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E-Health in primary care : from chronic disease management to person-centered e-Health : the necessity for blended care

Talboom-Kamp, E.P.W.A.

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eHealth in primary care

From chronic disease management to
person-centered eHealth:
the necessity for blended care



Esther P. W. A. Talboom-Kamp

“Imagination is
more important than
knowledge.”

Albert Einstein, 'Glimpses of the Great' 1930

Voor mijn kinderen Iris en Jorin

eHealth in primary care

From chronic disease management to
person-centered eHealth: the necessity for
blended care.

E.P.W.A. Talboom-Kamp

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eHealth in Primary Care

From chronic disease management to person-centered
eHealth: the necessity for blended care.

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Esther Patricia Willy Adria Talboom-Kamp

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Promotoren: **Prof. Dr. N.H. Chavannes**
Prof. Dr. M.E. Numans

Copromotoren: **Dr. N.A. Verdijk**
Dr. M.J. Kasteleyn

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Non-communicable chronic diseases

The number of individuals with chronic illness and multimorbidity is growing due to rapid ageing of the population and longer individual lifespan. By 2050 the number of people aged 80 or over will be tripled and all major areas of the world, except Africa, will have nearly a quarter or more of their populations aged 60 or above ^[1]. This aging will provoke an increase in the rate of chronic illnesses; in 2010 eighty-six percent of all health care expenses in the US were already spent on people with one or more chronic medical conditions ^[2]. In the Netherlands thirty-two percent of the total population had a chronic illness in 2014, which will rise to forty percent in 2030 ^[3]. Chronic illnesses are expected to be the primary cause of death and disability in the world by 2020 ^[4].

The increase in chronic diseases leads to a higher workload in care, which results in a growing need for structural changes of the health care system. This thesis addresses self-management programs including eHealth integrated into regular care, known as ‘blended care’. Both self-management as well as integrated eHealth are frequently suggested additions to the portfolio of solutions for the increasing burden of healthcare. More specifically, this thesis will focus on eHealth solutions for two chronic patient groups: patients with chronic obstructive pulmonary disease (COPD) and patients that use oral anticoagulants.

..... Integrated disease management

In the past decades, integrated disease management (*IDM*) was introduced with positive effects on the quality of care ^[5]. The aim of an IDM program is to reduce fragmentation and improve continuity and coordination of care, through several core components: education of patients, multidisciplinary approach, structured clinical follow-up, evidence-based clinical pathways and feedback information for healthcare providers regarding care for patients ^[5]. Healthcare providers co-operate to provide patients with chronic diseases with education, exercise, behavioral therapy, smoking cessation advice, medication, nutrition advice and follow-up. The last decades integrated disease management has evolved to person centered care in many countries. Co-creation of care between the patients, their families, care-givers, and health professionals is the core component of person-centered care ^[6], which is becoming a widely-used concept ^[7, 8, 9].

..... Self-management

Finding the best management for chronic diseases is imperative to deal effectively with increasing numbers of patients and escalating costs. Today's management of most chronic illnesses must be characterized by responsibility that patients need to take and by empowering the patients to take charge in measures improving their own health. Such management could entail better compliance in taking medication, effectively implementing essential lifestyle changes, or undertaking preventive actions. Patients, their caregivers, or both make daily decisions about these necessary actions ^[10]. Patients' involvement in the management of their own care is referred to as self-management, which has been defined as "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and life style changes inherent in living with a chronic condition". Effective self-management therefore includes the "ability to monitor one's condition and to affect the cognitive, behavioral and emotional responses necessary to maintain a satisfactory quality of life" ^[11]. This definition implies that self-management is more than the adherence to treatment guidelines because it also incorporates the psychological and social management of living with a chronic disease. Self-management provides more freedom for the patient, improves quality of life and self-efficacy and it lightens the burden of specialized centers ^[12, 13]. The core components of self-management include education, eliciting personalized goals, psychological coping strategies, formulating strategies to support adherence to treatment, behavioral change, together with practical and social support ^[14, 15]. Unfortunately, for many patients, optimal self-management is often difficult to achieve, as indicated by low adherence to treatment guidelines ^[16, 17], reduced quality of life, and poor psychological wellbeing, which are frequently reported across several chronic illnesses ^[18, 19, 20]. However, chronically ill patients who have experience with person-centered, high-quality chronic illness care that focuses on patient activation, decision support, goal setting, problem solving and coordination of care, are better self-managers ^[21]. Patients that use self-management programs are nowadays usually supported by tailor-made eHealth platforms ^[22].

..... eHealth

Given the impact of chronic illnesses on society, new and improved concepts of personalized disease management should be implemented and evaluated. One way of supervising and coaching patients is by use of electronic health

(*eHealth*), which helps patients manage and control their disease.

Generally, *eHealth* interventions are effective in stimulating self-management because they allow patients to cope better with their illness at the time and place of their choice, enabling them to adapt their lifestyle to their condition. Subsequently, *eHealth* support can reduce medical staff consultations ^[22]. The deployment of *eHealth* applications facilitates accessibility to healthcare which in turn enhances patients' understanding of their disease, their sense of control, and willingness to engage in self-management activities ^[23, 24].

Although patients' attitudes and receptiveness towards *eHealth* applications are promising with people of a certain age and education level ^[25, 26, 27], large-scale adoption of self-management and *eHealth* in daily practice lags behind expectations ^[28]. Implementation of *eHealth* applications and integration into regular care are still subject of research. Pre-conditions for starting *eHealth* are thorough organization within regular care, benefits for patients and technical sound applications. Organization of 'blended care' is difficult, mainly because clinicians experience barriers and resistance towards *eHealth*; therefore, the *eHealth* evidence base needs strengthening and a learning process (*including staff training*) must be instituted ^[29]. In addition, it is necessary to inform patients more adequately about the possibilities and consequences of *eHealth* ^[30]. Furthermore, poor user-friendliness of web-based applications and the lack of 'push' factors (*e.g. automated reminders, or messages from healthcare professionals*) are a common cause of low usage or decline in the usage of web-based applications ^[31]. In any *eHealth* study, a substantial proportion of users drop out before completion, or stop using the application, which should be analyzed to provide insight for real-life adoption problems ^[32]. One of the major challenges of *eHealth* in care is to make it beneficial and easy to use for healthcare providers and patients, otherwise professionals nor patients will use it ^[33].

..... COPD

Chronic obstructive pulmonary disease (*COPD*) is a slowly progressive lung disease, and one of the main causes of morbidity and mortality in high, middle, and low-income countries ^[34]. Worldwide nearly 3 million people die from *COPD* every year which, in 2012, was equal to about 6% of all deaths globally ^[35, 36]. The burden of *COPD* on patients' lives is enormous and the impact on society is substantial ^[37].

According to current COPD guidelines, symptoms and airflow obstruction should be monitored regularly to guide modification of treatment and for early identification of complications [38, 39]. Routine monitoring should contribute to achieving management goals in COPD: the delay of disease progression and alleviation of its manifestations. The most important primary care objective should be to improve the quality of life (QoL) of patients [40].

IDM for people with COPD does not only improve disease-specific QoL and exercise capacity, but can also reduce hospital admissions and hospital days per person [41]. IDM for COPD is of high quality but the responsibility for the program lies largely with the healthcare professional, with a modest role for the patient.

..... Oral Anticoagulation Patients

Venous thromboembolism (VTE) and atrial fibrillation (AF) are common causes of mortality and morbidity [42, 43, 44]. The economic and disease burden of AF [45, 46] and VTE [47, 48] is considerable; oral anticoagulation therapy (OAT) is crucial to prevent morbidity and adverse effects of AF and VTE [49]. Oral anticoagulation therapy (OAT) has shown to reduce thromboembolic events in AF, prosthetic heart valves, acute myocardial infarction, and other conditions and is effective as treatment of VTE. The major risks of OAT are bleeding complications with a rate of major bleeding among long-term users of vitamin K antagonists (VKAs) of 1.5% to 5.2% per year [50, 51, 52]. There is a narrow therapeutic range for OAT expressed as the International Normalized Ratio (INR); INR values over 4.5 increase the risk of major bleeding and values less than 2 increase the risk of thromboembolism [53, 54]. This is relevant as patients have substantial difficulties maintaining adequate adherence to VKA regimens with a significant effect on anticoagulation control [55]. OAT is only effective with high adherence to medication and an active role for the patient. Structured monitoring and coaching of patients using VKA is therefore essential. This may be carried out by specialized centers in primary care or hospitals [56]. Alternatively, patients might choose to self-manage their VKA-monitoring.

Recently other anticoagulants, Novel or Non-Vitamin-K-antagonist or Direct oral anticoagulants (NOACs or DOACs), have been introduced and are increasingly preferred as an alternative for VKA as they do not require frequent monitoring [57]. However, many data concerning effects of NOAC use

in routine clinical practice are still missing; disadvantages and risks have been reported. Monitoring of kidney function is necessary, and compliance to medication intake is very important for NOACs too ^[58, 59].

Self-management with eHealth in COPD and OAT

Self-management of COPD has been introduced as an effective method to improve the quality and efficiency of IDM, and to reduce healthcare costs ^[60, 61, 62]. Interventions to support self-management have shown reductions in hospital admissions, and fewer sick days because of exacerbations ^[63, 64]. Self-efficacy includes the emotional functioning and coping ability of an individual, to act or solve problems ^[65]. Self-efficacy is thought to be a strong predictor of health behaviors of COPD patients ^[66]. In a Dutch study on adherence to an online self-management application for patients with COPD or asthma, patients tended to use the online application on a regular basis when the healthcare professional provided coaching and training for them, whereas patients without assistance used the application only sporadically ^[67].

In the case of OAT, self-management includes monitoring INR values by patients (*self-monitoring*) and, as a possible next step, self-adjustment of the medication dosage (*self-dosage*). Research shows a reduction of thromboembolic events and a reduction in all-cause mortality for patients with self-management ^[68]. These improvements can be explained by the fact that patients are provided with greater responsibility in their disease management with an increase of awareness, commitment, and interest in their condition ^[69]. Adequate self-management is very important for all patients with OAT, despite the type of medicine they use. In a study on an internet-based self-management program for OAT patients, web-based and usual coaching by healthcare professionals remained very important for the quality of care ^[70].

Based on the described research results regarding integration of eHealth in regular care for COPD and OAT patients, we believe that online self-management support needs to be a fully integrated element of IDM with good assistance and coaching for patients. Because of the unanswered questions about the organization of 'blended care' and about the involvement of patients, we designed two implementation studies to learn more about the implementation of eHealth.

Aims of this thesis

The objective of the implementation studies described in this thesis, was to investigate the effect of chronic obstructive pulmonary disease (*COPD*) and Oral Anticoagulation Therapy (*OAT*) eHealth-supported programs applied in primary care.

Based on the available knowledge described, the aims of this thesis were:

- Evaluate the effect of different approaches of eHealth implementation on use of the eHealth platforms and patients' outcomes, particularly health status.
- Examine whether the effects found depend on (1) subjectively experienced practical added value for patients, thereby making their everyday lives easier; and (2) the level of organization as an integral part of existing care.

To achieve our research aims, we designed two studies on the implementation of self-management programs with eHealth, 'e-Vita COPD' and PORTALS.

..... The e-Vita COPD study

Because low usage of eHealth is an ongoing problem, we designed a multilevel study to investigate the implementation of a self-management web platform to support patients with COPD in primary care. As the web platform provides continuous education and contact with healthcare professionals, it is expected to help patients recognize and self-manage exacerbations better in an early phase, thereby helping to stabilize their health status.

This study, called 'e-Vita COPD', compares three different approaches to incorporate eHealth via web-based self-management platforms into the integrated disease management of COPD using a parallel cohort design.

First, an eHealth platform was highly integrated into regular care; second, a platform was integrated into regular care on a medium scale; third, a platform was not integrated into regular care. Also, participants are randomly allocated in two of the cohorts, using the same platform to different levels of personal assistance. The two levels of personal assistance for patients contained a group with high assistance and a group with low assistance. The main aim is to analyze the factors that successfully promote the use of a self-management web platform for patients with COPD.

From an organizational perspective, our hypothesis is that a self-management platform will be better adopted if the platform is an integrated part of IDM, with trained healthcare professionals who encourage patients to use the platform. From a human perspective, our hypothesis is that a self-management platform will be better adopted by patients if they receive sufficient personal assistance in how to use the platform.

..... The PORTALS study

As education is the basic approach in development of self-management skills for oral anticoagulation patients, we expect that the strategy to implement educational support largely affects the individual level of self-management and thereby clinical outcomes. To test this hypothesis, we designed the PORTALS study. The aim of this study was to analyze the effect of the implementation of a self-management program including eHealth by e-Learning versus a group training for oral anticoagulation patients. In addition, we aimed to investigate the relationship between the implementation strategy, health status, self-management skills and individual patient characteristics. In the design of the PORTALS study we considered self-monitoring and self-dosage of medication both as important self-management skills

..... About this thesis

This thesis describes the results of the e-Vita and PORTALS study. In chapter 2 of this thesis, our general viewpoint on the management of chronic diseases is presented. In chapter 3, 4 and 5 of the thesis the e-Vita COPD study is presented, with the design (*chapter 3*), the results on usage (*chapter 4*) and the results on health status (*chapter 5*). In chapters 6 and 7 of the thesis the PORTALS study is presented, with the design (*chapter 6*) and the results on health status and usage (*chapter 7*). In the general discussion (*chapter 8*) we consider our results, interpret them in the light of developments in the current literature and discuss our methods, consequences and implications of our findings.

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Chapter 2

An eHealth platform to manage chronic disease in primary care: an innovative approach

Esther PWA Talboom-Kamp | Noortje A Verdijk | Lara M Harmans |
Mattijs E Numans | Niels H Chavannes

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Abstract

The number of individuals with chronic illness and multimorbidity is growing due to the rapid ageing of the population and the greater longevity of individuals. This causes an increasing workload in care, which results in a growing need for structural changes of the health care system. In recent years, this led to a strong focus on promoting “self-management” in chronically ill patients. Research showed that patients who understand more about their disease, health, and lifestyle have better experiences and health outcomes, and often use less health care resources; the effect is even more when these patients are empowered to and responsible for managing their health and disease. In addition to the skills of patients, health care professionals need to shift to a role of teacher, partner, and professional supervisor of their patients. One way of supervising patients is by the use of electronic health (*eHealth*), which helps patients manage and control their disease. The application of eHealth solutions can provide chronically ill patients high-quality care, to the satisfaction of both patients and health care professionals, alongside a reduction in health care consumption and costs.

Introduction

The average age of the Dutch population is increasing rapidly in two distinct ways. The entire so called “baby boomer” generation, born between 1945 and 1965, will have reached the age of 65 and enter the post-active phase of their lives within the next twenty years. Following this, the population size of future generations will be smaller. By 2025, 21% of the Dutch population will consist of citizens older than 65 years, compared to approximately 10% at the turn of the millennium ^[1]. In addition, the life expectancy of the Dutch population has increased in recent years. Between 1980 and 2012, the life expectancy for men increased by almost seven years (*from 72.4 to 79.1 years*), and for women by almost four years (*from 79.1 to 82.8*) ^[2]. Technological developments in medicine and health care, as well as improved treatment methods, are the keys to the earlier detection and more adequate treatment of chronic diseases. As a result, older people are living longer despite their chronic diseases. Due to a combination of these developments, close-to-home primary health care is increasingly dominated by relatively old patients with one or more chronic diseases. Because of the resulting capacity implications for primary care, organizational health care processes will now have to be reviewed. Furthermore, new technologies will have to be tested and introduced, and it will be necessary to establish whether patients’ care needs can be better managed by promoting their own sense of responsibility.

We subscribe to the new definition of health by Huber et al ^[3]; health is no longer defined as a static situation but as the ability to adapt and to self-manage, in the face of social, physical, and emotional challenges. In this definition, self-management is an important and irreplaceable part of health and disease management.

From this perspective, chronic diseases require lifestyle changes and an approach that is referred to as “self-management”: the ability to actively participate in the management of health with the emphasis on complete physical well-being. This involves medical management; changing, maintaining, and creating meaningful behaviors and dealing with the emotions of suffering from chronic disease(s) ^[4]. The most important skills for self-management are problem solving, decision making, resource utilization, and taking action. The basic principle underlying self-management is that behavioral change cannot succeed without the patient taking responsibility ^[5].

In addition to skills of patients, another necessary ingredient for self-management is a good relationship between the patient and health care professional ^[4]. Until the first half of the 20th century, health care professionals were trained to diagnose and treat diseases. With the introduction of self-management, this role changed to being a teacher, partner, and professional supervisor. One way of supervising patients is by use of electronic health (*eHealth*), which helps patients manage and control their disease. The application of eHealth solutions can provide chronically ill patients high-quality care, to the satisfaction of both patients and care professionals, alongside a reduction in health care consumption and costs. One way of supporting self-management is the introduction of eHealth.

The pressure to implement self-management through eHealth is immense as the number of individuals with chronic illness and multimorbidity is growing fast, due to the rapid ageing and greater longevity of the population. The growing number of individuals suffering from major chronic illnesses faces many obstacles in coping with their condition, not the least of which is medical care that often does not meet their needs for effective clinical management, psychological support, and information ^[6]. Cumulatively, chronic diseases are the leading cause of death in many developed countries with cardiovascular and respiratory diseases dominating death statistics. Between 2005 and 2025, the number of heart failure and chronic obstructive pulmonary disease (COPD) cases in the Netherlands is expected to each rise by approximately 100,000, an increase of 45% and 33%, respectively ^[1].

..... The Case of Chronic Obstructive Pulmonary Disease

The World Health Organization (WHO) estimates that over 210 million people currently suffer from COPD. Three million people died worldwide from the disease in 2005. Although a change in smoking habits may alter this slowly, by 2020, COPD is expected to be the third most common cause of death worldwide ^[7]. Due to the increasing prevalence and complex treatment involved, COPD will account for a significant increase in health care costs, as well as for a growing capacity problem in care. In 2007, the number of COPD patients in the Netherlands was 276,100; between 2005 and 2025, this number is expected to increase by 38% ^[8].

Patients with COPD account for a higher consumption of care resources than people without COPD. On average, they visit their general practitioners (GPs) 12.7 times per year, of which 2.1 times are for COPD. In contrast, other

people visit their GPs 6.1 times per year^[8]. In 2005, the total cost for COPD- and asthma-related patient care was estimated at €799 million, placing COPD and asthma in the top ten of the most expensive diseases^[5,8].

The two early stages of COPD, The Global Initiative for Chronic Obstructive Lung Disease (*GOLD*) 1 and 2^[9], represent 80% of the total COPD population in the Netherlands. These patients are mainly examined and treated within primary care. In the years to come, more and more patients with COPD will be referred to primary care from secondary and tertiary care. Primary care has ample intervention options to offer patients with COPD that may lead to improvement of their condition. These include reactivation by support of physical therapists, smoking cessation programs, and self-management supported by bronchodilator medication. Various programs containing elements of these interventions have been implemented and tested for effectiveness in primary care^[10]. Several initial positive effects have been published so far, showing that these programs result in clinically relevant improvement in the areas of dyspnea, exercise tolerance, and quality of life after one year^[10-12].

It is well known that smoking cessation and exercise programs, as part of a multidisciplinary approach, are the most effective treatments for COPD^[13]. Integrated Disease Management (*IDM*) programs for patients with COPD promoting self-management and exercise result in improved disease-specific quality of life and exercise capacity, and a reduction in hospital admissions and days spent in hospital^[10-14]. However, this multidisciplinary approach is difficult to organize in primary care, and has, therefore, mainly been implemented and tested for effectiveness in secondary and tertiary care. Due to the organizational approach within the current health care processes, such programs have not been implemented for longer periods of time and have not produced intrinsic motivation on the part of patients to permanently switch to a healthy and active lifestyle. The main challenge within the next few years will be to strengthen the patients' own role in a responsible manner. Research has shown that self-management leads to better treatment of COPD; patients are more likely to adjust their lifestyles once they have acquired a sense of involvement in their disease. Fear of hospitalization and passive behavior hinder the early detection of exacerbations^[15]. Effing et al demonstrated that self-management education leads to a reduction in hospital admissions and fewer sick days resulting from exacerbations^[16]. Bourbeau et al showed that the application of self-management programs by patients with severe COPD results in a 40% reduction in hospital admissions^[17]. Individual action plans and proper

disease education for patients with moderately severe COPD improved the level of recognition and self-treatment of severe exacerbations; hence, the impact on the patients' health status due to exacerbations was reduced while promoting recovery ^[18]. In the bigger picture, effective self-management programs for patients with COPD may contribute to better quality of life and to a reduction in health care consumption ^[19], as well as health care costs ^[20].

An important success factor in several COPD self-management trials was that the self-management program had been effectively integrated into a disease management program, with a continuing and more remotely positioned role for health care professionals ^[21-23].

A few studies have been performed on eHealth interventions for patients with COPD ^[24-27]. While these studies mainly focused on the economic effects, they provided evidence of a decrease in the number of visits to the hospital, resulting in cost reduction. Pinnock et al examined the effectiveness of telemonitoring COPD parameters integrated into existing care programs; this intervention had no impact on the rate at which patients with COPD were admitted to the hospital. The quality of the telemonitoring process may not have sufficiently enabled patients to take control and the authors themselves suggest that the existing care process insufficiently improved during the study ^[28].

..... The Case of Venous Thromboembolic Disorders

Venous thromboembolism (VTE) is a common cause of potentially preventable mortality, morbidity, and high medical costs ^[29]. With ageing populations and persisting unhealthy lifestyles, the prevalence of VTE is rising rapidly ^[30]. Between 2005 and 2009, the number of patients with VTE in the Netherlands increased by 13%. In 2009, there were more than 385,000 patients with VTE in the Netherlands, more than half of whom suffered from atrial fibrillation ^[31]. Treatment of VTE consists of, among other interventions, anticoagulant therapy (AT) with vitamin K antagonists (VKA) to slow down the formation of blood clots ^[30]. AT requires frequent monitoring of the extent to which the blood clots, as well as regular visits to an anticoagulation clinic, laboratory, or physician, for venous puncture and analysis. For this group of patients, it can be hypothesized that self-management (*self-testing and self-measurement*) might increase the sense of involvement in their own care. In recent years, various methods have been implemented and tested for measuring the degree of anticoagulation (*international normalized ratio (INR)*) in the home setting by means

of self-measurement equipment. A meta-analysis by the Cochrane Collaboration in 2010 found that self-management (*including self-dosing*) by AT patients at home in combination with VKA treatment resulted in a decrease in thromboembolic complications and mortality at a constant frequency of bleeding complications ^[32]. This also applies to the Dutch situation with its extensive network of well-organized anticoagulation clinics ^[31].

Structured clinical trials with online self-management show a greater improvement in INR values within the therapeutic range (10%-23%) than self-management studies without online support (*improved time in therapeutic range (TTR) less than 4%*) ^[33,34]. Home measurement of INR and the reporting and dosing of weekly results online increase the TTR from 72% to 79% compared to conventional computer-assisted monitoring in an anticoagulation clinic ^[35]. Patient satisfaction proved to be higher using online remote monitoring of INR ^[36].

In anticoagulation clinics, it has been reported that fewer thromboembolic complications are reported if the self-management program is embedded in well-organized thrombosis care from a central thrombosis control center integrated in primary care ^[37,38].

..... Self-Management and eHealth

The changing and growing demand for care is causing health care costs to spiral upward in the Netherlands ^[5]. At the same time, there is an imminent shortage of professional health care workers, estimated to be between 280,000 and 800,000 in the Netherlands in 2025 ^[39]. These two aspects combined are increasing the pressure on health care, while at the same time compromising quality, accessibility, and sustainability. To ensure the provision of proper health care, a rearrangement of duties is required. “Traditional care” is reactive, mainly focused on the treatment of episodes of disease or derailment. However, changing care demands call for a more proactive policy. This can be achieved by the timely detection of diseases or complications and by continuously structured monitoring of patients for care gaps and adverse changes in their condition to ensure a faster response to changes and complications. Another element of a proactive policy consists of giving patients themselves a prominent role in coping with their illness and well-being ^[22-40].

The rising number of chronically ill patients and increasing workload in care bring along a growing need for structural change within the health care system. Based on this perspective, in recent years the focus has mostly been on promoting self-management in chronically ill patients. In doing

so, the objective is to give patients a more prominent role in dealing with their disease and sense of well-being; self-management is not only a convenient way to organize care differently, but also offers patients significant benefit. By providing patients with more knowledge about their disease and by active involvement in the process, patients are better able to accept and maintain a healthier lifestyle ^[41]. The effect is even more when these patients are empowered to and responsible for managing their health and disease ^[42]. Offering chronically ill patients innovative self-management solutions, such as eHealth, can support or even improve their independence. Many options exist for patients to get involved through websites and platforms; the quality and content vary greatly, as do the results ^[43]. Several studies have shown that based on this approach, patients are better able to cope with their illness at the time and place of their choosing, allowing them to better adapt their lifestyle to their condition while taking some of the burden off the medical staff ^[44]. The deployment of eHealth facilitates the accessibility to health care, which in turn enhances the patients' understanding of their disease, sense of control, and willingness to engage in self-management ^[45,46]. By applying eHealth solutions, chronically ill patients can be provided with high-quality care, to the satisfaction of both patients and health care professionals ^[47,48].

The results of eHealth-supported self-management depend on the patients' expectations and level of education. Beenkens, for instance, asked 485 patients in anticoagulation clinics why they had opted for eHealth ^[49], and it appeared that patients mainly expect to gain benefits in their well-being, for example in the form of less travel and waiting time, and more freedom of movement. This study also showed that highly educated patients are more inclined to adopt eHealth than those with a low level of education ^[49].

Research into self-management in patients with COPD showed that more relevant positive effects are measured in the group of "effective self-managers", predominantly characterized by relatively younger age, cardiac comorbidity, relatively more serious complaints, and living with others ^[50,51].

The Whole System Demonstrator (WSD) program is a large, randomized trial in England, in which 238 GP practices offered 6191 chronically ill patients various forms of telehealth or standard care. The telehealth systems in this study were designed to monitor vital signs, symptoms, and self-management behavior. The telehealth services were integrated within the existing GP practices and compared with a control group that was offered standard care. An evaluation after one year showed lower mortality rates and fewer acute admissions in the group using telehealth than observed in the standard

care control group ^[52]. It is possible that these differences were partly caused by an initial temporary increase in acute admissions in the control group. In another WSD evaluation, no differences were found between the telehealth group and the standard care group, measured by quality of life, anxiety, and depression symptoms ^[53].

Based on the initial results from the WSD program it can be assumed that patients receiving telehealth services are less likely to go for treatment at an accident and emergency department; further research is required to determine the underlying mechanism. Furthermore, anxiety and depression did not increase among patients using telehealth.

The randomized controlled trial (RCT) by Pinnock et al yielded the conclusion that the integration of telemonitoring within existing care had no effect on delayed hospitalization, on health-related quality of life, anxiety and depression, self-efficacy, and knowledge ^[28]. In their analysis, they argue that the added value generated by the WSD program can be partly explained by a general improvement in the quality of care, as a side-effect of implementation of telehealth ^[28].

The e-Vita COPD and PORTALS studys

Based on the available knowledge described, we formulated two research questions that we wish to answer using data from our large-scale implementation projects (*Textbox 1*). In these projects, we will record and evaluate the effects of eHealth interventions within integrated primary care in the two mentioned domains of chronic disease primary care-managed COPD (*e-Vita COPD*), and anticoagulant therapy in venous thromboembolic conditions (*PORTALS*).

Textbox 1. The two questions we aim to answer.

- What is the effect of the kind of eHealth implementation on use of the portals and patient outcomes?
- Does the effect depend on (1) subjectively experienced practical added value for patients, thereby making their everyday lives easier? and (2) The level of organization as an integral part of existing care?

We designed the multi-level study e-Vita to investigate different implementation methods of a self-management web portal to support and empower

patients with COPD in three different primary care settings; the level of integration of the web portal within the care program is different in the three settings. Using a parallel cohort design, the clinical effects of the implementation of the web portal will be assessed using an interrupted times series (*ITS*) study design and measured according to changes in health status with the Clinical COPD Questionnaire (*CCQ*). The different implementations and net benefits of self-management through eHealth on clinical outcomes will be evaluated from human, organizational, and technical perspectives. To our knowledge, e-Vita is the first study to combine different study designs that enable the simultaneous investigation of clinical effects (*changes in health status*), as well as effects of different implementation methods whilst controlling for confounding effects of the organizational characteristics.

We also used a parallel cohort design for the anticoagulation clinic patients in the PORTALS study. In this study, patient self-testing and patient self-management (*including a web portal*) will be offered to patients of a thrombosis service who currently receive usual care for long-term AT. To investigate determinants of optimal implementation, we will compare two different implementation methods (1) after inclusion where participants will be randomly divided in subgroups where one group will be trained and educated by e-Learning, and (2) the other group that will receive face-to-face group training. A third group, the non-self-management group consists of patients who continue to receive regular care.

In this PORTALS study, we will compare clinical outcomes and self-management skills of two different implementation methods. Second, the relationship between self-management skills, clinical outcomes, and individual characteristics will be investigated.

..... Hypotheses

Based on earlier eHealth research, we expect to see problems where patients' motivation is concerned when it comes to starting and continuing to use the patient platform ^[54]. If patients use the self-management platform on a regular basis, we expect to see a positive effect on quality of life, complications, and hospitalization rate in both groups.

For patients with COPD, we expect to see a relatively small improvement in their everyday lives using the digital platform. Resulting from this, we assume that the use of the platform will grow and take root less rapidly. Patients with VTE are linked to a center that determines their INR values on a regular basis, following which the clinic determines the dose of their

medication. This process has far-reaching effects on their daily lives. For these patients, a comprehensive self-management program supported by a digital platform will ease their dependence on the anticoagulation clinic and enhance their sense of self-reliance. Therefore, we expect these patients to use the digital platform more frequently. As a result, we expect even better improvements in both clinical outcomes and quality of life for patients with VTE.

The Potential Added Value of eHealth

It is too early to draw general conclusions about the impact of eHealth. The evidence of clinical and structural effects of eHealth interventions in patients with COPD and VTE is not clear-cut, partly because of the large differences in study design, interventions, and research methods. Furthermore, research methods into eHealth are a regular topic of discussion, as the focus on clinical outcomes often masks other beneficial effects. Chronic diseases require lifestyle changes and an approach that is referred to as self-management: the individual ability to properly deal with symptoms, treatment, and physical and social consequences. The basic principle underlying this approach is that behavioral change cannot succeed without the patient taking his or her responsibility ^[5]. eHealth is a useful method to implement self-management.

The rising number of chronically ill patients and increasing workload in care bring along a growing need for structural change within the health care system. Using eHealth as a method to implement self-management can provoke beneficial effects for both patients and caregivers.

We designed the studies e-Vita COPD and PORTALS, both parallel cohort designs with Web-based support for self-management, where we expect to see a positive effect on clinical outcomes and quality of life of patients through the implementation of a self-management patient platform integrated within primary care. We presume that behavioral change in both patients and caregivers is the basis for these positive effects. The implementation of eHealth will support caregivers to have a constructive coaching relationship with their patients and the use of eHealth will help patients take a more leading role towards their own health status and lifestyle.

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Abbreviations

- **AT:** anticoagulant therapy
- **COPD:** chronic obstructive pulmonary disease
- **eHealth:** electronic health
- **GP:** general practitioner
- **INR:** international normalized ratio
- **ITS:** interrupted times series
- **TTR:** time in therapeutic range
- **VKA:** vitamin K antagonists
- **VTE:** venous thromboembolism
- **WSD:** Whole System Demonstrator program

Chapter 3

e-Vita:

Design of an innovative approach to COPD disease management in primary care through eHealth application

Esther P. W. A. Talboom-Kamp | Noortje A. Verdijk | Coert M. G. Blom |
Lara M. Harmans | Irvin J. S. H. Talboom | Mattijs E. Numans | Niels H. Chavannes

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Abstract

..... Background

COPD is a highly complex disease to manage as patients show great variation in symptoms and limitations in daily life. In the last decade, self-management support of COPD has been introduced as an effective method to improve quality and efficiency of care, and to reduce healthcare costs. Despite the urge to change the organization of health care and the potential of eHealth to support this, large-scale implementation in daily practice remains behind, especially in the Netherlands.

..... Methods/Design

We designed a multilevel study, called e-Vita, to investigate different organizational implementation methods of a self-management web portal to support and empower patients with COPD in three different primary care settings. Using a parallel cohort design, the clinical effects of the web portal will be assessed using an interrupted times series (ITS) study design and measured according to changes in health status with the Clinical COPD Questionnaire (CCQ). The different implementations and net benefits of self-management through eHealth on clinical outcomes will be evaluated from human, organizational, and technical perspectives.

..... Discussion

To our knowledge this is the first study to combine different study designs that enable simultaneous investigation of clinical effects, as well as effects of different organizational implementation methods whilst controlling for confounding effects of the organizational characteristics. We hypothesize that an implementation with higher levels of personal assistance, and integrated in an existing care program will result in increased use of and satisfaction with the platform, thereby increasing health status and diminishing exacerbation and hospitalization.

Background

Chronic obstructive pulmonary disease (COPD) represents one of the main causes of morbidity and mortality, and worldwide nearly 3 million people die from COPD every year ^[1]. In the Netherlands, COPD was responsible for almost 5 % of the total deaths in 2011 ^[2]. More than 3 million people died worldwide of COPD in 2012, which is equal to 6 % of all deaths globally that year ^[3]. COPD is a highly complex disease to manage as patients show great variation in symptoms and limitations in daily life. This results in a position in the top ten of most expensive diseases for respiratory disease ^[2]. Within the last decade self-management support of COPD has been introduced as an effective method to improve quality and efficiency of care, and to reduce healthcare costs ^[4, 5, 6]. It has shown to improve the level of recognition of severe exacerbations ^[7]. Interventions to support self-management have shown reductions in hospital admissions and fewer sick days because of exacerbations ^[8, 9]. Studies have shown that eHealth interventions are effective in stimulating self-management. Patients are better able to cope with their illness at the time and place of their choosing, allowing them to adapt their lifestyle to their condition while eHealth support also reduces medical staff consultations ^[10]. The deployment of eHealth applications facilitates accessibility to healthcare, which in turn enhances the patients' understanding of their disease, sense of control, and willingness to engage in self-management ^[11, 12]. Although patients' attitudes and receptiveness towards eHealth applications are promising in certain groups of age and education ^[13, 14, 15], large-scale adoption of eHealth in daily practice is low. Despite the urge to change the organization of health care and the potential of eHealth to support this, large-scale implementation in daily practice remains behind on predictions, especially in the Netherlands ^[16].

Low adoption of eHealth in daily practice may be explained by the varying successes of eHealth programs ^[17, 18, 19, 20]—sometimes with a negative impact on quality of care and clinical effects ^[21]. In addition, the field of eHealth assessment is relatively new. The evaluation of eHealth research has several difficulties regarding evaluation methods and challenges of technology itself (usability and privacy), environmental issues that pose special problems for eHealth researchers, and logistic or administrative concerns of the selected evaluation method ^[11]. Therefore, specific frameworks have been developed for eHealth evaluation, including evaluation of eHealth over time and based on different development stages. For example, Kaufman et al. ^[22] suggest that evaluation of eHealth includes specification and needs of requirements, component development, integration of components, integration in clinical

setting and routine use. There are also frameworks that suggest that eHealth should be evaluated from different point of views. For example, Yusof et al.^[23] suggest that human, organizational, and technological aspects and net benefits are essential components of eHealth evaluation.

eHealth shows great potential for effective COPD management. Despite the difficulties of evaluation, research of eHealth interventions is highly valuable for further adoption of eHealth in daily practice. Positive as well as negative results are needed to improve quality, utility and effectiveness, to minimize the likelihood of harm, to promote innovation, conserve resources, encourage participation, to promote confidence among users, and to promote a positive public image^[24]. Therefore, we designed a multilevel study to investigate implementation of a self-management web portal to support patients with COPD in primary care. As the web portal provides continuous education and contact with health care professionals, we expect it to help patients to better recognize and self-manage exacerbations in an early phase, and thereby increase health status and diminish exacerbation and hospitalization. In this ongoing study, called e-Vita, we compare different organizational implementation methods in different primary care settings. We aim to investigate 1) the effect of self-management through eHealth on clinical outcomes and 2) the relationship between technological and organizational factors on the one hand and system use and user satisfaction on the other hand. We will therefore evaluate implementation and net benefits from human, organizational and technical perspectives (Figure 1).

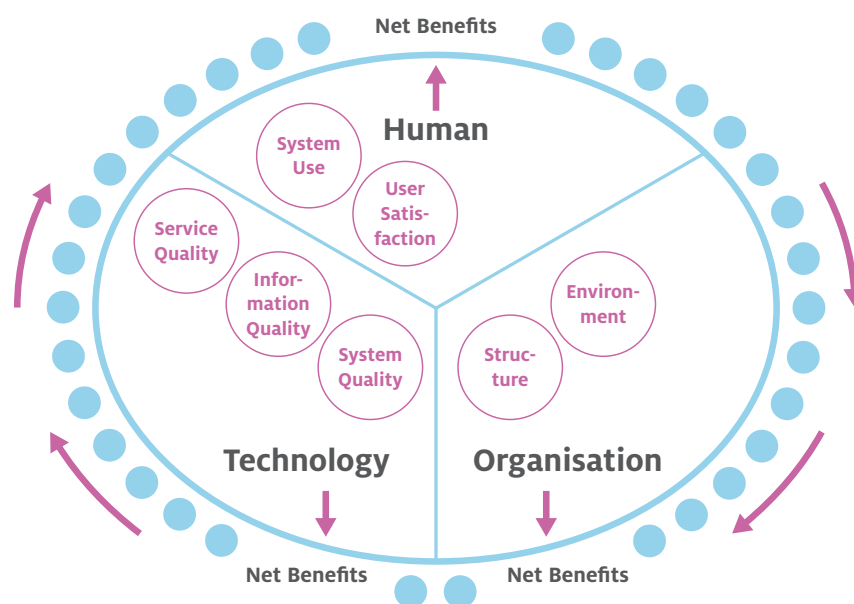


Figure 1. Model based on Yusof^[22]: different aspects of eHealth evaluation

..... Methods/Design

Our primary aim is to investigate the effect of use of patient portals on clinical outcomes in primary care COPD patients (net benefits, Figure 1). In addition, we aim to investigate the optimal organizational implementation method of the platform. Therefore, we will compare different organizational implementation methods in different care settings, and evaluate their use and user satisfaction. We hypothesize that an implementation setup with greater personal support, integrated into an existing care program will be preferred by patients and therefore be more likely to be used. As discussed in the introduction, the evaluation of eHealth is a challenge because of the different views to evaluate from (clinical, technical, and organizational). Moreover, eHealth is not a classical clinical isolated intervention (in this case a platform) with one output (here CCQ). Instead it affects care processes, communication and patients behavior. Finally we have a multilevel purpose to not only investigate effects but also organizational implementation methods. Therefore, we made a design for a quality improvement intervention. In this study, we aimed to include the importance of integration in the daily practice of primary care. Therefore, we chose an implementation study ^[25]. We designed a method to promote the uptake of our research findings into routine primary healthcare; with this design, we aim at studying the influences on healthcare professionals and patient behavior and at evaluating the process by which effects are achieved. Because the most powerful studies are prospective studies, we chose a prospective parallel cohort design. We asked three primary care groups to invite their COPD patients for the e-Vita study. Because there are several differences between the groups (Figure 3), we cannot compare the COPD cohorts by combining data across three different groups. We chose for an interrupted time series (ITS) design to evaluate clinical outcomes (CCQ) within each group. In ITS studies, data are collected at multiple time points before and after an intervention to detect whether the intervention has a significantly greater effect than any underlying secular trend ^[26]. ITS can detect changes that are delayed or intermittent. It can also determine if the change is permanent or temporary. In addition, it allows evaluation of variables which are changing before the intervention, for instance, by comparing slopes of trend lines before and after the intervention. Finally, ITS makes it easier to control for confounding variables and regression to the mean ^[27]. The ITS will be performed according to guidelines of the EPOC Cochrane group ^[25]. Although well-conducted randomized trials provide the most reliable evidence on the effectiveness of interventions, they are not

feasible for our setting of an implementation design with organizational changes in a real-life health care system within three different care groups with different demands. An advantage of an ITS design is that it allows for the statistical investigation of potential biases in the estimate of the effect of the intervention.

In addition to clinical outcomes, we also want to investigate the effect of different organizational implementation methods. Therefore, we will implement the platform in group 1 and 2 using different methods. Differences will be measured using a parallel cohort design. To be certain that intervention groups will be balanced in known and unknown prognostic factors in the long run we will use randomization within group 1 and 2. To rule out human influences we will randomize online for the level of support.

In this study, we combine different study methods within one research to investigate organizational implementation methods and net benefits of eHealth interventions from human, organizational, and technical view. To do so, we created a unique study that enables us to simultaneously investigate clinical effects, as well as effects of different organizational implementation methods whilst controlling for confounding effects on an organizational level. In Figure 2 the combined study design is shown.



Figure 2. Research design for the different groups and interventions of e-Vita COPD

Organizational and technical differences are depicted in Figure 2: three different care groups and two different web portals are included. Two different methods of implementation are distinguished within group 1 and 2: one with high level of personal assistance and one with low level of personal assistance. All patients in group 1 and 2 start with a personal instruction by the primary care nurse during a regular control visit. Patients will be randomly subdivided in two groups by computer by research assistants (randomization is computerized to prevent human influence) with high (a) and low (b) level of support. In group 1a, high level support implies home visits for patients by a research nurse who accompanies the use of the web portal. In group 2a, high level support implies telephone consultation for patients by a research nurse who accompanies use of the web portal. In group 1b and 2b low level support implies that the primary care nurse shows the patient only once how to use the web portal (the usual organizational implementation method in daily practice) without any follow-up instruction. In group 3 the web portal is offered as free use: patients will receive instructions from the web portal itself. There will be no active support from caregivers or research nurses.

The groups differ in organization, area, use of the web portal, and integration of the portal in a COPD disease management program (Figure 3); these characteristics are based on Dutch reports of care groups ^[28]:

- 1 Group 1 will start with COPD disease management simultaneous to implementation of the web portal. The web portal is integrated in the disease management program (integrated use).
- 2 Group 2 is used to working with a COPD disease management program. They will start with the web portal, which is integrated in their own disease management program (integrated use).
- 3 Group 3 is used to working with a COPD disease management program. They will start with the web portal, but the web portal is not integrated in their own disease management program (free use).

	Group 1	Group 2	Group 3
Multidisciplinary care group	-	+	+
Academic care group	-	-	+
Type of practice	Solo	Health Centre	Health Centre
Environment	Countryside	City	City
COPD care program	-	+	+
Use of portal	Integrated	Integrated	Free
Financial coverage of care program	+	+	+
# General practitioners	170	34	27

Figure 3. The different characteristics of Group 1, 2, and 3

As was described above, the implementation of the portal will be studied using a prospective parallel cohort design. The clinical effects of the web portal will be investigated using an interrupted times series (ITS) study design (Figure 4) and measured according to changes in health status with the Clinical COPD Questionnaire (CCQ, see Appendix 1). ITS design includes multiple observations over time that are ‘interrupted’ by interventions. The time intervals between the observations T₁, T₂, T₃, and T₄ are 6 months, to detect the change in CCQ in a trend and slope over the total period. The time intervals between the 3 measurements of each observation T₁, T₂, T₃, and T₄ is 2 weeks, based on the high responsiveness of CCQ ^[29]. The ITS will be performed according to guidelines of the EPOC Cochrane group ^[30]. The aim of an ITS design is to detect confounding trends by performing several measurements at specified time intervals, before and after the intervention. An advantage of an ITS design is that it allows for the statistical investigation of potential biases in the estimate of the effect of the intervention.

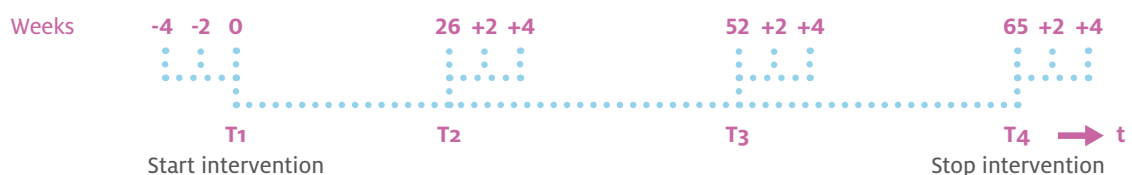


Figure 4. ITS design with CCQ

..... Participants

Three health care groups participate in this study. Therefore, COPD patients of general practices in these care groups are eligible. More specifically, patients are eligible when they are diagnosed with COPD according to GOLD criteria (post-bronchodilator FEV₁/FVC < 0.7) in accordance with the Dutch general practitioners (GPs) COPD Guidelines ^[31] and when they are treated for COPD in primary care. The study is intended to be inclusive rather than exclusive to achieve high external validity (applicability to daily practice). Patients are excluded if they are unable to fill in questionnaires, patients that have no access to internet, patients with terminal illness, immobile patients and patients with severe substance abuse.

..... Recruitment of patients and non-participation analysis

We started by recruiting primary care groups; group 1, group 2, and group 3 decided to participate in this study because they wanted to contribute to a project with a possible healthcare improvement. The general practitioners that are part of the care groups could volunteer to participate in the study; a selection of them did.

Because general practices as well as patients are free to volunteer, bias might occur in our research group. We will determine the differences in clinical status between study participants (included patients) and non-participants (eligible patients) by CCQ questionnaire, as well as gender and age differences.

..... Intervention

In Figure 5 all actions of the intervention are summarized:

- 1 In group 1 all caregivers (GPs as well as practice nurses) will be trained to provide COPD care according to an evidence based disease management program; subsequently they implement the COPD care program in their practices under supervision of a specialized nurse. Practice nurses will receive support by a research nurse to make sure their records of COPD patients are up-to-date and to prepare consultation with their patients according to the disease management program. In addition, all practice nurses will be trained to use the web portal and to communicate with patients according to the principles of self-management.

- 2 In group 2 all caregivers (GPs as well as practice nurses) will be trained shortly to ameliorate their skills in COPD care according to an evidence based disease management program that they already use. All practice nurses will be trained to use the web portal and to communicate with patients according to the principles of self-management. The training is developed and provided for by the e-Vita study group and is based on national and international guidelines.
- 3 In group 3 caregivers will not receive any training. Patients will receive a brochure how to use the web portal.

	fixed use Group 1		fixed use Group 2		free use Group 3	
Development of patient platform	+		+		+	
Training all caregivers in COPD care	+		+		-	
Training nurses to use web portal and self-management	+		+		-	
Make sure patient population is up-to-date	+		+		-	
Implementation COPD care program	+		-		-	
Intake by practice nurse	+		+		-	
Patients start use of portal	+		+		+	
Randomisation of patients	1*		2*			
1*: personal assistance research nurse 2*: assistance by telephone						

Figure 5. Interventions per group

The type of intervention is adopted by the care groups after thorough consideration and discussion. The e-Vita study group determined the type of platform and the level of support.

Next, we will offer patients an online interactive care platform or web portal. The portal provides disease specific education and tips that fit their personal disease management program. In addition, the portal provides tools to report and monitor personal health goals, actions and health-re-

lated quality of life that can be shared with the patients' own practice nurses. The portal in group 1 and 2 has better quality and more advanced possibilities for monitoring health goals with actions than the portal in group 3. The portal will be provided for a period of 15 months. Patients are informed by letter about the web portal. Patients in group 3 who agree to use the portal will receive instructions and log in information by e-mail. Patients in group 1 and 2 who agree to use the portal will be invited by their own practice nurses for intake. During intake the practice nurse defines a personal health goal together with the patient and gives instructions how and why to use the portal. Participants continue to receive regular COPD care by their GP and nurse practitioner according to the disease management program of the care group. Stable COPD patients visit their nurse practitioner yearly to check up on their disease management. The patient portal can be used by care professionals to prepare consultation or to monitor patients in-between their visits to their general practice. Third, a subgroup of participants (1a and 2a) will receive extra support to use the portal by home visits or with instructions by telephone. During the home visit and consultation it will be checked if patients are able to log on the portal, if they understand the possibilities of the portal, and if they have started working on their personal health goal using the portal.

.... Data collection

Data collection consists of self-reporting questionnaires that are integrated in the portal. Therefore, all data collection is provided digitally. In Figure 6 the measurement schedule is visualized. There are four measurements in this study during a period of 16 months. Due to the ITS design, CCQs will be offered three times at each measurement.

T in weeks	Sociodemographic characteristics	CCQ	MRC	EQ-5D	Satisfaction patient	Hospitalisation	Use portal
T1a = -4	X	X					
T1b = -2		X					
T1c = 0		X	X	X			
T2a = 26		X			X		
T2b = 26+2		X					
T2c = 26+4		X	X	X			X
T3a = 52		X					
T3b = 52+2		X					
T3c = 52+4		X	X	X			X
T4a = 65		X					
T4b = 65+2		X					
T4c = 65+4		X	X	X	X	X	X

Figure 6. ITS measurements per interval

Outcome parameters

..... Primary outcome

The primary outcome is clinical and expressed as health status, measured using the CCQ. The CCQ was originally designed by Van der Molen and consists 10 items with a 7-point Likert scale. The CCQ comprises 3 domains; symptom state (4 items), functional state (4 items) and mental state (2 items). Research showed that the CCQ is a reliable and valid questionnaire with Cronbach's alpha between 0.89 and 0.91 ^[29].

..... Secondary outcomes

From the human perspective, we will measure the following outcomes:

Disability associated with breathlessness: this is measured using the Medical Research Council (MRC) breathlessness scale (see Appendix 2), which comprises five statements that describe almost the entire range of respiratory disability: from none (Grade 1) to almost complete incapacity (Grade 5). It can predict survival ^[32] and it is advocated as complementary to FEV₁ in describing disability in those with COPD ^[33].

Quality of life (QoL): QoL will be assessed using EuroQol-5D (EQ-5D). This questionnaire contains 5 items with a 3-point Likert scale. A higher score reflects higher quality of life. The EQ-5D comprises 5 levels: mobility, self-care, daily activity, pain/discomfort and anxiety/depression. Research showed that the EQ-5D is a reliable and valid questionnaire ^[34]. The EQ-5D can be used to compute QALY's, which are necessary to evaluate cost-effectiveness.

Adoption of the portal: usage of the portal is monitored continuously by log files. User satisfaction is measured by purpose-designed questionnaires.

From the organizational perspective, we will measure the following outcome:

Costs: in this study, we include direct costs of the intervention and COPD care. Intervention costs include development costs of the patient platform and costs of the implementation process. Development costs are provided retrospectively by the owner of the portal. Implementation costs are administered by the research group and mainly include costs of home visits and interviews by telephone. The cost for COPD care (time of professional care) is extracted from the portal in which consultation in general practice will be registered in an agenda. In addition, hospitalization (caused by COPD exacerbation) will be based on reports of the patient and practice nurse in the portal. All costs are based on regular tariffs in Dutch healthcare.

..... Determinants

Self-efficacy: self-efficacy is measured using the General Self-Efficacy Scale (GSES), which will be displayed at baseline. This 10-item questionnaire was designed in 1981 by Schwarzer ^[35]. The items are scored on a four-point scale, in which a higher score reflects higher self-efficacy. Research in 28 countries showed that Cronbach's alpha varies between .76 and .90, of which mostly above .80. Self-efficacy is derived from the Social Cognitive Theory, which states that behavioral change is made possible by personal sense of control. Self-efficacy is the "belief in one's capabilities to organize and execute the courses of action required to produce given attainments". Research shows that self-efficacy is an important factor for self-management in behavioral change of the chronic ill, such as diabetics and cardiovascular patients. For example, in people with type 2 diabetes self-efficacy is an important factor influencing self-management behaviors; self-efficacy impacts adherence to treatment ^[36]. Sociodemographic characteristics: these are assessed by a purpose-designed online questionnaire. We include the following characteristics: age, socioeconomic status, marital status, and general use of online and digital products and services. Since decreased access to internet and decreased general health outcomes have been associated with lower socioeconomic status, minority racial/ethnic groups, older age, and poorer health we will include these characteristics in our study.

..... Power calculation

Health status of patients with COPD generally decreases over time. Recent research on disease management programs in COPD in primary care shows that a general increase of 1.5 to 2.0 points (SD 0.75) in CCQ can be expected during a 1 year period ^[37]. In our study, we offer patients a web portal in addition to their regular disease management program. We therefore expect that the regular deterioration in CCQ (from 1.5 to 2.0 points) will change to stabilization of health status at 1.5 CCQ points. Hence, we expect a significant difference in health status of 0.5 points in patients using the portal ($2.0 - 1.5 = 0.5$ points). To measure significant differences in health status (>0.5 CCQ points) at 80 % power, SD 0.75 and $\alpha = 0.05$, 37 patients must be included. Based on an estimated 20 % drop-out during the study, 45 ($37/0.80$) patients are needed. As we use two different organizational implementation methods within two of the care groups $2 \times 45 = 90$ patients must be included in those settings. In the third care group only one organizational implementation method (free use) is used. Hence, a total of 225 ($90 + 90 + 45$) patients are necessary to achieve sufficient statistical power.

..... Data analysis

Along with our research design, analyses will be multilevel:

- 1 To investigate the effect of the use of the web portal on the primary clinical outcomes, the ITS data will be analyzed. The preferred method to analyze ITS studies is a statistical comparison of time trends before and after the intervention. Time series analysis using ARIMA models is one way of analyzing the data, but there are several statistical techniques that can be used depending on the characteristics of the data, the number of data points available and whether autocorrelation is present. The final choice for the method to analyze the data will be made when the total set of data is available after consultation of a statistician.
- 2 To investigate the effects of organizational aspects uptake of the portal will be analyzed for care group 1, 2 and 3 using Chi Square tests (Fishers' Exact Test for categorical variables and F-tests for continuous variables) and (repeated measures) ANOVA analyzes. To analyze the effects of organizational aspects as described in the paper, the groups will be compared.
- 3 To investigate the effect of integration of the web portal in daily practice, outcomes within integrated (group 1 and 2) and the free use groups (group 3) will be analyzed using Chi Square tests (Fishers' Exact Test for categorical variables and F-tests for continuous variables) and (repeated measures) ANOVA analyzes.
- 4 To investigate the effect of different organizational implementation methods, outcomes within groups with high level support (1a and 2a) and low level support (1b, 2b and 3) will be analyzed using Chi Square tests (Fishers' Exact Test for categorical variables and F-tests for continuous variables) and (repeated measures) ANOVA analyzes.
- 5 To explore correlation between self-efficacy, sociodemographic characteristics on the one hand and adoption of the portal and clinical outcomes on the other hand, Pearson product-moment coefficients will be calculated across all research groups.
- 6 To make a cost-effectiveness analysis, the direct costs of the different organizational implementation methods will be defined and analyzed parallel to the effects of the portal in terms of Quality of Life (EQ-5D).

..... **Ethical principles**

Participation in the study provides several benefits: increasing costs and deficit of health care professionals stress the need for efficient health care processes. Benefits of eHealth regarding clinical effects and costs have repeatedly been demonstrated, but extensive integration in clinical practice stays behind. This project aims to explore organizational implementation methods for optimal integration of patient portals in primary care. Optimal integration stimulates patients in self-management and improves efficiency and accuracy administration and communication. We expect patients to improve their health status while decreasing health care use. Health care providers participating in these projects improve communication between different workers, adherence to guidelines, and thereby increase quality of care. The online portals will not be offered to patients who are unable to use the online portals. However, they will not be in disadvantage by receiving usual care.

Discussion

COPD is one of the main causes of morbidity and mortality in the world. Worldwide nearly 3 million people die from COPD every year ^[1]. COPD is a highly complex disease to manage as patients show great variation in symptoms and limitations in daily life. An important treatment of COPD is empowerment of patients: self-management may reduce hospital admission and significantly improves health status ^[38]; it can diminish the impact of exacerbations on health status and tends to accelerate recovery ^[39, 40]. eHealth tools for COPD patients have potential to raise self-management to higher levels. Patients' attitudes and receptiveness towards eHealth applications are promising ^[20] but lack of robust trials and inconclusive research results ^[17, 18, 19, 20] make it impossible to draw firm conclusions about clinical effectiveness or cost effectiveness.

In this study, we aim to empower COPD patients in primary care by providing a self-management web portal. We expect this portal to help patients to better recognize and self-manage exacerbations in an early phase, thereby increasing health status and diminishing exacerbation and hospitalisation. In addition, we aim to provide practical insights into a successful implementation of patient portals in real-life primary care settings. We will therefore compare different organizational implementation methods. We expect that an implementation setup with greater personal support will result in increased use of the online program.

This e-Vita study has several strengths. To our knowledge this is the first study to combine different study designs that enable simultaneous investigation of clinical effects, as well as effects of different organizational implementation methods whilst controlling for confounding effects of the organizational characteristics. Our hypothesis is that in well-organised primary care groups with highly skilled and motivated nurses and doctors there will be a higher use of the portal and therefore better health status. Secondly, our web portal is integrated in real life care settings and will therefore provide practical insights and knowledge of eHealth in daily practice. Third, this study adds Dutch evidence to the existing body of knowledge which is important because local political and financial factors have a major impact on successful integration in daily practice ^[41]. This study also includes several limitations: from a technical perspective, the development of the web portal is a difficult task due to lack of broad experience in the field. The technique of the web portal and decisions made during the design phase will largely affect our outcomes but are beyond the scope and influence of our study. From a human perspective, effects

through self-management imply behavioral changes. Behavioral changes require time, whereas the study period is limited to 15 months. Furthermore, patients in a primary care setting have a low burden of disease. From an organizational perspective, other projects in the primary care cooperation's can influence the speed and thoroughness of the implementation of our web portal.

..... Appendix 1

Table 1 CCQ

Please circle the number of the response that best describes how you have been feeling during the past week. (Only one response for each question)

	Never	Hardly	A few	Several times	Many times	Most of the time	All the time
1 Short of breath at rest?	0	1	2	3	4	5	6
2 Short of breath doing physical activities?	0	1	2	3	4	5	6
3 Concerned about your breathing getting worse?	0	1	2	3	4	5	6
4 Depressed (down) because of your breathing problems?	0	1	2	3	4	5	6
During the past week, how much of the time did you...							
5 Cough	0	1	2	3	4	5	6
6 Produce phlegm?	0	1	2	3	4	5	6
During the past week, how limited were you in activities because of your breathing problems when doing...							
	Not limited at all	Very slightly limited	Slightly limited	Moderately limited	Very limited	Extremely limited	Totally limited or unable to do
7 Strenuous physical activities (such as climbing stairs, hurrying, doing sports)?	0	1	2	3	4	5	6
8 Moderate physical activities (such as walking, housework, carrying things)?	0	1	2	3	4	5	6
9 Daily activities at home (such as dressing, washing yourself)?	0	1	2	3	4	5	6
10 Social activities (such as talking, being with children, visiting friends/relatives)?	0	1	2	3	4	5	6

..... **Appendix 2**

Table 2 MMRC

Do you ever experience breathlessness? Which of the following statement applies most to you?		Grade
<input type="radio"/>	I do not experience breathlessness	0
<input type="radio"/>	I am only troubled by breathlessness during strenuous exercise	1
<input type="radio"/>	I am only short of breath when hurrying on the level or walking up a slight hill	2
<input type="radio"/>	My breathlessness makes me walk slower on the level than most people my age, or results in the need to stop for breath after walking at my own pace after 15 min.	3
<input type="radio"/>	I need to stop for breath for a few minutes after walking 100 meter on the level	4
<input type="radio"/>	I am too breathless to leave the house, or need to catch my breath when undressing	5

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Abbreviations

- **ANOVA:** Analysis of variance
- **CCQ:** Clinical COPD questionnaire
- **COPD:** Chronic obstructive pulmonary disease
- **EQ-5D:** EuroQoL five dimensions questionnaire
- **FEV:** Forced expiratory volume
- **FVC:** Forced vital capacity
- **GOLD:** Global initiative for chronic obstructive lung disease
- **GP:** General practitioner
- **GSES:** General self-efficacy scale
- **ITS:** Interrupted times series
- **MRC:** Medical Research Council
- **QALY:** Quality-adjusted life year
- **QoL:** Quality of life
- **SD:** Standard deviation
- **WMO:** Wet Medisch-wetenschappelijk Onderzoek met mensen (Medical Research Involving Human Subjects Act)

Chapter 4

Self-management of COPD with web-based platforms

High level of integration in integrated disease management leads to higher usage in the e-Vita study

Esther P. W. A. Talboom-Kamp | Noortje A. Verdijk | Marise J. Kasteleyn |
Lara M. Harmans | Irvin J. S. H. Talboom | Mattijs E. Numans | Niels H. Chavannes

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Abstract

..... Background

Worldwide, nearly 3 million people die of chronic obstructive pulmonary disease (COPD) every year. Integrated disease management (IDM) improves disease-specific quality of life and exercise capacity for people with COPD, but can also reduce hospital admissions and hospital days. Self-management of COPD through eHealth interventions has shown to be an effective method to improve the quality and efficiency of IDM in several settings, but it remains unknown which factors influence usage of eHealth and change in behavior of patients.

..... Objective

Our study, e-Vita COPD, compares different levels of integration of Web-based self-management platforms in IDM in three primary care settings. The main aim of this study is to analyze the factors that successfully promote the use of a self-management platform for COPD patients.

..... Methods

The e-Vita COPD study compares three different approaches to incorporating eHealth via Web-based self-management platforms into IDM of COPD using a parallel cohort design. Three groups integrated the platforms to different levels. In groups 1 (high integration) and 2 (medium integration), randomization was performed to two levels of personal assistance for patients (high and low assistance); in group 3 there was no integration into disease management (none integration). Every visit to the e-Vita and Zorgdraad COPD web platforms was tracked objectively by collecting log data (sessions and services). At the first log-in, patients completed a baseline questionnaire. Baseline characteristics were automatically extracted from the log files including age, gender, education level, scores on the Clinical COPD Questionnaire (CCQ), dyspnea scale (MRC), and quality of life questionnaire (EQ-5D). To predict the use of the platforms, multiple linear regression analyses for the different independent variables were performed: integration in IDM (high, medium, none), personal assistance for the participants (high vs low), educational level, and self-efficacy level (General Self-Efficacy Scale (GSES)). All analyses were adjusted for age and gender.

..... Results

Of the 702 invited COPD patients, 215 (30.6%) registered to a platform. Of the 82 patients in group 1 (high integration IDM), 36 were in group 1A (personal assistance) and 46 in group 1B (low assistance). Of the 96 patients in group 2 (medium integration IDM), 44 were in group 2A (telephone assistance) and 52 in group 2B (low assistance). A total of 37 patients participated in group 3 (no integration IDM). In all, 107 users (49.8%) visited the platform at least once in the 15-month period. The mean number of sessions differed between the three groups (group 1: mean 10.5, SD 1.3; group 2: mean 8.8, SD 1.4; group 3: mean 3.7, SD 1.8; $P=.01$). The mean number of sessions differed between the high-assistance and low-assistance groups in groups 1 and 2 (high: mean 11.8, SD 1.3; low: mean 6.7, SD 1.4; $F_{1,80}=6.55$, $P=.01$). High-assistance participants used more services (mean 45.4, SD 6.2) than low-assistance participants (mean 21.2, SD 6.8; $F_{1,80}=6.82$, $P=.01$). No association was found between educational level and usage and between General Self-Efficacy Scale and usage.

..... Conclusions

Use of a self-management platform is higher when participants receive adequate personal assistance about how to use the platform. Blended care, where digital health and usual care are integrated, will likely lead to increased use of the online program. Future research should provide additional insights into the preferences of different patient groups.

Introduction

Chronic obstructive pulmonary disease (COPD) is a slowly progressive lung disease and one of the main causes of morbidity and mortality in high-, middle-, and low-income countries ^[1]. Worldwide, nearly 3 million people die of COPD every year; in 2012, this was equal to approximately 6% of all deaths globally ^[2,3].

According to current COPD guidelines, symptoms and airflow obstruction should be monitored regularly to guide modification of treatment and for early identification of complications ^[4,5]. Routine monitoring should contribute to achieving management goals in COPD (ie, to delay disease progression and alleviate its manifestations). The most important primary care objective should be to improve quality of life (QoL) ^[6].

In the past decade, integrated disease management (IDM) was introduced as a means of improving quality of care. An IDM program for COPD consists of different components of care in which various health care providers cooperate on education, exercise, behavioral therapy, smoking cessation, medication, nutrition advice, and follow-up. The responsibility for the program lies largely with the health care professional, with a modest role for the patient. For people with COPD, IDM not only improves disease-specific QoL and exercise capacity, but it can also reduce hospital admissions and hospital days per person ^[7].

..... Self-Management of Chronic Obstructive Pulmonary Disease

Self-management of COPD has been introduced as an effective method to improve the quality and efficiency of IDM, and to reduce health care costs ^[8,9,10]. Interventions to support self-management have shown reductions in hospital admissions and fewer sick days as a result of exacerbations ^[11] ^[12]. The core components of self-management include education, eliciting personalized goals, psychological coping strategies, formulating strategies to support adherence to treatment, and behavioral change, together with practical and social support ^[13,14]. Chronically ill patients who have experience with person-centered, high-quality chronic illness care that focuses on patient activation, decision support, goal setting, problem solving, and coordination of care are better self-managers ^[15]. Self-efficacy explores the emotional functioning and coping skills of an individual and is thought to be a strong predictor of health behavior of COPD patients; the General Self-Efficacy Scale (GSES) tool is a reliable and sensitive measure of self-efficacy for patients with COPD ^[16].

..... eHealth Interventions

Generally, eHealth interventions are effective in stimulating self-management because they allow patients to better cope with their illness at the time/place of their choosing, enabling them to adapt their lifestyle to their condition, while reducing medical staff consultations ^[17]. The deployment of eHealth apps facilitates accessibility to health care, which enhances patients' understanding of their disease, their sense of control, and willingness to engage in self-management ^[18,19]. Although patients' attitudes and receptiveness toward eHealth apps are promising in persons of a certain age and education level ^[20,21,22], large-scale adoption of self-management and eHealth in daily practice lags behind expectations ^[23].

Previous eHealth studies have revealed the challenges, barriers, and factors that make successful implementation difficult, yet many questions remain unanswered. Moreover, a major challenge of eHealth in care coordination is to make it beneficial and easy to use for health care providers and patients, otherwise neither will use it ^[24]. Also, online self-management support needs to be a fully integrated element of IDM. For example, in a Dutch study on adherence to an online self-management app for patients with COPD or asthma, patients tended to use the online application on a regular basis when the health care provider was involved, whereas patients without assistance used the app only sporadically ^[25]. For barriers related to clinicians, the eHealth evidence base needs strengthening, whereas for primary care practices a learning process (including staff training) needs to be instituted ^[26]. In addition, it is necessary to more adequately inform patients about the possibilities and consequences of eHealth ^[27]. Furthermore, poor user-friendliness of Web-based apps and the lack of "push" factors (eg, automated reminders or messages from health care professionals) are a common cause of low usage or decline in usage of Web-based apps ^[28]. In any eHealth study, a substantial proportion of users drop out before completion, or stop using the app; thus, attrition is a common problem and should be analyzed to provide data for real-life adoption problems ^[29]. Studies on the use of online self-management show that attrition tends to start when users "get lost" in the intervention ^[28-30].

Preconditions for starting eHealth are (1) it must be well organized within usual care (organizational perspective), (2) it should be beneficial and easy to use for patients (human perspective), and (3) the apps have to be technically sound (technical perspective).

..... Design of e-Vita COPD

Because low usage of eHealth is an ongoing problem, we designed a multilevel study to investigate the implementation of a self-management web platform to support patients with COPD in primary care ^[31]. Because the web platform provides continuous education and contact with health care professionals, it is expected to help patients better recognize and self-manage exacerbations in an early phase, thereby helping to stabilize their health status.

This study, called “e-Vita COPD,” compares three different approaches to incorporating eHealth via Web-based self-management platforms into the integrated disease management of COPD using a parallel cohort design. Also, participants are randomly allocated in two of the cohorts (1 and 2), using the same platform to different levels of personal assistance. All three cohorts incorporated the platforms to different levels; the two levels of personal assistance for patients were a group with high assistance and a group with low assistance. The main aim is to analyze the factors that successfully promote the use of a self-management web platform for patients with COPD.

From an organizational perspective, our hypothesis is that a self-management web platform will be better adopted if the platform is an integrated part of IDM, with trained health care professionals who encourage patients to use the platform. From a human perspective, our hypothesis is that a self-management platform will be better adopted by patients if they receive sufficient personal assistance in how to use the platform, and will be better adopted by patients with a higher level of self-efficacy (assessed by GSES) and a higher educational level. From a technical perspective, our hypothesis is that a self-management web portal will be better adopted if the platform is easy to use and has practical content.

Methods

..... Study Design

For this study, we used the CONSORT-eHEALTH checklist that describes how the intervention should be reported ^[32].

We designed a quality improvement intervention and chose an implementation study ^[33]. We designed a method to promote the uptake of our research findings into routine primary health care; with this design, we aimed at studying the influences on health care professionals and patient behavior and at evaluating the process by which these effects are achieved.

This research combined different study methods to investigate organizational implementation methods and the net benefits of eHealth interventions from a human, organizational, and technical viewpoint. Full methodological details were reported previously ^[31]. Figure 1 presents an overview of the combined study design with organizational and technical differences.



Figure 1. Design of the e-Vita COPD Study. High, medium, and none refer to the level of integration of the web platform into the patient's integrated disease management program. A: high assistance; B: low assistance.

Included in the study were three different care groups (groups 1-3) and two web portals. In group 1, the online e-Vita platform was offered as a highly-integrated part of the COPD IDM with a tailor-made intensive course program on COPD and eHealth for health care providers and patients. Group 2 had a medium level of integration with a standard basic course program for health care providers and patients. The COPD patients in groups 1 and 2 who agreed to use the platform were invited by practice nurses for intake in which they defined a personal health goal together and discussed how and why to use the platform. In group 3, the online platform was offered without integration into disease management; health care providers and patients received instructions from the web platform itself and received no training on COPD care.

Therefore, group 1 (high) had a high level of integration of the web platform into their IDM program, group 2 (medium) had a medium level of integration into their IDM program, and group 3 (none) had no integration.

Two different levels of assistance for patients were distinguished within group 1 (high) and 2 (medium): one with a high level of personal assistance and one with a low level of personal assistance. Patients in groups 1 and 2 were randomly subdivided into two groups with high and low levels of support. Randomization was carried out stratified on the care group (1:1) by computer. In group 1 (high integration-high assistance), a high level of support consisted of two home visits to patients by a research nurse who assisted in the use of the web portal. In group 2 (medium integration-high assistance), a high level of support consisted of telephone consultation between the patient and a research nurse who explained use of the web portal. In the low-assistance groups of groups 1 and 2, low-level support consisted of a primary care nurse showing the patient only one time how to use the web platform, without any follow-up instruction. Patients in group 3 that used the online self-management platform (called “Zorgdraad”) had no active support from health care professionals or research nurses. Both platforms were provided for the intervention period of 15 months.

..... Participants

Three health care groups participated in this study. Patients were eligible if they were diagnosed with COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (postbronchodilator forced expiratory volume in first second/forced vital capacity <0.7) in accordance with the COPD Guidelines of Dutch general practitioners (GPs) [34] and they were being treated for COPD in primary care. The study aimed to be

inclusive rather than exclusive, to achieve high external validity (applicability to daily practice). Patients were excluded if they were unable to fill in questionnaires, had no access to the Internet, had a terminal illness, were immobile, or were severe substance abusers.

..... Recruitment of Patients and Nonparticipation Analysis

We started by recruiting the primary care groups (groups 1-3). Healthcare professionals decided to participate in this study mainly because they wanted to join a project that offered possible health care improvement. In group 1, this was 19 of 170 GPs (11%); in group 2, 29 of 34 GPs (84%); and in group 3, all 27 GPs (100%).

Patients were invited to participate by letter. When they refused to participate, we defined them as nonparticipants. When participants in the e-Vita study logged in and used the web platform at least once, we defined them as “users.” Patients were defined as “lost to follow-up” if they did not log on to the platform after signing informed consent and if they did not complete the whole intervention period.

..... Intervention

The interventions in the three groups consisted of a self-management program including different levels of education for health care professionals, different levels of integration in the COPD care program, and different levels of personal assistance for patients. We used two Web-based platforms (e-Vita in groups 1 and 2, Zorgdraad in group 3) that were very similar, with the same basic features and functionalities. The education, the care programs, and the platforms were specifically designed for COPD patients; their needs and wishes were processed.

The online self-management platform e-Vita is an initiative of the Dutch foundation “Care Within Reach” [35]. The content was created by experts guided by interviews with COPD patients about their thoughts/feelings related to living with COPD and its treatment; the experiences of health care professionals related to the treatment of patients with COPD were also integrated. The main content of the platform consists of insight into personal health data, self-monitoring of health values, education, and a coach for attaining personal goals. The first release of the platform was in January 2014 with an update in May 2015 (which was during the intervention period).

All patients in groups 1 and 2 that used the e-Vita platform had access to a telephonic and digital helpdesk to address any problems. Patients in groups

1 and 2 that used e-Vita received automated online reminders via email from our research team for the self-reported questionnaires and messages. Patients in group 3 used the online self-management platform Zorgdraad (an initiative of the Dutch foundation Zorgdraad and the diagnostic center Saltro). The content was created by experts guided by their experience in treating patients with COPD. The main content of the platform is basic and consists of insight into personal health data, self-monitoring of health values, and education. All patients that used Zorgdraad received automated online reminders via email for the self-reported questionnaires.

..... **System and Services**

When logging on (username plus password) for the first time to e-Vita or Zorgdraad, every user saw a pop-up with a brief explanation about e-Vita or Zorgdraad and the services that could be found on the website. After the pop-up, the user was directed to the home page. From there, users could access all functionalities of the platform. The log-on procedure of both platforms is based on Dutch security legislation and guidelines (the Dutch Personal Data Protection Act).

The e-Vita platform (Multimedia Appendices 1 and 2) consisted of the following set of interrelated services, which could be accessed via the home page:

- An online coach for guidance when working on personal goals and planning of the personal actions.
- Self-monitoring personal health values and self-reported questionnaires, in which users could register the values they measured for the disease-specific health status Clinical COPD Questionnaire (CCQ) ^[36], the modified Medical Research Council scale (MRC scale) for dyspnea ^[37], the General Self-Efficacy Scale ^[38], sociodemographic characteristics, and EuroQol five-dimensions questionnaire on quality of life (EQ-5D) ^[39].
- An education module with text and movies about COPD.
- Extra information about COPD.
- Information about the team of health care professionals
- A module to send and receive messages to the health care professionals.

The Zorgdraad platform (Multimedia Appendix 3) has basic usability and content, with the following set of interrelated services:

- Self-monitoring personal health values and self-reported questionnaires, where users can register the same values as in the e-Vita platform.

- A basic education module with text and movies about COPD.
- Information about the team of health care professionals.
- A module to send and receive messages to the health care professionals.

..... Outcome Measures

Full details on outcome measures were reported previously ^[31]. The primary outcome of this study was the usage of the online self-management platform: we defined usage as every visit to e-Vita and Zorgdraad that was tracked objectively by collecting log data in log files. We focused on the log data in the intervention period of 15 months. The usage was divided into sessions and services; a session was defined as the total period between logging in and logging out of the system and a service was defined as a focused action within the system, as described for both platforms previously. For every action in e-Vita and Zorgdraad (button clicks, page views, and database transactions), the following information was collected by the web server and added to a log file: (1) the users' identification number, (2) time and day of the session, (3) the type of actions (services) taken, and (4) optional additional information about the actions (services). For these analyses, it was important to investigate not only the amount of use, but also the user's patterns.

Baseline characteristics were extracted from the log files of e-Vita and Zorgdraad, including age, gender, education level, and scores on the CCQ (range 0=very good health status to 6=extremely poor health status), MRC scale (range 1-5), EQ-5D, and GSES.

Data were collected that could plausibly be related to the study outcomes. In the analyses, the organizations of GPs (care groups PreventZorg, Zorg op Noord, and Leidsche Rijn Julius Gezondheidscentra), integration in IDM (integrated vs not integrated), and personal assistance for the participants (personal assistance vs no assistance) were used as determinants. Education was self-reported using eight response categories and converted into three levels based on the International Standard Classification of Education (ISCED): high (bachelor, master, doctor), medium (secondary and tertiary education), and low (no formal education, primary education) ^[40]. Self-efficacy was measured with the General Self-Efficacy Scale in a self-reported 10-item questionnaire. Total scores ranged from 0 to 10.

An attrition curve was drawn with the nonusage attrition; the percentage of users who used the platforms were plotted over time.

..... Statistical Methods

For the nonparticipation analysis, differences in age and gender between participants and nonparticipants were compared using a chi-square test and a Mann-Whitney U test after normality tests.

Categorical baseline characteristics were reported as numbers and percentages, normally distributed continuous variables as means with standard deviations (SD), and nonnormally distributed variables as medians with interquartile ranges (IQRs). Characteristics between the three groups were explored using chi-square tests and Kruskal-Wallis tests.

To predict the use of the e-Vita and Zorgdraad platforms, multiple linear regression analyses (mean number of sessions/services/mean session time/mean number of services per session) for the different independent variables were performed:

- Integration in integrated disease management including training by health care professionals by comparing groups 1 (high), 2 (medium), and 3 (none);
- Personal assistance given to patients by comparing the high-assistance groups of groups 1 (high) and 2 (medium) versus the low-assistance groups of groups 1 (high) and 2 (medium);
- Patients' scores on the GSES; and
- Patients' educational levels.

We analyzed the main effects because, theoretically, we presumed no interaction between factors. All analyses were adjusted for age and gender.

Attrition was measured by logging and evaluating the percentage of users that used one of the platforms every month during the intervention period plus three months. The area under the curve was calculated for a period of 18 months; after this period, usage dropped to zero for two groups. We used a calculating program to measure the area under the curve using definite integrals. All analyses were performed with SPSS version 22.0 (IBM Corporation, Armonk, NY, USA).

..... Results

In total, 942 diagnosed COPD patients from the medical files of the three care groups were selected to be eligible for the study (Figure 2). The GPs of these care groups excluded 240 COPD patients from participation due to (1) other diseases, (2) treatment in hospital, and (3) probably incompetent to participate in the program. In the end, 702 COPD patients were invited to start with the e-Vita platform; of these, 215 (30.6%) agreed to register

and provided informed consent. Reasons for declining to participate are presented in Figure 2.



Figure 2. Flowchart of inclusion of participants in the e-Vita COPD study. High, medium, and none refer to the level of integration of the web platform into the patient's integrated disease management program. A: high assistance; B: low assistance.

Of the 215 COPD patients included at baseline, 82 were in group 1 (high), 96 in group 2 (medium), and 37 in group 3 (none).

After randomization, 36 patients in group 1 were allocated to high-assistance group, 46 to low-assistance group; in group 2 44 patients were randomized to high-assistance group, and 52 to low-assistance group.

The total number of patients lost to follow-up was 132. Figure 2 shows the reasons for drop out in groups 1 and 2; patients in group 3 were not asked for their reasons. Of the 215 participants, 107 (49.8%) patients were identified as platform users: 43 in group 1, 42 in group 2, and 22 users in group 3 (Figure 3).

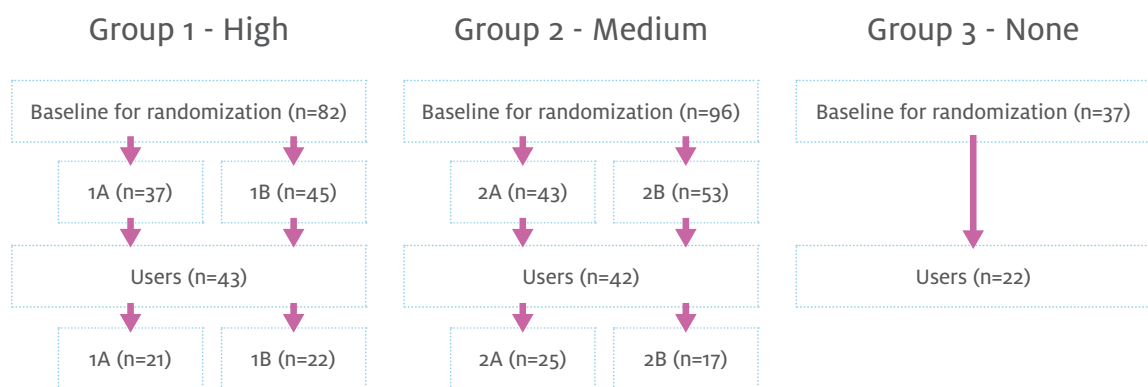


Figure 3. Flowchart of the platform users of the e-Vita COPD study. High, medium, and none refer to the level of integration of the web platform into the patient's integrated disease management program. A: high assistance; B: low assistance.

..... Nonparticipation Analysis

The age and gender of participants and nonparticipants are presented in Table 1. Participants and nonparticipants did not differ regarding gender (52.1%, 112/215 male vs 46.2%, 336/727 male, $P=.13$) or age (median 66.6, IQR 61.4-74.7 vs median 68.5, IQR 61.2-77.9 years, $P=.20$). Because only a few nonparticipants filled in a questionnaire on CCQ, the mean CCQ could not be determined for nonparticipants.

	Group 1 - High	Group 2 - Medium	Group 3 - None	Total
Non-participants				
N	209	383	135	727
Median age in years [IQR]	69.3 [61.1-77.5]	69.8 [61.6-78.5]	66.3 [60.3-74.4]	68.5 [61.2-77.9]
Males N (%)	108 (51.7)	167 (43.6)	61 (46.2)	336 (46.2)
Included patients (= baseline for randomization)				
N	82	96	37	215
Median age in years [IQR]	66.3 [61.1-75.7]	67.3 [62.6-76.6]	64.1 [61.5-69.2]	66.6 [61.4-74.7]
Males N (%)	51 (62.2)	41 (42.7)	20 (54.1)	112 (52.1)

Table 1. Characteristics and comparison of participants and nonparticipants of the e-Vita study.

..... Baseline Characteristics of Patients

Table 2 presents the baseline demographic and clinical characteristics of the included COPD population (median age 66.6 years; 52.1% was male). These patients had mildly symptomatic COPD which is reflected by a median MRC scale of 1.0 and a median CCQ of 1.2. Of all participants, 89 of 215 (41.4%) filled in the online questionnaire for education level; most participants had a middle education level (42.7%). The median General Self-Efficacy Scale was 3.3 and the median EQ-5D 0.86. The characteristics age ($X^2_2=5.4$, $P=.07$), education level ($X^2_4=2.2$, $P=.70$), General Self-Efficacy Scale ($X^2_2=1.74$, $P=.42$), and EQ-5D ($X^2_2=2.4$, $P=.28$) were similar in the three groups. There was a difference in the characteristics gender ($X^2_2=6.8$, $P=.03$), with more male patients in group 1; and a difference in CCQ ($X^2_2=6.5$, $P=.04$) and MRC scale ($X^2_2=11.3$, $P=.003$) with a higher CCQ and MRC scale in group 2.

	Group 1 - High		Group 2 - Medium		Group 3 - None	Total
	High	Low	High	Low		
N	36	46	44	52	37	215
Median age in years [IQR]	66.3 [61.0-79.2]	65.6 [61.3-73.4]	68.7 [64.0-78.3]	66.8 [60.3-75.1]	64.1 [61.5-69.2]	66.6 [61.4-74.7]
Males N (%)	19 (52.8)	32 (69.6)	17 (38.6)	24 (46.2)	20 (54.1)	112 (52.1)
Education level N questionnaires	14	21	22	19	13	89
Low N (%)	4 (28.6)	8 (38.1)	5 (22.7)	8 (42.1)	7 (53.8)	32 (36.0)
Medium N (%)	7 (50.0)	8 (38.1)	11 (50.0)	8 (42.1)	4 (30.8)	38 (42.7)
High N (%)	3 (21.4)	5 (23.8)	6 (27.3)	3 (15.8)	2 (15.8)	19 (21.3)
CCQ* [IQR]	1.0 [0.6-1.9]	1.2 [0.8-1.6]	1.3 [0.9-2.1]	1.4 [1.1-2.1]	1.3 [0.6-1.8]	1.2 [0.8-1.9]
MRC* [IQR]	1.0 [1.0-3.0]	1.0 [1.0-2.0]	2.0 [1.0-3.0]	2.0 [1.0-2.0]	1.0 [1.0-1.0]	1.0 [1.0-2.0]
GSES* [IQR]	3.4 [3.1-3.7]	3.3 [3.0-3.8]	3.3 [2.8-3.5]	3.3 [3.1-3.7]	3.4 [3.3-3.7]	3.3 [3.0-3.7]
EQ-5D* [IQR]	0.85 [0.7-1.0]	0.89 [0.81-1.0]	0.85 [0.72-1.0]	0.84 [0.71-1.0]	0.9 [0.84-1.0]	0.86 [0.78-1.0]

Table 2. Baseline demographic and clinical characteristics of the patients with COPD included in the e-Vita study.

..... Use of the Online e-Vita and Zorgdraad Platforms

Table 3 presents the 15-month usage pattern by patients using the log files of e-Vita and Zorgdraad. In total, 107 users visited the platform at least once in the 15-month period. The helpdesk received 101 calls; most questions concerned problems with the log-on procedure.

	Group 1 - High	Group 2 - Medium	Group 3 - None	Total	P	F _{2,100}
N	43	42	22	107		
Mean (SD) number of sessions	10.5 (1.3)	8.8 (1.4)	3.7 (1.8)	8.2 (8.7)	0.011	4.68
Mean (SD) session time (minutes)	3.5 (0.7)	4.8 (0.7)	6.7 (0.9)	4.8 (4.3)	0.025	3.83
Mean (SD) number of services total per user	45.2 (6.1)	27.9 (6.2)	6.7 (8.3)	(4.3) 28.8	0.001	7.18
Mean (SD) number of services per session total per user	3.9 (0.4)	4.1 (0.4)	2.1 (0.6)	3.6 (2.8)	0.022	3.97

Table 3. Usage patterns for groups 1, 2, and 3.

In the 15-month intervention period, the total number of sessions for the e-Vita platform was 830 (9.8 per user) and for the Zorgdraad platform 78 (3.7 per user). The mean number of sessions differed between the three groups ((group 1: mean 10.5, SD 1.3; group 2: mean 8.8, SD 1.4; group 3: mean 3.7, SD 1.8; $P=.01$) (Table 3). In groups 2 and 3, the mean session time was higher than in group 1; the difference between the three groups was significant ($P=.03$). In groups 1 and 2, the mean number of services in total was higher than in group 3 (group 1: mean 45.2, SD 6.1; group 2: mean 27.9, SD 6.2; group 3: mean 6.7, SD 8.3; $P=.001$) and the number of services per session in groups 1 and 2 was higher than in group 3 (group 1: mean 3.9, SD 0.4; group 2: mean 4.1, SD 0.4; group 3: mean 2.1, SD 0.6; $P=.02$).

Figure 4 shows use of the e-Vita for the two groups with high and low assistance; higher usage of the platform was related to a higher level of personal assistance.

The mean number of sessions differed between the high-assistance groups and the low-assistance groups in groups 1 and 2 (high assistance: mean 11.8, SD 1.3; low assistance: mean 6.7, SD 1.4; $F_{1,80}=6.55$, $P=.01$). Participants

in the high-assistance groups used more services (mean 45.4, SD 6.2) than participants in the low-assistance groups (mean 21.2, SD 6.8; $F_{1,80}=6.82$, $P=.01$). In the high-assistance groups, the mean number of services per session did not differ from the low-assistance groups (mean 4.1, SD 0.4 vs mean 3.8, SD 0.5; $F_{1,80}=0.36$, $P=.55$).

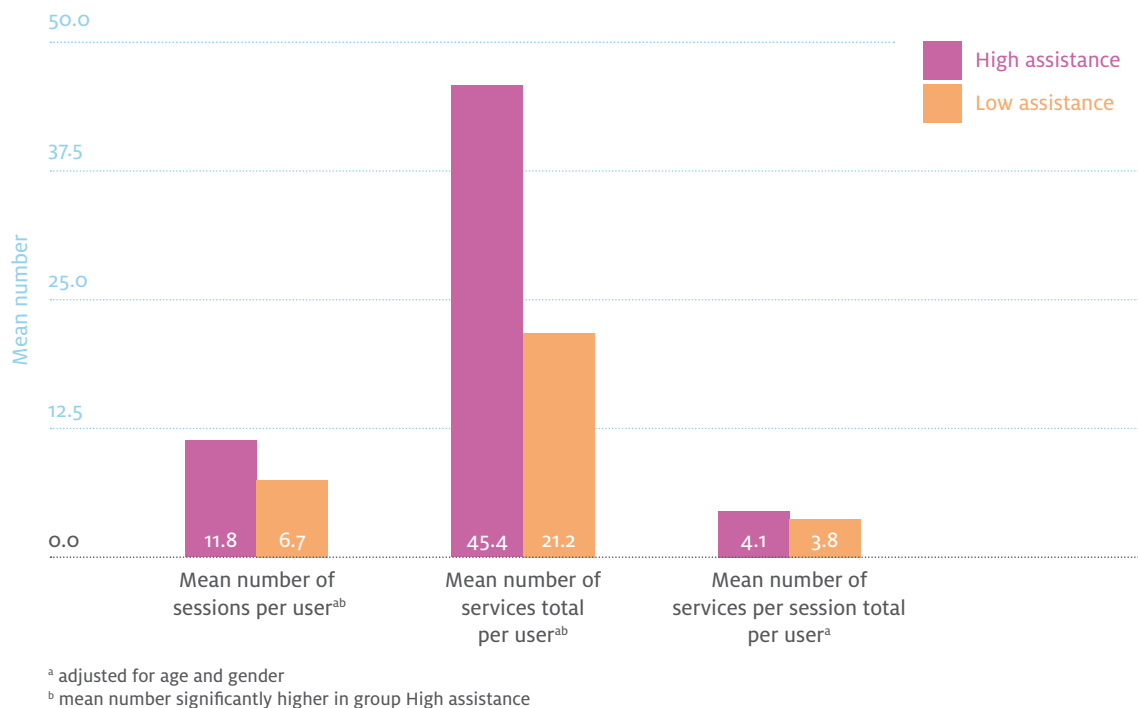


Figure 4. Usage patterns for high and low levels of assistance. a: mean number significantly higher in high assistance group b: adjusted for age and gender.

An overview of the online platform services visited during the intervention period is provided in Figure 5; for every service, the mean number per user is depicted. The log files revealed that all services were mainly used by group 1. Furthermore, it revealed that the e-Vita and Zorgdraad web platforms were predominantly used for online questionnaires, general information, and depicting wishes/goals related to their lifestyle, and to a lesser extent for online education, visiting the library, and looking for information about their health care professionals. Log files also showed that there was almost no interest in the measurement values CCQ and MRC scale. The email feature and an explanation of the test results of e-Vita were used to a moderate extent.

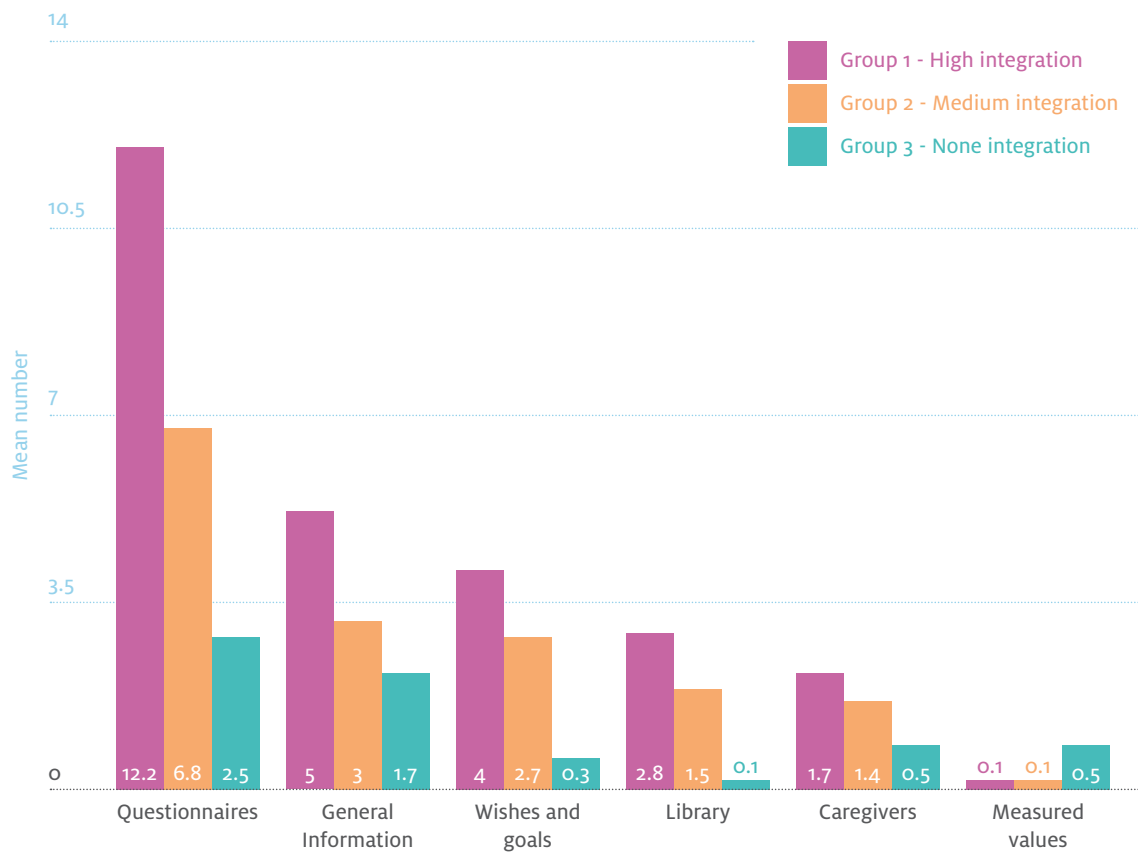


Figure 5. Usage patterns of the mean number of services per user in each group.

..... Educational Level and the General Self-Efficacy Scale

The association between the educational level and scores on the General Self-Efficacy Scale and the mean number of sessions are presented in Table 4. Educational level was not associated with the number of sessions ($P=.15$). No association was found between the General Self-Efficacy Scale and the mean number of sessions ($P=.79$).

	Unadjusted for age and gender		Adjusted for age and gender	
	B (95% CI)	P	B (95% CI)	P
Education	low -4.401 (-9.51 to 0.71) medium -1.265 (-5.90 to 3.39) high 0.000	0.195	low -5.304 (-10.86 to 0.26) medium -1.853 (-6.61 to 2.90) high 0.000	0.149
GSES	0.231 (-4.85 to 5.31)	0.928	0.674 (-4.43 to 5.78)	0.793

Table 4. Educational level and the General Self-Efficacy Scale (GSES) as predictors for web platform usage.

..... Attrition

The log files revealed that a substantial proportion of the users did not continuously use the platforms before completion of the study. Figure 6 shows the patterns of use of the web platforms in groups 1 to 3 during the intervention period, with the percentage of users on the y-axis, starting with 100% of the users, and the duration of usage on the x-axis. The area under the curve (AUC) until the 18th month for attrition in group 1 was 337.36, 254.70 in group 2, and 166.76 in group 3.

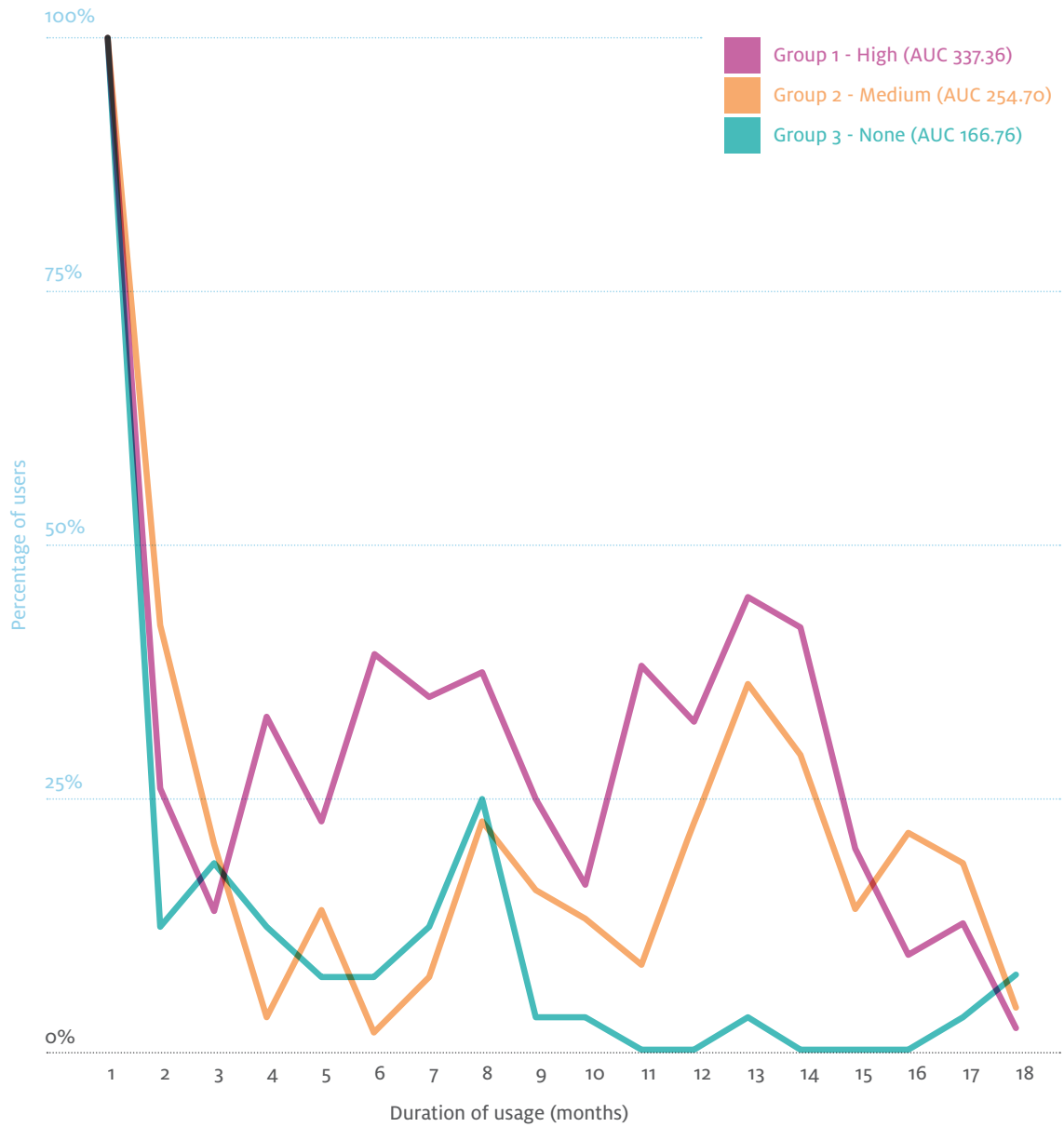


Figure 6. Attrition curve of group 1, 2 and 3.

Discussion

..... Main Results

In this study, usage of the COPD self-management Web-based platform is higher when the platform is an integrated part of IDM with trained health care professionals who encourage patients to use the platform. Furthermore, usage of the e-Vita COPD platform is higher when patients receive more personal assistance in learning how to use the platform. Usage of the self-management Web-based platform e-Vita (high and medium level of integration in IDM) is higher than that of Zorgdraad (no integration in IDM).

..... Interpretation and Findings

Despite high expectations and numerous initiatives around eHealth, implementation and use of eHealth apps are not yet common practice. Our primary aim was to analyze the factors that successfully promote the usage of two self-management web platforms for COPD patients. We compared different organizational implementation methods. An implementation setup with greater personal support is expected to increase the use of an online program.

Our findings highlight the importance of integrating a Web-based platform into IDM; usage of the self-management web platform is higher and more varied when the platform is an integrated part of IDM with appropriate personal coaching for patients. Patients in care groups with a high level of integration of the platform in IDM showed a higher number of sessions and a larger amount of visited services with more variation. Patients that received personal assistance also showed higher usage of the platform. Similar results were found in a study on COPD and asthma patients; the online app was used on a more regular basis with higher involvement of the health care provider and more assistance of the patients ^[25]. The e-Vita study on patients with diabetes mellitus showed minimal impact of implementing a personal health record including self-management support in primary diabetes care; recommendations were made to use additional strategies for patient motivation and engagement of professionals for a successful adoption of Web-based platforms ^[41,42].

In this study, we implemented extensive professional training of health care professionals on IDM and self-management supported by platforms; we also offered personal assistance for the users to guide them through the platform as well as push factors (automated reminders or messages by health care professionals). Both strategies are essential elements to influence the use of platforms.

The self-efficacy of users (GSES) was not a predictor for use of the platforms. The construct of perceived self-efficacy reflects an optimistic self-belief^[43]; a correlation can be understood based on the belief that one can change behavior, perform a novel or difficult task (eg, using a platform), or cope with adversity with a higher General Self-Efficacy Scale^[44,45]. In a healthy Dutch population, the mean General Self-Efficacy Scale is reported to be approximately 3.1^[38-46]; in our study population, the median General Self-Efficacy Scale was 3.3. Educational level was not a predictor of use of the e-Vita COPD platform. These predictors might be useful for future studies on and the development of platforms.

The EQ-5D values reflect the relative desirability of health states on a scale in which 1 refers to full health and 0 refers to death. In our study population, the median EQ-5D was 0.86 compared with 0.87 in a healthy Dutch population^[47].

In the three groups, there was no bias regarding baseline age, gender, education level, CCQ, MRC scale, GSES, and EQ-5D.

Analysis of attrition provided insight into the decrease in usage (eg, after 1 month, 10%-45% of the participants were actively using the platform). The periodic steep rise in the percentage of users might be explained by the email reminders sent by the platform to fill in the questionnaires; all users received continuous reminders during the intervention period. In group 3, all users received urgent and repeated requests to fill in questionnaires at the end of the intervention period, which probably explains the steep rise in the percentage of users at the end of the study. The attrition curve depicts the “push factors” that are required to remind participants to use the platform. This “law of attrition” (the phenomenon of participants stopping usage) is a common finding in eHealth evaluations and one of the fundamental and methodological challenges in the evaluation of eHealth apps^[29].

During this study, there were several lessons learned by the research team. First, it took a lot of effort to motivate health care professionals to work together with patients on self-management platforms; we experienced differences in communication skills among the health care professionals working with patients in a more modern, less hierarchic way. When patients started using the platform, it took great effort to stimulate the usage with several reminders, even though we established a high amount of attrition probably due to low usability of the platforms and logging problems.

..... Strengths and Limitations

This e-Vita COPD study has several strengths. To our knowledge, it is the first to combine different study designs thereby enabling simultaneous investigation of clinical effects, as well as the effects of different organizational implementation methods. Randomization was carried out for the level of assistance for patients. This study also adds evidence to the existing body of knowledge; this is important because local political and financial factors have a major impact on successful integration of eHealth in daily practice ^[48].

This study also has limitations. Although well-conducted randomized trials provide the most reliable evidence on the effectiveness of interventions, they are not feasible for our setting of an implementation design with organizational changes in a real-life health care system within three different care groups with different demands.

From a technical perspective, development of the Web-based platforms was difficult due to a lack of broad experience in the field. We used two different platforms with the same basic principles and functionalities. The platforms were new and the usability was not tested thoroughly before starting the study. The platform technique and the decisions made during the design phase were beyond the influence of our research group, but have affected our outcomes. From a human perspective, self-management skills imply behavioral changes. Behavioral changes require time, whereas the study period was restricted to 15 months. Furthermore, patients in a primary care setting have a low burden of disease (in this study, the mean CCQ score was 1.2) and motivation to use the platform might be negatively influenced by this fact. In respiratory medicine, there is a lack of research on patients with mild to moderate COPD despite that more than 80% of COPD patients suffer from this stage of disease and are often treated in primary care ^[49].

From an organizational perspective, other projects in primary care cooperatives can influence the speed and thoroughness of the implementation of our web portal. Finally, this study also has typical limitations found in eHealth trials. The loss to follow-up is high, as in all eHealth studies. Because general practices, as well as patients, were free to volunteer, bias might have occurred in our research groups. Users were self-selected and were presumably motivated to use the Web-based platform as would be expected in a real-life setting. The patients that were invited by GPs/nurses to participate in the study might differ from other patient groups. Furthermore, GPs excluded 26% of the COPD patients from this study. Of the 702 eligible patients, 215 (30.6%) were willing to participate and provided

informed consent, and 132 (61.4%) of the participants dropped out during follow-up. Even though nonparticipants did not differ in age and gender from participants, caution is required when generalizing these results to general practice. However, the practical applicability of our results for other primary care groups is positive (ie, the study provides practical insight into successful implementation of patient platforms). Nevertheless, primary care organizations should consider the different aspects of good organization of blended care and good quality of implementation.

More studies are needed (preferably with larger sample groups and among the nonusers) to gain more insight into the preferences of various patient groups. The substantial workload generated by integrating a Web-based platform in IDM emphasizes the importance of piloting and assessing workforce implications for primary care groups during the planning and implementation phase. These results provide additional insight into the organizational aspects of the implementation of platforms, including the need to assist patients in the use of Web-based platforms integrated in IDM.

Conclusions

Use of a self-management Web-based platform is higher when it is an integrated part of IDM, with trained health care professionals encouraging patients to use the platform. Use of a self-management platform is higher when participants receive adequate personal assistance about the use of the platform. The self-management Web-based platform e-Vita had higher usage than Zorgdraad, which is probably due to the superior organizational conditions of integrated care and because e-Vita is, technically, better customized for use. An implementation setup with blended care through integration of the online platform in IDM, together with greater personal support of the users, will likely lead to increased use of the online program. Future research should provide additional insights into the preferences of different patient groups

High level of integration in integrated disease management
leads to higher usage in the e-Vita Study

Appendix 1



Ik wil meer doen met Jette en Gijs



Daarom stop ik met roken

UITLOGGEN

Overzicht Dossier Plan Behandelteam Uitslagen

Uitslagen

CCQ

1,8

MRC

4

Wat betekenen deze uitslagen?

Training 3



Meer Lucht door sport

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed diam nonummy nibh euismod tincidunt.

START TRAINING

Vandaag 25 oktober

Training 1	Afgerond
Training 2	Ga verder met training
Training 3	Start training

Aandoeningen

COPD [Naar dossier](#)

Diabetis [Naar dossier](#)

Ik voel een aanval aankomen.

START HULP

Behandelteam

<



Huisarts
R. van Lierpen...



Fysio
Anne Milosovich



POH
S. van Doorn

ACTIVEER



Dietiste
T. van Beyens

>

Ik wil al mijn behandelteam zien



Joggen vermindert last van longpijn

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed diam nonummy.

[Lees meer](#)



Adem 10 keer diep in per dag

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[Lees meer](#)



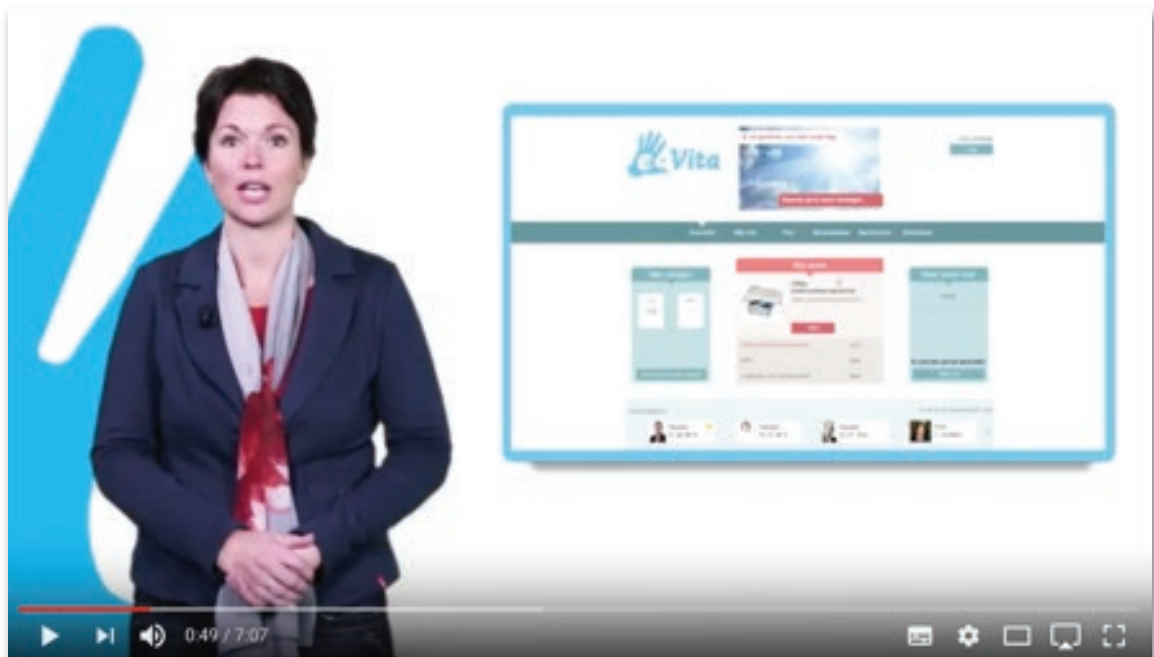
Activeer uw longen!

Lorem ipsum dolor sit amet, consectetur.

[Lees meer](#)

High level of integration in integrated disease management
leads to higher usage in the e-Vita Study

Appendix 2



Appendix 3



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Abbreviations

- **CCQ:** Clinical COPD Questionnaire
- **COPD:** chronic obstructive pulmonary disease
- **EQ-5D:** EuroQol 5D
- **GP:** general practitioner
- **GSES:** General Self-Efficacy Scale
- **IDM:** integrated disease management
- **MRC scale:** modified Medical Research Council dyspnea scale
- **QoL:** quality of life

Chapter 5

The Effect of Integration of Self-Management Web Platforms on Health Status in Chronic Obstructive Pulmonary Disease Management in Primary Care (e-Vita study): Interrupted Time Series Design

Esther PWA Talboom-Kamp | Noortje A Verdijk | Marise J Kasteleyn |
Lara M Harmans | Irvin JSH Talboom | Ingrid Looijmans-van den Akker |
Nan van Geloven | Mattijs E Numans | Niels H Chavannes

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Abstract

..... Background

Worldwide nearly 3 million people die from chronic obstructive pulmonary disease (COPD) every year. Integrated disease management (IDM) improves quality of life for COPD patients and can reduce hospitalization. Self-management of COPD through eHealth is an effective method to improve IDM and clinical outcomes.

..... Objectives

The objective of this implementation study was to investigate the effect of 3 chronic obstructive pulmonary disease eHealth programs applied in primary care on health status. The e-Vita COPD study compares different levels of integration of Web-based self-management platforms in IDM in 3 primary care settings. Patient health status is examined using the Clinical COPD Questionnaire (CCQ).

..... Methods

The parallel cohort design includes 3 levels of integration in IDM (groups 1, 2, 3) and randomization of 2 levels of personal assistance for patients (group A, high assistance, group B, low assistance). Interrupted time series (ITS) design was used to collect CCQ data at multiple time points before and after intervention, and multilevel linear regression modeling was used to analyze CCQ data.

..... Results

Of the 702 invited patients, 215 (30.6%) registered to a platform. Of these, 82 participated in group 1 (high integration IDM), 36 in group 1A (high assistance), and 46 in group 1B (low assistance); 96 participated in group 2 (medium integration IDM), 44 in group 2A (high assistance) and 52 in group 2B (low assistance); also, 37 participated in group 3 (no integration IDM). In the total group, no significant difference was found in change in CCQ trend ($P=.334$) before (-0.47% per month) and after the intervention (-0.084% per month). Also, no significant difference was found in CCQ changes before versus after the intervention between the groups with high versus low personal assistance. In all subgroups, there was no significant change in the CCQ trend before and after the intervention (group 1A, $P=.237$; 1B, $P=.991$; 2A, $P=.120$; 2B, $P=.166$; 3, $P=.945$).

..... Conclusions

The e-Vita eHealth-supported COPD programs had no beneficial impact on the health status of COPD patients. Also, no differences were found between the patient groups receiving different levels of personal assistance.

Introduction

Chronic obstructive pulmonary disease (COPD) is a slowly progressive lung disease and a main cause of morbidity and mortality in high-, middle-, and low-income countries ^[1]. Worldwide, nearly 3 million people die from COPD every year which, in 2012, was equal to 6% of all deaths globally ^[2,3].

According to current COPD guidelines, symptoms and airflow obstruction should be regularly monitored to modify treatment and identify complications at an early stage ^[4,5]. Monitoring should contribute to delaying disease progression and alleviate its manifestations; the most important primary care objective should be to improve quality of life (QoL) ^[6]. In primary care COPD studies, the mean score on the Clinical COPD Questionnaire (CCQ) reflects a mildly symptomatic COPD ^[7], and the health status of patients was found to decline over a longer period of time ^[8].

In the last decade, integrated disease management (IDM) was introduced to improve quality of care. An IDM program consists of different components of care in which different health care providers are cooperating and collaborating to provide efficient and good quality of care; IDM for COPD improves disease-specific QoL and exercise capacity and also reduces hospital admissions and hospital days per person ^[9].

To improve the quality and efficiency of IDM and reduce health care costs, self-management of COPD patients was introduced and has proven an effective method ^[10,11,12]. The core components of self-management include education, eliciting personalized goals, psychological coping strategies, improving compliance to treatment, behavioral change, and practical and social support ^[13,14]. Interventions to support self-management have shown reductions in hospital admissions and fewer sick days because of exacerbations ^[15,16]. Chronically ill patients who received person-centered care focusing on patient activation and goal setting are better self-managers ^[17], with self-efficacy as an important factor influencing self-management behaviors ^[18].

eHealth interventions are effective in stimulating self-management in chronic disease; patients are better able to cope with their illness and adapt their lifestyle, while eHealth support also reduces medical staff consultations ^[19]. The deployment of eHealth applications facilitates accessibility to health care, enhances patient understanding of their disease, sense of

control, and willingness to engage in self-management ^[20,21]. Although patient attitudes and receptiveness toward eHealth applications are promising in certain groups of age and education ^[22,23,24], large-scale adoption of eHealth in daily practice still lags behind predictions in comparison with the explosive growth of other digital tools like Facebook and Twitter ^[25] (also, during recent years, online banking acceptance has increased rapidly worldwide ^[26]). A major challenge of eHealth in care coordination is to make it beneficial and easy to use for both health care providers and patients ^[27]. It is important that online self-management support is a fully integrated element of IDM; COPD and asthma patients tended to use an online application on a regular basis when the caregiver was involved, whereas patients on their own used the application only sporadically ^[28]. For clinicians, the eHealth evidence base needs strengthening, while for primary care practices, a learning process including staff training needs to be instituted ^[29]. Since advances in eHealth are not clear for patients who have never used it, it is necessary to provide patients with more and better information about the possibilities and potential benefits of eHealth to increase their self-efficacy and provide a feeling of more personal control in daily life ^[30]. Furthermore, poor user-friendliness of Web-based applications and the lack of push factors (frequent reminders or messages by caregivers) are a common cause of low usage or decline in usage ^[31].

Despite high expectations and numerous eHealth initiatives, implementation and use of eHealth applications is not yet common practice. Therefore, this e-Vita study investigated the effect of usage of eHealth platforms on the health status of COPD patients treated in primary care. In this paper, we describe 3 eHealth-supported care programs with different components that support the treatment of COPD patients through digital coaching. Two programs were applied as blended care (ie, implemented within usual care to explore the potential for daily health care practice), and one program was applied with the self-management platform as an independent component.

In our e-Vita study, use of the self-management platforms was higher when the platform was an integrated part of IDM and with adequate personal assistance on how to use the platform ^[32]. We hypothesize that use of the platforms will improve self-management skills and thereby stabilize the health status of COPD patients, with a greater effect with higher usage.

Methods

Study Design

Full methodological details of this multilevel parallel cohort design have been reported previously ^[33]. For our implementation study in a real-life health care setting, we used an interrupted time series (ITS) design in a pragmatic trial in which data were collected at multiple time points before and after implementation to detect whether the intervention had a significantly greater effect than any underlying secular trend ^[34]. The ITS is performed according to the guidelines of the Effective Practice and Organization of Care Cochrane review group ^[35].

Figure 1 presents an overview of the study design. The study included 3 different care groups in primary care (groups 1 to 3); all patients started using the Web-based platforms (Multimedia Appendices 1 and 2).

In groups 1 and 2, we offered the patients blended care, and in group 3 the self-management platform was offered to the patients as an independent module. In group 1, the online platform was offered as a highly integrated part of the COPD IDM (High) with a tailor-made intensive course program on COPD for health care professionals that contained education on COPD, training about the possibilities of eHealth, and conversational techniques to approach patients in an equal and coaching way. All patients in group 1 started with a personal consultation with the primary care nurse with coaching on the necessity of self-management and explanations of their burden of disease and the eHealth program. Group 2 had a medium level of integration (Medium) with a basic course program for health care professionals on COPD that contained education on COPD and training about the possibilities of eHealth. All patients in group 2 started with a personal consultation with the primary care nurse with coaching and explanation of the self-management program. In groups 1 and 2, the first question the nurse asked was what patients would like to achieve in their daily life when they would have a lower burden of disease. With the platform, the patients could work with a coaching program on their personal goals, actions and health-related QoL ^[33]. In group 3, the online platform was offered without integration in COPD IDM (None); health care providers and patients received basic instructions on the platform.

Two different levels of assistance for patients were distinguished within groups 1 and 2: one with a high level of personal assistance (A) and the

other with a low level of personal assistance (B). Patients were randomly subdivided into 2 groups. In group 1A, high-level support implied home visits to patients by a research nurse who coached and assisted in use of the platform. In group 2A, high-level support implied telephone consultation (3 times during the intervention period, scheduled after 3, 6, and 9 months) between the patient and a research nurse who explained use of the platform. In groups 1B and 2B, low-level support implied that the primary care nurse showed the patient only once how to use the platform. Patients in group 3 who used the online self-management platform had no support from the caregivers or research nurses. Both platforms were provided for the intervention period of 15 months.

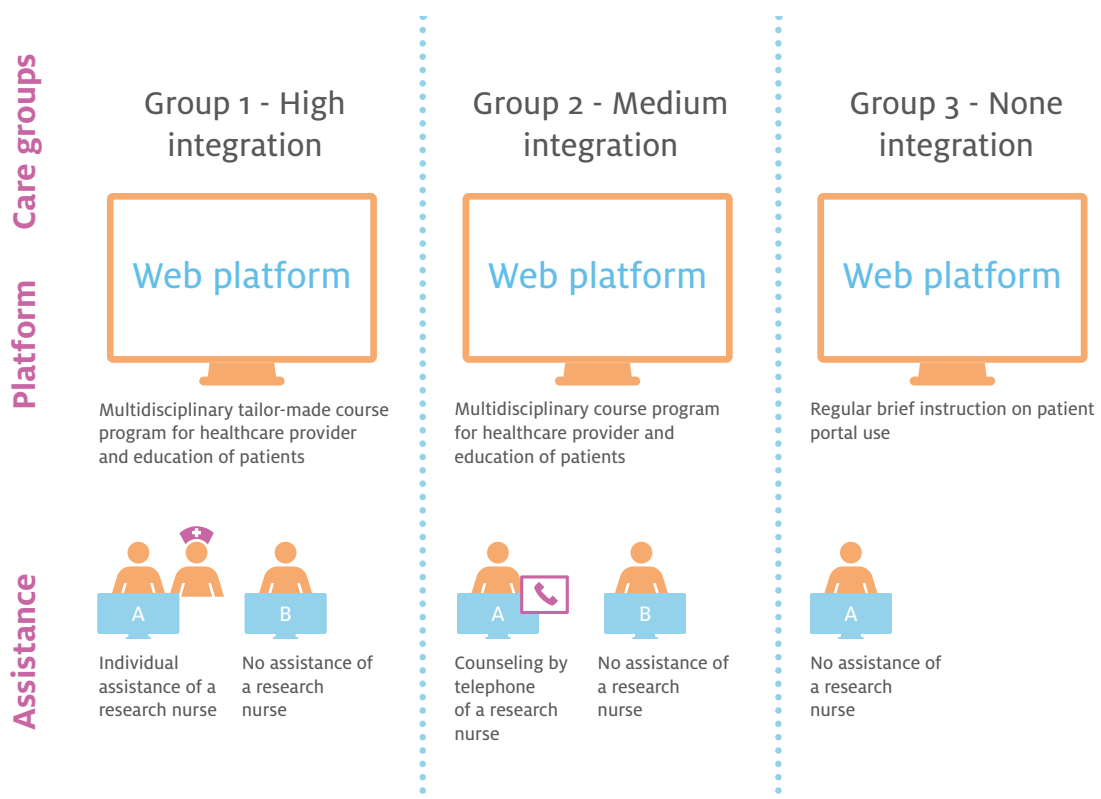


Figure 1. Design of the e-Vita COPD Study.

..... Participants

A total of 3 care groups participated. Patients were eligible when they were diagnosed with COPD according to the Global Initiative for Chronic Obstructive Lung Disease criteria (post-bronchodilator $FEV_1/FVC < 0.7$) in accordance with the COPD Guidelines of the Dutch College of General Practitioners^[36] and when they were being treated for COPD in primary care. Patients were excluded if they were unable to fill in questionnaires, had no access to the Internet, had a terminal illness, were immobile, or were severe substance abusers.

..... Recruitment of Patients

We started by recruiting the care groups: general practitioners in charge (GPs) in groups 1, 2, and 3 decided to participate because they wanted to contribute to possible health care improvement. Members of the care groups (GPs) volunteered to participate.

Patients were invited to participate by letter via their own GP. When participants of the e-Vita study logged in and used the web platform at least once, they were defined as users. Patients were defined as lost to follow-up if they did not log on to the platform for at least 12 months after signing informed consent or if they did not complete the digital questionnaires within the intervention period.

..... Ethics Approval and Consent to Participate

This study was conducted according to the principles of the Declaration of Helsinki (version 59, 2008) and in accordance with the Medical Research Involving Human Subjects Act. The study was approved by the Medical Ethics Committee of the Medical University Center of Leiden. All subjects provided written informed consent.

..... Intervention

The online self-management platforms were created by national experts on chronic disease management guided by interviews with COPD patients about their thoughts and feelings related to living with COPD; the experiences of professional COPD experts were also integrated. The main content of the platform consists of insight into personal health data, self-monitoring of health values (CCQ, Modified Medical Research Council Dyspnea scale ^[MRC]), education, and a coach for attaining personal goals. The educational and coaching programs were developed by the Lung Alliance of the Netherlands. The online self-management platform e-Vita is an initiative of the Dutch foundation Care Within Reach ^[37]. The patients received automated online reminders. Details on the online platforms are published elsewhere ^[33].

..... Outcome Measures

The primary outcome is a clinical one, expressed as health status (ie, the CCQ). This questionnaire was designed by Van der Molen ^[38] and consists of 10 items, each answered on a 7-point Likert scale. The CCQ comprises 3 domains: symptom state (4 items), functional state (4 items), and mental state (2 items). The CCQ total score is calculated as the mean of the sum of

all items (minimum 0, maximum 6), with a higher value indicating lower health status. The CCQ is a reliable and valid questionnaire with a Cronbach alpha of 0.89-0.91.

Data collected at baseline included age, gender, education level, and total scores on the CCQ, MRC [39], General Self-Efficacy Scale (GSES) [40], and Euro-Qol 5-dimension questionnaire (EQ-5D) [41]. Education was self-reported using 8 response categories ranging from no formal education to graduate or professional level and converted into 3 levels (low, medium, high). In the main analyses, personal assistance for the participants (high assistance vs low assistance) and integration in IDM (integrated vs not integrated) were used as determinants.

..... Data Collection

Data were extracted from the log files of the self-management platforms. Figure 2 shows the measurement schedule of the CCQ. During the 15-month intervention period, there were 4 measurement periods with 3 CCQ questionnaires at each period (3 data points before intervention and 9 data points after intervention) in order to apply ITS analysis.

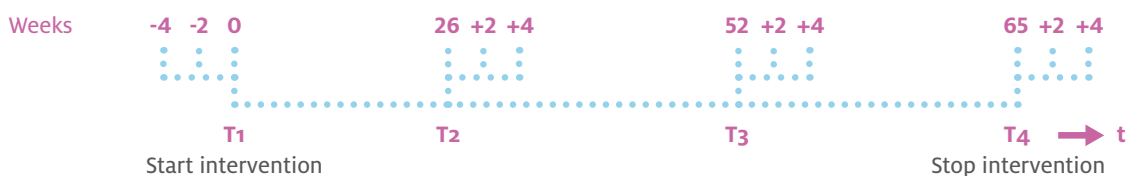


Figure 2. Interrupted time series measurements of the Clinical COPD Questionnaire per interval.

..... Sample Size Calculation

Generally, the health status of patients with COPD decreases over time. Studies on IDM in COPD in primary care show that a general increase in CCQ of 0.5 (SD 0.75) can be expected over a 1-year period [42,43]. In this study, we offered patients a web platform in addition to their regular IDM program. Therefore, we hypothesized that the regular increase in CCQ (0.5 points per year) would change to stabilization of health status as compared to literature [44].

To measure differences in health status (>0.5 CCQ points) at 80% power (SD 0.75 and $\alpha=0.05$), 37 patients needed to be included. Based on an estimated 20% drop-out during the study period, 45 (37/0.80) patients needed to

be included. As we used 2 different implementation methods (with and without personal assistance) in 2 of the care groups, $2 \times 45 = 90$ patients needed to be included in those groups. In the third care group, because only 1 implementation method was used, a total of 45 patients were required to achieve sufficient statistical power.

..... Statistical Methods

Categorical baseline characteristics were reported as numbers and percentages, normally distributed continuous variables as means with standard deviations (SD), and nonnormally distributed variables as medians with interquartile ranges (IQRs). Characteristics between the 3 groups were examined using chi-square tests and Kruskal-Wallis tests.

ITS analyses were used to study time trends before and after intervention. Due to the correlation between the repeated measurements within a patient, we used multilevel linear regression modeling (mixed models) to analyze CCQ data in the total group as well as in the groups with high and low levels of assistance and in the 5 subgroups.

The analyses allowed us to quantify the effect of the intervention on CCQ versus the observed preintervention period. Estimates for regression coefficients corresponding to 2 standardized effect sizes were obtained: a direct change in the level of the CCQ (also called step change or jump) and a change in trend of the CCQ before and after the intervention ^[34].

Included in the model for the total group and 5 subgroups as fixed effects were time, treatment, and the interaction between time and treatment; the model comparing the groups with high and low assistance additionally contained the assistance group factor and the interaction of this factor. All models included a random intercept per patient. When there was a substantial improvement in the Akaike Information Criterion (used to assess the model fit score), an additional random slope (time) was used.

Because of a nonnormal distribution of the CCQ data, the log of the CCQ data was used as outcome in the multilevel linear regression models. The analysis model did not test or correct for seasonality; although seasonality influences exacerbations of COPD, it has no effect on the CCQ ^[45,46]. We visually assessed normality of the residuals to evaluate the validity of the assumptions of the mixed models analysis.

Results

Inclusion

A total of 942 COPD patients were selected from 3 care groups (Figure 3). The GPs of these care groups excluded 240 COPD patients from participation due to other diseases, treatment in hospital, or incompetency to participate in the program. Finally, 702 COPD patients were invited, of whom 215 (30.6%) agreed and provided informed consent.

The number of patients lost to follow-up (no log on to the platform after signing informed consent or not completing the entire intervention period) was 132; results of the nonparticipation analysis are reported elsewhere^[33]. Figure 3 shows the reasons for loss to follow-up in groups 1 and 2; patients in group 3 were not asked for their reasons.

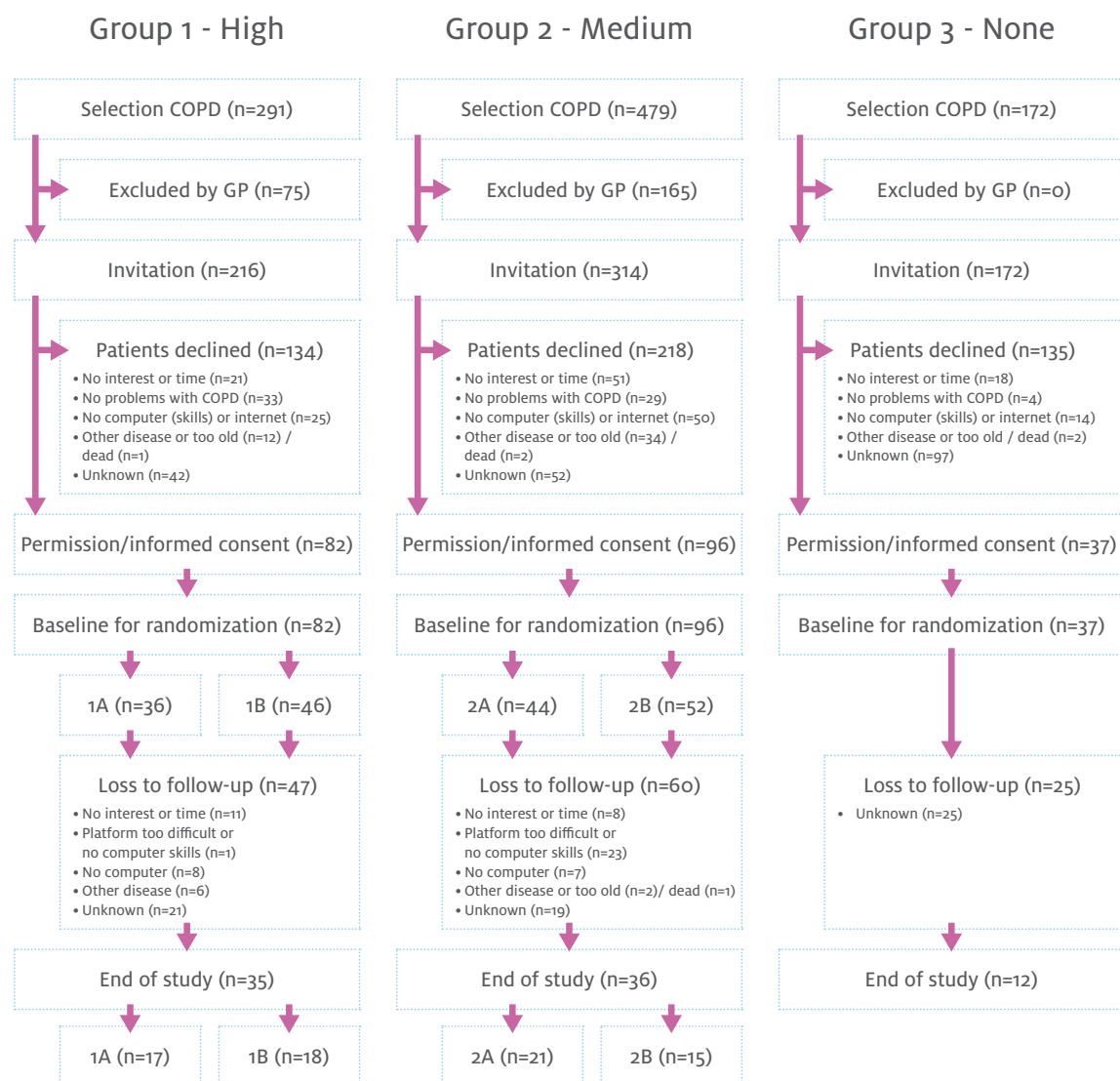


Figure 3. Flowchart of the e-Vita chronic obstructive pulmonary disease study.

..... Baseline Characteristics of Patients With Chronic Obstructive Pulmonary Disease

Table 1 presents the baseline demographic and clinical characteristics of the included COPD population (median age 66.6 years; 52.1% male). These patients had mildly symptomatic COPD which was reflected by a median MRC scale of 1.0 and a median CCQ of 1.2. Out of 215 participants, 89 (41.4%) filled in the online questionnaire for education level; most participants had a middle education level, reflected by a 4 or 5 on a scale of 1 to 7 (38/89, 42.7%). The median General Self-Efficacy Scale was 3.3, and the median EQ-5D was 0.86. The characteristics age ($X^2_2=5.4$, $P=.07$), education level ($X^2_4=2.2$, $P=.70$), General Self-Efficacy Scale ($X^2_2=1.7$, $P=.42$), and EQ-5D ($X^2_2=2.4$, $P=.28$) were similar in the 3 groups. There was a difference in the characteristic gender ($X^2_2=6.8$, $P=.03$), with more male patients in group 1, and a difference in CCQ ($X^2_2=6.5$, $P=.04$) and MRC scale ($X^2_2=11.3$, $P=.003$), with a higher CCQ and MRC scale in group 2.

	Group 1 - High		Group 2 - Medium		Group 3 - None	Total
	High	Low	High	Low		
N	36	46	44	52	37	215
Age, years, [IQR ^a]	66.3 [61.0-79.2]	65.6 [61.3-73.4]	68.7 [64.0-78.3]	66.8 [60.3-75.1]	64.1 [61.5-69.2]	66.6 [61.4-74.7]
Males N (%)	19 (52.8)	32 (69.6)	17 (38.6)	24 (46.2)	20 (54.1)	112 (52.1)
Education level N questionnaires (%)						
Low N	4 (28.6)	8 (38.1)	5 (22.7)	8 (42.1)	7 (53.8)	32 (36.0)
Medium N	7 (50.0)	8 (38.1)	11 (50.0)	8 (42.1)	4 (30.8)	38 (42.7)
High N	3 (21.4)	5 (23.8)	6 (27.3)	3 (15.8)	2 (15.8)	19 (21.3)
CCQ ^b	1.0 [0.6-1.9]	1.2 [0.8-1.6]	1.3 [0.9-2.1]	1.4 [1.1-2.1]	1.3 [0.6-1.8]	1.2 [0.8-1.9]
MRC ^c	1.0 [1.0-3.0]	1.0 [1.0-2.0]	2.0 [1.0-3.0]	2.0 [1.0-2.0]	1.0 [1.0-1.0]	1.0 [1.0-2.0]
GSES ^d	3.4 [3.1-3.7]	3.3 [3.0-3.8]	3.3 [2.8-3.5]	3.3 [3.1-3.7]	3.4 [3.3-3.7]	3.3 [3.0-3.7]
EQ-5D ^e	0.85 [0.7-1.0]	0.89 [0.81-1.0]	0.85 [0.72-1.0]	0.84 [0.71-1.0]	0.9 [0.84-1.0]	0.86 [0.78-1.0]

^aIQR: interquartile range.

^bCCQ: Clinical COPD Questionnaire.

^cMRC: Modified Medical Research Council Dyspnea score.

^dGSES: General Self-Efficacy Scale.

^eEQ-5D: EuroQoL 5-Dimension Questionnaire.

Table 1. Baseline characteristics of patients with chronic obstructive pulmonary disease in the e-Vita study.

..... Health Status Changes

Figure 4 A shows the effect of the intervention on CCQ in the total patient group. The decrease before the intervention was 0.5% per month and after the intervention 0.08% per month; this difference was not significant ($P=.334$). The estimated direct change in the level of the CCQ slopes at the moment of the intervention (jump) was -0.015 ($P=.421$) implying that the CCQ trend was 1.5% lower before the intervention.

Figure 4 B shows the effect of the intervention on CCQ in the groups with a high level of personal assistance (A) and a low level of personal assistance (B). In group A, the preintervention decrease was 0.8% per month and the decrease after the intervention was 0.05% per month; in group B, the preintervention decrease was 1.8% per month and the decrease after the intervention was 0.1% per month. No significant difference was found in CCQ changes going from preintervention to postintervention between groups A and B ($P=.429$). The direct change in the level of the CCQ slopes at the moment of the intervention (jump) was 0.017 in group A and -0.033 in group B (implying that the CCQ trend was 1.7% higher before the intervention in group A and 3.3% lower in group B). There was no significant difference in the jumps ($P=.207$).

Figure 4 C shows the effect of the intervention on the CCQ in the 5 sub-groups; no significant difference was found in the slope of the CCQ before and after the intervention (1A, $P=.237$; 1B, $P=.991$; 2A, $P=.120$; 2B, $P=.166$; 3, $P=.945$). The direct changes in the level of the CCQ slopes before and after the intervention (jump) were -0.0196 in group 1A, -0.0582 in group 1B, 0.0426 in group 2A, 0.0184 in group 2B, and -0.0874 in group 3 and were not significant.

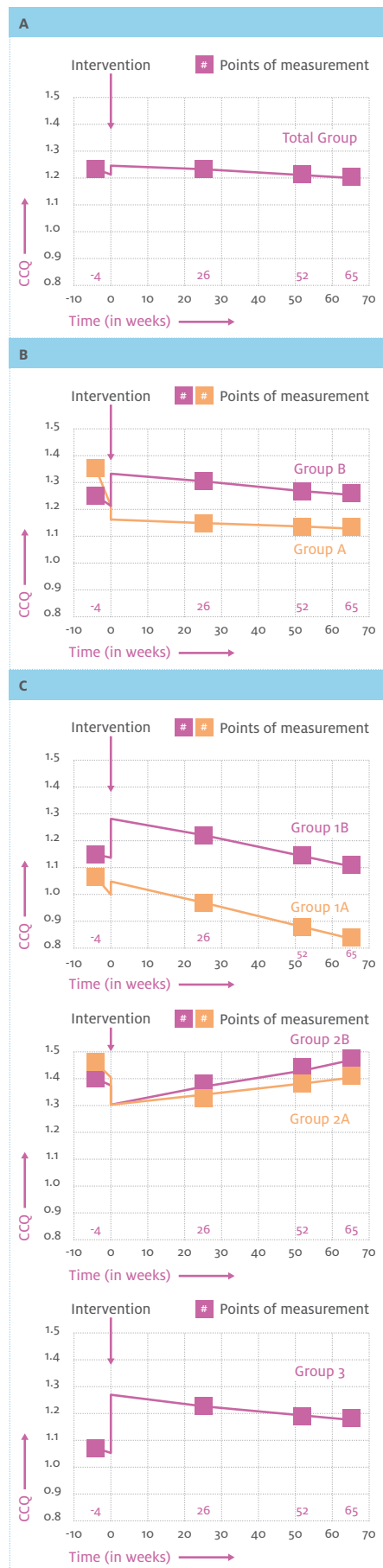


Figure 4. (A) Total group analysis of health status, (B) analysis of health status in groups receiving high and low levels of assistance, and (C) subgroup analyses of health status.

Discussion

..... Principal Findings

This study investigated the effect of use of eHealth platforms on the health status of COPD patients in primary care. No changes in health status were found before and after introduction of the eHealth-supported COPD programs, and no differences were found between care groups with a high versus a low level of personal assistance.

It is essential to carefully review the design strategies for integrating eHealth applications within disease management ^[47] by means of a thorough evaluation and analysis of the results. A recent study analyzed the effect of wearable devices that monitored and provided feedback on physical activity among young adults with obesity; providing a group with this device resulted in less weight loss over 24 months ^[48]. In a trial of elderly persons with a high risk for prehospitalization, telemonitoring was offered for monitoring and reporting symptoms but did not result in lower hospitalizations or emergency room visits (although mortality was higher in this telemonitoring group) ^[49]. High expectations of eHealth should be preceded by evaluations in pragmatic studies on implementation ^[50].

In our study, changes in health status CCQ were not within the range of a minimal clinically important difference ^[51]. QoL and health status are determined by a significant number of factors ^[46]. We expect that eHealth interventions will be effective in stimulating self-management and stabilizing health status in COPD patients when these patients use the platforms for a longer period of time. In earlier studies, a worsening in health status was found for primary care patients over a longer period of time ^[8]; this finding was not confirmed in our e-Vita study. In Dutch primary care, the standards of IDM are high, with a wide variety in the implementation of interventions ^[7]; this might explain the absence of a worsening of health status before the intervention in our study. The introduction and integration of eHealth within IDM will not make a significant difference in the short term due to the high standard of IDM.

In our study, the median baseline CCQ score of 1.2 was low compared with scores in other primary care COPD studies, which reflects mildly symptomatic COPD ^[7]. This limits the room for stabilization or improvement in our primary outcome (ie, ceiling effect).

In a patient population with more severe COPD (patient-data meta-analysis from 2016), self-management interventions improved health-related QoL at 12 months but not at 6 months ^[52]; this confirms our observation that long-term use of platforms is necessary for an effect on health status. In our research, the platforms are probably not sufficiently customized to the wishes or needs of COPD patients to provide sufficient motivation to use the platform on a regular basis for a longer period; in our e-Vita study, a significant number of users stopped using the platforms (attrition) ^[32].

The change in level of CCQ (positive/negative) at the start of the intervention might be explained by the participant rise in consciousness regarding their health status, thereby completing the questionnaire more critically after explanation from a health care professional. Similar to our study, in a randomized controlled trial (RCT) with asthma patients, the QoL was enhanced over the first 3 months after starting to use a self-management portal ^[53].

The effect of eHealth cannot easily be evaluated in a classical RCT; integrating eHealth in IDM is a complex intervention in a multidisciplinary care process. Pragmatic trials frequently include complex interventions and often involve the skills and experience of health care professionals ^[54] and are, therefore, more suitable for eHealth studies.

eHealth technologies for chronic conditions can be used to enhance self-management and revise the chronic care model; patients who actively participate in their care achieve valuable and sustained improvement in well-being ^[55,56]. Findings in many eHealth studies suggest that the use of a personal health record or self-management platform can promote an informed or activated patient and augment the chronic care model for self-management support and productive interactions even though a direct dosage-effect relationship (usually analyzed in a classical RCT) is not common in eHealth studies ^[57]. Also in our e-Vita study, interpretation of the results on use and health status cannot be made in a direct dosage-effect relationship. Use of the self-management platform was higher when the platform was an integrated part of IDM, with trained caregivers encouraging patients to use the platform and with personal assistance about how to use the platform, but without a significant change in health status. Based on current literature and the e-Vita COPD study, we conclude that eHealth-supported self-management integrated into usual care can help patients with COPD to manage their disease effectively.

Further studies based on this study and current literature are needed to establish the mechanisms most likely to ensure the successful development and implementation of Web-based self-management interventions, including considerations about how the intervention is integrated in IDM and how it enhances the patient's self-management behavior to stimulate long-term use of self-management platforms with a stabilizing effect on health status [11-58].

..... Strengths and Limitations

This e-Vita COPD study has several strengths. To our knowledge, it is the first to combine different study designs thereby enabling simultaneous investigation of the effect of eHealth and the effects of different organizational implementation methods on health status. Randomization was performed for the level of assistance provided to patients, allowing comparison of patient groups with high and low levels of assistance. Because the care groups 1, 2, and 3 were not randomized, no analysis of the differences between these groups can be made.

An advantage of the ITS design is that it detects changes that are delayed or intermittent and can determine whether the change is permanent or temporary. The design, including the 3 datapoints of CCQ before the intervention, also allows evaluation of variables which are changing by comparing slopes of trend lines before and after the intervention.

This study also has some limitations. Development of the platforms was relatively difficult due to lack of experience in this field. Also, decisions made during the design phase were beyond the influence of our group but affected the usability of the platforms. Self-management skills imply behavioral changes which require some time, whereas the present study period was restricted to 15 months. Furthermore, patients in a primary care setting have a low burden of disease (in this study, a median score on the CCQ of 1.2) and motivation to use the platform might be negatively influenced by this fact. In respiratory medicine there is a lack of research on patients with mild-to-moderate COPD despite that over 80% of COPD patients suffer from this stage of disease and are often treated in primary care [59]. Other projects among care groups (eg, patient education, start different IDMs) might influence the speed and thoroughness of the implementation of our platforms.

This study also has limitations typically associated with eHealth trials. For example, as GPs and patients were free to volunteer, bias might have occurred in our study groups. Users were self-selected and were, presumably, motivated to use the Web-based platform as would be expected in a real-life setting. Also, the patients selected to be invited by the GPs might differ from other patient groups. Furthermore, GPs excluded 25.5% of the COPD patients from this study. Of the 702 eligible patients, 30.6% were willing to participate and provided informed consent, and 61.4% of the participants dropped out during follow-up. Even though the nonparticipants did not differ in age or gender from the participants ^[32], caution is required when generalizing these results to general practice.

Like most Internet outcome studies, there were 2 types of attrition in our study; attrition from the intervention itself (lack of site utilization) and attrition from the follow-up assessments. This law of attrition (the phenomenon of participants stopping usage) is a common finding in eHealth evaluations and one of the fundamental and methodological challenges in the evaluation of eHealth applications ^[60]. To prevent both types of attrition, email reminders were sent by the platform to fill in the questionnaires. All users received urgent and repeated requests to fill in questionnaires by email and by telephone. The attrition curve was analyzed earlier and depicts the push factors that are required to remind participants to use the platform ^[32]. The loss to follow-up is high with a risk of biased results due to user bias; therefore, these results are only applicable for users of eHealth.

The study aimed to be inclusive rather than exclusive to achieve higher external validity. Patients were excluded if they were unable to fill in questionnaires, had no access to the Internet, had a terminal illness, were immobile, or were severe substance abusers. During the inclusion of patients, we found that patients did not want to start the study for several different reasons: no computer skills, old age, no problems with COPD, and other reasons. These reasons are typical for eHealth research in a primary care setting with a low burden of disease; participants were self-selected and were, presumably, motivated to use the Web-based platform as would be expected in a real-life setting. Therefore, the results of the study are not generalizable to all COPD patients but to those who are willing, motivated, and able to use eHealth. Nevertheless, we believe that this study is inclusive rather than exclusive, since there are almost no limitations for participation for this group of motivated patients.

However, the practical applicability of our results for other primary care groups is positive (ie, the study provides practical insight into successful implementation of patient platforms). Nevertheless, primary care organizations should take into account the different aspects of the organization of blended care and quality of implementation.

Although an RCT provides the most reliable evidence on the effectiveness of interventions, this was not feasible for our implementation study in a real-life health care setting with 3 different care groups. After randomization in groups 1 and 2, more patients were assigned to the groups with a low level of personal assistance (group 1B and 2B). After simple randomization, some discrepancy between the numbers in the comparison groups would be expected ^[61]. Such unpredictability reflects the essence of randomness. Moreover, the baseline characteristics did not differ significantly between groups with high and low assistance. Therefore, we expect no significant influence on the results.

To measure a significant difference in health status, 45 patients were needed in each subgroup; although these numbers were not met within each subgroup, analysis on the combined groups should be sufficiently powered to detect relevant differences. In addition, the number of data points collected before the intervention has a substantial impact on the strength of an ITS design. It is necessary to collect enough data points to be convinced that a stable estimate of the underlying secular trend has been obtained ^[62]. In our study, the 3 data points before the intervention represent a minimum number of data and may have influenced the effective power of our study.

..... Conclusion

There is growing interest in the potential of Web-based self-management platforms to deliver more individually tailored self-management support integrated into the everyday lives of COPD patients to improve their quality of life. In this study, the e-Vita eHealth-supported COPD programs had no significant impact on the health status of COPD patients, health status showed no significant change before or after the introduction of the eHealth-supported programs, and no differences were found between the patient groups receiving different levels of personal assistance.

..... Multimedia Appendix 1
Homepage e-Vita.



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Homepage Zorgdraad.

Leidsche Rijn



JuliusGezondheidscentra

START

BIBLIOTHEEK

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VRAGENLIJSTEN

MEETWAARDEN

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OVER

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Abbreviations

- **CCQ:** Clinical COPD Questionnaire
- **COPD:** chronic obstructive pulmonary disease
- **FEV:** forced expiratory volume
- **FVC:** forced vital capacity
- **GP:** general practitioner
- **GSES: General** Self-Efficacy Scale
- **IDM:** integrated disease management
- **IQR:** interquartile range
- **ITS:** interrupted time series
- **MRC:** Modified Medical Research Council
Dyspnea scale
- **RCT:** randomized controlled trial
- **QoL:** quality of life

Chapter 6

PORTALS: Design of an innovative approach to anticoagulation management through eHealth

Esther P. W. A. Talboom-Kamp | Noortje A. Verdijk | Irvin J. S. H. Talboom |
Lara M. Harmans | Mattijs E. Numans | Niels H. Chavannes

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Abstract

..... Background

For the monitoring of International Normalized Ratio (INR) values, venous thromboembolism (VTE) and atrial fibrillation (AF) patients can visit anticoagulation clinics, laboratories, or physicians for venous puncture. Point-of-care testing (POCT) made it possible for patients to monitor INR themselves (self-monitoring) and even self-adjust their medication dosage (self-dosage). Both skills are accepted as forms of self-management. eHealth applications can improve this self-management, resulting in better clinical outcomes.

..... Methods

Our study, called PORTALS, aims at identifying the optimal implementation strategy of training to improve self-management and explore factors that enhance good self-management skills. In addition, the relationship between the implementation strategy of training, clinical outcomes, and individual characteristics will be investigated. Of the 247 recruited participants, 110 chose to continue with regular care. 137 patients have been randomly divided in subgroups and compared using a parallel cohort design: one group will be trained and educated by e-Learning, and the other group will receive face-to-face group training.

..... Discussion

More insight in factors that enhance good self-management will help to improve clinical outcomes and patient satisfaction on anticoagulation therapy. Our study will provide practical insights and knowledge of eHealth in daily practice and of the importance of education on the adoption of self-management. We expect the self-management program including training to help patients to better manage their own INR values and medication use, thereby increasing health status and diminishing thromboembolic events and hospitalisation.

Background

Venous thromboembolism (VTE) and atrial fibrillation (AF) are common causes of mortality and morbidity, and are associated with high medical costs ^[1]. With the ageing population and persisting unhealthy lifestyles, the prevalence of VTE and AF is rising rapidly ^[2]. Treatment of VTE and AF patients consists of, among other interventions, anticoagulant therapy (AT) with vitamin K-antagonists to treat, slow down, or prevent formation of blood clots ^[2]. AT demands frequent monitoring of blood samples to measure its effects. Results are expressed as International Normalized Ratio or INR values. In 2009, there were over 385.000 patients in the Netherlands who were treated with anticoagulants, more than half of whom suffered from AF (211.000 patients) ^[3]. Between 2005 and 2009 the number of VTE patients in the Netherlands increased by 13%; the prevalence of AF patients increases every year, especially amongst males due to the rising survival rate of myocardial infarcts ^[4].

For the monitoring of INR, patients must visit anticoagulation clinics, laboratories, or physicians for venous puncture. This is one of the major disadvantages of anticoagulant therapy with vitamin K antagonists and, together with frequently occurring unstable anticoagulation, one of the reasons that other anticoagulants (novel oral anticoagulants, NOACs) are being developed and often preferred as an alternative ^[5]. However, since the alternatives show disadvantages and risks too, improving procedures around vitamin K antagonists attract attention ^[6].

Point-of-care testing (POCT) is one of these potential improvements: it generates rapid test results and has been widely implemented in the last decade. POCT made it possible for patients to monitor INR values themselves (self-monitoring) and, as a next step, to even self-adjust their medication dosage (self-dosage). The major benefit of this self-management approach is the increased involvement of patients in their own care process, thus resulting in improved adherence to AT, and thereby reduction of complications. Research showed that self-management in AT patients decreases the risk of thromboembolic complications and mortality at a constant frequency of bleeding complications ^[7]. Several published studies and systematic reviews have suggested methods of monitoring anticoagulation therapy may be equal to or better than standard monitoring by a physician. Patients who self-monitor or self-dose can improve the quality of their oral anticoagulation therapy ^[8]. When patients start with self-monitoring or self-dosage, they receive structured education and training in self-testing and adjustment of medication dosage. In addition, eHealth applications are developed in

the form of online web portals to share self-measured INR values with care professionals. These web portals also provide programs that support self-adjustment of medication dosage. Research showed that self-management with online support results in improved INR values (Time in Therapeutic Range, TTR, of 10–23%) compared to self-management without online support (less than 4% improvement of TTR) [9,10]. Moreover, patient satisfaction is higher when using online remote monitoring of INR [11]. Based on these results we conclude that eHealth applications do improve self-management of vitamin K antagonist anticoagulant therapy, resulting in better clinical outcomes. In the last few decades, self-management has become an important strategy for coping with chronic illnesses. Adequate self-management requires the individual ability to deal with symptoms, treatment, and physical and social consequences of a disease. The basic principle of self-management is that behavioral change cannot succeed without patients taking their responsibility [12]. Research on other chronic diseases such as diabetes [13], COPD [14], and heart failure [15] showed that personality aspects such as self-efficacy are important factors in successful self-management. This notion is derived from the social cognitive theory, which states that behavioral change is made possible by a personal sense of control. Self-efficacy has been described as the “belief in one’s capabilities to organize and execute the course of action required to produce given attainments”.

As education is the basic approach in development of self-management skills, we expect that the strategy to implement the educational support largely affects the individual level of self-management and thereby clinical outcomes. However, it is clear that self-management is not a ‘one-size-fits-all’ intervention. How can self-management skills then be optimized in large groups of individuals, such as patients with AT? Which factors positively influence the acceptance of self-management? To answer these questions for patients with AT we designed the PORTALS study.

Our goal is to analyze the effect of the implementation of e-Learning versus a group training on top of a program of self-monitoring or self-management. In addition, we will investigate the relationship between the implementation strategy of training, clinical outcomes, and individual patient characteristics. We consider both self-monitoring and self-adjustment of medication as important self-management skills. In this study we defined self-management skills as the usage of the self-management platform; the amount of login sessions. For this definition, the difference between self-monitoring and self-dosage is not relevant. Self-monitoring and self-dosage activities are registered within the same login session. Therefore, we make no dis-

inction between patient-self-dosage and patient-self-testing in this study. All skills are accepted as forms of self-management.

Methods

In this study, self-management will be offered to patients of the Saltro Thrombosis Service (outpatient anticoagulation clinic and laboratory), who currently receive usual care for long-term AT.

Usual care consists of frequent monitoring of blood samples to measure the effects of vitamin K-antagonists. These blood samples are taken by classical venipuncture at primary care locations or at home. Based on the INR, specialized medical doctors define the acquired dosage for individual patients and follow puncture; patients receive the advice and instruction on individual basis.

We used a parallel cohort design to investigate determinants of optimal implementation; we will compare the different training methods. After inclusion, participants will be randomly divided in subgroups: one group will be trained and educated by e-Learning (group 1) and the other group will receive face to face group training (group 2). Both the e-Learning and the group training consist of at least three components: i) disease-specific knowledge of VTE; ii) self-testing skills; iii) use of the web portal; and iv) self-adjustment of medication. The fourth module is voluntary. Hence, 2 groups of self-management patients will be formed. Patients who do not wish to start with self-management will be invited to participate in the non-self-management group, a parallel cohort group describing usual care (group 3). They continue to receive regular care of high quality. In Figure 1 the inclusion of the research groups is summarized.

Saltro Thrombosis Service Centre			
	Self-Management		Usual Care
Patients	Group 1	Group 2	Group 3
	#72	#72	#72
Instruction	e-Learning	Group Course	Basic Short Training
Platform	Self-management	Self-management	-

Figure 1. Subdivision within the Saltro Thrombosis Service into three groups; Groups 1 and 2 perform self-management; group 1 was instructed by e-Learning and group 2 by group course. Group 3 receives the usual care, with brief instructions

Due to the nature of this study (implementation research in a real-life care setting) a perfect RCT design is not feasible: patients cannot be forced to start self-management. Patients will however be randomized in group 1 (e-Learning) and group 2 (group training). Furthermore, patients unable to dose their medication are free to continue with only self-monitoring. This study will be performed using a parallel cohort design. Although bias may occur, the results of this study remain valuable because in daily practice biases will occur too when it comes to patients voluntarily choosing the type of care they are willing to receive. Based on our study design, comparison between e-Learning and group training for self-management (group 1 and 2) and non-self-management patients (group 3) is applicable considering specific conditions in the choice of the statistics. Parallel cohort group 3 provides valuable information about patients who are unable or unwilling to use online supported self-management programs.

..... Power calculation

In thrombosis patients clotting speed is expressed in INR values. Optimal INR values vary between individual norms. Therapeutic effects are expressed as the percentage of Time the patient is in the Therapeutic INR Range (TTR). A pilot study of 100 patients of the Saltro Thrombosis Service Centre shows that the average TTR is 84% (SD 10). Research shows that TTR improves significantly in self-management compared with usual care, with 5–13% increasing TTR [16]. To prove a relevant effect of the new implementation strategy of e-Learning or group training (>5%) at a power 80% and $\alpha = 0.05$, 63 patients must be included per group. Considering a 15% drop out, 72 (63/0.85) patients are needed per study group.

Previous studies reported a 21–77% response at inclusion of study [8,9–17]. Even if attrition rate at inclusion would be only 21%, there are sufficient eligible patients to reach an adequate sample size: at 21% attrition rate, 343 patients (72/0.21) must be approached per group to include sufficient participants in the study. As this study includes three research groups, a total of at least 1029 patients is needed to complete the study. Currently, 8950 patients receive usual care from the Saltro Thrombosis Service.

..... Participants

This study focuses on patients of the Saltro Thrombosis Service who voluntarily choose to start with self-management. The Thrombosis Service states several inclusion criteria for their patients to start with self-management. The first criterion is a long-term indication for anticoagulants as

the training period and investments exceed the regular three to six months of short-term anticoagulant prescription. In 2013, 85% of the patient population of the Thrombosis Service suffered from long-term indication for anticoagulants. Secondly, internet access is mandatory as monitoring of patients by the Saltro Thrombosis Service is provided by the web portal. In the Netherlands 95% of the people have internet access at home. The average age of patients of the Saltro Thrombosis Service is 65 years. In 2013, 61% of Dutch people over 65 used internet daily and over 75% used it during the last three months ^[18]. Of people aged between 55 and 65, 81% used internet daily ^[19]. Third, one must have stable INR values: during a period of at least five days at least two INR values must be within therapeutic range. Patients who meet the criteria for self-management will be approached for participation in the study. Because self-management is already a regular care process of the Saltro Thrombosis Service, the group training is also available for people who are not willing to enter the study. The e-Learning is dedicated for participants of the study as this is a new implementation method.

..... Recruitment of patients

Patients of the Saltro Thrombosis Service who receive regular care will be recruited. In 2013, 8950 patients received usual care from the Saltro Thrombosis Service, of which 85% with long-term indications. A random selection of 1632 patients was approached for participation in the study using three methods:

1. First, a randomly selected group of 475 patients was informed by letter. Of these, 233 patients responded and 59 were willing to participate in the study.
2. Second, we approached patients through personal invitation by nurses of the Saltro Thrombosis Service who collect blood by venipuncture. All nurses were trained by the research team to inform patients well about the study and research goals. During five months, nurses actively informed 692 patients about self-management. Of those, 139 patients were interested to participate in the study. In addition, 234 were interested in self-management too, but not in participation in the study.
3. Third, we recruited patients by telephone. Two trained research assistants called patients at home to inform them about the possibilities of self-management and about the study. By telephone 465 patients were approached,

of which 111 were willing to participate in the study. In addition, 52 patients signed up for self-management but were not willing to participate in the study.

Participants were only included in the study after written informed consent was received. Because not all patients signed an informed consent, 247 participants were finally included. Of these, 110 continued to receive regular care and 137 patients were randomly divided in group 1 and 2 using a computer program. In group 1 (e-Learning) 63 patients were included and in group 2 (group training) 74 patients were included. In Figure 2 recruitment is summarized.

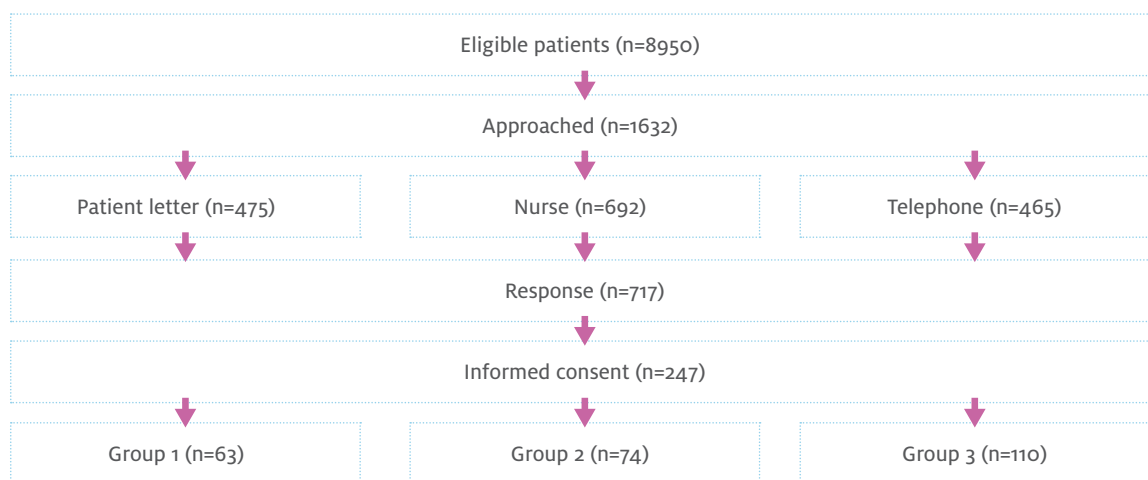


Figure 2. Schematic summary of recruitment; A schematic summary of the number of eligible patients, how many of them were approached, with what method they were approached, how many responded, how many are participating, and in which group

Patients who are willing to participate will receive rewards: a € 25,- gift card after completing the first set of questionnaires and a € 50,- gift card after completing the last set of questionnaires after 18 months.

..... Responder analysis

The total population of the Saltro Thrombosis Service on January 1st, 2014 was 10,209 patients of which 8,939 patients received regular care (eligible patients) and 1,271 self-management (894 self-monitoring and 377 self-dosage). 53% were men and 47% women. The mean age was 73 years (SD 14). In the study population 247 patients were included of which 72.9% were men and 27.1% women. The median age was 66.9 (IQR 59.5–72.7) years in the total group; 65 years in group 1 and 65.8 years in group 2, and 69.6 years in group 3. Analysis showed a significant difference in median age between the groups.

Younger men participated in the PORTALS trial compared to patients who declined participation. The average INR of the participants did not significantly differ from the eligible population at the start of the study. In Figure 3 the characteristics of the patients are summarized.

Saltro Thrombosis Service Centre				
	Self-Management		Usual Care	Eligible patients
Patients	Group 1	Group 2	Group 3	
Age in years* [IQR]	65.0 [56.2-67.7]	65.8 [56.4-70.4]	69.6 [64.0-74.9]	73
Males (%)	47 (74.6)	52 (70.3)	81 (73.6)	5410 (53)
INR	2.9	2.9	2.9	2.9

Figure 3. Characteristics of eligible patients versus included patients; The average age, percentage of males, and average INR of eligible patients versus included patients is shown

Among patients who were recruited by letter we asked non-participants to inform us about their reasons. 35 patients filled in the non-responders form 12 patients did not want to start self-management because they had no computer or internet access, 7 patients were satisfied with regular care and wanted to continue it, 6 patients felt they were too old, 10 patients had other reasons such as painful fingers (1), physical inabilities (2), training is too much effort (2), insecurity (2) or unknown reasons (3).

..... Allocation procedure

Participants were randomly selected for e-Learning (group 1) or group course (group 2) during the registration procedure for the training by a computerized program. Participation in group 3 was not randomized but free choice for patients.

In Figure 2 the total amount of included patients is summarized.

..... Intervention

This study investigates the effect of different implementation strategies on adequate training for self-management skills in patients with AT expressed in TTR, as well as potential determinants of the effect. We compare group training versus e-Learning. Patients who follow e-Learning have to pass at least three modules. The first module contains general education about anticoagulation including test questions. Patients can only successfully

pass this first module after all questions are answered correctly. They then receive a written confirmation. With this confirmation patients can pick up a self-testing device at one of the Saltro Thrombosis Service locations. Furthermore, patients get access to the second module that teaches them to use the self-testing device. After one or two weeks patients have an appointment with a nurse of the Thrombosis Service Centre to show their self-testing skills. If the skills are sufficient, the nurse explains the patients how to use the online web portal. The following three months a training period is applicable, during which patients measure their INR weekly and inform the Thrombosis Service using the web portal. After three months, patients have another control appointment to check their self-testing skills technique and adequate use of the web portal. If patients are able to provide reliable INR values by self-measurement and if they adequately use the web portal to inform the Thrombosis Service about testing results and relevant medical information, the self-monitoring training is ended. From that moment on, patients have control appointments with the nurse every six months. In addition, patients are offered to continue with training in self-adjustment of medication dosage. This training is only available in a group course. The group training consists of two meetings. During the first meeting patients are trained to use the device to measure their own INR and they are trained to use the web portal. Patients practice at home for three weeks. At the second meeting the capillary technique of patients is checked by nurses of the Thrombosis Service. In addition, patients receive general education about anticoagulation. The following three months a training period is applicable during which patients measure their INR weekly and inform the Thrombosis Service using the web portal. After three months patients have a control appointment with the nurse to check their capillary technique and to discuss the training period. If patients are able to provide reliable INR values by self-measurement and if they adequately use the web portal to inform the Thrombosis Service about testing results and relevant medical information, the self-management training is ended. From that moment on, patients have control appointments with the nurse every six months. In addition, patients are offered to continue with training in self-adjustment of medication dosage. This training is only available in a group course.

The regular care group receives traditional thrombosis care, which means a basic instruction by nurses of the Saltro Thrombosis Service in their own home. Patients are explained what locations they can go to for venous puncture. Based on analyses of the blood samples (INR values) experienced

thrombosis doctors give written instructions about medication dosage and lifestyle to the VTE patients. This also includes indication for follow-up puncture.

All training schedules are summarized in Figure 4.

Group 1	Group 2	Group 3
<ul style="list-style-type: none"> • General education (e-Learning) about anti coagulation + test • Self-testing device • Training (e-Learning) Self-testing • Three months of e-Learning + Self-testing 	<ul style="list-style-type: none"> • Group course + training • Self-testing + how to use webportal course • Three weeks practice at home • Group course about anti coagulation • Three months of training at home 	<ul style="list-style-type: none"> • Basic training
<ul style="list-style-type: none"> • Self-testing device 	<ul style="list-style-type: none"> • Self-testing device 	<ul style="list-style-type: none"> • Venipuncture at home or in facilities
<ul style="list-style-type: none"> • Control and quality check by nurse • Continuing self-management program + Control and quality check by nurse every six months 	<ul style="list-style-type: none"> • Control and quality check by nurse • Continuing self-management program + Control and quality check by nurse every six months 	<ul style="list-style-type: none"> • Written instructions by Thrombosis doctor

Figure 4. Time course for group 1, 2 and 3; The three groups and the time courses of their trainings, blood testing procedures, and instructions

.... Data collection

The data collection consists of questionnaires to measure the determinants and secondary outcomes, that patients of group 1 and 2 receive by e-mail. Patients in research group 3 (who do not work with the web portal) receive the same questionnaires either by e-mail or post. In case of non-response we will send two reminders by mail or email and will approach the patients once by telephone. In Figure 5 planning of measurements is summarized. There are four measurements in this study during a period of 18 months. INR values and thromboembolic events are monitored and registered daily by professionals of the Saltro Thrombosis Service. In addition health care use, the number of self-tests and use of the portal are continuously registered in the web portal. Data collection is summarized in Figure 5.

t in months	EQ-5D	GSES	Satisfaction patient	Sociodemographic characteristics	TTR	Events	Use Device	Use Portal	Health Care Use
T ₁ = 0			X	X	↓	↓	↓	↓	↓
T ₂ = 6	X		X		↓	↓	↓	↓	↓
T ₃ = 12	X		X		↓	↓	↓	↓	↓
T ₄ = 18	X	X	X		↓	↓	↓	↓	↓

Figure 5. Measurements over time; A schematic overview of the different types of measurements on T₁ = 0, T₂ = 6, T₃ = 12, and T₄ = 18 months

..... Outcome parameters

At first, we compare clinical outcomes (TTR) and complications between three groups; second we compare TTR, complications and self-management skills of two different implementation methods in group 1 and 2. Second, the relationship between self-management skills, clinical outcomes, and individual characteristics will be investigated.

..... Primary outcome

Health status is the primary outcome, expressed by TTR and severe complications (bleedings and thromboembolic events). TTR is computed as INR values within therapeutic range based on individual targets, calculated with the Rosendaal method ^[20]. INR values will be measured using a whole blood PT/INR monitor (CoaguChek, Boehringer Mannheim, Germany). Bleedings and thromboembolic events will be registered in patient files by professionals of the Saltro Thrombosis Service during the total study period of 18 months. Events can be reported by general practitioners and hospital professionals by e-mail or telephone, or by patients themselves using the online portal, e-mail, or telephone.

In this study, adequate self-management skills are defined as a) the ability to correctly measure one's own INR; b) the ability to use the online web portal to report all measured INR values; c) the ability to use the online web portal to report all relevant medical conditions and d) the ability to correctly calculate dosage schedules. The latter being only applicable if

patients voluntarily choose to self-adjust their own medication intake. Correct self-testing of INR will be judged by thrombosis nurses during yearly control visits. We registered the usage of the self-management platform, including sharing of information and calculation of medication dosage; the amount of login sessions will be used as a measure for self-management skills. The usage counts will be analyzed.

..... Determinants

We expect that the relationship between the level of self-management skills and clinical outcomes is influenced by socio-demographic, (psycho) social characteristics, and self-efficacy.

Self-efficacy is measured using the General Self-Efficacy Scale (GSES), which will be displayed at baseline. This 10-item questionnaire was designed in 1981 by Jerusalem en Schwarzer ^[21]. The items are scored by a four-point scale on which a higher score reflects higher self-efficacy. Research in 28 countries showed that Cronbach's alpha varies between .76 and .90, of which mostly above .80 ^[22].

Socio-demographic characteristics will be assessed by a purpose-designed questionnaire (online). As use of the web portal is part of the self-management program and as decreased access to internet and low general health outcomes have been associated with lower socioeconomic status, minority racial/ethnic groups, older age, and poorer health we will also include the following characteristics in our questionnaires: age, socioeconomic status, marital status, and general use of online and digital products and services.

..... Secondary outcomes

Quality of life (QoL) is assessed using the EuroQol-5D (EQ-5D). This questionnaire contains 5 items with a 3-point Likert scale. A higher score reflects a higher quality of life. The EQ-5D comprises 5 levels: mobility, self-care, daily activity, pain/discomfort, and anxiety/depression. Research showed that the EQ-5D is a reliable and valid questionnaire ^[23]. The EQ-5D can be used to compute QALY's, which are necessary to evaluate cost-effectiveness. Direct costs of both intervention methods will be included in this study. Intervention costs include development costs of e-Learning and costs of group courses. Development costs are provided retrospectively by the owner of the portal. Implementation costs are administered by the research group, and mainly consist of personnel costs and practice materials. Health care use of the Saltro Thrombosis Service is constantly registered in

this study the health care use of the Saltro Thrombosis Service is constantly registered.

..... Data analyses

1. Baseline characteristics between the 3 groups will be explored using Chi-square tests and Kruskal-Wallis tests.
2. To investigate the effect of different implementation methods of training versus the parallel cohort group, TTR and complications between groups will be analyzed using multilevel linear regression modelling (mixed models). First, outcomes will be compared between the three groups. A second analysis will be used to compare the difference in effect between e-Learning and group training (group 1 vs group 2) on TTR, complications and usage using mixed models. Analyses will be adjusted for age and gender.
3. To examine the impact of General Self-Efficacy Scale and education on the effect of different implementation methods, those variables will be included in the mixed models.

..... Ethical principles

Increasing costs and deficit of health care professionals stress the urge for efficient health care processes. Benefits of online supported self-management regarding clinical effects have been repeatedly demonstrated, but extensive integration in clinical practice stays behind. This study aims to explore implementation methods for optimal integration of online supported self-management in primary care. Optimal integration stimulates patients in self-management and improves efficiency and accuracy administration and communication. We expect patients to improve their health status while decreasing health care use. On the other hand, self-management will not be offered to patients who are unable to use internet. They will however not be in disadvantage by receiving usual care. All over, this study will be conducted according to the principles of the Declaration of Helsinki (version 59, 2008) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

..... Discussion

Adequate self-management requires the individual ability to deal with symptoms, treatment, and physical and social consequences of a disease. The basic principle is that behavioral change cannot succeed without

patients taking their responsibility ^[24]. Education is an important factor for the enhancement of self-management skills; research showed that patients who understand more about their disease, health, and lifestyle have better experiences and health outcomes and often use less health care resources. The effect is even bigger when these patients are empowered to and responsible for managing their health and disease ^[25].

In this study, we aim to empower patients with AT by providing self-management including a web portal and education. We expect this self-management program to help patients to better manage their own INR values and medication use, thereby increasing health status and diminishing thromboembolic events and hospitalization. Health status (INR and TTR) is the main outcome. We investigate the optimal implementation strategy of training of self-management and the relationship with personality and characteristics to provide practical insights in determinants of successful implementation of patient self-management portals in real-life thrombosis care settings.

By analyzing the non-participation reasons (35 patients), we can conclude that the possession of a computer, age and satisfaction with usual care are the most important reasons not to start with this study. These aspects can create a bias in the individual ability of the whole self-management group of patients how to deal with their disease.

This PORTALS study has several strengths. The self-management in combination with a web portal and different forms of education are integrated in real life care settings and will therefore provide practical insights and knowledge of eHealth in daily practice. We expect to learn what type of education can be a significant factor in the adoption of self-management. Furthermore, this study adds Dutch evidence to the existing body of knowledge which is important because local political and financial factors have a major impact on successful integration in daily practice ^[26]. This study also has several limitations: from a technical perspective, the development of the web portal is a difficult task due to lack of broad experience in the field. The content of the web portal will affect our outcomes, but is beyond the scope and influence of our study. From a human perspective, effects through self-management imply behavioral changes. Behavioral changes require time, whereas the study period is limited to 18 months.

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Abbreviations

- **AF:** Atrial fibrillation
- **COPD:** Chronic obstructive pulmonary disease
- **EQ-5D:** EuroQol-5D
- **GSES:** General Self-Efficacy Scale
- **INR:** International Normalized Ratio
- **NOACs:** Novel oral anticoagulants
- **POCT:** Point-of-care testing
- **RCT:** Randomised controlled trial
- **SD:** Standard deviation
- **TTR:** Time in therapeutic range
- **VTE:** Venous thromboembolism
- **WMO:** Wet medisch-wetenschappelijk onderzoek met mensen (Medical Research Involving Human Subjects Act)

Chapter 7

Effect of a combined education and eHealth programme on the control of oral anticoagulation patients (PORTALS study): a parallel cohort design in Dutch primary care

Esther PWA Talboom-Kamp | Noortje A Verdijk | Marise J Kasteleyn |
Lara M Harmans | Irvin JSH Talboom | Mattijs E Numans | Niels H Chavannes

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Abstract

..... Objectives

To analyse the effect on therapeutic control and self-management skills of the implementation of self-management programmes, including eHealth by e-Learning versus group training.

..... Setting

Primary Care Thrombosis Service Center.

..... Participants

Of the 247 oral anticoagulation therapy (OAT) patients, 63 started self-management by e-Learning, 74 self-management by group training and 110 received usual care

..... Intervention and methods

Parallel cohort design with two randomised self-management groups (e-Learning and group training) and a group receiving usual care. The effect of implementation of self-management on time in therapeutic range (TTR) was analysed with multilevel linear regression modelling. Usage of a supporting eHealth platform and the impact on self-efficacy (General Self-Efficacy Scale (GSES)) and education level were analysed with linear regression analysis. After intervention, TTR was measured in three time periods of 6 months.

..... Main outcome measures

(1) TTR, severe complications, (2) usage of an eHealth platform, (3) GSES, education level.

..... Results

Analysis showed no significant differences in TTR between the three time periods ($p=0.520$), the three groups ($p=0.460$) or the groups over time ($p=0.263$). Comparison of e-Learning and group training showed no significant differences in TTR between the time periods ($p=0.614$), the groups ($p=0.460$) or the groups over time ($p=0.263$). No association was found between General Self-Efficacy Scale and TTR ($p=0.717$) or education level and TTR ($p=0.107$). No significant difference was found between the self-management groups in usage of the platform (0–6 months $p=0.571$; 6–12 months $p=0.866$; 12–18 months $p=0.260$). The percentage of complications was low in all groups (3.2%; 1.4%; 0%).

..... Conclusions

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. The TTR was similar in self-management and regular care patients. With adequate e-Learning or group training, self-management seems safe and reliable for a selected proportion of motivated vitamin K antagonist patients.

Introduction

Venous thromboembolism (VTE) and atrial fibrillation (AF) are common causes of mortality and morbidity, with rising prevalence and medical costs.^[1–3] Oral anticoagulation therapy (OAT) reduces thromboembolic events in AF, prosthetic heart valves, acute myocardial infarction and other conditions, and is an effective treatment for VTE.^[4–6] The major risks of OAT are bleeding complications, with a rate of major bleeding among long-term users of vitamin K antagonists (VKAs) of 1.5%–5.2% per year.^[7–9] There is a narrow therapeutic range for VKA, expressed as the international normalised ratio (INR) with an optimal intensity, related to a low rate of events, between 2.5 and 4.9.^[10,11] This is relevant, as patients have considerable difficulty in maintaining adequate adherence to VKA regimens, with a significant effect on anticoagulation control.^[12] Structured monitoring and coaching of patients using VKA is essential. This may be carried out by specialised centres in primary care or in hospitals.^[13]

Alternatively, patients might choose to self-manage their VKA monitoring. In the case of VKA, self-management includes monitoring INR values by patients (self-monitoring) and, as a possible next step, self-adjustment of the medication dosage (self-dosage). Nowadays, patients are usually supported by improved eHealth supported self-management programme^[14] with more freedom, improved quality of life and self-efficacy and less burden of specialised centres.^[15,16] Research shows a reduction of thromboembolic events and in all-cause mortality for patients with self-management^[17] due to the fact that patients have greater responsibility, increased awareness, commitment and interest in their condition.^[18]

Adequate self-management is important for all patients with OAT to improve adherence to medication, irrespective of the type of anticoagulation medicine they use.^[19–21] The basic principle of self-management is behavioural change, which is necessary to improve the quality of life of patients and the primary outcomes of their health and disease.^[22] Research on chronic diseases such as diabetes,^[23] chronic obstructive pulmonary disease^[24] and heart failure^[25] has shown that aspects such as self-efficacy (belief in one's capabilities to organise and execute the course of action required to produce given attainments), educational level, socioeconomic status, age and gender are influencing factors in successful self-management and predictors in eHealth usage.^[26]

As education is the basic approach in the development of self-management skills, the strategy used to implement educational support is expected

to affect the individual level of self-management and, thereby, clinical outcomes. To test this hypothesis, we designed the PORTALS study. The aim of this study was to analyse the effect on anticoagulation control of an intervention consisting of an education programme in combination with the use of an online self-management portal. The general definition of self-management is the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition^[27]; in line with this definition, both self-monitoring and self-dosage of medication are considered important self-management skills in the PORTALS study (PORTal implementation within anTicoagulation care; AmpLification of self-management).

Methods

Study design

For the PORTALS study, we designed a quality improvement intervention and compared strategies in an implementation study.^[28] Two methods were developed to train long-term VKA patients of the Saltro Thrombosis Service (outpatient anticoagulation clinic and laboratory) in self-management routine care. Using this design, we aimed to examine the influence of the training strategy on clinical outcomes and usage of the supporting eHealth platform. Full methodological details are reported elsewhere^[29]; Table 1 presents an overview of the study design. A parallel cohort design was used to investigate determinants of optimal implementation of self-management by comparing two different training methods. After inclusion, participants were randomly divided into subgroups: one group was trained and educated by e-Learning (group 1) and the other group received face-to-face group training (group 2). Patients unable or unwilling to dose their medication were free to continue with only self-monitoring. Patients who did not wish to start with self-management were invited to participate in the non-self-management group, that is, a parallel cohort group receiving usual care (group 3). Group three provided valuable information about the patients who were unable/unwilling to use an online supported self-management programme. Based on our parallel cohort design, comparison between e-Learning and group training for self-management (group 1 and 2) and non-self-management patients (group 3) is applicable, considering the specific conditions in the choice of the statistics.

	Saltro Thrombosis Service Centre		
	Self-management		Usual Care
	Group 1	Group 2	Group 3
Patients	#72	#72	#72
Instruction	e-Learning	Group Course	Basic Short training
	Disease-specific knowledge Self-testing skills Use of the web-portal (voluntary) Self-adjustment of medication	Disease-specific knowledge Self-testing skills Use of the web-portal (voluntary) Self-adjustment of medication	
Platform	Self-management	Self-management	

Table 1 Overview of the study design: details of groups 1, 2 and 3

..... Participants

The present study focused on patients of the Saltro Thrombosis Service who voluntarily chose to start with self-management. The inclusion criteria for patients to start with self-management were a long-term indication for anticoagulants, internet access and stable INR values (at least three INR values in succession must be within therapeutic range). Patients who met the criteria for self-management were approached for participation in the study. Because self-management (including eHealth) is already an option for patients of the Saltro Thrombosis Service, the group training was also open to patients who were not willing to participate in the study. The e-Learning was reserved for participants of the present study, as this was a new implementation method. All patients provided written informed consent before participation in the study.

..... Patient involvement

Patients were neither involved in the design nor in defining research questions and outcome measures of the study; however, they were actively involved in the development of the self-management platform Portavita. To maximise the involvement of patients, we did not randomise the intervention groups (self-management and usual care); we chose a recruitment design in which patients of the Thrombosis Service voluntarily chose to start with self-management. During the study, patients could give feedback on the

intervention and on the self-management platform; their satisfaction was continuously monitored. Feedback from patients made it possible to optimise their care. All patients will be informed about the results of this study.

..... Recruitment of patients and non-participation

Patients of the Saltro Thrombosis Service who received regular care without a self-management programme were eligible for recruitment. In 2013, 8950 patients received usual care from the Saltro Thrombosis Service of which 85% had a long-term indication. From June 2013 onward, a random selection of 1632 patients was approached for participation in the present study using three methods, (1) information and invitation by letter, (2) personal invitation by specialised nurses and (3) invitation by telephone. Patients who did not wish to start with self-management were invited to participate in a parallel cohort group receiving usual care (group 3), thereby providing valuable information about non-participants. Baseline characteristics of all regular patients of the Saltro Thrombosis Service also provided valuable information about non-participants.

..... Intervention

The intervention in groups 1 and 2 consisted of a training programme in combination with the use of an online self-management portal called Portavita. In group 1, patients used an e-Learning that was specifically designed for the PORTALS study (see online multimedia supplementary appendix 1).

Group 1	Group 2	Group 3
General education (<i>e-Learning</i>) about anticoagulation + test Self-testing device Training (<i>e-Learning</i>) Self-testing + use of web portal Three months of e-Learning + Self-testing	Group course with training Self-testing + use of web portal Three weeks practice at home Group course about anti coagulation Three months of training at home	Basic training
Self-testing device	Self-testing device	Venipuncture at home or in facilities
Control and quality check by nurse Continuing self-management program + Control and quality check by nurse every six months	Control and quality check by nurse Continuing self-management program + Control and quality check by nurse every six months	Written instructions by thrombosis doctor

Table 2 Training methods in group 1, 2 and 3

Table 2 summarises the programme in all groups: the e-Learning modules in group 1, the group training modules in group 2 and the basic training in group 3. In group 1, the training was provided by e-Learning that started with a personal login procedure and an online instruction; the interim control and quality checks were carried out by specialised nurses of the Thrombosis Service. The group course in group two was carried out by specialised and expert healthcare professionals. Both training methods had the same content but were offered in a completely different manner. In the PORTALS study, the online self-management portal used is called Portavita (see online multimedia supplementary appendix 2). This application combines a patient portal and a healthcare provider portal. The healthcare portal leaves space for the OAT protocol, medication records and information about complications. The Portavita anticoagulation self-management patient portal has become widely accepted; it provides patients with a diary tool for self-monitoring and self-dosage, education; it also allows personal notes and healthcare professionals can send advice and notes to the patient. It implies that the patient analyses a drop of blood using a home INR monitor. The patient can access the web-based patient portal to enter the INR and specific information for the health professional (intervention, bleeding, change in medication, vacation, etc). Clinically validated inbuilt algorithms provide advice regarding the next dose and test interval. The only things needed are an internet connection and a device like a personal computer, tablet or smartphone. When logging on (username +password) for the first time to Portavita, every user was directed to the homepage. From there, users could access all functionalities of the portal. The logon procedure of this portal is based on Dutch security legislation and guidelines (the Dutch Personal Data Protection Act).

.... Data collection

INR values, thromboembolic events, bleedings, medication and indication were monitored and registered continuously by patients in the portal and by professionals of the Saltro Thrombosis Service. We measured the INR, complications and medication during a period of 6 months before and 18 months after starting the intervention (ie, 24 months in total). The data collection also consisted of questionnaires (at baseline and after each 3×6-month period) to measure the determinants and outcomes. Patients of group 1 and 2 received these questionnaires by email, and patients in group 3 by email or by post. In addition, the number of self-tests and use of the

portal were continuously registered in the portal. Data on the total population of the Saltro Thrombosis Service were also collected.

..... Outcome measures and determinants

The primary outcome of this study was therapeutic control expressed as the INR control over time and severe complications (bleedings and thrombo-embolic events). To summarise the INR control over time, the percentage of time in therapeutic range (TTR) of INR was used, calculated with the Rosendaal method.^[30] TTR values were calculated for two INR ranges (INR 2–3 and INR 2–3.5) because different calculations are used in Dutch and in international guidelines. TTR was measured at four moments: at 6 months before intervention and at 3×6-month periods (total of 18 months) after starting the intervention. Serious complications were defined as those needing treatment or medical evaluation. An independent thrombosis specialist was responsible for classifying serious complications at the end of the trial. The total follow-up period for all these measures was 24 months.

Furthermore, the self-management skills of participants were evaluated. Self-management skills were defined as usage of the self-management platform, reflected as the amount of login sessions. Self-monitoring and self-dosage are registered within the same login session. The usage counts were analysed. The determinants were self-efficacy and sociodemographic characteristics. Self-efficacy was measured at baseline using the General Self-Efficacy Scale (GSES), with items scored on a four-point scale with a higher score reflecting higher self-efficacy.^[31] Sociodemographic characteristics were assessed by an online questionnaire addressing the following characteristics: age, gender, education level, marital status, working status (labour) and quality of life (QoL), which was assessed using the EuroQol-5D (EQ-5D) and displayed at baseline. The EQ-5D is a five-item questionnaire with a higher score reflecting a higher QoL. Sample size and statistical methods To detect a relevant effect of the new implementation strategy of e-Learning or group training ($>5\%$)^[32] at a power 80% and $\alpha=0.05$, we calculated that a sample size of 63 patients was required per group. Considering a 15% dropout, 72 ($63/0.85$) patients were needed per study group. Baseline characteristics between the three groups were explored using χ^2 tests and Kruskal- Wallis tests.

To investigate the effect of the different implementation methods of training versus the parallel cohort group on TTR, multilevel linear regression

modelling (mixed models) was used. First, TTR outcomes were compared between the three groups. A second (mixed models) analysis was used to compare the difference in effect between e-Learning and group training (group 1 vs group 2) on TTR. The variable TTR was included as outcome in the model. The periods of TTR measurements (time), the group and the interaction term (time×group) were included as predictors. Both analyses were adjusted for age and gender.

To examine the impact of General Self-Efficacy Scale and education on the effect of the different implementation methods, multiple linear regression analyses were performed with TTR at time point 3 as outcome and General Self-Efficacy Scale and education as predictors. Analyses were adjusted for age and gender.

A linear regression analysis was used to analyse usage (mean number of login sessions) of the portal Portavita in groups 1 and 2.

Results

A total of 1632 VKA patients of the Saltro Thrombosis Service were invited to participate, of which 56% (n=915) declined (figure 1). Patients were invited in three different ways: by letter (n=475), by personal invitation during a visit to the Thrombosis Service (n=692) and by telephone (n=465). 717 patients were interested in participation in the study; 247 patients eventually signed an informed consent. During the process of inviting patients for the PORTALS study, patients were asked about their reasons for not participating: the main reasons were not having a computer or internet, no digital skills, the effort of participating in a trial and their high level of satisfaction with usual care. Participants were included in the study only after providing written informed consent but, because some patients failed to do this, 247 participants were finally included. Of these, 110 continued to receive regular care (group 3) and 137 patients were randomly divided into group 1 and 2 using a computer program. After randomisation, 63 patients were included in group 1 (e-Learning) and 74 in group 2 (group training). Figure 1 summarises the recruitment process, including the reasons for loss to follow-up.

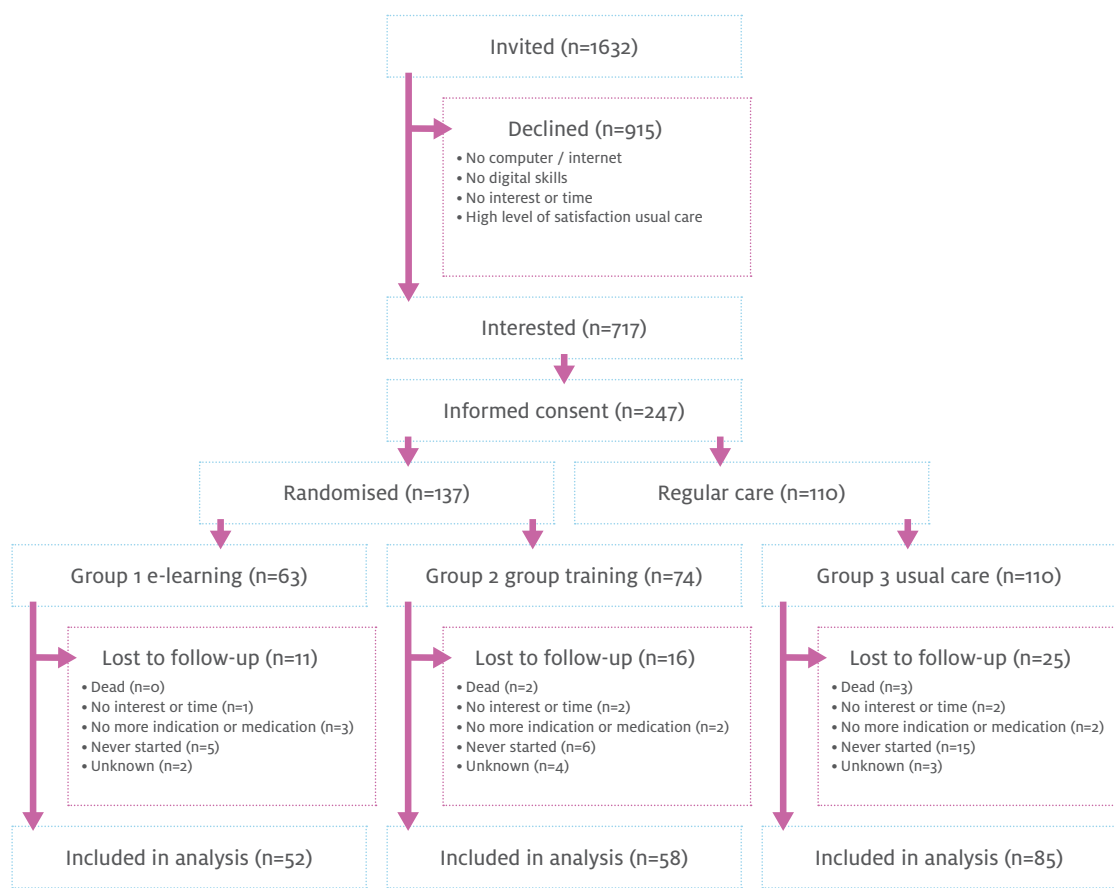


Figure 1 Flowchart of the PORTALS study

..... Characteristics of the total population of the thrombosis service

The characteristics of all VKA patients of the Saltro Thrombosis Service in 2015 are shown in table 3.

Total patients N	11132
Male N (%)	6009 (54.0)
Self-management N (%)	1986 (17.8)
Male self-management N (%)	1260 (63.4)
Medication	
Acenocoumarol N (%)	8360 (75.1)
Phenprocoumon N (%)	2761 (24.8)
Warfarin N (%)	11 (0.1)
Indications	
AF N (%)	7430 (66.8)
Ven thromboembolism N (%)	1673 (15.0)
Artificial valve N (%)	720 (6.5)
Other N (%)	1309 (11.8)
Severe complications	
Major bleedings N (%)	219 (2.0)
Thromboembolism N (%)	85 (0.8)

Table 3 Clinical characteristics of the population of the Saltro Thrombosis Service

..... **Baseline characteristics of study participants**

Table 4 presents the baseline characteristics of the participants: median age was 66.9 years, and median TTR was 54.7 (for INR range 2–3) and 79.1 (for INR range 2–3.5). Of these patients, 66% had an indication of AF and 77.3% used acenocoumarol as oral anticoagulation medication. No significant differences were found between the three groups for gender ($X^2_2=0.38$, $p=0.826$), TTR ($X^2_2=3.68$, $p=0.159$), indication ($X^2_2=8.33$, $p=0.215$) and marital status ($X^2_2=7.47$, $p=0.280$). The three groups differed significantly in age ($X^2_2=19.96$, $p=0.000$), baseline GSES ($X^2_2=15.08$, $p=0.001$) and EQ-5D ($X^2_2=6.66$, $p=0.036$), use of medication ($X^2_2=15.23$, $p=0.004$), education level ($X^2_2=23.72$, $p=0.000$) and work status ($X^2_2=13.01$, $p=0.043$) (table 4).

	Group 1	Group 2	Group 3	p-value	Total
N	63	74	110		247
Age in years* [IQR]	65.0 ^a [56.2-67.7]	65.8 ^a [56.4-70.4]	69.6 ^b [64.0-74.9]	0.00**	66.9 [59.5-72.7]
Males N (%)	47 (74.6)	52 (70.3)	81 (73.6)	0.826	180 (72.9)
TTR INR range 2-3 (%)* [IQR]	50.2 [39.1-67.1]	52.9 [39.0-68.6]	57.4 [40.1-75.1]	0.159	54.7 [39.8-70.7]
TTR INR range 2-3.5 (%)* [IQR]	76.3 [67.0-86.0]	77.1 [64.1-85.3]	85.6 [72.0-93.5]	0.159	79.1 [68.2-88.8]
GSES* [IQR]	3.5 ^a [3.1-3.8]	3.3 ^{a,b} [3.0-3.7]	3.1 ^b [2.9-3.5]	0.001**	3.3 [3.0-3.7]
EQ-5D* [IQR]	1.0 ^a [0.81-1.0]	0.84 ^{a,b} [0.78-1.0]	0.84 ^b [0.78-1.0]	0.036**	0.84 [0.81-1.0]
Indication	42 (66.7)	44 (59.5)	77 (70.0)	0.215	163 (66)
AF N (%)	13 (20.6)	18 (24.3)	11 (10.0)		42 (17)
Ven thromboembolism N (%)	2 (3.2)	3 (4.1)	4 (3.6)		9 (3.6)
Artificial valve N (%)	6 (9.5)	9 (12.2)	18 (16.4)		33 (13.4)
Other N (%)					
Medication				0.004**	
Acenocoumarol N (%)	51 (81) ^a	64 (86.5) ^a	76 (69.1) ^b		191 (77.3)
Phenprocoumon N (%)	10 (15.9) ^a	10 (13.5) ^a	34 (30.9) ^b		54 (21.9)
Warfarin N (%)	2 (3.2) ^a	0 (0) ^a	0 (0) ^a		2 (0.8)
Education level				0.00**	
Low N (%)	7 (12.1) ^a	13 (19.1) ^a	33 (35.9) ^b		53 (24.3)
Medium N (%)	24 (41.4) ^a	32 (47.1) ^a	46 (50.0) ^a		102 (46.8)
High N (%)	27 (46.6) ^a	23 (33.8) ^b	13 (14.1) ^c		63 (28.9)
Marital status				0.280	
Married N (%)	49 (84.5)	50 (73.5)	73 (79.3)		172 (78.9)
Widow N (%)	1 (1.7)	6 (8.8)	4 (4.3)		11 (5.0)
Divorced N (%)	1 (1.7)	6 (8.8)	4 (4.3)		11 (5.0)
Single N (%)	7 (12.1)	6 (8.8)	11 (12.0)		24 (11.0)
Labour				0.043**	
No paid work N (%)	28 (48.3) ^a	29 (42.6) ^a	39 (42.4) ^a		96 (44.0)
Paid work N (%)	19 (32.8) ^a	20 (29.4) ^a	14 (15.2) ^b		53 (24.3)
Household N (%)	8 (13.8) ^a	11 (16.2) ^a	23 (25.0) ^a		42 (19.3)
Incapacitated N (%)	3 (5.2) ^a	8 (11.8) ^a	16 (17.4) ^a		27 (12.4)

Table 4 Baseline characteristics of patients with VKA therapy in the PORTALS study

*Values are medians and corresponding Interquartile Ranges [IQR]

** Between-group differences ($P < 0.05$) are indicated by ** Each superscript (a,b,c) letter denotes a subset of sample categories which do not differ significantly from each other at the 0.05 level.

TTR is the therapeutic international normalized ratio (INR) range, General Self-Efficacy Scale is the General Self-efficacy Scale, EQ-5D EuroQol five dimensions questionnaire is a standardized instrument for use as a measure of health outcome. N Missing questionnaires: General Self-Efficacy Scale 29, EQ-5D 32, indication 0, medication 0, education 29, marital status 29, labour 29.

..... Therapeutic control before and after intervention

Figure 2A shows the TTR values using the INR 2-3 in the three groups, 6 months before the intervention and in the 3x6-month periods after the intervention; the TTR values using the INR 2-3.5 are presented in figure 2B (see online supplementary appendix 3). Analysis of the three groups showed no significant difference in TTR values over time ($F_{3,631}=0.755$, $p=0.520$), between the groups ($F_{2,211}=0.924$, $p=0.398$) or between the groups over time ($F_{6,631}=1.009$, $p=0.418$). Analysis of the two self-management groups showed no significant differences in TTR values between the four time periods ($F_{3,378}=0.602$, $p=0.614$). Also, no significant differences in TTR were found between group 1 and 2 ($F_{3,378}=0.548$, $p=0.460$) or between these two groups overtime ($F_{3,378}=1.335$, $p=0.263$).

The sensitivity analyses showed that using an INR of 2-3.5, instead of 2-3, had no marked effect on the results, although a significant time effect was found. Results are presented in figure 2B in Appendix 3. During the 18-month period after the intervention, across all three groups, a total of three severe complications occurred (3/247=1.2%): that is, two muscular bleedings in the e-Learning group (2/63=3.2%) and one cerebrovascular accident among patients receiving group training (1/74=1.4%); no complications occurred in the usual care group.

TTR (1) pre and after intervention

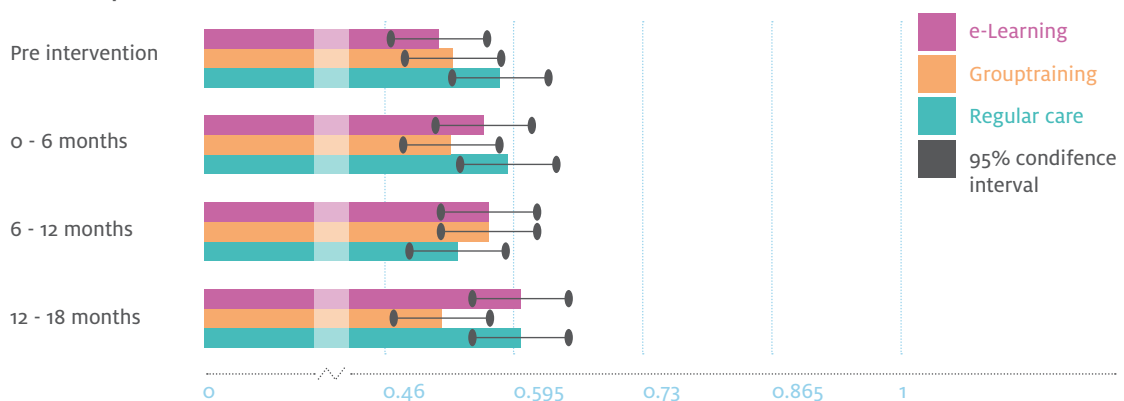


Figure 2A Health status based on TTR (for INR range 2-3) for the three groups. INR, international normalised ratio; TTR, time in therapeutic range.

..... Educational level and GSES

Educational level was not associated with the TTR in the last 6 months ($F_{2,198}=2.263$, $p=0.107$); education level did not modify the effect of the different implementation methods on TTR ($F_{4,198}=1.659$, $p=0.161$). No association was found between the General Self-Efficacy Scale and TTR in the last 6 months ($F_{1,198}=0.132$, $p=0.717$); General Self-Efficacy Scale did not modify the effect of the different implementations methods on TTR ($F_{2,198}=1.762$, $p=0.174$).

..... Usage of the platform

Figure 3 presents the usage by patients in groups 1 and 2 (using the log files of the Portavita platform) during the 18 months after start of the intervention. Patients logged on to the platform to register their INR; some also used it to establish their medication dosage or to communicate with healthcare professionals of the Thrombosis Service. There was no significant difference between groups 1 and 2 in usage of the platform during the three time periods (0-6 months: mean 20.75, SD 5.20, $F_{1,109}=0.091$, $p=0.764$; 6-12 months: mean 13.00, SD 7.0, $F_{1,109}=0.029$, $p=0.866$; 12-18 months: mean 12.5, SD 7.39, $F_{1,109}=1.28$, $p=0.260$).

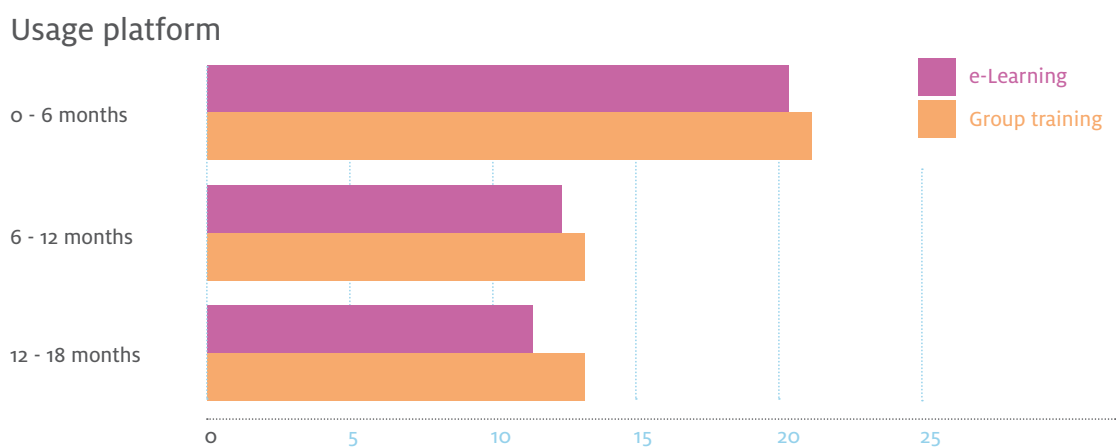


Figure 3 Usage of the platform in group 1 and group 2 after start of the intervention.

Discussion

In the present study, no differences were found in therapeutic control and usage of the platform between anticoagulation self-management patients trained by e-Learning and by group training. Moreover, the clinical results for self-management patients were similar to those of patients receiving regular care. Therefore, we conclude that, with adequate training through e-Learning or group training, self-management is safe and reliable for a selected proportion of motivated patients receiving VKA. The PORTALS study provides valuable information on different implementation methods of OAT self-management, including eHealth.

..... Strengths and limitations

This PORTALS study has several strengths. The study investigates the effect of different education programmes in a situation as close to ‘real life’ as possible, integrated in a self-management programme including eHealth, on clinical outcomes and self-management skills. The study also adds evidence to the existing body of knowledge on implementation of eHealth; this is important because local political/financial factors have a major impact on successful integration of eHealth in daily practice and because self-management is important for patients who will use VKAs in the future.^[33]

This study also has limitations. First, a randomised controlled trial (RCT) was not feasible in our setting of an implementation design in a real-life healthcare system with patients who have differing demands. Instead, an observational study was considered the best option for our context, that is, patients cannot be denied or forced to start with self-management. Furthermore, self-management skills imply behavioural changes. However, behavioural changes require time, whereas the study period was restricted to 18 months. This study also has limitations typically associated with eHealth trials. For example, as patients were free to volunteer, bias might have occurred in our study groups. Users were self-selected and were, presumably, motivated to use the education programme (including the web-based platform) as would be expected in a real-life setting. Of the 1632 invited OAT patients, 247 patients (15%) were willing to participate and provided informed consent. However, only 137 patients (8.4% of invited patients) wanted to participate in the self-management groups and were randomised; other studies have a similar low recruitment rate for self-management trials.^[34] This phenomenon might have affected the

measurability of differences and might also reduce differences between the groups. The high number of participants lost to follow-up in our study ('law of attrition'; the phenomenon of participants stopping usage) is a common finding in eHealth evaluations and one of the fundamental and methodological challenges in the evaluation of eHealth apps.^[35] The loss to follow-up is high with a risk of biased results due to user bias; therefore, these results are only applicable for users of eHealth.

The total population of the Thrombosis Service showed a lower percentage of men than the participants of the present study, although the distribution of indications/ medication was similar. In the total population, the percentage of severe complications was low (bleedings 2%, thromboembolism 0.8%); during our study period the percentage of complications was also low (group e-Learning =3.2%; group training =1.4%; group usual care =0%), indicating a high quality of thrombosis care.

During the process of inviting patients for the PORTALS study, we asked their reasons for not participating (main reasons were: not having a computer/internet, no digital skills, the effort of participating and their high level of satisfaction with usual care). The group with usual care differed significantly from the self-management groups on several baseline characteristics: that is, patients in usual care were older, had a lower education level and fewer of them had paid work. Also, they had a lower General Self-Efficacy Scale and EQ-5D and made less use of acenocoumarol. Patients in the total population of the Thrombosis Service and in the usual care group, might have different wishes and expectations towards care than patients that chose for a self-management programme; that is, self-management programmes are suitable for patients that are highly motivated and have skills for self-management tasks.

Finally, to measure a significant difference in therapeutic control, 72 patients were needed in each group. Although these numbers were not entirely met in group 1 (e-Learning), analysis of the groups should be sufficiently powered to detect relevant differences. In addition, the high number of INR data points collected before and after the intervention has a substantial impact on the strength of the design and the multilevel linear analysis.

Due to these limitations, caution is required when generalising our results to general practice. However, the practical applicability of our results for

other specialised OAT centres is positive, that is, the study provides practical insight into successful implementation of self-management programme consisting of high-quality training and usage of a patient platform.

..... Interpretation of findings

No overall significant differences in therapeutic control were found between the three groups; also, there was no difference in therapeutic control between the group with e-Learning and group training. Therapeutic INR control was good in all groups; in the last 6 months of the intervention period, all groups spent around 58% of time within the narrow therapeutic range 2-3 and 83% of time within the therapeutic range 2-3.5; this indicates high quality and is comparable to other studys.^[34-36] Anticoagulation control levels around 60% for TTR of INR range 2-3 are considered safe.^[36-38] In studies conducted outside specialised care facilities in several different regions, TTR ranged from 40% to 70%.^[13] The national guidelines for the INR range changed during the last 6 months of our PORTALS study; this had a negative impact on the TTR during our last measurement period. Complication rates also compared favourably with international data; our overall adverse event rate was low compared to other studys.^[39-41]

In comparison to literature, the baseline quality of OAT management in the present study can be considered high in all groups; therefore, further improvement through a self-management programme including education was difficult to achieve and the outcomes in the groups remained the same. Finally, both training methods were comparable on the effect of anticoagulation control; for patients and healthcare professionals this means that a good e-Learning programme is a good alternative for labour-intensive group trainings. Based on our study, we recommend considering self-management programmes supported by e-Learning as the preferred plan of action for self-management for anticoagulation patients. Furthermore, self-management with an e-Learning component is suitable for motivated patients with sufficient digital skills; in our opinion, regular anticoagulation care needs to remain available for the rest of the population.

Self-efficacy and educational level of users had no impact on therapeutic control for the different implementation methods. The construct of perceived self-efficacy reflects an optimistic self-belief^[31]; a correlation can be understood based on the belief that one can perform a novel or difficult task or cope with adversity (indicating a higher self-efficacy). In

the present study, self-efficacy was comparable to that in a healthy Dutch population.^[42,43]

The practical value of the Portavita portal is very high for patients because of the functionalities of self-monitoring, self-dosage and digital advice from professional healthcare providers. Because patients use the self-management programme, regular visits to medical facilities are unnecessary. Patients can manage their anticoagulation in their own time and in their own chosen place. Thus, using the self-management programme gives them (extra) freedom; this might be a strong motivating factor for using the programme. Also, the training programmes were sound and sustainable during the entire study period, probably stimulating patients to persevere with their self-management programme. Moreover, e-Learning and group training led to the same usage and, therefore, the same self-management skills. Therefore, we conclude that our e-Learning and group training provide a good start for OAT patients that voluntarily start with a self-management programme including eHealth.

Self-management programmes with eHealth technologies for chronic conditions can be used to enhance self-management and revise the Chronic Care Model; patients who actively participate in their care achieve valuable and sustained improvement in well-being.^[44,45] In many eHealth studies, use of a Personal Health Record or self-management platform can promote an informed/ activated patient and augment the Chronic Care Model for self-management support and productive interactions; even though a direct dosage–effect relation (usually analysed in a classical RCT) is not common in eHealth.^[46] Self-management programmes with good training and practical eHealth platforms have the potential to make chronic care personalised in a blended care model; every patient needs a different approach for optimal therapeutic control. Healthcare providers need to embrace a different role and release tight protocols.^[47] Individual patients have different expectations and wishes, which should be a topic of conversation with each patient. The general scientific basis for self-management applies perfectly to anticoagulation patients, which is confirmed in our study.

More studies are needed (preferably with larger sample groups, and including non-users) to gain more insight into the preferences of various patient groups, as well as the related costs.

The substantial workload generated by integrating a web-based platform

in an OAT self-management programme emphasises the importance of piloting and assessing workforce implications for OAT management centres. The present results provide additional insight into the organisational aspects of the implementation of education programmes into a self-management programme with a platform, including the need to educate and coach patients in the use of web-based platforms.

Conclusion

Our main finding is that there were no differences in therapeutic control and usage of a supporting eHealth platform between anticoagulation self-management patients trained by e-Learning and by group training. Moreover, we found that clinical results for self-management patients are comparable to those of patients receiving usual care. We conclude that with appropriate and sound training through e-Learning or group training, self-management seems safe and reliable for a selected proportion of motivated patients receiving oral anticoagulation treatment. The PORTALS study provides valuable information on different implementation methods of oral anticoagulation self-management, including eHealth.

..... Multimedia Appendix 1

HOME UITLOGGEN BEHEER REVIEW/1

E-LEARNING SALTRO Coursus Bloedstolling - © 2016 - 2

saltro
DIAGNOSTIEK IN DE ZORG

Menu

- 1. GEBRUIKSAANWIJZING CURSUS
- 2. INHOUD VAN DEZE CURSUS
- 3. DE HOOFDSTUKKEN VAN DEZE CURSUS
- 4. Hoofdstuk 1. Bloedstolling en trombose
- 5. Hoofdstuk 2. Antistolling
- 6. Hoofdstuk 3. Controle stollingstijd
- 7. Hoofdstuk 4. Leven met antistolling
- 8. Hoofdstuk 5. Tot slot...

Cursus BLOEDSTOLLING

Ten behoeve van patiënten van de trombosedienst

Bron: Federatie Nederlandse Trombosediensten

Deze cursus duurt ongeveer een half uur

< VORIGE VOLGENDE >

..... Multimedia Appendix 2

PORTA VITA Selfmanagement, S.

Homepage from Selfmanagement, S.

My details Contact Manual & Instructional videos Log out

Personal data

Patient number: SELF01992765

Most recent dosing schedule (provisional)

Dosing period	28-03-2017 until 17-04-2017	Measurement frequency	21 days
Anticoagulation medication	Acenocoumarol 1 mg	Tolerance	3 days
Dosing schedule created on	28-03-2017 by Selfmanagement, S.		
Dose according to step	25		

Important data

Dosing schedule based on INR 3,6 measured on Tue. 28-03-2017 at 06:46

Next Thrombosis Service check-up **Tue. 17-01-2017 at 09:00**

Next blood sampling date Tue. 18-04-2017

	wk. 13	wk. 14	wk. 15	wk. 16
Mon.		3 Apr. 2	10 Apr. 2	17 Apr. 2
Tue.	28 Mar. 1	4 Apr. 2	11 Apr. 1	18 Apr. 2
Wed.	29 Mar. 2	5 Apr. 2	12 Apr. 2	19 Apr. 2
Thu.	30 Mar. 2	6 Apr. 1	13 Apr. 2	20 Apr. 1
Fri.	31 Mar. 2	7 Apr. 2	14 Apr. 2	
Sat.	1 Apr. 1	8 Apr. 2	15 Apr. 1	
Sun.	2 Apr. 2	9 Apr. 2	16 Apr. 2	

Print dosing schedule Print holiday letter You will need Adobe Reader to view the holiday letters. You can download this program for free [here](#).

Subject (read message)

	New messages from	Date	Time
Er is een opmerking bij uw doseschema toegevoegd of gewijzigd	Trombosedienst Demo	19-01-2017	12:48
test	Trombosedienst Demo	12-01-2017	16:18

Terms and Conditions | Marking PORTA VITA Software Health

..... Appendix 3

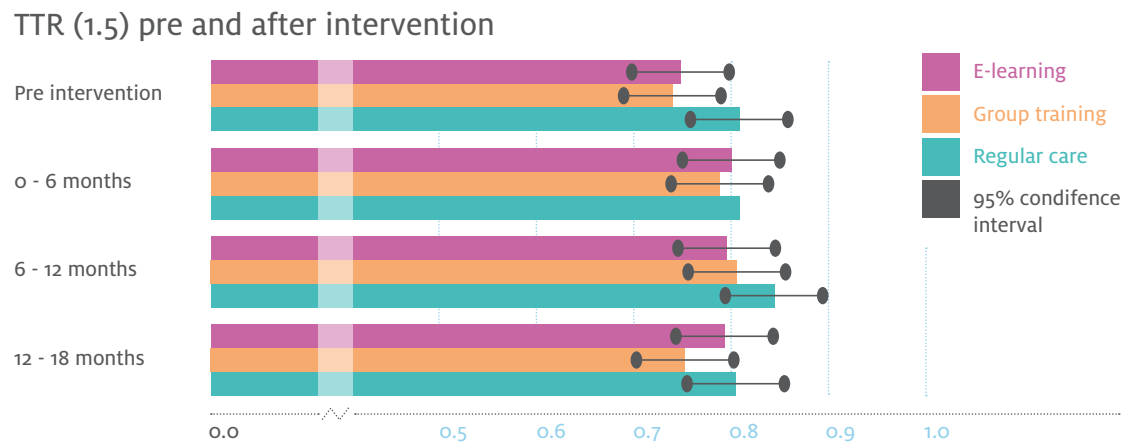


Figure 2B Health status based on TTR (for INR range 2–3.5) for the three groups. INR, international normalised ratio; TTR, time in therapeutic range

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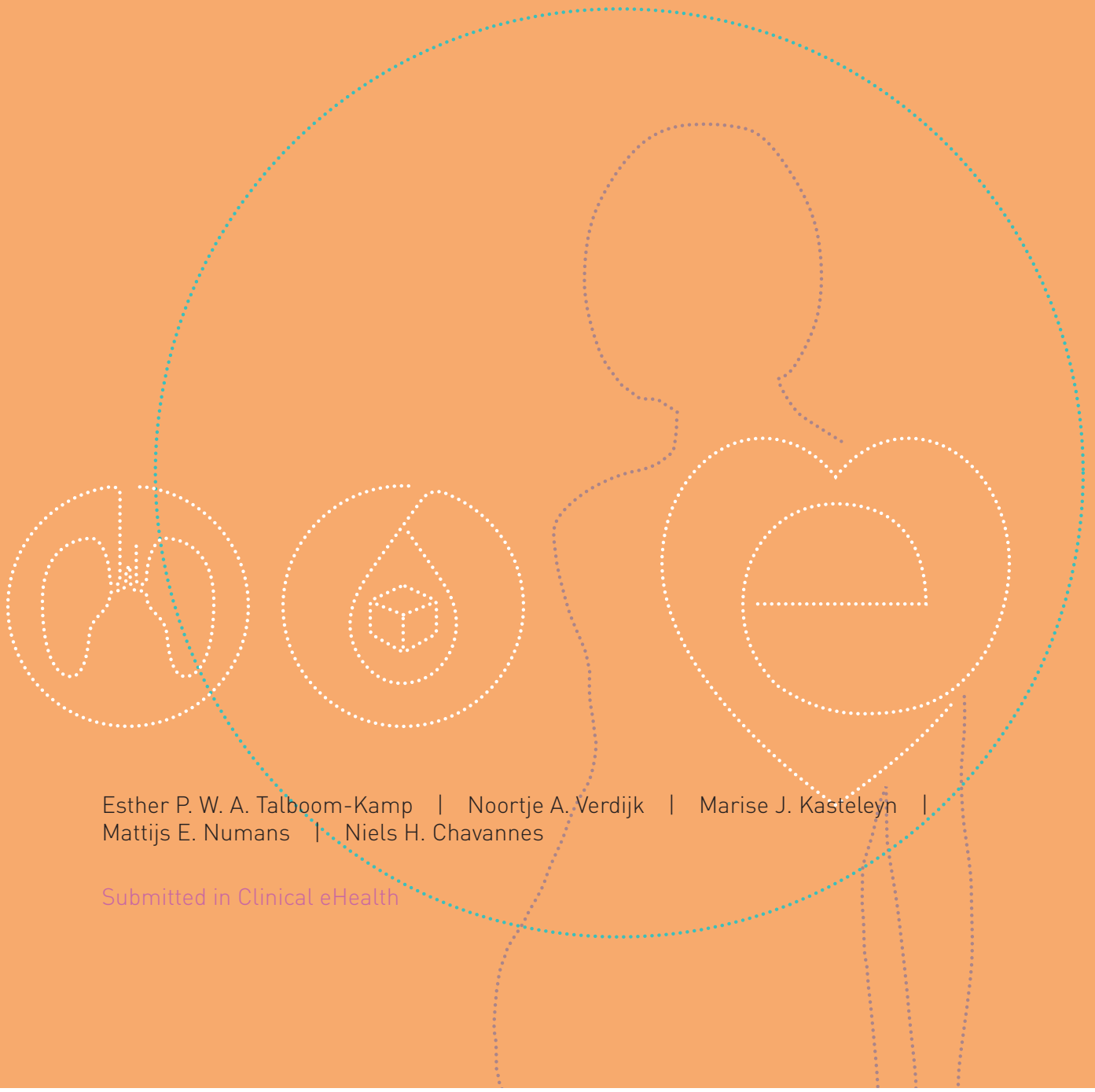
Chapter 8

Discussion

From chronic disease management to person-centered eHealth: the necessity for blended care

Esther P. W. A. Talboom-Kamp | Noortje A. Verdijk | Marise J. Kasteleyn |
Mattijs E. Numans | Niels H. Chavannes

Submitted in Clinical eHealth



Abstract

..... Background

A growing need for structural changes of the organization of the health care system has emerged from the fast-growing number of people with chronic illnesses. eHealth supported self-management programs offer a way to change the traditional approach into person-centered care.

..... Objective

Inclusion and evaluation of the studies e-Vita and PORTALS, which focused on the necessary elements for implementation of eHealth supported self-management for Chronic Obstructive Pulmonary Disease (COPD) and Oral Anticoagulation Therapy (OAT) patients.

..... Summary

Based on this narrative review of the e-Vita COPD study and the PORTALS study, we conclude that eHealth supported self-management integrated into usual care can help patients with COPD and OAT to manage their disease better. We assume that blended care with total integration of eHealth and usual care will provide better quality of care in the long term. While eHealth-supported self-management was not superior to usual care for health status, the studies reported no negative effects, suggesting that eHealth is a safe option for delivery of self-management support and high quality disease management.

Usage of the eHealth platforms is better under conditions of perfect integration into usual care and with personal assistance and coaching of patients. The usage is highest for the patients with platforms that add high practical value in day to day life.

The need to educate and coach patients in the use of web-based platforms and to educate healthcare professionals to take a different role, is of great importance. Furthermore, eHealth supported self-management programs need to be offered for a sufficient period to give patients the chance to change their behavior, and finally achieve a better health status.

..... Implications for future research and clinical practice

More studies are needed (preferably with larger sample groups, and including non-users) to gain more insight into the optimal combination of usual care and eHealth based self-management, the preferences and needs of various patients, the necessary education for healthcare professionals and patients, the best platform for patients that is easy to use, as well as the related costs.

Introduction

The number of individuals with chronic illness and multimorbidity is growing due to rapid ageing of the population and a longer life expectancy of individuals. By 2050 the number of persons aged 80 or over will be tripled and all major areas of the world, except Africa, will have nearly a quarter or more of their populations aged 60 or over ^[1]. This rise will be associated with an increase in the rate of chronic illnesses; already in 2010 eighty-six percent of all health care expenses in the US was intended for people with one or more chronic medical conditions ^[2]. In the Netherlands thirty-two percent of the total population had a chronic illness in 2014, which is thought to rise to forty percent in 2030 ^[3]. Chronic illnesses are expected to be the primary cause of death and disability in the world by 2020 ^[4].

The increase in chronic diseases leads to a higher workload in health care, a substantial impact on society and an enormous burden on patients' lives ^[5,6,7,8,9], which results in a growing need for structural changes of the organization of the health care system. High quality management of chronic illnesses can only be achieved if patients take responsibility. Therefore, it is important to empower them to take charge for their own health. This concept is reflected as self-management and provides more autonomy for the patient, improves quality of life and self-efficacy and it reduces the burden of specialized centers ^[10,11]. eHealth interventions can be effective to stimulate self-management ^[12,13]; patients that use self-management programs are nowadays usually supported by tailored eHealth platforms ^[14]. The necessity to implement self-management through eHealth is immense as the number of individuals with chronic illness and multimorbidity is growing fast. Self-management is not only a convenient way to organize care differently, it also offers patients significant benefit by providing them with more knowledge about their disease and involvement to be able to accept and maintain a healthier lifestyle. eHealth provides the means to facilitate communication between health care providers and patients, to transfer information and to facilitate the patient to become more self-managed. Research findings on eHealth supported self-management are conflicting within and between different conditions, with positive effects on self-management in some chronic diseases such as reduction in mortality in heart failure and improvement of glycemic control in diabetes, but with insufficient or inconsistent evidence of benefit for COPD, asthma and cancer ^[15].

Based on the available knowledge in literature, we identified relevant factors to stimulate the use of self-management eHealth platforms to

empower patients in self-management (Chapter 2). These proved to be: good organizational conditions with integration of self-management eHealth platforms in Integrated Disease Management (IDM), ‘blended care’ (combination of digital and regular care) ^[16,17]; conditions for education, coaching, training and support for healthcare professionals and patients ^[18]; and optimal technical conditions with a customized and user friendly eHealth platform ^[19]. Another necessary ingredient for self-management is a good relationship between the patient and health care professional with a role for the professional as a teacher or coach ^[20]. Unfortunately, the implementation of self-management (with or without eHealth) in daily practice is complex and difficult, partly because of inadequate consideration of the relevant attitudes and possibly skills of healthcare professionals, the obstacles of time and competing priorities and because of the plurals of all necessary factors to enhance self-management ^[21].

Because of these difficulties of implementation in daily practice, we aimed to investigate the effect of different approaches of eHealth implementation on the use of platforms and on health status. Moreover, we aimed to examine if the effect depends on (1) subjectively experienced practical added value for patients, thereby making their everyday lives easier; and (2) the level of organization as an integral part of existing care. Therefore, we designed the studies e-Vita and PORTALS to study the effectiveness of different implementation methods of eHealth platforms into disease management of Chronic Obstructive Pulmonary Disease (COPD) and Oral Anticoagulation Therapy (OAT) patients (Chapter 3 and chapter 4) ^[22,23]. We consider the results of both studies, we interpret them in the light of developments in the current literature and discuss the clinical implications of the findings.

Methods

..... Methods of the narrative review

In this narrative review, we included and evaluated two studies which focused on the necessary elements for implementation of eHealth supported self-management. We described the methods of the studies, the results and compared them with the literature.

..... **Methods of the included studys**

The e-Vita COPD study is a multi-level study of an eHealth intervention integrated in primary care disease management for Chronic Obstructive Pulmonary Disease (COPD) patients. In the e-Vita COPD study, three levels of integration into usual care were used; high and medium level of integration ('blended care') and no integration (independent self-management component). High level of integration meant tailored education for the healthcare professionals on COPD, theory and practice of self-management and coaching of patients; a tailored start of the intervention for patients supported by a specialized nurse; and the eHealth platform as an integrated element of the disease management program. Medium level of integration meant a standard education for the healthcare professionals on COPD, a tailored start of the intervention for patients supported by a specialized nurse, and the eHealth platform as an integrated element of the disease management program. No integration meant a single offer and question to patients to use the eHealth platform. Furthermore, we used different levels of personal assistance and training for the patients; the support varied from home visits by a research nurse who coached and assisted in use of the platform, telephone consultation by a research nurse who explained the use of the platform, no support at all and explanation of the primary care nurse how to use the platform. The supportive elements were used in different combinations (Chapter 3).

The PORTALS study is a study on the effectiveness of support by an eHealth platform for OAT. Three different programs were offered to three groups of patients, with standard usual care as the baseline for all patients. Two groups received a self-management program (including self-monitoring and self-dosage of medication) for OAT patients including the use of an eHealth platform, organized as blended care. For those two groups, different implementation methods were used; after inclusion patients were randomly divided in subgroups with e-Learning as their education and with group training as education. Both trainings were developed tailor-made by experts in OAT. The platform was necessary for the patients in the self-management groups to monitor the diagnostic test results of blood clotting and to calculate and determine the dosage of the medication. The third parallel cohort group received only regular care (Chapter 6).

..... Results

The e-Vita COPD showed that patients used the self-management web-based platform significantly more in the blended care groups (high and medium level of integration in IDM) than the patients in the group without any integration of the eHealth platform (no integration in IDM) (Chapter 4) ^[24]. The usage of the platform was higher when patients received more personal assistance in learning how to use the platform. Furthermore, no changes in health status were found before and after introduction of the eHealth platforms, and no differences were found between the groups with a high vs. a low level of personal assistance for patients. There was also no deterioration of the health status (Chapter 5).

The strength of this study lies in the combination of different study designs, thereby enabling simultaneous investigation of clinical effects, as well as the effects of different organizational implementation methods. The design was tailor-made for implementation in real-life healthcare settings, with a good support from healthcare professionals. Randomization was carried out for the level of assistance of patients.

The limitations are associated with the relatively new field of research in eHealth. The eHealth platforms are not perfectly matched to the needs of healthcare professionals and patients; usability, adaptability and compatibility with existing systems were insufficient. Because general practitioners, as well as patients, were free to volunteer, bias might have occurred in our research groups. Users were self-selected and were presumably motivated to use the platform, as would be expected in a real-life setting.

In the PORTALS study, no differences were found in health status and usage of the platform between anticoagulation self-management patients trained by e-Learning and by group training (Chapter 7). Moreover, the health status of self-management patients was equal to those of patients receiving regular care without any deterioration. From this study it was concluded that, with adequate training through e-Learning or group training, self-management is safe and reliable for a selected proportion of motivated patients receiving OAT. All approaches are equivalent and result in good clinical outcomes (Chapter 7).

The most important strength of the study is the investigation of the effect of different education programs in a situation as close to 'real life' as possible, integrated in a self-management program including eHealth, on clinical outcomes and self-management skills.

This study also has limitations typically associated with eHealth trials.

Patients were free to volunteer: bias might have occurred in our study groups. Users were self-selected and were, presumably, motivated to use the education program (including the web-based platform) as would be expected in a real-life setting.

Discussion

To understand more of the underlying mechanisms of a successful introduction of eHealth supported self-management programs, we interpret the results of the e-Vita COPD study and the PORTALS study in light of the current literature.

The results of the e-Vita COPD study showed the importance of blended care, combining face-to-face patient consultations with dedicated eHealth support, with a different usage of the platform in different patient groups, that depends on the level of blended care. In the patient group with the highest level of blended care and with the highest amount of training, patients used the platform the most, and they used more different components of the platform. In the PORTALS study, the usage of the platform remained high during the whole intervention period in both self-management groups with blended care. We conclude from both studies that blended care, with a thorough integration of eHealth into disease management programs including personal assistance for patients, leads to higher and better use of an eHealth platform. Most evidence in literature on blended care arises from the domain of mental health care. This evidence shows that face-to-face and online mental care should be combined in such a way that the potentials of both treatment modalities are used optimally, depending on patient abilities, needs, and preferences ^[25]. Most systematic reviews on depression found that online psychological treatments for depression are as effective as face-to-face psychological treatments and that offering support or guidance during online treatment increases its effectiveness and is associated with higher levels of completion ^[26,27,28]. Even in mental care, with years of experience and evidence in blended care, more insight is needed into what suits whom and how technology features and treatment operationalization via technology can be optimized ^[25]. In literature on chronic care, the impact of eHealth supported self-management on disease control and health care utilization was inconsistent, without a thorough description of and focus on the organization of blended care^[15]. Even though, more intensive and multifaceted interventions were associated with greater improvements in diabetes, heart failure, and asthma ^[15].

For blended care, motivation and training of healthcare professionals is an indispensable factor; it is important to teach and support them to deliver care in a person-centered way. Our studies show that coaching and training of both healthcare professionals and patients are important for the adoption of eHealth supported self-management programs. In the e-Vita and the PORTALS study, we started with training and support of the healthcare professionals in the self-management or blended care groups; they were trained on the medical aspects of the diseases and on the necessary skills to stimulate self-management. The need to approach their patients in an equivalent and coaching way, lead to the most vivid discussions; exercising with their colleagues in role plays, helped them to approach patients differently. The goal was that healthcare professionals could support and assist their patients in an appropriate coaching way.

In literature, several studies focused on several predictors for eHealth usage, as also described in the introduction. Results are fragmented across multiple subspecialty areas, but it is evident that embedding eHealth into healthcare involves complex processes of change ^[29]. Nevertheless, in most eHealth studies and reviews the provision of training and education to all those involved with implementation is a key success factor ^[30]. In a Dutch survey for primary care professionals it was concluded that future interventions on self-management programs should incorporate strategies to enhance motivation in unmotivated patients; to reach that goal, healthcare professionals should be better equipped to promote motivational change in their patients ^[31]. In a study on COPD and asthma patients, the online app was used on a more regular basis with a higher involvement of the health care provider and more assistance of the patients ^[32].

In our studies the results were inconsistent concerning the usage pattern of the platform during the intervention period. In the PORTALS study, the usage of the platform remained high during the whole intervention period in contrast to the e-Vita study and in contrast to most eHealth studies, there was no 'attrition'. Normally in eHealth studies, a substantial proportion of users drop out before completion, or stop using the application ^[33]. In literature, this drop out is explained by real-life adoption problems ^[33]; in our opinion it is important that patients experience practical added value in their daily life to stay motivated for using the eHealth platform. In the case of OAT patients, it is necessary to use the platform to monitor the diagnostic test results of blood clotting and to calculate and determine the dosage of the medication. For COPD patients, there is no need to use the

platform to facilitate daily life activities. For patients, the use of an eHealth platform should have the function to facilitate daily life to motivate them to use it permanently.

In literature, several studies focused on predictors for eHealth usage. In a process analysis of the actual usage of web-based applications, it became clear that innovations in health care will diffuse more rapidly when technology is employed that is simple to use and has applicable components for interactivity ^[34]. For clinically significant improvements in diabetes self-management a range of components need to be incorporated into telehealth interventions: patient education, health care provider education, self-monitoring profile, blood test goals, easy use of blood diagnostic data to modify behavior, feedback to patients, and 2-way interaction ^[35]. These components are relevant for all chronic illnesses and should be incorporated in platforms. In a study on eHealth usage among healthy adults, it was illustrated that lower SES, older, and male online US adults were less likely to engage in several eHealth activities compared to their counterparts ^[36]. We can confirm that in our PORTALS study, the percentage of male participants was significantly higher. In all eHealth studies these determinants are important to involve in the design; in our study, we analyzed demographic features on baseline and corrected for them in the statistical analysis.

In both studies, the eHealth supported self-management programs had no positive and no negative effect on the health status. Like in other literature we presume that the intervention period was too short to achieve a change in behavior for patients with subsequently an amelioration of the health status¹⁸. Although it did not lead to an improvement of health status during the study period, we expect that a long-term exposure to 'blended care' will lead to a better health status for COPD and OAT patients. In a recent systematic meta-review of chronic illnesses, telehealth-mediated self-management was not consistently superior to usual care, none of the reviews reported any negative effects, suggesting that telehealth is a safe option for delivery of self-management support, particularly in conditions such as heart failure and type 2 diabetes, where the evidence base is more developed ^[15]. Our findings of a long process of behavioral change and positive effect on health status match with the theory of 'health literacy', which means the individuals' capacity to obtain, process and understand basic health information and services that are needed to make appropriate health decisions ^[37]. People have a different basic level of health literacy. Further-

more, improving health literacy means more than transmitting information, and developing skills to be able to read folders and successfully make appointments; in the future emphasis should be given to more personal forms of communication, and community-based educational outreach, as well as more focus on equipping patients to overcome structural barriers to health ^[38]. eHealth of the future should be tailored for people with different health literacy, different chronic illnesses and be focused on empowering them to obtain a healthier lifestyle.

Chronic care of the future should contain an optimal involvement of the patient. Depending on their skills, the role of the patient should be tailor-made. Enhancement of self-management is necessary for patients to take charge of their own health and disease. eHealth is a practical tool to help patients have more control over daily decisions concerning their disease at the time and place of their choosing; the information concerning their health status facilitates to understand their disease, to have an adult conversation with their healthcare professional and to adapt an appropriate lifestyle. Self-management programs with eHealth technologies for chronic conditions can be used to enhance self-management and revise the Chronic Care Model; patients who actively participate in their care achieve valuable and sustained improvement in wellbeing ^[39,40]. In many eHealth studies, use of a Personal Health Record or self-management platform can promote an informed/activated patient and augment the Chronic Care Model for self-management support and productive interactions; even though a direct dosage-effect relation (usually analyzed in a classical RCT) is not common in eHealth ^[41]. Self-management programs with good training and practical eHealth platforms have the potential to make chronic care personalized in a blended care model; every patient needs a different approach for an optimal health status. Healthcare providers need to embrace a different role and release tight protocols in blended care ^[42]. Individual patients have different expectations and wishes, which should be a topic of conversation with each patient.

What's in it for healthcare professionals? A more challenging and satisfactory profession with a meaningful relationship with their patients.

What's in it for patients? Tailored and accessible care, digitally supported, with appropriate lead over their own health, lifestyle and illness.

eHealth based self-management improves quality of care. It does not replace usual care.

Recommendations for future research

The present results provide additional insight into the organizational aspects of the implementation of a self-management program with an eHealth platform, including training programs. The need to educate and coach patients in the use of web-based platforms and to educate healthcare professionals to take a different role, is of great importance. Furthermore, eHealth supported self-management programs need to be offered for a sufficient period to give patients the chance to change their behavior, and finally achieve a better health status. Therefore, more studies are needed (preferably with larger sample groups, and including non-users) to gain more insight into the optimal combination of usual care and eHealth based self-management, the preferences and needs of various patients, the necessary education for healthcare professionals and patients, the best platform for patients that is easy to use, as well as the related costs. The substantial workload generated by integrating a web-based platform in a self-management program emphasizes the importance of piloting and assessing workforce implications for care centers.

Conclusion

Based on this narrative review of the e-Vita COPD study and the PORTALS study, we conclude that eHealth supported self-management integrated into usual care can help patients with Chronic Obstructive Pulmonary Disease (COPD) and Oral Anticoagulation Therapy (OAT) to manage their disease better. We assume that blended care with total integration of eHealth and usual care will provide better quality of care in the long term. While eHealth-supported self-management was not superior to usual care for health status, the studies reported no negative effects, suggesting that eHealth is a safe option for delivery of self-management support and high quality disease management.

Usage of the eHealth platforms is better under conditions of perfect integration into usual care and with personal assistance and coaching of patients. The usage is highest for the patients with platforms that add high practical value in day to day life.

The need to educate and coach patients in the use of web-based platforms and to educate healthcare professionals to take a different role, is of great importance. Furthermore, eHealth supported self-management programs need to be offered for a sufficient period to give patients the chance to change their behavior, and finally achieve a better health status.

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Summary

The number of individuals with chronic illness and multi-morbidity is growing due to the rapid ageing of the population and a longer individual lifespan. This ageing will bring about an increase in the rate of chronic illnesses with a rapidly growing workload in care. Therefore, structural changes of the healthcare system, with an important role for self-management for patients (including electronic health; eHealth), are necessary (Chapter 1). Currently, the management of most chronic illnesses is characterised by the responsibility that individual patients need to take, and by empowering patients to 'take charge' regarding the measures required to improve their own health.

Nowadays, patients that follow self-management programs are usually supported by tailored eHealth platforms. Generally, eHealth interventions are effective in stimulating self-management because they allow patients to cope better with their illness at the time and place of their choosing, enabling them to adapt their lifestyle to their individual condition.

Despite promising pilots with eHealth and the positive experience of patients regarding eHealth, large-scale adoption of self-management and eHealth still lags behind in daily practice. An important reason for this backlog is the difficulty of organising 'blended care', in which eHealth is integrated into regular care. Several pre-conditions should be considered before starting the implementation of eHealth. In the studies described in this thesis we thoroughly considered, implemented and analysed these pre-conditions.

The objective of the implementation studies described in this thesis was to investigate the effect of the application of eHealth-supported programs for chronic obstructive pulmonary disease (COPD) and oral anticoagulation therapy (OAT) in primary care.

The aims of this thesis were:

- to examine whether the effects found depend on: 1) subjectively experienced practical added value for patients, thereby making their everyday lives easier; and 2) the level of organisation as an integral part of existing care.
- to evaluate the effect of different approaches of eHealth implementation on the use of eHealth platforms and patient outcomes, focusing on health status in particular.

To achieve these research aims, we designed two studies on the implementation of self-management programs with eHealth called i) *e-Vita COPD* and ii) *PORTALS (PORTal implementation within anTicoagulation care; Amplification of self-management)*.

Chapter 2 describes our viewpoint regarding the expected added value of eHealth-supported self-management for chronically ill patients. There has been an increasing focus on self-management in the aim to handle the growing need for appropriate care for this large group of patients. Research has shown that patients who understand more about their disease, health and lifestyle have better experiences and health outcomes, and often use less healthcare resources; this effect is even greater when these patients are empowered to be/are responsible for managing their own health and disease. In addition to the importance of patient skills, healthcare professionals need to shift to a role of teacher, partner, and professional supervisor of their patients. One way of supervising and coaching patients is to use eHealth, which helps patients manage and control their disease. The application of eHealth solutions can provide chronically ill patients with high-quality care, to the satisfaction of both patients and healthcare professionals, together with a reduction in healthcare consumption and related costs.

For this purpose, we designed two implementation studies on eHealth-supported self-management programs: one focusing on patients with COPD (**Chapters 3, 4 and 5**) and one for patients that use OAT for atrial fibrillation (AF) or for venous thromboembolism (VTE) (**Chapters 6 and 7**). The rationale for choosing these two diseases is twofold: the economic and disease burden of both these chronic diseases is considerable, and self-management has been introduced as an effective method to improve the quality of care for both conditions.

For patients using the self-management platform on a regular basis, we expected to see a positive effect on quality of life and complications in both groups. For patients with COPD, we expected to see a relatively small improvement in their everyday lives using the digital platform. Resulting from this, we assumed that the use of the platform would grow less rapidly and take root less rapidly. For OAT patients, a comprehensive self-management program supported by a digital platform will tend to lessen their dependence on the anticoagulation clinic and enhance their sense of self-reliance. Therefore, we expected these OAT patients to use the digital platform more frequently leading to an enhanced improvement in clinical outcomes.

Chapter 3 presents the design and methodology of the e-Vita COPD study. The management of COPD is highly complex, since patients show considerable variation in their symptoms and limitations in daily life. In the last decade, self-management support of COPD was introduced as an effective method to improve the quality and efficacy of care, and to reduce healthcare costs. Despite the urge to change the organisation of health care and the potential of eHealth to support this, large-scale implementation in daily practice still lags behind, especially in the Netherlands.

The e-Vita COPD study compared three different approaches to incorporating eHealth via web-based self-management platforms into integrated disease management (IDM) of COPD in primary care using a parallel cohort design. Three different groups integrated the platforms to different levels. In group 1, the online platform was offered as a highly integrated part of the COPD IDM with a tailored intensive course program on COPD for healthcare professionals that covered i) education on COPD, ii) training related to the possibilities of eHealth, and iii) conversational techniques to approach patients in a way that is equal and also supports coaching. All patients in group 1 started with a personal consultation with the primary care nurse, followed by coaching on the necessity of self-management and an explanation about the burden of their disease and the eHealth program. Group 2 had a medium level of integration with a basic course program for healthcare professionals on COPD that covered education on COPD, and training about the possibilities of eHealth. All patients in group 2 started with a personal consultation with the primary care nurse, followed by coaching and an explanation of the self-management program. With the platform, the patients could work with a coaching program on their personal goals, actions and health-related quality of life. In group 3, the online platform was offered without integration in COPD IDM; healthcare providers and patients received basic instructions about the platform. In the blended care groups (group 1 and 2), randomisation was performed to two different levels of personal assistance for the patients (i.e. high and low level assistance). All programs were offered for a period of 15 months.

Every visit to the web platforms was tracked by collecting log data (number of sessions, and use of the different services). At the first log-in, patients completed a baseline questionnaire including age, gender, education level, scores on the Clinical COPD Questionnaire (CCQ), the dyspnoea scale (MRC), and the quality-of-life questionnaire (EQ-5D). To compare the use of the platforms in the three different groups, multiple linear regression analyses were performed. The association between educational level and

usage, and between the General Self-Efficacy Scale (GSES) and usage, was analysed. An interrupted time series (ITS) design was used to collect CCQ data at multiple time points before and after intervention. Multilevel linear regression modelling was used to analyze the CCQ data emerging from the three groups over time.

This study combined different designs that enabled simultaneous investigation of the clinical effects, as well as the effects of different organisational implementation methods, whilst controlling for the confounding effects of the organisational characteristics. It was expected that when the eHealth program was integrated in existing care and patients received a high level of personal assistance, the use of the platform would be higher, thereby increasing the health status.

Although self-management of COPD through eHealth interventions has shown to be beneficial in several settings, it remains unknown which factors influence the usage of eHealth and, thereby, a change in patients' behaviour. In [Chapter 4](#) we analysed the factors that successfully promote the use of a self-management platform among COPD patients in the e-Vita study. The COPD patients were recruited from three groups in primary care: of the 702 COPD patients that were invited, 215 (30.6%) registered to a platform. Of the 82 patients in group 1 (high integration IDM), 36 were in group 1A (personal assistance) and 46 in group 1B (low assistance). Of the 96 patients in group 2 (medium integration IDM), 44 were in group 2A (telephone assistance) and 52 in group 2B (low assistance). A total of 37 patients participated in group 3 (non-integration IDM). In total, 107 users (49.8%) visited the platform at least once during the 15-month period. The mean number of sessions differed between the three groups (group 1: mean 10.5, SD 1.3; group 2: mean 8.8, SD 1.4; group 3: mean 3.7, SD 1.8; $p=0.01$). The mean number of sessions differed between the high-assistance and low-assistance groups in groups 1 and 2 (high: mean 11.8, SD 1.3; low: mean 6.7, SD 1.4; $F_{1,80}=6.55$, $p=0.01$). High-assistance participants used more services (mean 45.4, SD 6.2) than low-assistance participants (mean 21.2, SD 6.8; $F_{1,80}=6.82$, $p=0.01$).

No association was found between educational level and usage, or between General Self-Efficacy Scale and usage. Our findings highlight the importance of integrating an eHealth platform into IDM; usage of the self-management eHealth platform is higher and more varied when the platform is an integrated part of the care program with personal coaching for patients. Patients in care groups with a high level of integration of the platform in

IDM showed a higher number of sessions and a larger amount of visited digital services with more variation. Patients that received assistance also showed higher usage of the platform. We implemented extensive professional training of healthcare professionals on the COPD care program and self-management supported by eHealth platforms; we also offered personal assistance for the users to guide them through the platform, as well as specific push factors (automated reminders, or messages made by healthcare professionals). Both strategies are essential elements to stimulate the use of platforms.

Chapter 5 describes the effect of the integration of self-management web platforms on health status as measured with the CCQ among COPD patients in the e-Vita study. Patients' health status was examined using the CCQ in three primary care groups, i.e. with a highly, a medium, and a non-integrated eHealth platform. During the 15-month intervention period, there were four measurement periods with three CCQ questionnaires at each period (3 data points before intervention, and 9 data points after intervention). Higher CCQ values indicate a lower health status. The decrease of CCQ scores in the total group of patients before the intervention was 0.5% per month and after the intervention was 0.08% per month; this difference was not statistically significant. Furthermore, no significant difference was found in CCQ changes when going from pre-intervention to post-intervention between the groups with a high level of personal assistance for COPD and a low level of assistance. The changes in health status CCQ were not within the range of a minimal clinically important difference, meaning that no changes in health status were found before and after introduction of the eHealth-supported COPD programs, and no differences were found between the care groups with a high versus a low level of personal assistance. Despite these results of the e-Vita study, we expect that eHealth interventions will be effective in stimulating self-management and stabilising the health status of COPD patients when these patients use the platforms for a longer period. It is likely that the intervention period in our e-Vita study was too short to give patients sufficient time to change their lifestyle and behaviour in order to show an improved health status. Furthermore, in Dutch primary care the standards of regular COPD disease management are relatively high; this might explain the absence of an improvement of health status after the introduction and integration of eHealth within IDM. It appears that there was too little room for improvement, especially for these particular COPD patients in primary care with a ever-relatively low burden

of disease.

Chapters 6 and 7 of the thesis present the PORTALS study. Both VTE and AF are common causes of mortality and morbidity, with continually rising prevalence and medical costs.

OAT reduces thromboembolic events in AF and other conditions, and is an effective treatment for VTE. There is a narrow therapeutic range for OAT through vitamin K antagonists, with a high need for strict therapeutic adherence. This adherence and consequently the complications due to a deviant therapeutic range, are reduced when OAT patients are supported by self-management programs.

Chapter 6 describes the design and the intervention of the PORTALS study; this is an implementation study with a quality improvement intervention for OAT patients who receive regular thrombosis care. It is a parallel cohort design with two randomised self-management groups, and a group receiving regular care. Two methods to train long-term OAT patients in self-management were developed to improve the quality of care and introduce the use of an eHealth portal. After inclusion, patients interested in participating in a self-management program were randomly divided into a group with education and training by e-Learning, and another group that received face-to-face group training. Both the e-Learning group and the group training consisted of at least three components: i) disease-specific knowledge of VTE and AF; ii) self-testing skills; iii) use of an eHealth portal; and iv) self-adjustment of medication. Patients who did not wish to start with self-management were invited to participate in the non-self-management group, a parallel cohort that received usual care. Health status was the primary outcome, expressed by therapeutic control through International Normalized Ratio (INR) values over time; INR values were registered continuously and converted into the percentage of time within the therapeutic range (TTR) over three time periods (0-6 months, 6-12 months, and 12-18 months) during the intervention that lasted 18 months. Severe complications (bleedings and thromboembolic events) and the usage of the eHealth portal were monitored and registered continuously. Analysis of the usage of the portal (linear regression analysis) allowed us to indirectly estimate the self-management skills of the participants. TTR was analyzed with multilevel linear regression modelling. In this study, we aimed to empower patients with OAT by providing self-management, including an eHealth portal and education. We expected to learn what type of education could be a significant factor in the adoption of self-management. It was expected

that this self-management program would help patients to better manage their own INR values and medication use, thereby increasing their health status and diminishing severe complications.

Chapter 7 describes the effect of the combined education and eHealth programs on the therapeutic control of OAT patients in the PORTALS study. A total of 1,632 vitamin K antagonist patients of the Saltrø Thrombosis Service were invited to participate, of which 56% (n=915) declined. Of the 717 patients that were interested to participate in the study, 247 provided informed consent. Of these, 110 patients continued to receive regular care (group 3) and 137 were randomly divided into the self-management groups 1 (e-Learning, n=63) and 2 (group training, n=74). Analyses showed no significant differences in TTR between the three time periods ($p=0.520$), the three groups ($p=0.460$), or the groups over time ($p=0.263$). Comparison of e-Learning and group training showed no significant differences in TTR between the time periods ($p=0.614$), the groups ($p=0.460$), or the groups over time ($p=0.263$). No significant difference was found between the self-management groups in usage of the platform (0-6 months $p=0.571$; 6-12 months $p=0.866$; 12-18 months $p=0.260$). The percentage of complications was low in all groups (3.2%; 1.4%; 0%).

No overall significant differences in therapeutic control were found between the three groups. Furthermore, no differences were found between OAT patients trained by e-Learning or by a group course regarding TTR and usage of a supporting eHealth platform. The absence of improvement of the therapeutic control after the intervention seems to be (partly) caused by the fact that further improvement through a self-management program (including education) was difficult to achieve for this group of patients that already received high quality care; in comparison to literature, the baseline quality of OAT management in the present study could be considered high in all groups. Both of the training methods had a similar effect on anticoagulation control; for patients and healthcare professionals this implies that a good e-Learning program is a good alternative for labour-intensive group training. Therefore, we recommend to consider self-management programs supported by e-Learning as the preferred plan of action for the self-management for anticoagulation patients. Furthermore, self-management with an e-Learning component is suitable for motivated patients with sufficient digital skills; in our opinion, regular anticoagulation care needs to remain available for the remainder of the population.

In this study, the practical value of the eHealth portal was very high for

patients because of the functionalities of self-monitoring, self-dosage, and digital advice from professional healthcare providers. Patients could manage their anticoagulation in their own time in their own chosen place. Using this self-management program gave them freedom, which might have been a strong motivating factor to use the program during the entire intervention period.

We concluded that with appropriate and sound training through e-Learning or group training, self-management seems safe and reliable for a selected proportion of motivated patients receiving oral anticoagulation treatment.

In **Chapter 8** we discuss the implications of our findings regarding the e-Vita and the PORTALS study. We conclude that eHealth-supported self-management integrated into usual care can help patients with COPD and OAT to manage their disease. We assumed that blended care with total integration of eHealth and usual care will provide better quality of care in the long term. Even though eHealth-supported self-management was not superior to usual care regarding health status, the studies produced no negative effects, suggesting that eHealth is a safe option for delivery of self-management support and high-quality disease management.

The usage of eHealth platforms is better under conditions of perfect integration into usual care and with personal assistance and the coaching of patients. The usage is highest for patients with platforms that add high practical value in daily life.

Based on our findings, some recommendations can be made for additional research. Future eHealth applications should be tailored for individuals with varying health literacy, different chronic illnesses, and should focus on empowering them to obtain a healthier lifestyle. The need to educate and coach patients in the use of web-based platforms, and to educate healthcare professionals to take a facilitating role in an equivalent position, is of great importance. Furthermore, eHealth-supported self-management programs need to be offered for a sufficiently long period of time to give patients the chance to gradually change their behaviour and finally achieve a better health status. Therefore, more studies are needed, preferably with larger sample groups, and also including non-users. This will provide more insight into i) the optimal combination of usual care and eHealth-based self-management, ii) the preferences and needs of various types of patients, iii) the necessary education for healthcare professionals and patients, iv) the best platform

for patients that is easy to use, and v) the related costs.

The substantial workload generated by integrating a web-based platform in a self-management program emphasises the importance of piloting and assessing workforce implications for care centres.

Samenvatting

Het aantal mensen met chronische ziekten en multimorbiditeit stijgt vanwege de vergrijzing en omdat men steeds langer leeft. Deze toenemende levensduur zal een stijging teweegbrengen in het aantal chronisch zieken, en daarmee ook een snelle toename in de werkdruk in de zorg. Er zijn daarom structurele veranderingen in de gezondheidszorg nodig, waarbij een belangrijke rol is weggelegd voor zelfmanagement bij patiënten, inclusief “electronic health”: eHealth (Hoofdstuk 1). Bij de meeste chronische aandoeningen is de huidige moderne zorg vooral gericht op de verantwoordelijkheid die iedere individuele patiënt moet nemen, en op het stimuleren van patiënten om de eigen regie te voeren voor een betere gezondheid.

Patiënten die zelfmanagementprogramma's volgen, worden in de huidige tijd vaak ondersteund door specifieke eHealthplatforms (websites of applicaties). Over het algemeen zijn eHealth interventies effectief in het stimuleren van zelfmanagement omdat patiënten hun ziekte beter leren reguleren als ze daar zelf de tijd en plaats voor kunnen kiezen: ze kunnen hun leefstijl aan hun individuele aandoening aanpassen. Ondanks veelbelovende pilots met eHealth en de positieve ervaringen van patiënten blijft grootschalig gebruik van zelfmanagement en eHealth in de dagelijkse praktijk uit. Een belangrijke reden voor deze achterstand is de complexiteit van de organisatie van ‘blended care’, waarbij eHealth wordt geïntegreerd in de reguliere zorg. Er moeten aan allerlei voorwaarden worden voldaan voordat er kan worden gestart met de implementatie van eHealth. In de studies die zijn beschreven in dit proefschrift hebben we deze voorwaarden uitvoerig overdacht, geïmplementeerd en geanalyseerd.

De doelstelling van de implementatiestudies die in dit proefschrift zijn beschreven was om het effect van de toepassing van met eHealth ondersteunde programma's voor chronisch obstructieve longziekte (COPD) en orale antistollingstherapie (OAT) in de eerste lijn te onderzoeken.

De doelen van dit proefschrift waren:

- het effect evalueren van verschillende implementatiemethoden van eHealth op het gebruik van eHealthplatforms en patiëntuitkomsten, de gezondheidsstatus in het bijzonder.
- te onderzoeken of de gevonden effecten afhankelijk zijn van: 1) subjectief ervaren praktisch toegevoegde waarde van eHealth voor de patiënten, waarmee hun dagelijks leven wordt vergemakkelijkt; en 2) de mate van

integratie van eHealth als onderdeel van bestaande zorg.

Om deze onderzoeksdoelen te behalen, hebben we twee studies ontworpen met implementatie van zelfmanagementprogramma's met eHealth, genaamd i) e-Vita COPD en ii) PORTALS.

Hoofdstuk 2 beschrijft onze opinie over de verwachte toegevoegde waarde van zelfmanagement met ondersteuning van eHealth voor chronisch zieken. De aandacht voor zelfmanagement is enorm toegenomen in de hoop de juiste zorg voor deze grote patiëntengroepen te kunnen realiseren. Onderzoek heeft aangetoond dat patiënten die hun aandoening, gezondheid en leefstijl beter begrijpen ook betere ervaringen en gezondheidssuitkomsten hebben, en bovendien vaak ook minder zorg consumeren. Dit effect is nog groter wanneer deze patiënten in staat worden gesteld om zelf verantwoordelijkheid te nemen voor de regie over de eigen gezondheid en ziekte. Naast het belang van deze vaardigheden bij de patiënt, is het noodzakelijk dat zorgprofessionals zich ontwikkelen tot een rol van leraar, coach en supervisor van hun patiënten. Deze vorm van patiëntcoaching kan worden gefaciliteerd door eHealth, hetgeen patiënten in hun thuis-situatie helpt om hun ziekte te regisseren en controleren. Het gebruik van eHealthoplossingen kan chronisch zieken voorzien van hoogstaande zorg, tot grote tevredenheid van zowel patiënten als zorgprofessionals; ook kunnen de zorgconsumptie en daaraan gerelateerde kosten verlaagd worden. Voor dit doeleinde hebben we twee implementatiestudies opgezet naar door eHealth ondersteunde zelfmanagementprogramma's: de een kijkt naar patiënten met COPD (**Hoofdstuk 3, 4 en 5**) en de ander naar patiënten die OAT gebruiken voor atriumfibrilleren (AF) of veneuze trombo-embolie (VTE) (**Hoofdstuk 6 en 7**). De keuze voor deze twee aandoeningen is tweeledig: de economische lasten en de ziektelast van beide chronische aandoeningen zijn aanzienlijk en voor beide aandoeningen is zelfmanagement al eerder geïntroduceerd als effectieve methode om de kwaliteit van zorg te verbeteren. Bij patiënten die de zelfmanagementplatforms op regelmatige basis gebruiken, verwachtten we voor beide groepen een positief effect te zien op de kwaliteit van leven en complicaties. Omdat we bij COPD-patiënten een relatief kleine verbetering in het dagelijks leven door het digitale platform verwachtten, veronderstelden we dat het gebruik van het platform minder snel zou toenemen en minder goed zou beklijven. Voor OAT-patiënten zal een begrijpelijk zelfmanagementprogramma, ondersteund door een digitaal platform, de afhankelijkheid van de antistollingskliniek doen afnemen en een gevoel van zelfstandigheid bevorderen. We

verwachtten daarom dat OAT-patiënten het digitale platform vaker zouden gebruiken, wat tot een verbetering in de klinische uitkomsten zou leiden.

Hoofdstuk 3 behandelt het ontwerp en de methodologie van de e-Vita COPD studie. Er zit aanzienlijke variatie in de symptomen en dagelijkse belemmeringen van patiënten met COPD, wat het reguleren van de ziekte zeer complex maakt. In het afgelopen decennium is zelfmanagementondersteuning van COPD geïntroduceerd als een effectieve methode om de kwaliteit en doeltreffendheid van zorg te verbeteren en om zorgkosten te verminderen. Ondanks de noodzaak om de organisatie van de gezondheidszorg te veranderen en de potentie van eHealth om hierin te ondersteunen, blijft grootschalige implementatie in de dagelijkse praktijk uit, vooral in Nederland.

De e-Vita COPD studie vergeleek in een parallel cohort design drie verschillende manieren om eHealth in de eerste lijn via een digitaal zelfmanagementplatform aan te bieden in een geïntegreerd zorgprogramma (IDM) voor COPD. Drie verschillende groepen integreerden de platforms op verschillende niveaus. In groep 1 werd het digitale platform als een volledig geïntegreerd onderdeel van het COPD IDM aangeboden, met een op maat gemaakt, intensief cursusprogramma over COPD voor zorgprofessionals dat verdieping gaf in i) scholing over COPD, ii) training over de mogelijkheden van eHealth, en iii) gesprekstechnieken om patiënten te benaderen op een gelijkwaardige en coachende manier. Alle patiënten in groep 1 startten met een persoonlijk consult met de praktijkondersteuner, gevolgd door coaching over de noodzaak van zelfmanagement en uitleg over hun ziektelast en het eHealthprogramma. Groep 2 had een tussenniveau van integratie: een basis cursusprogramma over COPD voor zorgprofessionals met informatie over COPD, zelfmanagement en een training over de mogelijkheden van eHealth. Alle patiënten in groep 2 startten met een persoonlijk consult met de praktijkondersteuner, gevolgd door coaching en uitleg over het zelfmanagementprogramma. De patiënten konden op het platform met een begeleidend programma werken aan hun persoonlijke doelen, acties en ziektegerelateerde kwaliteit van leven. In groep 3 werd het digitale platform aangeboden zonder integratie in de reguliere zorg voor COPD. Zorgverleners en patiënten kregen basisinformatie over het platform. In de 'blended care' groepen (groep 1 en 2) is gerandomiseerd op twee niveaus van persoonlijke assistentie voor de patiënten (hoge en lage mate van assistentie). Alle programma's zijn aangeboden voor een periode van 15 maanden. Ieder bezoek aan de digitale platforms werd gelogd (aantal sessies en

het gebruik van de verschillende services). Bij de eerste login vulden de patiënten een vragenlijst in met onder andere leeftijd, geslacht, opleidingsniveau, scores op de klinische COPD-vragenlijst (CCQ), de MRC-dyspnoeschaal en een vragenlijst over de kwaliteit van leven (EQ-5D). Multiple lineaire regressie-analyses zijn uitgevoerd om het gebruik van de platforms in de drie verschillende groepen te vergelijken. De associatie tussen opleidingsniveau en gebruik, en tussen de General Self-Efficacy Scale (GSES) en gebruik zijn geanalyseerd. Een interrupted time series (ITS) ontwerp is gebruikt om CCQ data op meerdere momenten vóór en na de interventie te verzamelen. Multilevel lineaire regressiemodellering is gebruikt om de CCQ data van de drie groepen te analyseren.

Deze studie combineert verschillende ontwerpen om gelijktijdig onderzoek naar de klinische effecten te doen en naar de effecten van verschillende organisatorische implementatiemethoden, terwijl er wordt gecontroleerd voor de versturende effecten van de organisatorische karakteristieken. De verwachting was dat het gebruik van het platform hoger zou zijn als het eHealthprogramma was geïntegreerd in bestaande zorg en als de patiënten meer persoonlijke assistentie kregen, en dat daarmee de gezondheidsstatus zou stabiliseren.

Hoewel zelfmanagement van COPD middels eHealthinterventies in verschillende settings waardevol is gebleken, blijft het onduidelijk welke factoren het gebruik van eHealth (en daarmee ook een verandering in het gedrag van de patiënt) beïnvloeden. In [Hoofdstuk 4](#) analyseren we de factoren die het gebruik van een zelfmanagementplatform succesvol maken onder COPD-patiënten in de e-Vita studie. De COPD-patiënten kwamen uit drie eerstelijns zorggroepen: van de 702 COPD-patiënten die waren uitgenodigd voor deelname, registreerden zich er 215 (30.6%) bij een eHealthplatform. Van de 82 patiënten in groep 1 (hoge integratie IDM) zaten er 36 in groep 1A (persoonlijke assistentie) en 46 in groep 1B (lage mate van assistentie). Van de 96 patiënten in groep 2 (lage integratie IDM) zaten er 44 in groep 2A (telefonische assistentie) en 52 in groep 2B (lage mate van assistentie). In totaal zaten er 37 patiënten in groep 3 (niet geïntegreerd IDM). In totaal hebben 107 gebruikers (49.8%) het platform ten minste één keer bezocht in de periode van 15 maanden. Het gemiddelde aantal sessies verschilde tussen de drie groepen (groep 1: gem. 10.5, SD 1.3; groep 2: gem. 8.8, SD 1.4; groep 3: gem. 3.7, SD 1.8; $p=0.01$). Het gemiddelde aantal sessies verschilde tussen de groepen met hoge mate van assistentie en lage mate van assistentie in groep 1 en 2 (hoog: gem. 11.8, SD 1.3; laag: gem. 6.7, SD 1.4; $F_{1,80}=6.55$, $p=0.01$). Deelnemers met een hoge mate van assistentie gebrui-

kten meer diensten (gem. 45.4, SD 6.2) dan deelnemers met een lage mate van assistentie (gem. 21.2, SD 6.8; $F_{1,80}=6.82$, $p=0.01$). Er is geen associatie gevonden tussen het opleidingsniveau en het gebruik van het platform of tussen General Self-Efficacy Scale en gebruik.

Onze bevindingen onderstrepen het belang van integratie van een eHealth-platform in de reguliere zorg: het gebruik van het platform is hoger en gevarieerder wanneer het beter geïntegreerd is in het zorgprogramma, met persoonlijke coaching voor de patiënten. Bij patiënten in zorggroepen met hoge integratie van het platform in IDM was een hoger aantal sessies gemeenten en waren er meer en gevarieerdere digitale diensten gebruikt. Er was ook meer gebruik van het platform te zien bij patiënten die persoonlijke assistentie kregen. We hebben uitgebreide professionele training gegeven aan zorgprofessionals over het COPD-zorgprogramma en zelfmanagement met behulp van eHealth; ook hebben we persoonlijke assistentie om door het platform te worden geleid en specifieke 'push-factoren' (geautomatiseerde herinneringen of berichten van zorgprofessionals) aangeboden aan de gebruikers. Beide strategieën zijn essentiële elementen om het gebruik van platformen te stimuleren.

Hoofdstuk 5 schetst het effect van de integratie van digitale zelfmanagementplatforms op de gezondheidsstatus van COPD-patiënten in de e-Vita studie. De gezondheidsstatus van de patiënten is onderzocht aan de hand van CCQ van de geïnccludeerde COPD patiënten die verschillende gradaties van blended care ontvingen (hoog-, middel- en niet-geïntegreerde eHealth). Tijdens de interventieperiode van 15 maanden waren er vier meetperioden met drie CCQ-vragenlijsten per periode (3 datapunten voor de interventie en 9 datapunten na de interventie). Hogere CCQ-waarden geven een lagere gezondheidsstatus weer. De afname van de CCQ-score voor aanvang van de interventie over de totale patiëntengroep was 0.5% per maand en na de interventie was dit 0.08% per maand; dit verschil was statistisch niet significant. Daarnaast is er geen significant verschil gevonden in verandering in CCQ voor en na de interventie tussen de patientgroepen met een hoge mate van assistentie en een lage mate van assistentie. De veranderingen in gezondheidsstatus CCQ lagen niet binnen de range van een minimaal klinisch belangrijk verschil. Dat wil zeggen dat er geen veranderingen in gezondheidsstatus zijn gevonden voor en na de introductie van de door eHealth ondersteunde COPD programma's, en dat er geen verschillen zijn gevonden tussen de patientgroepen met een hoge mate versus een lage mate van persoonlijke assistentie.

Ondanks deze resultaten van de e-Vita studie verwachten we dat eHealth-interventies effectief zullen zijn in het stimuleren van zelfmanagement en het stabiliseren van de gezondheidsstatus van COPD-patiënten als zij het platform langere tijd gebruiken. Het is aannemelijk dat de interventieperiode in onze e-Vita studie te kort was om patiënten voldoende tijd te geven om hun leefstijl en gedrag aan te passen en zo een verbetering in gezondheidsstatus te zien. Daarnaast zijn de standaarden van reguliere zorg voor COPD in de eerste lijn in Nederland relatief hoog – dit zou kunnen verklaren waarom er geen verbetering in gezondheidsstatus werd gemeten na de introductie van integratie van eHealth. Er leek te weinig ruimte voor verbetering te zijn, vooral in deze groep eerstelijns COPD-patiënten met een relatief lage ziektelast.

Hoofdstuk 6 en 7 van dit proefschrift gaan over de PORTALS studie. Zowel VTE als AF zijn veelvoorkomende oorzaken van mortaliteit en morbiditeit, met oplopende prevalenties en medische kosten. OAT vermindert trombo-embolische voorvallen bij AF en andere aandoeningen, en is een effectieve behandeling voor VTE. Er is een nauwe therapeutische range voor OAT met vitamine K-antagonisten (VKA), waarbij strikte therapietrouw noodzakelijk is. De complicaties ten gevolge van een afwijkende therapeutische range worden verminderd als OAT-patiënten ondersteund worden door zelfmanagementprogramma's.

Hoofdstuk 6 beschrijft het ontwerp en de interventie van de PORTALS studie; een implementatiestudie met een kwaliteitsverbeterende interventie voor OAT-patiënten in de reguliere trombosezorg. We hebben gebruik gemaakt van een parallel cohortdesign met twee gerandomiseerde zelfmanagementgroepen en een groep met reguliere zorg. Er zijn twee methoden ontwikkeld om langetermijn OAT-patiënten in zelfmanagement te trainen om zo de kwaliteit van zorg te verbeteren en het gebruik van een eHealthportaal te introduceren. Na inclusie zijn de patiënten die geïnteresseerd waren in deelname in een zelfmanagementprogramma willekeurig verdeeld over een groep met scholing en training door e-Learning en een groep met een fysieke groepstraining. Het programma van beide groepen (e-Learning en groepstraining) bestond uit minimaal drie van deze onderdelen: i) ziektespecifieke kennis over VTE en AF; ii) zelfmeetvaardigheden; iii) gebruik van het eHealthportaal; iv) zelfdosering van medicatie. Patiënten die niet met zelfmanagement aan de slag wilden, zijn uitgenodigd om deel te nemen in de niet-zelfmanagementgroep, een parallel

cohort met reguliere zorg. De primaire uitkomstmaat was de gezondheidsstatus, uitgedrukt in therapeutische controle middels internationaal genormaliseerde ratiowaarden (INR-waarden) in de tijd; INR-waarden werden continu geregistreerd en omgezet in het percentage van tijd binnen de therapeutische range (TTR) over drie perioden (0-6 maanden, 6-12 maanden en 12-18 maanden) tijdens de interventieperiode van 18 maanden. Ernstige complicaties (bloedingen en trombo-embolische voorvallen) en het gebruik van het eHealthportaal werden continu geregistreerd. Door analyse van het gebruik van het portaal (lineaire regressie-analyse) konden we indirect een schatting maken van de zelfmanagementvaardigheden van de deelnemers. De TTR is geanalyseerd met multilevel lineaire regressie-modellering. Het doel van deze studie was om patiënten met OAT te ondersteunen door ze te voorzien van zelfmanagement, inclusief een eHealthportaal en scholing. We verwachtten vast te kunnen stellen welke vorm van scholing een belangrijke factor bij succesvol zelfmanagement kan zijn. De verwachting was dat dit zelfmanagementprogramma patiënten zou helpen om hun eigen INR-waarden en medicatiegebruik beter te reguleren, wat de gezondheidsstatus zou bevorderen en het aantal ernstige complicaties zou doen afnemen.

Hoofdstuk 7 omschrijft de effecten van de combinaties van scholingen en eHealthprogramma's op de therapeutische controle van OAT-patiënten in de PORTALS studie.

In totaal zijn er 1.632 VKA-patiënten van de Trombosedienst van Saltro uitgenodigd om deel te nemen, wat in 56% van de gevallen ($n=915$) is afgewezen. Van de 717 patiënten die wilden deelnemen aan de studie, hebben er uiteindelijk 247 informed consent gegeven. Van hen bleven 110 reguliere zorg ontvangen (groep 3) en zijn er 137 willekeurig verdeeld over de zelfmanagementgroepen 1 (e-Learning, $n=63$) en 2 (groepstraining, $n=74$). De analyses toonden geen significante verschillen in TTR tussen de drie perioden ($p=0.520$), de drie groepen ($p=0.460$) of de drie groepen in de tijd ($p=0.263$). Vergelijking tussen e-Learning en groepstraining toonde geen significante verschillen in TTR tussen de perioden ($p=0.614$), de groepen ($p=0.460$) of de groepen in de tijd ($p=0.263$). Er zijn geen significante verschillen gevonden tussen de zelfmanagementgroepen in het gebruik van het platform (0-6 maanden $p=0.571$; 6-12 maanden $p=0.866$; 12-18 maanden $p=0.260$). Het percentage complicaties was laag in alle groepen (3.2%; 1.4%; 0%).

Er zijn geen significante verschillen in therapeutische controle gevonden

tussen de drie groepen. Bovendien zijn er geen verschillen gevonden tussen OAT-patiënten die getraind waren met e-Learning of in een groepstraining wat betreft TTR en gebruik van een ondersteunend eHealthplatform. Dat de therapeutische controle na de interventie niet is verbeterd, lijkt (deels) te liggen aan het feit dat verdere verbetering door een zelfmanagement-programma (inclusief scholing) moeilijk te realiseren was voor deze groep patiënten die al zorg van hoge kwaliteit kreeg; in tegenstelling tot de literatuur was de kwaliteit van OAT-management in de huidige studie bij aanvang al relatief hoog in alle groepen. Beide trainingsmethoden hadden een vergelijkbaar effect op antistollingscontrole; voor patiënten en zorg-professionals betekent dit dat een goed e-Learningprogramma een geschikt alternatief is voor arbeidsintensieve groepstrainingen. Onze aanbeveling is daarom om bij voorkeur zelfmanagementprogramma's ondersteund door e-Learning te overwegen bij zelfmanagement van antistollingspatiënten. Zelfmanagement met een e-Learningcomponent is geschikt voor gemotiveerde patiënten met voldoende digitale vaardigheden; we zijn wel van mening dat reguliere antistollingszorg moet blijven bestaan voor een deel van de populatie.

In deze studie was de praktisch toegevoegde waarde van het eHealthportaal erg hoog voor patiënten, vanwege de functionaliteiten zelfmonitoring, zelfdosering en digitaal advies van zorgprofessionals. Patiënten konden hun antistolling op elke gewenste tijd en plaats regelen. Het gebruik van het zelfmanagementprogramma gaf hen vrijheid, wat waarschijnlijk een sterke motivator was om het programma tijdens de gehele interventieperiode te blijven gebruiken.

We kunnen hieruit concluderen dat zelfmanagement met adequate en solide training via e-Learning of groepstraining veilig en betrouwbaar lijkt voor een selecte groep gemotiveerde patiënten die orale antistollingsmiddelen gebruiken.

In **Hoofdstuk 8** bediscussiëren we onze bevindingen uit de e-Vita- en PORTALS studie. We concluderen dat zelfmanagement ondersteund door eHealth en geïntegreerd in de reguliere zorg patiënten met COPD en OAT kan helpen bij het reguleren van hun ziekte en gezondheid. We veronderstelden dat blended care met een volledige integratie van eHealth en reguliere zorg op de lange termijn de kwaliteit van leven zal verbeteren. Ondanks dat zelfmanagement ondersteund door eHealth geen voordeel leek te hebben boven reguliere zorg wat betreft gezondheidsstatus, toonden de studies ook geen negatieve effecten. eHealth zou dus een veilige optie

kunnen zijn voor zelfmanagementondersteuning en kwalitatief goed ziektemanagement.

Het gebruik van eHealthplatforms is beter wanneer het perfect is geïntegreerd in de gebruikelijke zorg, vooral wanneer patiënten persoonlijke assistentie en coaching ontvangen. Platforms worden meer gebruikt als ze hogere praktisch toegevoegde waarde hebben in het dagelijks leven van de patiënten.

Vanuit onze bevindingen kunnen enkele aanbevelingen worden gedaan voor vervolgonderzoek. eHealthapplicaties moeten op maat worden afgestemd op individuen met variabele basiskennis over gezondheid en op verschillende chronische ziekten; de platforms zouden zich moeten focussen op ondersteuning om de leefstijl te verbeteren. Het is heel belangrijk om patiënten op te leiden en te coachen in het gebruik van digitale platforms; daarnaast is het noodzakelijk om zorgprofessionals te scholen om een faciliterende en begeleidende rol aan te nemen. Zelfmanagement-programma's met eHealth dienen lang genoeg te worden aangeboden om patiënten de kans te geven hun gedrag geleidelijk te veranderen, en tot een betere gezondheidsstatus te komen. Er zijn daarom meer studies nodig, bij voorkeur met een groot aantal deelnemers en met niet-gebruikers. Dit zal meer inzichten geven in i) de optimale combinatie van reguliere zorg en zelfmanagement op basis van eHealth, ii) de voorkeuren en wensen van allerlei soorten patiënten, iii) de nodige scholing voor zorgprofessionals en patiënten, iv) het beste en meest gebruiksvriendelijke platform voor patiënten, en v) de gemoeide kosten.

De aanzienlijke werklast die de integratie van een digitaal platform in de reguliere zorg met zich meebrengt benadrukt het belang van het testen en evalueren van de gevolgen op de werkdruk binnen de zorgcentra.

Dankwoord

Het schrijven van een proefschrift lijkt op een lange, zware, mooie en leerzame reis. Ik heb gereisd met veel fantastische en inspirerende mensen die het mij gegund hebben deze reis af te ronden met een thesis. Eindelijk mag ik al deze mensen bedanken!

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Aan de eVita COPD studie hebben veel mensen meegewerkt in verschillende fases en op verschillende manieren.

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Zonder de dappere patienten die zich wilden wagen aan een innovatief onderzoek over eHealth was deze promotie niet gelukt. Ze zullen het waarschijnlijk niet lezen, maar ik ben ze zeer dankbaar!

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Gijs, als vriend van Iris ben je in ons gezin gerold. Het is net alsof het altijd zo geweest is. En daar ben ik heel blij om.

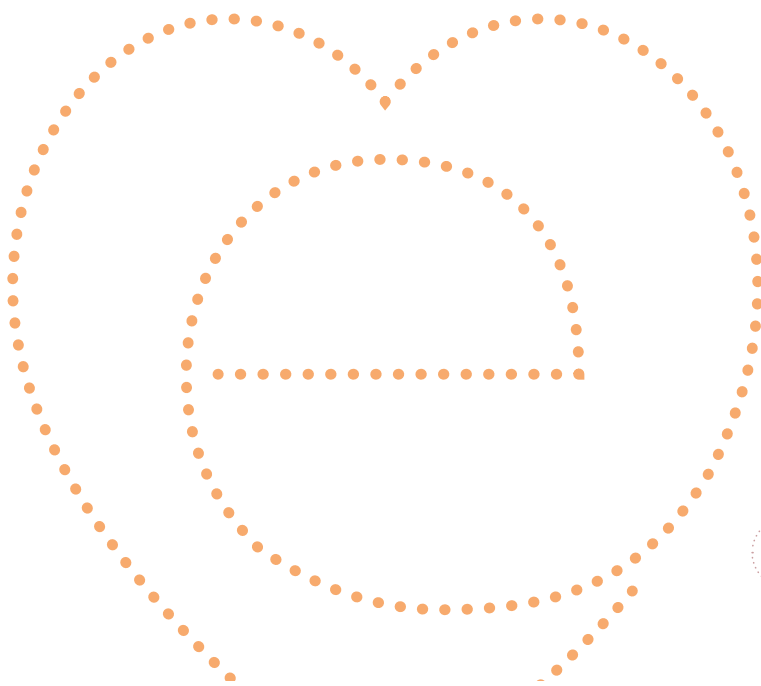
Lieve Iris en Jorin, de mooiste, slimste, sterkste, kwetsbaarste en meest bijzondere kinderen van dit heelal. Eindeloos veel dank voor jullie steun. Jullie hebben heel vaak verwonderd naar mij gekeken; waarom doe ik mijzelf een promotie aan terwijl het niet noodzakelijk is? Jullie hebben me met veel humor geholpen te relaxen en te relativieren. En jullie hebben allebei bijgedragen aan dit onderzoek. Een familieproject!

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Curriculum Vitae

Esther Talboom-Kamp was born on the 27th of May 1968 in Etten-Leur, the Netherlands. She graduated at the Katholieke Scholengemeenschap Etten-Leur in 1986. During her medical study at the Faculty of Medicine of the Erasmus University Rotterdam, she also worked on the department of Gynaecology and Obstetrics in a Czech hospital. After finishing medical school cum laude in 1993, she gained experience as a medical doctor in internal medicine and pulmonary disease in Hopital Tenon in Paris in 1993. Furthermore, she worked as a resident in internal medicine in a hospital until 1995.

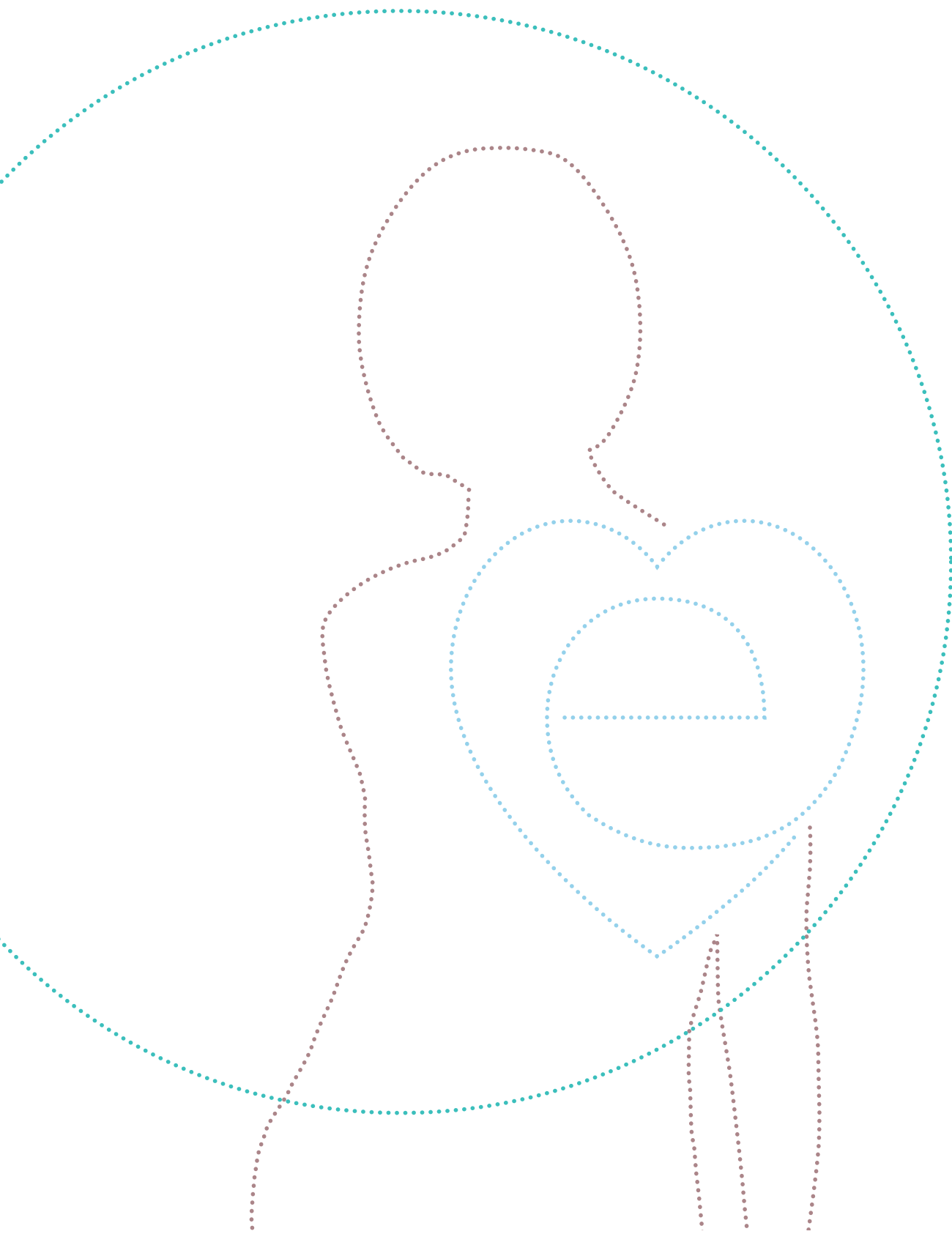
Her vocational training as a general practitioner started in 1995 at the faculty of general practice of the Erasmus University Rotterdam and she graduated as a general practitioner in 1998. From 1998 to 2008 she practiced as a general practitioner in a multicultural neighbourhood in Rotterdam. During this function, her interest in integrated care and self-management for patients developed over time. She had an active role implementing disease management programs for chronic patients in her practice. Furthermore, her interest in managerial responsibility developed in due course of time through various management and leadership functions in a large primary care organisation (Stichting Boog). In 2010, she obtained a master's degree in business administration at the Erasmus University. In 2008, she was appointed as a director of a diagnostic centre in the Netherlands. In 2010, she was elected as the most talented manager in healthcare and received a national award. In 2011, she started as chairman of the board at Saltro Diagnostics, a leading innovative diagnostic centre. In this executive function, she is responsible for the strategy and operational management of this laboratory with 600 employees.



In 2011, she joined the supervisory board of a consultancy agency called Raedelijs. Since 2014 she is a member of the board of the association which supports primary care in the Netherlands called InEen. Within this board, she is responsible for innovation of healthcare, human resources and diagnostics. Furthermore, she is a board member of a national platform that promotes and supports the implementation of self-management for chronic patients (Zelfzorg Ondersteund).

Next to her work as an executive, in 2009 she started the scientific research described in this thesis under the guidance of Professor Niels Chavannes, Doctor Noortje Verdijk, Professor Mattijs Numans and Doctor Marise Kasteleyn.

After finishing this PhD thesis, she will combine her executive functions with her scientific research work.



List of publications

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