

# REVISIÓN BIBLIOGRÁFICA **MAYO 2022:** Selección de artículos

## REVISTAS FARMACÉUTICAS

### AJHP American Journal of Health System Pharmacist

#### Effects of a pharmacy-driven medication history program on patient outcomes

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#### **Abstract**

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##### **Purpose**

Obtaining an accurate medication history is a vital component of medication reconciliation upon admission to the hospital. Despite the importance of this task, medication histories are often inaccurate and/or incomplete. We evaluated the association of a pharmacy-driven medication history initiative on clinical outcomes of patients admitted to the general medicine service of an academic medical center.

##### **Methods**

Comparing patients who received a pharmacy-driven medication history to those who did not, a retrospective stabilized inverse probability treatment weighting propensity score analysis was used to estimate the average treatment effect of the intervention on general medical patients. Fifty-two patient baseline characteristics including demographic, operational, and clinical variables were controlled in the propensity score model. Hospital length of stay, 7-day and 30-day unplanned readmissions, and in-hospital mortality were evaluated.

## Results

Among 11,576 eligible general medical patients, 2,234 (19.30%) received a pharmacy-driven medication history and 9,342 (80.70%) patients did not. The estimated average treatment effect of receiving a pharmacy-driven medication history was a shorter length of stay (mean, 5.88 days vs 6.53 days;  $P = 0.0002$ ) and a lower in-hospital mortality rate (2.34% vs 3.72%,  $P = 0.001$ ), after adjustment for differences in patient baseline characteristics. No significant difference was found for 7-day or 30-day all-cause readmission rates.

## Conclusion

Pharmacy-driven medication histories reduced length of stay and in-hospital mortality in patients admitted to the general medical service at an academic medical center but did not change 7-day and 30-day all-cause readmission rates. Further research via a large, multisite randomized controlled trial is needed to confirm our findings.

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## British Journal of Clinical Pharmacology

### Paracetamol dosing in hospital and on discharge for older people who are frail or have low body weight

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#### Abstract

#### Aim

To describe paracetamol dosing and liver function test (LFT) monitoring in older hospital inpatients who are frail or have low body weight.

#### Methods

Retrospective observational study, at a 790-bed metropolitan public health service in Australia. Patients aged  $\geq 70$  years, with body weight  $< 50$ kg or frailty index based on laboratory data (FI-Lab) score  $\geq 0.3$ , who were administered paracetamol during an admission with length-of-stay  $> 72$  hours, were included.

Data were extracted from electronic medical records. Paracetamol doses administered in hospital, and doses prescribed on discharge, were compared against consensus guidelines that recommended  $\leq 60$  mg/kg/day for older people weighing  $< 50$ kg, and  $\leq 3000$ mg/day for frail older people.

## Results

240 admissions (n=229 patients, mean age 84.7 years) were analysed. During 150 (62.5%) admissions, higher than recommended paracetamol doses were prescribed. On 138 (57.5%) occasions, patients were prescribed paracetamol on discharge, and 112/138 (81.2%) doses were higher than recommended. Most discharge prescriptions (97/138, 70.3%) were for regular administration. The median daily dose on discharge for patients <50kg was 83.7mg/kg (IQR 73.6-90.9mg/kg). For frail patients ≥50kg, the median daily discharge dose was 3990mg (IQR 3000-4000mg). LFTs were measured in hospital for 151/200 (75.5%) and 93/166 (56.0%) patients who received paracetamol for >48 hours and >5 days respectively.

## Conclusions

Majority of paracetamol doses prescribed for frail or low-weight older patients in hospital and on discharge were higher than recommended in consensus guidelines. LFTs were not measured for 44% patients who received paracetamol regularly for >5 days. Further studies are needed to explore long-term outcomes of this practice.

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## Does co-prescribing non-steroidal anti-inflammatory drugs and oral anticoagulants increase the risk of major bleeding, stroke and systemic embolism?

[Leonie S. Penner, Sean P. Gavan, Darren M. Ashcroft, Niels Peek, Rachel A. Elliott](#)

### Abstract

#### Aims

To examine the risk of gastro-intestinal (GI) bleeding, major bleeding, stroke and systemic embolism associated with prescribing non-steroidal anti-inflammatory drugs (NSAIDs) to adults receiving oral anticoagulant (OAC) therapy.

#### Methods

We conducted a population-based cohort study in adults receiving OAC therapy using linked primary care (Clinical Practice Research Datalink GOLD) and hospital (Hospital Episodes Statistics) electronic health records.

We used cause-specific Cox regression models with time-dependent NSAID treatment in a propensity score matched population to estimate the increased risk of GI bleeding, stroke, major bleeding, and systemic embolism associated with NSAID use.

## **Results**

The matched cohort contained 3,177 patients with OAC therapy alone and 3,177 with at least one concomitant NSAID prescription. Compared with OAC therapy alone, concomitant prescription of NSAIDs with OACs was associated with increased risk of GI bleeding (hazard ratio [HR] 3.01, 95% confidence interval [CI] 1.63 to 5.55), stroke (HR 2.71, 95% CI 1.48 to 4.96), and major bleeding (HR 2.77, 95% CI 1.84 to 4.19). The association with systemic embolism did not reach statistical significance (HR 3.02, 95% CI 0.82 to 11.07). Sensitivity analyses indicated that the results were robust to changes in exclusion criteria and the choice of potential confounding variables.

## **Conclusions**

When OACs are co-prescribed with NSAIDs, the risk of adverse bleeding events increases and, simultaneously, the protective effect of OACs to prevent strokes reduces. There is a need for interventions that reduce hazardous prescribing of NSAIDs in people receiving OAC therapy.

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## **Drug Safety**

### **Leveraging Machine Learning to Facilitate Individual Case Causality Assessment of Adverse Drug Reactions**

[Yauheniya Cherkas, Joshua Ide & John van Stekelenborg](#)

#### **Introduction**

Causality assessment of individual case safety reports (ICSRs) is an important step in pharmacovigilance case-level review and aims to establish a position on whether a patient's exposure to a drug is causally related to the patient experiencing an untoward adverse event. There are many different approaches for case causality adjudication, including the use of expert opinions and algorithmic frameworks; however, a great deal of variability exists between assessment methods, products, therapeutic classes, individual physicians, change of process and conventions over time, and other factors.

## **Objective**

The objective of this study was to develop a machine learning-based model that can predict the likelihood of a causal association of an observed drug–reaction combination in an ICSR.

## **Methods**

In this study, we used a set of annotated solicited ICSRs (50K cases) from a company post-marketing database. These data were enriched with novel supplementary features from external and internal data sources that aim to capture facets such as temporal plausibility, scientific validity, and confoundedness that have been shown to contribute to causality adjudication. Using these features, we constructed a Bayesian network (BN) model to predict drug–event pair causality assessment. BN topology was driven by an internally developed ICSR causality decision support tool. Performance of the model was evaluated through examination of sensitivity, positive predictive value (PPV), and the area under the receiver operating characteristic curve (AUC) on an independent set of data from a temporally adjacent interval (20K cases). No external validation was performed because of a lack of publicly available ICSRs with causality assessments for drug–event pairs.

## **Results**

The model demonstrated high performance in predicting the causality assessment of drug–event pairs compared with clinical judgment using global introspection (AUC 0.924; 95% confidence interval [CI] 0.922–0.927). The sensitivity of the model was 0.900 (95% CI 0.896–0.904), and the PPV of the model was 0.778 (95% CI 0.773–0.783).

## **Conclusion**

These results show that robust probabilistic modeling of ICSR causality is feasible, and the approach used in the development of the model can serve as a framework for such causality assessments, leading to improvements in safety decision making.

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## Pharmacoepidemiology and Drug Safety

### Use of Prescription Medications With Cardiovascular Adverse Effects Among Older Adults in the United States

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#### **Background**

Many commonly used prescription medications have cardiovascular adverse effects, yet the cumulative risk of cardiovascular events associated with the concurrent use of these medications is unknown. We examined the association between the concurrent use of prescription medications with known risk of a major adverse cardiovascular event (MACE) [“MACE medications”] and the risk of such events among older adults.

#### **Methods**

A multi-center, population-based study from the Atherosclerosis Risk in Communities (ARIC) study of a cohort of 3,669 community-dwelling adults aged 61 to 86 years with no history of cardiovascular disease who reported the use of at least one medication between September 2006 and August 2013 were followed up until August 2015. Exposure defined as time-varying and time-fixed use of 1, 2 or  $\geq 3$  MACE medications with non-MACE medications serving as negative control. Primary outcome was incident MACE defined as coronary artery revascularization, myocardial infarction, fatal coronary heart disease, stroke, cardiac arrest, or death.

#### **Results**

In fully adjusted models, there was an increased risk of MACE associated with use of 1, 2, or  $\geq 3$  MACE medications (1 MACE: hazards ratio [HR], 1.21; 95% confidence interval [CI], 0.94-1.57); 2 MACE: HR 1.89, CI 1.42-2.53;  $\geq 3$  MACE: HR 2.22, CI 1.61-3.07) compared to use of non-MACE medications.

These associations persisted in propensity score-matched analyses and among new users of MACE medications, never users of cardiovascular medications and subgroups of participants with increased risk of MACE. There was no association between the number of non-MACE medications used and MACE.

### **Conclusions and Relevance**

In this community-based cohort of older adults with no prior cardiovascular disease, the use of MACE medications was independently and consistently associated with an increased risk of such events in a dose-response fashion.

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## International Journal of Clinical Pharmacy

### Polypharmacy and potentially inappropriate medications in stroke rehabilitation: prevalence and association with outcomes

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#### **Abstract**

##### **Background**

Evidence is scarce regarding polypharmacy and potentially inappropriate medications (PIMs) in rehabilitation medicine. Aim To investigate the prevalence of polypharmacy and PIMs and their association with outcomes in stroke rehabilitation.

##### **Method**

A retrospective cohort study was conducted with 849 older inpatients post-stroke. Polypharmacy was defined as six or more medications, and PIMs were defined based on Beers criteria 2019.

Study outcomes included functional independence measure (FIM)-motor, FIM-cognitive, energy intake, dysphagia, length of hospital stay, and the rate of home discharge. To consider the effect of pharmacotherapy during rehabilitation, multivariate analyses were used to determine whether the presence of polypharmacy or PIMs at discharge was associated with outcomes.

### **Results**

After enrollment, 361 patients (mean age  $78.3 \pm 7.7$  years; 49.3% male) were analyzed. Polypharmacy was observed in 43.8% and 62.9% of patients, and any PIMs were observed in 64.8% and 65.4% of patients at admission and discharge, respectively. The most frequently prescribed PIMs included antipsychotics, benzodiazepines, and proton pump inhibitors. Polypharmacy was negatively associated with FIM-motor score ( $\beta = -0.062$ ,  $P = 0.049$ ), FIM-cognitive score ( $\beta = -0.076$ ,  $P = 0.014$ ), energy intake ( $\beta = -0.143$ ,  $P = 0.005$ ), and home discharge (OR: 0.458; 95% CI: 0.248, 0.847;  $P = 0.013$ ). PIMs were negatively associated with home discharge (OR: 0.375; 95% CI: 0.195, 0.718;  $P = 0.003$ ).

### **Conclusion**

Polypharmacy and PIMs are commonly found among older patients undergoing stroke rehabilitation. Moreover, polypharmacy was negatively associated with activities of daily living (ADL) but not with PIMs and ADLs, and both were associated with home discharge.

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## REVISTAS GERIÁTRICAS

### Journal of the American Geriatrics Society

#### **Oral anticoagulants and outcomes in adults $\geq 80$ years with atrial fibrillation: A global federated health network analysis**

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#### **Abstract**

##### **Background**

The objective of this study was to determine associations between use of oral anticoagulation (OAC) and stroke and bleeding-related outcomes for older people  $\geq 80$  years with atrial fibrillation (AF), and to determine trends over time in prescribing of OAC for this population.

##### **Methods**

A retrospective cohort study was conducted. People aged  $\geq 80$  years with AF receiving (1) no OAC; (2) warfarin; or (3) a non-vitamin-K antagonist oral anticoagulant (NOAC) between 2011 and 2019 were included. Propensity score matching was used to balance cohorts (no OAC, warfarin or a NOAC) on characteristics including age, sex, ethnicity, and comorbidities. Cox proportional hazard models were used to derive hazard ratios (HRs) and 95% confidence intervals (CIs).

##### **Results**

The proportion of people aged  $\geq 80$  years receiving any OAC increased from 32.4% ( $n = 27,647$ ) in 2011 to 43.6% ( $n = 110,412$ ) in 2019. After propensity score matching,  $n = 169,067$  individuals were included in the cohorts receiving no OAC or a NOAC. Compared to no OAC, participants receiving a NOAC had a lower risk of incident dementia (hazHR 0.68, 95% CI 0.65–0.71), all-cause mortality (HR 0.49, 95% CI 0.48–0.50), first-time ischaemic stroke (HR 0.87, 95% CI 0.83–0.91), and a higher risk of major bleeding (HR 1.08, 95% CI 1.05–1.11). Compared to participants receiving warfarin, participants receiving a NOAC had a lower risk of dementia (HR 0.90, 95% CI: 0.86–0.93), all-cause mortality (HR 0.74, 95% CI: 0.72–0.76), ischaemic stroke (HR 0.86, 95% CI: 0.82–0.90) and major bleeding (HR 0.88, 95% CI: 0.85–0.90). Similar results were observed when only including people with additional bleeding risk factors.

## Conclusions

The proportion of people aged  $\geq 80$  years receiving OAC has increased since the introduction of NOACs, but remains low. Use of a NOAC was associated with improved outcomes compared to warfarin, and compared to no OAC, except for a small but statistically significant higher risk of major bleeding.

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## Geriatrics and Gerontology International

### **Associations of polypharmacy and drugs with sedative or anticholinergic properties with the risk of long-term care needs certification among older adults in Japan: A population-based, nested case-control study**

[Naoaki Kuroda, Masao Iwagami, Shota Hamada, Jun Komiyama, Takahiro Mori, Nanako Tamiya](#)

#### Abstract

##### Aim

To estimate the risk of disability associated with high-risk prescribing, such as polypharmacy and drugs with sedative or anticholinergic properties, using long-term care needs certification as a proxy of incident disability.

##### Methods

A case-control study nested within a cohort of older adults (89% aged  $\geq 65$  years) was carried out between 2014 and 2019 using the combined medical claims and long-term care needs certification database of Tsukuba City, Japan. We identified 2123 cases who received their first long-term care certification, and matched them to 40 295 controls based on age, sex, residential area and observation period ( $\geq 36$  months). The risk of long-term care needs certification associated with high-risk prescribing exposure 7–30 months before the index month was estimated using conditional logistic regression adjusting for baseline comorbidities and health service use.

##### Results

Polypharmacy (5–9 drugs; adjusted odds ratio [aOR] 1.32, 95% confidence interval [95% CI] 1.18–1.47), hyperpolypharmacy ( $\geq 10$  drugs; aOR 1.87, 95% CI 1.57–2.23) and cumulative dose of drugs with sedative or anticholinergic properties (1–364 defined daily dose [DDD]; aOR 1.07, 95% CI 0.97–1.19; 365–729 DDD; aOR 1.25, 95% CI 1.07–1.45;  $\geq 730$  DDD; aOR 1.33, 95% CI 1.19–1.62) had dose-response relationships with long-term care certification risks.

## **Conclusions**

High-risk prescribing was associated with the risk of long-term care needs certification in the general older population. Further studies are warranted to examine whether a decrease in prescribing drugs with sedative or anticholinergic properties could reduce the long-term care burden on society.

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