

# REVISIÓN BIBLIOGRÁFICA JUNIO 2020: Selección de artículos

## REVISTAS GERIÁTRICAS

### DRUGS AND AGING

#### **Use of SGLT2 Inhibitors in Older Adults: Scientific Evidence and Practical Aspects.**

Joaquim Silva Custódio Jr, Jarbas Roriz-Filho, Catarina Addobbati Jordão Cavalcanti, Amanda Martins & João Eduardo Nunes Salles

#### **Abstract**

Diabetes mellitus (DM) is an increasingly prevalent condition that has a significant impact on health systems worldwide, particularly in older people. It is estimated that 30% of people aged > 65 years fulfil the diagnostic criteria for DM, with 90% having type 2 DM (T2DM). Generally, specific guidelines for the treatment of T2DM in older people address in a very limited manner the use of more recent therapies, such as sodium–glucose co-transporter-2 inhibitors (SGLT2i), which have important benefits for older people, such as a low risk of hypoglycemia, reduction of cardiovascular and renal risk, and an insulin-independent mechanism, allowing its use in disease of any duration. The SGLT2i class is well-tolerated, though some caution is also suggested, including adjustment of concomitant therapies, such as insulin and antihypertensives, especially loop diuretics. This review discusses the pathophysiological characteristics of the older patient with T2DM and evaluates the main benefits of and cautions for the use of SGLT2i in this population.

Disponibile en: <https://link.springer.com/article/10.1007/s40266-020-00757-y>

#### **Prescribed Doses of CYP2D6-Metabolized Drugs and Hemodynamic Responses in Relation to CYP2D6 Genotype Among Older Patients Exposed to Polypharmacy**

Rita Romskaug, Torgeir Bruun Wyller, Jørund Straand, Hege Kersten & Espen Molden

#### **BACKGROUND/OBJECTIVES**

Many drugs with dose-dependent effects on hemodynamic variables are metabolized by cytochrome P450 2D6 (CYP2D6). The aim of this study was to compare prescribed dosages and hemodynamic responses of such drugs in relation to pharmacogenetic variability in CYP2D6 metabolism among patients aged  $\geq 70$  years exposed to polypharmacy.

## Methods

We included 173 patients with detailed information about drug use. The patients were retrospectively subjected to *CYP2D6* genotyping, which comprised the most common variant alleles encoding reduced, absent, or increased *CYP2D6* metabolism. In order to compare dosages across different *CYP2D6*-metabolized drugs, all prescribed daily doses were harmonized to the 'percent of a daily defined dose' (DDD). The mean harmonized DDD was compared between genotype-predicted normal metabolizers (NMs) and patients with reduced or absent *CYP2D6* enzyme activity, defined as intermediate or poor metabolizers (IMs/PMs). Blood pressure, pulse, and patient proportions with orthostatism and bradycardia were also compared between genotype subgroups.

## Results

The genotype-predicted phenotype subgroups comprised 79 NMs (45.7%), 75 IMs (43.4%), and 16 PMs (9.2%). There were no differences in dosing of *CYP2D6* substrates between NMs and IMs/PMs ( $p = 0.76$ ). A higher proportion of *CYP2D6* IMs/PMs experienced orthostatism ( $p = 0.03$ ), while there were no significant subgroup differences for the other hemodynamic variables.

## Conclusions

In this real-life clinical setting of patients aged  $\geq 70$  years, dosing of *CYP2D6* substrates were not adjusted according to genotype-predicted *CYP2D6* metabolism. The increased occurrence of orthostatism in patients with reduced/absent *CYP2D6* metabolism may indicate that individualized dosing based on genotype has the potential to prevent adverse effects in these vulnerable patients.

Disponible en: <https://link.springer.com/article/10.1007/s40266-020-00763-0>

## GERIATRICS AND GERONTOLOGY INTERNATIONAL

### Effect of renin–angiotensin system on senescence

Masaki Mogi MD, PhD

#### BACKGROUND/OBJECTIVES

The renin–angiotensin system (RAS) plays crucial roles in the control of blood pressure and sodium homeostasis. Moreover, RAS also acts as a key player in cell and organ senescence, mainly by activation of the classical axis of angiotensin (Ang) converting enzyme (ACE)/Ang II/Ang II type 1 receptor via overproduction of reactive oxygen species. Overactivation of the classical RAS axis induces organ dysfunction in the vasculature, brain, kidney and skeletal muscle, resulting in atherosclerosis, stroke, chronic kidney disease and sarcopenia. Moreover, RAS has been shown to regulate lifespan, using gene-modification models. Recently, mice lacking the Ang II type 1 receptor were shown to exhibit an increase in lifespan compared with control mice. Here, the effect of RAS on age-related tissue dysfunction in several organs is reviewed, including not only the classical axis but also protective functions of RAS such as the ACE2/Ang (1–7)/Mas axis.

Disponible en: <https://onlinelibrary.wiley.com/doi/10.1111/ggi.13844>

## INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY

### **New use of psychotropic medication after hospitalization among people with dementia**

Tobias Möllers, Laura Perna, Hannah Stocker, Peter Ihle, Ingrid Schubert, Ben Schöttker, Lutz Frölich, Hermann Brenner

#### **Abstract**

##### **Objective**

Psychotropic medication is commonly used among people with dementia (PWD), but it shows modest efficacy and it has been associated with severe adverse events. Hospitalizations are an opportunity for medication management as well as treatment recommendations for outpatient physicians. The aim of this study was to assess factors associated with new use of psychotropic medication after hospitalization among PWD.

##### **Method**

We conducted a retrospective dynamic cohort study from 2004 to 2015 using claims data from a German health insurance company. PWD were identified by an algorithm that included ICD-10 diagnosis and diagnostic measures. The medication classes included were antidepressants, antipsychotics, anxiolytics or hypnotics/sedatives, and Alzheimer's medication. The assessment period was up to 30 days after discharge from the hospital across four hospitalizations.

##### **Results**

The main predictors for new use of psychotropic medication were similar across medication classes. Neuropsychiatric symptoms (NPS) and the need of care were associated with higher odds of new use of antidepressants, antipsychotics, and anxiolytics or hypnotics/sedatives. A hospital stay due to dementia was an independent predictor for new use across medication classes as well. Delirium increased the odds for new use of antipsychotics and anxiolytics or hypnotics/sedatives.

##### **Conclusions**

Factors associated with new use of psychotropic medication included delirium, NPS, and the need of care in PWD. The findings highlight the need for preventive interventions and non-medical treatment options in regards to delirium and NPS as well as for a more intensive use of screening tools for inappropriate medication use among PWD.

Disponible en: <https://onlinelibrary.wiley.com/doi/10.1002/gps.5282>

**REVISTAS FARMACÉUTICAS**

**British Journal of Clinical Pharmacology**

## One-year efficacy and safety of prasugrel and ticagrelor in patients with acute coronary syndromes: Results from a prospective and multicentre ACHILLES registry.

Juan Miguel Ruiz-Nodar, María Asunción Esteve-Pastor, Jose Miguel Rivera-Caravaca, Miriam Sandín, Teresa Lozano, Nuria Vicente-Ibarra, Esteban Orenes-Piñero, Manuel Jesús Macías, Vicente Pernías, Luna Carrillo, Elena Candela, Andrea Veliz, Antonio Tello-Montoliu, Juan Gabriel Martínez Martínez, Francisco Marín.

### Abstract

#### Objective

Prasugrel and ticagrelor have demonstrated higher efficacy than clopidogrel in their main clinical trials for patients with acute coronary syndrome (ACS). However, the long-term prognosis and different clinical characteristics related to the type of antiplatelet prescription in current clinical practice ACS patients have not been analysed in depth. The objective of this study was to analyse the clinical profile of ACS and the efficacy and safety of novel oral P2Y12 inhibitors in current clinical practice patients discharged after ACS.

#### Methods

We collected data from the ACHILLES registry, and an observational, prospective and multicentre registry of patients discharged after ACS. We analysed baseline characteristics, clinical profile and therapy during ACS admission and compared with the different treatments at discharge. After 1 year of follow-up, ischaemic and major bleeding events were analysed. Multivariate Cox regression analysis and Kaplan Meier curves were also plotted.

#### Results

Of 1717 consecutive patients, 1294 (75.4%) were discharged with a P2Y12 inhibitor without oral anticoagulation. Novel oral P2Y12 inhibitors were indicated in 47%. Patients treated with clopidogrel were elderly ( $69.1 \pm 13.4$  vs  $60.4 \pm 11.5$  years;  $P < .001$ ) and had a higher prevalence of cardiovascular risk factors. GRACE and CRUSADE scores were higher in the clopidogrel than in novel oral P2Y12 inhibitors group ( $P < .001$ ). After 1 year of follow-up, 64 (5.0%/year) patients had a new myocardial infarction, 127 (10.0%/year) had a major adverse cardiovascular event (MACE) and 78 (6.1%/year) died. Patients treated with clopidogrel had a significantly higher annual rate of cardiovascular mortality, MACE and all-cause mortality (all  $P < .001$ ) without differences in major bleeding ( $P = .587$ ) compared with novel oral P2Y12 inhibitors. After multivariate adjustment for the main clinical variables related to adverse prognosis in ACS patients, the discharge with novel oral P2Y12 inhibitors therapy was independently associated with lower risk of all-cause mortality (HR 0.49, 95% CI [0.24-0.98],  $P = .044$ ) and lower risk of MACE (HR 0.64, 95% CI [0.41-0.98],  $P = .044$ ).

#### Conclusions

In this prospective, observational and current clinical practice ACS registry, the use of novel oral P2Y12 inhibitors was associated with a reduction in adverse events compared with clopidogrel in patients with ACS. Novel oral P2Y12 inhibitors prescription at discharge was independently associated with lower all-cause mortality and MACE without differences in bleeding events. However, clopidogrel remained the most common P2Y12 inhibitor employed for ACS, especially in older and high-risk patients.

## Farmacia Hospitalaria.

### Specialized pharmaceutical care in social health centers in the times of COVID-19.

Juan F. Peris-Martí, Patricia Bravo-José , Carmen Sáez-Lleó , Elia Fernández-Villalba

#### **Abstract**

The COVID-19 pandemic is having a devastating effect on the nursing homes for dependent older people. The difficulty of management of this crisis is aggravated by the frailty of the people served and by the specific characteristics of the care area, mainly the fact of not being integrated into the health system. The objective of this work is to describe the pharmaceutical care developed by a hospital pharmacy service established in a nursing home and, from a more global perspective, analyze the strengths and weaknesses found from the various experiences of hospital pharmacy in all Spanish autonomous communities to deal with this pandemic. Specialized pharmaceutical care has provided rigor in the validation and treatments review processes from a comprehensive perspective, maximizing safety and collaborating in the establishment of the therapeutic intensity degree most appropriate to the individual situation, has ensured the availability of all necessary medications, has collaborated in the acquisition and management of personal protective equipment, has been able to adapt the dispensation processes to the internal nursing homes sectorization and has facilitated the coordination between the nursing home and the health system. It is clear that the crisis caused by COVID-19 has put relevance of the need to integrate the social-health level into the health system. And also, the contribution of specialized pharmaceutical care in improving healthcare coverage and coordination with health services has highlighted the urgency of developing the current legislation, prioritizing the establishment of pharmacy services able to provide specialized and specific care for this area, so that it meets healthcare needs and is integrated into the health system.

Disponible en: [https://www.sefh.es/fh/196\\_12especial1111493esp.pdf](https://www.sefh.es/fh/196_12especial1111493esp.pdf)

### Pharmaceutical care in hospitalized patients.

Daniel Sevilla-Sánchez, Montse Tuset-Creus.

#### **Abstract.**

During the pandemic caused by the SARS-CoV-2 virus, pharmacy services have had to adapt their service portfolio, and yet ensure efficient, equitable and quality pharmaceutical care. Given the limited scientific evidence available, most drugs have been used off-label or in the context of clinical trials, which should be the preferred option in order to create new evidence. Among kind different situations we have faced are the increase in workload, the expansion of coverage to new wards and ICUs and shortages, which have caused the use of alternative drugs and even other routes of administration. Given that COVID-19 affects elderly population with greater severity and many of them are polymedicated, great effort have been focused on monitoring interactions, both pharmacokinetic and pharmacodynamic (specially prolongation of the QT interval), monitoring correct concentrations of electrolytes, nutritional support, adaptation of chemotherapy treatment protocols and anticoagulant management, among others. The use of

personal protective equipment added difficulty for nursing work and some measures had been taken to minimize the number of entries into the rooms. Eventually, team's split to guarantee care, the challenge of teleworking, remote validation, telemedicine and telepharmacy for communication between professionals and patients, as well as training in this pandemic situation have been a challenge for our profession. These difficulties have risen up new learning opportunities we hope will be useful to us in the event we have to face similar situations in the future.

Disponible en: [https://www.sefh.es/fh/196\\_08especial0611513esp.pdf](https://www.sefh.es/fh/196_08especial0611513esp.pdf)

## Pharmacotherapy.

### **Effect of Preinjury Oral Anticoagulants on Outcomes Following Traumatic Brain Injury from Falls in Older Adults.**

Jason P. Hecht Zachary J. LaDuke Anne H. Cain-Nielsen Mark R. Hemmila Wendy L. Wahl

#### **Abstract**

#### **Background**

Warfarin has been the oral anticoagulant of choice for the treatment of thromboembolic disease. However, upwards of 50% of all new anticoagulant prescriptions are now for direct oral anticoagulants (DOAC). Despite this, outcome data evaluating preinjury anticoagulants remains scarce following traumatic brain injury (TBI). Our study objective is to determine the effects of preinjury anticoagulation on outcomes in older adults with TBI.

#### **Methods**

Patient data was obtained from 29 level 1 and 2 trauma centers from 2012 to June 30, 2018. Overall, 8312 patients who were aged 65 years or older, suffering a ground level fall, and with an Abbreviated Injury Scale score (AIS)-head of  $\geq 3$  were identified. Patients were excluded if they presented with no signs of life or a traumatic mechanism besides ground level fall. Statistical comparisons were made using multivariable analyses with anticoagulant/antiplatelet use as the independent variable.

#### **Results**

Of the total patients with TBI, 3293 were on antiplatelet agents (AP), 669 on warfarin, 414 on warfarin + AP, 188 on DOACs, 116 on DOAC + AP, and 3632 on no anticoagulant. There were 185 (27.7%) patients on warfarin and 43 (22.9%) on a DOAC with a combined outcome of mortality or hospice as compared to 575 (15.8%) in the no anticoagulant group ( $p < 0.001$ ). After adjusting for patient factors, there was an increased risk of mortality or hospice in the warfarin (OR 1.60; 95% CI 1.27 – 2.01) and DOAC group (OR 1.67; 95% CI 1.07 – 2.59) as compared to no anticoagulant. Warfarin+AP was associated with an increased risk of mortality or hospice (OR 1.61; 95% CI 1.18-2.21) that was not seen with DOAC+AP (OR 0.93; 95% CI 0.46-1.87) as compared to no anticoagulant.

## Conclusions

In older adults with TBI, preinjury treatment with warfarin or DOACs resulted in an increased risk of mortality or hospice whereas preinjury AP therapy did not increase risk. Future studies are needed with larger sample sizes to directly compare TBI outcomes associated with preinjury warfarin versus DOAC use.

Disponible en: <https://accpjournals.onlinelibrary.wiley.com/doi/abs/10.1002/phar.2435>

## Pharmacoepidemiology and Drug Safety

### **Opioid, gabapentinoid, and nonsteroidal anti-inflammatory medication use and the risks of atrial fibrillation and supraventricular ectopy in the Multi-Ethnic Study of Atherosclerosis.**

Barbara N. Harding Kerri L. Wiggins Paul N. Jensen Barbara McKnight Bruce M. Psaty Susan R. Heckbert James S. Floyd

## Abstract

### Purpose

Opioids, gabapentinoids, and nonsteroidal anti-inflammatory drugs (NSAIDs) may have adverse cardiovascular effects. We evaluated whether these medications were associated with incident clinically detected atrial fibrillation (AF) or monitor-detected supraventricular ectopy (SVE), including premature atrial contractions (PACs) and supraventricular tachycardia (SVT).

### Methods

We used data from the Multi-Ethnic Study of Atherosclerosis (MESA), a cohort study that enrolled 6814 Americans without clinically detected cardiovascular disease in 2000 to 2002. At the 2016 to 2018 examination, 1557 individuals received ambulatory electrocardiographic (ECG) monitoring. Longitudinal analyses investigated time-varying medication exposures at the first five exams (through 2011) in relation to incident clinically detected AF through 2015 using Cox proportional hazards regression models. Cross-sectional analyses investigated medication exposures at 2016 to 2018 examination and the risk of monitor-detected SVE using linear regression models.

### Results

The longitudinal cohort included 6652 participants. During 12.4 years of mean follow-up, 982 participants (14.7%) experienced incident clinically detected AF. Use of opioids, gabapentinoids, and NSAIDs were not associated with incident AF. The cross-sectional analysis included 1435 participants with ECG monitoring. Gabapentinoid use was associated with an 84% greater average frequency of PACs/hour (95% CI, 25%-171%) and a 44% greater average number of runs of SVT/day (95% CI, 3%-100%). No associations were found with use of opioids or NSAIDs in cross-sectional analyses.

## Conclusions

In this study, gabapentinoid use was associated with SVE. Given the rapid increase in gabapentinoid use, additional studies are needed to clarify whether these medications cause cardiovascular complications.

Disponible en: <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5036>

## Rivaroxaban was found to be noninferior to warfarin in routine clinical care: A retrospective noninferiority cohort replication study

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### Abstract

#### Purpose

To compare the effectiveness and safety of a drug in daily practice with the outcomes of a target non-inferiority trial by rigorously mimicking in an observational study the trial's design features.

#### Methods

This cohort study was conducted using the British Clinical Practice Research Datalink (CPRD) to emulate the ROCKET AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) trial. Patients with atrial fibrillation who were newly prescribed ( $\geq 12$  months of no use) either rivaroxaban or warfarin from October 2008 to December 2017 were included. Non-inferiority of rivaroxaban to warfarin in the prevention of stroke or systemic embolism was assessed in different analysis populations (intention-to-treat [ITT], per-protocol [PP], and as-treated populations) using a hazard ratio (HR) of 1.46 as the non-inferiority margin. Major bleeding (safety outcome) was also assessed and compared to that of the target trial. All outcomes were analyzed using Cox-proportional hazard analyses.

#### Results

We included 25,473 incident users of rivaroxaban ( $n=4,008$ ) or warfarin ( $n=21,465$ ). Similar to the trial, non-inferiority in the primary outcome was demonstrated in all three analysis populations: HR=1.04 (95%CI 0.84 to 1.30) (ITT), HR=0.98 (95%CI 0.70 to 1.38) (PP), and HR=1.11 (95%CI 0.86 to 1.42) (as-treated). Risk of major bleeding was also similar to the target trial.

#### Conclusion

The results of this study provide supportive evidence to the effectiveness of rivaroxaban and adds knowledge on the usefulness of emulating a non-inferiority trial to assess drug effectiveness.



Disponible en: <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5065>

## **Risk of incident dementia following metformin initiation compared with noninitiation or delay of antidiabetic medication therapy**

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Doug Barthold Sascha Dublin

### **Abstract**

#### **Purpose**

Emerging evidence suggests metformin compared with sulfonylurea is associated with an 8% to 10% lower risk for dementia. Guidelines recommend metformin as initial diabetes treatment, but there is still the question of treatment timing. Thus, the risk of dementia associated with initiating metformin compared with not initiating or delaying treatment was examined.

#### **Methods**

A retrospective cohort study (1996 to 2015) was conducted with electronic health records from Veteran Health Affairs (VHA;  $n = 112\,845$ ) and Kaiser Permanente Washington (KPW;  $n = 14\,333$ ) healthcare systems. Patients were aged  $\geq 50$  years, had a hemoglobin A1c (HbA1c) between 6.5 and  $<9.5$  mg/dL, and did not have dementia or fills for antidiabetic medications before cohort entry. Initiators started metformin monotherapy and noninitiators used no antidiabetic medications in the 6 months after the first qualifying HbA1c. The primary outcome was incident dementia. Propensity scores and inverse probability of treatment weighting (IPTW) controlled for confounding in Cox proportional hazards models.

#### **Results**

During a median follow-up of 6.2 years in VHA and 6.8 years in KPW, there were 7547 new dementia cases in VHA and 1090 in KPW. After IPTW, there was no association between initiation of metformin (vs no initial treatment) and incident dementia in VHA (HR = 1.04; 95% confidence interval [CI]: 0.95-1.13) or KPW (HR = 0.81; 95% CI: 0.51-1.28). Results did not differ by age, baseline HbA1c, or race.

#### **Conclusions**

Results do not support initiating metformin earlier to prevent cognitive decline and, thus, may dampen enthusiasm for metformin as a potential antidementia drug. Randomized clinical trials could help clarify the relationship between metformin and cognitive decline.

Disponible en: <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5014>

## **Sulphonylureas monotherapy and risk of hospitalization for heart failure in patients with type 2 diabetes mellitus: A population-based cohort study in China**

Yang Xu Tiansheng Wang Zhirong Yang Hongbo Lin Peng Shen Siyan Zhan

### **Abstract**

#### **Purpose**

The risk of heart failure associated with sulphonylureas is unclear. We evaluated the association between sulphonylureas and hospitalization of heart failure (HHF) in patients with type 2 diabetes mellitus (T2DM) in China.

#### **Methods**

A retrospective cohort study was implemented using the Yinzhou Regional Health Care Database (YRHCD). We identified 15 752 adult patients with T2DM who were newly exposed to sulphonylurea monotherapy (N = 12 487) or acarbose monotherapy (N = 3265) from January 2010 to September 2016. Cox proportional hazards models weighted by inverse probability of treatment weights were used to compare the risk of HHF between initiators of sulphonylurea and acarbose.

#### **Results**

During a median follow-up of 0.55 (0.49, 1.11) and 0.49 (0.35, 0.70) years for sulphonylureas and acarbose initiators separately, 320 patients developed HHF, with 279 events in sulphonylureas group, and 41 events in acarbose group. The incidence rates of HHF among sulphonylureas initiators and acarbose initiators were 22.2 (95% CI 19.6-24.9) and 18.3 (95% CI 13.2-24.9) per 1000 person-years, respectively. The adjusted hazard ratio (aHR) of HHF for sulphonylureas vs acarbose was 1.61 (95% CI 1.14-2.27). When stratified by history of heart failure, aHR was 1.55 (95% CI 0.79-3.06) in patients with a history of heart failure, and 1.64 (95% CI 1.10-2.45) in patients with no history of heart failure.

#### **Conclusions**

Our study suggested that use of sulphonylureas monotherapy compared with acarbose monotherapy for initial treatment of T2DM for approximately 0.5 years are significantly associated with a higher risk of HHF.

Disponible en: <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5024>

## **Comparative risk of Parkinsonism associated with olanzapine, risperidone and quetiapine in older adults-a propensity score matched cohort study**

Te-yuan Chyou Revathi Nishtala Prasad S. Nishtala

### **Abstract**

## **Purpose**

The purpose of this study was to examine the incidence of Parkinsonism in new users of second-generation antipsychotics (SGAs) in older adults ( $\geq 65$  years). In the secondary analyses, we examined the risk of Parkinsonism by type and dose of SGA and conducted age-sex interactions.

## **Method**

This population-based study included older adults who had a new-onset diagnosis of Parkinsonism and who started taking olanzapine, risperidone or quetiapine between 1 January 2005, and 30 December 2016. The Cox proportional hazard (COXPH) model with inverse probability treatment weighted (IPTW) covariates was used to evaluate the risk of new-onset Parkinsonism associated with SGAs, using quetiapine as the reference. We used the Generalized Propensity Score method to evaluate the dose-response risk of Parkinsonism associated with SGAs.

## **Results**

After IPTW adjustment for covariates, the COXPH model showed that compared to quetiapine, the use of olanzapine and risperidone were associated with an increased risk of Parkinsonism. The IPTW-hazard ratios are 1.76 (95% confidence interval 1.57-1.97) and 1.31 (95%CI 1.16-1.49), respectively. The dose-response risk of Parkinsonism was highest for olanzapine with a hazard ratio of 1.69 (95%CI 1.40-2.05) and the least for quetiapine with a hazard ratio of 1.22 (95%CI 1.14-1.31). The risk of Parkinsonism in the 65 to 74-year age group was higher for both sexes with risperidone compared to olanzapine, but the risk increased with olanzapine for both sexes in the 85+ age group.

## **Conclusion**

The study found that the risk of new-onset Parkinsonism in older adults is 31% and 76% higher with risperidone and olanzapine respectively compared to quetiapine.

Disponible en: <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5007>

## **International Journal of Clinical Pharmacy**

### **Aspirin compared to enoxaparin or rivaroxaban for thromboprophylaxis following hip and knee replacement**

Sadhbh Ní Cheallaigh, Aoife Fleming, Darren Dahly, Eimear Kehoe, John M. O'Byrne, Brid McGrath, Charles O'Connell & Laura J. Sahm

## **Abstract**

### **Background**

The risk of venous thromboembolism following major orthopaedic surgery is among the highest for all surgical specialties. Our hospital guidelines for thromboprophylaxis following elective primary total hip or knee replacement are based on American College of Chest Physicians

guidance. The most recent change to local guidelines was the introduction of the extended aspirin regimen as standard thromboprophylaxis.

### **Objective**

To establish the appropriateness of this regimen by comparing venous thromboembolism rates in patients receiving extended aspirin to previous regimens. Setting The largest dedicated orthopaedic hospital in Ireland.

### **Methods**

This was a retrospective cohort study. Data were collected from patient record software. All eligible patients undergoing primary total hip or knee replacement between 1st January 2010 and 30th June 2016 were included. Main outcome measure Venous thromboembolism up to 6 months post-operatively.

### **Results**

Of the 6548 participants (55.3% female, mean age 65.4 years ( $\pm$  11.8 years, 55.8% underwent total hip replacement), venous thromboembolism occurred in 65 (0.99%). Venous thromboembolism rate in both the inpatient enoxaparin group (n = 961) and extended aspirin group (n = 3460) was 1.04% and was 0.66% in the modified rivaroxaban group (n = 1212). Non-inferiority analysis showed the extended aspirin regimen to be equivalent to the modified rivaroxaban regimen. History of venous thromboembolism was the only significant demographic risk factor for post-operative venous thromboembolism (0.87% vs. 3.54%, p = 0.0002).

### **Conclusion**

In daily clinical practice, extended aspirin regimen is at least as effective as modified rivaroxaban for preventing clinically important venous thromboembolism among patients undergoing hip or knee arthroplasty who are discharged from the hospital without complications. Aspirin can be considered a safe and effective agent in the prevention of venous thromboembolism after total hip or total knee replacement.

Disponibile en: <https://link.springer.com/article/10.1007/s11096-020-01032-1>

## **Clinical Therapeutics.**

### **Misdosing of Non-Vitamin K Antagonist Oral Anticoagulants in Primary Care.**

Carlos Seíça Cardoso, MD, João André Sousa, MD, Pedro Simões, MD, Gustavo Santo, MD  
Fernando Silva, MD, João Sargento-Freitas, MD, PhD

#### **Abstract**

#### **Purpose**

Prescription patterns of non-vitamin K antagonist oral anticoagulants (NOACs) are unknown among primary care physicians, where most patients with nonvalvular atrial fibrillation (NVAf) are

diagnosed and followed up. The goal of this study was to evaluate overdosing and underdosing of NOACs in patients with NVAF followed up in primary care and determine their clinical predictors.

### **Methods**

This multicenter cross-sectional study included all patients with NVAF followed up in 13 primary care units in the center region of Portugal. Patients receiving antithrombotic regimens other than NOACs and patients with missing data were excluded.

### **Findings**

The study included 858 patients with NVAF on an NOAC regimen. Overall, 30.3% were prescribed an off-label dosage (25.4% with infratherapeutic dosing [ITD] and 4.9% with supratherapeutic dosing). Chronic kidney disease (odds ratio, 14.0; 95% CI, 5.4–36.5;  $P < 0.001$ ) and female sex (odds ratio, 2.6; 95% CI, 1.2–5.7;  $P < 0.001$ ) were independent predictors of supratherapeutic dosing. We also found a significant effect of chronic kidney disease on ITD (odds ratio, 0.22; 95% CI, 0.258–0.678;  $P < 0.001$ ).

### **Implications**

In primary care, NOACs are frequently prescribed with unadjusted dosages, generally infratherapeutic. Attention should be paid to women and patients with chronic kidney disease.

Disponible en: [https://www.clinicaltherapeutics.com/article/S0149-2918\(20\)30195-8/pdf](https://www.clinicaltherapeutics.com/article/S0149-2918(20)30195-8/pdf)

## **REVISTAS DE MEDICINA GENERAL**

### **JAMDA: JOURNAL OF THE AMERICAN MEDICAL DIRECTORS ASSOCIATION**

#### **Benzodiazepine Dispensing to Persons With Dementia in France, 2011-2016: A Nationwide Study**

Anais Couret, MSa, Adeline Gallini, PhD, Mathilde Poncet, Axel Renoux, Maryse Lapeyre-Mestre, PhD, Virginie Gardette, PhD

#### **Objectives**

To study temporal trends of benzodiazepine exposure among incident Alzheimer's disease and related dementia (ADRD) cohorts between 2011 and 2016.

#### **Design**

Repeated cross-sectional study

#### **Setting and participants**

Three nationwide incident ADRD cohorts (community-dwelling and institutionalized subjects) were identified in 2011, 2013, and 2016 through the French health insurance database. Subjects were followed 4 semesters around ADRD identification [Semester -2 (S-2) to Semester 2 (S2)]

### Measures

Odds ratios (ORs) for semestrial prevalent exposure, initiation, and adherence to benzodiazepine prescription recommendations (prescription duration <3 months, single reimbursement) were computed using multivariate logistic regressions for each cohort and according to benzodiazepine half-life

### Results

Among 262,024 community-dwelling subjects, as compared to 2011, overall benzodiazepine prevalence risk decreased slightly immediately after ADRD identification [S1: aOR2013 = 0.93 (0.91-0.95), aOR2016 = 0.95 (0.93-0.97)] and did not differ during S2. Among 72,013 institutionalized subjects, it increased over time [S2: aOR2013 = 1.16 (1.11-1.21), aOR2016 = 1.26 (1.21-1.32)]. Long half-life benzodiazepine prevalence risk decreased in the 4 semesters among recent cohorts, for both populations [S2: community-dwelling: aOR2013 = 0.77 (0.74-0.79), aOR2016 = 0.61 (0.59-0.64); institutionalized: aOR2013 = 0.74 (0.68-0.80), aOR2016 = 0.58 (0.54-0.63)]. Short half-life benzodiazepine prevalence risk increased [S2: community-dwelling: aOR2013 = 1.13 (1.10-1.16), aOR2016 = 1.22 (1.20-1.25); institutionalized: aOR2013 = 1.26 (1.21-1.32), aOR2016 = 1.44 (1.38-1.50)]. The same patterns were observed for benzodiazepine initiation. Adherence to benzodiazepine prescription recommendations (based on French prescription duration) worsened over years [prescription duration <3 months: aOR2013 = 0.90 (0.86-0.95), aOR2016 = 0.90 (0.85-0.95), single reimbursement: aOR2013 = 0.95 (0.91-1.00), aOR2016 = 0.94 (0.90-0.99)].

### Conclusions and implications

Long half-life benzodiazepine exposure was reduced whereas short half-life benzodiazepine exposure increased, and adherence to recommendations worsened (prescription duration longer than 3 months and more than a single reimbursement in recent cohorts). Efforts from prescribers and authorities are required in order to restrict psychotropic exposure among the ADRD population. Further research among institutionalized ADRD subjects could provide useful data to disentangle the effects of changes in prescribing practices and in patients' characteristics

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