	Tele-support	Muslims with diabetes were able to self-manage when fasting using tele-monitoring support and intervention, with decreased complications during Ramadan compared with pre-Ramadan
Offringa et al. 104, 2018	RCT	1799 patients	Mobile platform	Users of the mobile platform tested their BG more often and demonstrated greater improvement in blood glucose compared to users who did not use the mobile platform
Sani et al. 105, 2018	Quasi-experimental design	200 patients	Audio-visual messages via mobile phone and peer support	This study demonstrated that JILSE program is effective, feasible, and acceptable to Saudi diabetic patients
Kumar et al. 106, 2018	RCT	945 patients	Mobile phone messages	After the intervention, an average FBG declined from 163.7 to 152.8 mg/dl ($P = 0.019$) in intervention and from 150.5 to 149.2 mg/dl ($P = 0.859$) in control group
Dobson et al. 107, 2018	RCT	366 patients	Tailored, text message based, self-management support programme	A tailored, text message based, self-management support programme resulted in modest improvements in glycaemic control in adults with poorly controlled diabetes

Warren et al. 108, 2018	RCT	126 patients	Telemonitoring	There was a clinically meaningful and statistically significant benefit from the telehealth intervention at a lower cost; thus, telehealth was cost saving and produced greater health benefits compared with usual care
Fang et al. 109, 2018	RCT	129 patients	Text messaging	Regular smartphone communication had a favourable impact on cardiovascular risk factors in patients with type 2 diabetes mellitus
Wong et al. 110, 2018	Observational post-RCT study	104 patients	SMS intervention	The SMS intervention preserved the clinical benefits within the trial period but failed to transform from treatment efficacy to long-term effectiveness beyond 2 years after intervention
Sood et al. 111. 2018	Cluster RCT	282 patients	Teleconsultation	Patients in both groups showed a small decrease in haemoglobin A1c, with no statistical difference between the groups (telemedicine consultation -1.01% vs usual consultation -0.68%, $p = 0.19$)
Wong et al. 112, 2016	Markov model		SMS intervention	The SMS intervention for IGT subjects had the superiority of lower monetary cost and a considerable improvement in preventing or delaying the T2DM onset
Elsabrout et al. 113, 2018	Single cohort study	14 patients	Web based intervention	Self-reported medication adherence results demonstrated a modest increase at the delayed postintervention time. In addition, there was a large increase in engagement scores at the delayed postintervention time
Hashmi et al. 114, 2018	Quasi-experimental	62 physicians	mHealth	m-Health technology can be a useful educational tool to help with improving knowledge and practice of diabetic guidelines
Yang et al. 115, 2018		107 patients	Telemedicine via smartphone	GDM treatment based on the WeChat platform effectively reduces FBG and 2-h PBG and may improve pregnancy outcomes

Ramadas et al. 116, 2018	RCT	128 patients	Web-based dietary intervention	Most important impact of myDIDeA was on the overall DKAB score. This study is one of the first to demonstrate that an e-intervention can be a feasible method for implementing chronic disease management in developing countries
Bollyky et al. 117, 2018	RCT	330 patients	Remote lifestyle coaching (Livongo)	Livongo participation significantly improves BG control in people with T2D
Michaud et al. 118, 2018	Retrospective study	955 patients	Remote monitoring	RPM for post discharge patients with T2D might be a promising approach for HbA1c control with increased patient engagement
Moin et al. 119, 2018	Single cohort study	268 patients	Online based intervention	An intensive, multifaceted online DPP intervention had higher participation but similar weight loss compared to in-person DPP.
Castro Sweet et al. 120, 2018	Single cohort study	501 patients	Digital Health intervention	This Medicare population demonstrated sustained program engagement and improved weight, health, and well-being
Jeong et al. 121, 2018	RCT	338 patients	Telehomecare	Telehealthcare was as effective as conventional care at improving glycemia in patients with type 2 diabetes without serious adverse effects
Rasekaba et al. 122, 2018	Explanatory RCT	95 patients	Telemedicine	Telemedicine support for GDM care showed no impact on service utilisation and costs

Kooiman et al. 123, 2018	RCT	72 patients	Fitbit Zip and online program	Responders (56%, increasing minimally 1000 steps/d) had significantly decreased glycated haemoglobin compared with nonresponders (-0.69% ± 1.18% vs 0.22% ± 0.47%, respectively; P = .007)
Akinci et al. 124, 2018	RCT	65 patients	Internet-based exercise	In type 2 diabetes, supervised group-based and Internet-based exercise can improve equally glycaemic control, waist circumference, and quality of life, and both are better than simply counselling
Nanditha et al. 125, 2018	RCT	346 patients	SMS intervention	Sustained reduction in incident diabetes was apparent after cessation of active lifestyle intervention. This was possibly associated with continuing practice of improved lifestyle
Polgreen et al. 126, 2018	RCT	138 patients	Fitbit + text messaging	In a population of patients with diabetes or pre-diabetes, individualized reminders to wear their Fitbit and elicit personal step goals did not lead to increases in daily steps, although daily steps were higher on days when goals were set
Lee et al. 127, 2018	RCT	148 patients	Tailored mobile coaching	Addition of TMC to conventional treatment for diabetes improved glycaemic control, and this effect was maintained without individualized message feedback
Miremberg et al. 128, 2018	RCT	120 patients	Smartphone feedback system	Introduction of a smartphone-based daily feedback and communication platform between gestational diabetes mellitus patients and the multidisciplinary diabetes-in-pregnancy clinic team improved patient compliance and glycaemic control, and lowered the rate of insulin treatment
Levy et al. 129, 2018	Single cohort study	129 patients	Mobile Insulin Titration Intervention	This implementation study showed MITI to have continued success after transitioning from an RCT program into real-world settings

Burner et al. 130, 2018	Mixed methods analysis	44 patients	mHealth	mHealth is a feasible, acceptable, and promising avenue to improve social support and diabetes outcomes
Carolan-Olah et al. 131, 2019	RCT	110 patients	Web based intervention	Findings suggest that the education intervention had a positive impact on women's postpartum weight and attendance at OGTT by 12 weeks postpartum.
Sarmiento et al. 132, 2019	RCT	308 patients	SMS intervention	SMS reminders did not improve postpartum follow-up rate among GDM patients at 12 weeks postpartum
Zhang et al. 133, 2019	RCT	51 patients	Smartphone app	Our feasibility study showed that among medication-nonadherent patients with type 2 diabetes, a smartphone app intervention was acceptable, improved awareness of medication adherence, and reduced self-reported barriers to medication adherence, but did not improve clinical outcomes in a developed Asian setting
Dixon et al. 134, 2019	Single cohort study	740 patients	Virtual Type 2 Diabetes Clinic	These findings suggest that the VDC has potential to support individuals with T2D and their clinicians in diabetes management between office visits
Clarke et al. 135, 2019	RCT	780 patients	Web based intervention	Improvement in social and occupational functioning and the secondary outcomes was generally no greater for myCompass users than for users of the control program at 3 months postintervention
Hochberg et al. 136, 2016	RCT	27 patients	Text messaging	Participants who received messages tailored by the personalized policy increased the amount of activity (e.g., walking) and pace of walking over time

Caballero-Ruiz et al. 137, 2017	RCT	90 patients	Web based telemedicine system	Sinedie generates safe advice about therapy adjustments, reduces the clinicians' workload and helps physicians to identify which patients need a more urgent or more exhaustive examination and those who present good metabolic control
Wei et al. 138, 2015	RCT	28 patients	Remote glucose monitoring	In this pilot trial in insulin-treated type 2 diabetes, RGM did not affect glycaemic control after hospital discharge; however, the high rate of hypoglycaemia in the post discharge transition period and the higher frequency of insulin titration in patients who used RGM suggest a safety role for such monitoring in the transition from hospital to home
Van Ryswyk et al. 139, 2015	RCT	276 patients	SMS reminder system	The SMS reminder system did not increase postpartum OGTT, fasting plasma glucose or HbA1c completion, although high rates of test completion were measured in both groups
McManus et al. 140, 2018	RCT	170 patients	Walking group/Website; biweekly e-mails	Families Defeating Diabetes outcomes were not significantly different for INT maternal or paternal participants versus CON participants
Nobis et al. 141, 2018	RCT	260 patients	Web-based intervention	This web-based intervention for individuals with diabetes and comorbid depression demonstrated a high probability of being cost-effective compared with an active control group
Fottrell et al. 142, 2019	RCT	11454 patients	mHealth intervention	Our data provide strong evidence to support the use of community mobilisation based on PLA to prevent type 2 diabetes in this rural Bangladeshi population
Alonso-Dominguez et al. 143, 2019	RCT	204 patients	Smartphone app	The success of this multifactorial intervention should help inform future clinical approaches and application designs towards managing type 2 diabetes mellitus and improving patient outcomes

Hooshmandja et al. 144, 2019	Quasi-experimental	51 patients	Smartphone app	The results indicated the positive effect of the mobile application on self-care behaviour, FBS, and HbA1C
Parsons et al. 145, 2019	RCT	323 patients	TeleCare support	Structured self-monitoring of blood glucose provides clinical and statistical improvements in glycaemic control in Type 2 diabetes. No additional benefit, over and above the use of structured self-monitoring of blood glucose, was observed in glycaemic control with the addition of once-monthly TeleCare support
Borgen et al. 146, 2019	RCT	238 patients	The Pregnant+ app	The Pregnant+ app had no effect on 2-hour glucose level at routine postpartum OGTT. After controlling for parity, the difference in emergency caesarean section was not statistically significant
Naghibi et al. 147, 2015	RCT	228 patients	Cell phone	Regarding the study results on using cell phone, to utilize virtual training methods is recommended as an appropriate procedure for different health care, self-caring and follow-up training plans for various groups in society, especially diabetic and chronic patients
Zhang et al. 148, 2019	RCT	276 patients	Mobile app	In Chinese patients with poorly controlled diabetes, it was difficult to achieve long-term effective glucose improvement by using app self-management alone, but combining it with interactive management can help achieve rapid and sustained glycaemic control
Jantraporn et al. 149, 2019	RCT	53 patients	Telemonitoring	The study program was effective in decreasing HbA1c levels because the program enhanced patients' confidence in dietary control, which improved consumption behaviour
MacPherson et al. 150, 2019	RCT	66 patients	Mobile prompts	This study provides preliminary evidence regarding the potential influence of prompts on mHealth self-monitoring and self-reported exercise and the duration for which prompts may be effective as exercise behaviour change tools

Yu et al. 151, 2019	RCT	185 patients	Mobile app	Implementation of the MPA, Diabetes-Carer, is effective in improving the proportion of HbA1c <7% in patients with type 2 diabetes
Guo et al. 152, 2019	RCT	124 patients	Mobile health	Mobile health intervention management of gestational diabetes mellitus improves patients' compliance and blood glucose control, and reduces weight gain, thereby reducing the rates of complications in both pregnant women and foetuses during delivery during pregnancy
Kjos et al. 153, 2019	Single cohort study	51 patients	Mobile app	The mobile app may not affect adherence and adherence-related beliefs in a 6-month period
Benson et al. 154, 2019	RCT	118 patients	Telemonitoring	ENHANCED (diEtitiaNs Helping pAtieNts CarE for Diabetes) findings suggest that registered dietitian nutritionists following medication treatment protocols can effectively improve care for adults with type 2 diabetes and can serve an instrumental role as part of the health care team in providing evidence-based, patient-centred care
Xu et al. 155, 2019	RCT	65 patients	Phone Call and Text Message-Based Telemedicine Platform	EpxDiabetes helps to reduce HbA1c in patients with uncontrolled T2DM and fosters patient-provider communication; it has definite merit as an adjunct therapy in diabetes management
Gunawardena et al. 156, 2019	RCT	67 patients	Mobile app	The SGM, a mobile application specifically designed to support self-management of diabetes, appeared to show long-term improvement of A1c levels in patients with diabetes residing in Sri Lanka
Alotaibi et al. 157, 2019	RCT	20 patients	Mobile health	The pilot study of the SAED system showed that a mobile health technology can significantly improve the HbA1C levels among Saudi diabetic and improve their disease management plans

Al-Ofi et al. 158, 2019	RCT	57 patients	Telemonitoring	Telemonitoring can facilitate close monitoring of women with GDM and motivate patients to adopt a healthy lifestyle
Kim et al. 159, 2019	Single cohort study	165 patients	Web application	This hybrid diabetes self-management model is a viable tool for traditionally underserved groups with diabetes or prediabetes
Hochsmann et al. 160, 2019	RCT	36 patients	Smartphone game	A novel, self-developed smartphone game, delivering multidimensional home-based exercise and physical activity promotion, significantly increases daily physical activity (steps/day) and aerobic capacity in inactive type 2 diabetes patients after 24 weeks
Von Storch et al. 161, 2019	RCT	115 patients	Telemedicine-assisted self-management program	Patients with T2DM can benefit from telemedicine-assisted self-management programs, which may offer new options for treatment and prevention of disease progression
Lee et al. 162, 2019	Cluster RCT	240 patients	Telemonitoring	This study indicates that there is limited benefit of replacing telemedicine with the current practice of self-monitoring of blood glucose
Bramwell et al. 163, 2019	Observational study	92 patients	mHealth intervention	Importantly, this reduced frequency of contacts with patients, time per interaction and average time for titration ($p<0.01$)
Kim et al. 164, 2019	RCT	191 patients	Smartphone based intervention	The implementation of the mDiabetes for patients with inadequately controlled type 2 diabetes resulted in a significant reduction in HbA1c levels, with tolerable safety profiles

Garabedian et al. 165, 2019	Single cohort study	556 patients	Mobile glucose meter	Although uptake of the mHealth program was low, most members who started testing had initial glucose values that indicated a need for better glucose management and the majority of patients engaged with the program for over a year
Bender et al. 166, 2019	RCT	45 patients	mHealth	PilAm Go4Health was feasible and demonstrated potential efficacy in reducing diabetes risks in overweight Filipino Americans with T2D
Abbaspoor et al. 167, 2018	RCT	100 patients	Text messaging	The education through a short text message system seem couldn't control the blood sugar, but it could promote physical activity and food additives of pre-diabetic pregnant women
Or et al. 168, 2016	RCT	63 patients	Patient-Centred, Computer-Based Self-Monitoring System	No significant differences were observed between the groups in the fasting blood glucose level, the HbA1c level, or chronic disease knowledge

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List of meta-analysis on Digital Health for TD2M management in primary prevention

Author	Design	Studies included	Intervention	Conclusion
Huang et al. 22, 2015	Meta-analysis	18 studies	Telecare intervention	Patients monitored by telecare showed significant improvement in glycaemic control in type 2 diabetes when compared with those monitored by routine follow-up
Huang et al. 1, 2015	Meta-analysis	18 studies	Telecare intervention	Patients monitored by telecare showed significant improvement in glycaemic control in type 2 diabetes when compared with those monitored by routine follow-up
Lieber et al. 2, 2015	Meta-analysis	5 studies	Telemonitoring to improve HbA1c levels	The varying results may be due to specific factors in the trials that contributed to their large heterogeneity, and further trials are needed to support the role of telemonitoring in improving diabetes management in this population
Rasekaba et al. 3, 2015	Meta-analysis	3 studies	Telemedicine gestational diabetes	Telemedicine has the potential to streamline GDM service utilization without compromising maternal and foetal outcomes
Hou et al. 4, 2016	Meta-analysis	14 studies	Mobile apps	Apps may be an effective component to help control HbA1c and could be considered as an adjuvant intervention to the standard self-management for patients with type 2 diabetes
Hadjiconstantinou et al. 5, 2016	Meta-analysis	16 RCTs	Web-based intervention	While the meta-analyses demonstrated nonsignificant results for depression and distress scores, this review has shown that there is a potential for Web-based interventions to improve well-being outcomes in type 2 diabetes
Su et al. 6,2016	Meta-analysis	92 studies	Nutritional counselling as part of telemedicine	The inclusion of nutritional counselling as part of a telemedicine program does not make a significant difference to diabetes outcomes.

Cui et al. 7, 2016	Meta-analysis	6 studies	Smartphone apps	Smartphone apps offered moderate benefits for T2DM self-management
Ming et al. 8, 2016	Meta-analysis	7 studies	Telemedicine Technologies for Diabetes in Pregnancy	There is currently insufficient evidence that telemedicine technology is superior to standard care for women with diabetes in pregnancy; however, there was no evidence of harm
Arambepola et al. 9, 2016	Meta-analysis	15 studies	Automated Brief Messages	Automated brief messages strategies can improve health outcomes in people with type 2 diabetes
Faruque et al. 10, 2017	Meta-analysis	111 studies	Telemedicine	Compared with usual care, the addition of telemedicine, especially systems that allowed medication adjustments with or without text messaging or a Web portal, improved HbA1C but no other clinically relevant outcomes among patients with diabetes
Alharbi et al. 11, 2016	Meta-analysis	32 studies	Information Technology-Based Interventions	Information technology strategies combined with the other elements of chronic care models are associated with improved glycaemic control in people with diabetes
Bonoto et al. 12, 2016	Meta-analysis	13 studies	Mobile apps	The use of apps by diabetic patients could help improve the control of HbA1c. In addition, the apps seem to strengthen the perception of self-care by contributing better information and health education to patients
Christensen et al. 13, 2017	Meta-analysis	4 studies	Games	PA is important for diabetes management. The present review indicates that game-based interventions are not superior to ordinary PA in controlling HbA1c.
Yoshida et al. 14, 2018	Meta-analysis	34 studies	Health information technology	HITs can be an effective tool for glycaemic control among patients with type 2 diabetes

Heitkemper et al. 15, 2017	Meta-analysis	10 studies	Technology self-management interventions	These results are similar to in-person DSME in medically underserved patients, showing that well-designed HIT DSME has the potential to increase access and improve outcomes for this vulnerable group
Shen et al. 16, 2018	Meta-analysis	35 trials	Internet-based interventions	In conclusion, utilization of internet-based intervention is beneficial for patients with type 2 diabetes mellitus, and taking full advantage of this type of intervention may substantially reduce the incidence of complications and improve quality of life
Wu et al. 17, 2018	Meta-analysis	17 trials	Smartphone technologies	STs improved glycaemic control among T2DM patients, especially for patients at earlier disease stages (duration of diagnosis <8.5 years)
Wu et al. 18, 2018	Meta-analysis	19 RCTs	Telehealth	Telehealth holds promise for improving the clinical effectiveness of diabetes management.
Hou et al. 19, 2018	Meta-analysis	21 studies	Mobile applications	A reduction of 0.57% in HbA1c was found in type 2 diabetes patients. However, HCP functionality is important to achieve clinical effectiveness
Baskerville et al. 20, 2017	Meta-analysis	12 studies	Accelerometer or pedometer	People with Type 2 diabetes, provided with an accelerometer or pedometer, substantially increased their free-living physical activity
Lee et al. 21, 2018	Meta-analysis	4 systematic reviews	Telehealth remote patient monitoring	Current evidence suggests that telehealth is effective in controlling HbA1c levels in people living with type 2 diabetes
So et al. 22, 2018	Meta-analysis	7 studies	Telehealth interventions	This review showed positive effects of telehealth interventions for diabetes control self-management at the primary healthcare stage

Hu et al. 23, 2019	Meta-analysis	14 studies	Telemedicine	Compared to usual care, the use of telemedicine was found to improve HbA1c and reduce the risk of moderate hypoglycaemia in diabetic patients, but without significant difference in BMI
Haider et al. 24, 2019	Meta-analysis	11 RCTs	Lifestyle-focused text messaging	Lifestyle-focused text messaging is a low-cost initiative aimed at motivating patients with T2DM to adhere to a healthy lifestyle
Hadjiconstantinou et al. 25, 2018	Meta-analysis	16 meta-analysis	Web based interventions	While the meta-analyses demonstrated nonsignificant results for depression and distress scores, this review has shown that there is a potential for Web-based interventions to improve well-being outcomes in type 2 diabetes
Huang et al. 26, 2019	Meta-analysis	13 RCTs	Text messaging	This meta-analysis demonstrated that text message intervention indeed leads to a decline in HbA1c and improvement of blood glucose control
Huang et al. 27, 2019	Meta-analysis	25 studies	Telemedicine	Both patients with chronic disease and overweight/obese people could benefit from telemedicine interventions
Lee et al. 28, 2017	Network meta-analysis	107 studies	Telemedicine	The review indicates that most telemedicine strategies can be useful, either as an adjunct or to replace usual care, leading to clinically meaningful reduction in HbA1c

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List of trials on Digital Health for smoking cessation intervention in primary prevention

Author	Design	Sample Size	Intervention	Conclusion
Bottorff et al. 1, 2015	Single cohort study	117 men	Interactive video drama (IVD) series	Findings suggest that IVD interventions may be an important addition to men's smoking cessation programs
Chan et al. 2, 2015	Block RCT	1003 patients	Text messages	The abstinence rate in the TEL, SMS and CONTROL group was 22.2, 20.6 and 20.3%, respectively (P for TEL versus CONTROL = 0.32; P for SMS versus CONTROL = 0.40)
Harris et al. 3, 2015	Single cohort study	17 patients	Web-based contingency management program (CM) and a phone-delivered cessation counselling program (Smoking Cessation for Healthy Births [SCHB]	Based on this initial evaluation, the web-based CM and SCHB programs appeared to be feasible for use with rural pregnant smokers with acceptable program adherence for both approaches
Naughton et al. 4, 2015	Single cohort study	1750 patients	Tailored short message service (SMS)	A low-intensity, cheap cessation intervention promoted at very low cost, resulted in a small but potentially impactful uptake rate by pregnant smokers
Thrul et al. 5, 2015	Single cohort study	92 patients	Internet-based cell phone-optimized assessment technique (ICAT)	Similar to the few prior ICAT studies, compliance was low compared to traditional EMA studies

Richter et al. 6, 2015	RCT	556 patients	Integrated Telemedicine-ITM versus telephone counselling	TM increased utilization of cessation pharmacotherapy and produced higher participant satisfaction, but Phone counselling was significantly less expensive
Selby et al. 7, 2015	Survey	1240 patients	Web-assisted tobacco intervention	This study establishes the feasibility of using the Internet and free medication to enable smokers to engage physicians to treat this addiction
Houston et al. 8, 2015	RCT	176 patients	Online practice ePortal with an "e-referral tool"	The practice ePortal smokers received multiple reminders (increasing registration opportunities), and the practices could track patient progress
Jordan Filion et al. 9, 2015	RCT	181 patients	Text messaging for sleep and physical activity	This study provides preliminary evidence that a text message-based intervention may be a promising approach for improving sleep quantity among young adult smokers
Abroms et al. 10, 2015	Single cohort study	40 patients	Text messaging	Findings suggest that iStopSmoke was feasible and could be, with some additional revisions, acceptable to smokers in Israel
Ramo et al. 11, 2015	RCT	79 patients	Facebook Smoking Cessation Intervention	A Facebook quit smoking intervention is attractive and feasible to deliver, and early efficacy data are encouraging. However, the 1.5-fold greater use of electronic cigarettes over nicotine replacement products for quitting is concerning
Villanti et al. 12, 2015	Single cohort study	726 patients	Facebook Smoking Cessation Study	A more intensive phone baseline assessment protocol yielded a lower rate of enrolment, equivalent follow-up rates, and higher enrolment costs compared to a Web-based assessment protocol
Graham et al. 13, 2015	RCT	1236 patients	Internet and Telephone Treatment	Increased treatment utilization and associated changes in several psychosocial measures yielded higher abstinence rates

Davis et al. 14, 2015	Prospective observational study	26 patients	Mindfulness Web-based video	Results suggest that Mindfulness Training for Smokers can be provided via web-based video instruction with phone support and yield reasonable participant engagement on intervention practices and that intervention efficacy and mechanism of effect deserve further study
Cottrell et al. 15, 2015	Single cohort study	3381 patients	Simple telehealth	Satisfaction with AIM appeared optimal when patients were carefully selected for the protocol; professional users were familiar with the system; the programme addressed a problem with the previous service delivery that was identified by users and users took an active approach to achieve clinical goals
Thrul et al. 16, 2015	Observational study	79 patients	Smoking Cessation Intervention on Facebook	Participants not ready to quit in the next 30 days (in Precontemplation or Contemplation) engaged most when prompted to think about the pros and cons of behaviour change, while those in the Preparation stage engaged most when posts increased awareness about smoking and smoking cessation
Wittekind et al. 17, 2015	RCT	257 patients	Online intervention	Analyses revealed that the standard AAT, in particular, led to a significant reduction in cigarette consumption, cigarette dependence, and compulsive drive
Graham et al. 18, 2015	Single cohort study	492 patients	Online smoking cessation community	Community users were more likely to quit smoking at 3 months than nonusers. The estimated benefit from use of online community resources was even larger among subjects with high propensity to use them
Cheung, 19, 2015	RCT	136 patients	WhatsApp and Facebook Online Social Groups	The intervention via the WhatsApp social group was effective in reducing relapse probably because of enhanced discussion and social support
Nash et al. 20, 2015	Single cohort study	141,429 patients	Web-based vs integrated phone/Web cessation program	Web-Only were younger, healthier smokers of higher socioeconomic status who interacted more intensely with services in a single session, but were less likely to re-engage or access NRT benefits

Jones et al. 21, 2015	RCT	94 patients	Web-based intervention	This was the first study of web-based ACT for smoking cessation among smokers with depressive symptoms, with promising evidence of receptivity, efficacy, impact on a theory-based change process, and possible secondary effects on depression
Elfeddali et al. 22, 2016	RCT	434 patients	Web-based Attentional Bias Modification	Web-based ABM training is ineffective in fostering cognitive bias reduction and continued smoking abstinence
Brown et al. 23, 2016	RCT	3019 patients	Online Documentary Film to Motivate Quit Attempts	This trial found that an online documentary film (4Weeks2Freedom) designed to boost motivation and self-efficacy and to promote ex-smoker identity was ineffective in prompting quit attempts among an unselected panel of smokers from the UK
Fingrut et al. 24 ,2016	Single cohort study	368 patients	Phone, text, or email	Over 80% of ED smokers who accepted a referral to counselling services chose the phone or email modality. The lesser chosen text modality was more popular with younger patients
Calhoun et al. 25, 2016	RCT	413 patients	Internet-based intervention	Current results suggest that using an electronic medical record to identify smokers and proactively offering smoking cessation services that are consistent with US Public Health Guidelines can significantly reduce smoking in veterans
Carpenter et al. 26, 2016	Single cohort study	20 patients	Web-based contingency management (CM)	Results of this open pilot study suggest that mCM may be a useful adjunctive smoking cessation treatment component for reducing smoking among homeless veterans
Müssener et al. 27, 2016	RCT	1590 patients	Short Message Service Text-Based	With the limitation of assessing only the short-term effect of the intervention, the effects observed in this trial are comparable with those for traditional smoking cessation interventions

Stanczyk et al. 28, 2016	RCT	2099 patients	Video-based computer-tailored intervention	The video-based computer-tailored intervention was effective in obtaining substantial long-term abstinence compared to the text-based version and a brief generic text advice
Christofferson et al. 29, 2016	Single cohort study	1470 patients	Text messaging	SmokefreeVET may be effective at supporting abstinence among a real-world group of highly engaged users. Smoking cessation medication use was also associated with abstinence in SmokefreeVET users
Sarna et al. 30, 2016	Single cohort study	1386 patients	Web-based smoking cessation education	Nurses receiving web-based smoking cessation education significantly increased self-reports of frequency of providing interventions to patients who smoke
Bottorff et al. 31, 2016	Single cohort study	117 patients	Online, Men-Centred Smoking Cessation Intervention	The results of this research support efforts to integrate gender-sensitive approaches in smoking cessation interventions and indicate that this novel Web-based resource has potential in supporting men’s smoking cessation efforts
Zeng et al. 32, 2016	Single cohort study	84 patients	Smartphone app	Full adherence and use of specific ACT theory-based components of the app predicted quitting
Hoeppner et al. 33, 2016	Content analysis	225 apps	Publicly available smartphone smoking cessation app	Publicly available smartphone smoking cessation apps are not particularly "smart": they commonly fall short of providing tailored feedback, despite users' preference for these features
Sadasivam et al. 34, 2016	RCT	120 patients	Collective Intelligence Tailored Messaging System	he proportions of days when smokers agreed/strongly agreed (daily rating ≥4) that the messages influenced them to quit was significantly higher for PERSPeCT (73%, 23/30) than standard CTHC (44%, 14/30, P=.02)

Parks et al. 35, 2016	Survey	1218 patients	Telehealth Intervention	Results showed that IPC was strongly associated with initial quitline utilization and continuous smoking abstinence as measured by 30-day point prevalence rates at 7-month follow-up
Papandonatos et al. 36, 2016	RCT	399 patients	iQUITT Study	More than 1/3 of the participants who used the community both passively and actively achieved abstinence
Cutrona et al. 37, 2016	Single cohort study	759 patients	Online tobacco websites and online communities	Community visiting was not associated with quit rates in our study, but low use may have limited our power to detect differences
Smit et al. 38, 2016	RCT	414 patients	Web-Based Multiple Tailored Smoking Cessation Program	Web-based multiple computer-tailored smoking cessation program combined with a single face-to-face counselling session by a practice nurse may not be more effective than this computer-tailored program alone or than usual smoking cessation care in the general practice setting
Cole-Lewis et al. 39, 2016	Single cohort study	4243 patients	Social Network Behaviour and Engagement	These findings highlight the importance of the moderator for network engagement and provide helpful insights into the patterns and types of interactions participants are engaging in
Mason et al. 40, 2016	RCT	2000 patients	Text messaging	These results provide encouraging evidence of the efficacy of text messaging interventions to reduce smoking among adolescents and our intervention holds promise as a large-scale public health preventive intervention platform
Skov-Ettrup et al. 41, 2016	RCT	1810 patients	Telephone, internet and text messaging	Proactive telephone counselling was more effective than a self-help booklet in achieving prolonged abstinence for 12 months
Graham et al. 42, 2017	RCT	2657 patients	Online social networks	This study is the first to demonstrate that increased tie formation among members of an online social network for smoking cessation is prospectively associated with abstinence

Heminger et al. 43, 2016	Single cohort study	262 patients	Text messaging	Using interactive tools such as pledges and reporting on smoking status were predictive of cessation
Neri et al. 44, 2016	Observational study	4086 patients	Web based intervention	The 7-month 30-day PPA rate was 32% for quitline users and 27% for Web-based users
Businelle et al. 45, 2016	RCT	92 patients	Mobile phone	Real-time estimation of smoking lapse risk is feasible and may pave the way for development of mobile phone–based smoking cessation treatments that automatically tailor treatment content in real time based on presence of specific lapse triggers
Kathleen et al. 46, 2016	RCT	1488 patients	Web based intervention	Lack of difference between treatment arms suggests a strong effect for UC, WI was not effective, or both
Alessi et al. 47, 2017	RCT	90 patients	mHealth reinforcement	This study suggests that mHealth abstinence reinforcement is efficacious and may present temporal and spatial opportunities to research, engage, and support smokers trying to quit that do not exist with conventional (not technology-based) reinforcement interventions
Abroms et al. 48, 2017	RCT	497 patients	Text messaging	Results provide limited support of the efficacy of the Quit4baby text messaging program in the short term and late in pregnancy, but not in the postpartum period
Graham et al. 49, 2017	RCT	5290 patients	Web based intervention	This study demonstrated that an integrated approach to medication provision and social network integration, when delivered through an online program, can enhance adherence across all three recommended components of an evidence-based smoking cessation program

Bialous et al. 50, 2017	Single cohort study	436 nurses	Online education	Educating nurses on cessation interventions and tobacco control is pivotal to decrease tobacco-related disparities, disease, and death
Kim et al. 51, 2017	Single cohort study	16 patients	Facebook intervention	Our findings imply that receiving one like or posting on the Facebook-based intervention platform predicted smoking approximately one less cigarette in the past 7 days
Khalil et al. 52, 2017	RCT	101 patients	Web based intervention	Participants in the experimental condition were more likely to show a decrease in their intention to smoke than those in the control condition (beta=-0.18, P=.008)
Mavrot et al. 53, 2017	RCT	1120 participants	Tailored program delivered via the Internet and by e-mail	An individually tailored program delivered via the Internet and by e-mail in addition to a smoking cessation website did not significantly increase smoking cessation rates, but its increased motivation to quit and self-efficacy
Haug et al. 54, 2017	Cluster RCT	1471 patients	Technology-based, integrated smoking cessation and alcohol intervention	Overall, the integrated smoking cessation and alcohol intervention exhibited no advantages over a smoking cessation only intervention, but it might be more effective for the subgroup of adolescent smokers with higher alcohol consumption
Cobos-Campos et al. 55, 2017	RCT	320 patients	Text messaging	Health advice is effective for promoting changes in lifestyle, but these changes do not persist over time, so we have to use strengthening mechanisms, as e-health, and specifically, mobile phone-based interventions
Naughton et al. 56, 2017	RCT	407 patients	Text messaging	There was some evidence, although not conclusive, that a text-messaging programme may increase cessation rates in pregnant smokers when provided alongside routine NHS cessation care

Dallery et al. 57, 2017	RCT	94 patients	Internet based intervention	A contingency management/financial incentive program delivered via the internet improved short-term abstinence rates compared with an internet program without the incentives
Cheung et al. 58, 2017	RCT	467 patients	Facebook and WhatsApp groups	Online social groups provided a useful platform for the delivery of cessation support and encouragement of reporting abstinence, which support relapse prevention
Pechmann et al. 59, 2017	RCT	160 patients	Twitter delivered intervention	Tweet2Quit was engaging and doubled sustained abstinence. Its low cost and scalability make it viable as a global cessation treatment
Sadasivam et al. 60, 2017	RCT	759 patients	Online social network	This study demonstrates the successful recruitment of smokers to a TATI using a Facebook-based peer marketing strategy
Bricker et al. 61, 2017	Single cohort study	99 patients	Smartphone app	The revised app had high user receptivity, modest quit rates, and high smoking reduction rates. Program completion may be key to boosting the app's effectiveness
Bommelé et al. 62, 2017	RCT	757 patients	Tailored web-based intervention	The intervention increased hardcore smokers' receptivity to information about smoking cessation and decreased their cigarette consumption by about 1 cigarette per day
Reinwand et al. 63, 2017	RCT	672 patients	Website intervention	The website did not change perceptions of tobacco additives or smoking behaviour
Augustson et al. 64, 2017	RCT	8000 patients	Text messaging	Our findings suggest that a text message-based smoking cessation intervention can be successfully delivered in China and is acceptable to Chinese smokers, but further research is needed to assess the potential impact of this type of intervention

DeLaughter et al. 65, 2016	Single cohort study	30 patients	Gamification	Overall, playing the game resulted in small, but nonsignificant decreases in cravings, with changes greater for those had already quit for more than 48 hours
Krishnan et al. 66, 2018	RCT	102 patients	Mobile phone-based messaging support	There were no significant differences in smoking cessation, smoking reduction, and motivation to quit between study arms
Garrison et al. 67, 2018	RCT	325 patients	Smartphone app	Although mindfulness training via smartphone app did not lead to reduced smoking rates compared with control, our findings provide preliminary evidence that mindfulness training via smartphone app may help lessen the association between craving and smoking
Dar et al. 68, 2018	RCT	40 patients	Smartphone app for detection smoke episodes	The SmokeBeat algorithm correctly detected over 80% of the smoking episodes and produced very few false alarms
Liao et al. 69, 2018	RCT	1369 patients	Text messaging	Our findings demonstrate that a mobile-phone-based text messaging intervention (Happy Quit), with either high- or low-frequency messaging, led to smoking cessation in the present study, albeit in a low proportion of smokers, and can therefore be considered for use in large-scale intervention efforts in China
Ponciano-Rodriguez et al. 70, 2018	Single cohort study	132 patients	eHealth tool	The e-Health tool produced a high rate of smoking cessation
Barcelona de Mendoza et al. 71, 2018	Single cohort study	138 patients	Phone calls, emails and text messaging	There was a statistically significant increase in the number of participants who had quit smoking from program enrolment to discharge (5.1%–18.5%, p = 0.02)

Pearson et al. 72, 2018	RCT	3297 patients	Online smoking cessation community	Exposure to positive sentiment about NRT was associated with increased NRT use when smokers obtained it on their own
Cole et al. 73, 2018	Observational study	4022 patients	Web based intervention	To better balance cost with clinical effectiveness, funders of state-based tobacco cessation services may want to consider (1) allowing tobacco users to choose between phone- and web-based programs while (2) limiting longer NRT benefits only to multiple-call program participants
Graham et al. 74, 2018	RCT	5290 patients	Web based + social network intervention	Treatment assignment analyses showed no effects on abstinence for either adherence strategy
Bricker et al. 75, 2018	RCT	2637 patients	Web based intervention	WebQuit.org and Smokefree.gov had similar 30-day point prevalence abstinence rates at 12 months that were descriptively higher than those of prior published website-delivered interventions and telephone counsellor-delivered interventions
Yingst et al. 76, 2018	RCT	150 patients	Text messaging	Although there were no differences in quit rates between the intervention and control group, intervention group participants rated the text messaging system more favourably, were more likely to recommend the program to others, and were more likely to complete positive smoking cessation activities
Crane et al. 77, 2018	Explanatory RCT	28112 patients	Smartphone app	Despite very low follow-up rates using in-app follow up, both intention-to-treat/missing equals smoking and follow-up only analyses showed the full version of the Smoke Free app to result in higher self-reported 3-month continuous smoking abstinence rates than the reduced version
Forinash et al. 78, 2018	RCT	49 patients	Text messaging	Text messaging had minimal impact on improving smoking cessation rates in the obstetric population

De Ruijter et al. 79, 2018	RCT	121 nurses	eLearning	Results from our RCT showed that among PNs with more than average counselling experience, the e-learning program resulted in significantly better smoking cessation guideline adherence
Cupertino et al. 80, 2018	Single cohort study	164 patients	e-Health tools	Integration of e-Health tools in primary healthcare settings has the potential to improve knowledge about cessation treatments among smokers and integrate smoking cessation into routine of care
Sarna et al. 81, 2018	Single cohort study	283 nurses	Webcast education	An online educational programme, plus printed toolkit about tobacco dependence treatment increased nurses' delivery of smoking cessation interventions over time
Nomura et al. 82, 2019	RCT	115 patients	Telemedicine using internet-based video counselling	The application of telemedicine using internet-based video counselling as a smoking cessation program had a similar CAR from weeks 9 to 12 as that of the standard face-to-face clinical visit program
Gram et al. 83, 2019	RCT	7135 patients	Text messaging or Email	This nationwide, double-blinded, large, fully automated RCT found that 1 in 9 enrolled smokers reported 7-day PPA in both arms, 6 months post cessation. Our study found that identical smoking cessation interventions delivered by mobile text messaging and email may be equally successful at a population level
Daly et al. 84, 2019	Group RCT design	626 patients	Cell phone interventions	Cell phone interventions for low socioeconomic groups are a cost-effective use of healthcare resources. Intensive Care was the most cost-effective strategy both for men and women
Masaki et al. 85, 2019	Single cohort study	55 patients	Smartphone app	The addition of CASC to usual smoking cessation therapies resulted in high CARs, high patient retention rates, and improvement of cessation-related symptoms

Westmaas et al. 86, 2018	RCT	1070	Email	Stand-alone tailored, multiple emails providing support, motivation and information during a quit attempt are an easily deployable, inexpensive mode of providing effective cessation assistance to large numbers of smokers planning to quit
Iacoviello et al. 87, 2017	Single cohort study	416 patients	Smartphone app	In this initial single-arm trial, Clickotine users appeared to demonstrate encouraging indicators of engagement in terms of the number of app opens, number of program interactions, and continued engagement over time
Lim et al. 88, 2019	RCT	60 patients	Text messaging	SDT-based workplace smoking cessation program using individual counselling and tailored text messaging is effective in encouraging autonomous regulation and competence for workers
Vidrine et al. 89, 2019	RCT	624 patients	Mobile phone-based intervention	Findings indicate that assignment to an intervention consisting of text messaging alone may not increase cessation rates for socioeconomically disadvantaged smokers. However, text messaging plus proactive counselling may be an efficacious option
White et al. 90, 2019	RCT	54 patients	Web based intervention	Participants receiving cognitive behavioural treatment gained less weight when abstinent than those receiving the standard treatment
Boal et al. 91, 2016	Quasi-experimental	8726 patients	Text messaging	Text messaging may not confer additional benefits over and above those received through multi-modal, multi-call quitline programs
Danaher et al. 92, 2019	RCT	1271 patients	Smartphone vs Personal computer	This study provides evidence for optimizing intervention design for smartphones over a usual care internet approach in which interventions are designed primarily for use on nonmobile devices such as desktop computers, laptops. or tablets

Schlam et al. 93, 2019	RCT	30 patients	Gamification	Feasibility results encourage a fully powered trial of this easily disseminable intervention
Durmaz et al. 94, 2019	RCT	132 patients	WhatsApp support	WhatsApp support embedded in cessation service delivery increases the abstinence rate and has favourable effects on follow-up

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List of meta-analysis on Digital Health for smoking cessation intervention in primary prevention

Author	Design	Studies included	Intervention	Conclusion
Spohr et al. 1, 2015	Meta-analysis	13 studies	SMS Text Message Interventions	Smoking quit rates for the text messaging intervention group were 36% higher compared to the control group quit rates
Ybarra et al. 2, 2016	Meta-analysis	5 studies	Text messaging	Text messaging-based smoking cessation programs increase self-reported quitting rates across a diversity of countries and cultures
Griffiths et al. 3, 2018	Meta-analysis	12 studies	Digital health interventions with behavioural change techniques (BCT)	A meta-regression suggested that interventions using larger numbers of BCTs produced the greatest effects
Scott-Sheldon et al. 4, 2018	Meta-analysis	22 interventions	Text messaging	The evidence for the efficacy of text messaging interventions to reduce smoking behaviour is well-established
McCrabb et al. 5, 2019	Meta-analysis	45 studies	Internet-based smoking cessation intervention	Internet-based smoking cessation interventions increased the odds of cessation by 29 per cent in the short term and by 19 per cent in the long term

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List of trials on Digital Health for weight loss intervention in primary prevention

Author	Design	Sample Size	Intervention	Conclusion
Fukuoka et al. 1, 2015	RCT	61 patients	Mobile phone technology	The significant weight loss resulting from this modified combined mobile app and pedometer intervention for overweight adults warrants further investigation in a larger trial
Crane et al. 2, 2015	RCT	107 patients	Face-to-face sessions followed by Internet contacts	The novel REFIT intervention produced clinically significant weight losses. This approach holds promise as an alternative to traditional behavioural therapy for men
Plaete et al. 3, 2015	RCT	522 patients	eHealth intervention 'MyPlan	'MyPlan' was feasible and acceptable, and has the potential to increase PA levels, and fruit and vegetable intake.
Harden et al. 4, 2015	Single cohort study	1030 patients	Internet-Based Worksite Weight Loss Program	Twenty-two percent of the participants lost a clinically meaningful amount of weight (≥5% weight loss).
Watson et al. 5, 2015	RCT	65 patients	Internet-Based Weight Loss Program	Although the intervention group had high attrition levels, this study provides evidence that this Web-based program can be used to initiate clinically relevant weight loss and lower CVD risk up to 3-6 months
Unick et al. 6, 2015	Single cohort study	181 patients	Internet-based weight loss program	This study provides initial evidence that a 4-week WL of <2.0% places an individual at an increased risk of failing to achieve clinically significant WL following an Internet program.

Mundi et al. 7, 2015	Single cohort study	30 patients	Smartphone-Based Education Modules	The app was well-received based on subject satisfaction scores and revealed trends toward positive behaviour change and increased weight loss
Huber et al. 8, 2015	RCT	90 patients	Telecoaching	Telecoaching with a portion control plate can produce positive change in body habitus among obese primary care patients; however, changes depend upon sex
Ahn et al. 9, 2016	RCT	80 patients	Text messaging	The one-way text messaging intervention was a simple and effective way to manage obesity
Luger et al. 10, 2016	Single cohort study	1635 patients	Web based program	A favourable healthful dietary pattern at the beginning and after 3 months was positively associated with anthropometry
Brindal et al. 11, 2016	RCT	146 patients	Partial meal replacement program, point-of-care testing and face-to-face and smartphone app support	Overall, the program supported participants and was successful in achieving significant weight loss and improvements in health outcomes over 24 weeks
Smith et al. 12, 2016	Cost-effective analysis		Regular, brief, web-based individualized counselling	The ODPP may offer an economical approach to combating overweight and obesity
West et al. 13, 2016	RCT	398 patients	Online motivational interviewing chat sessions	Online MI chat sessions were not a viable strategy to enhance Web-based weight control treatment outcomes
Livingstone et al. 14, 2016	RCT	1607 patients	Internet-based, personalized nutrition intervention	Higher MedDiet scores at baseline were associated with healthier lifestyles and lower adiposity

Springvloet et al. 15, 2016	RCT	1349 patients	Web-based computer-tailored nutrition education	Both intervention versions were more effective in improving some of the self-reported dietary behaviours than generic nutrition information, especially in the risk groups, among both higher- and lower-educated participants
Lin et al. 16, 2016	RCT	124 patients	Tailored, interactive text messages	While attrition was high, this study supports a tailored, interactive text-message intervention to enhance weight loss among obese African American adults
Hutchesson et al. 17, 2016	RCT	301 patients	Web-based weight loss program	Enhanced features, including additional individualized feedback and reminders, are effective in enhancing self-monitoring behaviours in a Web-based weight loss program
Elbert et al. 18, 2016	RCT	146 patients	Mobile app intervention	The setting for applying cardio-metabolic prevention programmes is important given its likelihood to influence programme efficacy
Mummah et al. 19, 2016	RCT	17 patients	Mobile Technology	Vegethon demonstrated initial efficacy and user acceptability. A mobile app intervention may be useful for increasing vegetable consumption among overweight adults
Allman-Farinelli et al. 20, 2016	RCT	250 patients	Mobile Health Lifestyle Program	Delivery of an mHealth intervention for prevention of weight gain resulted in modest weight loss at 12 weeks with further loss at 9 months in 18- to 35-year-olds
Partridge et al. 21, 2015	RCT	214 patients	mHealth Lifestyle Program	The TXT2BFiT low-intensity intervention was successful in preventing weight gain with modest weight loss and improvement in lifestyle behaviours among overweight young adults
Oh et al. 22, 2015	RCT	422 patients	Mobile Phone-Based Care	The efficacy of SmartCare services was confirmed as the intervention group that received both SmartCare services and the existing treatment had superior results compared with the control group that only received the existing treatment

Nikolaou et al. 23, 2015	RCT	20,975 patients	eLearning	Both interventions were associated with prevention of the weight gain observed among control subjects. This low-cost intervention could be widely transferable as one tool against the obesity epidemic
Bertz et al. 24, 2015	RCT	167 patients	Frequent Self-Weighing with Electronic Graphic Feedback	CTM intervention was effective in preventing age-related weight gain in young adults over 1 year and thus offers promise to reduce overweight and obesity
Schweitzer et al. 25, 2015	RCT	148 patients	Electronic wellness program	Use of an electronic wellness program is feasible in college students and resulted in a decrease in saturated fat intake and an increase in observed fruit intake compared to a control group
Svetkey et al. 26, 2015	RCT	365 patients	Cell phone intervention	Despite high intervention engagement and study retention, the inclusion of behavioural principles and tools in both interventions, and weight loss in all treatment groups, CP did not lead to weight loss, and PC did not lead to sustained weight loss relative to Control
Ball et al. 27, 2016	RCT	58 patients	Digital Health Methods	In women with ASCVD risk completing a 3 month LEARN program, Digital Health administration resulted in similar decreases in weight loss as traditional methods, but more favourable cardiometabolic results
Ross et al. 28, 2016	RCT	80 patients	Self-monitoring technology plus brief phone-based intervention	These results suggest use of newer self-monitoring technology plus brief phone-based intervention improves adherence and weight loss compared with traditional self-monitoring tools
Ross et al. 29, 2016	Single cohort study	75 patients	12-week Internet-based, multicomponent behavioural weight loss program	An Internet-based behavioural weight management intervention can be successfully implemented in a worksite setting and can lead to clinically significant weight losses

Stumm et al. 30, 2016	RCT	49 patients	Telemonitoring Weight-Reduction Program	The relative weight changes after the first year had been, respectively, −13.4% and −11.4% in the “ABC discontinued” and “ABC continued” groups, and after the second year they decreased by, respectively, 4.4 and 2.8%
Hales et al. 31, 2016	RCT	51 patients	Social POD application	Use of the Social POD app resulted in significantly greater weight loss than use of a commercially available tracking app
Fischer et al. 32, 2016	RCT	163 patients	Text messaging	Text message support can lead to clinically significant weight loss in patients with prediabetes
Martin et al. 33, 2015	RCT	40 patients	Smartphone-based weight loss intervention	SmartLoss efficaciously promote clinically meaningful weight loss compared with an attention-matched control group
Kim et al. 34, 2015	RCT	205 patients	Tailored text message reminders	Tailored text message reminders did not have a significant effect on weight loss in obese men as part of a worksite weight loss program
Carter et al. 35, 2017	RCT	86 patients	Mobile application	The results of this post hoc exploratory analysis indicate that duration and frequency of app use is associated with improved weight loss
Lee et al. 36, 2016	Single cohort study	20 patients	Smartphone application	The application With U, designed and developed to allow friends to challenge each other to lose weight, affected both motivation to lose weight and the amount of weight loss
Chin et al. 37, 2016	Single cohort study	35921 patients	Smartphone application	This study demonstrated the clinical utility of an app for successful weight reduction in the majority of the app users; the effects were more significant for individuals who monitored their weight and diet more frequently

Rutledge et al. 38, 2017	Observational study	223 patients	Telehealth treatment (TeleMOVE)	In this observational study, TeleMOVE was at least as effective for weight loss as the more established multidisciplinary MOVE!
Skoyen et al. 39, 2015	Observational study	171 patients	Telehealth treatment (TeleMOVE)	TeleMOVE is a promising intervention, warranting a further investigation of its efficacy
Tu et al. 40, 2017	Observational study	159 patients	e-health lifestyle intervention	Findings demonstrate that improving adolescents' adherence to e-health lifestyle intervention can effectively alter the weight trajectory of overweight/obese adolescents
Phelan et al. 41, 2017	RCT	371 patients	Internet-based weight loss program	Among low-income postpartum women, an internet-based weight loss program in addition to the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC program) compared with the WIC program alone resulted in a statistically significant greater weight loss over 12 months
Celis-Moralis et al. 42, 2017	RCT	1269 patients	Internet delivered intervention	Among European adults, PN advice via internet-delivered intervention produced larger and more appropriate changes in dietary behaviour than a conventional approach
Toro-Ramos et al. 43, 2017	Single cohort study	100 patients	Smartphone app	This advanced smartphone app was a useful tool to maintain weight loss in overweight or obese people
Thomas et al. 44, 2017	RCT	154 patients	Internet based intervention	Physician referral to an Internet-based behavioural weight-loss intervention produced clinically significant weight loss for over half of the patients studied
Shin et al. 45, 2017	RCT	105 patients	Financial incentives + activity tracker + smartphone app	The addition of financial incentives to Smartcare was effective in increasing physical activity and reducing obesity

Spring et al. 46, 2017	RCT	96 patients	Technology supported intervention	Abbreviated behavioural counselling can produce clinically meaningful weight loss regardless of whether self-monitoring is performed on paper or smartphone, but long-term superiority over standard of care self-guided treatment is challenging to maintain
Naparstek et al. 47, 2017	RCT	136 patients	Internet-delivered obesity treatment	This study is the first to show that Internet-delivered obesity treatment improves depression risk and depressive symptoms in individuals with overweight or obesity
LaCaille et al. 48, 2016	A quasi-experimental non-equivalent control group design	407 participants	Multi-component worksite obesity prevention intervention	This low-intensity intervention was well-received by employees but had little effect on their weight over the course of 12 months
Godino et al. 49, 2016	RCT	404 patients	Social and Mobile Tools	Social and mobile technologies may facilitate limited short-term weight loss among young adults, but as utilized in this intervention, these approaches did not produce sustained reductions in weight
Little et al. 50, 2017	RCT		Web-based behavioural programme	A web-based behavioural programme and brief support results in greater mean weight loss and 10% more participants maintain valuable weight loss
Azar et al. 51, 2017	RCT	64 patients	Virtual small groups	Virtual small groups may be an effective means of allowing face-to-face group interaction, while overcoming some barriers to access
Thomas et al. 52, 2017	RCT	279 patients	Weight Watchers Online program alone (WWO) or with	WWO produced significantly more weight loss at 3 months relative to Control, but not at 12 months

			the ActiveLink® activity tracking device	
Hageman et al. 53, 2017	Single cohort study	301 patients	Web based intervention	Web-based interventions assisted women from rural communities in achieving 6-month weight loss, with weight regain by half at 30 months
Burke et al. 54, 2017	RCT	39 patients	Smartphone app + Facebook	All groups adhered to SM at levels comparable to or better than other weight loss studies and lost acceptable amounts of weight, with minimal intervention contact over 12 weeks
Turner-McGrievy et al. 55, 2017	RCT	81 patients	Wearable Bite counter device vs App	While frequency of diet tracking was similar between the App and Bite groups, there was greater weight loss observed in the App group
Silina et al. 56, 2017	RCT	123 patients	Text messaging	SMS messaging in clinically healthy overweight and obese subjects facilitates a slight decrease in weight, BMI and WC
Jakikic et al. 57, 2016	RCT	471 patients	Wearable device technology	Among young adults with a BMI between 25 and less than 40, the addition of a wearable technology device to a standard behavioural intervention resulted in less weight loss over 24 months
Soltani et al. 58, 2015	Single cohort study	14 patients	Text messaging	MOMTech was feasible within clinical setting and acceptable intervention to support women to limit GWG
Herring et al. 59, 2016	RCT	66 patients	Text messaging + Facebook	The intervention resulted in lower prevalence of excessive gestational weight gain

McClure et al. 60, 2016	RCT	60 patients	Mobile Health	The MyMAP intervention was found to be feasible and acceptable. Since the study was not powered for statistical significance, no conclusions can be drawn about the program's effects on smoking abstinence or medication adherence, but the overall study results suggest further evaluation in a larger randomized trial is warranted
Van der Pligt et al. 61, 2018	Single cohort study	28 patients	Online calorie tracking program, smartphone app	The online intervention reported in the present study shows promise with respect to reducing waist circumference in postpartum women
Fukuoka et al. 62, 2018	Single cohort study	51 patients	Fitbit app	The intervention showed the potential efficacy of this intervention, which should be formally evaluated in a randomized controlled trial
Van Horn et al. 63, 2018	RCT	281 patients	Technology-enhanced intervention	Technology-enhanced Dietary Approaches to Stop Hypertension diet and lifestyle intervention resulted in significantly less total gestational weight gain over 35 weeks with no adverse infant outcomes
Wilcox et al. 64, 2017	RCT	91 patients	mHealth	An intervention that aimed to deliver healthy diet, physical activity and GWG guidance utilising innovative technology can be feasibly implemented and produce positive physical activity and GWG outcomes
Siriwoen et al. 65, 2018	Quasi-experimental design	38 patients	Mobile health technology	This weight management program was effective for the prevention and control of overweight and obesity
Bennett et al. 66, 2018	RCT	351 patients	Digital obesity treatment	A digital obesity treatment, integrated with health system resources, can produce clinically meaningful weight-loss outcomes among socioeconomically disadvantaged primary care patients with elevated cardiovascular disease risk

Sindhu et al. 67, 2016	RCT	380 patients	Text messaging	We found no evidence that an SMS based weight maintenance intervention encouraging adults to weigh themselves weekly prevented weight regain at 3 or 9 months after completing a commercial weight loss programme
Zwickert et al. 68, 2016	RCT	60 patients	Text messaging	A low intensity text-message support programme is just as effective as higher intensity technological support for maintaining weight loss in obese adults
Lee et al. 69, 2018	Single cohort study	19 patients	Text messaging + peer group	Modest but statistically significant reductions were detected in weight and body mass index from baseline to 16 weeks
Wing et al. 70, 2017	RCT	599 patients	Self-regulation	Self-regulation with large or small changes both reduced weight gain in young adults over 3 years relative to control, but the large-changes intervention was more effective
Leahey et al. 71, 2016	RCT	75 patients	Internet delivered cost-benefit approach	These results suggest that an Internet delivered cost-benefit approach to weight loss maintenance may be effective for long-term weight control
Olson et al. 72, 2018	RCT	1689 patients	Weight gain tracker, and separate diet and physical activity goal-setting and self-monitoring tools	The addition of three behaviour change tools to an informational placebo control did not result in a difference in the proportion of women with excessive total GWG compared to the placebo control in this effectiveness trial of an online, self-directed intervention
Kurtzman et al. 73, 2018	RCT	196 patients	Social Incentives and Gamification	Using digital health devices to track behaviour with a partner led to significant weight loss through 36 weeks, but the gamification interventions were not effective at promoting weight loss when compared to control

Gomez-Marcos et al. 74, 2018	RCT	833 patients	Smartphone app	An intervention of nutritional counselling and PA plus the smartphone app with personalised recommendations compared to CG showed beneficial results in terms of reduction of abdominal obesity and the percentage of body fat in women, but not in men
Redman et al. 75, 2018	RCT	54 patients	eHealth intervention	An intensive lifestyle intervention for GWG can be effectively delivered via a mobile phone, which is both cost-effective and scalable
Recio-Rodriguez et al. 76, 2018	RCT	833 patients	Smartphone app	Better results were achieved in terms of modifying usual diet composition from counselling and the diet smartphone application compared to counselling alone
Brindal et al. 77, 2019	RCT	88 patients	Mobile phone app	Although some aspects of the intervention app such as usage and user feedback showed promise, there were few observable effects on behavioural and psychological outcomes
Cheung et al. 78, 2019	RCT	60 patients	Text messaging	Overall, results suggest that a text message and activity monitor intervention is feasible for a larger study or even as a potentially scalable population health intervention
Ventura et al. 79, 2019	RCT	59 patients	Telenutrition	Primary care referred telenutrition interventions have the potential to improve access to dietary counselling for obesity treatment in health disparate populations
Viglione et al. 80, 2019	RCT	45 patients	Technology assisted health coaching intervention	We found that a technology assisted health coaching intervention delivered within primary care using student health coaches was feasible and acceptable to Veteran patients
Gulayin et al. 81, 2019	Cluster RCT	357 patients	Smartphone app	Although the intervention did not reach a reduction in cholesterol levels, it had a significant positive impact on the promotion of adequate use of clinical practice guidelines

Thomas et al. 82, 2019	RCT	276 patients	Smartphone app	Mobile online delivery of behavioural obesity treatment can achieve weight loss outcomes that are at least as good as those obtained via the more intensive gold standard group-based approach
Goldstein et al. 83, 2019	RCT	276 patients	Smartphone app	Results provide evidence of a bidirectional association between self-monitoring and weight change. Better self-monitoring was consistently associated with better weight loss across intervention and tracking modalities
Sniehotta et al. 84, 2019	RCT	288 patients	Low-intensity technology-mediated behavioural intervention	There was no difference in the WLM of participants who received the NULevel intervention compared to participants who received standard lifestyle advice via newsletter
Patel et al. 85, 2019	RCT	84 patients	mHealth treatment	Responding early to an mHealth treatment is associated with higher engagement and greater likelihood of achieving clinically meaningful weight loss
Apinaniz et al. 86, 2019	RCT	110 patients	Mobile app	The use of AKTIDIET® to support health advice for weight loss cannot be recommended
Muralidharan et al. 87, 2019	RCT	741 patients	Mobile app	An mHealth intervention helped to achieve moderate weight loss. Future studies should explore the sustainability of this weight loss
Monroe et al. 88, 2019	RCT	36 patients	Technology-based, social support approach	Although feasible to implement, this technology-based, social support approach failed to enhance outcomes of a face-to-face, group-based behavioural weight-loss treatment

Stein et al. 89, 2017	Single cohort study	70 patients	Fully Automated Conversational Artificial Intelligence	This study showed that use of an AI health coach is associated with weight loss comparable to in-person lifestyle interventions
Kempf et al. 90, 2019	RCT	104 patients	Telemonitoring	TMC and/or telemonitoring support long-term weight reduction in overweight employees. The combination of both interventions points towards an additional effect
Nakata et al. 91, 2019	RCT	119 patients	Web-based intervention	Web-based intervention using an activity monitor failed to promote weight-loss maintenance, increased physical activity was associated with successful weight-loss maintenance
Stephens et al. 92, 2017	RCT	62 patients	Smartphone technology	The results of this weight loss trial support the use of smartphone technology and feedback from a health coach on improving weight in a group of diverse young adults
Teeriniemi et al. 93, 2018	RCT	532 patients	Web-based counselling	The combination of CBT-based group counselling and HBCSS-based weight management is feasible for overweight or obese individuals. Moreover, HBCSS alone could be disseminated to the population at large as an effective means of treating obesity.
Nevanpara et al. 94, 2015	Observational study	74 patients	Videoconferencing	Constructivism-based counselling delivered through videoconferencing was effective at improving eating behaviours

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List of meta-analysis on Digital Health for weight loss intervention in primary prevention

Author	Design	Studies included	Intervention	Conclusion
Liu et al. 1, 2015	Meta-analysis	14 studies	Mobile phone intervention and weight loss	These findings provide evidence that mobile phone intervention may be a useful tool for promoting weight loss among overweight and obese adults
Flores-Mateo et al. 2, 2015	Meta-analysis	12 studies	Mobile phone apps	Evidence from this study shows that mobile phone app-based interventions may be useful tools for weight loss
Siopsis et al. 3, 2015	Meta-analysis	14 studies	Text messaging	The small body of evidence indicates that text messaging interventions can promote weight loss. However, lack of long-term results indicate that further efficacy studies are required
Schippers et al. 4, 2017	Meta-analysis	12 studies	Mobile phone	The current body of evidence shows that interventions delivered via mobile phones produce a modest reduction in body weight when combined with other delivery modes
Cai et al. 5, 2016	Meta-analysis	11 RCTs	Pedometer intervention	Pedometer intervention promotes modest weight loss, but its association with physical activity requires further clarification
Joiner et al. 6, 2017	Meta-analysis	26 trials	eHealth intervention	There is promising evidence of the efficacy of DPP-based eHealth interventions on weight loss

Sherifali et al. 7, 2017	Meta-analysis	10 studies	eHealth	This review found evidence for benefits of eHealth technologies on weight management in postpartum women only
Job et al. 8, 2018	Meta-analysis	7 studies	Text-messaging	Evidence from the small number of studies reviewed suggests that extended contact, text message-delivered interventions are effective
Park et al. 9, 2019	Meta-analysis	20 RCTs	Mobile health	The use of mHealth for obese adults showed a modest short-term effect on body weight and BMI
Sherrington et al. 10, 2016	Meta-analysis	12 studies	Internet-delivered weight loss interventions	This suggests that personalized feedback may be an important behaviour change technique (BCT) to incorporate within internet-delivered weight loss interventions
Seo et al. 11, 2015	Meta-analysis	31 studies	Internet-based interventions	Internet-based interventions have a significant and promising effect on waist circumference change.

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List of trials on Digital Health for physical activity in primary prevention

Author	Design	Sample Size	Intervention	Conclusion
Mackenzie et al. 1, 2015	Single cohort study	17 patients	Free reminder software to install onto computers; social media to increase awareness	This small-scale pilot provides encouragement for the acceptability and feasibility of low-cost, multi-modal interventions to reduce workplace sitting in UK settings
Almeida et al. 2, 2015	RCT	452 patients	Tailored, computer-based, interactive personal action planning session	A brief, computer-based, interactive personal action planning session may be an effective tool to initiate PA within a health care setting, in particular as part of the ETT system
Schneider et al. 3, 2015	RCT	102 patients	Social networking Web site (Meetup™)	Results suggest that a Meetup™ group is feasible for increasing physical activity in dog owners
Compernolle et al. 4, 2015	RCT	267 patients	Web-based, computer-tailored, pedometer-based physical activity	A computer-tailored, pedometer-based PA intervention was effective in increasing both pedometer-based and self-reported PA levels, mainly in the at-risk participants
Van der Weegen et al. 5, 2015	RCT	199 patients	Mobile and Web-Based Monitoring and Feedback	The combination of counselling with the tool proved an effective way to stimulate physical activity. Counseling without the tool was not effective
Friederichs et al. 6, 2015	RCT		Web-based physical activity intervention	Overall, the web-based PA intervention grounded in SDT and MI did not outperform the traditional web-based PA intervention

Martin et al. 7, 2015	RCT	48 patients	Fully automated mobile health (mHealth)	An automated tracking-texting intervention increased physical activity with, but not without, the texting component
Finkelstein et al. 8, 2015	A randomized crossover design	27 patients	Mobile App	We concluded that mobile app monitoring inactivity and providing a real-time notification when inactivity period exceeds healthy limits was able to significantly reduce inactivity periods in overweight sedentary women
Litman et al. 9, 2015	A Moderated Mediation Analysis	726 patients	Mobile exercise apps	Exercise app users are more likely to exercise during their leisure time, compared to those who do not use exercise apps
Puig-Ribera et al. 10, 2015	RCT	264 patients	Workplace web-based intervention	W@WS is a feasible and effective evidence-based intervention that can be successfully deployed with sedentary employees to elicit sustained changes on "sitting less and moving more"
Cadmus-Bertram et al. 11, 2015	RCT	51 patients	Fitbit-Based Physical Activity	The Fitbit was well accepted in this sample of women and associated with increased physical activity at 16 weeks
Judice et al. 12, 2015	Cross-over RCT	10 patients	Computer prompts	Sitting time in overweight/obese adults can be reduced following a brief multi-component intervention based on prompts, telephone support, goal setting and behavioural self-monitoring
Mistry et al. 13, 2015	RCT	337 patients	Text messaging	There were no differences in action planning or physical activity based on the content or tailoring of text messages

Burn et al. 14, 2015	Markov model		Text messaging	At a cost-effectiveness threshold of 64 000 AUD, MobileMums would likely be a cost-effective use of healthcare resources in Queensland, Australia
Rote et al. 15, 2015	RCT	63 patients	Facebook social support group	These results demonstrate the potential effectiveness of using Facebook to offer a social support group to increase physical activity in young women
Benitez et al. 16, 2015	Single cohort study	24 patients	Web-based technology	Participants reported significant increases in self-efficacy as well as cognitive and behavioural processes of change
Wang et al. 17, 2015	RCT	67 patients	Wearable Sensor/Device (Fitbit One) and SMS Text-Messaging	These data suggest that the Fitbit One achieved a small increase in MVPA at follow-up and that the SMS-based PA prompts were insufficient in increasing PA beyond 1 week
Broekhuizen et al. 18, 2016	RCT	235 patients	Internet-Based Physical Activity Intervention	Our study shows that an Internet-based physical activity program was effective in improving quality of life in 60-70-year-olds after 3 months, particularly in participants that reached their individually targeted increase in daily physical activity
Al-Eisa et al. 19, 2016	Quasi-experimental study	58 patients	Motivation by “Instagram”	The use of Instagram with the home exercise program as a motivational modality could be attractive and effective to reinforce adherence and maintain an appropriate PA level
Harries et al. 20, 2016	A parallel group randomised controlled trial	165 patients	Smartphone app	Always-on smartphone apps that provide step-counts can increase physical activity in young to early-middle-aged men, but the provision of social feedback has no apparent incremental impact

Poirier et al. 21, 2016	RCT	265 patients	Activity Tracker- and Internet-Based Adaptive Walking Program	The program is effective in increasing daily steps. Participants benefited from the program regardless of their initial activity level
Van Dyck et al. 22, 2016	RCT	240 patients	Self-regulation eHealth intervention 'MyPlan1.0	Results show that our eHealth intervention is effective in recently retired adults
Gillman et al. 23, 2016	RCT	28 patients	Game-based and performance-tracking running app	Game-based and performance-tracking running apps may not have differential effects on goal motivation during exercise
King et al. 24, 2016	RCT	95 patients	Three Motivationally Targeted Mobile Device Applications	The results provide initial support for the use of a smartphone-delivered social frame in the early induction of both physical activity and sedentary behaviour changes
Rovniak et al. 25, 2016	RCT	308 patients	Online and In-Person Social Networks	Although the structure of procedures for targeting social networks varied across intervention groups, the functional effect of these procedures on physical activity was similar
Richards et al. 26, 2016	RCT	49 patients	E-mail messages	Results indicate that a simple SCT-based e-mail intervention is effective in increasing and maintaining an increase in dog walking among dog owners at 12-month follow-up
Rospo et al. 27, 2016	Single cohort study	68 patients	Mobile App	A 10,000 steps/day target-based app improved CRF similar to an ACSM guideline-based program whether it was implemented on a mobile app or in supervised gym sessions
Walsh et al. 28, 2016	RCT	58 patients	mHealth intervention	The results of this study demonstrate that a mobile phone app can significantly increase physical activity in a young adult sample by setting specific goals, using self-monitoring, and feedback

Direito et al. 29, 2016	RCT	51 patients	Mobile phone interventions	Although apps have the ability to increase reach at a low cost, our pragmatic approach using readily available commercial apps as a stand-alone instrument did not have a significant effect on fitness
Rabbi et al. 30, 2016	RCT	17 patients	Mobile phone application	MyBehavior is a simple-to-use mobile phone app with preliminary evidence of efficacy
Choi et al. 31, 2016	RCT	30 patients	mHealth	Pregnant women who were motivated to increase physical activity might find using mobile technologies in assessing and promoting PA acceptable
Cowdery et al. 32, 2015	RCT	40 patients	Exergaming	Exergame Apps and Physical Activity: The Results of the ZOMBIE Trial
Zhang et al. 33, 2015	RCT	217 patients	Online social media intervention	Social influence from anonymous online peers was more successful than promotional messages for improving physical activity.
Joseph et al. 34, 2015	RCT	29 patients	Print versus a culturally relevant Facebook and text message	A culturally relevant Facebook and text message delivered physical activity program was associated with several positive outcomes, including decreased sedentary behaviour, increased light- and moderate-lifestyle intensity physical activity, enhanced psychosocial outcomes, and high participant satisfaction
Mailey et al. 35, 2016	RCT	69 patients	Web-based intervention	These findings suggest web-based interventions can improve physical activity and self-worth among working mothers
Howe et al. 36, 2016	Single cohort study	560 patients	Pokémon GO	Pokémon GO was associated with an increase in the daily number of steps after installation of the game

Rebar et al. 37, 2016	RCT	514 patients	Web-based interventions with computer-tailoring	Web-based interventions with computer-tailoring and interactive features show promise as a method for increasing physical activity and reducing depressive symptoms
Herget et al. 38, 2016	RCT	28 patients	Media Supported Intervention	Overall program content was rated as "good" by participants, although high drop-out rates were observed
Kendzor et al. 39, 2016	Quasi-experimental evaluation	215 patients	Mobile Phone Intervention	A simple mobile phone intervention was associated with engaging in less sedentary time and more physical activity
Gomez-Quinonez et al. 40, 2016	RCT	373 patients	Web-Based Computer-Tailored Physical Activity Intervention	The overall effect was mainly caused by the more effective eHealth intervention. The mHealth app was rated inferior to the eHealth version with regard to usability and appreciation
Marcus et al. 41, 2016	RCT	205 patients	Internet-delivered individually tailored intervention	Findings from the current study suggest that this Internet-delivered individually tailored intervention successfully increased MVPA in Latinas compared to a Wellness Contact Control Internet Group
Joseph et al. 42, 2016	Single cohort study	25 patients	Culturally Adapted Internet-Enhanced Physical Activity	Findings of this exploratory study show some preliminary support for Internet-enhanced approaches to promote PA among overweight/obese AA women
Irwin et al. 43, 2016	RCT	135 patients	A brief, online group dynamics-based intervention	A brief, online group dynamics-based intervention may be an effective method of improving group cohesion in virtual PA groups

Muller et al. 44, 2016	RCT	42 patients	Text messaging	This study provides evidence that SMS text messaging is effective in promoting exercise in older adults from an upper-middle-income country
Gell et al. 45, 2015	RCT	87 patients	Text messaging	Intervention participants had higher step counts after 12 and 24 weeks compared to a control group; however, the difference was significant only at the midpoint of the intervention and was attributable to a decrease in steps for the control group
De Cocker et al. 46, 2016	RCT	213 patients	Web-Based Computer-Tailored Intervention	Our results point out the significance of computer tailoring for sedentary behaviour and its potential use in public health promotion, as the effects of the tailored condition were superior to the generic and control conditions
Smith et al. 47, 2016	RCT	45 patients	Web-Based Behavioural Intervention	Sedentary pregnant women should increase PA but may need additional dietary counselling to prevent excessive GWG
Alley et al. 48, 2016	RCT	83 patients	Web-Based Video-Coaching to Assist an Automated Computer-Tailored Physical Activity	Only small improvements were observed when video-coaching was added to computer-tailored advice in a Web-based physical activity intervention
Widmer et al. 49, 2016	Observational study	30974 patients	Online and smartphone-based portal	The current study demonstrates the success of DHI in a large, community cohort to modestly reduce CVD risk factors in individuals with high participation rate
Tucker et al. 50, 2016	RCT	40 patients	Text messaging	Sedentary and PA levels, fat mass, and weight improved for both groups, significantly only for the early text group

Nishiwaki et al. 51, 2017	RCT	17 patients	Twitter intervention	Lifestyle intervention can increase daily PA and reduce body fat more effectively when using an activity monitor and Twitter than an activity monitor alone
Larsen et al. 52, 2017	RCT	205 patients	Web-based physical activity intervention	While the Web-based physical activity intervention was more expensive than the wellness control, both were quite low cost compared to face-to-face or mail-delivered interventions
Blake et al. 53, 2017	RCT	296 patients	Text messaging	Minimal physical activity promotion delivered by SMS or e-mail can increase frequency and duration of active travel and duration of moderate intensity physical activity at work and for leisure, which is maintained up to 1 month after messaging ends
Adams et al. 54, 2017	RCT	96 patients	Adaptive goal setting and financial incentives with Fitbit Zip	Adaptive goals outperformed static goals (i.e., 10,000 steps) over a 4-month period. Small immediate rewards outperformed larger, delayed rewards
Xian et al. 55, 2017	Pre-post observational study	167 patients	Pokémon GO	Pokémon GO participation was associated with a significant increase in PA among young adults
Huberty et al. 56, 2017	RCT	80 patients	Text messaging	SMS may not be a "potent" enough strategy to improve PA
Vandelanotte et al. 57, 2017	Randomized Ecological Trial	1328 patients	Website	The website that provided more interactive and social features was more effective in improving physical activity in real-world conditions
Patel et al. 58, 2017	RCT	281 patients	Financial incentives + daily feedback	Financial incentives framed as a loss were most effective for achieving physical activity goals.

Yu et al. 59, 2017	Observational study	11,436 unique persons	Web based physical activity program	The program did not have a statistically significant impact on cholesterol or blood pressure
McConnell et al. 60, 2017	Observational study	40017 participants	Smartphone app	A smartphone-based study of cardiovascular health is feasible, and improvements in participant diversity and engagement will maximize yield from consented participant
Baillot et al. 61, 2017	Single cohort compared with historic data	6 patients	In-home telehealth	The TelePreSET group significantly increased their physical fitness compared to the usual care group
Hong et al. 62, 2017	RCT	23 patients	Video conferencing-based supervised resistance exercise	Video conferencing-based supervised resistance exercise had positive effects on sarcopenia-related factors such as total-body skeletal muscle mass, appendicular lean soft tissue, lower limb muscle mass, and the chair sit-and-reach scores among community-dwelling elderly adults
Muntaner-Mas et al. 63, 2017		32 patients	Whatsapp intervention	Comparison between training and mobile group showed that WhatsApp-based physical activity intervention was less effective than face-to-face condition
Finkelstein, 64, 2016	RCT	800 patients	Effectiveness of activity trackers with and without incentives	The cash incentive was most effective at increasing MVPA bout min per week at 6 months, but this effect was not sustained 6 months after the incentives were discontinued. At 12 months, the activity tracker with or without charity incentives were effective at stemming the reduction in MVPA bout min per week seen in the control group
Hartman et al. 65, 2017	RCT	205 patients	Internet based intervention	Intervention Group engaged in significantly more minutes of MVPA per week than the Control Group at the end of the maintenance period for both self-reported (mean diff. = 30.68, SE = 11.27, p = .007) and accelerometer measured

Dadaczynski et al. 66, 2017	RCT	144 patients	Pedometer-based interventions using gamification	Pedometer-based interventions using gamification elements can have positive effects not only on health promotion parameters but can also lead to an increase in PA behaviour
Kolt et al. 67, 2017	RCT	504 patients	Social networking + pedometers	More interactive Web 2.0 intervention, as well as the paper-based Logbook intervention, improved physical activity in the short term, but that effect reduced over time, despite higher levels of engagement of the Web 2.0 group
McCoy et al. 68, 2017	Observational study	82 patients	Text messaging	The intervention group increased walking and running. The control group increased running
Fournier et al. 69, 2017	Observational study	49 patients	SMS messaging	SMS delivery had a marginal effect on the maintenance of PA behaviours 1 year after the intervention
Buchholz et al. 70, 2017	Observational study	33 patients	Text messaging	Both physical activity and aerobic fitness improved
Cotton et al. 71, 2016	RCT	82 patients	Text messaging	Text messages have the potential to increase non-sedentary behaviours in university students. These messages can increase self-efficacy beliefs to take more breaks and reduce sitting time
Yu et al. 72, 2018	Single cohort study	802 patients	Pedometer-assisted walking intervention	The prescription pedometer-assisted walking intervention can effectively improve exercise adherence and manage weight
Korinek et al. 73, 2018	Single cohort study	20 patients	Smartphone app + Fitbit Zip	An adaptive step goal + rewards intervention using a smartphone app appears to be a feasible approach for increasing walking behaviour in overweight adult

Peyman et al. 74, 2018	Quasi-experimental study	360 patients	Digital health-based intervention	The mean score of knowledge, attitude and level of physical activity in the control group were not significantly different before and after the intervention
Liu et al. 75, 2018	Single cohort study	50 patients	Text messaging boosters	The study shows that incorporating goal-setting theory-based text message reminders can be useful to boost user compliance with self-monitoring fitness apps by reinforcing users' personal goals and enhancing cognitive factors associated with health behaviour change
Maylor et al. 76, 2018	RCT	48 patients	Work-based multicomponent intervention	This short multicomponent workplace intervention was successful in reducing prolonged sitting and increasing physical activity in the workplace, although total sitting time was not reduced and the impact on cardiometabolic health was minimal
Yancy et al. 77, 2018	RCT	191 patients	Text messaging	Compared with the active control of daily texting based on daily home weighing, lottery-based and direct monetary incentives provided no additional benefit for weight loss maintenance
Mouton et al. 78, 2015	RCT	149 patients	Web based intervention	Centre-based intervention was more likely to produce significant improvements of the PA level and the stage of change for PA change whereas web-based intervention was more likely to extend the awareness about PA
Brakenridge et al. 79, 2016	RCT	153 participants	Activity tracker	Organisational-support strategies with or without an activity tracker resulted in improvements in sitting, prolonged sitting and standing; adding a tracker enhanced stepping changes
Rowley et al. 80, 2019	RCT	170 patients	Internet-delivered pedometer intervention	Individually tailored, Internet-mediated PA interventions are an effective way to significantly increase PA in older adults

Gremaud et al. 81, 2018	RCT	146 patients	Fitbit Zip + mobile health platform	MapTrek is an effective approach for increasing physical activity at a clinically meaningful level in sedentary office workers, but as with accelerometer use alone, the effect decreases over time
Mascarenhas et al. 82, 2018	RCT	64 patients	Videoconferencing + smartphone app	We found that a group exercise intervention using videoconferencing and mobile apps was a feasible and acceptable way to deliver a physical activity intervention to mothers
Miragall et al. 83, 2018	RCT	76 patients	Internet based pedometer associated intervention	This study shows the effectiveness of a self-administered IMI using pedometers in increasing PA and enjoyment, and the effectiveness of the IMI alone in changing different theoretical constructs related to the PA behaviour
Mansi et al. 84, 2015	RCT	58 patients	Pedometer-driven walking intervention	This research provides important information for a larger (RCT) in the future: results demonstrated that a pedometer-driven walking intervention in combination with goal setting, and self-monitoring supported by weekly e-mails are feasible and potentially effective in increasing step count within the workplace setting over the short term
Hargraeves et al. 85, 2016	RCT	97 patients	Pedometer-driven walking intervention	Both groups had similar improvements in step counts and physical and psychological health after 12 weeks but only the SW group successfully maintained the increased step-counts 24 weeks post-intervention
Patel et al. 86, 2017	RCT	200 patients	Game-based intervention	Gamification designed to leverage insights from behavioural economics to enhance social incentives significantly increased physical activity among families in the community
Dunning et al. 87, 2018	RCT	21 patients	Text messaging	Sitting time was lower during the message-receiving period, but the difference between groups was no longer apparent after the intervention

Degroote et al. 88, 2018	Quasi experimental design	615 patients	eHealth Intervention 'MyPlan 1.0'	Significant intervention effects were found for total PA and moderate to vigorous PA with an increase for the intervention group compared to a decrease in the control condition
Robin et al. 89, 2018	RCT	89 patients	Text messaging	The results of this study extend the literature by providing evidence that imagery text delivered through cell phones can also be a successful strategy for increasing weekly minutes of APA among older adults
Moffitt et al. 90, 2015	RCT	59 patients	Pedometer + DVD intervention	The ACT intervention, delivered via DVD for the promotion of physical activity, proved a simple, efficient, and accessible method to encourage positive short-term increases in an important health-promoting behaviour
Alley et al. 91, 2018	RCT	504 patients	Web based intervention	Results partially support the use of Web 2.0 features to improve adults over 55 s' engagement in and behaviour changes from web-based physical activity interventions
Vandelanotte et al. 92, 2018	RCT	243 patients	Physical activity trackers and Web-based computer-tailored intervention	Integrating physical activity trackers into a Web-based computer-tailored intervention significantly increased intervention effectiveness
Lambert et al. 93, 2018	RCT	62 patients	Web based intervention	It was feasible to deliver eMotion in UK communities to inactive populations. eMotion has the potential to be effective and is ready for testing in a full-scale trial
Joosen et al. 94, 2018	Single cohort study	20 patients	mHealth system	This study demonstrates that an mHealth system can be implemented in a care home setting to motivate activity of the elderly, and that the biodata can be translated in a fitness score predicting the outcome of labour-intensive tests

Mitchell et al. 95, 2019	RCT	171 patients	Online intervention	While increased physical activity and decreased sedentary time were observed in both groups during the intervention period, maintenance was only observed for LPA at six-month follow-up in the intervention group
Linke et al. 96, 2019	RCT	205 patients	Web-based PA intervention	These results demonstrate that greater use of a tailored, Web-based PA intervention, particularly certain features on the site, was significantly related to increased PA levels in Latinas
Ni et al. 97, 2019	Observational study	65 patients	Pokémon Go	In this pilot study, Pokémon Go was associated with a transient increase in physical activity in the first week
Carr et al. 98, 2016	RCT	54 patients	Emails	The HP/HP group increased occupational physical activity and greater activity permissive workstation adherence was associated with improved health and work productivity outcomes
Donath et al. 99, 2015	RCT	38 patients	Screen prompts	Low-frequent and low-cost screen-based point of choice prompts (3 per day within 12 weeks) already result in notable increases of occupational standing time of approx. daily 30 min
Macniven et al. 100, 2015	Single cohort study	587 patients	Pedometer-based program	Although this pedometer-based program resulted in increases in physical activity and reductions in occupational sedentary behaviour, most participants were already meeting physical activity recommendations at baseline
Mathew et al. 101, 2019	Single cohort study	46 patients	Pedometer intervention	This study shows that a pedometer-driven walking intervention in the workplace setting is feasible and effective in increasing physical activity over a short term

Murawski et al. 102, 2019	RCT	160 patients	Mobile app	This remotely delivered intervention did not produce statistically significant between-group differences in minutes of moderate-to-vigorous intensity physical activity
Arrogi et al. 103, 2019	RCT	58 patients	stAPP smartphone-based intervention	The stAPP smartphone-based intervention constitutes a promising intervention tool to interrupt and reduce prolonged sitting behaviour
Feng et al. 104, 2019	RCT	156 patients	In home web-based intervention	This study supports the feasibility of a home-based, subject-controlled, exercise program in which P&I is regulated via real-time participant feedback, which may promote self-efficacy
Maher et al. 105, 2015	RCT	110 patients	An online, social networking physical activity intervention with pedometers	An online, social networking physical activity intervention with pedometers can produce sizable short-term physical activity changes
Spelt et al. 106, 2019	RCT	195 patients	Mobile app + wearable tracker	Results indicated that participants using the lifestyle e-coaching application reported significantly more often an increase in activity levels than a parallel control group
Fukuoka et al. 107, 2019	RCT	210 patients	Mobile app	The intervention groups substantially increased their physical activity. However, use of both the app and accelerometer for an additional 6 months after the initial 3-month intervention did not help to maintain increases in physical activity compared with continued use of the accelerometer alone
Direito et al. 108, 2019	Single cohort study	69 patients	Smartphone app	The adaptive proof-of-concept app was considered acceptable, with preliminary support for its positive effects on PA and SB

Haufe et al. 109, 2019	RCT	314 patients	Telemonitoring system	A 6-month exercise-focused intervention using telemonitoring systems reduced metabolic syndrome severity
Mora-Gonzalez et al. 110, 2019	RCT	117 patients	Gamification app	A gamification program, including the use of a game-based mobile app in a university setting, had a significant effect on the CRF in college students, in comparison with a CG that follows a traditional teaching methodology
Paul et al. 111, 2017	Single cohort study	16 patients	Mobile app	The STARFISH app was acceptable and straightforward to use for older adults
Dasgupta et al. 112, 2017	RCT	347 patients	Pedometer based	A simple physician-delivered step count prescription strategy incorporated into routine clinical practice led to a net 20% increase in step counts; however, this was below the 3000 steps/day targeted increment
Riordan et al. 113, 2019	Single cohort study	30 patients	Mobile app	The study did not demonstrate a statistically significant increase in physical activity using technology
Mitchell et al. 114, 2018	Single cohort study	32229 patients	Multicomponent intervention	Providing very small but immediate rewards for personalized daily step goal achievement as part of a multicomponent intervention increased daily step counts on a population scale, especially for physically inactive individuals and individuals who engaged more with the walking program

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List of meta-analysis on Digital Health for physical activity in primary prevention

Author	Design	Studies included	Intervention	Conclusion
Hutchesson et al. 1, 2015	Meta-analysis	84 studies	eHealth intervention	The findings support the use of eHealth interventions as a treatment option for obesity, but there is insufficient evidence for the effectiveness of eHealth interventions for weight loss maintenance or weight gain prevention
Hakala et al. 2, 2017	Meta-analysis	23 RCTs	Technology-based delivery of interventions	Technology-based delivery of interventions seems to be more effective than usual care in promoting physical activity, particularly in the interventions targeting patients
De Vries et al. 3, 2016	Meta-analysis	11 studies	Activity monitors	Behavioural physical activity interventions with an activity monitor increase physical activity in adults with overweight or obesity.
Qui et al. 4, 2015	Meta-analysis	15 RCTS	Step counter	Step counter use is associated with reduced sedentary time among adults
Direito et al. 5, 2017	Meta-analysis	21 RCTs	mHealth technology	Current mHealth interventions have small effects on PA/SB
Cotie et al. 6, 2018	Meta-analysis	20 studies	eHealth interventions	eHealth interventions are effective at increasing min week-1 of moderate-to-vigorous physical activity among working-age women from high income countries

Romeo et al. 7, 2019	Meta-analysis	9 studies	Smartphone app	This meta-analysis provides modest evidence supporting the effectiveness of smartphone apps to increase physical activity
Gal et al. 8, 2019	Meta-analysis	18 RCTs	Wearables and smartphone applications	This meta-analysis showed a small to moderate effect of physical activity interventions comprising wearables and smartphone applications on physical activity
Feter et al. 9, 2019	Meta-analysis	45 studies	Smartphone based interventions	Mobile phone-based PA interventions, inclusive those delivery by APP, were effective to increase minutes and steps per day in adults

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List of trials on Digital Health for cardiovascular risk reduction

Author	Design	Sample Size	Intervention	Conclusion
Tian et al. 1, 2015	Cluster RCT	2086 patients	Smartphone-based electronic decision support system	Results indicate that the simplified cardiovascular management program improved quality of primary care and clinical outcomes in resource-poor settings in China and India
Gaziano et al. 2, 2015			Mobile phone application	The mobile application emerged as the most cost-effective strategy because it could save more lives than the paper tool at minimal extra cost
Greving 3, 2015	RCT	330 patients	An internet-based, nurse-led intervention	An internet-based, nurse-led intervention in addition to usual care to improve vascular risk factors in patients with a clinical manifestation of a vascular disease does not result in a QALY gain at 1 year
Kim et al. 4, 2015	Single cohort study	48 patients	Internet-based lifestyle intervention on cardio-metabolic risks and stress	Internet-based one-on-one counselling and mobile phone text messages can assist individuals with targeted lifestyle modifications for metabolic syndrome
Jahangiry et al. 5, 2015	RCT	160 patients	Interactive web-based lifestyle intervention	The findings suggest that the web-based interactive program was beneficial for individuals with metabolic syndrome
Liu et al. 6, 2015	RCT	589 patients	Mobile phone-based intervention	Mobile phone-based intervention may therefore be a potential solution for reducing CVD risk in China

Ylimaki et al. 7, 2015	Single cohort study	53 patients	Internet-based and carried out via Skype or face-to-face	Changes in lifestyle were detected as a result of the intervention. These lifestyle changes may improve cardiovascular health in the long term
Naimark et al. 8, 2015	RCT	99 patients	Web-based app	We showed a positive impact of a newly developed Web-based app on lifestyle indicators during an intervention of 14 weeks
Reinwand et al. 9, 2015	RCT	1638 patients	eHealth Interventions	The more frequent as-recommended intervention use by unemployed, older, and ill participants may be an indication that these eHealth interventions are attractive to people with a greater need for health care information
Anand et al. 10, 2015	RCT	343 patients	Digital Health Intervention	Among South Asian individuals, a DHI was not associated with a reduction in MI risk score after 12 months and was not influenced by knowledge of genetic risk status
Bloss et al. 11, 2016	RCT	160 patients	Withings Blood Pressure Monitor; diabetes: Sanofi iBGStar Blood Glucose Meter; arrhythmia: AliveCor Mobile ECG) and an iPhone	There was little evidence of differences in health care costs or utilization as a result of the intervention. Furthermore, we found evidence that the control and intervention groups were equivalent with respect to most health care utilization outcomes
Aalbers et al. 12, 2016	Pre-post single cohort study	1212 patients	Self-Motivated eHealth Intervention	Among an adult Dutch population, this eHealth intervention resulted in lifestyle changes in behavioural risk factors associated with cognitive decline, and these improvements lasted over the period of 1 year
Gilson et al. 13 ,2016	Single cohort study	44 patients	Smartphone activity tracking application	Step counts were more successfully monitored than dietary choices in those drivers who used the Jawbone UP

Dixon et al. 14, 2016	RCT	641 patients	Telehealth	There is evidence to suggest that the Healthlines telehealth intervention was likely to be cost-effective at a threshold of £20 000 per QALY
Salisbury et al. 15, 2016	Pragmatic, multicentre, randomised controlled trial	641 patients	Telehealth	This evidence-based telehealth approach was associated with small clinical benefits for a minority of people with high cardiovascular risk, and there was no overall improvement in average risk
Storm et al. 16, 2016	RCT	790 patients	Web-based computer-tailored interventions	Our findings indicate the general effectiveness and practicality of Web-based computer-tailored interventions in terms of increasing self-reported habit strength for physical activity and fruit and vegetable consumption
Rubinstein et al. 17, 2016	RCT	637 patients	mHealth-based intervention	Our mHealth-based intervention did not result in a change in blood pressure that differed from usual care, but was associated with a small reduction in bodyweight and an improvement in some dietary habits
Ganesan et al. 18, 2016	Single cohort study	69219 patients	mHealth	Distributed mHealth implementation of a low-cost life-style intervention is associated with short-term, reproducible, large-scale improvements in physical activity, sitting, and weight
van den Brekel-Dijkstra et al. 19, 2016	Single cohort study	800 patients	Web-based cardiovascular risk assessment	The personalized prevention approach offers a system for integrated risk profiling and individualized health management that was well received in general practice
Recio-Rodriguez et al. 20, 2016	RCT	833 patients	Mobile Phone App	Leisure-time MVPA increased more in the app+counseling than counselling only group, although no difference was found when comparing the increase between the two groups

Brunetti et al. 21, 2016	Single cohort study	1000 patients	Telecardiology	The awareness, therapy, and control of cardiovascular risk factors in a Mediterranean real-world population are unsatisfactory
Smith et al. 22, 2016	Markov model		Internet delivered lifestyle program	The ODPP may offer an economical approach to combating overweight and obesity
Jahangiry et al. 23, 2017	RCT	160 patients	Internet based lifestyle program	These results indicate the positive impact of a lifestyle intervention by a web-based program on physical activity, dietary intake and several dimension of QoL
Ashton et al. 24, 2017	RCT	50 patients	eHealth intervention	The HEYMAN program demonstrated feasibility in assisting young men to make some positive lifestyle changes
Duan et al. 25, 2017	RCT	566 patients	Web-based intervention	This study provides evidence for the efficacy of a Web-based multiple health behaviour intervention among Chinese university students tested with different outcome variables
Gilson et al. 26, 2017	Single cohort study	19 patients	Smartphone app + activity tracker	Not all drivers benefitted from the program. However, positive changes for different health behaviours were observed in the majority of participants
Zhang et al. 27, 2017	RCT	80 patients	Smartphone app	This pilot study partially confirmed the positive effects of the SBCHDP programme in improving awareness and knowledge of CHD among the working population
Spark et al. 28, 2015	RCT	29 patients	Text messaging	In comparison to interventions without extended contact, results suggest text message-delivered extended contact may support the attenuation of weight regain and promote the maintenance of physical activity

Sperl-Hillen, 29, 2018	Cluster RCT	7914 patients	Clinical decision support	This EHR-integrated, web-based outpatient CDS system significantly improved 10-year CV risk trajectory in targeted adults
Barton et al. 30, 2018	RCT	182 patients	Telemedicine	Despite enhancing treatment adherence, this intervention was unsuccessful in countering clinical inertia, likely explaining its lack of effect on CVD risk factors
Choudhry et al. 31, 2018	RCT	4078 patients	Text messaging	A remotely delivered multicomponent behaviourally tailored intervention resulted in a statistically significant increase in medication adherence but did not change clinical outcomes
Van Doorn-Van Atten et al. 32, 2018	RCT	214 patients	Telemonitoring	This intervention leads to improved nutritional status in older adults at risk of undernutrition, and to improved diet quality and physical activity levels of community-dwelling elderly
Dodd et al. 33, 2018	RCT	162 patients	Smartphone application	There was no significant additional benefit from the provision of the smartphone application in improving HEI score (p = .452)
Staffileno et al. 34, 2018	Single cohort study	26 patients	eHealth tools	Our eHealth platform provides an alternative approach for reaching young AA women and was successful with respect to improving PA and dietary behaviours
Fjeldsoe et al. 35, 2016	RCT	228 patients	Text messaging	The GHSH extended care intervention led to significantly better anthropometric and physical activity outcomes than standard practice (no contact)
Lara et al. 36, 2016	RCT	70 patients	Web based intervention	The trial procedures and the LEAP intervention proved feasible and acceptable. Effectiveness and cost-effectiveness of LEAP to promote healthy lifestyles warrant evaluation in a definitive RCT

Brakenridge et al. 37, 2016	RCT	153 participants	Activity tracker	Organisational-support strategies with or without an activity tracker resulted in improvements in sitting, prolonged sitting and standing; adding a tracker enhanced stepping changes
Griffin et al. 38, 2018	Single cohort study	104 patients	Text messaging	A low-cost, text messaging initiative particularly targeting women residing in rural communities with high rates of poverty and obesity can promote weight loss and improve dietary and physical activity behaviours
Arens et al. 39, 2018	Observational study	166 patients	Novel App- and Web-Supported Diabetes Prevention Program	The approach of enhanced interaction of HCPs and patients via app- and web-based communication was a clear success and delivered favourable responder rates
Memon et al. 40, 2018	RCT	56 patients	Smartphone app	Financial incentives combined with a smartphone app designed to track physical activity did not promote physical activity or decrease obesity
Bosworth et al. 41, 2018	RCT	428 patients	Telehealth intervention	Despite increased access to pharmacist resources, we did not observe significant improvements in CVD risk for patients randomized to the intervention compared to education control over 12 months
Jones et al. 42, 2018	Single cohort study	40 patients	Text messaging	Use of text messages was widely accepted among participants. Significant CVD risk reductions and increased cancer screenings were noted
Mensorio et al. 43, 2019	Explanatory RCT	106 patients	Internet based intervention	This study demonstrates that the Internet is a viable alternative for the delivery and dissemination of interventions focused on promoting healthy habits, and a totally self-administered intervention can produce long-term positive results

Bonn et al. 44, 2019	RCT	209 participants	mHealth	The Health Integrator Intervention Study will evaluate if a personalized intervention combining mHealth and conventional programs for lifestyle change, with or without additional health coach sessions, can improve lifestyle behaviours and quality of life
Patel et al. 45, 2019	Quasi-experimental study	6579 patients	Multifaceted mobile technology-supported primary health care intervention	This study found that a multifaceted mobile technology-supported primary health care intervention was associated with greater use of preventive CVD medication and lower BP levels among high-risk individuals in a rural Indonesian population
Peiris et al. 46, 2015	Cluster RCT	38725 patients	computer-guided, quality improvement program	Computerized quality improvement tools offer an important, albeit partial, solution to improving primary healthcare system capacity for cardiovascular disease risk management
Spring et al. 47, 2018	RCT	212 patients	mHealth + remote coaching	Multicomponent mHealth diet and activity intervention involving connected coaching and modest initial performance incentives holds potential to reduce chronic disease risk.
Yousef et al. 48, 2019	Single cohort study	595 participants	Web based intervention	e-Coaching using MyCLIC is a low cost and effective method to perform lifestyle interventions and has the potential to reduce the 10-year cardiovascular disease risk
Peiris et al. 49, 2019	Single cohort study	62254 patients	Mobile health intervention	Strategy was well implemented with increased treatment rates among high risk individuals assessed by CHWs, however effects on BP were not demonstrated
Dandge et al. 50, 2019	Single cohort study	2456 patients	mHealth intervention strategy	This research demonstrates the feasibility and local acceptability of a mHealth intervention strategy anchored on NPHWs guided by physicians for detection, treatment and regular follow-up of individuals with hypertension and diabetes in a community setting in India

Garcia-Ortiz et al. 51, 2018	RCT	833 patients	Smartphone app	The participants with strongest app adherence showed better outcomes in terms of maintenance of healthy lifestyles at 12 months than those with weaker adherence
Gonzalez-Sanchez et al. 52, 2019	RCT	833 patients	Smartphone app	Adding an intervention with the use of an app for three months to standard counselling on diet and physical activity, does not provide additional benefits for improving CVRFs or the estimated CVR in the long term
Beratarrechea et al. 53, 2019	RCT	755 patients	mHealth tools	Use of mHealth tools identifies patients at high CVD risk in their home, increases the likelihood of participating in chronic CVD risk factor management, and strengthens referrals
Duscha et al. 54, 2018	RCT	20 patients	mHealth program	12-week mHealth program in PAD patients with IC can improve peak VO2 and claudication onset time

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List of meta-analysis on Digital Health for cardiovascular risk reduction

Author	Design	Studies included	Intervention	Conclusion
Mita et al. 1, 2016	Meta-analysis	16 studies	Social media in reducing risk factors for noncommunicable diseases	Further trials are warranted, especially to isolate the effect of social media use and to fully evaluate the effect of the social presence and media richness of social media platforms
Widmer et al. 2, 2015	Meta-analysis	51 studies	Digital Health intervention	Overall, these aggregations of data provide evidence that DHIs can reduce CVD outcomes and have a positive impact on risk factors for CVD
Armanasco et al. 3, 2017	Meta-analysis	35 studies	Text messaging	Text message interventions are capable of producing positive change in preventive health behaviours
Kassavou et al. 4, 2018	Meta-analysis	17 RCTs	Automated telecommunication	The BCTs 'tailored' and 'information about health consequences' were positively and significantly associated with ES
Beishuizen et al. 5, 2016	Meta-analysis	47 studies	Web-based interventions	Web-based interventions have the potential to improve the cardiovascular risk profile of older people, but the effects are modest and decline with time

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Annex 2: Digital health in secondary prevention of CAD

List of trials on Home rehabilitation of CAD

Author	Design	Sample Size	Intervention	Conclusion
Brubaker et al. 1, 2000	RCT	31 patients	Home-based (HB) maintenance exercise program after centre-based (CB) CR	These data indicate that the HB program was as effective as the CB program
Ades et al. 2, 2000	Multicentre, controlled trial	133 patients	Home-based, trans telephonically monitored cardiac rehabilitation	Patients with coronary heart disease can effectively participate in home-based, monitored cardiac rehabilitation, with exercise and quality of life improvements comparable to those demonstrated at on-site programs
Kodis et al. 3, 2001	Retrospective analysis	1042 patients	Home-based aerobic training in coronary artery bypass graft surgery patients	Stable post CABGS patients who receive a detailed exercise prescription to follow at home do as well as those in supervised rehabilitation
Tygesen et al. 4, 2001	RCT	62 patients	Intensive home-based exercise training	Intensive exercise training in cardiac rehabilitation increases exercise capacity and global HRV, which could be of prognostic significance

Arthur et al. 5, 2002	RCT	240 patients	Monitored, home-based exercise program	This study suggests that low-risk CABG surgery patients may be served as well or better with a monitored, home-based exercise program than with an institution-based program
Ueshima et al. 6, 2002	Single cohort study	10 patients	Home-based Exercise Using a Stepping Device with ECG Telemetry Monitoring	A computer-based ECG telemetry system combined with a stepping device facilitated an effective home-based exercise program in patients with previous MI
Gielen et al. 7, 2003	RCT	19 patients	Home-based exercise training	Home-based ET sustained part of the effects of hospital-based ET on endothelium-dependent vasodilation in coronary artery disease
Hamm et al. 8, 2004	RCT	623 patients	Combining supervised with unsupervised exercise sessions	The results of this study show that an outpatient cardiac rehabilitation program combining supervised with unsupervised exercise sessions and continuing for 38 weeks results in the greatest improvement in these selected outcomes
Izawa et al. 9, 2005	RCT	45 patients	Self-monitoring approach (SMA) on exercise maintenance	SMA during supervised CR may effectively increase exercise maintenance, SEPA, and objective physical activity at 12 months after myocardial infarction onset
Giallauria et al. 10, 2006	RCT	45 patients	Home-based CR of similar duration and were monitored by telecardiology	TC improves compliance, functional capacity and psychological profile of patients undergoing a home-based CRP, compared to patients enrolled in a home-based CRP without ecg-monitoring by Telecardiology
Kouidi et al. 11, 2006	Single cohort study	91 patients	Transtelephonic electrocardiographic monitoring	These data demonstrate that TEM provides a workable facility in cardiac rehabilitation for monitoring patients who are exercising in gyms

Senuzun et al. 12, 2006	Single cohort study	30 patients	Home-based cardiac exercise program (HBCEP)	These results suggest that a first-time HBCEP in Turkey can be successful in having patients adhere to a prescribed exercise program and reduce risk factors
Wu et al. 13, 2006	RCT	54 patients	Home exercise vs CR vs control group	Our results point out that a cardiac rehabilitation exercise program has a positive effect on heart rate recovery in patients having undergone CABG and is consistent with the autonomic improvement
Körtke et al. 14, 2006	RCT	170 patients	Telemedicine-based rehabilitation used in the home	Our data indicate that home-based rehabilitation is more effective than in-hospital rehabilitation for patients after cardiac surgery
Dalal et al. 15, 2007	Pragmatic randomized controlled trial with patient preference arms.	230 patients	Home-based cardiac exercise program (HBCEP)	Home-based cardiac rehabilitation with the Heart Manual was as effective as hospital-based rehabilitation for patients after myocardial infarction
Jolly et al. 16, 2007	RCT	555 patients	Home-based cardiac exercise program (HBCEP)	A home-based cardiac rehabilitation programme for low- to moderate-risk patients does not produce inferior outcomes compared with the traditional centre-based programmes
Taylor et al. 17, 2007	RCT	104 patients	Home-based cardiac exercise program (HBCEP)	The health gain and total healthcare costs of the present hospital-based and home-based cardiac rehabilitation programmes for patients after myocardial infarction appear to be similar
Grace et al. 18, 2005	Survey	141 patients	Home-based CR	Time-constrained, working cardiac patients were most likely to prefer home-based programs, yet patient preferences did not differ on the basis of age or sex

Carlson et al. 19, 2000	RCT	80 patients	Were gradually weaned to an off-site exercise regimen (MP)	These results suggest that a reduced cost MP was as effective as an established traditional rehabilitation in improving physiologic outcomes while demonstrating higher rates of exercise adherence and program participation
Robertson et al. 50, 2001	RCT	62 patients	Intensive home follow-up	Intensive home follow-up provided a cost-effective alternative to traditional cardiac rehabilitation programs
Salvetti et al. 21, 2008	RCT	39 patients	Home-based cardiac exercise program (HBCEP)	Programme seems to provide an efficient low-cost approach to cardiac rehabilitation in low-risk patients.
Butler et al. 22, 2009	RCT	110 patients	Pedometer based intervention	The pedometer-based intervention was successful in increasing physical activity in cardiac patients after a CRP
Jones et al. 23, 2009	Survey	26 patients	Home-based cardiac exercise program (HBCEP)	Patients in the hospital programme enjoyed the camaraderie of group exercise and patients in the home programme valued the wealth of information and advice in the Heart Manual and this gave them a feeling of being in control of their health
Johnson et al. 24, 2009	RCT	153 patients	Home walking intervention	HRQL improved in both groups but seemed to increase earlier among women in the intervention group.
Smith et al. 25, 2004	Survey	222 patients	Home-based cardiac exercise program (HBCEP)	This follow-up study suggests that low-risk patients whose CR is initiated in the home environment may be more likely to sustain positive physical and psychosocial changes over time than patients whose program is initially institution-based

Jolly et al. 26, 2009	RCT	555 patients	Home-based cardiac exercise program (HBCEP)	A home-based cardiac rehabilitation programme does not produce inferior outcomes when compared to traditional centre-based programmes as provided in the United Kingdom.
Blanchard et al. 27, 2010	Single cohort study	280 patients	Home-based cardiac exercise program (HBCEP)	The MVPA levels of patients attending home-based CR tend to vary depending on gender, whether or not metabolic syndrome was present, and prior MVPA levels
Furber et al. 28, 2010	RCT	215 patients	Pedometer-based telephone intervention	The pedometer-based telephone intervention could be offered as an effective and accessible option for patients not attending a CRP to increase and maintain their physical activity levels after hospitalisation
Marchionni et al. 29, 2003	RCT	270 patients	Home-based cardiac rehabilitation programmes	Post-MI Hosp-CR and Home-CR are similarly effective in the short term and improve TWC and HRQL in each age group
Lai et al. 30, 2011	RCT	32 patients	Home-based cardiac rehabilitation programme	In postmenopausal women with coronary heart disease, a home-based exercise program appears able to improve FC and HRV
Smith et al. 31, 2011	RCT	196 patients	Home-based cardiac rehabilitation programme	Home and hospital-based exercise training-maintained exercise capacity above pre-CR levels 6 years after CR
Korzeniowska-Kubacka et al. 32, 2011	Single cohort study	62 patients	Hybrid model: partly out-patient and partly home-based and tele-monitored	Hybrid rehabilitation improved physical capacity and positively influenced the sympatho-vagal balance in post-MI male patients with preserved left ventricular systolic function
Houle et al. 33, 2011	RCT	65 patients	Home-based cardiac rehabilitation program	This study supports development of the home-based cardiac rehabilitation program using socio-cognitive intervention associated with a pedometer after an acute coronary syndrome

Oerkild et al. 34, 2011	RCT	75 patients	Home-based cardiac rehabilitation program	Home-based CR is as effective as centre-based CR in improving exercise capacity, risk factor control and health-related quality of life
Worringham et al. 35, 2011	Single cohort study	134 patients	Smartphone, ECG and GPS based system for remotely monitoring exercise in cardiac rehabilitation	The system provided a feasible and very flexible alternative form of supervised cardiac rehabilitation for those unable to access hospital-based programs
Dalleck et al. 36, 2011	Observational study	226 patients	Telemedicine using videoconferencing	The results show the suitability of telemedicine for delivering cardiac rehabilitation for risk factor modification and exercise monitoring to patients who otherwise would not have access to it
Izawa et al. 37, 2011	RCT	126 patients	Self-monitoring of physical activity by hospitalized cardiac patients attending phase I cardiac rehabilitation	Self-monitoring of patient physical activity from phase I CR might effectively increase the physical activity level in preparation for entering a phase II CR program
Guiraud et al. 38, 2012	RCT	29 patients	Telephone support based on accelerometer recordings	Telephone support based on accelerometer recordings appeared to be an effective strategy to improve adherence to PA in noncompliant patients
Moholdt et al. 39, 2012	RCT	30 patients	Home-Based Aerobic Interval Training	Found no evidence for a different treatment effect between patients randomized to home-based AIT compared to patients attending organized rehabilitation
Scalvini et al. 40, 2009	RCT	47 patients	Home-based cardiac rehabilitation program	This type of home rehabilitation using telemedicine appears to be worth implementing in selected categories of patients.

Houle et al. 41, 2012	RCT	65 patients	Pedometer-based program	The use of a pedometer concomitantly with a socio-cognitive intervention improves adherence to physical activity and quality of life during the year after an acute coronary syndrome event
Oerkild et al. 42, 2012	RCT	40 patients	Home-based cardiac rehabilitation program	Participation in home-based CR improved exercise capacity among elderly patients with coronary heart disease, but there was no significant difference between the home intervention and the control group
Lee et al. 43, 2013	RCT	55 patients	Home-based cardiac rehabilitation program with wireless monitoring	CR using home-based exercise training with wireless monitoring led to improvement of exercise capacity and QOL relative to conventional care in ACS patients undergoing PCI
Zutz et al. 44, 2007	RCT	15 patients	Internet as a medium for delivery of an interactive "virtual" CRP (vCRP) to patients at a distance	The vCRP group significantly improved their HDL-C, triglycerides, total cholesterol: HDL-C ratio and exercise capacity
Clark et al. 45, 2013	Single cohort study	24 patients	Internet-based electronic Outpatient Cardiac Rehabilitation (eOCR) program	Each patient monitored at least five risk factors and read at least one of the secondary prevention articles
Brough et al. 46, 2014	Single cohort study	41 patients	Interactive web-based program	Observed important improvements in exercise capacity, QOL, and dietary habits in a group of participants following a Web-based CR program

Aamot et al. 47, 2014	RCT	90 patients	Home-based cardiac rehabilitation program	HIT was efficiently performed in three settings of cardiac rehabilitation, with respect to target exercise intensity, exercise attendance, and increase in peak VO2. Exercise mode was not essential for exercise capacity
Korzeniowska-Kubacka et al. 48, 2014	Observational study	52 patients	Hybrid CR: tele-monitored walking training at home	In post-MI women, a hybrid model of training improved physical capacity and was a similarly effective form of CR as a centre-based approach
Whittaker et al. 49, 2014	RCT	120 patients	Technology enabled home-based cardiac rehabilitation program	The cost of delivery by telehealth was slightly lower than for patients attending a rehabilitation service in person
Piotrowicz et al. 50, 2014	Single cohort study	365 patients	Home-based cardiac telerehabilitation	HTCR is a feasible, safe form of rehabilitation, well accepted by patients. The adherence to HTCR was high and promising.
Lear et al. 51, 2014	RCT	78 patients	Virtual Cardiac Rehabilitation Program Delivered at a Distance via the Internet	These results are promising and suggest that a low-cost technology such as the Internet can be used safely and effectively in remotely delivering cardiac rehabilitation
Wakefield et al. 52, 2014	Observational study	62 patients	Remote, Telephone-Based Delivery of Cardiac Rehabilitation	Many hospitals do not provide comprehensive CR services on-site; thus, remote CR is a viable alternative to bring services closer to the patient
Pfaeffli et al. 53, 2012	Survey study	41 participants	mHealth cardiac rehabilitation	Most participants thought a mHealth exercise program was an effective way to deliver exercise-based CR

Szaleweska et al. 54, 2015	Single cohort study	125 patients	Home-based cardiac telerehabilitation (HCR)	In patients with documented CAD, HCR is feasible and safe, and adherence is good
Ramadi et al. 55, 2015	Retrospective analysis	3488 patients	Home-based cardiac rehabilitation	The present findings indicate that when the patients were given a choice as to the delivery model (centre- vs home-based) used for their CR program, they were relatively successful in retaining the improvement in exercise capacity
Frederix et al. 56, 2015	RCT	80 patients	Physical activity telemonitoring	The study showed that, to maintain exercise tolerance and lower re-hospitalisation rate after hospital-based CR in CAD patients, a physical activity telemonitoring program might be an effective intervention
DuttaRoy et al. 57, 2015	RCT	62 patients	Home-based cardiac rehabilitation	Home-based HFE decreased circulating VEGF in patients with stable CAD, suggesting a reduced ischaemic burden
Pfaeffli et al. 58, 2015	RCT	123 patients	mHealth CR intervention	mHealth CR intervention plus usual care showed a positive effect on adherence to multiple lifestyle behaviour changes at 3 months in New Zealand adults with CHD compared to usual care alone
Pfaeffli et al. 59, 2015	RCT	171 patients	mHealth CR intervention	Adults with IHD were able to use an mHealth program and reported that text messaging is a good way to deliver exercise information
Li et al. 60, 2015	RCT	70 patients	Home-based cardiac rehabilitation	The low-intensity, home-based exercise led by an advanced practice nurse was effective in improving HRQOL and physical fitness

Sangster et al. 61, 2015	RCT	313 patients	Pedometer-based telephone coaching program	Low-contact, telephone-based interventions are a feasible means of delivering lifestyle interventions for underserved rural communities
Frederix et al. 62, 2015	RCT	140 patients	Patient-Specific Telerehabilitation Program With Text Messaging Support	Study showed that an additional 6-month patient-specific, comprehensive telerehabilitation program can lead to a bigger improvement in both physical fitness (VO2 peak) and associated HRQL
Najafi et al. 63, 2015	RCT	887 patients	Home-based cardiac rehabilitation	A well-designed hybrid CRP can be a viable alternative for hospital-based CRP in low- and middle-income countries where there are no appropriate health facilities in remote areas
Frederix et al. 64, 2015	RCT	140 patients	Patient-Specific Telerehabilitation Program with Text Messaging Support	Paper shows the addition of cardiac telerehabilitation to conventional centre-based cardiac rehabilitation to be more effective and efficient than centre-based cardiac rehabilitation alone
Vahedian-Azimi et al. 65, 2016	RCT	70 patients	Family-Centred Empowerment Model versus home-based cardiac rehabilitation	The family-centred empowerment model may be an effective hybrid cardiac rehabilitation method for improving the physical and mental health of patients post-MI
Brun Thorup et al. 66, 2016	Qualitative research design	33 participants	Pedometer use	Cardiac patients' motivation for walking was evident due to pedometer use. Even though not all aspects of motivation were autonomous, and self-determined, the patients felt motivated for walking
Borges et al. 67, 2016	Retrospective study	50 patients	Home-based cardiac rehabilitation	Self-regulated exercising following CR discharge seems to be effective to maintain gains in exercise capacity acquired during supervised centre-based programs

Chen et al. 68, 2016	RCT	64 patients	Home-based cardiac rehabilitation	There was a significant between-group, within-group, and interaction effect found in the MetS Z scores
Xu et al. 69, 2016	RCT	52 patients	Home-based cardiac rehabilitation	Our study suggests that an early, home-based CR program can greatly improve the ventricular function of AMI patients in a short period of time
Kidholm et al. 70, 2016	RCT	151 patients	Home-based cardiac telerehabilitation	Even though the rehabilitation activities increased, the program does not appear to be cost-effective
Wang et al. 71, 2016	Longitudinal quasi-experimental study	60 patients	Multimedia Exercise Training Program	Our inpatient multimedia exercise training program safely improved distance walked in the 6MWT, heart rate recovery, and self-efficacy at hospital discharge
Dithmer et al. 72, 2016	Single cohort study	10 patients	"The Heart Game": Using Gamification as Part of a Telerehabilitation Program	"The Heart Game" concept presents a new way to motivate heart patients by using technology as a social and active approach to telerehabilitation
Widmer et al. 73, 2017	RCT	80 patients	Digital health intervention	The current study demonstrated that complementary DHI significantly improves weight loss, and might offer a method to reduce CV-related ED visits plus rehospitalizations in patients after ACS undergoing CR
Ruivo et al. 74, 2017	RCT	32 patients	In-class Active Video Game Supplementation	The additional use of AVGs during CR sessions is feasible, safe, and significantly improved daily PA and EE
Dunn et al. 75, 2017	A descriptive longitudinal design	324 patients	Home-based cardiac telerehabilitation	Exercise may be effective in reducing moderate to severe hopelessness in patients with CHD

Noites et al. 76, 2017	RCT	32 patients	Phase IV Home-Based Cardiac Rehabilitation Program	This specific phase IV home-based exercise program seems to improve cardiorespiratory fitness, haemodynamics at peak exercise and heart rate recovery, an indicator of cardiac autonomic function
Bravo-Escobar et al. 77, 2017	RCT	28 patients	Home-based cardiac rehabilitation	The home-based cardiac rehabilitation programme with mixed surveillance appears to be as effective and safe as the traditional model in patients with ischemic heart disease who are at moderate cardiovascular risk
Matos-Garcia et al. 78, 2017	RCT	54 patients	Home walking intervention	Low-risk patients recently experiencing MI demonstrate impaired MIP and respiratory endurance compared with healthy participants
Kraal et al. 79, 2017	RCT	90 patients	Home-based cardiac rehabilitation	No differences between home-based training with telemonitoring guidance and centre-based training on physical fitness, physical activity level or health-related quality of life
Zhang et al. 80, 2017	Prospective study	95 patients	Community health service centre (CHSC)-based Cardiac Rehabilitation (CR)	Given the high participation and low withdrawal along with considerable improvements in HRQoL, psychological state and exercise capacity, CHSC was likely to be the optimal setting for implementing CR
Vieira, 81, 2017	RCT	33 patients	Virtual reality CR	The virtual reality format had a positive influence on body composition, specifically on the waist-to-hip ratio, in the first three months
Waite et al. 82, 2017	Single cohort study	22 patients	Pre-operative Rehabilitation (PREHAB) home-based exercise programme	This small exploratory evaluation suggests that providing a home-based PREHAB programme for frail patients undergoing CABG or Valve surgery may be able to improve functional ability and reduce hospital length of stay

Kraal et al. 83, 2014	RCT	50 patients	Home-based cardiac rehabilitation	Analysis shows that HT with telemonitoring guidance has similar short-term effects on exercise capacity and quality of life as CT in CR patients
Oliveira et al. 84, 2008	Observational study	30 patients	Home-based cardiac rehabilitation	Patients participating in the home-based intervention increased PA throughout the day; moreover, they performed enough moderate-intensity PA to meet health-related recommendations
Skobel et al. 85, 2017	RCT	118 patients	Smartphone-guided training system	A newly designed system for home-based CR appears feasible, safe and improves exercise capacity compared to national CR
Guiraud et al. 86, 2017	RCT	50 patients	Huber Motion Lab (HML) for strength training	Both protocols appeared to be well tolerated, safe and feasible for these CHD patients
Frederix et al. 87, 2017	RCT	126 patients	A combined telerehabilitation and centre-based programme	A combined telerehabilitation and centre-based programme, followed by transitional telerehabilitation induced persistent health benefits and remained cost-efficient up to 2 years after the end of the intervention
Frohmader et al. 88, 2018	Qualitative study	20 participants	Nurse supported Home-based cardiac rehabilitation	Patients believed the program assisted their recovery and were satisfied with the information, guidance and support received from mentors
Duscha et al. 89, 2018	RCT	25 patients	mHealth program	A 12-week mHealth program of physical activity trackers and health coaching following CR graduation can sustain the gains in peak VO2 and physical activity achieved by site-based CR

Chokshi et al. 90, 2018	RCT	105 patients	Wearable trackers, goal setting and incentives	Loss-framed financial incentives with personalized goal setting significantly increased physical activity among ischemic heart disease patients using wearable devices during the 16-week intervention, and effects were sustained during the 8-week follow-up
Vieira, 91, 2018	RCT	33 patients	Virtual reality CR	The virtual reality format had improved selective attention and conflict resolution ability, revealing the potential of CR, specifically with virtual reality exercise, on executive function
Harzand et al. 92, 2018	Single-arm, nonrandomized feasibility study	18 patients	Smartphone-enabled, home-based CR	Smartphone-enabled, home-based CR is feasible in veterans with heart disease and is associated with moderate to high levels of engagement and patient satisfaction
Rawstorn et al. 93, 2018	RCT	162 patients	REMOTE-CR Exercise-Based Cardiac Telerehabilitation Program	REMOTE-CR can extend the reach and impact of existing cardiac rehabilitation services by overcoming traditional participation barriers while preserving expert oversight
Torri et al. 94, 2018	Quasi-experimental design	53 patients	Long-term web-monitored exercise-based CR maintenance program	Our web-based home CR maintenance program was feasible, well-accepted, and effective in improving physical activity for 6 months and achieved higher overall adherence to cardiovascular risk targets than UC
Sunamura et al. 95, 2018	RCT	914 patients	Standard CR extended for 9 months with five to six telephone general lifestyle counselling sessions (CR+T)	Extending CR with extra behavioural counselling (group sessions or individual telephone sessions) does not confer additional benefits with respect to SCORE parameters
Melholt et al. 96, 2018	Survey	49 patients	Cardiac telerehabilitation	Online telerehabilitation portals may be used as a tool in patient education and cardiac rehabilitation

Frederix et al. 97, 2018	Cost–benefit analysis		Cardiac telerehabilitation in Belgium	Increased cardiac rehabilitation uptake rates can reduce the burden of disease, and the resulting benefits exceed its costs
Avila et al. 98, 2018	RCT	90 patients	Home-Based Rehabilitation with Telemonitoring Guidance	Adding a home-based exercise program with telemonitoring guidance following completion of a phase II ambulatory CR program results in further improvement of physical fitness and is equally as effective as prolonging a centre-based CR in patients with CAD
Bailly et al. 99, 2018	RCT	50 patients	Telephone follow-up	A physical activity program is cost-effective in providing a better quality of life and reducing health care consumption in cardiovascular patients
Ter Hoeve et al. 100, 2018	RCT	734 patients	Standard CR extended for 9 months with five to six telephone general lifestyle counselling sessions (CR+T)	Adding three pedometer-based, face-to-face group PA counselling sessions to standard CR increased daily step count and time in prolonged MVPA
Knudsen et al. 101, 2019	Matched control study	77 patients	Tele-rehabilitation	Tele-rehabilitation and hospital-based cardiac rehabilitation seemed to be equally successful in improving patient activation and health literacy
Kayser et al. 102, 2019	RCT	39 patients	Web-based tailored nursing intervention	From 40%-60% of acute coronary syndrome patients self-report insufficient levels of physical activity. No effect was found on the primary outcome of daily steps
Kim et al. 103, 2019	Observational study	114 patients	Home-based cardiac rehabilitation	9-month home-based CR program was more effective for fitness in men, but only the HDL-C showed positive improvement among the cardiovascular risk factors

Nabutovsky et al. 104, 2019	Cross-sectional study	200 patients	Remote digital cardiac rehabilitation	RDCR program was acceptable to most cardiac patients, including the elderly population, and could be a potential solution for patients who avoid traditional rehabilitation programs in medical centres
Fang et al. 105, 2019	RCT	80 patients	Home-based cardiac telerehabilitation (HBCTR)	Our observations indicated that the HBCTR program may be applied successfully in Chinese patients who had very little technical skills and its application may be highly cost-effective
Song et al. 106, 2019	RCT	96 patients	Smartphone-Based Telemonitored Exercise Rehabilitation	Telemonitored exercise rehabilitation is an effective rehabilitation mode for CHD patients in China
Uddin et al. 107, 2019	A quasi-randomized controlled trial	142 patients	Home-Based Cardiac Rehabilitation	In the context of a single-centre LMIC setting, this study demonstrated the feasibility of home-based CR programs and offers a model of service delivery that could be replicated on a larger scale
Spindler et al. 108, 2019	RCT	136 patients	Telerehabilitation	TR is comparable to conventional rehabilitation in motivating patients, preventing psychological distress and improving quality of life
Barnason et al. 109, 2019	RCT	43 patients	Weight management telehealth intervention	Findings demonstrated the usefulness and feasibility of using telehealth delivery of the WMI for cardiac rehabilitation participants in rural communities to improve weight management outcomes
Ge et al. 110, 2019	Single cohort study	1033 patients	Home-Based Cardiac Rehabilitation	Improvement of family support by educating both patients and families may be helpful in improving adherence to home-based CR programs

Maddison et al. 111, 2019	RCT	162 patients	Home-Based Cardiac telerehabilitation	REMOTE-CR is an effective, cost-efficient alternative delivery model that could—as a complement to existing services—improve overall utilisation rates by increasing reach and satisfying unique participant preferences
Laustsen et al. 112, 2019	Single cohort study	34 patients	Telemonitored exercise-based cardiac rehabilitation	This study demonstrated that the self-elected type of physical exercise in cardiac rehabilitation with telemonitoring improved all outcome measures both on the short and long-term, except for peak oxygen uptake at 12 months follow-up
Fang et al. 113, 2016	Qualitative study	150 patients	Home-based cardiac telerehabilitation (HBCTR)	Most patients lacked knowledge about HBCTR but volunteered to participate after they have learned about the program. Several personal and life-style factors influenced their acceptance of the program
Wang et al. 114, 2012	RCT	160 patients	Home-based rehabilitation	Home-based cardiac rehabilitation program for patients with acute myocardial infarction, using a self-help manual, improves health-related quality of life and reduces anxiety
Mutwalli et al. 115, 2012	RCT	49 patients	Home-based cardiac rehabilitation program	The home-based CR program improves health related QoL and risk factor profiles for patients following coronary arteries bypass graft to greater extent than the standard hospital care
Peng et al. 116, 2018	RCT	98 patients	Home-based telehealth exercise training program	The results reveal that telehealth exercise training is an effective alternative method for cardiac rehabilitation, especially under the conditions in China
Vernooij et al. 117, 2012	RCT	330 patients	Internet based vascular risk factor management	An internet based, nurse led treatment programme on top of usual care for vascular risk factors had a small effect on lowering vascular risk and on lowering of some vascular risk factors in patients with vascular disease

Jiang et al. 118, 2007	RCT	167 patients	Home-based CR	A cardiac rehabilitation programme led by a nurse can significantly improve the health behaviours and cardiac physiological risk parameters in coronary heart disease patients
Gallagher et al. 119, 2012	RCT	147 patients	Home walking program with pedometer	The HEELP resulted in weight loss and improved exercise behaviour in obese people with CHD and T2DM
Ozemek et al. 120, 2019	RCT	99 patients	Pedometer feedback intervention	The findings from this study demonstrate that using PF was superior to the usual time-based PA recommendations and to newsletter-based MM in patients starting a phase III CR program
Kaminsky et al. 121, 2013	RCT	18 patients	Pedometer step count goals	Providing pedometers with individualized step count goals to patients entering a CR program was superior to the usual time-based PA recommendations for increasing PA
Cupples et al. 122, 2013	Single cohort study	45 patients	Pedometer step count goals	May help increase and sustain PA after CR programme
Pinto et al. 123, 2011	RCT	130 patients	A telephone-based intervention	A telephone-based intervention can help maintain exercise, prevent regression in motivational readiness for exercise, and improve physical functioning in this patient population
Prescott et al. 124, 2019	RCT	1633 patients	Regular CR + mHealth CR	Risk factors and exercise capacity indicate the continued need for cardiac rehabilitation in these patients
Sankaran et al. 125, 2019	RCT	32 patients	HeartHab smartphone application	Persuasive design techniques integrated in HeartHab and tailoring of exercise targets were effective in motivating patients to reach their telerehabilitation targets

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List of meta-analysis on Home rehabilitation of CAD

Author	Design	Studies included	Intervention	Conclusion
Jolly et al. 1, 2006	Meta-analysis	24 studies	Home-based CR	Current evidence does not show home-based cardiac rehabilitation to be significantly inferior to centre-based rehabilitation for low-risk cardiac patients
Taylor et al. 2, 2010	Meta-analysis	12 studies	Home-based cardiac rehabilitation programmes	Home- and centre-based cardiac rehabilitation appear to be equally effective in improving the clinical and health-related quality of life outcomes in acute MI and revascularisation patients
Huang et al. 3, 2015	Meta-analysis	9 trials	Telehealth intervention delivered cardiac rehabilitation	Telehealth intervention delivered cardiac rehabilitation does not have significantly inferior outcomes compared to centre-based supervised program in low to moderate risk CAD patients
Zwisler et al. 4, 2016	Meta-analysis	19 trials	Home-based cardiac rehabilitation	Home-based CR results in short-term improvements in exercise capacity and health-related quality of life of heart failure patients compared to usual care
Rawstorn et al. 5, 2016	Meta-analysis	11 trials	Telehealth exercise-based CR	Telehealth CR appears to be at least as effective as centre-based CR for improving modifiable cardiovascular risk factors and functional capacity
Buckingham et al. 6, 2016	Meta-analysis	17 studies	Home-based cardiac telerehabilitation	Home-based and centre-based CR provide similar benefits in terms of clinical and health-related quality of life outcomes at equivalent cost for those with heart failure and following myocardial infarction and revascularisation

Claes et al. 7, 2017	Meta-analysis	7 studies	Home-based cardiac telerehabilitation	The results showed no significant differences in EC between HB rehabilitation and UC
Wu et al. 8, 2018	Meta-analysis	6 studies	Hybrid CR	Hybrid CR protocols showed comparable efficacy to the traditional model. Further well-designed studies are required to validate these findings, especially regarding the long-term outcomes

1. *Jolly K, Taylor R, Lip G, et al. "Home-based Cardiac Rehabilitation Compared with Centre-based Rehabilitation and Usual Care: A Systematic Review and Meta-analysis." International Journal of Cardiology 111.3 (2006): 343-51. Web.*
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5. *Rawstorn J, Gant N, Direito A, et al. "Telehealth Exercise-based Cardiac Rehabilitation: A Systematic Review and Meta-analysis." Heart (2016): Heart, 2 March 2016. Web.*
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7. *Claes J, Buys R, Budts W, et al. "Longer-term Effects of Home-based Exercise Interventions on Exercise Capacity and Physical Activity in Coronary Artery Disease Patients: A Systematic Review and Meta-analysis." European Journal of Preventive Cardiology 24.3 (2017): 244-56. Web.*
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List of trials on Lifestyle management in secondary prevention

Author	Design	Sample Size	Intervention	Conclusion
Faulkner et al. 1, 2000	RCT	30 patients	Weekly telephone contact by pharmacist for lipid therapy	Short-term telephone follow-up favourably affected compliance and lipid profile results up to 2 years after start of therapy.
Robinson et al. 2, 2000	Single cohort study	2827 patients	Telephone-based computerized system primarily managed by dietitians for lipid control	Whether a patient had LDL cholesterol < or = 100 mg/dl was not predicted by patient characteristics, drugs given, or by medication insurance coverage.
Lear et al. 3, 2001	RCT	49 patients	Long-term management of the lifestyles after CR with telephone	The study identified the challenges of lifestyle intervention and found that favourable risk factor modifications are possible for patients who have completed a CR
Guthrie et al. 4, 2001	RCT (4:1)	13100 patients	Effects of postal and telephone reminders	Results of this study suggest that early telephone and postal reminders do not improve compliance with drug treatment
Allen et al. 5, 2002	RCT	228 patients	Nurse case management of dyslipidaemia	Control of hypercholesterolemia in patients who have undergone coronary revascularization can be improved by a nurse case-management program
Vale et al. 6, 2002	RCT	245 patients	Coaching patients with coronary heart disease	The effectiveness of the coaching intervention is best explained by both adherence to drug therapy and to dietary advice given

Gleason et al. 7, 2002	Single cohort study	35 patients	Home-delivered, heart-healthy meals and snacks, combined with telephone diet education	This program could be a useful additive component to traditional medical nutrition therapy to improve dietary adherence
Gallagher et al. 8, 2003	RCT	196 patients	Telephone counselling	Women at risk for poor outcomes following hospitalization for a cardiac event can be identified
Barnason et al. 9, 2003	RCT	35 patients	Home communication intervention	Data from this pilot study can be used to strengthen the HCI intervention with more tailored strategies for vulnerable subgroups of CABG patients
Lear et al. 10, 2003	RCT	302 patients	Long-term management of the lifestyles after CR with telephone	One-year multi-factorial post-CRP intervention results in modest, non-significant benefits to global risk compared to usual care
Vale et al. 11, 2003	RCT	792 patients	Coaching patients with coronary heart disease via telephone and mailings	Coaching, delivered as The COACH Program, is a highly effective strategy in reducing TC and many other coronary risk factors in patients with coronary heart disease
Southard et al. 12, 2003	RCT	104 patients	Internet-based case management system	An Internet-based case management system could be used as a cost-effective intervention for patients with CVD
Froelicher et al. 13, 2004	RCT	277 patients	Telephone follow-up in smoking cessation	Cognitive behavioural intervention resulted in longer average times to resumption of smoking, but in these 2 groups of older women with limited social and financial resources, long-term success rates were similar

Hansen et al. 14, 2005	Survey	14 patients	Information needs of acute myocardial infarction patients	Most importantly, our participants' follow-up preferences favoured open telephone lines and telephone follow-up
Yates et al. 15, 2005	RCT	64 patients	Educational boosters by telephone	Although the effects of the booster interventions were not significant, there was evidence to suggest that a booster intervention, compared with usual care, had a positive effect on patients' physical functioning
Bambauer et al. 16, 2005	Single cohort study	79 patients	Telephone counselling intervention	Study patients reported greater SRH improvement resulting from the telephone-based intervention compared with control subjects
Holcslaw et al. 17, 2015	Survey	1000 patients	Telephone and mail interventions provided by a clinical pharmacy cardiac risk reduction service	Overall, survey respondents indicated a high level of satisfaction with the services provided by CPCRS. Based upon patient satisfaction, the results of this survey suggest that the use of telephone and mail systems to provide patient care can allow clinical pharmacy specialists to manage a large number of patients successfully
Carroll et al. 18, 2006	RCT	132 patients	Telephone counselling	Although the data did not validate the benefits of these self-efficacy interventions, future efforts at identifying changes in health outcomes may need to use more discrete measurements that are more sensitive to changes in the older unpartnered adult
Lear et al. 19, 2006	RCT	249 patients	Long-term management of the lifestyles after CR with telephone	A modest risk factor and lifestyle management intervention resulted in a significant reduction to global risk compared with usual care and should be considered after CRP
Mittag et al. 20, 2006	RCT	297 patients	Follow-up intervention rendered by telephone	Telephone counselling by specially trained nurses seems a cost-effective way to achieve a lasting reduction in cardiac risk factors and to maintain the effects of cardiac rehabilitation

Lapointe et al. 21, 2006	RCT	127 patients	Systematic telephone follow-up of patients	This trial did not support the role of nurse-managers and a system of telephone-based contacts to ensure the continuity of care and aggressive intervention
Lester et al. 22, 2006	RCT	235 patients	Informatics-based intervention to increase statin prescription	A visit-independent disease management tool resulted in significant improvement in secondary prevention of hyperlipidaemia at 1-month postintervention and showed a trend toward improvement at 1 year
Reid et al. 23, 2006	Single cohort study	1300 patients	Outpatient smoking counselling	Hospitalization for coronary artery disease provides an important opportunity to intervene with smokers when their motivation to quit is high
Hartford et al. 24, 2001	RCT	131 patients	Telephone counselling	Patients' anxiety was moderate to severe the day before discharge. It was significantly lower in the treatment group than in the control group at day 2 at home
Hansen et al. 25, 2007	RCT	288 patients	Telephone counselling	A nurse-led systematic telephone follow-up intervention significantly improved the physical dimension of health-related quality of life in patients in the intervention group compared with usual care patients
Holmes-Rovner et al. 26, 2008	Survey	525 patients	Post discharge telephone counselling	Telephone coaching post-hospitalization for ACS was modestly effective in accomplishing short-term, but not long-term life-style behaviour change
Aldana et al. 27, 2008	Single cohort study	763 patients	Video based education	For individuals empowered to make better choices regarding diet and exercise, significant improvements occurred in most coronary risk factors in as little as 4-6 weeks
Redfern et al. 28, 2009	RCT	144 patients	Telephone counselling	Participation in a brief CHOICE programme significantly improved the modifiable risk profiles and risk factor knowledge of ACS survivors over 12 months

Fernandez et al. 29, 2009	RCT	51 patients	Self-management intervention	Findings support the feasibility of implementing the health-related lifestyle self-management intervention for risk factor modification in patients with acute coronary syndrome
Parry et al. 30, 2009	RCT	95 patients	Individualized education and support via telephone	These preliminary results suggest that peer support may improve recovery outcomes following CABG
Jedinek et al. 31, 2009	RCT	656 patients	Coaching patients with coronary heart disease via telephone and mailings	The changes in CRF status and adherence to cardiac medications achieved at 6 months in The COACH Program are sustained for at least 18 months after cessation of The COACH Program
Schoen et al. 32, 2009	RCT	177 physicians	Internet-delivered continuing medical education (CME) intervention designed to improve care for post-MI patients	Physicians with more post-MI patients and rural practice location were found to predict enrolment in an Internet-delivered continuing medical education (CME) intervention designed to improve care for post-MI patients
Roth et al. 33, 2009	Observational study	699 patients	Telemedicine follow-up	The "SHL" Telemedicine subscribers had significantly higher survival rates at 1 year
Lindsay et al. 34, 2009	RCT	108 patients	Password-protected access to our health portal	This study offers insight into the potential implications for health changes of moderating arrangements for online health communities
Zhao et al. 35, 2009	RCT	200 patients	Structured home visits and telephone follow-ups	Study has constructed a transitional care model for patients with coronary heart disease in the context of the Chinese population which is effective in enhancing healthy lifestyle among these patients

Giallauria et al. 36, 2009	RCT	52 patients	Two-year multicomprehensive secondary prevention program	Long-term, multifactorial educational and behavioural intervention represents a valid strategy for improving cardiovascular risk profile in postinfarction patients
Kerr et al. 37, 2010	Mixed methods investigation	168 patients	Web-based interventions	The availability of a web-based intervention, with support for use at home or through public Internet services, did not result in a large number or all types of patients with CHD using the intervention for self-management support
Chen et al. 38, 2010	RCT	62 patients	Home-based deep-breathing training	Home-based deep-breathing training is effective in reducing depressive symptoms as compared with telephone support in patients with CHD
Ma et al. 39, 2010	RCT	689 patients	Pharmacist-delivered telephone counselling calls	Conclude that a pharmacist-delivered intervention aimed only at improving patient adherence is unlikely to positively affect outcomes
Sinclair et al. 40, 2005	RCT	324 patients	Post-discharge home-based support	Home-based nurse intervention may improve confidence and self-esteem and reduce early hospital readmissions.
Lewin et al. 41, 2002	RCT	142 patients	Self-management	Angina Plan appears to improve the psychological, symptomatic, and functional status of patients newly diagnosed with angina
Neubeck et al. 42, 2011	Mixed methods	66 patients	Internet interventions	Some patients have more confidence using the Internet; therefore, a range of multi-technological secondary prevention interventions should be considered based on individual need

Levine et al. 43, 2011	Cluster RCT	15847 patients	2-year internet-delivered intervention	A longitudinal, Internet-delivered intervention improved only 1 of 7 clinical indicators of cardiovascular management in ambulatory post-MI patients.
Neubeck et al. 44, 2011	RCT	144 patients	Telephone counselling	Participants in CHOICE maintained favourable changes in coronary risk profile at 4 years compared with control, indicating that CHOICE is an effective long-term intervention among those not accessing facility-based CR
Edworthy et al. 45, 2007	RCT	2643 patients	Videos and printed materials, Pharmacist counselling	The intervention program failed to improve outcomes in the present study
Quist-Paulsen, 46, 2003	RCT	240 patients	Telephone follow-up	A smoking cessation programme delivered by cardiac nurses without special training, significantly reduced smoking rates in patients 12 months after admission to hospital for coronary heart disease
Norris et al. 47, 2009	RCT	98 patients	Telephone follow-up	This pilot study demonstrated that early recognition strategies and referral protocols that address mental health needs are effective in decreasing the reported depressive symptomatology of this high-risk population
Harris et al. 48, 2003	Descriptive design	352 patients	Modified CR program in which nurse care managers used telephonic communication	Risk factor management, including testing of serum lipids and achieving goals for lipid reduction, for participants in both CR programs was superior to risk factor management for nonparticipants

Harkness et al. 49, 2005	Retrospective study	3536 patients	Pre-appointment telephone contact	These findings suggest that pre-appointment telephone contact by a cardiovascular nurse is a valuable tool to enhance attendance at a CR intake appointment after CABG
Reid et al. 50, 2012	RCT	141 patients	Motivational telephone counselling	Patients with CAD not participating in cardiac rehabilitation receiving a theory-based motivational counselling intervention were more physically active at follow-up than those receiving usual care
Reid et al. 51, 2012	RCT	223 patients	CardioFit Internet-based expert system	Patients with CHD using an Internet-based activity prescription with online coaching were more physically active at follow up than those receiving usual care
Blasco et al. 52, 2012	RCT	203 patients	Telemedicine service for the secondary prevention	A telemonitoring program, via mobile phone messages, appears to be useful for improving the risk profile in ACS survivors and can be an effective tool for secondary prevention, especially for overweight patients
Turkstra et al. 53, 2013	RCT	430 patients	Telephone-delivered CHD coaching	There was no intervention effect measured using the SF-36/SF-6D and ProActive Heart resulted in significantly increased costs
Meisinger et al. 54, 2013	RCT	340 patients	Nurse-based management	A nurse-based management among elderly patients with AMI had no significant influence on the rate of first unplanned readmissions or death during a one-year follow-up
Mok et al. 55, 2013	RCT	82 patients	Telephone follow-up	This study found positive changes in dietary behaviour and an increase in high-density lipoprotein level from participants who undertook the NFDI for self-management in dietary modification

Hawkes et al. 56, 2013	RCT	130 patients	Telephone-delivered secondary prevention program	Telephone-delivered secondary prevention programs can significantly improve health outcomes and could meet the treatment gap for myocardial infarction patients
Quilici et al. 57, 2013	RCT	499 patients	Motivational mobile phone short message service on aspirin adherence	Results of the present pilot study show that innovative tools, such as daily personalized SMS, improved the rate of antiplatelet intake after stent implantation
Steventon et al. 58, 2013	Matched control study	2698 patients	Telephone health coaching	The Birmingham OwnHealth telephone health coaching intervention did not lead to the expected reductions in hospital admissions or secondary care costs over 12 months, and could have led to increases
Nymark et al. 59, 2013	Matched control study	2698 patients	Telephone health coaching	This difference in costs constituted a 27% reduction in utilization and 22% reduction in cost of secondary care with the OwnHealth program
Rinfret et al. 60, 2013	RCT	300 patients	Telephone follow-up	A simple approach of four telephone calls to patients after DES implantation significantly improved 1-year drug adherence to near-perfect scores
Barley et al. 61, 2014	RCT	126 patients	Nurse-delivered personalized care intervention	Trial and intervention procedures appeared to be feasible and acceptable. PC allowed patients to work on unaddressed problems and appears cheaper than TAU
Mayer-Berger et al. 62, 2014	RCT	600 patients	Regular telephone reminders	This long-term secondary prevention programme with inpatient rehabilitation at the beginning and telephone reminder for a 3-year period was successful

O'Neill et al. 63, 2014	RCT	121 patients	Tele-health program (MoodCare) that integrates depression management into a cardiovascular disease risk reduction program	MoodCare was effective for improving depression in acute coronary syndrome patients, producing effect sizes exceeding those of some face-to-face psychotherapeutic interventions and pharmacotherapy
Forman et al. 64, 2014	Single cohort study	26 patients	Smartphone application	Integrating a mobile care delivery platform into CR was feasible, safe, and agreeable to patients and clinicians
Berndt et al. 65, 2014	RCT	625 patients	Telephone counselling	These findings suggest that intensive counselling is effective in increasing short-term abstinence rates, particularly in patients with lower SES
Yan et al. 66, 2014	RCT	124 patients	Telephone follow-up intervention	This telephone follow-up intervention can result in improved illness perception and lifestyle after MI.
Varnfield et al. 67, 2014	RCT	120 patients	Smartphone-based home care model	This smartphone-based home care CR programme improved post-MI CR uptake, adherence and completion
Cohen et al 68. 2014	RCT	502 patients	Telephone counselling	Compared with conventional care, the House of Education did not result in superior improvement in lifestyle-related cardiovascular risk factors after an acute coronary syndrome
Rollman et al. 69, 2009	RCT	302 patients	Telephone-delivered collaborative care for treating post-CABG depression	Compared with usual care, telephone-delivered collaborative care for treatment of post-CABG depression resulted in improved HRQL, physical functioning, and mood symptoms at 8-month follow-up

Saffi et al. 70, 2014	RCT	74 patients	Face-to-face sessions and telephone contact	Structured and systematic nurse-led lifestyle counselling effectively reduced cardiovascular risk score
Ben-Assa, 71, 2014	Single cohort study	897 patients	Telemedicine	Telemedicine technology shows considerable promise for reducing 30-day readmission rates of post-AMI patients
Schulz et al. 72, 2014	RCT	1733 patients	Web-based computer-tailored lifestyle intervention	Both the sequential and the simultaneous lifestyle interventions were likely to be cost-effective when it concerned the lifestyle factor, whereas the control condition was when it concerned quality of life
Antypas et al. 73, 2014	RCT	69 patients	Longitudinally tailored Internet- and mobile-based intervention for physical activity as an extension of a face-to-face cardiac rehabilitation stay	Results indicate that the tailored version of the intervention may have contributed to the long-term higher physical activity maintained after cardiac rehabilitation
Keyserling et al. 74, 2014	RCT	385 patients	Web-based lifestyle and medication intervention	Both intervention formats reduced CHD risk through 12-month follow-up. The web format was less expensive.
O'Neill et al. 75, 2014	RCT	297 patients	Telephone-delivered health coaching	The ProActive Heart programme effectively improves anxiety outcomes of patients following myocardial infarction
Park et al. 76, 2014	RCT	90 patients	Text messaging intervention to promote medication adherence	TM increased adherence to antiplatelet therapy demonstrated by MEMS and TM responses

Sheridan et al. 77, 2011	RCT	160 patients	Computerized decision aid and automated tailored adherence messages	A computerized intervention that involves patients in CHD decision making and supports adherence to effective prevention strategies can improve adherence and reduce predicted CHD risk
Tranmer et al. 78, 2004	RCT	200 patients	Telephone follow-up intervention	There were no significant group differences in HRQL, unexpected contacts with the health care system, or symptom distress
Kirchberger et al. 79, 2015	RCT	300 patients	A nurse-based management	A nurse-based management among elderly patients with AMI did not significantly affect time to unplanned readmissions or death during a three-year follow-up
Sherrard et al. 80, 2015	RCT	1608 patients	Interactive voice response (IVR) follow-up system	Follow-up by IVR produced positive outcomes in ACS patients
Widmer et al. 81, 2015	Single cohort study	42 patients	Digital Health Intervention	This study suggests that a guideline driven DHI CR program can augment secondary prevention strategies during usual CR by improving risk factors for repeat events
Seidl et al. 82, 2015	RCT	300 patients	A nurse-based management	This study could not provide evidence to conclude that the case management intervention was an effective and cost-effective alternative to usual care within a time horizon of 1 year
Hunger et al. 83, 2015	RCT	300 patients	A nurse-based management	The results of the KORINNA study indicate that nurse-based case management can improve blood lipid levels, functional status, and nutrition risk of aged patients with MI
Chow et al. 84, 2015	RCT	352 patients	Lifestyle-focused text messaging	Among patients with coronary heart disease, the use of a lifestyle-focused text messaging service compared with usual care resulted in a modest improvement in LDL-C level and greater improvement in other cardiovascular disease risk factors

Khonsari et al. 85, 2015	RCT	62 patients	An automated SMS-based reminder system	An automated SMS-based reminder system can potentially enhance medication adherence in ACS patients during the early post-discharge period
Maddison et al. 86, 2015	RCT	171 patients	A mobile phone intervention	A mobile phone intervention was not effective at increasing exercise capacity over and above usual care
Adams et al. 87, 2015	Cluster RCT	120 patients	Brief, structured, telephone tobacco cessation counselling (BST) delivered by clinical pharmacists	BST delivered by clinical pharmacists may not adequately affect patient motivation enough to increase tobacco cessation attempts in tobacco-dependent patients with CVD
Almeida et al. 88, 2015	RCT	452 patients	Interactive Computer Session	A brief, computer-based, interactive personal action planning session may be an effective tool to initiate PA within a health care setting, in particular as part of the ETT system
Ammenwerth et al. 89, 2015	Single cohort study	25 patients	MyCor telemonitoring programme	The MyCor telemonitoring programme Tirol for CHD patients has a high rate of acceptance among included patients
Kurhula et al. 90, 2015	RCT	517 patients	Telemonitoring and Mobile Phone-Based Health Coaching	A health coaching program supported with telemonitoring did not improve heart disease patients' or diabetes patients' quality of life or their clinical condition
O'Neill et al. 91, 2015	RCT	121 patients	Telephone-delivered health coaching	After 12 months, MoodCare was superior to UC for improving mental health outcomes for those with a clinical diagnosis of major depression

Furuya et al. 92, 2015	RCT	60 patients	Telephone follow-up	The educational programme with telephone follow-up is a promising intervention as it led to reduction in anxiety for those receiving the educational programme
Berndt et al. 93, 2016	RCT	625 patients	Telephone counselling	Assuming a willingness-to-pay of €20,000 per abstinent patient, telephone counselling would be a highly cost-effective smoking cessation intervention assisting cardiac patients to quit
Leemrijse et al. 94, 2016	RCT	374 patients	Telephone lifestyle intervention 'Hartcoach'	Hartcoach has modest impact on BMI, waist circumference, physical activity, intake of vegetables, self-management and anxiety
Wong et al. 95, 2016	Observational study	492 patients	Nurse-led, telephone-based, care coordination protocol	Care coordination improved the rate of transition of post-PCI patients to primary care and improved LDL control, with no difference in the rate of hospital admissions due to cardiovascular causes
Du et al. 96, 2016	RCT	964 patients	Telephone follow-ups after discharge	A cardiologist-coordinated intensive follow-up program markedly decreased cardiovascular risk factors, reduced medical costs, promoted medication adherence and improved the long-term prognosis
Fang et al. 97, 2016	Random sampling method	280 patients	Short message service	Short message service and messaging applications, such as Micro Letter, are effective means of providing discharged patients with reminders and coronary artery disease-related health information
Huber et al. 98, 2016	RCT	661 patients	Nurse-led telephone-based follow-up	Nurse-led telephone-based follow-up after ACS can be applied to a large proportion in an unselected clinical setting

Pfaeffli et al. 99, 2016	Pilot study	74 patients	Text messaging	Text messaging was seen as a simple and acceptable way to deliver nutrition information and behaviour change strategies
Alharbi et al. 100, 2016	RCT	134 patients	Telephone follow-up	The Healthy Eating and Exercise Lifestyle Program was an effective programme to achieve and sustain weight loss and increase exercise participation over 1 year
Mertens et al. 101, 2016	Cross-over design	24 patients	Mobile application	Logging data showed a significantly stronger adherence for the medication app than the paper system for both blood pressure recordings
Johnston et al. 102, 2016	RCT	174 patients	Smartphone application	In MI patients, use of an interactive patient support tool improved patient self-reported drug adherence and may be associated with a trend toward improved cardiovascular lifestyle changes and quality of life
Thakkar et al. 103, 2016	RCT	710 patients	Text messaging	The TEXT ME intervention improved recreational and travel physical activity, reduced sedentary times but had no effects on work-related physical activity
Wolf et al. 104, 2016	RCT	199 patients	eHealth Diary and Symptom-Tracking Tool	Found a significant effect on improved general self-efficacy and the composite score for patients using an eHealth diary and symptom-tracking tool in combination with PCC compared with traditional care
Cheng et al. 105, 2016	Markov model		Pedometer-based telephone coaching sessions	The results of this paper provide evidence of the long-term cost-effectiveness of home-based CR interventions for patients who are referred to CR but do not attend

Ho et al. 106, 2014	RCT	253 patients	A multifaceted intervention comprising pharmacist-led medication reconciliation and tailoring, patient education, collaborative care between pharmacist and patients' primary care clinician and/or cardiologist, and voice messaging	A multifaceted intervention comprising pharmacist-led medication reconciliation and tailoring, patient education, collaborative care between pharmacist and patients' primary care clinician and/or cardiologist, and voice messaging increased adherence to medication regimens
Burn et al. 107, 2017	Markov model		Text messaging	The provision of TEXT ME is predicted to lead to better health outcomes and an overall saving in costs for the health system.
Huber et al. 108, 2017	RCT	768 patients	Nurse-led telephone-based follow-up	Nurse-led telephone-based secondary prevention was significantly more efficient at improving LDL-C and diastolic BP levels than usual care
Seidl et al. 109, 2017	RCT	300 patients	A nurse-based management	The case management was cost-neutral and led to an important and significant improvement in health status among survivors
Zhang et al. 110, 2017	RCT	199 patients	Nurse management with telephone follow-up	This study provides evidence for the value of a nurse-led transitional care program using both the Omaha system and Pender's health promoting model as its theoretical framework
Yu et al. 111, 2015	RCT	160 patients	A health education booklet and telephone follow-ups	The study provided clues for healthcare professionals to develop interventions while undertaking clinical work with limited resources in China

Lounsbury et al. 112, 2015	Retrospective analysis	237 patients	Text-messaging	Patients enrolled in OP-CR who participated in a text-messaging program were younger, attended significantly more sessions and were significantly more likely to complete the program
Boroumand et al. 113, 2016	RCT	70 patients	Text-messaging	The text message and telephone follow-up program is effective in promoting the cardiac self-efficacy of patients with CAD.
Prince et al. 114, 2017	RCT	762 patients	Telephone-delivered interventions	FrancoForme is unique in targeting both the primary and secondary prevention of CVD and removes several of the barriers to participating in a conventional CVD prevention program for French-speaking patients
Minneboo et al. 115, 2017	RCT	824 patients	Multiple digital health approaches	Nurse-coordinated referral to a comprehensive set of community-based, widely available lifestyle interventions, with optional partner participation, leads to significant improvements in LRFs
Eyles et al. 116, 2017	RCT	66 patients	Smartphone application	The SaltSwitch smartphone app is effective in supporting people with cardiovascular disease to make lower salt food purchases
Akhu-Zeheya et al. 117, 2017	RCT	160 patients	Text messaging	It is recommended to apply Short Message System (SMS) via cell phone services to improve patient's adherence to a healthy diet and medication
Schwalm et al. 118, 2015	Cluster RCT	852 patients	Delayed Educational Reminders	There was no significant difference compared with usual care in the persistence to guideline-recommended medications post-STEMI

Pandey et al. 119, 2017	2 RCTs	84 patients	Text message reminders	Text message reminders significantly increased adherence to medication and exercise among post-MI patients receiving care in a structured cardiac rehabilitation program
Deighan et al. 120, 2017	Qualitative study	28 participants	The Digital Heart Manual	The Digital Heart Manual is user friendly and accessible to patients and health professionals, regardless of age, presenting a suitable alternative to the paper version
Usher-Smith et al. 121, 2017	Mixed-methods design	36 participants	Web-based intervention	This study shows that the level of engagement with a Web-based intervention is not influenced by the level of risk but by the individual's response to the risk information, their past experiences of behaviour change, the extent to which they consider the lifestyle information helpful, and whether they felt obliged to complete the intervention as part of a research study
Zhang et al. 122, 2017	RCT	80 patients	Smartphone application	This pilot study partially confirmed the positive effects of the SBCHDP programme in improving awareness and knowledge of CHD among the working population
Tang et al. 123, 2018	Quasi-experimental design that included pre- and post-test	94 patients	WhatsApp text messaging	Study concluded that WhatsApp was an effective health intervention in increasing coronary artery disease patient's knowledge and subsequently increasing their adherence to healthy lifestyles
Thakkar et al. 124, 2018	RCT	710 patients	Text-messaging	The study identified TEXT ME text messaging program did not increase use of Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) captured healthcare services

Wallin et al. 125, 2018	Mixed methods	117 participants	Internet-Based Cognitive Behavioural Therapy for Adults With Depression	Patients with a recent myocardial infarction and symptoms of depression and anxiety showed low treatment activity in this guided iCBT intervention with regard to completed modules, completed assignments, and internal messages sent to their therapist
Santo et al. 126, 2018	RCT	710 patients	Text-messaging	A lifestyle-focused text-message programme improved adherence to the dietary guideline recommendations, and specifically improved self-reported consumption of vegetables, fruits, fish, takeaway foods and salt intake
Duan et al. 127, 2018	RCT	136 patients	Web-based intervention for Multiple Health Behaviour Changes	Patients' psychological resources such as motivation, self-efficacy, planning, and social support as well as lifestyle can be improved by a Web-based intervention that focuses on both PA and FVC
Kimble et al. 128, 2018	RCT	39 patients	Self-Management Intervention	Angina symptom monitoring may be more difficult for women. Rehabilitation nurses should be proactive in addressing issues associated with women's AP symptom management
Colella et al. 129, 2018	RCT	185 patients	Telephone peer supported counselling	Healthcare providers need to continue to investigate novel interventions to enhance social support and reduce depression in cardiac patients
Lin et al. 130, 2018	Observational study	43 patients	Internet-based group therapy program using video conference	These results indicated that the Internet-based group therapy program using video conference is feasible and acceptable for the psychosocial rehabilitation of patients with coronary artery heart disease
Dogu et al. 131, 2018	Observational study	120 patients	Web-based Distance Training and Consultancy on Individual's Treatment	Web-based remote training and counselling prepared the individuals after myocardial infarction to the treatment and their well-being in a positive way

Neubeck et al. 132, 2018	RCT	203 patients	Telephone-based tailored risk-factor reduction	The 24-month CHOICEplus program did not confer additional benefit above the brief 3-month CHOICE intervention
Norlund et al. 133, 2018	RCT	239 patients	Internet-based cognitive behavioural therapy (iCBT)	iCBT treatment for an MI population did not result in lower levels of symptoms of depression or anxiety compared with TAU. Low treatment adherence might have influenced the result
Sakakibara et al. 134, 2017	Single cohort study	21 patients	Consumer m-health solution developed to facilitate peer support	Delivery of peer and self-management support using m-health technologies is well received and may improve self-management and social support
Ni et al. 135, 2018	RCT	99 patients	mHealth application for medication reminder	The feasibility of using mHealth to remind CHD patients to take their medications is high
Gallagher et al. 136, 2019	Mixed-methods study	282 patients	Mobile application	Target audience for CHD-specific apps is aged <56 years, employed, has completed high school and is an experienced app user
Zheng et al. 137, 2019	RCT	822 patients	Text messaging	Text messages supporting secondary prevention among patients with coronary heart disease did not lead to a greater reduction in blood pressure at 6 months
Molan et al. 138, 2019	Pre-test post-test design	67 patients	Patient website	The St Vincent's Heart Health website shows real promise as an educational tool for patients, as an adjunct to standard CR and for patients in remote settings
Turan Kavradim et al. 139, 2019	RCT	66 patients	Telephone follow-up	This study demonstrated that education and telephone follow-up intervention based on Roy Adaptation Model was had positive and significant results after 12 weeks compared with usual care

Mols et al. 140, 2019	RCT	294 patients	Nurse-led motivational telephone follow-up	Nurse-led motivational telephone follow-up did not influence adherence to antiplatelet medical therapy after PCI
Tongpeth et al. 141, 2019	RCT	70 patients	Avatar application for teaching	The education app was effective in improving individuals' ACS knowledge, attitudes, and beliefs
Santo et al. 142, 2019	RCT	163 patients	Smartphone application	Patients with CHD who used medication reminder apps had better medication adherence compared with usual care, and using apps with additional features did not improve this outcome further
Reid et al. 143, 2019	RCT	440 patients	Automated telephone follow-up (ATF) and nurse-counselling	TF-mediated follow-up helped smokers with CHD achieve abstinence during the intervention period
Jiang et al. 144, 2019	RCT	112 patients	Nurse-led individualized self-management program (NISMP) with telephone follow-up	The NISMP demonstrated positive effects on health behaviours, control of cardiac risk factors, and HRQoL among Chinese patients with AMI undergoing PCI
Xu et al. 145, 2019	RCT	240 patients	Clinical pharmacist intervention with telephone follow-up	Clinical pharmacist intervention had no significant effects on reduction in cardiovascular events among patients with CHD
Davis et al. 146, 2019	Single cohort study	9 patients	Telephone reinforcements for symptom recognition	The nurse-delivered intervention was feasible and acceptable to women in the study. Results support further testing and refinement of the intervention in a longitudinal randomized control study to determine efficacy and sustainability

Devi et al. 147, 2014	RCT	94 patients	Internet-based secondary prevention intervention	An Internet-based secondary prevention intervention could be offered to those with angina
Wang et al. 148, 2018	RCT	129 patients	4-week home-based self-help psychoeducation program	This study did not find any significant effect of our program on outpatients with coronary heart disease
Wang et al. 149, 2016	RCT	128 patients	Home-based self-management programme	The study may provide a useful tool to help health care professionals to meet the cardiac rehabilitative care needs of community-dwelling patients with myocardial infarction in Singapore
Gallagher et al. 150, 2017	Survey	282 patients	Mobile Technology Use	Mobile technology offers an important opportunity to improve access to secondary prevention for cardiac patients, particularly when modified to suit subgroups
Park et al. 151, 2015	Single cohort study	90 patients	Text messaging	TM medication reminders and/or health education did not improve medication self-efficacy
Yehle et al. 152, 2012	Qualitative study	27 participants	Web-based and mobile-based nutrition tools	Food for the Heart and MML may be tools that CHD patients would value in making food choices and adhering to dietary recommendations, especially if additional features are added to assist patients with changes
Sequist et al. 153, 2005	RCT	2199 patients	Electronic Clinical Reminders	An integrated electronic reminder system resulted in variable improvement in care for diabetes and CAD. These improvements were often limited, and quality gaps persist
Schweier et al. 154, 2014	Sequential controlled trial	571 patients	A web-based peer-modelling intervention	Usage of the lebensstil-aendern website corresponds to more positive lifestyle changes.

Mohammady et al. 155, 2011	Experimental design	117 patients	Comparing Computer-assisted vs. Face to Face Education	Both computer-assisted and face to face educational strategies had positive effects on improving adherence following myocardial infarction
Barnason et al. 156, 2009	RCT	232 patients	Symptom management telehealth intervention	Subjects were able to return to preoperative levels of functioning between 3 and 6 months after CABS and to increase their physical activity over reported preoperative levels of activity

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List of meta-analysis on telehealth in secondary prevention of CAD

Author	Design	Studies included	Digital Intervention	Conclusion
Neubeck et al. 1, 2009	Meta-analysis	11 trials	Telehealth	Telehealth interventions provide effective risk factor reduction and secondary prevention
Clark et al. 2, 2010	Meta-analysis	39 trials	Home-based secondary prevention programs	Home-based secondary prevention programs for CHD are an effective and relatively low-cost complement to hospital-based cardiac rehabilitation and should be considered for stable patients less likely to access or adhere to hospital-based services
De Waure et al. 3, 2012	Meta-analysis	5 trials	Telemedicine for the reduction of myocardial infarction mortality	Telemedicine may improve health outcomes of patients with AMI.
Kotb et al. 4, 2014	Meta-analysis	26 trials	Telephone Support Interventions	Compared to standard post-discharge care, regular telephone support interventions may help reduce feelings of anxiety and depression as well as, improve systolic blood pressure control and the likelihood of smoking cessation
Gandhi et al. 5, 2017	Meta-analysis	27 trials	Mobile Health Interventions	mhealth group compared with the usual care group had increased adherence to medical therapy, ability to reach blood pressure targets, exercise goals, and showed less anxiety and increased awareness of diet and exercise
Jin et al. 6, 2019	Meta-analysis	30 trials	Telehealth interventions for the secondary prevention	Telehealth interventions with a range of delivery modes could be offered to patients who cannot attend cardiac rehabilitation, or as an adjunct to cardiac rehabilitation for effective secondary prevention

Coorey et al. 7, 2019	Meta-analysis	10 trials	Mobile applications for cardiovascular disease self-management	Multiple behaviours and cardiovascular disease risk factors appear modifiable in the shorter term with use of mobile apps
McClure et al. 8, 2013	Meta-analysis	8 trials	Home-based secondary prevention programs	This meta-analysis provides evidence that home-based secondary prevention programs are effective in reducing anxiety level in CAD patients
Devi et al. 9, 2015	Meta-analysis	11 studies	Internet-based interventions for the secondary prevention	Effects on healthcare utilisation and cost-effectiveness are also inconclusive, and trials are yet to measure the impact of Internet interventions on compliance with medication
Adler et al. 10, 2017	Meta-analysis	7 studies	Mobile phone text messaging	While the results of this systematic review are promising, there is insufficient evidence to draw conclusions on the effectiveness of text message-based interventions for adherence to medications for secondary prevention of CVD
Su et al. 11, 2019	Meta-analysis	14 studies	eHealth cardiac rehabilitation	Health cardiac rehabilitation is effective in engaging patients in active lifestyle, improving quality of life and reducing re-hospitalization

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Annex 3: Digital health in heart failure management

List of trials on Telemonitoring and home care

Author	Design	Sample Size	Intervention	Conclusion
Hohmann et al. 1, 2019	Single cohort study	9 patients	Telemonitoring-capable LVAD	Real-time telemonitoring of LVAD pump flow, motor speed and power consumption is a promising tool in the follow-up of LVAD recipients.
Chaudry et al. 2, 2010	RCT	1653 patients	Telemonitoring was accomplished by means of a telephone-based interactive voice-response system	Among patients recently hospitalized for heart failure, telemonitoring did not improve outcomes.
Verdejo et al. 3, 2007	Single cohort study	12 patients	New heart failure (HF) sensor (HFS)	The HFS provides an accurate method for PAP assessment in the intermediate follow-up of HF patients.
Goldberg et al. 4, 2003	RCT	280 patients	Daily electronic home monitoring system	Despite no difference in the primary end point of rehospitalization rates, mortality was significantly reduced for patients randomized to the AlereNet system without an increase in utilization, despite specialized and aggressive heart failure care in both groups.
Cleland et al. 5, 2005	RCT	426 patients	Home telemonitoring (HTM)	Further investigation and refinement of the application of HTM are warranted because it may be a valuable role for the management of selected patients with heart failure.

Galbreath et al. 6, 2004	RCT	1069 patients	Disease management (DM) programs	Participation in DM resulted in a significant survival benefit, most notably in symptomatic systolic HF patients.
Mejhert et al. 7, 2004	Single cohort study	208 patients	Nurse based outpatient management programme	A nurse-based management programme is more effective than follow up in primary care in optimising medication for elderly patients with heart failure
O'Connell et al. 8,	Single cohort study	32 patients	Multidisciplinary disease management programs	Multidisciplinary heart failure program can improve functional status and reduce hospitalization and net costs compared with conventional care
Krumholz et al. 9, 2002	RCT	88 patients	Multidisciplinary disease management programs	A formal education and support intervention substantially reduced adverse clinical outcomes and costs for patients with HF.
Herschberger et al. 10, 2001	Single cohort study	108 patients	Outpatient heart failure management program	Our study shows the effectiveness of this heart failure outpatient management program.
Doughty et al. 11, 2002	RCT	197 patients	Integrated heart failure management	This integrated management programme for patients with chronic heart failure improved quality of life and reduced total hospital admissions and total bed days
Nanevicz et al. 12, 2000	Single cohort study	50 patients	Home telemonitoring system	This pilot study suggests that home telemonitoring is feasible and has clinical utility in diverse patient groups
Johnston et al. 13, 2000	RCT	212 patients	Remote video technology in the home health care	Remote video technology in the home health care setting was shown to be effective, well received by patients, capable of maintaining quality of care, and to have the potential for cost savings.

Hughes et al. 14, 2000	RCT	1966 patients	Team-Managed Home-Based Primary Care	The TM/HBPC intervention improved most HR-QoL measures among terminally ill patients and satisfaction among non-terminally ill patients.
De Lusignan et al. 15, 2001	Single cohort study	20 patients	Home telemonitoring	Home telemonitoring is an acceptable reliable intervention.
Jenkins et al. 16, 2001	Single cohort study	28 patients	Telemedicine technology	Both nurses and patients reported the need to have real nurse home visits along with telemedicine visits.
Stewart et al. 17, 2002	RCT	297 patients	Home-based intervention in congestive heart failure	The beneficial effects of HBI in reducing frequency of unplanned readmissions in CHF patients persist in the long term and are associated with prolongation of survival.
Blue et al. 18, 2001	RCT	165 patients	Specialized heart failure nurses	Specially trained nurses can improve the outcome of patients admitted to hospital with heart failure.
Stewart et al. 19, 2002	RCT	90 patients	Multidisciplinary, home-based intervention (HBI)	Post-discharge HBI is an important means for identifying and addressing early clinical deterioration
Artinian et al. 20, 2003	Single cohort study	18 patients	Web-based home care monitoring	These are promising pilot results that, if replicated in a larger sample, may significantly improve care and outcomes for patients with heart failure.
Vavouranakis et al. 21, 2003	Single cohort study	33 patients	Home-based intervention	Intensive home care of middle-aged patients with severe heart failure results in improved quality of life and a decrease in hospital readmission rates.

LaFramboise et al. 22, 2003	Single cohort study	95 patients	In-home telehealth communication device	These findings suggest that delivering a disease management program through a telehealth communication device is feasible and may be as effective as traditional methods.
Jerant et al. 23, 2001	RCT	37 patients	1) home telecare delivered via a 2-way video-conference device with an integrated electronic stethoscope; 2) nurse telephone calls; and 3) usual outpatient care.	Substantial reductions in hospital readmissions, emergency visits, and cost of care for patients with CHF might be achieved by widespread deployment of distance technologies to provide posthospitalization monitoring.
Scalvini et al. 24, 2005	RCT	426 patients	Trans-telephonic follow-up and electrocardiogram (ECG) monitoring	The results suggest that a telecardiology service can detect and prevent clinical instability, reduce rehospitalization and lower the cost of managing CHF patients.
Moyer-Knox et al. 25, 2004	Single cohort study	70 patients	Remote titration	The use of advanced practice nurses, titration protocols, and tele management technologies may improve the number of HF patients initiated and treated with appropriate doses of BB.
Roth et al. 26, 2004	Single cohort study	118 patients	Novel trans telephonic monitoring and follow-up program	Data are provided to demonstrate that a trans telephonic system allowing primary care at the patient's home can significantly reduce hospitalization rate
Finkelstein et al. 27, 2004	Survey	53 patients	Telehomecare	These programs can provide timely and quality home health nursing care with VVs augmenting traditional home visits.

Noel et al. 28, 2004	Single cohort study	104 patients	Home telehealth	Integrating home telehealth with the healthcare institution's electronic database significantly reduces resource use and improves cognitive status, treatment compliance, and stability of chronic disease for homebound elderly with common complex co-morbidities.
Capomolla et al. 29, 2004	RCT	133 patients	A telemonitoring service (TMS)	A management program delivered by a TMS can reduce health care demands by CHF patients.
Laramee et al. 30 ,2003	Single cohort study	287 patients	Early discharge planning, patient and family CHF education, 12 weeks of telephone follow-up, and promotion of optimal CHF medications.	These results suggest several limitations to the generalizability of the CHF CM-improved outcome link in a heterogeneous setting.
Riegel et al. 31, 2002	RCT	458 patients	Standardized telephonic case-management intervention	The reduction in hospitalizations, costs, and other resource use achieved using standardized telephonic case management in the early months after a heart failure admission is greater than that usually achieved
DeWalt et al. 32, 2004	Single cohort study	25 patients	Disease management program	A heart failure disease management program designed specifically for patients with low literacy skills is acceptable and is associated with improvement in self-care behaviour
Feldmann et al. 33, 2004	RCT	371 patients	Community-based home health care	The intervention was associated with a marginally significant reduction in the volume of skilled nursing visits (p = .074), and a reduction variation in the typical number of visits provided

Berg et al. 34, 2004	Concurrent matched-cohort study	533 patients	Disease-management heart failure program	The study demonstrates that a commercially delivered heart failure disease-management program significantly reduced hospitalizations, emergency department visits, and SNF days.
Scalvini et al. 35, 2005	Single cohort study	230 patients	Home telenursing	Home telenursing could be an important application of telemedicine and single-lead ECG recording seems to offer additional benefit in comparison with telephone follow-up alone.
Hudson et al. 36, 2005	Single cohort study	91 patients	Remote physiological monitoring (RPM)	The results indicate that RPM, as a component of a traditional disease management program, has a sustained, beneficial effect on participants' lifestyles after the monitoring period has ended.
Bertoli et al. 37, 2005	Single cohort study	2 patients	Home peritoneal ultrafiltration	After at least 12 months of treatment, we observed a significant improvement in quality of life and a reduction in morbidity and hospitalization in both patients.
DeBusk et al. 38, 2005	RCT	462 patients	Nurse care management provided structured telephone surveillance	Among patients with heart failure at low risk on the basis of sociodemographic and medical attributes, nurse care management did not statistically significantly reduce rehospitalizations
McDonald et al. 39, 2002	RCT	98 patients	Multidisciplinary care (MDC)	These data demonstrate for the first time the intrinsic benefit of MDC in the setting of protocol-driven, optimal medical management of HF.
Ledwidge et al. 40, 2003	RCT	98 patients	Multidisciplinary care (MDC)	MDC of HF remains cost-beneficial when combined with optimal, medical care.
Azevedo et al. 41, 2002	Single cohort study	339 patients	Multidisciplinary care (MDC)	The results support the fact that a multidisciplinary and permanently available medical staff might be of relevance in improving outcomes in HF patients.

Akosah et al. 42, 2002	Chart review	111 patients	Disease management program	A comprehensive disease management program for patients discharged with a diagnosis of CHF resulted in fewer rehospitalizations
Ramahi et al. 43, 2000	Single cohort study	133 patients	Specialized heart failure care	Care of patients with CHF in a specialized heart failure program was associated with significant increase in the utilization and doses of all beneficial cardiovascular drugs
Holst et al. 44, 2001	Single cohort study	42 patients	Comprehensive management program (CMP)	A CMP improves QOL and exercise capacity as well as substantially reducing hospital admissions in CHF pts.
Avlund et al. 45, 2009	Single cohort study	149 patients	Comprehensive Follow-up Home Visits	The results point at a need for the expertise of the interdisciplinary geriatric team in preparation of discharge among special groups of patients
Steward et al. 46, 2002	Cost-analysis		Specialist heart failure nurse management	Our findings suggest that such a service will not only improve quality of life and reduce readmissions in patients with congestive heart failure, but also reduce costs
Thompson et al. 47, 2005	RCT	106 patients	Hybrid program of clinic plus home-based intervention	Its beneficial effects on recurrent readmission and event-free survival are consistent with those applying either a home or clinic-based approach.
Schofield et al. 48, 2005	Single cohort study	92 patients	In-home telehealth message device	Our nurse-directed, care coordinated home telehealth management program was associated with improved early outcomes in a group of elderly male veterans with chronic HF.
Bradford et al. 49, 2005	Single cohort study	366 patients	Telemedicine	We find that patient willingness to pay has the expected negative relationship between price and the likelihood of purchase and that patients with CHF are less responsive to price changes than those with hypertension.

Kashem et al. 50, 2006	RCT	36 patients	Web-based Internet telemedicine	Surveillance through Internet-based telemedicine resulted in less hospitalization compared to control patients
Spaeder et al. 51, 2006	RCT	49 patients	Automated telemedicine system named TeleWatch (TW)	Remote monitoring with an automated telemedicine system can successfully facilitate titration of carvedilol in outpatients with New York Heart Association class II and III congestive heart failure.
Delgado et al. 52, 2003	Single cohort study	16 patients	Internet-based communication	Internet-based communication is a feasible tool for the management of heart failure patients, providing an effective medium through which health care professionals can interact with their patients.
Lopez Cabezas et al. 53, 2006	RCT	134 patients	Active telephone follow-up	Postdischarge pharmaceutical care allows for reducing the number of new admissions in patients with heart failure, the total days of hospital stay, and improves treatment compliance
Kasper et al. 54, 2002	RCT	200 patients	Multidisciplinary care in heart failure outpatients	This study demonstrates that a six-month, multidisciplinary approach to CHF management can improve important clinical outcomes at a similar cost
Inglis et al. 55, 2006	RCT	297 patients	Nurse-led, multidisciplinary, home-based intervention	HBI is a remarkably cost- and time-effective strategy over the longer term.
Lehmann et al. 56, 2006	RCT	20 patients	Telehealth	The findings demonstrated that patients managing their CHF via telehealth technology decreased their overall utilization of healthcare resources

Kimmelstiel et al. 57, 2004	RCT	200 patients	Disease management program	In a population with high background use of standard HF therapy, a DM intervention, uniformly delivered across varied clinical sites, produced significant short-term improvement in HF-related clinical outcomes
Ojeda et al. 58, 2005	RCT	153 patients	Disease management program	The positive effects of an intervention programme are clearly reduced when it is stopped, due to less strict control of the patients and a decrease in the use of drugs with proven efficacy in HF.
Atienza et al. 59, 2004	RCT	174 patients	Disease management program	This comprehensive hospital discharge and outpatient management program prolonged time to first event, reduced hospital readmissions, improved survival and quality of life of patients hospitalized for HF, while reducing cost of management.
Scalvini et al. 60, 2004	RCT	438 patients	Telecardiology system	These preliminary data suggest the applicability and the efficacy of both management models for CHF patients.
Wierzchowiecki et al. 61, 2006	RCT	160 patients	Telephone counselling and home-based interventions	The one-year multidisciplinary care programme for patients with chronic heart failure in Poznań demonstrated significant improvement of treatment results in terms of frequency of readmissions and length of hospital stay as well as improved QoL.
DeWalt et al. 62, 2006	RCT	123 patients	Picture-based educational materials, a digital scale, and scheduled telephone follow-up	A primary care-based heart failure self-management program designed for patients with low literacy reduces the risk of hospitalizations or death.
Fragasso et al. 63, 2007	Single cohort study	50 patients	Videophone-based method, employing an electronic stethoscope	Remote cardiopulmonary examination appears as a feasible method for assessing patients with heart failure

Del Sindaco et al. 64, 2007	RCT	173 patients	Home-based (patient's general practitioner visits) care	A hybrid DMP for elderly heart failure patients improves outcomes and is cost-effective over a long-term follow-up.
Ho et al. 65, 2007	Single cohort study	247 patients	Home- and clinic-based caring system	The home- and clinic-based caring system is capable of decreasing adverse outcomes, most notably hospitalization and length of stay, and could trigger significant cost savings in the management of heart failure.
Riegel et al. 66, 2006	RCT	134 patients	Telephone case management	Although disease management is effective in the mainstream HF patient population, in Hispanics this ill, elderly, and poorly educated, a different approach may be needed.
Dunagan et al. 67, 2005	RCT	151 patients	Telephone case management	A nurse-administered, telephone-based disease management program delayed subsequent health care encounters but had minimal impact on other outcomes.
GESICA investigators. 68, 2005	RCT	1518 patients	Telephone case management	This simple, centralised heart failure programme was effective in reducing the primary end point through a significant reduction in admissions to hospital for heart failure.
Holland et al. 69, 2007	RCT	293 patients	Home based intervention in heart failure patients.	This community pharmacist intervention did not lead to reductions in hospital admissions in contrast to those found in trials of specialist nurse led interventions in heart failure.
Whitten et al. 70, 2007	RCT	161 patients	Home based intervention in heart failure patients.	In regard to patient perceptions of home telecare, patients were satisfied with the technology and the way that care was delivered via this modality.
Pinna et al. 71, 2007	RCT	461 patients	Home telemonitoring of vital signs	This study, the largest so far, demonstrates that self-managed home telemonitoring of both vital signs and respiration is feasible in HF patients

Gambetta et al. 72, 2007	Double cohort study	282 patients	Self-directed tele management component	The results of the present study indicate that tele management is an important component of a disease management program in patients with HF.
Schwarz et al. 73, 2008	RCT	102 dyads	Telemonitoring	There were no significant differences due to telemonitoring for any outcomes.
Morguet et al. 74, 2008	Single cohort study	540 patients	Home-based telemedicine service programme	These data suggest that telemedicine may benefit patients following repeat percutaneous coronary intervention or cardioversion for atrial fibrillation.
Triller et al. 75, 2007	Single cohort study	154 patients	A home-based pharmaceutical care model	A home-based pharmaceutical care model for recently hospitalized patients with heart failure did not significantly improve the combined rate of death or rehospitalization.
Kashem et al. 76, 2008	RCT	48 patients	Internet-based telemedicine system.	Frequent monitoring and patient management using a telemedicine system may help to reduce hospitalizations, hospital days, and emergency department visits.
Wakefield et al. 77, 2008	RCT	28 patients	Telephone (n=14) and videophone (n=14) interactions	The results of this study did not support use of a videophone over the telephone.
Rondinini et al. 78, 2008	Single cohort study	44 patients	Nurse-led domiciliary intervention	The present study demonstrates that a domiciliary-based strategy in elderly patients affected by heart failure guarantees clinical stability and reduces hospitalizations as well as outpatient visits.
Balk et al. 79, 2008	Single cohort study	44 patients	Home TV-channel providing educational materials	Tele-guidance may play a role in the management of heart failure patients since it takes over some of the tasks of HF-nurses.

Antonicelli et al. 80, 2008	RCT	57 patients	Home telemonitoring	The improved results with home telemonitoring in CHF were probably due to better compliance and to closer monitoring of the patients.
Morguet et al. 81, 2008	Matched- control study	128 patients	Home telemonitoring	These preliminary data suggest that telemedical care and monitoring may reduce morbidity in patients with NYHA class II and III chronic heart failure.
Dansky et al. 82, 2008	Single cohort study	284 patients	Telehomecare	Results show a greater reduction in symptoms for patients using telehomecare compared to control patients.
Shah et al. 83, 2008	Single cohort study	130 patients	Telehomecare	More than a third of clinician time was spent on calls, during which >50% of patient contacts and HF education and >39% of diuretic adjustments occurred.
Patel et al. 84, 2008	RCT	31 patients	Telehomecare in early discharge	Reduction in cost of care for selected patients with CHF eligible for hospital care might be achieved by early discharge from hospital followed by home visits.
Nahm et al. 85, 2008	Single cohort study	44 patients	eHealth program that includes both telemonitoring and motivational components	The findings showed the participants' high readiness to use the proposed eHealth program if access and training were provided.
Myers et al. 86, 2006	Matched- control study	166 patients	Home-based telemonitoring	Daily home care telemonitoring reduced the frequency of home nursing visits, provided cost savings, and was associated with improved self-perceived quality of life.
Schmidt et al. 87, 2008	Single cohort study	62 patients	Medication telemonitoring	Medication telemonitoring might prove an effective method to improve medication intake and health in home care in a subset of patients with self-reported noncompliance.

Kwok et al. 88, 2008	RCT	105 patients	Home care	Community nurse-supported post-discharge programme was effective in preserving independence and was probably effective in reducing the number of unplanned re-admissions.
Dar et al. 89, 2009	RCT	105 patients	Home telemonitoring	Home telemonitoring in a typical elderly population of heart failure patients produces a similar outcome to 'usual' specialist care
Whitten et al. 90, 2009	Survey	50 patients	Home telemonitoring	Patients found the service easy to use and perceived the care they received via telehealth to be as good as regular in-person care.
Wakefield et al. 91, 2009	RCT	148 patients	Home telemonitoring	The intervention group patients were more likely to have had their medications adjusted during the 90-day intervention period.
Giordano et al. 92, 2009	RCT	460 patients	Home-based tele management (HBT) programme	This study suggests that one-year HBT programme reduce hospital readmissions and costs in CHF patients.
Laframboise et al. 93, 2009	Survey	13 patients	Home-based tele management (HBT) programme	Telehealth, a cost-effective way to promote improved health management, is suitable to most patients.
Ramaekers et al. 94, 2009	Sub analysis of RCT	111 patients	Home-based tele management (HBT) programme	Adherence in terms of fluid restrictions ($p = 0.012$), daily weighing ($p < 0.001$), physical exercising ($p = 0.034$), and alcohol restrictions ($p = 0.040$) improved significantly in the telemonitoring group.
Tomita et al. 95, 2009	RCT	40 patients	A secure and simple web-based recording system of vital signs	An effective program to change one’s behaviours in managing HF takes a multidisciplinary approach to create and provide

			and health behaviours and a mechanism for feedback	
Mortara et al. 96, 2009	RCT	461 patients	Home-based tele management (HBT) programme	Home or Hospital in Heart failure indicates that self-managed HT of clinical and physiological parameters is feasible in HF patients, with surprisingly high compliance.
Bowles et al. 97, 2009	RCT	313 patients	Telephone intervention (Telephone), and in-person visits vs. telemonitoring (Telemonitoring)	During the first 60 days, 10% of the Control group were rehospitalised, 17% of the Telephone group and 16% of the Telemonitoring group. Having heart failure and receiving more in-person visits were significantly related to readmission and time to readmission.
Kulshreshtha et al. 98, 2010	RCT	150 patients	Remote monitoring (RM) of homebound heart failure (HF)	This pilot study demonstrates that RM can be successfully implemented in non-homebound HF patients and may reduce readmission rates.
Maric et al. 99, 2010	Single cohort study	17 patients	Telemonitoring	A Web site that facilitates the telemonitoring of patients with HF was favourably accepted and its use in this pilot study was associated with improved self-care skills.
Delaney et al. 100, 2010	RCT	24 patients	Multicomponent home care intervention	This pilot study suggests that a full-scale trial of the HEART intervention is feasible.
Hebert et al. 101, 2010	RCT		Nurse-led disease management intervention	Over 12 months, the nurse-led disease management program was a reasonably cost-effective way to reduce the burden of heart failure in this community.
Antonicelli et al. 102, 2010	RCT	57 patients	Home patient telemonitoring	This study showed that a home-care model including telemonitoring of relevant clinical parameters may provide useful support in the management of patients with CHF.

McManus et al. 103, 2004	Observational study	60 patients	Home patient telemonitoring	In light of the rapidly increasing number of older patients living longer with chronic diseases, financial concerns, and the nursing shortage, telehealth contacts are a promising tool for maximizing resources, controlling costs, and improving multidisciplinary management of chronic diseases.
Woodend et al. 104, 2008	RCT	249 patients	Home patient telemonitoring	Telehealth technologies are a viable means of providing home monitoring to patients with heart disease at high risk of hospital readmission to improve their functional status and quality of life
Seibert et al. 105, 2008	RCT	147 patients	In-home telemedicine education and monitoring program	Telemedicine applications that allow specialists to view and communicate with patients remotely may help improve outcomes.
Chen et al. 106, 2010	RCT	550 patients	Home-based telephone intervention	These results suggest that the home-based intervention with nursing specialist-led telephone consultations may improve the clinical outcome and provide cost-savings for Chinese patients with heart failure.
Wade et al. 107, 2011	RCT	318 patients	Telemonitoring with case management	Despite effective implementation of an Internet-based telehealth intervention in an elderly HF population, there was no discernible impact on overall morbidity or mortality.
Boyne et al. 108, 2011	RCT	382 patients	Telemonitoring	No significant differences were found regarding the primary endpoint, possibly caused by a relative underpowering of the population combined with well-treated study groups.
Koehler et al. 109, 2011	RCT	710 patients	Remote telemedical management used portable	In ambulatory patients with chronic HF, RTM compared with usual care was not associated with a reduction in all-cause mortality.

			devices for ECG, blood pressure, and body weight	
Katra et al. 110, 2011	Single cohort study	180 patients	External multi-sensor system applied to the chest	This proof-of-concept study suggests that a chronotropic response that may be functionally debilitating during activities of daily living in HF patients can be detected and tracked in a point-of-care telemonitoring approach using a non-invasive, adherent device.
Giordano et al. 111, 2011	Single cohort study	358 patients	6-month home-based tele management (HBT)	Our experience confirms that HBT for patients with CHF is associated with favourable effects on hospital readmission for cardiovascular reasons
Konstam et al. 112, 2011	RCT	188 patients	Automated home monitoring (AHM) system	AHM and noAHM treatments demonstrated improved HRQL scores at 45 and 90 days after baseline assessment.
Adlbrecht et al. 113, 2011	RCT	190 patients	Home-based nurse care (HNC) and a HNC group in which decision-making was based on NT-proBNP levels (BNC)	NT-BNP-guided heart failure specialist care in addition to home-based nurse care is cost effective and cheaper than standard care, whereas HNC is cost neutral.
Lynga et al. 114, 2011	RCT	344 patients	Daily electronic transmission of body weight	Daily electronic transmission of body weight and monitoring three times a week did not decrease hospitalization or death in HF patients followed up at a HF clinic.
Pekmezaris et al. 115, 2011	RCT	168 patients	Remote patient monitoring (RPM)	RPM, when utilized in conjunction with a robust management protocol, was not found to significantly differ from live nursing visits in the management of HF in home care.
Boyne et al. 116, 2011	RCT	382 patients	Telemonitoring	Tailored telemonitoring was found to educate patients with HF and to improve their self-care abilities and sense of self-efficacy.

Thokala et al. 117, 2013	Markov model		Structured telephone support (STS) via human to machine (STS HM) interface, (2) STS via human to human (STS HH) contact and (3) home telemonitoring (TM), compared with (4) usual care.	Cost-effectiveness analyses suggest that TM was an optimal strategy in most scenarios, but there is considerable uncertainty in relation to clear descriptions of the interventions and robust estimation of costs.
Gellis et al. 118, 2012	RCT	102 patients	Telehealth care	Telehealth may be an efficient and effective method of systematically delivering integrated care in the home health sector.
Stewart et al. 119, 2012	RCT	280 patients	Home-based intervention (HBI)	HBI was not superior to CBI in reducing all-cause death or hospitalization.
Soreca et al. 120, 2012	Single cohort study	118 patients	Home echocardiographic examinations	Home echocardiography for monitoring of CHF patients does not improve the cardiovascular endpoints.
Austin et al. 121, 2012	Single cohort study	60 patients	Interactive voice response system (IVRS) with daily self-management and clinical monitoring messages	An IVRS self-management support system can be an effective technology to reduce CHF readmissions.
Domingo et al. 122, 2012	RCT	97 patients	Telemedicine program in a HF Unit.	Less than half of our patients participated in the telemedicine study. However, those who completed the study had confidence in the system, a high degree of satisfaction with the tools and positive behavioural changes.

Dendale et al. 123, 2012	RCT	160 patients	Telemonitoring-facilitated collaboration between general practitioner and heart failure clinic	Telemonitoring-facilitated collaboration between GPs and a heart failure clinic reduces mortality and number of days lost to hospitalization, death, or dialysis in CHF patients.
Lemay et al. 124, 2013	Single cohort study	594 patients	Home telemonitoring	Thus, in the telemonitoring programme, the pattern of usage by older patients was similar to that of the younger ones.
Prescher et al. 125, 2013	Survey	288 patients and 102 physicians	Telemedical care	RM will be a medical care concept for recently hospitalized HF- patients in the near future but the optimal telemedical setting of RM and the duration of this intervention have to be defined in further clinical trials.
Jehn et al. 126, 2013	Single cohort study	155 patients	Tele-accelerometry	Tele-accelerometry is feasible in patients with CHF and output parameters are indicative of exercise capacity.
Maisel et al. 127, 2013	Multicentre, single-arm, double-blinded observational prospective clinical trial	163 patients	Monitor daily concentrations of B-type natriuretic peptide (BNP)	This pilot study demonstrates that home BNP testing is feasible and that trials using home monitoring for guiding therapy are justifiable in high-risk patients.
Weintraub et al. 128, 2010	RCT	188 patients	Automated home monitoring and telephonic disease management	Short-term reductions in the heart failure hospitalization rate were associated with the use of automated home monitoring equipment.

Naylor et al. 129, 2004	RCT	239 patients	A 3-month APN-directed discharge planning and home follow-up protocol.	A comprehensive transitional care intervention for elders hospitalized with heart failure increased the length of time between hospital discharge and readmission or death, reduced total number of rehospitalizations
Soran et al. 130, 2008	RCT	315 patients	Computer-Based Telephonic Monitoring System	Our study results suggest that enhanced patient education and follow-up is as successful as a sophisticated home monitoring device with an interactive program in patients with HF
Berger et al. 131, 2010	RCT	278 patients	N-terminal pro-B-type natriuretic peptide-guided, intensive patient management	Compared with MC alone, additional BM improves clinical outcome in patients after HF hospitalization.
Barker et al. 132, 2012	RCT	120 patients	Pharmacist directed home medication reviews	Post-discharge pharmacy directed home medication review appeared to have no effect on mortality and health care utilisation above that achieved with standard care.
Piette et al. 133, 2008	Single cohort study	52 patients	Augmenting HF care management with weekly, automated assessment and behaviour change calls to patients, feedback via the Internet to an out-of-home informal caregiver or CarePartner (CP)	The CP program may extend the impact of HF telemonitoring beyond what care management programs can realistically deliver.
Sisk et al. 134, 2006	RCT	406 patients	Nurse Management	Nurse management can improve functioning and modestly lower hospitalizations in ethnically diverse ambulatory care patients who have heart failure with systolic dysfunction.

Ross et al. 135, 2004	RCT	107 patients	Web-based online medical record	providing patients with congestive heart failure access to an online medical record was feasible and improved adherence.
Fairbrother et al. 136, 2014	Survey	18 patients	Telemonitoring for chronic heart failure	Although popular with patients, professionals emphasised the importance of case selection and adequate training and support, both for patients and themselves, in order to maximise the expected benefits of the service, particularly with regard to enabling self-management.
Tsuyki et al. 137, 2004	RCT	276 patients	Education about HF, self-monitoring, adherence aids, newsletters, telephone hotline, and follow-up at 2 weeks, then monthly for 6 months after discharge	Simple interventions can improve ACE inhibitor use and patient outcomes.
Ramachandran et al. 138, 2007	RCT	50 patients	Telephonic helpline was established, and regular telephone calls made to reinforce the information and modify drug dosage	This study demonstrates that in the setting of a developing country, improvement in QOL by intensive management of heart failure patients through a heart failure programme with telephonic reinforcement and a helpline is greater than that usually achieved with drug therapy in a routine heart failure clinic.
Clark et al. 139, 2007	RCT	79 patients	Telephone-monitoring	This study shows that elderly CHF patients can adapt quickly, find telephone-monitoring an acceptable part of their healthcare routine
Smith et al. 140, 2008	RCT	1069 patients	Telephone-monitoring	The intervention was effective but costly to implement and did not reduce utilization.

Barth et al. 141, 2001	Experimental study		Telephone-monitoring	This type of nursing intervention can improve outcomes for patients after discharge from the hospital.
Gregory et al. 142, 2001	RCT	200 patients	Heart failure disease management (HFDM) program	The HFDM intervention, administered over 90 days to patients hospitalized for heart failure, succeeded in reducing the rate of heart failure hospitalizations
Jerant et al. 143, 2003	RCT	37 patients	(a) video-based home telecare; (b) telephone calls; and (c) usual care	Telenursing can reduce CHF hospitalizations and allow increased frequency of communication with patients.
Riley et al. 144, 2013	Qualitative study	15 patients	Telemonitoring	In summary, the majority of patients used telemonitoring daily and developed self-care skills in monitoring their heart failure.
Angermann et al. 145, 2012	RCT	715 patients	Standardized collaborative disease management	The primary end point of this study was neutral. However, mortality risk and surrogates of well-being improved significantly.
Boyne et al. 146, 2013	RCT	382 patients	Telemonitoring (TM)	The cost effectiveness analysis showed a high level of decision uncertainty, probably caused by the divergence between the participating institutions
Martinez et al. 147, 2013	Retrospective chart review	55 patients	Telephone-monitoring technology	Implementation of a pharmacist-managed HF medication titration clinic increased the percentage of patients achieving optimal ACEI, ARB, and β-blocker dosages
Henderson et al. 148, 2013	Pragmatic, cluster randomised controlled trial	3230 people with a long-term condition (heart failure,	Telehealth equipment and monitoring services for 12 months	The QALY gain by patients using telehealth in addition to usual care was similar to that by patients receiving usual care only, and total costs associated with the telehealth intervention were higher

		chronic obstructive pulmonary disease, or diabetes)		
Baker et al. 149, 2013	Retrospective matched cohort study.	1767 patients	Combined care management and telehealth	Care management coupled with content-driven telehealth technology has potential to improve health outcomes in high-cost Medicare beneficiaries.
Agrinier et al. 150, 2013	Single cohort study	1222 patients	Educational and home-visit monitoring programs	Coordinated DMP of HF might improve outcome cost-effectively when implemented in a real-world population setting, and was associated in Lorraine with a substantial modification of the trend of HF hospitalizations
Giordano et al. 151, 2013	Single cohort study	602 patients	Home-based telesurveillance program (HTP) including multidisciplinary management and remote telemonitoring	HTP was effective in improving CHF patient functional status, and an unsuccessful response to the intervention seems to be an independent marker of poor prognosis.
Ledwidge et al. 152, 2013	Single cohort study	87 patients	HeartPhone algorithm	An individualized approach to weight monitoring in HF with the HeartPhone algorithm improved prediction of HF deterioration.
Ferrante et al. 153, 2013	RCT	1518 patients	Telephone-monitoring technology	The benefit observed during the intervention period persisted and was sustained 1 and 3 years after the intervention ended.
Cui et al. 154, 2013	RCT	179 patients	Health Lines (HL) intervention and a third receiving Health	Findings demonstrate that the HL intervention from the Manitoba Provincial Health Contact program for CHF is an optimal intervention strategy for CHF management

			Lines intervention plus in-house monitoring (HLM)	
Singh et al. 155, 2013	Single cohort study	87 patients	Web-based viewing system for remote worldwide interpretation of echocardiography	This study demonstrates the feasibility of performing sonographer-driven focused echocardiographic studies for identifying the burden of structural heart disease in a community.
Wong et al. 156, 2013	Prospectively collected registry data	44 patients	Home-based advance care programme	Home-based advance care programme is potentially effective in reducing healthcare utilisation of end-stage HF patients, primarily by reducing HF rehospitalizations, and in probably saving costs as well.
Mueller et al. 157, 2002	Single cohort study	/	Diuretic treatment algorithm for advanced practice nurses as part of a tele management program	Preliminary data from the implementation of such an algorithm within an established HF program shows a decrease in hospitalizations rates and cost of care
Brannstrom et al. 158, 2014	RCT	36 patients	Integrated Palliative advanced home caRE and heart FailurE caRe	Person-centred care combined with active heart failure and palliative care at home has the potential to improve quality of life and morbidity substantially in patients with severe chronic heart failure.
Vuorinen et al. 159, 2014	RCT	94 patients	Home telemonitoring	Home telemonitoring did not reduce the number of patients' HF-related hospital days and did not improve the patients' clinical condition.
Villani et al. 160, 2014	RCT	80 patients	Handheld PDA	Mortality and hospital re-admissions for congestive heart failure were also reduced in integrated management patients

Boman et al. 161, 2014	RCT	38 patients	Robot-assisted remote echocardiographic examination and teleconsultation	The time from randomization until attaining a specialist consultation was also significantly reduced
Luttik et al. 162, 2014	RCT	189 patients	Home-based programmes	Patients discharged after initial management in a specialized HF clinic can be discharged to primary care for long-term follow-up with regard to maintaining guideline adherence and patient adherence.
Blum et al. 163, 2014	RCT	204 patients	Telemonitoring	Telemonitoring did not result in lower total costs, decreased hospitalizations, improved symptoms, or improved mortality.
De Souza et al. 164, 2014	RCT	252 patients	Home-based interventions for heart failure	A post-discharge, nurse-led management strategy significantly decreases the morbidity of ADHF patients in the public health system of a developing middle-income country.
Goldstein et al. 165, 2014	RCT	60 patients	Telehealth intervention (an electronic pill box) and an m-health intervention (an app on a smartphone) for improving medication adherence	Patients preferred the m-health approach.
Stewart et al. 166, 2014	RCT	280 patients	Home-based interventions for heart failure	Home-based intervention was, however, associated with significantly fewer all-cause deaths and significantly fewer days of hospital stay in the longer-term.
Brannstrom et al. 167, 2006	Qualitative study	14 patients	Palliative advanced home care	Being constructively dependent on palliative advanced home care facilitates everyday life at home.

Evangelista et al. 168, 2012	Prospective comparative study	36 patients	Outpatient palliative care consultation	A palliative care consultation may reduce symptom burden and depression and enhance QOL in patients with symptomatic heart failure.
Domingues et al. 169, 2011	RCT	48 patients	Education and telephone monitoring	An in-hospital educational nursing intervention benefitted all HF patients in understanding their disease, regardless of telephone contact after discharge.
Bocchi et al. 170, 2008	RCT	350 patients	Repetitive education at six-month intervals and monitoring	This heart failure disease management program model of patients under the supervision of a cardiologist is associated with a reduction in unplanned hospitalization, a reduction of total hospital days, and a reduced need for emergency care, as well as improved quality of life, despite modest program adherence over time.
Eilat-Tsanani et al. 171, 2016	Single cohort study	141 patients	Telehealth service	During the year of use in telehealth service for congestive heart failure parameters of hospitalization were improved, together with parameters of quality of life.
Ben-Assa et al. 172, 2014	Single cohort study	897 patients	Telehealth service	Telemedicine technology shows considerable promise for reducing 30-day readmission rates of post-AMI patients.
Maru et al. 173, 2015	RCT	280 patients	Home (HBI) versus clinic-based (CBI) management of chronic heart failure	Compared with CBI, HBI is likely to be cost-effective in elderly CHF patients with significant comorbidity.
Dorsch et al. 174, 2015	Single cohort study	24 patients	A Web application for self-monitoring heart failure	A Web application for self-monitoring heart failure over 12 weeks improved both NYHA classification and MLHFQ score.

Evangelista et al. 175, 2015	Single cohort study	21 patients	Remote monitoring systems	Our preliminary data show that the use of an RMS is feasible and effective in promoting activation, self-care, and QOL.
Riley et al. 176, 2015	Single cohort study	50 patients	Remote Heart Failure Monitoring	The findings from this project indicate that a remote HF monitoring program can be successfully implemented in a rural, underserved area.
Dierckx et al. 177, 2015	Retrospective analysis	333 patients	Home telemonitoring	Patients who choose HTM have a better prognosis than those who do not, but this does not appear to be mediated through greater prescription of key HF medications.
Albert et al. 178, 2007	RCT	112 patients	Video education	Video education prompts self-care behaviour adherence to control worsening signs/symptoms of volume overload.
Linne et al. 179, 2006	RCT	230 patients	Interactive CD-program	The lack of effect on the readmission rate could be due to an insufficient sample size but might also indicate that in pharmacologically well-treated patients there is little room for altering the course of the condition.
Liu et al. 180, 2012	RCT	159 patients	Oedema index-guided disease management	EI-based HF management program demonstrated an event-lowering effect superior to traditional nurse-led multidisciplinary care in 6 months after an acute HF episode.
Ducharme et al. 181, 2005	RCT	230 patients	Multidisciplinary congestive heart failure clinic	Compared with usual care, care at a multidisciplinary specialized congestive heart failure outpatient clinic reduced the number of hospital readmissions and hospital days and improved quality of life

Sethares et al. 182, 2004	RCT	70 patients	Tailored message intervention	A tailored message intervention changed the beliefs of the person with HF in regard to the benefits and barriers of taking medications, following a sodium-restricted diet, and self-monitoring for signs of fluid overload
Qian et al. 183, 2015	RCT	1427 patients	Telemonitoring	Compared with white patients, black patients with HF had better patient-reported health status shortly after HF admission but not at 3 or 6 months.
Wakefield et al. 184, 2015	Single cohort study	14 patients	Web-Based Symptom Monitoring Application	Most patients needed some assistance, but few patients were completely unable to complete some tasks.
Hagglund et al. 185, 2015	RCT	82 patients	New home intervention system (HIS, OPTILOGG (®)) consisting of a specialised software, a tablet computer (tablet) wirelessly connected to a weight scale	HF patients with a HIS tablet computer and scale improved in self-care and HRQoL. Days in hospital due to HF were reduced.
Pedone et al. 186, 2015	RCT	96 patients	Telemonitoring system (communicates oxygen saturation, heart rate, and blood pressure readings) and office-hours telephonic support provided by a geriatrician.	Telemonitoring of elderly people with HF is feasible and reduces the risk of death and hospitalization.
Bekelman et al. 187, 2015	RCT	384 patients	Patient-centred disease management (PCDM)	This multisite randomized trial of a multifaceted HF PCDM intervention did not demonstrate improved patient health status compared with usual care.

Rahimi et al. 188, 2015	Single cohort study	52 patients	User-centred home monitoring and self-management system	Despite no active medical intervention, patients felt that they benefited from the reassurance and sense of connectivity that the monitoring system provided.
Veenstra et al. 189, 2015	Single cohort study	102 patients	Optimized care program with telehealth	The number of unplanned admissions for heart failure decreased from on average 1.29 to 0.31 admissions per year after telehealth introduction.
Krum et al. 190, 2013	RCT	405 patients	Telephone support intervention (UC+I)	Although no difference was observed in the primary endpoint of CHAT (Packer composite score), UC+I significantly reduced the number of HF patients hospitalized among a rural and remote cohort.
Agboola et al. 191, 2015	Matched-control study	348 patients	Heart failure telemonitoring program, Connected Cardiac Care Program (CCCP)	CCCP was associated with significantly lower hospitalization rates up to 90 days and significantly lower mortality rates over 120 days of the program.
Laborde-Casterot et al. 192, 2016	Single cohort study	1816 patients	Multidisciplinary heart failure disease management	In a real-world setting, a multidimensional DMP for HF with structured patient education, home nurse monitoring, and appropriate physician alerts may improve survival when implemented after discharge from hospitalization due to worsening HF.
Sahlen et al. 193, 2016	RCT	72 patients	Palliative Advanced Home Care	The Palliative Advanced Home Care and Heart Failure Care working mode saves financial resources and should be regarded as very cost-effective.
Cassel et al. 194, 2016	Observational, retrospective study using propensity-based matching	368 patients	Home-Based Palliative Care Program	In the context of an alternative payment model in which the provider was "at risk" of bearing the costs of care, a proactive PC program helped to avoid the escalation in hospital use and costs

Gu et al. 195, 2016	Prospective study	329 patients	Community Health Service Center-Based Intervention with Home visits vs. telephone	It was concluded that CHSC might be the optimal setting for delivering care
Donate-Martinez et al. 196, 2016	Prospective study	74 patients	Primary-based telemonitoring programme	Our sample benefited from the Valcronic programme, experiencing an improvement in their HRQOL, a decreased use of health resources or high satisfaction levels.
McElroy et al. 197, 2016	Prospective study	443 patients after cardiac surgery	Web-based digital health kits (DHK)	In our study, adding DHKs to a formal RRP was not associated with a significant decrease in 30-d readmission rates.
Lee et al. 198, 2016	Nested matched case-control study	11985 patients	Post-discharge Follow-up	In adults discharged to home after hospitalization for HF, outpatient follow-up with a cardiology or general medicine provider within 7 days was associated with a lower chance of 30-day readmission.
Comin-Colet et al. 199, 2016	RCT	178 patients	Telemedicine included daily signs and symptoms based on telemonitoring and structured follow-up by means of video or audio-conference	Among patients managed in the setting of a comprehensive HF programme, the addition of telemedicine may result in better outcomes and reduction of costs.
Zan et al. 200, 2016	Single cohort study	21 patients	iGetBetter system, a secure Web- and telephone-based heart failure remote monitoring program	This pilot study demonstrated the feasibility of a low-intensive remote monitoring program leveraging commonly used mobile and portable consumer devices in augmenting care for a fairly young population of ambulatory patients with heart failure.

Nundy et al. 201, 2016	Single cohort study	15 patients	Text Messaging Intervention	We observed a high rate of satisfaction and preliminary evidence of improvements in heart failure self-management.
Athilingam et al. 202, 2016	A descriptive survey design	37 participants	Mobile health application "HeartMapp" for chronic heart failure (CHF) self-management	Having access to CHF symptom monitoring and education readily available in a mobile app may motivate individuals to engage in the prescribed self-management skills to ultimately attain desired outcomes, which warrants further exploration.
Rozen et al. 203, 2016	Single cohort study	45 participants	Tele-coaching for patients	Overall, patients increased knowledge over a 30-day period. Tele-coaching by social workers holds promise as a feasible model for health education for high-risk populations.
Evans et al. 204, 2016	Single cohort study	41 participants	Wireless wristwatch-based monitoring device	The findings indicate that a health monitoring system designed for older adults can and will be used for an extended period of time
Chen et al. 205, 2018	RCT	62 patients	Multidisciplinary disease management programs	A HF MDMP can improve QoL, depressive symptoms and self-care behaviours in China.
Steventon et al. 206, 2016	Single cohort study	716 patients	Telehealth	Telehealth was not associated with a reduction in secondary care utilisation.
Ong et al. 207, 2016	RCT	1436 patients	Remote Patient Monitoring After Discharge	Among patients hospitalized for HF, combined health coaching telephone calls and telemonitoring did not reduce 180-day readmissions.
Hale et al. 208, 2016	RCT	29 patients	Remote Medication Monitoring System	Telehealth medication adherence technologies, such as the MedSentry medication monitoring system, are a promising method to improve patient self-management

Young et al. 209, 2016	RCT	100 patients	Home-based activation intervention on self-management	Significantly higher patient-reported SM adherence was not accompanied by lower clinical biomarkers or readmission rates.
Liu et al. 210, 2015	RCT	131 patients	Videotape or a teaching booklet to educate HF patients, combined with telephone or telemonitoring	Our study reveals that self-care programs administered by HF patients can reinforce educational objectives and improve patient ability to effectively perform self-care.
Howie-Esquivel et al. 211, 2015	RCT	1033 patients	Home follow-up phone calls	The TEACH-HF intervention was associated with significantly fewer hospital readmissions and savings in bed days.
Gross-Schulman et al. 212, 2017	Single cohort study	101 patients	Automated Remote Monitoring System	This study demonstrated that the HF-ARMS is safe and nearly clinically equivalent to traditional human remote monitoring in a low-income, underserved population at 95% lower cost.
Barbita et al. 213, 2017	Single cohort study	3000 patients	Telehomecare	Research shows that the program reduces emergency department visits and hospital admissions
Nguyen et al. 214, 2017	Survey	28 participants	Supportive technology	Patients were willing to engage in HF self-care however they relied on CPs who were more willing to ask questions about HF.
Gallagher et al. 215, 2017	Quantitative surveys and qualitative interviewing	17 GPs	Teleconsultation	These data from an initial experience with Heart Failure Virtual Consultation present a very positive impact of this strategy on the provision of heart failure care

Grace et al. 216, 2017	Qualitative study	26 interviews	Autonomous zero-effort monitoring	Patient perception towards autonomous monitoring devices was positive, lending credence to zero-effort technology as a viable and promising approach.
Punchik et al. 217, 2017	Retrospective analysis	196 patients	Home care for homebound patients with CHF	Home care for homebound adults with CHF can reduce healthcare utilization and healthcare costs.
Gonzalez-Guerrero et al. 218, 2014	RCT	117 patients	Disease management programs (DMPs) for HF elderly patients attending a geriatric day care hospital (GDCH)	A developed DMP in a GDCH improves the event-free survival and the quality of life in elderly patients with HF.
Leventhal et al. 219, 2011	RCT	42 patients	Outpatient inter-professional management programme	An inter-professional disease management programme is possible in the Swiss healthcare setting but effects on outcomes need to be confirmed in larger studies.
Brotons et al. 220, 2009	RCT	283 patients	Home-based intervention	A home-based intervention for patients with heart failure reduced the aggregate of mortality and hospital readmissions and improved quality of life.
Aguado et al. 221, 2010	RCT	106 patients	Single home-based educational intervention	Patients with heart failure who receive a home-based educational intervention experience fewer emergency department visits and unplanned readmissions with lower healthcare costs.
Wootton et al. 222, 2009	RCT	288 patients	Telephone-supported care coordination	There were no significant differences in costs of care between the intervention (coordinated care) and control groups of veterans.
Madigan et al. 223, 2013	RCT	99 patients	Home health care with telemonitoring	Therefore, for older adults with heart failure, telemonitoring may be an important adjunct to home health care services to improve health status.

Copeland et al. 224, 2010	RCT	458 patients	Telephone-supported care coordination	A risk-stratified intervention for patients with CHF resulted in potential behavioural improvements but no survival benefit.
Cartwright et al. 225, 2013	RCT	3230 patients	Telehealth	Second generation, home based telehealth as implemented in the Whole Systems Demonstrator Evaluation was not effective or efficacious compared with usual care only.
Jones et al. 226, 2012	Case-control analysis nested in a HF self-care randomized trial	303 patients	Heart failure (HF) self-care intervention	Adherence to weight monitoring and diuretic self-adjustment was associated with lower odds of HF-related ED visits or hospitalizations.
Fergenbaum et al. 227, 205	Cost-effective analysis	6 RCTs	Home for the Management of Chronic Heart Failure	Care in the home in CHF seems to be more effective and less costly compared with UC.
Yu et al. 228, 2015	RCT	178 patients	Nurse-Implemented Transitional Care	The translation of individual-centred nurse-implemented TC to the Chinese culture and healthcare context of Hong Kong appears beneficial.
Martin-Lesende et al. 229, 2013	RCT	58 patients	Telemonitoring	This study shows that telemonitoring of in-home patients with HF and/or CLD notably increases the percentage of patients with no hospital admissions
Smeulders et al. 230, 2009	RCT	317 patients	'Chronic Disease Self-Management Programme' (CDSMP)	The CDSMP significantly improved physical activity among CHF patients for up to 6 months after the end of the programme

Otsu et al. 231, 2011	RCT	102 patients	Self-Management Programme'	Further long-term care is necessary for outpatients with CHF in order to prevent their deterioration and to maintain their health status
Martensson et al. 232, 2005	RCT	153 patients	Nurse-led intervention	A nurse-led intervention directed toward patients with heart failure in a primary health care setting resulted in limited effects between the groups, although the physical and mental status were retained during 12 months of follow-up to a greater extent than in the control group.
Heisler et al. 233, 2013	RCT	267 patients	Reciprocal peer support (RPS)using a telephone platform	Among patients recently hospitalized for HF, more than half of RPS participants had no or minimal engagement with the RPS program, and the program did not improve outcomes compared with usual HF nurse care management.
Steventon et al. 234, 2012	RCT	3230 patients	Telehealth	Telehealth is associated with lower mortality and emergency admission rates.
Delaney et al. 235, 2013	RCT	100 patients	Telemonitoring and self-care education intervention	The primary outcome of 90-day post–home care discharge hospitalization was significantly reduced in the intervention group compared to controls
Tompkins et al. 236, 2010	RCT	390 patients	Telemonitoring transmitted vital signs	The main finding was a tendency for lower total number of hospital days for patients assigned to telemonitoring.
Soran et al. 237, 2010	RCT	315 patients	Computer-based telephonic monitoring system	Our study results suggest that enhanced patient education and follow-up is as successful as a sophisticated home monitoring device with an interactive program
Kurtz et al. 238, 2011	RCT	138 patients	Automated home telephone self-monitoring	Automated home telephone self-monitoring reduced rehospitalization in patients with advanced HF.

Troughton et al. 239, 2011	Single cohort study	84 patients	Direct left atrial pressure monitoring	Accurate and reliable LAP measurement using a chronic implanted monitoring system is safe and feasible in patients with advanced heart failure.
Shearer et al. 240, 2007	RCT	90 patients	A telephone-delivered empowerment intervention	The knowledge gained from this study provides a beginning understanding of strategies to enhance health care providers' ability to facilitate self-management of HF among patients diagnosed with HF.
Harrison et al. 241, 2002	RCT	/	Hospital-to-home transition	There were significant improvements in health-related quality of life (HRQL) associated with Transitional Care and less use of emergency rooms.
Strömberg et al. 242, 2006	RCT	154 patients	Computer-based education	Computers can be a useful tool in heart failure education, but to improve compliance a single-session educational intervention is not sufficient.
Strömberg et al. 243, 2002	Qualitative study	42 patients	Education on CD-ROM	The nurses reported that the patients were positive towards the computer and seemed to understand the information and that the patient education was less time-consuming, when the patients could seek knowledge on their own.
Heisler et al. 244, 2007	Single cohort study	20 patients	Interactive voice response-facilitated telephone peer support	IVR peer-support intervention is feasible and is acceptable to patients
Hopp et al. 245, 2006	RCT	37 patients	Home care telehealth intervention	The use of telehealth services as an adjunct to traditional home care is associated with greater improvements in mental health status and a trend toward lower use of inpatient and outpatient healthcare services.

Bennett et al. 246, 2017	Single cohort study	29 patients	Novel under-the-mattress piezoelectric sensor	Respiratory rate was the most important risk-adjusted associate of readmission for HF.
Pfister et al. 247, 2017	Prospective case-control study	600 patients	Structured heart failure management programme	The inclusion of Turkish minority patients into a heart failure management programme is feasible with higher consent rate than in Germans.
Jayaram et al. 248, 2017	RCT	1521 patients	Telephonic monitoring	Telemonitoring results in statistically significant, but clinically small, improvements in health status when compared with usual care.
Albert et al. 249, 2017	Cross-sectional, multicentre, international design	206 patients	Telemonitoring	48.2% preferred smart phones for telemonitoring, especially when traveling (54.8%), with new/worsening symptoms (50%), for everyday use (50%), and connecting with doctors (48.5%).
Gallagher et al. 250, 2017	RCT	40 patients	Telemonitoring Adherence to Medications	Adherence telemonitoring was acceptable to most patients with HF. Diuretic nonadherence was common even when patients knew they were being monitored.
Rozen et al. 251, 2017	Single cohort study	50 patients	Telehealth platform allowing for daily, real-time reporting of health status and video conferencing	Adherence to this telehealth protocol was excellent and consistent, even among high-risk patients.
Scuffham et al. 252, 2017	RCT	787 patients	Heart failure management programme (INT-HF-MP)	During 12-months follow-up, an INT-HF-MP did not reduce healthcare costs or improve health outcomes relative to SM

Baker et al. 253, 2011	RCT	605 patients	Progressive, reinforcing telephone education	Telephone reinforcement of learning goals and self-care behaviours improved knowledge, health behaviours, and HF-related QOL compared to a single education session.
Grady et al. 254, 2014	RCT	902 patients	Self-management counselling	We conclude that in our cohort of patients, the self-management intervention had no benefit over enhanced education in improving domains of HRQOL and HRQOL for specified HF subgroups.
Maru et al. 255, 2017	Markov model		Home based management	Compared with CBI (outpatient specialized HF clinic-based intervention), HBI (home-based predominantly, but not exclusively) could potentially be cost-effective over the long-term
Dadosky et al. 256, 2018	Prospective nonrandomized trial	323 patients	Medtronic Zephyr BioModule	We conclude that tele management can be used to achieve reduced readmission rates even in high-risk populations requiring SNF level of care after HF hospitalization.
Grustham et al. 257, 2018	Markov model		Home telemonitoring (HTM) and nurse telephone support (NTS)	This modelling study demonstrated that HTM and NTS are viable solutions to support patients with chronic heart failure.
Olivari et al. 258, 2018	RCT	239 patients	Remote monitoring	In the intention-to-treat analysis, during the 12-month follow up of elderly patients hospitalised for HF, remote monitoring had no impact on the primary endpoint but it significantly improved patients' quality of life.
Herrmann et al. 259, 2018	Single cohort study	28 patients	Haemodynamic telemonitoring	The efficacy of the interventional MitraClip procedure on clinical symptoms can be confirmed by haemodynamic telemonitoring

Athar et al. 260, 2018	RCT	97 patients	Personalized Approach to Patient Education	A personalized HF tool did not affect rates of self-reported HF treatment adherence or survival without readmission or ED visit.
Koehler et al. 261, 2018	RCT	1571 patients	Telemedical interventional management	The TIM-HF2 trial suggests that a structured remote patient management intervention, when used in a well-defined heart failure population, could reduce the percentage of days lost due to unplanned cardiovascular hospital admissions and all-cause mortality.
Lycholip et al. 262, 2018	RCT	177 patients	Telemedical interventional management	TM did not have an advantage on self-care improvement. Poor physical aspect of quality of life, lower LVEF, and lower NYHA class were associated with self-care worsening.
Jeong et al. 263, 2018	RCT	35 patients	Telephone Support and Telemonitoring	Findings support that nurse-led telephone support may be effective for improvements in health behaviour, systolic blood pressure, and hypertension self-care in disadvantaged older adults under remote monitoring.
Segan et al. 264, 2018	Qualitative study	31 patients	Self-care strategies	Barriers to self-care included patient education, timely recognition of signs and symptoms of HF with an appropriate escalation plan, non-adherence and polypharmacy.
Ng et al. 265, 2018	RCT	84 patients	Home-Based Palliative Heart Failure Program	The program has potential to reduce distress for some of the symptoms.
Sponga et al. 266, 2018	Single cohort study	20 patients	Teleconsultation	Our early experience shows that this monitoring and management system achieves encouraging positive feedback in terms of perceived safety, reducing the anxiety for a ‘device-depending survival status’ by daily video calls

Moertl et al. 267, 2013	Markov Model		NT-proBNP-guided, intensive HF patient management	NT-proBNP-guided, intensive HF patient management in addition to multidisciplinary care not only reduces death and hospitalization but also proves to be cost-effective.
Chan et al. 268, 2008	Markov Model		Heart failure disease management	Heart failure disease management programs are likely cost-effective in the long-term along the whole spectrum of patient risk.
Idris et al. 269, 2015	RCT	28 patients	The Health Connect system integrates traditional telemedicine with virtual provider appointments	Virtual appointments empower patients to advocate for their own health by providing numerous opportunities for education and feedback.
Wang et al. 270, 2011	RCT	27 patients	Self-care program	The HFSC program for patients with heart failure improved their heart failure symptoms and resulted in increased functional status and better quality of life.
Kraai et al. 271, 2016	RCT	177 patients	ICT-guided disease management	ICT-guided-DMS+telemonitoring for the management of HF patients did not affect the primary and secondary endpoints.
Harkness et al. 272, 2014	Cross-sectional design	100 patients	Self-care management	Findings from this study highlight the difficulty older heart failure patients have with self-care management and the need to include formal screening for MCI
Wong et al. 273, 2018	RCT	84 patients	Home-based palliative care program	Results suggest that a transitional home-based palliative care program is more cost-effective than customary palliative care service.
Kenealy et al. 274, 2015	RCT	171 patients	Telecare	Strongly positive patient and staff experiences and attitudes complement and contrast with small or non-significant quantitative changes.

Maru et al. 275, 2018	RCT	611 patients	Nurse-led Intervention	Compared with standard care, the NIL-CHF intervention was not a cost-effective strategy as life-years and QALYs were slightly lower in the NIL-CHF group.
Ruschel et al. 276, 2018	RCT	611 patients	Nurse-led home visit (HV)	In Brazil, an intervention based on nurse-led home visits of patients with HF showed a favourable cost-effectiveness profile
McDonald et al. 277, 2018	RCT	107 patients	Daily home BNP monitoring	The HOME HF study demonstrates the feasibility of home BNP measurement and shows the potential value of BNP as an index of emerging clinical deterioration
Herold et al. 278, 2018	Matched cohort study	2622 patients	Telemonitoring	The probabilities to survive after 1 and 2 years were significantly increased in the intervention group.
Padula et al. 279, 2019	RCT	313 patients	Caregiver education	Caregivers training for early recognition of symptoms/signs of worsening heart failure may be effective in reducing hospitalizations
Frederix et al. 280, 2019	RCT	142 patients	Telemonitoring	An initial six-month telemonitoring programme was not associated with reduced all-cause mortality in CHF patients at long-term follow-up but resulted in a reduction in the number of days lost due to heart failure readmissions.
Plakogannis et al. 281, 2019	A retrospective manual chart review	131 patients	Post discharge call	Postdischarge phone calls, specifically made by pharmacy students, demonstrated a positive impact on reducing HF-associated hospital readmissions
Berman et al. 282, 2019	Single cohort study	21 patients	Pharmacist-Driven Heart Failure In-Home Counseling	Pharmacist intervention, as part of the health care team, during this tenuous time has shown to make a valuable impact.

Lopez-Liria et al. 283, 2019	Single cohort study	50 patients	Remote device-monitoring system (TM)	The patients followed up through hospital visits showed a greater increase in MLHF-HRQoL after 12 months
Gingele et al. 284, 2019	RCT	301 patients	Telemonitoring	Telemonitoring did not significantly influence the long-term outcome in our study. Therefore, extending the follow-up period of telemonitoring studies in HF patients is probably not beneficial.
Mizukawa et al. 285, 2019	RCT	59 patients	Nurse-Led Collaborative Management Using Telemonitoring	We conclude that CM has the potential to improve psychosocial status in patients with HF and prevent rehospitalization due to HF.
Jiang et al. 286, 2019	Single cohort study	10 patients	HOMe-based HEart failure self-Management Programme	A self-management psychosocial education approach is the preferred choice for many patients with chronic diseases. The effectiveness of the HOM-HEMP will next be tested in a full-scale randomised control trial.
Jaarsma et al. 287, 2008	RCT	1023 patients	Disease management program	Neither moderate nor intensive disease management by a nurse specializing in management of patients with HF reduced the combined end points of death and hospitalization
Morcillo et al. 288, 2005	RCT	244 patients	Home-Based Intervention	The simple educational program used in this study, consisting of a single visit one week after hospital discharge in the patient's home, resulted in a substantial decrease in the number of hospital admissions and emergency room visits.
Dracup et al. 289, 2014	RCT	602 patients	Self-care	A face-to-face education intervention did not significantly decrease the combined end point of cardiac death or hospitalization for HF

Hole et al. 290, 2014	Single cohort study	24 patients	Outpatient heart failure clinics	Quality of life assessed with MLHF improved after follow-up at outpatient HF clinics.
Pekmezaris et al. 291, 2019	RCT	104 patients	Telehealth self-monitoring (TSM)	These findings suggest that TSM is not effective in reducing utilization or improving QoL for underserved patients with HF.
Cabas et al. 292, 2019	Retrospective, quantitative study	138 patients	Home Telemonitoring	The findings from this study may provide healthcare providers with a better understanding of the outcomes of home telemonitoring for treating adult Hispanic patients with HF.
Gingele et al. 293, 2019	RCT	382 patients	Telemonitoring	Tailored telemonitoring stabilised the functional status of HF patients but did not improve HRQoL.
Lloyd et al. 294, 2019	Single cohort study	12 patients	Web-based, tablet computer-accessed, secure application	This study suggests that mobile technology is feasible, acceptable, and has potential for cost-effective opportunities to manage heart failure patients safely at home.
Koulaouzidis et al. 295, 2019	RCT	124 patients	Telemonitoring	TM is associated with lower any-cause mortality and also has the potential to reduce the number of days lost to hospitalisation and death.
Dang et al. 296, 2017	RCT	61 patients	Mobile Phone Intervention	A mobile phone-based disease management program may help improve self-care efficacy and QoL in a minority population and offers a modality to help reduce ethnic disparity.
Nouryan et al. 297, 2018	RCT	89 patients	Telemonitoring	Significantly improved all-cause ED utilization, LOS, and QoL were found for HTM; other differences were not significant.

Scherr et al. 298, 2009	RCT	120 patients	Telemonitoring using mobile phones	Telemonitoring using mobile phones as patient terminals has the potential to reduce frequency and duration of heart failure hospitalizations.
Klack et al. 299, 2013	Survey	117 participants	Telemonitoring	The perceived drawbacks are attributed to a general uncertainty about the reliability of telemedical systems, in combination with concerns about personal data privacy, security, and loss of control.
Sohn et al. 300, 2012	Retrospective analysis	1124 patients	Personalized healthcare	The findings suggest that, besides a reduction of costs, by participating in "Telemedicine for the Heart" patients with chronic heart failure experienced a reduced number of hospital stays, optimized medical therapy, better quality of life, and reduced mortality.
Veroff et al. 301, 2012	RCT	480 patients	Impact of video and written education	Broad application of inexpensive behaviour changes interventions, such as a DVD/booklet program, should help to facilitate important, routine self-care behaviours for individuals with heart failure.
Dilles et al. 302, 2012	Survey	65 patients	Computer assisted learning (CAL) program	Both educational strategies increased knowledge and improved self-care.
Brandon et al. 303, 2009	RCT	20 patients	Advanced-practice-nurse (APN)-led telephone intervention	The results of this study support the idea that an ALTI positively impacts outcomes of patient with HF
Smith et al. 304, 2005	Single cohort study	10 patients	Videotape education	These results indicate the need for further testing of the videotape as a potentially cost-effective method of teaching about HF self-management

Evangelista et al. 305, 2006	Qualitative study	69 patients	Web-based education and counselling program	Authors found that elderly persons with limited computer skills can and will use Web resources to obtain information when given adequate instructions on how to access the Web pages.
Wu et al. 306, 2006	Single cohort study	58 patients	Internet patient-physician communication tool	While the majority of patients discontinued use, 45% of the patients used the system and continued to use it on average for 1.5 years.
Kline et al. 307, 2007	Experimental, longitudinal, repeated-measures design	88 patients	Supportive-educative and mutual goal setting	Although no significant difference was demonstrated in participants' understanding of heart failure, the supportive-educative group showed a significantly increased self-efficacy in managing heart failure symptoms.
Westlake et al. 308, 2007	Matched control study	80 patients	Web-based education and counselling program	This approach may be potentially beneficial in delivering educational and behavioural support to this high-risk group in ways that are affordable and accessible.
Wongpiriyayothar et al. 309, 2011	Two-group pre-test–post-test experimental research design with random assignment to groups	22 patients	Telephone education	CTP is a strategy that helps patients with HF to decrease dyspnoea and improve physical functioning.
Piette et al. 310, 2015	RCT	36 patients	Mobile health support	mHealth+CP CarePartners reported less caregiving strain than controls at both 6 and 12 months

Koberich et al. 311, 2015	RCT	64 patients	Telephone education	The easy to implement and short educational intervention has a positive effect on self-care behaviour for patients with heart failure
Siabani et al. 312, 2015	RCT	231 patients	Home-based educational strategy	The home-based face-to-face education by CHVs improved self-care maintenance and self-care management in patients with CHF
Baptiste et al. 313, 2016	Single cohort study	41 patients	Nurse-led heart failure education program	Findings suggest that the nurse-led evidence-based HF education program improved self-care behaviours and decreased 30-day readmissions.
Ritchie et al. 314, 2016	RCT	478 patients	E-Coach technology-assisted care transition system	E-Coach was associated with significantly fewer days in the hospital
Al-Sutari et al. 315, 2017	RCT	144 patients	Educational program	The findings of this study demonstrate that individualized heart failure education, which is supported by follow-up phone calls and self-care manual, is an effective approach
Scherr et al. 316, 2006	Single cohort study	20 patients	Mobile phone-based surveillance	It may be a useful tool for patients with heart failure as well as hypertensive patients.
Seto et al. 317, 2010	Survey	110 patients	Mobile phone-based surveillance	Patients and clinicians want to use mobile phone-based remote monitoring and believe that they would be able to use the technology.
Winkler et al. 318, 2011	Single cohort study	30 patients	Portable home devices for electrocardiogram, blood pressure, body weight and self-assessment measurements	Mobile phone technology is suitable for continuous and secure medical data transmission.

Seto et al. 319, 2012	Semi-structured interviews	22 patients	Mobile phone-based surveillance	The success of a telemonitoring system is highly dependent on its features and design.
Seto et al. 320, 2012	RCT	100 patients	Mobile phone-based surveillance	Our findings provide evidence of improved quality of life through improved self-care and clinical management from a mobile phone-based telemonitoring system.
Cano-Martin et al. 321, 2014	Markov Model		Mobile app for the self-management	This means that CardioManager may be able to save more than 9,000 € per patient to the local Health Care System of Castile and Leon
Karhula et al. 322, 2015	RCT	471 patients	Mobile Phone-Based Health Coaching	A health coaching program supported with telemonitoring did not improve heart disease patients' or diabetes patients' quality of life or their clinical condition.
Doorenbos et al. 323, 2016	RCT	80 patients	Patient activation-education, telephone-based intervention	The GoC intervention resulted in more GoC conversations and higher quality communication between HF patients and providers without increased anxiety or depression
Li et al. 324, 2017	Survey	540 patients	SMS Self-care Messages	As a way of promoting HF self-care, SMS intervention combining educational and reminder function might be well accepted by HF patients in China.
Pahlevan et al. 325, 2017	Single cohort study	72 patients	Non-invasive iPhone Measurement of Left Ventricular Ejection Fraction	Analysis of carotid waveforms using intrinsic frequency methods can be used to document left ventricular ejection fraction with accuracy comparable with that of MRI.
Cajita et al. 326, 2017	Survey	129 patients	mHealth	Researchers should consider using the participatory approach in developing their interventions to ensure that their mHealth-based interventions will not only address the patient's HF self-management needs but also be easy enough to use even for those who are less technology savvy.

Foster et al. 327, 2018	Single cohort study	10 patients	mHealth	Feasibility study points to the incorporation of mobile applications to support self-care as promising research that can be useful to aid middle to older individuals in performing effective HF self-care
Portz et al. 328, 2018	Survey	30 patients	Mobile Application for Tracking Symptoms	The HF app is an acceptable tool for older patients with HF to self-manage their symptoms, identify patterns, and changes in symptoms, and ultimately prevent HF readmission.
Koole et al. 329, 2019	Single cohort study	55 patients	mHealth telemonitoring	The first results indicate that this program is feasible with high adherence.
Baik et al. 330, 2019	Cross-sectional study	168 patients	Web-based mHealth application	Patient-centred interventions should focus on modifiable risk factors that reduce dyspnoea, improve functional status, and enhance engagement in social roles to improve the health status of patients with heart failure.
Riegel et al. **331, 2006**	RCT	134 patients	Telephone case management	These results have important implications because of the current widespread enthusiasm for disease management.
Cole et al. 332, 2006	Single cohort study	24 patients	Nurse telephonic disease management	Based on patient acceptance and clinicians' reports, the program appeared feasible and possibly effective.
Holst et al. 333, 2007	Sub-analysis RCT	60 patients	Telephone follow-up	The self-care behaviour and quality of life in patients with heart failure did not change during one year of monthly telephone follow-up after a single session education

Steckler et al. 334, 2011	Single cohort study	79 patients	Telephone titration of heart failure medications	Telephonic titration of HF medications was feasible and safe and was achieved in 97% patients on ACEI/ARB and β-blockers.
Padja et al. 335, 2012	RCT	1535 patients	Health coaching by telephony	Individualized health coaching by telephony, as implemented in the trial was unable to achieve majority of the disease management clinical measures.
Bohme et al. 336, 2012	Single cohort study	259 patients	Telephone counselling	The results are auspicious and, if sustained, are expected to bring about long-term health benefits for our study's participants.
Ota et al. 337, 2013	Single cohort study	104 patients	Telephone counselling	Our experience is that direct, physician-patient telephone contact is feasible with a panel of around 100 HF patients for one provider.
Piamjariyakul et al. 338, 2013	Mixed methods design	10 caregivers	Telephone coaching program	The program was feasible to implement.
Steventon, 339, 2013	Single cohort study	2698 patients	Telephone coaching program	The Birmingham OwnHealth telephone health coaching intervention did not lead to the expected reductions in hospital admissions
Idouye et al. 340, 2015	Single cohort study	1095 patients	Automated follow-up calls	Patients at an elevated risk of readmission can be identified based on the trend of their responses to automated follow-up calls.
Yu et al. 341, 2015	RCT	160 patients	Telephone follow-up calls	The study provided clues for healthcare professionals to develop interventions while undertaking clinical work with limited resources in China.

Harter, 342, 2016	RCT	10815 patients	Telephone coaching program	While TBHC seems to reduce hospitalization only in specific patient groups, it may reduce mortality in patients with chronic somatic conditions.
Bell et al. 343, 2016	RCT	851 patients	Pharmacist Counseling Intervention	A tailored, pharmacist-delivered health literacy-sensitive intervention did not reduce post-discharge unplanned health care utilization overall.
Tiede et al. 344, 2017	Sub analysis RCT	184 patients	Telephone-based health coaching	Our results suggest that telephone-based health coaching has no effect on QoL, anxiety and depression of heart failure patients, but helps in improving certain risk behaviours and changes the locus of control to be more externalised.
Murtaugh et al. 345, 2017	Single cohort study	98730 patients	Early and Intensive Nursing Services	Our results call for closer coordination between home health and medical providers in the clinical management of HF patients immediately after hospital discharge.
Moon et al. 346, 2018	Quasi-experiment in non-equivalent control group design	38 patients	Telephone-Based Self-management Program	The findings indicate that the telephone-based self-management program is an effective intervention to improve self-management in heart failure patients.
Schlöglhofer et al. 347, 2018	Retrospective, single centre study	107 patients	Telephone follow-up calls	Continuous, standardized communication with VAD outpatients is important for early detection of upcoming problems and leads to significantly improved survival.
Oscaliles et al. 348, 2019	RCT	201 patients	Discharge guidance and telephone follow-up	Discharge guidance with telephone follow-up was effective and resulted in greater therapeutic adherence, as well as in decrease of re-hospitalization and death rates in patients with heart failure.

Negarandeh et al. 349, 2019	RCT	80 patients	Tailored tele-monitoring intervention	This study showed that tele-monitoring improved self-care behaviours in Iranian patients with heart failure but did not reduce their readmission rates.
Azzolin et al. 350, 2015	Single cohort study	23 patients	Home-based nursing interventions	Results show improved patient knowledge of heart failure
Martin et al. 351, 2017	Retrospective analysis	131 patients	Home Telehealth and Nursing Care	Further prospective research is required to determine best practices and multidisciplinary protocols to further reduce rehospitalization rates in this population.
Lundgren et al. 352, 2018	Qualitative study	13 patients	Internet-based cognitive behavioural therapy	Guided ICBT adapted for persons with HF and depressive symptoms was not statistically superior to participation in a Web-based DF.
Seto et al. 353, 2019	Feasibility study	15 patients	Heart Failure Telemonitoring System in Home Care Nursing	Lessons learned included the need to incentivize physicians, to ensure streamlined processes for recruitment and communication, to target appropriate patient populations, and to create a core clinical group
Ware et al. 354, 2019	A mixed-methods explanatory sequential design	24 patients	Mobile Phone–Based Heart Failure Telemonitoring Program	Decline in adherence rates over time is consistent with findings from other studies. However, this study also found adherence to be the highest and most consistent over time in older age groups and progressively lower over time for younger age groups
Jaana et al. 355, 2019	A longitudinal study design	23 patients	Telemonitoring use by seniors with chronic heart failure	The patients involved in this study perceived value of using telemonitoring, did not expect it to be difficult to use, and did not encounter adoption barriers. There was a significant improvement in patients' confidence in their ability to evaluate their symptoms, address them, and evaluate the effectiveness of the measures taken to address these symptoms

Kotooka et al. 356, 2019	RCT	181 patients	Home telemonitoring	Home telemonitoring for Japanese patients with heart failure was feasible; however, beneficial effects in addition to those of usual care were not demonstrated
Grustam et al. 357, 2018	Markov Model		Home telemonitoring (HTM) and Nurse telephone support (NST)	This modelling study demonstrated that HTM and NTS are viable solutions to support patients with chronic heart failure. NTS is cost-effective in comparison with UC at a WTP of €9000/QALY or higher. Like NTS, HTM improves the survival of patients in all NYHA classes and is cost-effective in comparison with UC at a WTP of €14,000/QALY or higher
Kao et al. 358, 2016	Retrospective analysis	623 patients	Telehealth and Care Management Program	The Health Buddy Program, a content-driven telehealth system coupled with care management, was associated with significantly better survival and reduced hospitalization in Medicare beneficiaries with HF
Athilingam et al. 359, 2017	RCT	18 patients	Mobile Health Intervention	The trends demonstrated in this pilot feasibility study warrant further exploration on the use of HeartMapp to improve HF outcomes.

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List of meta-analysis on Telemonitoring and home care

Author	Design	Studies included	Intervention	Conclusion
Donseth et al. 1, 2004	Meta-analysis	54 articles	Disease management programmes (DMPs)	DMPs are effective at reducing re-admissions among elderly patients with HF.
Inglis et al. 2, 2011	Meta-analysis	30 studies	Telemonitoring (TM) and structured telephone support (STS)	Telemonitoring and STS both appear effective interventions to improve outcomes in patients with CHF.
McAllister et al. 3, 2004	Meta-analysis	29 studies	Multidisciplinary strategies for the management of heart failure patients	Multidisciplinary strategies for the management of patients with HF reduce HF hospitalizations. Those programs that involve specialized follow-up by a multidisciplinary team also reduce mortality and all-cause hospitalizations.
Pandor et al. 4, 2013	Meta-analysis	21 RCTs	Remote monitoring and structured telephone support (STS)	STS HH and TM with medical support provided during office hours showed beneficial trends, particularly in reducing all-cause mortality for recently discharged patients with heart failure.
Roccaforte et al. 5, 2005	Meta-analysis	33 RCTs	Disease management programmes (DMP)	DMP reduce mortality and hospitalisations in HF patients

Xiang et al. 6, 2013	Meta-analysis	33 studies	Telehealth programmes	Telehealth programmes demonstrated clinical effectiveness in patients with CHF compared with usual care.
Nakamura et al. 7, 2014	Meta-analysis	13 studies	Remote monitoring	RPM is effective in chronic heart failure and rapid intervention was the most important factor in the RPM model.
Feltner et al. 8, 2014	Meta-analysis	47 studies	Transitional care interventions	Home-visiting programs and MDS-HF clinics reduced all-cause readmission and mortality; STS reduced HF-specific readmission and mortality.
Philips et al. 9, 2014	Meta-analysis	18 studies	Discharge planning plus post discharge support for older patients with CHF	Comprehensive discharge planning plus post discharge support for older patients with CHF significantly reduced readmission rates and may improve health outcomes such as survival and QOL without increasing costs.
Kotb et al. 10, 2015	Meta-analysis	30 RCTs	Telemedicine for individuals with heart failure	Compared to usual care, structured telephone support and telemonitoring significantly reduced the odds of deaths and hospitalization due to heart failure.
Van Spall et al. 11, 2017	Meta-analysis	53 RCTs	Transitional care services	Nurse home visits and DMCs decrease all-cause mortality after hospitalization for HF. Along with NCM, they also reduce all-cause readmissions, with no significant difference in comparative effectiveness.
Knox et al. 12, 2017	Meta-analysis	26 studies	Telemedicine enhanced chronic heart failure disease management	These findings provide preliminary support for the use of telemedicine in the management of heart failure without jeopardising patient well-being.
Lin et al. 13, 2017	Meta-analysis	39 studies	Telemedicine	Telemedicine was shown to be beneficial

Jonkman et al. 14, 2016	Meta-analysis	20 studies	Self-management	This study shows that self-management interventions had a beneficial effect on time to HF-related hospitalization or all-cause death and HF-related hospitalization alone and elicited a small increase in HF-related quality of life.
Or et al. 15, 2017	Meta-analysis	50 studies	Consumer health information technology (CHIT)	The narrative synthesis indicated that only a small proportion of the trials reported positive effects of CHITs over usual care.
Yun et al. 16, 2018	Meta-analysis	37 RCTs	Telemonitoring	TM intervention reduces the mortality risk in patients with HF, and intensive monitoring with more frequent transmissions of patient data increases its effectiveness.
Pekmezaris et al. 17, 2018	Meta-analysis	26 studies	Home telemonitoring	Home telemonitoring decreased the odds of all-cause mortality and heart failure–related mortality at 180 days but not at 365 days.
Lambrinou et al. 18, 2012	Meta-analysis	19 RCTs	Nurse-led discharge planning	The results of the current meta-analysis highlight the potential of HF-MPs with nurse-driven pre-discharge interventions to reduce hospital re-admissions.
Tse et al. 19, 2018	Meta-analysis	72 studies	Telemonitoring and hemodynamic monitoring	Telemonitoring and hemodynamic monitoring reduce hospitalization in both short- and long-term in heart failure patients.

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List of trials on Telerehabilitation in Heart Failure

Author	Design	Sample Size	Intervention	Conclusion
Oka et al. 1, 2000	RCT	40 patients	Home-based walking and resistance training program	The exercise intervention improved fatigue (p = 0.02), emotional function (p = 0.01), and mastery (p = 0.04).
Harris et al. 2, 2003	RCT	46 patients	Functional electrical stimulation (FES)	FES produces beneficial changes in muscle performance and exercise capacity in patients with CHF. Within this study, the benefits were similar to those observed following bicycle training.
Gary et al. 3, 2004	RCT	32 patients	Home-based exercise	Home-based, low-to-moderate intensity exercise, in addition to education, is an effective strategy for improving the functional capacity and quality of life in women with DHF.
Smart et al. 4, 2005	Single cohort study	30 patients	Heart rate monitors and exercise diaries	Telemonitoring is feasible for following adherence to home exercise training.
Daskapan et al. 5, 2005	RCT	22 patients	Home-based exercise	Supervised and home-based exercise training enhanced exercise capacity in patients with chronic heart failure.
Evangelista et al. 6, 2006	RCT	99 patients	Home-based walking program	Findings demonstrate the beneficial effects of a low-level, home-based walking program on weight loss in overweight and obese patients with advanced HF.

De Mello Franco et al. 7, 2006	RCT	29 patients	Home-based exercise training	Home-based training following supervised training is a safe strategy to maintain improvements in QoL
Gary et al. 8, 2006	RCT	32 patients	Home-based exercise training	Nevertheless, these findings indicate that exercise self-efficacy workload and adherence may increase as exercise tolerance increases.
O'Connor et al. 9, 2009	RCT	2331 patients	Usual training +home-based exercise	In the protocol-specified primary analysis, exercise training resulted in nonsignificant reductions in the primary end point of all-cause mortality or hospitalization and in key secondary clinical end points.
Dracup et al. 10, 2009	RCT	173 patients	A home-based walking program	A home-based walking program that incorporated aerobic and resistance exercise did not result in improved clinical outcomes at 1-year follow-up in this cohort of patients with systolic HF.
Karpolat et al. 11, 2009	RCT	74 patients	Home-based exercise training	Both the hospital-based and home-based exercise groups improved significantly in functional capacity, quality of life, depression symptoms, and LVEF.
Jehn et al. 12, 2009	Single cohort study	50 patients	Accelerometer-based quantification of 6-minute walk test	Accelerometers are reliable in measuring physical performance during the 6MWT in CHF patients.
Padela et al. 13, 2009	RCT	32 patients	Home-based nurse-coached inspiratory muscle training	Significant differences in PI(max), dyspnoea, and respiratory rate were found
Jolly et al. 14, 2009	RCT	169 patients	Home-based exercise programmes	Home-based exercise training programmes may not be appropriate for community-based heart failure patients.

Piotrowicz et al. 15, 2010	RCT	152 patients	Home-based telemonitored cardiac rehabilitation	In patients with HF, HTCR is equally as effective as SCR and provides a similar improvement in quality of life.
Quittan et al. 16, 2001	RCT	42 patients	Neuromuscular electrical stimulation of thigh muscles	Neuromuscular electrical stimulation of thigh muscles in patients with refractory heart failure is effective in increasing muscle strength
Corvera-Tindel et al 17, 2004	RCT	79 patients	Home walking exercise program	In patients with heart failure, a progressive home walking exercise program is acceptable, increases walking distance, and decreases global rating of symptoms.
Flynn et al. 18, 2009	RCT	2331 patients	Usual training +home-based exercise	Exercise training conferred modest but statistically significant improvements in self-reported health status compared with usual care without training.
Inglis et al. 19, 2006	RCT	297 patients	Home-based exercise programmes	HBI is a remarkably cost- and time-effective strategy over the longer term.
Webb-Peploe et al. 20, 2000	Cross-over trial	24 patients	Home-based exercise programme	Patients with idiopathic dilated cardiomyopathy showed a significant increase in exercise time
Hambrecht et al. 21, 2000	RCT	73 patients	Home-based ergometer exercise training	In patients with stable chronic heart failure, exercise training is associated with reduction of peripheral resistance and results in small but significant improvements in stroke volume and reduction in cardiomegaly
McKelvie et al. 22, 2002	RCT	181 patients	Home-based exercise programme	Exercise training improves peak oxygen uptake and strength during supervised training.

Sabelis et al. 23, 2004	RCT	29 patients	Hospital training +home-based exercise	Physical training led to normalization of the stimulated plasma vWF release.
Gielen et al. 24, 2003	RCT	20 patients	Home-based exercise programme	Exercise training significantly reduced the local expression of TNF-alpha, IL-1-beta, IL-6, and iNOS in the skeletal muscle of CHF patients.
Senden et al. 25, 2005	RCT	77 patients	Hospital training +home-based exercise	In CHF patients, home-based training in conjunction with a supervised strength and endurance training program is safe, feasible and effective
Cowie et al. 26, 2011	RCT	60 patients	Home walking exercise program	Hospital-based training enabled participants to walk for longer periods.
Chien et al. 27, 2011	RCT	51 patients	Home-based exercise programme	Home-based exercise improved quality of life and physical function significantly but not psychological status in these patients.
Servantes et al. 28, 2012	RCT	50 patients	Home-based exercise programme	Home-based exercise training is an important therapeutic strategy in chronic heart failure patients with sleep apnoea
Sato et al. 29, 2012	Single cohort study	40 patients	Home-based exercise programme	The number of steps and energy expenditures outside the hospital were correlated with improved exercise capacity.
Cowie et al. 30, 2014	RCT	46 patients	Home walking exercise program	Both training programmes incurred similar costs, which were offset by a reduction in emergency admission costs, compared with controls.

Piotrowicz et al. 31, 2015	RCT	131 patients	Home-based telemonitored cardiac rehabilitation	The study demonstrated that in heart failure patients HTCR provided a similar improvement in total QoL index as SCR.
Smolis-Bak et al. 32, 2015	RCT	52 patients	Telemonitoring guided home-based training programs	A structured exercise training program in the hospital and home-based with telemonitoring was safe option of additional treatment and improved directly physical fitness and, quality of life
Piotrowicz et al. 33, 2015	RCT	111 patients	Home-based telemonitored Nordic walking	In HF patients, including those with CIEDs, home-based telemonitored NW is safe and effective. NW was well accepted by patients and adherence was high and promising.
Selman et al. 34, 2015	A controlled, non-randomised trial	15 patients	Tele-Yoga	Tele-Yoga is an acceptable and appropriate intervention in people with HF and COPD
Prescher et al. 35, 2016	Single cohort study	155 patients	Tele-6MWT	Tele-6MWT has a high predictive value with respect to hospitalization as a result of HF or death from any cause and the results were comparable with the prognostic impact of a conventional 6MWT
Hollriegel et al. 36, 2016	RCT	37 patients	Hospital training +home-based exercise	Exercise training over 12 months resulted in an improvement in exercise capacity and reversing of left ventricular remodelling in patients with advanced CHF
Cowie et al. 37, 2012	RCT	60 patients	Home walking exercise program	Both training programmes significantly improved exercise capacity, though neither significantly improved QoL.
Jehn et al. 38, 2013	Single cohort study	155 patients	Tele-accelerometry	Tele-accelerometry is feasible in patients with CHF and output parameters are indicative of exercise capacity.

Piotrowicz et al. 39, 2012	Single cohort study	75 patients	ECG telemonitoring during home-based cardiac rehabilitation	Cardiac rehabilitation at home was improved by utilizing the tele-event-Holter ECG facility.
Piotrowicz et al. 40, 2016	RCT	111 patients	Home-based telemonitored Nordic walking	Positive effect of the sympatho-parasympathetic balance obtained during the home CCR based on Nordic walking training results from the additive effects of the reversion of depression and physical capacity improvement in CHF patients.
Safihari-Hafizi et al. 41, 2016	RCT	40 patients	Home-based exercise programme	We have shown that a home-based cardiac rehabilitation program involving interval and resistance training is associated with improved aerobic capacity and quality of life
Lundgren et al. 42, 2016	RCT	111 patients	Internet-based cognitive behavioural therapy	Guided ICBT adapted for persons with HF and depressive symptoms was not statistically superior to participation in a Web-based DF.
Hwang et al. 43, 2017	RCT	53 patients	12-week, home-based telerehabilitation program	Telerehabilitation was not inferior to a hospital outpatient-based rehabilitation program in patients with chronic heart failure.
Donesky et al. 44, 2017	Controlled non-randomized trial	14 patients	Tele-Yoga	TeleYoga was acceptable and adherence was good; however, technical issues were an important hindrance to participation.
Hwang et al. 45, 2017	Mixed-methods design	17 patients	12-week, home-based telerehabilitation program	Participants in this study reported high visual clarity and ease-of-use, but provided suggestions for further improvements in group-based video telerehabilitation for HF.
Hwang et al. 46, 2017	Single cohort study	17 patients	Assessing functional exercise capacity using telehealth	The use of telehealth for the assessment of functional exercise capacity appears to be valid and reliable in patients with heart failure.

Fayazi et al. 47, 2013	Matched groups study	60 patients	Home walking exercise program	The home-based walking showed improvement in the performance, exercise tolerance time and quality of life in heart failure patients
Okumus et al. 48, 2018	Single cohort study	45 patients	SenseWear arm band	Correlation between activity monitor data and 6MWD, most of SF-36 sub-group scores, MLHF scores and NEADL index scores suggest that activity monitor can be used in the evaluation of patients with PH.
Chen et al. 49, 2018	RCT	37 patients	Home-based exercise programme	Home-based cardiac rehabilitation offered the most improved results in functional capacity, QOL, and a reduced the rate of readmission within 90 days.
Kim et al. 50, 2017	Single-centre, non-randomized, prospective study	82 patients	Educated Home-based Exercise Training	Hospital-based ET was beneficial for HF patients, improving functional capacity and QOL. However, no significant advantages were observed in terms of a composite endpoint compared to home-based ET.
Abdelbasset et al. 51, 2019	RCT	69 patients	Home-based exercise	Both exercise programs had positive effects in reducing the severity of depression in HF patients.
Dalal et al. 52, 2019	RCT	216 patients	Home-based rehabilitation	The novel REACH-HF home-based facilitated intervention for HFrEF was clinically superior in disease-specific HRQoL at 12 months and offers an affordable alternative to traditional centre-based programmes to address current low cardiac rehabilitation uptake rates for heart failure.
Piotrowicz et al. 53, 2019	RCT	850 patients	Telerehabilitation in Heart Failure Patients (TELEREH-HF)	In this trial, the positive effects of a 9-week program of HCTR in patients with heart failure did not lead to the increase in percentage of days alive and out of the hospital and did not reduce mortality and hospitalization over a follow-up period of 14 to 26 months.

Palau et al. 54, 2019	Single cohort study	45 patients	Home-based inspiratory muscle training	In symptomatic and deconditioned older patients with heart failure with preserved ejection fraction, a home-based inspiratory muscle training programme improves aerobic capacity
Deka et al. 55, 2019	RCT	30 patients	Internet-based pilot study	Delivering social support by internet-based synchronized face-to-face video is feasible with heart failure patients.
Tousignant et al. 56, 2019	Single cohort study	4 patients	Telerehabilitation with live-feed biomedical sensor signals	This study proved the feasibility of using telerehabilitation with real-time biomedical sensors as an alternative or a complement to the conventional CR program.
Van Dissel et al. 57, 2019	RCT	34 patients	Home-based, self-selected exercise training	In symptomatic adults with moderate or severe CHD, home-based exercise training of their preference appeared safe, with good compliance and favourable effects on exercise capacity.
Deka et al. 58, 2018	Single cohort study	30 patients	Fitbit® Charge HR (FCHR)	Wrist-worn activity monitors can be useful for objective measurement of exercise adherence and monitoring of physical activity in patients with heart failure in a community setting.
Bhasipol et al. 59, 2018	Single cohort study	11 patients	Home cardiac rehabilitation program	Once-a-week outpatient hospital-based exercise program followed by supervised home-based exercise program showed a significant benefit in improvement of exercise capacity in adults with complex cyanotic congenital heart disease
Hwang et al. 60, 2018	RCT	53 patients	Home cardiac rehabilitation program	Heart failure telerehabilitation appears to be less costly and as effective for the health care provider as traditional centre-based rehabilitation.
Lang et al. 61, 2018	RCT	50 patients	Home-based rehabilitation intervention	Our findings support the feasibility and rationale for delivering the REACH-HF facilitated home-based rehabilitation intervention for patients with HFpEF and their caregivers

Ambrosy et al. 62, 2018	RCT	2331 patients	Home-based training	Ambulatory HF patients with a reduced EF had impaired health status at baseline which was associated with increased morbidity and mortality
Peng et al. 63, 2018	RCT	98 patients	Home-based telehealth exercise training program	The results reveal that telehealth exercise training is an effective alternative method for cardiac rehabilitation, especially under the conditions in China.
Babu et al. 64, 2011	RCT	30 patients	Structured Home-based Program	Early in-patient rehabilitation followed by an eight-week home-based exercise program improves function and quality of life in patients with congestive heart failure
Wall et al. 65, 2011	RCT	19 patients	Home-based, supervised exercise	The home-based exercise intervention caused a significant change in perceived fatigue between study groups (p=0.015), after 6 months of study participation, with the control group less fatigued than the intervention

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63. *Peng X, Su Y, Hu Z, et al. Home-based telehealth exercise training program in Chinese patients with heart failure: A randomized controlled trial. Medicine (Baltimore). 2018;97(35):e12069. doi:10.1097/MD.0000000000012069*
64. *Babu AS, Maiya AG, George MM, et al. Effects of Combined Early In-Patient Cardiac Rehabilitation and Structured Home-based Program on Function among Patients with Congestive Heart Failure: A Randomized Controlled Trial. Heart Views. 2011;12(3):99–103. doi:10.4103/1995-705X.95064*
65. *Wall HK, Ballard J, Troped P, et al. "Impact of Home-based, Supervised Exercise on Congestive Heart Failure." International Journal of Cardiology 145.2 (2010): 267-70. Web.*

List of meta-analysis on Telerehabilitation of Heart Failure patients

Author	Design	Studies included	Intervention	Conclusion
Hwang et al. 1, 2009	Meta-analysis	19 studies	Home-based exercise programmes	Home-based exercise programmes have been shown to benefit people with heart failure in the short term.
Zwisler et al. 2, 2016	Meta-analysis	19 trials	Home-Based Cardiac Rehabilitation	Home-based CR results in short-term improvements in exercise capacity and health-related quality of life of heart failure patients compared to usual care
Imran et al. 3, 2019	Meta-analysis	31 studies	Home-Based Cardiac Rehabilitation Alone and Hybrid with Center-Based Cardiac Rehabilitation	HBCR and hybrid CR significantly improved functional capacity, but only HBCR improved hr-QOL over usual care. However, both are potential alternatives for patients who are not suitable for CBCR.

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Annex 4: Home-hospitalisation of Heart failure patients

List of trials on Home-hospitalisation of Heart failure patients

Author	Design	Sample Size	Intervention	Conclusion
Bechich et al.1, 2000	Observational study	110 patients	Home-hospitalisation	In elderly patients with non-complicated HF, the intervention of an HH unit reduces conventional hospital admissions
Mendoza Ruiz de Zuazu et al. 2, 2003	Observational study	158 patients	Home-hospitalisation	Our data confirm Hospital at Home as a valid option to conventional hospital admission for the management of patients with congestive heart failure
Mendoza et al, 3, 2009	RCT	71 patients	Home-hospitalisation	Hospital at home care allows an important reduction in the costs during the index episode compared with hospital care, whilst maintaining similar outcomes with respect to cardiovascular mortality and morbidity and quality of life at 1-year follow-up
Patel et al. 4, 2008	RCT	31 patients	Home-hospitalisation	Reduction in cost of care for selected patients with CHF eligible for hospital care might be achieved by early discharge from hospital followed by home visits
Tibaldi et al. 5, 2009	RCT	101 patients	Home-hospitalisation	Substitutive hospital-at-home care is a viable alternative to traditional hospital inpatient care for elderly patients with acutely decompensated CHF

Roig et al. 6, 2006	Observational study	61 patients	Home-hospitalisation	Although mortality in end-stage heart failure patients remained very high, use of a specialized advanced heart failure care program decreased the number of hospitalizations, days per hospitalization, and emergency room visits, and reduced the cost of care

1. *Bechich S, Sort Granja D, Arroyo Mateo X, et al. [Effect of home hospitalization in the reduction of traditional hospitalization and frequency of emergencies in heart failure]. Rev Clin Esp. 2000 Jun;200(6):310-4.*
2. *Mendoza Ruiz de Zuazu H, Regalado de los Cobos J, Altuna Basurto E, et al. [Treatment of congestive heart failure in the setting of hospital at home. Study of 158 patients]. Med Clin (Barc). 2003 Mar 29;120(11):405-7.*
3. *Mendoza H, Martin MJ, Garcia A, et al. 'Hospital at home' care model as an effective alternative in the management of decompensated chronic heart failure. Eur J Heart Fail. 2009 Dec;11(12):1208-13. doi: 10.1093/eurjhf/hfp143. Epub 2009 Oct 29.*
4. *Patel H, Shafazand M, Ekman I, et al. Home care as an option in worsening chronic heart failure. European Journal of Heart Failure 10 (2008) 675–681*
5. *Tibaldi V, Isaia G, Scarafiotti C, et al. Hospital at home for elderly patients with acute decompensation of chronic heart failure: a prospective randomized controlled trial. Arch Intern Med. 2009 Sep 28;169(17):1569-75. doi: 10.1001/archinternmed.2009.267.*
6. *Roig E, Perez-Villa F, Cuppoletti A, et al. Specialized Care Program for End-Stage Heart Failure Patients. Initial Experience in a Heart Failure Unit. Rev Esp Cardiol. 2006 Feb;59(2):109-16.*

List of meta-analysis on Home-hospitalisation of Heart failure patients

Author	Design	Studies included	Intervention	Conclusion
Qaddoura et al. 1, 2015	Meta-analysis	3 RCTs	Home-hospitalisation (HaH)	In the context of a limited number of modest-quality studies, HaH appears to increase time to readmission, reduce index costs, and improve HrQOL among patients requiring hospital-level care for HF.

1. *Qaddoura A, Yazdan-Ashoori P, Kabali C, et al. Efficacy of Hospital at Home in Patients with Heart Failure: A Systematic Review and Meta-Analysis. PLoS One. 2015;10(6):e0129282. Published 2015 Jun 8. doi:10.1371/journal.pone.0129282*

Annex 5: Digital health in cardiac arrhythmia diagnosis and management

List of trials on Smartphone for arrythmia detection

Author	Design	Sample Size	Intervention	Conclusion
Webster et al. 1, 2008	Single cohort study	47 patients with chest pain	Telemedicine service consisting of ECG interpretation and advice on the management of chest pain offshore was offered to oil rig installations	The use of email for ECG transmission proved to be highly effective in managing chest pain offshore.
Brunetti et al. 2, 2008	Single cohort study	27,841 patients	ECG evaluation according to a previously fixed inclusion protocol. Data recorded were transmitted with mobile telephone support to a telecardiology "hub" active 24-h a day.	This first region-wide leading experience shows the feasibility and reliability of telecardiology applied to a public emergency health-care service
Alis et al. 3 2009	Single cohort study	30 patients	Lifelink, a mobile real-time telemonitoring and diagnostic facility to command and control remote medical devices through mobile phones.	The method successfully categorized the 30 subjects without user intervention into the following cases: normal (at 86.7% accuracy), congestive heart failure (86.7%), and atrial fibrillation (80.0%).

Lin et al. 4, 2010	Single cohort study	20 atrial fibrillation patients	The acquired ECG signals are instantaneously transmitted to mobile devices, such as netbooks or mobile phones through Bluetooth	Clinical testing reveals that the proposed system is approximately 94% accurate, with high sensitivity, specificity, and positive prediction rates for ten normal subjects and 20 AF patients.
Gradl et al. 5, 2012	Single cohort study		Application for Android™-based mobile devices that allows real-time electrocardiogram (ECG) monitoring	More than 99% of all QRS complexes were detected correctly by the algorithm. Overall sensitivity for abnormal beat detection was 89.5% with a specificity of 80.6%.
Lee et al. 6 ,2012	Single cohort study	25 patients	A pulsatile photoplethysmogram (PPG) signal from a fingertip using the built-in camera lens	Using this criterion, they achieved an accuracy of 100% for both detecting the presence of either AF or normal sinus rhythm.
Bilgi et al. 7, 2012	Single cohort study	305 patients	Interpretations of electrocardiogram (ECG) images taken by a mobile phone and sent as multimedia message was investigated.	Sending the ECG images via a multimedia message service may be a practical and inexpensive telecardiology procedure.
Kirtava et al. 8, 2012	Single cohort study	35 patients	A three-lead ECG loop recorder was used in automatic mode with a Nokia Symbian phone. Automatically recorded arrhythmia events were transmitted from the loop recorder by Bluetooth to a phone and then by 3G to the Vitasystems server and were available to Georgian physicians via e-mail/Internet.	In remote areas mobile telemonitoring of patients will improve quality of care by timely provision of a second opinion in cases when local expertise is not sufficient.

Brunetti et al, 9, 2013	Single cohort study	27,841 patients	ECG evaluation according to a previously fixed inclusion protocol. Data recorded were transmitted with mobile telephone support to a telecardiology "hub" active 24-h a day.	AF with symptoms other than palpitations is a common finding in elderly EMS patients. Tele-cardiology support improves the sensitivity of diagnosis of AF in elderly EMS patients and is useful in at-home identification of subjects with AF and atypical presentation.
Lau et al, 10, 2013	Single cohort study	204 patients	Accuracy of the iPhone ECG as a diagnostic screening tool for the detection of AF by comparing it with a contemporaneous 12-lead ECG interpreted by a cardiologist.	This technology enables a high-quality single lead ECG to be recorded quickly and easily on a standard iPhone. The high sensitivity, specificity and accuracy of the algorithm, and widespread distribution of smartphones, make this device ideal for community screening.
McManus et al, 11, 2013	Single cohort study	76 patients	A smartphone-based application to detect an irregular pulse from AF	They found that a novel algorithm analysing signals recorded using an iPhone 4S accurately distinguished pulse recordings during AF from sinus rhythm.
Pak-Hei Chan, 12. 2016	Single cohort study	1013 patients	A single-lead ECG was recorded by using the AliveCor heart monitor with tracings reviewed subsequently by 2 cardiologists to provide the reference standard.	The Cardiio Rhythm smartphone PPG application provides an accurate and reliable means to detect AF in patients at risk of developing AF and has the potential to enable population-based screening for AF.
Huang et al. 13, 2014	Single cohort study	48 ECG cases	WE-CARE, an intelligent telecardiology system using mobile 7-lead ECG devices.	The clinical results clearly showed that our solution achieves a high detection rate of over 95% against common types of anomalies in ECG, while it only incurs a small detection latency around one second, both of which meet the criteria of real-time medical diagnosis.

Spethmann et al. 14, 2014	Single cohort study	10 marathon runners	Holter Tele-electrocardiogram and a standard smartphone connected via Bluetooth	Online electrocardiogram surveillance during marathon running is a promising preventive concept.
Lowres et al. 15, 2014	Single cohort study	1000 patients	iPhone electrocardiogram (iECG) in pharmacies	Screening with iECG in pharmacies with an automated algorithm is both feasible and cost-effective.
Orchard et al. 16, 2014	Single cohort study	88 patients	A single-lead iPhone electrocardiograph (iECG) with a validated AF algorithm	AF screening in general practice is feasible.
Kwon et al. 17, 2014	Single cohort study	15 patients	A brassiere-based reliable electrocardiogram (ECG) monitoring sensor system, for supporting daily smartphone healthcare applications	89.53% of QRS peaks were detected on average. The questionnaire-based user study with 15 participants showed that the CardioGuard sensor was comfortable and unobtrusive.
Le Page et al. 18, 2015	Single cohort study	954 patients	ECG recorded using the AliveCor (CA, USA) device attached to an Apple (CA, USA) iPhone 4 or 5.	in conclusion, this novel ECG application was quick and easy to use and led to the new diagnoses of arrhythmia, bundle branch block, LVH and cardiomyopathy in 23 (2.4%) of the total patients screened.
Kakria et al. 19, 2015	Single cohort study	40 patients	Real-time heart monitoring system	The performance analysis shows that the proposed system is reliable and helpful due to high speed.

Haberman et al. 20, 2015	Single cohort study	381 patients	Wireless, single-lead real-time ECG monitoring supported by iOS and android devices	Smartphone ECG accurately detects baseline intervals, atrial rate, and rhythm and enables screening in diverse populations.
Chong et al. 21, 2015	Single cohort study	99 patients	Smartphone-based arrhythmia discrimination algorithm	This clinical application results show that the proposed method detects NSR with specificity of 0.9886 and discriminates PVCs and PACs from AF with sensitivities of 0.9684 and 0.9783, respectively.
Baquero et al. 22, 2015	Single cohort study	5 patients	The bipolar arrangement of the AliveCor monitor coupled to smart phone technology.	This study demonstrates the feasibility of creating a 12 lead ECG with a smart phone
Peritz et al. 23, 2015	Single cohort study	6 patients	AliveCor monitoring	AliveCor monitoring has the potential to enhance evaluation of symptomatic athletes by allowing trainers and team physicians to make diagnosis in real-time and facilitate faster return to play.
Muhlestein et al. 24, 2015	Single cohort study	6 patients	Smartphone ECG.	This study confirmed the potential of a smartphone ECG for evaluation of acute ischemia and the feasibility of studying this technology further to define the diagnostic accuracy, limitations and appropriate use of this new technology.
Shih et al. 25, 2015	Single cohort study	120 participants	Mobile wireless monitoring technology and IT	This efficient and inexpensive monitoring method can also prevent arrhythmias in unscreened competitors, the danger of collision among staff and competitors, and preserves oxygen by eliminating additional on-foot monitoring staff.

Orchard et al. 26, 2016	Single cohort study	976 patients	30-second iECG, which has a validated algorithm for detecting AF in real time	Screening with iECG during influenza vaccination by primary care nurses is feasible and well accepted by practice staff. Addressing barriers is likely to increase uptake.
Koenig et al. 27, 2016	Single cohort study	68 patients	Accuracy of a heart rate (HR) measurement algorithm applied to a pulse wave	In conclusion, the overall accuracy of HR and HRV indices of pulse wave analysis, based on video signals of a smartphone, with the developed algorithm was sufficient for preclinical screening applications.
Scheurermeyer et al. 28, 2016	Single cohort study	298 patients	De-identified photographs of each EKG via a mobile phone camera	Systematic text messaging of ED EKGs from a small community hospital to a referral centre is a rapid, accurate, portable, and inexpensive method of data transfer.
Lowres et al. 29, 2016	Single cohort study	42 patients	Phone handheld electrocardiogram (iECG)	Providing patients with an iECG is a non-invasive, inexpensive, convenient and feasible way to monitor for AF recurrence in post-cardiac surgery patients.
Garabelli et al. 30, 2016	Single cohort study	99 patients	Smart phone heart monitors	The SHM is accurate in measuring QTc interval in sinus rhythm when compared to 12-lead ECG in healthy volunteers.
McManus et al. 31, 2016	Single cohort study	121 patients	Smartphone app for AF detection	Smartphone-based app demonstrated excellent sensitivity (0.970), specificity (0.935), and accuracy (0.951) for real-time identification of an irregular pulse during AF.
Yano et al. 32, 2016	Single cohort study	370 patients	Hand-held devices such as smartphones can record short-duration (e.g., 1-minute) ECGs	Daily snapshot ECG monitoring over 365 days detects half of patients who developed AT/AF as detected by CIED, and shorter intervals of monitoring detected fewer AT/AF patients.

Poh et al. 33, 2017	Single cohort study	40 patients	Freely available smartphone application, Cardiio app (Cardiio, Inc., Cambridge, MA)	The Cardiio app provided accurate heart rate measurements from the finger and face, both at rest and after exercise.
Ghanbari et al. 34, 2017	Single cohort study	10 patients	Mobile application (miAfib) to assess symptoms, positive affect and negative affect on multiple occasions throughout the day based on iOS platform.	Participants reported that they found the application easy to use and would consider using the application in the future.
Yasin et al. 35, 2017	Single cohort study	21 haemodialysis patients	Smartphone equipped with inexpensive FDA-approved electrodes for three 2min intervals	A single-lead ECG acquired using electrodes attached to a smartphone can be processed to calculate the serum potassium in patients undergoing haemodialysis remotely.
Hickey et al. 36, 2017	Single cohort study	23 patients	mHealth technology with self-management approaches	Cardiac mHealth self-monitoring is a feasible and effective mechanism for enhancing AF/AFL detection that improves quality of life.
Maurizi et al. 37, 2017	Single cohort study	117 patients	D-Heart® is a portable device that enables the acquisition of the ECG on multiple leads which streams via Bluetooth to any smartphone.	D-Heart® proved effective and accurate stratification of ECG abnormalities comparable to the 12-lead ECGs, thereby opening new perspectives for low-cost community cardiovascular screening programs in low-income settings.
Chan et al. 38, 2017	Single cohort study	13122 patients	Smartphone-based wireless single-lead ECG	Community screening for AF with SL-ECG was feasible and it identified a significant proportion of citizens with newly diagnosed AF.

Plews et al. 39, 2017	Single cohort study	29 patients	Smartphone photoplethysmography (PPG) and heart-rate sensor	Both PPG and heart-rate sensors provide an acceptable agreement for the measurement of rMSSD when compared with ECG.
Brunner et al. 40, 2017	Single cohort study	3028 patients	Smartphone-based ECG and breath alcohol concentration (BAC) measurements	Acute alcohol consumption is associated with cardiac arrhythmias and sinus tachycardia in particular. This partly reflects autonomic imbalance as assessed by significantly reduced respiratory sinus arrhythmia.
Oginosawa et al. 41, 2017	Prospective, multicentre, observational study	185 patients	SmartShock Technology®(SST) discrimination algorithm	Compared with previous algorithms, the SST discrimination algorithm significantly lowered the rate of inaccurate detection of VT in recipients of dual-chamber ICD or CRT-D.
Guo et al. 42, 2017	Single cohort study	209 patients 113 intervention 96 control	Mobile AF (mAF) App was designed to incorporate clinical decision-support tools	mAF App, integrating clinical decision support, education, and patient-involvement strategies, significantly improved knowledge, drug adherence, quality of life, and anticoagulation satisfaction.
Jakkola et al. 43, 2018	Case-control study	300 patients 150 intervention 150 control	3-minute mechanocardiography recording was acquired from each subject with a Sony Xperia smartphone placed on the sternum, and a simultaneously obtained 5-lead telemetry electrocardiography	Smartphone mechanocardiography reliably detects AF without any additional hardware and provides a new easy-to-use and accessible concept for AF screening.
Pipitprapat et al. 44, 2018	Single cohort study	140 patients	HR detected by the smartphone apps (App1 = Instant HR, App2 = Cardiio: HR Monitor and App3 = Runtastic HR Monitor) with	HR measurements from all applications were correlated well with ECG monitoring. However, it was less accurate in case of irregular rhythm such as atrial fibrillation.

			simultaneous standard ECG monitoring	
Dimarco et al, 45, 2018	Single cohort study	148 patients	Kardia Mobile personalised smartphone electrocardiogram (ECG)	Kardia Mobile diagnosed the cause of intermittent palpitations in the majority of patients referred for specialist evaluation.
Yan et al. 46, 2018	Single cohort study	217 patients	(AF) screening using an iPhone camera to detect and analyse photoplethysmography signals	The Cardiio Rhythm smartphone application showed high sensitivity and specificity, with low negative likelihood ratio for AF from facial photoplethysmography signals.
Gaibazzi et al. 47, 2018	Single cohort study	30 participants	The Heart Sentinel™ app (HS-app) is conceived to detect cardiac arrest during outdoor sports, automatically alerting contacts via SMS with GPS position data.	A simple smartphone app, using commercially available heart rate monitors, is promising to detect cardiac arrest caused by VF during sports
Koshy et al. 48, 2018	Single cohort study	51 patients	Smartphone-based electrocardiograms (ECGs) for arrhythmia screening	Combining the device automated diagnostic algorithm with cardiologist interpretation of only uninterpretable traces yielded excellent results and provides an efficient, cost-effective workflow for the utilization of a smartphone-based ECG in clinical practice.
Rozen et al. 49, 2018	Single cohort study	98 patients	Cardiio Rhythm Mobile Application (CRMA) for AF detection	CRMA demonstrates promising potential in accurate detection and discrimination of AF from normal sinus rhythm in patients with a history of AF.

Narashima et al. 50, 2018	Single cohort study	38 patients	Smartphone-based electrocardiographic (ECG) recorder/event recorder	Kardia Mobile is noninferior to an external loop recorder for detecting arrhythmias in the outpatient setting
Lahdenoja et al. 51, 2018	Single cohort study	39 patients	Smartphone-only solution for the detection of atrial fibrillation	An accuracy of 97.4% in AFib versus healthy classification (a sensitivity of 93.8% and a specificity of 100%).
Mena et al. 52, 2018	Single cohort study	100 patients	Mobile electrocardiogram (ECG) monitoring	The system could be useful for detecting cardiac abnormalities in the home environment, while keeping costs down and increasing access to healthcare services for older persons.
Chan et al. 53, 2018	Single cohort study	244 patients	Nongovernmental organization-led community-based AF screening program	The effectiveness of the program in subsequently leading them to receive appropriate oral anticoagulation therapy is weakened by the lack of a more structured downstream management pathway.
Reading et al. 54, 2018	Qualitative study	13 patients, 6 health providers and 2 researcher coordinators	Interview	The findings of this study provide initial requirement specifications for the design of applications that engage patients in this unique population of adults with AF.
William et al. 55, 2018	Single cohort study	52 patients	Kardia Mobile Cardiac Monitor (KMCM) detects atrial fibrillation (AF) via a handheld cardiac rhythm recorder	The KMCM system provides sensitive and specific AF detection relative to 12-lead ECGs when an automated interpretation is provided. Direct physician review of KMCM recordings can enhance diagnostic yield, especially for unclassified recordings.

Reverberi et al. 56, 2019	Single cohort study	100 patients	RITMIA™ app	The automated RITMIA™ algorithm very accurately differentiated AF from SR before and after elective ECV. The only hardware required by this method is a cheap consumer-grade Bluetooth heart rate monitor of the chest-strap type
Selder et al. 57, 2019	Single cohort study	5982 patients	AliveCor Kardia Mobile	This study reports on the first symptom-driven remote arrhythmia monitoring program in the Netherlands. Less than 10% of the ECGs were uninterpretable.
Yakel et al. 58, 2019	Single cohort study	24 participants	Accuracy of a free heart rate monitoring application on two smartphone platforms	The applications chosen for both platforms to monitor heart rate were found to be fairly accurate, especially at rest.
Brasier et al. 59, 2019	Prospective, two-centre, international, clinical validation study	592 patients	Compared a PPG-based algorithm against a cardiologist's iECG diagnosis to distinguish between AF and sinus rhythm	This is the first prospective clinical two-centre study to demonstrate that detection of AF by using a smartphone camera alone is feasible, with high specificity and sensitivity.
Himmelreich et al. 60, 2019	Single cohort study	214 patients	AliveCor KardiaMobile	In a primary care population, a smartphone-operated, 1L-ECG device showed excellent diagnostic accuracy for AF/AFL and good diagnostic accuracy for other rhythm abnormalities.
Towhari et al. 61, 2019	Single cohort study	211 patients	Smartphone-based Electrocardiogram Recorders	The ECG rhythms produced by smartphone accessory have a good diagnostic accuracy in diagnosing arrhythmias.

Frisch et al. 62, 2019	Single cohort study	10 patients	Multi-lead tracings using a commercial mECG device	Compared to a single lead recording, multi-lead mECGs significantly improved cardiologists' diagnostic accuracy and confidence in their interpretation approaching that of a standard 12-lead ECG.
Reed et al. 63, 2019	Single cohort study	243 patients	Smartphone-based event recorder (AliveCor)	Use of a smartphone-based event recorder increased the number of patients in whom an ECG was captured during symptoms over five-fold to more than 55% at 90 days.
Goldenthal et al. 64, 2019	RCT	238 patients 115 intervention 123 control	AliveCor KardiaMobile ECG monitor	The use of mobile ECG self-recording devices allows for earlier detection of AF/AFL recurrence and may empower patients to engage in shared health decision-making.
Tarakji et al. 65, 2015	Single cohort study	60 patients	AliveCor heart monitor (AHM) case and a traditional trans telephonic monitor (TTM)	The AHM is an alternative method for monitoring patients with AF after the ablation procedure. Most patients found it easy to use.
Orchard et al. 66, 2019	Single cohort study	1805 patients	eHealth Tools to Provide Structured Assistance for Atrial Fibrillation	The eHealth tools showed promise. Adherence to guideline-based oral anticoagulant prescription was significantly higher in patients diagnosed during the study period, although the EDS was only used in a minority.
MacNiven et al. 67, 2019	Semi-structured interviews	23 staff members	An electrocardiogram (ECG) attached to a mobile phone (iECG) screening device for atrial fibrillation (AF)	The iECG device was well accepted within ACCHSs and was feasible to use to screen for AF among Aboriginal patients. Implications for public health:

Zaprutko et al. 68, 2019	Single cohort study	525 ECGs	Kardia Mobile with a dedicated application (Kardia app)	Kardia app is capable of fast screening and detecting AF with high sensitivity and specificity. The possible diagnosis of AF deserves additional cardiological evaluation.
Halcox et al. 69, 2017	RCT	1001 patients	AliveCor Kardia monitor attached to a WiFi-enabled iPod to obtain ECGs (iECGs)	Screening with twice-weekly single-lead iECG with remote interpretation in ambulatory patients ≥65 years of age at increased risk of stroke is significantly more likely to identify incident AF than RC over a 12-month period.
Krivoshei et al. 70, 2017	Single cohort study	80 patients	Plethysmography sensor of an iPhone 4S	The algorithm tested reliably discriminated between SR and AF based on pulse wave signals from a smartphone camera only.
Williams et al. 71, 2015	Single cohort study	99 patients	AliveCor® device	The AliveCor® device should be considered as an option for early identification of patients with unknown AF
Chan et al. 72, 2017	Single cohort study	2052 patients	Head-to-Head Comparison of the AliveCor Heart Monitor and Microlife WatchBP Office AFIB	The introduction of these devices into routine practice could have a substantial impact on reducing the stroke burden.
Newham et al. 73, 2017	Single cohort study	20 patients	AliveCor® device	The novel smartphone-based event recorder is an efficient tool for achieving symptom rhythm correlation in patients with palpitations
Harrington et al. 74, 2018	Single cohort study	93 patients	Novel iPhone 4S application	Our findings show that this smartphone application is able to accurately detect and classify an irregular pulse from signals in the fingertip of patients with AF and PACs/PVCs.

Syvaoja et al. 75, 2018	Single cohort study	22 VF rhythms	Mobile phone analysis	The recordings of normal ECG rhythm and VF within an area the size of a mobile phone are of sufficient quality and could be used in 'rhythm-based' OHCA recognition.

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List of trials on Ambulatory monitoring with new tools

Author	Design	Sample Size	Intervention	Conclusion
Gorjup et al. 1, 2000	Single cohort study	463 calls	Transtelephonic transmission of electrocardiograms (ECGs)	Transtelephonic ECG transmission enables direct communication between general practitioner or patient and cardiologist.
Orlov et al. 2, 2001	Single cohort study	74 patients	Wireless one channel limited (3-lead) home electrocardiogram (ECG) transmission system and ambulatory devices data transmission using telephone lines	CG screening can be significantly simplified and made widely acceptable at home and distant sites using wireless monitoring tools and telephone line transfer of the signal.
Uldal et al. 3, 2004	Single cohort study	44 patients	Mobile telemedicine unit (MTU)	Following the pilot study, the local Russian health administration stated that the MTU should always be included on emergency trips to the districts.
Inglis et al. 4, 2004	Single cohort study	152 patients	Nurse-led, multidisciplinary, home-based intervention (HBI)	These data provide sufficient preliminary evidence to support the hypothesis that the benefits of HBI in relation to the management of HF may extend to "high risk" patients with chronic AF in whom morbidity and mortality rates are also unacceptably high.
Scalvini et al. 5 ,2005	Single cohort study	310 patients	Cardiac event recording	More patients therefore received a clear diagnosis, and more quickly, when using event recording than with Holter monitoring.
Senatore et al. 6, 2005	Single cohort study	72 patients	Transtelephonic ECG is better than standard ECG and 24-h Holter recordings in evaluating AF relapses after RCA, thus	Transtelephonic electrocardiographic monitoring

			decreasing the short-term success of ablation from 86% to 72%.	
Roche et al. 7, 2002	Prospective cohort study	65 patients	Automatic long-term event recorders	In patients still complaining of palpitations after one negative 24-hour Holter, numerous, prolonged, and often asymptomatic episodes of PAF can be revealed by long-term automatic event recorders.
Rubel et al. 8, 2005	Single cohort study	697 patients	Novel, very affordable, easy-to-use, portable, and intelligent Personal ECG Monitor (PEM)	The clinical evaluation indicates that the EPI-MEDICS concept may save lives and is very valuable for prehospitalization triage.
Alte et al. 9, 2006	Single cohort study	7008 patients	Portable electrocardiogram (ECG)	The functionality and ergonomics of ECG cards appear to be sufficiently developed for large-scale use in epidemiological studies.
Wittkowsky et al. 10, 2006	Retrospective, observational cohort design	234 patients 117 in-hospital visits 117 telephone follow-ups	Telephone vs in-office visits in an anticoagulation clinic setting.	Telephone-based management of oral anticoagulation through a pharmacist-staffed anticoagulation clinic yielded clinical outcomes that were at least as favourable as those associated with traditional office-based visits.
Schickendantz et al. 11, 2006	Single cohort study	37 patients	Wireless Holter transmission	Wireless Holter recordings are useful in detecting dysrhythmias with rare occurrence, are less expensive and less invasive compared with implantable loop recorders and offer the patient rather wide geographic ranges with sufficient signal quality.

Terschuren et al. 12, 2007	Single cohort study	3 patients	One lead ECG meter	The GP reported a positive effect on her work, with time saved because of less travelling for home visits.
Webster et al. 13, 2008	Single cohort study	47 patients	Telemedicine service consisting of electrocardiogram (ECG)	The use of email for ECG transmission proved to be highly effective in managing chest pain offshore.
Atarashi et al. 14, 2008	Double-blind, placebo-controlled trial	123 patients	Trans-telephonic ECG findings	During a 4-week observation, 2848 ECGs, comprising 894 (31.4%) symptomatic and 1954 (68.6%) asymptomatic tracings, and, during 31 days of treatment, 3471 ECGs, comprising 874 (25.2%) symptomatic and 2587 (74.8%) asymptomatic tracings, were transmitted.
Janse et al. 15, 2008	Single cohort study	41 patients	Event recorder 1 month prior to the ablation for the period of 4 months. Event strips were sent by telephone on a daily basis	Our data demonstrate that for the evaluation of effectiveness of PV ablation, the lack of symptoms during follow-up is not a valid indication. Objective rhythm monitoring in order to detect asymptomatic AF should be performed.
Vanagas et al. 16, 2008	Single cohort study	34 patients	Telephonic electrocardiography (ECG) consultations	Tele-ECG service of routine ECGs can be useful in recognition of silent ischemia or arrhythmias and facilitating diagnosis.
Redmond et al. 17, 2008	Single cohort study	24 patients	Remote home monitoring system	The results show that in the majority of cases, the capture of ECG in an unsupervised home environment is achievable.
Zaliunas et al. 18, 2009	Single cohort study	34 patients	Tele-ECG device	Our study showed the potential of telemedicine facilities to overcome the problems of access that makes the technique so potentially useful, but for telemonitoring application at patient homes in a wider population

Kaleschke et al. 19, 2009	Single cohort study	508 patients	Simple, patient-operated electrocardiographic system	Recordings made by this patient-operated ECG device allow to detect arrhythmias and other ECG changes with high accuracy compared with a standard ECG.
Scherr et al. 20, 2008	Single cohort study	18 patients	New "leadless" ambulatory monitor	The "leadless" ECG monitor is associated with high patient compliance and results in high quality ECG recordings.
Olson et al. 21, 2007	Single cohort study	122 patients	Continuous mobile cardiac outpatient telemetry (MCOT)	MCOT can detect asymptomatic clinically significant arrhythmias, and was especially useful to identify the cause of presyncope/syncope, even in patients with a previous negative workup
Joshi et al. 22, 2005	Single cohort study	100 patients	Mobile cardiac outpatient telemetry (MCOT) system	MCOT increases the sensitivity of detecting atrial fibrillation without symptoms by providing a longer period of monitoring and automatic detection without the need for patient activation.
Klemm et al. 23, 2006	Single cohort study	80 patients	Transmitted trans telephonic (T-) ECG recordings	Assessment of success after AF ablation cannot be based on the absence of symptoms due to a high prevalence of asymptomatic episodes.
Balmelli et al. 24, 2003	Single cohort study	101 patients	Patient-triggered cardiac event recorders (CER)	Cardiac event recorders with a continuous automatic arrhythmia detection function are a well-tolerated device for sporadic, potentially arrhythmia-related symptoms.
Valle et al. 25, 2010	Single cohort study	179 cases	Electrocardiogram tele transmission	Calls regarding cardiovascular disease are infrequent but require an effective response. Recording and transmitting an ECG to the TMAS is technically feasible and enables treatment to be started with specific drugs

Tan et al. 26, 2010	Single cohort study	31 patients	HeartWave500 (HW), a novel web-based ambulatory ECG monitoring device	There is a trend toward a shorter monitoring time for HW. The ability of HW to record and transmit via the web, the earlier review of data and low unreadable data make HW an attractive alternative to TT.
Liu et al. 27, 2010	Single cohort study	92 patients	Transtelephonic electrocardiogram (TTECG)	The TTECG monitoring was superior to the standard electrocardiogram and 24-hour Holter recordings in evaluating AF recurrence after ablation.
Andrade et al. 28, 2011	Single cohort study	82 Brazilian towns	Microcomputer with a digital electrocardiograph, with the possibility of transmitting ECG tracings and communicating with the on-duty cardiologist at the University hospital	The implementation of a Telecardiology system as support to primary care in small Brazilian towns is feasible and economically beneficial and can be used as a regular program within the Brazilian public health system.
Wu et al. 29, 2012	Single cohort study	70 patients	Trans-telephonic electrocardiograph system.	Most paroxysmal AF episodes were asymptomatic, and the TTE system could easily detect these episodes.
Shacham et al. 30, 2012	Retrospective analysis	649 patients	Telemedical system ('SHL'-Telemedicine)	Telemedicine for rapid out-of-hospital diagnosis and provision of objective documentation and instructions for appropriate management of paroxysmal AF is feasible
Von Wangenheim et al. 31, 2012	Survey	564 patients	Large-scale asynchronous telemedicine network	The present findings also showed that both patients and healthcare professionals felt that introducing these new technologies was a positive step
Huang et al. 32, 2013	Single cohort study	86 patients	Cloud-based cardiac care system to monitor cardiac arrhythmias	The cloud-base ECG group had a lower number of hospitalizations during the 2-month follow-up than those in the Holter group (0.02±0.15 vs. 0.08 ± 0.31, p = 0.038

Kirtava et al. 33, 2012	Single cohort study	35 patients	Mobile telemedicine	Mobile telecardiology represents feasible methodology to monitor arrhythmias in outpatients in Georgia
Brunetti et al. 34, 2013	Single cohort study	Two thousand and fifteen ECGs	ECGs were sent by telephone connection to a regional tele-cardiology "hub"	Remote tele-medicine support for cardiology urgencies with pre-hospital electrocardiogram in prison detainees is feasible.
Dary et al. 35, 2013	Single cohort study	200 patients	Self-monitors at home, via a Holter worn	For 33% of patients, telemonitoring improves diagnosis and treatment of AF and ensures the best use of treatment in real time, by adapting doses according to the heart rhythm, rate and conduction time.
Kabe et al. 36, 2014	Single cohort study	24 patients	Portable internet-enabled ECG recording system	The iECG could serve as a useful support tool for monitoring heart health in Japanese workers residing abroad with risk factors of CVDs.
Rekosz et al. 37, 2015,	Retrospective analysis	26,208 ECGs	Tele-transmission and teleconsultation system (TTaTC)	Standard ECG TTaTC with a physician improved BMRT diagnostic capacities and exerted a beneficial impact on cardiovascular patient segregation and target hospital selection
Klein-Wiele et al. 38, 2016	Retrospective analysis	184 patients	Patient-activated event recorders (ER)	The investigated cross-sector telemetric network is a feasible approach to detect arrhythmia in patients with palpitations and may have high impact on further treatment, notably in those at risk for stroke due to AF.
De Asmundis et al. 39, 2014	Single cohort study	625 patients	Patient-activated electrocardiography (ECG) recorders	The studied system proved to be an efficient event recorder providing the diagnosis of the clinical arrhythmia in 89% of patients with paroxysmal palpitations or dizziness.

Turakhia et al. 40, 2015	Single-centre prospective screening study	75 patients	Continuous ambulatory electrocardiographic (ECG) monitoring	Outpatient extended ECG screening for asymptomatic AF is feasible, with AF identified in 1 in 20 subjects and sustained AT/AF identified in 1 in 9 subjects, respectively.
Attanasio et al. 41, 2015	Single cohort study	1404 patients	Patient-Activated Event Recording System	For patients with tachycardic palpitations, the external “leadless” event recorders are effective in achieving a symptom–rhythm correlation.
Hoefman et al. 42, 2005	RCT	253 patients	Patient-Activated Event Recording System	Patient-activated loop recorders are feasible and effective diagnostic tools in patients with palpitations or light-headedness in primary care.
Wu et al. 43, 2003	Single cohort study	660 patients	Patient-Activated Event Recording System	Patient-activated event recorders provided a good diagnostic yield in patients with different presentations of cardiac arrhythmia, and women had lower diagnostic yield in atrial flutter-fibrillation.
Rosenberg et al. 44, 2013	Single cohort study	74 patients	Zio® Patch, a single use, non-invasive waterproof long-term continuous monitoring	The Zio® Patch was well tolerated, and allowed significantly longer continuous monitoring than a Holter, resulting in an improvement in clinical accuracy
Anczykowski et al. 45, 2016	Single cohort study	790 patients	Trans-telephonic event-recorder monitoring (Tele-ECG)	Tele-ECG monitoring is effective in the diagnosis of suspected symptomatic CA. A diagnosis can usually be achieved within 1 week and has implications on patients' care.
Rothman et al. 46, 2007	Prospective clinical trial	266 patients	Mobile cardiac outpatient telemetry system (MCOT) with a patient-activated external looping event monitor (LOOP)	MCOT provided a significantly higher yield than standard cardiac loop recorders in patients with symptoms suggestive of a significant cardiac arrhythmia.

Locati et al. 47, 2016	Single cohort study	395 patients	External high-capacity loop recorder (SpiderFlash-T(®), Sorin)	The 4-week external ECG monitoring can be considered as first-line tool in the diagnostic work-up of syncope and palpitation.
Epifanio et al. 48, 2014	Single cohort study	112 patients	External event monitoring (web-loop).	We found no association between major symptoms and significant cardiac arrhythmia in patients submitted to event recorder monitoring.
Gula et al. 49, 2007	Single cohort study	78 patients	External loop recorder (ELR)	ELRs should be worn for at least 30 days to maximize their diagnostic yield. Patients who are unfamiliar with technology, live alone, or have low motivation to reach a diagnosis have a lower diagnostic yield from ELRs for assessment of syncope.
Muller et al. 51, 2009	Single cohort study	48 patients	Telemonitoring with an external loop recorder	The external loop recorder was very effective at detecting paroxysmal atrial fibrillation.
Schuchert et al. 52, 2003	Single cohort study	24 patients	Telemonitoring with an external loop recorder	The external loop recorder was not very useful for arrhythmia detection in patients with syncopal events, no overt heart disease, and a negative tilt table test because the cardiac rhythm was stored in only 1 of 8 (13%) patients with recurrent syncope.
Kimura et al, 53, 2017	Single cohort study	30 patients	Compared the AF ablation outcomes among periodic clinic electrocardiography (ECG), 24-h Holter ECG, and telemonitoring ECG	The AF ablation outcomes with twice daily telemonitoring ECG might differ from those with clinic ECG when the duration of the blanking period is 0-3 months.
Bush et al. 54, 2017	Single cohort study	1678 participants	Transtelephonic electrocardiography	Tele-ECG identifies significantly more AF cases in a population-based setting compared to conventional ECG. The impact of AF diagnosed only by extended monitoring differs from conventionally diagnosed AF.

Hendriks et al. 55, 2013	RCT	712 patients	Nurse-led care consisted of guidelines based, software supported integrated chronic care	Nurse-led care of patients with AF is superior to usual care provided by a cardiologist in terms of cardiovascular hospitalizations and cardiovascular mortality.
Staszewsky et al. 56, 2018	Single cohort study	289 patients	30-s single-lead electrocardiogram (ECG) with a telemedicine device	The screening scheme appears technically feasible and acceptable both to professionals and citizens/participants.
Ganapathy et al. 57, 2019	Single cohort study	753 teleconsults	Tele-emergency services (TES)	Preliminary analysis confirms that delivering TES in inhospitable terrains in a Public Private Partnership mode is doable and is welcomed by the community.
Ribeiro et al. 58, 2019	Single cohort study	2470424 ECGs	Telehealth Network of Minas Gerais	Large database that comprises all ECGs performed by a large telehealth network can be useful for further developments in the field of digital electrocardiography, clinical cardiology and cardiovascular epidemiology.
Lown et al. 59, 2018	Case-control study	418 participants	Inexpensive, wearable, consumer electrocardiography (ECG) sensing devices (Polar-H7 [PH7] and Firstbeat Bodyguard 2 [BG2])	The consumer devices performed as well or better than WatchBP and AliveCor and have the capability to store or transmit ECG data which could be used to confirm AF.
Evans et al. 60, 2017	Prospective Observational study	50 patients	Mobile electrocardiogram (ECG)	Using mobile ECG technology in screening for AF in low-resource settings is feasible and can detect a significant proportion of AF cases that will otherwise go undiagnosed.
Desteghe et al. 61, 2017	Single cohort study	445 patients	Two handheld single-lead electrocardiogram (ECG) devices	Using AliveCor or MyDiagnostick handheld recorders requires a structured screening strategy to be effective and cost-effective in a hospital setting.

Tison et al. 62, 2018	Multinational cardiovascular remote cohort study	9750 patients	Commercially Available Smartwatch	This proof-of-concept study found that smartwatch photoplethysmography coupled with a deep neural network can passively detect AF but with some loss of sensitivity and specificity against a criterion-standard ECG.
Svensson et al. 63, 2015	Single cohort study	7173 participants	Handheld ECG recorder	Mass screening for AF in a 75- to 76-year-old population identifies a significant proportion of participants with untreated AF. Initiation of stroke prophylactic treatment was highly successful in individuals with newly diagnosed AF.
Hendrikx et al. 64, 2014	Prospective, observational, cross-sectional study.	95 patients	30-second handheld ECG (Zenicor EKG® thumb)	Intermittent short ECG recording for four weeks is more effective in detecting AF and PSVT in patients with ambiguous symptoms arousing suspicions of arrhythmia than 24-hour Holter ECG.
Barrett et al. 65, 2014	Single cohort study	146 patients	Zio Patch (iRhythm Technologies, Inc, San Francisco, Calif) is a novel, single-lead electrocardiographic (ECG)	Prolonged duration monitoring for detection of arrhythmia events using single-lead, less-obtrusive, adhesive-patch monitoring platforms could replace conventional Holter monitoring in patients referred for ambulatory ECG monitoring.
Tavernier et al. 66, 2018	Single cohort study	252 patients	Hand-held device storing a bipolar ECG	On top of routine clinical care, daily short-term rhythm strip recordings identified another 13% of elderly hospitalised patients with AF, leading to an overall prevalence of 46% in hospitalised patients.
Doliwa et al. 67, 2009	Single cohort study	718 patients	Thumb ECG	Short-term ECG is able to diagnose AF with a high sensitivity, specificity and simple application making detection of asymptomatic AF possible for screening purposes

Doliwa et al. 68, 2012	Single cohort study	23 patients	Handheld trans telephonic ECG	Short-term ECG registrations over extended time periods seem to be a more sensitive tool, compared with short continuous ECG recordings, for detection of AF episodes.
Kearley et al. 69, 2015	Single cohort study	1000 patients	Comparative diagnostic accuracy of modified BP monitor and single-lead ECG devices	WatchBP performs better as a triage test for identifying AF in primary care than the single-lead ECG monitors as it does not require expertise for interpretation and its diagnostic performance is comparable to single-lead ECG analysis by cardiologists
Wiesel et al. 70, 2014	Single cohort study	199 patients	Microlife and Omron BPMs for electrocardiographic readings for AF detection	The specificity of both devices is acceptable, but only the Microlife BPM has a sensitivity value that is high enough to be used for AF screening in clinical practice.
Welton et al. 71, 2017	Systematic review and cost-effective analysis		Screening strategies for atrial fibrillation	A national screening programme for AF is likely to represent a cost-effective use of resources. Systematic opportunistic screening is more likely to be cost-effective than systematic population screening.
Jacobs et al. 72, 2018	Straightforward decision tree and a joining Markov model		MyDiagnostick®	Screening for AF in primary care with a handheld, single-lead ECG during seasonal influenza vaccination is very likely to be cost saving for identifying new cases of AF in the Dutch population aged 65 years and over.
Marazzi et al. 73, 2012	Single cohort study	503 patients	Microlife (®) BP A200 Plus (Microlife) and the OMRON(®) M6 (OMRON) home BP devices, in detecting AF	These results indicate that OMRON M6 is more accurate than Microlife BP A200 Plus in detecting AF in patients with essential hypertension.

Vaes et al. 74, 2015	Phase II diagnostic accuracy study in a convenience sample	191 patients	MyDiagnostick®	The MyDiagnostick is an easy-to-use device that showed a good diagnostic accuracy with a high sensitivity and specificity for atrial fibrillation in a convenience sample in primary care.
Tieleman et al. 75, 2015	Single cohort study	192 patients	MyDiagnostick®	The high AF detection performance of the MyDiagnostick, combined with the ease of use of the device, enables large screening programmes for detection of undiagnosed AF.
Engdahl et al. 76, 2013	Single cohort study	848 patients	Hand-held ECG	Stepwise risk factor-stratified AF screening in a 75-year-old population yields a large share of candidates for oral anticoagulation treatment on AF indication.
Hendrikx, 77, 2013	Single cohort study	989 patients	10-second handheld ECG recordings	Intermittent handheld ECG recording over a four-week period had a detection rate of 3.8% newly diagnosed AF, in a population of 928 out-of-hospital patients having at least one additional risk factor for stroke.
Kaasenbrood et al. 78, 2016	Single cohort study	3269 patients	MyDiagnostick®	Screening seems feasible with an easy to use single-lead, hand-held ECG device with automatic AF detection during influenza vaccination in primary care and results in a '1-day' yield of 1.1% new cases of AF
Proietti et al. 79, 2016	Single cohort study	65 747 participants	ECG handheld machine	In this Belgian national screening programme, prevalence of AF was 1.4%. The use of an ECG handheld machine is feasible to identify a significant number of new AF cases, most with a high thrombo-embolic risk.

Claes et al. 80, 2012	Single cohort study	13.564	A one-lead electrocardiogram	AF was present in 2.2% of the respondents. At least 60% of AF group had an increased risk for thrombo-embolism.
Battipaglia et al. 81, 2016	Single cohort study	855	MyDiagnostick	The MDK provided a rapid and accurate rhythm analysis and has potential implications in preventing ischaemic cardio-embolic stroke.
Schreiber et al. 82, 2014	Single cohort study	174 patients	A novel, single use continuous recording patch (Zio®Patch)	The Zio®Patch cardiac monitoring device can efficiently characterize symptomatic patients without significant arrhythmia and has a higher diagnostic yield for arrhythmias than traditional 24-48-hour Holter monitoring.
Wiesel et al. 83, 2013	Single cohort study	139 patients	Blood pressure (BP) measurements using an automatic AF-detecting BP monitor	This can be used to detect new AF, allowing treatment with anticoagulation to reduce the future risk for stroke.
Stergiou et al. 84, 2009	Single cohort study	73 patients	Self-home BP monitoring	These data suggest that an electronic device for self-home BP monitoring has an excellent diagnostic accuracy and might, therefore, be used as a reliable screening test for the early diagnosis.
Kollias et al. 85, 2018	Single cohort study	100 patients	Novel 24-hour ambulatory blood pressure (ABP) monitor	Thus, in elderly hypertensives, a 24-hour ABP recording with at least 26% of the readings suggesting AF indicates a high probability for AF diagnosis and should be regarded as an indication for performing 24-hour Holter monitoring.
Wiesel et al. 86, 2004	Single cohort study	125 ECGs	Modified sphygmomanometer	In this analysis, the sensitivity was 100%, the specificity 91%, and the diagnostic accuracy 92% for detecting AF.

Zenk et al. 87, 2004	Single cohort study	10 patients	Accuracy of an electronic stethoscope	The results of this study suggest that telemedicine-directed auscultation of patients may be just as successful as in person examination for the detection of cardiac arrhythmias.
Merilathi et al. 88, 2009	Single cohort study	17 participants	System consisting of both wearable and ambient technologies	The users gave positive feedback in almost all their responses in a questionnaire.
Winkler et al. 89, 2011	Single cohort study	60 patients	New handheld ECG device	The new algorithm is suitable for automated preanalysis of the ECG data with regard to AF. It could be used for rapid selection of ECGs with relevant rhythm abnormalities from a large pool.
Baig et al. 90, 2013	Comprehensive survey		Wearable and wireless ECG monitoring systems	The main drawbacks of deployed ECG monitoring systems including imposed limitations on patients, short battery life, lack of user acceptability and medical professional's feedback, and lack of security and privacy of essential data have been also discussed.
Singh et al. 91,2014	Single cohort study	450 patients	Handheld tele-electrocardiogram (ECG)	It can be safely concluded that tele-ECG is a portable, cost-effective, and convenient tool for diagnosis and monitoring of heart diseases and thus improves quality and accessibility, especially in rural areas.
Jeroudi et al. 92, 2015	Single cohort study	10 ECGs	Remote electrocardiogram interpretation with the use of Google Glass technology	Further improvements are needed before Google Glass can be reliably used for remote electrocardiographic analysis.
Couderc et al. 93, 2015	Single cohort study	11 patients	Contactless facial video monitoring	Our preliminary results support the concept that contactless video-based monitoring of the human face for detection of abnormal pulse variability due to AF is feasible.

Ousaka et al. 94, 2019	Single cohort study	5 patients	Real-time ECG tele-monitoring system, as an initial trial to assess operative possibility in a full marathon	Three out of five cases we monitored showed reasonable measurement of ECG with centralized observation in full marathon.
Gula et al. 95, 2009	Single cohort study	92 patients	External loop recorder (ELR)	Familiarity with technology correlates with successful use of the ELR but does not necessarily correlate with the ability to reach a diagnosis.
Omboni et al. 96, 2016	Single cohort study	220 patients	Automatic blood pressure measurement	Opportunistic screening of AF by BP measurement is feasible to diagnose this arrhythmia in unaware participants, particularly in those older than 65 years
Rockx et al. 97, 2005	RCT	100 patients	External loop recorder (ELR)	External loop recorders are an economically attractive alternative.
Castelletti et al. 98, 2018		36 patients	BodyGuardian™ (BG), a wearable remote monitoring system	This wearable monitoring system reliably identifies a prolonged QT interval and probably also subjects at risk for diLQTS.
Lee et al. 99, 2018	Single cohort study	17 patients	Highly flexible wearable cardiac sensor (WiSP)	A clinical feasibility study conducted in atrial fibrillation patients demonstrates that the WiSP device effectively measures cardiac signals matching the Holter monitor and is more comfortable.
Gajda et al. 100, 2018	Single cohort study	142 patients	Heart rate monitors (HRMs)	We conclude that the HRM is not a suitable tool for monitoring heart arrhythmias in athletes
Breteler et al. 101, 2018	Single cohort study	25 patients	Wireless sensor	The wireless sensor is capable of accurately measuring heart rate, but accuracy for respiratory rate was outside acceptable limits.

Perez et al. 102, 2019	Single cohort study	419297 patients	Smartwatch-based irregular pulse notification algorithm	The probability of receiving an irregular pulse notification was low.
Wasserlauf et al. 103, 2019	Single cohort study	24 patients	AF-sensing watch (AFSW; Apple Watch with KardiaBand)	An AFSW is highly sensitive for detection of AF and assessment of AF duration in an ambulatory population when compared with an ICM
Lo et al. 104, 2019	Single cohort study	111 patients	CardioChip - a single-channeled, low-powered, miniature ECG	The results suggested that CardioChip ECG is comparable to medical industry standard ECG.
Steinhubl et al. 105, 2018	RCT	2659 patients	Self-applied wearable electrocardiogram (ECG) patch	Among individuals at high risk for AF, immediate monitoring with a home-based wearable ECG sensor patch, compared with delayed monitoring, resulted in a higher rate of AF diagnosis
Molinari et al. 106, 2004	Single cohort study	106942 patients	Transtelephonic electrocardiography	Telecardiology improves the decision making of general practitioners, avoids unnecessary hospitalizations, reduces the time before treatment in cardiac emergencies, rationalizes health-care costs and promotes home care.
Kouidi et al. 107, 2006	Single cohort study	91 patients	Transtelephonic electrocardiography	These data demonstrate that TEM provides a workable facility in cardiac rehabilitation for monitoring patients who are exercising in gyms.

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List of meta-analysis on Ambulatory monitoring with new tools

Author	Design	Studies included	Intervention	Conclusion
Ramkumar et al. 1, 2017	Meta-analysis	18 studies	Single lead portable electrocardiographic monitoring	Portable ECG devices may offer an efficient screening option for AF compared with 24 hours Holter monitoring.
Taggar et al. 2, 2016	Meta-analysis	21 studies	Accuracy of methods for detecting an irregular pulse and suspected atrial fibrillation	BPMs and non-12-lead ECG were most accurate for detecting pulse irregularities caused by atrial fibrillation
Stergiou et al. 3, 2012	Meta-analysis	12 studies	Automated blood pressure measurement in atrial fibrillation	There is limited evidence and significant heterogeneity in the studies that validated automated blood pressure monitors in atrial fibrillation.
Belkin et al. 4, 2018	Meta-analysis	28 studies	New-Onset Device-Detected Atrial Tachyarrhythmia	New-onset DDAT is common, affecting close to one quarter of all patients with implanted pacemakers or defibrillators

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List of trials on Prehospital emergency ECG

Author	Design	Sample Size	Intervention	Conclusion
Scalvini et al. 1, 2002	Single cohort study	952 patients	Transmit a 12-lead electrocardiogram (ECG) via a telephone line	The telecardiology service showed a sensitivity of 97.4%, a specificity of 89.5% and a diagnostic accuracy of 86.9% for chest pain.
Terkelsen et al. 2, 2002	Single cohort study	250 patients	Telemetry equipped ambulances had 12-lead electrocardiograms (ECGs)	It was technically feasible to use telemedicine for remote prehospital diagnosing of patients suspected of AMI.
Drew et al. 3, 2004	Single cohort study	5 patients	Prehospital ST monitoring with telephone transmission	Prehospital ST monitoring appears feasible.
Clemmensen et al. 4, 2004	Single cohort study	24 patients	Prehospital ST monitoring with GSM transmission	Should become routine. Time to reperfusion was decreased
Pedley et al. 5, 2005	Single cohort study	229 patients	Mobile telemetry to facilitate pre-hospital thrombolysis	Telemetry offers essential back-up to paramedics adopting a challenging and extended role. Strategies can be developed to deal with signal strength and equipment failure.
Schwaab et al. 6, 2005	Single cohort study	158 patients	12-lead electrocardiogram (ECG) recorded by the patient and transmitted to a cardiology call centre via telephone	The tele-ECG technique seems a promising approach to reducing pre- and in-hospital time delays to the initiation of thrombolytic therapy.

Wollard et al. 7, 2005	Single cohort study	213 patients	Continuous telemetry system linking rural ambulances to a coronary care unit	Continuous telemetry systems may significantly reduce call to treatment times for patients recommended for pre-hospital thrombolysis in a rural setting.
Clemmensen et al. 8, 2005	Single cohort study	408 patients	Prehospital ST monitoring with GSM transmission	These preliminary data suggest that transmission of prehospital 12-lead ECGs directly to the attending cardiologist using handheld devices is a technologically sound concept without major safety concerns and markedly reducing time to reperfusion in patients with STEMI.
Vaught et al. 9, 2006	Single cohort study	92 patients	Transmission of EMS electrocardiographs (ECGs)	Initial gains in the time from hospital arrival to percutaneous coronary intervention, attributed to acquisition of the ECG in the prehospital setting, were not sustained over 10 years.
Chongtham et al. 10, 2006	Single cohort study	41 patients	Telecardiology-guided initiation of therapy	Utilizing telecardiology advances, district hospital physicians, in collaboration with cardiologists at the tertiary centre, can provide adequate standard diagnosis at the pre-coronary care unit level and also provide adequate therapy for acute myocardial infarction.
Ohtsuka et al. 11, 2007	Single cohort study	20 patients	Camera phones to transmit electrocardiogram (ECG) images.	ECG image transmission by camera phone can be efficiently used in the diagnosis of acute coronary syndrome.
Strauss et al. 12, 2007	Single cohort study	25 patients	Paramedic trans telephonic communication to cardiologist of clinical and electrocardiographic assessment	Paramedic trans telephonic communication to cardiologist of clinical and electrocardiogram assessment resulted in a 54-minute reduction in door-to-balloon time for patients with STEMI.
Dhruva et al. 13, 2007	Single cohort study	80 patients	Wireless technologies used to transmit prehospital electrocardiograms (ECGs)	A fully automated wireless network that transmits ECGs simultaneously to the ED and offsite cardiologists for the early evaluation and triage of patients with suspected STEMI can decrease D2I times to <90 min and has the potential to be broadly applied in clinical practice.

Adams et al. 14, 2006	Single cohort study	277 patients	Prehospital wireless transmission of electrocardiograms	Prehospital wireless electrocardiographic transmission to a cardiologist's hand-held device significantly decreased emergency department door-to-reperfusion time, thus achieving the American College of Cardiology/American Heart Association guideline for patients with STEMI.
Sejersten et al. 15, 2008	Single cohort study	565 patients	Prehospital electrocardiogram (ECG) transmission	Transmission of a prehospital 12-lead ECG directly to the attending cardiologist's mobile telephone decreased door-to-PCI time by >1 hour when patients were transported directly to PCI centres, bypassing local hospitals.
Leibrandt et al.16, 2000	Single cohort study	20 cases	Transmission of 12-lead electrocardiograms from remote locations to hand-held computers	Cardiologists' decisions did not vary significantly when viewing either traditional paper electrocardiograms or LCD screen electrocardiograms.
Sanchez-Ross et al. 17, 2011	Single cohort study	92 patients	Fully automated wireless network (STAT-MI) for transmission of electrocardiograms (ECGs)	A fully automated, field-based, wireless network that transmits ECGs automatically to offsite cardiologists for the early evaluation and triage of patients with STEMI shortens D2B times, reduces infarct size, limits ejection fraction reduction, and shortens LOS.
Rokos et al. 18, 2009	Single cohort study	2712 patients	Pre-hospital ECG	Ten independents regional SRC networks demonstrated a combined 86% rate of D2B <or=90 min, and each region individually surpassed the American College of Cardiology D2B Alliance benchmark.
Baron-Esquivias et al. 19, 2011	Single cohort study	506 patients	Transtelephonic electrocardiography	Transtelephonic electrocardiography combined with awareness of the risk factors of patients presenting with chest pain is useful for the diagnostic management of these patients in health care facilities without the means to interpret electrocardiograms.

Gonzalez et al. 20, 2011	Single cohort study	263 patients	Cellular videophone (VP) assisted interpretation of ECG	Cellular VP-assisted transmission and interpretation in real-time of prehospital ECG has high interphysician reliability, similar to the printed ECG interpretation.
Zanini et al. 21, 2008	Double cohort study	399 patients 263 patients no pre-hospital ECG 136 pre-hospital ECG	Prehospital setting with telemedicine equipment and transferred directly to the interventional centre	The present study shows a reduction in treatment delay and in-hospital mortality by prehospital ECG and direct referral to catheterization laboratory.
Ortolani et al. 22, 2007	Single cohort study	121 patients 79 patients no pre-hospital ECG 42 pre-hospital ECG	Ambulance-telemedicine-based triage	Prehospital triage with direct transportation to the intervention laboratory is associated with shorter treatment delay and better clinical outcome in patients with STEMI complicated by cardiogenic shock.
Sillisen et al. 23, 2008	Single cohort study	152 patients	Prehospital 12-lead electrocardiogram (ECG) transmission	Transmission of prehospital ECG is technically feasible and reduces time to pPCI in ST-segment elevation acute myocardial infarction patients.
Brunetti et al. 24, 2009	Single cohort study	27,841	ECG evaluation. Data recorded were transmitted with mobile telephone support to a	Telemedicine protocols would probably be useful in lowering the number of improper hospitalizations and shortening delay in the diagnosis process of some heart diseases.

			telecardiology "hub" active 24-h a day.	
Vaisanen et al. 25, 2003	Single cohort study	18 patients	Prehospital ECG transmission	An advanced mobile phone is as fast and reliable as a conventional table fax in receiving ECGs.
Bergrath et al. 26, 2011	Single cohort study	157 EMS missions	Multifunctional telemedicine system in an emergency medical service	Use of the telemedical system in EMS is feasible and the quality of the transmitted images and video was satisfactory. However, technical reliability and availability need to be improved prior to routine use.
Brunetti et al. 27, 2011	Single cohort study	27,841	ECG evaluation. Data recorded were transmitted with mobile telephone support to a telecardiology "hub" active 24-h a day.	A regional single telecardiology hub providing prehospital ECG for a sole regional public EMS provides an example of a prehospital ECG network optimizing quality of ECG report and uniformity of EMS assistance in a large region-wide network.
Larochelle et al. 28, 2011	Single cohort study	1140 ECGs	Pre-hospital 12- lead ECG transmission	More widespread implementation of this technology in the future, especially in rural settings, could have significant effects on the mortality and morbidity of myocardial infarction
Werman et al. 29, 2011	Single cohort study	90 patients	Prehospital transmission of the electrocardiogram	Prehospital transmission of diagnostic-quality ECG can be reliably performed by non-=paramedic providers.
Rao et al. 30, 2010	Single cohort study	386 patients	The EMS personnel obtained a 12-lead ECG during initial assessment in the field from patients with chest pain. The ECG was immediately transmitted to	Utilizing the prehospital ECG as a tool to bypass ER triage significantly decreases D2B times in patients with STEMI.

			the ER physician by cellular link to a computer receiving station.	
Diercks. 31 et al. 2009	Single cohort study	7,098 patients	Pre-hospital electrocardiograms (ECGs)	Only one-quarter of these patients transported by EMS receive a pre-hospital ECG.
Clemmensen et al. 32, 2013	Single cohort study	4000 prehospital ECGs annually transmitted	Pre-hospital electrocardiograms (ECGs)	With the optimal collaboration within a STEMI network including local hospitals, university clinics, EMS and military helicopters using the same telemedicine system and field triage of STEMI patients, most patients can be treated within the time limits suggested by the current guidelines.
Papai et al. 33, 2014	Single cohort study	397 patients	Transtelephonic electrocardiography	The findings illustrate that TTECG is a valuable tool which may potentially improve the regional management of STEMI patients.
Brunetti et al. 34, 2014	Single cohort study	297 patients	Pre-hospital electrocardiogram triage	Pre-hospital triage with tele-cardiology ECG in an EMS registry from an area with more than one and a half million inhabitants was associated with shorter time-to-balloon and higher rates of timely treated patients, even in 'rural' areas.
Rasmussen et al. 35, 2014	Single cohort study	15 992 patients diagnosed using telemedicine.	Telemedicine for prehospital diagnosis in triaging and treatment of STEMI.	The use of telemedicine for prehospital diagnosis and triage of patients directly to the catheter laboratory is feasible and allows 89% of patients living up to 95 km from the invasive centre to be treated with PPCI within 120 min of the emergency medical service call.
Rusworth et al. 36, 2015	Single cohort study	2,025 patients	Pre-Hospital ECG E-Transmission	This study has demonstrated that a specialist triage service based on e-transmission of ECGs in patients with suspected STEMI can be implemented in a diverse geographical setting.

Brunetti et al. 37, 2015	Single cohort study	356 patients	Pre-hospital electrocardiogram delivered by tele-medicine support	Trend toward a lower mortality may be observed in AMI patients treated with primary angioplasty after pre-hospital electrocardiogram triage by telemedicine support, more evident in high risk subjects.
Quinn et al. 38, 2014	Single cohort study	288 990 patients	Prehospital ECG (PHECG)	Findings from this national MI registry demonstrate a survival advantage in STEMI and non-STEMI patients when PHECG was used.
Savage et al. 39, 2014	Single cohort study	281 patients	Paramedics in the field identified patients with ST elevation myocardial infarction on a 12-lead electrocardiograph, activated the cardiac catheter laboratory team from the field	Pre-hospital intervention at our centre had a powerful effect in reducing the time to reperfusion in patients with STEMI undergoing primary percutaneous intervention.
Chan et al. 40, 2012	Single cohort study	167 patients	Pre-Hospital ECG E-Transmission	Pre-hospital triage strategy was associated with improved survival rate in patients undergoing primary PCI in a regional STEMI program.
Brown et al. 41, 2008	Single cohort study	78 patients	Prehospital 12-lead electrocardiogram	This study demonstrates that prehospital electrocardiographic diagnosis of STEMI markedly reduces door-to-balloon time
Sorensen et al. 42, 2011	Single cohort study	759 patients	Prehospital 12-lead electrocardiogram	Pre-hospital electrocardiographic (ECG) diagnosis and direct referral for primary PCI enables STEMI patients living far from a PCI centre to achieve a system delay comparable with patients living in close vicinity of a PCI centre.
Martinoni et al. 43, 2011	Single cohort study	3901 patients	Pre-hospital electrocardiogram (PH-ECG)	In this registry, PH-ECG significantly decreased first medical contact-to-balloon time.

Takeuchi et al. 44, 2015	Single cohort study	76 patients	Novel mobile cloud 12-lead ECG system	The Doctor Car system with the Mobile Cloud ECG was useful for reducing the door-to-balloon time.
Tanguay et al. 45, 2015	Single cohort study	208 patients	Prehospital telemedicine program	This study demonstrated that a regionalized prehospital system for STEMI patients could achieve the recommended 90-min interval benchmark for PCI
Verbeek et al. 46, 2012	Retrospective analysis	325 patients	Serial prehospital 12-lead electrocardiograms	A single prehospital ECG would have identified only 84.6% of STEMI patients. This suggests caution using a single prehospital ECG to rule out STEMI. Three serial ECGs acquired over 25 minutes is feasible and may be valuable in maximizing prehospital diagnostic yield, particularly where emergent access to PCI exists.
Ong et al. 47, 2012	Single cohort study	2653 patients	Out-of-hospital 12-lead ECG recording and transmission	Out-of-hospital ECG transmission should be adopted as best practice for management of chest pain.
Kawakami et al. 48, 2016	Single cohort study	393 patients	Prehospital ECG	Reperfusion delay was shorter in patients using MTS than in patients without it.
Dieker et al. 49, 2010	Single cohort study	581 patients	Pre-hospital triage with ECG	After ambulance-based diagnosis of STEMI, direct transport to an intervention centre with pre-hospital notification of the catheterization laboratory more than triples the proportion of patients treated within the time window of the guidelines.
Pedersen et al. 50, 2009	Single cohort study	616 patients	Field triage	This study shows that field triage of STEMI patients to pPCI significantly reduces treatment delay and improves outcome.

Sivagangabalan et al. 51, 2009	Single cohort study	624 patients	Ambulance field triage	Field triage of patient with STEMI decreased revascularization times, which preserved LV function, and improved early survival.
Tanguay et al. 52, 2017	Retrospective analysis	640 patients	Prehospital telemedicine program	Our system of transmitted prehospital ECG and STEMI interpretation by emergency physicians at an online medical control centre showed a total false-positive and inappropriate CCL activation rate of 14% over the 8-year study period.
Cheung et al. 53, 2018	Single cohort study	841 patients	Pre-hospital electrocardiogram triage with telemedicine	Prehospital ECG is technologically feasible in Hong Kong and shortens the D2B time. However, shorter reperfusion time was only recorded during daytime hours.
Chao et al. 54, 2018	Retrospective analysis	84 patients	Smartphone transmission of electrocardiography images	The additional use of a smartphone application to transmit ECG information to interventional cardiologists by EPs facilitated communication and reduced the decision time to CCL activation and percutaneous intervention.
Chauhan et al. 55, 2018	Single cohort study	819 patients	Smartphone-based tele-electrocardiography	This is an effective low-cost strategy and is easily replicable anywhere in the world.
O'Donnell et al. 56, 2019	Single cohort study	379 cases	Towards prompt electrocardiogram acquisition in triage. Acute Coronary Syndrome Application (AcSAP)	Testing of the AcSAP suggests that it accurately identifies patients who require an ECG within 10 min. As such, it has the potential to support the meeting of clinical guidelines for ECG acquisition.
Gibson et al. 57, 2019	RCT	907 patients	Implantable Cardiac Alert System for Early Recognition of ST-Segment Elevation Myocardial Infarction	The implantable cardiac system detects early ST-segment deviation and alerts patients of a potential occlusive event.

Kerem et al. 58, 2014	Single cohort study	99 patients	Pre-hospital electrocardiogram triage with telemedicine	Prehospital STEMI identification allows for prompt catheterization laboratory activation, leading to decreased reperfusion times
Meadows-Pitt et al. 59, 2013	Single cohort study	367 patients	Prehospital 12-lead electrocardiograms	Door-to-balloon times can be reduced when chest pain patients are transported to the emergency department by ambulance.
Daudelin et al. 60, 2010	Single cohort study	6994 patients	Prehospital 12-lead ECG	Feedback reports and quality improvement improved prehospital ECG performance for patients with acute coronary syndrome and ST-elevation myocardial infarction and increased aspirin administration without prehospital transport delays.
Cannon et al. 61, 2014	Single cohort study	2,021 patients	Prehospital 12-lead ECG	Over one-quarter of STEMI patients presenting without chest pain did not receive prehospital ECGs and had significantly longer FMC to device times.

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List of meta-analysis on Prehospital emergency ECG

Author	Design	Studies included	Intervention	Conclusion
Brunetti et al. 1, 2017	Meta-analysis of non-randomized studies	11 studies	Pre-hospital electrocardiogram triage with telemedicine	Pre-hospital triage with telemedicine is associated with a near halved time to treatment in AMI. The benefit is larger in terms of absolute time to treatment reduction in populations with larger delays to treatment.

1. *Brunetti, ND, De Gennaro L, Correale M, et al. "Pre-hospital Electrocardiogram Triage with Telemedicine near Halves Time to Treatment in STEMI: A Meta-analysis and Meta-regression Analysis of Non-randomized Studies." International Journal of Cardiology 232 (2017): 5-11. Web.*

List of trials on Digital Health for anticoagulation treatment in AF

Author	Design	Sample Size	Intervention	Conclusion
Waterman et al. 1, 2000	Survey	300 patients	Telephone-based Anticoagulation Service	A telephone-based ACS can be endorsed by primary-care physicians and improve patients' satisfaction with and knowledge about their antithrombotic therapy.
Lamminen et al. 2, 2002	Single cohort study	40 patients	Personal health care and the new media in anticoagulant treatment	Part of the population receiving anticoagulant treatment is ready to move to a more personal treatment routine involving home measurements in follow-up tests.
Witt et al. 3, 2003	Single cohort study	614 patients	A centralized, telephone follow-up Clinical Pharmacy Anticoagulation Service	The management of excessive anticoagulation by a centralized telephone follow-up anticoagulation service staffed by clinical pharmacists resulted in improved clinical outcomes compared to traditional management.
Finkelstein et al. 4, 2003	Single cohort study	29 patients	Home Automated Telemanagement (HAT) system for patients on oral anticoagulation therapy	Results demonstrated high acceptance of the HAT system by patients receiving long term anticoagulation therapy regardless of their previous computer experience or socioeconomic background.
Chaudhry et al. 5, 2004	Survey	187 patients	Point-of-care international normalized ratio (POC INR) testing	The authors conclude that nurse managed POC INR testing is quick, convenient, less painful, and more satisfying for patients
Abdelhafiz et al. 6, 2004	Open-label, prospective study	402 patients	Outpatient anticoagulation clinic	Based on this analysis, the risks of long-term oral anticoagulation therapy in an outpatient anticoagulation clinic appear to reflect the results of clinical trials.

Goldberg et al. 7, 2005	Single cohort study	156 patients	Monitoring oral anticoagulant therapy by telephone communication	The study is significant in that it documents that trans-telephonic communication is feasible safe and cost-effective and that the clinical results are at least as good as those obtained by traditional consultation.
Witt et al. 8, 2005	Retrospective, observational cohort study	6645 patients 3323 intervention 3322 control	Clinical pharmacy anticoagulation service	A centralized, telephonic, pharmacist-managed anticoagulation monitoring service reduced the risk of anticoagulation therapy-related complications compared to that with usual care.
Matchar et al. 9, 2002	Multi-site randomized trial	262 patients 144 intervention 118 control	The intervention cluster received an anticoagulation service that satisfied specifications for high-quality anticoagulation care	The effect of the anticoagulation service was limited by the utilization of the service, the degree to which the referring physician supports strict adherence to recommended target ranges for the INR, and the ability of the anticoagulation service to identify and to respond to out-of-range values promptly.
Chamberlain et al. 10, 2001	Retrospective study		Continuous anticoagulation care at the Family Medicine of Southwest Washington	More anticoagulation patients treated by the anticoagulation clinic model at FMSW received an INR test at least every 6 weeks than those treated by the traditional care model, and more of their INR results were within target range +/- 0.1 when compared with the traditional care model.
O'Shea et al. 11, 2008	Single cohort study	60 patients	Direct-to-patient expert system and home INR monitoring	This novel approach of internet-supervised patient self-management improved time in therapeutic range compared to an anticoagulation clinic.

Ryan et al. 12, 2009	Single cohort study	162 patients	Supervised patient self-testing of warfarin therapy using an internet-based expert system.	The use of an internet-based, direct-to-patient expert system for the management of PST improves the control of OAT as compared with AMS management.
Christensen et al. 13, 2011	RCT	669 patients	Expert computer system for the control of oral anticoagulation therapy, accessible by the patients via their own computer	Home measurement of INR and the reporting and dosing of results online once a week increase TTR from 72% to 79% as compared to conventional computer-assisted monitoring in an anticoagulation clinic.
Gadisseur et al 14, 2004	RCT	118 patients	Patient self-management of oral anticoagulant care	General treatment satisfaction was already high under routine care (5.11 on a scale of 1-6) and increased further through self-monitoring of the INR (+0.19) and full self-management (+0.32).
Watzke et al. 15, 2000	Prospective study	102 patients	Patient self-management of oral anticoagulant care	The achieved mean INR was almost identical with the target INR in the patients on self-management but was significantly (p <0.005) below the target INR in the high intensity anticoagulation group
Cromheecke et al. 16, 2000	Randomised controlled crossover study	50 patients	Patient self-management of oral anticoagulant care	Self-management of INR in the population in this study is feasible and appears to result in control of anticoagulation that is at least equivalent to management by a specialist anticoagulation clinic.
Fitzmaurice et al. 17, 2002	RCT	49 patients	Patient self-management of oral anticoagulant care	These are the first UK data to demonstrate that patient self-management is as safe as primary care management for a selected population.

Harper et al. 18, 2011	Prospective comparative study	41 patients	Home international normalized ratio testing and decision support provided through the Internet.	Self-testing with online computer decision support achieved anticoagulant control at least as good as laboratory management.
Regier et al. 19, 2006	Bayesian Markov model		Patient self-management of oral anticoagulant care	This model suggests that self-management is a cost-effective strategy for those receiving long-term oral anticoagulation therapy for atrial fibrillation or for a mechanical heart valve.
Menéndez-Jándula et al. 20, 2005	RCT	737 patients	Patient self-management of oral anticoagulant care	Compared with conventional management by an anticoagulation clinic, self-management of oral anticoagulant treatment achieved a similar level of control.
Sunderj et al. 21, 2004	RCT	140 patients	Self-management (SM) of warfarin by patients	SM was not significantly better than PM in maintaining therapeutic anticoagulation. SM was feasible and appeared safe in the present study population.
Khan et al. 22, 2004	RCT	120 patients	Self-management (SM) of warfarin by patients	Quality-of-life measurements and health beliefs about warfarin were unchanged (apart from emotional role limitation) with education or education and self-monitoring. Patient education regarding anticoagulation therapy could be a cost-effective initiative and is worthy of further study.
Lafata et al. 23, 2000	5-year Markov model		Patient self-management of oral anticoagulant care	Model results indicate that over a 5-year period, compared with usual care, anticoagulation clinic testing results in a total of 1.7 fewer thromboembolic events and 2.0 less haemorrhagic events per 100 patients.
Dimberg et al. 24, 2012	Retrospective cohort study	791 patients	AuriculA is a Swedish National web-based anticoagulation dosing system	Computerised dosing assistance within the Swedish national quality registry AuriculA improves or maintains a high treatment quality with warfarin as measured by TTR.

Jowett et al. 25, 2009	Trial-based cost-effectiveness analysis	13 219 patients	Computer-assisted anticoagulant dosage	Results indicate that computer-assisted dosage with the two programs (dawn ac and parma 5) is cheaper than manual dosage and is at least as effective clinically, indicating that investment in this technology represents value for money.
Wieloch et al. 26, 2011	National quality registry	18 391 patients	AuriculA is a Swedish National web-based anticoagulation dosing system	Compared with prospective randomized trials of warfarin treatment, TTR in the AuriculA population was higher. Complications were low, probably due to the organization of anticoagulation treatment in Sweden.
Simmons et al. 27, 2012	Single cohort study	44 patients	Novel patient self-management program for warfarin therapy	This novel PSM model appears to be a feasible method of managing warfarin therapy in carefully selected patients
Grunau et al. 28, 2011	Pragmatic open-label randomized crossover trial	11 patients	Patient self-management of warfarin therapy	Patient self-management was not demonstrated to be superior to standard care but was easily implemented and was the method preferred by patients.
Gardiner et al. 29, 2006	RCT	104 patients	Patient self-management (PSM) or patient self-testing (PST) alone	The quality of warfarin control in both PST and PSM may be superior to that achieved by conventional management in a specialised hospital anticoagulation clinic.
Boman et al. 30, 2012	RCT	40 patients	Monitored using the telemedicine device	Telemedicine reduced the total processing time for INR monitoring and has the potential to improve the management of patients undergoing anticoagulant treatment at PHCs.
Almeman et al. 31, 2013	Single cohort study	70 patients	Computer-Aided Warfarin Dosing	It appears that the software improves the effectiveness of warfarin dosing in patients.

Bereznicki et al. 32, 2013	Single cohort study	16 patients	Patient self-testing (PST)	PST supported by an online system for supervision was associated with improved INR control compared to usual care in a small group of elderly patients
Hassan et al. 33, 2013	Single cohort study	448 patients	Telephone-based anticoagulation management	Telephone-based management of warfarin therapy in the homebound setting is feasible. It can lower the cost of health care expenditures compared to other modalities of anticoagulation management.
Jenner et al. 34, 2015	Single cohort study	44 patients	Warfarin patient self-management (PSM)	Developing and administering a warfarin PSM education program for patients with atrial fibrillation was feasible.
McCahon et al. 35, 2015	Retrospective multicentre matched control study	126 patients	Patient self-management (PSM) of oral anticoagulation therapy	PSM outside trial conditions is as clinically effective as routine UK care.
Zuern et al. 36, 2015	Single cohort study	65 patients	Algorithm for discontinuation of OAC after ablation based on the AF burden documented by implantable cardiac monitors (ICM).	Rhythm monitoring by ICM in patients who have stopped OAC after catheter ablation of AF or ablation of possible AF triggers seems to be a safe and promising method to monitor for AF recurrence. Within 1.3 years after ablation, about two-thirds of patients were able to stay off OAC.
Singh et al. 37, 2015	Patient interviews	38 patients	Clinical video telehealth (CVT) technology	Through the use of CVT technology, high-quality anticoagulation services and patient satisfaction were maintained, and the allocation of clinical pharmacy specialist resources was optimized.

Prochaska et al. 38, 2015	Prospective, multi-centre, observational cohort study	760 patients	Telemedicine-based coagulation service	Treatment in a telemedicine-based coagulation service substantially improved quality of OAC therapy with regard to TTR level, frequency of stable anticoagulation control, and TTR variability.
Matchar et al. 39, 2015	RCT	787 patients	Patient-self testing (PST) via home monitoring	More frequent PST improved TTR and reduced the proportion of poorly managed patients.
De Santis et al. 40, 2014	Retrospective analysis	29,457 patients	Point-of-care, home international normalized ratio (INR) monitoring	Point-of-care patient self-testing at home achieves high-quality warfarin therapy outside of clinical trials and compares favourably with the results achieved in randomized trials or in anticoagulation clinic settings.
Matchar et al. 41, 2010	RCT	2922 patients	Weekly self-testing at home or monthly high-quality testing in a clinic	As compared with monthly high-quality clinic testing, weekly self-testing did not delay the time to a first stroke, major bleeding episode, or death to the extent suggested by prior studies.
Pandya et al. 42, 2016	Pragmatic (mix-method) approach	33 resources	Web-based education resources	The implied inclination of some resources towards particular anticoagulant therapies and imbalanced information about the importance of anticoagulation in AF might misinform and confuse patients.
Steinhaus et al.43, 2016	Markov model		Implantable Cardiac Monitor-Guided Intermittent Anticoagulation	Based on a pilot study, a strategy of ICM-guided anticoagulation with NOACs may be cost-saving relative to expected outcomes with continuous anticoagulation, with similar quality-adjusted survival.

Martin et al. 44, 2015	RCT	2718 patients	Atrial arrhythmia monitoring to guide anticoagulation	In patients with implanted defibrillators, the strategy of early initiation and interruption of anticoagulation based on remotely detected AT did not prevent thromboembolism and bleeding.
Lee et al 45, 2016	Single cohort study	18 patients	Mobile Applications for Seniors to enhance Safe anticoagulation therapy (MASS)	The results showed use of MASS improved older adults' knowledge of OAT.
Lee et al. 46, 2014	Patient interview	11 patients	Mobile health technology and health games for self-management	These findings indicate that our older adults on warfarin therapy are interested in mHealth technology specific to warfarin medication management and health games.
Passman et al. 47, 2016	Multicentre, single-arm study	59 patients	Implantable Cardiac Monitor-Guided Intermittent Anticoagulation	A targeted strategy of ICM-guided intermittent NOAC administration is feasible. A large-scale trial is necessary to evaluate the safety of this approach.
Phibbs et al, 48, 2016	RCT	2922	Patient self-testing (PST) using portable at-home INR monitoring devices	Weekly PST is a cost-effective alternative to monthly HQACM and a preferred testing frequency compared to twice weekly or monthly PST
Prochaska et al. 49, 2017	Prospective multicentre cohort study	760	e-health-based anticoagulation management systems	In this study, e-health-based management of OAC therapy was associated with a lower frequency of OAC-specific and non-specific adverse events.
Talboom-Kamp et al. 50, 2017	Parallel cohort design with two randomised self-	247 patients	Combined education and eHealth programme on the control of oral anticoagulation patients	No differences were found between OAT patients trained by e-learning or by a group course regarding therapeutic control (TTR) and usage of a supporting eHealth platform.

	management groups			
Stavrakis et al. 51, 2017	RCT	58 patients	Intermittent anticoagulation based on daily rhythm monitoring	Intermittent anticoagulation based on daily rhythm monitoring is feasible and may decrease bleeding in low-risk patients with paroxysmal AF.
Stoudenmire et al. 52, 2014	Retrospective cohort study	110 patients	Telephone versus office-based management of warfarin	Patients monitored via telephone had a higher incidence of extreme INR values than patients followed in-office, which may lead to an increased incidence of adverse outcomes in the long-term.
Blissit et al. 53, 2015	Single-centre, retrospective study	200 patients	Face-to-face (FF) vs telephone (TELE) visits	Mean TTR results for each group were greater and above the threshold that has been commonly described in the literature as quality control, suggesting a progression in implementation of telephone-based anticoagulation management.
Desteghe et al. 54, 2018	RCT	120 patients	Online tailored education platform for atrial fibrillation	Tailored online education is an effective strategy to improve AF- and procedure-related knowledge with lasting effects up to 12 weeks post-procedurally.
Desteghe et al. 55, 2017	Single cohort study	15 patients	App (Health Buddies) was developed as a tool to improve adherence to non-vitamin K antagonist oral anticoagulants (NOACs)	Only a small proportion of the current AF population seems eligible for the innovative Health Buddies app in its current form. Although the app was positively rated by its users, a large subset of patients was not willing to participate in this study or to use the app.
Stephan et al. 56, 2018	Single cohort study	30 patients	Mobile application to support shared decision about thromboembolic prophylaxis in atrial fibrillation.	The use of a mobile application during medical visits on anticoagulation in atrial fibrillation improves disease knowledge, enabling a shared decision with low decisional conflict.

Desteghe et al. 57, 2018	Randomized, single-blind, crossover, controlled trial	48 patients	Telemonitoring-based feedback	Telemonitoring resulted in high NOAC adherence due to the notion of being watched, as evidenced by the rapid decline during the observation period.
Ferguson et al. 58, 2019	Single cohort study	74 nurses	mHealth intervention to improve nurses' atrial fibrillation and anticoagulation knowledge	The EVICOAG intervention improved nurses' knowledge of atrial fibrillation and anticoagulation and influenced their uptake and use of stroke and bleeding risk assessment tools in clinical practice.
Brasen et al. 59, 2019	RCT	84 patients	Home Management of Warfarin Treatment	Using criteria-driven interactions enabled a considerable reduction in interactions per month. The two groups were comparable in terms of treatment effect and safety.
Nieto et al. 60, 2019	Single cohort study	6280 patients	Videoconferencing and self-testing	Our findings emphasize that in Chile, where the number of patients receiving anticoagulant treatment increases every year, telemedicine, by committed teams, improves the use of oral anticoagulants and is able to increase quality indicators of anticoagulant treatment care.
Nilsson et al. 61, 2014	Single cohort study	2068 patients	Patient-self-management (PSM) of oral anticoagulant therapy	Among patients treated with self-managed oral anticoagulant therapy, males achieve a higher effectiveness than females in terms of time spent in therapeutic INR range
Nagler et al. 62, 2014	Single cohort study	1140 patients	Patient-self-management (PSM) of oral anticoagulant therapy	PSM of properly trained patients is effective and safe in a long-term real-life setting and robust across clinical subgroups.
Ward et al. 63, 2015	Single cohort study	296 patients	Patient-self-management (PSM) of oral anticoagulant therapy	The findings show that, even with little training, people on OAT can successfully self-monitor, and even self-manage, their INR.

Siebenhofer et al. 64, 2008	RCT	195 patients	Self-management of oral anticoagulation	Long-term self-management of oral anticoagulation is superior for the prevention of major thromboembolic and bleeding complications and for the quality of oral anticoagulation control compared to routine care for a mean follow-up period of three years.
Siebenhofer et al. 65, 2012	RCT	141 patients	Self-management of oral anticoagulation	Treatment related quality of life in elderly patients performing self-management of OAC was similar as for patients in routine care setting, with a tendency of higher general treatment satisfaction, after three years of follow up.
Frischi et al. 66, 2007	Single cohort study	330 patients	Self-management of oral anticoagulation	PSM is suitable and safe for the patients identified by their family physicians and successfully trained by our training centre.
Dignan et al. 67, 2013	RCT	310 patients	Self-management of oral anticoagulation	Patient self-management performed at least as well as usual care in maintaining the INR within the target range, without any safety concerns.
Verret et al. 68,	RCT	114 patients	Self-management of oral anticoagulation	A self-management warfarin program led by pharmacists resulted in significant improvement in the quality of life of patients receiving warfarin therapy as well as a reduction in the time required for anticoagulation monitoring
Bleyth et al. 69, 2000	RCT	325 patients	Multicomponent program of management of warfarin therapy	A multicomponent comprehensive program of warfarin management reduced the frequency of major bleeding in older patients.
Voller et al. 70, 2005	RCT	202 patients	Self-management of oral anticoagulation	Management of oral anticoagulation by INR self-management in patients with atrial fibrillation is not inferior to conventional care.

Li et al. 71, 2019	Single cohort study	30 patients	Novel anticoagulation management system (Anticlot Assistant) based on a smartphone application (App)	Patient compliance is critical important for good outcomes and it might increase with improvements in education and more widespread use of information technology.
Mascarenhas et al.72, 2016	Single cohort study	70 patients	Insertable cardiac monitor (ICM)	In AF patients with high bleeding risk, ICM-guided rhythm control with AADs and assessment of AF burden may allow safe discontinuation of OACs.
Boriani et al. 73, 2012	Single cohort study	3438 patients	Implantable cardioverter-defibrillators	The ANGELS of AF project demonstrate the possibility to improve OAC use in accordance with available guidelines for stroke risk reduction in AF by supplying attending physicians with reports about patient's risk factors and AF information from continuous ICD monitoring.
Waks et al. 74, 2019	Single cohort study	48 patients	Implantable cardioverter-defibrillators	Among patients with rare AF episodes and low-to-moderate stroke risk, PM/ICD-guided DOAC administration is feasible and decreased anticoagulation utilization by 75%.
Mascarenhas et al.75, 2019	Single cohort study	145 patients	Cardiovascular implantable electronic devices (CIEDs)	Non-valvular atrial fibrillation patients, AF burden assessment by CIEDs allows an individualised disease-guided approach to safe withdrawal of long-term OAC in patients with high bleeding risk who do not wish to continue long-term anticoagulation
Eggebrecht et al. 76, 2019	RCT	750 patients	Telemedicine-based Coagulation Service	The lower frequency of adverse events in anticoagulated patients managed by the telemedicine-based CS compared to RMC translated into a substantial cost-saving.

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List of meta-analysis on Digital Health for anticoagulation treatment in AF

Author	Design	Studies included	Intervention	Conclusion
Heneghan et al. 1, 2006	Meta-analysis	14 RCT	Patient self-management of oral anticoagulant care	Self-management improves the quality of oral anticoagulation. Patients capable of self-monitoring and self-adjusting therapy have fewer thromboembolic events and lower mortality than those who self-monitor alone
Sakurai et al. 2, 2019	Meta-analysis	4 studies	Computerized Guideline-Oriented Clinical Decision Support System	Computerized guideline oriented CDSS may be effective for appropriate antithrombotic therapy as compared with control in patients with atrial fibrillation.
Lee et al. 3, 2018	Meta-analysis	7 studies	Telehealth interventions improve oral anticoagulation management	Based on very low-quality evidence, telehealth interventions may lower the risk of major thromboembolic events, but not other clinically important outcomes.
Bloomfield et al. 4, 2011	Meta-analysis	22 studies	Patient self-management (PSM) or patient self-testing (PST) alone	Compared with usual care, PST with or without PSM is associated with significantly fewer deaths and thromboembolic events, without increased risk for a serious bleeding event, for a highly selected group of motivated adult patients requiring long-term anticoagulation with vitamin K antagonists.

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Annex 6: Digital health for cardiovascular implantable devices

List of trials on Remote monitoring of CRT devices and defibrillators (RCT)

Author	Design	Sample Size	Intervention	Conclusion
Halimi et al. 1, 2012	RCT	379 patients 184 intervention 195 control	The intervention group, discharged from the hospital 24 h after a first PM implant or 4-6 h after replacement, and followed for 4 weeks with Home-Monitoring (HM)	Early discharge with HM after PM implantation or replacement was safe and facilitated the monitoring of patients in the month following the procedure.
Landolina et al. 2, 2012	RCT	200 patients 99 intervention 101 control	Remote monitoring	Remote monitoring reduces emergency department/urgent in-office visits and, in general, total healthcare use in patients with ICD or defibrillators for resynchronization therapy.
Varma et al. 3, 2014	RCT	1339 patients 908 intervention 431 control	Remote home monitoring	Automatic remote monitoring better preserves patient retention and adherence to scheduled follow-up compared with IPE.

Lüthje et al. 4, 2015	RCT	176 patients 87 intervention 89 control	Fluid monitoring (FM) combined with remote monitoring (RM)	In a single-centre randomized pilot study of RM in combination with FM, no significant influence on HF-related hospitalizations, ICD shocks, or mortality was found.
De Simone et al. 5, 2015	RCT	987 patients 499 intervention 488 control	Internet-based remote interrogation system	Compared with the standard follow-up through in-office visits, remote monitoring is associated with reduced death and cardiovascular hospitalizations in patients with ICD in clinical practice.
Sardu et al. 6, 2016	Multicentre, randomised study	183 patients 89 intervention 94 control	Telemonitoring (TM) of ICDs	At multivariate analysis, TM was the only factor predicting heart failure hospitalisation (hazard ratio 0.6, 0.42-0.79, 95% CI, $p = 0.002$), without affecting overall mortality and cardiac deaths events.
Dougherty et al. 7, 2016	RCT	160 patients 84 intervention 76 control	Home walking exercise. Adherence was tracked using Polar heart rate (HR) monitors, pedometers, home exercise logs, and telephone follow-up.	Adherence to aerobic exercise frequency and duration was high with few dropouts, resulting in higher peakVO2.
Morgan et al. 8, 2017	RCT	1650 patients	Remote management of heart failure using implantable electronic devices	Among patients with heart failure and a CIED, RM using weekly downloads and a formalized follow up approach does not improve outcomes.

Boriani et al. 9, 2017	International, prospective, multicentre, randomized controlled trial.	865 patients 437 intervention 428 control	Remote home monitoring	In heart failure patients implanted with a CRT-D, remote monitoring did not reduce mortality or risk of CV or device-related hospitalization.
Habibovic et al. 10, 2017	RCT	289 patients 143 control 146 intervention	WEB-based distress management program for ICD patients	Web-based treatment was not superior to usual care on the long-term regarding patient reported outcomes.
Lopez-Villegas et al. 11, 2018	RCT	50 patients 25 intervention 25 control	Tele-monitoring (TM) in patients with pacemakers	The NORDLAND trial shows that HRQoL is improved after implant in both groups. Without significant differences with regards to effectiveness and safety.
Hansen et al. 12, 2018	Prospective, randomised, multicentre study	210 patients 102 intervention 108 control	Remote monitoring system for implantable cardiac devices	In HF patients with ICDs/CRT-Ds, quarterly remote follow-up only over 12 months was non-inferior to regular personal contact. Addition of quarterly telephone follow-ups to remote monitoring does not appear to offer any clinical advantage.

Versteeg et al. 13, 2019	RCT	595 patients	Remote monitoring plus a yearly in-clinic ICD check-up	The REMOTE-CIED trial results show that patient-reported health status and ICD acceptance do not differ between patients on RPM and patients receiving in-clinic check-ups alone in the first 2 years after ICD implantation.
Garcia-Fernandez et al. 14, 2019	Multicentre prospective RCT	445 patients 220 home-monitoring + remote interrogations 225 + in office	Remote monitoring	RM-ALONE protocol common for ICD and PM surveillance, consisting of RM + RI every 6 months has proven safe and efficient in reducing hospital visits and staff workload.
Hindricks et al. 15, 2014	RCT	664 patients 331 control 333 intervention	(ICDs) or (CRT-Ds) with telemonitoring function	Automatic, daily, implant-based, multiparameter telemonitoring can significantly improve clinical outcomes for patients with heart failure.
Al-Khatib et al. 16, 2010	RCT	151 patients 76 intervention 75 control	Remote monitoring	We showed no significant reduction in cardiac-related resource utilization with remote monitoring of ICDs

Varma et al. 17, 2010	RCT	1339 patients 908 intervention 431 control	Remote home monitoring	Home monitoring is safe and allows more rapid detection of actionable events compared with conventional monitoring in patients with implantable electronic cardiac devices.
Crossley et al 18, 2011	RCT	1997 patients	Wireless remote monitoring	Wireless remote monitoring with automatic clinician alerts as compared with standard in-office follow-up significantly reduced the time to a clinical decision in response to clinical events
Boriani et al. 19, 2013	RCT	154 patients 78 intervention 76 control	Remote home monitoring	RM in CRT-D patients with advanced heart failure allows physicians to promptly react to clinically relevant automatic alerts and significantly reduces the burden of in-hospital visits.
Guédon-Moreau et al. 20, 2013	RCT	473 patients 239 intervention 234 control	Remote home monitoring	Our observations indicate that long-term HM of ICD is at least as safe as standard ambulatory follow-ups.
Crossley et al 21, 2009	RCT	897 patients 602 remote monitoring	Remote home monitoring	The strategic use of remote pacemaker interrogation follow-up detects actionable events that are potentially important more quickly and more frequently than trans telephonic rhythm strip recordings.

		295 telephonic monitoring		
Hindricks et al. 22, 2014	RCT	155 patients 78 quarterly follow-up 77 yearly follow-up	Remote home monitoring	In prophylactic ICD recipients under automatic daily remote monitoring, the extension of the 3-month in-office follow-up interval to 12 months appeared to safely reduce the ICD follow-up burden during 27 months after implantation.
Bohm et al. 23, 2016	RCT	1002 patients 505 intervention 497 control	Early automated fluid status alert notification via telemedicine	Among ICD patients with advanced HF, fluid status telemedicine alerts did not significantly improve outcomes.
Varma et al. 24, 2018	RCT	1339 patients 908 intervention 431 control	Automatic remote home monitoring	Automatic remote HM demonstrated robust transmission reliability. Daily transmission load may be sustained without reducing battery longevity.
Mabo et al. 25, 2012	RCT	538 patients	Long-term remote monitoring of pacemakers	Remote monitoring was a safe alternative to conventional care and significantly lowered the number of ambulatory visits during long-term follow-up of permanently paced patients.

Martin et al. 26, 2015	RCT	2718 patients	Remote rhythm monitoring	In patients with implanted defibrillators, the strategy of early initiation and interruption of anticoagulation based on remotely detected AT did not prevent thromboembolism and bleeding.
Van Veldhuisen et al. 27, 2011	RCT	335 patients	Measurement of intrathoracic impedance with an implanted device with an audible patient alert	Use of an implantable diagnostic tool to measure intrathoracic impedance with an audible patient alert did not improve outcome and increased heart failure hospitalizations and outpatient visits in heart failure patients.
Abraham et al. 28, 2011	RCT	550 patients	Wireless implantable haemodynamic monitoring (W-IHM) system	Our results are consistent with, and extend, previous findings by definitively showing a significant and large reduction in hospitalisation for patients with NYHA class III heart failure who were managed with a wireless implantable haemodynamic monitoring system.
Abraham et al. 29, 2016	RCT	550 patients	Wireless implantable haemodynamic monitoring (W-IHM) system	Management of NYHA Class III heart failure based on home transmission of pulmonary artery pressure with an implanted pressure sensor has significant long-term benefit in lowering hospital admission rates for heart failure.
Bourge et al. 30, 2008	Prospective, multicentre, randomized, single-blind, parallel-controlled trial	264 patients	Implantable continuous hemodynamic monitor-guided care	The implantable continuous hemodynamic monitor-guided care did not significantly reduce total HF-related events compared with optimal medical management.
Domencini et al. 31, 2016	RCT	80 patients	Telemedicine included daily signs and symptoms based on telemonitoring and structured follow-up by means of video or audio-conference	In this study, an empirical HF treatment guided by IIM alerts did not reduce emergency treatment of HF. However, it seems to have a positive impact on quality of life.

Adamson et al. 32, 2014	RCT	550 patients	CardioMEMS Heart Sensor	Hemodynamically guided management of patients with HF with preserved EF reduced decompensation leading to hospitalization compared with standard HF management strategies.
Krahnke et al. 33, 2015	RCT	550 patients	Implantable pulmonary artery pressure monitoring device	HF management incorporating hemodynamic information from an implantable PA pressure monitor significantly reduces HF and respiratory hospitalizations in HF subjects with comorbid COPD compared with standard care.
Adamson et al. 34, 2016	RCT	550 patients	CardioMicroelectromechanical system (CardioMEMS) Heart Sensor	Pulmonary artery pressure-guided HF management in Medicare-eligible patients led to a 49% reduction in total HF hospitalizations and a 58% reduction in all-cause 30-day readmissions.
Constanzo et al. 35, 2016	RCT	550 patients	Ambulatory Pulmonary Artery Pressure Monitoring	Incorporation of a PA pressure-guided treatment algorithm to decrease filling pressures led to targeted changes, particularly in diuretics and vasodilators
Martinson et al. 36, 2017	RCT	550 patients	Pulmonary artery pressure-guided heart failure management	Standard economic modelling suggests that pulmonary artery pressure-guided management of HF using the CardioMEMS™ HF System is cost-effective from the US-payer perspective.
Givertz et al. 37, 2017	RCT	550 patients	Pulmonary Artery Pressure-Guided Management	PA pressure-guided HF management reduces morbidity and mortality in patients with HFrEF on GDMT, underscoring the important synergy of addressing hemodynamic and neurohormonal targets of HF therapy.
Adamson, 38, 2011	RCT	400 patients	Continuous hemodynamic monitoring	The primary safety end point was met, but the rate of HF equivalents was not different between groups. REDUCE hf was unable to test clinical efficacy end

				points adequately. The device combining IHM-ICD technology was safe and functioned appropriately

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List of trials on Remote monitoring of CRT devices and defibrillators (Observational/retrospective)

Author	Design	Sample Size	Intervention	Conclusion
Schoenfeld et al. 1, 2004	Prospective analysis	59 patients	Patients were asked to transmit device data twice, at least 7 days apart, as scheduled by the clinic. Monitor functionality was assessed, and ease of using the system components was evaluated via questionnaires completed by patients and clinicians	Clinician review of data transmissions revealed several clinically significant findings, including silent AF discovery, assessment of antiarrhythmic drug efficacy in a previously diagnosed AF patient, previously unobserved atrial under sensing, and ventricular tachycardia. ICD patients found the monitor easy to use.
Joseph et al. 2, 2004	Prospective analysis	124 patients	124 patients with single chamber ICDs were monitored by remote RIM and by annual outpatient ICD analysis.	Remote ICD interrogation provides frequent, convenient, safe and comprehensive monitoring. Device and patient related problems were reliably detected and reduced the frequency of outpatient visits.
Kollmann et al. 3, 2007	Observational study	44 patients	A total of 62 electrocardiogram (ECG) recordings were transmitted using a mobile pacemaker (PM) follow-up unit. Using the automatic classification algorithm, 32 PMs were classified as 'OK' and eight PMs were classified as 'not OK'.	The results indicate that the proposed PM follow-up concept has the potential to work as an efficient screening method and may spare a significant number of patients the burden of having to travel to specialized PM clinics.
Nielssen et al. 4, 2008	Observational	260	Home-monitoring of ICD	Home monitoring is feasible and associated with an early detection of medical and technical events.

Lunati et al. 5, 2008	Observational	217	Remote follow-up systems	Six months after implant, reprogramming of device parameters is significantly less frequent, making the use of remote follow-up systems a practical alternative for patients and physicians.
Santini et al. 6, 2009	Observational	67 patients	Patients implanted with CRT-D for more than 6 months received the CareLink monitor and were trained to perform device interrogation.	Remote follow-up is an efficient method to manage tachyarrhythmias and heart failure episodes in CRT-D patients. Early reaction to clinical events may improve overall patient care.
Sacher et al. 7, 2009	Observational	34 Brugada patients	REmote monitoring ['Home Monitoring' (HM), Biotronik, Germany] system	Remote ICD monitoring in patients with BS decreases outpatient consultations and may help prevent ISs.
Spencker et al. 8, 2009	Observational	54 patients	Role of home monitoring to reduce inappropriate shocks due to lead failures	In 91% of all lead-related ICD complications, the diagnosis could be established correctly by an alert of the HM system.
Theuns et al. 9, 2009	Observational	146 patients	Remote monitoring of implantable cardioverter defibrillators (ICD)	Remote monitoring of ICD patients is feasible. Despite the large number of data transmissions, remote monitoring imposed a minimal additional burden on the clinical workload.
Hauck et al. 10, 2009	Single-centre prospective observational study	69 patients	Telemedical ICD monitoring	This pilot study demonstrates that HM enables early detection of ICD failure and appears to enhance patient safety.

Ricci et al. 11, 2013	Multicentre prospective observational study	1650 patients	Remote monitoring [Biotronik Home Monitoring (HM)] was based on primary nursing: each patient was assigned to an expert nurse for management and to a responsible physician for medical decisions. In-person visits were scheduled once a year.	Home Monitoring was highly effective in detecting and managing clinical events in CIED patients in daily practice with remarkably low manpower and resource consumption.
De Asmundis et al. 12, 2013	Single-centre prospective observational study	54 patients	Remote monitoring of implantable cardioverter defibrillators (ICD)	HM substantially improves the clinical management of patients with cardiac arrhythmogenic disease by early recognition of device-related inappropriate therapies and subsequent anticipation of treatment adaptation.
Drak-Hernandez et al. 13, 2013	Retrospective observational study	109 patients	Implantable loop recorders with remote monitoring via monthly telephone transmissions and yearly visits	Remote monitoring of patients with an implantable loop recorder can significantly shorten the time to diagnosis and targeted treatment, without adversely affecting patient safety.
Ricci et al. 14, 2013	Prospective, cohort, observational study	209 patients	Remote monitoring of cardiac implantable electronic devices	Social and economic impacts to patients attending routine device checks in hospital can be significantly reduced by using a remote monitoring strategy.
Perings et al. 15, 2013	Single-centre prospective observational study	109 patients	Remote monitoring of implantable cardioverter defibrillators (ICD)	Integrated follow-up care guided by remote monitoring allows to direct the more significant follow-ups towards ECs and routine follow-ups towards GCs.

Folino et al. 16, 2013	Single-centre prospective observational study	72 subjects (mean age 87 ± 8 years)	Remote pacemaker monitoring	Remote follow-up of pacemakers is a reliable, effective, and cost-saving procedure in elderly, debilitated patients.
Papavasileiou et al. 17, 2013	Single-centre prospective observational study	154 patients	Remote monitoring of implantable cardioverter defibrillators (ICD)	The clinician's work burden is high in patients with remote monitoring. In order to expand remote monitoring in all patients, reimbursement policies should be considered.
Zoppo et al. 18, 2014	Multicentre prospective observational study	472 patients	Web-based application, Discovery Link A Finder, in improving AF detection in CIED patients.	The A Finder web-based software, applied on top of standard in-hospital and remote monitoring, improved AF detection and enabled OAC treatment to be undertaken.
Morichau-Beauchant et al. 19, 2014	Retrospective study	355 patients	Remote monitoring of implantable cardioverter defibrillators (ICD)	RM allows early management of asymptomatic events and a reduction in scheduled ambulatory follow-up consultations in daily clinical practice
Marcantoni et al. 20, 2015	Non-randomized prospective study	207 patients 79 intervention 128 control	Remote home monitoring	Remote monitoring systems improved outcomes in patients with supraventricular arrhythmias by reducing the risk of cardiovascular events, but no benefits were observed in patients with ventricular arrhythmias.

Pürerfellner et al. 21, 2015	Nonrandomized, prospective, multicentre trial	30 patients	Reveal LINQ is a miniaturized insertable cardiac monitor (ICM) with wireless telemetry for remote monitoring	The miniaturized Reveal LINQ ICM supports arrhythmia detection and monitoring, achieving adequate sensing performance without safety issues.
Guédon-Moreau et al. 22, 2015	Observational study	562 patients	Remote home monitoring	An optimized RM organization based on automated alerts and decisional trees enabled a focus on clinically relevant events and a decrease in the consumption of resources without compromising the quality of ICD recipients' care.
Nägele et al. 23, 2014	Nonrandomized, prospective, multicentre trial	1533 patients	Biotronik Home Monitoring systems transmit an 'IEGM Online'	The Lumax and IEGM Online HD Evaluation study demonstrates that remote IEGM analysis is reasonably accurate in a remote monitoring system that transmits shorter IEGM than the full-length programmer IEGM
De Ruvo et al .24, 2016	Nonrandomized, prospective, multicentre trial	211 patients	Remote home monitoring	Although all RM systems effectively detected major events, daily transmission was associated with a higher probability of early event detection.
Portugal et al. 25, 2016	Retrospective cohort study	312 patients 121 intervention 191 control	Device-based remote monitoring	RM was independently associated with increased long-term survival and a lower incidence of a composite endpoint of hospitalization for HF or cardiovascular mortality.

Facchin et al. 26, 2016	Observational study	1251 patients	Device-based remote monitoring	Our experience shows that remote monitoring in a pacemaker population can safely replace in-clinic follow-up, avoiding unnecessary in-hospital device follow-up.
Mittal et al. 27, 2016	Retrospective cohort study	106,027 patients	Remote home monitoring	Improved survival in patients enrolled promptly into RM following CIED implantation
Weidemann et al. 28, 2016	Prospective, cohort, observational study	16 patients	Implanted loop recorder for continuous heart rhythm surveillance	Clinically relevant arrhythmias that require further device and/or medical therapy are often missed with Holter ECGs in patients with advanced stage Fabry cardiomyopathy, but they can be detected by telemonitoring with an implantable loop recorder.
Campana et al. 29, 2016	Prospective, single arm, multicentre cohort study	801 patients	Remote monitoring (RM) at the end of battery life	Our results showed that automatic RM reduced the frequency of scheduled in-hospital visits prior to ICD replacement.
Liberska et al. 30, 2016	Prospective, single-arm, cohort study	305 patients	Remote home monitoring	Remote monitoring of implantable devices is feasible, safe, and effective in supervising patients with CRT-D devices.
Lau et al. 31, 2016	Pre-post intervention trial.	301 patients	Early home-based walking program for first-time implantable cardioverter-defibrillator recipients	Early ambulation after an initial ICD was safe and effective, with few ICD shocks and improved efficacy.

Souissi et al. 32, 2016	Prospective, single-arm, cohort study	115 patients	Implantable cardioverter-defibrillator remote monitoring (RM) permits prompt detection of lead fracture.	Remote monitoring helps to reduce the burden of ISs related to ICD lead fractures.
Lim et al. 33, 2016	Prospective, single-arm, cohort study	57 patients	Remote home monitoring	Remote monitoring of CIED is safe and feasible. It has possible benefits to patient safety through earlier detection of arrhythmias or device malfunction, permitting earlier intervention.
Boulé et al. 34, 2016	Prospective, single-arm, cohort study	109 patients	Remote home monitoring	Remote monitoring systems that generate alerts following anti tachycardia pacing (ATP) delivery could reduce emergency presentations for ICD shock by 24%, as ATP is a key predictor of impending shock delivery.
Parahuleva et al. 35, 2017	Retrospective study	64 patients 217 intervention 147 control	Remote home monitoring	Early discharge with the HM system after ambulatory CIED implantation was safe and not inferior to the classic medical procedure. Thus, together with lower costs, HM and its modifications would be a useful extension of the present concepts for ambulatory implanted CIEDs.
Kurek et al. 36, 2017	Matched cohort study	822 patients	Remote monitoring (RM) of implantable cardioverter-defibrillators (ICDs)	RM of HF patients with ICDs/CRT-Ds significantly reduced long-term mortality in a real-world clinical condition.
Buchta et al. 37, 2017	Prospective, single-arm, cohort study	842 patients	Remote home monitoring	Remote monitoring in patients with implanted ICD or CRT-D devices reduces the cost for the national healthcare provider.

Portugal et al. 38, 2017	Propensity score-matched cohort study	168 patients 84 control 84 intervention	Remote home monitoring	In a propensity score-matched cohort of ICD recipients with long-term follow-up, RM was associated with a lower rate of a combined endpoint of hospital admission for heart failure or cardiovascular death.
Israel et al. 39, 2017	Prospective, single-arm, cohort study	123 patients	Implantable loop recorders (ILR) with automatic AF detection algorithms	AF can be documented in approximately 25 % of patients with the diagnosis of ESUS after careful work-up within a year of monitoring by an ILR and daily remote interrogation.
Kramer et al. 40, 2017	Observational study	26 509 patients	LATITUDE remote monitoring system	Change in physical activity between baseline and 6 months following CRT implantation is strongly associated with survival.
Al-Chekakie et al. 41, 2017	Prospective, double-arm, cohort study	14183 control 4106 intervention	Standard ICD remote monitoring can be supplemented with weight and blood pressure data	In patients using standard ICD RPM, the added transmission of weight and blood pressure data was not associated with improved outcomes.
Dalouk et al. 42, 2017	Retrospective analysis	523 patients 287 intervention 236 control	Telemedicine video-conferencing clinic	Video-conferencing ICD follow-up for patients in areas where electrophysiology subspecialty care is not available leads to outcomes that are noninferior to CIC follow-up.
Smeets et al. 43, 2017	Observational study	282 patients	Remote monitoring functions, including bioimpedance for fluid status monitoring.	No significant differences between both groups were observed in terms of the number of follow-up visits in the outpatient heart failure clinic, the number of hospital admissions with a primary diagnosis of heart failure, or mean length of hospital stay.

Palmisano et al. 44, 2018	Observational study	770 patients	Daily physical activity (PA), as measured by implanted devices	In HF patients with ICD, a low level of daily PA was associated with a higher risk of atrial arrhythmias, regardless of the patients' baseline characteristics. In addition, a lower daily PA predicted death or HF hospitalization.
Ploux et al. 45, 2018	Observational study	4457 patients	Recognition of implantable cardioverter defibrillator (ICD) lead malfunction with RM	ICD remote monitoring with systematic review of all transmitted data is associated with a very low rate of inappropriate shocks related to lead failure.
Nishii et al. 46, 2018	Observational study	1873 patients	Recognition of implantable cardioverter defibrillator (ICD) lead malfunction with RM	RM can detect lead failure earlier, before clinical adverse events. However, CIEDs often diagnose lead failure as just arrhythmic events without any warning.
Söth-Hansen et al. 47, 2018	Prospective four-arm study	1802 patients	Remote home monitoring	Significant and clinically relevant differences in time delay from event detection to acknowledgment exist between RM systems.
Bogyi et al. 48, 2019	Single-centre, retrospective, observational study	231 patients	Remote home monitoring	In this single-centre, retrospective study of optimally treated heart failure patients undergoing CRT-D implantation, the use of remote monitoring systems was associated with a significantly better survival rate.
Maier et al. 49, 2019	Observational study	497 patients	Remote monitoring functions, including bioimpedance for fluid status monitoring.	Overall performance in predicting imminent decompensation by monitoring TI alone is limited due to its high inter-patient variability.
Kort et al. 50, 2019	Prospective observational	30 patients	Continuous telemonitoring with an implantable loop recorder	The use of an ILR could potentially impact patient management

	Dutch multicentre study			
Varma et al. 51, 2015	Prospective observational multicentre study	269,471 patients	Remote monitoring	RM is associated with improved survival, irrespective of device type (including PMs), but demonstrates a graded relationship with the level of adherence. The results support the increased application of RM to improve patient outcomes.
Saxon et al. 52, 2010	Prospective observational multicentre study	185,778 patients	Remote monitoring	Remote follow-up of device data is associated with excellent survival, but arrhythmias that result in device therapy in this population are associated with a higher mortality risk compared with patients who do not require shock therapy
Akar et al. 53, 2013	Prospective observational multicentre study	39 158 patients	Remote monitoring	RPM technology is used in less than half of eligible patients. Lack of enrolment into RPM systems is the major cause of underutilization
Lazarus et al. 54, 2007	Observational study	11,624 patients	Telemonitoring system	This broad clinical application of a new monitoring system strongly supports its capability to improve the care of cardiac device recipients, enhance their safety, and optimize the allocation of health resources.
Akar et al. 55, 2015	Prospective observational multicentre study	37742 patients	Remote monitoring	Among patients undergoing initial ICD implant, RPM use is associated with significantly lower risk of adverse outcomes.
Yu et al. 56, 2005	Single-centre, prospective, observational study	33 patients	Implantable system capable of measuring intrathoracic impedance	Intrathoracic impedance is inversely correlated with pulmonary capillary wedge pressure and fluid balance and decreased before the onset of patient symptoms and before hospital admission for fluid overload.

Whellan et al. 57, 2010	Prospective, multicentre observational study	694 patients	Combined heart failure device diagnostics	Monthly review of HF device diagnostic data identifies patients at a higher risk of HF hospitalizations within the subsequent month.
Gudmundsson et al. 58, 2016	Single-centre, prospective, observational study	43 patients	Implantable cardioverter-defibrillator providing daily intrathoracic impedance were equipped with telemonitoring scales	Decompensation is marked by a decrease in intrathoracic impedance and increase in body weight the preceding 30 days.
Conraads et al. 59, 2011	Prospective, multicentre observational study	501 patients	OptiVol® intrathoracic fluid monitoring	An intrathoracic impedance-derived fluid index had low sensitivity and PPV in the early period after implantation of a device in chronic HF patients.
Ypenburg et al. 60, 2007	Prospective observational study	115 patients	Intrathoracic impedance measurement has been introduced in the InSync Sentry biventricular implantable cardioverter-defibrillator	Intrathoracic impedance measurement as present in the InSync Sentry biventricular implantable cardioverter-defibrillator may be a useful tool for monitoring pulmonary fluid status.
Ritzema et al. 61, 2010	Prospective, multicentre observational study	40 patients	Physician-directed patient self-management system targeting left atrial pressure	Physician-directed patient self-management of left atrial pressure has the potential to improve hemodynamic, symptoms, and outcomes in advanced heart failure.
Magalski et al. 62, 2002	Single cohort study	32 patients	implantable hemodynamic monitor	This implantable pressure transducer is accurate over time and provides a means to precisely monitor the hemodynamic condition of patients with CHF in a continuous fashion.

Ritzema et al. 63, 2007	Single cohort study	80 patients	Permanently implantable, direct left atrial pressure (LAP) monitoring	Ambulatory monitoring of direct LAP with a new implantable device was well tolerated, feasible, and accurate
Braunschweig et al. 64, 2002	Single cohort study	4 patients	Implantable haemodynamic monitor	Haemodynamic changes due to increased volume load can be detected with an implantable haemodynamic monitor.
Ohllson et al. 65, 2001	Single cohort study	21 patients	Continuous ambulatory monitoring	This multicentre feasibility study demonstrated the accuracy and stability of sensors implanted in the right ventricle.
Rozenman et al. 66, 2007	Single cohort study	10 patients	Continuous ambulatory monitoring	This pilot study demonstrates, for the first time, that acoustic wireless communication with a miniature implanted sensor is feasible and provides repeated PA pressure measurement.
Adamson et al. 67, 2003	Single cohort study	33 patients	Implantable haemodynamic monitor	Long-term ambulatory pressure measurements from an IHM may be helpful in guiding day-to-day clinical management, with a potentially favourable impact on CHF hospitalizations.
Ellery et al. 68, 2006	Single cohort study	123 patients	Novel cardiac resynchronization therapy (CRT) devices have a Home Monitoring capability	These interim findings suggest that Home Monitoring data may predict events leading to hospitalization and encourage further research.

Kjellstrom et al. 69, 2005	Single cohort study	148 patients	Implantable haemodynamic monitor (IHM)	A patient survey showed that the technology was user-friendly and that the training material provided sufficient information for patients and their families to install and use the transmission equipment at home
Hoppe et al. 70, 2009	Single cohort study	31 patients	Acoustic wireless communication with an implant directly measuring pulmonary artery (PA) pressures	Meeting the prespecified safety objective of this study warrants a randomised trial to fully evaluate the potential of home monitoring by this miniature PA implant in guiding long-term management in CHF.
Mullens et al. 71, 2010	Single cohort study	194 patients	Internet Based Remote Intrathoracic Impedance Monitoring	Our pilot observations suggested that Internet-based remote monitoring of Z trends from existing device interrogation uploads is feasible as part of a daily routine of HF disease management.
Zile et al. 72, 2008	Single cohort study	70 patients	Implantable hemodynamic monitor	The IHM was shown to be safe and was associated with a very low system-related and procedure-related complication rate in DHF patients.
Page et al. 73, 2007	Double cohort study	67 patients	Implantable device-based system to monitor	A new diagnostic expert system that holds promise for the long-term ambulatory monitoring of CHF was developed.
Charach et al. 74, 2013	Single cohort study	60 patients	Internal thoracic impedance (ITI) was monitored by the RS-205.	The RS-205 is suitable for monitoring patients at high risk of CPE development. It enables detection of CPE and the monitoring of patients at all stages of CPE.
Packer et al. 75, 2006	Single cohort study	212 patients	Impedance cardiography	These results suggest that when performed at regular intervals in stable patients with HF with a recent episode of clinical decompensation, ICG can identify patients at increased near-term risk of recurrent decompensation.

Stevenson et al. 76, 2010	Single cohort study	161 patients	Chronic ambulatory intracardiac pressures	Despite current management, many patients with advanced HF live on a plateau of high filling pressures from which later events occur.
Luthje et al. 77, 2007	Single cohort study	62 patients	Intrathoracic impedance monitoring	Intrathoracic impedance based alert events are associated with a significant increase in NT-proBNP concentration.
Small et al. 78, 2009	Single retrospective cohort study	326 patients	CRT-D with impedance-monitoring capabilities	Serial decreases in intrathoracic impedance sufficient to generate a fluid index threshold crossing as well as the net duration that the index remained above threshold during a 4-month monitoring period were associated with subsequent risk of ADHF hospitalization.
Catanzariti et al. 79, 2009	Single cohort study	532 patients	Monitoring intrathoracic impedance with an implantable defibrillator	The ICD reliably detected CE and yielded low rates of unexplained and undetected events.
Vollmann et al. 80, 2007	Single cohort study	373 patients	Monitoring intrathoracic impedance with an implantable defibrillator	A device-based algorithm that alerts patients in case of decreasing intrathoracic impedance facilitates the detection of HF deterioration.
Tang et al. 81, 2012	Retrospective analysis	21217 patients	Medtronic CareLink (®) Discovery Link	Threshold crossing of impedance trends detectable by implanted devices is associated with relatively increased mortality risk even after adjusted for demographic, device-detected AF, or defibrillator shocks
Forleo et al. 82, 2013	Single cohort study	80 patients	Device monitoring of heart failure	The present study confirms the feasibility and clinical usefulness of this novel multivector impedance monitoring system.

Binkley et al. 83, 2012	Single cohort study	75 patients	Multivector impedance to monitor pulmonary congestion	This multivector impedance algorithm was effective in tracking PE clinical events in this patient population.
Maines et al. 84, 2007	Case-control study,	27 patients	Intrathoracic fluids accumulation monitoring	The OptiVol feature is a useful tool for the clinical management of HF patients as it can result in early treatment during the pre-clinic stage of HF decompensation and in a significant reduction of hospital admissions for congestive HF.
Jermyn et al. 85, 2017	Single cohort study	77 patients	Remote pulmonary artery pressure (PAP) monitoring	Hemodynamic-guided HF management leads to significant improvements in NYHA class and HF hospitalization rate in a real-world setting compared with usual care
Heywood et al. 86, 2017	Single cohort study	2000 patients	Remote pulmonary artery pressure (PAP) monitoring	2000 general-use patients managed with hemodynamic-guided heart failure care had higher PA pressures at baseline and experienced greater reduction in PA pressure over time compared with the pivotal CHAMPION clinical trial.
Zile et al. 87, 2017	Retrospective analysis	790 patients	Implantable Hemodynamic Monitor	Implantable hemodynamic monitor-derived baseline ePAD and change from baseline ePAD were independent predictors of mortality in chronic heart failure patients.
D'Onofrio et al. 88, 2017	Prospective, case-control, multicentre study	254 patients	Structured program for β-blocker titration in CRT-D patients	The program for β-blocker up-titration increased the number of patients reaching the target dose and improved the response to the therapy.
Soga et al. 89, 2011	Prospective clinical observational study	123 patients	Fluid Assessment Based on Intrathoracic Impedance Monitoring	IIM-based fluid index in patients with HF due to LV systolic dysfunction was effective in predicting worsening HF

Boehmer et al. 90, 2017	International, multicentre, nonrandomized study	900 patients	Multisensor Chronic Evaluation in Ambulatory Heart Failure Patients	The HeartLogic multisensor index and alert algorithm provides a sensitive and timely predictor of impending HF decompensation.
Desai et al. 91, 2017	Retrospective analysis	1114 patients	Ambulatory Hemodynamic Monitoring	As in clinical trials, use of ambulatory hemodynamic monitoring in clinical practice is associated with lower HFH and comprehensive HF costs
Maier et al. 92, 2019	Single cohort study	457 patients	Implant-based remote monitoring	Overall performance in predicting imminent decompensation by monitoring TI alone is limited due to its high inter-patient variability.
Lopez-Villegas et al. 93, 2016	Controlled, non-randomized, non-blinded clinical trial	82 patients	Remote monitoring of pacemakers	The PONIENTE trial suggests that the remote monitoring of pacemakers in older adults is an equivalent option to hospital monitoring
Lieback et al. 94, 2011	Single cohort study	32 patients	Remote monitoring using implantable devices	Provided that patient compliance is strictly supervised, reliable data flow from sensors requiring patient involvement is possible.
Watanabe et al. 95, 2013	Single cohort study	215 patients	Implantable cardioverter defibrillator home monitoring	RM-based forecasts appear sufficiently accurate to safely individualize RFU. Most patients have a positive attitude towards RM.
Geller et al. 96, 2019	Single cohort study	987 patients	Implant-based multi-parameter telemonitoring	Daily multiparameter telemonitoring has a potential to reduce clinical endpoints in patients with chronic systolic heart failure both in ICD and CRT-D subgroups.

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List of trials on Remote monitoring of CRT devices and defibrillators (Cost-effective analysis)

Author	Design	Sample Size	Intervention	Conclusion
Fauchier et al. 1, 2005	Retrospective	502 patients	Costs of conventional follow-up (FU) of ICD were calculated without and compared with the expected cost of FU with home monitoring. Calculations included number of visits, including physician's fees, electrocardiograms, and specific ICD surveillance, and transportation costs.	Over the 5 years of expected life of the device, the decrease in costs for FU visits was estimated at 2,149 dollars. With an additional cost of 1,200 dollars for the HM system, saving began after a mean FU of 33.5 months.
Raatikainen et al. 2, 2008	Prospective study	41 patients	Internet-based remote monitoring	Remote monitoring offers a safe, feasible, time-saving, and cost-effective solution to ICD follow-up.
Bikou et al. 3, 2010	Prospective study	20 patients	Remote monitoring system was used to interrogate ICD devices via telephone	The cost of remote follow-up for 100 ICD patients/year was calculated to be €44,267, or about 16% of the cost of conventional in-clinic follow-up.
Burri et al. 4, 2013	Markov cohort model and data relating to events and costs identified via a systematic review		Remote monitoring system was used to interrogate ICD devices	HM is cost neutral over 10 years. This is mainly accomplished by reducing the number of battery charges and inappropriate shocks, resulting in fewer device replacements, and by reducing the number of in-clinic FU visits.
Guédon-Moreau et al. 5, 2014	RCT	310 patients	Remote monitoring system was used to interrogate ICD devices	From the French health insurance perspective, the remote management of ICD patients is cost saving.

Lorenzoni et al. 6, 2014	Observational two cohort study	582 patients	Remote control (RC) of pacemaker and ICD	RC potentially provides a risk reduction for stroke because it allows an early detection of new-onset AF. Moreover, it is also a cost-saving means of follow-up.
Bulava et al. 7, 2016	Prospective observational study	198 patients	Telemonitoring of patients with implantable cardioverter-defibrillators	HM system has been cost-effective for health insurance companies in patients with single- or dual-chamber ICDs.
Ladapo et al. 8, 2016	Prospective observational study	3314 patients	Remote home monitoring	Remote monitoring of patients with CIEDs may be associated with reductions in health care utilization and expenditures compared with exclusive in-office care.
Piccini et al. 9, 2016	Nationwide cohort study	92,566 patients	Remote monitoring (RM) of cardiac implantable electronic devices (CIEDs)	RM is associated with reductions in hospitalization and health care utilization. Since only about a third of patients with CIEDs routinely use RM, this represents a major opportunity for quality improvement.
Ricci et al. 10, 2017	Prospective, controlled, observational study	209 patients	Remote home monitoring	RM of patients with cardiac implantable electronic devices (CIEDs) is cost saving from the perspectives of the HCS, patients, and caregivers.
Schmier et al. 11, 2017	Markov cohort model		Implantable wireless pulmonary artery pressure remote monitor, the CardioMEMS HF System	Compared with standard of care, the CardioMEMS HF System was cost-effective when leveraging trial data to populate the model.
Capucci et al. 12, 2017	Prospective, non-randomized, multicentre trial	858 patients	Remote monitoring of ICD	There is a reduction in direct healthcare costs of RM for HF patients with ICDs, particularly CRT-D, compared with standard monitoring.

Hummel et al. 13, 2019	Observational study	15254 patients	Remote monitoring of ICD (Boston Scientific)	Remote monitoring is a cost-effective approach for the lifetime management of patients with implantable cardioverter-defibrillators.
Perl et al. 14, 2013	RCT	151 patients	Patient management using the BIOTRONIK Home Monitoring®-System	Remote home monitoring of pacemaker and ICD devices was safe, reduced overall hospital visits, and detected events that mandated unscheduled visits.
Heidbuchel et al. 15, 2015	RCT	312 patients	Remote follow-up (FU) of implantable cardiac defibrillators (ICDs)	For all the patients as a whole, FU-related costs for providers are not different for remote FU vs. purely in-office FU, despite reorganized care.
Zanaboni et al. 16, 2013	RCT	200 patients	Remote follow-up (FU) of implantable cardiac defibrillators (ICDs)	Remote management of heart failure patients with implantable defibrillators appears to be cost-effective compared to the conventional method of in-person evaluations.
Calo et al. 17, 2013	RCT	233 patients	Remote monitoring on ordinary follow-up of implantable cardioverter defibrillators	The time spent by the hospital staff was significantly reduced in the RM group. If the costs for the device and service are not charged to patients or the provider, patients could save about USD 190 per patient/year while the hospital could save USD 51 per patient/year.
Cowie et al. 18, 2017	Markov model		Real-time pulmonary artery pressure monitoring	The analysis indicates that integrating wireless PAP monitoring into the management of UK HF patients is likely to be a cost-effective addition to the HF treatment pathway for appropriate patients.
Sandhu et al. 19, 2016	Markov model		The CardioMEMS device, an implantable pulmonary artery pressure monitor	In populations similar to that of the CHAMPION trial, the CardioMEMS device is cost-effective if the trial effectiveness is sustained over long periods.

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List of trials on Remote monitoring of CRT devices and defibrillators (Meta-analysis)

Author	Design	Studies included	Intervention	Conclusion
Parthiban et al. 1, 2015	Meta-analysis	9 RCTs	Remote monitoring (RM) of implantable cardioverter-defibrillators (ICD)	Meta-analysis of RCTs demonstrates that RM and IO follow-up showed comparable overall outcomes related to patient safety and survival, with a potential survival benefit in RCTs using daily transmission verification.
Klersy et al. 2, 2016	Meta-analysis	11 RCTs	Implantable device telemonitoring	Compared with standard of care, device telemonitoring is associated with a marked reduction in planned hospital visits.
Hindricks et al. 3, 2017	Pooled data	2405 patients	Daily remote monitoring of implantable cardioverter-defibrillators	In a pooled analysis of the three trials, home monitoring reduced all-cause mortality
Adamson et al. 4, 2017	Meta-analysis	5 studies	Ambulatory Pulmonary Artery Pressure Monitoring	Haemodynamic-guided HF management using permanently implanted sensors and frequent filling pressure evaluation is superior to traditional clinical management strategies

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List of trials on Arrhythmia detection with implantable devices +ILR

Author	Design	Sample Size	Intervention	Conclusion
Montenero et al. 1, 2004	Single cohort study	9 patients	ILR	The ILR may be a helpful tool in monitoring pts undergoing ablation. Dedicated AF detection characteristics could give additional value to the device.
Varma et al. 2, 2005	Retrospective analysis	276 patients	Remote telemetry of implantable devices	HM enabled rapid anticoagulation decisions. In recipients of implantable devices, automatic wireless telemetry with HM was efficient and reliable.
Glotzer et al. 3, 2003	Single cohort study	312 patients with sinus node dysfunction	Pacemakers were programmed to log an Atrial high rate events (AHRE)	AHRE detected by pacemakers in patients with SND identify patients that are more than twice as likely to die or have a stroke
Israel et al. 4, 2004	Single cohort study	110 patients	Pacemaker with dedicated functions for AF detection and electrogram storage was implanted	This prospective study demonstrates a high incidence of recurrent AF despite optimized antiarrhythmic therapy.
Swerdlow et al. 5, 2000	Single cohort study	80 patients	Atrial implantable cardioverter-defibrillator	A new ICD detects AT/AF accurately and continuously. Therapy may be programmed for long-duration AT/AF, with a low risk of under detection.
Pollak et al. 6, 2001	Single cohort study	56 patients	Intraatrial electrograms (EGMs) of DDD pacemakers	Pacemaker diagnostic data with intraatrial EGMs can diagnose specific atrial tachyarrhythmias and identify other pacemaker-sensed events.
Pokushalov et al. 7, 2011	Single cohort study	72 patients	ILR	. Concomitant AF ablation during CABG is effective in the treatment of AF, as assessed through 1 year of continuous monitoring.

Quirino et al. 8, 2009	Single cohort study	102 patients	Dual-chamber pacemakers equipped with diagnostic features for AF	Many pacemaker patients with paroxysmal AF can develop AF-like symptoms in the absence of device-stored AF.
Hanke et al. 9, 2009	Single cohort study	45 patients	Novel implantable continuous cardiac rhythm monitoring (IMD) device (Reveal XT 9525).	For "real-life" cardiac rhythm documentation, continuous heart rhythm surveillance instead of any conventional 24HM follow-up strategy is necessary.
Botto et al. 10, 2009	Retrospective analysis	568 patients	Continuous monitoring	In patients with recurrent AF episodes, risk stratification for thromboembolic events can be improved by combining CHADS (2) score with AF presence/duration.
Hindricks et al. 11, 2010	Single cohort study	247 patients	Implantable leadless cardiac monitor (ICM)	In this ICM validation study, the dedicated AF detection algorithm reliably detected the presence or absence of AF and the AF burden was accurately quantified.
Ziegler et al. 12, 2006	Retrospective analysis	574 patients	Continuous monitoring with pacemaker	Intermittent and symptom-based monitoring is highly inaccurate for identifying patients with any or long-duration AT/AF and for assessing AT/AF burden.
Ricci et al. 13, 2009	RCT	334 patients	Impact of dual- vs. single-chamber defibrillators on atrial fibrillation (AF) occurrence	Dual-chamber ICDs compared with single-chamber ICDs reduced the incidence of an endpoint composed by permanent AF, AF-related hospitalizations
Verma et al. 14, 2007	Single cohort study	86 patients	Permanent pacemakers (PPM)	Detection of atrial tachyarrhythmias by a PPM occurred in 30% of patients without symptomatic AF recurrence.
Steven et al. 15, 2009	Single cohort study	37 patients	Pacemaker/implantable cardioverter defibrillator (ICD) implantation	Continuous atrial monitoring reveals AF ablation success rates comparable with those assessed by clinical evaluation.

Ghali et al. 16, 2007	Multicentre, prospective study	427 patients	Dual chamber multiprogrammable pacemakers	In patients receiving pacemakers for atrio-ventricular block or sinus node dysfunction, the prescription pattern for anticoagulation and antiarrhythmic drugs is influenced by the detection of asymptomatic AHRE.
Martinek et al. 17, 2007	Single cohort study	14 patients	Implanted pacemaker device	Continuous monitoring provided by an implantable device is able to detect significantly more AF episodes than routine FU.
Purerfellner et al. 18, 2004	Retrospective analysis	409 patients	Implanted device	Accurate detection and discrimination of FFRWs validates the reliability of AT diagnostic data and decreases the risk of inappropriate device therapy.
Mehra et al. 19, 2004	Single cohort study	643 patients	Implanted device	In patients implanted with pacemakers for management of bradyarrhythmia who have a history of AT, a significantly positive but weak correlation was observed between changes in rhythm control measures
Kristensen et al. 20, 2004	Single cohort study	28 patients	Pacemaker telemetry	The specificity and sensitivity for detection of AT recorded by the pacemaker telemetry in this study was 100% and 90%, respectively. The false-positive rate was 0%.
Capucci et al. 21, 2005	Single cohort study	725 patients	DDDRP pacemaker	In a cohort of patients with bradycardia and AF, arterial embolism was common in patients with ischemic cardiopathy, hypertension, diabetes mellitus, and in patients with known stroke risk factors.
De Voogd et al. 22, 2006	Single cohort study	57 patients	Automatic mode switching (AMS) of pacemakers	The total duration of AF is correctly represented by the total duration of AMS and can be considered a reliable measure of total AF duration.
Fitts et al. 23, 2000	RCT	97 patients	Thera DR pacemaker	The diagnostic atrial tachyarrhythmia detection feature in newer pacemakers is an effective method for evaluating the time course of paroxysmal AF in patients with implantable pulse generators.

Passman et al, 24, 2004	Single cohort study	40 patients	Medtronic Thera or Kappa 700 permanent pacemakers underwent Holter monitoring	In patients with tachycardia-bradycardia syndrome and permanent pacemakers having these mode switching algorithms, mode switching events are reliable surrogate markers for atrial tachyarrhythmias.
Leshem-Rubinow et al. 25, 2011	Single cohort study	604 patients	Cardio R loop recorder	The Cardio R device enables prompt ECG confirmation/exclusion of a probable arrhythmic cause of symptoms, enabling rapid intervention for cardiac-relevant complaints.
Jons et al. 26, 2011	Single cohort study	271 patients	ILR	Using an implantable cardiac monitor, the incidence of new-onset AF was found to be 4-fold higher than earlier reported.
Ng et al. 27, 2004	Single cohort study	50 patients	Reveal® Plus implantable loop recorder	Automatic detection of asymptomatic arrhythmia did not appear to improve the diagnostic utility of the ILR in our series.
Schwartzman et al. 28, 2006	Single cohort study	29 patients	ILR	Using the ILR, serial, long-term characterization of electrocardiographic events preceding AF onset was feasible, and typically demonstrated a varied pattern within individuals.
Bloch et al. 29, 2010	Single cohort study	1393 patients	Implantable cardiac monitor	Clinically significant bradyarrhythmia and tachyarrhythmias were documented in a substantial proportion of patients with depressed left ventricular ejection fraction after acute myocardial infarction.
Nierop et al. 30, 2000	Single cohort study	35 patients	ILR	Syncope recurrences decreased significantly after implantation of the device, especially in the younger patients. Noncompliant patients had a high mortality rate.
Sivakumaran et al. 31, 2003	RCT	100 patients	ILR	Loop recorders have a much higher diagnostic yield for patients with syncope or presyncope as compared with Holter monitors.

Seidl et al. 32, 2000	Single cohort study	132 patients	ILR	An implantable loop recorder is useful for establishing a diagnosis when symptoms are recurrent but too infrequent for conventional monitoring techniques.
Solano et al. 33, 2004	Two-hospitals, observational, prospective study	2052 patients	ILR	The mechanism of syncope is different in patients with and without SHD; diagnostic yield and safety are similar in both groups.
Entem et al. 34, 2009	Single cohort study	140 patients	ILR	Long-time experience with the ILR confirmed the utility of this device in the diagnosis of unexplained syncope in clinical practice.
Boersma et al. 35, 2004	Single cohort study	34 patients	ILR	The ILR is a valuable and effective tool to establish an arrhythmic cause for unexplained syncope.
Lombardi et al. 36 ,2005	Single cohort study	34 patients	ILR	These data indicate that ILR monitoring facilitates the identification of mechanisms responsible for recurrences and therapeutic management in subjects with syncope or pre-syncope and negative traditional neurological and cardiovascular work-up.
Krahn et al. 37, 2001	RCT	40 patients	ILR	A prolonged monitoring strategy is more likely to provide a diagnosis than conventional testing in patients with unexplained syncope.
Ashby et al. 38, 2002	Retrospective analysis	48 patients	ILR	The implantable loop recorder was effective in making a cardiological or non-cardiological diagnosis for unexplained syncope or presyncope in 52.1% of the patients.
Farwell et al. 39, 2004	Single cohort study	421 patients	ILR	LR significantly increased the rate of diagnosis in an unselected Western population with recurrent syncope.

Ip et al. 40, 2012	Single cohort study	45 patients	Leadless implantable cardiac monitor (ICM).	The ICM provides an objective measure of AF ablation success and may be useful in making clinical decisions.
Glotzer et al. 41, 2009	Prospective, observational study	2486 patients	ILR	The thromboembolic event rate was low compared with patients with traditional AF with similar risk profiles. The data suggest that TE risk is a quantitative function of AT/AF burden.
Eitel et al. 42, 2011	Single cohort study	64 patients	ILR	The rate of AF detection on ILR-AF may be higher compared with standard AF monitoring
Schmidt et al. 43, 2007	Single cohort study	20 patients	Implantable cardiac defibrillator	AF causes DeltaZ drop in pacemaker and ICD recipients.
Kubala, et al. 44, 2012	Single cohort study	11 patients	ILR	The ILR contributed to the exclusion of a ventricular arrhythmia as a mechanism of an atypical syncope in patients with electrocardiographic BS and the suspension of the ICD implant.
Brignole et al. 45 ,2007	Single cohort study	392 patients	ILR	A strategy based on early diagnostic ILR application, with therapy delayed until documentation of syncope allows a safe, specific, and effective therapy in patients
Shanmugam et al. 46, 2012	Single cohort study	560 heart failure (HF) patients	Cardiac resynchronization therapy (CRT)	In a high-risk cohort of HF patients, device-detected atrial arrhythmias are associated with an increased incidence of thromboembolic events.
Santini et al. 47, 2011	Single cohort study	1193 heart failure (HF) patients	Cardiac resynchronization therapy (CRT)	In HF patients with CRT-D, device-detected AT/AF is associated with a worse prognosis. Continuous device diagnostics monitoring, and Web-based alerts may inform the physician of AT/AF occurrences
Mittal et al. 48, 2013	Single cohort study	20 patients	ILR	The data show that many (but not all) patients develop new AF within the first 4 months of flutter ablation.

Dijkman et al. 49, 2000	Single cohort study	64 patients	Dual chamber implantable cardioverter defibrillator (ICD)	Dual chamber detection algorithms evaluated in a subset of diagnostically difficult arrhythmias allow safe detection of double tachycardias but require further extension and programmability to improve VT: SVT discrimination rules.
Parachuri et al. 50, 2011	Single cohort study	50 patients	ILR	A diagnosis of syncope was ultimately made in nearly one third of patients with unexplained syncope. Patients frequently did not activate their ILR at the time of recurrent syncope.
Kapa et al. 51, 2013	Single cohort study	44 patients	ILR	In AF ablation patients, ILR can detect more arrhythmias than CM. However, false detection remains a challenge. With adequate oversight, ILRs may be useful in monitoring these patients after ablation.
Ermis et al. 52, 2003	Retrospective analysis	50 patients	ILR	The ILR auto-activation feature proved effective in providing a high probability basis for syncope and enhanced the diagnostic effectiveness of the device compared with patient activation alone
Arrocha et al. 53, 2004	Single cohort study	40 patients	ILR	Automatic ILR recording and wireless technique is feasible for remote ECG monitoring by ILRs. However, sensitive criteria for recording and transmission may result in an excessive ECG burden.
Furukawa et al. 54, 2011	Single cohort study	47 patients	ILR	Remote monitoring enhances the diagnostic effectiveness of Reveal, limiting the risk of memory saturation due to the high number of false detections and reducing the time to diagnosis.
Charitos et al. 55, 2012	Observational study	47 patients	ILR	IRM follow-up is significantly inferior to CM. IRM strategies will not identify AF recurrence in a great proportion of patients at risk.
Pokushalov et al. 56, 2011	Single cohort study	286 patients	ILR	Patients with recurrences after the first AF ablation are likely to respond to a second early ablation when AF is triggered by supraventricular arrhythmias or premature contractions.

Giada et al. 57, 2007	Single cohort study	50 patients	ILR	In subjects without severe heart disease and with infrequent palpitations, ILR is a safe and more cost-effective diagnostic approach than conventional strategy.
Farwell et al. 58, 2006	Single cohort study	201 patients	ILR	Investigation by the ILR significantly increases the diagnostic rate and ECG directed treatments in a typical unselected syncopal population
Leclercq et al. 59, 2010	Single cohort study	120 patients	Cardiac resynchronization therapy (CRT) devices	More than 20% of the overall HF patient population treated with CRT suffer PAT episodes.
Tse et al. 60, 2005	Retrospective analysis	226 patients	Dual chamber rate responsive pacemaker (DDDR)	These data suggest the use of a pacemaker diagnostic counter to detect AF episodes in pacemaker patients, especially in those without a prior history of AF, can assist in identifying patients
Lacunza-Ruiz et al. 61, 2013	Prospective, multicentre registry of patients	743 patients	ILR	One-third of patients obtained a final diagnosis with the ILR, independent of the baseline characteristics.
Volosin et al. 62, 2013	Single cohort study	2190 patients	ILR	The majority (63.9%) of detected tachycardias contained true tachycardia. Sensitivity to detect induced VT/VF was 99.3%.
Edvardsson et al. 63, 2011	Prospective, multicentre, observational study	570 patients	ILR	The ILR revealed or contributed to establishing the mechanism of syncope in the vast majority of patients.
Pezawas et al. 64, 2008	Single cohort study	70 patients	ILR	The presence of structural heart disease has little predictive value for the occurrence or type of arrhythmia in patients with unexplained syncope.

Schlingloff et al. 65, 2013	Single cohort study	70 patients	ILR	In the patients having an ILR after surgical atrial ablation, initial compliance regarding data transmission was low. A substantial time effort was necessary to obtain sufficient data on cardiac rhythm.
Drak-Hernandez et al. 66, 2013	Retrospective analysis	109 patients	ILR	Remote monitoring of patients with an implantable loop recorder can significantly shorten the time to diagnosis and targeted treatment, without adversely affecting patient safety.
Stollberger et al. 67, 2013	Retrospective analysis	3 patients	ILR	From our limited experience we consider monitoring by a loop-recorder as a useful tool to detect arrhythmias in noncompaction-patients
Charitos et al. 68, 2014	Retrospective analysis	647 patients	ILR vs. intermittent rhythm monitoring (IRM)	IRM-derived AF burden estimates are unreliable estimators of the true AF burden. Particularly for paroxysmal AF patients, IRM-derived AFB estimates should not be used to evaluate outcomes after AF interventions.
Israel et al. 69, 2006	Single cohort study	254 patients	Dual-chamber pacemakers	ATs occur in pacemaker patients significantly more frequently than estimated by ECG/Holter recordings.
Pokushalov et al. 70, 2012	Single cohort study	613 patients	ILR	AF% ≥4.5% at 2 months assessed by continuous monitoring is a powerful predictor of subsequent AF recurrences after initial ablation
Ziegler et al. 71, 2006	Retrospective analysis	574 patients	Pacemaker	Intermittent and symptom-based monitoring is highly inaccurate for identifying patients with any or long-duration AT/AF and for assessing AT/AF burden.
Ziegler et al. 72, 2012	Single cohort study	1386 patients	Implantable cardiac rhythm devices	Whether patients with CHADS(2) risk factors but without a history of AF might benefit from implantable monitors for the selection and administration of anticoagulation for primary stroke prevention merits additional investigation.

Tondo et al. 73, 2014	Single cohort study	143 patients	Continuous cardiac monitor	Continuous ECG monitoring is a valuable tool for long-term follow-up after AF catheter ablation facilitating reliable assessment of symptomatic and asymptomatic AF episodes.
Lorenzoni et al. 74, 2014	Two cohort study	582 patients	Pacemakers (PMs) and implantable cardioverter defibrillators (ICDs)	Remote control potentially provides a risk reduction for stroke because it allows an early detection of new-onset AF. Moreover, it is also a cost-saving means of follow-up.
Gersak et al. 75, 2012	Prospective nonrandomized study	50 patients	ILR	Using 24 × 7 continuous loop recording, the CP demonstrated success in treating persistent and longstanding persistent AF patients.
Nagel et al. 76, 2014	Single cohort study	11 patients with atrial switch operation for transposition of the great arteries	Implantable cardiac device	Remote monitoring enables early detection of tachyarrhythmia followed by optimization of medical treatment and potentially life-saving anti-tachycardic intervention in adults after atrial repair of TGA.
Silva et al. 77, 2015	Prospective observational study	100 patients waiting for renal transplant	ILR	In medium-term follow-up of RTCs, ILR helped detect a high incidence of AE, most of which did not have clinical relevance
Bergau et al. 78, 2015	Retrospective analysis	30 patients	ILR	To improve effectiveness of detecting AF episodes, it is useful to implant subpectorally.
Purerfellner et al. 79, 2015	Single cohort study	30 patients	Miniaturized Reveal LINQ insertable cardiac monitoring system	The miniaturized Reveal LINQ ICM supports arrhythmia detection and monitoring, achieving adequate sensing performance without safety issues.

Mittal et al. 80, 2015	Single cohort study	151 patients	Miniaturized Insertable Cardiac Monitor	The cumulative experience from a controlled clinical trial and a "real-world" registry demonstrate that the new ICM can be inserted with very low incidence of AEs.
Mittal et al. 81, 2013	Single cohort study	20 patients	ILR	Our data show that many (but not all) patients develop new AF within the first 4 months of flutter ablation. Since external ECG monitoring for this duration is impractical, the ILR has an important role for long-term AF surveillance.
Turakhia et al. 82, 2015	Single cohort study	9850 patients	Cardiac implantable electronic devices	In this population with continuous heart rhythm recording, multiple hours of AF had a strong but transient effect raising stroke risk.
Gunda et al. 83, 2015	Single-centre, prospective, observational study	217 patients	Novel insertable LinQ device	We found that with the current implantable techniques, the novel insertable LinQ device is associated with increased risk of complications.
El-Chami et al. 84, 2016	Single cohort study	23 patients	Insertable Cardiac Monitor Technology	Better detection of recurrent AF might identify patients at risk for stroke who would benefit from continuing anticoagulation.
Yang et al. 85, 2016	Single cohort study	32 patients	ILR	The value of ILR in assessing the efficacy of AF RFCA was superior to that of traditional methods.
Nolker et al. 86, 2016	Single cohort study	90 patients	ILR	The SJM Confirm DM2102 can accurately and repeatedly detect paroxysmal AF episodes of at least 2 minutes in length.
Mittal et al. 87, 2016	Single cohort study	3759 patients	LINQ intracardiac monitor	The performance of LINQ ICM is dependent on the AF incidence rate in the population being monitored, the programmed sensitivity of AF algorithm, and the duration of detected AF episodes.

Podd et al. 88, 2016	RCT	50 patients	REVEAL (®)XT implantable cardiac monitors (ICMs) vs permanent pacemakers (PPMs)	Permanent pacemakers Holters are the most accurate method of evaluating arrhythmia burden and the therapeutic efficacy of novel AF therapies.
Sanders et al. 89, 2016	Nonrandomized, prospective, multicentre trial	151 patients	LINQ intracardiac monitor	The new AF detection algorithm in the Reveal LINQ ICM accurately detects the presence or absence of AF.
Sarkar et al. 90, 2012	Retrospective analysis	1561 patients	Cardiac resynchronization therapy	Evaluation of AF burden and rate control information on a monthly basis can identify patients at risk for HF hospitalization in the next 30 days.
Wilke et al. 91, 2016	Retrospective analysis	30 patients	Continuous monitoring	AF is common in patients with HCM who need a CRM device.
Pecha et al. 92,2016	Single cohort study	206 patients	ILR	Continuous rhythm monitoring provides reliable outcome data and helps to guide antiarrhythmic therapy.
Davis et al. 93, 2012	Decision analytic model		ILR	Implantable loop recorder monitoring is likely to be a cost-effective strategy in people presenting to the UK NHS
Providencia et al. 94, 2014	Markov Model	197 patients	ILR	The utilization of ILR leads to an earlier diagnosis and lower number of syncope hospital admissions and investigations, thus allowing significant cost offsets in the Portuguese setting.
Podoleanu et al. 95, 2014	RCT	78 patients	ILR	In patients with unexplained syncope, the early use of an ILR has a superior diagnostic yield compared with the conventional evaluation strategy, with lower healthcare-related costs.

Da Costa et al. 96, 2013	RCT	78 patients	ILR	In this randomized prospective study, the ILR strategy proved largely superior to conventional follow-up in detecting recurrent events, with a potential impact on therapeutic management.
Kabra et al. 97, 2009	Retrospective analysis	86 patients	ILR	In patients with potentially arrhythmic symptoms, ILR plays an important role not only in diagnosing an arrhythmia, but also to rule out an arrhythmic cause.
Pierre et al. 98, 2008	Single cohort study	95 patients	ILR	Implantable loop recorder is a useful diagnostic tool for recurrent syncope of unknown aetiology.
Silveira et al. 99, 2016	Retrospective analysis	62 patients	ILR	ILR proved to be safe and efficient.
Kanters et al. 100, 2016	Markov model		ILR	Inserting the miniaturized version of the ICM is simpler and faster, and the procedure can take place outside the cathlab in a less resource intensive environment.
Weidemann et al. 101, 2016	Single cohort study	16 patients with Fabry cardiomyopathy	ILR	Clinically relevant arrhythmias can be detected by telemonitoring with an implantable loop recorder.
Damiano et al. 102, 2016	Single cohort study	47 patients	ILR	ILR was equivalent at detecting atrial tachycardia when compared with Holter monitoring or ECG.
Yano et al. 103, 2016	Single cohort study	370 patients	Cardiac resynchronization therapy	Daily snapshot ECG monitoring over 365 days detects half of patients who developed AT/AF as detected by CIED, and shorter intervals of monitoring detected fewer AT/AF patients
Ricci et al. 104, 2016	Single cohort study	1650 patients	Cardiac resynchronization therapy	In a large CIED population followed remotely for up to 4years, the incidence of thromboembolic events was less than half the estimations based on the CHA2DS2VASc risk profile.

Conti et al. 105, 2017	Prospective, single-arm, open-label, multicentre	395 patients	Miniaturized Insertable Cardiac Monitor	A clinically meaningful incidence of device detected AF in this study will inform clinical decisions regarding ICM use for AF screening in patients at risk.
Ibrahim et al. 106, 2017	Single cohort study	346 patients	ILR	An ILR has excellent diagnostic yield for syncope, palpitations, and suspected AF
Philippsen et al. 107, 2017	Single cohort study	82 patients	Insertable Cardiac Monitor	The incidence of subclinical AF in this group of patients was surprisingly high. Continuous monitoring with ICM detected significantly more AF episodes than 72-h Holter monitoring
Banghu et al. 108, 2016	Single centre, prospective, observational cohort study	70 patients	ILR	Patients who have cardiac arrhythmia are significantly more likely to experience future falls.
Maggi et al. 109, 2014	Single cohort study	58 patients	ILR	Implantable loop recorder monitoring provides additional diagnostic value in 'difficult' patients
Azocar et al. 110, 2011	Single cohort study	85 patients	ILR	The stepped use of electrophysiologic study (EPS) and ILR in negative patients enables us to safely achieve a high diagnostic yield, given that VT is usually diagnosed during EPS.
Armstrong et al. 111, 2003	Single cohort study	15 patients	ILR	Reveal offers additional diagnostic yield in complex elderly subjects with suspected cardiovascular causes of syncope or unexplained falls
Boriani et al. 112, 2014	Pooled analysis	5 prospective studies (10016 patients)	Cardiac implanted electronic devices (CIEDs)	Device-detected AF burden is associated with an increased risk of ischaemic stroke in a relatively unselected population of CIEDs patients.

Diederichsen et al. 113, 2017	RCT	1420 patients	ILR	The Reveal LINQ™ ICM can be inserted with a very low risk of complications, both in the traditional electrophysiology laboratory setting and in an outpatient procedure room.
Ciconte et al. 114, 2017	Single cohort study	66 patients	Subcutaneous leadless implantable cardiac monitors (ICMs)	Continuous monitoring using this novel device, equipped with a dedicated detection algorithm, yields an accurate and reliable detection of AF episodes.
Deharo et al. 115, 2006	Single cohort study	25 patients	ILR	In highly symptomatic patients with vasovagal syncope, the heart rhythm observed during spontaneous syncope does not correlate with the head-up tilt test
El Hage et al. 116, 2017	Survey	46 haemodialysis patients	ILR	The prevalence of arrhythmia-related symptoms is high in haemodialysis patients and the majority would consider an implantable cardiac monitor if recommended by their physicians.
Reiffel et al. 117, 2017	Prospective, single arm, multicentre study	446 patients	ILR	The incidence of previously undiagnosed AF may be substantial in patients with risk factors for AF and stroke
Witt et al. 118, 2015	Single cohort study	394 patients	Cardiac implanted electronic devices (CIEDs)	In patients without any history of AF, detection of early AHREs after CRT implantation is associated with a significantly increased risk of clinical AF and thromboembolic events
Van Gelder et al. 119, 2017	Single cohort study	2580 patients	Cardiac implanted electronic devices (CIEDs)	Subclinical atrial fibrillation >24 h is associated with an increased risk of ischemic stroke or systemic embolism.
Swiryn et al. 120, 2016	Single cohort study	5379 patients	Cardiac implanted electronic devices (CIEDs)	In the RATE Registry, rigorously adjudicated short episodes of AT/AF, as defined, were not associated with increased risk of clinical events compared with patients without documented AT/AF.

Amara et al. 121, 2017	RCT	595 patients	ILR	Remotely monitored patients were diagnosed and treated earlier for ATA, and subsequently had a lower ATA burden.
Roberts et al. 122, 2017	Single cohort study	30 patients	ILR	The findings confirm the high mortality rate seen in haemodialysis populations and contrary to initial expectations, bradyarrhythmia emerged as a common and potentially significant arrhythmic event.
Lacour et al. 123, 2017	Single cohort study	19 patients	ILR	This study demonstrates that the BioMonitor 2-AF is a safe and effective tool for continuous cardiac monitoring.
Romanov et al. 124, 2018	Single cohort study	165 patients	ILR	AF is a frequent but largely underestimated cardiac arrhythmia after AMI.
Reinsch et al. 125, 2018	A single-centre, prospective, observational study	30 patients	ILR	Implantation of the novel BioMonitor 2 ILR is fast and uncomplicated. Initial sensing values are good and improve over time.
Lortz et al. 126, 2016	Retrospective analysis	30 patients	ILR	The consistent detection of events is an important safety feature of an ICM and linked to secure R-wave sensing.
Maines et al. 127, 2018	Single cohort study	154 patients	ILR	The remote monitoring feature of the Reveal LINQTM allowed earlier diagnosis of asymptomatic but serious arrhythmias in a significant proportion of patients.
Ooi et al. 128, 2018	Single cohort study	30 patients	ILR	The results of the BioMonitor 2 Pilot study confirm the excellent sensing amplitudes

Sulke et al. 129, 2016	RCT	246 patients	ILR	Implantable loop recorder monitoring achieved a more rapid diagnosis in unexplained syncope than usual care.
Sanpaio et al. 130, 2018	Single cohort study	129 patients	Pacemaker	Pacemakers' event monitors underestimate the occurrence of ventricular arrhythmias detected by Holter.
Sakhi et al. 131, 2018	Retrospective single-centre study	94 patients	ILR	In comparison to patients without heart disease, the diagnostic yield of an ILR was lower in patients with inherited primary arrhythmia syndrome and the prevalence of ILR-diagnosed nonsustained VT was higher in patients with structural heart disease.
Schernthaner et al. 132, 2008	Retrospective single-centre study	55 patients	ILR	The ILR helped efficaciously to determine the correct diagnosis and appropriate treatment of recurrent syncope.
Magnussson et al. 133, 2018	Retrospective single-centre study	173 patients	ILR	Time to diagnosis is unpredictable and prolonged ILR monitoring is warranted in addition to optimal use of other diagnostic tools.
Pürerfellner et al. 134, 2018	Single cohort study	138 patients	ILR	An enhancement that adapts sensitivity for AF detection reduced inappropriately detected episodes and duration with minimal reduction in sensitivity.
Yeung et al. 135, 2018	Single cohort study	25 patients	ILR	Extended cardiac monitoring of patients with severe OSA may facilitate the identification of newly detected AF.
Chanda et al. 136, 2015	Single cohort study	20 patients	Pacemaker	In patients with severe OSA without a known history of AF, 7 days of extended cardiac monitoring with an ECG event recorder did not detect clinically meaningful, silent AF.

Mazza et al. 137, 2017	Single cohort study	160 patients	Pacemaker	In pacemaker patients, device-diagnosed severe SA was independently associated with a higher risk of AF (≥6 h/day) and new-onset AF
Roy-Chaudhury et al. 138, 2018	Single cohort study	66 patients	ILR	Clinically significant arrhythmias are common in hemodialysis patients
Rodes-Cabau et al. 139, 2018	Single cohort study	103 patients	ILR	A high incidence of arrhythmic events was observed at 1-year follow-up in close to one-half of the patients with LBBB post-TAVR.
Lewalter et al. 140, 2018	Single cohort study	1003 patients	Implantable cardiac monitor	ICM either revealed progression of 1st-degree AV block to a higher-grade block (53%) or detected an already existing more severe bradycardia warranting an IPG in 40.5% patients.
Li et al. 141, 2018	A single-centre retrospective study	95 patients	Implantable cardiac monitor	ICM (Reveal LINQ™) offers substantial expected and unexpected clinical utility in patients with a variety of clinical presentations.
Wechelselberger et al. 142, 2018	Single cohort study	419 patients	Implantable cardiac monitor	We suggest AF detection duration >6 min and AF burden >0.1% as a standardized outcome definition for AF studies to come in the future.
Palmisano et al. 143, 2018	Single cohort study	770 patients	Cardiac implanted electronic devices (CIEDs)	In HF patients with ICD, a low level of daily PA was associated with a higher risk of atrial arrhythmias, regardless of the patients' baseline characteristics.
Wang et al. 144, 2015	Retrospective analysis	260 patients	Cardiac implanted electronic devices (CIEDs)	Patients who accumulated an AT duration exceeding 5% (18 days) of the total time in any of the 1-year periods are more likely to have an ischaemic stroke
Gonzalez et al. 145, 2014	Single cohort study	224 patients	Permanent pacemakers	Subclinical atrial high rate episodes are commonly encountered in pacemaker patients with no history of AF and are independent predictors of cardiovascular mortality.

Isath et al. 146, 2019	A single centre, retrospective study	542 patients	Permanent pacemakers	Ventricular high rate episodes are frequently encountered on remote monitoring of pacemakers
Forkmann et al. 147, 2019	Single cohort study	126 patients	ILR	Continuous cardiac monitoring after AF ablation provides important information regarding early recurrence episodes and their prognostic impact.
Verma et al. 148, 2019	Single cohort study	387 patients	ILR	ICM monitoring to identify AF guides both immediate and long-term patient management in a population at high risk for stroke.
Sogaard et al. 149, 2019	Single cohort study	212 patients	Implantable cardiac monitor	Our analysis confirms that the physician can rely on Home Monitoring to be informed of all possibly significant arrhythmias during long-term follow-up.
Piorkowski et al. 150, 2019	Single cohort study	92 patients	BioMonitor 2	Safety and efficacy of the new device has been demonstrated.
Perino et al. 151, 2019	Retrospective analysis	10212patients	Cardiac implanted electronic devices (CIEDs)	Among veterans with cardiac implantable electronic devices, device-detected AF is common
Dodeja et al. 152, 2019	Retrospective analysis	22 patients	ILR	ILRs are a useful adjunct for arrhythmia monitoring in the ACHD population with clinically relevant events in 41% of patients.
Rinciog et al. 153, 2019	Markov model		ILR	The use of ICMs to identify AF in a high-risk population is cost-effective for the UK NHS.
Scacciatella et al. 154, 2019`	Single cohort study	195 patients	ILR	A 6-month loop-recorder monitoring may improve the patient-oriented decision-making.

Lim et al. 155, 2019	Single cohort study	475 patients	ILR	ILR implantation in the outpatient setting by suitably trained nurses is safe and leads to significant financial savings.
Diederichsen et al. 156, 2019	Single cohort study	597 patients	ILR	A considerable burden of previously unknown AF was detected when long-term monitoring was applied in at-risk patients.
Kipp et al. 157, 2017	Retrospective analysis	125 patients	Injectable ILR	Implantation of injectable ILR in an ambulatory care setting by APPs following a single dose of intravenous antibiotics and standard manufacturer technique yielded a low complication rate with high acute procedural success.
Lacunza-Ruiz et al. 158, 2019	Prospective registry	128 octogenarians	ILR	The implantable loop recorder seems to be an effective and safe tool in the management of syncope in the octogenarian population.
Afzal et al. 159, 2019	Single cohort study	695 patients	ILR	Incidence of FP during remote monitoring with nominal settings on this ILR was substantial, ranging from 46% to 86% depending on the indication for implantation.
Mamchur et al. 160, 2019	RCT	32 patients	ILR	In patients with paroxysmal AF, the diagnostic value of both non-invasive ambulatory monitoring and ILR is comparable.
Padmanabhan et al. 161, 2019	Single cohort study	312 patients	ILR	ILR monitoring is effective in achieving symptom-rhythm correlation and results in changes in management in nearly half of implanted patients.
Diederichsen et al. 162, 2019	Single cohort study	590 patients	ILR	Although previously unknown AF was highly prevalent, the burden was low, and progression was limited.

Sanfins et al. 163, 2003	Retrospective analysis	10 patients	ILR	Eight patients activated events, out of a total of 45 episodes, and five patients reported two or more symptoms.
Turley et al. 164, 2009	Retrospective analysis	564 patients	ILR	Ten-year experience with the ILR confirms its utility in establishing a pacemaker indication as the cause for syncope or pre-syncope
Sayed et al. 165, 2015	Single cohort study	20 patients	ILR	The discovery that bradyarrhythmia heralded terminal cardiac decompensation in most patients with severe cardiac AL amyloidosis supports a study of prophylactic pacemaker insertion in this patient population.
Inamdar et al. 166, 2006	Single cohort study	100 patients	ILR	Five-year experience with the ILR in 100 consecutive patients confirms the utility of this device in the diagnosis of recurrent, infrequent, unexplained syncope or presyncope.
Vitale et al. 167, 2010	Single cohort study	159 patients	ILR	The estimated indications were four times higher than those observed. Moreover, in about one quarter of the cases, the use of ILRs proved to be potentially inappropriate according to guideline indications.
Kadmon et al. 168, 2012	Retrospective analysis	75 patients	ILR	The ILR has a high diagnostic yield.
Bovin et al. 169, 2012	Retrospective analysis	44 patients	ILR	ILR was an effective tool to establish an arrhythmic cause of the recurrent, unexplained syncope, and useful in ruling out arrhythmia as a cause of syncope.
Bartoletti et al. 170, 2013	Retrospective analysis	107 patients	ILR	Our results show that the new-generation device offer a higher diagnostic yield, mainly as a result of its improved automatic detection function and is associated with fewer adverse outcomes.

Kang et al. 171, 2013	Single cohort study	18 patients	ILR	ILR may be a valuable and effective diagnostic tool for patients with unexplained syncope.
Linker et al. 172, 2013	Retrospective analysis	514 patients	ILR	Patients who only underwent an "initial work-up" had fewer investigations and a lower incidence of injury or hospitalization.
Merlos et al. 173, 2013	Single cohort study	97 patients	ILR	Recurrent syncope is common in patients in whom a diagnosis is not established after the full battery life of an ILR.
Edvardsson et al. 174, 2014	Single cohort study	570 patients	ILR	Gender and/or age had relevance for the clinical evaluation, rate of recurrence, and subsequent specific treatment but not for the diagnostic yield of the ILR.
Ahmed et al. 175, 2015	Retrospective analysis	200 patients	ILR	A history of injury secondary to syncope and female sex were independent predictive factors for bradycardia necessitating PM implantation in patients receiving an ILR for syncope with or without ECG conduction abnormalities.
Edvardsson et al. 176, 2015	Cost-analysis	570 patients	ILR	Important opportunities to reduce test-related costs before an ILR implant were identified, e.g. by more appropriate use of tests recommended in the initial evaluation, by decreasing repetition of tests, and by avoiding early use of specialized and expensive tests
Unterhuber et al. 177, 2016	Retrospective analysis	84 patients	ILR	We found an important number of patients who showed a disappearance of syncope during an observation period of 2-3 and 4 years.
Kanjwal et al. 178, 2018	Retrospective analysis	450 patients	ILR	Postural orthostatic tachycardia syndrome patients with unusually frequent syncope should be considered for ILR implantation if other monitoring modalities like 48-hour Holter monitor or event recorder are inconclusive

Arcinas et al. 179, 2019	Retrospective analysis	222 patients	ILR	Atrial fibrillation was a common diagnostic rhythm in this cohort of adults, aged 65 and older, with ILRs for unexplained syncope.
Huemer et al. 180, 2019	Retrospective analysis	106 patients	ILR	Bradycardia is a frequent finding in patients undergoing ILR implantation due to un- explained syncope.
Brignole et al. 181, 2001	Single cohort study	52 patients	ILR	In patients with BBB and negative electrophysiological study, most syncopal recurrences have a homogeneous mechanism that is characterized by prolonged asystolic pauses, mainly attributable to sudden-onset paroxysmal AV block.
Mieszczanska et al. 182, 2001	Single cohort study	12 patients	ILR	ILR implantation is a simple, useful and safe method
Moya et al. 183, 2001	Single cohort study	111 patients	ILR	In most patients, the likely cause was neurally-mediated, and the most frequent mechanism was a bradycardic reflex
Menozzi et al. 184, 2002	Single cohort study	35 patients	ILR	The patients with unexplained syncope, structural heart disease, and negative electrophysiologic study had a favourable medium-term outcome with no case of death
Donoteo et al. 185, 2003	Single cohort study	36 patients	ILR	In patients with adenosine-sensitive syncope, the mechanism of syncope is heterogeneous, although bradycardia is the most frequent finding.
Mason et al. 186, 2003	Single cohort study	43 patients	ILR	Results suggest that early use of an ILR for the evaluation of unexplained syncope in an office-based electrophysiology practice is an effective approach in patients with and without structural heart disease.

Krahn et al. 187, 2004	Single cohort study	60 patients	ILR	Long-term monitoring of patients with unexplained syncope with automatic arrhythmia detection demonstrated that significant asymptomatic arrhythmias were seen more frequently than anticipated
Moya et al. 188, 2011	Single cohort study	323 patients	ILR	In patients with syncope, BBB, and mean left ventricular ejection fraction of 56 ± 12%, a systematic diagnostic approach achieves a high rate of aetiological diagnosis and allows to select specific treatment.
Moscato et al. 189, 2014	Single cohort study	11 patients	Continuous monitoring of cardiac rhythms in left ventricular assist device patients	Continuous monitoring of cardiac rhythms from available pump data is possible.
Lauschke et al. 190, 2017	Single cohort study	152 patients	A new implantable cardiac monitor (BioMonitor, Biotronik)	BioMonitor effectively detects patients with bradycardia, tachycardia, AF, or asystole.
Lima et al. 191, 2016	Single cohort study	300 patients	Pacemaker with remote monitoring (PRM)	AF monitoring by means of pacemaker is a valuable tool for silent AF detection and continuous remote monitoring allows early AF recurrence detection and reduces the number of days with AF.
Jędrzejczyk-Patel et al. 192, 2016	Single cohort study	304 patients	Remote monitoring	Nearly two-thirds of CRT-D patients had AHR episodes within 2.5 years after implantation.
Cabrera et al. 193, 2011	Single cohort study	585 patients	Remote monitoring	Atrial fibrillation is common in patients fitted with pacemakers.
Cheung et al. 194, 2006	Single cohort study	262 patients	Remote monitoring	Within 1 year of PPM implantation, AF is detected in 24% of patients without history of AF.

Marijon et al. 195, 2010	Single cohort study	198 patients	Remote monitoring	This first prospective electrogram-based evaluation of AT incidence demonstrated that 27% of patients developed > or =1 episode of sustained AT lasting > or =5 minutes in the 12 months after CRT-P device implantation.
Hayn et al. 196, 2013	RCT	177 patients	Remote monitoring	We conclude that alternating telemedical and in-clinic follow-ups brings no additional risks for patients.
Comoretto et al. 197, 2017	Observational study	42 patients	Remote device monitoring	Remote device monitoring has a significant impact on HRQoL in pacemaker patients, increasing its levels up to 6 months after implant.
Abudan et al. 198, 2019	Single cohort study	251 patients	AliveCor Kardia	The AliveCor Kardia device has an excellent safety profile when used in conjunction with most CIEDs. The quality of recordings was preserved in this population.
Lazarus et al. 199, 2019	Single cohort study	567 patients	Calendar-based intracardiac electrogram recordings (IEGM)	An active IEGM improves the clinical value of remote pacemaker follow-up.
Ren et al. 200, 2013	Single cohort study	101 patients	Remote monitoring of implantable pacemakers	In patients implanted with PM capable of remote wireless data transmission, initial home setup of the wireless monitoring device was frequently unsuccessful.
Ricci et al. 201, 2015	Retrospective analysis	201 patients	Daily remote monitoring of pacemaker	In normal practice, energy demand of HM, if present, was overshadowed by programming optimization likely favoured by continuous monitoring.
Schwab et al. 202, 2018	Single cohort study	283 patients	Remote monitoring of DR-ICDs	Remote monitoring of DR-ICDs allows for the quantification of the course of the pacing parameters and AB.

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List of Meta-analysis of on Arrhythmia detection with implantable devices and ILR

Author	Design	Studies included	Intervention	Conclusion
Burkowitz et al. 1, 2016	Meta-analysis	3 RCT	Implantable cardiac monitor	Prolonged monitoring with ICMs is an effective tool for diagnosing the underlying cardiac cause of unexplained syncope and for detecting AF in patients with CS.
Mahajan et al. 2, 2018	Meta-analysis	11 studies	Cardiac implanted electronic devices (CIEDs)	Subclinical AF strongly predicts clinical AF and is associated with elevated absolute stroke risk albeit lower than risk described for clinical AF.
Belkin et al. 3, 2016	Meta-analysis	28 studies	New-Onset Device-Detected Atrial Tachyarrhythmia	New-onset DDAT is common, affecting close to one quarter of all patients with implanted pacemakers or defibrillators
Solbiati et al. 4, 2017	Meta-analysis	49 studies	ILR	About a half of unexplained syncope subjects implanted with an ILR were diagnosed, and around 50% of them had an arrhythmia.

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2. *Mahajan R, Perera T, Elliott AD, et al. "Subclinical Device-detected Atrial Fibrillation and Stroke Risk: A Systematic Review and Meta-analysis." European Heart Journal 39.16 (2018): 1407-415. Web.*
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4. *Solbiati M, Casazza G, Dipaola F, et al. "The Diagnostic Yield of Implantable Loop Recorders in Unexplained Syncope: A Systematic Review and Meta-analysis." International Journal of Cardiology 231 (2017): 170-76. Web.*

List of trials on Patient and staff experiences of remote monitoring of CIED

Author	Design	Sample Size	Digital Intervention	Conclusion
Dickerson et al. 1, 2005	Virtual focus group	13 patients	The study took place through an online virtual focus group and e-mail interviews	Providers must be aware of the value added when patients use the Internet for self-care management of their chronic illness. Through information searches and sharing stories, patients gain insight into possibilities and potential outcomes of living with an ICD.
Ricci et al. 2, 2008	Observational study	117 patients	A pacing expert nurse consulted daily the website and submitted critical cases to physician.	Home Monitoring technology allowed optimization of medical treatment and device programming with low consumption of health-care resource.
Masella et al. 3, 2008	Observational study	67 patients	Remote monitoring service for the follow-up of implanted cardiac devices	The telemonitoring service was more efficient than conventional face-to-face follow-up in terms of the time savings: both for physicians (4.7 minutes versus 15 minutes for remote and conventional monitoring) and for patients (6.6 minutes versus 116.3 minutes)
Przybylski et al. 4, 2009	Observational study	27 patients	Remote monitoring of implantable cardioverter-defibrillators (ICD)	Remote monitoring of ICD recipients in Poland does not present technical difficulties and enables early detection of serious events in ICD patients.

Heidbuchel et al. 5, 2008	Retrospective study	159 patients	Remote monitoring of device function	ICD remote monitoring can potentially diagnose >99.5% of arrhythmia- or device-related problems if combined with clinical follow-up by the local general practitioner and/or referring cardiologist. It may provide a way to significantly reduce in-office follow-up visits
Serber et al. 6, 2010	Survey	146 patients	A patient satisfaction survey describing the participants' experience was used as a measure of acceptability in this non-experimental, survey, pilot study.	Participants were satisfied with the webcast technology, enabling broader access to patients.
Ando et al. 7, 2010	Observational	203 patients	Remote monitoring system for implantable cardiac devices	The CareLink Network was well accepted by both the patients and physicians.
Cronin et al. 8, 2012	Observational	434 patients	Remote monitoring system for implantable cardiac devices	Analysis of RM transmissions has significant implications for the device clinic workflow. Nonactionable transmissions are rapidly processed, allowing clinicians to focus on clinically important findings.
Petersen et al. 9, 2012	Survey	385 patients	CareLink® (Medtronic) remote monitoring	Ninety-five percent of the patients were content with the remote FU. Only 25% had unscheduled transmissions and most unscheduled transmissions were for appropriate reasons.

Vogtmann et al. 10, 2013	Observational	121 patients	Automated, daily Home Monitoring (HM) of pacemaker and implantable cardioverter-defibrillator	Centralized HM was feasible, reliable, safe, and clinically useful. Basic screening and communication of relevant arrhythmic and technical events required a total of 30 min (TN) and 1.1 min (physician) daily per 100 patients monitored.
Ottenberg et al. 11, 2013	Focus group	9 patients	Focus groups of patients with an ICD who received an RM system	Patient adherence to RM systems can be improved by explaining perceived benefits and addressing barriers to use.
Morichelli et al. 12, 2014	Survey	169 patients	Remote monitoring system for implantable cardiac devices	ICD patients showed a high level of acceptance and satisfaction for RM. Patients with CRT-D perceived the greatest benefit.
Habibovic et al. 13, 2014	RCT	289 patients	Web-based distress management program	In this Web-based intervention trial, no significant intervention effects on anxiety, depression, health-related quality of life, device acceptance, shock anxiety, or ICD-related concerns were observed.
Ricci et al. 14, 2014	Multicentre prospective observational study	1650 patients	Remote monitoring [Biotronik Home Monitoring (HM)]	HM implemented in the HomeGuide workflow model required <1 hour/month every 100 patients to detect the majority of actionable events with limited administrative workload.

Laurent et al. 15, 2014	Survey	571 patients	Remote monitoring system for implantable cardiac devices	Clear understanding was associated with a higher acceptance of HM, although it was unrelated to the data transmission rate.
Rosenfeld et al. 16, 2014	Observational	14,848 patients	Remote monitoring system for implantable cardiac devices	There is room for improvement in RM usage among enrolled patients. Younger patients, smaller clinics, and certain geographic areas may be targets for research into interventions to further improve the use of RM.
Taraki et al. 17, 2018	Retrospective analysis	48,016 patients	App-based remote monitoring	Most patients in this large and first-of-its kind reported cohort used smart devices to successfully activate app-based RM technology and remained adherent per guidelines irrespective of age or sex.
De Filippo et al. 18, 2018	Observational	106 patients	Remote monitoring Subcutaneous ICD (S-ICD)	The level of patient compliance with remote checks is high with current technology for RM of S-ICD. The vast majority of data transmissions are consistently performed on a weekly basis on the day scheduled.
Srivatsa et al. 19, 2019	Survey	85 patients	Remote home monitoring	Survey respondents preferred clinic to remote interrogation because they believe clinic appointments allow better interaction.

Artico et al. 20, 2019	Survey	466 patients	Remote home monitoring	Our results highlighted patients' satisfaction, who also felt safer, with the remote monitoring, its ease of use, and the absence of any disturbances in patients' everyday activities or in their privacy.
Villani et al. 21, 2019	Survey	268 patients	Smartphone-compatible devices	The patients' interests were mainly directed at receiving information related to technical data of the implantable cardiac device and not to the overall management of the disease, underlying the insufficient awareness of patients towards the key role of self-control health status and the promotion of a healthy lifestyle.
Timmermans et al. 22, 2019	Survey	300 patients	Remote home monitoring	In general, patients were highly satisfied with RPM, but a subgroup preferred in-clinic follow-up.
Marzegalli et al. 23, 2008	Observational study	67 patients	Remote home monitoring	The ease of use, satisfaction, and acceptance of the CareLink Network in European clinical practice appears elevated both for patients and for clinicians.
Ricci et al. 24, 2010	Survey	119 patients	Home Monitoring (HM) remote control system	A high level of acceptance and satisfaction after 1-year remote control by HM was detected by the five-point scale HoMASQ, which showed a good internal reliability.
Mairesse et al. 25, 2015	Survey		Remote monitoring (RM) of cardiac implantable electronic devices (CIEDs)	Physicians regard RM of CIEDs as a clinically useful technology that affords significant benefits for patients and healthcare organizations.

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2. *EP Europace, Volume 10, Issue 2, February 2008, Pages 164–170, https://doi.org/10.1093/europace/eum289*
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5. *EP Europace, Volume 10, Issue 3, March 2008, Pages 351–357, https://doi.org/10.1093/europace/eun010*
6. *Heart Lung. 2010 Mar-Apr;39(2):94-104. doi: 10.1016/j.hrtlng.2009.06.003. Epub 2009 Aug 25.*
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8. *Heart Rhythm. 2012 Dec;9(12):1947-51. doi: 10.1016/j.hrthm.2012.08.002. Epub 2012 Aug 3.*
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13. *Psychosom Med. 2014 Oct;76(8):593-602. doi: 10.1097/PSY.0000000000000096.*
14. *J Cardiovasc Electrophysiol. 2014 Nov;25(11):1216-23. doi: 10.1111/jce.12482. Epub 2014 Jul 28.*
15. *Arch Cardiovasc Dis. 2014 Oct;107(10):508-18. doi: 10.1016/j.acvd.2014.06.009. Epub 2014 Sep 11.*
16. *Pacing Clin Electrophysiol. 2014 Jul;37(7):820-7. doi: 10.1111/pace.12358. Epub 2014 Jan 31.*
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23. *Marzegalli M, Lunati M, Landolina M, et al. Remote monitoring of CRT-ICD: the multicentre Italian CareLink evaluation–ease of use, acceptance, and organizational implications. Pacing Clin Electrophysiol 2008;31:1259–64.Ricci RP, Morichelli L, Quarta L,et al. Long-term patient acceptance of and satisfaction with implanted device remote monitoring. Europace 2010;12:674–9.*
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