**Supplemental Table 1.** Numbers of medication by class prescribed to hospitalised Calgary seniors 2013-2021.

|  |  |
| --- | --- |
| **Medication Class** | **Count** |
| **Statin** | 2706992 |
| **PPI** | 2477437 |
| **Calciumblocker** | 2343022 |
| **Betablocker** | 2120849 |
| **Appropriatebetablocker\*** | 1866600 |
| **Aceinhibitor** | 1786653 |
| **Antiplatelet** | 1724720 |
| **NSAID** | 1661178 |
| **Thyroxine** | 1537833 |
| **ARB** | 1363172 |
| **Aspirin** | 1317398 |
| **Opioid** | 1263059 |
| **Acetaminophen** | 1194105 |
| **SSRI** | 1076966 |
| **Loopdiuretic** | 996801 |
| **Metformin** | 962475 |
| **Antidepressantmore** | 915163 |
| **Hypnoticz** | 791259 |
| **A1blocker** | 727397 |
| **Anticholmusc** | 692128 |
| **Corticosystemic** | 678234 |
| **Neuroleptic** | 677408 |
| **Vitkantagonist** | 661224 |
| **Beta2agonist** | 582813 |
| **Laxative** | 574443 |
| **SNRI** | 563657 |
| **Hypocalcaemia** | 562393 |
| **Benzodiazepine** | 529618 |
| **Bisphosphonate** | 522139 |

**Supplemental Table 2.** First admission. Gender, age, comorbidities, numbers of medications, PIMs, PPOs, Charlson Index and correlations with readmission or mortality within 6 months of discharge (data for 129443 admissions).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | |
| **Unadjusted ORs and 95%CIs** | | | | | | |
|  | OR | 95%CI | p | OR | 95%CI | p |
| Gender | 1.17 | 1.14-1.20 | <.001 | 1.07 | 1.03-1.11 | <.001 |
| Age at admission | 1.01 | 1.01-1.02 | <.001 | 1.07 | 1.07-1.07 | <.001 |
| Number of comorbidities | 1.06 | 1.05-1.06 | <.001 | 1.21 | 1.20-1.21 | <.001 |
| Post admission Rx number | 1.13 | 1.12-1.13 | <.001 | 1.07 | 1.06-1.07 | <.001 |
| Total STOPP PIMs | 1.17 | 1.16-1.17 | <.001 | 1.04 | 1.03-1.05 | <.001 |
| START Omissions (PPOs) not corrected | 1.51 | 1.47-1.55 | <.001 | 2.47 | 2.57-2.56 | <.001 |
| START Omissions (PPOs) correctly prescribed | 1.43 | 1.39-1.47 | <.001 | 1.03 | 0.99-1.07 | .109 |
| AGS Beers PIMs | 1.12 | 1.11-1.12 | <.001 | 1.11 | 1.11-1.12 | <.001 |
| Charlson Index | 1.12 | 1.12-1.13 | <.001 | 1.46 | 1.45-1.47 | <.001 |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | |
|  | OR | 95%CI | p | OR | 95%CI | p |
| Post admission Rx number | 1.12 | 1.12-1.12 | <.001 | 1.04 | 1.04-1.05 | <.001 |
| Total STOPP PIMs | 1.16 | 1.15-1.16 | <.001 | 0.99 | 0.96-1.00 | <.001 |
| START PPOs not prescribed | 1.39 | 1.35-1.42 | <.001 | 1.56 | 1.50-1.63 | <.001 |
| START PPOS correctly prescribed | 1.26 | 1.23-1.30 | <.001 | 0.51 | 0.49-0.53 | <.001 |
| AGS Beers | 1.11 | 1.11-1.11 | <.001 | 1.08 | 1.07-1.08 | <.001 |

**Supplemental Table 3.** Second admission. Numbers of medications, PIMs, PPOs, and correlations with readmission or mortality within 6 months of discharge (data for 64441 admissions).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | |
|  | OR | 95%CI | p | OR | 95%CI | p |
| Post admission Rx number | 1.11 | 1.11-1.12 | <.001 | 1.01 | 1.1-1.02 | <.001 |
| Total STOPP PIMs | 1.15 | 1.14-1.15 | <.001 | 0.98 | 0.98-0.99 | <.001 |
| START PPOs not corrected | 1.41 | 1.36-1.46 | <.001 | 1.44 | 1.37-1.51 | <.001 |
| START PPOS correctly prescribed | 1.36 | 1.31-1.41 | <.001 | 0.52 | 0.50-0.55 | <.001 |
| AGS Beers | 1.10 | 1.10-1.11 | <.001 | 1.07 | 1.06-1.07 | <.001 |

**Supplemental Table 4.** Third admission. Numbers of medications, PIMs, PPOs, and correlations with readmission or mortality within 6 months of discharge (data for 35206 admissions).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | |
| Post admission Rx number | 1.10 | 1.09-1.10 | <.001 | 1.00 | 0.99-1.01 | <.667 |
| Total STOPP PIMs | 1.14 | 1.13-1.15 | <.001 | 0.98 | 0.97-1.00 | <.004 |
| START PPOs not corrected | 1.41 | 1.35-1.48 | <.001 | 1.33 | 1.25-1.41 | <.001 |
| START PPOS correctly prescribed | 1.42 | 1.36-1.49 | <.001 | 1.04 | 1.04-1.04 | <.001 |
| AGS Beers | 1.09 | 1.08-1.10 | <.001 | 1.06 | 1.05-1.06 | <.001 |

**Supplemental Table 5.** Fourth admission. Numbers of medications, PIMs, PPOs, Charlson Index and correlations with readmission or mortality within 6 months of discharge (data for 20354 admissions).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | |
|  | OR | 95%CI | p | OR | 95%CI | p |
| Post admission Rx number | 1.10 | 1.09-1.10 | <.001 | 0.98 | 0.98-0.99 | <.001 |
| Total STOPP PIMs | 1.15 | 1.14-1.17 | <.001 | 0.96 | 0.95-0.98 | <.001 |
| START PPOs not corrected | 1.35 | 1.28-1.44 | <.001 | 1.30 | 1.21-1.40 | <.001 |
| START PPOS correctly prescribed | 1.50 | 1.41-1.59 | <.001 | 0.56 | 0.52-0.61 | <.001 |
| AGS Beers | 1.09 | 1.08-1.101 | <.001 | 1.04 | 1.03-1.05 | <.001 |

**Supplemental Table 6.** Fifth admission. Number of medications, PIMs, PPOs, Charlson Index and correlations with readmission or mortality within 6 months of discharge (data for 12271 admissions).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | |
|  | OR | 95%CI | p | OR | 95%CI | p |
| Post admission Rx number | 1.08 | 1.07-1.09 | <.001 | 0.97 | 0.96-0.98 | <.001 |
| Total STOPP PIMs | 1.13 | 1.12-1.15 | <.001 | 0.97 | 0.95-0.98 | <.001 |
| START PPOs not corrected | 1.38 | 1.28-1.49 | <.001 | 1.23 | 1.12-1.34 | <.001 |
| START PPOS correctly prescribed | 1.49 | 1.38-1.60 | <.001 | 0.63 | 0.57-0.68 | <.001 |
| AGS Beers | 1.07 | 1.06-1.09 | <.001 | 1.03 | 1.03-1.04 | <.001 |

**Supplemental Table 7.** Sixth admission. Numbers of medications, PIMs, PPOs, Charlson Index and correlations with readmission or mortality within 6 months of discharge (data for 7577 admissions).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | | |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | | |
|  | OR | 95%CI | p | | OR | 95%CI | p |
| Post admission Rx number | 1.08 | 1.07-1.09 | <.001 | | 0.95 | 0.94-0.96 | <.001 |
| Total STOPP PIMs | 1.14 | 1.12-1.16 | <.001 | | 0.97 | 0.95-0.99 | <.001 |
| START PPOs not corrected | 1.47 | 1.34-1.62 | <.001 | | 1.24 | 1.11-1.40 | <.001 |
| START PPOS correctly prescribed | 1.64 | 1.49-1.81 | <.001 | | 0.68 | 0.61-0.76 | <.001 |
| AGS Beers | 1.08 | 1.07-1.09 | 1<.001 | | 1.02 | 1.01-1.04 | <.001 |

**Supplemental Table 8.** Seventh through 39th admissions. Numbers of medications, PIMs, PPOs, Charlson Index and correlations with readmission or mortality within 6 months of discharge (data for 10994 admissions).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Readmission within 6 months** | | | **Mortality within 6 months** | | |
| **ORs and 95%CIs adjusted for age at admission, gender (male) and comorbidities** | | | | | | |
|  | OR | 95%CI | p | OR | 95%CI | p |
| Post admission Rx number | 1.06 | 1.06-1.07 | <.001 | 0.95 | 0.94-0.96 | <.001 |
| Total STOPP PIMs | 1.13 | 1.12-1.15 | <.001 | 0.94 | 0.93-0.96 | <.001 |
| START PPOs not corrected | 1.23 | 1.14-1.34 | <.001 | 1.14 | 1.04-1.26 | <.001 |
| START PPOS correctly prescribed | 1.53 | 1.41-1.65 | <.001 | 0.71 | 0.65-0.78 | <.001 |
| AGS Beers | 1.07 | 1.06-1.08 | <.001 | 1.00 | 0.99-1.01 | <.892 |

**Supplemental Table 9.** Population of Calgary ages 65 to 100+, Canadian Census 2022.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Population of Calgary 2022 Canadian Census** | | | | | | |
| **Counts** | | | | **Rates in total population** | | |
| Age | Total | Male | Female | Total | Male | Female |
| 65-69 | 62120 | 30410 | 31710 | 4.8 | 4.7 | 4.8 |
| 70-74 | 46495 | 22225 | 24270 | 3.6 | 3.4 | 3.7 |
| 75-79 | 28965 | 13485 | 15485 | 2.2 | 2.1 | 2.4 |
| 80-84 | 19405 | 8370 | 11035 | 1.5 | 1.3 | 1.7 |
| 85-89 | 12620 | 4995 | 7625 | 1.0 | 0.8 | 1.2 |
| 90-94 | 6225 | 2115 | 4110 | 0.5 | 0.3 | 0.6 |
| 96-99 | 1375 | 390 | 990 | 0.1 | 0.1 | 0.2 |
| ≥100 | 195 | 45 | 155 | 0.0 | 0.0 | 0.0 |
| Total | 177405 | 82035 | 95375 | 13.6 | 12.6 | 14.5 |

Source: https://www12.statcan.gc.ca/census-recensement/2021/dp-pd/prof/index.cfm?Lang=E.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

|  |  |  |
| --- | --- | --- |
|  | Item No | Recommendation |
| Title and abstract | 1 | (*a*) Admissions of 129,443 persons 65 to 108 years old to the four acute care Calgary hospitals 2014-2021 and correlations of risk factors, “potentially inappropriate medications” and “potential prescribing omissions” with 155,758 readmissions (range 2 to 39 readmissions) and mortality. |
| (*b*) ABSTRACT  The goals of this retrospective cohort study of 129,443 persons 65 to 108 years old admitted to the four Calgary acute care hospitals over nine years (2013-2021) were to ascertain the correlations of “potentially inappropriate medications” (PIMs) and “potential prescribing omissions” (PPOs) and risk factors for readmissions and mortality. Processing and analysis codes were built in Oracle Database 19c (PL/SQL), R and Excel. The percentage dying during their hospital stay rose from 3.03% during the first to 7.2% during the 6th admission. The percentage dying within 6 months of discharge rose from 9.4% after the first to 24.9% after the sixth admission. The relative risk of admission rose from 49.8% after the first to 61.8% after the fifth admission.  The most frequent primary admitting diagnoses were cardiac (34,277), orthopedic procedures (25,610), infections (22,364), pulmonary (15,637), CNS (13,308), renal (8,890), gastro-intestinal (6,505) and 5,897 for partial; excision/destruction of the prostate. Costs 2013-2021 totaled $7,477,391,068 excluding physician fees.  The odds ratios (adjusted for age, gender and comorbidities) for readmission were post admission number of medications (1.16; 1.12-1.12), STOPP PIMs (1.16; 1.15-1.16); AGS Beers PIMs (1.11; 1.11-1.11) and START omissions not corrected with a prescription (1.39 (1.35-1.42). Paradoxically START omissions corrected with a prescription correlated with readmissions (1.26;1.23-.1.30). Possible explanations are that these patients still had a burden of illness related to the prescribed medications (many START medications are cardiac or other illnesses) and the correction had not had enough time to work or the patient had not taken the medications (too costly?)  The odds ratios (adjusted for age, gender and comorbidities) for mortality were post admission number of medications (1.04; 1.04-1.05), STOPP PIMs (0.99; 0.96-1.00); AGS Beers PIMs (1.08; 1.07-1.08) and START omissions not corrected with a prescription (1.56 (1.50-1.63). START omissions corrected with a prescription correlated with a dramatic reduction in mortality (0.51; 0.49-0.53).  The odds ratios for readmissions for the second through the 39th admission were consistently higher if START PPOs were not corrected: second admission (1.41; 1.36-1.46); third admission (1.41;1.35-1.48); fourth admission 1.35;1.28-1.44); fifth admission 1.38; 1.28-1.49); sixth admission (1.47;1.34-1.62) and 7th through 39th admission (1.23; 1.14-1.34).  For all admissions when a prescription was given to correct START PPOs with a prescription the ORs for mortality within six months of discharge were dramatically improved (0.51; 0.49-0.53). This was also true for the second admission (0.52; 0.50-0.55; fourth admission (0.56; 0.52-0.61; fifth admission (0.63; 0.57-0.68); sixth admission (0.68; 0.61-0.76); and 7th through 39th admissions (0.71; 0.65-0.78).  Key activities of the home care team of the family physician, deprescribing pharmacist and home care nurse are to prescribe to correct PPOs and assess the patient’s and carer’s understanding of their illnesses and medications and enhance in major ways their ability and enthusiasm for self-care and participate closely and frequently by frequent reassessments being key resources for more self-care.  A next key step forward is to obtain the genomics of the P450 system for all seniors to ascertain which of their medications are enhancers or inhibitors of specific metabolic enzymes or compete to use the same P450 enzymes to avoid adverse drug events or under- or over-treatment. This is particularly important in light of the increase in medications as readmissions increase demonstrated in this study. The US NIH has invested many millions developing precision medicine with genomically guided prescribing in major hospitals and academic centres. |
| Introduction | | |
| Background/rationale | 2 | Potentially inappropriate medications and potential prescribing omissions are key problems for seniors’ hospital readmissions and mortality |
| Objectives | 3 | 1. To measure in this retrospective database of 129,443 first admissions of Calgary seniors spanning 2013-2021, the relative contributions of risk factors identified in the literature review for mortality and the 155,758 readmissions: (a) demographics (age, sex); (b) medical status (number of illnesses, number of medications, Charlson scores, PIMs, PPOs, corrected PPOs, and higher risk illnesses such as cardiac, pulmonary and cancer).  2. To identify cohorts at highest risk of mortality and readmission.  3. To identify the costs of readmissions and how much of these costs could be freed up for teams of family physicians, pharmacists and home visiting nurses to maintain patients as long as possible in their own homes and avoid readmissions. |
| Methods | | |
| Study design | 4 | The Province of Alberta’s DIMR staff anonymised admission, hospital and discharge records (file DAD) of all individuals ≥ 65 years admitted to the four main acute care hospitals in Calgary with ICD-10 diagnoses and ICC procedure codes in the Province of Alberta DIMR database, and prescribing data in the Patient Information System (PIN). The STOPP/START medications (an 2022 updated list was provided by Professor Denis O’Mahony, personal communication) and the 2019 AGS BEERS criteria were linked to ATC codes. |
| Setting | 5 | Retrospective database of 129,443 first admissions of Calgary seniors spanning 2013-2021 and the 155,758 readmissions |
| Participants | 6 | (*a*) All individuals ≥ 65 years admitted to the four main acute care hospitals in Calgary 2013-2021. Cohort database study, all data entered by hospital personnel. |
| (*b*) **N/A** |
| Variables | 7 | Demographics (age, sex); (b) medical status (number of illnesses, illnesses (Medical Councill of Canada codes), number of medications, Charlson scores, PIMs, PPOs, corrected PPOs, readmissions, mortality. |
| Data sources/ measurement | 8\* | The Province of Alberta’s DIMR staff anonymised admission, hospital and discharge records (file DAD) of all individuals ≥ 65 years admitted to the four main acute care hospitals in Calgary with ICD-10 diagnoses and ICC procedure codes in the Province of Alberta DIMR database, and prescribing data in the Patient Information System (PIN). |
| Bias | 9 | All output data were independently checked by two authors. |
| Study size | 10 | All individuals ≥ 65 years admitted to the four main acute care hospitals in Calgary 2013-2021. No exclusions. |
| Quantitative variables | 11 | The Alberta Health Services DAD and PIN data were combined using patient identifier and admission time windows and any duplicate records in the provided source files were eliminated in the course of processing. |
| Statistical methods | 12 | (*a*) There is no publicly available software for applying STOPP/START or AGS BEERS criteria on electronic medical records. The processing and analysis codes developed in the course of this research project were built using a combination of Oracle Database 19c (PL/SQL), R and Excel and statistical analyses (logistic regressions) were conducted within those databases. |
| (*b*) Patient outcomes were analysed by age, sex, number of medications on admission and discharge, number of comorbidities, Charlson Index, PIMs, PPOs and corrected PPOs. |
| (*c*) Missing data were not replaced because the dataset was anonymised by Alberta Health Services and we had no access to individual patient charts. |
| (*d*) All patients admitted to the four Calgary acute care hospitals were entered in a unified data system. If patients went out of province and their records were not thereafter incorporated into the AHS database we had no way of knowing about any out of province medical events. |
| (*e*) Logistic regressions adjusted raw outcome data for age on admission, sex and number of comorbidities |
| Results | | |
| Participants | 13\* | Retrospective database of 133,738 first admissions of Calgary seniors spanning 2013-2021 and the 161,968 readmissions. No exclusions |
| (b) No non-participation. All patients were entered into the AHS database on admission and discharge. |
| (c) Table 1 shows key data on admission. |
| Descriptive data | 14\* | (a) Patients were all individuals ≥ 65 years admitted to the four main acute care hospitals in Calgary 2013-2021. No exclusions. |
| (b) No missing data for key outcome variables. |
| (c) All admissions from 2013-2021. |
| Outcome data | 15\* | Data for the numbers of admissions are determined by the numbers of three files LAB\_UC-2022, PIN-US\_2022 and DAD\_UC\_2022 with DAD-UC-2022 containing 295,236 admissions. |
| Main results | 16 | (*a*) The odds ratios for readmissions for the second through the 39th admission were consistently higher if START PPOs were not corrected: second admission (1.41; 1.36-1.46); third admission (1.41;1.35-1.48); fourth admission 1.35;1.28-1.44); fifth admission 1.38; 1.28-1.49); sixth admission (1.47;1.34-1.62) and 7th through 39th admission (1.23; 1.14-1.34).  For all admissions when a prescription was given to correct START PPOs with a prescription the ORs for mortality within six months of discharge were dramatically improved (0.51; 0.49-0.53). This was also true for the second admission (0.52; 0.50-0.55; fourth admission (0.56; 0.52-0.61; fifth admission (0.63; 0.57-0.68); sixth admission (0.68; 0.61-0.76); and 7th through 39th admissions (0.71; 0.65-0.78). |
| Other analyses | 17 |  |
| Discussion | | |
| Key results | 18 | Odds ratios were adjusted for age, sex and comorbidities. The odds ratios (adjusted for age, gender and comorbidities) for readmission were post admission number of medications (1.16; 1.12-1.12), STOPP PIMs (1.16; 1.15-1.16); AGS Beers PIMs (1.11; 1.11-1.11) and START omissions not corrected with a prescription (1.39 (1.35-1.42). Paradoxically START omissions corrected with a prescription correlated with readmissions (1.26;1.23-.1.30). Possible explanations are that these patients still had a burden of illness related to the prescribed medications (many START medications are cardiac) or other illnesses) and the correction had not had enough time to work or the patient had not taken the medications (too costly?)  The odds ratios (adjusted for age, gender and comorbidities) for mortality were post admission number of medications (1.04; 1.04-1.05), STOPP PIMs (0.99; 0.96-1.00); AGS Beers PIMs (1.08; 1.07-1.08) and START omissions not corrected with a prescription (1.56 (1.50-1.63). START omissions corrected with a prescription correlated with a dramatic reduction in mortality (0.51; 0.49-0.53). |
| Limitations | 19 | There was a difference of ~10,000 in the numbers of patients in the Alberta health Services files LAB\_UC-2022, PIN-US\_2022 and DAD\_UC\_2022 with DAD-UC-2022 containing 295,236 admissions. This affected only very specialised analyses as when we attempted a LACE analysis for readmissions (which we did not use). |
| Interpretation | 20 | The next step is to use money saved from readmissions to fund activities of the home care team of the family physician, deprescribing pharmacist and home care nurse to prescribe to correct PPOs and assess the patient’s and carer’s understanding of their illnesses and medications and enhance in major ways their ability and enthusiasm for self-care and participate closely and often by frequent reassessments and whether more key resources are needed for more self-care.  A next key step forward is to obtain the genomics of the P450 system for all seniors to ascertain which of their medications are enhancers or inhibitors of specific metabolic enzymes or compete to use the same P450 enzymes to avoid adverse drug events or under- or over-treatment. This is particularly important in light of the increase in medications with each readmission demonstrated in this study. |
| Generalisability | 21 | The study is generalisable to the Calgary population as a whole because the numbers of patients by age group and gender admitted to the four Calgary acute care hospitals are representative of the Calgary population as measured by the 2022 Canadian Census.  The study population is also similar to the five-year age groupings of Alberta, Canada and the US and could be generalised to those jurisdictions with appropriate caution for differences in ethnic composition, access to medical care and prescribed medications. |
| Other information | | |
| Funding | 22 | No funding. |