TRNC

NEAR EAST UNIVERSITY

INSTITUTE OF HEALTH SCIENCES

Drug Related Problems in Elderly Patients with Cardiovascular Diseases at University Hospital in Northern Cyprus

A THESIS SUBMITTED TO THE GRADUATE INSTITUTE OF HEALTH SCIENCES NEAR EAST UNIVERSITY

By:

Mouaz Yousfan

In Partial Fulfillments of the Requirements for the Degree of Master of Science in Clinical Pharmacy

Northern Cyprus, Nicosia

2018

TRNC

NEAR EAST UNIVERSITY

INSTITUTE OF HEALTH SCIENCES

Drug Related Problems in Elderly Patients with Cardiovascular Diseases at University Hospital in Northern Cyprus

By:

Mouaz Yousfan

Advisor**:**

Assist. Prof. Dr.sc. Arijana Meštrović, MPharm

Co-Advisor:

Dr. AbdiKarim Abdi

Northern Cyprus, Nicosia

2018

DEDICATION

I dedicate this work to Almighty Allah for giving me the knowledge, wisdom, and strength.

Also, to my dad, mom and my entire family for giving me all supports I need.

Special thanks for both, my adviser Assist. Prof. Arijana Meštrović and my teacher Assoc.Prof.Dr. Bilgen Basgut

Approval

Thesis submitted to the Institute of Health Sciences of Near East University in partial fulfillment of the requirements for the degree of **Master of Science in Clinical Pharmacy.**

Thesis Committee:

Chair of the committee: **Prof. Dr. Nurettin Abacıoğlu**

Near East University

Sig: ……

Advisor: **Assist. Prof. Dr.sc. Arijana Meštrović**

Near East University

Sig: ……

Member: **Assoc. Prof. Dr. Bilgen Basgut**

Near East University

Sig: ……

Member: **Assoc. Prof. Dr. Emre Hamurtekien**

Near East University

Sig: ……

Co-advisor: **Dr. Abdikarim Abdi**

Near East University

Sig: ……

Approved by: ` **Prof. HüsnüCan BAŞER**

Director of Health Sciences Institute

Near East University

Sig: ……..

ACKNOWLEDGMENTS

I owe my sincerest gratitude and much respect to my adviser and mentor **Assist. Prof. Arijana Meštrović,** for her remarkable support, advice, and words of encouragement throughout each step of this work.

I am very grateful to **Assoc. Prof. Bilgen Basgut**, the Head of the Clinical pharmacy department at Near East University for her teaching, her time with us and support that she gave me during my study. She wasn't just teacher, but mother and friend

I'm thankful for my Co-adviser **Dr. Abdikarim Abdi**, he was always in responded to guide me to right way

A special thanks to the faculty of pharmacy at **NEU** and its Deanship for their assistance and opportunity to proceed my graduate studies in their distinguished faculty

Finally, I am very thankful to my family members, father **Dr.Abduljabbar**, mother: **Samira**, brothers: **Dr.Ayman, Dr.Ahmad, Dr.Aabdullah** whose support, prayers, and trust are the great factors that push me forward to acquire success.

Lovely thanks for my life partner **Dr.Layal Hawasli** for her inspiration.

Abstract

Introduction: Drug-related problems (DRPs) are among the leading causes of morbidity and mortality, especially in elderly patients. Cardiovascular diseases are common in elderly patients. Cardiovascular diseases (CVDs) are the most important cause of death globally. An estimated 17.5 million people died from CVDs in 2012, which is 31% of all global deaths. (WHO 2016) Studying DRPs in those patients will decrease medications error and improve patient care and quality of life, but interventions and studying in those problems by the pharmacist will not be enough without the healthcare provider corporate.

Aim: The aim of this study is to assess the prevalence and distribution of DRPs in Near East University Hospital (NEUH) in male and female patients aged older than 65 years, who were admitted to the hospital with only cardiovascular diseases.

Methods: A retrospective study have been done in NEUH archive. The data of the 8-months period (01 July 2017 till 01. March 2018) were collected, where 231 patient's medical cases were registered and reviewed. A total of 106 patients were included in the study according to the inclusion criteria. DRPs were documented and identified by using Pharmaceutical Care Network Europe (PCNE) DRP classification system V 8.02. Data was reviewed by clinical pharmacist and specialist physician, and documented by the researcher

Result: Out of a 106 patients, 65 cases (61.3%) DRPs. The most frequently reported DRPs were adverse drug event (possible) occurring in 52.2% of cases.

Conclusion: DRPs may occur in more than half of elderly patients with cardiovascular diseases. Identifying DRPs and reducing them will increase health status and patient safety for the elderly population. And we need prospective studies with interventions to evaluate the outcomes in the patients, clinical pharmacist in the healthcare system will help to reduce the incidence of the DRP events.

CONTENTS

Title Pages ……..ii

Dedication ……..iii

Acknowledgments ……...……..v

Abstract ……vi

Figures ……...…ix

Tables……x

Abbreviations……xi

1. Introduction ……1

1.1 Drug-Related Problems (DRPs)……1

1.1.1 Definitions ……...1

1.1.2 Categories of Drug-Related Problems……..3

1.1.3 Drug-Related Problems in Hospitals……6

1.1.4 Associated factors to drug-related problems……...7

1.2 Geriatric patients ……...9

1.2.1 DEMOGRAPHIC CONSIDERATIONS……9

1.2.2 Physiologic Changes in the elderly……..11

1.2.3 COMPLEX GERIATRIC MEDICAL PROBLEMS……14

1.3 Cardiovascular diseases ……...15

1.3.1 Global burden of cardiovascular disease……15

1.3.2 Cardiovascular Physiology Changes with Aging……...15

1.3.3 Cardiovascular diseases associated with ageing……18

1.3.4 Drug Related Problems in Patients with Cardiovascular Diseases……...20

1.4 Clinical Pharmacy Services in Hospitals……21

1.5 Previous studies……...…..22

2. Methodology …….……25

2.1 PCNE's Drug-Related Problems Classification System…….....25

2.2 Inclusion Criteria……..27

2.3 Exclusion Criteria…….……27

2.4 Sample Size and Data Collection…….……27

2.5 Statistical Analysis……...…….…....28

2.6 Guidelines and references used ……...…..…..28

2.7 Ethical Consideration…….…..28

3. Results ……..…..29

3.1 Characteristics of the Patients……..…...29

3.2 Drug-related problems data ……...….31

3.3 Causes of the problem ……...…...32

3.4 Relationship between ages and number of problems……...…..34

3.5 Relationship between numbers of medications with number of problems……..……36

3.6 Medications with DRPs……..……..38

4. Discussion……..……..39

5. Conclusions……..……42

6. References……43

Appendixes……...51

FIGURES

Fig 1: Medication Errors and Adverse Drug Events……2

Fig 2. Young children and older people in global population……9

Fig 3. PCNEs Drug-Related Problems Classification System……26

Fig 4. Disease related to DRPs……29

Fig 5. Relationship between age and number of problems……..35

Fig 6. Relationship between numbers of medicines with number of problems……...37

Fig 7. Medicines with DRPs…….38

Tables

Table 1: The percentage of elderly people in the World……10

Table 2: Physiologic Changes in the elderly……..13

Table 3: Aging Changes in the Cardiovascular System and Their Consequences…….17

Table 4: Problems analysis ……31

Table 5: Cause Frequencies……32

Table 6: Causes analysis……..33

Table 7: Relationship between ages and number of problems……....34

Table 8: Relationship between numbers of medicines with number of problems……..36

ABBREVIATIONS

ACE/ARB: Angiotensin converting enzyme / Angiotensin receptor blockers

AF: Atrial fibrillation

CHF: Congestive heart failure

CP: Clinical pharmacist

CPS: Clinical pharmacy services

CVD: Cardiovascular disease

DRP: Drug-related problem

ESCP: European society of clinical pharmacy

ME: Medication error

NEUH: Near East University Hospital

PCNE: Pharmaceutical care network of Europe

PPI: Proton ump inhibitor

SD: Standard deviation

SPSS: Statistical package for the social sciences

TRNC: Turkish Republic of Northern Cyprus

WHO: World Health Organization

1 INTRODUCTION AND BACKGROUND:

1.1 Drug-Related Problems (DRPs):

1.1.1 Definition:

A DRP exists when the patient experience or is likely to experience either a disease or a symptom having a present or suspected relationship with the medicine. Eight different categories of DRPs are described each category presented. This categorization serves a number of functions, such as (1) to clarify how adverse drug reactions form but one category of extant DRPs, (2) to make noticeable the pharmacist's role for the future, (3) to serve as a focus for developing a systematic process whereby the pharmacist engage significantly to the overall positive result of patients, (4) to make pharmacy practice vocabulary understood by healthcare professionals, and (5) to assess in the development of standards of practice for pharmacist. (DJCP *Ann Pharmacotherapy* 1990; 24:1093-7)

A DRP is an undesirable patient experience that involves drug therapy and that actually or potentially interferes with a desired patient outcome. The use of word “problem" in the term, "drug-related problem" is used to indicate a drug-related event adjustable detection, treatment, or more appropriable, prevention, and should not be explained in the common usage where it vaguely communicates the idea that "something (puzzle, paradox, perplexity) is incorrect here.

Adverse drug event (ADE): is an event that is "Noxious and unintended and occurs at doses used for prophylaxis, diagnosis, therapy, or modification of physiologic functions." (WHO A. T., 2009).

Adverse drug reaction (ADR): An undesirable response associated with the use of a drug that either compromise therapeutic efficacy, enhances toxicity, or both. (WHO A. T., 2009)

Medication error (ME): Any preventable event that may cause inappropriate medication usage or jeopardize patient safety. (WHO A. T., 2009)

Drug-related problems (DRPs): is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. (PCNE, 2017)

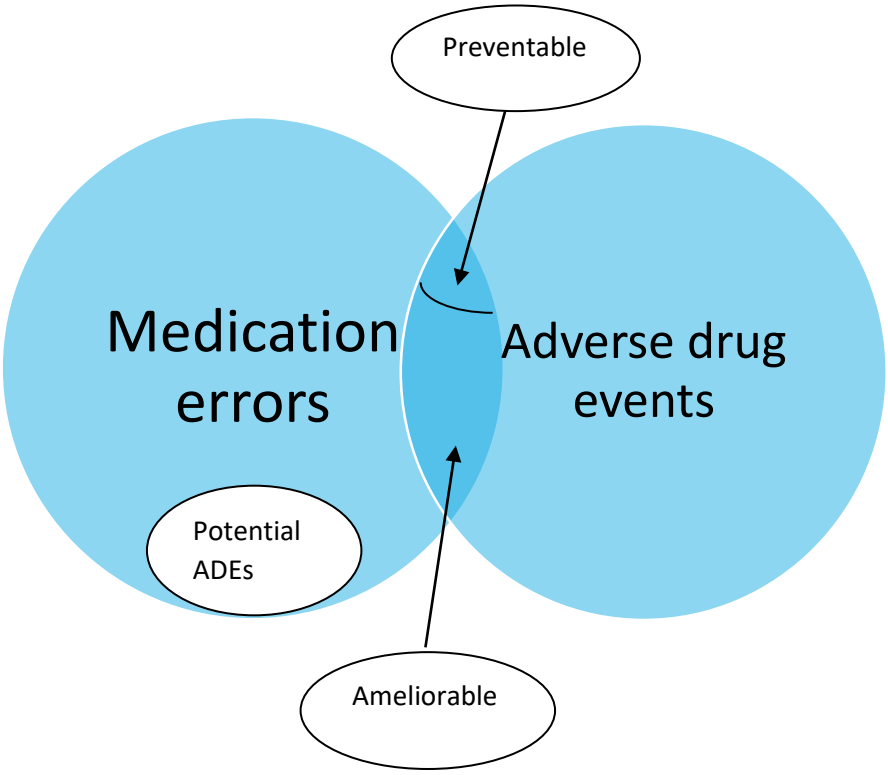


Fig 1: Medication Errors and Adverse Drug Events (Morimoto, 2004)

1.1.2 Categories of Drug-Related Problems

DRPs are identified and characterized by the following distinctions:

1. Untreated indications

The patient has a medical condition that requires drug therapy, but the patient is not receiving a drug to treat it. A number of common circumstances develop where the patient is in need of drug therapy but is not receiving it. For example, a patient is being appropriately treated for a peripheral vascular disease but is not receiving treatment for a developing anaemia. Here, the focus of treatment is on the primary condition and the new problem has not been identified or treated

2. Improper drug selection

The patient has a medical condition and wrong drug is being taken. Sometimes the drug therapy used to treat a patient's medical condition is determined to be ineffective, or a drug therapy likely to be more effective exists but is not being used. Additionally, some patients receive a particular drug therapy in the presence of an allergy to that drug or receive drug therapy when contraindications exist. Other obvious situations present themselves to the clinician

3. Sub therapeutic dosage

The patient has a medical condition, but too little of the correct drug is being taken. Although it may be a fundamental, positive tenet of homeopathic medicine, too little (suboptimal) drug may be classified as a DRP when the desired outcome for a patient is not being realized (i.e., infection is not responding to suboptimal antibiotic treatment), if a drug dose is not individualized for a specific patient, taking into consideration all of the appropriate drug, disease, and patient-specific information, then the dose may be deemed less than optimal.

4. **Over dosage**

The patient has medical condition for which too much of the correct drug is being taken. All of the situations described in the previous section may also result in the opposite effect-too much of the correct drug. Clearly finding the balance is the major enterprise. In situations where a patient's dose is increased rapidly and the rate of increase itself may cause complications, we have another instance of this type of DRP. For example, rapid escalation of nicotinic acid doses are very often associated with severe cutaneous reactions

5. **Adverse drug reactions**

The patient has medical condition resulting from an adverse drug reaction. There are two type of adverse drug reactions,

- Type A reactions are consistent with the pharmacologic actions of the drug, occur commonly, are usually Dose-dependent, and are fairly predictable.
- Type B reactions represent allergic and idiosyncratic reactions that are independent of drug pharmacology. These are rare, not dose-related, and cannot be predicted.

6. **Drug interactions**

The patient has a medical condition resulting from a Drug-drug, drug-food, and drug-laboratory interaction. The possibility of a patient experiencing an adverse event resulting from a physical/chemical interaction between a particular drug and food consumed is always present. For example, milk intake will inhibit the absorption of oral iron preparations.

7. **Medication use without indication**

The patient is taking a medication for no medically valid indication. Patients do not receive the intended drug for a number of reasons, those within the patient's control and those outside of it. Noncompliance with a drug regimen occurs for reasons that fall into both of these categories depending upon the nature of the cause.

8. Indication without medication

The patient has a medical condition that is the result of not receiving the prescribed drug. This category tends to be far too frequently overlooked as a DRP. This is possible because self-treatment, substance abuse, and the like are major factors in defining the situation. Tobacco, alcohol, and coffee consumption, for example, can and do lead to this type of problem. Narcotic abuse is, of course, the extreme form of drug administers with no legitimate medical indication, although the patient may very well insist that the drug abuse is a valid solution to a pain problem.

(Linda M. Strand, 1990) (PCNE)

The classification system of the DRPs is an important tool for clinical practice to contribute in identifying, resolve, and to prevent problems. (Ginny D. Crisp, 2011)

The goal of pharmaceutical care is to improve the patient's quality life through the achievement of specific (predefined), medication-related therapeutic outcomes. (Abraham, 2012)

Those outcomes are

1. Cure of a patient's disease.
2. Elimination or reduce a patient's symptomatology.
3. Prevent or slowing of a disease process.
4. Prevention of a disease or symptomatology

(Strand, 1990)

The PCNE's V (8.02) DRPs classification system was chosen in this study to identify the DRPs. *(see the methodology section)*

1.1.3 Drug-Related Problems in Hospitals

For a lot of diseases, drug therapy enhances health and quality of life. However, inappropriate use of medicine may be harmful and could cause new symptoms. Since the drug therapy is complex, thus giving appropriate drug prescribing is challenging. Accordingly, in clinical medicine, a wide range of drug-related problems (DRPs) may arise. DRPs include cost-effectiveness of the treatment, a recent study in the US estimated that the cost of treating conditions caused by inappropriate medication, medication misuse and polypharmacy cost the United States more than $177 billion in unnecessary visits to the doctor, the emergency room, and the hospital every year. (Marabella, 2015) Optimization of drug therapy may, by preventing DRPs, influence health expenses, potentially save lives and enhance quality patient's life. (Viktil, 2004)

A lot of studies and publications published in the last 15 years ago show that the medication errors and/or adverse drug events in hospitalized patients, focusing on the frequency of, risk factors for and avoidance of such problems associated with pharmacotherapy, specified that medication errors occurred in a mean of 5.7% of all event of drug administration, but with a high variability among the 35 studies retrieved. This variability was clarified by the methods by which medication errors were detected and by the way drugs were administered. Errors happened throughout the whole medication process, with administration errors accounting for more than half of all errors. Important risk factors included insufficient pharmacological knowledge of health professionals, errors in the patient charts or documentation by nurses and inadequate pharmacy services. (LaPointe NM1, 2003)

Adverse events, on the other hand, affected 6.1 patients per 100 hospitalized and also showed a high variability among the 46 studies retrieved. This variability could also be explained by drugs with a narrow therapeutic range, use of anticoagulants or diuretics, polypharmacy, elderly patients, renal elimination of drugs and duration of the stay in the hospital. (uhl-Melcher, 2007)

1.1.4 Associated factors to drug-related problems

i. **Gender:** Female gender has shown in a lot of studies that they are more likely to have increased risk for DRPs. The females have physiological differences in immunological and hormones that mean when they exposure to drugs-weight dependent usually higher in females, which may affect drug response. Also females have more active liver enzyme like CYP3A4 which is responsible for metabolism of many drugs. (Makkar, 1993).

ii. **Age:** studies consider the age (elderly/pediatric) as a risk factor for the prevalence of DRPs. The ratio of body fat increases, the renal function is decreasing, hepatic enzymes decrease and eliminations goes slower. Fat soluble elements are retained in the body. To avoid DRPs in the elderly, both pharmacodynamics and pharmacokinetics have to be carefully assessed when prescribing medicine Examples of inappropriate drugs for older people are benzodiazepines with a long half-life, tramadol, anticholinergic substances, and propiomazine. (Mörike K, 2008).Diseases increase while with age increase (Mörike K, 2008) .A study investigated risk factors for DRPs and determined polymorbidity, renal impairment, dementia, and cardiovascular diseases are significant factors for having DRPs. Moreover, renal function is an important parameter for choosing an appropriate drug and dosage modification. (Kaufmann, 2014)

iii. **The number of drugs**: the number of drugs is a risk factor for increased in adverse drug event/ reactions, however, increasing number of drugs that are also lead to reduced compliance among patients.

Polypharmacy is defined as using more than five drugs at the same time. (Peterson, 2017). A study in Sweden showed that patients over 75 years old are treated with an average of 4.7 drugs and approximately 10% have 10 drugs or more. One study investigated the covariation between DRPs and the number of drugs. With every unit increase in the number of drugs The DRPs increased linearly with 8.6 %. (Viktil, 2007)

The DRPs which we mentioned previously are not isolated from each other. All associated factors can happen in one patient and one factor can increase the probability for a second factor. For example, in elderly patients' diseases prevalence increases, the risk of polypharmacy increases and renal function decreases. (Hamid, 2014) There is another example for reducing renal function like patients with age-related diagnoses such as hypertension and DM. (McDonnell, 2002)

In summary, many factors such as renal impairment, polypharmacy, age and diagnoses are suggested to be associated with DRPs

1.2 Geriatric patients

1.2.1 DEMOGRAPHIC CONSIDERATIONS

According to the World Health Organization (WHO) the percentage elderly in developed countries is 15%, whereas 3-4% for oldest (80 years and older) group the variation in percentage of elderly population reflects the variation in mortality rate which a direct indicator of variation in health care system quality from place to another (Aging, 2010) In 2012, the global population reached 7 billion people, aged 65 and over was 562 million (8.0 percent). In 2015, the population of the elderly increased by 55 million and the proportion of the elderly population reached 8.5 percent of the total population. From 2015 to 2050 it is equivalent to an average increase of 27.1 million older people (Wan He, March 2016).

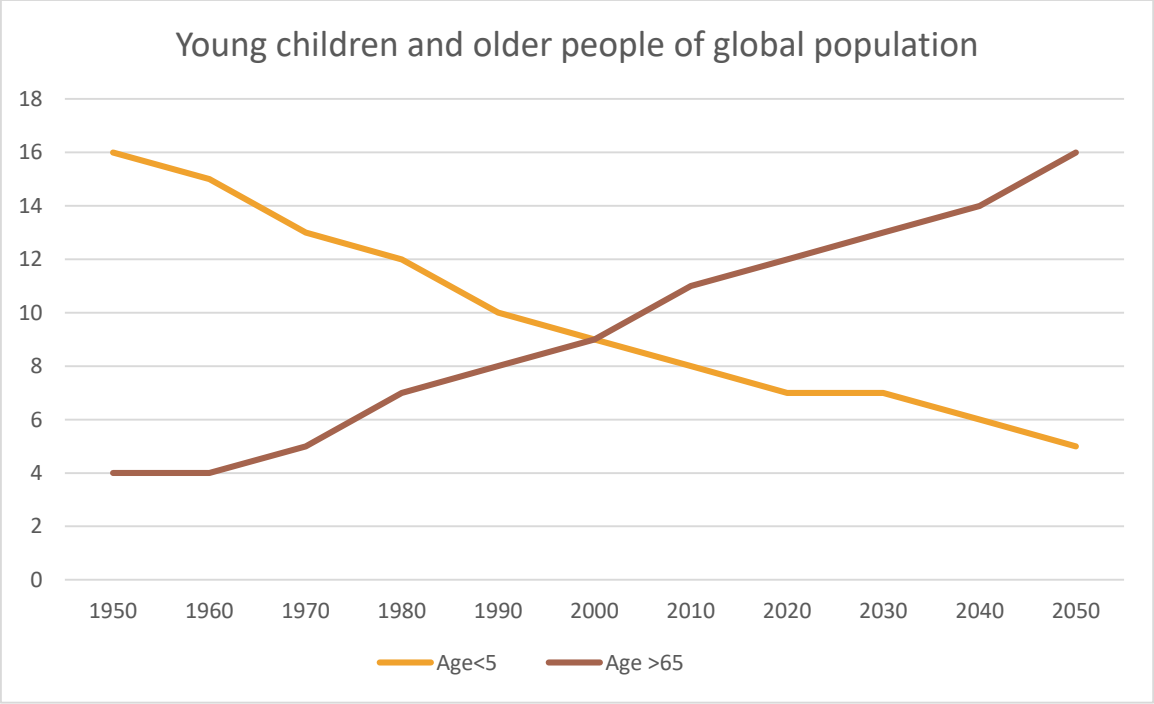


Fig2: Source, United Nations. World Population Prospects: The 2010 Revision.

The increase in the elderly population rate associated with economical and healthy challenges made this aged part of the population under view the most of researchers and studies to improve health levels in elderly ages. (Liu X, 1996). On the average, the individuals who are 65 to 69 years old take nearly 14 prescriptions per year and individuals who aged 80 to 84 years take an average of 18 prescriptions per year (Tom G. Bartol, 2015).

Table 1: The percentage of elderly people through the world

Region	**Years**	**% of population**		
		≥ 65 years	**≥ 75 years**	**≥ 80 years**
Europe	1990	13.7	6.1	3.2
	2010	17.5	8.4	4.9
	2025	22.4	10.8	6.4
Asia	1990	4.8	1.5	0.6
	2010	6.8	2.5	1.2
	2025	10.0	3.6	1.8
USA	1990	12.6	5.3	2.8
	2010	14.0	6.5	4.0
	2025	20.1	8.5	4.6

1.2.2 Physiologic Changes in the elderly

There is a lot of age-related physiologic changes occur which may cause reductions in functional reserve capacity and affect drug pharmacokinetics and pharmacodynamics, thus increase the rate of medication-related problems (U.S Food and Drug Administration, August 1994). The age-associated changes may cause a clear reduction in the capacity of functional reserve like ability to respond to physiologic challenges and stresses.

The changes in cardiovascular are decreased myocardial sensitivity to β-adrenergic stimulation, cardiac output, baroreceptor activity, and increased total peripheral resistance and left ventricular hypertrophy. However Homeostatic mechanisms in the cardiovascular and nervous systems are less efficient, Central nervous system changes are; decreased weight and volume of the brain, cognitive decline, memory impairment, predisposition to falls and autonomic baroreceptor dysfunction. All those lead to decease in drug metabolism and excretion. (murray, 1997)

Chronic alterations in hepatic blood flow occur with aging process. Clearance of a large number of drugs declines and also decreases in liver mass, in liver blood flow, in a number of functional hepatocytes, reduction in function of certain mixed function oxidase enzymes. With increasing age, hepatic blood flow falls and so does hepatic volume. Moreover, binding of some agents normally carried on albumin may decrease. In contrast, increasing age has relatively modest effects on hepatic drug metabolism and these are highly selective. (S, 1994)

Some of these changes are:

- **Metabolism**

The liver can use various types of reactions to complete the transformation process like oxidative reactions (phase 1)it is typically involve various types of Cytochrome P450 mono oxygenize (CYP450) enzymes, this phase have important role in drug metabolism

The Phase 2 reactions involve conjugation and the products of conjugation reactions may have an increased molecular weight and they are usually inactive, unlike phase 1 reactions, which seldom produce active metabolites. (Miller SW., 2007)

In elderly the studies shows the alteration in metabolism happened in phase1are more likely as a result of reduced hepatic volume than reduced hepatic enzymatic activity (Sotaniemi EA, 1997)

- **Distribution**

Distribution defined as" where the drug may go after it enters the bloodstream". (Turnheim K., 2004).There are various factors that influence the drug volume of distribution, which includes protein binding, pH, the molecular size, and the water or lipid solubility (Mangoni AA, 2004)

The aging effect on how the drug is distributed in the body. the muscle mass declines and the proportion of body fat may increase; so the drugs that are more fat soluble will have a greater volume of distribution in an older age. (Shi, 2011)

- **Absorption**

Although earlier studies reported significant age-related changes in the gastrointestinal tract including increase gastric PH and gastric empting, the drugs absorbed which undergo the first-pass metabolism also may increase in older people. However, there is evidence in decreasing the first-pass effect on hepatic and/or the gut wall metabolism that may result in increasing the bioavailability and higher the plasma concentrations of the drugs, that's why transdermal administration is becoming commonly increased and is used for several medications prescribed to the elderly patients. Alterations in the stratum corneum and lipid composition of the skin, changes in sebaceous gland activity, and changes in the dermis and epidermis may affect drug absorption for some lipophilic drugs appear to be less affected by aging than do hydrophilic medication. (L, 1992)

- **Elimination**

The primary elimination of drugs from the body occurs via renal excretion. As with metabolism, as the half-life of the drugs is increased as the renal function is reduced. Also as the body ages and the renal functions declines sometimes by a significant degree. (Jackson, 2007).Alteration in renal function in elderly, spicily glomerular filtration rate, affects the excretion of many drugs such as in lithium, the 50% dosage reduction seemed necessary to recompense in lithium excretion and to reduce lithium side effects to a level comparable to that acceptable in younger patients (Hewick et al). Knowing which drugs are excreted via renal and knowing the way of adjusting the doses of those drugs is imperative to ensuring the safety and affectivity of drug dosing in all patients (Turnheim K., 2004).

Table 2: Physiologic Changes in the elderly

Metabolism	**Distribution**	**Absorption**	**Elimination**
↓Microsomal hepatic oxidation ↓Clearance ↓1st pass metabolism ↑Steady state levels ↑Half life ↑Active metabolites level	↓ Cardiac out put ↓ Hepatic blood flow ↓Renal blood flow ↓ Body water content ↓ Serum albumin ↓for water soluble drug ↑Adipose tissue	↓saliva secretion ↑Gastric PH ↑Gastric emptying time ↓ Gastric surface area ↓Gastrointestinal motility ↓Active transport mechanism	↓ Renal perfusion ↓Renal size ↓GFR ↓Tubular secretion ↓Tubular reabsorption excretion

1.2.3. COMPLEX GERIATRIC MEDICAL PROBLEMS

Aging is known be associated with high prevalence of multiple chronic diseases and that lead to use of complex therapeutic regimes, changes in pharmacokinetics and pharmacodynamics that are related to the age, Pharmacodynamics changes can be defined as alterations in concentration–response relationships or receptor sensitivity. There is evidence of altered drug response or sensitivity in the older adults. Four mechanisms have been suggested:

- Changes in the numbers of the receptor
- Changes in the affinity for receptor
- The alterations of post-receptor
- The impairment of the homeostatic mechanisms that are age-related

(Swift, 1990)

20% of elderly (more than 65) have multiple disease processes that functionally limit normal activity. Geriatricians refer to them as the "frail elderly" like, those

Whose functional disabilities are so great as to prevent their carrying out independently one or more of the activities of daily living, But, After the age of 85, 46% of those living in the community, This is the group of patients that present the most series and challenging problems to the physician and all healthcare providers. (DH, 1988) Particularly for the treatment of chronic diseases, elderly patients were found to use about three times more drugs than younger patients (Vinks et al, 2006).

The lack of a consistent drug list, and inadequate prescription and monitoring of drug therapy and the lack of continuity in physician contacts are also some of the reasons for complexity of treating elderly. Poly-pharmacy and increased sensibility are causing adverse drug events (ADE), drug-drug interactions and medication errors in the elderly (Gustafsson M, 2016). In Sweden, deaths associated with drug-related problems (DRPs) are estimated to 3000 annually and 6-16 % of the hospital admissions can be derived to drugs (Peterson CC, 2017).

1.3 Cardiovascular diseases

1.3.1 Global burden of cardiovascular disease

Approximately 50 million deaths occur in the world each year, with almost 80% of these (39million) occurring in developing countries, it has been estimated that approximately one quarter of all deaths in developing countries and almost half of all deaths in developed countries are attributable to cardiovascular disease(CVD).

Worldwide there are more deaths from coronary heart disease (CHD) (5.2 million) than from stroke, cardiovascular diseases (CVDs) are the most important cause of death globally. An estimated 17.5 million people died from CVDs in 2012, which is 31% of all global deaths. (WHO 2016) In developed countries, cardiovascular disease account for approximately 10%of direct health care costs, and more than half of these diseases occur in people aged 65 years and older. (Rice, 1985)These costs generally represent between 0.5% and 1% of the country's gross national product. In developing countries these is little information on the economic consequences of ill-health in old age, the extra burden on the household as a result of cardiovascular mortality and morbidity in an elderly person has not yet been adequately documented. (WHO, 1995)

1.3.2 Cardiovascular Physiology Changes with Aging

There are some changes in the cardiovascular system happened with ageing, and that is a result of alterations in cardiovascular physiology. Those changes must be differentiated from the effects of pathology, such as coronary artery disease, that occur with increasing frequency of elderly. Those changes happened to everyone but not the same rate, therefore there is tow ages according to studies chronologic age and physiologic age. Like the decrease in elasticity and an increase in stiffness of the arterial system. That leads to an increased afterload on the left ventricle, an increase in systolic blood pressure, and left ventricular hypertrophy, also

changes in the left ventricular wall that prolongs relaxation of the left ventricle in diastole. And also there is a dropout of atrial pacemaker cells resulting in a decrease in intrinsic heart rate. (Melvin D. Cheitlin, 2003)

Physiologic ageing is characterized by slow loss of organs function. With ageing there is also an increasing of diseases such as coronary artery disease (CAD), renal, cerebrovascular disease and pulmonary disease that can accelerate the loss of function.

This is explained by the prevalence of CAD in autopsy studies showed that there were over than 60% of the patients who died at age (60) or older had at least one coronary artery disease that had a 75% or greater occlusion. (ELVEBACK, 2015)

Other studies showed that about 20% of elderly patients with age 80 years or more have clinically evident of CAD; the majority of elderly patients with significant obstructive CAD are asymptomatic. (Wenger, 1992)

Table 3 : Aging Changes in the Cardiovascular System and Their Consequences

CHANGE	CONSEQUENCE
Decreased compliance of the arterial tree	Increased afterload on left ventricle and development of LVH
Myocardial cell hypertrophy, increased interstitial fibrosis, dropout of cardiac myocytes, and delayed inactivation of ICa-L channels	Increased cytosolic Ca++ Maintenance of contractility Prolongation of action potentials Delayed relaxation Decreased left ventricular compliance
Apoptosis of sino-atrial pacemaker cells, fibrosis, and loss of His bundle cells.	Slower intrinsic heart rate Varying degrees of AV block
Decreased responsiveness to β adrenergic stimulation and reactivity to baroreceptors and chemo receptors	Increased circulating catecholamines

AV=atrioventricular; LVH=left ventricular hypertrophy; ICa-L=L-type Ca++ current

(Melvin D. Cheitlin, 2003)

1.3.3 Cardiovascular diseases associated with ageing

Hypertension

Hypertension refers to a clinical entity (blood pressure) is used in the context of discussion on risk factor. The measurement of blood pressure requires careful attention to methods of measurement, in elderly propel group, elevated blood pressure is common. Systolic blood pressure increases with age, at least until the eighth decade of life
In the contrast, diastolic blood pressure rise only until about 50 years of age. These divergent trends in systolic and diastolic blood pressure lead to an increase in pulse pressure with age and increase prevalence of isolated systolic hypertension. (WB, 1998)

In elderly patients the pathophysiological accompaniments of ageing and hypertension may alter the responses to medicine. Elderly hypertensive patients show lower stroke volume, cardiac output, and intravascular volume and higher peripheral vascular resistance than younger patients. Baroreceptor reflex function is damage in elderly patients, and postural hypotension is widespread and may be exacerbated with medicine. (Beard, 1992)

Trials on hypertension treatment in the elderly explain that blood pressure control leads to significant reductions in clinical endpoints of stroke, myocardial infarction and cardiovascular death. In the Systolic Hypertension in the Elderly Program (SHEP), over 4000 patients (mean age 72) with stage II hypertension were randomized to placebo or hypertensive management. Treatment given to 45 Patients to achieve an average systolic blood pressure of 143 mmHg had a 36% relative risk reduction in stroke (P = .0003) at 4.5 years. In the Hypertension in the Very Elderly Trial (HYVET), a randomized, placebo-controlled study for patients older than 80 years, the 21% relative risk reduction in mortality with 2 years *P = .02* prompted the trial to be stopped prematurely.46 The HYVET blood pressure target was less than 150/80mmHg. (Beckett NS, 2008)

Atrial Fibrillation

Atrial fibrillation is the most common clinically significant arrhythmia in ageing and the incidence of atrial fibrillation increases with prolonged age (WS, 2008). For treating atrial fibrillation there are two important issues rate-control versus rhythm-control strategies and anticoagulation, (9) randomized, controlled trials have compared pharmacologic rhythm-control and rate-control strategies. (4) Of these trials have been combined in a meta-analysis

of over (5000) patients, although 4060 patients were registered in a single trial, the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study, and the results of the meta-analysis closely matched the results of the AFFIRM trial. (DG, 2002)

And another study done to show the relation between AF and mortality, AF was present in 22% of 106,780 persons aged 65 years and older with acute MI in the Cooperative Cardiovascular, patients with AF had a higher (hospitalized patients) mortality 25% vs. 16%, 30-day mortality 29% vs. 19%, and one year mortality 48% vs33%. (N, 2007)

Heart Failure

Heart failure is a common problem in elderly, each year approximately 1% of the population and 20%of hospital admission patients older than 65 years suffer from HF. (Jessup, 2003)

Although heart failure has a variety of causes, the most common factor in the elderly is chronic heart disease, and the next is hypertension. the morbidity of Heart Failure in the geriatric is related to decreased cardiac reserve, and the number of comorbid illnesses, such as chronic kidney disease and atrial fibrillation. Heart Failure mortality is high, with up to one third of geriatric patients dying within 1-year of their initial Heart Failure hospitalization. (Croft, 1999)

Heart failure occurs equally frequently in men and women, although the survival rate is poor for men, even for women, only about 15% survive for 10 years. (JK, 1990) There has been little improvement in case fatality following the onset of heart failure during the past few decades, despite the decline in HF mortality and marked improvement in hypertension control. (Flather, 2005)

1.3.4 Drug Related Problems in Patients with Cardiovascular Diseases

Cardiovascular disease is public health problem and one of the most important causes of premature death throughout the world, that's why it have increased healthcare costs.

However, CVDs accompanied with comorbidities and complications that makes the patients take multiple drugs, therefore, they are abler for exposed to drug-related problems (DRPs).

As a result, DRPs can happen at any stages of medication process from prescription to follow-up treatment. Most of the problem usually occurs on administration, dispensing and during the patient's use of a medicinal product. (Abdela, 2016)

A prospective, observational, interventional study has been done in India for 7 months in hospitalized cardiovascular patients admitted in cardiology department for all patients with cardiovascular diseases above 18 years old have been included in the study. Among 112 patients, total of 53 DRPs were found in 44 patients. The incidence of DRPs was high (55.35%) in patients aged between 41-60 years. (Shareef, 2014)

A study has been done in Gondar University Hospital, Ethiopia it was a cross-sectional study, structured systematic data review was designed focusing on patients with CVDs (both out and inpatients) older than 18 years old, from April to June 2015

A total of 227 patients with CVDs were reviewed with a mean age of 52.0 ± 1.7 years. Patients who're diagnosed with heart failure (71, 31.3%). Diuretics (199, 29.5%) were the most commonly prescribed drugs. A total of 265 DRPs were identified, 63.4% of patients have at least one DRP (1.17 ± 1.1). The most common DRPs were found to be an inappropriate selection of drug (36.1%) and dose (24.8%). The most identified risk factors causing DRPs were: Need of additional drug therapy and lack of therapeutic monitoring. (Ousman Abubeker Abdela, 2016)

1.4 Clinical Pharmacy Services in Hospitals

Since the cardiovascular disease responsible for causing death (48%) in worldwide. In 2008, CVDs cause 36 million deaths. (WHO, Noncommunicable diseases country profiles, 2011) Clinical pharmacy services (CPS) assist in reducing hospital mortality rates. Clinical pharmacy definition is ‘‘area of pharmacy concerned with the science and practice of rational medication use’’ (ACCP, 2008)

CPS are essential for the delivery of pharmaceutical care. Pharmaceutical care is defined as ‘‘the pharmacist’s contribution to the care of individuals in order to optimize medicines use and improve health outcomes ‘‘ (ACCP, 2008)

The clinical pharmacists have a significant role in preventing and discovering errors. Like, medication errors, DRPs and patients counseling. Medication errors in United States hospitals were evaluated. A database was constructed from the 1992 National Clinical Pharmacy Services database. Both simple and multiple regression analyses were employed to determine relationships and associations. A total of 429,827 medication errors were evaluated from 1081 hospitals. Medication errors occurred in 5.22% of patients admitted to these hospitals each year; those errors were discovered by clinical pharmacists. (Bond, 2002)

A Systematic Review has been done to evaluate the clinical service extracted from databases (2609 studies) in February 2011 with no time limitation included. They include all studies for those whose received direct care from a clinical pharmacist in the CVD therapeutic area or for CVD risk factors The majority of outcomes reported in their review (68.6%) found that clinical pharmacy services were associated with better improvement in patient clinical outcomes compared with health care services that did not involve pharmacists in direct patient care. (Abdulaziz Altowaijri, 2013)

Also, prospective interventional study estimated in university hospital, CPSs were provided for inpatients by independent clinical pharmacists and documented over 4 months. The study includes all patients who were admitted to the hospital in cardiology or cardiovascular surgery departments, a total of 133 patients were admitted to the wards during the 4-month study period. Clinical pharmacists reviewed all the patients, and 81 patients (60.9%) had at least one DRP. Total of 217 DRPs were identified (mean DRP per patient1.6 ± 1.7), 95%. (Al-Baghdadi, 2017)

1.5 Previous studies

- A prospective, observational, interventional study has been done in India for 7 months in hospitalized cardiovascular patients admitted in cardiology department for all patients with cardiovascular diseases above 18 years old have been included in the study. Among 112 patients, a total of 53 DRPs were found in 44 patients. The incidence of DRPs was high (55.35%) in patients aged between 41-60 years. (Shareef, 2014)

- A study has been done in Gondar University Hospital, Ethiopia it was a cross-sectional study, structured systematic data review was designed focusing on patients with CVDs (both out and inpatients) older than 18 years old, from April to June 2015

  A total of 227 patients with CVDs were reviewed with a mean age of 52.0 ± 1.7 years. Patients who're diagnosed with heart failure (71, 31.3%). Diuretics (199, 29.5%) were the most commonly prescribed drugs. A total of 265 DRPs were identified, 63.4% of patients have at least one DRP (1.17 ± 1.1). The most common DRPs were found to be an inappropriate selection of drug (36.1%) and dose (24.8%). The most identified risk factors causing DRPs were: Need of additional drug therapy and lack of therapeutic monitoring. (Ousman Abubeker Abdela, 2016)

- Also, prospective interventional study estimated in university hospital in Northern Cyprus, CPSs were provided for inpatients by independent clinical pharmacists and documented over 4 months. The study includes all patients who were admitted to the hospital in cardiology or cardiovascular surgery departments, a total of 133 patients were admitted to the wards during the 4-month study period. Clinical pharmacists reviewed all the patients, and 81 patients (60.9%) had at least one DRP. A total of 217 DRPs were identified (mean DRP per patient1.6 ± 1.7), 95%. (Al-Baghdadi, 2017)

- A cross-sectional study has been done in Rotterdam, the Netherlands for 4971 subjects aged 55 to 94 years. To investigate the distribution of cognitive function in elderly people and to assess the impact of clinical manifestations of atherosclerotic disease on this distribution. All participation rates in the study were 80%. Cognitive test data were available for 90% of them. Increasing age and lower educational level were associated with poorer cognitive function. Previous vascular events, the presence of plaques in the carotid arteries, and presence of peripheral arterial atherosclerotic disease were associated with worse cognitive performance independent of the effects of age and education. the study concluded that atherosclerotic disease accounts for considerable cognitive impairment in the general population. (Breteler, 1994)
- Articles reviewed and summarized for diagnostic approaches and treatment recommendations for congestive heart failure, cardiac valvular disease, coronary artery disease and arrhythmias in elderly patients. The result was that the ageing process is associated with predictable anatomic and physiologic alterations in the cardiovascular system. Consequently, the manifestations of heart disease in the geriatric population differ from those found in younger patients. Additionally, outcomes of cardiac diseases and therapeutic options change with advancing age because of such factors as alterations in drug metabolism. (Duncan, 1996)
- A retrospective study has been done in Tayside hospitals in Scotland. To assess the incidence of DRPs in elderly patients, all elderly people admitted to hospital were screened by a pharmacist; individual case reviews were prepared for all those with a potential DRP and reviewed by a three-member panel which made a final decision on the presence of a DRP and its contribution to admission.1011 elderly patient admissions over than 9-month period, the main outcome was that the incidence of DRPs was 144/1011 (14.2%), with 54/1011 (5.3%) of the admissions identified as

being definitely or probably drug-related, Over 66% of admissions due to adverse effects of NSAIDs were considered to be definitely preventable. (Cunningham, 1997)

- Between November 2009 and January 2010, a prospective longitudinal study investigated the incidence and preventability of DRPs in a single cardiac transplant centre. Three independent reviewers used validated scoring systems to determine the incidence and preventability of drug-related hospital admissions. DRPs were classified by type, pharmacologic class, and impact on length of stay. The result was that during the 3-month study period, 48 cardiac transplant patients were hospitalized. DRPs accounted for 40% (19/48) of these admissions and 58% (11/19) were adjudicated to be preventable. Common DRPs included supratherapeutic (32%) and subtherapeutic (16%) dosage, adverse drug reaction (32%), drug interaction (5%), and nonadherence (5%). Pharmacologic classes implicated included immunosuppressant (63%), antimicrobial (11%), electrolyte/fluid (11%), and anticoagulant (5%). Average length of stay in drug-related compared to non-drug-related admissions was 11.4 versus 8.5 days ($p = 0.458$). When annualized, 44 hospitalizations or 500 hospital days may have been prevented. (Repp, 2012)

2 Methodology

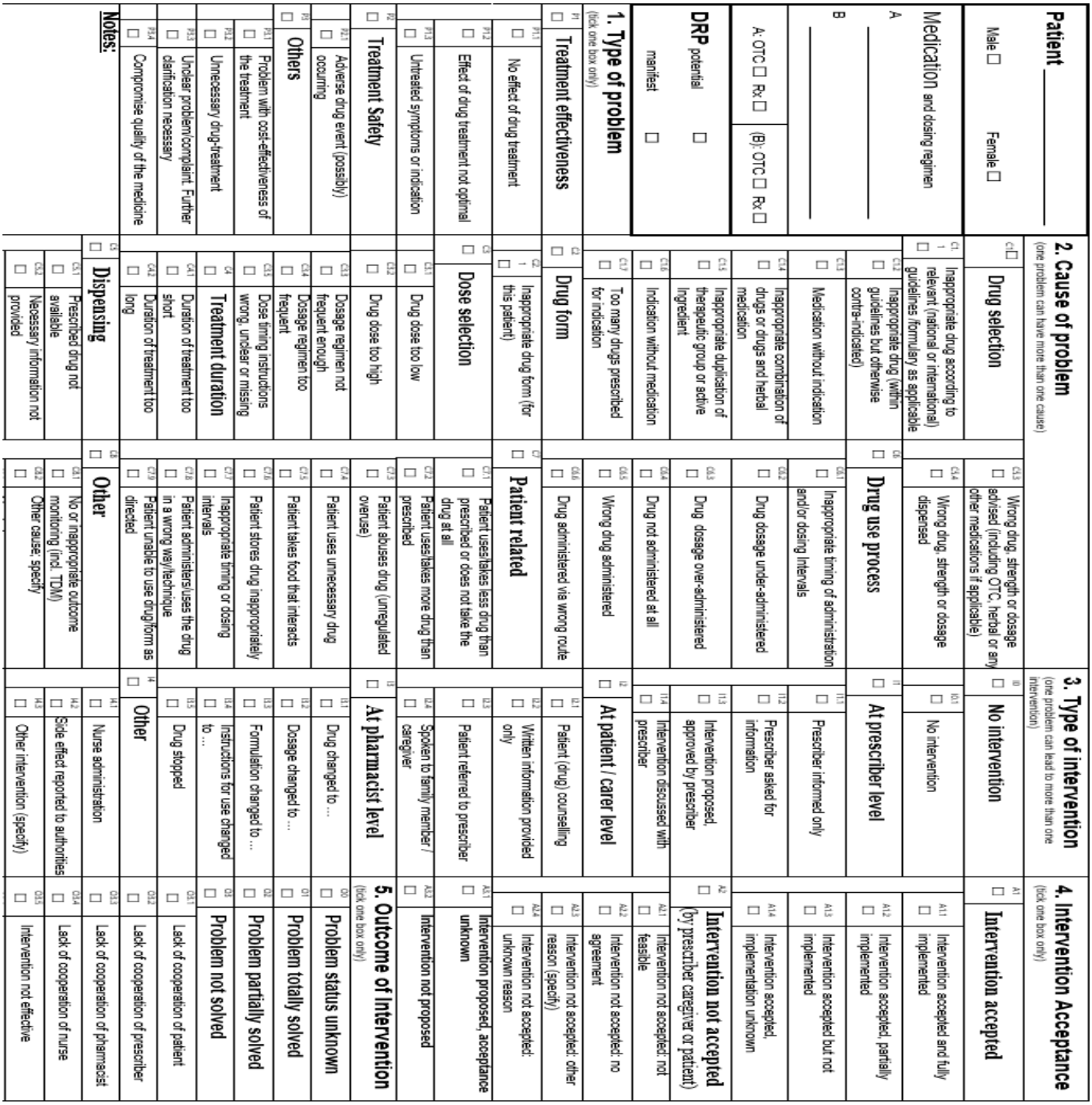
The retrospective observational study was carried out on male and female geriatric patients (aged 65 years and more) who admitted with cardiovascular disease in Near East University Hospital in North Cyprus. The data of the past 8-months (01 July 2017 till 01. March 2018) were collected during 01 April – 01 June 2018. Identifying the DRP cases was done by using the form of PCNE v8.02. That form has already been used in the Near East University hospital, to classify the causes and problems, of the DPRs. The descriptive statistics (Mean ± SD, Percentage) represent the data.

2.1 PCNE's Drug-Related Problems Classification System

The Pharmaceutical Care Network of Europe published in January 1999 a drug-related problem classification scheme. Over the years the PCNE's classification system was devolved and improved by experts, the latest version 8.01 has been published in the 5th of November 2017 and has been used in this study. This classification version is hierarchical coded system and has three primary domains for problems (P-code) (Treatment effectiveness, Treatment safety, Others) eight primary domains, for causes (C code) (drug selection, drug form, dose selection, treatment duration, dispensing, drug use process, patient related, other), and five primary domains for Interventions (I code) (no intervention, at prescriber level, at patient/care level, at pharmacist level, other). Moreover, on the more detailed level, there are 8 subgroups for problems, 37 subgroups for causes and 17 subgroups for interventions, and 20 subdomains for intervention acceptance.

The following form is the form that has been used in our study:

Fig 3: PCNEs Drug-Related Problems Classifiction



2.2 Inclusion Criteria

- Elderly patients (more than 65years old)
- Cardiovascular disease patients using at least one cardiovascular medicine
- The patients who have been hospitalized in NEUH during the last 09 months for at least one day or more
- Patients who have complete documented files

2.3 Exclusion Criteria

- Patients who wasn't taking cardiovascular medicine
- Patients younger than 65 years old
- Patients who are not hospitalized in NEUH at least one day

2.4 Sample Size and Data Collection

The data have been collected from the medical files of all hospitalized elderly patients during the last 09 months (01 July 2017 till 01. March 2018)

Patient's age, gender, principal diagnosis, concomitant disease states, medical history, concurrent medications, dosage, and medications taken prior to admission have been recorded. Other data collected include biochemistry and haematology results, microbiological culture and sensitivity tests, and plasma drug concentrations when these are available. Normal laboratory values for the hospital have been used to determine the presence of abnormalities. Renal function has estimated from creatinine clearance (Cockcroft and Gault 1976). DRPs experienced by the patients on admission and during their inpatient stay, together with the suspected drugs have extracted from their medical records.

Hospitalized Patients who have CVDs or those are at risk of developing a CVD based on Framingham CVD risk assessment scores (age, gender, smoker total cholesterol and systolic BP) who admitted to NEUH during the months July 2017 till the end of February 2018. The medical files have reviewed and analysed to identify any possible Drug Related problems.

2.5 Statistical Analysis

Data analyses have conducted using Microsoft Excel 2016 and SPSS (Statistical Package for the Social Science) programming version 24.0. (To estimate DRP in elderly patients with cardiovascular diseases) The Continuous data have presented as mean (± standard deviation) or median (range), Mann Whitney test was used to test for significant difference between the number of medications taken and the risk of DRPs, while absolute information will be presented as frequency and percentages (%).

2.6 Guidelines and references used to determine DRPs

- Lexicomp (Online database was used to analyse potential drug-drug interactions).
- Beers criteria 2015 (which is Potentially Inappropriate Medication Use in Older Adults, has been developed to assist healthcare providers in improving medication safety in older adults. Our purpose is to inform clinical decision-making concerning the prescribing of medications for older adults in order to improve safety and quality of care).
- The PCNE's Drug-related problems v 8.01 was used to classify the type of DRPs, Causes, Interventions and the outcomes when applicable.

2.7 Ethical Consideration

Privacy of the patient was assured during the study. The study was approved by the Near East Institutional Review Board (IRB) of Near East University Hospital that assigned this research as being just an observational study. Private patient data were not recorded. Only the patient name, age, and gender were used during the study.

The medical record and patient's profile approved to be obtained from the NEU archive and Nuclus system data basis of hospital.

3 Results

3.1 Characteristics of the Patients

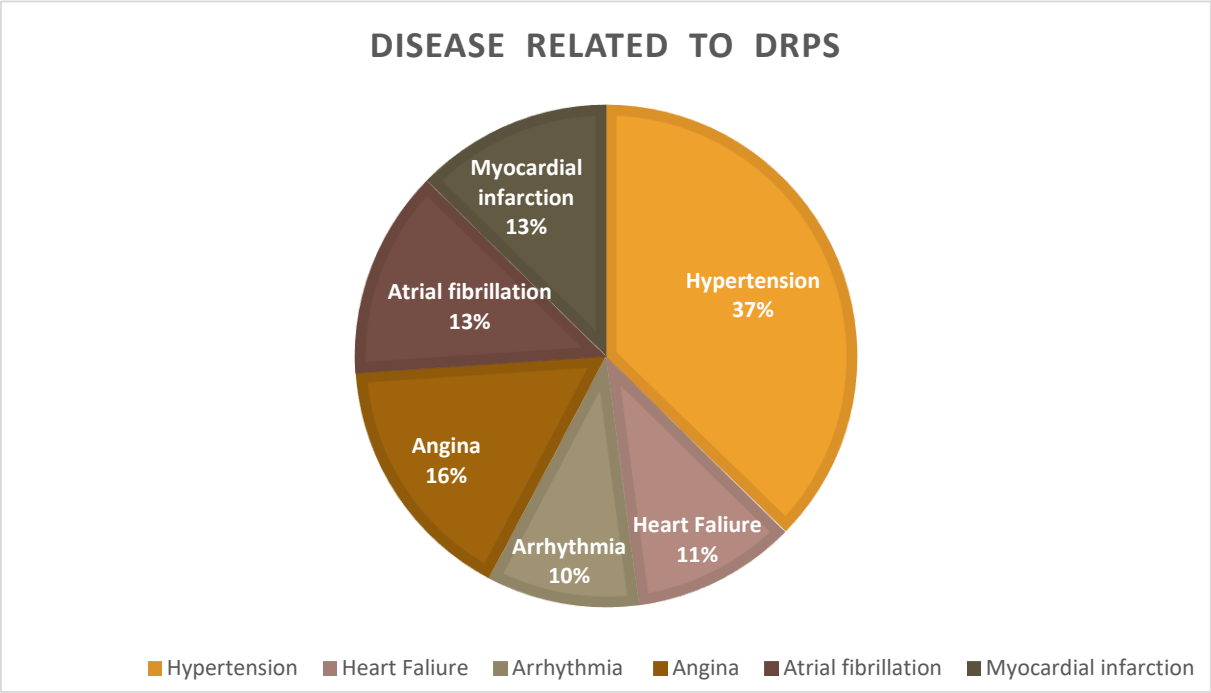
There were 231 patient's medical cases had registered in NEUH archive from (01 July 2017 till 01. March 2018), 106 cases patients were included in this research, 68 of the patients were male and 38 patients were female, with an average age of 76.6 years (SD= 7.4).

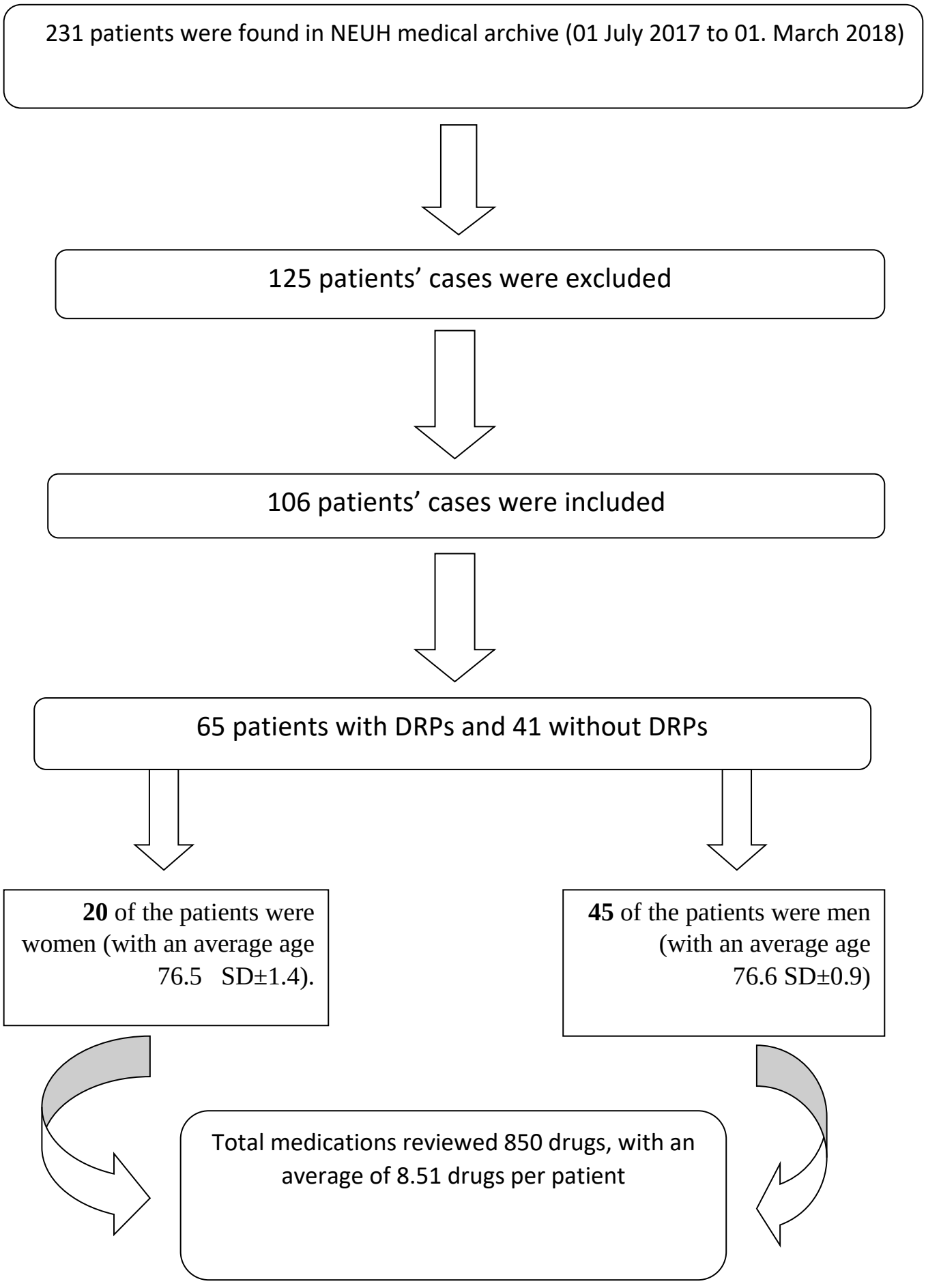
65 patients were identified to have drug-related problem.45 of the patients were men (with an average age 76.6 SD= 0.9) and 20 of them were women (with an average age 76.5 SD=1.4). With average of medication were (8.51) per patient and the average of diagnoses for each patient (1.4)

The patients who are included in this study had an average of 1.4 active medical conditions. For each patient, one medical condition was classified to be the primary disease of the case which was associated with the drug-related problem incidence and increased its complications.

37 % of the drug-related problems cases occurred in hypertension patients

Fig 4: Disease related to DRPs




231 patients were found in NEUH medical archive (01 July 2017 to 01. March 2018)
125 patients' cases were excluded
106 patients' cases were included
65 patients with DRPs and 41 without DRPs
20 of the patients were women (with an average age 76.5 SD±1.4).
45 of the patients were men (with an average age 76.6 SD±0.9)
Total medications reviewed 850 drugs, with an average of 8.51 drugs per patient

3.2 Drug-related problems data

Out of 106 total patents cases were included, 65 cases **(61.3%**) of drug-related problems were identified, reviewed by one clinical pharmacist and one specialist physician, and documented by the researcher.

In those 65 cases, we found 92 drug-related problems (more than one DRPs for one patient)

The most frequently identified DRPs were adverse drug event (possible) occurring (P2.1) (52.2%). Followed by unnecessary drug treatment (P3.2) (18.5%).

Unclear problem or complaint represented (P3.3) (12%).

Untreated symptoms or indication (P1.3) (8.7%), followed by the effect of drug treatment not optimal (P1.2) (7.6%) and problems with cost-effectiveness (1.1%)

Table 4 : Problem analysis

	Frequency	Percentage
Effect of drug treatment not optimal (P1.2)	7	7.6
Untreated symptoms or indication (P1.3)	8	8.7
Adverse drug event (possible) occurring (P2.1)	48	52.2
Problem with cost effectiveness (P3.1)	1	1.1
Unnecessary drug treatment (P3.2)	17	18.5
Unclear problem or complaint (P3.3)	11	12.0
Total	**92**	**100.0**

3.3 Causes of the problem

The cause “medication error” section domain is vital for identifying the type of errors (might be more than one) that caused the incidence of the drug-related problem. Identifying those causes is important to highlight the way of problems happened to be easier to solve.

Only one error was identified to be the leading cause of each drug-related problem registered.

The drug selection (C1) was the most identified error to cause a drug-related problem 83.7%, followed by dose selection (C3) 10.9% and drug form (C2) 4.3%.

Table 5 : Causes Frequencies

Category	Frequency	Percent
Drug selection (C1)	77	83.7
Drug form (C2)	4	4.3
Dose selection (C3)	10	10.9
Treatment duration (C4)	1	1.1
Total	**92**	**100.0**

Table 6 : Causes analysis

Causes Categories	Frequency	Percent
Inappropriate drug according guidelines (C1.1)	4	4.3
inappropriate drug according guidelines but contra indication (C1.2)	29	31.5
Medication without indication (C1.3)	21	22.8
inappropriate combination of drug or drugs and herbal (C1.4)	5	5.4
Inappropriate duplication of therapeutic group (C1.5)	6	6.5
indication without medication (C1.6)	9	9.8
Too many drugs prescribed for indication (C1.7)	3	3.3
Inappropriate drug form (C2.1)	4	4.3
Drug dose too low (C3.1)	6	6.5
Drug dose too high (C3.2)	3	3.3
Dosage regimen too frequent (C3.4)	1	1.1
duration of treatment too short (C1.4)	1	1.1
Total	92	100.0

3.4 Relationship between ages and number of problems

The number of patients aged 65 -80 years old with one problem was 35 patients, with two problems was 8 patients, with three problems was 1 patients and with four problems was 1 patient.

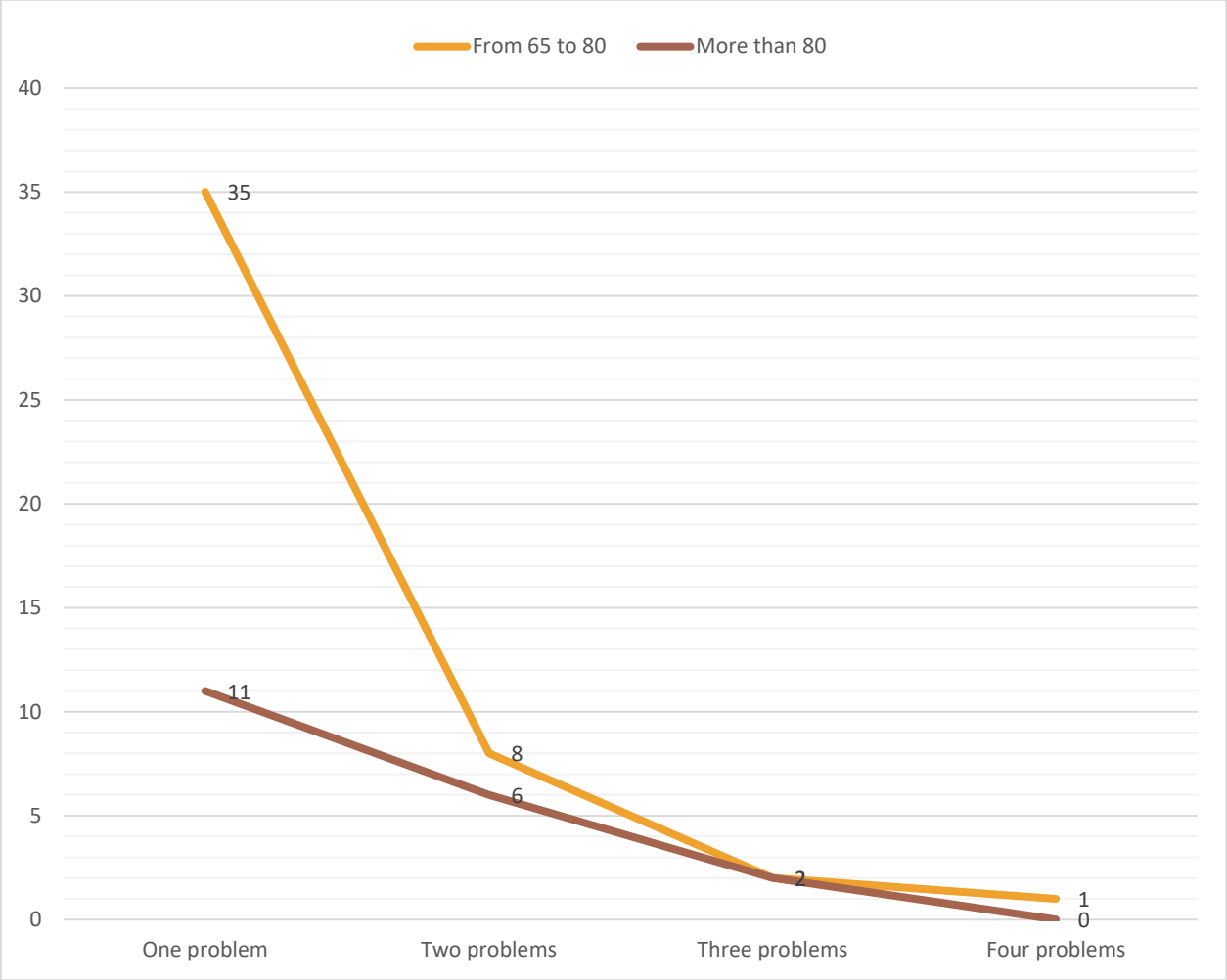
The patients whose age over than 80 years old with one problem was 11 patients, with two problems was 6 patients, with three problems was 2 patients and no one with four problems.

The total of one problem for both 65-80, over than 80 was 46 out of 65 cases.

Table 7 : Relationship between ages and number of problems

		No. problems				Total
		1	2	3	4	
Ages	from 65 to 80	35	8	2	1	46
	Over than 80	11	6	2	0	19
Total		46	14	4	1	65

Fig 5: Relationship between age and number of problems



3.5 Relationship between numbers of medications with number of problems

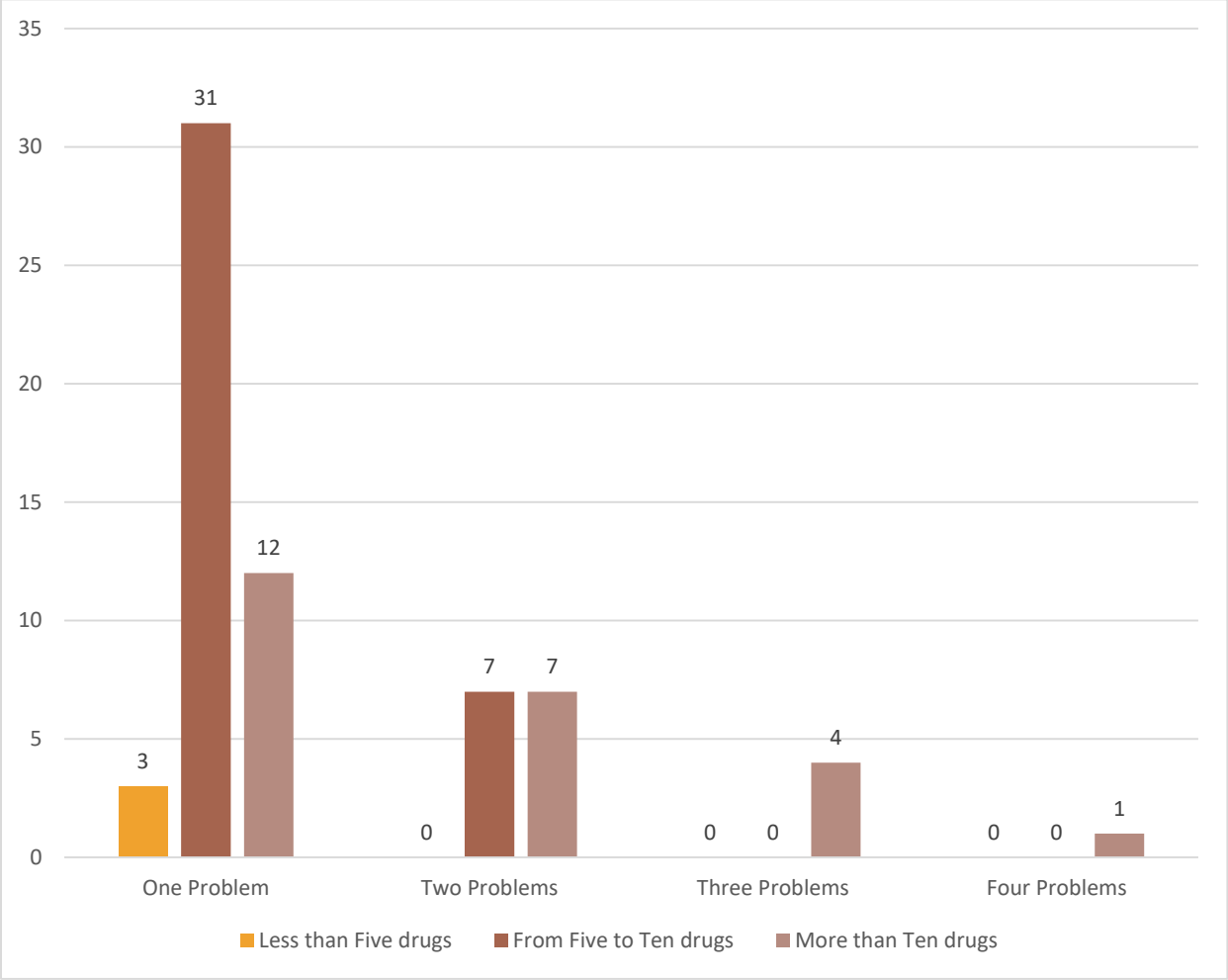
By reviewing 65 patients we classified their drugs in three categories, the number of patients who was taking from five drugs up to ten with one problem was (31) patients, with two problems the number was (7) patients.
But, the number of patients who was taking more than ten drugs with three problems was (4) patients.

The following chart clarifies number of medication with number of problems.

Table 8 : Relationship between number of medications with number of problems

		No. problems				Total
		1	2	3	4	
NO. medication	Less than five drugs	3	0	0	0	3
	From five to ten drugs	31	7	0	0	38
	More than ten drugs	12	7	4	1	24
Total		46	14	4	1	65

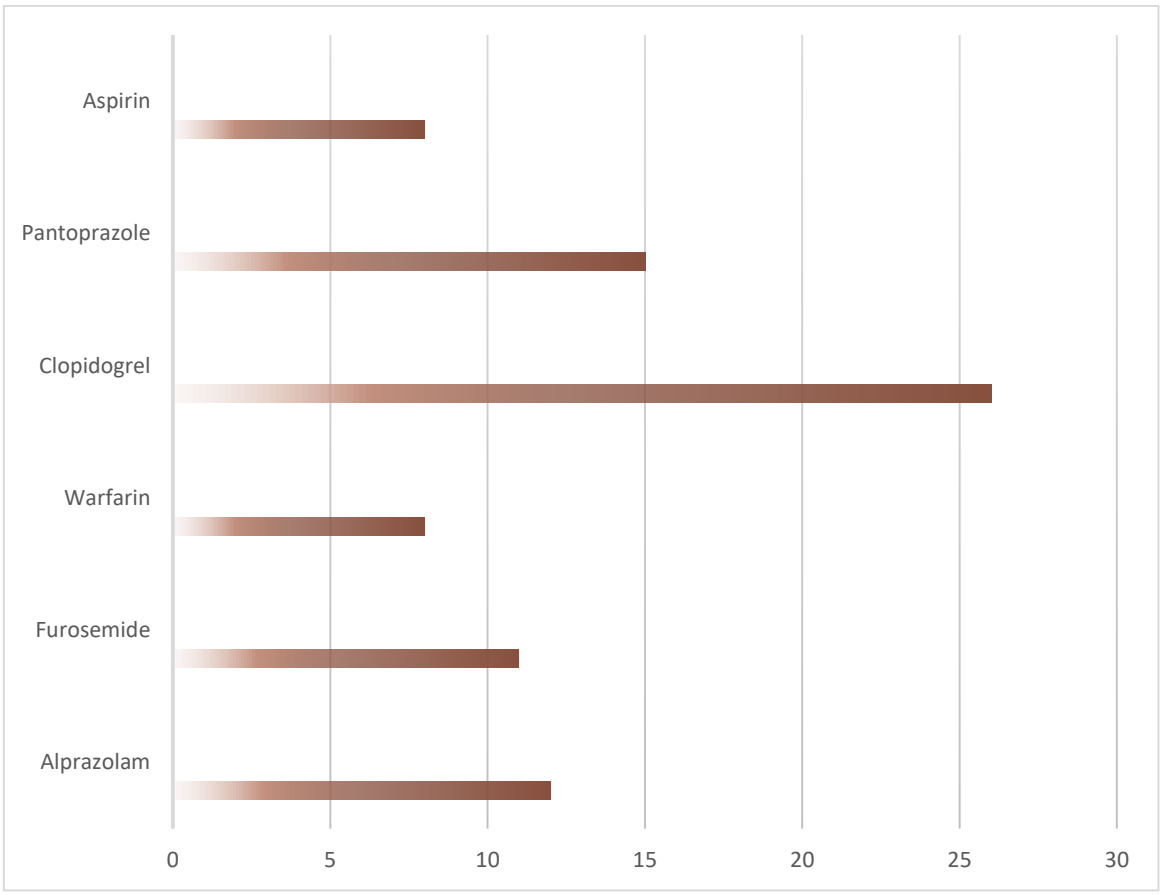
Fig 6: Relationship between numbers of medications with number of problems (columns)



3.6 medications with DRPs

By reviewing the medication for our patients, we specified causing the most DRP medications.

Fig 7: **medications with DRPs**



4 DISCUSSIONS

Out of 106 patients (68 were male and 38 were female), 65 (**61.3**%) patients had at least one DRP. The total number of DRPs identified was 92.With 67% of males had at least one DRPs and 52% of females had at least one DRPs. Age and gender may not be as important as the number of drugs prescribed as predictors of experiencing a DRP in patients with polypharmacy, in our study we included the elderly patients (65 years old and over) and excluded the others. (See methodology section). The average patient age was 76.6 years old (SD 7.4). Polypharmacy was obvious as the average number of medicines prescribed per patient was 8.51.

The number of an active medical conditions were 1.4 per patient which corresponds to obvious multiple morbidities. Also, in the present study, DRPs increased with increasing numbers of medications per patient, and with increasing number of chronic conditions per patient. The four primary medication classes associated with DRPs were anticoagulants (26%), PPIs (14.9%), antidepressants (12%) and diuretics (11%). Antidepressants and PPIs were the main DRPs type adverse drug event (possibly) occurring, the cause was inappropriate drug according guidelines but contra indication (C1.2) 31.5%. PPIs and antibiotics had the same type and cause of DRPs, which were given as unnecessary treatment with no specific. The low dose of diuretics prescribed was the major cause of the noted problems associated with the effect of drug not optimal

ACE/ARB inhibitors are the first-line of treatment for CHF. (Yancy, 2013) However, ACEI and antiplatelet drugs were the major medication classes that clinical pharmacists suggested be added to patients' treatment plans (indication without medication).

Treatment cost-effectiveness, unclear problem/complaint and patient related category were the least identified DRPs might be due to the limitations of the study and the difficulty to contact with patients.

Those problems happen because of the lack of clear guidelines for treating cardiovascular patients in the hospital, and no clinical pharmacist role in reviewing drugs for each patient

In comparing ages with number of problems we found that the number of problems increases while the ages increase (Mean=1.75 for patients over than 80 years old) and (Mean=1.18 for patients ages between 65 and 80 years old), due to polypharmacy and number of morbidity. But, we cannot generalize this because of its need more studies and small number of patients

Those results consider normal in comparing with other studies. Several studies in cardiology clinics showed a different number of DRPs per patient. For example, an 8-month study in the general medicine and cardiology departments in a tertiary care hospital in Coimbatore, India reported a mean of 4.9 DRPs per patient. Also, 394 DRPs were identified in 80 patients (Abraham, Drug related problems and reactive pharmacist interventions for inpatients receiving cardiovascular drugs, 2014).

While a 5-week study in a cardiology clinic at a teaching hospital in Nitra, Slovakia, reported a mean of 1.3 DRPs per patient. Also, 73 medication records were analyzed where minimally one DRP was found in 27 (37%) medication records, and 36 DRPs were identified. (B, 2015)

These studies varied between countries with their hospitals by patient number, study duration, presence of a clinical pharmacist prior to the study, physician collaboration and many other factors.

- Limitations of the study

This study has the following limitations: first, our study is retrospective, that's prevented us from applying intervention and sees the outcomes clinically in patients. Second, the only source of our information was the patient's files that not allowed us to contact with patients and indicate other problems. Third, our time limit and small number of the sample we can't generalizing our study findings. We recommend further controlled multicenter studies, where interventions are evaluated regarding both updated therapy guidelines and clinical endpoint, to further characterize DRPs incidence.

5 Conclusions

Drug-related problems among geriatric patients especially with cardiovascular disease are common, because of their polypharmacy and multi-diseases with ageing those problems could be avoided by including more pharmacists whose play a major role in providing healthcare with their knowledge in drugs and their associated problems.

The identification and documentation of DRPs are an important part that will eventually lead to reduce and solve the frequently incidence drug-related problems.

The most frequently reported DRPs among this population were the adverse drug event (possible) occurring (52.2%).

The most apparent cause that contributed to the DRPs incidence was the Drug selection.

At least including one pharmacist in the health centers will increase the chance to avoid drug and dose selection-related problems. According to this study, the pharmacists identified 61.3% of DRPs cases.

6 REFERENCES

A, A. H. (2014). A systematic review of hospitalization resulting from medicine-related problems in adult patients. pp. 202-17.

Abdela, O. A. (2016). Risk factors for developing drug-related problems in patients with cardiovascular diseases attending Gondar University Hospital, Ethiopia. *J Pharm Bioallied Sc* , 289.

Abdulaziz Altowaijri. (2013). A Systematic Review of the Clinical and Economic Effectiveness of Clinical Pharmacist Intervention in Secondary Prevention of Cardiovascular Disease. *JMCP* .

ACCP. (2008). The definition of clinical pharmacy. Pharmacotherapy. *American College of Clinical Pharmacy* .

ACG Egberts, v. d. (2007). Drug-related problems: definitions and classification. *EJHPPractice* , 62-64.

ADUSUMILLI PK, A. R. (2014). DRUG RELATED PROBLEMS: AN OVER VIEW OF VARIOUS CLASSIFICATION SYSTEMS. *Asian Journal Pharmaceutical and Clinical Research* , 7-10.

Age-related changes in pharmacokinetics and pharmacodynamics:. (n.d.).

Aging, N. I. (2010). Global Health and Aging. *Journal of Gerontological Nursing, .*

AK, D. (1996). Cardiovascular disease in elderly patients. *Mayo clin* .

Al-Baghdadi, H. (2017). Introducing clinical pharmacy services to cardiovascular clinics at a university hospital in Northern Cyprus. *Int J Clin Pharm* , 10-1007.

Alomar, M. J. (2014). Factors affecting the development of adverse drug reactions (Review article). *Saudi Pharmaceutical Journal* , 83-94.

Anderson GD, L. A. (2009). Optimizing pediatric dosing: a developmental pharmacologic approach. *Pharmacotherapy* , 680-690.

B, K. (2015). Medication review in inpatients at cardiology clinic/Prehodnotenie terapie u hospitalizoe. Acta Facultatis. 62.

BALIDEMAJ, F. (2013). Assessment of Pharmacists' Role in Non-Governmental Organizations and Their Humanitarian Effort in Refugee Camps Worldwide. *UNIVERSUM COLLEGE WORKING PAPER SERIES* .

Basger BJ1, M. R. (2014). Application of drug-related problem (DRP) classification systems: a review of the literature. *European Journal of Clinical Pharmacology* , 799-815.

Beard, K. (1992). *Management of elderly patients with sustained hypertension.* BMJ.

Beckett NS, P. R. (2008). Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* , 1887-98.

Bedouch P, A. B. (2008). Drug-related problems in medical wards with a computerized physician order entry system. *Journal of Clinical Pharmacy and Therapeutics* , 187-195.

Birarra MK, H. T. (2017). Assessment of drug-related problems in pediatric ward of Zewditu Memorial Referral Hospital, Addis Ababa, Ethiopia. *International Journal of Clinical Pharmacy* , 1039-1046.

Bond, C. A. (2002). Clinical Pharmacy Services, Hospital Pharmacy Staffing, and Medication Errors in United States Hospitals. *Bond et al* .

Boss et al, G. R. (1981). Age-related physiological changes and their clinical significance. . *Western Journal of Medicine,* , 135(6), 434.

Budnitz DS, S. N. (2007). Medication use leading to emergency department visits for adverse drug events in older adults. *Annals of Internal Medicine* , 755-765.

Bushra R, B. S. (2015). ADVERSE DRUG REACTIONS: FACTORS AND ROLE OF PHARMACIST IN THEIR PREVENTION. *Journal of Ayub Medical College Abbottabad* , 702-706.

Buurma, E. I. (2004). Drug related problems identified by European community pharmacists in patients discharged from hospital. *Pharmacy World and Science* , 353-360.

CDC, C. f. (2013). *INTESTINAL PARASITE GUIDELINES FOR DOMESTIC.* U.S. Department of Health and Human Services.

Cipolle, R. J. (2012). *Pharmaceutical Care Practice, Edition3, CHAPTER 5. Drug Therapy Problems* . McGraw-Hill Education.

Clavenna A, B. M. (2009). Adverse drug reactions in childhood: a review of prospective studies and safety alerts. *BMJ Journals* , 724-728.

CMS, C. f. (2015). *Adverse Drug Events – What Do We Really Mean?* England Quality Innovation Network.

CW, Y. (2013). guideline for the management of heart failure. *AHA* .

Daynes L. (2016). The health impacts of the refugee crisis: a medical charity perspective. *Clinical Medicine* , 437-440.

De Gregori S, D. G. (2009). Drug transporters and renal drug disposition in the newborn. *The Journal of Maternal-Fetal & Neonatal Medicine* , 31-37.

DG, W. (2002). A comparison of rate control and rhythm control. *N Engl J Med* , 1825.

DH, s. (1988). New issues in geriatric care. *ann intern mwd* , 718-32.

Dipak Chandy, W. S. (2013). Current perspectives on treatment of hypertensive patients with chronic obstructive pulmonary disease. *Integrated Blood Pressure Contro* , 101-109.

DP, R. (1985). the economic costs of illness. *health care finance* , 61-80.

EFRA. (2015). *Cost of exclusion from healthcare, the case of migrants.* European Union Agency for Fundamental Rights.

El-Eraky H, T. S. (2003). Effects of sex on the pharmacokinetic and pharmacodynamic properties of quinidine. *Br J Clin Pharmacol* , 198-204.

Emily R. Hajja, A. C. (2007). Polypharmacy in Elderly Patients. *The American Journal of Geriatric Pharmacotherapy* , 345-351.

Eran Klein, D. B. (2013). Postmarketing adverse drug reactions. *Neurology: Clinical Practice* , 288-294.

Ernst FR, G. A. (2001). Drug-related morbidity and mortality: updating the cost-of-illness model. *Journal of the American Pharmacists Association* , 192-199.

Fog AF, K. G. (2017). Drug-related problems and changes in drug utilization after medication reviews in nursing homes in Oslo, Norway. *Scandinavian Journal of Primary Health Care* , 1-7.

G, C. (1997). Drug-related problems in elderly patients admitted to Tayside hospitals, methods for prevention and subsequent reassessment. 375-82.

Ginny D. Crisp, J. I. (2011). Development and testing of a tool for assessing and resolving medication-related problems in older adults in an ambulatory care setting: the individualized medication assessment and planning (iMAP) tool. *The American Journal of Geriatric Pharmacotherapy* , 451-460 V9.

Gustafsson M. (2016). Optimizing drug therapy among people with dementia: the role of clinical pharmacists. *(Doctoral dissertation, Umeå universitet)* , 1.

Hajjar ER, H. J. (2003). Adverse drug reaction risk factors in older outpatients. *The American Journal of Geriatric Pharmacotherapy* , 82-89.

Hamid, A. (2014). A systematic review of hospitalization resulting from medicine-related problems in adult patients. pp. 202-17.

Hasniza Zaman, L. C. (2013). Drug-related problems in type 2 diabetes mellitus patients with dyslipidemia. *BMC Public Health* , 13:1192.

Hewick et al, D. S. (n.d.). Age as a factor affecting lithium therapy. *British journal of clinical pharmacology* , 4(2), 201-205.

Horowitz IN, T. K. (2007). Hypoalbuminemia in critically ill children. *Archives of Pediatrics & Adolescent Medicine* .

Hussain Al Rahbi, R. M.-S. (2014). *Interventions by pharmacists in out-patient pharmaceutical care.* 101-106: Saudi Pharmaceutical Journal.

Huysmans K, D. W. (2014). Drug related problems in Belgian community pharmacies. *Journal De Pharmacie De Belgique* , 4-15.

Ibáñez L, L.-B. A. (2009). Abdominal fat partitioning and high-molecular-weight adiponectin in short children born small for gestational age. *The Journal of Clinical Endocrinology and Metabolism* , 1049-1052.

Jackson, H. D. (2007). Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *British Journal of Clinical Pharmacology* , 1365.

JB, C. (1999). heart failure survival among older adults in the United States. *Arch Intern Med* , 505-10.

JK, G. (1990). trend in hospitaliztion rates for heart failure. *hyattsville* , 769-773.

Johnson JA, B. J. (1995). Drug-related morbidity and mortality. A cost-of-illness model. *Archives of Internal Medicine* .

Jose J, R. P. (2006). Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacological Research* , 226-233.

Katja M. Hakkarainen, K. H. (2012). Percentage of Patients with Preventable Adverse Drug Reactions and Preventability of Adverse Drug Reactions – A Meta-Analysis. *PLOS One* , 33-39.

Kaufmann CP1, S. D. (2014). Determination of risk factors for drug-related problems: a multidisciplinary triangulation process. p. 006376.

KK, V. (2007). Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. pp. 187-95.

KL, R. (2012). Drug-related problems and hospital admissions in cardiac transplant recipients. *Ann pharmacother* , 307.

Klotz. (2009). Pharmacokinetics and drug metabolism in the elderly. *Drug Metabolism Reviews* , 67-76.

Knapp DE, T. D. (1987). *Second Annual Adverse Drug/Biologic Reaction Report: 1986.* 1499-1503: Food and Drug Administration FDA.

L, W. (1992). Drug therapy in the elderly. *South* , 127.

LaPointe NM1, J. J. (2003). Medication errors in hospitalized cardiovascular patients. (pp. 1461-6). Arch Intern Med.

Lazarou J, P. B. (1998). Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *The Journal of the American Medical Association* , 1200-1205.

Lazarou J, P. B. (1998). Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *The Journal of the American Medical Association* , 1200-1205.

LILA ELVEBACK. (2015). Continued high incidence of coronary artery diseaseat autopsy in Olmsted County, Minnesota,. *CONS CALIFORNIA DIG LIB* .

Linda M. Strand, P. C. (1990). DRUG-RELATED PROBLEMS: THEIR STRUCTURE AND FUNCTION.

Liu X, T. E. (1996). Probabilities and lifetime durations of short-stay hospital and nursing home use in the United States, 1985.

LM, S. (1990). Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm* , 533-43.

M, J. (2003). Heart failure. *N Engl J Med* .

M. M. Breteler. (1994). Cardiovascular disease and distribution of cognitive function in elderly people: the Rotterdam Study. *BMJ* .

Makkar RR1, F. B. (1993). Female gender as a risk factor for torsades de pointes associated with cardiovascular drugs. JAMA.

Malkawi, U. S. (2013). *At a glance: Health data for Syrian refugees.* UNHCR.

Mangoni AA, J. S. (2004). *Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications* (Vol. 57:6Y14). Br J ClinPharmacol.

McDonnell. (2002). Hospital admissions resulting from preventable adverse drug reactions. pp. 1331-6.

MD, F. (2005). -mortality and cardiovascular hospital admission in elderly. . *Eur Heart J* .

Melvin D. Cheitlin, M. (2003). Cardiovascular Physiology—. *THE AMERICAN JOURNAL OF GERIATRIC CARDIOLOGY* .

Miller SW. (2007). *Therapeutic drug monitoring in the geriatric patient. In: Murphy JE, ed. Clinical Pharmacokinetics* (4th ed.). Bethesda, MD: American Society of Health-System Pharmacists.

Mohamed Azmi Hassali, O. T.-T. (2016). Role of Pharmacists in Health Based Non-Governmental Organizations (NGO): Prospects and Future Directions. *Pharmaceutica Analytica Acta* , 1049-1056.

Molham's Volunteering Team. (2017). Retrieved from https://molhamteam.com

murray. (1997). Medication appropriateness index: putting a number on an old problem in older patients. *ann pharmacother* , 643-4.

N, D. (2007). *Gender-related differences in presentation, treatment, and outcome of patients with atrial fibrillation.* Coll Cardio.

NK, W. (1992). Cardiovascular disease in the elderly. *Curr Probl Cardiol* , 609.

O, U. (2015). Patient risk factors for developing a drug-related problem in a cardiology ward. *Ther Clin Risk Manag* , 11-9-15.

Oberbauer et al, R. K. (1993). Pharmacokinetics of indomethacin in the elderly. *Clinical pharmacokinetics,24(5)* , 428-434.

Ofotokun I, P. C. (2003). Sex differences in adverse reactions to antiretroviral drugs. *Topics in HIV Medicine Journal* , 55-59.

Oleg O. Bilukha, D. J. (2014). *Nutritional Status of Women and Child Refugees from Syria — Jordan.* Morbidity and Mortality Weekly Report.

Olsson, S. (2015). Pharmacovigilance in resource-limited countries. *Expert Review of Clinical Pharmacology , 4*, 449-460.

Ousman Abubeker Abdela, A. (2016). Risk factors for developing drug-related problems in patients with cardiovascular diseases attending Gondar University Hospital, Ethiopia. *J Pharm Bioallied* , 289-295.

oxford, u. (1993). *world development report.* new york: world bank.

Patel P, Z. P. (2002). Drug-related visits to the emergency department: how big is the problem? *Pharmacotherapy* , 915-923.

PCNE, P. C. (2017). *Drug-related problems classification.* Retrieved from Pharmaceutical Care Network Europe Foundation: http://www.pcne.org/upload/files/152_PCNE_classification_V7-0.pdf

PCNE, P. C. (2017). *PCNE drug related problem classification*. Retrieved from PCNE: http://www.pcne.org/working-groups/2/drug-related-problem-classification

Pellicer A, B. M. (2009). Early systemic hypotension and vasopressor support in low birth weight infants: impact on neurodevelopment. *Pediatrics Journal* , 1369-1375.

Peterson CC. (2017). Characterization of drugrelated problems and associated factors at a clinical pharmacy-naïve hospital. *in the northern part of Sweden* , .

Peterson, C. (2017). Characterisation of Drug-Related Problems and Associated Factors at a Clinical Pharmacist Service-Naïve Hospital in Northern Sweden. pp. 97-107.

Portnoi, V. A. (1979). Digitalis delirium in elderly patients. . *The Journal of Clinical Pharmacology* , 19(11), 747-750.

Rana Abu Farha, A. S. (2017). The impact of drug related problems on health-related quality of life among hypertensive patients in Jordan. *Pharmacy Practice (Granada)* , 995-1001.

Rigby et al, J. W. (1985). A comparison of the pharmacokinetics of atenolol, metoprolol, oxprenolol and propranolol in elderly hypertensive and young healthy subjects. . *British journal of clinical pharmacology,* , 20(4),327-331.

RR, A. (2012). Drug Related Problems and Reactive Pharmacist Interventions for Inpatients Receiving Cardiovascular Drugs. *Am J Pharm Tech Res* .

RR, A. (2014). Drug related problems and reactive pharmacist interventions for inpatients receiving cardiovascular drugs. *IJBMSP* .

S, S. (1994). Drug disposition and hepatotoxicity in the elderly. *J Clin Gastroenterol* , 232-7.

Sadek, G. (2014). *Legal Status of Refugees: Egypt, Jordan, Lebanon, and Iraq.* The Law Library of Congress, Global Legal Research Center.

Schoderboeck L, A. M. (2009). The "window of susceptibility" for inflammation in the immature central nervous system is characterized by a leaky blood-brain barrier and the local expression of inflammatory chemokines. *Neurobiology of Disease* , 368-375.

Shah Jainam V.a, P. K. (2016). *A Study of Role of Clinical Pharmacist in Medication Review and Patient Education.* . International Journal of Pharma Sciences and Research.

Shannon Doocyr, E. L.-Z. (2015). Prevalence and care-seeking for chronic diseases among Syrian refugees in Jordan. *BMC Public Health* , 1097-1114.

Shareef, J. (2014). Assessment of Drug Related Problems in Patients with Cardiovascular Diseases in a Tertiary Care Teaching Hospital. *JPC* .

Shi S1, M. K. (2008). The clinical implications of ageing for rational drug therapy. pp. 183-99.

Shi, S. &. (2011). Age-related changes in pharmacokinetics. *Current drug metabolism* , 12(7), 601-610.

Sight, U. f. (2017). *Healthcare in Refugee Camps and Settlements*. Retrieved from www.uniteforsight.org: https://www.cdc.gov/immigrantrefugeehealth/profiles/congolese/healthcare-access/index.html

Solheim K. (2005). Patterns of community relationship: nurses, non-governmental organizations and internally displaced persons. *International Nursing Review* , 60-67.

Somogyi et al, A. H. (1990). Amiloride disposition in geriatric patients: importance of renal function. *British journal of clinical pharmacology, ,* 29(1), 1-8.

Sotaniemi EA, A. A. (1997). *Age and cytochrome P450–linked drug metabolism in humans.* Clin Pharmacol Ther.

Swift, C. G. (1990). Pharmacodynamics: changes in homeostatic mechanisms, receptor and target organ sensitivity in the elderly. . *British medical bulletin* , 46(1), 36-52.

T Strunk, A. C. (2011). Innate immunity in human newborn infants: prematurity means more than immaturity. *The Journal of Maternal-Fetal & Neonatal Medicine* , 25-31.

Tom G. Bartol, N. (2015, July 02). Which Drugs Should Be Deprescribed in the Elderly? *Medscape Nurses* , p. 2.

Turnheim K. (2004). *Drug therapy in the elderly* (Vol. 39:1731Y1738). Exp Gerontol.

U., K. (2009). Pharmacokinetics and drug metabolism in the elderly. *Drug Metabolism Reviews* .

U.S Food and Drug Administration. (August 1994). *Guidline for industry: Studies in Support of Special population. Geriatrics.*

uhl-Melcher, A. K. (2007). Drug-Related Problems in Hospitals. (p. 5916). Adis Data Information .

UN. (2015). *International migration report.* United nation.

UNHCR. (2017, November). *Statistics* . Retrieved from http://www.unhcr.org/figures-at-a-glance.html

UNHCRemergency. (2017). *Health in camps.* UNHCR.

UNHCRreport. (2016). *Regional Refugee & Resilience Plan 2016-2017.* UNHCR.

Viktil, H. S. (2004). The majority of hospitalised patients have drug-related problems: results. Eur J Clin Pharmacol.

Viktil, K. K. (2006). Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *British Journal of Clinical Pharmacology* , 187-195.

Vinks et al, T. H. (2006). Identification of potential drug-related problems in the elderly: the role of the community pharmacist. *Pharmacy world & science* , 28(1), 33-38.

Wan He, D. G. (March 2016). *An Aging World: 2015.* Bureau, U.S. Census, Washington: U.S. Government Publishing Office.

WB, k. (1998). *incidence and hazrd of hypertension in elderly.* 5-10.

WHO. (1995). *epidemiology and prevention of CVD in elderly poeople.* Geneva.

WHO. (2011). *Noncommunicable diseases country profiles.*

WHOannex, A. T. (2009). *Glossary of Patient Safety Concepts and References.* World health organization.

WHOeuro. (2017). *Migration and health: key issues.* Retrieved from World health organization Europe: http://www.euro.who.int/en/health-topics/health-determinants/migration-and-health/migrant-health-in-the-european-region/migration-and-health-key-issues#292936

WHOprogrammes. (2016). *Global Tuberculosis Report.* Retrieved from World Health Organization:

WS, A. (2008). pathophysiology, and treatment of atrial. *Cardiol Rev* , 181-8.

Zaal RJ, J. M.-v. (2013). *Identification of drug-related problems by a clinical pharmacist in addition to computerized alerts.* 753-765: International Journal of Clinical Pharmacy.

Zaal RJ1, J. M.-v. (2013). Identification of drug-related problems by a clinical pharmacist in addition to computerized alerts. *International Journal of Clinical Pharmacy* , 753-765.

Zeinab Hijazi, I. W. (2014). *Addressing Regional Mental Health Needs and Gaps in the Context of the Syria Crisis.* International Medical Corps.

Appendixes

Near East University Hospital

Drug related problems in elderly patients with cardiovascular diseases at University Hospital in Northern Cyprus

Advisor: Assis. Prof. Dr: Arijana M Co-advisor:Dr. Abdikarim A investigator: Mouaz Y

Demographic information

Patient no.	H.unit	Wt.kg	Date	Age "YRS"	Gender
			/ /		M F

Past medical history	Current diagnosis	Staying periods	Sr.cr

Medical charts

No	Trade name	Generic name	Dose & duration	Indication	Time& day
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					

BP	PO2	HR	EF	Additional information
/				
Other abnormal lab results				
				Name Phone no.

EK: 638-2018

YAKIN DOĞU ÜNİVERSİTESİ
BİLİMSEL ARAŞTIRMALAR DEĞERLENDİRME ETİK KURULU

ARAŞTIRMA PROJESİ DEĞERLENDİRME RAPORU

Toplantı Tarihi : 29.03.2018
Toplantı No : 2018/56
Proje No : 549

Yakın Doğu Üniversitesi Eczacılık Fakültesi öğretim üyelerinden Assis. Prof. Dr Arijana Meštrović'in sorumlu araştırmacısı olduğu, YDU/2018/56-549 proje numaralı ve **"Drug Related Problems İn Elderly Patients With Cardiovascular Diseases At University Hospital İn Northern Cyprus"** başlıklı proje önerisi kurulumuzca değerlendirilmiş olup, etik olarak uygun bulunmuştur.

1. Prof. Dr. Rüştü Onur (BAŞKAN)
2. Prof. Dr. Nerin Bahçeciler Önder (ÜYE)
3. Prof. Dr. Tamer Yılmaz (ÜYE)
4. Prof. Dr. Şahan Saygı (ÜYE)
5. Prof. Dr. Şanda Çalı (ÜYE)
6. Prof. Dr. Nedim Çakır (ÜYE)
7. Prof. Dr. Kaan Erler (ÜYE) Katılmadı
8. Doç. Dr. Ümran Dal Yılmaz (ÜYE)
9. Doç. Dr. Nilüfer Galip Çelik (ÜYE)
10. Yrd. Doç.Dr. Emil Mammadov (ÜYE)

Patient_____

Male ☐ Female ☐

Medication and dosing regimen

A _____

B _____

A: OTC ☐ Rx ☐ (B): OTC ☐ Rx ☐

DRP potential ☐

manifest ☐

1. Type of problem
(tick one box only)

- P1 ☐ **Treatment effectiveness**
  - P1.1 ☐ No effect of drug treatment
  - P1.2 ☐ Effect of drug treatment not optimal
  - P1.3 ☐ Untreated symptoms or indication
- P2 ☐ **Treatment Safety**
  - P2.1 ☐ Adverse drug event (possibly) occurring
- P3 ☐ **Others**
  - P3.1 ☐ Problem with cost-effectiveness of the treatment
  - P3.2 ☐ Unnecessary drug-treatment
  - P3.3 ☐ Unclear problem/complaint. Further clarification necessary
  - P3.4 ☐ Compromise quality of the medicine

Notes:

2. Cause of problem
(one problem can have more than one cause)

- C1 ☐ **Drug selection**
  - C1.1 ☐ Inappropriate drug according to relevant (national or international) guidelines/formulary as applicable
  - C1.2 ☐ Inappropriate drug (within guidelines but otherwise contra-indicated)
  - C1.3 ☐ Medication without indication
  - C1.4 ☐ Inappropriate combination of drugs or drugs and herbal medication
  - C1.5 ☐ Inappropriate duplication of therapeutic group or active Ingredient
  - C1.6 ☐ Indication without medication
  - C1.7 ☐ Too many drugs prescribed for indication
- C2 ☐ **Drug form**
  - C2.1 ☐ Inappropriate drug form (for this patient)
- C3 ☐ **Dose selection**
  - C3.1 ☐ Drug dose too low
  - C3.2 ☐ Drug dose too high
  - C3.3 ☐ Dosage regimen not frequent enough
  - C3.4 ☐ Dosage regimen too frequent
  - C3.5 ☐ Dose timing instructions wrong, unclear or missing
- C4 ☐ **Treatment duration**
  - C4.1 ☐ Duration of treatment too short
  - C4.2 ☐ Duration of treatment too long
- C5 ☐ **Dispensing**
  - C5.1 ☐ Prescribed drug not available
  - C5.2 ☐ Necessary information not provided
  - C5.3 ☐ Wrong drug, strength or dosage advised (including OTC, herbal or any other medications if applicable)
  - C5.4 ☐ Wrong drug, strength or dosage dispensed
- C6 ☐ **Drug use process**
  - C6.1 ☐ Inappropriate timing of administration and/or dosing Intervals
  - C6.2 ☐ Drug dosage under-administered
  - C6.3 ☐ Drug dosage over-administered
  - C6.4 ☐ Drug not administered at all
  - C6.5 ☐ Wrong drug administered
  - C6.6 ☐ Drug administered via wrong route
- C7 ☐ **Patient related**
  - C7.1 ☐ Patient uses/takes less drug than prescribed or does not take the drug at all
  - C7.2 ☐ Patient uses/takes more drug than prescribed
  - C7.3 ☐ Patient abuses drug (unregulated overuse)
  - C7.4 ☐ Patient uses unnecessary drug
  - C7.5 ☐ Patient takes food that interacts
  - C7.6 ☐ Patient stores drug inappropriately
  - C7.7 ☐ Inappropriate timing or dosing intervals
  - C7.8 ☐ Patient administers/uses the drug in a wrong way/technique
  - C7.9 ☐ Patient unable to use drug/form as directed
- C8 ☐ **Other**
  - C8.1 ☐ No or inappropriate outcome monitoring (incl. TDM)
  - C8.2 ☐ Other cause; specify
  - C8.3 ☐ No obvious cause

3. Type of intervention
(one problem can lead to more than one intervention)

- I0 ☐ **No intervention**
  - I0.1 ☐ No intervention
- I1 ☐ **At prescriber level**
  - I1.1 ☐ Prescriber informed only
  - I1.2 ☐ Prescriber asked for information
  - I1.3 ☐ Intervention proposed, approved by prescriber
  - I1.4 ☐ Intervention discussed with prescriber
- I2 ☐ **At patient / carer level**
  - I2.1 ☐ Patient (drug) counselling
  - I2.2 ☐ Written information provided only
  - I2.3 ☐ Patient referred to prescriber
  - I2.4 ☐ Spoken to family member / caregiver
- I3 ☐ **Atpharmacistlevel**
  - I3.1 ☐ Drug changed to ...
  - I3.2 ☐ Dosage changed to ...
  - I3.3 ☐ Formulation changed to ...
  - I3.4 ☐ Instructions for use changed to ...
  - I3.5 ☐ Drug stopped
- I4 ☐ **Other**
  - I4.1 ☐ Nurse administration
  - I4.2 ☐ Side effect reported to authorities
  - I4.3 ☐ Other intervention (specify)

4. Intervention Acceptance
(tick one box only)

- A1 ☐ **Interventionaccepted**
  - A1.1 ☐ Intervention accepted and fully implemented
  - A1.2 ☐ Intervention accepted, partially implemented
  - A1.3 ☐ Intervention accepted but not implemented
  - A1.4 ☐ Intervention accepted, implementation unknown
- A2 ☐ **Intervention not accepted** (byprescriber caregiver orpatient)
  - A2.1 ☐ Intervention not accepted: not feasible
  - A2.2 ☐ Intervention not accepted: no agreement
  - A2.3 ☐ Intervention not accepted: other reason (specify)
  - A2.4 ☐ Intervention not accepted: unknown reason
- A3.1 ☐ **Intervention proposed, acceptance unknown**
- A3.2 ☐ **Intervention not proposed**

5. Outcome of Intervention
(tick one box only)

- O0 ☐ **Problem status unknown**
- O1 ☐ **Problem totally solved**
- O2 ☐ **Problem partially solved**
- O3 ☐ **Problem not solved**
  - O3.1 ☐ Lack of cooperation of patient
  - O3.2 ☐ Lack of cooperation of prescriber
  - O3.3 ☐ Lack of cooperation of pharmacist
  - O3.4 ☐ Lack of cooperation of nurse
  - O3.5 ☐ Intervention not effective
  - O3.6 ☐ No need or possibility to solve problem

Examples of Treatment Safety: adverse drug event (possibly) occurring					
Drug A	**Drug B**	Severity	clinical significance	Recommendation	Frequency
Pantoprazole Omeprazole	**Clopidogrel**	Moderate	Reduced therapeutic efficacy of Clopidogrel	Monitor the therapeutic efficacy of clopidogrel during concomitant treatment	7
Spironolactone **Valsartan**	**Potassium chloride**	Major	Hyperkalemia	Serum potassium and renal function should be checked regularly	2
Warfarin	**Enoxaparin**	Major	Risk of bleeding	Any agent that can enhance the risk of hemorrhage including other anticoagulants should be discontinued prior to initiation of LMWH	2
Diltiazem	**Metoprolol**	Major	Additive reductions in heart rate, cardiac conduction, and cardiac contractility (combination may be useful and effective in some situations)	TDM Monitoring of patient hemodynamic response	1
Haloperidol	**Diltiazem**	Moderate	Orthostatic hypotension and syncope associated with vasodilation	A lower starting dosage and slower titration of the Haloperidol	1
Haloperidol **Tiotropium**	**Ipratropium**	Moderate	Additive anticholinergic effects such as mydriasis, blurred vision, heat intolerance, fever, dry mouth, tachycardia,	Inhaled anticholinergic preparations should preferably not be used in combination with other anticholinergic agents	2

Atorvastatin	**Diltiazem**	Moderate	Increase the plasma concentrations of Atorvastatin (increased risk of musculoskeletal toxicity and Myopathy)	Use the lowest effective statin dose	2
Aspirin	**Ticagrelor**	Moderate	Decrease the effectiveness of ticagrelor in preventing thrombotic events in patients with acute coronary syndromes	Daily maintenance dose of 75 to 100 mg is recommended	2
Amiodarone	**Furosemide**	Major	Risk of ventricular arrhythmias, including ventricular tachycardia	Serum electrolytes should be evaluated	1
Spironolactone	**Ramipril**	Major	Hyperkalemia	Serum potassium and renal function should be checked regularly	1
Clopidogrel	**Dabigatran**	Major	Risk of bleeding complications associated with the use of dabigatran.	Monitoring to bleeding complications,	1
Spironolactone	**Metoprolol**	Moderate	Hyperglycemia and Hypertriglyceridemia	Monitoring of serum potassium levels, blood pressure, and blood glucose	1
Citalopram	**Metoprolol**	Moderate	Bradycardia, Hypotension, and Complete heart block	TDM of Metoprolol	1
Citalopram	**Spironolactone**	Moderate	Hyponatremia	Monitoring of potential signs and symptoms of hyponatremia such as nausea, vomiting, headache, malaise, lethargy, irritability, difficulty concentrating, memory impairments	1
Quetiapine	**Spironolactone**	Moderate	Orthostatic hypotension and syncope	TDM of Quetiapine	1

			associated with vasodilation		
Enoxaparin	**Apixaban**	Major	Risk of bleeding	Close clinical and laboratory observation for bleeding complications	1
Furosemide	**Sucralfate**	Moderate	Reduce the absorption and therapeutic effects of oral furosemide	Oral furosemide and sucralfate doses should be separated by at least 2 hours.	1
Quetiapine	**Donepezil**	Moderate	Range from mild cognitive impairment to delirium	Avoid combination	1
Warfarin	**Sucralfate**	Moderate	Reduce its therapeutic effect of Warfarin	take the anticoagulant at least 2 hours before or 6 hours after the sucralfate to minimize a potential interaction	1
Allopurinol	**Ramipril**	Major	Risk of severe hypersensitivity reactions, neutropenia, agranulocytosis, and serious infections.	Monitoring of white blood cell counts is recommended	2
Cefuroxime	**Pantoprazole**	Moderate	Reduce the oral bioavailability of Cefuroxime	Avoid combination	1
Spironolactone	**Potassium sulfate**	Moderate	Fluid and electrolyte disturbances (cardiac arrhythmias, seizures, and renal impairment.)	Hospitalization and intravenous fluid hydration	2
Aspirin	**Apixaban**	Major	Risk of bleeding	Monitored for increased anticoagulant effects and bleeding complications	1
Doxazosin	**Tamsulosin**	Moderate	Postural hypotension, Dizziness, Headache, Syncope, Priapism, and Nasal congestion	Avoid combination	1

Severity	Frequency
Major	12
Moderate	25