How can pharmacists contribute to a more effective care of patients with hypertension or diabetes?

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Abstract

Introduction: Pharmacy services that include counseling of patients have been shown to be effective in improving disease states. Such consultative services can either take place face-to-face or the pharmacist can be working remotely through telepharmacy. People living in the rural parts of Sweden have a relative high mortality in myocardial infarction and diabetes. With regard to this fact, this study focus on how consultative pharmacy services can improve the health of patients with hypertension – which have an elevated risk of suffering from myocardial infarction – and diabetics.

Objective: The questions addressed are: How can patient oriented consultative telepharmacy services in the primary care contribute to better outcomes for patients with hypertension? How can patient oriented consultative pharmacy services in the primary care or at pharmacies be used to improve the outcomes for diabetes patients?

Method: A literature study was undertaken using PubMed to find publications that evaluated pharmacy services that included counseling of patients with hypertension or diabetes. The searches were made between March 25 and April 30, 2015.

Results: Two out of three studies that analyzed telepharmacy services for hypertension patients showed a significant decrease in blood pressure for the patients receiving pharmacist interventions. Out of the 10 diabetes studies identified, 9 showed positive results with either improved blood glucose values or in reaching the blood glucose goal.

Discussion: Although the studies analyzed have some limitations, e.g. low participant number and lack of control groups, they are encouraging regarding extending the pharmacists role in helping patients managing their diseases by providing consultative services. The longevity of the positive effects needs to be analyzed further.

Conclusions: Pharmacist have the potential to contribute to a more effective care of patients suffering from hypertension or diabetes through patient counseling. Larger, longer and better controlled studies are however needed to confirm the results.

Key words: Pharmacy services, telepharmacy, hypertension, diabetes
Introduction

Rural Sweden

Out of Sweden’s population of about 9.7 million, less than 300,000 inhabitants live in rural municipalities (1). These municipalities are 39 in total and are defined as having less than 7 inhabitants per square kilometer and less than 20,000 inhabitants in total. Most of these municipalities are located in the inland of the middle and northern parts of the country (2). The population in these areas are constantly decreasing at the same time as the average age is increasing. In the year 2030, it is estimated that the number of people that are able to work will be outnumbered by those that are not. Already today, in some municipalities, the number of people over 80 years old exceeds 10% of the inhabitants (1).

When it comes to the social situation in the rural areas, there are few high income takers and the education level – especially among the men – is low. There is also a high proportion of people living under the social security norm. Both the men and women living in these parts of the country feel mentally well but physically unwell and their health is also worse with high incapacity rates compared to other parts of Sweden. The rural population has a low intake of vegetables, high alcohol consumption and a high proportion of obese people. This probably contributes to the shorter life expectancy and high mortality in myocardial infarction and diabetes seen in the rural areas (2).

Myocardial infarction and hypertension

There is, as mentioned above, a high mortality in myocardial infarction in rural Sweden (2). During a myocardial infarction, the heart does not receive enough oxygen which can lead to necrosis of the heart tissue and death. There are several factors that increase the risk of having a myocardial infarction. The ones that are effectible are: hypertension, smoking, diabetes, central obesity, stress, and a high ApoB/ApoA-1 ratio (dyslipidemia) (3). Hypertension is a major risk factor and the risk of dying from ischemic heart disease is decreased by half with every 20 mmHg reduction in systolic blood pressure (SBP) (4). Hypertension is also estimated to be the risk factor with most attributed deaths worldwide and the prevalence of hypertension increases with age. The blood pressure goal in Sweden is 140/90 mmHg and both medications and lifestyle changes can lower the blood pressure. Non-pharmacological interventions include lowering of stress, and decreased energy and salt intake, as well as a moderate alcohol consumption (5).
**Diabetes mellitus**
As mentioned above, diabetes is an over-represented cause of death in rural parts of Sweden (2) and it is also a risk factor for myocardial infarction (3). Diabetes mellitus is a chronic disease that is defined by hyperglycemia. There are several different types of diabetes, the most common being type 1 and type 2. Under-treated diabetes mellitus leads to microvascular and neuropathic complications.

The blood glucose value can be determined with an HbA1c blood test that measures the amount of irreversibly glycosylated hemoglobin that circulates in the blood. The HbA1c test tells you what the blood glucose was 2-3 month before the test (6). The American Diabetes Association (ADA) recommends that the HbA1c value should be below 7.0%. The recommendation in Sweden are that the HbA1c value should be less than 52 mmol/mol, which is equivalent to 6.0% (6).

In addition to the pharmacological treatment of diabetes, the lifestyle of diabetes patients can affect the clinical outcome of the disease. Both weight loss, exercise, and smoking cessation can improve blood glucose values as well as reduce cardiovascular risk factors. A variety of diets have also been shown to improve blood glucose values for diabetics, e.g. Mediterranean diet and low-carbohydrate diets (7,8).

**Diabetes comorbidities**
Diabetes mellitus patients have an increased risk of contracting other diseases. The most common comorbidities are obesity, hypertension, and dyslipidemia, but diabetics are also more prone to suffer from myocardial infarction (see above), depression, anxiety, and arthritis (9). The ADA recommendations for treatment of hypertension and dyslipidemia and prevention of heart failure are foremost lifestyle changes with reduced weight (if the patient is overweight or obese), increased exercise, a moderate intake of alcohol and reduced intake of sodium, saturated fat and cholesterol. If these actions are not enough, medications are prescribed to treat these conditions (10).

**Consultative pharmacy services**
Pharmacy services are services carried out by certified pharmacists. These not only involve preparation and dispensing of drugs, but also include consultative services to patients and institutions. Pharmacy services that include counseling of patients have been shown to be effective in improving disease states, e.g. lowering blood pressure and cholesterol. It has been estimated that interventions performed by pharmacists leads to a decrease in SBP of 8.4 mmHg while interventions by nurses only reduce it with 4.8 mmHg. Pharmacist interventions have also been demonstrated to increase the quality of
life and adherence (11). Since dispensing of medications has become more effective over the last decades, the community pharmacist with their pharmaceutical expertise could be used more effectively. This would be beneficial for patients and reduce the load on other health care professionals. The UK government for example, wants the community pharmacists to have a greater role when it comes to helping chronically ill patients managing their disease (12)

**Telepharmacy**

The consultative pharmacy services can either take place face-to-face or the pharmacist can be working off-site. This later type of pharmacy service is called telepharmacy and the most common way of communication is via telephone or over the internet by video-conferencing (11,13). Telephone based contact with healthcare professionals have been shown to be an effective way of changing patient behaviors. Telepharmacy not only provide rural areas access to pharmacists but it can also be more convenient for the patients since the counseling is made at home – telepharmacy thus saves both travel costs and time (11). One prerequisite for telepharmacy to work optimally is, however, that the population has well-functioning telephone and internet networks.

By learning how pharmacists better can be utilized in the primary care and at pharmacies – both face-to-face with the patients and off-site – the care of patients can potentially be improved with better life quality but also reduced costs for society. This study emanated from the health situation in rural Sweden and focuses on pharmacy services that provide counseling of patients with hypertension (a group that has an elevated risk of suffering from myocardial infarction) or diabetes. For the former patient group, telepharmacy services were analyzed since these might be of particular use when the distances to health services are long.

**Objective**

The questions addressed in this literature study are: How can patient oriented consultative telepharmacy services in the primary care contribute to better outcomes for patients with hypertension? How can patient oriented consultative pharmacy services in the primary care or at pharmacies be used to improve the outcomes for diabetes patients?
Method

This literature study was based on publications found between March 25 and April 30, 2015. PubMed was searched for articles with the search terms stated below (see Table 1). Publications that analyzed how pharmacists could improve the health status for people suffering from hypertension or diabetes through counseling were selected. The pharmacists needed to be directly in contact with the patient during the intervention. Case studies, studies with preliminary results, and review articles were excluded. In addition, the articles needed to be available via the University Library at Umeå University.

Table 1. Search terms used in PubMed and selected publications.

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Results

Telepharmacy services for patients with hypertension
Consultative telepharmacy services that aim at lowering the blood pressure of patients with hypertension have been tried in USA. Three studies were identified that analyzed such services (see Appendix A for summary). Two of the studies were telephone-based and one study included a web based pharmacy service. None of the studies were undertaken in rural areas.

Blood pressure control
Green et al. (25) investigated if a web based pharmacy service could improve the treatment if hypertensive patients in a randomized controlled trial. The study was located to 10 medical centers in USA between 2005 and 2007. The patients that were included in the study had a SBP between 140-199 mmHg a diastolic blood pressure (DPB) between 90-190 mmHg and no other serious disease e.g. diabetes. The 730 participants all were given pamphlets describing the disease, importance of taking medication, and how the life-style effects the outcome. The participants were divided into 3 groups (see Figure 1): i) a control group received usual care (247 patients), ii) a group that received a home blood pressure monitor and training in using a web service that enables refilling of prescriptions, appointment booking, healthcare contact, and viewing of portions of one’s electronic medical record (EMR) (246 patients), iii) a group that received the same intervention as the previous but in addition also received pharmacist care management (237 patients). The participants in this last group first received a telephone call from a pharmacist who toke the participant’s medical history and set up an action plan including at least one life-style change that the patient was going to make (patient selected). After the telephone call, the pharmacist contacted the participants once every two weeks via the web service. During this contact, the participant provided the blood glucose readings, and medical concerns and progress of the life-style change was discussed. The pharmacist made recommendations (including medical adjustments) and changed the action plan if necessary. The web contact continued until the patient reached the blood pressure goal of <135/85 mmHg. At the 12 month follow-up, no significant difference was seen between the two groups that had not received pharmacist consultations when it came to control of the blood pressure. In the usual care group, 31% of the participants were at goal and 36% in the group that had received a blood pressure monitor and web services (p=0.20). In the group that had received the pharmacist care management, however, 56% of the participants had
controlled blood pressure after the intervention. That is significantly better than in the other two groups (p<0.001 for both comparisons) (25).

![Diagram showing the number of participants in each group of the Green et al. (25) study and the type of intervention they received. The participants were placed in the different groups randomly. The patients that were lost during the trial either withdrew, were not contactable, moved, missed visits, left the health plan, became too ill, or died. BP = blood pressure. Figure adapted from Green et al. (25).]

**Figure 1.** Showing the number of participants in each group of the Green et al. (25) study and the type of intervention they received. The participants were placed in the different groups randomly. The patients that were lost during the trial either withdrew, were not contactable, moved, missed visits, left the health plan, became too ill, or died. BP = blood pressure. Figure adapted from Green et al. (25).

Margolis et al. (24) investigated the impact that a home blood pressure telemonitor in combination with follow up calls from a pharmacist had on hypertension patients. The study was made at 16 clinics in the metropolitan area of Minneapolis-St. Paul, USA, with start in 2009. Pharmacists at 8 of the clinics were part of the telemonitoring intervention while the other pharmacists gave usual care. The intervention group consisted of 228 patients and the control group of 222. All 450 patients had a SBP ≥140 mmHg or a DBP of ≥90 mmHg. If the patient also had diabetes or chronic kidney disease, the blood pressure inclusion criteria was ≥130 mmHg systolic or ≥80 mmHg diastolic. The intervention group got one initial face to face visit with a pharmacist, during which the patient was educated about the condition and instructed on how to use the blood pressure telemonitor. The patients were also informed about the blood pressure goal, which was set to SBP <135 mmHg and DBP <85 mmHg, for patients with comorbidities the goal was <125/75 mmHg. After the initial meeting, the pharmacists called the patients once every 2 weeks until the blood pressure was under control for 6 weeks in a row. After that the telephone calls were made less often until 12 months of the
The intervention had passed, after which the support from the pharmacists ended. During the telephone calls, the pharmacists talked about life-style changes and medical adherence. The pharmacists also analyzed the blood pressure measurements and made necessary medical adjustments. The control group received usual care. Significantly more patients in the intervention group reached the blood pressure goal after both 6, 12, and 18 months compared to the control group. At 12 months, 71.2% of the intervention group had reached the goal compared to 52.8% of the control group (p=0.005). The corresponding numbers at 18 months were 71.8% and 57.1% (p=0.003) (24).

A randomized controlled trial was conducted in the metropolitan area of Denver, USA, by Magid et al. (26) to investigate if a combination of education, home blood pressure monitoring, interactive voice response (IVR) phone system, and clinical pharmacist management could improve the blood pressure for patients with uncontrolled hypertension. Patients in both the intervention and control groups were educated about hypertension. The 145 patients in the control group were then encouraged to follow up with their primary care provider to get their blood pressure under control. The 138 patients in the intervention group were to measure their blood pressure 3-4 times/week and report the obtained values once a week via the IVR phone system. If the participants had not made a report in 10 days, they got an automated reminder call. If they still had not reported their blood pressure in 4 more days, they were phoned by a pharmacist. After reporting their blood pressure, the patient had the option to listen to an educational message and request a phone call from a pharmacist to discuss any question that had arisen. If the average reported blood pressure was above 135 mmHg systolic or 85 mmHg diastolic for patients without diabetes or chronic kidney disease or above 125 mmHg and 75 mmHg respectively for patients with these illnesses, a pharmacist called the patient. During the telephone call, the adherence to the medication as well as life-style changes were discussed. If necessary, the pharmacist made adjustments in the medication regimen with physician oversight. At baseline, the blood pressure for the patients in the intervention group was significantly higher than in the control group. The average SBP and DBP in the intervention group were 150.5±19.5 and 89.4±13.6, and in the control group 143.8±16.8 and 85.3±11.1 respectively (p<0.01 for SBP and p=0.02 for DBP). After 6 month of intervention, similar number of patients had reached the blood pressure goal in both groups – 36.0% in the intervention group and 35.2% in the control group (p=0.89). The average blood pressures were also similar with the SBP being 137.4±19.4 in the intervention group and 136.7±17.0 in the control group (p=0.85), and DBP being 82.9±12.9 and 81.1±11.7 respectively (p=0.14) (26).
Life style changes and other secondary outcomes
Two of the above studies also included secondary outcomes (24,25). Green et al. (25) and Margolis et al. (24) looked at life style changes such as exercise and diet. Green et al. (25) did not see any differences between the study groups and the only difference that Margolis et al. (24) showed was that the intervention group added less salt to the food. Margolis et al. (24) also looked at the medication adherence among the participants. In the intervention group, the adherence increased during the first months of the intervention but at the end of the study this difference had disappeared (24). Green et al. (25) also analyzed the quality of life, but could not detect that the interventions improved this parameter for the patients.

Pharmacy services for diabetes mellitus patients
Ten studies that analyzed the benefits of consultative pharmacy services for diabetes patients were identified (see Appendix B for summary). All but one study were undertaken in urban areas and the majority in USA. The design of the studies differed, from randomized controlled trials to retrospective trials and the number of participants also varied between studies.

Blood glucose control
Out of the 10 publications that studied the blood glucose values of diabetes patients that retrieved some kind of pharmacy service, 9 showed improvement in HbA1c values or in achieving the diabetes goal (see definition below) compared to a control group if present (17,19,21,22) or on their own if a control group was not included in the study (14,16,18,20,23). The ADA guidelines for diabetes patients is an HbA1c value below 7% (27), and this value is normally used as goal in published studies. The 7% will therefore hereon forward be referred to as blood glucose goal if nothing else is stated.

In Florida, USA, a retrospective study was made by Pepper et al. (19) to assess if inclusion of a pharmacist in the diabetes care team improved clinical outcomes for diabetes patients. Medical records (from 2006-2010) for 86 patients at 2 clinics that included clinical pharmacists in the care team were compared with medical records for the same number of patients at clinics that did not use a clinical pharmacist but instead had teams consisting of physicians, nurses, and diabetes educators. The pharmacist’s job in the care team was to educate patients with advanced or uncontrolled diabetes about the disease, nutrition, and exercise, but also to make medical adjustments in collaboration with the caring physician. Between the initial and final visits (3 months), the average decrease in HbA1c after cofounders had been adjusted for, was significantly greater for the group that had been counseled by a pharmacist compared to the patients in the control group.
The intervention group went from having an HbA1c value of 9.68% to 8.19% while no difference was seen for the control group. The differences between the groups were however not statistically significant when comparing the number of patients that reached the diabetes goal (p=0.25) (19).

Ip et al. (22) made a similar retrospective study, where pharmacists were included in the care team. Patients with type 2 diabetes and an HbA1c value $\geq 7.0\%$ were included in the study. The intervention group, which consisted of 147 patients, had an initial face-to-face meeting with a pharmacist. During this meeting, the patient was given dietary and exercise recommendations as well as education about self-care. The pharmacist also made modifications to the pharmacotherapy if needed. After the initial meeting, the patient was followed-up either by face-to-face visits or via telephone until their therapeutic goals were reached. The 147 participants in the control group received usual care. After 12 month of intervention, the HbA1c had decreased from 9.5% to 6.9% in the intervention group. The control group also decreased their HbA1c values from 9.3% to 8.4%. The difference between the groups was statistically significant (p<0.001). Significantly more in the intervention group (62.6% vs 28.6%) also reached the blood glucose goal (p<0.001) (22).

The only European study found was the one made by Mehuys et al. (17) in Belgium. This was a randomized controlled trial where the intervention involved education and counseling of patients with type 2 diabetes. The intervention group consisted of 135 participants that were educated about the disease, medication, life-style, as well as counseling to improve the adherence. The participants were also reminded to make foot and eye exams. The intervention lasted for 6 months and took place when the participants made their prescription refills. The 135 participants in the control group received the normal pharmacist care. At the end of the study, the HbA1c values had decreased significantly for the intervention group from 7.7% (±1.7) to 7.1% (±1.1), p<0.001. This was not the case for the control group where the corresponding values were 7.3% (±1.2) and 7.2% (±1.0), p=0.162. The number of patients that reached the blood glucose goal increased in both groups. In the intervention group, the number of participants at goal went from 41.5% to 52.6%, and from 42.9% to 49.4% in the control group. The differences between the groups was however not statistically significant (p=0.187). A follow-up measurement of the blood glucose was made 18 month after the intervention ended. Not all participants was part of this follow-up, values were obtained from 71.4% of the intervention participants and 71.9% of the participants in the control group. What was found was that the HbA1c did not differ significantly between the
Another pharmacy coaching program for diabetes patients was tried by Wertz et al. (16) in Cincinnati, USA, with start in 2008. The studied patients were either currently employed at or retired from the city of Cincinnati or Kroger Co. The employees and retirees were offered to participate in the program. The ones that accepted became part of the intervention groups while a subset of those that declined from the city of Cincinnati that matched the intervention group were used as controls. Each participant met with a community pharmacist several times (average 6 visits for employees and 9.5 for retirees) during on average 14 months. The participants (307 diabetics) were educated about their disease and their adherence and treatment goals discussed. The pharmacists also made feet assessments and monitored blood pressure, weight, lipid values and glucose control. When necessary, the pharmacists recommended medication changes. At the end of the study, the HbA1c values for the intervention group had decreased from 7.9% to 7.1% (p<0.05) and the number of patients that reached the treatment goal went from 44% to 62% (p<0.05). There are however no corresponding values for the control group stated. The total medical costs for the diabetes patients were more or less the same between the intervention and control groups, however, the costs were differently distributed. The intervention group had increased costs of medications and office visits while the costs for the control group came from hospitalizations (16).

The only study analyzed here that were conducted in Australia, was made by Mitchell et al. (18) and included 524 diabetes patients that were offered 5 visits to their local pharmacy where they received assessment, counseling, and education by a pharmacists. At each monthly visit, the pharmacist downloaded the patient’s glucose readings and generated graphs from these. The graphs were then used during the following discussion where the self-monitoring of blood glucose, medication adherence and potential problems, life-style changes, and goals for the next visit were addressed. Of the participants, 74% completed all the visits and after the 6 months intervention, the average blood glucose values had significantly decreased from 9.5% (±4.4) to 8.7% (±2.1), p<0.001. This study did not include a control group. At the end of the study, most participants were happy with the service. The ones that had recently gotten their diagnosis found that their knowledge about their condition was improved while the participants that had lived with the disease for a number of years instead thought that their motivation was improved by the discussion with the pharmacist (18).
A study similar to the one above was made by Pinto et al. (15). Like the previous study, no control group was included and the diabetes patients were offered 5 visits with a pharmacist. One difference between these two studies is that in the latter, the visits were spread out over a 1 year period. During these visits, the pharmacist performed medication therapy reviews, provided the patient with his or hers complete medical record, made a medication-related action plan, and educated the patient about the disease and medication (e.g. adverse effects and interactions). The pharmacists also made referrals and interventions with recommendations to the caring physician. Only 38 of the 101 participants completed the study. Unlike the study by Mitchell et al. (18), no major changes regarding the HbA1c values were seen but for the patients that came to all appointments (p=0.866) the number of hypoglycemic events significantly decreased (p=0.009) (15).

At a free clinic for uninsured in a rural county of South Carolina, USA, Sease et al. (14) conducted a study where volunteering pharmacists provided diabetes patients education about the disease, consultation on lifestyle changes, and assessment on appropriateness of the drug therapy, over a 2 year period. The pharmacists had one initial meeting with the patients and then, unlike the two studies above, as many follow up meetings that were necessary to reach the patients goals. No control group was included in this study. At the end of the intervention, a significantly reduction in HbA1c was seen for the 95 participating patients, from 10.7% (±2.4) to 8.1% (±1.9), p<0.0001. Significantly more of the participants also met the goal regarding the diabetes treatment at the end of the study compared to baseline (p<0.0001). At the end of the study 35.8% of the patients met the diabetes compared to 0% at the start. The authors estimated that if a patient decreased the HbA1c value with at least 1%, that would have saved $1,118 (14).

A retrospective evaluation of a pharmacy service in Texas, USA, was performed by Anaya et al (23). The pharmacist intervention took place between 2001 and 2005 at an outpatient clinic. Primary physicians referred diabetes patients to the pharmacist who educated the patients about the disease, made medication changes, and further referrals if necessary. A total of 110 patients were part of the study, no control group was included. The average number of consultations with the pharmacist were 5.9±3.7 during one year after the initial visit. The HbA1c values decreased significantly during the intervention from 8.9% (±2.0) to 8.2% (±1.8), p≤0.001. The cost of hospitalizations and emergency department costs were also compared. One year before the intervention started, the average cost per patient had been $2,434 (±4,612). The corresponding number during the intervention was $636 (±1,438), which is a significant decrease (p=0.015) (23).
Jennings and Marx (20) made a retrospective study where a clinical pharmacy service to diabetes patients at a community pharmacy in Utah were analyzed. Most patients that were referred to the service from the associated community clinic had poorly controlled diabetes. At the first visit, the therapeutic regimen was assessed and the pharmacist made necessary adjustments. The pharmacist also evaluated the patient’s ability to use a glucometer and inject insulin. The patient was told to check the blood glucose two times a day. The pharmacist went through the goals of the therapy and suggests lifestyle changes. The patient was also provided educational information. After the initial visit, the pharmacist called the patient once a week to follow up on the treatment and made adjustments if necessary. This continued until the patient reached the therapeutic goal.

Out of the patients referred to the service between 2009 and 2010, records for 111 were analyzed. No control group was included. After 6 months of participating in the pharmacy service, the average HbA1c decreased significantly from 10.1% (±2.0) to 8.1% (±1.8), \( p<0.001 \), the number of patients reaching an HbA1c value below 7.0% also increased significantly as did the individuals having a value over or at 9.0% (\( p<0.001 \)) (20).

All of the above studies involve one-on-one counseling by a pharmacist. One randomized controlled trial have however assessed if pharmacist-led intensive behavioral and pharmacological shared medical appointments could be beneficial for diabetes patients that also suffer from hypertension and hyperlipidemia. This study by Cohen et al. (21), was performed at the Veterans Affairs Medical Center in USA and the intervention consisted of group sessions with 4-6 participants in each group. Each group session was divided into two parts: The first part focused on education and was held by either a clinical pharmacist, nurse, dietitian, or physical therapist. The second half of the meeting consisted of group discussions led by the pharmacist. The discussions addressed risk factor control, obstacles that might occur, and possible solutions. The first 4 sessions were held once a week and the following 5 meetings were held once a month. Each of the 50 participant had exercise and dietary goals and kept a food-log and were provided with a pedometer. At the end of the study, significantly more participants in the intervention group (40.8%) had reach the HbA1c goal compared to the control group (20.4%), \( p=0.028 \) (21).

**Risk factor control and adherence**

Six of the studies that evaluated how pharmacy services could help diabetes patients decrease their blood glucose values also analyzed how the services reduced risk factors
and improved the medical therapy adherence for these patients. Wertz et al. (16) and Mitchell et al. (18) show the same, namely that the adherence improved. The intervention by Wertz et al. (16) also improved the adherence to medication for hypertension and dyslipidemia. Three of the studies reported that there were no change in smoking, weight or exercise (15,18,20). However, the study by Mehuys et al. (17) showed that the intervention group exercised significantly more at the end of the trial compared to the control group (p=0.045). The study by Mitchell et al. (18) also showed a decrease in the risk of barriers for a successful treatment, e.g. late refills, taking the wrong dose, and missing dose.

**Comorbidities**

Many of the diabetes patients also suffer from high blood pressure and hypercholesterolemia. Several of the studies discussed above investigated if the interventions performed by the pharmacists improved the state of these comorbidities.

When it comes to the blood pressure, the studies by Cohen et al. (21) and Ip et al. (22) both show that significantly more of the participants in the intervention groups reached the blood pressure goal compared to the control groups. The result from the Pepper et al. study (19), however, showed no significant difference between the intervention group and the control group when it came to blood pressure. For the patients that suffered from both diabetes and hypertension in the study by Pinto et al. (15), the blood pressure decreased with 14 mmHg systolic and 12 mmHg diastolic. Sease et al. (14) showed that both the systolic and diastolic blood pressure were reduced and that significantly more of the patients met the blood pressure goals at the end of the study compared to the start. Similarly, in the study by Wertz et al. (16), the percentage of patients reaching the goals for blood pressure improved. The results from the Pinto et al. (15), Sease et al. (14), and Wertz et al. (16) studies were not compared to control groups.

Regarding dyslipidemia, neither Pepper et al. (19) nor Cohen et al. (21) could show a significant difference between their intervention and control groups when it came to the cholesterol values. In contrast to this, the study by Ip et al. (22) showed that LDL cholesterol was significantly decreased compared to the control group (p<0.001). The studies by Sease et al. (14) and Wertz et al. (16) also reported an improvement in cholesterol values at the end of the studies, while Anaya et al. did not (23). As mentioned above, the results in neither of these three studies were compared to a control group (14,16,23).
Discussion

Current projects in rural Sweden
This study had as its starting point, the health situation in rural Sweden where the physical health is worse than in other parts of the country (2). Many of the rural municipalities are located in the northern parts of the country and county councils here are also working to assure that their inhabitants are receiving the same health care as the rest of the population (1). Example of projects that are undertaken are cognitive behavioral therapy (CBT) via videoconferencing or web camera, and remote measurement of e.g. blood pressure, blood glucose, and PK (INR) (28,29). What all of the current projects have in common are that they are conducted by other health care professionals than pharmacists. Counseling by pharmacist, however, have in other countries been shown to improve the health of patients (11). In this report, the latest studies regarding the benefits of pharmacist counseling for patients with diabetes were analyzed. The counseling services can also be performed by remotely located pharmacist and the benefits of such telepharmacy services for patients with hypertension were investigated as well.

Telepharmacy
In other countries different telepharmacy services are used or have been tried. Telepharmacy services require well-functioning mobile phone networks and/or internet connection. Sweden has a good mobile net coverage with 99% of the population included and the network operators are working on reaching 90% geographic coverage (30). This constitutes a good basis for telepharmacy services, services that might be of use in rural parts of Sweden where the population is aging and thereby becoming more disease prone.

Telepharmacy services for patients with hypertension
In this report, telepharmacy services for patients with hypertension have been reviewed. All of the hypertension studies were randomized controlled trials with approximately 200 participants in each group (24–26). This is not a large number of patients and larger studies would have been desirable to get more convincing results. It is hard to analyze the Magid et al. study (26) since the base line blood pressure differed significantly between the groups. However, what can be concluded is that the telepharmacy intervention at least was not worse than the usual care. The interventions in the Green et al. (25) and Margolis et al. (24) studies both showed that the telepharmacy interventions facilitated more patients to reach their blood pressure goal. Especially the
Margolis et al. study (24) is encouraging since a difference still could be seen 6 months after the intervention ended. It would have been interesting to see how long lasting the effects from both this study (24) and the Green et al. study (25) were, and if follow up with interventions more rarely, e.g. twice a year, could improve the longevity of the positive effects.

**Consultative services for diabetics**

In 2007 a meta-analysis was published by Machado et al. (31) that showed pharmacist interventions could reduce the HbA1c values of diabetes patients. However, the quality of the included studies were not optimal and the authors suggested that more researched should be done on the topic (31). In this thesis, more recent studies that investigated the pharmacist role in helping diabetics managing their disease through counseling were analyzed. Like the studies analyzed by Machado et al. (31), the majority of studies included here are positive in their outcomes but they also had varying design and quality. Five of the studies were lacking a control group (14,15,18,20,23) and one study included a control group but that was not compared to when it came to the blood glucose outcome (16). This must be seen as weaknesses for these studies since there is no way of knowing what would have happened without the interventions. With regard to this, the results from the Mehuys et al. (17), Pepper et al. (19), Cohen et al. (21), and Ip et al. (22) must be seen as the strongest since they all included control groups that the intervention data were compared to.

Mehuys et al. (17), Pepper et al. (19), and Ip et al. (22) directly looked at the HbA1c values and they showed a greater reduction in the blood glucose value in the intervention groups compared to the control groups. However, when comparing the number of participants that reached the blood glucose goal, no statistical difference was seen by Mehuys et al. (17) or Pepper et al. (19). In contrast to these studies, the interventions conducted by Cohen et al. (21) and Ip et al. (22) led to more patients reaching the blood glucose goal compared to the control groups. The question in diabetes treatment is also what is most important: reaching the blood glucose goal or decreasing the blood glucose as much as possible. As mentioned, the Mehuys et al. (17) and Pepper et al. (19) studies showed a greater reduction in blood glucose values in the intervention group but no difference in the numbers of participants that reached the goal. It has been shown that a 1% decrease in HbA1c value reduces the risk of suffering from microvascular complications by 33%, myocardial infarction by 18%, and diabetes death by 25% (16). With this in mind, it seems like every reduction that can be made in the blood glucose values are of value and maybe that is a better measurement than obtaining the 7% goal.
As with the hypertension studies, the number of participants in the face-to-face interventions were quit low. None of the four studies discussed above had more than 147 participants in any one group (17,19,21,22). As discussed previously, this is not a very large amount of participants. Another weakness is that these studies did not look at the long term effects of the interventions. It would have been interesting to see how long lasting the positive outcomes were. Larger and longer studies that investigate the benefits with consultative face-to-face services for diabetics are therefore desirable.

**Effects on comorbidities**

A majority of the diabetes studies reviewed here showed encouraging results when it came to blood glucose values (although some of the studies lacked control groups). However, it was not only the blood glucose that was improved – when comorbidities existed, these were also mainly positively affected by the pharmacy services. Five out of 6 studies that looked at blood pressure showed a decrease (14–16,21,22), and 3 out of 6 studies also reported better cholesterol values at the end of the interventions (14,16,22,23). This, in combination with the overall positive results from the hypertension studies, points at an important role for pharmacist in helping patients managing their diseases.

**Effects of pharmacy services on life-style and adherence**

A successful self-management is needed to obtain the best possible prognosis for hypertension patients and especially diabetes patients. This, however, requires both cognitive and behavioral changes. For example are life-style modifications such as increased exercise, changed diet, and foot care important for diabetics, as well as medication compliance, self-monitoring of blood glucose values, and regular health care visits. If patients are going to succeed in undertaking these alterations, they need knowledge, skills, and motivation – something that the pharmacy interventions tried to provide.

Although many of the studies reviewed in this report have positive primary outcomes – such as lowered blood pressure or blood glucose – almost none can show improvement in life style, e.g. exercise and smoking habits (15,16,18,20,25). The only exceptions were the studies by Margolis et al. (24), who noted a decreased use of salt among the hypertensive participants in the intervention group, and Mehuys et al. (17) that saw an improvement in exercise among the diabetics. It thus seems hard to change people’s habits through pharmacy services, however, most of the studies did not use motivational interviewing as a method. The only publication (to my knowledge) that incorporated
motivational interviewing was the one made by Mitchell et al. (18), which showed positive results (although a control group was not included). An ongoing study in North Carolina, USA, by Zullig and colleagues (32) are investigating how this technique can be used in a telepharmacy service for hypertension and hyperlipidemia patients. The intervention will provide the participants with monthly telephone calls over a 1 year period and aims at helping the participants to gain self-efficacy, implement healthy behaviors and maintain these over time. The pharmaceutical intervention is to be tailored after each patient’s specific needs, e.g. smoker will be helped with smoking cessation and obese participants with weight loss (32). It will be really interesting to see the outcome of this study and if the participants succeed better than the ones presented here when it comes to improving their life-style alterations.

The adherence to medication regimen was analyzed in 3 of the publications with varying results (16,18,24). What was interesting was that the adherence in the hypertension study was better in the intervention group in the beginning of the studies but then the difference disappeared at the end of the trial (24). This was also seen in a study by López-Carbezas, which analyzed a pharmacy service for heart failure patients (33). For the two diabetes studies on the other hand, the adherence at the end of the studies had improved (16,18). What is worth mentioning is that the study made by Mitchell et al. (18) did not include a control group which makes it hard to say how the adherence would have turned out without the pharmacist intervention. This study was also shorter than the hypertension and heart failure ones, with a 6 month intervention period vs 12 months (18,24,33). The study by Wertz et al. (16) did include a control group and that group did not show any change in adherence throughout the study while the participants in intervention group significantly increased theirs. The intervention period differed between the participants in this study but was on average 14 month (16). From these findings it is hard to draw any conclusions on if pharmacy services such as those reviewed here have any big impact on the medical adherence of patients. The ongoing study by Zullig et al. (32) (mentioned above) also include analysis of the participants adherence so perhaps it can shed some light on the impact pharmacists can have when it comes to medical adherence.

**Economic impact of the pharmacist interventions**

The scope of this study was not to look at the potential economic savings that pharmacy services can lead to. However, telepharmacy services in particular have a potential of being cost saving, not only for the health care system when fewer patient visits are needed, but also for the patients when e.g. travel costs are reduced (11). Sease et al. (14)
estimated that a decrease in HbA1c values with at least 1% would save $1,118 per patient. The face-to-face pharmacy service tried by Wertz et al. (16) did not decrease the costs for the diabetes patients but the cost distribution became altered by the intervention. In the control group, most of the costs came from hospitalizations while the patients in the intervention group instead had increased costs for medications and office visits (16). In agreement with the Wertz et al. (16) study, Anaya et al. (23) showed that the costs of hospitalization and emergency department visits for the diabetes patients significantly decreased with almost 4 times during the intervention. Unfortunately, this study did not include the costs for the pharmacy service, medications, and other visits to health care providers and the results were not compared to a control group (23).

**Inspiration for rural Sweden**

The starting point for this study was the health situation in rural Sweden. None of the studies included were performed in Sweden and only one study in a rural area (14), but they present pharmacy services that can potentially be beneficial for hypertension and diabetes patients living in the rural parts of Sweden.

As mentioned previously, most of the studies included were made in USA. The health care and social security systems in Sweden and USA are different, which could affect the outcomes if the interventions are applied in Sweden. Studies undertaken in rural Sweden are therefore wanted to see if the positive effects seen in other countries can be repeated here.

**Limitations**

The result in this report are based on the publications found. It is possible that the outcome would have differed somewhat if the literature search had been done differently. E.g. only the database PubMed was used to identify studies. Another factor that can have skewed the result are the limitations used in the searches. Only publications available via the Umeå University library were included, leading to exclusions of publications in the Journal of the American Pharmacists Association, which the library does not subscribe to. In total, 3 articles (34–36) are missing from the analysis due to this, however, the abstracts indicate that they all show similar results as the publications included with a decrease in HbA1c after the interventions. A 10 year cut-off was used when searching for diabetes publications. A meta-analysis analyzing the role of pharmacists in diabetes care was published in 2007 (31), wherefore articles with this topic older than 10 years were not included here.
Conclusion

Two out of three studies that analyzed consultative telepharmacy services for patients with hypertension showed that the interventions lead to a significant decrease in blood pressure. Nine out of 10 studies that investigated the benefits of face-to-face consultative pharmacy services for diabetics also showed positive results with either lowering in blood glucose values or in achieving the blood glucose goal. The studies thus demonstrate that extending the role of pharmacists beyond dispensing medications to counseling can be beneficial for patients with diabetes and hypertension. Larger, longer and better controlled studies are however needed to confirm the results.

Acknowledgement

I would like to thank my supervisor Helena Holmgren for all the valuable input and for steering me in the right direction when I was lost.
References


## Appendix A

Summary of the hypertension studies. BP = blood pressure and Home BP = home blood pressure monitoring.

<table>
<thead>
<tr>
<th>Authors, Country &amp; Design</th>
<th>Intervention</th>
<th>Number of participants &amp; Disease state</th>
<th>Main conclusions</th>
</tr>
</thead>
</table>
| Green et al. (25) USA Randomized controlled trial | Control group: Usual care  
Web intervention group: Web services, home BP  
Web+pharmacist intervention group: Web services, home BP, pharmacist care management via web, drug therapy adjustments  
12 month intervention duration | Control group: 247  
Web group: 246  
Web+pharmacist: 237  
SBP 140-199 mmHg  
DBP 90-190 mmHg  
No other serious disease | Significantly more in the web+pharmacist group reached BP goal compared to control group and web group.  
No significant difference between control and web groups. |
| Margolis et al. (24) USA Randomized controlled trial | Control group: Usual care  
Intervention group: Telephone consultations, home BP, drug therapy adjustments  
12 month intervention duration, follow up after 18 months | Control group: 222  
Intervention group: 228  
SBP ≥140 mmHg  
DBP ≥90 mmHg  
If diabetes or chronic kidney disease  
SBP ≥130 mmHg  
DBP ≥80 mmHg | Significantly more reached goal in intervention group.  
At 18 month 71.8% were at goal in intervention group and 57.1% in control group. |
| Magid et al. (26) USA Randomized controlled trial | Control group: Usual care  
Intervention group: Home BP, clinical pharmacist consultation via telephone, drug therapy adjustments  
6 month intervention duration | Control group: 145  
Intervention group: 138  
Uncontrolled hypertension  
N.B. Baseline BP was significantly higher for intervention group | Approximately the same number of patients reached the BP goal in the both groups (36.0% in the intervention group vs 35.2% in the control group). |
## Appendix B

Summary of the diabetes studies.

<table>
<thead>
<tr>
<th>Authors, Country &amp; Design</th>
<th>Intervention</th>
<th>Number of participants &amp; Disease state</th>
<th>Main conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pepper et al. (19) USA Retrospective controlled trial</td>
<td>Control group: Usual care  Intervention group: Education and medical adjustments  3 months intervention duration</td>
<td>Control group: 86  Intervention group: 86  Advanced or uncontrolled type 2 diabetes</td>
<td>Significantly larger decrease in HbA1c compared to control group.  No difference in goal achievement between the groups.</td>
</tr>
<tr>
<td>Ip et al. (22), USA Retrospective controlled trial</td>
<td>Control group: Usual care  Intervention group: Consultations and medical adjustments  Intervention until goal or 12 months</td>
<td>Control group: 147  Intervention group: 147  Type 2 diabetes and HbA1c≥7%</td>
<td>Significantly larger reduction in HbA1c and improved goal achievement in intervention group compared to control group.</td>
</tr>
<tr>
<td>Mehuys et al. (17), Belgium Randomized controlled trial</td>
<td>Control group: Usual care  Intervention group: Education and counseling  6 months intervention duration</td>
<td>Control group: 135  Intervention group: 135  Type 2 diabetes</td>
<td>Significant decrease in HbA1c in intervention group but not control group.  No significant difference in reaching goal.</td>
</tr>
<tr>
<td>Wertz et al. (16), USA Quasi-experimental pre/post longitudinal trial</td>
<td>Control group: Usual care  Intervention group: Counseling, education and drug therapy adjustments  14 months average intervention duration</td>
<td>Control group: 274  Intervention group: 307  Diabetes</td>
<td>Decreased HbA1c and more reached goal in intervention group.  Intervention group not compared to control group in the publication.</td>
</tr>
</tbody>
</table>
Summary of the diabetes studies continued from previous page. Home BG = Home blood glucose monitoring.

<table>
<thead>
<tr>
<th>Study Authors, Location, Study Type, Group</th>
<th>Number of Patients</th>
<th>Type of Diabetics</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitchell et al. (18), Australia, Uncontrolled trial</td>
<td>524</td>
<td>Uncontrolled type 2 diabetes</td>
<td>Significant decrease in HbA1c.</td>
</tr>
<tr>
<td>Pinto et al. (15), USA, Uncontrolled trial</td>
<td>101</td>
<td>Type 2 diabetes</td>
<td>No significant reduction in HbA1c. Only 38 patients came to all visits</td>
</tr>
<tr>
<td>Sease et al. (14), USA, Uncontrolled trial</td>
<td>95</td>
<td>Type 2 diabetes</td>
<td>Significant decrease in HbA1c. Significantly more reached goal.</td>
</tr>
<tr>
<td>Anaya et al. (23), USA, Retrospective evaluation</td>
<td>110</td>
<td>Type 1 and type 2 diabetes</td>
<td>Significant decrease in HbA1c.</td>
</tr>
<tr>
<td>Jennings &amp; Marx (20), USA Retrospective controlled trial</td>
<td>111</td>
<td>Uncontrolled diabetes</td>
<td>Significant decrease in HbA1c. Significantly more reached goal.</td>
</tr>
<tr>
<td>Cohen et al. (21), USA, Randomized controlled trial</td>
<td>Control group: 49, Intervention group: 50</td>
<td>Uncontrolled type 2 diabetes together with hypertension and hyperlipidemia</td>
<td>Significantly more patients reached goal compared to control group</td>
</tr>
</tbody>
</table>