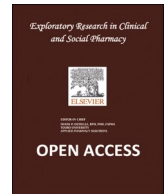


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# Exploratory Research in Clinical and Social Pharmacy

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## Hypertension management and drug-related problems. A case report of the 23-year history of Mr. Jonas

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### ABSTRACT

Arterial hypertension is a lifelong disease, which management is recognized as the most effective way to reduce cardiovascular mortality. Even though there is extensive evidence on the benefits of lifestyle modification and antihypertensive treatment, many patients with hypertension do not reach blood pressure targets. This paper aims to review the history of antihypertensive treatment of one patient and identify the drug related problems that occurred over the study period. In this case report, the patient's health record was studied, guidelines checked and a semi-structured interview conducted. Drug related problems were identified and possible pharmacist interventions were introduced. Drug related problems that could have contributed to the lack of hypertension control were adherence, side effects and disease-drug interaction. Identified pharmacists' interventions ranged from managing self-medication, to collaboration with general practitioner to change prescribing, and counselling the patient on medication use, including adherence. Even though the drug related problems were not that serious in the studied case, the patient could have valued from pharmacist intervention.

### 1. Background

Globally, it is estimated that 32% of adult men and 34% of adult women have hypertension.<sup>1</sup> Arterial hypertension (AH) is considered the number one risk factor for mortality and morbidity from cardiovascular diseases (CVDs). Despite the extensive evidence of benefits of lifestyle interventions and antihypertensive treatment, many patients with AH do not reach target blood pressures.<sup>2,3</sup> Treatment coverage is at most 80% and control rates were <70% in high income countries.<sup>4</sup> Suboptimal adherence with medication, which includes failure to initiate pharmacotherapy, to take medications as often as prescribed, and to persist on therapy

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are long-term are factors contributing to the poor control of blood pressure.<sup>5</sup> Patients' beliefs about hypertension and its treatment, low health literacy and lack of social support are some of the underlying barriers for lack of adherence.<sup>6,7</sup>

Successful control of hypertension can be achieved through comprehensive prevention strategies at the individual and population level. International guidelines emphasize the importance of an interdisciplinary team approach in the management of CVD.<sup>8</sup> A team approach that includes a pharmacist appears to represent the most efficient healthcare delivery model, as pharmacist interventions have been shown effective for most patients with cardiovascular diseases.<sup>9</sup> Examples of effective pharmacist interventions include counselling, health education, and medication review.<sup>10</sup> But practical integration of pharmacists in multidisciplinary teams to manage CVD seem to be advancing only slowly. Therefore, we use a clinical case following a patient with hypertension over a long time, to illustrate and discuss the role of the pharmacist in management of those problems. The case report is from Lithuania, a country where around 32% of the adult population has a diagnosis of arterial hypertension<sup>11</sup> which makes hypertension one of the most prevalent chronic diseases in the country.<sup>12</sup>

The aim of this clinical case report is to explore the history of a male (65 years) patient with hypertension, to review his over 20 years' antihypertensive treatment and identify the drug related problems that occurred over time with a focus on the role of the pharmacist in managing those problems.

## 2. Case presentation

Mr. Jonas is a white Lithuanian man, first diagnosed with hypertension in November 1998. Over the studied period, Mr. Jonas had 207 general practitioner (GP) visits recorded, with an average 9 visits a year. At the first record visit in 1998, Mr. Jonas is a 41 years old chief executive at higher education school who visited the GP with symptoms of flickering in the eyes and numbness in the limbs. Lipids and glucose level were not documented at that time. His blood pressure (BP) was measured as 150/110 mmHg. There was no information in the record how BP was measured. The GP prescribed a beta blocker atenolol 25 mg twice a day for 25 days. No further GP visits were documented until January 2000, when he visited the GP with complaints of dryness of the mouth and thirst. In that year, Mr. Jonas was diagnosed as being hypertensive (160/100 mmHg), having elevated glucose level (5.9 mmol/l (106 mg/dl) and being obese. No medicines were prescribed then. From March 2001 onwards he was prescribed antihypertensive medication, initially a beta blocker (nebivolol 5 mg) and a calcium channel blocker (nitrendipine 20 mg). From that point Mr. Jonas renewed his prescriptions for antihypertensives regularly. Over the following years, his antihypertensive medication was changed from time to time, switching within and between drug classes, ranging from monotherapy to triple therapy. His BP ranged between 130/100 mmHg and 160/100 mmHg in this period. From 2010 onwards, he received some of his antihypertensives as fixed-dose combination.

In 2008, he was prescribed rilmenidine, a centrally acting agent rarely used in hypertension management, for about 5 years. He was found to have dyslipidemia and was prescribed fenofibrate for two months in 2007 and atorvastatin for three months in 2008. Over the years, cardiovascular disease risk was not formally assessed. There were no hospitalizations due to hypertension. He also had a thyroidectomy and levothyroxine treatment was started in 2010. The patient was diagnosed with type 2 diabetes in 2019 and metformin 1000 mg was prescribed twice a day. The patient stayed with the same primary care practice over the whole study period. The treating GP changed in 2016.

Fig. 1 shows the timeline of the prescribed antihypertensives and Fig. 2 the timeline of his diagnoses between 1998 and 2021.

The patient was also prescribed some other medications over time, including pentoxifylline for flickering in the eyes and numbness in the limbs, nimesulide and diclofenac for upper back and neck pain. Some episodes of infectious diseases were recorded with antibiotics and antivirals prescribed. His health record reveals use of some over-the-counter (OTC) medicines and food supplements that were suggested to him, such as the cough medicine ambroxol and some medicines to relieve flu symptoms such as pseudoephedrine, along with magnesium, vitamin B6 and Omega-3 supplements. For some stomach pain episodes' omeprazole and ranitidine were prescribed concordantly. The record also showed that silymarin 140 mg tablets were prescribed several times for fatty liver. In 2021, the patient took 3 medications chronically. Diagnoses, the medicines prescribed, and last test results recorded are presented in Table 1.

## 3. Drug related problems over time

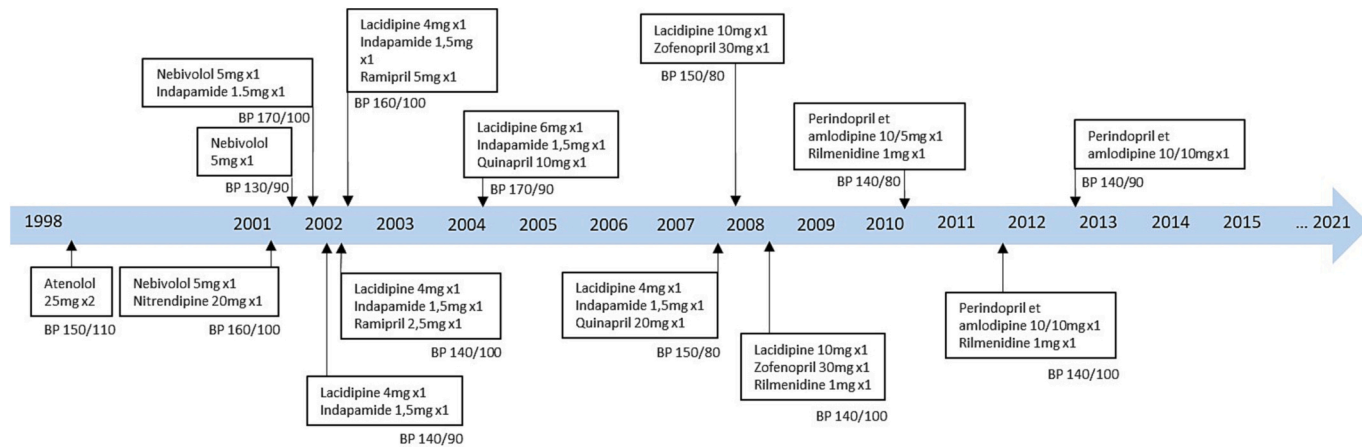
A general practitioner (JP, unrelated to the patient) and a pharmacist, (IT, daughter of the patient), both not previously involved in patient's treatment, studied the patient's medical record from the GP practice, taking relevant treatment guidelines for hypertension into account.

Over the span of the 23 years, European hypertension management guidelines had changed several times.<sup>13–16</sup> The changes of drug classes and combinations prescribed for the patient, might be due to those changes. In general, prescribing was in line with the guidelines, even the use of rilmenidine was recommended as an additional treatment in Lithuanian guidelines when it was prescribed. The main reason for the frequent GP visits was probably the need for medicines to be prescribed as reimbursed medicines could be prescribed for the maximum period of 3 months till the beginning of 2014.<sup>17</sup>

The patient gave written consent. A semi structured interview was conducted with the patient and patients' comments on distinguished episodes were collected (Table 2). The patients' medical record and the patient information from an interview was used to identify drug related problems in the studied period.

Drug related problems were classified using PCNE Classification for Drug-Related Problems V9.1.<sup>18</sup> Possible interventions were also suggested using the same PCNE tool. Identified problems, causes and possible pharmacist's interventions are presented in Table 3.

According to medical health record patient was not consulted on lifestyle change (diet, smoking cessation) and no educational intervention to address cardiovascular risk or cardiovascular disease/hypertension management was recorded. The patient did not

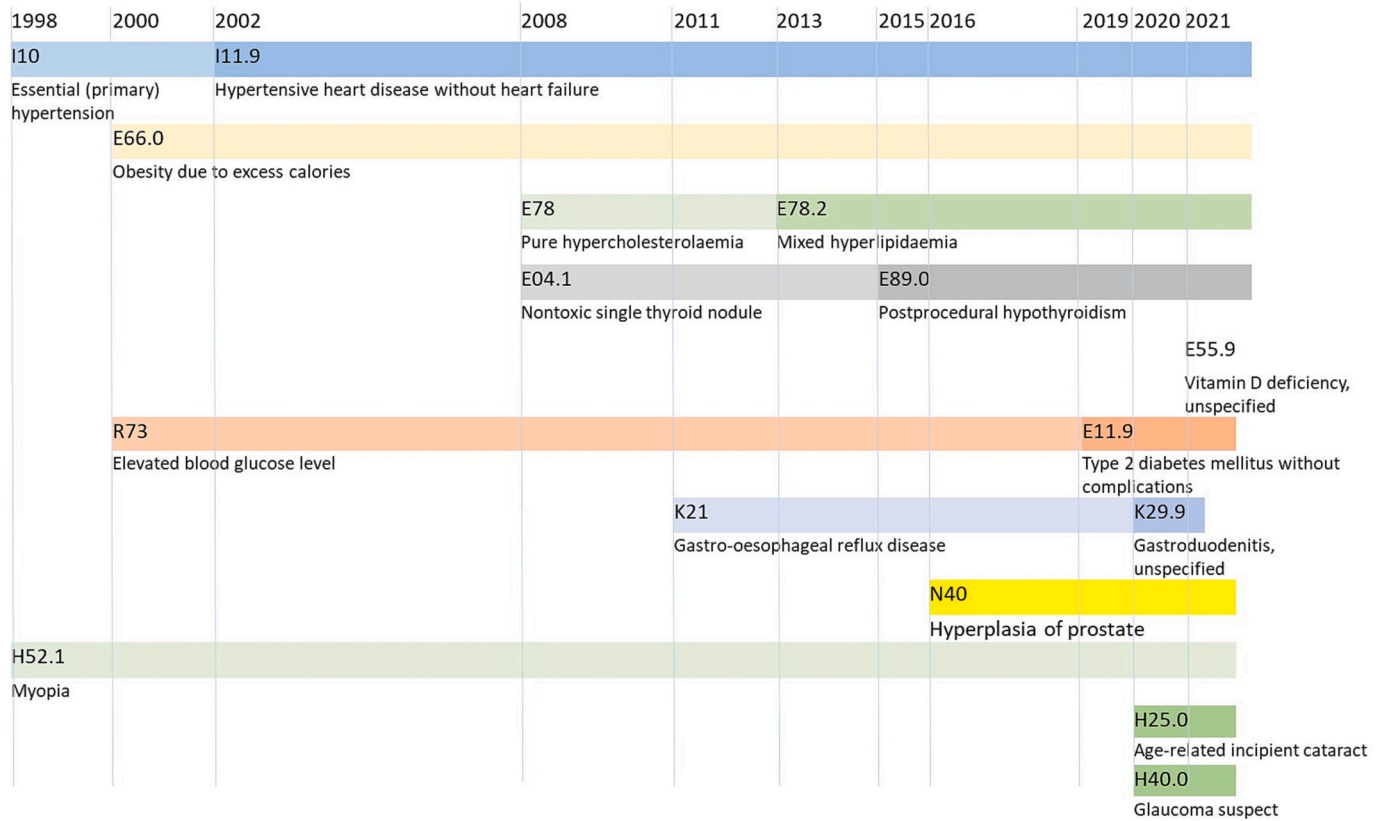


**Fig. 1.** Time line of antihypertensive medicines initiated and office blood pressure (BP) at time of prescription The atenolol was only prescribed once; the other medicines were prescribed regularly until the treatment was changed.

\* Fixed combinations.

BP – office blood pressure where first number is systolic blood pressure (SBP), second – diastolic blood pressure (DBP), measurements in mmHg.

Note: only time points when the treatment was initiated or changed are showed in this time line; patient continued to use prescribed medications, accept atenolol started 1998.



**Fig. 2.** Chronic non-communicable diseases recorded in the patients' medical record from 1998 to 2021.

Note: diagnoses that have been suspected, but rejected or specified and acute diagnoses like pain, infectious diseases are not recorded in this figure.

**Table 1**  
Diagnoses recorded and medicines prescribed at the end of 2021.

| Diagnose code* | Diagnose   | Medication                           | ATC code | Use recommendation              | Test results  | Norms  |
|----------------|--|--------------------------------------|----------|---------------------------------|---|--|
| I11.9          | Hypertensive heart disease without heart failure | Perindopril et amlodipine 10/10 mg** | C09BB04  | Once a day in the morning       | SBP 144 mmHg<br>DBP 85 mmHg   | <135<br><85  |
| E11.9          | Type 2 diabetes mellitus without complications   | Metformin 1000 mg**                  | A10BA02  | Twice a day morning and evening | TC 4.10 mmol/l<br>(158,55 mg/dl)<br>LDL 2.42 mmol/l<br>(93.58 g/dl)<br>TG 1.5 mmol/l<br>(58.00 mg/dl)<br>HbA1c 5.4%<br>CREA 65 mcmol/l*** | 0.90-<br>8.40<br>0.00-<br>3.37<br>0.00-<br>1.70<br>4,0-6,0<br>59-104 |
| E89.0          | Postprocedural hypothyroidism                    | Levothyroxine 75 µg**                | H03AA01  | Once a day in the morning       | TSH 4.14 mIU/ml   | 0.25-<br>5.00  |
| E55.9****      | Vitamin D deficiency, unspecified                | Colecalciferol 25000TV               | A11CC05  | Once a week (8 weeks)           | –   | –  |
| K29.9          | Gastroduodenitis, unspecified                    | Esomeprazole 40 mg                   | A02BC05  | Once a day (2 month)            | –   | –  |
| E66.0          | Obesity due to excess calories                   | –                                    | –        | –                               | –   | –  |
| H40.0          | Glaucoma suspect                                 | –                                    | –        | –                               | –   | –  |
| H52.1          | Myopia   | –                                    | –        | –                               | –   | –  |
| H25.0          | Age-related incipient cataract                   | –                                    | –        | –                               | –   | –  |

SBP – systolic blood pressure, DBP – diastolic blood pressure, TC- total cholesterol, LDL – low density cholesterol, TG- triglycerides, HbA1c - haemoglobin A1c, TSH - thyroid-stimulating hormone, CREA – creatinine.

\* ICD-10-AM (The International Statistical Classification of Diseases and Related Health Problems).

\*\* medications taken chronically.

\*\*\* possible because CREA was in norms, other renal function tests were not performed.

\*\*\*\* no record of vitamin D concentration test was found.

recall that he was informed about cardiovascular risk either. His first diet and physical activity recommendation were recorded in 2005 by his general practitioner.

#### 4. Discussion

Over the time span of 23 years of hypertension, Mr. Jonas' treatment has been revised several times. Mr. Jonas visited the doctor regularly. During this time the patient developed comorbidities such as diabetes and hyperlipidaemia. He had a thyroidectomy, but was never hospitalized due to hypertension. According to the recorded office-blood pressure measurements, the patient never reached the target BP. At least eight drug related problems, four of which were related to hypertension treatment were identified.

The drug related problems were adherence, side effects, and disease drug interaction. Those drug related problems are very common in practice<sup>19</sup> and are very typical in a lifelong disease treatment. The problems identified were clinically not very serious, but

**Table 2**  
Patient's comments about different episodes.

| Episode from the medical record  | Patient's comments from the semi-structured interview  |
|--|--|
| Initiation of treatment with BB (Atenolol)                                     | Patient did not remember the episode when he was first prescribed antihypertensive treatment.  |
| Continuation of treatment with BB (Nebivolol)                                  | Patient was provided with some leaflets about DASH diet and home BP monitoring, but he failed following the recommendations. He was in a responsible stressful job position. He took medicines prescribed daily, but did not feel ok, his home BP was not stable, he had experienced headaches, tension and tinnitus often. Patient had doubts whether these were because of his job or the treatment.   |
| Starting free combination therapy with ACEi plus CCB (Quinapril and Lacidipin) | He often failed to take medicines three times a day. This medication regimen was difficult to adapt to the work/day schedule.  |
| Use of OTC medicines with Pseudoephedrine                                      | When he used hot flu drink his BP increased. He thought it was because of virus infection and didn't link it with the medicine taken. In later years he used the same medicine for similar flu symptoms until he was recommended other medicines in the pharmacy.  |
| Possible adverse drug reactions  | No side effects were noted by patient. When pharmacist had specified some possible events, patient reported that sometimes/rarely: <ul style="list-style-type: none"> <li>• his head spins when he stands up quickly, and sudden movements are avoided</li> <li>• drowsiness takes over in the middle of the day, especially after eating.</li> <li>• has a dry mouth.</li> <li>• patient reported that he gets up 2-3 times at night to go to the toilet, but this does not bother him.</li> <li>• patient had no constipation, in fact quit opposite.</li> </ul> |
| Adherence to medications   | Patient admitted that sometimes he forgets to take his morning metformin dose, but not other medicines. Overall patient was satisfied with the treatment and felt that his condition is under control.   |

BB – beta blocker, ACEi – angiotensin converting enzyme inhibitor, CCB – calcium channel blocker, OTC – over-the-counter.

**Table 3**  
Drug related problems and possible pharmacist's interventions identified.

| Year      | Description  | Problem                                      | Cause  | Possible pharmacist's interventions   |
|-----------|--|--|--|---|
| 1998      | Patient diagnosed with hypertension and prescribed with beta blocker; treatment was discontinued                                 | P1.3 Untreated symptoms or indication        | C7.1 Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason | I2.1 Patient (drug) counselling   |
| 2000-2002 | Patient prescribed with beta blocker; patient complaining having headache at every visit to GP                                   | P2.1 Adverse drug event (possibly) occurring | C1.1 Inappropriate drug according to guidelines/formulary  | I1.3 Intervention proposed to prescriber<br>I2.1 Patient (drug) counselling<br>I3.1 Drug changed to other antihypertensive. |
| 2004-2005 | Combination of ACEi, CCB and diuretic prescribed; gaps from 20 to 40 days with no medication were detected in the health record. | P1.2 Effect of drug treatment not optimal    | C7.1 Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason | I2.1 Patient (drug) counselling   |
| 2007      | Pseudoephedrine combination*prescribed; BP increased   | P2.1 Adverse drug event (possibly) occurring | C1.1 Inappropriate drug according to guidelines/formulary<br>C5.3 Wrong drug, strength or dosage advised (OTC)       | I1.1 Prescriber informed only<br>I2.1 Patient (drug) counselling<br>I3.1 Drug changed to other symptoms relieving OTC       |
| 2017      | Patient prescribed with omeprazole and ranitidine at the same time.  | P3.1 Unnecessary drug-treatment              | C1.4 Inappropriate duplications of therapeutic group or active ingredient  | I1.4 Intervention discussed with prescriber<br>I3.5 Drug paused or stopped  |
| 2017-2020 | Silymarin was prescribed and recommended to be used from time to time further for "fatty liver"                                  | P3.1 Unnecessary drug-treatment              | C1.2 No indication for drug  | I1.4 Intervention discussed with prescriber<br>I3.5 Drug paused or stopped  |
| 2021      | Patient forgets to take his Metformin tablets  | P1.2 Effect of drug treatment not optimal    | C7.1 Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason | I2.1 Patient (drug) counselling   |
| 2021      | Indication for Cholecalciferol 25000TV was not supported by test results   | P3.1 Unnecessary drug-treatment              | C1.2 No indication for drug  | I1.4 Intervention discussed with prescriber<br>I3.1 Drug changed to food supplement   |

\* Pseudoephedrine combinations are OTC medicines in Lithuania, yet it could also be prescribed by the doctor and in this case is considered as prescribed, as it is recorded in the medical record of the patient.

had impact on the patient's overall wellbeing. Furthermore, some of the drug related problems contributed to the lack of hypertension control which increased the patient's risk for CVDs. Other drug related problems were not related to hypertension treatment, but were related to the patient's co-morbidities and polypharmacy. Unnecessary drug use is also common in practice.<sup>20,21</sup>

We identified a number of possible pharmacist-led interventions to solve the drug related problems. These interventions ranged from managing self-medication to collaboration with the GP to change prescribing and counselling of the patient on medication use, including adherence. While managing self-medication is a daily routine of pharmacists' work, other interventions require additional efforts and service implementation. Medication review interventions have been found to be effective, not only in detecting and solving drug related problems, but also improving cardiovascular disease management - control of blood pressure, cholesterol, and type 2 diabetes mellitus<sup>22</sup> and SBP<sup>23,24</sup>. Medication reviews vary from a brief revision of the prescribed medicines to more complex interventions involving interdisciplinary teams (patients, physicians and other health care professionals), which allow the detection of pharmacological interactions and medicine-related problems such as adverse drug reactions, effectiveness problems, non-adherence, and self-medication. More advanced interventions require an integrated, interdisciplinary approach and improve professionals' guideline adherence, support informed decision-making and patient-centred care.<sup>8,25</sup> Pharmacist-led interventions in hypertension have been shown to improve adherence.<sup>26,27</sup> Examples include employing special medication packaging, dose modification, patient self-monitoring of medication-taking and written instructions.<sup>28</sup> More specifically, when antihypertensive treatment is started patient education, including addressing motivation, teaching blood pressure monitoring and emphasizing medication adherence could be provided. A recent study showed that such adherence enhancing interventions improved patients' BP control and medication adherence and increased adherence correlated with improved BP control.<sup>29</sup> Additional pharmacist intervention could also have addressed life style changes<sup>30</sup>, including smoking cessation.<sup>31</sup>

In some countries pharmacists already play an important role in management of chronic diseases.<sup>32</sup> A number of advanced services are common and offered in >50 countries worldwide, including medication reviews, disease management programmes (diabetes, hypertension, asthma) as well as measuring of clinical parameters (blood pressure, blood sugar, body mass index etc.). Cardiovascular disease primary and secondary prevention is done mainly through patient education and counselling, medication safety management, medication review, monitoring and reconciliation, detection, and control of specific risk factors, e.g., smoking cessation. Screening individuals at-risk who are not on medication are provided in some pharmacies in 26, first time dispensing interventions (New Medicines Service) in 5 and therapeutic adherence support in 4 European countries. Medication review services such as medication therapy management, home medicines review and medicines use review have been offered by community pharmacists in several countries.<sup>33,34</sup>

In Lithuania no services beyond dispensing are implemented in pharmacies except inhaler technique service for asthma or COPD patients. The only service that might directly enhance adherence is authorization to dispense 30 days' supply of prescription medicines to chronic patients with evidence of previous prescription. This intervention only addresses a logistical barrier to adherence – renewal of medicines, but not other factors contributing to medication adherence.<sup>35</sup>

Despite the evidence that pharmacists can improve clinical outcomes in a wide array of chronic diseases<sup>36</sup> there are structural barriers and barriers due to the perception of pharmacists and or other health professionals to implement services. For example, in Lithuania, pharmacists are seen as pharmaceutical care specialists that do not provide health care or disease management services.<sup>37</sup> This influences the perception of pharmacists' competencies and limits pharmacy services to dispensing only thus preventing pharmacy intervention programs or pharmacist involvement in interdisciplinary teams in Lithuania. The main structural barriers for pharmacy services include lack of comprehensive access to medical records and lack of remuneration. A related issue is poor, sometimes non-existent, collaboration between the different healthcare professionals.<sup>38</sup>

A case report, as a research design has limitations, yet describes important scientific observations that are encountered in practice to expand our knowledge base. Limitations of this report include possibility of recall bias and that some drug related problems were missed. Also, no information on pharmacies' activities in practice was recorded. Furthermore, we focused on the possible role of the pharmacist in this case, but this is not the only way to analyse hypertension management. Health care improvement could come from different stakeholders and other health care professionals could also contribute to chronic disease management.<sup>39</sup>

## 5. Conclusion

This case illustrates a range of drug related problems that Mr. Jonas experienced during his 23-years of hypertension treatment history. Even though the drug related problems were not very serious in the studied case, the patient could have benefitted from pharmacist-led interventions.

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## Declaration of Competing Interest

One author declares the following personal relationships which may be considered as potential competing interests: Indre Treciokiene is a daughter of the patient studied.



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