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Ulrika Andersson



#### **DOCTORAL DISSERTATION**

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**Title:** E-health in the treatment of hypertension in primary care

#### Abstract

**Background:** Hypertension is a major risk factor for cardiovascular disease, affecting more than a billion people around the world. Despite the good availability of effective antihypertensive drugs and the proven effect of lifestyle modifications, more than half of the people with the diagnosis do not have a controlled blood pressure (BP). Health care in Sweden is changing, and patients are expected to take on a bigger role and be more involved in their own treatment in a more person-centred health care system. Digital tools can support patients' self-management of chronic conditions, such as hypertension. By empowering and enabling patients to find insight and motivation to adhere to treatment, better BP control can be achieved in the population. Aim: The overall aim of this thesis is to evaluate if the treatment of hypertension in primary care can improve by supporting patients to self-manage their condition, using an interactive web-based system, which may facilitate person-centred health care. Methods: A randomised controlled trial entitled PERson-centredness in Hypertension management using Information Technology (PERHIT) was performed in four Swedish regions in primary care, including more than 900 patients. The patients in the intervention group received a BP monitor and used an interactive web-based support system at home for eight consecutive weeks. Patients self-reported, once daily, via their mobile phone; BP and pulse, and rated their wellbeing, physical activities, symptoms, and side effects during the day. They could receive graphical feedback on their BP values and self-reports through a secure web portal and were offered to receive motivational messages. A follow-up consultation with the patient's nurse or physician was conducted after eight weeks and after 12 months. **Results:** The proportion of participants with a controlled BP increased after eight weeks, with a significant difference between the groups favouring the intervention group, 48.8% compared to 39.9% (P=0.006). The long-term effects were uncertain. Using the system could promote a constructive and person-centred partnership between patient and professional. Most of the participants were positive about using the system, but all did not agree. Increased day-to-day home BP variability (BPV) was significantly associated with increased pulse pressure (P=0.015) and decreased eGFR (P=0.049), as markers for target organ damage. Furthermore, self-reported higher wellbeing, lower restlessness and less stress, and higher adherence to medication, were all associated with lower same-day BP levels. The associations between same-day BP and symptoms were weaker, but significant for headache. Conclusions: The findings suggest that the interactive self-management system can be used as a tool for a person-centred approach in hypertension care and can improve BP control in primary care. It can promote a constructive partnership between patient and professional. However, the e-health solution alone is insufficient for effective hypertension management. Successful implementation relies on health care professionals' willingness to embrace new methods and technology.

**Keywords:** blood pressure, digital intervention, e-health, home monitoring, hypertension, mobile phones, patient-professional partnership, person-centred care, primary health care, self-management

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## **Abstract**

#### Introduction

Hypertension is a major risk factor for cardiovascular disease, affecting more than a billion people around the world. Despite the good availability of effective antihypertensive drugs and the proven effect of lifestyle modifications, more than half of the people with the diagnosis do not have a controlled blood pressure (BP). Health care in Sweden is changing, and patients are expected to take on a bigger role and be more involved in their own treatment in a more person-centred health care system. Digital tools can support patients' self-management of chronic conditions, such as hypertension. By empowering and enabling patients to find insight and motivation to adhere to treatment, better BP control can be achieved in the population.

#### Aim

The overall aim of this thesis is to evaluate if the treatment of hypertension in primary care can improve by supporting patients to self-manage their condition, using an interactive web-based system, which may facilitate person-centred health care.

#### Methods

A randomised controlled trial entitled PERson-centredness in Hypertension management using Information Technology (PERHIT) was performed in four Swedish regions in primary care, including more than 900 patients. The patients in the intervention group received a BP monitor and used an interactive web-based support system at home for eight consecutive weeks. Patients self-reported, once daily, via their mobile phone; BP and pulse, and rated their wellbeing, physical activities, symptoms, and side effects during the day. They could receive graphical feedback on their BP values and self-reports through a secure web portal and were offered to receive motivational messages. A follow-up consultation with the patient's nurse or physician was conducted after eight weeks and after 12 months.

#### Results

The proportion of participants with a controlled BP increased after eight weeks, with a significant difference between the groups favouring the intervention group, 48.8% compared to 39.9% (P=0.006). The long-term effects were uncertain. Using the system

could promote a constructive and person-centred partnership between patient and professional. Most of the participants were positive about using the system, but all did not agree. Increased day-to-day home BP variability (BPV) was significantly associated with increased pulse pressure (P=0.015) and decreased eGFR (P=0.049), as markers for target organ damage. Furthermore, self-reported higher wellbeing, lower restlessness and less stress, and higher adherence to medication, were all associated with lower same-day BP levels. The associations between same-day BP and symptoms were weaker, but significant for headache.

#### Conclusions

The findings suggest that the interactive self-management system can be used as a tool for a person-centred approach in hypertension care and can improve BP control in primary care. It can promote a constructive partnership between patient and professional. However, the e-health solution alone is insufficient for effective hypertension management. Successful implementation relies on health care professionals' willingness to embrace new methods and technology.

## List of Papers

### Paper I

Andersson U, Bengtsson U, Ranerup A, Midlöv P, Kjellgren K. Patients and Professionals as Partners in Hypertension Care: Qualitative Substudy of a Randomized Controlled Trial Using an Interactive Web-based System Via Mobile Phone. *Journal of Medical Internet Research*. 2021; 23(6): e26143.

#### Paper II

**Andersson** U, Nilsson PM, Kjellgren K, Hoffmann M, Wennersten A, Midlöv P. PERson-centredness in Hypertension management using Information Technology: a randomized controlled trial in primary care. *Journal of Hypertension*. 2023; 41(2): 246-253.

#### Paper III

Andersson U, Nilsson PM, Kjellgren K, Harris K, Chalmers J, Ekholm M, Midlöv P. Variability in home blood pressure and its association with renal function and pulse pressure in patients with treated hypertension in primary care. *Journal of Human Hypertension*. 2024; 38(3): 212-220.

## Paper IV

**Andersson** U, Nilsson PM, Kjellgren K, Ekholm M, Midlöv P. Associations between daily Home Blood Pressure Measurements and Self-reports of Lifestyle and Symptoms in Primary Care: the PERHIT Study. Accepted for publication by *Scandinavian Journal of Primary Health Care*.

## **Abbreviations**

ARV Average real variability

BP Blood pressure

BPV Blood pressure variability

CKD Chronic kidney disease

CV Coefficient of variation

CVD Cardiovascular disease

DBP Diastolic blood pressure

eCRF Electronic case report form

eGFR Estimated glomerular filtration rate

ESH The European Society of Hypertension

GPCC Gothenburg Centre for Person-centred Care

HBPM Home blood pressure monitoring

HDBP Home diastolic blood pressure

HSBP Home systolic blood pressure

HCP Health care professional

ICT Information and Communication Technology

PHCC Primary health care centre

PP Pulse pressure

RAAS Renin angiotensin aldosterone system

RCT Randomised controlled trial

SBP Systolic blood pressure

SD Standard deviation

TOD Target organ damage

VIM Variation independent of the mean

WHO World Health Organization

## Introduction

In my work as a general practitioner at Vårdcentralen Löddeköpinge in Skåne I meet a lot of patients with hypertension, at yearly check-ups, but also when they visit for other reasons. Hypertension care can sometimes seem like an uncomplicated task. Blood pressure (BP) is easily measured and there are effective medications available. Despite this, many of my patients still have a high BP, even if they regularly come to the health care centre. When scratching the surface, you will find that hypertension care is more complicated than it seems, and there are considerable challenges in improving hypertension management.

Hypertension is the most important modifiable risk factor for cardiovascular disease (CVD), affecting more than one billion people around the world. An increase of 20 mmHg in systolic BP (SBP) or 10 mmHg in diastolic BP (DBP) doubles the risk of dying of stroke or ischaemic heart disease. It is well known that hypertension can be effectively treated with lifestyle changes or with antihypertensive medication. Despite this, less than half of everyone with diagnosed and treated hypertension have a well-controlled BP. Healthy habits are hard to maintain, prescribing physicians do not uptitrate treatment to a sufficient extent, and patients' adherence to treatment is suboptimal.

Health care in Sweden, and around the world, is changing. The traditional roles of patients and professionals are being questioned and challenged, with an increased focus on patients' participation and involvement in their health care treatment. With an ageing population and increasing prevalence of chronic conditions, our society needs to provide more efficient health care with fewer means.

Digital solutions can be used to facilitate the transformation of health care and enable support to patients to successfully self-manage their health conditions, such as hypertension. The market for e-health solutions is enormous, with many different stakeholders. It is crucial to ensure scientific evaluation and validation in the process of introducing new technologies and digital tools in health care since there is no room for solutions without a positive effect, which may burden the already strained health care system even more.

In this thesis, I describe results from a trial where an interactive web-based self-management system for hypertension management was tested. With this as a base, I discuss hypertension management in primary care, using e-health. There are three different focus areas in the thesis: hypertension, e-health, and person-centred care (PCC).

## Background

## Hypertension

## History of hypertension

The first known measurement of BP is attributed to Reverend Stephen Hales, who in 1733 managed to measure arterial BP in a horse. A century later, the French physician Poiseuille demonstrated that arterial BP is maintained in small arteries by using a mercury manometer and a cannula inserted in the experimental animal's artery.3 During the same period, high BP was observed in patients with kidney disease, but it took a few more decades before it was reported that hypertension could occur in apparently healthy individuals.<sup>4</sup> The first non-invasive measurement of BP was performed in the mid-19th century and during the following decades, the sphygmomanometer was refined and improved. BP measurement could by then be performed in humans, although not generally accepted in clinical practice. In 1896, the Italian physician, Riva-Rocci, introduced a sphygmomanometer applied to the upper arm, using a mercury manometer, which rendered precise and rapid measurements of SBP, while remaining harmless to the patient.<sup>3</sup> Nine years later, the Russian surgeon Korotkoff described the auscultatory technique to gauge SBP and DBP, using the Riva-Rocci sphygmomanometer. This technique to measure BP is still used today, although the mercury manometer has usually been replaced with less health-hazardous devices. The term "essential hypertension" first appeared in the early 1900s, indicating that elevation of BP was seen as a necessary and compensatory reaction in the body. The idea that high BP should be treated was not without controversy. In 1967, the first randomised controlled trial on hypertension treatment versus placebo was published, with convincing evidence of benefits from treatment.<sup>6</sup> The first group of modern antihypertensive drugs developed were diuretics, which were introduced in the 1950s.<sup>5</sup> During the following decades, the major classes of antihypertensive drugs used today were discovered; β-blockers, calcium antagonists, angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB) and α-1 receptor blockers. <sup>5</sup> The knowledge about the benefits of different classes of antihypertensive drugs increased with large trials during the 1990s and early 2000s. One of them was the AngloScandinavian Cardiac Outcome Trial (ASCOT) which showed that amlodipine and/or ACEi was superior to atenolol and/or thiazide in preventing cardiovascular events and all-cause mortality, as well as reducing new onset of diabetes mellitus, in patients with hypertension and increased risk of CVD.<sup>7</sup> The Losartan Intervention For Endpoint reduction in hypertension (LIFE) study showed that losartan was better than atenolol in reducing the incidence of CVD in patients with hypertension and better tolerated, with the same BP-lowering effect.<sup>8</sup> With several major trials and cohort studies, such as The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)<sup>8</sup>, the Framingham project<sup>9</sup> and the Systolic Blood Pressure Intervention Trial (SPRINT)<sup>10</sup>, our knowledge about BP as a risk factor for cardiovascular disease and its treatment has increased significantly. Nevertheless, hypertension continues to be a major health problem around the world. There is still much we do not know about hypertension, and the research field is still growing.

## Definition and prevalence

Hypertension is defined by the World Health Organization (WHO) as having a mean SBP  $\geq$ 140 mmHg or DBP  $\geq$ 90 mmHg or taking antihypertensive medication. The definition is arbitrary and not without dispute; the latest American guidelines define hypertension as a mean  $\geq$ 130/80 mmHg in adults, thus leading to a substantially larger population with the condition. Increased BP above 115/75 mmHg is linearly associated with increased cardiovascular mortality and morbidity.

In this thesis, hypertension is defined as ≥140/90 mmHg, in line with European guidelines and WHO definition. <sup>11,13</sup> The BP values refer to a mean of repeated readings in the clinic. Hypertension can be divided into primary (or "essential") and secondary hypertension. Only a small fraction of all hypertension diagnoses consist of secondary hypertension. It should mainly be suspected in younger patients with a sudden onset of resistant or malignant hypertension and is caused by a specific pathophysiology, such as primary aldosteronism or renal disease. <sup>13</sup> This thesis concerns primary hypertension.

BP is pulsatile and usually described by its extreme pressure values: the highest value when the heart contracts, SBP, and the lowest value when the heart is relaxed before the next contraction, DBP. It can also be described as a steady component, mean arterial pressure (MAP), and a pulsatile component, pulse pressure (PP). PP is the difference between SBP and DBP and represents the oscillations around MAP. It depends on how the volume ejected by the left ventricle in systole is accommodated by the large arteries, thus affected by the stiffness of the arteries. With older age, SBP increases steadily. DBP increases until the age of 50-60 years, whereafter it plateaus and

then slightly decreases, due to ageing blood vessels with increased arterial stiffness. <sup>15</sup> PP thus increases with age and is an independent predictor of cardiovascular events. <sup>16,17</sup>

Globally, hypertension is estimated to affect 33% of the adult population (aged 30-79) and the incidence increases with age. Even though the age-adjusted prevalence of hypertension in high-income countries has decreased during the last 30 years, from 38% in 1990 to 32% in 2019, the total number of persons in the world with hypertension has doubled, from 650 million to 1.3 billion at the same time. About one billion of these people live in low- and middle-income countries where the prevalence has increased somewhat, but the large increase is mainly due to a growing population around the world, with a higher proportion of people of old age. In Sweden, the prevalence of hypertension is estimated to be 30%. Men are overrepresented in the population with hypertension globally as well as in Sweden; 36% of Swedish men have hypertension compared to 25% of Swedish women (aged 30-79).

### Pathogenesis

Unlike secondary hypertension, primary hypertension is not derived from one specific cause. The development of primary hypertension is due to an intricate interplay of genetic, environmental and lifestyle factors, and to date, we do not have the complete picture. To understand the pathogenesis of hypertension, one must start with the physiology of BP.

BP is the force exerted on the walls of the arteries by the blood flow. It is determined by the amount of blood pumped by the heart every minute (cardiac output) and by the total peripheral vascular resistance. Peripheral resistance is affected by the elasticity and the diameter of the blood vessels. Cardiac output in turn is determined by the heart rate and the stroke volume (the volume of blood pumped with every cardiac contraction). <sup>14</sup> BP can be expressed as

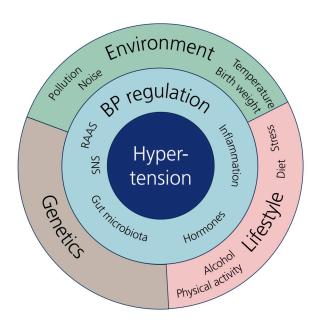
BP = cardiac output  $\cdot$  peripheral resistance

Increased BP is thus the result of increased cardiac output and/or peripheral resistance. Increased cardiac output and normal peripheral resistance are seen in children and younger adults with hypertension, whereas in adults with established hypertension, increased peripheral resistance is observed, and cardiac output is usually normal or reduced.<sup>20</sup>

Various mechanisms affect cardiac output and peripheral resistance and collectively contribute to elevated BP. Genetic factors account for 30-60% of the individual risk of

developing hypertension.<sup>21</sup> Even with advances in recent years, only a small fraction of the genetic variations associated with hypertension are identified.<sup>22</sup>

Environmental and lifestyle factors that influence BP are, for example, stress, increased salt intake, physical inactivity, obesity, and excess intake of alcohol. <sup>12</sup> Influences in early life can also be of consequence for future risk of hypertension. <sup>23</sup> For example, birth weight is considered inversely related to the risk of adult hypertension. <sup>24</sup> In recent years, gut microbiota has gained interest in hypertension research, as it seems to be both associated with the development of hypertension and affected by hypertension. <sup>25</sup> Development of hypertension is also affected by intrinsic factors such as vascular conditions and endothelial dysfunction, as well as sympathetic activation, activation of the renin-angiotensin aldosterone system (RAAS), renal mechanisms, inflammation, and oxidative stress. <sup>19</sup> Some of the mechanisms involved in hypertension development are illustrated in Figure 1.



**Figure 1.**Mechanisms involved in the development of hypertension, modified from <sup>13</sup>. RAAS, renin-angiotensin-aldosterone system; SNS, sympathetic nervous system.

### Hypertension management in primary care in Sweden

Most patients with hypertension in Sweden are treated in primary health care. 26 Health care in Sweden is funded by taxes and organised in 21 different regions. Health care professionals (HCP) have regional clinical guidelines to rely on, which are based on international guidelines, but the interpretation and prioritisation processes may vary according to local conditions. Hellberg et al showed that there are differences in hypertension management between different primary health care centres (PHCCs) and different regions in Sweden. About half of the included PHCCs in the study had teams with nurses and physicians dedicated to hypertension management.<sup>27</sup> Team-based hypertension care has been shown to improve treatment results. <sup>28,29</sup> There were also large differences in how BP measurements were conducted, and the authors identified that there was generally room for improvement in this area.<sup>27</sup> BP control has improved for patients with treated hypertension in recent years, but there is still a need for further improvement. National surveys in Sweden have shown that 44-49% of the patients with hypertension had a BP lower than 140/90 mmHg in 2017.<sup>2,30</sup> Globally, the situation is similar: a large survey from 2018 showed that 46.3% of the participants receiving treatment for hypertension did not have a controlled BP.<sup>31</sup>

The European Society of Hypertension (ESH) updated its guidelines for the management of arterial hypertension in 2023.<sup>13</sup> The guidelines cover all aspects of hypertension management, from correct diagnosis to adequate treatment. After diagnosis of hypertension and once the target BP is reached and stable, the guidelines recommend one or two follow-up visits per year. Home BP measurement/monitoring (HBPM) is recommended prior to follow-up visits and on a regular basis. HBPM has several benefits over office BP readings: it predicts CVD risk better than office BP; it is easily reproducible and well-tolerated by patients.<sup>13</sup> A home BP of 135/85 mmHg corresponds to an office BP value of 140/90 mmHg.<sup>32</sup>

With a reduction of 10 mmHg in SBP, the risk of major CVD is lowered by 20%.<sup>33</sup> Recommended treatment of hypertension is lifestyle modifications and drug treatment. Lifestyle modifications include increased physical activity, smoking cessation, stress reduction, a healthy diet with limited salt intake and low alcohol consumption, and weight reduction if needed.<sup>34,35</sup> Recent international hypertension management recommendations also include the use of digital tools and wearables in hypertension treatment to support behaviour change and facilitate communication between patients and professionals.<sup>35</sup>

### Symptoms and perceptions of hypertension

Hypertension is often considered a symptomless condition and is sometimes referred to as "the silent killer". 36 However, patients with hypertension do not necessarily agree with this suggestion. Studies have shown that many patients frequently experience symptoms that they attribute to hypertension, such as headache, dizziness, and heart palpitations. <sup>37,38</sup> The symptoms reported by patients with hypertension are commonly also reported by patients without hypertension, thus clouding the picture.<sup>39</sup> It may be difficult to discern the origin and cause of the symptoms, for example, hypertension or the treatment may cause headache, but pain may also inflict a rise in BP. 40 Moreover, the association between experienced symptoms and BP levels has been shown to be weak in several studies. 41,42 In 1985, Meyer, Leventhal and Gutman applied the Common-Sense Model to hypertension, and described that people with the condition construct common-sense beliefs of the condition, based on their previous experience of illness.<sup>43</sup> Most of the participants in their study believed that hypertension and BP elevations were associated with symptoms and that the condition was of limited duration, and adherence to treatment was found to be related to the belief in the beneficial effect of treatment on symptoms. 43 Even though almost 40 years have passed since Meyer's study, the findings are still relevant, as confirmed in more recent studies. 44-46 Bengtsson et al described that HCPs' views on symptoms concerning hypertension may differ from patients, resulting in different expectations of the effect of treatment on perceived symptoms.<sup>47</sup> Studies show that some patients base their decisions about adherence to treatment on how they feel and their experiences of symptoms. 48-50 With non-specific symptoms and weak associations to actual BP levels, basing hypertension treatment on the experience of symptoms may lead to inaccurate treatment decisions.

Psychological symptoms such as anxiety and stress are also attributed to hypertension by patients. In a systematic review of patients' perspectives on hypertension, it was stated that many patients across different ethnic groups saw stress as an important explanation for developing hypertension. Many patients perceive that stress and nervousness are closely linked to hypertension - as a cause, a consequence, or an exacerbating factor. As a result of this, patients may decide to discontinue their antihypertensive treatment when not feeling stressed or nervous.

Patients' perceptions of hypertension are important for adherence and persistence to treatment, as shown in a Swedish study by Qvarnström et al from 2019.<sup>52</sup> The authors concluded that patients who discontinued their antihypertensive treatment more frequently believed that hypertension was not a chronic condition and were less aware of the protective effect of antihypertensive treatment.<sup>52</sup> The perceptions of hypertension may differ in different countries and cultures, whereby cultural beliefs

may influence adherence.<sup>53</sup> To improve the management of hypertension in clinical practice, it is necessary for HCPs to familiarise themselves with the patient's perceptions and knowledge of the condition. It is also important to identify if and how the patient is prepared to change their behaviour to maintain a controlled BP.<sup>54</sup>

Non-adherence to antihypertensive treatment is a well-known problem in hypertension management. According to the ESH guidelines, one in three to four patients with hypertension do not adhere to treatment <sup>13</sup>, but some studies report non-adherence to be as high as 50%. <sup>55</sup> Non-adherence results in elevated BP and increased risk of negative health consequences. Reasons for non-adherence differ, and patients' perception of hypertension and symptoms matter, even though that is somewhat neglected in the current literature. <sup>55,56</sup> Patients' beliefs and experiences of symptoms are not discussed in hypertension guidelines, where symptoms are mainly mentioned as effects of target organ damage. <sup>13</sup> Other factors that may influence adherence to treatment are, among others, patient-professional relationship, economy, social status and support, number of prescribed drugs, and side effects. <sup>57</sup> Financial reasons for non-adherence are probably less frequent in Sweden than in other countries where the patients need to cover health care costs and medication themselves. <sup>58</sup>

## Blood pressure variability

One less explored field in hypertension research is BP variability (BPV) and its clinical importance. The variation of BP over the short and long term is a normal phenomenon and a cardiovascular regulatory response to internal and external behavioural and environmental factors. However, an increased BPV is a prognostic marker for cardiovascular morbidity and mortality, independent of mean BP. As an independent risk marker, BPV may become a potential therapeutic target. There are some indications that antihypertensive drugs with long-lasting effects, such as calcium antagonists, might be a good choice in individuals with elevated BPV. However, this hypothesis is based on results from *post-hoc* analyses, hence why further research is needed for recommendations in clinical practice. As an independent of the post-hoc analyses, hence why further research is needed for recommendations in clinical practice.

BPV can be measured during different time intervals and categorised accordingly. Very short-term BPV is beat-to-beat variability and requires invasive intra-arterial measuring methods. Short-term variability is defined as variability over 24 hours and can be assessed by ambulatory BP monitoring (ABPM). Mid-term variability is equivalent to day-to-day variability and may be based on HBPM. Long-term BPV can be assessed by repeated office BP measurements and is also called visit-to-visit BPV. <sup>64</sup> The different measurement methods of BPV are not interchangeable, as there seems to be a low

correlation between the different measurement methods and low concordance in diagnosing patients with high BPV.<sup>65</sup>

There is no consensus regarding which index or thresholds should be used for BPV. Some of the most frequently used indices are presented in Table 1. Since BPV generally increases with increased mean BP, it is recommended to incorporate mean BP in the index.<sup>66</sup>

**Table 1.** BPV indices.

Index	Explanation
Standard deviation (SD)	Square root of variance
Coefficient of variation (CV)	SD divided by mean BP multiplied by 100
Variability independent of the mean (VIM)	SD/mean <sup>x</sup> , where x is obtained by a fitting curve through a plot of SD against mean using the model SD=a*mean <sup>x</sup>
Average real variability (ARV)	Average of absolute differences between consecutive BP values
Range	The difference between max and min BP values

HBPM has the advantage of being easily accessed and well-accepted by patients. Increased day-to-day BPV is associated with several factors in treated hypertensive patients: advanced age, female sex, increased arterial stiffness, elevated mean BP values, low BMI, low heart rate, excessive alcohol intake, cigarette smoking, CVD, diabetes, diabetic nephropathy, and sedentary lifestyle.<sup>67</sup>

With many unanswered questions, BPV has long been considered of mere interest for research, without any implication in clinical practice. However, in 2023, a European consensus paper was published by the ESH, suggesting consideration of BPV in clinical practice. <sup>66</sup> With the introduction of wearable cuffless devices for BP measurement, in the form of wristwatches, unobtrusive continuous BP monitoring becomes possible. Cuffless devices are not recommended by current guidelines since they are not considered accurate enough, but it should only be a matter of time before we get there. <sup>13</sup> This development may contribute to shedding new light on aspects of BPV and its clinical implications.

## E-health

## Definition and development

Globally, two-thirds of the population use a mobile phone, and in Sweden, 95% of the population between 16 and 85 years use the internet.<sup>68,69</sup> Digital technologies bring opportunities for accessible and affordable health solutions and delivery of health services, but also new concerns and potential threats. The development of digital solutions for health care has been immense during the last decades and the terminology and concepts in the field are constantly evolving. WHO describes digital health as:

The field of knowledge and practice associated with the development and use of digital technologies to improve health.<sup>70</sup>

Digital health is often used as an umbrella term, covering the concept of e-health. The distinction between digital health and e-health is not clear though, and the terms are used interchangeably in scientific literature. In this thesis, the term e-health is primarily used. The first generally accepted definition of e-health was published in 2001 by Gunther Eysenbach, who defined e-health as a medical and public health field,

referring to health services and information delivered or enhanced through the Internet and related technologies.<sup>71</sup>

Eysenbach's definition is still considered valid and frequently cited. He emphasised that e-health is a broader term than just dealing with the internet,

a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve health care locally, regionally, and worldwide by using information and communication technology.  $^{71}$ 

As described by Eysenbach, e-health can be seen as a new way of thinking and communicating about health care, locally and globally, thus revolutionising health care. The word e-health was first used in the fields of industry and marketing in an era of other e-words, such as e-mail, e-solutions and e-commerce. The "e" then referred to "electronic", but can, according to Eysenbach, stand for other things, for example, efficiency, empowerment, enabling and equity, thus incorporating the potential of the concept.<sup>71</sup>

The functions of e-health have been described as threefold: 1) inform, track, and monitor health parameters, 2) interaction and communication between health care participants, and 3) data utilisation to improve health and health services.<sup>72,73</sup> E-health

thus covers everything from electronic health records and big data to implantable electronic devices.<sup>74</sup> It includes usage of mobile phone applications (apps) and wearables, such as smartwatches, in health care, which can be classified as mobile health (m-health). There is a huge market for health care apps and the number of apps has increased immensely in recent years, but few available apps are scientifically tested and validated.<sup>75,76</sup>

If e-health as a concept has existed for a little more than 20 years, the concept of telemedicine is significantly older and can be considered somewhat of a predecessor to e-health. Telemedicine encompasses the use of telecommunication technology in health care, and dates back to the time of the telegraph.<sup>77</sup> It involves any medical activity performed over a distance.<sup>78</sup> E-health has been suggested as a more modern term for the concept of telemedicine, although telemedicine is still used today, together with, or separate from e-health.<sup>79</sup>

In Sweden, there are high hopes for the opportunities that e-health offers in health care. The Swedish government has together with the Swedish Association of Local Authorities and Regions (Sveriges Kommuner och Regioner) jointly produced the initiative *Vision for eHealth 2025*, with the goal that Sweden should by 2025 be:

best in the world at using the opportunities offered by digitisation and e-health to make it easier for people to achieve good and equal health and welfare, and to develop and strengthen their own resources for increased independence and participation in the life of society.<sup>80</sup>

#### Benefits and risks with e-health

E-health inspires optimism and faith in a revolutionised health care system, where everyone is included and connected. The benefits can be numerous, with increased patient participation, personalised medicine, and prerequisites for increased self-management and shared decision-making.<sup>73</sup> E-health can also contribute to access to health care in remote areas, and in low-resource settings. During the covid-19 pandemic, the benefits of digital encounters became apparent.<sup>81,82</sup> There are hopes and expectations that e-health will facilitate the increasing demands on health care due to a growing population and increase of chronic conditions.<sup>83</sup>

With many potential benefits, it is important to acknowledge that there may also be concerns and drawbacks with e-health. Different actors have different agendas for e-health. For the individual, e-health can mean increased participation and accessibility. For politics and society, it can be a way to make health care more effective and reduce costs. For e-health platform developers and the industry, e-health can be lucrative.<sup>84</sup>

With these different agendas, it is important to discuss and clarify the purpose and possible benefits of e-health solutions. There are concerns that e-health interventions are based on assumptions about benefits without evidence to back them up. <sup>85</sup> E-health solutions often come with the pretences of saving time and money through more effective utilisation of resources, although the evidence is mixed. <sup>86</sup> Significantly more scientific evaluation and validation of e-health solutions is essential before implementation in clinical care.

Although e-health has great potential to decrease health inequality, one must consider the risk of further excluding those already at risk of social health inequalities when implementing e-health solutions. E-health solutions usually require some sort of health and digital literacy not held by everyone, and if this is not recognised and acted on, there is a risk of increasing health inequality.<sup>87</sup>

## Person-centred care

Person-centred care (PCC) can be described as an ethical approach to health care rather than a health care model. It is not something that can be implemented; it is something to aspire to. This ethical approach can guide practical actions performed by HCPs. 88 The Health Foundation in the UK has described a framework with four principles of PCC: personalised, coordinated and enabling care where the person is treated with dignity, compassion, and respect. 89 The Gothenburg Centre for Person-centred Care (GPCC) describes PCC as a partnership between patient and HCP, founded in the patient's narrative and leading to shared documentation in the form of a personal health plan. 90 It includes a collaborative and equalitarian partnership between patient and provider, different from the traditional health care model with the patient as a passive recipient of care. In this thesis, PCC is viewed according to the perspective provided by GPCC. 90

Different nomenclature exists in the field, and sometimes the word patient-centred is used interchangeably with person-centred. Both terms are used to describe health care models with a holistic approach, tailored to the individual's needs, preferences, and values, as opposed to the traditional paternalistic health care model. <sup>91</sup> The goal of patient- and person-centred care may differ though, where a "functional life" is the goal of patient-centred care, and a "meaningful life" is the goal of PCC. PCC is thus a broader concept than patient-centred care and is used to highlight the importance of considering the whole life of the person. <sup>92</sup>

PCC has its roots in the philosophical tradition of personalism, inspired by, among others, the French philosopher Paul Ricoeur. The base in PCC is the concept of the person with individual abilities, knowledge, priorities, resources, capabilities, and a social context. The designation "patient" is the role the person takes on in health care contexts. The patient is always a person, but the person is not a patient in other contexts. PCC is increasingly recognised as an efficient and satisfying health care approach, for both patients and professionals. 93,94

### Partnership and technology

In PCC, the knowledge held by the patient, involving their experience of symptoms and illness in their context, is equally esteemed as the medical knowledge held by the professional. Patients are the experts regarding their own lives, and professionals are experts in the medical field. With their shared expertise, the patient and the professional can together decide on what is important for the patient and form a health plan based on that. The patient and the professionals can preferably work as partners. 90,95 The traditional health care roles with the professional telling the patient what to do may be transformed, and the patient can take on the role of the principal caregiver with the professional as a consultant.

A partnership cannot exist without some antecedents: there must be mutual capability, with willingness and openness for a respectful relationship. From the professional, competence and clinical knowledge are required, as well as empathy. 96,97 In the literature about partnership in health care, shared knowledge, shared power, shared decision-making, and patient autonomy are described as partnership attributes. 98 Empowerment of the patient is considered a consequence of partnership, with enhanced self-management and improved health outcomes for the patient. 98

When introducing e-health solutions in health care, the relationship between patient and professional may be altered. Wildevuur et al<sup>99,100</sup> has described how the partnership between patient and professional is affected and enabled by Information and Communication Technologies (ICT). They have founded their research on the problem that most ICT applications, which aim to support chronic disease self-management, do not take the partnership between patient and professional into consideration. Most ICT applications are not developed in collaboration with stakeholders and may overlook the perspective of either the patient or the professional, which are both needed for meaningful outcomes. The authors conclude that ICT-enabled PCC need to involve shared decision-making, personalisation of ICT, improvement of health-related quality of life, and efficiency, both for the patient and the professional, to strengthen the partnership and improve patient self-

management.<sup>100</sup> When introducing ICT in chronic disease management, the partnership between patient and professional requires adjustments. Using ICT may result in increased potential for self-management, shared analysing of data, and a change in the experience of the partnership, with less physical contact and new pathways for initiation of treatment, all depending on the patient's ability and trust in technology. Other actors need to be introduced, such as intelligent device specialists, which leads to new relationships being formed.<sup>101</sup>

In a paper by Boer et al<sup>102</sup>, the triangular relationship shaped by digital solutions between patient, e-health, and professional is discussed. With e-health, the direct contact between patient and professional can change, and this might affect the holistic assessment obtained by meeting face-to-face and physical examination. On the other hand, some patients may feel more at ease discussing sensitive subjects via a digital connection. E-health and AI-created algorithms are also discussed in relation to shared-decision making, which can be supported or compromised. Through increased access to health knowledge, and support of self-monitoring and -management, e-health may support shared-decision making, but compromises may arise if general algorithms are used that do not incorporate patient preferences and values, which should be the starting point in the primary care process.<sup>102</sup>

## Self-management

Every person who has a chronic condition self-manages their disorder every day, for example by choosing what to eat and drink, whether to exercise or not, and whether to take prescribed medication. <sup>95</sup> The choices they make determine how well they manage their condition. Bokhour et al<sup>50</sup> describe that patients' explanatory model, that is, their understanding and beliefs about the condition, symptoms, and treatment, together with their daily lived experience including their social context, habits, and other health problems, affect how they self-manage their condition. Misconceptions and lack of insight about hypertension influence the patient's self-management activities and can lead to non-adherence and non-persistence to treatment. <sup>103</sup> According to Bokhour, interventions aimed at improving self-management should include more than education and assessment to be effective. The patient's perceptions and experience need to be acknowledged and the intervention needs to be tailored accordingly. <sup>50,104</sup>

Self-management interventions in hypertension care usually involves self-monitoring of BP, which preferably is done at home and can then also be referred to as HBPM. As mentioned above, HBPM has several benefits and is recommended by hypertension guidelines. <sup>13</sup> Self-monitoring also requires the patient to actively engage in hypertension

management, which may favour self-management.<sup>105</sup> In a meta-analysis and systematic review<sup>106</sup>, it was reported that self-monitoring on its own does not affect BP, even though it does bring other benefits, such as better estimation of BP and increased adherence. Self-monitoring was effective in lowering BP if it was combined with interventions offering additional support provided by HCPs, such as tailored education, lifestyle recommendations, or titration of antihypertensive drugs, which is in line with Bokhour's findings regarding self-management.<sup>50,106</sup> The same research group confirmed in a later systematic review and meta-analysis that self-monitoring of BP is effective also for patients with hypertension and comorbidities, such as diabetes or obesity.<sup>107</sup>

### Self-management and e-health

There are several studies with digital solutions aimed at improving hypertension management through support of self-management. Systematic reviews have shown that the interventions have a favourable effect on BP levels. 108,109 The interventions can contain different features and strategies to engage patients. Education regarding hypertension and a healthy lifestyle is commonly present, combined with self-monitoring, goal setting, reminders, motivational encouragement, and social or professional support. 108,110 Li et al described in a systematic review that interventions in hypertension self-management should be tailored to the patient's preferences and include multifaceted functions and interactivity to be more effective. 108

## Pilot project

The research project described in this thesis originates from a pilot project in Sweden named Mobiles phones in Hypertension Management (MIHM). The aim of MIHM was to develop and validate an interactive digital tool for self-management of hypertension, with the purpose of increasing patient adherence to medication and lifestyle changes, through increased patient participation and sharing of knowledge about hypertension. <sup>47,111,112</sup>

The project MIHM was built on research done by Kjellgren et al, with population-based as well as qualitative studies on preconditions of patient adherence to antihypertensive treatment in clinical practice. The authors found that patients' understanding of hypertension and their medication was less than satisfactory and that the patients had a passive role in the interaction with the professionals. The patients in their studies generally perceived symptoms and medication could reduce the

frequency and intensity of hypertension-related symptoms but could in turn generate symptoms as side effects of medication.<sup>37</sup> Since hypertension was usually considered an asymptomatic condition by professionals, it was reasoned that these contrasting views may be problematic in hypertension management and may cause a barrier to adherence.<sup>47</sup>

To ensure that the digital tool was relevant for the intended users, patients with hypertension and professionals participated in the process of developing the system, together with a group of interdisciplinary researchers. The project was well rooted in a person-centred perspective and used the Common-Sense Model as a theoretical base. <sup>116</sup> During the development of the system it became clear that patients wanted to know more about BP and its relation to symptoms, treatment, and side effects. They wanted to feel in control of their condition, and the system was developed to meet these needs. <sup>47</sup> In total, 50 patients with hypertension participated in the project. MIHM showed positive results, with improved BP levels after using the digital tool for eight weeks. SBP and DBP decreased significantly, with 7.0 and 4.9 mmHg respectively. <sup>117</sup> The patients described greater insight and understanding of hypertension and how their BP values were related to daily life, resulting in increased motivation to adhere to treatment. <sup>118,119</sup> The project is described in detail in the thesis by Ulrika Bengtsson <sup>116</sup>, and additional papers. <sup>118–120</sup>

## Aims

The overall aim of this thesis is to evaluate if the treatment of hypertension in primary care can improve by supporting patients to self-manage their condition, using an interactive web-based system via mobile phones, which may facilitate person-centred health care.

## Specific aims

- To explore the partnership between patients and health care professionals and further the roles of patient and professional when using an interactive webbased system for self-management of hypertension via the patient's mobile phone. (Paper I)
- 2. To study the effect of a person-centred approach supported by e-health technology on the proportion of individuals being treated for hypertension obtaining a BP goal of less than 140/90 mmHg, by improving the management of hypertension in daily life. (Paper II)
- 3. To explore BPV based on daily home measurements in hypertensive patients from primary care, and to identify factors associated with increased BPV. Furthermore, we aimed to investigate whether estimated glomerular filtration rate (eGFR) and PP, as markers of target organ damage (TOD), were associated with day-to-day BPV. (Paper III)
- 4. To explore associations between patients' daily self-measured BP during eight weeks and concurrent self-reported values of wellbeing, lifestyle, symptoms, and medication intake, in primary care. (Paper IV)

## Materials and Methods

This thesis comprises three quantitative and one qualitative study. The material for all four studies comes from the randomised controlled trial PERson-centredness in Hypertension management using Information Technology (PERHIT). An overview of the papers is presented in Table 2.

**Table 2.**Overview of the papers included in the thesis.

Paper	1	II	III	IV
Study design	Qualitative study	Randomised controlled trial	Observational study	Observational study
Participants	22 patients and 15 professionals participating in the RCT	949 patients with treatment for hypertension in primary care	454 patients in the intervention group of the RCT	454 patients in the intervention group of the RCT
Data collection method	Focus group interviews	Office BP, pulse, height, weight, blood samples and questionnaires at baseline, 8 weeks, and 12 months	Baseline BP, pulse, height, weight, blood samples and questionnaires Patients self- reported variables (BP, pulse, lifestyle- related factors, symptoms)	Baseline BP, pulse, height, weight, blood samples and questionnaires Patients self- reported variables (BP, pulse, lifestyle- related factors, symptoms)
Outcomes	Experiences of partnership and roles after using the system	Proportion of patients with a BP <140/90 mmHg	Exploration of BPV and associated factors, and associations between BPV and TOD	Associations between daily BP and self-reports
Data analysis	Descriptive statistics Thematic analysis	Descriptive statistics Pearson's chi <sup>2</sup> -test	Descriptive statistics Multiple linear and logistic regression analyses	Descriptive statistics Repeated- measures linear mixed-effect models

### Research design and setting

The randomised controlled trial PERHIT was performed in primary health care in four regions in southern Sweden. In total, 949 patients from 31 PHCCs were included. The data collection period ranged from 2018 to 2021. 121

Unit heads of eligible PHCCs in the four regions were contacted and invited to participate in the trial. Information meetings were held at the PHCCs who responded with interest in participating. The participating HCPs were instructed on study procedures and in how to use the digital web-based tool in the trial. The HCPs recruited patient participants for the trial and were instructed to recruit patients with treated hypertension regardless of BP level or digital literacy. Inclusion criteria were:

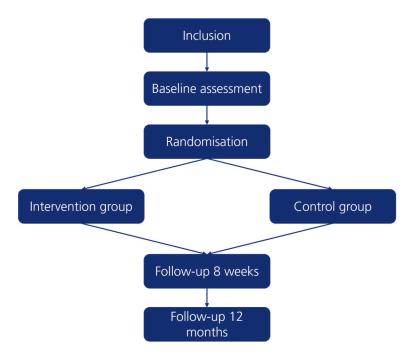
- 18 years or older
- Diagnosis of hypertension with at least one antihypertensive drug prescribed
- Able to understand Swedish in written and oral form

#### Exclusion criteria were:

- Pregnancy-induced hypertension
- Terminal illness
- Secondary hypertension
- Cognitive impairment
- Psychotic disorder
- Impaired vision (the participants needed to be able to read messages on their mobile phone)

After inclusion in the trial, the participating patients were allocated equally to either the intervention or the control group. Block randomisation was used to ensure that the distribution between the intervention and control groups was even at every PHCC. All patients participated in the baseline assessment, and two follow-up visits were booked: after eight weeks and after 12 months. Each visit, which was held at the PHCC, included measuring BP and heart rate, height and weight, blood tests (creatinine, cystatin C, HbA1c and cholesterol) and filling in questionnaires. The questionnaires were filled in by the patients at the PHCC and some of the questionnaires were repeated at each follow-up visit. The study design is illustrated in Figure 2. Monitoring and quality control were performed by two research nurses, who visited the PHCCs regularly during the study period and were available to answer questions from the

participating professionals. The monitor nurses visited the PHCCs after start-up, to ensure that study protocol was followed, documentation was correct and that the site had access to the right resources. A closing visit was also carried out, to ensure that the electronic case report form (eCRF) was completed and that all essential documents were in place.



**Figure 2.** Flowchart of PERHIT.

The participants allocated to the intervention group received a BP monitor (Microlife BP A6 BT; Microlife, Widnau, Switzerland) and instructions on how to use it correctly at home. They also installed a program on their mobile phone called CQ (developed by Circadian Questions AB, Sweden). They were instructed to use the program daily for eight consecutive weeks. The reports could be made during a specified time window every evening, and the participants got reminders via the program. First, the participants answered questions in the program and then they measured their BP and heart rate with the BP monitor and reported the numbers. The questions in the program were about lifestyle, medication intake, symptoms, side effects, and quality of life, and are presented in Table 3.

**Table 3.** Questions and possible responses in CQ.

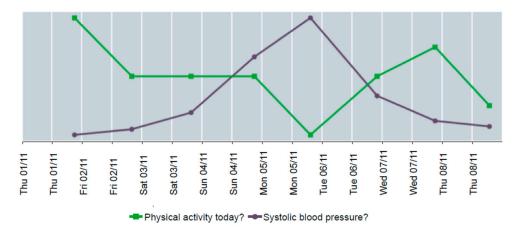
Item	Question*	Response format (steps)
Wellbeing	How do you feel today?	Very bad - Very good (5)
Medication intake	Taken your BP medicine today?	Yes – Some of it - No (3)
Tiredness	Tired today?	Very much - Not at all (5)
Dizziness	Dizzy today?	Very much - Not at all (5)
Headache	Headache today?	Very much - Not at all (5)
Palpitations	Heart palpitations today?	Very much - Not at all (5)
Restlessness	Restless today?	Very much - Not at all (5)
Sleep	How did you sleep last night?	Very bad - Very good (5)
Physical activity	Physically active today?	Very much - Not at all (5)
Stress	Felt stressed today?	Very much - Not at all (5)
Ankles**	Swollen ankles today?	Very much - Not at all (5)
Dry mouth**	Dry mouth today?	Very much - Not at all (5)
Cough**	Cough today?	Very much - Not at all (5)
Toilet use frequency**	Had to urinate often today?	Very often - No (5)
Systolic BP	Systolic (top) blood pressure?	Value
Diastolic BP	Diastolic (bottom) blood pressure?	Value
Pulse	Pulse today?	Value

<sup>\*</sup>The questions were concise to accommodate various mobile phone displays. Participants received supplementary details about the questions in the information material distributed during their initial visit. The questions have been translated from Swedish.

All the answers in CQ were stored in a secure database and not on the person's mobile phone, as this would constitute a security risk.

During the intervention period, the participants could log in to a secure website and see their reported values in graphs. This was an important part of the intervention, allowing the participants to reflect on how their lifestyle and their BP were connected. The HCP could also log in to the website and see all the values for their respective patients. They could thus potentially monitor the patients' BP at home. An example of a graph is displayed in Figure 3.

<sup>\*\*</sup>The questions about side effects were answered twice a week and were chosen for each participant by the installation of the program on the phone, to be relevant to their treatment regime.



**Figure 3.** Example of a graph displaying reports of physical activity and SBP during one week.

Another part of the intervention was motivational messages, which were optional and sent to the participants through CQ. The messages were short and were intended to be a reminder of healthy behaviours, with no option to reply. At the start-up, the patients could choose which type of motivational messages they wanted to receive, to make sure that the messages were relevant to them.

The participating patients had access to informative videos about correct BP-measurement techniques via the study website, where they could also find links to webpages with lifestyle advice for hypertension. A brochure with information on how to register answers in CQ and how to access the graphs was handed out to the participants after inclusion in the study, and the same information was also available on the study website. All patient and professional participants had access to technical support via telephone during daytime hours.

The components of the intervention in this thesis are referred to as the system, thus including the program on the mobile phone, BP measurement and the graphical feedback through a secure website.

At the eight-week follow-up visit, the HCPs were instructed to discuss the experiences of using the system with the participants in the intervention group. They could use the graphs on the website as a basis for the consultation.

The participants in the control group were treated with care as usual and did not receive access to the system or a BP monitor via the current study.

### Study participants and procedures

#### Paper I

During the trial period, focus group interviews were held with patients who had completed the intervention and attended their eight-week follow-up visit. Participating HCPs were also interviewed in separate focus groups. Four PHCCs were strategically selected to represent different socioeconomic areas. One PHCC was located in a small town, one in a suburb of a larger city and two in middle-sized cities. Available patients at the PHCCs were asked by the HCP to participate in the interviews. The HCPs were from the same PHCCs as the patients, but since usually only one or two nurses or physicians were available for interviews from each PHCC, other HCPs from nearby PHCCs who also participated in the trial were invited to join. As preparation for the focus group interviews, semi-structured interview guides were developed: one for the interviews with patients and one for interviews with HCPs. The interview topics are presented in Table 4.

**Table 4.** Interview topic list.

Topic	Subtopic
Hypertension and support	Hypertension treatment at present, drugs or lifestyle (patients)
	Support received regarding hypertension in usual care (patients)
	Perceptions about hypertension treatment (professionals)
PCC and partnership	Perceptions of PCC
	Perceptions of partnership/collaboration between patients and professionals, in general, and specifically during the intervention
	Experiences from the follow-up consultation after the intervention period
	Experiences of discussing patient support needs in hypertension care
	Perceptions of the patient's role in hypertension treatment
Using the technology	Experiences of using the digital system and how it was used during the intervention
	Views of motivational messages
	If/how using the system affected everyday life (patients)
	If/how using the system affected working methods in hypertension care (professionals)
	Experiences of using digital tools for chronic disease in health care in general

The focus group interviews were held between June 2019 and January 2020. Four interviews were held with patients, with four to seven participants attending each interview. Three interviews were held with HCPs, with four to six participants at each

interview. I was the moderator of all the focus group interviews and Ulrika Bengtsson assisted and took notes during the interviews. The interviews were recorded by audio and video.

#### Paper II

For the main outcome of the trial, an intention-to-treat analysis was performed. The proportions of patients with controlled BP, defined as less than 140/90 mmHg, were compared between the intervention group and the control group after eight weeks and 12 months. The BP measured at the PHCC was used as the main outcome since office BP is commonly used in clinical studies concerning hypertension. The HCPs were instructed at the start-up meetings on how to correctly measure BP to ensure systematic measurements, with the BP taken in a sitting position after five minutes of rest. The same BP monitor as the participants in the intervention group brought with them home was used at the office. The mean value of three consecutive measures was used and manually documented in the eCRF.

The study design did not involve instructions regarding prescription of antihypertensive drugs. It was up to the patient's physician to decide on adding or removing antihypertensive drug treatments during the study period, for the participants in the intervention group as well as for the participants in the control group.

The HCP filled out the information about antihypertensive drugs used by the patient at the three visits, using the ATC-code for drugs.

#### Papers III and IV

In the analyses of BPV and associations between BP and self-reports, the participants in the intervention group who had recorded 10 or more daily reports in CQ were included. We reasoned that at least 10 values were needed for the analyses. The maximum number of reports was 57, the first day was numbered as 0.

In Paper III, eGFR was used as a marker for chronic kidney disease (CKD) and PP as a marker for arterial stiffness, both indicators of TOD in hypertension. PP and eGFR were chosen as the information was available in the dataset.

### Statistical analyses

Descriptive statistics were applied in all four studies to illustrate the characteristics of the study population. Statistical significance was set to P < 0.05 for all analyses.

#### Paper II

To ensure statistical significance, a power calculation had been conducted prior to the start of the trial. Previous literature gave an estimate of a decrease in SBP of 5.5 mmHg between baseline and 12 months. A mean difference of 5 mmHg was assumed, and a standard deviation of 20 mmHg in both groups. With a 20% dropout, 423 included patients were required in each group for 90% statistical power, at the 5% significance level.

Pearson's chi<sup>2</sup>-test was used to test for significant differences in office BP between the intervention and the control group. To test for significant differences in the number of antihypertensive drugs between the intervention and the control group, Wilcoxon Rank Sum Test was used. Wilcoxon signed Rank Test was also used to test for significant differences between the three points in time in the same group.

The data in this study were analysed using IBM SPSS statistics (Version 27).

#### Paper III

Coefficient of variation (CV) was chosen as the main index for BPV in the analyses since it has been used in several previous studies. Calculations of BPV with SD, ARV and VIM were also performed and presented.

To test for associations between BPV and baseline characteristics and self-reported variables, the participants were divided into fifths based on CV of home SBP. Linear (continuous variables) or logistic (categorical variables) regression models were performed, with the fifths of BPV as a continuous independent variable and the baseline characteristics as the dependent variables to test for trends in the baseline characteristics. Regression models were also performed with the mean values of the self-reports from CQ as dependent variables. The analyses were adjusted for age and sex.

There are different ways to calculate eGFR. Internationally, the most used is the CKD-EPI equation, recommended by KDIGO-guidelines. <sup>122</sup> In this study, we used the average of the CAPA and LMrev equations, which are developed in Sweden and have been shown to perform better than other eGFR estimations in our population. <sup>123</sup>

Linear regression models were used to test for a significant association between BPV and eGFR and PP, respectively. The CV of SBP was used as a continuous dependent variable and eGFR or PP as the independent variable. The models were adjusted for age, sex, smoking, BMI, cholesterol level, HbA<sub>1c</sub>, reported alcohol consumption at baseline, mean physical activity and baseline SBP (the latter only in the model with eGFR). Similar analyses for BPV and PP were also conducted with subgroups of participants based on antihypertensive treatment.

To further test for the association between BPV and PP and eGFR as markers of TOD, PP and eGFR were dichotomised into low and high groups and odds ratios were calculated using multiple logistic regression models. Low eGFR was defined as less than 60 mL/min/1.73m² and high PP as greater than or equal to 60 mmHg, consistent with previous research.<sup>13</sup>

#### Paper IV

Baseline characteristics were compared between men and women using Student's t-test for continuous variables and Pearson's chi<sup>2</sup>-test for categorical variables.

Repeated-measures linear mixed-effect models were used to examine the effect of the self-reported variables of quality of life, adherence, lifestyle, and symptoms on BP. Separate models with SBP or DBP as dependent variables were set up with all 10 variables included as independent variables and as fixed effects. The participants were included as random effects. The correlation structure was set to AR(1) to account for the autoregressive pattern of the residuals in the repeated measures design.

All statistical analyses in Papers III and IV were performed in R Statistical Software (version 4.1.2; R Core Team (2021) and RStudio version 2022.2.2.485; RStudio Team (2022)).

### Qualitative analysis

#### Paper I

The audio recordings of the interviews were transcribed verbatim by a professional transcriptionist. The transcripts were then checked against the audio recordings to make sure they were correct. The recordings were also listened through several times and initial notes were made. The video recordings were only used as an aid for memory during the analysis phase and were not further analysed. Thematic analysis according

to Braun and Clarke<sup>124</sup> was used to allow for both an inductive and a deductive approach to the material. Initial codes were created without a predefined coding frame. For the coding process, Nvivo software (version 12, QSR International) was used. The initial codes were organised into common categories. Inspired by previous research in the area, the categories and initial codes were arranged in themes and subthemes focusing on different aspects of partnership and technology. The themes and subthemes were repeatedly discussed and reviewed by the authors. A narrative description of every theme was created as well as a thematic map. Finally, the themes and subthemes were named appropriately, and descriptive excerpts were identified to distinguish the themes more clearly.

### Ethical considerations

The PERHIT study was approved by the regional ethical review board in Lund (2017/311 and 2019/00036).

All the participants were given oral and written information about the study and signed a consent form before enrolment.

The risk of adverse effects for patients participating in the trial was considered low. The study did not include any additional drug treatment and the risk of high or low BP was the same as with usual care. One might speculate that daily measurement of BP may cause anxiety for some people – if they have an excessive focus on BP. The risk with this is considered acceptable considering the benefit that increased knowledge and insights about high BP might have on CVD risk. One might also speculate that signals of the reminders and messages from the program used in the study may come at inappropriate times, such as while driving. However, it must be considered up to the participant to act appropriately in such situations.

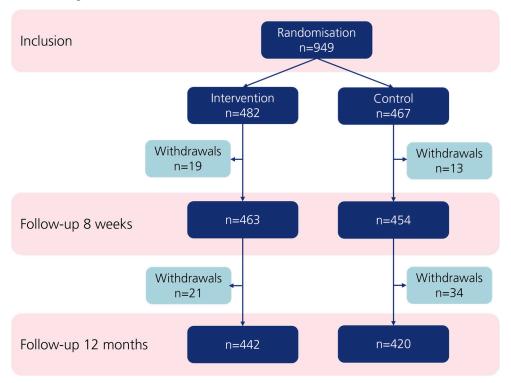
The participants in the focus group interviews signed an additional consent form specifically for the focus group interviews after they had received oral and written information about the study. The transcripts of the audio recordings were made anonymously, and the results of the analysis could not be traced to the participants. The audio and video recordings were stored safely with no risk of spreading to unauthorised persons.

The PERHIT trial was registered with ClinicalTrials.gov [NCT03554382].

### Results

### Main results of the PERHIT trial (Paper II)

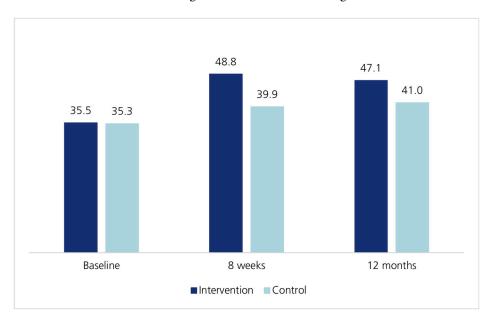
In total, 949 patients were included in PERHIT. Due to different reasons, 87 participants withdrew during the study period, and a total of 862 patients completed the trial (Figure 4).



**Figure 4.** Flow chart of included patients in the PERHIT trial. Reasons for withdrawal from the study: patients' choice (n=32), decision by HCP (n=8), lost to follow-up (n=3), other (n=44).

The participants were randomised into the two arms of the study and there were no significant differences in baseline characteristics between the intervention and the control group.

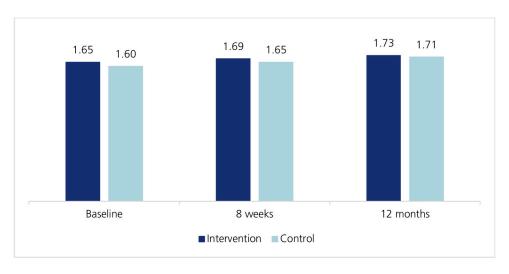
The primary outcome was the proportion of participants with a BP <140/90 mmHg after eight weeks and after 12 months. At baseline, there was no difference between the groups. After eight weeks, there was a significant difference (P=0.006), but after 12 months, the difference was not significant (P=0.071), see Figure 5.



**Figure 5.** Proportion (%) of participants with BP <140/90 mmHg.

The BP was also measured at home by the participants in the intervention group. On the first day of the intervention, 25% (107 of 432) of the participants had a BP <135/85 mmHg. The second day, the corresponding number was 37% (167 of 448). On the last day of the intervention, after eight weeks, 49% (124 of 254) of the participants had a BP <135/85 mmHg.

The mean number of prescribed antihypertensive drugs increased significantly (P<0.001) in both the intervention and the control group during the study period. There was no significant difference between the groups (Figure 6).

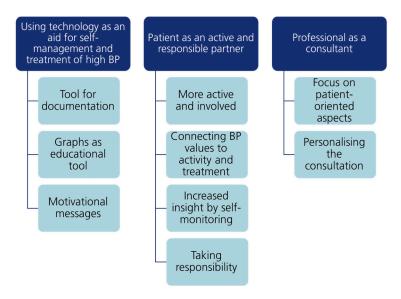


**Figure 6.** Mean number of antihypertensive drugs.

### Participants' experiences (Paper I)

In total, 22 patients and 15 HCPs participated in the focus group interviews. Most patients were men (64%), and the average age was 65 years old. All patients originated from Sweden. Of the professionals, 10 (67%) were women. Seven of them were nurses, six were physicians, and two were assistant nurses. They had, on average, 17 years of experience working with patients with hypertension.

The thematic analysis of the focus group interview resulted in three themes and nine subthemes, presented in Figure 7. The three main themes were each connected with an actor: the patient, the professional and the technology. The subthemes described the different actions identified.



**Figure 7.**Overview of themes and subthemes.

#### The Technology

The patients described that the system was easy to use. Some were apprehensive at first but found no difficulties in using it during the intervention. It was not considered a burden to self-report every evening, some patients revealed that they missed it when the intervention was completed.

The technology was viewed as an aid for the treatment and self-management of high BP. It enabled documentation of BP values and related factors and could facilitate communication about hypertension. It could be used by both patients and professionals to evaluate the effect of changes in medication treatment. Some professionals thought that the system used in the study was too time-consuming and not worth using. The professionals were encouraged to look at the graphs together with the patient at the follow-up visit after eight weeks, but everyone did not do that. When the graphs were viewed, they were perceived as an educational tool. One professional described how she used the graphs together with the patient as a base for the discussion at the follow-up consultation:

We went through the graphs and explained and discussed about... how they were and just like you said before, this if they forgot a tablet if you say, and it happens that they do, that they saw the effect of it and likewise the exercise, so that you had a dialogue with them. (HCP 2)

The motivational messages produced different reactions from the patients – some appreciated them and found them inspirational, some found them annoying since there was no way to respond or generate further information, and some did not pay attention to them as they were lost in the steady stream of incoming notifications on their mobile phone.

#### The Patient

Both the professionals and the patients experienced that the patients were more active and involved in the consultation at the follow-up after eight weeks compared to usual consultations. The patients were more prepared with questions and discussion topics and found this to be confirmed by the professional who was experienced as more attentive.

Yes, I thought I had another approach, because I had prepared a little extra maybe, that I will ask about this or I will bring this up and wonder why it was so or... so that I was probably... more maybe on my toes, that I... well, tried to be active in the conversation. (Patient 8)

Patients described that they found insights into what affected their BP through daily measurements and reflection upon daily activities. They viewed it as their responsibility to keep track of their BP and to act if the values were too high or low. Some participants described that participating in the study motivated them to make lifestyle changes. They believed that they were aware of the importance of healthy habits before, but it was only now that they took it to heart.

#### The Professional

The HCPs described that using the system facilitated a more lifestyle-oriented conversation with the patient, with a stronger focus on the individual patient's needs and wishes. The patients expressed that the conversation came to be about things that were important to them. The HCPs could take a more consultative role in the meeting.

When working with patients in the study, some of the HCPs felt that they learned more about the patients and could hold a discussion in a more personalised way. Some professionals experienced that they learned new ways of talking about BP and hypertension management by using the system.

No, personally, I probably think that I have benefited from this kind of teaching in this, in that you had...and addressed to the person you have in front of you. That it was like

a little lesson there, how to talk, you have something to go after, you can show, talk about like that particular person's... what to say... statistics or what to say. (HCP 13)

By using the system, the patient and the HCP could share knowledge. The patients contributed with their experience and the professionals with medical knowledge. The consultation became more equal when the patient was more knowledgeable and prepared, implying shared power and collaborative decision-making as a basis for a partnership between patient and professional.

### Blood pressure variability (Paper III)

Higher home BPV was associated with higher age, office BP and heart rate, and smoking. BPV was lower for participants with low alcohol consumption and treatment with calcium antagonists. Higher mean home BP, mean heart rate and mean PP were also associated with higher BPV. The participants with the highest BPV reported slightly more dizziness and palpitations (Table 5).

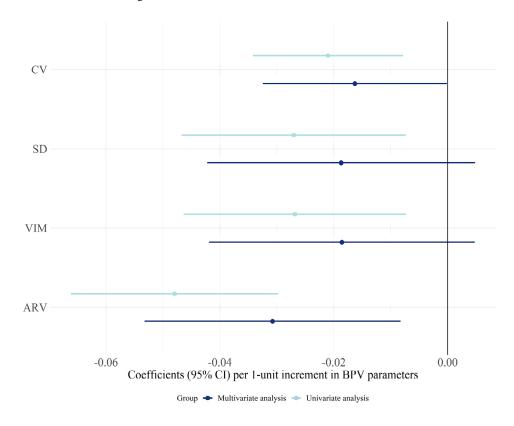
**Table 5.**Baseline characteristics and CQ variables according to fifths of CV of home SBP. Only displaying significant associations.

	CV of home SBP, %					
	1 <sup>st</sup> fifth 2.4 – 5.4	2 <sup>nd</sup> fifth 5.4 – 6.3	3 <sup>rd</sup> fifth 6.3 – 7.2	4 <sup>th</sup> fifth 7.2 – 8.4	5 <sup>th</sup> fifth 8.4 – 15.5	P-value
N	91	91	90	91	91	
Age (years), SD and range	59.2 ±10.6 30-77	62.0 ±9.9 31-80	63.0 ±9.3 25-82	63.7 ±9.3 33-83	64.4 ±8.6 43-85	<0.001
Proportion with BP <140/90 mmHg, n (%)	38 (30.8)	43 (47.3)	33 (36.7)	20 (22.0)	31 (34.1)	<0.001
Office SBP (mmHg), mean and SD	139.3 ±12.3	140.7 ±15.0	143.0 ±16.3	150.1 ±17.5	145.3 ±17.4	<0.001
Office DBP (mmHg), mean and SD	84.5 ±8.3	84.3 ±9.6	83.6 ±8.4	85.8 ±9.1	85.2 ±9.2	0.008
Ca-antagonists, n (%)	41 (45.1)	29 (31.9)	35 (38.9)	29 (31.9)	26 (28.6)	0.024
Current smoker, n (%)	2/89 (2.2)	3/89 (3.4)	4/90 (4.4)	5/91 (5.5)	9/88 (10.2)	0.013
Alcohol <1 standard drinks per week, n (%)	38/89 (42.7)	42/88 (47.7)	32/90 (35.6)	26/89 (29.2)	28/88 (31.8)	0.006
Alcohol ≥10 or standard drinks per week, n (%)	4/89 (4.5)	2/88 (2.3)	7/90 (7.8)	6/89 (6.7)	8/88 (9.1)	0.056
CQ variables						
HSBP (mmHg), mean and SD	132.9 ±8.3	132.5 ±9.5	135.6 ±10.9	138.4 ±11.6	138.8 ±12.8	<0.001
HDBP (mmHg), mean and SD	79.3 ±6.5	78.0 ±6.5	78.4 ±7.6	79.6 ±7.4	80.0 ±8.2	0.001
PP* (mmHg), mean and SD	53.7 ±8.4	54.8 ±8.8	57.3 ±9.0	58.9 ±10.2	58.8 ±10.6	<0.001
Heart rate (beats/min), mean and SD	70.3 ±9.1	70.2 ±9.5	71.1 ±9.6	72.4 ±9.5	74.1 ±9.6	<0.001
Dizziness**, mean and SD	1.1 ±0.2	1.1 ±0.2	1.2 ±0.3	1.2 ±0.3	1.2 ±0.4	0.023
Palpitations**, mean (SD)	1.1 ±0.3	1.1 ±0.2	1.2 ±0.3	1.2 ±0.3	1.2 ±0.4	0.018

<sup>\*</sup>PP was calculated from the participants' reports of SBP and DBP. \*\*1=not at all, 5=very much.

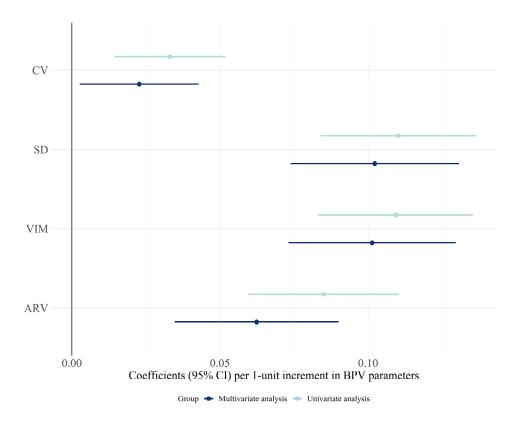
There was a significant association between higher BPV and lower eGFR, even after adjusting for age, sex, smoking, baseline SBP, BMI, cholesterol level, HbA<sub>1c</sub>, reported alcohol consumption at baseline and mean physical activity (P=0.049) in the linear

regression model (Figure 8). The logistic regression model showed no significant association between high CV of SBP and low eGFR.



**Figure 8.**Linear regression analysis of the relationship between different parameters for BPV and eGFR. Multivariable analysis included age, sex, smoking, baseline SBP, BMI, cholesterol level, HbA1c, reported alcohol consumption at baseline and mean physical activity as independent variables.

Higher PP was significantly associated with higher BPV (P=0.027 for CV of SBP) in the multivariable linear regression model (Figure 9). Similar results were seen in the logistic regression model with high CV of SBP and high PP.



**Figure 9.**Linear regression analysis of the relationship between different parameters for BPV and PP. Multivariable analysis included age, sex, smoking, BMI, cholesterol level, HbA1c, reported alcohol consumption at baseline and mean physical activity as independent variables.

# Associations between BP measurements and self-reported variables (Paper IV)

The median number of self-reports during the 57 days was 53 (at least one variable). The missing values constituted 13% and were clustered to a few participants. Adherence to medication was high in the study, only 2.9% of the reports of medication intake were negative.

The linear mixed-effect models showed a significant association between SBP or DBP and wellbeing, medication intake, headache, restlessness, physical activity, and self-reported stress (Table 6).

**Table 6.**Linear mixed-effect models for association between SBP and DBP and self-reported variables.

	Systolic BP			Diastolic BP			
Variables	Estimate	P-value	95% CI	Estimate	P-value	95% CI	
Intercept	143.78	< 0.001	141.26 - 146.29	81.84	< 0.001	80.20 - 83.49	
Wellbeing	-1.04	< 0.001	-1.330.76	-0.41	< 0.001	-0.600.22	
Medication intake	-5.19	< 0.001	-6.673.71	-2.63	< 0.001	-3.601.66	
Tiredness	-0.12	0.276	-0.35 - 0.10	-0.11	0.154	-0.25 - 0.04	
Dizziness	-0.21	0.264	-0.57 - 0.16	-0.16	0.189	-0.40 - 0.08	
Headache	0.38	0.010	0.09 - 0.68	0.39	< 0.001	0.19 - 0.58	
Palpitations	0.15	0.475	-0.26 - 0.56	0.16	0.255	-0.11 - 0.43	
Restlessness	0.84	< 0.001	0.49 - 1.19	0.42	< 0.001	0.19 - 0.65	
Sleep	-0.02	0.884	-0.22 - 0.19	0.02	0.717	-0.11 - 0.16	
Physical activity	-0.63	< 0.001	-0.790.47	-0.13	0.012	-0.240.03	
Stress	1.06	< 0.001	0.83 - 1.30	0.59	< 0.001	0.43 - 0.75	

As seen in Tables 7 and 8, the results were different for men and women for some variables. Physical activity was only associated with BP levels for men. Wellbeing was not significantly associated with DBP for women. Restlessness had a bigger impact on BP for women than for men. Tiredness was associated with BP for women, not for men, but the impact on BP was small compared to other variables. Dizziness was only associated with DBP for men.

**Table 7.** Linear mixed-effect model for association between SBP and self-reported variables for women and men.

	Women			Men		
Variables	Estimate	P-value	95% CI	Estimate	P-value	95% CI
Intercept	137.35	<0.001	133.67 - 141.01	148.50	<0.001	145.07 - 151.92
Wellbeing	-0.95	< 0.001	-1.350.55	-1.14	< 0.001	-1.550.73
Medication intake	-3.16	0.005	-5.370.95	-6.72	<0.001	-8.704.74
Tiredness	-0.34	0.038	-0.650.02	0.09	0.580	-0.22 - 0.39
Dizziness	0.001	0.997	-0.52 - 0.53	-0.38	0.138	-0.89 - 0.12
Headache	0.28	0.173	-0.12 - 0.69	0.48	0.024	0.06 - 0.89
Palpitations	0.41	0.161	-0.16 - 0.98	-0.03	0.917	-0.61 - 0.55
Restlessness	1.03	< 0.001	0.49 - 1.57	0.68	0.004	0.22 - 1.14
Sleep	0.003	0.982	-0.28 - 0.28	-0.06	0.690	-0.34 - 0.23
Physical activity	-0.24	0.057	-0.48 - 0.01	-0.89	< 0.001	-1.100.68
Stress	1.11	<0.001	0.78 - 1.45	1.02	<0.001	0.69 - 1.35

**Table 8.** Linear mixed-effect model for association between DBP and self-reported variables for women and men.

	Women			Men		
Variables	Estimate	P-value	95% CI	Estimate	P-value	95% CI
Intercept	77.77	< 0.001	75.33 - 80.21	84.97	< 0.001	82.75 - 87.19
Wellbeing	-0.23	0.094	-0.50 - 0.04	-0.60	< 0.001	-0.860.34
Medication intake	-1.71	0.025	-3.190.22	-3.35	<0.001	-4.622.07
Tiredness	-0.23	0.030	-0.450.02	0.02	0.812	-0.17 - 0.22
Dizziness	0.06	0.723	-0.28 - 0.41	-0.37	0.025	-0.700.05
Headache	0.43	0.002	0.15 - 0.70	0.35	0.010	0.09 - 0.62
Palpitations	-0.02	0.899	-0.41 - 0.36	0.35	0.066	-0.02 - 0.73
Restlessness	0.50	0.007	0.14 - 0.87	0.33	0.028	0.04 - 0.63
Sleep	-0.03	0.786	-0.22 - 0.17	0.06	0.491	-0.12 - 0.25
Physical activity	0.08	0.345	-0.09 - 0.24	-0.28	< 0.001	-0.410.14
Stress	0.65	< 0.001	0.43 - 0.88	0.54	< 0.001	0.32 - 0.75

### Discussion

### Summary of the main findings

Paper I: The relationship between patients and professionals, and their respective roles, may change when using the interactive web-based system described in this thesis. The patients viewed themselves as more active and motivated, and the professionals could be more of a consultant during the follow-up consultation. The consultation was described as more equal than in usual practice, thus potentially affecting the partnership between patient and professional. Not all professionals were positive about using the system. For an e-health intervention like the one described in this thesis to work, it is important to motivate and interest the intended users. Without it, the technology may not be used as intended and instead be perceived as a burden.

Paper II: More patients with hypertension reached their target BP when using the interactive system described in the study compared to usual care. The results were significant in the short term, but unsure in the long term. The positive results are interpreted as a result of lifestyle changes and increased adherence to treatment, and not dependent on up-titrated drug treatment since this did not differ between the groups.

Paper III: Higher day-to-day BPV was associated with higher PP and lower eGFR in patients with antihypertensive treatment. High BPV was associated with older age, smoking, high mean BP, and increased heart rate. Low BPV was associated with low alcohol consumption and treatment with calcium antagonists.

Paper IV: Self-reported daily life experiences and behaviours were associated with BP levels for the participants in our study. Higher wellbeing, less stress and restlessness, and higher medication adherence, were associated with lower same-day BP. Physical activity was significantly associated with BP for men, but not for women. The associations between same-day BP and symptoms were weaker, but significant for headache.

### Meaning of findings

The findings of this thesis support the use of e-health to promote patients' self-management in hypertension care, in agreement with previous research. The improvement in the proportion of participants with a BP <140/90 mmHg can be considered modest – after the intervention still less than half of the participants had a controlled BP. Even so, the results are important, as hypertension is a prevalent cardiovascular risk factor and every step in the right direction in hypertension management is meaningful. The findings reflect the challenge of achieving controlled BP in hypertension management.

Outside of the effect on physiological parameters, such as BP level, there are other values of importance in clinical interventions. The experiences of the intended users, the patients and the professionals, are imperative to consider before implementation. In our focus group interviews, we found that most patients and professionals were positive about using the system. It could influence the relationship between patients and professionals and pave the way for a constructive partnership. It also became clear that there were different opinions about the intervention, and some of the professionals preferred traditional care over using a digital tool like this one.

Papers III and IV describe secondary analyses from the PERHIT trial. The design of the intervention with daily BP measurements at home for eight weeks offered the possibility of studying BPV and associated variables. The association between BPV and TOD is described in previous publications<sup>66</sup>, and in our study we noticed an association between BPV and TOD for patients with antihypertensive treatment. This knowledge can contribute to our understanding of the role of BPV in the development of CVD.

In Paper IV, we described associations between BP levels and the participants' same-day behaviours and experiences. The results can be of importance for practitioners interested in motivating patients to treatment adherence. Not unexpectedly, adherence to medication represented the strongest association with same-day BP. Wellbeing, stress and restlessness were also strongly associated with BP levels, which may deserve attention in hypertension care.

### Methodological considerations, strengths and limitations

A randomised controlled trial is the gold standard when testing the effectiveness of a new intervention <sup>126</sup>, such as the web-based system in the PERHIT trial. Ideally, participants should be blinded to which treatment they are allocated, but for obvious

reasons that was not possible in our study. As is recommended, a power calculation was conducted prior to the trial. The total number of patients recruited in the trial slightly surpassed what was required according to the power calculation. A strength of the trial is that it was conducted in primary care, where most patients with hypertension are treated, and the results are therefore valid in real-life settings.

The main outcome of this trial was the proportion of patients with a BP less than 140/90 mmHg, based on office BP in the short and long term. Other values could have been chosen as the primary outcome, such as mean BP values, but we used the current endpoint since it was considered the most clinically relevant. Except for office BP, home BP values were also available for the participants in the intervention group. The proportion of participants with an office BP <140/90 mmHg was similar to the proportion of participants with home BP <135/85 mmHg after eight weeks, which was expected since home BP is usually about 5 mmHg lower than office BP.<sup>32</sup> No comparison can be made of home BP values with the control group since they did not measure their BP at home.

With a block randomisation, it was ensured that there were about the same number of included participants in both groups at every site, thus avoiding skewness of the results due to differences between the PHCCs. The proportion of participants with controlled BP in the control group improved during the study period, from 35% at baseline to 41% after one year. It is possible that just participating in a hypertension study affected the participants, even if randomised to the control group. The focus on hypertension became greater as the participants came for extra visits at the PHCC. It is also possible that the control group was affected by the professionals, since the same HCP met the participants in both groups. In the focus group interviews, some of the professionals described that they were inspired to use new ways of communicating about BP after working with the system. This may have affected our results, making it harder to detect a significant difference between the groups. To avoid this kind of contagious bias, another study design would be needed. Randomisation could have been done on the PHCC level instead, but then the risk of differences between the PHCCs could have constituted a bias.

In this discussion, it is important to consider what is clinically relevant. If many patients need to use the system for it to be effective for a few patients, that is, if the numbers needed to treat are high, then the clinical effectiveness of the intervention can be considered low. We saw a positive effect of using the system, but it may be that some groups of patients benefit more from using it than others. We have not been able to determine which groups this might be though. It is possible that the patients included in this trial were already more motivated and adherent to treatment than the average

patient with hypertension and that the effect would have been different in patients with other preconditions.

The intervention in the PERHIT study comprised several different components: selfmonitoring of BP, self-reporting, and motivational messages in the web-based system. From the results, we cannot establish which component was accountable for the positive effect. To find out, the study would have to be designed differently. For example, a third arm could have been included, with participants who were given a BP monitor and instructed to self-monitor but did not have access to the web-based system. Previous research has stated that self-monitoring results in lower BP, but additional support is required. 106,127 Some patients who participated in the focus group interviews reported that they were unaware of the possibility to log in and view the reported answers in graphs, even though they should have been informed about it and it also appeared clearly in the written information. When this information was lost, one could speculate that the intervention was reduced to mere self-monitoring. However, some of the patients who did not log in to view the graphs reported that they made their own notes and related differences in their BP levels to what they had done during the day. Thus, the opportunity to reflect on one's day and contemplate on BP in relation to activities of daily life was likely an important component of the intervention.

When experiences of participants in research projects are to be described, a qualitative research approach is required. Different methods can be used, questionnaires, individual interviews, or group interviews. The advantage of focus group interviews is that the participants through discussion develop their thoughts together, and other aspects can come to light than during individual interviews. <sup>128</sup> As with all qualitative research, the aim is not to generalise the findings but to clarify the thoughts and feelings of the participants and to understand the individual's reality and experiences in their context. <sup>129</sup> The people who agree to participate in interviews may be more positive to and interested in the study, which may affect the results. With this in mind, we did conclude that some views and experiences were recurring during the focus group interviews, and that some opinions differentiated between the participants. After the interviews were conducted, we considered that there was saturation in the data.

In Paper III, BPV was explored through a secondary analysis of the data. The data were not collected for the purpose of analysing BPV and related factors. The analysis had to be adapted to the data that was available, and the results must be interpreted with this in mind. We used PP as a marker for arterial stiffness and eGFR as a marker for CKD. Another commonly used marker for CKD is the urine albumin/creatinine ratio<sup>13</sup>, but this was not available in our study. The PP represents a surrogate marker for stiffness in the large arteries. The gold standard for assessing arterial stiffness is to measure aortic pulse wave velocity<sup>130</sup>, which is not done commonly in clinical practice and was not

conducted in this study. In our study, treatment with calcium antagonists was associated with lower BPV, but we cannot draw any conclusions regarding which treatment is preferred in increased day-to-day BPV. Calcium antagonists have been associated with lower BPV in other observational studies as well<sup>131,132</sup>, but so far, no large enough RCT has been conducted with this as the primary aim.

In Paper IV, we described associations between self-reported BP and variables relevant to hypertension. As the reports were made every evening, the risk of recall bias was low. The BP was manually entered into the system, which increased the risk of incorrect input. This was intentional though, giving the participants a chance to reflect on the numbers when manually entering the digits. The study was not designed to establish causation between BP and the included factors. For some factors, causation is established in previous literature. Medication adherence, physical activity and stress are known to affect BP levels in patients with hypertension. 133-135 In our study, we do not know what type of exercise or stress the participants referred to, and it is possible that the reported association is not only one-way. The participants may have been more inclined to be physically active or felt less stressed when their BP was lower. However, this can be considered irrelevant, since the intention of the intervention was to enable the participants to explore variations in their BP and associations to relevant experimental and behavioural factors. We believe that the patients could find insights and motivation to make behavioural changes favouring BP control. This is supported by the results of focus group interviews in Paper I. For the symptoms, only headache was significantly associated with BP, to a lower extent than the other significant variables. To further explore the associations, an analysis could be conducted between BP and the previous or next-day variables.

Apart from the methodological considerations mentioned above, there are some general limitations of the thesis that need to be acknowledged. One inclusion criterion in the PERHIT study was that the participants needed to understand Swedish to make use of the system. More than 95% of the included patients stated that they originated from Sweden, and thus we did not test the system in a diverse ethnic population. The participation in the trial of one PHCC in a multicultural area had to be terminated due to errors in the execution of the study, largely due to language difficulties. We do not know how usable the system would be in other cultural environments.

As mentioned above, there is a risk of recruitment bias in this trial. The patients who agree to participate may already be motivated to have healthier habits or have an interest in health-related issues. They may also be more motivated to use e-health solutions than other patients with hypertension. The HCPs who recruited the patients may have chosen patients who they believed were well suited for the intervention, or who they thought benefited the most from using the system, even though the instructions given

for the study stated that all patients who met the study criteria should be considered for participation. The risk of selection bias applies to all similar studies and is practically unavoidable.

### Findings compared to other studies and literature

#### Blood pressure

The proportion of participants with controlled BP in the study at baseline was remarkably low, considering that the patients included were already on medical treatment for hypertension. However, compared to other studies, this is not very surprising. As mentioned above, less than half of the individuals on antihypertensive treatment have been shown to have a controlled BP in Swedish surveys. <sup>2,30</sup> After one year, the proportion of participants with controlled BP had decreased slightly in the intervention group, compared to after eight weeks. The effect of lifestyle interventions usually declines over time <sup>136</sup>, and it is possible that the results would improve if the intervention was repeated at regular intervals, for instance, once a year.

In the pilot project, a larger decrease in SBP and DBP was seen after eight weeks of using the system.<sup>117</sup> Since the pilot project was smaller, with fewer PHCCs involved, the research team had more contact with every PHCC and could guide the intervention more. From the focus group interviews described in Paper I, we know that the system was not used completely as intended in all PHCCs, which may have affected the results.

The intervention did not include any instructions for the prescribing physician or the patient on the up-titration of antihypertensive medications. As demonstrated, the mean number of drugs prescribed for each patient increased equally in the intervention and the control group during the year of the study. The increase may be coherent with usual care, as an up-titration of antihypertensive drugs would be expected with time in this population, or it may have been affected by the participation in the study. Regardless, we can conclude that the positive effect seen on controlled BP was not due to increased prescription of antihypertensive drugs, which is a different result compared to other studies on self-management of hypertension.<sup>137</sup> In the HOME BP trial, a digital intervention for self-management of hypertension showed positive results on BP. The intervention comprised self-monitoring, titration of antihypertensive drugs, lifestyle advice and behavioural support, and addressed both patients and professionals. A positive effect on BP was seen, and the authors concluded that the effect was due to an increased titration of drugs and adherence to treatment.<sup>137</sup> Hallberg et al reported in a publication from the pilot project MIHM that the patients described increased

motivation to adhere to treatment and a healthy lifestyle, after using the self-management system. This is similar to what the patients conveyed in our focus group interviews. Some patients described that they had made, or planned to make, lifestyle changes. The positive effect on BP seen in this study is thus likely due to a healthier lifestyle, and increased adherence to treatment.

Other interventions on e-health systems in hypertension management have shown positive effects. A Japanese research team has developed a digital therapeutics system with an interactive mobile app, designed to aid lifestyle changes to reduce BP. 138 The system was tested by patients with untreated hypertension and was found to have a significant effect on BP in the short term, although the addition of BP-lowering drugs was required to sustain the positive effect for more than 12 weeks. An apprehension with this study may be that the digital system was personally adapted to the patients' conditions, but not to their preferences. The system entailed information and education but did not include the patient's perceptions and experiences, which, according to Bokhour et al<sup>50</sup>, is needed in hypertension self-management. The Japanese trial is not unique in this regard, much of the literature regarding hypertension management describes interventions lacking incorporation of a person-centred perspective, which may be beneficial for long term effects. 110,139,140 The patient participation based on their preferences in the PERHIT trial was described in a paper by Vestala et al.<sup>141</sup> There were indications that the intervention increased the preference-based participation in selfcare and treatment, but the long-term effects were reversed. This may suggest that the results of the intervention would benefit from being repeated regularly.

#### Using the system

As stated above, many e-health solutions for self-management of hypertension are designed to educate and inform patients but lack an interactive feature in the system. <sup>110</sup> The system used in this trial is designed to engage the patients, by actively reflecting on their day every evening in relation to their BP, and through graphical feedback of the self-reports. <sup>47,111</sup> Through the graphs the patients can gain insights into what affects their BP. This engagement of the patients is regarded as an interactive feature, together with the possibility for the patient and the professional to view the graphs together. This part of the intervention was appreciated by both patients and professionals in the pilot study. <sup>119</sup>

Using the system every evening for eight weeks may seem like a burdensome request. However, the participants in the focus group interviews described that even though they at first saw the intensive reporting as a difficult task, they soon got used to it and found it easy. Some even reported that they missed the procedure when the intervention

ended. As reported in Paper IV, the average number of daily reports was high, with a low percentage of missing reports, supporting that the participants were not burdened by the daily task. This view is also supported by interviews with patients in the pilot project, who found the system easy to use and relevant for them. By using the system, they found insights and understanding of hypertension, which yielded motivation for healthy habits and adherence to treatment. Similar results were described in a study by McBride et al, when testing a smartphone app for self-monitoring BP and graphical feedback of the values. 142

The system is developed to be used as a tool in person-centred hypertension management. When using the system, the patient brings the data and can share it with their physician at the consultation. Through the data, the patient can narrate his or her reality and experience of hypertension. Both the patient and the professional can exchange knowledge and interpretations. Questions, perceptions, and views can come to light, and the counselling and treatment can be tailored to the patient's needs, which is in line with PCC. The system does not guarantee that the working method becomes person-centred; the HCP needs to be motivated and interested, and well-educated in the technical system. They should also possess some previous knowledge about a person-centred approach. The term PCC is increasingly used in Swedish health care, and person-centredness is emphasised in current official Swedish health care reports. It therefore seems reasonable that more HCPs in Swedish health care have knowledge of what PCC implies.

#### Blood pressure and daily life

With data from the 50 patients in the pilot project MIHM, Taft et al conducted a similar analysis as ours, exploring associations between BP and same-day behaviour and experiences. The results were similar, with associations between lower BP and less stress, more physical activity, better wellbeing, and medication intake. In our larger study, we also found associations between BP levels and restlessness and headache. Taft et al concluded that the system could enable patients to monitor their BP in relation to the included factors. It could also help inform patients that symptoms are poor indicators of BP levels, stressing the importance of medication adherence. We did see a significant association between BP and headache, although with a lower impact than for the other significant associations. Headache is commonly associated with BP, and antihypertensive treatment has, in some studies, reduced the prevalence of headache. However, the association remains ambiguous, given that several studies have reported an absence of correlation between headache and BP levels.

Acute as well as chronic stress of different origins is associated with increased BP, and psychosocial stress is considered a risk factor for hypertension. <sup>135,146</sup> In our study, high reported stress was associated with 4.2 mmHg higher SBP than low reported stress, consistent across sexes. Restlessness, which may be experienced concomitantly with stress, correlated with 3.4 mmHg higher SBP. Wellbeing, inversely related to BP, showed a similar impact as stress, with a high rating associated with 4.2 mmHg lower SBP. These findings support the notion that stress and wellbeing influence BP levels, emphasising the potential positive impact of stress reduction and promoting wellbeing on hypertension management.

Regular physical activity has a positive effect on BP control, but also a single dose of exercise causes a temporary reduction in BP, referred to as post-exercise hypotension. 147,148 In our study, there was a significant association between SBP and physical activity, as expected, but the results differed when analysing men and women separately. The association was significant for men (P<0.001) but close to significant for women (P=0.057). We do not know what type of physical activity or with which intensity the participants referred to, as the self-reports were subjective. The reports were made in the evening, and the potential post-exercise hypotension could have passed by that time. We can therefore not draw any further conclusions, but through our results it seems that when women report physical activity, the association to BP is weaker.

#### Blood pressure variability

The BPV in our study varied between 2.4 and 15.5 when reported as CV of SBP. There is no generally accepted threshold for high BPV. Juhanoja et al suggested that a CV of SBP >11.0 may be appropriate, since the cardiovascular risk increases above this. <sup>149</sup> This value corresponds to the highest fifth in our study.

The findings in Paper III were largely consistent with previous literature regarding factors associated with BPV.<sup>66</sup> The elasticity and compliance of large arteries decrease with age, leading to arterial stiffness and subsequently increased BPV.<sup>150</sup> Older age, higher mean BP, alcohol intake and smoking are frequently associated with increased BPV.<sup>67</sup> Some of our findings diverge from previous findings, for example, we did not find an association with female sex. Furthermore, in our study, there was an association between increased BPV and higher heart rate, not with low heart rate as previously described.<sup>67</sup>

This study found no significant link between participants reporting physical activity and BPV, a finding that is in line with previous studies. <sup>151,152</sup> A healthy lifestyle has

been associated with lower BPV in a study by Maseli et al $^{153}$ , but lifestyle-related variables, including BMI, cholesterol, and HbA $_{1c}$ , in addition to physical activity, did not differ among different levels of BPV in our study. This can be attributed to differences in study populations, as we included patients with treated hypertension whereas the Maseli et al study focused on young, healthy adults. $^{153}$ 

There was a significant association between BPV and eGFR, which is in line with a previous study by Kubozono et al.<sup>154</sup> However, the logistic regression model did not show a significant association between low eGFR and high BPV. There was also a significant association between BPV and PP, supporting the findings of Imai et al that PP is a predictor of BPV.<sup>155</sup> Our findings were not consistent for different indices of BPV. One could argue that ARV seems to be the best index for day-to-day BPV according to our results, as this shows a stronger significant association to eGFR and PP. The choice of BPV index and measurement method continues to be an ongoing challenge, necessitating further research for a comprehensive understanding of BPV and its implications in clinical practice.

### E-health in primary care

In the TASMINH4 study 156, the addition of telemonitoring to self-monitoring compared to usual care was tested in primary care in the UK, for patients with uncontrolled BP. Self-monitored BP values guided antihypertensive titration by the prescribing physician. Data transfer occurred via paper or electronic means (telemonitoring) with reminders and alerts. The authors concluded that using selfmonitoring for titration of antihypertensive drugs was effective with or without telemonitoring. 156 After the intervention, the participants were interviewed, and facilitators and barriers to self-monitoring and telemonitoring were identified. Although telemonitoring offered several benefits and was usually preferred by HCPs and patients, it was reasoned that the option of paper-based transfer of BP values was still valuable. Some patients preferred the analogue option, but primarily, it was easier to integrate into the present clinical system. 157 The TASMINH4 trial was conducted from 2015 to 2016, and since then things may have changed in favour of facilitating digital tools into clinical care in the UK. Based on personal experience, this is not yet the reality in primary care in southern Sweden though. From the focus group interviews in our study described in Paper I, it became clear that some of the HCPs were not interested in using digital tools in hypertension care. They expressed apprehension about using the system in clinical reality, and one reason was that it was too timeconsuming. As the system was not integrated into the technical health care systems, it

became an extra burden to work in different electronic systems. This could also potentially increase the risk of mistakes, when data needs to be manually transferred between systems.<sup>83</sup> The introduction of e-health solutions should take place with sufficient education and training for the HCP, but examples from Swedish health care show that it is often insufficient.<sup>158</sup> Frennert et al described that with the introduction of e-health solutions, the workload increased for nurses, since the technology often did not replace pre-existing work tasks but instead added new routines or increased the amount of information which needed to be processed. This increased workload was considered invisible as it was not noticed at an organisational level.<sup>159</sup> E-health solutions are often promoted as effective and feasible in hypertension care<sup>160</sup>, but it might be important to also include the invested workload by the professionals when evaluating interventions.

The expected benefits of digital solutions are based on the willingness of proposed users to use the technology as intended. According to a health care survey of the Swedish population from 2022, 45% of the respondents stated that they were positive about health care, consultation, and treatment with the help of digital technology and 31% were negative. A small majority, 56%, stated that they were positive to treatment at home, through home visits or digital technology. These numbers indicate that e-health interventions will not be a "one size fits all" solution. Health care needs to continue to be accessible also for those who do not want to or cannot participate in digital care. As seen in this study, the intervention resulted in better BP control, but to a limited extent. A system such as this one can become a tool among several in the clinic, for those who are willing to use it, and for the patients who benefit from it.

There are high hopes for e-health solutions for improving hypertension management with a person-centred approach, globally and in Sweden. In Europe, a large EU-funded project called HSMonitor is underway with pilot testing at five different sites, of which one is Region Jämtland-Härjedalen in Sweden. The project is very ambitious and targeted at tackling hypertension care on different levels, from self-management to health care organisation. <sup>162</sup> Other e-health solutions for hypertension management are already implemented in many regions in Sweden, such as self-monitoring. In some regions, pilot testing of self-monitoring is ongoing, while in others implementation is taking place. <sup>163</sup> The effects on hypertension care and BP levels are yet to be evaluated.

E-health tools supporting patients' self-monitoring and self-management of chronic conditions are undoubtedly going to be a part of primary health care in the future. As described in this thesis, there can be many benefits with e-health solutions, and conditions for more person-centred care and improved BP control can be supported. That said, digitalisation of health care will not solve all problems facing society with an ageing population and an increase of chronic medical conditions. Careful

considerations are necessary so that the technology used is truly improving health care on every level, for the patients, the HCP and society. Watchfulness is necessary to not exclude patients who are not part of the digital community and to not further burden an already strained primary care. It can be easy to get caught up in the digitalisation frenzy where digitalisation in itself may appear to be the goal. The primary focus must still be an effective and person-centred health care system, and e-health should be used to facilitate this.

### Conclusions and possible clinical implications

- The results presented in this thesis from the trial PERHIT advocate that the
  interactive system for self-management of hypertension used in the study can
  contribute to better BP control for patients with hypertension in primary care,
  but the long-term effects are uncertain.
- In general, the patients were positive about using the system. The effect of the system on BP was likely due to other changes made by the participants than only increased antihypertensive drug treatment since this did not differ between the groups.
- The use of the system depends on the approach of the HCPs and their willingness to make use of new working methods and technology. The system can be used as a tool for PCC, but that requires motivation or knowledge about PCC on the part of the HCP. Most of the professionals we interviewed were positive about using the system. However, some disagreed.
- BPV is associated with hypertension TOD. Even though it has no clinical
  implication at present, increased BPV will likely be a target for treatment in
  the future, to optimise cardiovascular risk reduction.
- In hypertension management it may be beneficial to address the association between BP and daily-life behaviour and experience, in which the selfmanagement system may be of use.
- E-health solutions can be an important part of hypertension management but will not be the one and only solution. Other aspects of health care still need to be acknowledged and in front light, such as interpersonal relationships and enough allocated time for every consultation.

### Future perspectives

Concerning the context of this thesis, the benefits and limitations of using the system described can be further explored. The system was considered beneficial for BP control, but it is unclear which group of patients could benefit the most from using it. It is possible that the effect of using the system differed between PHCCs, depending on the motivation and interest of the professionals using it. As previously described, some participants did not use the system as intended. We reasoned that the HCPs' motivation and ability to inform and inspire the patient is of crucial importance. Another way of reasoning is that the digital solution needs to be simplified so that there is no room for errors. Other professional disciplines such as user experience designers could be involved to further develop the system and make it more fool-proof. For the system to be of use to all patients, who may benefit from using it, it should also be further adaptable to every patient's needs. For example, to be available in other languages or for patients with impaired vision. As reasoned above, there is a risk of further increasing health inequality if considerations are not made to include all groups of patients.

The long-term effects of using the self-management system are still unknown and could be investigated with follow-ups of the participants. The cost-effectiveness of using the system will be evaluated in further studies. It would also be interesting to explore the effects of repeating the intervention at regular intervals. Another idea is to combine self-management support with an intervention aimed at improving therapeutic inertia, that is, prescribing physicians not increasing antihypertensive medication when indicated, and to explore the effect on BP control. The system presented in this thesis can potentially be tailored and of use also in other chronic conditions, such as diabetes or COPD, but this would require further testing.

Beyond the scope of this thesis, one can ponder on the future development of digital health. There is a growing phenomenon in society of increased self-awareness through digital self-measurement. Smartwatches and wearables enable ample self-tracking of health parameters by those who are interested and have the means; a phenomenon that public health care could incorporate and make use of. When cuffless devices such as smartwatches and wristbands for BP measurement become reliable enough to be used in hypertension management, BP assessments in primary care can be transformed. Not only can the person gain an insight into BP real-life levels throughout the day, but the potential source of error of basing antihypertensive treatment on isolated office BP measurements can be eliminated. With these devices also come the possibilities of studying BP variations in new ways. It may bring further knowledge to the role of BPV as a target for treatment in clinical practice. As with e-health in general, the use of

wearables may benefit some, but further exclude others who do not have the means or the capacity to use the devices. In line with PCC, health care should be tailored to the individual's preferences and needs, and self-tracking could be utilised when preferred. If validated and efficient equipment and digital systems are provided by public health care, to those who need it and when needed, the potential of e-health can be maximised.

Changes are needed in hypertension management, to improve BP control and reduce the risk of CVD. Using digital tools is one way forward, but there are also other potential strategies. Since hypertension and atherosclerotic CVD are highly prevalent in the population, actions requiring low resources but reaching many people are appealing. One such strategy that has shown promise is the use of polypills; a combination of several drugs in one tablet. For example, one or more antihypertensives but also a statin, and low-dose aspirin. Trials have shown that polypills can improve adherence and risk factor control.<sup>56</sup> Polypills seem to be effective also in primary prevention of CVD.<sup>164</sup> A way forward may be to provide polypills to the many patients with mild to moderate cardiovascular risk and focus on intensive and individualised treatment for the patients at the highest risk. At present, polypills are not available in Sweden, and more research is needed before introduction clinical practice.

Greenstein et al present the idea that low-dose polypills for cardiovascular prevention could be available over the counter, for those who choose to self-medicate. <sup>165</sup> Personcentred care should be based on the patient's personal preferences, including level of self-care, and if those who are willing and capable are enabled to self-track, self-manage and maybe even self-medicate, more time and resources may be freed in health care for those in highest need of professional medical care.

## Epilogue

I started as a PhD student in 2018, after attending a course in research methodology for resident physicians, given by the Center for Primary Health Care Research at Lund University. Patrik Midlöv contacted me and asked if I wanted to enrol as a PhD student, working with the PERHIT trial. I took the opportunity gladly and began my journey as a researcher. The journey has not always been straightforward. One of the first things I did as a PhD student was to participate in the course "The concept "Person" and person-centred care - philosophical foundation", given by GPCC at University of Gothenburg. This course was like no other course I had attended during my medical education. Fostered in the school of logical empiricism in the medical sciences, other worldviews and paradigms were foreign to me. I liked statistics and things you can number and measure, which were nowhere to be found in the philosophical discourse of personhood. Although it was a struggle, the course was very valuable for my future research and my professional development as a GP. By participating in the course, I learnt about what person-centred care entails, and that even if we may think that we already are, we might not always be working in a personcentred way in primary care. During my journey, I have learnt a lot about research and health care in general, and that other worldviews, research paradigms as well as the lifeworld of patients, are important to acknowledge and consider. My knowledge in the area has expanded hugely during my time as a PhD-student and I hope that this thesis can contribute to further developing hypertension management in primary care, with a person-centred approach and by exploiting the potential of e-health.

# Svensk sammanfattning

## Bakgrund

I Sverige har var tredje vuxen person högt blodtryck (hypertoni), vilket definieras som ett medelblodtryck ≥140/90 mmHg. Hypertoni kan behandlas genom att ändra levnadsvanor; äta en hälsosam kost med lågt innehåll av salt, vara fysiskt aktiv, dricka ingen eller måttligt med alkohol, stressa mindre, och gå ner i vikt om det behövs. Dessutom finns flera vältolerabla och effektiva läkemedel mot hypertoni. Trots detta har de flesta patienter med insatt behandling fortfarande för högt blodtryck. Det har flera förklaringar, dels är följsamheten till insatt behandling för låg hos många patienter, dels är behandling ordinerad av läkare ofta otillräcklig och skulle behöva intensifieras. Många patienter vet inte så mycket om högt blodtryck eller vad som påverkar detta, och då kan det vara svårt att motivera sig till att ändra sina levnadsvanor eller ta sina mediciner, framför allt i avsaknad av symtom.

I Sverige håller vården på att förändras och det talas mycket om personcentrerad vård. Med det menar man en hälso- och sjukvård som utgår från patienten som person. Vården ska anpassas till personens kunskap, resurser och behov. Vårdpersonalen och patienten bör samarbeta på ett jämlikt sätt för att uppnå ett meningsfullt liv för patienten. I personcentrerad vård kan det också ingå att patienten tar ett större ansvar för sin hälsa, med stöd av vårdpersonalen. Ett sätt för patienterna att ta ansvar för sin hälsa kan vara genom att använda digitala hjälpmedel, vilket också kan kallas e-hälsa. Denna e-hälsa definieras användandet informationssom av kommunikationsteknologi i hälso- och sjukvårds sammanhang. Det kan finnas stora vinster med att använda e-hälsa; patienter kan bli mer delaktiga i sin vård, och vård kan bli tillgänglig på avstånd och utan fysiska besök. Den kan dock också finnas risker med e-hälsa; såsom att patienter med låg tillgång till och kunskap om digitala hjälpmedel får svårare att nå fram till vården.

Ett personcentrerat arbetssätt och digitala verktyg kan leda till förbättrad vård för patienter med högt blodtryck. Insikter och kunskap om sitt tillstånd kan leda till ökad motivation att följa behandling med mediciner och förändrade levnadsvanor för patienten. Detta var utgångspunkten för den randomiserade kontrollerade studien

"PERson-centredness in Hypertension management using Information Technology (PERHIT)", där ett webbaserat system för att stödja patientens egen hantering av högt blodtryck testades i svensk primärvård.

#### Material

Denna avhandling bygger på fyra delstudier där materialet kommer från studien PERHIT. Mer än 900 patienter med behandling för hypertoni från 31 olika vårdcentraler i södra Sverige inkluderades i studien av läkare och sjuksköterskor på vårdcentralerna. Efter inklusion i studien randomiserades deltagare till två grupper, interventionsgrupp och kontrollgrupp. Alla deltagarna fyllde i enkäter, lämnade blodprov och mätte blodtryck och puls vid det första besöket. Deltagarna i interventionsgruppen fick en blodtrycksmätare med sig hem och installerade ett program, CQ, på sin mobiltelefon. De uppmanades att varje kväll under åtta veckor mäta sitt blodtryck och svara på frågor i CQ. Frågorna var relaterade till högt blodtryck och deltagarna valde det alternativ som de upplevde överensstämde med hur deras dag hade varit. Till exempel handlade frågorna om fysisk aktivitet, stress, upplevelse av symtom och medicinintag. De skrev också in blodtryck och puls i CQ. Deltagarna kunde under interventionstiden logga in på en säker websida och se sina rapporterade värden i grafer, och kunde på så sätt relatera sina upplevelser och aktiviteter till blodtrycket. Efter åtta veckor kom deltagarna tillbaka till vårdcentralen för ett uppföljande samtal med sin sjuksköterska eller läkare. De fick då chansen att diskutera sina erfarenheter med vårdpersonalen och kunde använda graferna som diskussionsunderlag. För deltagarna i kontrollgruppen fortsatte vården som vanligt under studietiden. Alla deltagarna återkom efter ett år för uppföljande kontroll. Det primära utfallsmåttet var andelen patienter som uppnådde målblodtryck <140/90 mmHg efter åtta veckor och efter ett år.

### Metod och resultat

#### Delstudie 1

Fokusgruppintervjuer genomfördes med deltagare i interventionsgruppen på utvalda vårdcentraler efter att dessa hade avslutat den åtta veckor långa interventionsperioden, samt med vårdpersonal som deltagit i studien. Syftet med studien vara att undersöka om partnerskapet, eller samarbetet, mellan patient och professionsföreträdare, och även

patientens och den professionellas roll, påverkades av interventionen. Totalt deltog 22 patienter och 15 läkare och sköterskor i fyra respektive tre fokusgruppintervjuer. Materialet analyserades med tematisk analys, vilket resulterade i tre övergripande teman associerade med ingående aktörer: "Använda teknologin som hjälpmedel för egen hantering och behandling av blodtryck", "Patienten som aktiv och ansvarstagande partner" och "Den professionella som konsult". Varje tema beskrevs med flera underteman. De flesta deltagare var positiva till att använda digitala system, men vissa tyckte att det tog för mycket tid och inte tillförde tillräckligt för att vara värt att användas.

#### Delstudie 2

I denna studie undersöktes det primära utfallsmåttet i PERHIT-studien, vilket var andelen av deltagare med kontrollerat blodtryck (<140/90 mmHg) i interventionsgruppen jämfört med kontrollgruppen, efter åtta veckor och efter ett år, med Pearsons chi²-test. Vid starten av studien hade 35,5% och 35,3% av deltagarna ett blodtryck <140/90 mmHg, i interventions- respektive kontrollgruppen. Efter åtta veckor sågs en signifikant skillnad mellan grupperna, då hade 48,8% i interventionsgruppen och 39,9% i kontrollgruppen ett kontrollerat blodtryck. Det sågs även en skillnad efter ett år, då 47,1% i interventionsgruppen och 41,0% i kontrollgruppen hade ett kontrollerat blodtryck, men skillnaden var då inte signifikant. Antalet förskrivna läkemedel ökade i båda grupperna under studietiden men det var ingen skillnad mellan grupperna.

#### Delstudie 3

Deltagarna i interventionsgruppen uppmanades mäta sina blodtryck dagligen under åtta veckor. Detta gav tillfälle till att studera hur blodtrycket varierade för patienterna under denna tid. En stor variabilitet i blodtrycksvärden har visat sig vara en riskmarkör för hjärtkärlsjukdom, oberoende av hur högt blodtrycket är i genomsnitt. Det finns ingen standard för hur blodtrycksvariabilitet ska mätas, och det kan därför beskrivas på olika sätt. I denna studie använde vi variationskoefficienten för systoliskt blodtryck hemma dagligen för att beskriva blodtrycksvariabiliteten. blodtrycksvariabilitet var associerat med hög ålder, högt blodtryck och puls, samt rökning. Låg blodtrycksvariabilitet var associerat med låg alkoholkonsumtion och behandling med kalciumantagonister. Deltagarna med hög blodtrycksvariabilitet rapporterade något mer yrsel och hjärtklappning än övriga. Blodtrycksvariabilitet var signifikant associerat med pulstryck och glomerulär filtrationshastighet, ett mått på njurfunktion, som användes som parametrar för organskada.

#### Delstudie 4

Denna studie undersökte om det fanns samband mellan deltagarnas rapporterade blodtryck och deras egna rapporter om livskvalitet, medicinintag, livsstil och symtom från samma dag, med hjälp av linjär blandad modell för upprepade mätningar. Signifikanta samband mellan systoliskt och/eller diastoliskt blodtryck och medicinintag, välmående, stress, rastlöshet, fysisk aktivitet och huvudvärk kunde anges. Det starkaste sambandet uppmättes mellan blodtryck och medicintag, där total följsamhet (tagit sin medicin helt) medförde 5 mmHg lägre blodtryck än ingen följsamhet (ej tagit sin medicin). När deltagarna rapporterade hög stress eller lågt välmående var blodtrycket 4 mmHg högre än när de rapporterad ingen stress eller högt välmående. Resultaten skilde sig åt till viss del åt för män och kvinnor, bland annat var sambandet mellan fysisk aktivitet och blodtrycksnivå signifikant för män men inte för kvinnor.

## Slutsatser och patientnytta

Användandet av det webbaserade systemet för egen hantering av högt blodtryck gav positiva effekter med högre andel patienter med kontrollerat blodtryck efter åtta veckor, men långtidseffekterna var osäkra. Effekten av systemet berodde sannolikt även på andra förändringar som deltagarna gjorde än enbart ökad läkemedelsbehandling, eftersom denna inte skilde sig signifikant mellan grupperna. De flesta patienter och personal var positiva till att använda systemet. Patienterna blev mer aktiva i sin vård och användandet av teknologin kunde medverka till att samarbetet och kommunikationen mellan patient och professionsföreträdare blev bättre och mer jämlikt. Vi kunde visa på signifikanta associationer mellan deltagarnas blodtryck och deras dagliga rapporter. De starkaste sambanden sågs mellan blodtryck och medicinintag samt upplevd stress och välmående. Systemet kan användas som ett verktyg i personcentrerad vård, men det krävs motivation och kunskap om personcentrerad vård hos vårdpersonalen för en optimering av modellen.

Vi har identifierat variabler som är associerade med blodtrycksvariabilitet och såg också att blodtrycksvariabilitet vid dagliga hemblodtrycksmätningar är associerat med organskador hos patienter med behandlad hypertoni. Blodtrycksvariabilitet har idag ingen fastlagd klinisk betydelse men forskningen går framåt och kunskapen om blodtrycksvariabilitet kommer sannolikt att kunna bidra till framtida behandlingsstrategier för att minska risken för hjärtkärlsjukdomar ytterligare.

Digitala verktyg rekommenderas i hypertonibehandling, vilket denna avhandling ger ytterligare stöd för. Dock kommer digitala verktyg inte att vara den enda lösningen på problem med högt blodtryck. Andra aspekter inom hälso- och sjukvården måste även i framtiden uppmärksammas och framhävas, såsom mellanmänskliga relationer och tillräckligt med tid avsatt för varje konsultation.

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### About the author

**ULRIKA ANDERSSON** is a general practitioner working at Löddeköpinge primary health care centre. Her research interests lay in management of chronic conditions and digital health in primary care. This thesis is based on a randomised controlled trial, in which a web-based system for self-management of hypertension was tested in primary care. The proportion of patients with a controlled blood pressure improved, and it was concluded that e-health can contribute to a constructive partnership between patients and professionals with a person-centred



approach. The study was unique as the patients self-reported behaviour and experiences as well as their blood pressure daily during eight weeks. The associations between daily blood pressure and self-reported symptoms and lifestyle variables were studied, as well as blood pressure variability during eight weeks with daily measurement.



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