T.R.N.C

NEAR EAST UNIVERSITY

INSTITUTE OF HEALTH SCIENCES

Applying Beers Criteria for Elderly Patients to Assess Rational Drug Use in Northern Cyprus

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BY:

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Master of Science in Clinical pharmacy

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DEDICATION

Dedicated to my great parents, supportive sisters, brothers

and all of my family andfriends.

Especially my cousin SalwaSaifan andDr. Aisha Yahya.

Who encourage me to higher ideas of life,

took pains and sacrificed their comforts for my brilliant

future.

And because of their support, help, prayers, and love I got

what I'm in.

I dedicate this work and give special thanks to my best

Teacher

Assoc. Prof. Dr. BilgenBasgut

Approval

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Abstract

Several sets of potential inappropriate prescriptions (P.I.P) criteria have been published which is designed specifically for older patients. Beers believed that ensuring the proper medication use in older patients must be a health care priority and should work as an advocate for responsible medication prescribing in the elderly patient. The potential inappropriate prescribing may occur when the risks outweigh the benefits of a prescription. In this study we are using beers criteria to assess the prescriptions of geriatric patients in Near East University Hospital North Cyprus.

In this study we carried a cross-sectional prospective analysis for 451 patients, were a sample consisting of119 geriatric patients prescriptions, that wereadmitted to Near East University Hospital in North Cyprus was withdrawn to assess degree of adherence with expert geriatric guidelines i.e. the Beers Criteria. Out of these 119 patients107 were eligible for assessment while 12 were excluded 9due to their incomplete data, 2 patients were terminally ill and 1 patient died during collecting data and thus were all excluded. The study was carried out between 25thSeptember and 25thOctober 2016. Special forms were used for collection of data.

The utilization of the most frequently criteria for the older patient medication “beers criteria 2015" was found well as 82% of 1039 prescribed medicine were adherent, however un preventable poly-pharmacy of elders and incidence of PIMs were seen high too as reported from elsewhere necessitating multidisciplinary approaches and incorporation of pharmaceutical care to further enhance adherence and improve drug safety in geriatric patients.

Key Words: Elderly, Geriatrics, Beers, criteria, Prescription, STOP, Rational drug use.

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LIST OF ABBRREVATIONS

S. #	ABBREVATIONS	EXPLANATION
1	AARP	American association of retired person
2	ADWE	Adverse Drug withdrawal event
3	AGS	American Geriatrics Society
4	BC	Beers Criteria
5	CME	Continuous Monitoring Emission System
6	Crcl	Creatinine Clearance
7	CYP450	Cytochrome P450 monooxygenase
8	DRP	Drug Related Problems
9	GI	Gastro-intestinal
10	IPET	Improved Prescribing in the Elderly Tool
11	IRB	Institutional Review Board
12	MAI	Medication Appropriateness Index
13	MTM	Medication Therapy Management
14	NP	Nurse Practitioner
15	OTC	Over the counter
16	pH	power of hydrogen
17	PIM	Potential Inappropriate Medication
18	PIP	Potential Inappropriate Prescription
19	START	Screening Tool to Alert to Right Treatment
20	STOPP	Screening Tool of Older Person Prescriptions

21	SPSS	Statistical Package for the Social Science
22	US	United State
23	WHO	World Health organization

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Chapter 1: Introduction

1.1 Changes and challenges in treating elderly patients

The life expectancy has increased over the past 100 years. The world population continues to grow older rapidly as fertility rates have fallen to low levels in most world regions and generally death rates tend to be lower. 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). About 80% of the world's elderly adults found in developing countries with a dearth quality of medical care (United Nations, 2013). 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). Figure 1 (International Data Base, December 2013), Figure 2 (U.S. Census Bureau).

A study in Canada recently showed that in a group of elderly patients, 15 (range, 6-28) was the average number of medications taken with 8.9 drug-related problems occurring per patient. When these problems were analyzed, they found out that 2.5 of those 8.9 problems were as a result of drugs that were not needed. 28% of hospitalizations in seniors in the United States are caused by medication-related problems (Tom G. Bartol, 2015) .

A number of age-related physiologic changes occur which may cause reductions in functional reserve capacity and could affect drug pharmacokinetics and pharmacodynamics, thus increase the rate of medication-related problems. This information's gap can improve with the implementation of Food and Drug Administration guidelines, the Geriatrics associations and studies for older adults (U.S Food and Drug Administration, August 1994) .

1.1.2 The Elderly Physiologic Changes

There are many progressive functional declines in most organs of the body with advancing age. The age-associated physiologic changes may cause a clear reduction in the capacity of functional reserve (for example the ability to respond to physiologic challenges and stresses)

and cause reductions in the ability to preserve homeostasis, thus may make elders more susceptible to decompensation in stressful situations.[(Kane RL, 2004), (Cusack BJ, 2004)] The systems that appear to be most affected are cardiovascular, musculoskeletal, and central nervous systems (Masoro EJ., 2003) .

There are a reasonable number of age-related physiologic changes that occur and could affect the drug pharmacokinetics and pharmacodynamics (U.S Food and Drug Administration, August 1994).

The changes in body composition are decreased total body water, lean body mass, muscle mass and increased body fat. Also changes in drug binding proteins, such as serum albumin and increases in the α1-acid glycoprotein.

The cardiovascular changes are decreased myocardial sensitivity to β-adrenergic stimulation, baroreceptor activity, cardiac output and increased total peripheral resistance and left ventricular hypertrophy.

Central nervous system changesare; decreased weight and volume of the brain, cognitive decline, memory impairment, predisposition to falls and autonomic baroreceptor dysfunction**.**

Endocrine changes are thyroid gland atrophy, increased incidence of diabetes mellitus and increased incidence of thyroid disease, post-menopausal concerns in women secondary to reduced endogenous estrogen production and a decrease in endogenous melatonin production by the pineal gland.

Gastrointestinal changes are an increase in gastric pH (more basic or alkaline intra-luminal pH), a decrease in gastrointestinal blood flow, delayed gastric emptying and decreased intestinal transit or decrease in gut peristalsis.

Hepatic changes are an overall decrease in liver mass, in liver blood flow, in a number of functional hepatocytes, reduction in function of certain mixed function oxidase enzymes and decreased production of endogenous clotting factors by the liver.

Respiratory tract changes are a decrease in respiratory muscle strength, decrease in chest wall compliance, decrease in total alveolar surface, decrease in lung vital capacity, a decrease in maximal breathing capacity and decrease in peak expiratory flow rate.

Renal changes are an overall decrease in renal mass, number of functional nephrons, glomerular filtration rate, renal blood flow, filtration fraction and tubular secretion with reduced basal renin levels.

Sensory changes are hearing loss, decreased visual acuity and accommodation of the lens of the eye resulting in farsightedness.

1.2 Pharmacokinetic changes that are related with age

With the advancement in age and because of the change in the body weight, several changes in pharmacokinetics may present in many elderly people, especially the changes in the volume of distribution and renal clearance (Hilmer SN, 2007) .

Pharmacokinetics is defined as" how the body processes the drug after administering it". Every drug has its specific pharmacokinetic profile which is based on specific parameters such as age, gender, body weight, body mass index, liver function, and renal function. When a specific drug is studied in specific patient types such as elderly patients, the understanding for the pharmacology will be better. Though the more popper doses can be established and the profile of a clear adverse effect can be determined.

Most of the elderly patients have several different diseases and they take many different medications which cannot be discontinued. Thus, to developan effective pharmacotherapeutic plan for an elderly patient is required to get a clear understanding of the pharmacokinetics principles (the absorption, the distribution, the metabolism, and the elimination) and how the pharmacokinetics of a drug may alter in the geriatric population and this consideration. (Turnheim K., 2004), (Hutchison LC, 2007), (Miller SW., 2007), (Greenblatt DJ, 2002).

1.2.1 Absorption

Most of the drugs are taken orally; that's why the number of age-related changes in the gastrointestinal physiology may affect the absorption of medications (Iber FL, 1994). The age-related changes can reduce the GI motility and also the GI blood flow. Gastric acid secretion is also reduced in older adults and this result in an elevation in the gastric pH. The

increase in the gastric pH and the reduction in gastric blood flow can cause reduced drug absorption, whereas the reduction in the GI motility can result in increased drug absorption. The ageing absorptive changes which can show a fluctuating gastric pH also can be influenced by medication use and may alter significantly the absorption of drugs as well as its onset of action [(Kapadia A, 2010)].

The drugs absorbed which undergo the first-pass metabolism also may increase in older people. However, there is an 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.

The net effect of all these changes is little difficult to predict and may it vary depended on the nature of drug that is being prescribed. Ageing changes that affects the drug absorption are generally considered minimal, but the elderly patients are at risk of developing other problems that may affect the absorption (Hutchison LC, 2007), (Mangoni AA, 2004), (Kapadia A, 2010).

1.2.2 Distribution

Drug distribution defined as" where the drug may go after it enters the bloodstream". For the orally drugs, the distribution phase begins after the absorption and the first-pass metabolism. And some drugs are also widely distributed into tissues, body fluids, and to the central nervous system by crossing the blood brain barrier. Some other drugs are never distributed well. (Turnheim K., 2004) (Hutchison LC, 2007) (Miller SW., 2007).

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), (Kapadia A, 2010).

The aging process could have a significant effect on how the drug is distributed in the body. In relation to the ages, 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 adult compared to a young adult. But for drugs that are distributed in the muscle tissue, the volume of distribution can be reduced and the aging process also may be associated with a

theoretical reduction in the total body water, which can affect the water-soluble drugs volume of distribution. Generally, the older adults produce fewer albumins that bind with drugs in the bloodstream. The reduction in the protein binding can result in increased free drug concentration, which causes increase in the pharmacologic effect in an elderly individual. (Greenblatt DJ, 2002).

P-glycoprotein can affect the transport of drugs that crosses the blood–brain barrier. Studies have demonstrated that there is a decrease in P-glycoprotein activity in the blood– brain barrier with aging. Thus, the brain of aged individuals may be more exposed to higher levels of drugs and toxins than normal levels of them.[(Toornvliet R, 2006)]

All of these effects may greatly influence the drug distribution and this determines the necessary dose that can produce a desired pharmacologic effect or unwanted adverse effects. The drug toxicity can result from the failure of taking these changes into consideration (Greenblatt DJ, 2002).

An important component to consider is how a drugs' volume of distribution may be altered in the elderly patient, which can help to determine more proper drug dose for all individuals. The drugs that have sufficient study for elderly patients to determine how the volume of distribution will change as a result of aging, can be dosed more precisely in this population. However, for drugs that lack such information, the dose should be reduced and should titrate to a specific effect.[(McLean AJ, 2004), (Roehl B, 2006)]

1.2.3 Metabolism

As we know, the liver is the primary organ responsible for the metabolism of the drug. Also, it can both synthesize various proteins, substrates enzymes and can convert chemicals (xenobiotics) from one form to another, this cause conversion of substances which are believed to be harmful to the body to a form which can be eliminated more easily. In general, the final by-product of the liver metabolism is water soluble and is readily eliminated via the kidney.

The liver can use various types of reactions to complete the transformation process. One of them is oxidative reactions (phase 1) which may occur via oxidation, reduction, hydrolysis, or

in one of the other types of the chemical conversions. Phase 1 reactions typically involve various types of Cytochrome P450 monooxygenase (CYP450) enzymes, which play roles 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. .[(Hutchison LC, 2007) (Miller SW., 2007)

Alteration of the normal metabolic process can affect the pharmacokinetics of drugs significantly. We note that one of the most remarkable characteristic factors of hepatic function in elderly adults is the increase in inter-individual variability compared with other age groups (Herrlinger C, 2001).

The data suggest that the age-related declines in the metabolism of phase 1 are more likely as a result of reduced hepatic volume than reduced hepatic enzymatic activity (Sotaniemi EA, 1997). Also decreased phase1 metabolism (e.g., hydroxylation, dealkylation) leads to a decrease in drug clearance and increase in the terminal disposition half-life (t1/2) in elders for medications. Phase 2 metabolism which includes, glucuronidation, acetylation of medications appears to be relatively unaffected by the advancing age. The hepatic enzyme induction or inhibition does not appear to be affected by the age-related changes. Aging decreases in hepatic blood flow may decrease significantly the metabolism of drugs which have high hepatic extraction ratios (Dilger K, 2000).

1.2.4 Elimination

The primary elimination of drugs from the body occurs via renal excretion. The difference between the hepatic changes observed with aging and the renal changes can be predictive, thus drug dose adjustment may be based on a renal function that is either measured or calculated. 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. This decline occurs due to several aging physiological changes, which include the blood flow reduction to the kidneys, a decrease in the mass of kidney, and a reduction in the functioning size and number (Mangoni AA, 2004).

The calculations of renal function based on laboratory measurements (as serum creatinine) or other data can estimate a patient's renal function. In older adults, a low level of serum creatinine is not always indicative of normal renal function. Because older adults have a lower muscle mass than younger people, so low serum creatinine may not always indicate normal renal function but can be indicative of a reduction in muscle mass. For some patients in whom the serum creatinine may not be an exact indicator of renal function, collecting an actual 24-hour creatinine may be accurate (Hutchison LC, 2007), (Miller SW., 2007).

The reduction in glomerular filtration rate is a noted consequence of aging and the renal elimination impact of medications cannot be overstated. 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 effectivity of drug dosing in all patients(Turnheim K., 2004).

1.3 Pharmacodynamic changes that related with age

Pharmacodynamics can be defined as" the study of how a specific drug may affect the body. All drugs have their specific mechanisms of action and their adverse effects which may be caused by pharmacological interactions in the body. Due to the aspects of physiological aging, elderly adults may become at high risk of inducing less or more sensitivity to particular medications. There is evidence of altered drug response or sensitivity in the older adults. Four mechanisms have been suggested: (a)the changes in the numbers of the receptor, (b) changes in the affinity for receptor, (c)the alterations of post-receptor, and (d)the impairment of the homeostatic mechanisms that are age-related (Cusack BJ, 2004), (Guay D, 2003).

To predict the extent of the drug-related pharmacodynamic changes will be difficult because the older adults may be sensitive to the drugs' pharmacological actions. Whenever new medications are initiated, care should be taken and by starting the lower drug doses and by titrating the dose as tolerated maybe, helps to prevent and decrease the unwanted effects of drug-related pharmacodynamic. By understanding about monitoring patients for a specific therapeutic response and understanding many drug-related adverse effects can help healthcare practitioners to determine the desired pharmacodynamic effect. Also by the proper titration of doses and monitoring of patient will ensure that the correct therapy is prescribed (Toornvliet R, 2006).

1.4 The Challenges of Drug Therapy in the Older Adults

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, co-morbidity and polypharmacy, all make the elderly a special group of patients who should be treated with more attention (Wan He, March 2016).

The other causes are the lack of continuity in physician contacts, the lack of a consistent drug list, and inadequate prescription and monitoring of drug therapy are also some of the reasons for drug-related problems. A drug-related problem (DRP) known as ‘‘an undesirable patient experience that involves all drug therapy which actually or potentially interferes with the desired patient outcome’’ (Tom G. Bartol, 2015).

There are three important and potentially preventable negative outcomes that are caused by drug-related problems that are adverse drug withdrawal events (ADWEs), which are sets of symptoms or of signs caused by the removal of a drug; therapeutic failure (means inadequate or inappropriate drug therapy and that not related to the natural progression of disease); though the adverse drug reactions (ADRs), can be defined as the reactions that are noxious and unintended to occur at dosages that are normally used in humans for the prophylaxis, diagnosis, or therapy (Handler SM, 2006), (Institute of Medicine, 2006).

1.4.1 Overuse

Polypharmacy can be described as either the concomitant use of multiple drugs or the administration of more medications as indicated clinically and it is usually common among older adults [(Stewart RB, 1994)]. Polypharmacy may become problematic for older adults due to its increasing risk of geriatric syndromes (for example falls, cognitive impairment), diminished functional status, and healthcare costs (Roth MT, 2005), (Montamat SC, 1992), (Hermida J, 2006).

Community-based surveys reveal that older adults take an average of two to nine prescription and nonprescription medications each day. Drug-use studies showed that polypharmacy occurs in 55% to 59% of older outpatients (Schmader K, 1994), (Lipton HL, 1994)]. A study of frail veterans at hospital discharge reported that 44% of patients were taking one or more

unnecessary medications, with 25% of patients starting the medication(s) during hospitalization. Outside of the community, a nursing facility survey found that institutionalized older persons took an average of 6.69 routine medications and 27.1% took nine or more medications on a regular basis. Increased use of dietary supplements, such as herbal products, vitamins, and minerals, may add to the increase in polypharmacy. In a nationwide survey, Kaufman et al., found that 59% of women and 46% of men older than 65 years used a vitamin or mineral supplement and 14% of these women and 11% of these men, used an herbal product and multiple medication use has been strongly associated with ADRs (Kaufman DW, 2002).

Polypharmacy is a controversial issue and has been found to be related to an increased risk of drug–drug interactions, higher morbidity in the older population, higher numbers of hospital admissions, lower compliance and increased institutionalization. A comprehensive literature review on the topic shows that polypharmacy is increasing in the elderly and is a major cause of morbidity and mortality in the elderly population worldwide (Stewart RB C. J., 1994), (Hajjar EH, 2005).

1.4.2 Inappropriate Prescribing

Inappropriate prescribing is defined as" prescribing medications that are outside the bounds of accepted medical standards" (Guay D, 2003). Alternatively, inappropriate prescribing can also be defined as" prescribing drugs whose use should be avoided due to their risk outweighs which their potential benefit (Fick DM, 2003). The inappropriate prescribing occurs commonly in older outpatients, it was reported in one study that 92% of patients were taking ≥1 medication with ≥ 1 inappropriate ratings based on clinical review applying explicit criteria (Hanlon JT A. M., 2004)]. Other Studies which use explicit drug use review criteria have found that between 15% and 21% of community well older adults take ≥ 1 medications that have a dose, duration, duplication, or drug interaction problem (Hanlon JT, 2002), (Lindblad CI, 2006).

1.4.3 Underuse

Underuse medications is an important and increasingly recognized problem in elders, it defined as the omission of drug therapy that is indicated for the treatment or prevention of a disease condition. A study related to the community-dwelling elders found that 50% of 372 vulnerable adults were not prescribed an indicated medication. One of the most common problems were that the lack of a gastroprotective agent for high-risk nonsteroidal anti-inflammatory drug users, no calcium and/or vitamin D for those with osteoporosis and no angiotensin-converting enzyme inhibitor for patients with diabetes and proteinuria.

Underuse has an important relationship with an older adults' negative health outcomes, which includes functional disability, health services use and death (Kaufman DW, 2002).

1.4.4 Nonadherence to Medication

Medication adherence as defined by (W.H.O) is "the extent of the person's behavior—taking from a healthcare provider the medication corresponds with agreed recommendations. The range of 40% to 80% was the prevalence rate of medication nonadherence in older adults (Kapadia A, 2010). According to the AARP (formerly the American Association of Retired Persons) and also, a study in the Medicare population, the cost is one common reason that causes the older adults not to fill their prescriptions. Although, because of some possible adverse effects, the older patients also may not adhere to their regimens, an inability to read the labels of the product or a lack of full understanding of information about the prescribed drugs (Korrapati MR, 1997). Some limited retrospective data suggest that nonadherence is may associate with increased health service use and ADRs. A study that was done in 2001, found that nonadherence was one of the possible factors that may cause more than 10% of older adult hospital admissions (Brenner SS, 2003). As well as the study of Col et al. which evaluated 315 of older patients admitted to a hospital and concluded that 11.4% of admissions resulted from nonadherence. Because of the errors in patient adherence, Gurwitz et al. found that 21% of ADRs in elderly outpatients were preventable. On the positive side, a study found that the fewer hospitalizations were associated with increased medication adherence and decreased cost in patients with chronic medical conditions (Krupka E, 2006), (Ujhelyi MR, 1997).

Chapter 2: Validated drug utilizationreview tools

Adults 65 years old or older are at high risk of complications of drug therapy and the vulnerability to poor quality medication prescribing patterns and potentially inappropriate medications (PIM) due to the age-related changes, the comorbidities, polypharmacy, and the medication interactions. These complications include also mortality and morbidity, ADE, dementia, and falls (Roth, 2009).

For more than 20 years, the PIM usage in adults' ≥ 65 has been researched in more than 500 studies in the outpatient settings, the long-term care settings, and the inpatient settings. The results showed an association between certain medications and the poor patient outcomes such as delirium, falls, and gastrointestinal bleeding (Agency for Healthcare Research and Quality, 2012). The PIMs guidelines have been developed in many countries, such as the United States, Canada, France, Ireland , Australia , Norway , and South Korea .

There are three groups which the PIMs in older adults can be categorized: the inappropriate medications regardless of comorbidities, the medications that may exacerbate some diseases, and medications that can interact with other medications that are using (McLeod PJ, 1997).

According to the recommendation by the Institute of Medicine, the appropriate prescribing patterns, and the improvement of care satisfies the following domains: (a) fewer ADEs with patients having safe care experience, (b) the standard of care delivery is evidence based when effective care, and (c) the care involves the patient as an informed consumer when the patient-centered care (Joshi, 2008).

The assessment of the appropriateness of prescribing can be with process or outcome measures that are explicit (criterion-based) or implicit (judgment-based). The explicit indicators usually developed from published reviews, expert opinions, and consensus techniques. These measures are drug or disease oriented and may apply with little or no clinical judgment. According to the implicit approaches, the clinician can employ patient-specific information and published evidence to form judgments about the appropriateness. The focus is based on the patient more than on drugs or diseases. The sensitive patients are more potentially in the implicit approaches, but they are time-consuming, according to the users' knowledge and attitudes. Because no ideal measure exists, the strengths and the weaknesses of all approaches should be taken into account. Nowadays there are four tools

which are used to evaluate PIM prescribing in older adults. The Beers' Criteria, Screening Tool of Older Persons (STOPP) are explicit approaches, Improved Prescribing in the Elderly Tool (IPET), and Medication Appropriateness Index (MAI).

2.1 Beers criteria:

Since 1990, several sets of potential inappropriate prescriptions (P.I.P) criteria have been published which is designed specifically for older patients (Dimitrow MS, 2011). Dr. Mark Beers believed that ensuring the proper medication use in older patients must be a health care priority and should work as an advocate for responsible medication prescribing in the elderly patient. The potential inappropriate prescribing may occur when the risks outweigh the benefits of a prescription (Hill-Taylor B, 2013).

The Beers Criteria initially developed in 1991by Dr. Mark Beers through a consensus panel of experts by using the Delphi method with the focusing on a medication use in nursing home residents (Beers MH, 1991) and the list/criteria must continually be reviewed and updated because prescription drug availability is not static. Therefore, the Beers list was expanded to include all geriatric care settings, such as inpatient or outpatient and primary care (Davidoff AJ, 2015). It was also updated and expanded to include all geriatric care settings in 1997 and in 2003 (Beers MH, 1997). In 2012, an expert panel convened in collaboration with the American Geriatrics Society to update the Beers criteria and released updates in 2012 and 2015 (Lau DT, 2009).

The updated 2012 Beers Criteria consist of 53 classes of medications which are divided into three groups: PIMs to be avoided in older adults, PIMs to be avoided in older adults with diseases and syndromes that the drugs can exacerbate and medications which should be used with caution. The changes in the 2015 update are not extensive as those of the previous update, but two major components have been added: drugs for the dose adjustment is required based on kidney function and drug–drug interactions. Because such lists would be too extensive, the new additions are intended to be comprehensive (American Geriatric Society 2015 Beers Criteria Update Expert Panel, 2015).

The BC is not a substitute for clinical judgment and individualized care, but is meant as a guide for health care providers to make clinical decisions and to develop a policy to improve quality, safety and conduct research and training (Resnick B, 2012). An important note is that the medications addressed in the BC are not absolute contraindications. Nurse practitioners (NPs) should be familiar with the lists by incorporating the knowledge of potentially inappropriate medications (PIMs) into practice. The BC is designed to be used across all the geriatrics patients' settings, primary care, chronic and acute, but not for population 65 years of age who are in hospice and palliative care.

The Beers Criteria goal is to improve the care, effectiveness and safety of prescription practices for older patients by decreasing the PIMs. Yet, as stated previously, as new medications are added to the list, monitoring, education, and clinical interventions need to continue.

The AGS has noted that the BC should never be used to supersede individualized patient care and clinical judgment (American Geriatric Society 2015 Beers Criteria Update Expert Panel, 2015). It serves as a "warning light" to identify the medications that have an unfavorable balance of benefits and harms in older adults, particularly when compared with pharmacological and nonpharmacological alternatives. However, there are some situations in which use of medications included in the criteria can be appropriate. The criteria are designed to support, rather than supplant, good clinical judgment then, widespread efforts to educate clinicians (Micheal A. Steiman, 2015).

Presently the implementation and uptake of the BC have not been without problems. Therefore many clinicians misunderstand the purpose of the criteria and they mistakenly believe that the criteria are deeming all uses of the listed drugs to be inappropriate. Moreover, the quality of care can be negatively affected by restricting access to medications included in the criteria and they can negatively affect use in appropriate ways and create unnecessary burden and trouble for prescribers (Anderson K, 2014).

2.1.1 Key principles to guide optimal use of the AGS 2015 Beers Criteria

They hope that patients, caregivers, clinicians, health systems leaders, and payers will use these guidelines to direct implementation efforts that yield maximal benefits from the AGS 2015 Beers Criteria while minimizing unintended harms.

Key Principle 1: Medications are potentially inappropriate, not definitely inappropriate. In some cases the drug is almost always a poor choice. However, there are some older adults in whom use of these medications is appropriate.

Key Principle 2: Read the rationale and recommendations statements for each criterion. Many medications are considered potentially inappropriate only in certain circumstances or in most circumstances but with some exceptions.

Key Principle 3: By understanding why the medications are included in the AGS 2015 Beers Criteria and adjusting the approach of medications accordingly

Key Principle 4: The AGS 2015 Beers Criteria is a starting point for a comprehensive process to identify and improve medication appropriateness and safety (Steinman MA H. J., 2010).

Key Principle 5: Access to medications included in the AGS 2015 Beers Criteria should not be excessively restricted by prior authorization and/or health plan coverage policies.

Key Principle 6: The AGS 2015 Beers Criteria are not equally applicable to all countries.

2.2 Screening tool of older persons (STOPP)

Beers criteria have approved the published literature on inappropriate prescribing in late life. Then in 2008 the first version of STOPP/START criteria was published. It was developed in Ireland by a multidisciplinary team of Irish geriatricians, primary care physicians, pharmacists, and pharmacologists. It has steadily gained significance as an alternative set of PIM criteria. Like Beers criteria, STOPP criteria describe the evidence of potentially inappropriate medications (PIMs).

STOPP contain the PIM prescribing in older adults that include drug–drug and drug–disease interactions, the drugs that may affect elderly patients at risk of falls, and duplicate drug class prescriptions.

It's arranged according to relevant physiological systems, and each criterion is followed by an explanation as for why the prescription is potentially inappropriate (Masoro EJ., 2003). They were updated in 2015 to include drugs affecting or may affect renal function, as the update of the AGS Beers Criteria. (Winbery S, 2011).

2.3 Improved prescribing in the elderly tool (IPET)

It is referred as "Canadian Criteria", the IPET consists of a list of the most 14 prevalent prescription errors which has known from a long list of inappropriate prescription. It is developed by an expert Canadian Consensus Panel in 1997. Furthermore, as with the Beers' criteria, there is an insufficient convincing evidence that exists regarding IPET's efficacy to reduce the ADR incidence, and reduce the excessive health resource utilization or decreases mortality (Steinman MA, 2010) .

2.4 Medication appropriateness index (MAI)

MAI is a measurement of prescribing appropriateness developed by Dr. Joseph Hanlon and colleagues. MAI assesses elements of prescribing: the indication, the effectiveness, the dose, the practical directions, the correct directions, the drug–disease interactions, the drug–drug interactions, the duration, the duplication, and the cost. The most three components that can be used to detect the unnecessary polypharmacy and PIM prescribing are indication, effectiveness, and duplication, (Chapron DJ. Drug disposition and response, 2000).

The MAI has major advantages: testing in both the inpatient and ambulatory settings, exhibiting excellent intra-rater and inter-rater reliability, and facing and contesting validity. Also, it addresses multiple components of prescribing appropriateness and may be applied to all medication in the context of the patient. However, the tool is more time-consuming (~10 minutes per drug assessed) and cannot assess the under-prescribing (untreated indications) (Chapron DJ. Drug disposition and response, 2000).

2.5 Previous studies

Bilyeu, Gumm, Fitzgerald, Fox, and Selig (2011) initiated a nurse quality improvement intervention program for patients admitted to an inpatient unit. Before the intervention, researchers reviewed charts of 100 patients to identify medications prescribed to each patient. Each medication was compared to the Beers Criteria. As a result of the 2-month project, for the 46% of the PIMs identified in the cohort, providers chose to either discontinue the medication, or change the medication to a safer dose, or safer medication. According to Bilyeu et al. (2011), the nurses' unexpected outcomes related to quality care issues. The nurses involved in the program reported increased confidence using the Beers Criteria to identify potentially inappropriate medications, increased compliance with medication reconciliation, heightened awareness of potentially inappropriate medications and the relationship to adverse drugs effects, and a sense of empowerment to implement interventions that provide safer and higher quality outcomes for inpatients.

In India, a study was undertaken to study the prescribing pattern of various drugs in geriatric patients and also evaluate inappropriate prescribing with the help of beers criteria. According to a study that was done from the period of January 2013 to April 2013 in Rajah Muthiah Medical College hospital, Annamalai University, inpatient who are 65 years and older of both gender were reviewed. Most commonly prescribed drugs were gastrointestinal drugs followed by cardiovascular drugs. Polypharmacy was high which is usually unavoidable in elderly and according to Beer's criteria the study suggests that drugs that were avoided in elderly are among the most frequently inappropriately prescribed drug.

Also, a retrospective study aimed at examining potentially inappropriate medication prevalence and factors that affect the use of PIMs was done in Womack Army Medical Center Internal Medicine Unit at U.S military hospital between December 2012 and September 2013 by Edward K.Osi. The lists of admission and discharge medication of patients aged ≥ 65 years was reviewed by a clinical pharmacist using the 2012 Beers criteria. Among the PIM top three classes at admission were antihistamine followed by nonsteroidal anti-inflammatory drugs and benzodiazepines. Patients who took more than ten medications were more likely to have a PIM.

Another study which had a purpose to determine the prevalence and patterns of PIM prescription in Korean older adults according to 2012 Beers criteria by using data from Korean health insurance review and assessment database of an outpatient prescription from January 1, 2009, to December 31, 2011. The study confirmed that the PIM prescription is more common among elder Koreans and the female sex, comorbidity, severity and polypharmacy were the most risk factors for PIM. The clinical decision support system should be developed to decrease the prevalence of PIM prescriptions.

Also a study carried out in Cork, Ireland to compare Beers (2003, 2012) and STOP/START version 1 (v1) and (v2) according to the effect on the incidence of potentially inappropriate prescribing medication, polypharmacy and clinical relevance of medication changes. They found out that the number of medications was most reduced by STOP/START v2. In addition, STOP/START v2 identified more instance of potential major clinical relevance.

An Italian study aimed to assess the occurrence of polypharmacy and hyper-polypharmacy and the risk of potentially inappropriate prescription PIP among elderly patient and very elderly patient in different health care settings of the Friuli-Venezia Giulia region in the North East at Italy in March 2014. The assessment was done according to the Beers criteria. A total of inpatients, outpatients, and nursing homes were included the polypharmacy and hyper-polypharmacy among elderly and very elderly are associated with the risk of multiple PIPs and showed that the most PIPs result from the benzodiazepines. Also the study showed that female sex aged > 79 years, hyper-polypharmacy and chronic kidney disease which were associated with high risk of having two more PIPs.

Other study conducted in Nepal evaluated the prescribing pattern, prescribing potentially inappropriate medicine and polypharmacy in elderly population to contribute in process of the awareness of rational use of drugs by the observational study which was done for hospitalized geriatric patients in Nepal. The world health organization and Beers 2012 update criteria were used to assess the prescribing pattern and inappropriate respectively and using Medscape for drug-drug interaction. The study result showed that majority of hospitalized elderly patient received polypharmacy with drugs which have serious of drug-drug interaction. The potentially inappropriate medicines prescribed were 7.2%.

From June 2013 to August 2012, Dr. B.P Amedkar of Medical College and Hospital carried out a study to show prescribing pattern of many various drugs in elderly patients and evaluate inappropriate prescription using Beers criteria. Most of the cases were from respiratory system followed by cardiovascular system and the most commonly prescribed drugs were antimicrobials. The polypharmacy was observed high and the drugs which must be avoided in elderly are among more frequently inappropriately prescribed drugs.

Chapter 3 . Methodology

A cross sectionalprospective study was carried out on both male and female geriatric patients (aged 65 years and more) in Near East University Hospital in North Cyprus between September and October 2016. Within the time frame of my study, the total number of admitted elderly patients above 65 years of age was 119 patients.

The inclusion criterion was :

1- Patients who are aged 65 years or older
2- Patents who were hospitalized between September and October 2016 whether in general clinic or geriatric.

Exclusion criteria:

1- Patients who were at hospice care and who were receiving palliative care.
2- Patients who were discharged before completing their data collection or had no medications.
3- Patients who died during the collection data.

Sample size and data Collection

The study population consists of 119 patients. 107 patients were eligible for inclusion whereas 12 patients were excluded- (9 of them were excluded due to incomplete data and 3 patient died during the course of collecting data).

Data was collected through review of case sheets of all elderly patients admitted. Case sheets of all admitted elderly patients who were inpatient, discharged or to be discharged from the hospital were reviewed each day during the study period. Such review of case considered only once for each patient.

Data were obtained from the patient medical records and collected in a structured pre-form which included patients' age, gender, date of admission, date of review, diagnosis, creatinine clearance and all medications prescribed.

Identification of potentially inappropriate medications:

The medications were prescribed in trade name then I verified their generic name by using www.drug.com for international drugs. All medications were assessed for PIM using 2015 Beers criteria. The medications in the record listed in beers criteria were considered as PIM according to major component of beers criteria which include:

1- Changes to PIMs and Older Adults.
2- Changes to Drug-Disease and drug-Syndrome PIMs.
3- Drugs to be used with cation.
4- Drug-Drug Interactions.
5- PIMs Based on Kidney Function.

Statistical analysis:

Collected data was entered in Microsoft Office Excel 2010 and analyzed by using Statistical Package for the Social Sciences SPSS statistical software (version 20, IBM, SPSS).

The methods used to analyze the data include an analysis of descriptive statistic variables such as frequency, percentages and crosstabs for the categorical variables and the correlation test. The chosen level of significance is $p < 0.05$.

Ethical Consideration:

Confidentiality was assured during the study and also patients' privacy. The study was approved by the Near East Institutional Reviews Board (IRB) of Near East University Hospital that assigned this research as being just observational study and just initials were used during the study.

Chapter 4. Results:

Demographics

Out of 451 patients admitted to the hospital and scanned for inclusion during the period of this study,119 patients were classified as elderly patients, 107 of them were included; 62 (57.9%) being males and 45 (42.1%) being females [Table.1]. Total admitted elderly patients were classified to two age groups 65-75 and>75. Most common elderly patients admitted during study period were aged 65-75 N= 59 (55.1%), followed >75N=481 (44.9%). [Table.1]

Based on the patients' file information, most of the patients were admitted to cardiology clinic *N*=42, followed bygeriatrics *N*=11, respiratory clinic *N*=11, internal clinic *N*=11, surgery *N*=11, then infections *N*=9, oncology *N*=8and neurology *N*=4 [Table.1].

Prescription Pattern and Polypharmacy

The total number of medicines prescribed to the 107 patients was 1039, with a median of 9. The number of prescribed drugs had no correlation with the age within the geriatrics.

Polypharmacy was found in *N*=85 patients, the variation in polypharmacy with relation to age: Patients aged 65-75 years was *N*=45 and patients aged >75years was N=40 [Table.2. Fig.1].

Table I. General Information	
Sex:	
Male	62(57.9%)
Female	45 (42.1%)
Age:	
65-75	59 (55.1%)
>75	48 (44.9%)
Total Number of drugs	**1039**
Range	22.00
Mean	9.7

Prevalence of poly-pharmacy	85 (79.4%)
Distribution of patients across clinics	
Geriatric	11 (10.3%)
Cardiology	42 (39.3%)
Surgery	11 (10.3%)
Internal	11 (10.3%)
Respiratory	11 (10.3%)
Infection	9 (8.4%)
Oncology	8 (7.5%)
Neurology	4 (3.7%)

Table.2. **Age * polypharmacy Cross tabulation**

			polypharmacy		Total
			1	2	
Age	65-75	Count	14	45	59
		% of Total	13.1%	42.1%	55.1%
	> 75	Count	8	40	48
		% of Total	7.5%	37.4%	44.9%
Total		Count	22	85	107
		% of Total	20.6%	79.4%	100.0%

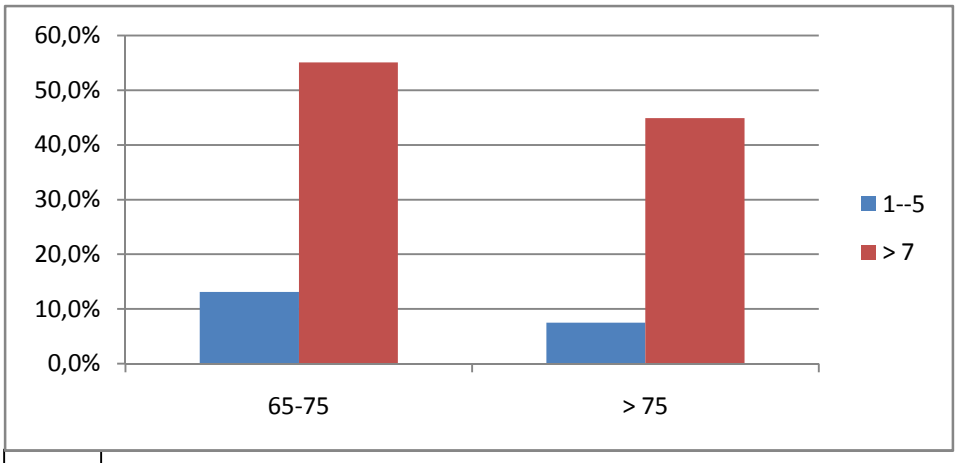

Fig.1

Beers criteria

Out of the total of 1039 medicines prescribed, 176 (16.9%) were potentially inappropriate as determined by Beer's criteria groups during hospitalization while 103(9.9%) PIMs of total discharge medications were observed.

For PIMs used during hospitalization, 88(50%) PIMs were identified as medications to be avoided in older adults 38(21.6%) PIMs there the second group drug-disease and drug-syndrome interaction there were, in the drugs used with caution group there were 32(18.2%) PIMs, the forth group drug-drug interactions there were 3 (1.7%) and in the fifth group that based in kidney function there were 14 (7.95%) of PIMs [Table.3].

On discharge; the PIMs of the first group which is medications avoided in older adults there were 67(38.1%) PIMs, the second group drug-disease and drug-syndrome interaction there were 31(17.61%) PIMs, in the drugs used with caution group there were 21(11.9%) PIMs, the forth group drug-drug interactions there were 1 (.6%) and in the fifth group that based in kidney function there were 5 (2.84%) of PIMs. [Table.4]

Of patients on PIMs; during hospitalization, at least one PIM was prescribed to 29 (27.1%) patients. N=26 (24.3 %) of the patients were prescribed with two PIMs, N=17 (15.9%) were prescribed with three PIMs, N=5 (4.7%) were prescribed with four PIMs and N=4 (3.7%) were prescribed with five and more PIMs according to Beers criteria .

While for same patients on discharge, at least one PIM was prescribed to 25 (23.4%) of them. N=22 (20.6 %) of the patients were prescribed with two PIMs, N=8 (7.5%) were prescribed with three PIMs, and N=2 (1.9%) were prescribed with five PIMs according to Beers criteria.

Most potentially inappropriate medicines during hospitalization were administered in cardiology patients *N*=34(31.4%), followed by respiratory patients *N*=13(12.2%), internal medicine patients *N*=11(10.2%), then surgery *N*=7(6.6%), infections *N*=5(4.7%) and oncology *N*=5 (4.7%), geriatrics *N*=4(3.7%) and neurology *N*=3(2.8%) patients.

PIM medications

Proton pump inhibitors were most prescribed PIMs (n=68) for patients during hospitalization and on discharge. According to Beers criteria they are classified as first group Potentially inappropriate. In this omeprazole was prescribed most though stopped on discharge. Enoxaparin was the second common prescribed drug which classed as PIM, however it was stopped in all cases on discharge. Diuretics such as Furosemide was the third most common PIM prescribed even on discharge for significant (n=14) patients. Antipsychotic like (Alprazolam, Diazepam, Citalopram, Olanzapine, Clonazepam, Mirtazapine, Sertraline) were respectfully significantly prescribed PMIs (N=24) during hospitalization and on discharge. These drugs are classed as drugs that increase symptoms such as anticholinergic symptoms and falls in elderly especially when they take more than two.

Corticosteroids were prescribed 12 times during hospitalizations mostly in respiratory patients and on discharge have been stopped.

Table.3. PIMs Drugs

Drug	Repetition	Family
1. Famotidine	3	histamine H_2 receptor antagonist
2. Ranitidine	3	histamine-2 blockers
3. Amiodarone	4	antiarrhythmic
4. Digoxin	4	antiarrhythmic
5. Atropine	1	Anticholinergic
6. Doxazosin	2	alpha-adrenergic blockers
7. Terazosin	1	alpha-adrenergic blockers
8. Aspirin	1	NASID
9. İbuprofen	1	Nonsteroidal anti-inflammatory drug (NSAID)
10. Tramadol	2	narcotic-like pain reliever.
11. Nitrofurantoin	1	Antibiotic
12. Modafinil	1	wakefulness-promoting agent.
13. Scopolamine	1	Anti-motion sickness
14. Metoclopramide	1	Dopamine receptor blocker

Potentially Inappropriate Medication

During hospitalization, according to the first group in Beers criteria which is potentially inappropriate medications there were 88(50%) of PIMs included in this group. 10 (11.4%) of the drugs were recommended as avoid, 12 (13.6%) drugs were recommended as avoid as first

choice, 64 (72.7%) drugs were recommend as avoid with exceptions and 2 (2.3%) of the drugs that have other recommendation.

64 (72.7%) drugs were recommend as avoid with exceptions and 2 (2.3%) of the drugs that have other recommendation.

The quality of evidence of the recommendation in this group was 63 (71.6%) which is high, 24 (27.3%) which is moderate and 1 (1.1%) is low. Also in this group the strength of all recommendations were strong 88 (100%) [Table.3].

While on discharge according to the first group in Beers criteria which is potentially inappropriate medications there were 67(38.1%) of PIMs included in this group. 9(13.4%) of the drugs were recommended as avoid, 11 (16.9%) drugs were recommended as avoid as first choice, 45(67.2%) drugs were recommend as avoid with exceptions and 2 (3%) of the drugs that have other recommendation.

The quality of evidence of the recommendation in outpatient in this group were43(64.3%) which is high, 23(34.3%) which is moderate and 1(1.5%) is low. Also in this group the strength of all recommendations were strong 67(100%) [Table.4].

Drug-Disease or Drug-Syndrome Interactions.

While hospitalized, according to the second component in Beers criteria for PIMs that may exacerbate the disease or syndrome, 38 (21.59%) drugs matched. 19 (48.7%) of drugs were interact with delirium. The drugs that may interact with history of fall and history of syncope were 5 (3.9%) , 5(3.9%) drugs , seizure and lower urinary syndrome were 4 (3.1%), 4(3.1%) drugs, and insomnia and parkinsonism were 1 (0.8%) , 1 (0.8%) .

20 (52.6%) of the drugs were recommended as avoid, 13 (34.2%) drugs were recommended as avoid as first choice and 5 (13.2%) drugs were recommended as avoid with exceptions.

The quality of evidence of the recommendation at this component was 2 (5.3%) which is high, 34 (89.3%) which were moderate and 2 (5.3%) is low. Also in this group the strength of recommendations were strong 35 (92.1%) and 3 (7.9%) were with low strength [Table.3].

19(61.3%) of the drugs were recommended as avoid, 9(29%) drugs were recommended as avoid as first choice and 3(9.7%) drugs were recommended as avoid with exceptions.

The quality of evidence of the recommendation in this component was 2(6.5%) which is high and29(93.5%) which were moderate. Also in this group the strength of recommendations were strong 28(90.3%) and 3(9.7%) were with low strength [Table.4].

Drugs Use with Caution

During hospitalisation there were 32 (18.2%) drugs that should be used with caution in elderly patients. 1 (3.1%) of them had high quality of evidence and 32 (96.9%) drug had moderate quality of evidence. The recommendations were 31 (96.9%) strong and 1 (3.15) was low [Table.3].

While on discharge there were 21(11.93%) drugs that should be used with caution in elderly patients. 1 (4.8%) of them had high quality of evidence and 20(95.2%) drug had moderate quality of evidence. The recommendations were 20(95.2%) strong and 1(4.8%) was low [Table.4].

Drug-Drug Interactions

The non-anti-infective drugs that should be avoided in older adults were 3(1.7%). 2(66.7%) recommended avoid with high quality of evidence and 1(33.35%) should avoid with exceptions with moderate quality of evidence.All drug recommendations were strong[Table.3].

The non-anti-infective drugs that should be avoided in older adults were 3(1.7%). 2(66.7%) recommended avoid with high quality of evidence and 1(33.35%) should avoid with exceptions with moderate quality of evidence.All drug recommendations were strong[Table.3].While in outpatients only 1 avoided drug at this group with high evidence and strong strength of recommendation [Table.4].

Medications and Kidney Function

Non-Infective medications that should be avoided or have their dosage reduced with varying levels of kidney functions in hospitalized were found as 14 (7.95%). The medication

recommended as avoid were 5(35.7%), and the medications that should reduce the dose were 9(64.3%).

The quality of evidence of each recommendation were 1 (7.1%) high, 12 (85.7%) moderate and 1 (7.1%) low although the strength of recommendation was all strong [Table.3].

During hospitalization total PIMs found in this category were5(2.84%). The medications recommended as avoid were 4(80%) while the medications that should reduce the dose were 1(20%).

Table.4. Beers criteria group's potentially inappropriate medications for Inpatients

Group	Number of PIM	Recommendations					Quality of evidence			Strength of recommendation		
		Avoid	Avoid as 1st choice	Avoid with exceptions	Use with caution	Reduce dose	High	moderate	low	Strong	moderate	low
Drugs to be avoid	88(50%)	10(11.4%)	12(13.6%)	64(72.7%)	2(2.3%)	--	63(71.6%)	24(27.3%)	1(1.1%)	88(100%)	--	--
Drug-disease interaction	38(21.59%)	20(52.6%)	13(34.2%)	5(13.2%)	--	--	2(5.3%)	35(89.3%)	2(5.3%)	35(92.1%)	--	1(7.9%)
Use with cation	32(18.2%)	--	--	--	32(100%)	--	1(3.1%)	31(96.9%)	--	31(96.9%)	--	1(3.1%)
Drug-drug interaction	3(1.7%)	1(33.3%)	--	2(66.7%)	--	--	2(66.7%)	1(33.3%)	--	3(100%)	--	--
Based in kidney function	14(7.95%)	5(35.7%)	--	9(64.3%)	--	9(35.7%)	1(7.1%)	12(85.7%)	1(7.1%)	14(100%)	--	--

Table.5. Beers criteria group's potentially inappropriate medications for Outpatients

Group	Number of PIM	Recommendations					Quality of evidence			Strength of recommendation		
		Avoid	Avoid as 1st choice	Avoid with exceptions	Use with caution	Reduce dose	High	moderate	low	Strong	moderate	Low
Drugs to be avoid	67(38.1%)	9(13.4%)	11(16.4%)	45(62.2%)	2(3%)	--	43(64.3%)	23(34.3%)	1(1.5%)	67(100%)	--	--
Drug-disease interaction	31(17.6%)	19(29%)	9(29%)	3(9.7%)	--	--	2(6.5%)	29(93.5%)	--	28(90.3)	--	3(9.7%)
Use with cation	21(11.9%)	--	--	--	21(100%)	--	1(4.8%)	20(95.2%)	--	20(95.2%)	--	1(4.8%)
Drug-drug interaction	1(0.6%)	1(100%)	--	--	--	--	1(100%)	--	--	1(100%)	--	--
Based in kidney function	5(2.84%)	4(80%)	--	--	--	1(20%)	1(20%)	3(60%)	1(20%)	5(100%)	--	--

Chapter.5. Discussion:

Beers criteria is frequently used in elderly for evaluation of the appropriateness of prescribing specific drugs in elderly, it was developed at 1991 and recently updated in 2015.

Prescribing patterns need to be evaluated periodically to assure rational drug prescribing and use by assuring conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. Thus watching for guidelines utilization and feed backing health providers can aid in rationalizing drugs use, which is a mission clinical pharmacist; owe both their communities and other healthcare providers.

In the present study, 107 prescriptions, 1039 medications were analyzed with the aim of delineation prescription pattern in elderly, determining whether PIMs were prescribed to them, and evaluating the drugs that need monitoring and use with caution.

The majority of patients in present study were men aged 65-70 years, were using minimum 1 drug and maximum 23 drugs and mostly admitted to the cardiology clinic.

Of interest the present study showed an inverse relation between polypharmacy and age within geriatric patients as polypharmacy was observed generally in 79.4% in all cases. However the present study did not show a relative relation between the number of drugs prescribed and the patient's age unlike Ghosh R findings.(Ghosh R., 2003).

Because this is one of the first study of potentially inappropriate medications according to the new updating of beers criteria 2015, we cannot compare our findings with those of published studies which have mainly involved the beers criteria 2012 (Veena D., 2012), (sangharshila B., 2016).

As also observed by Klejda H et al, no association was observed between the frequency of PIM and increasing age or sex (Klejda H., 2015)

According to beers criteria components it revealed that (16.9%) of total drugs prescribed during hospitalization were inappropriate with 75.7% of patients having at least one PIMs and 11 drugs being used in average.

Most PIM were observed in cardiology patients followed by respiratory and internal medicine patients.

As observed in similar published literature, this study also shows a correlation between the number of PIMs and polypharmacy [Table.5].

Table.6. Correlation PIM with Polypharmacy

		polypharmacy	#PIMoutpatient	#PIMinpatient
polypharmacy	Pearson Correlation	1	.188	.273**
	Sig. (2-tailed)		.052	.004
	N	107	107	107
#PIMoutpatient	Pearson Correlation	.188	1	.538**
	Sig. (2-tailed)	.052		.000
	N	107	107	107
#PIMinpatient	Pearson Correlation	.273**	.538**	1
	Sig. (2-tailed)	.004	.000	
	N	107	107	107

**. Correlation is significant at the 0.01 level (2-tailed).

The drugs were classified according to its type of inappropriateness that was recommended at beer's criteria 2015 components. During hospitalization 50% of PIMs belonged to the first group (number 1) which includes the potential inappropriate medications in elderly patient. 72.7% of these drugs were recommended as TO BE AVOIDED with exceptions. With 71.6% high quality of evidence and 100% had a strong strength of recommendation. While for outpatients 38.1% of PIMs belonged to the same group. 67.2% of these drugs were recommended as TO BE AVOIDED with exceptions.

These groups of component involve drugs that need monitoring or avoiding the use for more than selected period. Also some drugs should not use as first choice and some should avoided in elderly adults.

In this study also during hospitalization we found that 21.6% of PIMs drugs may interact with disease and some syndromes. The most selected syndrome that may be increased was delirium. 52.6% of the drugs were classified as to be avoided with 89.3% of recommendations being supported by high quality of evidence and 92.1% of them being classified as strong recommendations. Also there were 18.2% PIMs which should be used with caution.

However on discharge we found that 17.6% of PIMs drugs may interact with disease and some syndromes. 61.3% of the drugs were classified as to be avoided with 93.5% of recommendations being supported by moderate quality of evidence and 90.3% of them being classified as strong recommendations. Also there were 11.9% PIMs which should be used with caution.

Beers criteria 2015 was remind the drug-drug interaction of drugs are not anti-infective, in our study the recommendation were strong. Also the new component of medication and level of kidney function, that only 7.95% medication were selected, 64.3% of them should reduce their dose in case of Crcl< 30 mg/min. While it's 2.84% on discharge.

According to guideline utilization and expert panels recommendations adaption the findings of this study seems comparable to ranges reported by other observers in different parts of the world, of all 1039 prescribed medicine 16.9% were classified PIM compared to 32.19% reported recently by Abraham et alWhile high prevalence of PIMs in inpatients was found in our study (75.5%) and in outpatients was (64.5) quite similar to findings of Osei et al (73% for in patients) and (50% for outpatients) in an American military hospital.

Many things can lead to such high prevalence easy access to medications in Turkey both OTC and non OTC, multiple diseases, polypharmacy, multiple different hospitalizations with lack of geriatric specialty clinics, also lack of clinical pharmacists and MTM services which may cut prevalence of PIM in geriatric patients and probably lack of medication review services by pharmacists or other qualified healthcare provider. All these and others may further increase the prevalence of PIM among such vulnerable population (Hunt, Kreiner, & Brody, 2012), (The American Pharmacists Association, the National Association of Chain Drug Stores Foundation, 2008)

Strategies to overcome these finding and further enhance geriatric patient care may include specialized Pharmacists regular medication chart reviews, frequent awareness activities such as workshops and hospital seminars and healthcare providers CME's addressing newly released guidelines such as Beers criteria 2015.

Also frequently monitoring practices in healthcare settings and feedback reporting healthcare providers and also encouraging multidisciplinary healthcare practice involving clinical

pharmacists beside physicians and nurses may all lead to more optimized and rational care for geriatric population.

To our knowledge, this study is the first study to assess the medications of elderly patients in Northern Cyprus. Our study is one of the first studies that evaluate drugs of old patient according to the newest updating, “the Beers criteria 2015” worldwide and specifically in Turkey and North Cyprus.

The high prevalence of PIM in geriatric patients reported from this study necessitates a nation wade assessment and responsible bodies to act to reduce and adopt strategies that may cut and overcome such high prevalence. Furthermore, the sampled population in this study was from different clinics and represented wide range of pathologies and chronic illness populations.

Yet a major limitation of our study is the fact that it was uni-centered hence limiting the generalizability of its results nationwide, also time limitations existed leading to enroll a larger sample of patients. Also prevalence of PIM reported could be less than real prevalence sincewe use the 2015update of Beers criteria which contain PIMs’ recommendation as use with caution or reduce dose.

Another limitation also is the providers’ knowledge and awareness of the latest Beers Criteria, which is significantly different than beers 2012 and thus did not have sufficient time to adapt and incorporate it, such unawareness should be addressed by frequent CMEs.
Further studies should be carried nationwide in Multi-center approach, also such assessments should consider awareness statue and thus assess both pre and post awareness CMEs, also other healthcare facilities and setting should have such assessments continuously, while also its important to trace readmission in geriatrics specially due medications so to follow up medications that are classified as used with caution and also be vigilant for new possible candidates to be classified as PIMs.

Conclusion

By assessing the applying of Beers criteria 2015 update in Near Est Hospital in North Cyprus, the prevalence of PIMs according to beers criteria 2015 was acceptable whether for inpatients or outpatients related to some other studieswith the endeavor of the hospital to improve the geriatrics treatment plan.

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