The Characteristics of Older Persons Who Present at a Tertiary Emergency Unit; In Particular, the Contribution of Adverse Drug Events: a Prospective Cross-Sectional Study

By

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<tr>
<td>ACE</td>
<td>Angiotensin Converting Enzyme</td>
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<td>ADE</td>
<td>Adverse Drug Event</td>
</tr>
<tr>
<td>BADL</td>
<td>Basic Activities of Daily Living</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CT</td>
<td>Computer tomography</td>
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<td>CVA</td>
<td>Cerebrovascular Accident or Stroke</td>
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<tr>
<td>DOB</td>
<td>Date of Birth</td>
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<tr>
<td>DVT</td>
<td>Deep Venous Thrombosis</td>
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<td>EU</td>
<td>Emergency Unit</td>
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<tr>
<td>GIT</td>
<td>Gastrointestinal tract</td>
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<tr>
<td>IADL</td>
<td>Instrumental Activities of Daily Living</td>
</tr>
<tr>
<td>IHD</td>
<td>Ischaemic Heart Disease</td>
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<tr>
<td>MET</td>
<td>Metabolic Equivalent</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Non-steroidal Anti-inflammatory Drugs</td>
</tr>
<tr>
<td>PVD</td>
<td>Peripheral Vascular Disease</td>
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<tr>
<td>RALES</td>
<td>Randomised Aldactone Evaluation Study</td>
</tr>
<tr>
<td>RECORD trial</td>
<td>Randomised Evaluation of Calcium OR vitamin D trial</td>
</tr>
<tr>
<td>RR</td>
<td>Risk Ratio</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>UTI</td>
<td>Urinary Tract Infection</td>
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Abstract

Introduction

Older persons (aged 65 years or older) present to their health care professionals with problems that represent a combination of multiple specific disease pathologies, the individual specific features of the ageing process and the resultant functional, cognitive and the social strains that may be inherent with later life. To improve both morbidity and mortality patients are prescribed medications by their health carers. The intended benefits of these medications may be offset by medication related adverse events. Older persons have been identified to be at an increased risk of suffering drug related adverse events which may contribute to patient disease. The Emergency Unit (EU) is commonly the point where patients whose illness warrants hospitalization are initially evaluated and managed.

Objectives

A prospective cross-sectional study was undertaken to determine the characteristics of older persons presenting to a tertiary EU and evaluate the burden and risk factors for adverse drug events (ADEs).

Results

Older persons comprised 17% of the patient burden of the EU during the 104 day study period. Data was obtained on 517 patient presentations resulting in audit coverage of 84%. The mean age was 74 years (range 65 to 95).

The majority of older persons (58%) presented after hours and waited an average of one hour before medical assessment. A third of patients demonstrated significant dependence on assistance with multiple basic activities of daily living at their baseline
functional status. The majority of older persons (83%) identified a family member as their primary caregiver.

Older persons presented to the emergency unit with diseases predominantly involving the cardiovascular, neurological and respiratory systems. Patients took an average of 4 prescription medications and 82% were assessed as having adherence with their medication.

ADEs contributed to EU presentation in 20% of the patient presentations. The most frequently implicated drug classes were cardiovascular (36%), anti-thrombotic (25%), analgesic (18%) and anti-diabetic (8%). Multivariate logistic regression analysis of predictors for ADEs showed that taking 5 or more prescription medications significantly increased the risk of an adverse drug event (RR 2.6; 95% CI 1.6 – 4.1) (p<0.001).

Patients taking angiotensin converting enzyme inhibitors (RR 2.6; 95% CI 1.3 – 5.2) (p=0.009), the non-steroidal anti-inflammatories (RR 4.1; 95% CI 2.1 - 8.0) (p<0.0001) and warfarin (RR 3.1; 95% CI 1.6 – 6.3) (p=0.001) were more likely (in multivariate analysis) to be identified with an ADE. Patients presenting with a gastrointestinal bleed had a higher risk an identified adverse drug event (RR 7.2; 95% CI 3.5 – 14.8) (p<0.001). Patients suffering an ADE were more likely to require hospitalisation (p=0.04).

**Conclusion**

Older persons represent a disproportionately large percentage of the emergency unit patient load due to their accumulated disease burden. The busy emergency unit provides an opportunity for recognising the unique health care needs of older persons. This recognition forms the basis for improving care of the older person.

Recognising the high incidence of adverse drug events in the older EU population facilitates the promotion of appropriate drug prescription. This approach aims to prevent the benefits of pharmacological intervention being outweighed by its risks, particularly in frail older patients who paradoxically may receive the highest benefit from drug therapy.
Chapter 1 – Introduction, Literature Review, Study Rationale and Objectives

1.1. General aspects of older persons and the emergency unit

Older persons (ages 65 years or older) present to their health care professionals with complex problems. These problems represent a combination of multiple specific disease pathologies, individual specific features of the ageing process (these relate to highly variable intra-individual age-related changes of various organ systems and their physiological reserves), as well as the resultant functional, cognitive and social strains (including lack of community support, poor access to transport, and poverty) inherent with later life. The process of ageing is not homogenous between different individuals; as people age so they grow increasingly different from one another. This is in contrast to younger patients, who present with predominantly disease related manifestations and tend to maintain similar physiological characteristics. Ill older persons can thus pose as significant clinical challenges to their health care providers. These challenges may be most significant in the busy Emergency Unit (EU).

The EU is commonly the initial point of evaluation and first line management for patients whose illness warrants hospitalization. This is true for the South African public health sector, providing health care to approximately 80% of the population, where the majority of non-elective hospital admissions are derived from the EU [1]. No published data from South Africa has documented the characteristics of older persons who present to the EU.

In the later stages of life patient goals shift emphasis from more than just the prolongation of life and cure of disease. Older persons place a substantial emphasis on comfort, function and the ability to live independently [2]. Knowledge of baseline characteristics of older persons in the EU (general demographic information, functional status, predominant clinical problems, waiting times, and admission rates) would provide data for the development and implementation of a more patient centered service.
Older persons comprise 5.0% of the total population of South Africa (in the Western Cape Province they comprise 5.6% of the total population) [3]. Older people form a minority subgroup of the total population, however because of their accumulated disease burden and disability they may represent a disproportionately larger percentage of EU patients.

A baseline understanding of the scope of clinical problems present in the older EU population also provides the information required for the development and implementation of a program to improve geriatric evaluation and management. At present there is relatively little specialist geriatric support in South Africa (there are presently less than 10 qualified specialist geriatricians) and in most medical training institutions Geriatrics does not form part of the core curriculum. This dearth of specialist geriatric medicine means that the complex and special needs of older persons may not be adequately met. Obtaining clinical information regarding the characteristics of older persons and their utilization of clinical services will allow for targeting of these areas for specific training and clinical support measures. By improving support and training it is possible that the ill older person with a multitude of problems presenting to a busy EU after hours may represent less of a daunting challenge. Junior staff frequently cover these units and may have had very limited or no prior training regarding aspects of the evaluation and management of older persons.

1.1.1. International studies on older persons and the emergency unit

Internationally there is limited data exploring the characteristics and utilization of EU’s by older persons available. A large United Kingdom based study (examining patient presentations) with nearly 3 million EU attendances identified older persons to be more likely to attend with non-injury, particularly cardiac-related conditions, to require admission to hospital, to require ambulance transport to the hospital and arrive for evaluation in the morning and early afternoon [4]. A much smaller Australian study (mainly examining EU outcomes) showed that older persons presenting with cardiac failure or neurological diseases were more likely to suffer functional decline or death. Other characteristics that were associated with poorer outcome in that study were: being referred by a non-family member, having social problems and requiring admission [5]. A
United States based study showed that compared to younger persons, older persons presenting to the EU presented with conditions requiring a higher degree of urgency, had more comorbid conditions, were more likely to remain for a longer time period in the EU, had higher admission rates and were more likely to have higher laboratory and radiological investigation rates [6].

1.1.2. Specific problems with care of the older patient in the Emergency Unit

Recognised deficiencies with the care of older persons in the EU include: failure to recognise problems that could benefit from more careful assessment, failure of referral to appropriate community support services, and failure to communicate to the primary physician of the problems identified and the interventions implemented at the EU visit [7, 8].

Failure to recognise problems in older EU patients may be due to the atypical manifestations of diseases in the older person. The gradual diminution of an older person’s physiological reserve due to either age or disease related changes results in progressive constriction of each organ system’s capacity to maintain homeostasis in the face of challenge [9]. Any insult may thus initially manifest as a symptom or sign attributable to the weakest system. For example, pneumonia may present as either heightened confusion in patients with dementia or cognitive impairment, falls in a patient with musculoskeletal compromise or incontinence in patients with poor urinary storage reserve or compromised mobility. Specific disease processes may also manifest with less symptoms and signs. For example, older patients with pneumonia present with a mean of three fewer symptoms than their younger counterparts. Despite the varied manifestations of pneumonia in the older person the astute clinician with appropriate training easily recognises a raised respiratory rate and considers pneumonia as a possible diagnosis [10].

The law of diagnostic parsimony does not apply to older persons. This law states that a single unifying diagnosis should be sought to explain all of a patient’s clinical findings. In older persons who frequently have multiple comorbidity the application of this law in clinical practice will result in important comorbid conditions being overlooked [2].
Poor communication with the primary physician may also hinder successful assessment and prevent implementation of interventions initiated in the EU. Often older persons may utilise the EU because they feel they are "too unwell" to visit their primary physician [11]. Bypassing this referral process may result in the primary physician being unaware of their deterioration. The lack of referral information also disadvantages the EU personal as important background information may be missing. Upon discharge from the EU communication back to the primary physician is also required. All too often this is overlooked as older patients may be rapidly discharged from the EU without adequate referral documentation or follow-up arrangements. Simple and low-cost initiatives aimed at improving care of the older EU patient include telephone follow-up of older patients discharged home or telephonic follow-up supplemented by selective visits and mobilization of relevant support services [7].

Functional assessment of all older patients is part of routine care. Approximately 25% of persons older than 65 years and more than 50% of those older than 85 years need the help of another person to perform activities of daily living. These activities include: bathing, dressing, eating, toileting, transportation, shopping, preparation of food, managing finance and administering medications. Information regarding functional status can be used as a baseline measure for future functional decline. Knowledge of an individual's baseline functional status and any subsequent disease-related decline allows the clinician to guide the patient with selecting appropriate future medical or surgical interventions. Subsequent rehabilitation planning, support services and long term care or placement options are also guided by a patient's functional status. Often new functional decline may be the only manifestation of a new illness [12]. Older patients discharged from the EU have been shown to have greater deterioration in their ability to care for themselves than younger adults [11]. Failure to refer older patients to appropriate support services which include: home-based care, physiotherapy, occupational therapy, speech therapy and in-patient rehabilitation and respite facilities may contribute to this functional decline. Under-recognition of the needs of the ill older person due to inadequate functional assessment and ageist attitudes may contribute to this under-referral.
Waiting times for patient assessment by medical staff, as well as time spent in the EU before being admitted or discharged may be a useful quality of care indicator. The older patient may be at risk of both being overlooked in favour of younger patients (because of ageist staff perceptions) and having staff fail to recognise the severity of their illness. Lying immobile on a hard stretcher for a prolonged period in a busy EU may increase the risk of delirium, pressure ulcers, aspiration, malnutrition and dehydration. Development of these complications worsen patient outcome [13, 14].

Other specific aspects of the care of ill older persons may go unattended in the busy EU. These may include: poor mobility, inability to communicate clearly their care preferences or discomforts (for example confused or demented patients), toileting difficulties, sensory disabilities (hearing and sight), and inability to maintain hydration and nutritional status. Patient dignity and autonomy may also be compromised in the busy EU.

1.2. Drugs and the older patient in the emergency unit

Pharmacological therapy with prescription drugs represents one of the most important interventions in attempting to maintain the health of a diseased individual. As more data documenting the beneficial effects of drugs becomes available, so the older patient (with a high burden of diseases) receives recommendations from their health care providers to take increasing numbers of medications. The spectrum of chronic diseases commonly found in older persons includes: chronic cardiovascular (hypertension, ischaemic heart disease, stroke, arrhythmias, peripheral vascular disease, heart failure), musculoskeletal (osteoarthritis, gout, rheumatoid arthritis), respiratory (chronic obstructive pulmonary disease, asthma), metabolic (diabetes), neurological (dementia, Parkinsonism) and neoplastic diseases. Medications may be used for these diseases to provide symptomatic relief. For example: non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief in osteoarthritis and digoxin in heart failure. Alternatively medications may be used to alter the natural course of the disease, thus improving both morbidity and mortality. Examples of such medications include: beta blockers for heart failure and ischaemic heart disease, angiotensin converting enzyme (ACE) inhibitors for hypertension and heart failure, aspirin for stroke and ischaemic heart disease, and warfarin for atrial fibrillation [15- 20]. Multiple medication use increases the risk of an
adverse event [19, 20]. The older person may be at greater risk of suffering iatrogenic adverse events from this good intentioned pharmaceutical therapy [19, 21]. These adverse events may be significant enough resulting in presentation to the EU for assessment. Factors besides polypharmacy (the use of multiple drugs including ‘over-the-counter’ preparations) that are believed to be responsible for increased adverse drug events in the older person are: increased drug-drug interactions, pharmacokinetic changes (related mainly to age related alterations in body composition, renal and hepatic processing of drugs), pharmacodynamic changes (changes in the end-organ responsiveness to drugs) and medication adherence [15, 22, 23].

1.2.1. Important age-related pharmacological aspects of commonly utilized drug classes in the older person and their consequences

- **Non-steroidal Anti-inflammatory Drugs**

These agents are used primarily for their analgesic, antipyretic and anti-inflammatory properties. They inhibit cyclo-oxygenase, the enzyme required for prostaglandin synthesis. Analgesic effects are comparable to those of paracetamol and low-efficacy opioids [23]. Gastrointestinal tract (GIT) toxicity manifests as dyspepsia or ulceration, with or without complications such as bleeding or perforation. The mechanisms of this injury are both direct and indirect. Direct chemical injury occurs to the gastric epithelium and direct microvascular injury to the vascular endothelium. Indirect injury occurs by inhibiting prostaglandins, these prostaglandins are responsible for maintaining gastric mucosal integrity [24]. Concomitant use of alcohol worsens this GIT toxicity [25].

Prostaglandins also have an important role in promoting renal perfusion. NSAIDs thus also impair renal perfusion causing sodium and fluid retention which may worsen already existing hypertension and heart failure [15]. The age-related decline in renal function makes older persons more susceptible to adverse events. Dehydration markedly enhances the risk of renal damage. Older persons have reduced total body water compared to younger persons, increasing their risk of dehydration [26]. There is also evidence emerging that cyclo-oxygenase-2
inhibitors may result in unopposed prostacyclin inhibition, a prothrombotic activity. This may explain their association with an increased risk of cardiovascular events [24].

- **Warfarin**

Warfarin is an anticoagulant that acts by inhibiting the vitamin K-dependent coagulation factors. It is 99% protein bound and is eliminated by the cytochrome p450 hepatic microsomal enzyme system [23, 28]. Hepatic dysfunction can increase this anticoagulant effect by impaired clotting factor synthesis and decreased metabolism. Concomitant drugs that are also metabolised by the cytochrome p450 system will either increase or decrease the anticoagulant effect depending on their effect on enzyme inhibition or induction [23]. A diet with inconsistent amounts of vitamin K may also be responsible for an inconsistent anticoagulant efficacy. Older patients may have inconsistent dietary habits [26, 27]. Low serum albumin, either due to malnutrition or disease, increases free warfarin with increased anticoagulant effect. Older patients have an age-related decrease in liver weight and hepatic blood flow (up to 40%), both of these factors reduce hepatic drug metabolism which in turn increases the anticoagulant effect of warfarin [23,29]. Vascular integrity may also become impaired with age and this may potentially contribute to a higher risk of bleeding in older patients taking warfarin [15].

- **Angiotension converting enzyme inhibitors [23]**

These agents act by inhibiting the conversion of angiotensin I to angiotensin II, which is a powerful vasoconstrictor and modifies intrarenal blood flow. They also block the degradation of bradykinin, a potent vasodilator. Their excretion is renal, hence dosage modification is required if glomerular filtration rate is reduced to less than 20-30ml/minute [23]. Resultant hypotension may be an important adverse event in patients with cardiac failure, renal artery stenosis or patients who are relatively intravascularly depleted [23].

Patients treated with loop diuretics maintain their blood pressure by activation of the renin angiotensin aldosterone system. Sudden inhibition of this system by
ACE inhibitors may thus result in hypotension [23]. By inhibiting the production of aldosterone, ACE inhibitors may result in hyperkalaemia. This adverse event is particularly significant if potassium-sparing diuretics are being used concomitantly or in diabetic patients who may have a type 4 renal tubular acidosis [30].

Older patients frequently have occult renovascular disease. Initiation of ACE inhibitor therapy may reduce renal perfusion in patients with bilateral renal artery stenosis precipitating renal failure [23]. Concomittant use of NSAIDs potentially predisposes to renal failure by inhibiting renal prostaglandin related renal perfusion [15].

- **Beta blockers**
  These agents act by blocking beta-adrenoreceptors primarily in the heart, bronchi, peripheral vasculature, pancreas and liver. They reduce myocardial oxygen demand by their negative inotropic and chronotropic effects [23]. Adverse events in the elderly may be related to resultant symptomatic bradycardia [31]. This may manifest as syncope or pre-syncope from reduced cerebral perfusion. Cardiac failure may be worsened via their negative inotropic effects. Abrupt withdrawal may result in rebound tachycardia increasing myocardial oxygen demand precipitating ischaemic symptoms [23]. Propanolol and metoprolol are lipid soluble agents and can cross into the central nervous system where they may cause depression. Patients with reversible airways disease should not be given beta blockers as these agents may worsen airway obstruction by inhibiting bronchial beta receptors. Hypoglycaemic symptoms may be masked by the inhibition of catecholamine responses by beta blockers [23]. Atenolol is also known to impair glucose tolerance and may also promote an adverse lipid profile (by reducing serum high density lipoprotein (HDL) and increased triglycerides) [23].

- **Digoxin**
  This cardiac glycoside has a positive inotropic effect which is mediated by increasing intracellular myocardial calcium via inhibition of the Na+/K+ ATPase
pump. It also enhances parasympathetic activity slowing conduction through the atrioventricular node. The large volume of distribution, long half-life and renal elimination of this drug places older patients (who may have both age and disease-related renal impairment) at a higher risk of toxicity. Lean patients have an increased risk of toxicity due to the large volume of distribution of digoxin. The older person using potassium depleting drugs (certain diuretics and corticosteroids) may be at increased risk of adverse events, as hypokalaemia and hypomagnesaemia predispose to toxicity [23].

- Oral blood glucose lowering agents (hypoglycaemics) – sulphonylureas

These agents act by stimulating the release of endogenous insulin from functioning pancreatic beta-cells [23]. The older person is more susceptible to hypoglycaemic events [15]. Elimination may be hindered in the older person due to age related renal and hepatic impairment. Older persons with an erratic food intake are also at increased risk of hypoglycaemia. Commonly used agents, both glibenclamide and gliclazide, are highly protein bound. Hypoalbuminaemia will therefore increase free drug levels with resultant increased therapeutic effects. Other protein bound drugs may also be displaced resulting in increased free (active) drug levels [23].

Additional contributors to adverse events in patients using drugs include concomitant alcohol consumption and the patient’s nutritional status. Alcohol induces hepatic enzymes when consumed chronically. This may increase the metabolism of certain drugs thus reducing their efficacy (for example warfarin). Acute alcohol ingestion can impair the hepatic metabolism of drugs [32]. Nutritional status can affect drug metabolism by altering the distribution volume of certain drugs. Hypoalbuminaemia due to malnutrition also reduces protein binding which may increase the amount of free (active) drug available. Certain drugs can contribute to poor nutrition by impairing the appetite of older persons for example digoxin and metformin [27].

Injury as a result of the use of a drug is defined as an adverse drug event (ADE) [33]. The term “event” rather than “reaction” or “effect” is preferred as it is not always possible
to ascribe certain causality to drug related clinical presentations. Since the publication of the influential report by the United States Institute of Medicine in 2000, *To Err is Human*; adverse drug events have been identified as an important patient safety priority internationally [33]. ADEs in older persons have been shown to contribute to between 7 and 14% of their Emergency Unit visits [35-39]. ADEs can worsen, contribute to or even cause the geriatric syndromes of falls, cognitive decline, incontinence, depression and cause dehydration. Subsequent sequelae to these conditions may be functional deterioration, hospitalization, nursing home placement and an impaired quality of life [40, 41]. The contribution of ADEs to the presentation of older persons to the EU for the public health sector in South Africa is not yet known.

Longitudinal data available from Australia shows the rate of ADEs to be on the rise, with the age standardised rate of adverse drug reaction-related hospital stays having increased from 2.5/1000 person years in 1981 to 12.9/1000 person years in 2002. The largest increase occurring in those aged 80 years and older, with a tenfold increase in men and a sevenfold increase in woman [42].

1.3. **Rationale for performing a clinical audit of older persons in the EU**

South Africa is currently undergoing a rapidly population ageing which is predicted to continue for at least the short- to medium future [43]. The calculated growth rate of the total population of South Africa in 2005 was 0.7%. This rate is predicted to decline to 0.3% by 2015 largely due to the influence of the HIV pandemic [44]. In contrast the annual growth rate in the over 60 year old population group was 2.3% in 2005 and is expected to increase marginally or remain constant. This means that approximately 1 in 20 persons in South Africa are currently older than 65 years. This figure will double to 1 in 10 persons by 2025 [43]. Studies exploring health care aspects relevant to the older person are required to facilitate adequate planning and management strategies.

There have been relatively few studies looking at the older person's presentation to the EU worldwide [4]. Considering the dearth of information of older persons presenting to the EUs in South Africa, this study set out to determine the characteristics of older persons presenting to the EU of a large tertiary level regional hospital (Groote Schuur
Hospital) and specifically to determine the impact of ADEs on older person’s presentation to the EU.

1.4. **The Groote Schuur Hospital Emergency Unit**

Groote Schuur Hospital has a regional tertiary level emergency unit that receives adult patients (age 13 and above) from approximately half of the Cape Town Metropolitan Region. It is an academic center affiliated with the University of Cape Town Faculty of Health Sciences. All non-traumatic medical and surgical emergencies presenting to this hospital are initially assessed in this unit. A separate dedicated unit manages all acute trauma related emergencies. Referrals are derived from either primary level facilities (Hanover Park, Van Guard Drive, Woodstock, and Silvertown Community Health Centers) located within its local referral area or from nearby secondary level hospitals (New Somerset, Victoria, Brooklyn Chest and GF Jooste Hospitals) and rarely from other secondary or tertiary level hospitals serving the greater Cape Town Metropolitan area (Tygerberg, Paarl, Hottentots Holland, Karl Bremer Hospitals).

During weekdays (Monday to Friday) the medical staff works three shifts. These are 08h00 to 16h00, 16h00 to 23h00 and 23h00 to 08h00. Staffing of the EU during the day generally comprises 1-2 consultants, 3 registrars and 2-3 junior staff whilst in the evenings there are 1-2 registrars and 2 junior staff and at night only 1 registrar and 1-2 junior staff. Consultants on duty are qualified specialist physicians. The registrars are medical doctors enrolled in specialty training in either the emergency medicine or general medicine departments. Junior medical staff comprises medical officers and medical interns rotating through the EU.
1.5. **Study objectives**

To ascertain the characteristics of older persons who present to a tertiary Emergency Unit with respect to the following aspects:

1.5.1. The baseline demographic, functional status and certain social aspects of older persons presenting to the emergency unit for evaluation.

1.5.2. The spectrum of problems that cause older persons to present to the emergency unit for evaluation.

1.5.3. To determine the burden of adverse drug events in the older person, to identify risk factors for these events, and to ascertain which drugs pose a higher risk for adverse events.
Chapter 2 - Study Design and Methods

2.1. Study design

A prospective cross-sectional study. (Prospective clinical audit).

2.2. Study population

Patients aged 65 years and older presenting for care at the tertiary emergency unit of Groote Schuur Hospital. All non-traumatic emergencies presenting to the hospital are assessed and stabilised in this unit. For this study the age of 65 years and older was selected. This is a convention used in classifying older persons eligible for geriatric services in the literature, as well as being the commonly recognised local age criterion classifying patients as admissible to the geriatric medicine service.

2.3. Sampling method

The audit included all patients aged 65 years and above who presented to the emergency unit during a three month period (11th February 2005 to the 22nd of May 2005).

The following patients were excluded from the study:

- Patients with traumatic injuries, these patients are assessed and managed in a separate unit (Trauma Unit) at Groote Schuur Hospital.
- Patients presenting to the EU over the weekends.
- Patients who died in the EU before audit information could be obtained.
- Patients who were already in-patients at other facilities and were referred to the tertiary facility for the purpose of undergoing a special investigation for example computer tomography (CT) scanning, magnetic resonance (MRI) scanning or ventilation perfusion lung scanning.
2.4. Measurement tools

A proforma specifically designed for the study was used for patient data collection [Appendix A]. Patient data was entered onto the pre-printed data capture sheets by the emergency unit attending doctor or the researcher (an emergency unit affiliated physician) and checked for completion by the researcher. The data obtained is routinely required for patient assessment and is charted in any older person assessed in the emergency unit.

2.5. Variables and definitions

The following variables were recorded during the audit process:

- Demographic information: Date of birth, hospital folder number, gender.

- Date of presentation, time of presentation, time of assessment by doctor.

- Baseline functional status with respect to the patient being dependent for assistance with:
  1. Basic Activities of Daily Living (BADLs): washing, dressing, eating and transfers.
  2. Instrumental Activities of Daily Living (IADLs): doing their own shopping, cooking, ability to independently use transportation and manage their own finances.

If the patient required assistance with one or more of the above they were scored as dependent in that category.

- Identification of the primary caregiver as either: a spouse, other family member, friend, residential or institutional nursing care, or as having no caregiver available.

- Assessment of the patient’s effort tolerance was made by utilizing information given by patient or caregiver about the amount and nature of activity they were able to perform. Physical energy demands of various activities are often compared in units called metabolic equivalents, or METs. The MET is a ratio comparing the energy consumption of a specified activity to energy consumption at rest. For example sitting quietly exerts a physical energy demand of 1 MET. The following 4 categories were selected to reflect relative work loads in terms of METS [45]:
  - Bed bound = patients work capacity equal to or less than 1 MET
  - Difficulty dressing = patients work capacity between 1.0 and 2.5 METS
- Inability to carry two bags of groceries on the flat, or walk up twenty stairs = patient unable to perform a work capacity of 2.5 to 4.0 METS.

- Able to climb more than twenty stairs without stopping or carry two bags of groceries = patient able to perform work capacity of more than 4.0 METS.

- The body habitus of the patient as assessed by the primary physician and categorised as either: obese, normal, thin or emaciated. Formal measurement of body weight and height was not performed.

- The clinical problems present as identified on a predetermined check-list. This list was derived from a pilot study performed in the emergency unit of Somerset hospital (a district level hospital) in 2004 (unpublished) and was determined to reflect common presentations, problems and diagnoses prevalent amongst older patients presenting to an EU.

- Social habits: non-users, current or previous users of alcohol or tobacco products.

- Medications taken by the patient; including over-the-counter, herbal, traditional and vitamin preparations (information obtained from the patient, caregiver and prior prescription information as available).

- Medication adherence was assessed using reporting by the patient or caregiver, considered together with the combination of clinical and biochemical parameters (for example measured serum drug levels, electrocardiogram findings, etc.) at the time of EU evaluation in support of either adherence or non-adherence.

- In the opinion of the attending physician or researcher whether an ADE contributed to the patient’s presentation to the emergency unit. This clinical judgment required confirmation by causality assessment scoring. (See 3.6.)

- If an adverse drug event was identified, details of the event were recorded.

- Patient outcome; either admission or discharge.

- Prolonged stay (more than 6 hours) of the patient in the EU between initial assessment and either admission or discharge. The time period of 6 hours was chosen as this reflects a window in which basic investigations (x-rays, electrocardiograms, and blood investigations) can generally be easily obtained in this EU. This would allow for a decision to be reached regarding appropriate management and disposal of the patient. A time period of longer than 6 hours may
reflect more complex investigation, management and decision making or a delay in providing for discharge or admission of the patient.

2.6. **Adverse drug event causality assessment**

Any substance (drug) taken with the intention of conferring a therapeutic benefit is capable of resulting in an unwanted or adverse event. The process of establishing that an individual drug taken has caused an observed adverse event is called causality assessment and needs to be done in a reliable and reproducible manner. A variety of drug causality assessment tools are described in clinical practice [46]. The definitions for adverse drug events and the causality assessment tools used in this study are detailed below:

2.6.1. Definition of an adverse drug event:

"an injury resulting from medical intervention related to a drug"

or simplified to: "harm resulting from the use of a drug" [33].

2.6.2. Adverse drug events identified in the South African Medicines Formulary (6th) edition were considered for causality assessment [23].

2.6.3. Causality assessment and definition of an adverse drug event was performed according to two recognised clinical methods as summarised below (A and B):

A). **Causality assessment by grades of causation** (Nebeker et al., 2004)[33, 46]

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Certain</td>
<td>A clinical event, including an abnormal laboratory test result, that occurs in a plausible time relationship to drug administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge)* should be clinically plausible. The event must be</td>
</tr>
</tbody>
</table>
pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.

- **Probable/likely** A clinical event, including an abnormal laboratory test result, that occurs within a plausible time sequence to administration of the drug, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a reasonable response on withdrawal (dechallenge)*. Rechallenge information is not required to fulfill this definition.

- **Possible** A clinical event, including abnormal laboratory test result, that occurs within a plausible time sequence to administration of the drug but could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear. Causality may be upgraded from this category once more information is available.

- **Unlikely** A clinical event, including an abnormal laboratory test result, whose temporal relationship to drug administration makes a causal relationship improbable and in which other drugs or chemicals or underlying disease provides plausible explanations.

*For adverse drug events caused by withdrawal or reduced dose of a drug, *rechallenge* is restoring the previous drug dose and *dechallenge* is reducing the drug dose or withdrawing the drug again.
B). Amended Hallas criteria for causality (Howard et al. 2003) [47]

1. Known adverse drug reaction, toxic reaction, response to omission of treatment or inadequate treatment.

2. Reasonable temporal relationship between commencement or cessation/omission of treatment and onset of problem.

3. Risk of further problems likely to be reduced by dose reduction, increase, discontinuation, closer monitoring or commencement of treatment.

4. Not explained by any other known condition of predisposition to the patient, or this condition/predisposition is likely to be exacerbated by the presence/absence of the drug.

5. For drug toxicity:
   o symptoms re-appear upon re-exposure.
   o laboratory tests show toxic drug levels or drug induced metabolic disturbances that explain the symptom/s.
   o symptom/s resolve on dose reduction or discontinuation of the drug.

For drug omission:
   o symptom/s resolve upon reintroduction of the drug or dose increase.

If 5 criteria = definite
If 4 criteria = probable
If 3 criteria = possible
If 2 or less criteria then not drug related or unevaluable.

In this study adverse drug events graded as possible, probable and certain/definite on both scoring systems were considered as clinically important and analyzed.
2.7. **Data analysis**

Data was entered into a Microsoft Access (2002) database and then coded for further analysis. Statistical analysis was performed using the Statistica version 7 (StatSoft Inc. 2005), and the SAS (SAS Institute Inc., Cary, North Carolina) version 8 (for multivariate analyses) statistical packages. Categorical data were compared using the Chi squared test.

To determine the inter-criteria test agreement for the calculation of adverse drug event causality, the kappa value was calculated using the Medcalc version 8.0 package. Calculating the difference between two known means was performed using the t-test (Medcalc version 8.0).

Univariate and multivariate analysis was performed using logistic regression models. Univariate and multivariate models were fitted to determine factors associated with the likelihood of developing ADEs. Factors considered for inclusion in the analysis were: age, sex, drug intake, body habitus, functional status for BADLs, number of clinical problems, adherence to medications and number of presentations during the study period. Continuous variables were categorised using their mean value. Factors identified to have a significant ($P$ value of $<0.05$) association with the likelihood of developing ADEs in the univariate models were used to build multivariate models and were included in the multivariate logistic regression model if significant in the univariate model. The Wald statistic was used as a test of the significance of the regression coefficient for the risk ratio in the univariate models.

2.8. **Ethical issues**

Ethics approval was obtained from the Research Ethics Committee University of Cape Town Faculty of Health Sciences for conduction of the clinical audit. Reference number 112/2005 [Appendix B]. This study was a review of audit data, and thus the results had no influence on the management of the patients. Informed patient consent was obtained prior to completion of the data capture form. Research was conducted according to the principles as set out by the World Medical Association Declaration of Helsinki [48].
2.9. **Funding**

The audit received no external funding.

2.10. **Conflict of Interest**

None.
Chapter 3 – Study Results

3.1. Results – General Audit Population

3.1.1. General audit statistics and coverage

The audit period was 77 days out of a 104 day period, between 11th February 2005 and 22nd May 2005. During this period there were a total of 5149 presentations to the emergency unit, of these 897 presentations were by patients aged 65 or older. Older persons therefore made up 17.4% of the patient load of the Emergency Unit during the audit period.

Of the 897 presentations 280 were excluded for the following reasons:

- Patients died before complete audit data was obtained (18 patients).
- Patients already in-patients at secondary level facilities and are referred to the tertiary facility for the purpose of a special investigation (e.g. CT scanning) (59 patients).
- Patients presenting on non-audit days (203 patients).

This left 617 older patients available for auditing. Audit data was captured on 517 of these patients, resulting in audit coverage of 84%. Audit data was not obtained for 100 patients who presented because EU physicians were unable to complete the data capture proforma. Calculating the accuracy of this sample size (517 patients) as being representative of the total auditable population (617 patients) using a confidence interval of 95% results in a confidence level of 1.7%. In other words we can be 95% certain that the true audit population’s characteristics are within 1.7% of those observed in the sampled audit population [49].
3.1.2. **Number of repeat presentations**

The 517 presentations captured reflected visits made by 468 different patients. Forty three patients presented more than once to the EU during the audit period as shown in table 1.

<table>
<thead>
<tr>
<th>Number of presentations</th>
<th>Number of patients</th>
<th>Contribution to total presentations</th>
<th>Percent (%) of patient number</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>1</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>12</td>
<td>0.8</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>76</td>
<td>8</td>
</tr>
<tr>
<td>1</td>
<td>425</td>
<td>425</td>
<td>91</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>468</strong></td>
<td><strong>517</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

3.1.3. **Age and gender of audit population**

Mean age of the study population was 74 years (range 65 to 95).

When divided into the different old age categories, the sample comprised:

- The young-old (65-74 years) 298 (58%)
- The old-old (75-84 years) 178 (34%)
- The oldest-old (85+ years) 41 (8%)

Out of the 517 presentations, 303 (59%) were made by women.
3.1.4. Waiting times and the hour of presentation to the emergency unit

3.1.4.1. Time of presentation
The proportion of presentations made by patients according to the different medical doctor shifts is detailed in table 2.

Table 2. Number of presentations by patients according to medical doctor shift times

<table>
<thead>
<tr>
<th>Time of shift</th>
<th>No. presentations</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>23h00 to 08h00</td>
<td>96</td>
<td>19</td>
</tr>
<tr>
<td>08h00 to 16h00</td>
<td>177</td>
<td>34</td>
</tr>
<tr>
<td>16h00 to 23h00</td>
<td>204</td>
<td>39</td>
</tr>
<tr>
<td>Time of arrival not recorded</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>517</td>
<td>100</td>
</tr>
</tbody>
</table>

3.1.4.2. Waiting time before assessment by doctor
Time of assessment by a medical doctor was recorded in 225 of the 477 (44%) patients with a recorded arrival time. These 225 patients waited a total time of 13386 minutes, with an average waiting time of 59.5 minutes per patient (Standard deviation 113 minutes).

3.1.4.3. Waiting time in the Emergency Unit before disposal
The audit documented whether patients waited more than 6 hours in the EU. Out of 517 patient presentations to the EU, 322 (62%) remained in the EU for longer than 6 hours.
3.1.5. **Baseline functional status**

3.1.5.1. **Basic Activities of Daily Living (BADL's)**

These included: washing, dressing, eating and transfers. One hundred and sixty (31%) patients were significantly dependent on a caregiver for help with one or more of these tasks on a daily basis. In four patients (<1%) BADL data was missing.

3.1.5.2. **Instrumental Activities of Daily Living (IADL's)**

These included: shopping, cooking, transport and managing finances. Three hundred and twenty six patients (63%) were dependent on caregiver assistance for one or more of these activities on a regular basis. Five patients (1%) had missing data.

3.1.5.3. **Effort tolerance**

Effort tolerance was divided into four categories as shown in table 3. Comparison with metabolic equivalent units and the predicted level of disability is shown [45].

**Table 3. Baseline effort tolerance of older patients presenting to the emergency unit**

<table>
<thead>
<tr>
<th>Effort tolerance</th>
<th>Number of presentations</th>
<th>Percent of total</th>
<th>Metabolic unit equivalents (mets)</th>
<th>Level of disability predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed Bound</td>
<td>51</td>
<td>10%</td>
<td>(\leq 1) met</td>
<td>Overt disability</td>
</tr>
<tr>
<td>Difficulty dressing</td>
<td>117</td>
<td>23%</td>
<td>(&gt;1-2.5) mets</td>
<td>Overt disability</td>
</tr>
<tr>
<td>Unable to do stairs, or carry 2 bags of groceries</td>
<td>251</td>
<td>48%</td>
<td>(&gt;2.5-4.0) mets</td>
<td>Subclinical disability</td>
</tr>
<tr>
<td>Climbs &gt; 20 steps</td>
<td>90</td>
<td>17%</td>
<td>(&gt;4.0) mets</td>
<td>Fit</td>
</tr>
<tr>
<td>No data</td>
<td>8</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.1.6. **Primary caregiver availability**

Of the patients: 131 (25%) were looked after by a spouse, 298 (58%) by other family members, 39 (8%) were residents in an institutional facility, 12 (2%) were cared for by friends and only 32 (6%) had no caregiver available. Data was missing for 5 (1%) patients.

3.1.7. **Lifestyle aspects**

3.1.7.1. **Smoking**

In men 49 (23%) were current smokers, while 85 (40%) were previous smokers. Only 64 (30%) reported never smoking.

In women 43 (14%) were current smokers, while 76 (25%) were previous smokers. One hundred and forty eight (49%) reported having never smoked.

Data was missing for 19 (7%) men and 36 (12%) women.

Men were significantly more likely than women to be past or current smokers (p<0.001).

3.1.7.2. **Alcohol use**

In men 30 (14%) acknowledged current alcohol consumption, while 27 (13%) were previous drinkers. One hundred and thirty eight (65%) reported never taking alcohol.

In women only 8(3%) admitted to current alcohol consumption, while 3 (<1%) reported previous alcohol intake. Two hundred and fifty five women (84%) denied previous alcohol use.

Data was missing for 19 (9%) men and 37 (12%) women.

Men were significantly more likely than women to have consumed alcohol (p<0.001).
3.1.7.3. **Body habitus**

Body habitus of the population is reflected in table 4.

<table>
<thead>
<tr>
<th>Body habitus category</th>
<th>Men</th>
<th>%</th>
<th>Women</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese</td>
<td>21</td>
<td>10</td>
<td>67</td>
<td>22</td>
</tr>
<tr>
<td>Normal</td>
<td>107</td>
<td>50</td>
<td>171</td>
<td>56</td>
</tr>
<tr>
<td>Thin</td>
<td>68</td>
<td>32</td>
<td>56</td>
<td>19</td>
</tr>
<tr>
<td>Emaciated</td>
<td>15</td>
<td>7</td>
<td>7</td>
<td>2.3</td>
</tr>
<tr>
<td>No data</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>214</td>
<td>100</td>
<td>303</td>
<td>100</td>
</tr>
</tbody>
</table>

Compared to women, men were significantly more likely to be underweight (thin or emaciated) (p<0.0001).

3.1.8. **Clinical problems**

As determined by the predetermined problem list the total number of problems for the audited sample was 1661. The average number of problems per patient presentation was 3.2 (range 0-6).

Table 5 shows the incidence of clinical problems in the sampled population.
Table 5. Incidence of problems present in older emergency unit patients

<table>
<thead>
<tr>
<th>Clinical problem</th>
<th>No. of patients</th>
<th>Percentage of total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>346</td>
<td>67.0%</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>214</td>
<td>41.4%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>165</td>
<td>31.9%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>131</td>
<td>25.3%</td>
</tr>
<tr>
<td>Stroke</td>
<td>91</td>
<td>17.6%</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>78</td>
<td>15.1%</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>77</td>
<td>14.9%</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>69</td>
<td>13.3%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>59</td>
<td>11.4%</td>
</tr>
<tr>
<td>Confusion</td>
<td>54</td>
<td>10.4%</td>
</tr>
<tr>
<td>Gastrointestinal tract bleeding</td>
<td>43</td>
<td>8.3%</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>34</td>
<td>6.6%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>30</td>
<td>5.8%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>26</td>
<td>5.0%</td>
</tr>
<tr>
<td>Asthma</td>
<td>24</td>
<td>4.6%</td>
</tr>
<tr>
<td>Dehydration</td>
<td>24</td>
<td>4.6%</td>
</tr>
<tr>
<td>Dementia (known)</td>
<td>23</td>
<td>4.4%</td>
</tr>
<tr>
<td>Seizures</td>
<td>23</td>
<td>4.4%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>21</td>
<td>4.1%</td>
</tr>
<tr>
<td>Urinary obstruction</td>
<td>19</td>
<td>3.7%</td>
</tr>
<tr>
<td>Constipation</td>
<td>16</td>
<td>3.1%</td>
</tr>
<tr>
<td>Syncope</td>
<td>16</td>
<td>3.1%</td>
</tr>
<tr>
<td>Depression</td>
<td>14</td>
<td>2.7%</td>
</tr>
<tr>
<td>Gastrointestinal obstruction</td>
<td>6</td>
<td>1.2%</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>6</td>
<td>1.2%</td>
</tr>
<tr>
<td>Bed sores</td>
<td>5</td>
<td>1.0%</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>5</td>
<td>1.0%</td>
</tr>
<tr>
<td>Fall</td>
<td>3</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

3.1.9. **General audit population medication use**

3.1.9.1. **Total prescription medication use**

Total number of prescription drugs taken was 2059 prescribed drugs for the 517 presentations, an average use of 4 medications per presentation (range 0-10).
3.1.9.2. Over-the-counter, vitamin and/or herbal medication use

Total number of different non-prescription preparations taken was 277, an average of 0.5 preparations per presentation (range 0-5).

3.1.9.3. Medication adherence

Medication adherence was reported in 422 (82%) of the 517 presentations. Patients admitted to not taking their medication in 33 (6%) presentations, while in 41 (8%) there was clinical evidence to support a suspicion that the patient was not maintaining adherence, for example a resting tachycardia in a patient on beta blockers in the absence of an alternate explanation, a normal prothrombin index in a patient who reported taking their prescribed warfarin, or collateral history from a reliable source that supported poor adherence. Adherence data was not recorded in 21 (4%) of the presentations. Thus in a total of 74 (14%) presentations the patient was determined to be non-adherent with their medication.

On bivariate analysis adherence did not differ significantly according to caregiver status (p=0.46).

3.1.10. Outcome

Three hundred and twenty two (62%) of the 517 presentations required admission to the hospital for ongoing care, 188 (36%) were discharged and the remaining 7 (1%) patients were transferred to another facility for ongoing management or further evaluation.

There was no significant difference in waiting time within the EU between those patients who required admission and those who were discharged (p=0.12).
3.2. Results – Adverse Drug Events

3.2.1. Contribution of adverse drug events
An adverse drug event was judged to have contributed to the presentation of the patient in 104 (20%) of the 517 presentations. Multiple adverse drug events were identified as having a causal relationship to the patient’s presentation in 14 (3%) presentations.

3.2.2. Causality assessment of adverse drug events
Forty two (40%) of the 104 presentations with an ADE were rated as probable by the causality assessment method used by Nebeker et al., 2004 [33]. Sixty two (60%) were of possible causality.

Using the causality method recommended by Howard et al., 2003 [47], forty one (39%) were of probable causality, while 63 (61%) were of possible causality.

Agreement between the two scoring systems was very good with $\kappa=0.9$.

3.2.3 Baseline demographic and clinical characteristics of patients with and without adverse drug events
Univariate analysis showed a significant difference between the groups for the following characteristics: (1) having a prescription drug intake of five or more drugs, (2) having three or more clinical problems, and (3) patients who were adherent with their medications (Table 6).

In the multivariate logistic regression analysis, having a prescription drug intake of five or more drugs retained significance ($p<0.001$), while adherence and having three or more clinical problems lost significance ($p$-values of 0.09 and 0.11 respectively). Table 7 shows the risk ratios of the characteristics shown to be significantly related to ADEs.

Adherence to prescription medication was higher in patients taking 5 or more medications 88% (188 out of 212) compared with patients taking less than 5 medications 77% (234 out of 305). This difference was significant ($p=0.008$).
Table 6. Baseline demographic and clinical characteristics of patients who had adverse drug events (n=104) and those who did not (n=413)

<table>
<thead>
<tr>
<th></th>
<th>Patients with ADE n(%)</th>
<th>Patients without ADE n(%)</th>
<th>P-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age group (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>62 (60)</td>
<td>236 (57)</td>
<td>0.84</td>
</tr>
<tr>
<td>75-84</td>
<td>35 (34)</td>
<td>143 (35)</td>
<td></td>
</tr>
<tr>
<td>&gt;85</td>
<td>7 (7)</td>
<td>34 (8)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>35 (34)</td>
<td>179 (43)</td>
<td>0.07</td>
</tr>
<tr>
<td>Female</td>
<td>69 (66)</td>
<td>234 (57)</td>
<td></td>
</tr>
<tr>
<td><strong>Body habitus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>27 (26)</td>
<td>119 (30)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>23 (22)</td>
<td>65 (16)</td>
<td>0.49</td>
</tr>
<tr>
<td>Thin</td>
<td>53 (51)</td>
<td>225 (54)</td>
<td></td>
</tr>
<tr>
<td>Emaciated</td>
<td>1 (1)</td>
<td>4 (1)</td>
<td></td>
</tr>
<tr>
<td><strong>Basic activities of daily living</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>71 (68)</td>
<td>282 (68.3)</td>
<td>0.32</td>
</tr>
<tr>
<td>Dependent</td>
<td>31 (30)</td>
<td>129 (31.2)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (2)</td>
<td>2 (0.5)</td>
<td></td>
</tr>
<tr>
<td><strong>OTC use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48 (46.1)</td>
<td>156 (37.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>No</td>
<td>56 (53.9)</td>
<td>257 (62.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Prescription drug intake</strong></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt; 5 drugs</td>
<td>38 (36)</td>
<td>267 (65)</td>
<td></td>
</tr>
<tr>
<td>≥ 5 drugs</td>
<td>66 (64)</td>
<td>146 (35)</td>
<td></td>
</tr>
<tr>
<td><strong>Presence of clinical problems</strong></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>≤ 3 problems</td>
<td>47 (45)</td>
<td>259 (63)</td>
<td></td>
</tr>
<tr>
<td>&gt; 3 problems</td>
<td>57 (55)</td>
<td>156 (37)</td>
<td></td>
</tr>
<tr>
<td><strong>Adherence to medication</strong></td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Yes</td>
<td>93 (89)</td>
<td>329 (80)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11 (11)</td>
<td>84 (20)</td>
<td></td>
</tr>
<tr>
<td><strong>Number of presentations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>99 (95)</td>
<td>326 (89.6)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3 (3)</td>
<td>35 (9.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>3</td>
<td>2 (2)</td>
<td>2 (0.5)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td></td>
</tr>
</tbody>
</table>

* χ² test. †OTC: over-the-counter drugs.
Table 7. Risk ratios of adverse drug events
Characteristics associated with an ADE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>P-value*</td>
</tr>
<tr>
<td>&gt; 5 drug intake</td>
<td>3.2(2.0-5.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt; 3 clinical problems</td>
<td>2.0(1.3-3.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Poor adherence</td>
<td>0.4(0.2-0.8)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Wald's statistic
Univariate and multivariate logistic regression analysis

3.2.4. Drugs and drug classes causally implicated in adverse drug events

The different individual prescription drugs causing ADEs together with the events caused are shown in table 8.

The thirteen most frequently used prescription drug/drug classes used by patients who did and did not develop ADEs are shown in table 9.

The drug class categories of cardiovascular, anti-thrombotics, analgesics and hypoglycaemics together accounted for 77% of the total observed ADEs as shown in table 10.

Use of an angiotensin converting enzyme inhibitor (p=0.009), non-steroidal anti-inflammatory (p<0.0001) and warfarin (p=0.001) were associated with a significant likelihood of having an ADE, independent of whether they specifically caused an ADE. (Table 11)
<table>
<thead>
<tr>
<th>Drugs</th>
<th>Events</th>
<th>No of events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin converting enzyme inhibitor</td>
<td>Hyperkalaemia</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Hypotension</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Renal impairment</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Angioedema</td>
<td>2</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Diarrhoea</td>
<td>1</td>
</tr>
<tr>
<td>Aspirin</td>
<td>GIT bleed</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Microcytic Iron deficiency anaemia</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia</td>
<td>1</td>
</tr>
<tr>
<td>Atropine</td>
<td>Confusion</td>
<td>1</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Hypoglycaemia (masked symptoms)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Worsening heart failure</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Withdrawal worsening angina</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hypotension</td>
<td>1</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Skin reaction</td>
<td>1</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Hyperglycaemia</td>
<td>1</td>
</tr>
<tr>
<td>Digoxin</td>
<td>GIT bleed</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Toxic (clinically symptomatic and/or toxic serum levels)</td>
<td>8</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Dehydration</td>
<td>3</td>
</tr>
<tr>
<td>Insulin</td>
<td>Hypoglycaemia</td>
<td>1</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Movement disorder</td>
<td>1</td>
</tr>
<tr>
<td>Nifedipine XL</td>
<td>Hypotension</td>
<td>1</td>
</tr>
<tr>
<td>Non-steroidal anti-inflammatories</td>
<td>Worsening heart failure</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>GIT bleeding/anaemia</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Renal impairment</td>
<td>1</td>
</tr>
<tr>
<td>Opioids</td>
<td>Confusion</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Respiratory depression</td>
<td>1</td>
</tr>
<tr>
<td>Oral hypoglycaemics</td>
<td>Hypoglycaemia</td>
<td>9</td>
</tr>
<tr>
<td>Other: Methotrexate, Salazopyrine, Clexane</td>
<td>Various</td>
<td>3</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Cerebellar dysfunction with toxic serum levels</td>
<td>1</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Coma</td>
<td>1</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Worsening heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Bleeding</td>
<td>12</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>118</strong></td>
</tr>
</tbody>
</table>

GIT: Gastrointestinal tract
Table 9. Medications used in patients who developed an adverse drug event (n=104) versus those who did not (n=413)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Patients developed adverse events (n=104)</th>
<th>Patients did not develop adverse events (n=413)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n(%)</td>
<td>n(%)</td>
<td></td>
</tr>
<tr>
<td>ACE Inhibitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>41(39.4)</td>
<td>264(63.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>63(60.6)</td>
<td>149(36.1)</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>56(53.9)</td>
<td>248(60.1)</td>
<td>0.25</td>
</tr>
<tr>
<td>Yes</td>
<td>48(46.1)</td>
<td>165(39.9)</td>
<td></td>
</tr>
<tr>
<td>Beta Blocker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>61(58.7)</td>
<td>303(73.4)</td>
<td>0.003</td>
</tr>
<tr>
<td>Yes</td>
<td>43(41.3)</td>
<td>110(26.6)</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>85(81.7)</td>
<td>380(94.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>19(18.3)</td>
<td>23(5.6)</td>
<td></td>
</tr>
<tr>
<td>Oral hypoglycaemics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>75(72.1)</td>
<td>329(79.7)</td>
<td>0.096</td>
</tr>
<tr>
<td>Yes</td>
<td>29(27.9)</td>
<td>84(20.3)</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>95(91.4)</td>
<td>388(94.0)</td>
<td>0.34</td>
</tr>
<tr>
<td>Yes</td>
<td>9(8.6)</td>
<td>25(6.0)</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>82(78.9)</td>
<td>387(93.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>22(21.1)</td>
<td>26(6.3)</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>94(90.4)</td>
<td>394(95.4)</td>
<td>0.047</td>
</tr>
<tr>
<td>Yes</td>
<td>10(9.6)</td>
<td>19(4.6)</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>100(96.2)</td>
<td>404(97.8)</td>
<td>0.33</td>
</tr>
<tr>
<td>Yes</td>
<td>4(3.8)</td>
<td>9(2.2)</td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34(32.7)</td>
<td>188(45.5)</td>
<td>0.018</td>
</tr>
<tr>
<td>Yes</td>
<td>70(67.3)</td>
<td>225(54.5)</td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>100(96.2)</td>
<td>400(96.8)</td>
<td>0.72</td>
</tr>
<tr>
<td>Yes</td>
<td>4(3.8)</td>
<td>13(3.2)</td>
<td></td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>96(92.3)</td>
<td>390(94.4)</td>
<td>0.42</td>
</tr>
<tr>
<td>Yes</td>
<td>8(7.7)</td>
<td>23(5.6)</td>
<td></td>
</tr>
<tr>
<td>Non-steroidal anti-inflammatory drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>86(82.7)</td>
<td>387(93.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>18(17.3)</td>
<td>26(6.1)</td>
<td></td>
</tr>
</tbody>
</table>

*χ² test

†ACE = Angiotensin converting enzyme
Table 10. Frequency of adverse drug events for the four most common drug categories

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Percentage of total ADEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular (beta-blockers, ACE inhibitors, digoxin, diuretics, calcium channel blockers)</td>
<td>36%</td>
</tr>
<tr>
<td>Anticoagulant/antiplatelet (warfarin, low dose aspirin)</td>
<td>25%</td>
</tr>
<tr>
<td>Analgesic (nonsteroidal anti-inflammatory drugs, opioids)</td>
<td>18%</td>
</tr>
<tr>
<td>Hypoglycaemics (insulin, oral agents)</td>
<td>8%</td>
</tr>
</tbody>
</table>

ACE = Angiotensin converting enzyme

Table 11. Risk Ratio (RR) of drugs associated with the likelihood of having an adverse drug event

<table>
<thead>
<tr>
<th>Drug</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95%CI)</td>
<td>P-value*</td>
</tr>
<tr>
<td>ACE Inhibitor</td>
<td>2.7 (1.8-4.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>1.9 (1.2-3.0)</td>
<td>0.004</td>
</tr>
<tr>
<td>NSAIDs#</td>
<td>3.4 (1.9-6.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypoglycaemic agents</td>
<td>1.6 (1.0-2.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Corticosteroids, oral</td>
<td>2.2 (1.0-4.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>Diuretics</td>
<td>1.7 (1.1-2.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>Warfarin</td>
<td>3.8 (2.0-7.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Wald’s statistic

ACE = Angiotensin converting enzyme
NSAIDs = nonsteroidal anti-inflammatory drugs

Univariate and multivariate logistic regression analysis
3.2.5. **Adverse drug events and identified clinical problems**

A simple cross tabulation was performed for the most common clinical problems (having an incidence greater than 10%) to see whether adverse drug events differed for each problem or condition.

3.2.5.1. **The following problems were significantly associated with adverse drug events:**

- Hypertension (p=0.05)
- Heart failure (p=0.0033)
- Diabetes (p=0.011)
- Stroke (p=0.0073)
- Atrial fibrillation (p=0.014)
- Gastrointestinal bleeding (GIT) (p<0.0001)

3.2.5.2. **The following problems were NOT associated with an adverse drug event:**

- Chronic Obstructive Pulmonary Disease (COPD) /Asthma (p=0.44)
- Neoplasia (p=0.44)
- Ischaemic heart disease (p=0.18)
- Confusion (p=0.26)
- Musculoskeletal pain syndrome (p=0.19)

3.2.5.3. **Multivariate analysis of clinical problems associated with adverse drug events**

In the multivariate logistic regression analysis (adjusting for previously determined non-drug confounding variables of: number of drugs, number of clinical problems, adherence and admission requirement) the clinical problems of stroke and gastrointestinal bleeding were significantly related to the presence of an adverse drug event. Risk ratios are shown in table 12.
Table 12. Risk ratio of an adverse drug event being identified in patients according to their clinical problem (As determined by multivariate logistic regression analysis)

<table>
<thead>
<tr>
<th>Clinical Problem</th>
<th>Multivariate analysis</th>
<th>RR (95%CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td>1.4 (0.75-2.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>1.5 (0.9-2.6)</td>
<td>0.13</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
<td>1.7 (0.9-2.9)</td>
<td>0.08</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td>0.4 (0.2-0.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
<td>1.5 (0.7-2.9)</td>
<td>0.26</td>
</tr>
<tr>
<td>GIT* Bleeding</td>
<td></td>
<td>7.2 (3.5-14.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*GIT = Gastrointestinal

3.2.6. Contribution of adverse drug events to hospital admissions

Patients having an ADE were significantly more likely to require admission to hospital, 70% versus 60% for patients without an ADE (p=0.04).

ADE’s contributed to 74 (23%) of the total 322 admissions.
Chapter 4 - Interpretation and Discussion of Results

4.1. General audit population

4.1.1 General audit results

This study shows that older persons contribute a significant burden towards the patient load of the EU. A recently published United Kingdom based study looked at nearly 3 million patient attendances to the EU. This showed that persons aged 65 years and over accounted for 18% of attendances, which is similar to the 17.4% shown in this study [4]. In the United Kingdom persons over 65 years comprise 16% of the total population [50]. In the Western Cape Province persons over 65 years comprise approximately 5.6% of the total population of 4.6 million [3]. Presentations by older patients in the Western Cape are thus disproportionate to their proportion of the general population. This is likely due to a combination of factors which include both age related accumulated disease burden and impecunity. Older persons have less social and financial resources and therefore are unable to access either state primary care facilities, private health care facilities or other community support services.

4.1.2. Number of repeat presentations and it implications

It has been proposed that repeated presentations to the emergency unit by older persons may be used as an indicator of quality of care provision. The reasoning for this is that patients with repeat presentations may comprise: (1) patients who develop new problems, (2) patients with persistent old problems, (3) patients who present again because of adverse events related to therapy changes and (4) patients who return because their initial evaluation and management was inadequate or incorrect. Repeat visits by patients made up 9.2% of the total patient visits. Thus almost one in ten of the older EU population will have repeated visits in a 3 month period. Does this rate reflect poor quality of care provision by the EU? Data from the United Kingdom (UK) shows that rates of EU repeat presentation for older persons in the same year may be up to 38%. In the following year this readmission rate falls to 9%, and within five years is within the 3% repeat presentation rate observed for the general population [43]. In a short (one month duration) Australian study repeat presentations occurred in 10% of study patients (age >75 years) [5]. While direct comparison is not strictly possible, it would appear that our
EU's data for repeat presentation is comparable to that of some of the more affluent first world settings.

Patients identified as repeat presenters (having ≥ 2 presentations in a year) to the EU could be targeted for interventions to lower their admission rates. Published work by Roland et al., 2005 [51] has shown that such intervention is unlikely to be effective because of a rapidly reducing rate of repeat presentation in subsequent years. It is thought that a high mortality in this high risk population may account for an apparent ineffectiveness of interventions aimed at reducing EU repeat visits. The implications of this observation is that when planning an intervention aimed at reducing rates of EU/hospital presentation, monitoring the rates of repeat presentation is not a reliable variable. Interventions aimed at reducing EU repeat visits would need to be compared against a carefully selected control group to assess their effectiveness.

4.1.3. Time of presentation

Older patients may present at any time to the EU, but the majority of presentations (58%) with a documented time of initial presentation occurred outside of the “normal working hours” (08h00 to 16h00). The most favoured time of presentation was during the evening shift (39%). On-site EU consultant input is generally only available during the day shift. The implications for this are that older patients with more complex problems may be kept overnight waiting for consultant input regarding their care. Support of this is provided by the finding that 62% of older patients remained in the EU for a period longer than 6 hours. This delay of either discharge or admission may have implications for a frail older patient confined to lying on a hard stretcher for a protracted period of time. The EU setting may not provide a formal nursing routine that pays attention to aspects of care relevant to an older patient in the acute hospital setting for example: delirium prevention, pressure care, adequate hydration, nutrition, aspiration prevention, temperature regulation, and other important issues such as patient dignity and comfort. Comparable UK data of patients presenting to the EU shows that patients over 65 years favoured presenting in the mornings and early afternoon 09h00 to 16h00 [4], this is different from this study. A possible reason for this may be that older people in South Africa are more reliant on family members to bring them to hospital and that these persons may work during the day. Additionally, it is possible that the limited ambulance services are overloaded during the day and only bring older patients, who may be
assigned a lower priority, at less peak times. A third explanation for the bulk of presentations occurring outside of "normal" working hours is thought to be the possibility of poor patient access to primary care health. This could contribute to opportunistic EU visits as EUs are readily accessible on a 24 hour basis.

A marker of the efficiency of an EU may be the interval between initial arrival and assessment by a doctor. Study data was only available for less than half of the presentations. The average waiting time was one hour, this provides a quality control measure against which future efficiency measures may be compared. Possible factors that could contribute to a prolonged waiting time include: (1) junior staff may be intimidated by the multitude of problems the older person may have, (2) the older person may appear less ill initially, (3) they may not be seen as a priority by junior staff or (4) older persons may also be less vocal than younger patients thus attracting less attention.

4.1.4. Functional status and caregiver availability

Baseline (prior to current illness) functional status (patient's ability to carry out activities of daily living) generally reflects a patient's level of independent survival. Persons dependent on assistance with their basic activities of daily living may require 24 hour supervision depending on the nature and number of basic activities of daily living they require help with. In the study population a third of the patients had limiting disability rendering them dependent on 24 hour care assistance. Impaired effort tolerance causing overt disability may also impact on the ability to live independently.

Caregiver availability data obtained from this study highlights the large role family play in caring for the older population. More than 80% of the patients were cared for by a family member, while only 8% were residents in an institutional facility. This provides an impetus for continued expansion of services that assist and support family members, for example the Community/Home-Based Care Program which provides basic nursing care needs by formal or informal caregivers to patients in their own homes. The initial family contact at the EU presentation provides an important opportunity for establishing communication necessary to implement both care plan and future discharge planning. This aspect may be a component overlooked by initial attending staff.
4.1.5. **Primary caregiver**

The majority of older patients presenting to the emergency unit in this study identified either a spouse (25%) or family member (58%) as their primary caregiver. This has important implications in the management and the discharge planning of functionally dependent older patients. Often the family may be unable to cope with the additional care burden secondary to an acute illness resulting in a deterioration of a patient's functioning. In order to sustain our predominantly family-based model of older person care our health system needs to be able to provide respite support. At present there is generally severe limitation to this service with few facilities and few trained support staff.

4.1.6.1. **Lifestyle aspects - General**

Older men in this study are significantly more likely to be previous or current smokers \((p<0.001)\), to consume alcohol \((p<0.001)\) and/or be judged to be underweight \((p<0.0001)\) than their women counterparts.

4.1.6.2. **Lifestyle aspects - Alcohol use**

Firm data on alcohol consumption in the older person is lacking but some data has suggested a prevalence rate of up to 14% for alcohol use disorders in older patients who are assessed in the EU [52]. Recognised sociodemographic risk factors for an alcohol use disorder in the older person includes male gender, socially isolated, single, separated or divorced [52]. This study confirms that male gender is more likely to be associated with alcohol consumption.

This study likely underestimates the rate of male current alcohol consumers (14%). Two reasons for under-recognising alcohol-related illness in older persons are: they are less likely to disclose alcohol use and health care workers have a lower index of suspicion when assessing older persons, thus failing to elicit a significant history. This study’s data may support the former suggestion, as 65% of men reported having never used alcohol.

4.1.6.3. **Lifestyle aspects - Body habitus**

Malnutrition is defined as a state of being poorly nourished. This may be due to either a lack of one or more nutrients (undernourished) or an excess of nutrients (over nutrition).
Between 29%-61% of the older patient hospital population will suffer from malnutrition at any one time [27]. This study population has an estimated malnutrition rate of 49% in men and 44% in woman. Men were significantly more likely to be undernourished than women (p<0.0001). In this study formal and validated nutritional assessment was not performed because of logistic and resource constraints. The assessment of body habitus in a subjective manner does not permit firm conclusions to be drawn.

4.1.7. Clinical problems

The spectrum of problems manifest in older persons in this study is compared with that of two other EU studies in Table 13 [4, 5]. Disease affecting the cardiovascular system is the most common problem in older persons presenting to the EU. Gastrointestinal system involvement appears under represented in this study's patients. The development of management protocols should focus on conditions/clinical problems that occur more frequently in older EU patients. However, the nature of multiple problems in a single older patient may (average of 3.2) caution against protocols that do not attempt to consider the interaction of other comorbid conditions with any single problem to which a protocol may be targeted.

Table 13. Comparison of the relative frequencies of common system disease involvement in older Emergency Unit patients (Values given are a percentage (%) frequency of total disease burden)

<table>
<thead>
<tr>
<th>System involvement</th>
<th>Groote Schuur EU (South Africa)*</th>
<th>United Kingdom</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(excl. hypertension)</td>
<td>27.2</td>
<td>17.5</td>
<td>14.8</td>
</tr>
<tr>
<td>Neurological</td>
<td>12.7</td>
<td>8.2</td>
<td>6.7</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>4.7</td>
<td>6.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Respiratory</td>
<td>7.4</td>
<td>10.9</td>
<td>10.9</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>5.5</td>
<td>12.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>2.4</td>
<td>6.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Percentage of total</td>
<td>59.9</td>
<td>61.3</td>
<td>57.1</td>
</tr>
</tbody>
</table>

*Groote Schuur data obtained from table 5.

[United Kingdom data from reference 4 and Australian data from reference 5].
When the spectrum of clinical problems present in the older EU population is compared with the ten most common single causes of death of patients 60 years and older in the Western Cape it closely reflects the mortality burden (table 14). See Appendix C for more detailed mortality information in the Western Cape as obtained from the National Burden of Disease Study, 2000 [53].

In comparison a study reporting on medical patients admitted to a tertiary hospital in the Eastern Cape during 1986-87 showed a total older patient mortality rate of 5.4% with respiratory diseases comprising 22%, stroke 13% and cardiovascular disease 12% of the total mortality [54]. Respiratory disease contributed more than cardiovascular disease to the mortality in this predominantly periurban setting.

Table 14. Six leading causes of death in the Western Cape compared with the Emergency Unit incidence of the same problems

<table>
<thead>
<tr>
<th>Disease</th>
<th>Contribution to total mortality (age &gt;60, %)</th>
<th>Emergency unit frequency (% of patients affected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>22.2</td>
<td>41.4</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6.2</td>
<td>31.9</td>
</tr>
<tr>
<td>Stroke</td>
<td>15.5</td>
<td>17.6</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>11.2</td>
<td>14.9</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>6.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2.7</td>
<td>5.8</td>
</tr>
</tbody>
</table>

Falls are under-represented in this study as patients commonly present to the Trauma unit and not the EU. Falls are increasingly being recognised as an important non-specific feature of geriatric acute illness as well as an associated risk factor for significant ADEs [20].

The contentious issue of "social problems" was not considered in this study. Doctors are often reluctant to label patients with this problem. The literature sites figures of between 4.6 and 19% of older patients with a predominantly "social problem" component to their EU presentation [5]. Thus social work services are mandatory for an EU to appropriately manage older patients.
The clinical problem of confusion in this study was used to denote patients who were not oriented to time, place or person in the EU and who were not known previously to have a diagnosis of dementia (patients known with dementia were placed in their own clinical problem category). The confused problem category therefore comprised both undiagnosed demented patients and patients with an acute confusional state (delirium). During the study period 54 confused and 23 known dementia patients were assessed. Thus 77 of the 517 (15%) patients had cognitive dysfunction. Patients with mild cognitive dysfunction (not known with dementia and not overtly confused) may have been overlooked by EU staff not routinely screening for cognitive impairment.

4.1.8.1. Aspects of medication use in the study population

Studies looking at medication use in the older population site a mean number of prescription medications as between 4 and 5 for both ambulatory, institutional and community dwelling patients [20, 37, 39, 55-57]. These studies were all conducted in more affluent first world countries (France, United States of America, Denmark, Canada and the Netherlands). This study population has a comparable average number of prescription medications (4 per patient).

The use of 'over-the-counter', vitamin and/or herbal medications by patients is increasingly being recognised as a contributor to the burden of drugs patients are subjected to. In this study the low reported average of only 0.5 preparations per patient may reflect a combination of both under reporting by the patient (fear of reaction from the doctor) and the low socioeconomic status of these patients (precludes purchasing of these often relatively costly preparations).

4.1.8.2. The role of medication adherence

A study by Malhorta et al., 2001 [38] in India showed that poor adherence accounted for 7.6% of older person presentations to a tertiary EU. Factors identified in that study to be associated with poor adherence were: poor recall of the medication regimen, consulting multiple physicians, female gender, polypharmacy (taking 3 or more medications), drug costs, and patient selection of alternate and non-conventional forms of treatment.
To be considered adherent patients are accepted to be taking more than 80% of their medications more than 80% of the time. A significant proportion of older patients have poor adherence. An example of this is the recent RECORD trial based in the United Kingdom (with over 5000 participants, mean age 77 years) [58]. This secondary prevention population based trial measured adherence by postal questionnaire during the two year trial period. At the end of the 24 month period only 60% of patients taking tablets (combinations or Vitamin D, calcium carbonate or placebo) did so on more than 80% of days. In a non-trial setting this is likely to be less, and estimates of poor adherence figures for older persons in the EU setting range between 26 and 59% [38].

While this study did not seek to specifically address the issue of non-adherence the self reported adherence rate of 82% is comparable to that reported in the RECORD trial. This may be an overestimation of adherence. Older patients may report adherence as a fear of poor adherence disclosure may evoke a negative reaction from their health care provider. Eliciting a history of poor adherence should be done in a non-judgmental manner and consider all factors involved in the "chain" of medication provision ranging from: adequate pharmacy supplies, delivery, sufficient cognition to administer their medication or alternatively appropriate caregiver supervision and lastly the ability to ingest the medication. In patients identified as having an ADE only one event (worsening of angina) was attributable to patient poor adherence. Interestingly, this patient was unable to have their prescription filled due to inadequate stock of beta blockers at their community health centre. Subsequent withdrawal tachycardia induced by abruptly stopping his beta blocker contributed to his presentation with angina.

4.1.9. Outcome

Older patients have been recognised as one of the main groups at risk of a poor outcome after attendance at an EU. Reasons cited for this include their significant disease burden, severity of their presenting problems, and lack of community support upon discharge [5]. In a study by Downing and Wilson 2005 [4] in the United Kingdom they reported an admission rate of 46.1% for patients over 65 years and only 14.1% for patients less than 65 years. United Kingdom EU's also assess injuries which comprise 33.1% of their cohorts' problems. In this study over 60% of older patients presenting to the EU required admission. Our three tier health system (primary, secondary and tertiary
level care facilities) may account for this high admission rate as very ill patients are referred for tertiary level care.

4.2. **Adverse drug events**

4.2.1. **Contribution of adverse drug events**

The study's findings confirm a high incidence of ADEs in older persons presenting to the EU. The rate of 20% is amongst the highest reported in the literature, possibly due to the study actively seeking ADEs in a group of high risk patients. However, it is well recognised that the protean manifestations and clinical presentation of ADEs in older patients may account for some events remaining unrecognised.

4.2.2. **Causality assessment of adverse drug events**

The large variation in the reported rates of ADEs in the EUs (6.7-14.2%) may be attributable to methodological differences on the causality assessment of ADEs in the different studies. Recently attempts have been made to standardise ADE terminology and determination, and the present study followed these recommendations [33]. The setting of the EU places a restriction on the level of causality assessment achieved for any suspected ADE. In this study, levels of "possible" or "probable" causality were achieved. The "certain" or "definite" level of causality requires rechallenge criterion to be satisfied. Rechallenge is often precluded in the EU setting for safety and efficiency reasons.

The study showed age not to be a specific risk factor for ADEs, but rather the number of concurrent prescription medications to be the best predictor of an ADE. The number of coexistent diseases is directly related to the number of medications taken.

4.2.3. **Prescription drug classes implicated in adverse drug events**

Drug classes associated with ADEs in this study have been consistently identified in similar EU studies for their risk of causing ADEs in older patients. In the literature the reported contribution to total ADEs per drug class in the older EU population are: analgesics
(NSAIDs and opioids) 15-36%, cardiovascular drugs (including diuretics, beta-blockers, ACE inhibitors and digoxin) 5-41.8%, antithrombotics (low dose aspirin and warfarin) 7.9-13.3% and hypoglycaemic agents 6.6-31% [21, 35-39, 42, 56, 59]. Interpretation of the contribution of each drug class to the total burden of ADEs requires caution.

Accumulated trial data shows that agents such as beta-blockers, ACE inhibitors, aspirin, warfarin and hypoglycaemic medications have significant beneficial effects on morbidity and mortality [16, 17, 60-62]. Despite optimal prescription and monitoring of these beneficial agents, a certain rate of ADEs will be observed. The number of beta-blocker related ADEs (17%) in this study suggests that this class of drugs, proven to be highly beneficial in ischaemic heart disease and cardiac failure [16, 62], may be incorrectly prescribed despite an appropriate indication. In the public sector of the Western Cape atenolol and propranolol are the only beta-blockers available at primary and secondary level care. There is insufficient evidence that the use of atenolol or propranolol in heart failure confers the benefit reported with carvedilol, metoprolol or bisoprolol. The concept of class effect refers to a hypothesis that drugs within a pharmaceutical class all work similarly, have similar advantages and disadvantages, and are therefore to a large extent interchangeable [63]. The class effect does not necessarily apply to the older patient population with their complex pathophysiology. The practice of intra-drug class substitution in the older person in settings where original trial validated drugs are not available may increase the risk of ADEs [63]. Essential drug lists present in both the public and private health care sectors add the risk of dictating forced intra-class substitution. There is a concern that this practice will cause increased resultant adverse events which may potentially cost much more in health outcomes and overall expenditures rather than restricting costs [63].

Other drugs used extensively in the older patient have not been shown to offer any survival benefit and are used mainly for symptomatic benefit only. These drugs include non-steroidal anti-inflammatory agents, digoxin and psychoactive agents such as low dose tricyclic antidepressants [18, 64, 65]. The risks in these drugs may frequently outweigh any benefit, particularly when used in patients with significant comorbidity. Increasingly safer substitutes are available for example: paracetamol for chronic pain and the newer anti-depressant agents in place of the tricyclic antidepressants. In the case of digoxin, correct dosage prescription for corrected renal function, or substitution with a beta-blocker for heart rate control may reduce ADEs. In the future more widely
available non-pharmacological measures (eg. circumferential pulmonary-vein ablation for chronic atrial fibrillation [66]) may permit a reduction in the use of potentially toxic pharmacological agents.

A published study by Cunningham et al., 1997 [35] explored the issue of an intervention strategy aimed at reducing the incidence of NSAID ADE related hospitalisation. In their setting NSAIDs accounted for 42% of their total ADE's (15 of 36 events) with 87% of these being judged as preventable. The study intervention used a combination of: (1) written educational intervention targeting referring general practitioners, (2) patient information leaflet given to patients prescribed NSAIDs, and (3) oral presentations educating trainee general practitioners. A 7% drop in the prescription rate was noted after the intervention but this did not achieve significance. This was most likely due to both a short study period of only 9 months and the relatively low numbers of NSAID related drug side effects initially observed.

4.2.4 Medication adherence and adverse drug events

Adherence with medication is an intuitive risk for the likelihood of developing an ADE. There was a significant (risk ratio 0.4) protective effect of poor adherence against an ADE in this study. Poor adherence as a protective trend was observed in the multivariate analysis (p=0.09).

Poor adherence was shown to be significant (p<=0.008) in patients taking less than 5 prescription medications in comparison to patients taking 5 or more. In contrast the opposite was reported in the study by Malhotra et al. 2001 [38], there was a higher risk of poor adherence in patients taking 3 or more medications (p=0.0001). Continuous variable categorisation may account for these apparently discrepant results. In this study continuous variables were categorised according to their mean values for the multivariate analysis, hence the choice of the category of 5 or more prescription drug versus less than 5 prescription drugs. Reporting bias is another factor which may influence the above observed discrepancy. Patients who are poorly adherent with one or more of their medications may not report these medications to their attending doctor, thus appearing to be on fewer medications.
4.2.5. **Clinical problems and adverse drug events**

The following clinical problems with an incidence of over 10% in the study population were identified to have a significant risk of adverse events: (1) hypertension and heart failure (patients taking ACE inhibitors, beta blockers, diuretics, warfarin and digoxin), (2) patients with diabetes (use of oral hypoglycaemic agents and insulin), (3) patients with atrial fibrillation (require antithrombotics, either warfarin or aspirin), and (4) gastrointestinal (GIT) bleeding (aspirin and NSAID use). The multivariate analysis identified the clinical problem of GIT bleeding to have the highest risk of being related to an ADE (risk ratio 7.2).

Interestingly stroke was negatively associated with ADE risk in this study group. In other words stroke appeared to significantly protect the patient against an ADE (relative risk 0.4; 95% CI=0.2-0.9). A possible explanation for this surprising finding may be that stroke patients are under treated and thus have a lower risk of an ADE. Stroke patients took a mean number of 3.6 prescription medications compared to the average total sample mean of 4.0 prescription medications. This difference between the means of 0.4 was not statistically significant (p=0.44) using the t-test, thus stroke patients are not under treated. An alternate explanation for this observation is that ADEs in stroke patients may have been more occult and therefore not identified.

A clinical presentation with confusion was not significantly associated with the identification of an ADE in this study. Data collection did not distinguish between acute confusion (delirium) and chronic confusion (undiagnosed dementia). This should have been performed because drugs alone have been shown to account for 12-39% of cases of delirium [67]. There is a possibility that ADEs in the confused patient may have been under recognised in this study.

### 4.2.6. Contribution of adverse drug events to hospital admissions

A patient with an ADE is significantly more likely to require hospital admission. During the study period ADEs contributed to 23% of older patient admissions to Groote Schuur Hospital. Thus the observed rate of ADEs would account for over 250 admissions per
year. Data from the United Kingdom shows that drugs contributed to 11% of older patient hospital admissions. This data was obtained in the early 80s and 90s, and may not be comparable with recent data as a result of changing prescription trends [22].

4.2.7. The role of alcohol and adverse drug events

The role of alcohol and its possible predisposition for contributing to ADEs could not be determined due to significant (10.8%) missing data.

The contribution of alcohol to ADEs has been previously recognised in a large survey [32] which showed that up to one in five older persons were using alcohol in conjunction with a drug known to interact with alcohol. While the majority of patients reported in the study by Pringle et al., 2005 [32] were in nursing homes, the spectrum of medication use was comparable to most populations of older persons with chronic diseases commonly found in their age group. Common medications which have significant interactions with alcohol are: sedatives (where alcohol enhances the sedative effect), non-steroidal anti-inflammatories (which have an increased risk of gastric mucosal irritation when used with alcohol) and concomitant use with drugs metabolised by the liver (e.g. warfarin, anticonvulsants and rifampicin among others) (resulting in unpredictable drug levels which may be variably altered depending on the alcohol mediated hepatic enzyme induction or inhibition).

4.2.8. Comparison of adverse drug event rates with other local data both published and unpublished

A literature review revealed only one published South African study. The prospective study conducted in 1982 documented adverse drug events in a group of 300 white male and female patients admitted to the general medical wards of Addington hospital in Kwazulu Natal [68]. Of the patients, 178 were age 60 years or older. Patient admission was attributed to an ADE in 4.6% of presentations. The mean age of these patients was 72 years with only 2 of the 14 patients being less than 65 years of age. Of the 14 presentations, drugs most frequently implicated were: warfarin 2 (14%), digoxin 3 (21%), aspirin 2 (14%), and beta blockers 2 (14%). Despite 23 years elapsing, similar drug groups remain frequent contributors to adverse drug events in older patients.
In an unpublished clinical audit performed during 2004 at a secondary level hospital (New Somerset Hospital, Green Point, Cape Town) 27 of the 249 patients age 65 years or older presenting to the EU were reported to have an ADE that contributed to, or resulted in their presentation. Of the 27 ADEs reported: 7 (26%) were due to NSAIDs, 5 (19%) due to ACE Inhibitors, 4 (15%) due to anticoagulants (includes both aspirin and warfarin), 3 (11%) due to digoxin, 2 (7%) due to beta-blocker, 2 (7%) hypoglycaemic medications and 4 (15%) central nervous system agents. Once again similar drug classes were observed to account for the bulk of ADEs.
Chapter 5 - Conclusions and Recommendations

5.1. General aspects

This study highlights the disproportionate presentations of the older person to the EU and emphasizes the need for geriatric care and education. The EU is one of the busiest geriatric settings, the fledgling African specialties of emergency medicine and geriatric medicine need to recognize the opportunities that our emergency units provide for improving care of the older person.

Aspects that could be targeted include: (1) improved screening for common problems (for example cognitive evaluation of a patient repeatedly presenting with disease decompensation attributable to poor adherence), (2) improved recognition of the unique needs of the older person (for example poor access to transport which makes it difficult to come back on the following morning for results or additional medications), (3) improved patient dignity and autonomy in a busy service with long waiting periods, (4) improving diagnostic evaluation of the complicated and very ill older patient (doctors may inappropriately focus on an aspect unrelated to the core problem with unnecessary resource utilization in pursuit of these problems), (5) implementing simple and effective primary and secondary prevention strategies (for example post-fall evaluation), (6) appropriate drug prescribing and monitoring and (7) improved communication with primary care providers. Many patients may use the EU for health care because of problems accessing primary health care services. Improving the access of these services may reduce EU utilization by older persons.

5.2. Adverse drug events

ADEs are a common contributor to illness in the older person. When assessing an older patient, one should always consider the possibility of an ADE contributing to the patient’s symptomatology. There is no doubt that the older patient with a high burden of disease will receive substantial benefit from the use of appropriate medications with proven efficacy. Emphasis of appropriate medication use is the first step in the pendulum of medication benefit versus risk of harm swinging in favour of benefit.
The substantial benefit from effective and appropriate medication usage may be ignored when the concept of "accidental drug injury" is overemphasized. This was possibly the case in the "To err is human" report published by the Institute of Medicine [34]. The term adverse drug event detracts from any "accident" and provides a non-judgemental term against which benefit can be emphasized. Data is required to provide guidance regarding risk versus benefit for effective medication prescription and use. This data needs to be disseminated to medical practitioners to allow appropriate implementation.

5.2.1. **Methods of reducing adverse drug events in the local setting – recommended prescribers points**

Targeted educational interventions have been shown to reduce the incidence of prescription of high risk drugs [35]. Based on the ADEs identified, this study supports the previous recommendations which may reduce the risk of ADEs in older persons:

- **NSAIDs** should be avoided in older persons. They should be used only if strongly clinically indicated in fit older patients with no renal or cardiac disease. Treatment duration should not exceed a few days. Chronic pain in the older person requires a more comprehensive evaluation and management plan than the simple prescription of symptomatic therapy.

- **Digoxin** should not be used in older patients with a risk of hypokalaemia, renal impairment or at doses greater than 0.125mg daily for men and 0.0625mg-0.125mg daily for women. Patients reporting a loss of appetite should have their digoxin stopped as this may be the first sign of toxicity in the older person. Any patient assessed for an acute illness in the EU taking digoxin should be considered for digoxin toxicity. Digoxin toxicity can occur in older persons with normal serum levels. Recently the optimal serum level for digoxin has been lowered to the range of 0.5 to 0.8ng/ml (previous range 1.0 to 1.5ng/ml) [18]. Only once other causes of tachycardia (dehydration, anaemia, pain and heart failure) have been managed may digoxin therapy considered for rate control. Beta-blockers, if tolerated, should be the first agent of choice for rate control.

- The **principle indication for warfarin use** is as either primary or secondary stroke prevention of patients in atrial fibrillation. Atrial fibrillation causes approximately 35% of strokes in patients aged over 80 years. In large stroke prevention trials
the main risk factors identified for stroke in patients with atrial fibrillation were: advancing age, female sex, previous stroke or transient ischaemic attack, hypertension and diabetes [69, 70]. Pre-requisites for warfarin therapy are a motivated patient or caregiver as well as an adequate health care setting that monitors the patients blood International Normalised Ratio (INR). Associated morbidities are more important than age alone for reliably predicting risk related to the use of warfarin. Improved monitoring is required for tighter INR control in the older person aiming for between 2.0 to 2.5 for nearly all indications. Despite the best monitoring, a proportion of patients will still experience bleeding related to warfarin use. This risk is inherent with the use of warfarin and should be clearly outweighed by the risk of repeat thromboembolism. The present risk/benefit ratio for primary stroke prevention is unclear and data to provide further clarification is pending [60]. However, in patients with previous stroke, warfarin use for secondary prophylaxis has significant benefit. The decision to warfarinise a patient thus requires the mature judgment of the attending physician, patient and the caregiver or family.

- Beta blockers are highly beneficial in the older patient with ischaemic heart disease or stable heart failure [16]. This study showed a high rate of beta-blocker related adverse events. However atenolol was used in the study setting and it may not share the same safety profile of other beta-blockers proven to be effective in heart failure trials (carvedilol, metoprolol, bisoprolol). Clinical dosage titration with atenolol is rapid, while agents shown to be of benefit in heart failure trials require slow titration. The use of beta-blockers in patients with ischaemic heart disease and stable heart failure (no oedema) is recommended as there is satisfactory evidence of benefit in the older person. Atenolol should be avoided in patients with heart failure. Drug titration in heart failure patients needs to be slow and the beta-blockers that are proven safe and effective in clinical trials should be used. For this to occur agents (such as carvedilol, metoprolol and bisoprolol) need to be available in the primary care setting and not only at tertiary centers. The majority of older patients are required to obtain their medications from primary care facility pharmacies.

- Angiotensin converting enzyme inhibitors are highly effective intervention in the older person with hypertension, heart failure and for the prevention of
progression of renal impairment associated with proteinuria (such as that occurring with diabetic or hypertensive nephropathies). Initiation dosages in the older person need to be low and documentation of serum potassium and serum renal parameters (creatinine and/or urea) is mandatory. Blood monitoring is required prior to initiation, after initiation and on follow-up in patients at higher risk of renal decompensation and/or hyperkalaemia. High risk patient groups include: diabetic patients, patients with renal impairment, vasculopaths and patients with any superimposed acute illness.

- Aspirin therapy in older patients at very high risk of a cardio- or cerebrovascular event is a highly effective intervention. However it is important to note that safety data on patients over 70 years of age is relatively scant. The high risk of atherothrombotic events in older persons likely balances out the high risk of gastrointestinal bleeds maintaining a favourable risk to benefit ratio. For example in patients with an estimated annual risk of 4 to 8% for serious vascular events, aspirin would prevent 10 to 20 fatal and non-fatal vascular events for every 1000 patients for one year treated, this would be offset by 5-6 upper gastrointestinal (GI) complications (bleeding or pain) for patients with no previous upper GI complaints. In patients with a previous history of complicated or uncomplicated ulcer the risk of GI complications would be in excess of benefit, with rates of 35 and 22 per 1000 person years respectively for patients in the age category of 70 to 79 years [71]. Older persons initiating aspirin therapy should avoid concomitant use of NSAIDs. Anemia should be investigated and managed before initiation of aspirin therapy. Concomitant therapy with proton pump inhibitors in patients at higher risk of GI complications is commonly practiced but there is currently a lack of definitive evidence to support this practice [71].

- In the state sector the principal oral hypoglycaemic agents used are gliclazide and glibenclamide. Both agents are cleared by renal excretion, which is commonly impaired in the older patient due to an age related gradual decline in renal function. Glibenclamide should be avoided in the older diabetic patient as it has a longer excretion half-life, and the present form of preparation does not allow for the very low dosing required by older patients.
5.2.2. **Effective strategies which could be implemented at the primary health care level aimed at reducing the risk of ADEs:**

- Improving access of older persons to monitoring of: (1) INR's (allows safer clinical use of warfarin), (2) digoxin levels (prevents morbidity and mortality in patients using digoxin), (3) glycaemic control (preventing both hyperglycaemia and hypoglycaemia in diabetic patients) and (4) serum potassium and (5) creatinine levels (for patients on ACE inhibitors and guidance regarding appropriate prescribing for patients with significant renal impairment).

- Educational campaigns and prescription warnings regarding the use of NSAIDs.

- The availability of safer, easily titratable and efficacious beta blockers for patients with heart failure.

- Continuing medical education for primary care physicians, education of undergraduate medical students in geriatric medicine and the development of protocols for treatment of older persons.

5.3. **Strengths and weaknesses of this study**

5.3.1. **Weaknesses of this study:**

1. Limited to one tertiary academic institution thus the results may not be representative of other facilities.

2. Patients who presented during the weekend were not audited. This population may have differed slightly from the study population. They may have been more frail and reliant on family members not available during the week to bring them to the hospital.

3. Despite the use of causality criteria to confirmation the presence of an ADE, the diagnosis of an ADE remains a subjective assessment and some ADEs may have been overlooked.

4. Data was not available for some patients presenting to the EU who may have had different characteristics or risk profile. These patients include the 18 patients who died before complete assessment, as well as the 16% of the study.
population not sampled. A potential bias could occur if patients identified as having an ADE were preferentially audited. This bias may be offset by an unknown number of overlooked/missed ADE's. Older patients are recognised to have protean manifestations of ADEs which may be easily attributed to other illness.

5. Determination of adherence in this study relied on a judgment made by the attending doctor based on available information from the patient, caregiver and/or clinical and biochemical parameters. This is a simple, inexpensive and useful method in the busy real-world clinical setting; however it is susceptible to distortion by the patient. Additional bias may have occurred if the attending doctor identified a patient with poor adherence and then failed to include the possibility of an ADE contributing to the patient's presentation. This bias would result in a relative under-reporting of ADEs.

6. The cross-sectional design of this study is another limitation, as patients in this study were not followed up beyond their acute assessment.

5.3.2. Strengths of this study:

1. The prospective nature and manner in which ADEs were detected by the admitting doctor and/or investigator while the patient was still present in the EU. This enabled evaluation at the time of the event rather than a judgement made at a later date where information pertaining to the event may be incomplete or could not be extracted from the clinical records.

2. This audit included frail high risk older patients with multiple clinical problems taking multiple medications. Such patients are rarely included in formal randomised controlled drug trials. Randomised drug trials excluding high risk patients may overestimate the safety of certain drugs used alone or in combination. A good example of this is the RALES study published in 1999 [72] which strongly recommended the use of spironolactone in combination with ACE inhibitors to reduce the mortality of patients with heart failure. There was a 2% incidence of hyperkalaemia in the original study. Subsequent published work has shown that older patients in real world clinical settings have rates of severe hyperkalaemia (serum potassium >6.0 mmol/l) of 10-11% and rates of
hyperkalaemia (serum potassium > 5.5 mmol/l) up to 36% in those using the combination of spironolactone and an ACE inhibitor for treatment of their heart failure [30, 73].

5.4. Future areas of research

This study only evaluated the medications patients were taking before or at the time of presentation. A nationwide survey in the United States conducted between 1992 and 2002 demonstrated, despite the publication of explicit criteria for inappropriate medication use in the older person in 1997, a stable rate of 12.6% of older persons being prescribed inappropriate medication (or over 16.1 million inappropriate prescriptions) during EU visits [74]. Further work is needed to explore the issue of inappropriate prescription of medications in the South African EU setting.

A systematic review of geriatric interventions aimed at reducing EU visits conducted by McCusker and Vernor 2006 [8] suggested that interventions implemented in a hospital setting (either in the EU or as an in-patient), or recruiting patients from these settings did not have an overall effect on EU utilization. Interventions conducted in outpatient or home-care settings were successful in reducing EU utilization. The improved continuity of care and the provision of an alternate location to the EU for the management of acute problems may account for this. Many patients may utilize the EU because of poor access to primary care facilities at an earlier stage. Data is however required to support this proposal. If confirmed, further work would guide the development of methods of improved access of older persons to their appropriate care services.

With age renal and liver function may deteriorate. This study could not explore renal impairment as a valid risk factor due to the lack of premorbid baseline renal function. Furthermore there is presently no clinically reliable indicator of hepatic function and reserve relevant to the setting of drug safety determination. Further ADE research would need to include these as possible risk factors for ADE development in the older person.
An acceptable versus an unacceptable rate of ADEs for a drug class has not been determined and warrants further research, particularly in the context of older persons. Benefit must significantly outweigh risk to justify the cost of drug use. It remains to be determined whether a proportion of ADEs may have been prevented with more careful monitoring. In our resource (both economic and personnel) constrained health care system, cost saving shortcuts involving a reduction in monitoring may prove to be more costly in the long term.
Chapter 6 - References


60. Morgan SV. Between the devil and the deep blue sea – balancing the risks and potential benefits of warfarin for older people with atrial fibrillation. Age Ageing 2004; 33: 544-547.


Appendix A

Groote Schuur Hospital Emergency Unit - Geriatric Audit Form
Please complete on all patients assessed in the Ante room who are over 65 years. As far as possible, please complete all details.

<table>
<thead>
<tr>
<th>Hospital Sticker</th>
<th>Date: ____________________________</th>
<th>Time of presentation: ____________________________</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOB:</td>
<td>Gender:</td>
<td>Time of assessment: _____________________________</td>
</tr>
<tr>
<td>Suburb:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1). BASELINE LEVEL OF FUNCTION: (prior to deterioration causing current assessment)
- Activities of Daily Living (ADL’s): washing, dressing, eating, transfers
- Instrumental ADL’s eg: shopping, finances, transport, cooking

<table>
<thead>
<tr>
<th>Effort tolerance:</th>
<th>Independent</th>
<th>Dependent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Climbs &gt; 20 steps or carry heavy groceries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to do steps or groceries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty dressing/washing self</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed bound</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2). PRIMARY CAREGIVER: None | Spouse | Family | Institutional | Friends |

3). BODY HABITUS: Obese | Normal | Thin | Emaciated |

4). PROBLEM LIST: Mark appropriate if present; more than one may be applicable
Respiratory: Pneumonia | Asthma | COPD |
Cardiovascular: Syncope | IHD | PVD | Hypertension | Heart Failure | Atrial fibr. |
Central nervous: CVA | Confusion | Dementia (known) | Seizures |
Abdominal: GIT bleeding | Obstruction | Dyspepsia | Constipation |
Genitourinary: UTI | Retention | Obstruction |
Musculoskeletal: Bed sores | DVT | Musculoskeletal Pain Syndrome |
Other: Fall | Neoplasia | Diabetes | Dehydration |
Psychiatric: Depression |
SMOKER | ALCOHOL |

5). MEDICATIONS: please list fully with dosages as far as possible.
Compliance: Yes | No | Suspected non-compliance |
Prescription medications: ____________________________ |

Over the counter preparations (eg. analgesics, cold/flu preparations, laxatives, etc.):
Herbal/Vitamin or Traditional preparations: ____________________________ |

DID A MEDICATION ADVERSE EVENT CONTRIBUTE TO PATIENTS PRESENTATION?
<table>
<thead>
<tr>
<th>NO</th>
<th>YES - Please specify</th>
</tr>
</thead>
</table>

6). OUTCOME: Admitted to GSH | Discharged | Transferred | In C15 more than 6 hours |

66
Appendix B – Ethics approval letter

UNIVERSITY OF CAPE TOWN

Research Ethics Committee
E53 Room 44.1, Old Main Building
Groote Schuur Hospital, Observatory,
7925
Queries: Xolile Fula
Tel: (021) 406-6492 Fax: 406-6411
E-mail: Xfula@curie.uct.ac.za

10 March 2005

REC REF: 112/2005

Dr B Tipping
Geriatrics

Dear Dr Tipping

CLINICAL ELDERLY PATIENTS ASSESSED IN THE EMERGENCY UNITS OF GROOTE
SCHUUR AND SOMERSET HOSPITALS

Thank you for your letter to the Research Ethics Committee dated 28 February
2005.

It is a pleasure to inform you that the Research Ethics Committee has formally
approved the above mentioned study:

Please quote the REC. REF in all your correspondence

Yours sincerely

PROF T. ZABOW
CHAIRPERSON
Appendix C– Population mortality aetiology and demographics of the Western Cape

1. Ten leading single causes of death among adults by sex, Western Cape 2000

Male 60+ years, N = 8,738

- Ischaemic heart disease: 20.4%
- Stroke: 13.4%
- COPD: 8.5%
- Trachea/bronchial cancer: 7.8%
- Tuberculosis: 4.0%
- Diabetes mellitus: 4.1%
- Prostate cancer: 3.8%
- Stomach cancer: 2.4%
- Hypertensive heart disease: 2.3%
- Lower respiratory infections: 2.3%

Female 60+ years, N = 8,626

- Ischaemic heart disease: 23.0%
- Stroke: 17.5%
- Diabetes mellitus: 8.4%
- Hypertensive heart disease: 4.8%
- COPD: 4.1%
- Trachea/bronchial cancer: 5.9%
- Breast cancer: 3.7%
- Lower respiratory infections: 3.0%
- Nephritis/nephrosis: 2.3%
- Septicaemia: 1.9%
2. Twenty leading single causes of death by sex (all ages), Western Cape 2000

3. Age structure of the Western Cape population, 2000