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EVALUATION OF DRUG - RELATED PROBLEMS IN PATIENTS WITH ARTERIAL HYPERTENSION

Master thesis

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EVALUATION OF DRUG-RELATED PROBLEMS IN PATIENTS WITH ARTERIAL HYPERTENSION

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## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUMMARY</td>
<td>5</td>
</tr>
<tr>
<td>SANTRAUKA</td>
<td>7</td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td>9</td>
</tr>
<tr>
<td>DEFINITIONS</td>
<td>11</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>12</td>
</tr>
<tr>
<td>AIM AND WORK TASKS</td>
<td>13</td>
</tr>
<tr>
<td>1. LITERATURE REVIEW</td>
<td>14</td>
</tr>
<tr>
<td>1.1. Theoretical background</td>
<td>14</td>
</tr>
<tr>
<td>1.1.1. Hypertension</td>
<td>14</td>
</tr>
<tr>
<td>1.1.2. Drug therapy problems</td>
<td>14</td>
</tr>
<tr>
<td>1.2. Scientific articles review</td>
<td>16</td>
</tr>
<tr>
<td>1.2.1. Treatment of Hypertension</td>
<td>16</td>
</tr>
<tr>
<td>1.2.2. Comorbid diseases and their influence on hypertension</td>
<td>18</td>
</tr>
<tr>
<td>1.2.3. Assessment and identification of drug therapy problems</td>
<td>20</td>
</tr>
<tr>
<td>1.2.4. Possible causes of drug related problems</td>
<td>22</td>
</tr>
<tr>
<td>1.2.5. Impact of pharmacist interventions on improving blood pressure control</td>
<td>23</td>
</tr>
<tr>
<td>1.2.6. Physician – pharmacist collaborative treatment model for the management of hypertension</td>
<td>27</td>
</tr>
<tr>
<td>2. METHODOLOGY</td>
<td>29</td>
</tr>
<tr>
<td>2.1. Study design, area and period</td>
<td>29</td>
</tr>
<tr>
<td>2.2. Study population</td>
<td>29</td>
</tr>
<tr>
<td>2.3. Inclusion and exclusion area</td>
<td>29</td>
</tr>
<tr>
<td>2.3.1. Inclusion criteria</td>
<td>29</td>
</tr>
<tr>
<td>2.3.2. Exclusion criteria</td>
<td>29</td>
</tr>
<tr>
<td>2.4. Sample size determination</td>
<td>30</td>
</tr>
<tr>
<td>Section</td>
<td>Title</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>2.5</td>
<td>Sampling techniques</td>
</tr>
<tr>
<td>2.6</td>
<td>Data collection procedure and instruments</td>
</tr>
<tr>
<td>2.7</td>
<td>Study variables and outcome measures</td>
</tr>
<tr>
<td>2.7.1</td>
<td>Dependent (Outcome) variable</td>
</tr>
<tr>
<td>2.7.2</td>
<td>Independent (Exposure) variable</td>
</tr>
<tr>
<td>2.7.3</td>
<td>Outcome measures</td>
</tr>
<tr>
<td>2.8</td>
<td>Data analysis</td>
</tr>
<tr>
<td>2.9</td>
<td>Ethical consideration</td>
</tr>
<tr>
<td>3.1</td>
<td>General information about participants</td>
</tr>
<tr>
<td>3.1.1</td>
<td>Control of blood pressure at home</td>
</tr>
<tr>
<td>3.1.2</td>
<td>Laboratory tests and BP</td>
</tr>
<tr>
<td>3.2</td>
<td>Analysis of risk factors</td>
</tr>
<tr>
<td>3.2.1</td>
<td>Smoking</td>
</tr>
<tr>
<td>3.2.2</td>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>3.2.3</td>
<td>Physical activity</td>
</tr>
<tr>
<td>3.2.4</td>
<td>Comorbid diseases</td>
</tr>
<tr>
<td>3.3</td>
<td>Complications and ADRs</td>
</tr>
<tr>
<td>3.4</td>
<td>Treatment of hypertension</td>
</tr>
<tr>
<td>3.5</td>
<td>Evaluation of drug – related problems</td>
</tr>
<tr>
<td>3.5.1</td>
<td>Drug interactions</td>
</tr>
<tr>
<td>4</td>
<td>STUDY LIMITATIONS</td>
</tr>
<tr>
<td>5</td>
<td>CONCLUSION</td>
</tr>
<tr>
<td>6</td>
<td>PRACTICAL RECOMMENDATIONS</td>
</tr>
<tr>
<td>7</td>
<td>REFERENCES</td>
</tr>
</tbody>
</table>
SUMMARY

Master Thesis of E. Biryukova “Evaluation of drug-related problems in patients with arterial hypertension“. Scientific supervisor Lect. Dr. R. Minkutė; Lithuanian University of Health Sciences, Faculty of Pharmacy, Department of Clinical Pharmacy. – Kaunas

The aim of the thesis. To determine the type of drug–related problems and their most common reasons for patients who suffer from arterial hypertension.

Objectives of the research.

1) To determine the drug–related problems in the investigative patients’ groups.
2) To analyze the identified problems and compare with the results from other studies.
3) To identify risk factors which affect DRP in hypertensive patients.
4) To make recommendations for the patient to prevent possible problems.

Methodology. This study was questionnaire–based which was conducted between July to August 2016 in Kaliningrad, Russia and from January to February 2017 in Kaunas, Lithuania. A convenient sampling method was used and a total of 100 hypertensive patients were included in the study. DRPs were identified based on strand classification system and trustable literature. Data were analyzed using Excel and SPSS software program. Descriptive statistics were generated in the form of numbers and percentage. To summarize the quantitative variables, mean and standard deviation (SD) were calculated, and for the qualitative variables, frequencies and percentages were used.

Results. The frequency of DRPs was identified 92% vs. 100% in the investigative group in Kaunas and Kaliningrad, respectively. One hundred and fourteen DRPs were identified in each city, an average of 2.3 DRP for each participant. Identified DRPs were unnecessary drug therapy (7.9% vs. 3.5%), needs an additional drug therapy (14.1% vs. 31.6%), ineffective therapy (25.4% vs. 15.8%), adverse drug reaction (27.2% vs. 17.5%), and non–adherence (25.4% vs. 31.6%) in Kaliningrad and Kaunas, respectively. Prevalence of risk factors for BP in the evaluated population was minimal: 82% vs. 72% respondents don’t smoke, 62% vs. 88% don’t consume alcohol; however, only 32% vs. 20% are doing sports and 90% vs. 84% has comorbid diseases in Kaliningrad and Kaunas, consequently.

Conclusion. A number of drugs and number of comorbidities significantly affect drug–related problems. The study showed that almost all the patients in the study have drug therapy problems. For that reason,
patients with multiple diagnosis and patients using multiple drugs should be closely monitored for drug –
related problems, to avoid clinically significant harmful consequences. The monitoring of medicines use is
an effective way to decrease the number of DRPs and to ensure safety and efficacy.
SANTRAUKA

E. Biryukova magistro baigiamasis darbas „Su vaistų vartojimu susijusių problemų įvertinimas pacientams, sergantiems arterine hipertenzija“, mokslinė vadovė lekt. dr. R. Minkutė; Lietuvos sveikatos mokslų universiteto Farmacijos fakulteto Klinikinės farmacijos katedra. – Kaunas

**Tyrimo tikslas:** Nustatyti su vaistų vartojimu susijusias problemas ir jų priežastis pacientams, kurie serga arterine hipertenzija.

**Tyrimo uždaviniai:**

1) Nustatyti su vaistų vartojimu susijusias problemas tiriamojoje pacientų grupėje
2) Išanalizuoti nustatytas problemas ir palyginti rezultatus su kitais moksliniais tyrimais
3) Identifikuoti rizikos veiksnius, kurie gali turėti įtakos su vaistų vartojimu susijusioms problemoms esant hipertenzijai
4) Pateikti rekomendacijas pacientams, norint išvengti galimų problemų


**Rezultatai:** Nustatytas su vaistų vartojimu susijusių problemų dažnis tiriamojoje grupėje buvo 92 % ir 100 % Kaune ir Kaliningrade, atitinkamai. Po šimtų keturiolika tokių problemų nustatyta kiekviename mieste – vidutiniškai 2,3 problemas kiekvienam pacientui. Identifikuotos su vaistų vartojimu susijusios problemas: nereikalingas vaistų vartojimas (7,9 % ir 3,5 %), papildomo vaisto poreikis (14,1 % ir 31,6 %), neveiksmingas gydymas (25,4 % ir 15,8 %), nepageidaujamas vaisto poreikis (27,2 % ir 17,5 %) ir nurodymų nesilaikymas (25,4 % ir 31,6 %) atitinkamai Kaliningrade ir Kaune. Hipertenzijos rizikos veiksnių paplitimas tiriamojoje grupėje buvo nedidelis: 82 % ir 72 % respondentų nerūko, 62 % ir 88 % nevartojo alkoholio; tačiau tik 32 % ir 20 % sportuoja bei 90 % ir 84 % serga gretutinėmis ligomis atitinkamai Kaliningrade ir Kaune.
**Išvados.** Vaistai ir gretutinės ligos turėjo reikšmingą įtaką su vaistų vartojimu susijusioms problemoms. Tyrimas parodė, jog beveik visi respondentai turėjo farmakoterapinių problemų. Dėl šios priežasties, pacientai, sergantys daugeliu ligų ir vartojantys daug vaistų, turėtų būti atidžiai stebimi, kad būtų galima išvengti su vaistų vartojimu susijusių problemų ir kliniškai svarbių, žalingų pasekmių. Vartojamų vaistų stebėjimas yra efektyvus būdas mažinant su vaistų vartojimu susijusių problemų dažnį ir užtikrinant saugų ir veiksmingą gydymą.
ABBREVIATIONS

ADR – Adverse drug reaction

BP – Blood pressure

BMI – Body mass index

CORFIS - Cardiovascular Risk Factors Intervention Strategies

DBP - Diastolic blood pressure

DRPs – Drug – related problems

DTPs – Drug therapy problems

ECG – Electrocardiography

ESH – European Society of Hypertension

GP – General Practitioner

HBPM – Home blood pressure monitoring

HCT - Hydrochlorothiazide

HTN – Hypertension

ITT analysis - Intention-to-treat analysis

JNC - Joint National Committee

MTM - Medication therapy management

OTC – Over – the-counter drug

PCIs - Pharmaceutical care issues

PCP – Primary Care Provider

PharmD-PCP - Pharmacist - primary care physician
PP analysis - Per-protocol analysis

PPCC - Physician-pharmacist collaborative care

p. r. n (PRN) – as needed

SBP - Systolic Blood Pressure

SD – Standard Deviation

SPSS - Statistical Package for the Social Sciences

TBC – Team – Based Care

TBC-HTA - Team - Based Care for Improving Hypertension management

T2DM - Type 2 diabetes

WHO – World Health Organization
DEFINITIONS

Drug therapy problems - undesirable events or risks experienced by the patient that involve or are suspected to involve drug therapy, that inhibit or delay him or her from achieving the desired goals of therapy, and require professional judgment to resolve [1].

Hypertension is defined by persistent elevation of arterial blood pressure (BP) [2]. The Seventh Report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classifies adult BP as shown in Table 1 [3].
INTRODUCTION

Evaluation of drug-related problems (DRPs) is a very important topic in the pharmaceutical field, which would aid to resolve the consequences caused by negative drug therapy. The purpose of identifying drug-related problems is to help patients to reach their goals of therapy and achieve the best possible outcomes from drug therapy [1]. Hypertensive patients are one of those who are suffering from undesirable events of drug therapy.

Hypertension is one of the leading causes of cardiovascular diseases worldwide, and it is defined as the constant deviation of the blood pressure (BP) in the arteries. To add, hypertension is a chronic disease, which is diagnosed most commonly in persons aged 50 and older. According to World Health Organization (WHO): “The prevalence of raised blood pressure (SBP≥140 or DBP≥90), age-standardized 18+, completed in percentage (%), which was performed in 2015, prevalence in Lithuania in male is 36.1%, in female 23.1% and in Russia in male 32.6% and in female 22.3%, respectively [4].” As well as WHO has assessed that about 62% of cerebrovascular disease and 49% of ischemic heart disease are a major concern all over the world. Elevated blood pressure has assessed to cause 7.1 million deaths each year, considering 13% of all deaths globally [5]. Hypertension is one of the leading causes of cardiovascular diseases worldwide. Various researches have indicated that more than half of the hypertensive patients on treatment are still suffering from increased blood pressure (over 140/90 mm Hg), despite the availability of efficient medical therapy.

This is mainly because of drug therapy issues which are involved but not restricted to non-compliance, adverse drug reactions (ADRs), inappropriate choice of drug and drug interactions. The types of drug-related problems in hypertensive patients, and their effect on blood pressure control are still unknown. In this study, the evaluation of drug-related problems in patients suffering from hypertension and their associations between DRPs and blood pressure control were investigated.
AIM AND WORK TASKS

The aim: Find out what kind of drug-related problems and their reasons prevalent in arterial hypertension suffering patients.

Tasks:

1) To determine the drug-related problems in the investigative patients’ groups.

2) To analyze the identified problems and compare with the results from other studies.

3) To identify risk factors which affect DRP in hypertensive patients.

4) To make recommendations for the patient to prevent possible problems.
1. LITERATURE REVIEW

1.1. Theoretical background

1.1.1. Hypertension

Hypertension (HTN), in other words, it is high blood pressure. This condition occurs when the force of blood exerted by the arterial blood vessel exceeds a blood pressure of 140/90 mm Hg. Ninety percent of HTN cases is classified as primary hypertension, with unknown causative etiology. Another type of HTN is secondary, which can be caused by kidney disease or hormonal problems or induced by oral contraceptives, pregnancy, or other causes [6]. Below you can see the table 1, which describes a classification of blood pressure in adults.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>and</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120 – 139</td>
<td>or</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140 – 159</td>
<td>or</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160</td>
<td>or</td>
</tr>
</tbody>
</table>

BP – blood pressure

Untreated HTN can lead to many possible complications. As an example: stroke, ischemic heart disease, heart failure and kidney failure [6]. Patients with noncomplicated primary hypertension are commonly asymptomatic at an initial stage. Patients with secondary hypertension may make complaints against symptoms presumptive of the underlying disorder. Generally, the only indication of primary hypertension on physical examination is elevated blood pressure. Two or more measurements of blood pressure are taken during the clinical encounter. That is how the diagnosis of hypertension is made [2].

1.1.2. Drug therapy problems
Drug therapy problems are significant for the pharmaceutical care practitioner. The evaluation of drug therapy problems is the target of the assessment and shows the main decisions made in that step of the patient care process. Although drug therapy problem evaluation is technically part of the assessment procedure, it performs the very particular input made by pharmaceutical care practitioners [1].

Drug therapy problems are an outcome of a patient’s drug-related needs that have gone dissatisfied. They are fundamental to pharmaceutical care practice. If not resolved, drug therapy problems have clinical consequences [1].

All the patient problems including medications can be classified into one of seven types of drug therapy problems (Table 2). These include the need for additional, synergistic, or preventive medications, treatment failures, any and all side effects, toxic reactions, as well as adherence problems and noncompliance [1].

Table 2. Seven categories of drug therapy problems [1]

<table>
<thead>
<tr>
<th>Drug therapy problems</th>
<th>Description of the drug therapy problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Unnecessary drug therapy</td>
<td>The drug therapy is unnecessary because the patient does not have a clinical indication this time.</td>
</tr>
<tr>
<td>2. Needs additional drug therapy</td>
<td>Additional drug therapy is required to treat or prevent a medical condition.</td>
</tr>
<tr>
<td>3. Ineffective drug</td>
<td>The drug product is not effective for producing the desired response for this patient.</td>
</tr>
<tr>
<td>4. Dosage too low</td>
<td>The dosage is too low to produce the desired response for this patient.</td>
</tr>
<tr>
<td>5. Adverse drug reaction</td>
<td>The drug is causing an adverse drug reaction.</td>
</tr>
<tr>
<td>6. Dosage too high</td>
<td>The dosage is too high resulting in undesirable effects.</td>
</tr>
<tr>
<td>7. Adherence</td>
<td>The patient is not able or not willing to take the drug regimen as instructed.</td>
</tr>
</tbody>
</table>

The first two categories of drug therapy problems are correlated with the therapeutical indication. The third and fourth categories of drug therapy problems are linked with an effectiveness of pharmacotherapy. The fifth and sixth categories of drug therapy problems are associated with the safety of medicines. The seventh category deals with patient compliance.
First six categories of drug therapy problems characterize clinical problems that the patient faces arising from the actions of drug therapy on his or her health. These six categories are distinct from the seventh. That one category, adherence or noncompliance, results from the actions the patient makes regarding his or her readiness or capability to apply the medication as instructed.

1.2. Scientific articles review

Studies worldwide signify that in spite of the availability of effective drug therapy, more than fifty percent of hypertensive patients on treatment have blood pressures over 140/90 mm Hg threshold [7, 8]. This is regularly because of drug – related problems which include but not limited to, ADRs, drug interactions, improper drug selection, and non-compliance [9].

The presence of DRP among hypertensive patients could restrict or postpone patients from reaching desired therapeutic goals [10]. Significant numbers of patients do not get the highest benefit of medical treatment, resulting in unsatisfactory health outcomes, decreased the quality of life, increased health care costs and deteriorating public assurance in health system [7, 11].

Definitely, interventions to enhance drug – related problems are needed to overcome the harms imposed by the problem. If such interventions are to be successfully designed, targeted, and cost - effective, it is crucial to understand the complex reasons for drug – related problem and to analyze those that are changeable in hypertensive patients [10].

Assessment of drug – related problems is essential for pharmaceutical care practitioner, especially for a hypertensive patient. It helps to resolve undesirable events of drug therapy during treatment. As drug - related problems are prevalent among hypertensive patients, pharmacists should be involved in the monitoring of patients' pharmacotherapy to identify and resolve pharmacotherapy issues.

1.2.1. Treatment of Hypertension

In a study of Nasution et al. [12], the utilization pattern of antihypertensive drugs varies of which amlodipine (47.7%), followed by captopril (22.4%) and their combination (16.8%) the most were frequently provided antihypertensive drugs to the hypertensive patients. Combination therapy of
hydrochlorothiazide and amlodipine was given to 5.6% of the hypertensive patients. As well, combination therapy of HCT (hydrochlorothiazide) and amlodipine was only provided to 2.8% of the patients. Each of the rest antihypertensive combinations was only provided to one patient. The utilization pattern of the antihypertensive drugs in the treatment of the hypertensive patients is mostly affected by the disease severity as recommended by the National Formulary as well as JNC 7 (Joint National Committee) [3].

Few studies on utilization of antihypertensive drugs in patients with hypertension have been undertaken elsewhere. A prospective, randomized, controlled study found that the most widely provided antihypertensive drug to patients with hypertension was captopril (80.2%) [13]. A similar study found that calcium channel blocker (amlodipine), beta blocker (atenolol or metoprolol or carvedilol), and angiotensin receptor blocker (telmisartan) were the most frequently prescribed drugs in hypertensive patients [14].

In another one study conducted by Nascimento et al. [15], the more utilized medications were those necessary for the treatment of the most reported diseases, such as the medications acting on the cardiovascular system, corresponding to 145 (34.9%) mentions. Following are in descending order diuretics (10.6%), acting over the renin – angiotensin system (7.5%), beta – blockers and calcium channel blockers (5.0%).

As well as in the similar research [16] in the intervention group, 103 new antihypertensive drugs were initiated, 94 dose changes were made (80 dose increases, 14 dose decreases), and 76 antihypertensive drugs were discontinued. Additionally, 12 patients were prescribed with low-dose acetylsalicylic acid and 14 were prescribed with statins by the pharmacist. Thiazide diuretics were taking (55%), angiotensin receptor blocker (42%), ACE inhibitors (38%), calcium channel blockers (37%), and beta – blockers (19%) after 6-month intervention.

In Hussein et al. [10] study the average number of anti-hypertension medications prescribed was 1.58 ± 0.69 with a minimum of one and maximum of four, while the average number of the total drug was 2.96 ± 1.065 (range = 1 – 6). From patients on follow-up, 99 (51.6%) patients were on monotherapy and the rest 93 (48.4%) received a combination of anti-hypertensive drugs. In monotherapy, ACE inhibitor (Enalapril) was most commonly prescribed (72.7% of monotherapy) while in combination therapy, a two-drug combination consisting of calcium channel blockers (Nifedipine) and ACE inhibitors (Enalapril) were given to the majority of patients (53.8% of combination therapy).
McLean et al. [17] have claimed that changes in antihypertensive medication use, notably, the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers did not change in either group (65.2% vs. 67.0% in usual care and 61.7% vs. 59.1% in intervention group, respectively).

1.2.2. Comorbid diseases and their influence on hypertension

One of the important issues is a comorbidity of hypertension and diabetes mellitus, as well as hyperlipidemia. Type 2 diabetes (T2DM) patients with hypertension are at increased risk for suffering from drug–related problems; because they often receive multitherapy, which may cause undesirable effect and complications.

The combination of diabetes and hypertension distinctly increases the potential risk of earlier occurrence of cardiovascular disease. Even though hypertension is a greater risk factor for macrovascular cardiovascular events in patients with diabetes than glucose control; control of BP in patients with diabetes is often substandard, with less than 12% reaching the currently recommended target blood pressure (130/80 mm Hg) [17].

The outcomes of McLean et al. research [17] showed the significance of community pharmacist and nurse teams working in collaboration with patients and physicians to achieve better blood pressure control. Since there are plenty of patients with hypertension who are not attending their physician and because primary care physicians are already overcrowded, such approaches should be taken into a serious consideration. However, there was observed a significant reduction in systolic blood pressure with slight changes in the use of antihypertensive therapy, which suggests that improvements in compliance with patients’ prescribed drug therapy and/or lifestyle changes may have contributed to the benefits we observed.

A total of 227 eligible patients were randomized to intervention and control arms. The mean patient age was 64.9 years, 59.9% were male, and the mean baseline systolic/diastolic BP was 141.2/77.3 mm Hg at baseline. The intervention group had an adjusted mean greater reduction in systolic BP at 6 months of 5.6 mm Hg compared with controls. In the subgroup of patients with a systolic BP greater than 160 mm Hg at baseline, BP was reduced by an adjusted mean of 24.1 mm Hg more in intervention patients than in controls [17].
Study of Cardiovascular Risk Intervention by Pharmacists - Hypertension [17] provides a valid proof that a community pharmacist working collaboratively with nurse team, with patients and primary care physicians can achieve a significant effect on hypertension management in patients with diabetes mellitus and suboptimal BP control. Even in those patients who have diabetes and hypertension comorbidity that is relatively well controlled, a pharmacist – nurse cooperation intervention resulted in a clinically important improvement in blood pressure.

In Chua et al. [18] study, the term PCIs (pharmaceutical care issues) was used instead of DRPs to embrace a broader spectrum of issues and as well because pharmaceutical care was provided by pharmacists to the participants. This study was a part of the large controlled trial called the Cardiovascular Risk Factors Intervention Strategies (CORFIS) trial. A total of 477 participants in the CORFIS research were involved in this part of the study, 320 (67.1%) had hypertension, but particularly HTN had 79 (16.6%), HTN and diabetes mellitus had 54 (11.3%), HTN and hyperlipidemia had 88 (18.4%), HTN, diabetes mellitus and hyperlipidemia had 99 (20.8%). These three chronic diseases often occur together.

Of the 477 participants, 53.7% (256 participants) had at least one PCI, giving a total of 706 issues. Non-compliance to medications was the most common drug – related problem (146 of 235 issues, 62.1%). Other drug-use problems involved participants administrating their medications at inappropriate doses or frequencies or incorrect timing with respect to meals. As an example, metformin and aspirin were taken before meals and sulphonylureas were taken at bedtime [18].

ADRs included side effects of medications as reported by the participants. Therapy failure was considered when participants’ blood pressure, blood glucose levels or lipid levels were not at target levels in spite of being on pharmacological treatment. When in fact, drug choice problem in this research included participants who had been seen by the physicians but still with high blood pressure, high blood glucose or high cholesterol level and were not on any medications. Dosing problems were either too high or too low of prescribed medication. Non-compliance to drug therapy was assigned to obliviousness or to participants having hesitations or misapprehension purpose and effectiveness of their medications. Some study participants reported that they were not clear regarding the dosage and use of their medications while others were unwilling to take their medications due to fear of side effects. The eight cases of lifestyle modifications included participants who were current smokers and were counseled on smoking cessation [18].
A Cohen’s Kappa statistic was obtained which meant good arrangement in classification between the two experts. Of the 706 PCIs, 52% were classified as probably clinically insignificant, 38.9% with minimal clinical significance, 8.9% as definitely clinically significant and could cause harm to the patient health while one issue (0.2%) where a participant informed about anal bleeding ascribed to aspirin usage, this PCI was classified as life-threatening. 53.7% had at least one PCI, these included drug-use problems (33.3%), insufficient awareness and knowledge about disease condition and medication (20.4%), ADRs (15.6%), therapeutic failure (13.9%), drug choice problems (9.5%) and dosing problems (3.4%). Non-compliance to drugs topped the list of drug-related problems, accepted by incorrect administration of medical preparations. The main causes of PCIs were impairment of disease state which brought to the failure of therapy, and also the presentation of new symptoms or indications. Of the 338 PCIs where changes were recommended by the pharmacist, 87.3% were performed as recommended. The most common intervention performed by the pharmacists was the medication counseling to the patient (38.8%), followed by the referral of patients to the prescribers (20.8%), educating patients concerning their disease states (12.0%), recommending a change in the dose or frequency of the medications or to add another medication (5.8%) and to monitor the patient’s condition (5.0%) [18].

This study [18] assessed the types of PCIs faced by patients with diabetes, hypertension or hyperlipidemia. It also demonstrates the importance of pharmacists working in collaboration with other healthcare providers especially the primary care physicians in identifying and resolving drug-related problems to achieve optimal clinical outcomes for patients with chronic diseases.

1.2.3. Assessment and identification of drug therapy problems

A cooperative collaboration between clinical pharmacists and a clinical pharmacist and a clinical pharmacologist was created, in order to make them work together, address DRP’s questions in internal medicine by screening medical records, attend medical rounds and provide advice for pharmacotherapy optimization [19].

Despite most studies evaluating DRPs are retrospective, Guignard et al. study [20] offer the advantage of being prospective. Researchers sought to optimize the impact of pharmacist intervention by prioritizing DRPs to be reported to primary care physicians during rounds.
In Guignard et al. study [19] participated in total 145 patients, and 383 DRPs were identified (mean: 2.6 DRPs per patient). Research reported that the most represented types of DRPs in internal medicine wards were unwanted drug interactions (21%), untreated indications (18%), overdosages (16%), and drugs with no valid indication (10%). The following interventions have been chosen: no intervention (51%), the verbal advice of treatment optimization (42%), and written consultation (7%). The acceptance rate of physicians was 84% and their satisfaction was high. It was concluded that the presence of a specialized pharmacotherapy expertise during medical rounds was useful and well accepted by internal medicine ward prescribers in poly morbid and poly medicated patients, as well as they, helped to prevent DRPs.

One more research [20] has been conducted in Poland concerning assessment and identification DRPs among ambulatory patients diagnosed with arterial hypertension. Fifth – year pharmacy students took part during their internship in community pharmacy. Students questioned patients and collected data, which was analyzed retrospectively. Results of the research were surprising – 1214 DRPs were identified in 222 participants, on average 5.5 DRPs per patient. The most common DRPs were: potential interaction – 594 (49%), ADRs – 256 (21%), therapy failure – 167 (14%), drug dose is too low or dosage regime not frequent enough – 91 (7%). The researcher concluded that since DRPs are very common in hypertensive patients, community pharmacists should be involved in the monitoring of patients pharmacotherapy to identify and resolve drug therapy issues.

The 390 patients had 858 comorbid medical conditions. 50–57% of the patients had diabetes and/or chronic kidney disease. Even though pharmacists considered other comorbid medical conditions and medications during encounters with patients, the time and intensity of care delivered concentrated generally on hypertension and may not encompass a comprehensive medication therapy management (MTM) assessment to account for all of a patient’s drug therapy treatment goals. These patients took 897 antihypertensive medications. A total of 443 pharmacist recommendations were made to initiate a new antihypertensive medication and 283 recommendations to stop antihypertensive medications. Pharmacists made 329 recommendations to increase the dose and 94 recommendations to decrease the dose of antihypertensive medications. Patient interventions focused on medication compliance (43.2% of encounters) and lifestyle modifications. A total of 392 reported ADRs were assessed (83.7%) not related to the use of medications (e.g., cellulitis, pneumonia, alcoholism leading to pancreatitis), including 64 that were possibly medication-related adverse events [21].
Hirsch et al. [22] have gathered two clinical pharmacists and an internal medicine physician, who would serve as the medical director of the clinic, in order to create a clinical collaborative practice protocol using updated hypertension management literature for the pharmacist - primary care physician (PharmD-PCP) and national hypertension guidelines MTM group.

At the initial visit, almost half (45.2%) of the PharmD-PCP MTM collaborative care patients had a drug therapy problem identified at their initial pharmacist visit with one-third requiring a medication change. The two most prevalent problems were the needs an additional therapy (42.4%) and dosage is too low (33.3%). The percentage of patients with drug – related problems and consequent medications changes were much lower after six months care (20.0%, and 11.3% respectively). At nine months only two patients required a medication adjustment (increased dosage). A drug – related problem was identified for almost half of the patients; the two most common being a need for additional therapy and/or a dosage increase [22].

1.2.4. Possible causes of drug related problems

Chan et al. [23] report the causes and interventions for the 427 DRPs assessed in their study. Most (86%) had only one underlying cause. The total number of causes was 490 (1.1 ± 0.4 per problem). Out of six domains with 34 categories, 25 different categories had a least one cause reported. Causes of DRPs varied by the problem identified. For example, the most common cause of the “drug not taken/administered” problem was “patient has concerns with drugs” while the most common cause of the “inappropriate duplication of drug” problem was “inappropriate drug selection”.

Hussein et al. [10] provide evidence that marital status, a number of medications and number of complications significantly affects DTP (drug therapy problem). Single patients have high DTP than ever married couples. Results of this study indicated that patients with multiple diagnoses and patients using polypharmacy should be more carefully monitored for DTPs, to prevent serious harmful consequences. To distinguish and resolve the problem of drug interaction, both pharmacies have to assign skilled pharmacist and to be provided with drug interaction software if it’s possible.

Forgetting is one of the main reasons for non – compliance (19.5%). So patients should be encouraged to use different methods for remembering to take their medication such as a use of mobile alarm and alarm clock. As well as there are plenty applications for gadgets, it may remind which tablet to
take and at what time. Financial access has been deemed as one of the important barriers to adherence. Physicians should consider the financial status of their patients in prescribing antihypertensive medications to implement affordability, e.g. prescription of generics should be encouraged [10].

Chua et al. [18] have claimed that non-compliance to medications was attributed to forgetfulness or to participants having doubts or misconception about the purpose and effectiveness of their medications. Some participants of this study reported that they were not clear regarding the dosage and use of their medications while others were unwilling to take their medications due to fear of side effects. The main causes of DRPs were deterioration or improvement of disease state which led to therapy failure, and also the presentation of new symptoms or indication. This demonstrates the role of pharmacists in chronic diseases patients monitoring. The manifestation of side effects such as a cough, gastrointestinal problems and symptoms of hypoglycemia as well as patients’ concerns with drugs and undue worries about ADRs were also common causes of DRPs.

1.2.5. Impact of pharmacist interventions on improving blood pressure control

Recent student pharmacist-led research has begun to explore how student pharmacists can be a part of medication reconciliation services in patient care institution at a level that contributes to the evaluation and resolution of drug – related problems. Following each patient visit, pharmacy students revised the medication list in the electronic medical record, clarified discrepancies, and identified the appearance of drug therapy problems with patient’s physician. The most common DTP identified was an untreated indication. The total amount of interventions in hypertensive patients were 101, 15%. The most frequent intervention was concerning medication efficacy (42, 30%) [24].

The Center for Advancement of Pharmacy Education determines the ability to identify and resolve drug therapy problems as an origin educational outcome of student pharmacists [25].

Lubowski et al. [26] did specifically look at the impact of students delivering medication reconciliation in a community hospital and detected that students were able to evaluate and resolve drug – related problems. While this research in the acute care facilities has shown that student involvement in medication reconciliation has had a positive influence on the identification and resolution of drug – related problems.
According to Stewart et al. [24], it is reasonable to expect that clinically significant results could appear from some of the interventions made by pharmacy students, especially recommendations associated with the induction of drug therapy for the treatment of disease states like hypertension. The role of pharmacy students in the arrangement of medication reconciliation goes beyond the formulation of an accurate medication list and initiates an opportunity to identify drug-related problems that potentially effect on patient outcomes.

The United States Community Preventive Services Task Force has currently advised team-based care models, involving pharmacists, to improve BP control [27]. Pharmacists are extremely available healthcare professionals and a useful resource in the management of hypertension [17].

It is postulated that allowing pharmacists to independently prescribe drug therapy may result in even better patient outcomes than interventions based solely on providing recommendations. Since 2007, the Health Professions Act of Alberta, Canada has permitted pharmacists to apply for authority to prescribe [28].

Recent randomized trial by Tsuyuki et al. [16] was created to analyze the hypothesis that pharmacist prescribing for patients who are coming to community pharmacy with uncontrolled hypertension would result in improved BP reduction over usual care. This research was the first randomized trial of independent pharmacist prescribing in community pharmacy patients with hypertension. Results showed significant reductions in systolic and diastolic BPs, -18, 3 mm Hg and -8, 0 mm Hg, respectively. As well there were improvements in the proportion of patients reaching recommended BP targets compared between intervention and usual care (58% vs. 37%). Given the authorization of community pharmacies and a high burden of illness from hypertension, these findings could have an important impact on public health. The results of this study demonstrated that pharmacist intervention in addition to usual care, results in a clinically important reduction of BP and a valuable improvement in the proportion of patients with initially uncontrolled hypertension achieving their target BP, even though a very high proportion, 78%, were already taking antihypertensive therapy at baseline. Policy makers should take in consideration that pharmacist role can be expanded role, including prescribing, to address the burden of hypertension.

Independent pharmacist prescribing has been in place in the United Kingdom since 2006 [30]. The results from this research, the first randomized, controlled trial of pharmacist prescribing, and enormous evidence from 39 non-prescribing trials [30] help recent efforts to extend pharmacists’ capacity
of practice to be involved in drug therapy management activities in an effort to address clinical inertia in hypertension management [31].

Shireman T. [32] has analyzed three community pharmacist interventions, two of which were conducted in Canada and the third one was conducted in the United States [33]. This research [32] showed that community pharmacists can actually improve BP control, and compliance, as well in the United States [34]. The results were specifically important because the patient population existed particularly of black race people with uncontrolled hypertension. Another community chain pharmacy-based program, in addition, demonstrated beneficial effects on BP control and compliance, [35] and the Asheville Project, community cooperation between insurance plans, hospitals, and community pharmacists, similarly demonstrated the decline of BP, even though that was not their only targeted outcome [36].

What needs to be done is to get pharmacists involved in effective approaches, especially community pharmacists, to be strongly engaged in hypertension management [32]. Approximately 61% of the 286 400 pharmacists in the United States work in a community pharmacy [37]. There is an overwhelming ratio here if pharmacists will step out, analyze the cases of the patients, and follow up on the reduction of hypertension burden.

Pharmacists are well approachable healthcare professionals and actually a beneficial resource to enhance hypertension management by providing medication management in cooperation with physicians and by encouraging patients in medication intake [38 – 40]. Evidence proves that pharmacists – working alone or in teams – are effective for the management of hypertension [41, 42]. New approaches to hypertension care, involving pharmacists [43] could be a promising approach to improve BP management and control.

Santschi et al. [44] determined that a cooperative model involving community pharmacists and health care physicians concentrated on the management of drug compliance was possible in the Swiss medical care system and enhanced blood pressure control among uncontrolled hypertensive patients [45]. Collaborative care model of hypertension has currently been advised by the United States Community Preventive Services Task Force [46].

Therefore, health care professionals of ambulatory clinic designed the Team - Based Care for Improving Hypertension Management (TBC-HTA) randomized controlled study. This research [44] was created to assess if a TBC interprofessional intervention, including nurses and community pharmacists
working in cooperation with physicians, to enhance BP control among uncontrolled treated hypertensive patients under real-life conditions. In addition, Team – Based Care model of hypertension could propose a chance for an effective approach for hypertension treatment and BP control in real-life conditions and will inform policymakers on strategies to implement.

Collaboration between physicians, pharmacist and other health care practitioners, as well as encouragement of patient to a systematic control of blood pressure results in effectiveness improvement of hypertension pharmacotherapy [47 – 50]. Earlier studies have proved that engagement of pharmacists in taking care of patients with hypertension can improve their blood pressure and increase patients’ quality of life [51 – 53].

Research by Skowron et al. [54] provided evidence that community pharmacists in Poland have not yet carried out the pharmaceutical care into their practice. The health care service in Poland expects pharmacists only to dispense medication according to physicians’ prescription, pharmacists are not obligated to educate patient or check effectiveness or safety of their pharmacotherapy. Nevertheless, the Polish pharmacists conducted a study about community pharmacists how their assessment would influence on pharmaceutical care on patients knowledge, quality of life and BP control.

The significant difference in knowledge about disease between study and control group was observed at the end of the study. The pharmaceutical care improved patients’ knowledge about the disease. Pharmacists in the study group, who has provided pharmaceutical care, had a higher level of pharmacotherapy knowledge and professional satisfaction than the control group. Subjects in the study group at the end of the research were receiving a higher number of medications compared to the control group. However, pharmaceutical care had beneficial effect on therapy results, because at the last meeting normal values of arterial blood pressure (≤140/90 mmHg) achieved in 22 out of 28 patients (79%) in the study group, and in 31 out of 56 patients (55%) in the control group according to intention-to-treat (ITT) analysis. Among the patients included in the full pharmaceutical care program (PP analysis), the normal blood pressure was recorded in 8 out of 10 patients (80%) from the study group, and in 6 out of 8 patients (75%) in the control group [55].

It was concluded by Skowron et al. [54] that more patients who received pharmaceutical care had controlled BP comparing to the group of patients who were using standard pharmaceutical service model. The pharmaceutical care as well had a positive impact on the patients’ knowledge about the disease, risk factors, and lifestyle modifications. Additionally, pharmacists, who contribute pharmaceutical care
improved their pharmacotherapy knowledge and had better satisfaction from their work. Implementation of pharmaceutical care into the pharmacy practice benefits both, patients and pharmacists.

1.2.6. Physician – pharmacist collaborative treatment model for the management of hypertension

Recent research by Ernst ME [56] reached a conclusion that offering 24-hour ambulatory BP monitoring as part of the physician-pharmacist collaborative care (PPCC) hypertension clinic may reduce disapprovals on behalf of patients with suspected white-coat hypertension. In a cluster-randomized trial [57] of 402 patients with uncontrolled hypertension at baseline, a PPCC model made great results in more than twice the control rate of standard care from a physician (64% vs. 30% control rates, respectively) after 6 months of treatment.

The Collaboration among Pharmacists and Physicians to Improve Outcomes Now (CAPTION) trial [58] was designed in order to see how pharmacist intervention may affect the improvement of blood pressure control and resolution of drug – related problems impeding progress toward blood pressure goals. It was important to evaluate this pharmaceutical care model in minority populations because hypertension causes more heart disease, strokes, and kidney disease in racial minorities than in whites [59]. A significant amount of pharmacists’ time was spent resolving drug - related problems directly with patients to improve medication safety and effectiveness and to enhance medication compliance.

Among the 390 patients, there were 2811 encounters with pharmacists that involved 3.44 hours/patient for face-to-face care visits plus 1.55 hours/patient for pre-visit and post-visit work (average 0.58/patient/month). Significantly more dose increases or medication additions occurred in the intervention group (2.6 ± 2.5) than the control group (0.8 ± 0.9). The intensity of work is represented in interventions to resolve drug therapy problems with patients (43% of encounters) and with physicians (1169 recommendations, with an acceptance rate by physician 1153 [98.6%]), resulting in improvement of patients’ blood pressure goals achieved (from 0% at baseline to 43% at 9 months as measured by the study coordinators). More specific detail about the types of drug therapy changes in the control and intervention groups were previously published [22].

For example, a study of 179 patients with uncontrolled hypertension (101 MTM vs. 78 control), with pharmacists making recommendations to the physician (96% accepted), 89.1% of the MTM group
were at goal at 9 months vs. 52.9% in the control group [60]. Similarly, in a trial more closely aligned with ours where the pharmacist was able to initiate and change medications under a collaborative protocol, 62% of MTM patients vs. 44% of control patients were treated to a goal at 12 months [61].

Recognizing the pharmacist’s contribution to improving drug therapy management in collaboration with physicians, and given the shortages of Primary Care Providers (PCPs) and the aging population, incorporating pharmacists into the primary care team to provide MTM services can be a successful strategy for managing medication therapy and improving patient outcomes and possibly extending primary care capacity.
2. METHODOLOGY

2.1. Study design, area and period

This analytical study was initiated with a mixed questionnaire of opened and close-ended format questions in order to obtain drug – related problems in hypertensive patients (n=100). In Kaliningrad, Russia all the patients were interviewed personally, but in Kaunas, Lithuania, in order to facilitate the communication between the interviewer and the respondents, help from Lithuanian pharmacists was required. This research was conducted from July to August 2016 and January to February 2017 in community pharmacies located in Kaliningrad and Kaunas. A structured questionnaire was used to collect data. During this survey, co-morbidities (diabetes, increased cholesterol, angina pectoris, stroke, bad vision, kidney and liver problems) and risk factors (alcohol abuse, tobacco use; polypharmacy (≥5 drugs) for drug-related problems for each patient were recorded. To add, other data such as sex, age, weight, height, the number of prescribed medications as well as OTC medications and food supplements were also recorded (Annex 1, 2).

2.2. Study population

All hypertensive patients who were willing to be interviewed and who were attending “Aptechniy punkt”, Leonova 34, Kaliningrad and Camelia vaistine, Laisves al. 55, Kaunas were included in this study.

2.3. Inclusion and exclusion area

2.3.1. Inclusion criteria

1. Hypertensive patients who agreed and were willing to respond.
2. Patients above 18 years old.

2.3.2. Exclusion criteria

1. Pregnancy induced hypertension.
3. Unwillingness or inability to provide consent to participate.

2.4. Sample size determination

This research is limited only to patients who fulfill the criteria and present to community pharmacies in Kaliningrad and Kaunas during data collection (from July to August 2016 and January to February 2017) were questioned. The margin of error has been chosen as 5% since it is the first research performed, 90% is a confidence level. Since there is a lack of similar studies in the particular countries, concerning drug–related problems, \( \hat{\rho} \) is a guessed value based on past experience, and it has been assumed that the \( \hat{\rho} \) is 10%. According to this numbers, calculations have been made. Sample size using statistical formula \( ME = z \sqrt{\frac{\hat{\rho}(1-\hat{\rho})}{n}} \), equals to 98 people [62].

- ME is the desired margin of error.
- \( z \) is the z-score, e.g. 1.645 for a 90% confidence interval.
- \( \hat{\rho} \) is our prior judgment of the correct value of \( \rho \).
- \( n \) is the sample size (to be found).

2.5. Sampling techniques

Convenience sampling method was used to collect data. Patients who were found during the study period and fulfill the criteria were sampled.

2.6. Data collection procedure and instruments

A structured questionnaire consisting of both closed ended and open ended questions was used during this research. Each patient was questioned about their age, gender, weight, height, at what age he/she was diagnosed with hypertension, average BP, BP measurement at home, first – degree relative with hypertension, duration of treatment, lifestyle factors (smoking, alcoholism, and physical activities),
the administered antihypertensive drugs, as well as other medical preparations and food supplements, comorbid diseases, complications of hypertension, ADRs, adherence questions were assessed.

During the assessment, drug information for chronic medications was collected in detail for the past half a year period, including drug classes, Russian/English, Lithuanian/English brand names, dosage, and frequency. Short term and p.r.n. (pro re nata, reference to dosage of prescribed medication that is not scheduled) medications were excluded as the prescribing period could have been finished before the period when all survey data was collected. Also, the use of dietary supplements was recorded, due to the fact that some are known to interact with prescription medications as well as to have distinct ADRs.

2.7. Study variables and outcome measures

2.7.1. Dependent (Outcome) variable

Dependent (Outcome) variable includes adherence to anti-hypertensive drugs, unnecessary drug therapy, needs of additional drug therapy, ADR, drug interaction and inappropriate dosing (dose too low or too high).

2.7.2. Independent (Exposure) variable

Socio-demographic characteristics (i.e. age, sex, height, weight), and clinical characteristics (i.e. analyzes and tests, the number of co-morbidity diseases, complications, the number of medications and food supplements and duration of treatment and lifestyle factors).

2.7.3. Outcome measures

The primary outcome was the types of DRPs were encountered by the participants, as identified by the researcher. The secondary outcomes were the reasons and clinical significance of DRPs.

2.8. Data analysis

A target sample size of 100 patients in total was estimated as sufficient to detect drug – related problems in hypertensive patients. 50 patients were interviewed in Kaliningrad and 50 patients in Kaunas,
respectively. Characteristics of the patients were descriptively analyzed. Various parameters were calculated in order to analyze the data: mean values (X±SD) of age, weight, BMI; percentages of comorbid diseases, complications, possible ADR reasons, and antihypertensive drugs. Before statistical analysis calculation of body mass index was performed for each participant (BMI = \( \frac{mass \ (kg)}{elg \cdot \ell^2 \ (m)} \)). BMI less than 18.5 is underweight, between 18.5 and 25 is normal, between 25 and 30 is overweight, and above 30 is obese. All the treatment options were systemized by the hypertensive medication groups, and analyzed, as well as all patient answers were coded to ease the statistical analysis procedure.

Possible DRPs, but limited only to antihypertensive drugs provided to the patients, were identified and analyzed (unnecessary drug therapy, needs additional drug therapy, ineffective drug, dosage too low, adverse drug reaction, dosage too high, non-adherence) [1] by referring to guidelines for the management of hypertension provided by The Seventh Report of the Joint National Committee (JNC 7) on Prevention, detection, evaluation, and treatment of high BP [3]. Since one participant may have multiple drug – related problems, individual-level and problem-level analysis were done separately. All data collected were feed into the computer and analyzed using Microsoft Excel and Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA), version 17.0 software. Descriptive statistics were generated in form of numbers and percentage. To summarize the quantitative variables, mean and standard deviation (SD) were calculated, and for the qualitative variables, frequencies and percentages were used. The results were presented in the form of tables and figures.

2.9. Ethical consideration

In order to perform this study before collecting the required data, ethical permission was obtained from LUHS Bioethics Center (Annex 3), which has approved the ethical and methodological aspects of the project, and all patients signed a written informed consent form to participate in this study. All participants in this survey were informed about the purpose of the study; their right to refuse was maintained. Ethical conduct was maintained during data collection and throughout the research process. Information secrecy and confidentiality have been maintained.
3. RESULTS AND DISCUSSION

3.1. General information about participants

As you can see the Figure 1 below, in the pharmacy in Kaliningrad female hypertensive patients were willing more to be interviewed about their disease. A total of 50 patients were included in Kaliningrad, women with a mean age of 65 years (range 39–89 years, SD 15 years), and men with a mean age of 65 years (range 24 – 80 years, SD 14 years). According to the answers obtained from the respondents, the mean age of detection of hypertension for men is 51±12 years, and for women 51±13 years. The diagnosis was made in the following cases: on the follow – up (42% vs. 16%), due to the symptoms (42% vs. 48%), and due to the other reasons (16% vs. 36%) in Kaliningrad and Kaunas, subsequently.

![Figure 1. Percentage of participants by gender in Kaliningrad, n=50](image.png)

The same amount of respondents (n=50) was included in Kaunas (Figure 2), women with a mean age of 61 years (27 – 91 range years, SD 17 years), and men with a mean age of 58 years (37 – 84 range years, SD 16 years). Diagnosis of hypertension was performed at the mean age of men was 47±12 years and for women 51±14 years, subsequently.
66% and 68% of participants had first-degree relatives who had hypertension in Kaliningrad and Kaunas.

There is a strong effect of age on total cardiovascular risk models. It is so strong that younger adults (particularly women) are unlikely to reach high-risk levels even when they have more than one major risk factor and a clear increase in relative risk. By contrast, many elderly men (e.g. >70 years) reach a high total risk level whilst being at a slightly increased risk relative to their peers [63].

However, results from this study didn’t show a significant difference in average blood pressure between genders. Female average blood pressure was 142/87 mm Hg, the same was for a male in Kaunas, and just a small difference was in Kaliningrad, 139/87 mm Hg in female and 137/87 mm Hg in male, respectively.

Results from the Table 3 exhibits that prevalence of overweight and obese patients are high in both genders and in both cities, which indicates that obesity [BMI ≥30 kg/m² (height²)] is a significant risk factor for hypertension. However, in Kaliningrad, there is more overweight and obese male rather than in Kaunas, but the situation with female weight is quite similar, normal weight 27% vs. 20%, overweight 47% vs. 67%, obese 27% vs. 13% in Kaliningrad and Kaunas, respectively.
Table 3. BMI results in Kaliningrad and Kaunas

<table>
<thead>
<tr>
<th>City</th>
<th>Gender</th>
<th>BMI</th>
<th>Amount of participants, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaliningrad</td>
<td>Male (19)</td>
<td>underweight</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>normal</td>
<td>2 (10.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>overweight</td>
<td>6 (31.6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>obesity</td>
<td>11 (57.9%)</td>
</tr>
<tr>
<td></td>
<td>Female (31)</td>
<td>underweight</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>normal</td>
<td>8 (25.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>overweight</td>
<td>15 (48.4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>obesity</td>
<td>8 (25.8%)</td>
</tr>
<tr>
<td>Kaunas</td>
<td>Male (20)</td>
<td>underweight</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>normal</td>
<td>8 (40.0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>overweight</td>
<td>4 (20.0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>obesity</td>
<td>8 (40.0%)</td>
</tr>
<tr>
<td></td>
<td>Female (30)</td>
<td>underweight</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>normal</td>
<td>6 (20.0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>overweight</td>
<td>20 (66.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>obesity</td>
<td>4 (13.3%)</td>
</tr>
</tbody>
</table>

There have been performed eight studies with a total of 2,100 participants that looked at the effect various diets had on blood pressure. Participants lost 4 kilograms on average and due to that their blood pressure was lowered. The systolic value fell by 4.5 mmHg, the diastolic by 3 mmHg [64].

3.1.1. Control of blood pressure at home

In Kaunas, 84% of participants reported that they control blood pressure at home while the rest 16% didn’t. In contrast, 94% measure their BP and 6% don’t in Kaliningrad.

Home blood pressure monitoring (HBPM) among hypertensive adults was evaluated using the 2012 American Heart Association Cardiovascular Health Consumer Survey. The prevalence of
hypertension was 25.5% and 53.8% of that reported HBPM. Approximately 63% of hypertensive adults 65 years and older reported HBPM followed by 51% and 34.6% (35-64 and 18-34 years, respectively). Age and the belief that lowering BP could reduce cardiovascular disease risk were significant factors associated with HBPM. Half of the adult hypertensive patients reported HBPM and its use was greater among those who reported a positive attitude toward lowering blood pressure to reduce cardiovascular disease risk [65].

On Table 4, there are comparative results between Kaliningrad and Kaunas interviewers about the frequency of BP control at home. As you can see, the answers were quite close between cities, except two parameters: once a week 26% vs. 8%, and once in two weeks 6% vs. 22%. The most often option for both cities was once a day.

**Table 4. How often patients control blood pressure at home?**

<table>
<thead>
<tr>
<th>Frequency of BP measurement</th>
<th>Kaliningrad, N (%)</th>
<th>Kaunas, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twice a day</td>
<td>6 (12.0%)</td>
<td>7 (14.0%)</td>
</tr>
<tr>
<td>Once a day</td>
<td>22 (44.0%)</td>
<td>21 (42.0%)</td>
</tr>
<tr>
<td>Every second day</td>
<td>6 (12.0%)</td>
<td>7 (14.0%)</td>
</tr>
<tr>
<td>Once a week</td>
<td>13 (26.0%)</td>
<td>4 (8.0%)</td>
</tr>
<tr>
<td>Once in two weeks</td>
<td>3 (6.0%)</td>
<td>11 (22.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>50 (100%)</td>
<td>50 (100%)</td>
</tr>
</tbody>
</table>

Several sources claim that optimal measurement of BP at home should be done twice a day, in case if the patient has hypertension [66, 67]. The first measurement should be in the morning before eating or taking any medications, and the second in the evening [67]. Once the GPs (general practitioners) are happy with the patients’ blood pressure levels, the patient can take regular readings about 2 – 3 times a week [68].

Viera et al. [69] study results have shown that approximately 19% check their BP every day or almost every day; 26% check their BP a few times per week, and 29% check their BP a few times per month. For nearly one-third, their primary reason for using HBPM was because their doctor recommended it. Over one-half said they used HBPM because they were 'just interested in knowing' their BP. In another study [70] 15.7% of patients measure their BP 3 or more times per week, 22.3% 2 times per week, 37.1% 2 – 4 times per month, 24.9% monthly or less.
Table 5 shows the frequency to visit GP. As you may observe, only two parameters are close between Kaliningrad and Kaunas, once per month 6.0% vs. 8.0% and once per 6month 20.0% vs. 32.0%. The most common answer in Kaliningrad was once per 6 months (32.0%), but other options were quite frequent as well. The most popular answer in Kaunas was once per year (52.0%), the second one was once per 6 months (32.0%).

**Table 5. How often do you attend follow-up?**

<table>
<thead>
<tr>
<th>Frequency of attending follow-up</th>
<th>Kaliningrad, N (%)</th>
<th>Kaunas, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>once per month</td>
<td>3 (6.0%)</td>
<td>4 (8.0%)</td>
</tr>
<tr>
<td>once per 3 months</td>
<td>16 (32.0%)</td>
<td>4 (8.0%)</td>
</tr>
<tr>
<td>once per 6 months</td>
<td>10 (20.0%)</td>
<td>16 (32.0%)</td>
</tr>
<tr>
<td>once per year</td>
<td>14 (28.0%)</td>
<td>26 (52.0%)</td>
</tr>
<tr>
<td>once in 2 years</td>
<td>7 (14.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>50 (100%)</td>
<td>50 (100%)</td>
</tr>
</tbody>
</table>

ESH guidelines [63] recommend that once the target BP is reached, a visit interval between 3- and 6-month is reasonable. For stable patients, home blood pressure monitoring and electronic communication with the physician may also provide an acceptable alternative [71, 72]. It is nevertheless advisable to assess risk factors and asymptomatic organ damage at least every 2 years.

**3.1.2. Laboratory tests and BP**

In Kaliningrad, 96% of the participants have answered “Yes” to the question concerning ECG, Cholesterol blood test or other investigations? Comparatively to this result, 88% participants have answered positively in Kaunas. The most common analyses were: ECG (electrocardiography), cholesterol test (lipid panel), and blood glucose test. Only one respondent has mentioned test for Potassium, Magnesium, and Iron.

ESH guidelines recommend [63] following routine tests to identify the presence of additional risk factors and search for secondary hypertension: haemoglobin and/or haematocrit, fasting plasma glucose,
serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, fasting serum triglycerides, serum potassium and sodium, serum uric acid, serum creatinine (with estimation of GFR), urine analysis: microscopic examination; urinary protein by dipstick test, test for microalbuminuria, and 12-lead ECG.

The analysis which was most frequently assigned for patients by GP were an essential one in order to confirm the diagnosis of hypertension and to check the heart for any other diseases as well as the lipid panel test and blood glucose test is needed to exclude comorbid diseases and adjust the treatment for hypertensive patients.

3.2. Analysis of risk factors

3.2.1. Smoking

Particularly this risk factor was quite the same in results between the cities: 82% vs. 72% interviewed have answered “No” to the question concerning smoking in Kaliningrad and Kaunas, respectively. Those patients who have admitted the fact that they smoke were 18% in Kaliningrad, on average those participants were smoking 14 cigarettes per day, and in Kaunas that 28% have said that they are smoking 11 cigarettes per day on average.

Blood pressure in male participants who were smoking in Kaliningrad was 140/90 mm Hg, which determines stage 1 hypertension and in female participants, it was 130-139/85-90 mm Hg, prehypertension stage. In Kaunas, women were only smoking out of respondents, and their BP got divided into three parameters, those who has blood pressure 130-135/80-90 mm Hg (prehypertension), 145-170/95-105 mm Hg (stage 1 hypertension), and ≥160/≥100 mm Hg (stage 2 hypertension).

In comparison, almost all the non-smokers got into one out of three stages of hypertension (prehypertension, stage 1 and stage 2 hypertension) in both genders and both cities – no difference between smokers and non-smokers identified. Only 4.88% out of non-smokers had a normal BP in Kaliningrad, in contrast, 27.8% in Kaunas.

However, insistence on smoking cessation is mandatory in order to improve cardiovascular risk, and because cigarette smoking has an acute pressor effect that may raise daytime ambulatory blood pressure [63].
Dong – Qing et al. [73] have shown in their results that individuals who were heavy smokers (76.62 ± 13.28 mmHg) had higher diastolic blood pressure, compared with medium and light smokers (72.33 ± 12.98 and 70.28 ± 10.31 mmHg). There was a higher prevalence of diastolic hypertension (21.62% vs. 5.75% and 7.14%). Furthermore, there was a higher risk for diastolic hypertension in heavy smokers (adjusted) compared with light smokers. There was, however, no significant difference in systolic blood pressure or prevalence of systolic hypertension among the different smoking groups.

Average 24-hour blood pressure and daytime BP were significantly higher in the smoking period than in the nonsmoking period. No significant differences were observed in nighttime BP between the two periods. These results have demonstrated that cigarette smoking increased the daytime and average 24-hour BP, and the increases observed in daytime BP was associated with the attenuation of parasympathetic nerve activity [74].

### 3.2.2. Alcohol consumption

Both cities have similar results in alcohol consumption, but in both cases, the majority of participants didn’t consume alcohol.

**Table 6. Comparison of alcohol consumption**

<table>
<thead>
<tr>
<th>Alcohol consumption</th>
<th>Units</th>
<th>Kaliningrad, N (%)</th>
<th>Kaunas, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-1</td>
<td>31 (62.0%)</td>
<td>44 (88.0%)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>17 (34.0%)</td>
<td>2 (4.0%)</td>
</tr>
<tr>
<td></td>
<td>4-6</td>
<td>2 (4.0%)</td>
<td>2 (4.0%)</td>
</tr>
<tr>
<td></td>
<td>7-12</td>
<td>0%</td>
<td>2 (4.0%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>50 (100%)</td>
<td>50 (100%)</td>
</tr>
</tbody>
</table>

In Kaunas the participants who were consuming alcohol got divided into two stages of hypertension: 140-145/90-98 mm Hg (stage 1 hypertension) and ≥160/≥100 mm Hg (stage 2 hypertension). In Kaliningrad, there were three stages: normal blood pressure 110/75 mm Hg, prehypertension 130-135/85-90 mm Hg, and stage 1 hypertension 140-150/90-92 mm Hg.
The connection between alcohol consumption, blood pressure levels and the prevalence of hypertension is linear. Regular alcohol use raises BP in treated hypertensive subjects. Hypertensive men who drink alcohol should be advised to limit their consumption to no more than 20–30 g, and hypertensive women to no more than 10–20 g, of ethanol per day. Total alcohol consumption should not exceed 140 g per week for men and 80 g per week for women [63].

Wakabayashi et al. [75] have proved that SBP of men was significantly higher in moderate and heavy drinkers than in nondrinkers, and SBP of women was significantly higher in heavy drinkers but not in moderate drinkers than in nondrinkers. DBP of men and women was significantly higher in light, moderate and heavy drinkers than in nondrinkers. The differences in systolic and diastolic blood pressure between drinkers and nondrinkers were greater in men than in women. In another research [76] diastolic blood pressure was significantly higher in drinkers than in non-drinkers (101.6±11.5mmHg vs. 96.8±8.2mmHg).

3.2.3. Physical activity

Concerning the question: “Are you doing any sports?” positively have answered 32% vs. 20% in Kaliningrad and Kaunas, respectively. In both cities as an example of sports correspondents doing were: bicycle, physiotherapy, kinesiatrics, and swimming.

3.2.4. Comorbid diseases

In the questionnaire, there was provided one question: “Have you ever suffered from any of the following conditions?” with several diseases, which are the most common in hypertensive patients. Those were: diabetes, hypercholesterolemia, angina pectoris, intermittent claudication, poor vision renal and hepatic problems, and other option, where the patient should have mentioned if he/she has another disease out of the list.

In Kaliningrad, 10% of people questioned didn’t have any other comorbid diseases and the same was in Kaunas 16%, nevertheless, the other 90% and 84% had, and in most cases more than one. That’s
why it was hard to systemize the comorbid diseases between the patients, but it was taken into consideration in order to evaluate drug-related problems, so it has been calculated the percentage of it.

**Table 7. Prevalence of comorbid disease in hypertensive patients**

<table>
<thead>
<tr>
<th>Comorbid disease</th>
<th>Kaliningrad (%)</th>
<th>Kaunas (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>28%</td>
<td>12%</td>
</tr>
<tr>
<td>Increased cholesterol</td>
<td>38%</td>
<td>40%</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>44%</td>
<td>20%</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>Poor vision</td>
<td>56%</td>
<td>12%</td>
</tr>
<tr>
<td>Renal disorders</td>
<td>28%</td>
<td>16%</td>
</tr>
<tr>
<td>Hepatic disorders</td>
<td>14%</td>
<td>12%</td>
</tr>
</tbody>
</table>

However, there were several patients (10%) with the same comorbid diseases, such as diabetes, increased cholesterol, angina pectoris, poor vision, and renal disorders. As well as 6% have indicated about only one comorbid disease as angina pectoris, and another 6% had poor vision in Kaliningrad. Among other diseases were: varicose, cholecystitis, gallstones, obesity, and epilepsy. Those diseases, which were mentioned above don’t have a direct connection to hypertension, so it won’t cause drug therapy problem related to hypertension.

In Kaunas, the most common combination of comorbid disease was hypercholesterolemia and kidney disorder (8%) or liver disorder (8%). 40% of participants chose other option, and those diseases were: hypothyroidism, heart failure, ischemic heart disease, osteoporosis, glaucoma, acidosis, rheumatism, gallstones, gastritis, and gout. Moreover, 6% of all respondents have claimed that they suffer from glaucoma and another 6% from osteoporosis.

Comparing results from both cities, it was noticed that patients in Kaliningrad are having more comorbid diseases rather than in Kaunas: angina pectoris 44% vs. 20%, intermittent claudication 10% vs. 0%, poor vision 56% vs. 12%. Though, the results may be so because the mean age of correspondents in Kaliningrad is higher than in Kaunas, and patients in Kaunas have mentioned glaucoma as other diseases, not as a poor vision.
### 3.3. Complications and ADRs

In Kaliningrad and Kaunas (56% vs. 76%) didn’t have any complication from hypertension. 10% of respondents experience renal problems, as well as 10%, had a stroke in Kaliningrad, additionally, 6% of participants had those two complications at the same time, in contrast in Kaunas no one informed about such complications, but 4% suffer from retinopathy comparatively to 0% in another city. In both places, 20% have reported about cardiovascular complications. Other complications were: myocardial infarction and hypertensive crisis (18% vs. 8% in Kaliningrad and Kaunas).

In Santos et al. [77] research was found that 4.6% of the patients had coronary disease. It was the second most frequent complication among the patients. With regard to acute myocardial infarction, history was obtained in 4.4% of patients. Prevalence of stroke among hypertensive patients was 3.0%.

In another study, 67% percent of patients had cerebrovascular disease (stroke), 11% had a stroke and hypertensive heart disease, 8% had a stroke, hypertensive heart disease and chronic kidney disease (all three), and 5% had a stroke with chronic kidney disease [78].

Concerning the question related to side effects caused by hypertension medication, 14 possible ADRs were listed. 38% vs. 48% have reported that they have never noticed any undesirable events in Kaliningrad and Kaunas, respectively. All the rest have informed about different side effects. On the Table 8 may be seen the percentage of side effects in each city.

*Table 8. Prevalence of ADRs*

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Kaliningrad (%)</th>
<th>Kaunas (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>Skin rash</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>Cold hands and feet</td>
<td>14%</td>
<td>16%</td>
</tr>
<tr>
<td>Swollen ankles</td>
<td>20%</td>
<td>4%</td>
</tr>
<tr>
<td>Leg cramps</td>
<td>14%</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>24%</td>
<td>20%</td>
</tr>
<tr>
<td>Weakness</td>
<td>30%</td>
<td>12%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>18%</td>
<td>16%</td>
</tr>
<tr>
<td>Headache</td>
<td>24%</td>
<td>16%</td>
</tr>
</tbody>
</table>
Extraurination | 18% | 0
Constipation | 14% | 12%
Insomnia/sleep problems | 18% | 12%

Prevalence of possible side effects is notably higher in Kaliningrad in the following parameters: skin rash, swollen ankles, leg cramps, headache, weakness, and extra urination, but information of ADR was provided by participants, and it doesn’t have a proof by physician or pharmacist, since most of the patient were elderly, those symptoms may appear due to the age or some other factors.

3.4. Treatment of hypertension

From all respondents, only 2% (in Kaliningrad) vs. 24% (in Kaunas) didn’t use any treatment for their hypertension. The observed average was 2±1 medications per person, median 2 (range = 0-5) in Kaliningrad and 1.44±1 medications per person, median 1 (range = 0-4) in Kaunas.

Table 9. Antihypertensive drugs provided to the hypertensive patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Kaliningrad (%)</th>
<th>Kaunas (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE</td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td>ACE + β – blocker</td>
<td>0</td>
<td>4%</td>
</tr>
<tr>
<td>ACE + β – blocker + Diuretic</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>ACE + CCB</td>
<td>20%</td>
<td>0</td>
</tr>
<tr>
<td>ACE + CCB + Diuretic</td>
<td>6%</td>
<td>0</td>
</tr>
<tr>
<td>ACE + Diuretic</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>ACE + Imidazoline receptor agonist</td>
<td>0</td>
<td>4%</td>
</tr>
<tr>
<td>ARB</td>
<td>0</td>
<td>4%</td>
</tr>
<tr>
<td>ARB + β – blocker</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>ARB + β – blocker + diuretic</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>ARB + CCB</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>ARB + CCB + α- blocker</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>ARB + Diuretic</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>Drug Combination</td>
<td>Frequency</td>
<td>Percentage</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>B – blocker</td>
<td>4%</td>
<td>20%</td>
</tr>
<tr>
<td>B – blocker + Diuretic</td>
<td>0</td>
<td>8%</td>
</tr>
<tr>
<td>B – blocker + Imidazoline receptor agonist</td>
<td>0</td>
<td>4%</td>
</tr>
<tr>
<td>CCB</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>CCB + β - blocker</td>
<td>6%</td>
<td>0</td>
</tr>
<tr>
<td>CCB + β – blocker + Diuretic</td>
<td>0</td>
<td>4%</td>
</tr>
<tr>
<td>CCB + Diuretic</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>Imidazoline receptor agonist</td>
<td>4%</td>
<td>0</td>
</tr>
</tbody>
</table>

ACE inhibitor – angiotensin-converting-enzyme inhibitor; ARB – angiotensin II receptor antagonist; CCB – calcium channel blocker

Hypertensive drugs which are listed in an alphabetic order in the Table 9 above are provided to the patients with hypertension. As shown in the Table 9, the most frequently provided antihypertensive group was ACE inhibitor in combination with Calcium channel blockers (20%), followed by ACE inhibitors (10%), combination therapy of ACE inhibitor with β – blockers and diuretic (10%), and ACE inhibitor with diuretic (10%) in Kaliningrad. In contrast, the most popular option in Kaunas was β – blockers (20%), followed by a combination of the ACE inhibitor with a diuretic (12%), an ACE inhibitor with β – blocker and diuretic (8%), and β – blocker with a diuretic (8%). However, two treatment options were quite similar in both cities which are based on the combination therapy of ACE inhibitor with β – blocker and diuretic (10% vs. 8%) and ACE inhibitor in combination with a diuretic (10% vs. 12%) in Kaliningrad and Kaunas. If to compare results of the present medication treatment in both cities, prevalence of ACE inhibitors is higher in Kaliningrad (10% vs. 4%), β – blockers is higher in Kaunas (20% vs. 4%), and equals ARB in combination with β – blockers (4%. vs. 4%) in both cities. Other treatment options were provided either in Kaliningrad or in Kaunas.

In the Byrd et al. research [79] a combination of a thiazide and a potassium-sparing diuretic accounted for 47.6% of initial combination therapy, and a combination of a thiazide and ACE inhibitor accounted for another 41.4%. Of patients initiated on antihypertensive treatment with 2 drugs, 86% of the first antihypertensive prescriptions were for fixed-dose combination products. Less common combinations of antihypertensive medication classes included a thiazide and a beta blocker (5.3% of all combination therapy), and an ACE inhibitor and a beta blocker (2.6% of initial combination therapy). The remaining 3.1% of initial combination therapy was comprised of a wide variety of infrequent combinations, such as...
ACE inhibitor/loop diuretic (0.54%), thiazide/calcium channel blocker (CCB) (0.56%), ACE inhibitor/CCB (0.17%), and thiazide/angiotensin receptor blocker (ARB) (0.14%).

Concerning Table 10, the percentage of antihypertensive medication groups was calculated, and results were surprising. The percentage was calculated including combination and monotherapy and according to a number of people who are taking antihypertensive medications (49 people in Kaliningrad and 38 people in Kaunas). Prevalence of ARB is twice higher in Kaliningrad rather than in Kaunas (20.4% vs. 10.5%), as well as the popularity of CCB more than 9 times greater (49% vs. 5.3%). Nevertheless, β – blockers (68.4%) were the most often prescribed one in Kaunas, in comparison only 28.6% were prescribed with β – blockers in Kaliningrad.

Table 10. Prevalence of antihypertensive medication by group

<table>
<thead>
<tr>
<th>Antihypertensive drug</th>
<th>Kaliningrad (%)</th>
<th>Kaunas (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE</td>
<td>51.1%</td>
<td>42.1%</td>
</tr>
<tr>
<td>ARB</td>
<td>20.4%</td>
<td>10.5%</td>
</tr>
<tr>
<td>A - blocker</td>
<td>4.1%</td>
<td>0</td>
</tr>
<tr>
<td>B – blocker</td>
<td>28.6%</td>
<td>68.4%</td>
</tr>
<tr>
<td>CCB</td>
<td>49%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Diuretic</td>
<td>38.8%</td>
<td>42.1%</td>
</tr>
<tr>
<td>Imidazoline receptor agonist</td>
<td>4.1%</td>
<td>10.5%</td>
</tr>
</tbody>
</table>

3.5. Evaluation of drug – related problems

Table 11 consists of descriptive data concerning the frequency of DRPs in hypertensive patients. A total of 114 DRPs were identified in each city in 100 patients in Kaliningrad (n=50) and Kaunas (n=50). 2.3 DRPs per patient were represented in both cities, DRPs experienced by hypertensive patients vary from 1 to 4 occurrences. In 4 (8%) participants weren’t found any drug – related problems, in 10 (20%) patients there was only one type DRP, while it was two types in 14 (28%), three types in 12 (24%) patients, and four types in 10 (20%) in Kaunas. In 12 (24%) patients there was found only one type of drug – related problems, while it was two types in 17 (34%), three types in 16 (32%) patients, and four types in 5 (10%) in Kaliningrad.
Among the identified DTPs, one of the most frequently occurred DTP (14.1% vs. 31.6%) fell into the second category which is a need for additional drug therapy. The first major reason that caused the need for an additional drug therapy problem in Kaunas was due to the fact that 24% of the patients didn’t use any hypertensive medication. The second major reason was the need for an additional cholesterol level decrease drug therapy. However, in Kaliningrad, it was the most frequent reason for the second category of DTP.

Another common drug – related problem was ineffective drug therapy. Prevalence of this category was higher in Kaliningrad rather than in Kaunas (25.4% vs. 15.8%). The therapy was evaluated ineffective when the average BP didn’t meet the therapeutic goal of BP, as well as when the patients’ blood pressure was ≥140/≥90 mm Hg. Although 98% of participants in both cities have claimed that their treatment is effective.

The total number of ADRs was 31 in 50 patients in Kaliningrad, and 20 in another 50 patients in Kaunas which account 27.2% vs. 17.5% of total DRPs. The most commonly identified ADRs were a dry cough, dizziness, weakness, fatigue, headache, cold hands and feet, constipation, and sleeping disturbances (Table 8).

Therapeutic non-adherence was recorded in 29 patients (25.4%) in Kaliningrad and in 36 patients (31.6%) in Kaunas. The respondents’ adherence was affected by different factors. There were two major factors: patient memory (forget) and feel better. 17 (34%) vs. 20 (40%) patients were missing the dose, but still had normal BP, 26 (52%) vs. 36 (72%) patients had a high BP but felt good in Kaliningrad and Kaunas, respectively. As well as 14 (28%) patients in both cities had a duplicated non – compliance problem.

Table 11. The frequency of drug – related problems

<table>
<thead>
<tr>
<th>Drug – related problem</th>
<th>Kaliningrad, N (%)</th>
<th>Kaunas, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Unnecessary drug therapy</td>
<td>9 (7.9%)</td>
<td>4 (3.5%)</td>
</tr>
<tr>
<td>2. Needs additional drug therapy</td>
<td>16 (14.1%)</td>
<td>36 (31.6%)</td>
</tr>
<tr>
<td>3. Ineffective drug</td>
<td>29 (25.4%)</td>
<td>18 (15.8%)</td>
</tr>
<tr>
<td>4. Dosage too low</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5. Adverse drug reaction</td>
<td>31 (27.2%)</td>
<td>20 (17.5%)</td>
</tr>
<tr>
<td>6. Dosage too high</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Guignard et al. [19] research have shown similar results, 145 patients were included, and 383 DRPs were identified (mean: 2.6 DRPs per patient). The most frequent DRPs were drug interactions (21%), untreated indications (18%), overdosages (16%) and drugs used without a valid indication (10%).

In Hussein et al. [10] study 155 patients had at least one drug-related problem and a total of 452 DRPs were identified in them. The most common drug therapy problem identified in this study was drug interaction (n=259, 58.7%), followed by non-compliance and ADR constituting 19.5% and 18.6% respectively. Underdose accounts, only 0.9% of all drug therapy identified.

On the table 12 are described possible DRP causes which were present in the hypertensive patients who were interviewed in this study.

**Table 12. Possible DRP causes**

<table>
<thead>
<tr>
<th>Drug – related problem</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Unnecessary drug therapy</td>
<td>- The drug therapy is unnecessary because the patient does not have a clinical indication at this time.</td>
</tr>
<tr>
<td></td>
<td>- Duplicate therapy: multiple drug products are being used for a condition that requires only single drug therapy.</td>
</tr>
<tr>
<td>2. Needs additional drug therapy</td>
<td>- Untreated indication</td>
</tr>
<tr>
<td>3. Ineffective drug</td>
<td>- More effective drug available</td>
</tr>
<tr>
<td></td>
<td>- Condition refractory to drug</td>
</tr>
<tr>
<td>4. Adverse drug reaction</td>
<td>- The drug product causes an undesirable reaction that is not dose – related.</td>
</tr>
<tr>
<td></td>
<td>- A drug interaction causes an undesirable effect that is not dose – related.</td>
</tr>
<tr>
<td>5. Adherence</td>
<td>- The patient prefers not to take the medication</td>
</tr>
<tr>
<td></td>
<td>- The patient forgets to take medication</td>
</tr>
<tr>
<td></td>
<td>- The patient does not understand the instructions.</td>
</tr>
</tbody>
</table>
3.5.1. Drug interactions

Anti-hypertensive was prescribed concomitantly with other drugs with known potential drug interaction risk. A total of 97 vs. 56 drug – drug interactions (DDI) was found in 28 vs. 18 participants in Kaliningrad and Kaunas, respectively. 3.5 vs. 3.1 drug – drug interaction per patient in Kaliningrad and Kaunas. 26 (26.8%) of DDIs were major, and 71 (73.2%) were minor in Kaliningrad. Most common drug interaction identified in Kaunas was moderate DDI which account 36 (64.3%), followed by major 18 (32.1%), and minor type of drug interaction which was only 2 (3.6%).

The most frequent major DDI was related to Aspirin, 46.1% vs.66.7% out of total major DDI in Kaliningrad and Kaunas. However, the most common combination in Kaunas was Aspirin with Clopidogrel which may result in increased risk of bleeding, and in Kaliningrad, it was Aspirin with Metformin, which may result in increased risk of hypoglycemia, and Aspirin with Torsemide, which may result in reduced diuretic effectiveness and possible nephrotoxicity.

As well as one of the most common moderate interactions in Kaunas was Aspirin with Metoprolol, this may result in increased blood pressure. In Kaliningrad, it was Enalapril with Indapamide, which may result in a reduction of blood pressure.

Smoking and drinking populations were checked for drug – tobacco and drug – ethanol interactions. In Kaunas were found only two drug – tobacco interactions, which were the concurrent use of clopidogrel and tobacco. This interaction may result in increased antiplatelet effect of clopidogrel. In Kaliningrad in total were found 3 drug – tobacco interactions and 15 drug – ethanol interaction. 8 out of 15 interactions were the concurrent use of aspirin and ethanol, which may lead to increased risk of gastrointestinal bleeding. The rest interactions were related to the simultaneous use of metformin, verapamil, and insulin. Drug – tobacco interactions were presented because of concomitant use of clopidogrel and verapamil and smoking. Since verapamil is a CYP1A2 substrate, use of tobacco with it may result in decreased exposure of CYP1A2 substrates.

In contrast, in another study [10] drug interaction risk was found in 127 patients (66.1% of the study sample). The most frequently prescribed combination of this kind was an ACE inhibitor (Enalapril) with the oral hypoglycemic drug in 72 patients. Most common DDI type was moderate drug interaction which accounts 88.4% followed by a minor (8.9%) and major type of drug interaction which was only 2.7%.
4. STUDY LIMITATIONS

Although the research has reached its aims, there were some avoidable limitations. Because of nature of our study, the identification and assessment of the DRPs were based on the data received from the patients’ responses with reference to established literature and guidelines.

Another issue is that multiple causes can be involved in DRPs and each of the factors listed as important may be underestimated since only the most likely cause for each DRP was given. To estimate the responsibility of professionals, patients or the organization of the health system and to evaluate the contribution of each factor to the development of a specific DRP, longitudinal studies are required.

Despite these limitations, and due to the lack of research concerning this topic in both countries, it was believed that the data may be useful for evaluation of DRPs in the countries where research was conducted. Future studies with population-representative samples are needed to determine the significance of DRPs among hypertensive patients in particular countries.
5. CONCLUSION

1. The data obtained in this study show that high proportion of patients 100% vs. 92% had DRPs which is too high in Kaliningrad and Kaunas, subsequently. Adverse drug reaction was the main DRP identified in Kaliningrad while unnecessary drug therapy was the least cause of DRP. In contrast, in Kaunas the most frequently occurred DRP fell into needs for additional drug therapy and non–adherence category.

2. This study is comparable with another study [12], and it has different results such as the most commonly occurred DRP (47%) was indication without drug therapy, ineffective therapy was observed in 21.2% of the overall DRPs, and non-adherence of the hypertensive patients to the prescribed medications was 13.6% of the DRPs occurred.

3. Various classes of antihypertensive drugs were used by hypertensive patients. The most frequently used antihypertensive drugs were ACE+CCB combination in Kaliningrad, and beta – blockers in Kaunas.

4. Most of the participants didn’t smoke and drink alcohol, the prevalence of physical activity was low due to the age of participants. The most important risk factor was comorbid diseases, since that more than eighty percent in both cities had other chronic diseases. The results of this study suggest that the number of prevailing diseases added to the decrease of functional capacity, sedentarism, bad life habits, and polypharmacy are important factors of DRPs in the evaluated group.

5. According to identified DRPs in the investigative group recommendations for the hypertensive patients to ensure safe and effective treatment is necessary.
6. PRACTICAL RECOMMENDATIONS

1. Any prescriptive medication should be taken according to the dosage which was recommended by GP, and OTC according to pharmacist recommendation.

2. Any unnecessary medication or self–medication should be avoided in order not to cause any adverse event or drug–drug interactions. If patient experiences any ADR or undesirable event, it should be reported immediately to GP or consulted in the closest pharmacy, if GP is not available.

3. Medication shouldn’t be forgotten to take, in the case of hypertensive medication, it is very significant to take everyday medication, even better to take it at the same time. In case, if patient is predisposed to forgetfulness, there are plenty of application for gadgets which reminds which pill and at what time to take, as well as it can be a simple alarm which will ring and recall taking medication or it can be a diary where every time patient takes a pill, puts a note. Even though patients BP is not high, it is obliged to take medication at the appropriate time of the day as it was prescribed.

4. Another important aspect is to be acquainted with lifestyle modifications in hypertensive patients, which means smoking cessation, no alcohol abuse, lose weight (in the case of overweight or obesity), have physical activities according to the health status, and maintain healthy nutrition with appropriate sodium intake (DASH diet). It is necessary to be instructed about lifestyle changes and be willing to obtain knowledge concerning this topic by asking GP or pharmacist to become educated in healthy lifestyle subject.
7. REFERENCES


Опрос о гипертонии (повышенное кровеносное давление)

**Данные пациента**

1. Пол: М./Ж
2. Дата рождения:
3. Вес (кг):
4. Рост (м):

**Анкета о гипертонии**

1. Когда вам поставили диагноз гипертонии?
2. Почему вам измеряли кровеносное давление, в тот момент, когда вам поставили диагноз? Например: регулярное обследование, по скольку были какие-то симптомы, или какая-то другая причина.
3. Какое было ваше давление на тот момент?

Верхнее: [ ] mmHg   Нижнее: [ ] mmHg, Не помню [ ]

4. Какое ваше среднее кровеносное давление?

Верхнее: [ ] mmHg   Нижнее: [ ] mmHg

5. Какая терапевтическая цель вашего кровеносного давления? (Какого давления добивается ваш лечащий врач?)

Верхнее: [ ] mmHg   Нижнее: [ ] mmHg

6. Вы отслеживаете кровеносное давление дома?

Да [ ]   Нет [ ]

Если ДА, как часто вы отслеживаете кровеносное давление?

a) Раз в день
b) Каждый второй день
c) Раз в неделю
d) Каждые две недели
7. Делали ли вы кардиограмму, сдавали кровь на холестерин или какие-либо другие анализы или тесты?

Если ДА, то расскажите о результатах ваших анализов и тестов

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<th>Дата</th>
<th>Анализ</th>
<th>Результат</th>
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8. Как часто вы ходите на обследование к врачу?
   a) Раз в месяц
   b) Раз в три месяца
   c) Раз в полгода
   d) Раз в год

9. Курите ли вы сигареты, сигары или трубочный табак?
   Да ☐    Нет ☐
   Если ДА, то сколько в день?

10. Употребляете ли вы алкоголь, Если ДА, то сколько стаканов (напитков) в неделю?
    a) 0-1
    b) 1-3
    c) 4-6
    d) 7-12
    e) >12

11. Занимаетесь ли вы спортом?
    Да ☐    Нет ☐
    Если ДА, то каким спортом ____________ и как часто ____________?

12. Страдали/страдаете ли вы от следующих заболеваний?
    a) Диабет
b) Повышенный холестерин
c) Стенокардия
d) Мышечная боль
e) Плохое зрение
f) Почечные заболевания
g) Болезни печени
h) Другое: ________________

13. were there any complications or comorbidities from hypertension?
   a) No
   b) Renal disease
   c) Stroke
   d) Diabetic retinopathy
   e) Cardiovascular complications
   f) Other: ________________

14. Did you notice any side effects?
   a) Cough
   b) Asthma
   c) Rash
   d) Cold hands and feet
   e) Swollen ankles
   f) Leg cramps
   g) Dizziness
   h) Weakness
   i) Fatigue
   j) Headache
   k) Increased urination
   l) Constipation
   m) Depression
   n) Insomnia/Insomnia
15. Есть ли у вас близкие родственники, кто страдает гипертонией? Да / Нет

Если ДА, то кто этот человек? ________________________________


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17. Какие лекарства вы принимаете от гипертонии? Укажите название, дозировку, и как часто вы принимаете лекарство.

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<thead>
<tr>
<th>Лекарство</th>
<th>Дозировка</th>
<th>Частота</th>
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18. Изменилось ли ваше лечение с момента первоначального диагноза?

Если ДА, какое лечение было изначально? И почему оно изменилось?

19. Пожалуйста, перечислите все лекарства и БАДы, которые вы регулярно употребляете и ранее не упомянули.

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20. Лечение вам помогает?

Да □     Нет □

21. У вас когда – нигде было нормально давление, но вы пропустили дозу (таблетку)?
(Если ДА: Сколько доз вы пропустили? _______________ И какое было давление_______________, если вы помните).

22. У вас когда – нигде было нормальное давление, но были другие жалобы?

Да □     Нет □
(Если ДА: Какие жалобы были? ________________)

23. У вас когда – нигде было высокое давление, но вы чувствовали себя хорошо?

Да □     Нет □
(Если ДА: Какое было давление в тот момент? _______________)
HIPERTENZIJOS KLAUSIMYNAS

Paciento duomenys

1. Lytis: V/M
2. Gimimo data:
3. Svoris (kg):
4. Ūgis (cm):

Hipertenzijos klausimynas:

1. Kada buvo diagnozuota hipertenzija?
2. Dėl kokios priežasties tuo metu buvo matuojamas kraujo spaudimas? Pvz.: įprastas patikrinimas, dėl pasireiškusių simptomų ar dėl kitų priežasčių.
3. Koks buvo kraujo spaudimas tuo metu?

Sistolinis: mmHg   Diastolinis: mmHg Neprisimenu: 

4. Koks vidutinis kraujo spaudimas yra šiuo metu?

Sistolinis: mmHg   Diastolinis: mmHg

5. Koks yra terapinis siekiamas kraujo spaudimas?

Sistolinis: mmHg   Diastolinis: mmHg

6. Ar kontroliuojate savo kraujo spaudimą namuose?

Taip  Ne 

Jei atsakėte taip, kaip dažnai kontroliuojate per dieną?

a) Kartą per dieną
b) Kas antrą dieną
c) Kartą per savaitę
d) Kartą per dvi savaites

7. Ar kada nors esate atlikę EKG, cholesterolio kiekio kraujyje nustatymą ar kitus testus?

Jei “Taip”, užpildykite lentelę nurodant apie atliktą testą, datą ir rezultatus.
8. Kaip dažnai atliekate patikrą?
   a) Kartą per mėnesį
   b) Kartą per tris mėnesius
   c) Kartą per pusę metų
   d) Kartą metuose

9. Ar rūkote cigaretes, cigarus, pypkių tabaką?
   Taip   Ne
   Jei “Taip”, kiek kartų per dieną?

10. Ar vartojate alkoholį? Jei taip, kiek vienetų per savaitę vidutiniškai suvartojate?
   a) 0-1
   b) 1-3
   c) 4-6
   d) 7-12
   e) >12

11. Ar sportuojate?
   Taip   Ne
   Jei Taip, ką sportuojate?

12. Ar turite gretutinių ligų, išvardintų apačioje?
   i) Cukrinis diabetas
   a) Padidėjęs cholesterolio kiekis
   b) Angina
   c) Protarpinis šlubavimas
d) Prasta rega
e) Inkstų ligos
f) Kepenų ligos
g) Kita: 

13. Are sate turėję komplikacijų dėl hipertenzijos?
a) Ne
b) Inkstų ligos
c) Insultas
d) Retinopatija
e) Širdies-kraujagyslių sistemos ligos
f) Kita: 

14. Ar pastebėjote vaistų nuo arterinės hipertenzijos šalutines reakcijas?
a) Kosulys
b) Astma
c) Odos išbėrimas
d) Šaltos galūnės
e) Patinusios čiurnos
f) Mėšlungis
g) Galvos svaigimas
h) Silpnumas
i) Nuovargis
j) Galvos skausmas
k) Padidėjęs šlapimo kiekis
l) Vidurių užkietėjimas
m) Depresija
n) Nemiga/problematiškas miegas

15. Ar turite giminaičių, kuriems yra/buvo diagnozuota hipertenzija? Taip/Ne
   Jei “Taip”, kas tas asmuo? 

16. Ar Jums teko kada nors nenuvykti darba, ar buvote apribojės savo gyvenimo būdu ilgiau nei vieną
mėnesį dėl šios ligos?
Jei "Taip", pateikite detalęs informaciją žemiau.

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17. Žemiau pateikite detalęs informaciją apie gydymą. Įrašykite vaistų pavadinimą, dozavimą ir dažnį.

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18. Ar gydymo planas pasikeitė nuo to laiko, kai buvo diagnozuota hipertenzija?
Jei "Taip", koks gydymas buvo skirtas prieš tai? Kodėl jis buvo pakeistas?

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19. Išvardinkite žemiau visus vaistus ir maisto papildus, kurie prieš tai nebuvo paminėti šiam klausimyne, kuriuos vartojate reguliai dėl šios ar kitos diagnozės.

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20. Ar dabartinis gydymas yra efektyvus?
Taip [ ] Ne [ ]
21. Ar kadanors turėjote normalų kraujo spaudimą, net jeigu praleidote suvartoti vaistų dozę?
Taip ☐ Ne ☐
(Jei taip: Kiek dozių praleidote? _______________ ir koks buvo krauojo spaudimas ________________, jeigu atsimenate).

22. Ar kada nors turėjote normalų kraujo spadimą, tačiau buvo kitų nusiskundimų?
Taip ☐ Ne ☐
(Jei taip: Kokie buvo nusiskundimai? _____________________)

23. Ar kadanors turėjote aukštą kraujo spaudimą, tačiau jautėtės gerai?
Taip ☐ Ne ☐
(Jei taip: Koks tuo metu buvo krauojo spaudiams? _____________________)
DĖL PRITARIMO TYRIMUI


Bioetikos centro vadovas

[Signature]

doc. E. Peičius
DĖL PRITARIMO TYRIMUI


Bioetikos centro vadovas