CARDI
Centre for Ageing Research
and Development in Ireland

An evaluation of the inappropriate prescribing in older residents in long term care facilities in the greater Cork and Northern Ireland regions using the STOPP and Beers' criteria.

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Background

Older individuals generally suffer from multiple co-morbidities and this makes this patient group particularly vulnerable to inappropriate prescribing (IP). IP has been reported to be a substantial cause of morbidity and mortality and has been identified as a major contributing factor to increased healthcare utilisation. One method of evaluating or identifying inappropriate or sub-optimal prescribing practice is to use validated evidence-based explicit criteria to define instances of potential IP. Two sets of criteria have gained international recognition, i.e. Beers' criteria and "Screening Tool of Older Peoples Prescriptions (STOPP)".

Aim

The aim of this study was to determine the prevalence of potential IP in older nursing home residents on the island of Ireland.

Methods

A total of 315 residents ≥65 years were randomly selected from fourteen nursing homes from County Cork, Ireland and were age and gender matched with 315 residents from a Northern Irish nursing home dataset. Exclusion criteria included terminally ill or respite patients. Both the Beers' and STOPP criteria were applied to the patient profiles of the 630 residents in both Northern Ireland (NI) and the Republic of Ireland (RoI).

Results

Of the residents reviewed (n=630), 472 (74.9%) were female; the median age was 84 (IQR: 78-89) of the entire dataset. The total number of medicines prescribed for the RoI dataset was 3,730 (median 11, IQR 9-13) and for the NI population was 3,394 (median 10, IQR 7-13). In the RoI dataset, 73.0% of residents had at least one potentially inappropriate medication (PIM) identified by STOPP criteria and 54.3% had at least one PIM identified by the Beers' criteria. In the NI dataset 67.0% of residents had at least one PIM identified by STOPP criteria and 56.8% of residents had at least one PIM identified by the Beers' criteria.

Conclusion

Potential IP is a major area of concern and has been implicated throughout the literature as a substantial burden to health services internationally. In this study STOPP criteria demonstrated superior capability over the Beers' criteria in the identification of instances of potential inappropriate prescribing (PIP) in these nursing home / long term care facility residents.

1.0   Introduction

Most of the research (Tables 1-3) to date has outlined the prevalence of potentially inappropriate prescribing (PIP) in community dwelling older patients. Elderly individuals residing permanently in long term care facilities have generally been excluded from these studies. In 2006, it was reported that 5.5% of the Irish population aged over 65 years were permanently residing in long term care facilities and 2007 census data reported that 22.7% of people aged over 85 years were resident in such facilities (Barry *et al.* 2006; Central Statistics Office 2007). Given the anticipated growth in the Irish older population expected over the next few decades, there will probably be corresponding increases in the number of older individuals requiring long term care. Several studies in the recent literature evaluating PIP in residents residing in these facilities have demonstrated large rates of PIP occurrence (Tables 1-3). The aim of this study is to determine and compare the rates of PIP in older Irish residents residing in these settings both in Northern Ireland and the Republic of Ireland.

1.1   The Ageing Population

People over 65 years commonly suffer from multiple co-morbidities and routinely prescribed multiple medications to treat these different conditions when compared to their younger counterparts (Barry *et al.* 2006). Epidemiological data from Europe indicates that older people 65 years and older take 2.3 times more medication than younger counterparts (Barry *et al.* 2006). In a 2002 study it was estimated that approximately 11.5% of the Irish population is 65 years and over and it is reported that this portion of the population regularly receives almost 47% of all the prescribed medications in Ireland (Barry *et al.* 2002). This proportion of the population that live to over 65 years has increased over the last 50 years, with the number of older people almost tripling, and it is expected that it may almost triple again over the next 50 years (World population ageing 1950-2000). This predicted increase in the older population could potentially result in a major socio-economic problem and it warrants consideration as it means that caring for older individuals could become more significant and demanding (Barry *et al.* 2006).

A number of frailer older individuals who suffer from multiple chronic co-morbidities are unable to effectively care for themselves and often require admission to a long term care facility so as to receive adequate continual care. It is estimated that approximately 5.5% of Irish people aged over 65 years are permanently resident in long term care facilities, with an even higher percentage of older elders requiring long term care. This is illustrated by the 2007 census report which found that 22.7% of individuals aged over 85 years were resident in long term care facilities (Central Statistics Office 2007).

The fact that older individuals generally are more likely to suffer from multiple chronic morbidities, which usually require the use of long term complex medication regimens to treat each individual condition, places this patient group at increased risk of experiencing an adverse drug event (ADE) or a drug-drug interaction (Liu *et al.* 2003). This fact, coupled with an expected increase in an individual's longevity which is predicted over the next 50 or so years, could potentially mean that the medication usage by the older patient group will probably increase and place an already vulnerable patient group at an increased risk of inappropriate prescribing

(IP). Polypharmacy has been identified throughout the literature as a significant predictor of IP prevalence. A number of studies have reported a high prevalence of IP in the older population, which in turn has been identified as a major contributory factor in patients experiencing an adverse drug event (ADE). An increased incidence of ADE has been reported to correlate with increased mortality, morbidity and healthcare utilisation (Hamilton *et al.* 2009). Similarly, it has been reported that older patients who reside in long term care facilities are particularly vulnerable to IP. These individuals generally suffer from an increased incidence of functional disabilities as well as suffering from more acute and chronic co-morbidities as opposed to community dwelling older counterparts. This high incidence of multiple morbidities usually means that this patient group requires long term complex medication regimens (Rancourt *et al.* 2006).

1.2   Pharmacotherapy

Optimal prescribing is a crucial aspect of gerontology. The main aim of prescribing is to cure disease, eliminate or reduce symptoms relating to an underlying disease state and improve functional capacity of the patients (Hanlon *et al.* 2001).

1.2.1 Appropriate Prescribing

Appropriate prescribing is a general concept that encompasses a variety of different prescribing values and practices. Appropriate prescribing is essentially a phrase used to quantify / measure the quality of prescribing (Spinewine *et al.* 2007). Several important factors need to be taken into consideration when defining appropriate prescribing practices for a patient (Spinewine *et al.* 2007):
- What the patient wants,
- What the patient needs and;
- Scientific rationalism (including the clinical pharmacology of certain drugs).

However prescribing in older patients is complicated by a number of factors and these usually need to be taken into consideration when prescribing for such a patient (O'Mahony *et al.* 2008):
- Life expectancy of the patient,
- The right therapeutic approach in patients with poor prognosis and;
- Selection of the pharmacotherapy with the most favourable risk/benefit ratio.

1.2.2 Inappropriate Prescribing

Inappropriate Prescribing (IP) is a universal term used to describe a number of sub-optimal prescribing practices but essentially is the use of a particular medicine for which the risks associated with its use outweigh the potential benefits especially when there are as effective, safer alternatives available for treatment of the same condition (Beers *et al.* 1997; Spinewine *et al.* 2007). The definition of inappropriateness is usually considered to be relative rather than absolute; this relates to the fact that under certain circumstances medications which are deemed generally inappropriate might in fact have an appropriate indication e.g. furosemide as monotherapy to treat hypertension when other anti-hypertensives have failed (Fialova *et al.* 2005).

IP has become an area of major concern in the older population (Barry *et al.* 2006). It has been widely documented that certain drugs should be used cautiously in this patient group, and it is generally best to completely avoid them in older patients if a safer alternative is available.

The concept of IP encompasses several aspects of prescribing as follows:
- Over prescribing of medication i.e. polypharmacy, relates to the practice of prescribing multiple medications or more medications that are clinically required.
- Over prescribing also encompasses the practice of prescribing medications at higher doses or frequencies for periods longer than are clinically indicated.
- IP entails the prescribing of a medication where the risks of an adverse event associated with its use outweigh the clinical benefits, especially when there is evidence to support the use of a safer more effective alternative therapy for the same condition i.e. an unfavourable risk benefit ratio.
- IP also encompasses the prescribing of medications with high inherent risk of adverse drug-drug or adverse drug-disease interactions.
- The practice of prescribing certain medications that are not clinically beneficial or indicated for a specific patient.
- The prescribing of medications which may fulfil an intended therapeutic purpose but for which a more effective agent is available.
- Prescribing of a drug or drug class that are likely to exacerbate a clinical problem in older patients, e.g. the use of benzodiazepines in older patients with a past history of falls.
- Underuse of medications or under prescribing, is the failure to prescribe a clinically beneficial medication to a patient for whom there is no valid reason not to prescribe the said medication and for which there is no contra indication to this beneficial pharmacotherapy e.g. when a patient suffers from a particular condition and there is no drug prescribed to treat this indication, or the dose of the drug is not sufficient to effectively treat this condition.

(Barry *et al.* 2007; Fialova *et al.* 2005; Gallagher *et al.* 2007; Rojas-Fernandez *et al.* 2003; Spinewine *et al.* 2007; Steinman *et al.* 2006)

1.2.3 Inappropriate Medications

A potential inappropriate medication (PIM) is a medication which possesses an unfavourable risk-benefit ratio i.e. a medication for which the risks associated with using a particular medication outweighs the benefits of using said medication, especially when there are effective, safer alternatives available. The term potential is important as in some cases the prescriber may have considered alternative therapies but for a reason unknown to the researcher may have chosen to proceed with a given course of treatment.

A number of medications exhibit an increased potential to cause problems in older individuals and these medications have been categorised as potentially inappropriate for use in older patients. Medications which are identified as high risk or potentially inappropriate in older patients do not cause problems in all older patients but do have an increased potential to cause harm (Chukta *et al.* 2004).

In general a PIM in older patients is defined as a medication which (O'Mahony *et al.* 2008):
- Has no clear evidence based indication,
- Has a substantial higher risk of causing an ADE and;
- Is not considered cost effective.

1.2.4 Screening Tools to Assess Inappropriate Medications

Screening tools to assess the appropriateness of prescribing identified in the literature contain either explicit or implicit criteria or a combination of both. Explicit criteria are specific statements of inappropriateness, originating from evidence based guidelines, reviews, expert opinions and consensus techniques. Explicit criteria are generally drug or disease orientated and require a limited degree of clinical judgment. In contrast, implicit criteria are clinical judgment based and are not specific to any particular drug or disease. Clinicians using implicit criteria use patient-specific data and published work to make judgments about the appropriateness of medication usage in patients (Spinewine *et al.* 2007).

1.2.4.1 Explicit criteria

Several studies have been conducted to determine and formulate lists of explicit criteria. These are generally given names of the study investigators or group in which they were conducted. Some of these studies are described below:

McLeod
McLeod *et al.* developed a Canadian consensus-based, explicit list of criteria to identify PIP in older patients in 1997. The criteria were validated by a panel of 32 experts in geriatric pharmacotherapy from diverse locations in Canada and consisted of clinical pharmacologists, geriatricians, GPs and pharmacists. The final list of criteria contains 38 scenarios of PIP (18 medications contraindicated in older adults, 16 drug-disease interactions and 4 drug-drug interactions that should be avoided in the older person) (McLeod *et al.* 1997). The criteria are divided into four main headings: medicines for the Cardiovascular System (CVS) (n=8), psychotropics (n=12), non-steroidal anti-inflammatory drugs (NSAIDs) (n=11) and miscellaneous (n=7). Each criterion was qualified with a statement of a risk to patients and an

alternative therapy was suggested. For example, under the CVS, the prescribing practice of calcium-channel blockers (CCBs) to treat hypertension for patients with a history of heart failure was considered inappropriate as it may worsen heart failure. A diuretic and/or an Angiotensin-converting Enzyme (ACE) Inhibitor were recommended to replace the CCBs for this criterion. Scenarios where certain medicines were not appropriate, given a patient's condition, were listed along with some drug-drug interactions to be avoided.

This screening tool did not address under-prescribing of indicated medicines (PPOs) and did not state medication dosages that should be avoided in older patients. Three criteria have been superseded with newer evidence and eight of the medicines listed relating to six of the criteria in the screening tool are not available in either Northern Ireland (NI) or the Republic of Ireland (RoI).

Improving Prescribing in the Elderly Tool (IPET)
Naugler *et al.* formulated the Improving Prescribing in the Elderly Tool (IPET) (Naugler *et al.* 2000). It is a Canadian guideline which was derived from the criteria developed by McLeod *et al.*, based on the most prevalent instances of PIP found in a geriatric unit using the McLeod criteria. IPET lists 14 different drug/disease interactions which should be avoided in the older person but does not address the occurrence of potential prescribing omissions (PPOs). This tool has not been widely or extensively used in determining PIP, possibly owing to its brevity and that one of the listed instances of PIP has been superseded with newer evidence i.e. it states that β blockers should not be used in patients with CCF (Foody *et al.* 2002).

Beers' Criteria
Beers' criteria, a United State (US) based guideline, was originally formulated in 1991 (Beers *et al.* 1991). This screening tool contains a list of 30 medicines that should not be used in older patients. It was compiled for nursing home residents who are considered frailer, older and sicker than the general elderly population. The authors therefore cautioned that modifications may be necessary if the criteria were to be applied to older patients in a non-nursing home setting. The 1991 criteria were updated and expanded in 1997 to make the criteria more applicable to the general older population (Beers 1997).

The guidelines consist of two different lists or situations in which medicines should be avoided; one considering diagnosis (CD) and one independent of diagnosis (ID). Doses or frequencies of administrations that should not be exceeded were also listed. The 1997 criteria were revised and updated in 2003 (Fick *et al.* 2003). A 12-member expert panel consisting of psychopharmacologists, pharmaco-epidemiologists, clinical geriatric pharmacologists and clinical geriatricians from diverse geographical locations in the US completed the study which used a modified Delphi technique to reach consensus for each criterion. Eleven criteria that were listed in the 1997 tool were excluded from the 2003 list, one from the ID lists (phenylbutazone) and ten from the CD lists. Twenty five medicines were added to the ID list and 19 were added to the CD list. Four criteria were modified. The new criteria list 48 medicines ID and 20 medicines CD that should be avoided. It also rates the severity of the PIM into instances of "high severity" or "low severity" and provides a qualifying statement as to why the scenario is considered potentially inappropriate. For example, the prescribing of amiodarone is a PIP of "high severity"

ID as amiodarone is associated with QT interval problems and risk of provoking torsades de pointes and there is a lack of efficacy in older adults (Fick *et al.* 2003).

Beers' criteria were adapted as a standard by Centers for Medicare and Medicaid Services in 1999 for nursing home care patients and were included in the 2005 National Health Care Quality Report as a measure of use of inappropriate medications in the elderly (Hustey 2008). Beers' criteria do not address errors of prescribing omission and list several medicines as inappropriate that are not available or prescribed in Northern Ireland and the Republic of Ireland.

Screening Tool of Older People's potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right i.e. appropriate, indicated but often omitted Treatments (START)

Screening Tool of Older People's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right i.e. appropriate, indicated but often omitted Treatments (START) were formulated collaboratively by the Department of Geriatric Medicine, Cork University Hospital (CUH) and the School of Pharmacy, University College Cork (UCC) (Gallagher *et al.* 2008). The new screening tool addresses common instances of PIP (STOPP) and potential prescribing omissions (PPOs) (START).

The STOPP tool lists 65 instances of PIP and is divided into ten sections according to the physiological systems to which the instance of PIP relate. The START tool lists 22 common instances of PPOs divided into six physiological systems to which the PPOs pertain. The initial list of criteria was formulated based on a combination of evidence and common instances of PIP and PPOs observed throughout clinical working practice.

The STOPP and START tools were validated by the Delphi validation method. Eighteen experts in geriatric pharmacotherapy from diverse geographical locations throughout Ireland and the UK rated their level of agreement with each criterion on a five-point Likert scale. The experts included consultants in geriatric medicine, psychiatry of old age, clinical pharmacologists, senior academic primary care physicians and senior hospital pharmacists with an interest in geriatric medicine.

Agreement was achieved by the first Delphi validation round for all of the 22 criteria in the START tool and therefore all of these were included in the final published version of the START tool. Two postal rounds of the STOPP tool were required as the panel did not reach full consensus on the first round, the initial STOPP tool contained 68 criteria and the final STOPP tool contained 65 criteria.

A number of studies have reported on the prevalence of IP in the older population from different health care settings. Table 1-3 below summarise the published papers to date which have evaluated the incidence of IP in older patients using the Beers' and STOPP criteria.

Table 1 Summary table of studies which have used the Beers' Criteria in a European setting

Study	Country	Care setting /age category	No of patients	Criteria	Outcomes
De Oliveira et al. '06	Portugal	Community-dwelling elders ≥65 yrs	213	1997 Beers ID Criteria & 2003 Beers ID Criteria	37.7% of the dataset were prescribed at least one inappropriate drug as defined by the 1997 Beers' criteria and 38.5% as defined by the 2003 beers criteria
Rajska-Neumann et al. '07	Poland	Community-dwelling elders ≥75 yrs	680	1997 Beers ID Criteria	28.2% of the subjects were prescribed at least one inappropriate drug.
De Wilde et al. '03	United Kingdom	Community-dwelling elders ≥65 yrs	162,000	2003 Beers ID&CD Criteria	32.3% of the subjects were prescribed at least one inappropriate drug.
Van Der Hooft et al. '97-'01	Holland	Community dwelling elderly ≥ 65	18,030-29,605.	1997 Beers ID &CD Criteria & 2003 Beers ID & CD Criteria	A PIP prevalence rate of 16.8-18.5% was reported when the 1997 Beers' criteria were used to assess PIP and a PIP prevalence of 19.1-20.0% was reported when the 2003 beers criteria were used to define PIP.
Ay et al. '05	Turkey	Community dwelling elderly ≥ 70	1,019	1997 Beers ID & CD Criteria	In this study it was reported that 9.8% of the dataset were prescribed at least one inappropriate drug.
Pitkala et al. '02	Finland	Community dwelling elderly ≥65 yrs	2,511	1997 Beers ID & CD Criteria	It was reported that 12.5% of the patients studied were on at least one PIM.
Fialova et al. '05	Europe	Community dwelling elderly ≥65 yrs	2707	Modified 1997 Beers ID &CD Criteria & Modified 2003 Beers ID & CD Criteria	9.8% of the dataset were prescribed at least one inappropriate drug as defined by the 1997 Beers criteria and 16.9% as defined by the 2003 Beers criteria
Barry et al. '06	Ireland	Community-dwelling elders ≥65 yrs	350	2003 Beers ID Criteria & IPET	34% of the dataset received at least one PIM according to the Beers criteria, whereas a PIP prevalence of 22% was reported for IPET
Gallagher et al. '08	Ireland	Community-dwelling elders ≥65 yrs	597	2003 Beers ID & CD Criteria	32% of the patients in the dataset received at least one PIM according to Beers' criteria
Gallagher et al. '08	Ireland	Community-dwelling elders ≥65 yrs	715	STOPP Criteria & 2003 Beers ID & CD Criteria	In this dataset 34% of the patients were prescribed at least one PIM according to STOPP and 25%of the patients were prescribed a PIM according to the Beers' criteria
Ryan et al.' 09	Ireland	Community dwelling elderly ≥ 65 yrs	500	2003 Beers ID & CD Criteria & IPET	In this study a PIP prevalence rate of 13% was reported for the Beers Criteria and 10.4% for IPET
Ryan et al.' 09	Ireland	Community dwelling elderly ≥ 65	1,329	STOPP Criteria & 2003 Beers ID & CD Criteria	Beers' identified one or more PIMs in 18.4% of patients, whereas the STOPP criteria reported a PIP prevalence rate of 21.4%

Table 2 Summary table of Irish studies which have used the explicit criteria to investigate PIP prevalence

Study	Country	Care setting /age category	No of patients	Criteria	Main Outcomes
Barry et al. '06	Ireland	Community-dwelling elders ≥65 yrs	350	2003 Beers ID Criteria & IPET	34% of the dataset received at least one PIM according to the Beers criteria, whereas a PIP prevalence of 22% was reported for IPET
Gallagher et al. '08	Ireland	Community-dwelling elders ≥65 yrs	597	2003 Beers ID & CD Criteria	32% of the patients in the dataset received at least one PIM according to Beers' criteria
Gallagher et al. '08	Ireland	Community-dwelling elders ≥65 yrs	715	STOPP Criteria & 2003 Beers ID & CD Criteria	In this dataset 34% of the patients were prescribed at least one PIM according to STOPP and 25%of the patients were prescribed a PIM according to the Beers' criteria
Ryan et al. '09	Ireland	Community dwelling elderly ≥ 65 yrs	500	2003 Beers ID & CD Criteria & IPET	In this study a PIP prevalence rate of 13% was reported for the Beers Criteria and 10.4% for IPET
Ryan et al. '09	Ireland	Community dwelling elderly ≥ 65	1,329	STOPP Criteria & 2003 Beers ID & CD Criteria	Beers' identified one or more PIMs in 18.4% of patients, whereas the STOPP criteria reported a PIP prevalence rate of 21.4%
Cahir et al. '10	Ireland	Community dwelling elderly ≥70 yrs	338802	STOPP Criteria	It was reported that 36% of the patients studied were on at least one PIM.
Hamilton et al. '10	Ireland	Community dwelling elderly ≥65 yrs	500	STOPP Criteria & 2003 Beers ID & CD Criteria	This study found that 52% of the dataset was on at least one PIM as defined by the STOPP criteria and 27% of them were on at least one PIM as defined by the Beers' criteria.

Table 3 Summary table of studies which have used the STOPP Criteria

Study	Country	Care Setting /Age Category	No of patients	Criteria	Main Outcomes
Ryan *et al.* '09	Ireland	Community dwelling elderly ≥ 65	1,329	2003 Beers ID & CD Criteria STOPP Criteria & 2003 Beers ID & CD Criteria	a PIM according to the Beers' criteria Beers' identified One or more PIMs was identified in 18.4% of patient, whereas the STOPP criteria reported a PIP prevalence rate of 21.4%
Cahir *et al.* '10	Ireland	Community dwelling elderly ≥70 yrs	338802	STOPP Criteria	It was reported that 36% of the patients studied were on at least one PIM.
Lang *et al.* '10	Switzerland	Hospitalised elders ≥65 yrs	150	STOPP Criteria	A PIP prevalence of 77% was reported in this dataset of hospitalised elders.
Hamilton *et al.* '10	Ireland	Community dwelling elderly ≥65 yrs	500	STOPP Criteria & 2003 Beers ID & CD Criteria	This study found that 52% of the dataset was on at least one PIM as defined by the STOPP criteria and 27% of them were on at least one PIM as defined by the Beers' criteria.

2.0 Aims

The aims of this study were to:

1. Assess the prevalence of potentially inappropriately prescribed (PIP) medicines in residents 65 years and older in long term care facilities in both Northern Ireland (NI) and the Republic of Ireland (RoI) using both the STOPP screening tool and the Beers criteria; to evaluate prescribing practices between NI and RoI and to evaluate the prevalence of inappropriate prescribing in both jurisdictions.
2. Evaluate the effectiveness of both screening tools for identification of inappropriate prescribing (IP) in both population groups and evaluate the applicability of STOPP as a screening tool in both jurisdictions.
3. Analyse prescribing practices between the Northern Ireland and the Republic of Ireland and to make relevant recommendations to the chief medical officer of the care facilities in the RoI dataset.
4. Economically quantify the ingredient costs of the potential inappropriate medicines (PIMs) in both jurisdictions.

2.1 Objectives

The objectives of this study were to:

1. Quantify rates of PIMs amongst a random selection of older long-term residential patients in both NI and greater Cork regions using the STOPP criteria and Beers' criteria.
2. Compare the efficacy of these two tools for PIM identification in both populations and evaluate the applicability of the STOPP criteria in both jurisdictions.
3. Economically quantify the ingredient costs in both jurisdictions of the PIMs identified.
4. Evaluate the opinions of long term care residence with regards to their pharmacotherapy treatments.

3.0 Method

Ethical approval was granted for this study by the Clinical Research Ethics Committee of the Cork Teaching Hospital and University College Cork (Appendix 1 & 2). All publicly funded nursing homes/ community hospitals within one hour travelling time from Cork City (n=15) were written to and asked to be involved in the study. Fourteen facilities agreed to take part in the study, one facility declined.

Data pertaining to residents in Northern Ireland was collected as part of the Fleetwood Northern Ireland study; further information is given below.

3.1 Data collection

3.1.1 Republic of Ireland

In the Republic of Ireland (RoI) arm of the study all the medical information data for each individual resident was collected using a computerised collection proforma created in Microsoft Access^{TM} 2007 which was developed in partnership with representatives from the Pharmaceutical Care Research Group from the School of Pharmacy, University College Cork and the Clinical Pharmacy Research Group, School of Pharmacy, Queen's University Belfast. This proforma was piloted on 20 residents and was subsequently modified in order to improve usability.

Data collection was undertaken by a research assistant from the Pharmaceutical Care Research Group from the School of Pharmacy, University College Cork, who was sufficiently trained in data collection and application of the STOPP criteria and the Beers' criteria. The data collection was carried out over a 10 month period on a part-time basis between December 2009 and September 2010. Type of data collected included the current medication prescribed, medical diagnosis (current and past), the most up to date biochemical data as well as information relating to present and past history of falls. The medical information of the residents was recorded in the Access$^{®}$ database and was later exported to Predictive Analytics SoftWare Statistics (PASW) (SPSS Inc. Chicago, Ill.) version 18.0 for statistical analysis.

The medical notes of all residents in the fourteen facilities were prospectively reviewed and were allocated a unique identification number (1-732) at the point of recruitment for data analysis purposes. The data was then subsequently anonymised to all except for the research assistant for confidentiality purposes. All relevant diagnosis and medical histories were recorded in the electronic proforma for each individual resident. During the data collection and analysis aspect of the study random checks of the work was conducted by the principal investigator, Dr Stephen Byrne, to ensure consistency of results. Other co-investigators on this project were contactable at all times to liaise with the research assistant if and when queries arose.

3.1.2 Northern Ireland

The data relating to the residents for the Northern Ireland (NI) arm of the study had been previously compiled in a dataset using Microsoft Access® 2007 as part of the 2006-2007 Northern Irish Fleetwood study (Patterson *et al.* 2010) and subsequently exported into Predictive Analytics SoftWare Statistics (PASW) (SPSS Inc. Chicago, Ill.) version 18.0 for statistical analysis.

In the NI arm of the study all the patient identifiable information had been previously anonymised and each resident had already been allocated an individual identification number. Subsequently all the disease states, medical conditions and medications for both datasets were then recoded using internationally recognised coding systems in order to aid data analysis.

Data was collected for 732 residents in the RoI arm of the study and this data was subsequently age and gender matched with the 334 residents from the NI dataset. A total of 315 residents from each dataset were successfully matched; it was not possible to match 19 of the NI 334 residents. Data were matched by stratification of residents' age and gender using PASW. The results to follow will report on the findings of the matched datasets.

3.1.3 Diagnoses codes

The disease states in the study were coded using the World Health Organisation's (WHO) disease states classification system, the International Classification of Diseases 10 (ICD-10), to the second level in order to standardise the data between the two datasets. These codes were used for data analysis purposes.

3.1.4 Medication codes

The medications were coded using the WHO hierarchal Anatomical Therapeutic Chemical (ATC) Classification System (11th edition, 2008) (Appendix 3). Each medicine was assigned a seven digit code in accordance with the ATC classification system. This classification system divides medicines into different groups according to the organ or system on which they act and/or their therapeutic and chemical characteristics by assigning them an individualised seven alpha-numerical code.

E.g.   Atorvastatin = C10AA05
where: C = Cardiovascular System
            C10 = Lipid Modifying Agents
            C10A = Lipid Modifying Agents, Plain
            C10AA = HMG CoA reductase inhibitors
            C10AA05 = Atorvastatin

These codes were then used in data analysis; coding in this fashion facilitated analysis of medicines by class or by individual agents.

3.1.4 Determining the level of co-morbidity

The Charlson's Comorbidity Index (CCI) (Appendix 4) was applied to each patient's profile of the residents from both datasets. The CCI is a weighted index that takes into account the number and seriousness of co-morbid disease in determining a resident's health status (Charlson *et al*. 1987). It consists of a list of 17 clinical conditions that are ranked on a score of 1-6 in terms of the seriousness of co-morbid disease (e.g. residents with a history of a myocardial infarction have a score of 1, while residents with concurrent malignant tumours have a score of 6 (Appendix 4).

3.2   Determining the prevalence of PIP

The screening tools used to identify PIP were: Beers criteria (Appendix 5) and STOPP (Appendix 6). Each screening tool was applied to all the patient profiles of all residents in each dataset. For criteria that listed a class of medicines as potentially inappropriate, the most recent British National Formulary (BNF 59th Edition) available to the research assistant during the study period was consulted in order to classify the medicines (March 2010).

3.3   Calculation of the Net Ingredient Cost (NIC)

The net ingredient cost (NIC) was calculated for each medication identified as potentially inappropriate by each screening tool. The prices for the medications in the RoI dataset were obtained from the Irish Pharmacy Union's (IPU) January 2010 price list. If a medicine was prescribed by brand the cost price of the cheapest version of this brand (i.e. parallel imports) was used and if a medicine was prescribed generically the price of the cheapest available generic was used. For the NI dataset the prices for the medications were obtained from the January 2010 Northern Irish Drug Tariff and for any medications not listed in the Drug Tariff the price was obtained from the Health and Social Care Business Services Organisation January 2010 Pricing Book. The NIC price was calculated for a period of 28 days and for medications prescribed as required (pro re nata) "prn", the price of a 7 day supply was used. The NIC was then used to estimate the cost implications of PIP as identified by each individual screening tool. The total price was calculated for the instances of PIPs including and excluding "prn" medications on a monthly and annual basis both in euro and in sterling for both jurisdiction to allow for ease of comparison. The overall price of the monthly and annual instances of PIP identified by each tool across the entire dataset was also calculated in both euro and sterling. The conversion rate used for the purpose of this study was £1 = €1.135. The pricing represents only the NIC and did not reflect the entire costs involved as, for example, dispensing costs and VAT (where applicable) were not included.

3.4 Statistical Analysis

To determine the type of data i.e. parametric or non-parametric, the normality of the data was established by a review of the age distribution histogram and the boxplot and by performing Kolmogorova-Smirnova and Shapiro-Wilk tests. A significant result (p<0.05) indicates a non-normal distribution. The data was determined to be non-parametric based on its skewness and kurtosis (Table 4).

A Chi Square analysis was conducted to determine if there was any association between categorical data in the datasets i.e. gender and a Charlson co-morbidity of zero and instances of PIP as defined by Beers and STOPP for residents in both jurisdictions.

Mann Whitney U tests were performed to measure if there was any significant difference between median values in the number of medicines (including and excluding prn medicines) and the number of PIMs in both jurisdictions. A one-tailed Spearman's rho correlation coefficient test was performed to determine if there was any correlation between the dependent and independent variables e.g. number of medicines prescribed, gender, age and the occurrence of PIP. A p value of <0.05 was deemed to be significant.

Table 4 Skewness and kurtosis of the datasets

	Kolmogorov-Smirnov			Shapiro-Wilk		
	Statistic	Df	p	Statistic	Df	p
Age	0.062	630	0.000	0.986	630	0.000

df: Degrees of freedom

4.0 Results

4.1 Demographics

The total number of residents in the study was 630, 315 residents from both jurisdictions. The median age of the entire resident dataset was 84 (IQR: 78-89). The 80-84 year old category had the highest proportion of residents (27.3%), followed by the 85-89 year old category (24.4%). T here was an equal number of male and female residents in the 70-74 age category. There were more males than females in the 65-69 age category and for all the other age categories there were more females than males (
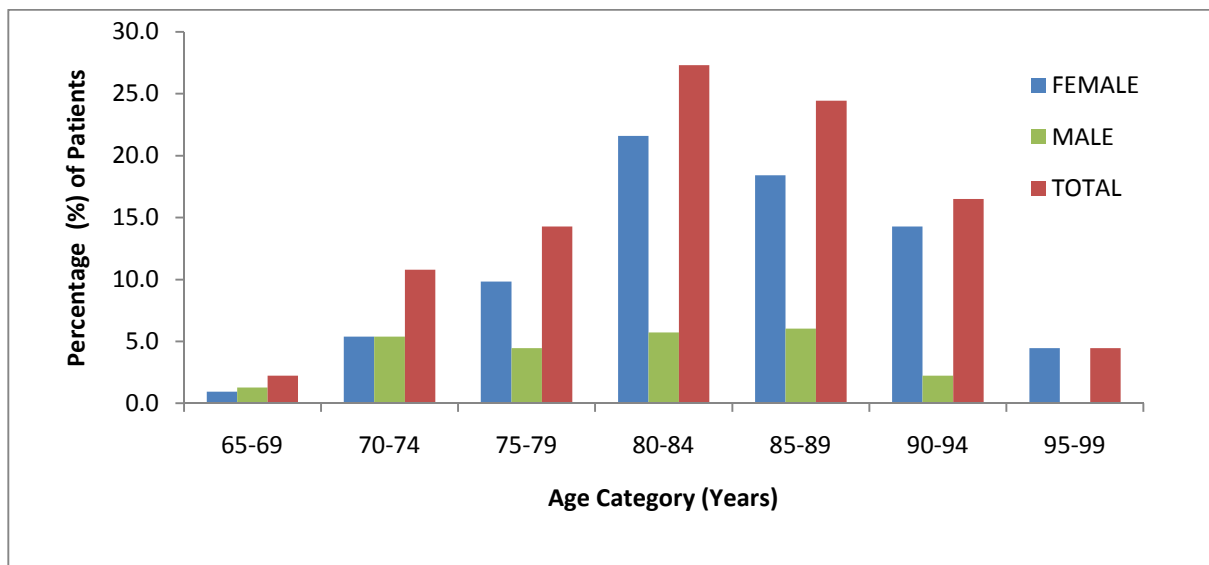Figure 1). The gender distribution in the matched datasets was female 74.9% and male 25.1%.

Figure 1 Population and gender distribution by age category.

Table 5 Demographics of the age and gender matched combine datasets

Demographics	RoI Dataset (n=315)	NI Dataset (n=315)	Matched Dataset (n=630)
Male	79 (25.1%)	79 (25.1%)	158 (25.1%)
Female	236 (74.9%)	236 (74.9%)	472 (74.9%)
Age Mean*	83.42	83.42	83.42
Age Range*	65-99	65-99	65-99
Age SD*	±7.048	±7.048	±7.048
No. of medicines prescribed	3,730	3,394	7,124
No. of regular medicines prescribed	2,683	2,246	4,929
No. of "prn" medicines prescribed	1,047	1,148	2,195
Median number of medicines prescribed	11	10	11
Min-Max of medicines prescribed	2-25	1-26	1-26
IQR of medicines prescribed	9-14	7-13	8-14
Mean of medicines prescribed	11.84	10.77	11.31
Median number of regular medicines	8	7	8
Min-Max of regular medicines	1-19	0-20	0-20
IQR of regular medicines	6-10	5-9	5-10
Mean of regular medicines	8.52	7.13	7.82

*Calculated in years

4.2   Number of medications prescribed

A total of 7,124 medicines were prescribed between the two datasets with 3,730 medications being prescribed in the RoI dataset, and 3,394 medications being prescribed in the NI dataset. The overall median number of medications per resident for the combined datasets was 11 (IQR 8-14), and the median number of medications per resident for the RoI dataset was 11 (IQR 9-13) and for the NI dataset was 10 (IQR 7-13).

The main differences in the median number of medicines prescribed per age category between the two datasets was for the 80-84 years age category, where the median number of medicines prescribed for the RoI dataset was 12 and for the NI dataset was 10; in the 85-89 years age category the median number of medicines for the RoI dataset was 12 and for the NI was 10 and in the 90-94 years age category the median number of medications was 10 for the RoI dataset and 9 for the NI dataset (

Figure 2)

A Mann-Whitney U test revealed that there was a small significant difference, (p=<0.05) although somewhat small, between the number of medications from the RoI dataset (Md=11, n=315) and NI dataset (Md=10, n=315), U= 41,605, z=-3.515, p=0.000, r=0.14.
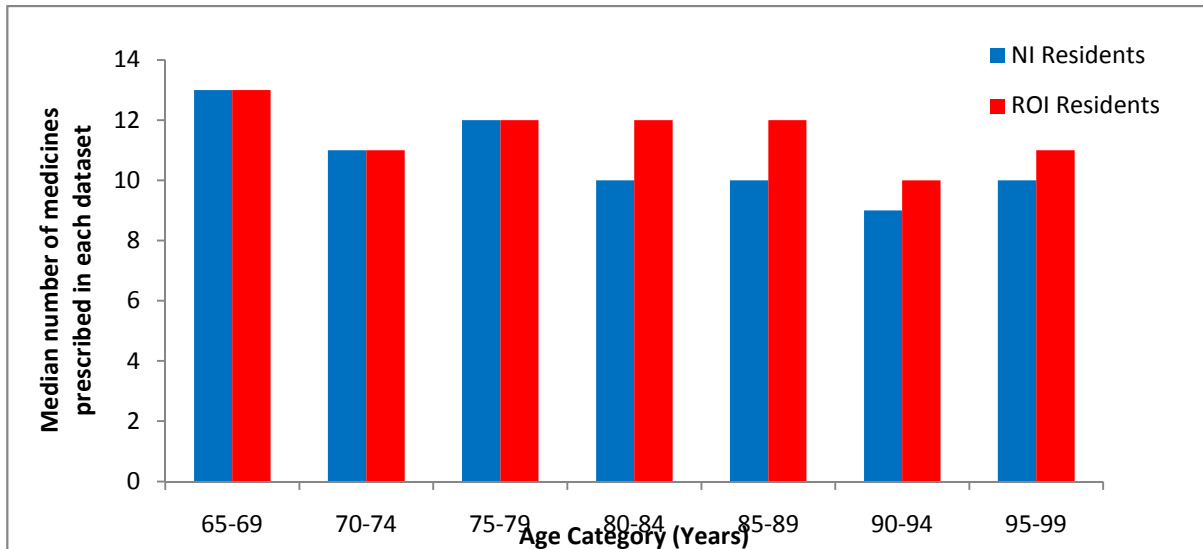
Figure 2 Median number of medicines prescribed by age category for both datasets

A Spearman's rho correlation test found that in the RoI dataset there was a significant negative correlation between the age and the number of medications that residents in this dataset were prescribed i.e. as age increased the number of medications decreases (rs=-0.125, p<0.05). Also as expected a significant positive correlation was also found for the Charlson co-morbidity index (CCI) score and the number of medications prescribed (rs=0.112, p<0.05). Similarly in the NI dataset a negative correlation was found between the number of medications a resident received and age, but this was not found to be significant (rs= -0.079 p=0.164). There was also a significant correlation between the CCI score and the number of medications (rs= 0.146 p<0.05) (Table 6).

Table 6 Correlations between demographic variables and the number of medications that residents from both datasets were prescribed

	Age	Female Gender	CCI score
Number of medications in the RoI dataset	rs=--0.125 p<0.05	rs=0.042 p=0.457	rs=0.112 p<0.05
Number of medications in the NI dataset	rs=-0.079 p=0.164	rs=0.107 p=0.059	rs=0.146 p<0.05

Key: CCI: Charlson Comorbidity Index

4.3 Medicines prescribed by physiological system

As shown in Figure 3, the highest percentage of medicines prescribed for the entire dataset (29.7%) was for the Central Nervous System (CNS), as well as being the highest percentage of medicines prescribed within each individual dataset. A higher percentage of CNS medicines was prescribed for residents from the RoI dataset than for residents from the NI dataset (RoI: 32.6%, NI: 26.5%).

Medications classified by the World Health Organisation (ATC code) for the alimentary tract (AT) and metabolism system were the second most commonly prescribed category of medicines (23.5%) across the entire dataset, with a higher percentage of medicines from this class being prescribed in the RoI dataset compared to NI dataset (RoI: 24% and NI: 22.9%).

Residents from RoI dataset also received a higher percentage of prescriptions written for medicines for the genito-urinary system (RoI: 1.6% and NI: 0.9%), respiratory system (RoI: 6.0% and NI: 5.7%) and the anti-infective drug category (RoI: 1.4% and NI: 0.8%) respectively.

Residents from the NI dataset received a higher percentage of prescriptions written for medicines for the cardiovascular system (CVS) (RoI: 12.9% and NI: 15.1%), muscle-skeletal (MS) system (RoI: 2.5% and NI: 3.6%), medicines for the blood and for blood forming organs category (RoI: 6.8% and NI: 7.8%) and dermatological products (RoI: 3.7% and NI: 6.3%). An equal percentage of medicines from the systemic hormone drug category (RoI: 1.9% and NI: 1.9%) was prescribed in each dataset (Figure 3).

4.4 Medicines prescribed for the CNS

Figure 4 illustrates the percentage of the medicines prescribed for each class of CNS medicines of the total CNS medicines prescribed to the entire dataset. The RoI dataset had a higher percentage of analgesic agents prescribed compared to the NI dataset: (RoI: 26.3% and NI: 24.0%).

A higher percentage of antidepressants (RoI: 14.6% and NI: 17.8%), hypnotics (RoI: 12.6% and NI: 17.3%) was prescribed in the NI dataset compared to the RoI dataset. Conversely, a higher percentage of antipsychotics (RoI: 13.7 % and NI: 11.5%), opioids (RoI: 9.7% and NI: 9.32%) and anxiolytics (RoI: 11.3% and NI: 9.8%) was prescribed in the residents from the RoI dataset over the NI dataset. A higher percentage of anti-epileptics (RoI: 5.4% and NI 3.4%) was prescribed in the RoI dataset when compared to the NI dataset.

There was a higher percentage of dopaminergic agents (RoI: 3.0% and NI 3.3%) and anti-dementia type agents (RoI: 1.8% and NI 2.4%) prescribed in the NI dataset compared to the RoI dataset. There was no difference in the percentage of anticholinergic agents prescribed across both datasets (RoI: 0.4% and NI 0.4%).
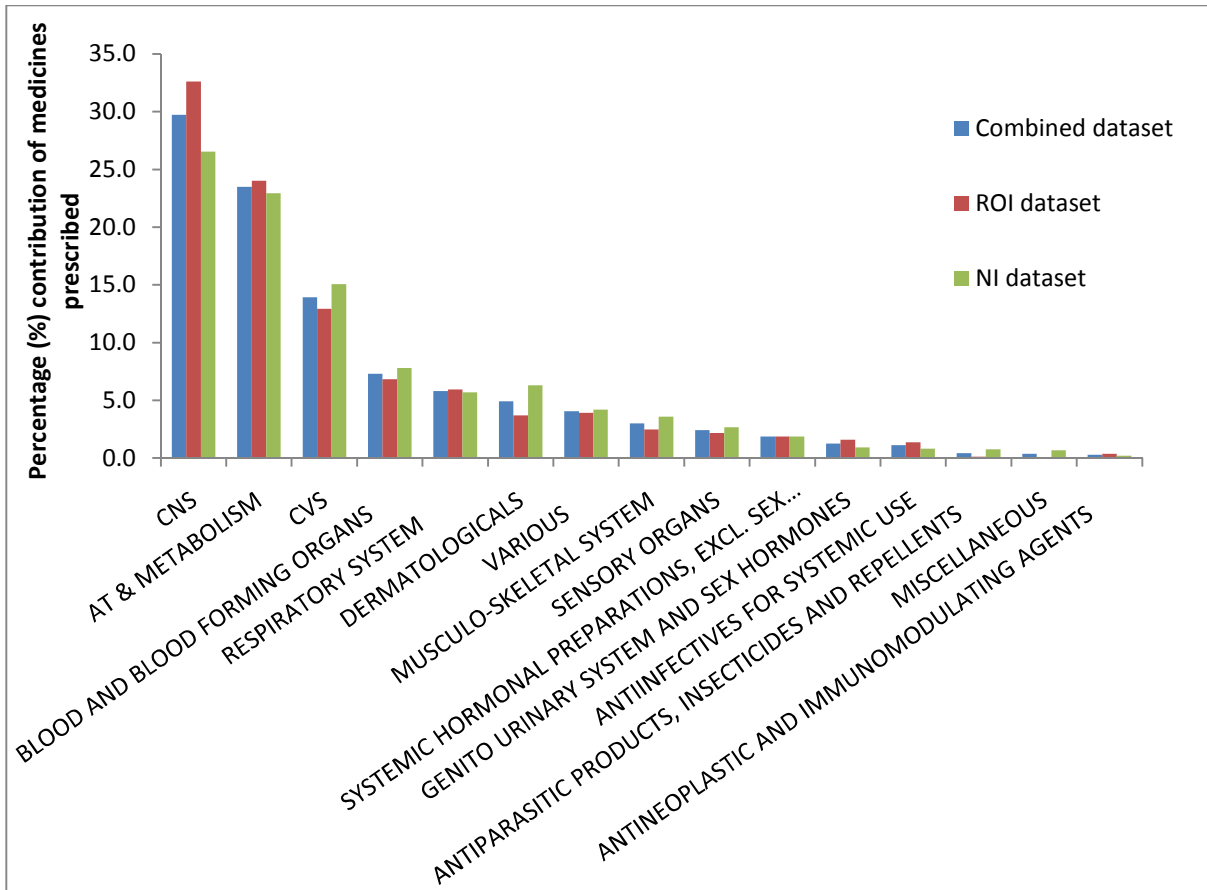
Figure 3 Contribution (%) of each physiological system to the overall prescribing both as a total usage and within each dataset
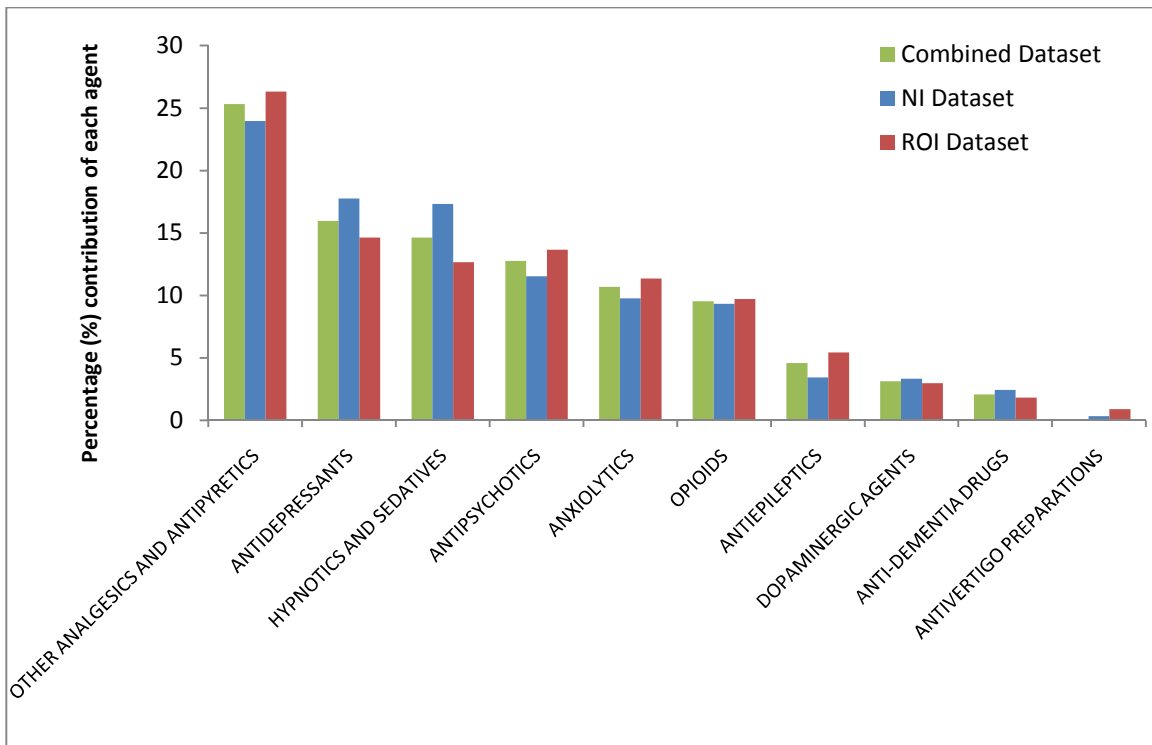

Figure 4 Percentage (%) of each individual class of medicines to the overall prescribing within the CNS

4.5 Medicines prescribed for the alimentary tract (AT) and metabolism

Figure 5 below illustrates the breakdown of the medicines prescribed for each class of medicine as per alimentary (AT) and metabolic drug class, as a percentage of the total metabolic and AT medicines prescribed to the entire dataset and in each individual dataset.
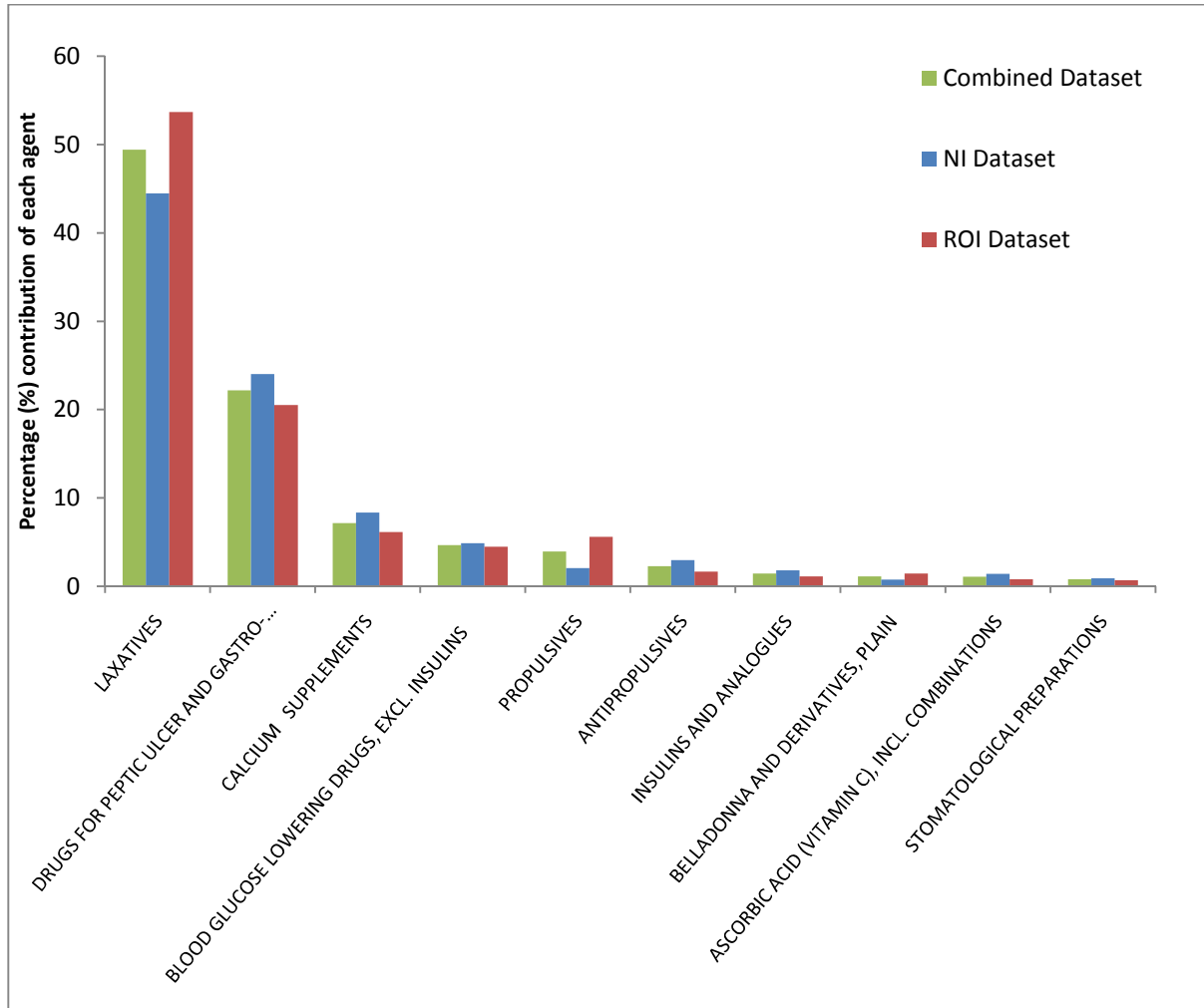
Figure 5 Percentage of medicines prescribed as per the alimentary and metabolic ATC codes, both as a total usage and within each dataset.

A higher percentage of laxatives (RoI: 53.7% and NI: 44.5%), propulsives (RoI: 5.6% and NI: 2.1%) and belladonna type medicines and their derivatives (RoI: 1.5% and NI: 0.8%) was prescribed in the RoI dataset in comparison to the NI dataset.

A higher percentage of medicines for gastro-oesphageal reflux disorders and peptic ulcer disease (RoI: 20.5% and NI: 24.0%), anti-propulsives (RoI: 1.7% and NI: 3.0%), calcium containing agents (RoI: 6.1% and NI: 8.4%), blood glucose lowering agents (RoI: 4.5% and NI: 4.9%), insulin and its analogues (RoI: 1.1% and NI: 1.8%) and vitamin C containing combinations (RoI: 0.8% and NI: 1.4%) was prescribed in the NI dataset compared to the RoI dataset. There was very little difference in the percentage of stomatological preparations (RoI: 0.9% and NI: 0.7%) prescribed between the two datasets (Figure 5).

4.6   Medicines prescribed for the CVS

Figure 6 illustrates the breakdown of the medicines prescribed for each class of CVS medicines, as a percentage of the total CVS medicines prescribed to the entire dataset and in each individual dataset.
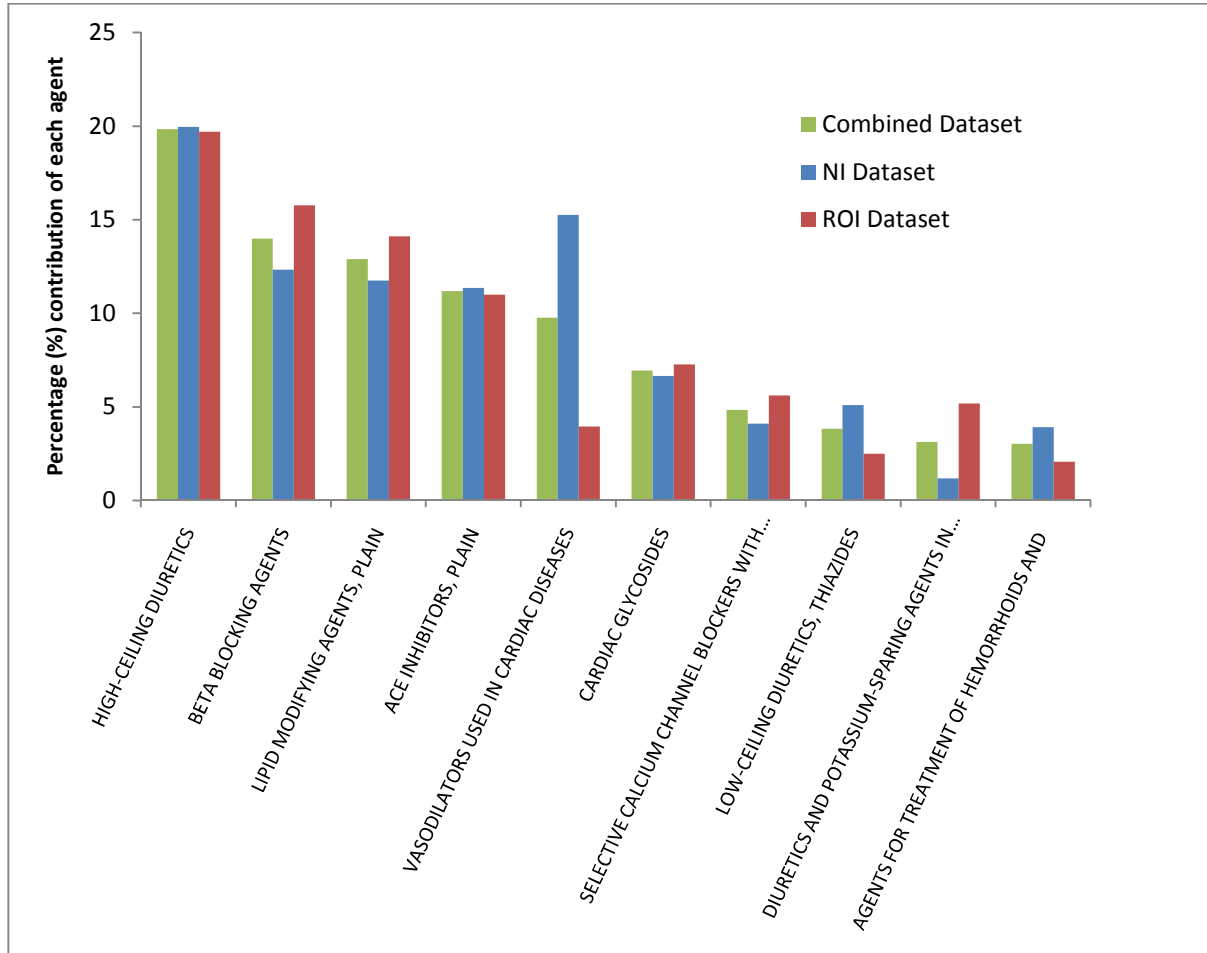
Figure 6 Percentage (%) of medicines prescribed as per the CVS ATC codes, both as a total usage and within each dataset.

Slightly more high ceiling type diuretics (RoI: 19.7% and NI: 20.0%) were prescribed in the NI dataset compared to the RoI dataset.

A higher percentage of β blockers (RoI: 15.8% and NI: 12.3%) and lipid modifying agents (RoI: 14.1% and NI: 11.7%) was prescribed in the RoI dataset in comparison with the NI dataset.

There was very little difference in the percentage of Angiotension 2 inhibitors (RoI: 11.0% and NI: 11.4%).

A higher percentage of cardiac glycosides (RoI: 7.3% and NI: 6.7%), calcium channel blockers (RoI: 5.6% and NI: 4.1%) and thiazide diuretics (RoI: 2.5% and NI: 5.1%) was prescribed in the NI dataset when compared with the RoI dataset.

A significantly higher percentage of vasodilator agents used for cardiac disease was prescribed in the NI dataset compared to RoI (RoI: 3.9% and NI: 15.3%).

A higher percentage of agents for the treatment of haemorrhoids and related agents was prescribed in the NI dataset in comparison to the RoI dataset (RoI: 2.1% and NI: 3.9%).

4.7 Medicines prescribed for the blood and for blood forming organs as per ATC classification system

A higher percentage of iron preparations (RoI: 15.7% and NI: 24.2%) was prescribed in the NI Irish dataset, whereas a higher percentage of vitamin B12 and folic acid type preparations (RoI: 20.8% and NI: 10.9%) was prescribed in the RoI Irish dataset over the NI Irish dataset.

There was very little difference in the percentage of irrigation solution (RoI: 0.4% and NI: 1.1%) and antifibrinolytic agents (RoI: 11.0% and NI: 11.4%) prescribed between the two datasets. Approximately the same percentage of antithrombotic agents (RoI: 63.5% and NI: 63.8%) was prescribed in both the NI and RoI datasets (
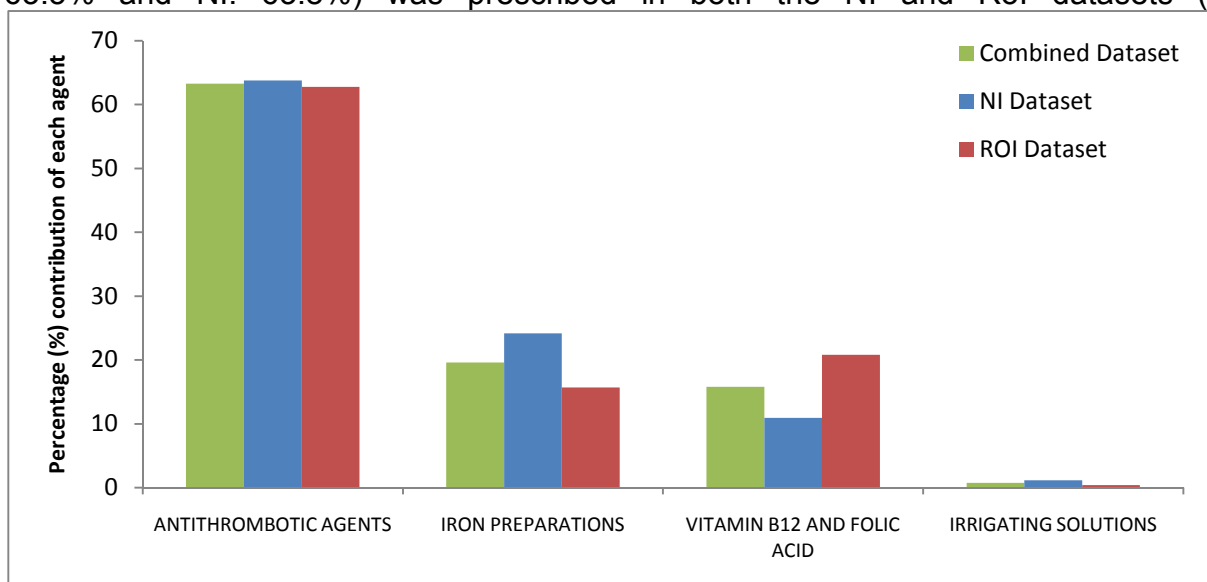
Figure 7).
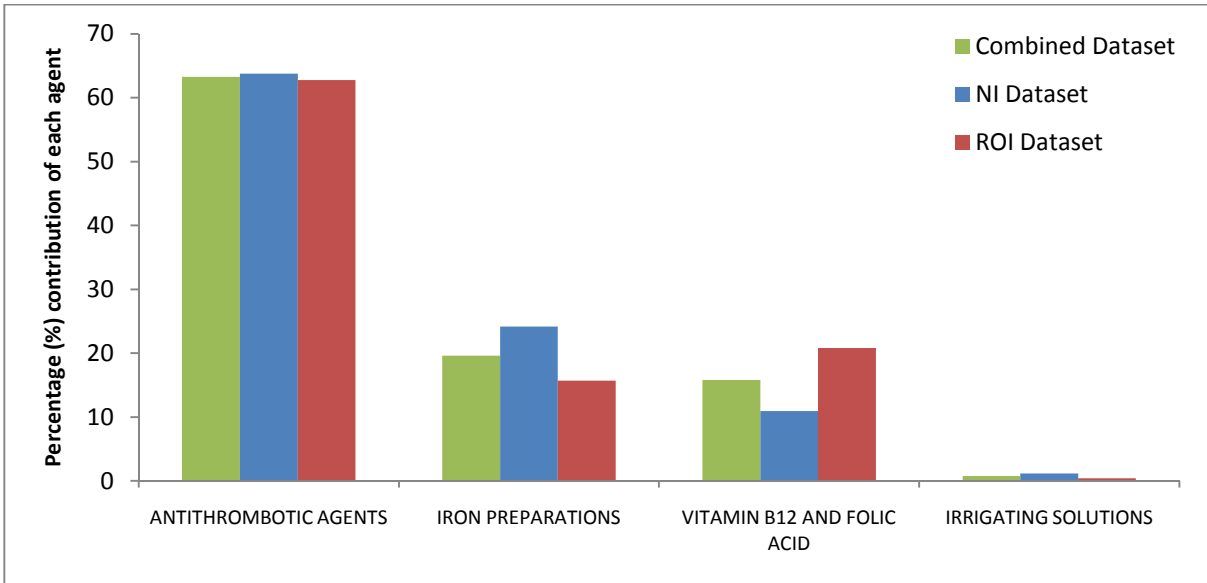
Figure 7 Percentage (%) of medicine prescribed as per the blood and for blood forming organs ATC codes, both as a total usage and within each dataset.

4.8   Medicine prescribed for the Respiratory System

A higher percentage of decongestants and nasal preparations (RoI: 38.7% and NI: 35.9%), adrenergics inhaler (RoI: 16.7% and NI: 0.5%) and systemic adrenergics (RoI: 4.5% and NI: 1.6%) was prescribed in the RoI dataset than in the NI dataset.

Whereas a higher percentage of systemic antihistamines (RoI: 0.5% and NI: 1.4%), throat preparations (RoI: 14.4% and NI: 15.1%), cough suppressants (RoI: 0% and NI: 2.1%), expectorants (RoI: 1.4% and NI: 2.7%), other miscellaneous systemic agents for obstructive airway diseases (RoI: 2.7% and NI: 3.1%), inhaled agents for the treatment of obstructive airways disease (RoI: 2.7% and NI: 4.2%) and systemic nasal decongestants (RoI: 18.5% and NI: 33.9%) was prescribed in the NI dataset than in the RoI dataset (
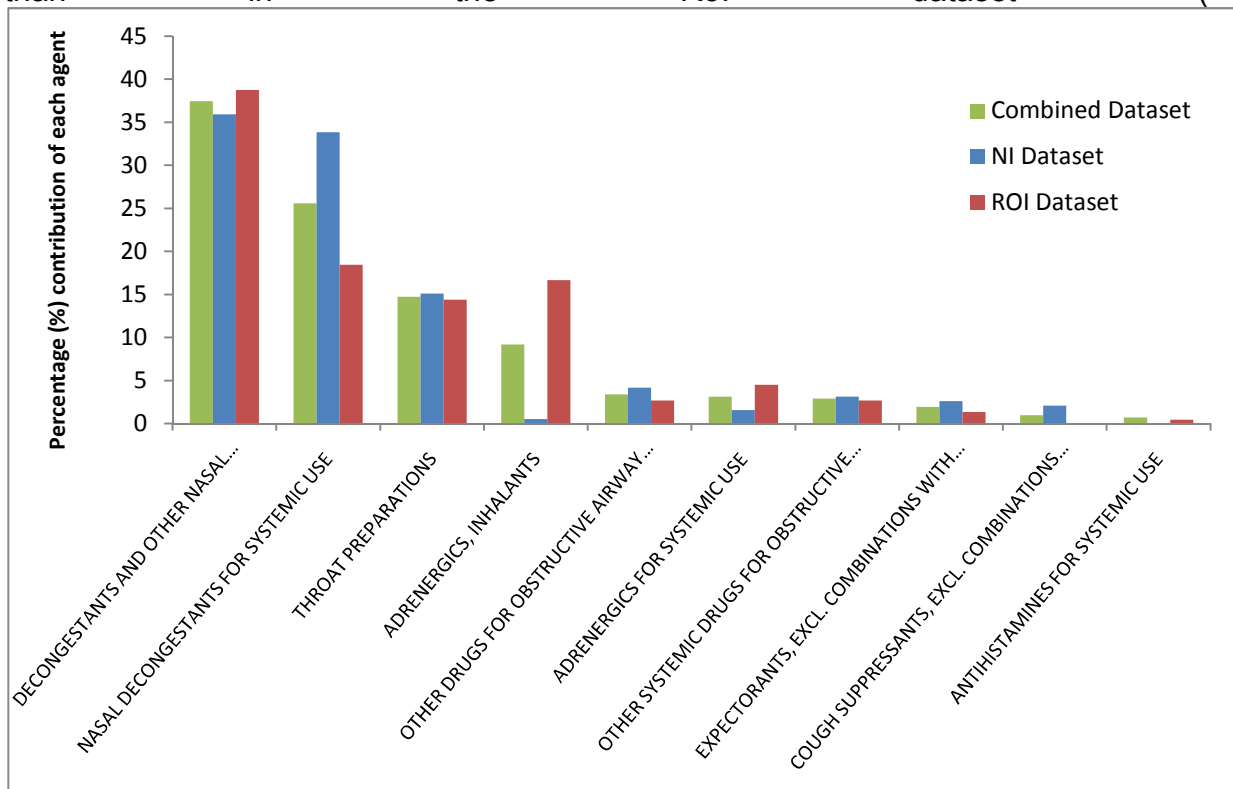
Figure 8).

Figure 8 Percentage (%) of each of the medicines for the Respiratory system prescribed to the overall prescribing of these medicines, both as a total usage and within each dataset.

4.9   Medicines prescribed for dermatological conditions

A higher percentage of topical antifungal preparations (RoI: 21.7% and NI: 10.8%), topical corticosteroids based preparations (RoI: 17.4% and NI: 7.5%), topical anti-psoriatic preparations (RoI: 2.9% and NI: 1.4%), topical corticosteroid combination preparations (RoI: 3.6% and NI: 3.3%) and preparations from the other miscellaneous dermatological preparation category (RoI: 22.5% and NI: 4.7%) was prescribed in the RoI dataset than in the NI dataset.

Whereas in the NI dataset a higher percentage of topical anti-pruritics (RoI: 2.2% and NI: 2.8%), topical antibiotics (RoI: 2.2% and NI: 4.2%), topical antibiotic–corticosteroid based preparations (RoI: 0.7% and NI: 4.2%), topical antiseptic–corticosteroid based preparations (RoI: 1.5% and NI: 13.6%), and emollients and protective type preparations (RoI: 25.4% and NI: 42.3%) was prescribed than in the RoI   dataset   (

Figure 9)

31

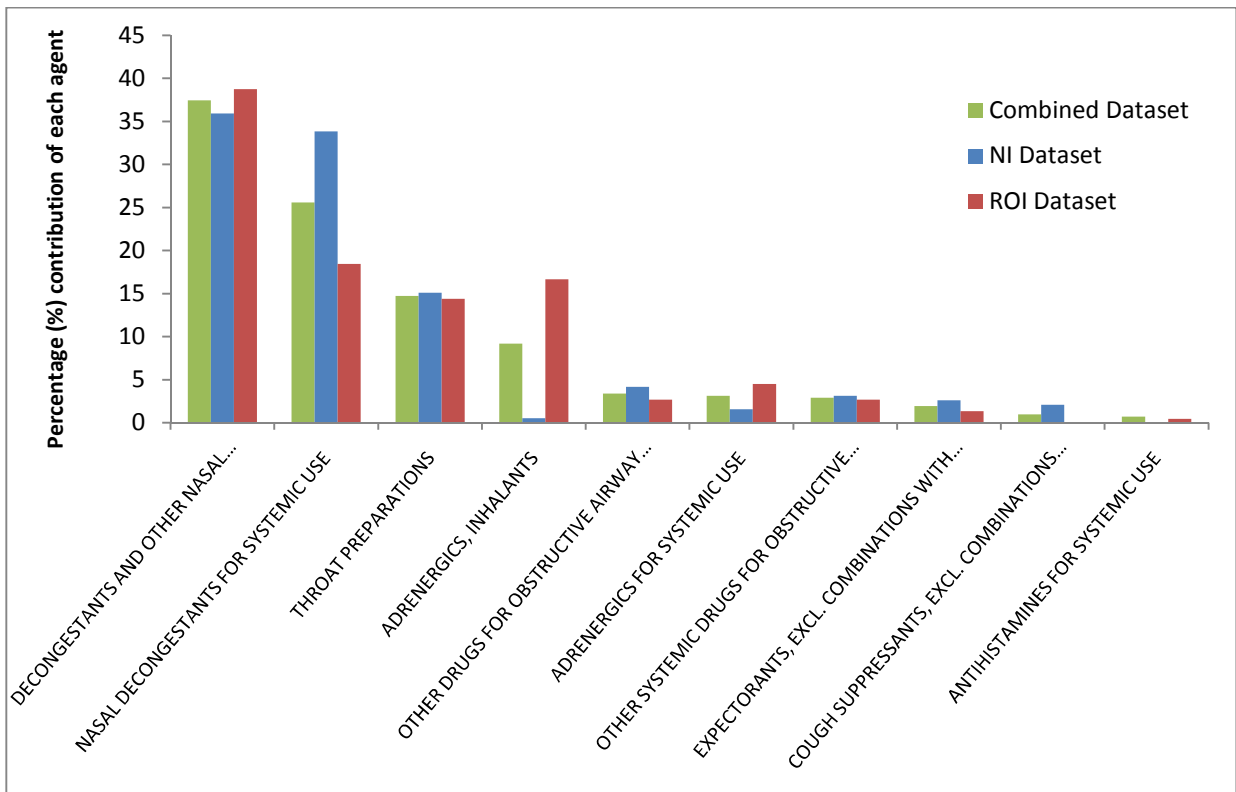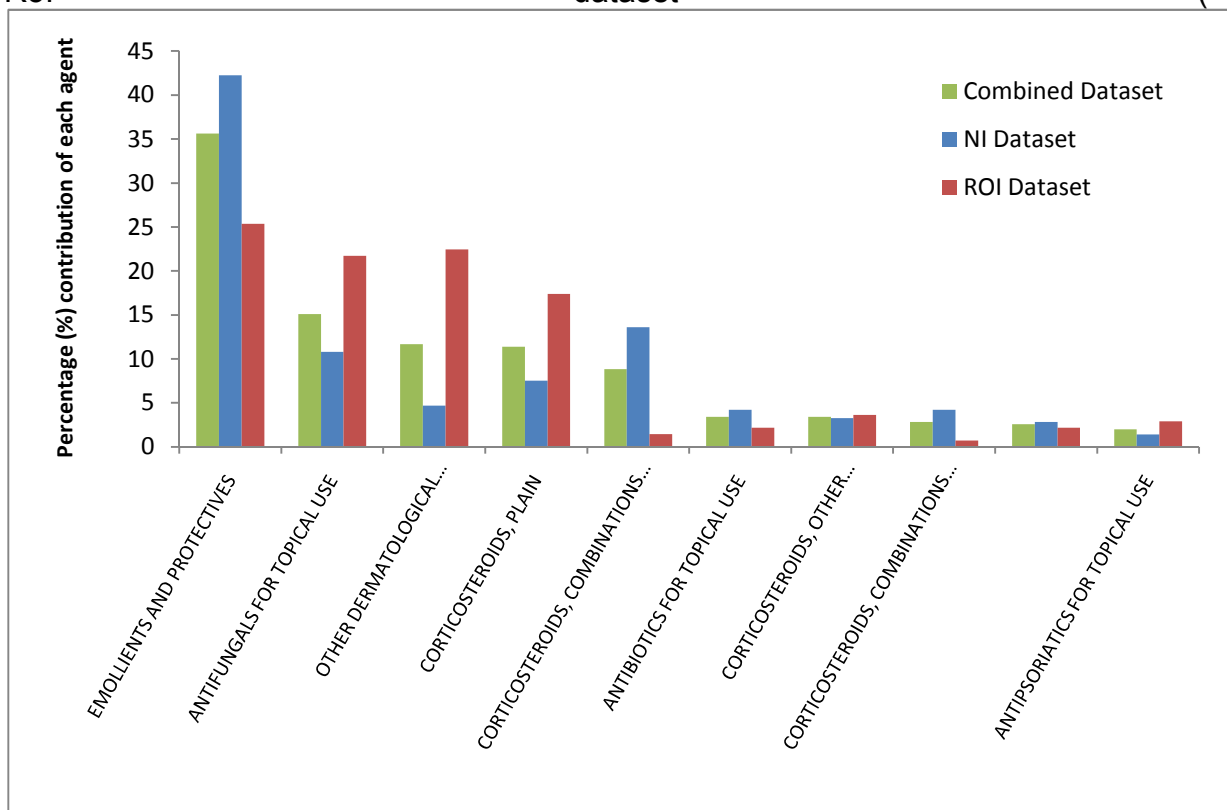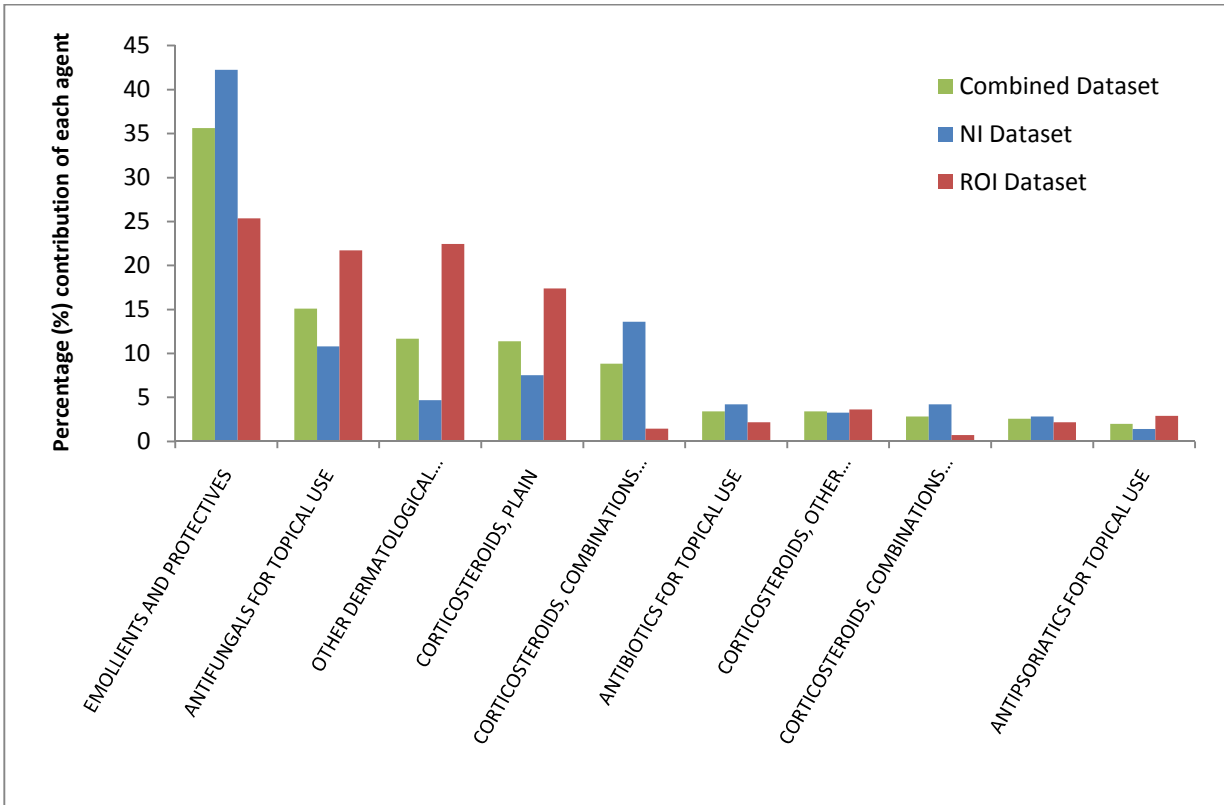**Figure 9 Percentage (%) of each of the medicines for dermatological conditions prescribed to the overall prescribing of these medicines, both as a total usage and within each dataset.**

4.10 Co-morbidity data in combined datasets

The Charlson Co-morbidity Index (CCI) scores were calculated for all study participants and were found to be consistent across each dataset, with less than 20% of residents in each dataset not scoring on the CCI index, indicating the relative frailty and high incidence of chronic illness in this patient population (Table 7). Chi Square analysis did not reveal any significant association between the gender of residents in each dataset that scored zero on the CCI index (χ^2= 2.246, p= 0.134).

Table 7 CCI of the entire dataset and each individual dataset

CCI	NI Dataset (n=315)	RoI Dataset (n=315)	Total (n=630)
CCI 0	50 (15.87)	39 (12.38)	89 (14.13)
Male:Female	*17:33*	*11:28*	*28:61*
CCI 1	126 (40.00)	97 (30.79)	123 (19.52)
Male:Female	*30:96*	*28:73*	*58:169*
CCI 2	91 (28.89)	64 (20.32)	155 (24.60)
Male:Female	*21:70*	*19:45*	*40:115*
CCI 3	29 (9.21)	65 (20.63)	94 (14.92)
Male:Female	*3:26*	*14:51*	*17:77*
CCI 4	11 (3.49)	31 (9.84)	42 (6.67)
Male:Female	*5:6*	*7:24*	*12:30*
CCI 5	8 (2.54)	13 (4.13)	21 (3.33)
Male:Female	*3:5*	*4:9*	*7:14*
CCI 6	-	5 (1.59)	5 (0.79)
Male:Female		*0:5*	*0:5*
CCI 7		1 (0.32)	1 (0.16)
Male:Female		*0:1*	*0:1*

Key: CCI: Charlson Comorbidity Index

4.11 Prevalence of PIP measured per dataset as defined by the Beers and STOPP criteria

Table 8 below summarises the rates of PIP including and excluding as required "prn" when the Beers' criteria were applied to residents' information for each dataset.

A Chi-square test for independence indicated that there was a significant association between the jurisdictions and the occurrence of PIP as defined by the Beers' criteria when instances of PIP relating to "prn" medications were excluded ($\chi2=28.558$, p<0.05) but when "prn" medicines were included an association was not reported ($\chi2=0.411$, p=0.521). An association between the rate of PIP obtained for the application of the STOPP criteria and locality was found but it was reported not to be significant when "prn" medicines were included ($\chi2=2.729$, p= 0.099) or when the instances of PIP relating to "prn" medicines were removed ($\chi2=2.459$, p= 0.117).

Table 8 below outlines the rate of PIP per dataset and it includes both the prevalence of PIP for both datasets including and excluding "prn" medicines. In the NI dataset the PIP prevalence reported for the Beers criteria was 56.8% (48.6% excluding "prn" medicine) and the PIP prevalence reported for STOPP in the NI dataset was 67.0% (60.0% excluding "prn" medicines). In the RoI dataset the PIP prevalence reported for the Beers criteria was 54.3% (41.6% excluding "prn" medicine) and the PIP prevalence rate identified by STOPP reported for the RoI dataset was 73.0% (66.0% excluding "prn" medicines) (Table 8).

Table 8 The rates of PIP calculated per dataset

	NI Dataset	RoI Dataset
Beers' Criteria (%)	56.8%	54.3%
Beers' criteria excluding prn medicines (%)	48.6%	41.6%
STOPP Criteria (%)	67.0%	73.0%
STOPP Criteria excluding prn medicines (%)	60.0%	66.0%

4.11.1 Application of the Beers' criteria to the Northern Irish and Republic of Ireland datasets

When the Beers' criteria were applied to the patient profiles of the residents in the RoI dataset they identified 384 instances of potential inappropriate prescribing (PIP) relating to 259 PIMs (108 independent of diagnosis (ID) and 276 considering diagnosis (CD) in a total of 171 (54.3%) residents when "prn" type medications were included and 275 (74 ID and 201 CD) instances of PIP relating to 180 PIMs in 131 residents (41.6%) when instances of PIP relating to "prn" type medicines were excluded. In the RoI dataset more males had one or more instances of PIP (62.0%)

compared to the female population (51.7%); this trend remained constant even after the instances of PIP relating to "prn" medicines were removed (46.8% of males and 39.8% of females respectively) (Table 9).

Sixty nine (21.9%) residents had one instance of PIP prescribed, forty five (14.3%) residents had two instances of PIP and fifty seven (18.1%) residents had three or more instances of PIP. When prn medicines were removed fifty nine (18.7%) residents had one instances of PIP, thirty four (10.8%) had two, thirty eight (12.1%) had three or more instances of PIP (Table 9).

Table 9 Number of residents with instances of PIPs identified by Beers' criteria in the RoI dataset

Number of PIP instances	Male (n=79)	Female (n=236)	Total (%) (n=315)	Male ex prn PIMs (n=79)	Female ex. Prn PIMs (n=236)	Total ex prn PIMs (%) (n=315)
1	21 (26.6)	48 (20.3)	69 (21.9)	17 (21.5)	42 (17.8)	59 (18.7)
2	14 (17.7)	31 (13.1)	45 (14.3)	13 (16.5)	21 (8.9)	34 (10.8)
≥3	14 (17.7)	43 (18.2)	57 (18.1)	7 (8.9)	31 (13.1)	38 (12.1)
Total Residents	49 (62.0)	122 (51.6)	171 (54.3)	37 (46.9)	94 (39.8)	131 (41.6)
Total PIP instances			**384**			**275**

When the Beers' criteria were applied to the NI resident profiles they identified 381 instances of PIP (183 ID and 198 CD) relating to 265 PIMs in a total of 179 (56.8%) residents. When the instances of PIP relating to "prn" medicines were removed it resulted in 283 instances of PIP (136 ID and 147 CD) relating to 204 PIMs in 153 (48.5%) residents.

Sixty nine (21.9%) residents had one instance of PIP prescribed, 58 (18.4%) had two and 38 (16.5%) residents had three or more instances of PIP. When "prn" medicines were removed 74 (23.5%) residents had one instance of PIP, 48 (15.2%) had two, 31 (9.8%) had three or more instances of PIP (Table 10).

Table 10 Number of residents with instances of PIPs identified by Beers' criteria in the NI dataset

Number of PIP instances	Male (n=79)	Female (n=236)	Total (%) (n=315)	Male ex prn PIMs (n=79)	Female ex. Prn PIMs (n=236)	Total ex prn PIMs (%) (n=315)
1	18 (22.8)	51 (21.6)	69 (21.9)	20 (25.3)	54 (22.9)	74 (23.5)
2	12 (15.2)	46 (19.5)	58 (18.4)	10 (12.7)	38 (16.1)	48 (15.2)
≥3	14 (17.7)	38 (16.1)	52 (16.5)	8 (10.1)	23 (9.7)	31 (9.8)
Total Residents	44 (55.7)	135 (57.2)	179 (56.8)	38 (48.1)	115 (48.7)	153 (48.5)
Total PIP instances			**381**			**283**

Overall, only 28 (12 CD and 16 ID) of the 68 Beers' criteria (41.2%) were used to identify these instances of PIP including "prn" medicines in the RoI dataset and 26 (12 CD and 14 ID) (Table 11-12) of the 68 Beers' criteria (38.2%) when "prn" medicines were excluded. In the NI dataset 26 (7 CD and 19 ID) of the 68 Beers' criteria (38.2%) were utilised to identify instances of PIP when "prn" medicines were included and excluded.

In the RoI dataset prescribing of benzodiazepines accounted for 51 (47.2%) of the inappropriate medicines identified by the Beers' ID criteria when "prn" medicines were included and accounted for 34 (45.9%) when "prn" medicines were excluded. In the NI dataset the prescribing of benzodiazepines accounted for 84 (45.9%) of the inappropriate medicines identified by the Beers' ID criteria when "prn" medicines were included and accounted for 45 (33.1%) when "prn" medicines were excluded.

Fluoxetine was prescribed on 5 occasions (1.6% of residents) in the RoI dataset and accounting for 4.6% (6.8% excluding "prn" medicines) of the total instances of PIP identified by Beers' ID criteria but was prescribed on 31 occasions (9.8% of residents) in the NI dataset and accounted for 16.9% (22.8% excluding "prn" medicines) of total instances of PIP identified by Beers' ID criteria.

In the RoI dataset a total of 276 instances of PIP (201 instances excluding "prn") and in the NI dataset a total of 198 instances of PIP (147 instances excluding "prn") were identified using Beers' CD. In both datasets the highest proportion were benzodiazepines in residents with a history of concurrent falls, in the RoI dataset 95 (34.4%) instances of PIP were identified when "prn" medicines were included and 54 (26.9%) instances of PIP when "prn" medicines were excluded. In the NI dataset residents using benzodiazepines with a history of concomitant falls was also the most prominent reason for PIP in the Beers CD list with 107 (54.0%) instances of PIP being identified when "prn" medicines were included and 73 (49.7%) instances of PIP identified when "prn" medicines are excluded. When the Beers' ID and CD were combined, instances of PIP relating to benzodiazepines accounted for 38.0% (32.0% excluding "prn" medicines) of the total instances of PIP identified in the RoI dataset and 50.1% (41.7% excluding "prn" medicines) in the NI dataset (Table 11-12).

Table 11 The instances of PIP identified by Beers' criteria independent of diagnosis

Medication	Total Rol PIP	Total Rol PIP ex prn	Total NI PIP	Total NI PIP ex prn
Independent of Diagnosis				
Oxybutynin *(unless XL)*	2	2	2	2
Flurazepam	9	9		
Amitriptyline	9	9	14	13
Doxepin	1	1	1	1
Short acting benzodiazepines: (Doses >)				
Lorazepam 3mg				
Temazepam	5	5	16	15
Triazolam				
Long Acting benzodiazepines:				
Chlordiazepoxide				
Diazepam	35	18	68	30
Long-acting benzodiazepines	2	2		
Disopyramide	1		4	4
Digoxin			2	2
Belladonna alkaloids	13	3	5	5
Chlorpheniramine	8	3	19	13
Diphenhydramine				
Promethazine			3	3
Hydroxyzine			1	1
All barbiturates (except Phenobarbital) except when used to control seizures			1	1
Long term long $t_{1/2}$ NSAIDs: Naproxen			1	1
Fluoxetine	5	5	31	31
Bisacodyl	1		2	2
Amiodarone	5	5	7	6
Nitrofurantoin	7	7	2	2
Doxazosin	4	4	3	3
Estrogen	1	1	1	1
Total Independent of Diagnosis	108	74	183	136

Table 12 The instances of PIP identified by Beers' criteria considering diagnosis

Medication	Total Rol PIP	Total Rol PIP ex prn	Total NI PIP	Total NI PIP ex prn
Considering Diagnosis				
Heart failure				
High sodium content medicines				
Peptic ulcer disease				
NSAIDs	7	4		
Blood clotting disorder				
NSAID	1	0		
Asprin	1	1		
Dipyridamole	1	1		
Clopidogrel	1	1		
Bladder outflow obstruction				
Anticholinergics	3	1	2	1
Antidepressants	5	5	3	3
Muscle relaxants	4	3		
Stress Incontinence				
TCAs	7	7	1	1
Benzodiazepine	12	7	4	2
Anticholinergics	10	7	2	2
Alpha blockers	7	7		
Arrhythmia				
TCA	1	1		
Parkinsons Disease				
Conventional Antipsychotics	3	3		
Cognitive Impairment				
Muscle relaxants	5	4	1	1
Anticholinergics	19	11	27	19
Barbiturates			1	1
Depression				
Long term benzodiazepine	44	44	22	22
Fall & Syncope				
Benzodiazepines	95	54	107	73
TCAs	5	5	20	18
Obesity				
Olanzapine	1	1		
COPD				
Long acting benzodiazepines	4	3	6	2
β-blocker: propranolol			1	1
Constipation				
CCBs	11	11	1	1
TCAs	7	7		
Anticholinergics	22	13		
Total Considering Diagnosis	276	201	198	147
Total Independent of Diagnosis & Considering Diagnosis	384	275	381	283

Key: >: Greater than, $t_{1/2}$: half life, NSAIDs: Non-Steroidal Anti-Inflammatory Drugs, COPD: Chronic Obstructive Pulmonary Disease, CCBs: Calcium Channel Blockers, TCAs: Tricyclic Antidepressants

4.11.2 The application of the STOPP criteria to both datasets

In the RoI dataset the STOPP criteria identified a total of 568 instances of PIP relating to 500 PIMs in 230 (73.0%) residents when "prn" medicines were included and 429 instances of PIP relating to 375 PIMs in 208 (66.0%) residents when "prn" were excluded. Eighty seven residents (27.6%) had one instance of PIP, 59 (18.7%) residents had two instances of PIP and 84 (26.7%) residents had three or more instances of PIP. When instances of PIP relating to "prn" medicines were removed 96 (30.5%) residents had one instance of PIP 60 (19.0%) residents had two instances of PIP and 52 (16.5%) residents had three or more instances of PIP.

In the NI dataset STOPP identified a total of 478 instances of PIP relating to 420 PIMs in 211 (67.0%) residents when "prn" medicines were included and 356 instances of PIP relating to 298 PIMs in 189 (60.0%) residents when instances of PIP relating to "prn" were removed. Eighty six residents (27.3%) residents had one instance of PIP, 56 (17.8%) residents had two instances of PIP and 69 (21.9%) residents had three or more instances of PIP.

When instances of PIP relating to "prn" medicines were removed, 97 patients (30.8%) had one instance of PIP, 48 (15.2%) patients had two instances of PIP and 44 (14.0%) patients had three or more instances of PIP.

In the RoI dataset slightly more of the male population were prescribed one or more instances of PIP (78.5%) than the female population (71.2%); this trend remained constant even after the instances of PIP relating to "prn" medicines were removed 72.2% of males and 63.9% of females being prescribed one or more instances of PIP (

Table **13**).

Whereas in the NI dataset slightly more females (67.4%) were prescribed one or more instances of PIP than the male population (65.8%) when the "prn" medicines were included but when instances of PIP relating to "prn" medicines were removed more males (62.0%) than females (59.3%) appeared to be prescribed one or more instances of PIP (Table 14).

A Mann-Whitney U test showed that there was no statistically significant difference between the number of instances of PIP identified by STOPP for each resident between the two datasets (z=-1.892, p=.058)

Table 13 The number of residents from RoI dataset with instances of PIP identified by STOPP

Number of PIP instances	Male (n=79)	Female (n=236)	Total (%) (n=315)	Male ex prn PIMs (n=79)	Female ex. Prn PIMs (n=236)	Total ex prn PIMs (%) (n=315)
1	28 (35.4)	59 (25.0)	87 (27.6)	27 (34.2)	69 (29.2)	96 (30.5)
2	14 (17.7)	45 (19.1)	59 (18.7)	18 (22.8)	42 (17.8)	60 (19.0)
≥3	20(25.3)	64 (27.1)	84 (26.7)	12 (15.2)	40 (16.9)	52 (16.5)
Total residents	62 (78.5)	168 (71.2)	230 (73.0)	57 (72.2)	151 (63.9)	208 (66.0)
Total PIP instances			**568**			**429**

Table 14 The number of residents from NI dataset with instances of PIP identified by STOPP

Number of PIP instances	Male (n=79)	Female (n=236)	Total (%) (n=315)	Male ex prn PIMs (n=79)	Female ex. Prn PIMs (n=236)	Total ex prn PIMs (%) (n=315)
1	24 (30.4)	62 (26.3)	86 (27.3)	25 (31.6)	72 (30.5)	97 (30.8)
2	13 (16.4)	43 (18.2)	56 (17.8)	15 (19.0)	33 (14.0)	48 (15.2)
≥3	15 (19.0)	54 (22.9)	69 (21.9)	9 (11.4)	35 (14.8)	44 (14.0)
Total residents	52 (65.8)	159 (67.4)	211 (67.0)	49 (62.0)	140 (59.3)	189 (60.0)
Total PIP instances			**478**			**356**

In the RoI dataset, of the 65 criteria in STOPP, 39 (60.0%) were used to identify PIP whereas in the NI dataset only 30 (46.15%) of the 65 criteria were used. The highest prevalence of PIP in the RoI and NI datasets relates to STOPP criterion H: "Drugs that adversely affect fallers" n=143 and n=189 respectively. This was followed by medicines whose primary effect was on the central nervous system (CNS) in the RoI dataset n=143 and in the NI dataset n=91 (Figure 10). Prescribing of duplicate drug classes accounted for a total of 29 PIMs, the endocrine system accounted for six and only one IP was identified for the respiratory system (
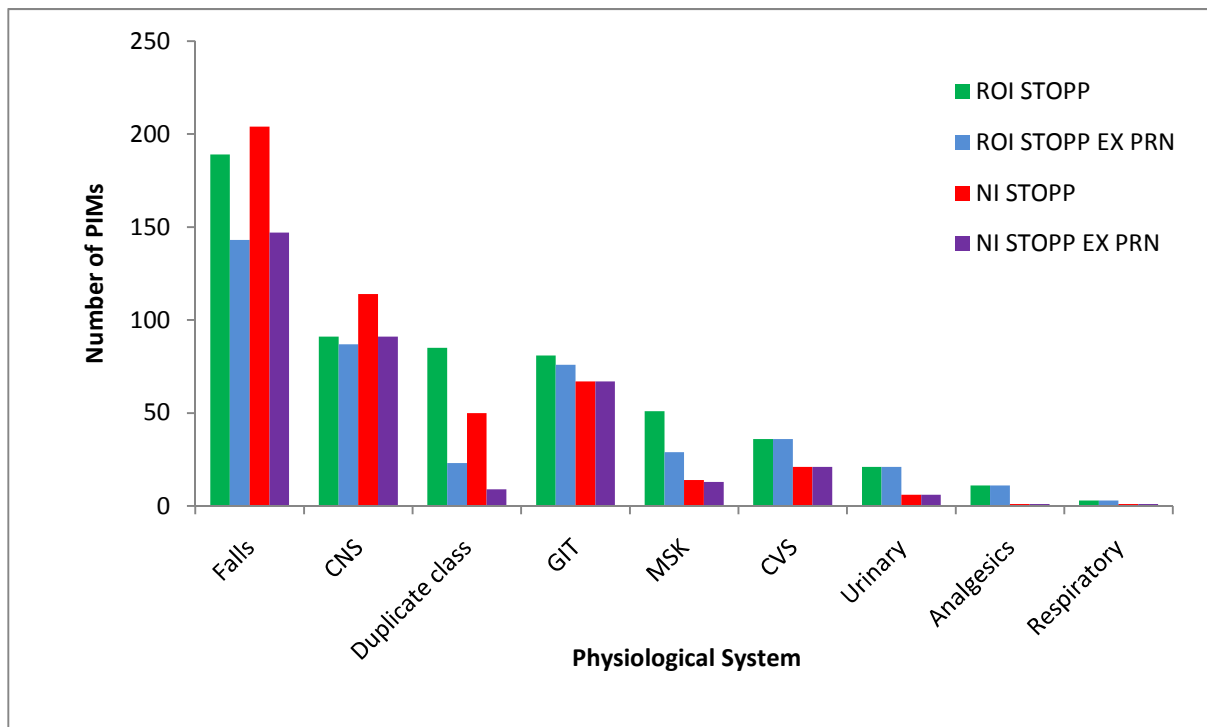
Table **15**).

Figure 10 The instance of PIP per physiological system.

Table 15 The number of instances of PIP identified by the STOPP criteria in the RoI and NI datasets.

CRITERIA	RoI Total	RoI Total ex "prn" medicines	NI Total	NI Total ex "prn" medicines
Cardiovascular System				
Loop diuretic & ankle oedema	5	5	3	3
Loop diuretic 1st line for hypertension	10	10	3	3
CCBs & constipation	11	11		
beta-blocker & COPD			1	1
Aspirin >150mg daily			1	1
Aspirin: not indicated	9	9	16	16
Diltiazem or verapamil &Class III or IV heart failure	1	1		
Central Nervous System				
TCAs & dementia	3	3	4	4
TCAs & cardiac conductive	1	1	2	2
abnormalities	6	6		
TCAs & constipation	7	5	19	5
TCAs & opiate or CCB			1	1
TCA & prostatism				
Long term long half life	29	29	32	32
benzodiazepine	13	13	29	22
Neuroleptics as long-term hypnotics				
i.e. > 1 month	16	15	4	2
Neuroleptics in Parkinsons Disease	2	1		
Phenothiazines & epilepsy	5	5	1	1
Anticholinergics for extra-pyramidal	9	9	22	22
side effects				
>1 week 1st generation antihistamines				
Respiratory System				
Theophylline monotherapy for COPD	2	2		
Systemic corticosteroids instead of			1	1
inhaled for COPD				
Nebulised ipratropium with glaucoma	1	1		
Gastro Intestinal System				
Diphenoxylate/ codeine phosphate for chronic diarrhoea	1	1		
Diphenoxylate/ loperamide/ codeine phosphate for acute infective gastroenteritis				
Metoclopramide/ prochlorperazine & Parkinsonism	2	1		
PPI for PUD at full therapeutic dosage for > 8 weeks	74	74	66	66
Anticholinergic antispasmodic & chronic constipation	4		1	1

CRITERIA	RoI Total	RoI Total ex "prn" medicines	NI Total	NI Total ex "prn" medicines
Musculoskeletal System				
NSAID & hypertension	30	15	4	4
Long term continuous NSAID for OA	5	5	3	3
NSAID & Heart Failure	7	1	2	1
Aspirin & Warfarin & NSAID	3	2		
NSAID & chronic renal impairment	1	1	2	2
Long term corticosteroid (>3 months) as monotherapy for RA or OA	5	5	3	3
Genitourinary System				
Bladder antimuscarinic drugs & dementia	4	4	4	4
Antimuscarinic drugs & chronic glaucoma	1	1	1	1
Antimuscarinic drugs & chronic constipation	7	7		
Antimuscarinic drugs & urinary outflow problems	7	7	1	1
α-blockers in males & frequent incontinence	2	2		
α-blockers & long term urinary catheter in situ				
Falls				
Benzodiazepines	94	56	107	73
Neuroleptic drugs	57	52	55	45
1st generation antihistamines	7	4	26	13
Long term opiates	31	31	16	16
Analgesics				
Use of powerful opiate as 1st line therapy for mild-moderate pain	1	1	1	1
Long term opiates in those with dementia	*10*	*10*		
Duplicate class	85	23	50	9
Total PIMs	**568**	**429**	**478**	**356**

Key: COPD: Chronic Obstructive Pulmonary Disease, CCBs= Calcium Channel Blockers, PPI: Proton Pump Inhibitor, PUD: Peptic Ulcer Disease, TCA: Tricyclic Antidepressant, OA: Osteoarthritis, NSAID: Non Steroidal Anti-inflammatory.

4.13 Variables associated with PIP in older residents

In the RoI dataset a significant correlation was found between the number of medicines prescribed and the occurrence of PIP identified using Beers' criteria (rs= 0.372, p<0.01) and STOPP (rs=0.356, p<0.01) using Spearman's rho correlation test. There was also a significant correlation between being on more than five medicines (internationally accepted standard of polypharmacy) and the occurrence of PIP identified by the STOPP (rs= 0.135, p<0.01) criteria but not for the Beers' criteria. A negative correlation between age and CCI score and the occurrence of PIP using Beers' criteria and STOPP but this was found to be statistically non-significant..

Table 16. Demographic variables and the occurrence of PIP using Beers' criteria, STOPP in the RoI dataset

Republic of Ireland Dataset	Age	Female Gender	No. of medicines prescribed	CCI score	>5 meds	≥80 years
PIP & STOPP	rs=-0.023 p=0.682	rs=-0.071 p=0.207	rs=0.356 p<0.01	rs=-0.050 p=0.376	rs=0.135 p<0.05	rs=-0.053 p=0.347
PIP & STOPP ex prn	rs=-0.076 p=0.176	rs=-0.075 p=0.186	rs=0.292 p<0.01	rs=-0.014 p=0.803	rs=0.0100 p=0.078	rs=-0.005 p=0.929
PIP & Beers	rs=-0.013 p=0.814	rs=-0.090 p=0.111	rs=0.372 p<0.01	rs=-0.072 p=0.201	rs=0.052 p=0.358	rs=-0.046 p=0.417
PIP & Beers ex prn	rs=-0.051 p=0.367	rs=-0.062 p=0.276	rs=0.318 p<0.01	rs=-0.074 p=0.193	rs=0.006 p=0.918	rs=-0.006 p=0.919

Key: CCI: Charlsons Comorbidity Index

Similarly in the NI dataset there was a significant correlation found between the number of medicines prescribed and the occurrence of PIP identified using Beers' criteria (rs= 0.376, p<0.01) and STOPP (rs=0.356, p<0.01) using Spearman's rho correlation test. There was also a significant correlation found between being on more than 5 medicines and the occurrence of PIP identified by the Beers' (rs= 0.267, p<0.01) and STOPP (rs= 0.258, p<0.01) criteria. There was also a significant correlation found between being female and the occurrence of PIP identified by the Beers' (rs= 0.131, p<0.05) criteria, but this correlation was not found for PIP identified by the STOPP criteria. Similar to the findings in the RoI dataset there was a negative correlation found between age and CCI score and the identification of PIP by Beers (rs= -0.45, p=0.426) and STOPP (rs= -0.034 p=0.551) but this was found to be statistically non-significant. This negative correlation between PIP identified by the STOPP and Beers criteria could in part be due to the fact that younger elders were being prescribed more medicines (Table 17).

Table 17 Demographic variables and the occurrence of PIP using Beers' criteria, STOPP in the NI dataset

Northern Irish Dataset	Age	Female Gender	No. of medicines prescribed	CCI score	>5 meds	≥80 years
PIP & STOPP	rs= -0.034 p=0.551	rs= -0.011 p=0.207	rs= 0.356 p<0.01	rs= -0.03 p=0.376	rs= -0.258 p<0.01	rs= -0.010 p=0.863
PIP & STOPP ex prn	rs= -0.072 p=0.203	rs= -0.024 p=0.672	rs= 0.245 p<0.01	rs= -0.033 p=0.555	rs= -0.195 p<0.05	rs= -0.053 p=0.352
PIP & Beers	rs= -0.045 p=0.426	rs= 0.131 p<0.05	rs= 0.376 p<0.01	rs= -0.74 p=0.192	rs= 0.267 p<0.01	rs= -0.42 p=0.462
PIP & Beers ex prn	rs=-0.59 p=0.300	rs=-0.05 p=0.927	rs=0.267 p<0.01	rs=-0.033 p=0.554	rs=-0.220 p<0.01	rs=-0.012 p=0.826

Key: CCI: Charlson's Comorbidity Index

In the RoI dataset the number of instances of PIP identified was significantly lower using the Beers' criteria than STOPP (Wilcoxon signed ranks test Z= -6.075; p<0.01) and in the NI dataset the number of instances of PIP identified was significantly lower using the Beers' criteria than STOPP (Wilcoxon signed ranks test Z= -4.135; p<0.01).

4.14   The Net Ingredient Cost of PIP rates calculated per dataset

The monthly net ingredient cost (NIC) for the PIMs identified by Beers in the NI dataset was £1,380.23 (€1,566.56) and when PIMs related to "prn" medicines were removed the NIC calculated was £1,314.58 (€1,492.05). The annual NIC for the PIMs identified by Beers in the NI dataset was £16,562.76 (€18,798.73) and the annual NIC when the PIMs relating to "prn" medicines were excluded was £15,774.96 (€17,904.58). In the RoI dataset the NIC for the PIMs identified by Beers was €2,227.68 (£1,962.71) and when the PIMs relating to "prn" medicines were removed the NIC calculated was €2,160.02 (£1,903.10). The annual NIC for the PIMs identified by Beers in the RoI dataset was €26,732.16 (£23,552.56) and the annual NIC when the PIMs related to "prn" medicines were excluded was €25,920.24 (£22,837.22) (Table 18).

The monthly NIC for the PIMs which were identified by STOPP in the NI dataset was calculated to be £3,953.28 (€4,486.98) and when PIMs relating to "prn" medicines were removed it was £3,237.89 (€3,675.01). T he annual NIC for the PIMs identified by STOPP in the NI dataset was £47,439.41 (€53,843.74) and the annual NIC when the PIMs related to "prn" medicines were excluded was £38854.68 (€44100.06).

In the RoI dataset the NIC for PIMs identified by STOPP was €9,305.84 (£8,198.97) and when PIMs related to "prn" medicines were removed it was €8,644.33 (£7,616.154) per month. The annual NIC for the PIMs identified by STOPP in the RoI dataset was €111,670.08 (£98,387.74) and the annual NIC when the PIMs related to "prn" medicines were excluded was €103,731.96 (£91,393.80) (Table 18).

The overall combined annual total NIC for the entire dataset (RoI and NI combined) for PIMs identified by the Beers' criteria was €45,530.89 (£40,115.32) and when "prn" related PIMs were excluded the total NIC was €43,824.82 (£38,612.18). The overall combined annual total NIC for the entire dataset (n=630) for PIMs identified by STOPP was €165,513.82 (£145,827.16) and when PIMs relating to "prn" medicines were excluded the annual total NIC calculated was €147,832.02 (£130,248.48) (Table 18).

Table 18 The Net Ingredient Cost of PIM calculated per dataset

	NI Dataset	Annual NI NIC	RoI Dataset	Annual RoI NIC	Total Irish Monthly NIC	Total annual Irish NIC
NIC Beers' criteria (€) (£)	1,566.56 1,380.23	18,798.73 16,562.76	2,227.68 1,962.71	26,732.16 23,552.56	3,794.24 3,342.94	45,530.89 40,115.32
NIC Beers' criteria excluding prn medicines (€) (£)	1,492.05 1,314.58	17,904.58 15,774.96	2,160.02 1,903.10	25,920.24 22,837.22	3,652.07 3,217.68	43,824.82 38,612.18
NIC STOPP (€) (£)	4,486.98 3,953.28	53,843.74 47,439.41	9,305.84 8,198.97	111,670.08 98,387.74	13,792.82 12,152.26	165,513.82 145,827.16
NIC STOPP excluding prn medicines (€) (£)	3,675.01 3,237.89	44,100.06 38,854.68	8,644.33 7,616.15	103,731.96 91,393.80	12,319.34 10,854.04	147,832.02 130,248.48

Key: NIC: Net Ingredient Cost
The January 2010 exchange rate of 1.135 was used to calculate the price

5.0   Discussion

Some of the general key findings from this study were:

1. the positive correlations of residents from both datasets being prescribed multiple medicines and the occurrence of PIPs as defined by both the STOPP and the Beers' criteria;
2. a negative correlation between the age of a resident (in both datasets) and their CCI score and the occurrence of PIP as defined by both criteria;
3. a positive correlation in the NI dataset between the female gender and the occurrence of PIPs as defined by the Beers' criteria (not observed in the RoI dataset with either set of criteria nor with the STOPP criteria in the NI dataset).

Key medicines / medication classes implicated as PIMs in both datasets

Inappropriate prescribing of long-acting benzodiazepines in older patients has been highlighted repeatedly in the literature over the last 25 years, in particular given the link with falls and fracture risk and the difficulties with successful withdrawal (*Parr et al.* 2008; Pimlott *et al.* 2003; Wang *et al*. 2001). Despite this, long-acting benzodiazepines continue to be initiated and repeatedly prescribed for older patients in primary and secondary care in Ireland and other countries (de Oliveira Martins *et al.* 2006; de Wilde *et al.* 2007; Rajska-Neumann *et al.* 2007; Ryan *et al.* 2009; van der Hooft *et al.* 2005). These realities suggest that long-acting benzodiazepines should not be initiated in older patients, given their high propensity for psychological and physical dependency (Chutka *et al.* 2004; Lader 1991; Mangoni *et al.* 2004; Turnheim 2003). Despite this, benzodiazepines were the most commonly occurring instances of PIP in both datasets i.e. the breached criteria related to the STOPP criteria H1- "use of benzodiazepines in individuals with a history of falls" (in the RoI n=97 and in the NI dataset n=107). It has been widely documented that the use of benzodiazepines in individuals already predisposed to falls can further contribute to future falls. This occurs primarily due to the CNS sedative effect of this class of medications but may also be due to their muscle relaxing properties, which can lead to weakening of the muscles of the lower back and upper legs, therefore directly affecting a resident's stability. This medication class can often prove quite problematic in older individuals who already exhibit a lower level of stability (Bourin *et al.* 2010; Cumming *et al.* 1998; Landi *et al.* 2005; Pariente *et al.* 2008; Ray *et al.* 2000).

Adverse effects relating to the inappropriate use of long term neuroleptics as hypnotics, as well as their use in individuals suffering from certain underlying conditions i.e. Parkinson's disease has been widely documented in the literature as a significant problem especially in older individuals (Alexopoulos *et al.* 2004; Maixner *et al.* 1999; Ruths *et al.* 2003; Stevenson *et al.* 2010). This class of medications contributed to a total of 177 PIP instances (88 in the RoI dataset and 89 in the NI dataset) as defined by the STOPP criteria.

Neuroleptics, long acting anticholinergic and long term opioids have also been documented throughout the literature as quite problematic and contributing to falls / ADEs. It is widely documented that specific medication classes are associated with an increased risk of falls and/ or related hip fractures (Lawlor *et al.* 2003; *Masud et al.* 2001; Passaro *et al.* 2000; Whooley *et al.* 1999; Woolcott *et al.* 2009). In both datasets a high incidence of PIP relating to these medications was identified (Table

15). In general, medications or medication class which predisposes an already vulnerable patient group to further falls should be avoided whenever possible.

A high incidence of PIP associated with the use of high dose proton pump inhibitors (PPIs) "criteria C4 as per STOPP" was also apparent in both datasets (n=74 in the RoI and n=66 in the NI dataset). It may be argued that long-term, high-dose PPI treatment in older people is relatively harmless in terms of ADEs and this may be true in practice. However, a number of relatively rare but potentially important ADEs have been identified as being associated with this class of medications. Yang *et al.* found that long-term use of PPIs at high doses was associated with an increased risk of hip fracture, due to their interference with calcium absorption and bone resorption (Yang *et al.* 2006). PPIs are also associated with an increased risk of infection with Clostridium difficile (Dial *et al.* 2005). The inappropriate use of long term PPIs is of global concern. In a review conducted by Forgacs *et al.*, the authors stated that 64% of hospital inpatients in Australia, 33% of hospital inpatients in Ireland and 65% of hospital inpatients in the UK, were taking PPIs outside the countries' licensed indication for the medication (Forgacs *et al.* 2008).

Continuation of high-dose PPI treatment without clear indication is expensive and almost always unnecessary. The surge in PPI prescribing in recent years is a cause of major budgetary concern. Annual expenditure on unnecessary PPI treatment is estimated to be £100m within the National Health Service (NHS) in the UK, and £2bn globally (Forgacs *et al.* 2008). In Ireland, annual expenditure on PPIs increased from approximately €8 million in 1995 to €64 million in 2002, accounting for over 10% of the total expenditure on drugs funded by the Irish government in 2002 (McGowan *et al.* 2005). In the current climate of major fiscal pressure on health resources, the overuse of PPIs becomes more relevant in terms of overall drug expenditure by governments globally.

Comparison of the detection rates of PIP between each screening tool
In the RoI dataset the number of instances of PIP identified by the Beers' criteria was found to be significantly lower than with the STOPP criteria (Wilcoxon signed ranks test Z= -6.075; p<0.001) similarly in the NI dataset the Beers' criteria identified a significantly lower number of instances of PIP compared to the STOPP criteria (Wilcoxon signed ranks test Z= -4.135; p<0.01). The superiority of the STOPP criteria in identifying instances of PIP has previously been reported in both primary and secondary care settings (Gallagher *et al.* 2008; Ryan *et al.* 2009). The STOPP and Beers' criteria gave a level of detection which varied considerably. In the RoI dataset, 60.0% of the STOPP (Section 4.11) and 41.2% of the Beers' criteria were breached, whereas in the NI dataset 46.2% of the STOPP and 38.2% of Beers' criteria were breached (Section 4.11). A Mann-Whitney U test demonstrated that there was no statistically significant difference between the PIP incidence as defined by STOPP between the two dataset.

Other recent studies have demonstrated that the STOPP criteria are significantly superior in the detection of ADEs causing hospitalisation versus Beers' criteria (Gallagher *et al.* 2008; Gillespie *et al.* 2010). This suggests that STOPP may be a more relevant PIP detection tool in secondary care setting than Beers' criteria. The findings from this study also demonstrate the superiority of STOPP over Beers in the identification of potential PIMs in long term care facilities, although the reproducibility

of these findings needs to be tested in other long term care facilities, in the RoI, NI and internationally.

Comparison of the NIC of PIP between each screening tool

Inappropriate prescribing, whilst having medical and social consequences, by inference, also can contribute to significant economic costs. The monthly NIC of medicines identified as potentially inappropriate in the RoI dataset using the STOPP criteria (€9,305.84 (£8,198.97)) was greater than that identified by the Beers' criteria (€2,227.68 (£1,962.71)) (Table 18). Similarly in the NI dataset the NIC of instances of PIP identified by the STOPP criteria (£3,953.28 (€4,486.98) were greater than those identified by the Beers' criteria (£1,380.23 (€1,566.56) (Table 18). These differences in price reported for the instances of PIP in the RoI compared to NI could be attributed to two reasons; one reason for this variation in price may be because nearly half the medications for the residents in NI were prescribed generically (48.5%), with less than a third being prescribed generically in the RoI dataset (28.4%); the majority were prescribed by brand which are generally more expensive than equivalent generics. Another reason for this significant difference in the price could be attributed to the fact that the NIC of the majority of medications in the RoI is significantly more expensive than the equivalent drugs NIC in NI. Some examples of the NIC differences between the two datasets were as follows:

- In NI the NIC of a 28 day supply of lanzoprazole 30mg once daily was £2.79 (€3.17), whereas in the RoI an equivalent supply of the cheapest available generic of lansoprazole "Zomel®" the NIC was €22.05 (£25.03), but for the majority of the patients in the RoI prescribed the proprietary brand "Zoton®" the NIC for a 28 day supply was €38.70 (£34.10).
- In NI the NIC of a 28 day supply of Risperidone 0.5mg was £1.89 (€2.15), whereas in the Republic of Ireland the NIC of an equivalent supply was €8.77 (£7.73).
- In NI the NIC for a 28 day supply of olanzapine "Zyprexa® 2.5mg once daily" was £21.85 (€24.80), but the equivalent NIC of the same medication in the RoI was €47.16 (£41.55).
- In NI the NIC for a 28 day supply of the opioid patch; "Durogesic® 50mcg/hr one every three days" was £96.72 (£109.78), but the equivalent NIC to supply this medicine in the RoI was €156.90 (€138.24).

Using the NIC to define cost means that other variables such as VAT and dispensing fees which can distort the overall price are ignored. Although this NIC itself may vary from country to country, using just one cost, the NIC, allows direct comparison regarding the magnitude of the differences in costs calculated for each screening tool. From an economic perspective, STOPP identified more costly medicines as potentially inappropriate than Beers' criteria.

As STOPP is physiological system based, it is much easier to use than the Beers' criteria. All medicines listed on the STOPP are available in the Republic of Ireland and the UK and all explicit rules of avoidance are supported by peer reviewed evidence and are difficult to dispute. STOPP was easy to use and was time efficient. On average, STOPP criteria were fully deployed within approximately 3 minutes, although there was a short but significant learning curve with STOPP until one was fully familiar with the criteria.

Long term care facilities

The potential for the development of a pharmacist-led medication usage review (MUR) service for patients residing permanently in long term care facilities has not yet been explored in RoI. This study intended to estimate the scale of the overall incidence of PIPs and from this future work could focus on the development of such a MUR service. This study investigated the rate of PIP in residents from nursing homes / long term care facilities in the greater Cork region and Northern Ireland and found that a significant proportion of older residents in both datasets were prescribed at least one instance of PIP (RoI: 54.3% and NI: 56.8% using Beers' criteria (Table 8) and RoI: 73.0% and NI: 67.0% using the STOPP criteria (Table 8)). The rate of PIP reported for patients residing in long term care facilities was considerably high, but is consistent with another study carried out by Ryan et al. in 2009 which reported a STOPP PIP prevalence of 57%, when the "prn" medicines were excluded, of residents in three long term care facilities in the greater Cork Region

In terms of the medication usage of residents in long term care facilities, this study showed that residents in these facilities in both the RoI and NI were commonly prescribed medications for disorders of the CNS, which were prescribed more frequently than medicines for the CVS (Figure 4 and 6). Almost a third of the PIP identified by the STOPP tool in the RoI was due to medicines prescribed for the CNS (32.2%) and over a third of PIP identified by the STOPP tool in the NI dataset were attributable to medications from this class, not counting the CNS medicines involved in the PIP identified for "duplication of therapy" class (Table 8). Several studies have shown that the prescribing of medicines for the CNS in these patients contributes significantly to the medication problems identified for these patients (Alexopoulos *et al.* 2004; Maixner *et al.* 1999; Ruths *et al.* 2003; Stevenson *et al.* 2010).

With respect to the applicability of criteria to these datasets of residents, the STOPP criteria performed favourably over the Beers' criteria in terms of the identification rate of PIMs. In the NI dataset a Wilcoxon signed ranks test demonstrated a significant difference in the number of instances of PIP identified by each tool (z= -4.135; p<0.01; Section 4.11.2). Similarly, a Wilcoxon signed rank test demonstrated a significant difference in the instances of PIP identified by each tool in the RoI dataset (z=-6.075; p<0.01; Section 4.11.2). More of the STOPP criteria were utilised to identify PIMs than the Beers' criteria, reiterating points made previously that many of the Beers' criteria are redundant in the Irish and European setting. While this current study did not investigate the association between the occurrence of PIP and hospitalisation, studies using Beers' criteria in older patients residing in long-term care facilities have previously found significant correlations between PIP and hospitalisation (OR=1.69; p-value<0.01) and death (OR=1.78; p-value<0.01) (Lau *et al.* 2005). Thus, the need to improve prescribing quality in these patients is imperative.

6.0   Conclusion / Summary

In this study, patients from NI and RoI datasets of older residents in long term care facilities were studied. Overall the rates of PIP were found to be similar. Due to the small sample size used in this study it is not possible to generalise these findings to long term care facilities across the entire island of Ireland. A much larger, randomised controlled trial would be required in order to fully quantify the prevalence of PIP. Although residents in each dataset were prescribed similar classes of medicines, variation in the choice of medicines within particular classes existed between datasets. The overall PIP rate identified for the RoI dataset was 54.3% using the Beers' criteria (41.6% excluding "prn" medicines) and 73.0% (66.0% excluding "prn" medicines) using the STOPP criteria, compared to that of an overall PIP rate identified in the NI dataset of 56.8% (48.6% excluding "prn" medicines) using the Beers' criteria and PIP rate of 67.0% (60.0% excluding "prn" medicine) using the STOPP criteria. The total number of medicines prescribed was positively associated with the identification of PIP as defined by both sets of criteria. Prevention of IP in late life is crucial for avoidance of potential ADEs, as well as limiting costs of medication. The routine application of a screening tool like STOPP could offer a reasonably inexpensive and time efficient method of pharmacotherapy optimisation. One interesting finding in both datasets was that advancing age was actually significantly associated with a reduction in the number of medicines prescribed, which contradicts most of the evidence in the published literature. Whether this association would still exist if residents were under 65 or if community dwelling elders had been included in the study is questionable.

Prescribing is both an art and a science, and prescribing in older patients can often prove especially complicated and daunting. Although care plans, guidelines and algorithms exist to somewhat standardise prescribing patterns and practices, these are only intended to complement a physician's clinical knowledge and it is crucial that they are balanced against the expertise and experience of each individual doctor so that the needs and circumstances of each individual resident can always be taken into consideration.

Further research in terms of a randomised controlled trial to measure the impact of these screening tools on patient-specific outcomes is also under investigation.

6.1   Limitations

A major drawback of this study was that the medicines identified as inappropriate according to set criteria were potentially inappropriate and the residents were not actually examined to determine if there was any level of harm evident from the PIM identified.

The PIP rates identified by the criteria may be a conservative estimate, since over the counter (OTC) medicines were not included in the analysis. OTC medicines were excluded because the relevant information was not collected in the Northern Ireland arm of the study; also residents in the nursing home setting receive continual care and very rarely have access to OTC medications. Also a number of issues were raised relating to the interpretation of different diagnosis/conditions between the two datasets. As the two datasets were recorded by a number of different researchers, the detail of information recorded (medical diagnosis, biochemical data) may have

varied between both datasets e.g. a resident has a history of constipation but requires long term laxative therapy, one person could report that this resident suffers from long term constipation, while another may not have recorded this as an ongoing problem because a physician has not diagnosed the resident with chronic constipation. This is also the case for individuals who consistently exhibit a low cognitive function e.g. one person may classify a resident as having dementia whereas another might just say s/he is cognitively impaired. This variation in diagnosis could significantly influence the PIP occurrence rate as a number of the criteria in the STOPP and Beers' CD list of criteria take diagnosis into consideration and therefore this can result in false positive or conversely false negative results.

Although the NIC gives a clear indication of the cost of medicines prescribed, it is not indicative of all costs involved and also it is a conservative estimate as when a medication was prescribed generically, the price calculated was for the cheapest available generic and so the overall NIC costs in theory could have been significantly greater. On the other hand when a medications was prescribed "prn" the price was calculated for a seven day supply and some residents might not have received seven days of the medication in any given month or conversely some residents could receive more than a seven day supply in the month, although this was somewhat counter balanced by the fact that the NIC relating to the PIP was quoted for both the total number of instances of PIP including and excluding "prn" medicines. A much more robust trial is necessary to determine the economic and tangible clinical benefits in terms of reduction of ADEs (e.g. falls), cost, hospitalisation and mortality from routine screening of medicines using the STOPP tool.

Further work

This work has highlighted a number of areas of prescribing concern, for example, the long term use of both benzodiazepines and hypnotics, in older residents residing in long term care facilities. Each of these individual areas should be further investigated to determine the underlying reason(s) for the prescribing concerns in these areas and strategic methods of addressing and preventing further issues should be developed on a national level.

As with other screening tools identified in the literature, STOPP criteria are in need of continued updating and revision. This update of the STOPP criteria is already under way and we are looking at the possibility of incorporating a severity level with regards to the instance of IP. In addition, each prescribing indicator should be supported by an evidence based recommendation to advise clinicians on appropriate alternatives to the identified PIM. Any alterations made to the current existing screening tools should be validated by the Delphi validation method, in accordance with the methods used for the initial version.

Funding

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Appendix 1

Our Ref: ECM 4 (jj) 08/12/09

4th November 2009

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
Cavanagh Pharmacy Buidling
University College Cork
Cork

Re: Inappropriate prescribing in the elderly, a review of nursing home prescriptions.

Dear Dr Byrne

Expedited approval is granted to carry out the above study in:

The following documents were approved:

> ➤ Application Form
> ➤ Data Collection Form.

Waiver of consent is granted.

We note that the co-investigators involved in this study will be:

> ➤ Mr David O'Sullivan, Dr Denis O'Mahony and Professor Carmel Hughes.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Ollscoil na hÉireann, Corcaigh - National University of Ireland, Cork.

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Our Ref: ECM 3 (III) 11/05/10

15th April 2010

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
Cavanagh Pharmacy Buidling
University College Cork
Cork

Re: Inappropriate prescribing in the elderly, a review of nursing home prescriptions.

Dear Dr Byrne

The Chairman approved the following amendment application:

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Appendix 2

Our Ref: ECM 3 (e) 07/09/10

30th July 2010

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
School of Pharmacy
Cavanagh Pharmacy Buidling
University College Cork
Cork

Re: Inappropriate prescribing in the elderly, a review of nursing home prescriptions.

Dear Dr Byrne

The Chairman approved the following amendment application:

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Appendix 3

ATC Codes

A   Alimentary tract and metabolism

B   Blood and blood forming organs

C   Cardiovascular System

D   Dermatologicals

G   Genito urinary system and sex hormones

H   Systemic hormonal preparations, excluding sex hormones and insulins

J   Anti-infectives for systemic use

L   Anti-neoplastic and immunomudulating agents

M   Musculo-skeletal system

N   Nervous System

P   Anti-parasitic products, insecticides and repellents

R   Respiratory system

S   Sensory organs

V   Various

Appendix 4

Charlson's Comorbidity Index

Assigned Weights for diseases	Conditions
1	Myocardial Infarction Congestive Heart Failure Peripheral Vascular Disease Cerebrovascular Disease Dementia Chronic Pulmonary Disease Connective Tissue Disease Ulcer Disease Mild Liver Disease Diabetes
2	Hemiplegia Moderate to Severe Renal Disease Diabetes with End Organ Damage Any Tumour Leukemia Lymphoma
3	Moderate or Severe Liver Disease
6	Metastatic Solid Tumour AIDS

Appendix 5

Beers' criteria considering diagnosis

Considering diagnosis	
Diagnosis	**Drug**
Heart failure	Disopyramide and high sodium content drugs
Hypertension	Phenylpropanolamine hydrochloride, pseudoephedrine, diet pills and amphetamines
Gastric of duodenal ulcers	NSAIDs and aspirin
Seizures or epilepsy	Clozapine, chlorpromazine, thioridazine and thiothixene
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipryidamole, ticlodipine and clopidogrel
Bladder outflow obstruction	Anticholinergics and antihistamines, GI antispasmodic drugs, muscle relaxants, oxybutynin, flavoxate, anticholinergics, antidepressants, decongestants and tolteridine.
Stress incontinence	α-blockers, anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride) and long-acting benzodiazepines.
Arrhythmias	Tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride)
Insomnia	Decongestants, theophylline, methylphenidate, MAOI's and amphetamines
Parkinson disease	Metoclopramide, conventional antipsychotics and tacrine
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, muscle relaxants and CNS stimulants: dextroamphetamine, methylphenidate, methamphetamine and pemolin.
Depression	Long-term benzodiazepine use. Sympatholytic agents: methyldopa, reserpine and guanethidine.
Anorexia and malnutrition	CNS stimulants: dextroamphetamine, methylphenidate, methamphetamine, pemolin and fluoxetine
Syncope or falls	Short to intermediate acting benzodiazepine and tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride)
SIADH/hyponatraemia	SSRIs: fluoxetine, citalopram, fluvoxamine, paroxetine and sertraline
Seizure disorder	Bupropion
Obesity	Olanzapine
COPD	Long-acting benzodiazepines: chlordiazepoxide, chlordiazepoxide- amitriptyline, clidinium-chlordiazepoxide, diazepam, quazepam, halazepam and chlorazepate. ß-blockers: propranolol.
Constipation	Calcium channel blockers, anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride and amitriptyline hydrochloride)

Beers' criteria independent of diagnosis

Drug	Drug
Propoxyphene and combination products	Diphenhydramine
Indomethacin	Ergot mesyloids and cyclandelate
Pentazocine	Ferrous sulphate >325mg
Trimethobenzamide	All barbiturates (except Phenobarbital) except when used to control seizures
Muscle relaxants and antispasmodics: methocarbamol, carisprodol, oxybutynin, chloroxazone, metaxalone and cyclobenzaprine (do not consider extended release oxybutynin)	Long-term use of full dosage, longer half-life, non-COX-selective NSAIDs: naproxen, oxaprozin and piroxicam.
Flurazepam	Ticlopidine
Amitriptyline, chlordiazepoxide-amitriptyline and perphenazine-amitriptyline	Ketorolac
Doxepin	Amphetamines and anorexic agents
Mepobramate	Meperidine
Doses of short acting benzodiazepines: doses greater than lorazepam 3mg; oxazepam 60mg; alprazolam 2mg; temazepam 15mg; triazolam 0.25mg.	Daily fluoxetine
Chlordiazepoxide, chlordiazepoxide-amitriptyline, clidinium-chlordiazepoxide, diazepam, quazepam, halazepam and chlorazepate	Long-term use of stimulant laxatives: bisacodyl, cascara sagrada and neoloid except in the presence of opiate analgesic use
Long-acting benzodiazepines	Amiodarone
Disopyramide	Orphenadrine
Digoxin (should not exceed 0.125mg daily, except when treating atrial arrhythmias	Guanethidine
Short-acting dipyridamole. Do not consider the long-acting dipyridamole except in patients with artificial heart valves	Guanadrel
Methyldopa and methyldopa-hydrochlorothiazide	Cyclandelate
Reserpine at doses >0.25mg	Isoxsurpine
Chlorpropramide	Nitrofurantoin
Gastrointestinal antispasmodic drugs:dicyclomide, hyoscyamine, propantheline, belladonna alkoloids and clinidium-chlordiazepoxide	Doxazosin
Anticholinergics and anthistamines: Chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine, tripelennamine and dexchlorpheniramine	Methyltestosterone
Thioridazine	Mesoridazine

Appendix 6

STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age.

A. Cardiovascular System

1. Digoxin at a long-term dose > 125µg/day with impaired renal function* *(increased risk of toxicity)*.

2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure *(no evidence of efficacy, compression hosiery usually more appropriate)*.

3. Loop diuretic as first-line monotherapy for hypertension *(safer, more effective alternatives available)*.

4. Thiazide diuretic with a history of gout *(may exacerbate gout)*.

5. Non cardioselective Beta-blocker with Chronic Obstructive Pulmonary Disease (COPD) *(risk of increased bronchospasm)*.

6. Beta-blocker in combination with verapamil *(risk of symptomatic heart block)*.

7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure *(may worsen heart failure)*.

8. Calcium channel blockers with chronic constipation *(may exacerbate constipation)*.

9. Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or proton pump inhibitor *(high risk of gastrointestinal bleeding)*.

10. Dipyridamole as monotherapy for cardiovascular secondary prevention *(no evidence for efficacy)*

11. Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or Proton Pump Inhibitor *(risk of bleeding)*.

12. Aspirin at dose > 150mg day *(increased bleeding risk, no evidence for increased efficacy)*.

13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event *(not indicated)*.

14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease *(not indicated)*.

15. Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration *(no proven added benefit)*.

16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration *(no proven benefit)*.

17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder *(high risk of bleeding)*.

∗ Serum Creatinine > 150 µmol/L, or estimated GFR <50ml/min.

B. Central Nervous System and Psychotropic Drugs.

1. Tricyclic antidepressants (TCA's) with dementia *(risk of worsening cognitive impairment)*.

2. TCA's with glaucoma *(likely to exacerbate glaucoma)*.

3. TCA's with cardiac conductive abnormalities *(pro-arrhythmic effects)*.

4. TCA's with constipation *(likely to worsen constipation)*.

5. TCA's with an opiate or calcium channel blocker *(risk of severe constipation)*.

6. TCA's with prostatism or prior history of urinary retention *(risk of urinary retention)*.

7. Long-term (i.e. > 1 month), long-acting benzodiazepines e.g. chlordiazepoxide, fluazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites e.g. diazepam *(risk of prolonged sedation, confusion, impaired balance, falls)*.

8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics *(risk of confusion, hypotension, extra-pyramidal side effects, falls)*.

9. Long-term neuroleptics (> 1 month) in those with parkinsonism *(likely to worsen extra-pyramidal symptoms)*

10. Phenothiazines in patients with epilepsy *(may lower seizure threshold)*.

11. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications *(risk of anticholinergic toxicity)*.

12. Selective serotonin re-uptake inhibitors (SSRI's) with a history of clinically significant hyponatraemia *(non-iatrogenic hyponatraemia <130mmol/l within the previous 2 months)*.

13. Prolonged use (> 1 week) of first generation antihistamines i.e. diphenydramine, chlorpheniramine, cyclizine, promethazine *(risk of sedation and anti-cholinergic side effects)*.

C. <u>Gastrointestinal System</u>

1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause *(risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognised gastroenteritis)*.

2. Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity *(risk of exacerbation or protraction of infection)*

3. Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism *(risk of exacerbating Parkinsonism)*.

4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks *(dose reduction or earlier discontinuation indicated)*.

5. Anticholinergic antispasmodic drugs with chronic constipation *(risk of exacerbation of constipation)*.

D. <u>Respiratory System.</u>

1. Theophylline as monotherapy for COPD. *(safer, more effective alternative; risk of adverse effects due to narrow therapeutic index)*

2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD *(unnecessary exposure to long-term side-effects of systemic steroids)*.

3. Nebulised ipratropium with glaucoma *(may exacerbate glaucoma)*.

E. <u>Musculoskeletal System</u>

1. Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H2 receptor antagonist, PPI or misoprostol *(risk of peptic ulcer relapse)*.

2. NSAID with moderate-severe hypertension *(risk of exacerbation of hypertension)*. 3. NSAID with heart failure *(risk of exacerbation of heart failure)*.

4. Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthtitis *(simple analgesics preferable and usually as effective for pain relief)*

5. Warfarin and NSAID together *(risk of gastrointestinal bleeding)*.

6. NSAID with chronic renal failure[*] *(risk of deterioration in renal function)*.

7. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis or osterarthritis *(risk of major systemic corticosteroid side-effects)*.

8. Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol *(allopurinol first choice prophylactic drug in gout)*

∗ Serum Creatinine > 150 µmol/L, or estimated GFR 20-50ml/min.

F. <u>Urogenital System</u>

1. Bladder antimuscarinic drugs with dementia *(risk of increased confusion, agitation)*.

2. Antimuscarinic drugs with chronic glaucoma *(risk of acute exacerbation of glaucoma)*.

3. Antimuscarinic drugs with chronic constipation *(risk of exacerbation of constipation)*.

4. Antimuscarinic drugs with chronic prostatism *(risk of urinary retention)*.

5. Alpha-blockers in males with frequent incontinence i.e. one or more episodes of incontinence daily *(risk of urinary frequency and worsening of incontinence)*.

6. Alpha-blockers with long-term urinary catheter *in situ* i.e. more than 2 months *(drug not indicated)*.

G. <u>Endocrine System</u>

1. Glibenclamide or chlorpropamide with type 2 diabetes mellitus *(risk of prolonged hypoglycaemia)*.

2. Beta-blockers in those with diabetes mellitus and frequent hypoglycaemic episodes i.e. ≥ 1 episode per month *(risk of masking hypoglycaemic symptoms)*.

3. Oestrogens with a history of breast cancer or venous thromboembolism *(increased risk of recurrence)*

4. Oestrogens without progestogen in patients with intact uterus *(risk of endometrial cancer)*.

H. <u>Drugs that adversely affect fallers.</u>

1. Benzodiazepines *(sedative, may cause reduced sensorium, impair balance)*.

2. Neuroleptic drugs *(may cause gait dyspraxia, Parkinsonism)*.

3. First generation antihistamines *(sedative, may impair sensorium)*.

4. Vasodilator drugs with persistent postural hypotension i.e. recurrent > 20mmHg drop in systolic blood pressure *(risk of syncope, falls)*.5. Long-term opiates in those with recurrent falls *(risk of drowsiness, postural hypotension, vertigo)*.

I. <u>Analgesic Drugs</u>

1. Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain *(WHO analgesic ladder not observed)*.

2. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives *(risk of severe constipation)*.

3. Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome *(risk of exacerbation of cognitive impairment)*.

J. <u>Duplicate Drug Classes</u>

Any duplicate drug class prescription e.g. two concurrent opiates, NSAID's, SSRI's, loop diuretics, ACE inhibitors *(optimisation of monotherapy within a single drug class should be observed prior to considering a new class of drug)*.

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