

# REVISIÓN BIBLIOGRÁFICA **OCTUBRE 2019**: Selección de artículos

## REVISTAS GERIÁTRICAS

### **BMC GERIATRICS**

Impact of training and structured medication review on medication appropriateness and patientrelated outcomes in nursing homes: results from the interventional study InTherAKT

Angelika Mahlknecht, Laura Krisch, Nadja Nestler, Ulrike Bauer, Nina Letz, Daniel Zenz, Jochen Schuler, Laura Fährmann, Georg Hempel, Maria Flamm & Jürgen Osterbrink

#### **Abstract**

#### **Background**

Uncoordinated interprofessional communication in nursing homes increases the risk of polypharmacy and inappropriate medication use. This may lead to augmented frequency of adverse drug events, hospitalizations and mortality. The aims of this study were (1) to improve interprofessional communication and medication safety using a combined intervention and thus, (2) to improve medication appropriateness and health-related outcomes of the included residents.

#### Methods

The single-arm interventional study (2014–2017) was conducted in Muenster, Germany and involved healthcare professionals and residents of nursing homes.

The intervention consisted of systematic education of participating healthcare professionals and of a structured interprofessional medication review which was performed via an online communication platform. The primary endpoint was assessed using the Medication Appropriateness Index MAI. Secondary endpoints were: cognitive performance, delirium, agitation, mobility, number of drugs, number of severe drug-drug interactions and appropriateness of analgesics. Outcomes were measured before, during and after the intervention. Data were analyzed using descriptive and inference-statistical methods.

#### **Results**

Fourteen general practitioners, 11 pharmacists, 9 nursing homes and 120 residents (n = 83 at all testing times) participated. Overall MAI sum-score decreased significantly over time (mean reduction: -7.1, CI95% -11.4--2.8; median = -3.0; dCohen = 0.39), especially in cases with baseline sum-score  $\geq$  24 points (mean reduction: -17.4, CI95% -27.6 - 7.2; median = - 15.0; dCohen = 0.86). MAI sum-score of analgesics also decreased (dCohen = 0.45). Mean number of severe drug-drug interactions rose slightly over time (dCohen = 0.17). The proportion of residents showing agitated behavior diminished from 83.9 to 67.8%. Remaining secondary outcomes were without substantial change.

#### Conclusion

Medication appropriateness increased particularly in residents with high baseline MAI sum-scores. Cognitive decline of participating residents was seemingly decelerated when compared with epidemiologic studies. A controlled trial is required to confirm these effects. Interprofessional interaction was structured and performance of medication reviews was facilitated as the online communication platform provided unlimited and consistent access to all relevant and updated information.

Trial registration DRKS Data Management, ID: DRKS00007900.

Disponible en: <a href="https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-019-1263-3">https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-019-1263-3</a>



## **REVISTAS FARMACÉUTICAS**

## DRUG SAFETY

Comparative Effectiveness and Safety of Direct Oral Anticoagulants in Patients with Atrial Fibrillation: A Systematic Review and Meta-Analysis of Observational Studies

Antonios DourosMadeleine DurandCarla M. DoyleSarah YoonPauline ReynierKristian B. Filion

#### **Abstract**

#### **Background**

There are no head-to-head randomized controlled trials comparing different direct oral anticoagulants (DOACs). Thus, we systematically reviewed and meta-analyzed observational studies assessing the comparative effectiveness and safety of DOACs for stroke prevention in patients with atrial fibrillation (AF).

#### Methods

We systematically searched MEDLINE and EMBASE up to February 2019 for observational studies comparing different DOACs head-to-head in patients with AF. Two independent reviewers identified studies, extracted data, and assessed the risk of bias using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool. Random-effects models were used to meta-analyze data across higher-quality studies.

#### Results

We identified 25 cohort studies including 1,079,565 patients with AF treated with DOACs. Meta-analysis of the 19 studies at moderate risk of bias yielded a similar risk of ischemic stroke for rivaroxaban versus dabigatran (six studies; hazard ratio [HR] 0.93; 95% confidence interval [CI] 0.83–1.04; I2: 0%), apixaban versus dabigatran (five studies; HR 0.94; 95% CI 0.82–1.09; I2: 0%), and apixaban versus rivaroxaban (four studies; HR 1.07; 95% CI 0.93–1.23; I2: 0%). Regarding major bleeding, there was an increased risk for rivaroxaban versus dabigatran (six studies; HR 1.33; 95% CI 1.20–1.47; I2: 22%) and decreased risks for apixaban versus either dabigatran (eight studies; HR 0.71; 95% CI 0.64–0.78; I2: 0%) or rivaroxaban (eight studies; HR 0.56; 95% CI 0.48–0.65; I2: 69%).

#### **Conclusions**

As head-to-head trials comparing different DOACs do not exist, available evidence derives exclusively from observational studies. These data suggest that while dabigatran, rivaroxaban, and apixaban have a similar effect on the risk of ischemic stroke, apixaban may be associated with a decreased risk of major bleeding compared with either dabigatran or rivaroxaban.

Disponible en: https://link.springer.com/article/10.1007%2Fs40264-019-00842-1



## THE ANNALS OF PHARMACOTHERAPY

## Associations Between Potentially Inappropriate Medications and Adverse Health Outcomes in the Elderly: A Systematic Review and Meta-analysis

Xiao Xuan Xing, Chen Zhu, Hua Yu Liang, Ke Wang, Yan Qi Chu, Li Bo Zhao, De Chun Jiang, Yu Qin Wang, Su Ying Yan

#### Abstract

#### **Background**

Adverse drug outcomes in the elderly have led to the development of lists of potentially inappropriate medications (PIMs), such as the Beers criteria, and these PIMs have been studied widely; however, it is still unclear whether PIM use is predictive of adverse outcomes in older people.

#### Objective

To qualitatively examine the associations between exposure to PIMs from the general Beers criteria and the Screening Tool of Older Persons' Prescriptions list and adverse outcomes, such as adverse drug reactions (ADRs)/adverse drug events (ADEs), hospitalization, and mortality.

#### Methods

Specified databases were searched from inception to February 1, 2018. Two reviewers independently selected studies that met the inclusion criteria, assessed study quality, and extracted data. Data were pooled using Stata 12.0. The outcomes were ADRs/ADEs, hospitalization, and mortality.

#### **Results**

A total of 33 studies met the inclusion criteria. The combined analysis revealed a statistically significant association between ADRs/hospitalizations and PIMs (odds ratio [OR] = 1.44, 95% CI = 1.33-1.56; OR = 1.27, 95% CI = 1.20-1.35), but no statistically significant association was found between mortality and PIMs (OR = 1.04; 95% CI = 0.75-1.45). It is interesting to note that the results changed when different continents/criteria were used for the analysis. Compared with the elderly individuals exposed to 1 PIM, the risk of adverse health outcomes was much higher for those who took  $\geq$ 2 PIMs.

#### **Conclusion and Relevance**

We recommend that clinicians avoid prescribing PIMs for older adults whenever feasible. In addition, the observed associations should be generalized to other countries with different PIM criteria with caution.

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## INTERNATIONAL JOURNAL OF CLINICAL PHARMACY

## Development of a trigger tool for the detection of adverse drug events in Chinese geriatric inpatients using the Delphi method

Qiaozhi Hu Zhou Qin Mei Zhan Bin Wu Zhaoyan Chen Ting Xu

#### **Abstract**

#### **Background**

The global trigger tool is a method of retrospective medical record review that identifies possible harm in hospitalized patients using "triggers". Elderly patients with multiple co-morbid illnesses are especially vulnerable to adverse drug events (ADEs) that have high prevalence rates.

#### Objective

The purpose of this study was to develop an appropriate trigger tool to detect ADEs in Chinese geriatric inpatients by combining a literature review with the Delphi method.

#### Setting

Chinese geriatric inpatients.

#### **Methods**

Two steps were used to develop the trigger tool. First, we conducted a comprehensive literature review for existing ADE triggers (adult or elderly) to form the initial triggers for the Delphi process. Second, a group of clinical experts, including physicians, clinical pharmacists and nurses, was established to score candidate triggers for utility according to the usefulness and feasibility of implementing triggers in clinical practice.

#### Main outcome measures

The frequency of the full mark, arithmetic mean and coefficient of variation of each trigger.

#### **Results**

An initial set of 51 triggers was selected by literature review for evaluation. The group of experts was composed of 18 clinical experts: 13 physicians, 4 clinical pharmacists, and 1 nurse. Based on the two-phase Delphi process, 42 triggers in five categories (laboratory index, plasma concentration, antidotes, clinical symptoms and intervention) were retained.

#### Conclusion

The 42-trigger tool was developed to identify ADEs in Chinese geriatric inpatients. A pilot study that tests the list of triggers to identify ADEs in Chinese geriatric inpatients is the next step for establishing a specific trigger tool for Chinese geriatric inpatients.

Disponible en: https://link.springer.com/article/10.1007/s11096-019-00871-x



## **Evaluating the Connect with Pharmacy web-based intervention to reduce hospital readmission for older people**

Fatima R. N. Sabir Justine Tomlinson Barry Strickland-Hodge Heather Smith

#### Abstract

#### **Background**

The patient transition from a hospital to a post-discharge healthcare setting has potential to disrupt continuity of medication management and increase the risk of harm. "Connect with Pharmacy" is a new electronic web-based transfer of care initiative employed by Leeds Teaching Hospitals NHS Trust. This allows the sharing of discharge information between the hospital and a patient's chosen community pharmacy.

#### **Objective**

We investigated whether the timely sharing of discharge information with community pharmacies via "Connect with Pharmacy" reduced hospital readmission rates in older patients.

#### Method

To evaluate intervention efficacy, hospital admission data was retrospectively collected. For primary analysis, admission rates were tracked 6-months prior (baseline) and 6-months post-intervention. Secondary measures included effect on total length of stay if readmitted, emergency department attendance and duration, and impact of polypharmacy.

#### Main outcome measure

The rate of non-elective hospital readmissions, 6-months post-intervention.

#### **Results**

In the sample (n = 627 patients; Mean age = 81 years), emergency readmission rates following the intervention (M = 1.1, 95% CI [0.98, 1.22]) reduced by 16.16% relative to baseline (M = 1.31, 95% CI [1.21, 1.42]) (W = 54,725; p < 0.001). There was no reduction in total length of stay. Subsidiary analysis revealed a post-intervention reduction in number of days spent in hospital lasting more than three days ( $\chi$ 2 = 13.37, df = 1, p < 0.001). There were no statistically reliable differences in the remaining secondary measures.

#### Conclusion

The results showed a reduction in readmissions and potential post-intervention length of stay, indicating there may be further benefits for our older patients' experiences and hospital flow.

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## Using telehealth to enable collaboration of pharmacists and geriatricians in residential medication management reviews

Leila Shafiee Hanjani Nancye M. Peel Christopher R. Freeman Leonard C. Gray

#### **Abstract**

#### **Background**

Practical issues impede optimum collaboration between pharmacists and other clinical specialists in the current Australian residential medication review services which potentially affect efficiency, timeliness and quality of outcomes.

#### **Objective**

This mixed methods study aimed to explore the potential value of an existing telehealth platform to enable collaboration of pharmacists and geriatricians in residential medication reviews.

#### Setting

Long term care facilities in Australia.

#### Method

Twenty vignettes of aged care residents were prepared and independently reviewed by five pharmacists and five geriatricians using a telehealth platform to record their recommendations for medications. The geriatricians were subsequently asked to re-consider their recommendations after being provided with a pharmacist's report.

#### Main outcome measure

The level of agreement between pharmacists and between geriatricians, changes in the mean number of medications after pharmacists' and geriatricians' reviews, number of changes in geriatricians' recommendations after viewing a pharmacist's report, and pharmacists' and geriatricians' feedback.

#### **Results**

Both pharmacists and geriatricians had fair agreement about their recommendations for medications (kappa of 0.30 and 0.31 respectively). The mean number of medications over 20 cases was significantly reduced from a baseline of 14.9 to 13.4 by pharmacists, and to 12.3 by geriatricians after their reviews. There was disagreement between geriatricians and pharmacists on 430/1485 (29%) recommendations on medications; after viewing a pharmacist's report, geriatricians changed their mind in 51 occasions. Geriatricians found the pharmacist report useful in 72% of the cases. The majority of the pharmacists (4/5) were prepared to use the online system routinely.

#### Conclusion

The tested telehealth platform has the potential of being used as a part of routine practice to improve accessibility of the service and to enable synchronous collaboration among healthcare professionals.

Disponible en: https://link.springer.com/article/10.1007/s11096-019-00890-8



### REVISTAS DE MEDICINA GENERAL

## **JAMA**

Association of Treatment With Metformin vs Sulfonylurea With Major Adverse Cardiovascular Events Among Patients With Diabetes and Reduced Kidney Function

Christianne L. Roumie, Jonathan Chipman, Jea Young Min, et al.

#### **Abstract**

**Importance** Before 2016, safety concerns limited metformin use in patients with kidney disease; however, the effectiveness of metformin on clinical outcomes in patients with reduced kidney function remains unknown.

**Objective** To compare major adverse cardiovascular events (MACE) among patients with diabetes and reduced kidney function who continued treatment with metformin or a sulfonylurea.

Design, Setting, and Participants Retrospective cohort study of US veterans receiving care within the national Veterans Health Administration, with data supplemented by linkage to Medicare, Medicaid, and National Death Index data from 2001 through 2016. There were 174 882 persistent new users of metformin and sulfonylureas who reached a reduced kidney function threshold (estimated glomerular filtration rate <60 mL/min/1.73 m2 or creatinine ≥1.4 mg/dL for women or ≥1.5 mg/dL for men). Patients were followed up from reduced kidney function threshold until MACE, treatment change, loss to follow-up, death, or study end (December 2016).

**Exposures** New users of metformin or sulfonylurea monotherapy who continued treatment with their glucose-lowering medication after reaching reduced kidney function.

Main Outcomes and Measures MACE included hospitalization for acute myocardial infarction, stroke, transient ischemic attack, or cardiovascular death. The analyses used propensity score weighting to compare the cause-specific hazard of MACE between treatments and estimate cumulative risk accounting for the competing risks of changing therapy or noncardiovascular death.

Results There were 67 749 metformin and 28 976 sulfonylurea persistent monotherapy users; the weighted cohort included 24 679 metformin and 24 799 sulfonylurea users (median age, 70 years [interquartile range {IQR}, 62.8-77.8]; 48 497 men [98%]; and 40 476 white individuals [82%], with median estimated glomerular filtration rate of 55.8 mL/min/1.73 m2 [IQR, 51.6-58.2] and hemoglobin A1c level of 6.6% [IQR, 6.1%-7.2%] at cohort entry). During follow-up (median, 1.0 year for metformin vs 1.2 years for sulfonylurea), there were 1048 MACE outcomes (23.0 per 1000 person-years) among metformin users and 1394 events (29.2 per 1000 person-years) among sulfonylurea users. The cause-specific adjusted hazard ratio of MACE for metformin was 0.80 (95% CI, 0.75-0.86) compared with sulfonylureas, yielding an adjusted rate difference of 5.8 (95% CI, 4.1-7.3) fewer events per 1000 person-years of metformin use compared with sulfonylurea use.

**Conclusions and Relevance** Among patients with diabetes and reduced kidney function persisting with monotherapy, treatment with metformin, compared with a sulfonylurea, was associated with a lower risk of MACE.

Disponible en: <a href="https://jamanetwork.com/journals/jama/article-abstract/2751397">https://jamanetwork.com/journals/jama/article-abstract/2751397</a>



## **NEW ENGLAND JOURNAL OF MEDICINE**

#### **Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes**

Stefanie Schüpke, Franz-Josef Neumann, Maurizio Menichelli, Katharina Mayer, Isabell Bernlochner, Jochen Wöhrle, Gert Richardt, Christoph LiebetrauBernhard Witzenbichler, David Antoniucci, Ibrahim Akin, Lorenz Bott-Flügel, et al., for the ISAR-REACT 5 Trial Investigators\*

#### **Abstract**

#### **BACKGROUND**

The relative merits of ticagrelor as compared with prasugrel in patients with acute coronary syndromes for whom invasive evaluation is planned are uncertain.

#### **METHODS**

In this multicenter, randomized, open-label trial, we randomly assigned patients who presented with acute coronary syndromes and for whom invasive evaluation was planned to receive either ticagrelor or prasugrel. The primary end point was the composite of death, myocardial infarction, or stroke at 1 year. A major secondary end point (the safety end point) was bleeding.

#### **RESULTS**

A total of 4018 patients underwent randomization. A primary end-point event occurred in 184 of 2012 patients (9.3%) in the ticagrelor group and in 137 of 2006 patients (6.9%) in the prasugrel group (hazard ratio, 1.36; 95% confidence interval [CI], 1.09 to 1.70; P=0.006). The respective incidences of the individual components of the primary end point in the ticagrelor group and the prasugrel group were as follows: death, 4.5% and 3.7%; myocardial infarction, 4.8% and 3.0%; and stroke, 1.1% and 1.0%. Definite or probable stent thrombosis occurred in 1.3% of patients assigned to ticagrelor and 1.0% of patients assigned to prasugrel, and definite stent thrombosis occurred in 1.1% and 0.6%, respectively. Major bleeding (as defined by the Bleeding Academic Research Consortium scale) was observed in 5.4% of patients in the ticagrelor group and in 4.8% of patients in the prasugrel group (hazard ratio, 1.12; 95% CI, 0.83 to 1.51; P=0.46).

#### **CONCLUSIONS**

Among patients who presented with acute coronary syndromes with or without ST-segment elevation, the incidence of death, myocardial infarction, or stroke was significantly lower among those who received prasugrel than among those who received ticagrelor, and the incidence of major bleeding was not significantly different between the two groups. (Funded by the German Center for Cardiovascular Research and Deutsches Herzzentrum München; ISAR-REACT 5 ClinicalTrials.gov number, NCT01944800. opens in new tab.)

Disponible en: https://www.nejm.org/doi/full/10.1056/NEJMoa1908973