

# REVISIÓN BIBLIOGRÁFICA MAYO 2021: Selección de artículos

## **REVISTAS GERIÁTRICAS**

### **BMC Geriatrics**

Neutrophil-lymphocyte ratio as a predictor of delirium in older internal medicine patients: a prospective cohort study

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#### **Abstract**

#### **Backgrounds**

Delirium is a common neuropsychiatric syndrome in older hospitalized patients. Previous studies have suggested that inflammation and oxidative stress contribute to the pathophysiology of delirium. However, it remains unclear whether neutrophil-lymphocyte ratio (NLR), an indicator of systematic inflammation, is associated with delirium. This study aimed to investigate the value of NLR as an independent risk factor for delirium among older hospitalized patients.

#### **Methods**

We conducted a prospective study of 740 hospitalized patients aged ≥ 70 years in the geriatric ward of West China Hospital of Sichuan University. Neutrophil and lymphocyte counts were collected within 24 h after hospital admission. Delirium was assessed on admission and every 48 h thereafter. We used the receiver operating characteristic analysis to assess the ability of the NLR for predicting delirium. The optimal cut-point value of the NLR was determined based on the highest Youden index (sensitivity + specificity − 1). Patients were categorized according to the cut-point value and quartiles of NLR, respectively. We then used logistic regression to identify the unadjusted and adjusted associations between NLR as a categorical variable and delirium.

#### Results

The optimal cut-point value of NLR for predicting delirium was 3.626 (sensitivity: 75.2 %; specificity: 63.4 %; Youden index: 0.386). The incidence of delirium was significantly higher in patients with NLR > 3.626 than NLR  $\leq$  3.626 (24.5 % vs. 5.8 %; P < 0.001). Significantly fewer patients in the first quartile of NLR experienced delirium than in the third (4.3 % vs. 20.0 %; P < 0.001) and fourth quartiles of NLR (4.3 % vs. 24.9 %; P < 0.001). Results from the multivariable logistic regression models showed that NLR was independently associated with delirium.

#### Conclusions



NLR is a simple and practical marker that can predict the development of delirium in older internal medicine patients.

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Cost-utility analysis of a consensus and evidence-based medication review to optimize and potentially reduce psychotropic drug prescription in institutionalized dementia patients

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#### **Abstract**

#### **Background**

Growing evidence shows the effects of psychotropic drugs on the evolution of dementia. Until now, only a few studies have evaluated the cost-effectiveness of psychotropic drugs in institutionalized dementia patients. This study aims to assess the cost-utility of intervention performed in the metropolitan area of Barcelona (Spain) (MN) based on consensus between specialized caregivers involved in the management of dementia patients for optimizing and potentially reducing the prescription of inappropriate psychotropic drugs in this population. This analysis was conducted using the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP) tool.

#### **Methods**

The MAFEIP tool builds up from a variety of surrogate endpoints commonly used across different studies in order to estimate health and economic outcomes in terms of incremental changes in quality adjusted life years (QALYs), as well as health and social care utilization. Cost estimates are based on scientific literature and expert opinion; they are direct costs and include medical visits, hospital care, medical tests and exams and drugs administered, among other concepts. The healthcare costs of patients using the intervention were calculated by means of a medication review that compared patients' drug-related costs before, during and after the use of the intervention conducted in MN between 2012 and 2014. The cost-utility analysis was performed from the perspective of a health care system with a time horizon of 12 months.

#### **Results**

The tool calculated the incremental cost-effectiveness ratio (ICER) of the intervention, revealing it to be dominant, or rather, better (more effective) and cheaper than the current (standard) care. The ICER of the intervention was in the lower right quadrant, making it an intervention that is always accepted even with the lowest given Willingness to Pay (WTP) threshold value (€15,000).

#### **Conclusions**



The results of this study show that the intervention was dominant, or rather, better (more effective) and cheaper than the current (standard) care. This dominant intervention is therefore recommended to interested investors for systematic application.

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## Drugs and Aging

## Antimuscarinic Cascade Across Individual Cholinesterase Inhibitors in Older Adults with Dementia

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#### **Abstract**

#### **Background**

Acetylcholinesterase inhibitors (AChEIs) have been associated with an increased risk of starting antimuscarinic treatment to treat overactive bladder (OAB)—an example of a prescribing cascade. Limited comparative data exist regarding the prescribing cascade of antimuscarinics across individual AChEIs in older adults with dementia.

#### **Objective**

This study examined the association between individual AChEI use and antimuscarinic cascade in older adults with dementia.

#### Methods

We conducted a new user retrospective cohort study from January 2005 to December 2018 using data from the TriNetX electronic medical record database, a federated electronic medical records network in the US. The cohort included patients 65 years or older with a diagnosis of dementia using AChEIs (donepezil, galantamine, or rivastigmine). Individual AChEIs were identified with index dates from 1 January 2006 to 31 June 2018, with a 1-year washout period. The study excluded patients with any antimuscarinic use and OAB diagnosis 1 year before the AChEI index date. The primary outcome of interest was the prescription of antimuscarinics within 6 months of the AChEI index date. A Cox proportional hazard model was used to assess the association between individual incident AChEI use and antimuscarinic prescribing cascade after controlling for several covariates.

#### **Results**

The study included 47,059 older adults with dementia who were incident users of AChEls. Most of these patients were initiated with donepezil (83.1%), followed by rivastigmine (12.3%) and galantamine (4.6%). Overall, 8.16% of the study cohort had incident OAB diagnosis or antimuscarinic prescription. Antimuscarinics were initiated by 1725 (3.7%) older adults with dementia within 6 months of AChEl prescription, and cascade varied widely across individual



agents—donepezil (3.9%), rivastigmine (2.6%), and galantamine (2.9%). Cox proportional hazard analyses revealed that donepezil users had an increased risk of receiving antimuscarinics (adjusted hazard ratio 1.55, 95% confidence interval 1.31–1.83) compared with rivastigmine. The findings were consistent in sensitivity analyses.

#### Conclusion

This study found that donepezil use is more likely to lead to antimuscarinic cascade than rivastigmine. Future studies are needed to determine the potential consequences of this cascade in dementia.

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## Revista Española de Geriatría y Gerontología

#### Anemia y fragilidad en ancianos españoles. Estudio FRADEA

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#### Introduction

The objective was to examine the prevalence of anemia according to the state of frailty and to analyze the relationship between anemia, hemoglobin concentration and frailty in a cohort of Spanish older adults.

#### Material and methods

Cross-sectional substudy of the FRADEA (Frailty and Dependency in Albacete) cohort, a population-based concurrent cohort study conducted in people older than 69 years of Albacete (Spain). Of the 993 participants included in the first wave, 790 were selected with valid data on anemia and frailty. Anemia was defined according to the criteria of the World Health Organization (hemoglobin less than 13 g/dL in men and 12 g/dL in women). Frailty was assessed using the Fried's phenotype. The association between anemia, hemoglobin concentration and frailty was determined by binary logistic regression adjusted for age, sex, educational level, institutionalization, comorbidity, cognitive status, body mass index, polypharmacy, creatinine, glucose and total white blood cell count.

#### Results

The mean age was 79 years. The prevalence of anemia was 19.6%. The prevalence of anemia was significantly higher in frail subjects (29.6%) compared to prefrail (16.6%) and robust ones (6%), p<0.001. The average hemoglobin concentrations were significantly lower in frail (12.7 g/dL), compared to the prefrail (13.5 g/dL) and robust participants (14.4 g/dL), p < 0.001. In the fully adjusted regression model, anemia was associated with frailty (OR 1.95; 95% CI: 1.02-3.73, p<0.05),



and similarly, the average hemoglobin concentrations showed a significant association with frailty (OR 0.79; 95% CI: 0.66-0.96, p < 0.05).

#### Conclusion

Anemia in older adults, defined according to WHO criteria, is independently associated with frailty.

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## Geriatrics and Gerontology International

#### Effect of clinical pharmacists' interventions on dementia treatment

#### adherence and caregivers' knowledge

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#### **Abstract**

#### Aim

Poor adherence with dementia medications is common among patients and caregivers, owing to the absence of perceived effect, polypharmacy, and adverse effects. The aim of this study was to evaluate the effect of clinical pharmacists' interventions on the adherence to dementia treatment and the caregivers' knowledge of dementia.

#### Methods

This study was conducted at a geriatric outpatient clinic of the university hospital between October 2018 and April 2019. The Morisky Green Levine Adherence Scale (MGLS) to patients or caregivers and the Dementia Knowledge Assessment Tool Version Two (DKAT2) to caregivers were applied at the beginning of the study and 4 months later by a clinical pharmacist. After the scales were applied in the first interview, verbal information about the importance of adherence to dementia treatment, and incorrect answers of caregivers in DKAT2 were provided by the clinical pharmacist.

#### **Results**

A total of 94 patients and 91 caregivers were included in the study. High adherence to treatment was determined in 70.2% of the patients in the first interview and in 95.7% in the second interview (P < 0.001). The mean score of DKAT2 was  $15.53 \pm 2.44$  in the first interview, while the median score of DKAT2 in the second interview was  $19.11 \pm 1.25$  (P < 0.001).

#### Conclusion



The intervention of clinical pharmacists significantly increased the adherence to dementia treatment and the caregivers' knowledge of dementia. Close monitoring of dementia patients and caregivers by clinical pharmacists and collaboration with a multidisciplinary team play an important role in dementia care

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## **REVISTAS FARMACÉUTICAS**

## AJHP American Journal of Health System Pharmacist

Impact of clinical decision support therapeutic interchanges on hospital discharge medication omissions and duplications

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#### **Abstract**

#### Disclaimer

In an effort to expedite the publication of articles related to the COVID-19 pandemic, AJHP is posting these manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time.

#### **Purpose**

Automatic therapeutic substitution (ATS) protocols are formulary tools that allow for provider-selected interchange from a nonformulary preadmission medication to a formulary equivalent. Previous studies have demonstrated that the application of clinical decision support (CDS) tools to ATS can decrease ATS errors at admission, but there are limited data describing the impact of CDS on discharge errors. The objective of this study was to describe the impact of CDS-supported interchanges on discharge prescription duplications or omissions.

#### **Methods**

This was a single-center, retrospective cohort study conducted at an academic medical center. Patients admitted between June 2017 and August 2019 were included if they were 18 years or older at admission, underwent an ATS protocol—approved interchange for 1 of the 9 included medication classes, and had a completed discharge medication reconciliation. The primary outcome was difference in incidence of therapeutic duplication or omission at discharge between the periods before and after CDS implementation.



#### **Results**

A total of 737 preimplementation encounters and 733 postimplementation encounters were included. CDS did not significantly decrease the incidence of discharge duplications or omissions (12.1% vs 11.2%; 95% confidence interval [CI], –2.3% to 4.2%) nor the incidence of admission duplication or inappropriate reconciliation (21.4% vs 20.7%; 95% CI, –3.4% to 4.8%) when comparing the pre- and postimplementation periods. Inappropriate reconciliation was the primary cause of discharge medication errors for both groups.

#### Conclusion

CDS implementation was not associated with a decrease in discharge omissions, duplications, or inappropriate reconciliation. Findings highlight the need for thoughtful medication reconciliation at the point of discharge.

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## British Journal of Clinical Pharmacology

Potentially inappropriate prescribing and its associations with healthrelated and system-related outcomes in hospitalised older adults: A systematic review and meta-analysis

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#### **Abstract**

#### Aims

To synthesise associations of potentially inappropriate prescribing (PIP) with health-related and system-related outcomes in inpatient hospital settings.

#### Methods

Six electronic databases were searched: Medline Complete, EMBASE, CINAHL, PyscInfo, IPA and Cochrane library. Studies published between 1 January 1991 and 31 January 2021 investigating associations between PIP and health-related and system-related outcomes of older adults in hospital settings, were included. A random effects model was employed using the generic inverse variance method to pool risk estimates.

#### Results

Overall, 63 studies were included. Pooled risk estimates did not show a significant association with all-cause mortality (adjusted odds ratio [AOR] 1.10, 95% confidence interval [CI] 0.90–1.36; adjusted hazard ratio 1.02, 83% CI 0.90–1.16), and hospital readmission (AOR 1.11, 95% CI 0.76–1.63; adjusted hazard ratio 1.02, 95% CI 0.89–1.18). PIP was associated with 91%, 60% and 26%



increased odds of adverse drug event-related hospital admissions (AOR 1.91, 95% CI 1.21–3.01), functional decline (AOR 1.60, 95% CI 1.28–2.01), and adverse drug reactions and adverse drug events (AOR 1.26, 95% CI 1.11–1.43), respectively. PIP was associated with falls (2/2 studies). The impact of PIP on emergency department visits, length of stay, and health-related quality of life was inconclusive. Economic cost of PIP reported in 3 studies, comprised various cost estimation methods.

#### **Conclusions**

PIP was significantly associated with a range of health-related and system-related outcomes. It is important to optimise older adults' prescriptions to facilitate improved outcomes of care.

Disponible en: <u>https://doi.org/10.1111/bcp.14870</u>

## Farmacia Hospitalaria

Guía de administración de antineoplásicos orales en pacientes con trastornos de la deglución

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#### **Abstract**

#### **Objective:**

To review the available literature on the administration of oral antineoplastic drugs in patients with swallowing disorders and systematize the information obtained.

#### Method:

Between September 2019 and April 2020, two hospital pharmacists drew up a list of the oral antineoplastic drugs available in Spain, which was then distributed to three hospital pharmacists, each of whom carried out a literature search and a review. An analysis was made of the prescribing information and searches were performed in Pubmed, Micromedex, Uptodate, the Cancer Care Ontario website, different pharmaceutical bulletins, feeding tube administration guidelines, and tertiary information sources. Lastly, the pharmaceutical industry was contacted. The group systematized the information obtained, after which a fourth hospital pharmacist and an independent physician reviewed the work carried out.

#### **Results:**

A total of 64 oral antineoplastic drugs were reviewed. Relevant information was obtained for 48 drugs, of which 44 were amenable to administration to these patients (69% of the investigated drugs). A systematization of the information found was carried out. Conclusions:

Despite having found different methods for preparing and administering most of the oral antineoplastic drugs reviewed, the information compiled was rather scarce and with a low level of evidence. Further studies, based on pharmacokinetic and stability studies, are necessary in this



field as there is a sore need for oral liquid pharmaceutical forms or extemporaneous preparations allowing administration of oral antineoplastic drugs to these patients.

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### **REVISTAS MEDICINA GENERAL**

## Atención Primaria

## Calidad de vida relacionada con la salud en pacientes consumidores de benzodiacepinas

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#### **Objective**

To describe the health-related quality of life (HRQoL) in benzodiazepine users and to verify whether there is an association with the characteristics of the treatment, its effectiveness, and the sociodemographic variables.

#### Design

Descriptive cross-sectional study.

#### Location

Family medicine consultations.

#### **Participants**

Four hundred and fifty 2patients over 18 years of age consuming benzodiazepines or similar drugs.

#### Main measurements

HRQoL was assessed using the EuroQol5-D questionnaire. Other variables: symptoms of anxiety or insomnia, sociodemographic variables and characteristics of the treatment.

#### Results

The mean score in health status was 62.80 (95% CI: 60.69-64.86), lower in people without studies (59.27±21.97 SD; P=.004) and lower social category ( $60.02\pm21.27$  SD; P<.001). Regarding the social rate (EQ index), a mean score of 0.6025 (95% CI: 0.5659-0.6391) was obtained, higher in people with higher education ( $0.6577\pm0.3574$  SD; P=.001), plus social category ( $0.7286\pm0.3381$  SD; P<.001) and age less than 65 years ( $0.6603\pm0.3426$  SD; P<.001). The variables that were associated with the



value of the EQ index by means of multiple regression were absence of anxiety/insomnia, belonging to higher social classes, age less than 65 years and less consumption of anxiolytics/hypnotics.

#### **Conclusions**

Patients who use benzodiazepines show, despite treatment, a moderate HRQL, lower than that obtained in the general population or in primary care patients. The situation is more favorable in the youngest, in those who do not present anxiety/insomnia, in those belonging to higher social classes and when the consumption of drugs is lower.

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## BMJ: British Medical Journal

## Treatment timing and the effects of rhythm control strategy in patients with atrial fibrillation: nationwide cohort study

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Abstract

#### **Objective**

To investigate whether the results of a rhythm control strategy differ according to the duration between diagnosis of atrial fibrillation and treatment initiation.

#### Design

Longitudinal observational cohort study.

#### Setting

Population based cohort from the Korean National Health Insurance Service database.

#### **Participants**

22 635 adults with atrial fibrillation and cardiovascular conditions, newly treated with rhythm control (antiarrhythmic drugs or ablation) or rate control strategies between 28 July 2011 and 31 December 2015.

#### Main outcome measure



A composite outcome of death from cardiovascular causes, ischaemic stroke, admission to hospital for heart failure, or acute myocardial infarction.

#### **Results**

Of the study population, 12 200 (53.9%) were male, the median age was 70, and the median follow-up duration was 2.1 years. Among patients with early treatment for atrial fibrillation (initiated within one year since diagnosis), compared with rate control, rhythm control was associated with a lower risk of the primary composite outcome (weighted incidence rate per 100 person years 7.42 in rhythm control v 9.25 in rate control; hazard ratio 0.81, 95% confidence interval 0.71 to 0.93; P=0.002). No difference in the risk of the primary composite outcome was found between rhythm and rate control (weighted incidence rate per 100 person years 8.67 in rhythm control v 8.99 in rate control; 0.97, 0.78 to 1.20; P=0.76) in patients with late treatment for atrial fibrillation (initiated after one year since diagnosis). No significant differences in safety outcomes were found between the rhythm and rate control strategies across different treatment timings. Earlier initiation of treatment was linearly associated with more favourable cardiovascular outcomes for rhythm control compared with rate control.

#### **Conclusions**

Early initiation of rhythm control treatment was associated with a lower risk of adverse cardiovascular outcomes than rate control treatment in patients with recently diagnosed atrial fibrillation. This association was not found in patients who had had atrial fibrillation for more than one year

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