

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

## **REVISTAS FARMACÉUTICAS**

### **AJHP American Journal of Health System Pharmacist**

#### **Frequency and clinical outcomes of pharmacist-driven switching from warfarin to direct oral anticoagulants in an underserved patient population: A retrospective cohort study**

[Rebekah R Bartholomew, PharmD, BCACP, Brie N Noble, BS, Jennifer J Stanislaw, PharmD, BCACP, Megan Viehmann, PharmD, BCACP, Megan C Herink, PharmD, MBA, BCPS, Jon P Furuno, PhD](#)

#### **Abstract**

##### **Disclaimer**

In an effort to expedite the publication of articles, AJHP is posting 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**

Direct oral anticoagulant (DOAC) medications have improved safety, efficacy, and laboratory monitoring requirements compared to warfarin. However, available data are limited on the frequency and clinical outcomes of pharmacist-driven warfarin-to-DOAC switches. We aimed to quantify the frequencies and rationale of warfarin-to-DOAC switches in an underserved population. We also assessed clinical outcomes and compliance with recommended laboratory monitoring after switches.

##### **Methods**

This retrospective cohort study included adult (age 18 years or older) patients on warfarin who were assessed by a clinical pharmacist for switch appropriateness to a DOAC. Study data were collected via manual chart review and included demographics, comorbid illnesses, switch status, the rationale for or against switching, incidence of thromboses and bleeds within 6 months of the switch assessment, and the time to the first complete blood count and renal and hepatic function tests after the switch. Statistical analysis utilized descriptive statistics, including the mean and SD, median and interquartile range, and frequencies and percentages.

## Results

Among 189 eligible patients, 108 (57%) were switched from warfarin to a DOAC. The primary rationales for switching were less monitoring (64%) and labile international normalized ratio (32%). The main reason against switching was DOAC inappropriateness (53%), such as in morbid obesity (14%). Patient preference was commonly cited in both groups (54% and 36%, respectively). The overall incidence of thrombotic events (9%) and bleeds (15%) after switch assessment was low. Laboratory monitoring after switches was consistent with current recommendations.

## Conclusion

No increase in harm was observed 6 months after switch assessment when pharmacists at a family medicine clinic switched underserved patients from warfarin to DOACs.

Disponible en: <https://doi.org/10.1093/ajhp/zxac375>

## Evaluating reduction in medical costs associated with pharmacists' presence in the emergency department using a novel cost avoidance framework

[Matthew Poremba, PharmD, Kelsey Champa, PharmD, Erin Reichert, PharmD, BCPS](#)

## Abstract

### Disclaimer

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### Purpose

The purpose of this study was to evaluate the cost avoidance associated with emergency medicine pharmacist (EMP) presence in the emergency department (ED) using a novel cost avoidance framework.

### Summary

This single-center, retrospective, observational study examined EMP interventions from November 1, 2021, through March 31, 2022. EMPs prospectively selected up to 10 shifts in which to log interventions during the study period. Interventions were categorized into 25 cost avoidance categories, 10 of which incorporated recently proposed probability variables. All categories were organized into 4 broad cost avoidance domains, including resource utilization, individualization of patient care, adverse drug event prevention, and hands-on care.

During the study period, 894 interventions were logged, which accounted for \$143,132 in cost avoidance (lower probability value of \$124,186, upper probability value of \$168,858), with a median cost avoidance per shift of \$1,671 (interquartile range, \$1,025 to \$2,451). On the basis of 240 shifts, the estimated annual total cost avoidance per pharmacist was extrapolated to be \$401,040.

### **Conclusion**

While the mean cost avoidance of \$161.10 per intervention observed in our study was less than that in prior cost avoidance studies due to the conservative and potentially more realistic estimates used, implementation of this cost avoidance framework still showed substantial cost avoidance associated with EMP presence in the ED.

**Disponible en:** <https://doi.org/10.1093/ajhp/zxac376>

## **British Journal of Clinical Pharmacy**

### **Hyperbaric oxygen should be used for carbon monoxide poisoning**

[Kinjal Sethuraman, Stephen R. Thom](#)

#### **Abstract**

This short review addresses the mechanisms of injury mediated by carbon monoxide (CO) and current information on efficacy of hyperbaric oxygen therapy (HBOT). Recent clinical series involving large, country-wide databases and prospective randomized trials are summarized. We conclude that there is an abundance of basic science and preclinical and clinical research supporting the use of HBOT for acute CO poisoning. With appropriate consideration for pathology and therapeutic mechanisms, HBOT at a dose of 2.5–3.0 atm absolute is a necessary treatment for this toxidrome.

**Disponible en:** <https://doi.org/10.1111/bcp.15605>

## **Risk factors for and preventability of drug-related hospital revisits in older patients: A post-hoc analysis of a randomized clinical trial**

Thomas G. H. Kempen, Anton N. Hedman, Nermin Hadziosmanovic, Karl-Johan Lindner, Håkan Melhus, Elisabet I. Nielsen, Johanna Sulku, Ulrika Gillespie

### **Abstract**

#### **Aim**

The aims of this study were (1) to identify older patients' risk factors for drug-related readmissions and (2) to assess the preventability of older patients' drug-related revisits.

#### **Methods**

Post hoc analysis of a randomized clinical trial with patients aged  $\geq 65$  years at eight wards within four hospitals in Sweden. (1) The primary outcome was risk factors for drug-related readmission within 12 months post-discharge. A Cox proportional hazards model was made with sociodemographic and clinical baseline characteristics. (2) Four hundred trial participants were randomly selected and their revisits (admissions and emergency department visits) were assessed to identify potentially preventable drug-related revisits, related diseases and causes.

#### **Results**

(1) Among 2637 patients (median age 81 years), 582 (22%) experienced a drug-related readmission within 12 months. Sixteen risk factors (hazard ratio  $>1$ ,  $P < 0.05$ ) related to age, previous hospital visits, medication use, multimorbidity and cardiovascular, liver, lung and peptic ulcer disease were identified. (2) The 400 patients experienced a total of 522 hospital revisits, of which 85 (16%) were potentially preventable drug-related revisits. The two most prevalent related diseases were heart failure ( $n = 24$ , 28%) and chronic obstructive pulmonary disease ( $n = 13$ , 15%). The two most prevalent causes were inadequate treatment ( $n = 23$ , 27%) and insufficient or no follow-up ( $n = 22$ , 26%).

#### **Conclusion**

(1) Risk factors for drug-related readmissions in older hospitalized patients were age, previous hospital visits, medication use and multiple diseases. (2) Potentially preventable drug-related hospital revisits are common and might be prevented through adequate pharmacotherapy and continuity of care in older patients with cardiovascular or lung disease.

Disponible en: <https://doi.org/10.1111/bcp.15621>

## Drug Safety

### Post-Authorization Safety Study of Hospitalization for Acute Kidney Injury in Patients with Type 2 Diabetes Exposed to Dapagliflozin in a Real-World Setting

Catherine B. Johannes, Daniel C. Beachler, J. Bradley Layton, Heather E. Danysh et al

#### **Introduction**

Dapagliflozin is a sodium-glucose cotransporter 2 inhibitor approved to treat type 2 diabetes mellitus (T2DM), among other conditions. When dapagliflozin was approved in Europe for treating T2DM (2012), potential safety concerns regarding its effect on kidney function resulted in this post-authorization safety study to assess hospitalization for acute kidney injury (hAKI) among dapagliflozin initiators in a real-world setting.

#### **Objective**

The aim of this study was to evaluate the incidence of hAKI in adults with T2DM initiating dapagliflozin compared with other glucose-lowering drugs (GLDs).

#### **Methods**

This noninterventional cohort study identified new users of dapagliflozin and comparator GLDs from November 2012 to February 2019 from three longitudinal, population-based data sources: Clinical Practice Research Datalink (CPRD; United Kingdom), the HealthCore Integrated Research Database (HIRD; United States [US]), and Medicare (US). Electronic algorithms identified occurrences of hAKI, from which a sample underwent validation. Incidence rates for hAKI were calculated, and incidence rate ratios (IRRs) compared hAKI in dapagliflozin with comparator GLDs. Propensity score trimming and stratification were conducted for confounding adjustment.

#### **Results**

In all data sources, dapagliflozin initiators had a lower hAKI incidence rate than comparator GLD initiators (adjusted IRRs: CPRD, 0.44 [95% confidence interval (CI), 0.22–0.86]; HIRD, 0.76 [95% CI, 0.62–0.93]; Medicare, 0.69 [95% CI, 0.59–0.79]). The adjusted IRR pooled across the data sources was 0.70 (95% CI, 0.62–0.78). Results from sensitivity and stratified analyses were consistent with the primary analysis.

#### **Conclusions**

This study, with > 34,000 person-years of real-world dapagliflozin exposure, suggests a decreased risk of hAKI in patients with T2DM exposed to dapagliflozin, aligning with results from dapagliflozin clinical trials.

Disponible en: <https://link.springer.com/article/10.1007/s40264-022-01263-3>

## **Mortality in Patients with Parkinson's Disease-Related Psychosis Treated with Pimavanserin Compared with Other Atypical Antipsychotics: A Cohort Study**

[J. Bradley Layton, Joan Forns, Lisa J. McQuay, Heather E. Danysh, Colleen Dempsey, et al](#)

### **Introduction**

Pimavanserin is approved in the USA to treat hallucinations and delusions associated with Parkinson's disease psychosis (PDP).

### **Objectives**

We evaluated mortality in patients with PDP after initiation of pimavanserin or comparator atypical antipsychotics, overall, over time, and across subgroups.

### **Methods**

A cohort of patients aged  $\geq 65$  years in the USA with PDP newly initiating pimavanserin or a comparator atypical antipsychotic (clozapine, quetiapine, risperidone, olanzapine, aripiprazole, brexpiprazole) was identified in 2016–2019 Medicare claims data. All-cause mortality in the propensity score–matched treatment groups was compared with hazard ratios (HRs) and 95% confidence intervals (CIs) estimated with Cox-proportional hazards models. Cumulative incidence curves and time period–specific models evaluated risk over time. Subgroup and sensitivity analyses were performed, including a sub-cohort of long-term care (LTC) or skilled nursing facility (SNF) residents.

### **Results**

We identified 2892 pimavanserin initiators and 19,083 comparator initiators (overall 47% female, mean age = 80.9 years, LTC/SNF residents = 30%). Before matching, pimavanserin users had fewer severe comorbidities and more anti-Parkinson medication use than comparators. Matching resulted in 2891 patients in both groups, and all covariates were well balanced. In the matched cohort, the HR for mortality for pimavanserin versus comparator was 0.78 (95% CI 0.67–0.91), with the lowest time period–specific HRs in the first 180 days. Hazard ratios were similar across sensitivity analyses and subgroups. In LTC/SNF residents, the HR was 0.78 (95% CI 0.60–1.01).

## Conclusion

The observed mortality rates were lower among patients treated with pimavanserin compared with those treated with other atypical antipsychotics.

Disponible en: <https://link.springer.com/article/10.1007/s40264-022-01260-6>

## European Journal of Clinical Pharmacology

### Effectiveness and safety of vonoprazan-based regimens compared with those of proton pump inhibitor (PPI)-based regimens as first-line agents for Helicobacter pylori: a meta-analysis of randomized clinical trials

[Yingchao Sun, Lei Yue, Weiling Hu](#)

#### Purpose

Vonoprazan (VPZ), a reversible H<sup>+</sup>–K<sup>+</sup> ATPase inhibitor, has a relatively fast and sustained acid-suppression action that is unaffected by diet or gene polymorphisms. Several randomized controlled trials have evaluated the difference in the eradication rate of Helicobacter pylori (HP) between VPZ-based and proton pump inhibitor (PPI)-based regimens. The present review aimed to (1) evaluate the efficacy, safety, and compliance of VPZ-based regimens compared with those of PPI-based regimens as first-line treatments for HP infection and (2) perform a subgroup analysis to examine the influence of differences in clarithromycin-resistance status, treatment duration, treatment regimens, and research region on treatment outcomes.

#### Methods

We conducted a systematic literature search on PubMed, Embase, Cochrane Library, Web of Science, and ChiCTR Register. Systematic searches, study selection, data extraction, risk of bias assessment, and statistical analysis were performed according to pre-registered protocol on the PROSPERO (CRD42022336608).

#### Results

Eight studies and 2956 HP-infected patients were enrolled. Only first-line therapy and RCT study were considered. VPZ-based group had a superior eradication efficacy compared to PPI-based group by intention-to-treat (ITT) (pooled risk ratio (RR): 1.14, 95% CI: 1.08–1.21,  $p < 0.00001$ ) and per-protocol analysis (pooled RR: 1.13, 95% CI: 1.07–1.20,  $p < 0.00001$ ). This finding was further validated by subgroup analysis depending on treatment regimens, duration, region, and clarithromycin resistance. In addition, there was no significant difference in adverse events ( $p = 0.33$ ) and compliances ( $p = 0.30$ ) between the regimens.

## Conclusion

The VPZ-based regimens showed a superior eradication efficacy compared to the already frequently used PPI-based regimens. Furthermore, VPZ-based therapy showed comparable tolerability and incidence of adverse events.

Disponible en: <https://link.springer.com/article/10.1007/s00228-022-03430-y>

## Abuse, dependence and withdrawal associated with fentanyl and the role of its (designated) route of administration: an analysis of spontaneous reports from Europe

[Kathrin Jobski, Carsten Bantel, Falk Hoffmann](#)

## Purpose

Fentanyl, a highly potent synthetic opioid used in cancer and non-cancer pain, is approved for various routes of administration. In Europe, fentanyl consumption increased substantially in the last decades but information on abuse, dependence and withdrawal associated with fentanyl is scarce, especially with respect to its different formulations.

## Methods

We analysed case characteristics of spontaneous reports of suspected fentanyl-associated abuse, dependence or withdrawal from European countries recorded in the EudraVigilance database up to 2018 with respect to the (designated) routes of administration and potential indications.

## Results

A total of 985 reports were included (mainly from France and Germany) with 43% of cases referring to transdermal fentanyl. Median age was 45 years (48.8% female) and 21.6% had musculoskeletal disorders. Only 12.6% of those using transdermal fentanyl had a cancer diagnosis compared to 40.2% and 26.8% of those using intranasal and oral transmucosal fentanyl, respectively. Depression was common (10.7%) and highest in cases with musculoskeletal disorders (24.9%) as was the use of benzodiazepines. Overall, 39.5% of reports resulted in a prolonged hospital stay and for 23.2% a fatal outcome was recorded. The respective proportions were especially high in cases with musculoskeletal disorders (56.3% with prolonged hospitalisation) and in those using transdermal fentanyl (35.2% fatalities).

## Conclusions

In suspected cases of abuse, dependence or withdrawal, fentanyl was mainly used for non-cancer pain indications and most often as transdermal formulations. Depression and prolonged hospitalisations were common, especially in patients with musculoskeletal disorders, indicating a vulnerable patient group and complex treatment situations.

Disponible en: <https://link.springer.com/article/10.1007/s00228-022-03431-x>



## Clinical Pharmacology & therapeutics

### Beyond the Michaelis-Menten: Accurate Prediction of Drug Interactions through Cytochrome P450 3A4 Induction

[Ngoc-Anh Thi Vu](#), [Yun Min Song](#), [Quyen Thi Tran](#), [Hwi-yeol Yun](#), [Sang Kyum Kim](#), [Jung-woo Chae](#), [Jae Kyoung Kim](#)

#### **Abstract**

U.S. Food and Drug Administration (FDA) guidance has recommended several model-based predictions to determine potential drug-drug interactions (DDIs) mediated by cytochrome P450 (CYP) induction. In particular, the ratio of substrate AUCs (AUCR) under and not under the effect of inducers is predicted by the Michaelis-Menten (MM) model, where the MM constant ( $K_m$ ) of a drug is implicitly assumed to be sufficiently higher than the concentration of CYP enzymes that metabolize the drug ( $ET$ ) in both the liver and small intestine. Furthermore, the fraction absorbed from gut lumen ( $F_a$ ) is also assumed to be one because  $F_a$  is usually unknown. Here, we found that such assumptions lead to serious errors in predictions of AUCR. To resolve this, we propose a new framework to predict AUCR. Specifically,  $F_a$  was re-estimated from experimental permeability values rather than assuming it to be one. Importantly, we used the total quasi-steady-state approximation to derive a new equation, which is valid regardless of the relationship between  $K_m$  and  $ET$ , unlike the MM model. Thus, our framework becomes much more accurate than the original FDA equation, especially for drugs with high affinities such as midazolam or strong inducers such as rifampicin, so that the ratio between  $K_m$  and  $ET$  becomes low (i.e., the MM model is invalid). Our work greatly improves the prediction of clinical DDI, which is critical to preventing drug toxicity and failure.

Disponible en: <https://doi.org/10.1002/cpt.2824>

## Annals of Pharmacotherapy

### Efficacy and Safety of Sacubitril/Valsartan Compared With ACEI/ARB on Health-Related Quality of Life in Heart Failure Patients: A Meta-Analysis

Hua-rong Yang, MSc, Xiao-di Xu, MSc, [...], and Bo-ting Zhou, PhD

#### **Abstract**

##### **Background:**

Data on the effects of sacubitril/valsartan compared with angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARB) on health-related quality of life (HRQoL) are limited.

##### **Objective:**

To evaluate the comparative effects between sacubitril/valsartan and ACEI/ARB on HRQoL, a systematic review and meta-analysis were performed.

##### **Methods:**

PubMed, EMBASE, Web of Science, and ClinicalTrials.gov were searched from inception to March 2, 2022 for randomized controlled trials that compared the HRQoL scores, including Kansas City Cardiomyopathy Questionnaire (KCCQ), Minnesota Living with Heart Failure Questionnaire (MLHFQ), or Medical Outcomes Study Short-Form Health Survey 12 or 36 (SF-12/36), between sacubitril/valsartan and ACEI/ARB. After screening, studies that met the inclusion criteria were eventually included and analyzed.

##### **Results:**

A total of 8 studies with 17 390 patients (8693 patients used sacubitril/valsartan, and 8697 patients used ACEI/ARB) were included in this study. Five of these studies used KCCQ, 1 used SF-12/36, 1 used MLHFQ, and 1 used both KCCQ and SF-12/36. The KCCQ overall summary score and its subscales were significantly higher in sacubitril/valsartan compared with ACEI/ARB in heart failure patients with reduced ejection fraction, but were similar in heart failure patients with preserved ejection fraction. Sacubitril/valsartan conferred similar HRQoL scores in MLHFQ and SF-12/36 to ACEI/ARB. The most frequently reported adverse event for sacubitril/valsartan is hypotension and the risk is higher than for ACEI/ARB.

##### **Conclusions:**

Sacubitril/valsartan may have the potential to improve HRQoL in heart failure patients with reduced ejection fraction compared with ACEI/ARB. Hypotension is the most common adverse event with sacubitril/valsartan compared with ACEI/ARB. The results of this study may contribute to the rational use of sacubitril/valsartan.

**Disponible en:** <https://doi.org/10.1177/10600280221140575>

## Gaps in Evidence-based Treatment of Concurrent Attention Deficit Hyperactivity Disorder and Opioid Use Disorder: A Scoping Review

Olivia L. Ramey, PharmD , Andrea E. Bonny, MD, [...], and Milap C. Nahata, MS, PharmD

### **Abstract**

#### **Objectives:**

To describe the effectiveness of medications for the treatment of opioid use disorder (OUD) and attention deficit/hyperactivity disorder (ADHD).

#### **Data Sources:**

Literature search of PubMed, Embase, Web of Science, CINAHL, Medline, PsycINFO, and Google Scholar was performed for studies published from inception to October 25, 2022.

#### **Study Selection and Data Extraction:**

Studies were included if patients were diagnosed with OUD and ADHD and had pharmacotherapy for either condition. Abstracts, commentaries, reviews, case reports, case series, non-English articles, and animal studies were omitted.

#### **Data Synthesis:**

This review found 18 studies. Treatment of ADHD was evaluated for impact on ADHD and OUD outcomes, while treatment of OUD was evaluated for OUD-related outcomes. Outcomes assessed included markers for symptom intensity, adherence, and treatment failure. While results were mixed, treatment of ADHD was largely associated with improvements in ADHD severity and retention in OUD treatment programs. ADHD severity was associated with higher rates of illicit substance abuse and worse OUD-related outcomes. It could not be determined which medications for treatment of OUD should be prioritized.

#### **Relevance to Patient Care and Clinical Practice:**

This review summarized key findings from studies that treated ADHD or OUD among dually diagnosed patients and highlighted methodological considerations for future research.

#### **Conclusions:**

Treatment of ADHD is warranted among patients with OUD and ADHD to improve retention in OUD treatment programs and reduce illicit substance abuse. Pharmacotherapy for the treatment of ADHD or OUD should continue to be determined based on patients' characteristics and the capabilities of the treatment program.

**Disponible en:** <https://doi.org/10.1177/10600280221141065>

## **Ponesimod: An Oral Second-Generation Selective Sphingosine 1-Phosphate Receptor Modulator for the Treatment of Multiple Sclerosis**

Amal Alnaif, PharmD, Isabelle Oiler, PharmD, and Manoranjan S. D'Souza, MD, PhD

### **Abstract**

#### **Objective:**

To describe the safety, efficacy, and potential role in therapy of ponesimod, which was recently approved by the Food and Drug Administration (FDA) as a therapeutic option for the treatment of multiple sclerosis (MS).

#### **Data Sources:**

A PubMed literature search using the following terms: ponesimod and MS (January 1, 2012-October 31, 2022). FDA product labeling was also reviewed for pertinent data sources.

#### **Study Selection and Data Extraction:**

All relevant English-language articles examining efficacy and/or safety of ponesimod were considered for inclusion.

#### **Data Synthesis:**

Ponesimod is an orally administered second-generation sphingosine 1-phosphate (S1-P) receptor modulator classified as a disease modifying treatment (DMT) for MS. Clinical studies have shown that ponesimod prevents relapse in patients with relapsing-remitting MS (RRMS) and has superior efficacy compared with teriflunomide. Nasopharyngitis, upper respiratory tract infections, headache, high blood pressure, and liver dysfunction were some of the common adverse effects associated with ponesimod. Dyspnea, bradyarrhythmias, atrioventricular conduction delays, and macular edema were some of the rare but serious adverse effects associated with ponesimod.

#### **Relevance to Patient Care and Clinical Practice in Comparison With Existing Agents:**

Some advantages of ponesimod over other S1-P receptor modulators approved for RRMS include selectivity for the S1-P1 receptor and short half-life, which allows for quick reversal of immunosuppressive effects. However, data from long-term efficacy and safety studies and more direct comparison studies with other DMTs are required.

#### **Conclusion:**

Currently available data suggest that ponesimod is a useful addition to other high-efficacy DMTs available to treat patients with MS.

**Disponible en:** <https://doi.org/10.1177/10600280221140480>

## Pharmacoepidemiology & Drug Safety

### Pharmacogenetics of warfarin and healthcare costs – real-world data analysis

[Jaakko Lähteenmäki](#), [Anna-Leena Vuorinen](#), [Mika Lehto](#), [Mikko Niemi](#), [Markus M. Forsberg](#)

#### **Abstract**

#### **Purpose**

Variants in CYP2C9 and VKORC1 genes have been associated with individuals' sensitivity to warfarin. The aim of this study was to investigate the differences of healthcare costs of genetically normal and genetically sensitive warfarin responder groups.

#### **Methods**

This was a retrospective study linking genotype data from three Finnish biobanks (THL Biobank, Auria Biobank, Helsinki Biobank) with healthcare encounter data of the Finnish Institute of Health and Welfare (THL), drug dispensation data from the Social Insurance Institution of Finland (Kela) and laboratory data from Finnish hospital districts and municipalities. We compared the normal and sensitive warfarin responder groups in terms of healthcare costs related to bleeding and thromboembolic events, INR tests and medication purchases.

#### **Results**

We found a trend towards increased bleeding-related hospital costs in the sensitive warfarin responder group (881 patients) when compared with the normal responders (1627 patients) with a per patient difference of 150.9 €/yr (95% CI: -55.1, 414.6 €/yr,  $p=0.087$ ). INR test costs were higher in the sensitive responder group with a difference of 7.2 €/yr (95% CI: -1.5, 16.4 €/yr,  $p=0.047$ ). Medication costs were significantly lower in the sensitive responder group with a difference of -14.4 €/yr (95% CI: -15.8, -12.9 €/yr,  $p<0.001$ ).

#### **Conclusions**

The difference in the costs of bleeding-related hospitalization between genetically sensitive and normal warfarin responders may justify genotype-guided warfarin dosing. Further studies with larger sample sizes would be needed to verify the result.

Disponible en: <https://doi.org/10.1002/pds.5585>

## Revista Clínica Española

### Valor pronóstico de una reevaluación precoz de la fracción de eyección reducida en insuficiencia cardíaca aguda

[J.M. Salvador-Casabóna,b,c,, D. Grados-Sasoa,b, I. Lacambra-Blascoa, I. Giménez-Lópezc, J.I. Pérez-Calvoc,d](#)

#### **Antecedentes y objetivo**

La mejoría en la fracción de eyección de ventrículo izquierdo (FEVI) en la insuficiencia cardíaca (IC) se relaciona con un mejor pronóstico. Identificar estos sujetos precozmente tras una descompensación, el umbral necesario de mejoría de FEVI y sus factores predictores resultan de gran interés.

#### **Pacientes y métodos**

Se reevaluaron prospectivamente 110 pacientes hospitalizados por IC en una visita ambulatoria precoz (media 38días).

#### **Resultados y conclusiones**

En sujetos con FEVI deprimida (<50%) un 50,7% presentaron una mejoría de FEVI  $\geq 5\%$  entre el episodio agudo y la visita ambulatoria. Esta mejoría en FEVI deprimida resultó ser útil para identificar pacientes con buen pronóstico (reingreso por IC +mortalidad cardiovascular,  $p=0,022$ ), pero no en FEVI preservada ( $\geq 50\%$ ). Los pacientes con FEVI mejorada presentaban significativamente menor edad, el debut de IC, mejor strain longitudinal global (SLG) y función renal. Un modelo de regresión logística multivariante seleccionó al SLG, el debut de IC y un menor tamaño ventricular izquierdo como predictores de mejoría de FEVI  $\geq 5\%$  (AUC=0,85).

Disponible en: [10.1016/j.rce.2022.10.003](#)

### Etiología de la osteonecrosis avascular de cadera y hombro. Cribado de la enfermedad de Gaucher

[J.Á. Cuenca-Gómez, C. Ocaña-Losada, P. Crujeirasb,c,d, D. Rodriguesb,c,d, M. Martínez-Espinosa](#)

## **Introducción**

La osteonecrosis avascular (ONA) de cadera y de hombro es una enfermedad poco estudiada y no se conocen bien los factores de riesgos predisponentes para desarrollarla. Existe un porcentaje alto de pacientes diagnosticados como osteonecrosis idiopática. Este estudio tiene como objetivo investigar la prevalencia de los posibles factores etiológicos de la ONA y realizar un cribado de la enfermedad de Gaucher en los pacientes diagnosticados de ONA idiopática.

## **Material y métodos**

Estudio observacional retrospectivo y unicéntrico de los pacientes que hayan presentado al menos un episodio de osteonecrosis avascular de la cadera o del hombro en el Hospital de Poniente (Almería, España) desde enero de 2010 a diciembre de 2019. Se recogieron datos clínicos y analíticos. Los pacientes en cuya historia clínica no se describían factores etiológicos fueron cribados para enfermedad de Gaucher.

## **Resultados**

Se incluyeron un total de 81 pacientes, de los cuales 58 eran hombres. La edad media de presentación de ONA fue de 45,9 años. Presentaron necrosis unilateral de cadera ( $n = 43$ ), necrosis bilateral de cadera ( $n = 34$ ), necrosis bilateral de cadera y unilateral de hombro ( $n = 3$ ) y necrosis unilateral de hombro ( $n = 1$ ). Los potenciales factores etiológicos más frecuentes fueron tabaquismo (46,9%) y obesidad (17,3%). Se realizó un cribado de la enfermedad de Gaucher en 10 pacientes, que resultó ser negativo.

## **Conclusiones**

En nuestro estudio los principales potenciales factores etiológicos de aparición de la ONA fueron el tabaquismo y la obesidad. Existe un porcentaje alto de pacientes diagnosticados de osteonecrosis avascular idiopática. Creemos que en estos casos se debería realizar un estudio más exhaustivo de los factores de riesgo menos frecuentes.

**Disponible en:** [10.1016/j.rce.2022.10.006](https://doi.org/10.1016/j.rce.2022.10.006)

## JAMA Internal Medicine

### REVISTAS GERIÁTRICAS

## Age and Ageing

### Simultaneously reassuring and unsettling: a longitudinal qualitative study of community anticipatory medication prescribing for older patients

[Ben Bowers, Kristian Pollock, Stephen Barclay](#)

#### **Abstract**

##### Background

The prescription of injectable anticipatory medications is widely accepted by clinicians to be key in facilitating effective last-days-of-life symptom control. Community end-of-life care and admission avoidance is particularly strongly advocated for older patients. However, patient and informal caregiver views and experiences of anticipatory medication have been little studied to date.

##### Objective

To understand older patients', informal caregivers' and clinicians' views and experiences of the prescribing and use of anticipatory medications.

##### Setting

Patients' homes and residential care homes. Six older patients, nine informal caregivers and six clinicians.

##### Methods

Multi-perspective, longitudinal interview study based on 11 patient cases. Semi-structured interviews ( $n = 28$ ) were analysed thematically.

##### Results

Three themes were identified: (i) living in the present whilst making plans: anticipatory medications were used by clinicians as a practical tool in planning for uncertainty, while patients and informal caregivers tried to concentrate on living in the present; (ii) anticipation of dying: it was rare for patients and informal caregivers to discuss explicitly the process and experience of dying with clinicians; and (iii) accessing timely care: the use of anticipatory medications generally helped symptom control. However, informal caregivers reported difficulties in persuading nurses to administer them to patients.



## Conclusions

Anticipatory medications are simultaneously reassuring and a source of unease to older patients and their informal caregivers. Prescriptions need careful discussion and tailoring to their preferences and experience. Nurses' decisions to administer medication should consider informal caregivers' insights into patient distress, especially when patients can no longer communicate their needs.

**Disponible en:** <https://doi.org/10.1093/ageing/afac293>

## Archives of Gerontology and Geriatrics

### Interaction between geriatric syndromes in predicting three months mortality risk

[M.M.OudabM.C.SchutP.E.SpiesaH.J.van der Zaag-LoonenbS.E.de RooijcdA.Abu-HannacB.C.van Munsterb](#)

#### **Abstract**

##### Objectives

Capturing frailty using a quick tool has proven to be challenging. We hypothesise that this is due to the complex interactions between frailty domains. We aimed to identify these interactions and assess whether adding interactions between domains improves mortality predictability.

##### Methods

In this retrospective cohort study, we selected all patients aged 70 or older who were admitted to one Dutch hospital between April 2015 and April 2016. Patient characteristics, frailty screening (using VMS (Safety Management System), a screening tool used in Dutch hospital care), length of stay, and mortality within three months were retrospectively collected from electronic medical records. To identify predictive interactions between the frailty domains, we constructed a classification tree with mortality as the outcome using five variables: the four VMS-domains (delirium risk, fall risk, malnutrition, physical impairment) and their sum. To determine if any domain interactions were predictive for three-month mortality, we performed a multivariable logistic regression analysis.

## Results

We included 4,478 patients. (median age: 79 years; maximum age: 101 years; 44.8% male) The highest risk for three-month mortality included patients that were physically impaired and malnourished (23% (95%-CI 19.0–27.4%)). Subgroups had comparable three-month mortality risks based on different domains: malnutrition without physical impairment (15.2% (96%-CI 12.4–18.6%)) and physical impairment and delirium risk without malnutrition (16.3% (95%-CI 13.7–19.2%)).

## Discussion

We showed that taking interactions between domains into account improves the predictability of three-month mortality risk. Therefore, when screening for frailty, simply adding up domains with a cut-off score results in loss of valuable information.

**Disponible en:** <https://doi.org/10.1016/j.archger.2022.104774>

## Resistance training-induced improvement in physical function is not associated to changes in endocrine somatotropic activity in prefrail older adults

[Anna Schaupp](#) [Martin Bidlingmaier](#) [Sebastian Martini](#) [Martin Reincke](#) [Sabine Schluessel](#) [Ralf Schmidmaier](#) [Michael Drey](#)

## **Abstract**

### Context

Resistance training improves muscle function in prefrail and frail elderly. The role of the somatotropic axis in this physiologic process remains unclear. Insulin-like growth factor I (IGF-I) and its associated proteins Insulin-like growth factor binding protein 3 (IGFBP3) and acid labile subunit (ALS) build a circulating ternary complex that mediates growth hormone (GH) effects on peripheral organs and can serve as a measure of endocrine somatotropic activity.

### Objective

The aim of this study was to assess the association between resistance training-induced changes in physical performance and basal levels of IGF-I, IGFBP-3 and ALS in prefrail older adults.

### Methods

69 prefrail community-dwelling older adults, aged 65 to 94 years, were randomly assigned to a 12-week period of strength or power training or to a control group. The study was registered at clinicaltrials.gov as NCT00783159. Serum concentrations of IGF-I, IGFBP-3 and ALS were measured at rest before and after the intervention. Hormonal differences were examined in relation to changes in physical performance assessed by the Short Physical Performance Battery (SPPB).

### Results

While resistance training led to significant improvements in SPPB score it did not induce significant differences in somatotrophic hormone concentrations. Pre- and post-intervention changes in IGF-I, IGFBP-3, ALS or IGF/IGFBP-3 molar ratio were not related to the intervention mode, even after adjustment for age, sex, nutritional status, as well as SPPB and hormone concentrations at baseline.

### Conclusion

Training-induced improvements in physical performance in prefrail older adults were not associated with significant changes in endocrine somatotrophic activity.

Disponible en: <https://doi.org/10.1016/j.archger.2022.104792>

## BMC Geriatrics

### Effectiveness and cost-effectiveness of a telemedicine programme for preventing unplanned hospitalisations of older adults living in nursing homes: the GERONTACCESS cluster randomized clinical trial

[Caroline Gayot, Cécile Laubarie-Mouret, Kevin Zarca, Maroua Mimouni, Noelle Cardinaud, Sandrine Luce, Isabelle Toven, Isabelle Durand-Zaleski, Marie-Laure Laroche, Pierre-Marie Preux & Achille Tchalla](#)

### **Abstract**

#### Objective

The GERONTACCESS trial evaluated the utility and cost-effectiveness of a gerontological telemedicine (TLM) programme for preventing unplanned hospitalisation of residents living in nursing homes (NHs) in regions lacking medical facilities and/or qualified medical providers (“medical deserts”).

### Design

GERONTACCESS was a 12-month, multicentre, prospective cluster-randomised trial conducted in NHs. The intervention group underwent TLM assessments every 3 months. The control group received the usual care. In both groups, comprehensive on-site assessments were conducted at baseline and the final visit. Care requirements were documented throughout the study.

### Setting and participants

NH residents aged  $\geq 60$  years with multiple chronic diseases.

### Methods

The study outcomes were the proportion of patients who experienced avoidable and unplanned hospitalisation, and the incremental cost savings per quality-adjusted life years from baseline to the 12-month follow-up.

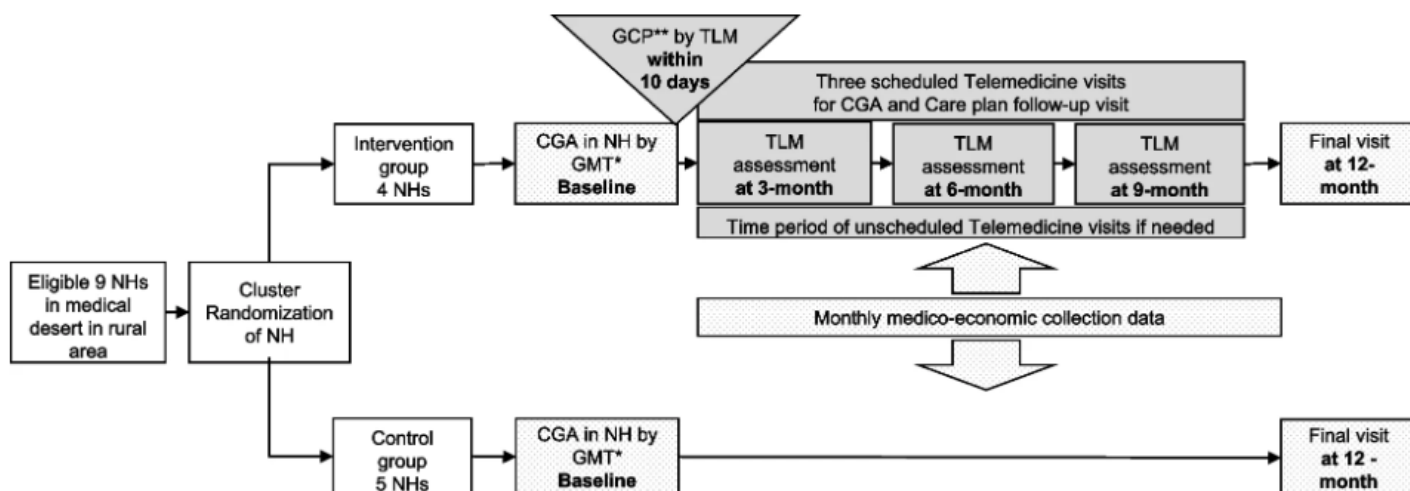
### Results

Of the 426 randomised participants (mean  $\pm$  standard deviation age,  $87.2 \pm 7.6$  years; 311 [73.0%] women), 23.4% in the intervention group and 32.5% in the control group experienced unplanned hospitalisation (odds ratio [OR] = 0.73, 95% confidence interval [CI] 0.43 to 0.97;  $p = 0.034$ ). Each avoided hospitalisation in the intervention group saved \$US 3,846.

### Conclusions and implications

The results of GERONTACCESS revealed that our gerontological, preventative TLM program significantly reduced unplanned hospitalisations. This innovative intervention limited disease progression and promoted a healthy lifestyle among NH residents.

### Trial registration



The design of the GTLM programme: GERONTACCESS study protocol. \*geriatric mobile team. \*\*gerontological care plan (formulated by the multidisciplinary geriatric mobile team staff and sent to the NH physician within 10 working days)

Disponible en: <https://doi.org/10.1186/s12877-022-03575-6>

## The risk factors for deep venous thrombosis in critically ill older adult patients: a subgroup analysis of a prospective, multicenter, observational study

Li Li, Junhai Zhen, Liquan Huang, Jia Zhou, Lina Yao, Lingen Xu, Weimin Zhang, Gensheng Zhang, Qijiang Chen, Bihuan Cheng, Shijin Gong, Guolong Cai, Ronglin Jiang & Jing Yan

### **Abstract**

#### Background

Older adult patients mainly suffer from multiple comorbidities and are at a higher risk of deep venous thrombosis (DVT) during their stay in the intensive care unit (ICU) than younger adult patients. This study aimed to analyze the risk factors for DVT in critically ill older adult patients.

#### Methods

This was a subgroup analysis of a prospective, multicenter, observational study of patients who were admitted to the ICU of 54 hospitals in Zhejiang Province from September 2019 to January 2020 (ChiCTR1900024956). Patients aged > 60 years old on ICU admission were included. The primary outcome was DVT during the ICU stay. The secondary outcomes were the 28- and 60-day survival rates, duration of stay in ICU, length of hospitalization, pulmonary embolism, incidence of bleeding events, and 60-day coagulopathy.

#### Results

A total of 650 patients were finally included. DVT occurred in 44 (2.3%) patients. The multivariable logistic regression analysis showed that age ( $\geq 75$  vs 60-74 years old, odds ratio (OR) = 2.091, 95% confidence interval (CI): 1.308-2.846,  $P = 0.001$ ), the use of analgesic/sedative/muscarinic drugs (OR = 2.451, 95%CI: 1.814-7.385,  $P = 0.011$ ), D-dimer level (OR = 1.937, 95%CI: 1.511-3.063,  $P = 0.006$ ), high Caprini risk score (OR = 2.862, 95%CI: 1.321-2.318,  $P = 0.039$ ), basic prophylaxis (OR = 0.111, 95%CI: 0.029-0.430,  $P = 0.001$ ), and physical prophylaxis (OR = 0.322, 95%CI: 0.109-0.954,  $P = 0.041$ ) were independently associated with DVT. There were no significant differences in 28- and 60-day survival rates, duration of stay in ICU, total length of hospitalization, 60-day pulmonary embolism, and coagulation dysfunction between the two groups, while the DVT group had a higher incidence of bleeding events (2.6% vs. 8.9%,  $P < 0.001$ ).

#### Conclusion

In critically ill older adult patients, basic prophylaxis and physical prophylaxis were found as independent protective factors for DVT. Age ( $\geq 75$  years old), the use of analgesic/sedative/muscarinic drugs, D-dimer level, and high Caprini risk score were noted as independent risk factors for DVT.

**Disponible en:** <https://doi.org/10.1186/s12877-022-03599-y>

## DRUGS AND AGING

### Deprescribing Medications that Increase the Risk of Falls in Older People: Exploring Doctors' Perspectives Using the Theoretical Domains Framework (TDF)

[Reham A. Kalim, Conal J. Cunningham, Sheila A. Ryder & Niamh M. McMahon](#)

#### **Abstract**

##### Background

Falls can lead to hospitalisation and death in older people. Polypharmacy is a major risk factor, and deprescribing fall-risk increasing drugs (FRIDs) is one of several possible important preventive measures. The objective of this study was to explore the factors that influence doctors when deprescribing FRIDs in a hospital setting.

##### Method

Semi-structured interviews were conducted with consultant geriatricians and hospital doctors experienced in dealing with patients aged 65 years or older, at a large academic teaching hospital (~ 1000 beds), Dublin, Ireland. The interviews were directed by an interview guide and audio recorded and transcribed verbatim, with subsequent thematic analysis in NVivo 12 software.

##### Results

A total of 18 participants were interviewed. Barriers to deprescribing included: insufficient time, incomplete patient records, changing medications initiated by other specialists and difficulties following up patients after discharge. Facilitators included: enhanced documentation through electronic patient records, the support of other healthcare professionals such as clinical pharmacists, and patients' engagement, which is considered essential for the success of the deprescribing process's outcome.

##### Conclusion

Deprescribing FRIDs in older adults in the hospital setting is challenging. Implementation of the process in practice requires combined effort from stakeholders to tackle everyday work environment challenges. Future studies are required examining the clinical effect of the suggested interventions and exploring patients' involvement in deprescribing decisions.

### Key Points

Deprescribing fall-risk increasing drugs in the hospital setting can be challenging. However, tackling challenges such as incomplete documentation and sub-optimal communication between teams and across primary and secondary care, has the potential to enhance the feasibility of implementing the deprescribing process.

Pharmacists and nurses can assist and support doctors completing the time-intensive process of medication review and deprescribing.

Shared decision making, in a patient-centred approach, is considered essential for the ongoing success of the intervention.

Disponible en: <https://doi.org/10.1007/s40266-022-00985-4>

## EUROPEAN GERIATRIC MEDICINE

### Pharmacist-driven antimicrobial stewardship program in a long-term care facility by assessment of appropriateness

[María Rosa Cantudo-Cuenca, Alberto Jimenez-Morales & Juan Enrique Martínez-de la Plata](#)

#### **Abstract**

##### Aim

Antimicrobials are the most frequently prescribed drugs in long-term care facilities (LTCF). Antibiotic stewardship programs (ASP) are coordinated interventions promoting the responsible use of antibiotics to improve patient outcomes and reduce antibiotic-resistant bacteria. The objectives are to evaluate the effectiveness of a pharmacist-led ASP in a LTCF, to characterize antibiotic therapy and assess the appropriateness of antibiotic prescriptions. Inappropriate use of antibiotics is high in LTCF so it is essential to implement an ASP to improve appropriateness.



## Methods

A prospective quasi-experimental study to implement an ASP in a LTCF. Antibiotic prescriptions for suspected infections initiated in any setting for LTCF residents were included. We assessed appropriateness and prospective audits and feedback of each inappropriate antimicrobial prescription were carried out. Associations of variables with appropriate antibiotic prescribing were estimated using logistic regression.

## Results

A total of 416 antibiotic prescriptions were included. The mean consumption of antibiotics was reduced from 63.2 defined daily doses per 1000 residents days (DRD) in the preintervention period to 22.8 in the intervention period (– 63.8%), with a significant drop in fluoroquinolones (81.4%). Overall, 46.6% of antibiotic prescriptions were judged inappropriate, mainly because of a use not recommended in treatment guidelines (63.2%). Multivariable analysis showed that empirical therapy, some classes of antibiotics (cephalosporins, fluoroquinolones, fosfomycin calcium, macrolides) and prescription initiation in the emergency department were independent predictors of antimicrobial inappropriateness.

## Conclusions

Pharmacist-led ASP in a LTCF has being effective in reducing consumption of antibiotics by improving appropriateness of treatment decisions. However, ASP should include interventions in the emergency department because of the high inappropriate use in this setting.

DRD, mean/month (SD)	Preintervention <sup>a</sup>	Intervention <sup>b</sup>	% reduction	p value
Total antibiotics	63.2 (15.1)	22.8 (13.7)	63.8	< 0.001
Penicillins (amoxicillin, cloxacillin)	4.6 (3.4)	3.3 (2.2)	28.3	0.282
Amoxicillin-clavulanic acid	20.8 (5.0)	4.3 (3.3)	79.3	< 0.001
Cephalosporins	9.6 (6.9)	5.8 (4.9)	39.6	0.052
Fluoroquinolones	18.8 (9.5)	3.5 (2.4)	81.4	< 0.001
Fosfomycin calcium	1.4 (0.9)	0.6 (1.0)	57.1	0.002
Fosfomycin-tromethamine	1.7 (1.0)	1.1 (0.6)	35.3	0.058
Macrolides	2.8 (2.7)	2.3 (7.0)	17.9	0.013
Sulfonamides	1.6 (1.3)	0.9 (0.6)	43.8	0.070
Other antibiotics	1.9 (1.7)	1 (1.6)	47.4	0.055
Costs of antibiotics (euros), median/trimester (IQR)	818.9 (688.7–987.4)	438.0 (237.7–720.6)	46.5	0.013

DRD defined daily doses (DDD) per 1000 residents per day, IQR interquartile range, SD standard deviation

<sup>a</sup>January 1, 2018–June 30, 2019

<sup>b</sup>July 1, 2019 to December 31, 2020

Disponible en: <https://doi.org/10.1007/s41999-022-00715-4>

## Consensus validation of a screening tool for cardiovascular pharmacotherapy in geriatric patients: the RASP CARDIO list (Rationalization of Home Medication by an Adjusted STOPP list in Older Patients)

Hannah De Schutter, Julie Hias, Laura Hellemans, Karolien Walgraeve, Jos Tournoy, Peter Verhamme, Peter Sinnaeve, Rik Willems, Walter Droogné, Christophe Vandenbriele, Lucas Van Aelst, Thomas Vanassche & Lorenz Van der Linden

### **Abstract**

#### Purpose and aim

Cardiovascular agents commonly used in geriatric patients, are linked to potentially avoidable harm and might hence be a suitable substrate for medication review practices. Therefore, we sought to update and validate the content of the cardiovascular segment of the previously published Rationalization of Home Medication by an Adjusted STOPP list in Older Patients (RASP) List. We aim to update and validate the content of the cardiovascular segment of the RASP list, a previously validated explicit screening tool to improve geriatric polypharmacy.

#### Methods

A three-step study was conducted by the pharmacy department in collaboration with the geriatric medicine and cardiology department at the University Hospitals Leuven, Belgium. First, the cardiovascular segment of the RASP list version 2014 was updated taking into account published research, other screening tools and the input of end-users. Secondly, this draft was reviewed during three panel discussions with five expert cardiologists and three clinical pharmacists, all of whom had relevant expertise in geriatric pharmacotherapy. Thirdly, the content was validated using a modified Delphi Technique by a panel of European hospital pharmacists, cardiologists, geriatricians and an internal medicine physician.

#### Results

After the first and second step, the RASP\_CARDIO list comprised 94 statements. Consensus ( $\geq 80\%$  agreement) of all statements and one new statement about gliflozins in heart failure was achieved by a panel of seventeen experts across four European countries after two validation rounds. The final construct comprised a list of 95 statements related to potentially inappropriate prescribing of cardiovascular agents.

#### Conclusion

The RASP\_CARDIO list is an updated and validated explicit screening tool to optimize cardiovascular pharmacotherapy in geriatric patients.

**Disponible en:** <https://doi.org/10.1007/s41999-022-00701-w>

## Journal of the American Geriatrics Society

### Frailty phenotype as a predictor of bleeding and mortality in ambulatory patients receiving direct oral anticoagulants

Matteo Candeloro MD, Marcello Di Nisio MD, PhD, Nicola Potere MD, Lorenzo Di Pizio MD, Enzo Secinaro MD, Claudia De Flaviis MD, Camilla Federici MD

#### **Abstract**

##### Background

Limited prospective data exist about the clinical relevance of frailty in patients with atrial fibrillation (AF) or venous thromboembolism (VTE) receiving direct oral anticoagulants (DOACs). The aim of this study was to evaluate whether frailty phenotype identifies DOAC-treated patients at higher risk of adverse clinical outcomes.

##### Methods

Consecutive, adult outpatients treated with DOACs for AF or VTE were prospectively enrolled. Patients were classified as frail, pre-frail, or non-frail according to frailty phenotype. Study outcomes were clinically relevant bleeding, including major and clinically relevant non-major bleeding, arterial and venous thromboembolism, and all-cause mortality.

##### Results

236 patients (median age 78 years, 44% females) were included, of whom 156 (66%) had AF and 80 (34%) VTE. Ninety-eight (41%) patients were frail, 115 (49%) pre-frail, and 23 (10%) non-frail. Inappropriately high or low dose DOAC was used in 33% of frail and in 20% of non-frail or pre-frail patients. Over a median follow-up of 304 days, the incidence of clinically relevant bleeding, thromboembolism, and mortality were 20%, 4%, 9% in frail, and 10%, 3%, and 2% in pre-frail, respectively, while no study outcome occurred among non-frail patients. Risk ratios (95% confidence intervals) for these outcomes in frail versus pre-frail and non-frail patients were respectively 2.5 (1.8, 3.7), 1.9 (0.9, 4.0), and 6.3 (2.9, 13.6).

##### Conclusion

In a prospective cohort of ambulatory patients receiving DOAC treatment for AF or VTE, frailty phenotype identified patients at higher risk of bleeding and all-cause mortality. Frailty assessment could be valuable to guide targeted interventions potentially improving patient prognosis.

**Disponible en:** [10.1111/jgs.18001](https://doi.org/10.1111/jgs.18001)

## Journal of Clinical Interventions In Aging

### Preoperative Risk Factor Analysis and Dynamic Online Nomogram Development for Early Infections Following Primary Hip Arthroplasty in Geriatric Patients with Hip Fracture

Cheng X, Liu Y, Wang W, Yan J, Lei X, Wu H, Zhang Y, Zhu Y

#### **Abstract**

##### Background:

Hip arthroplasty is in increasing demand with the aging of the world population, and early infections, such as pneumonia, surgical site infection (SSI), and urinary tract infection (UTI), are uncommon but fatal complications following hip arthroplasty. This study aimed to identify preoperative risk factors independently associated with early infections following primary arthroplasty in geriatric hip fracture patients, and to develop a prediction nomogram.

##### Methods:

Univariate and multivariate logistical analyses were performed to identify the independent risk factors for early infections, which were combined and transformed into a nomogram model. The prediction model was evaluated by using the area under the receiver operating characteristic curve (AUC), Hosmer–Lemeshow test, concordance index (C-index), 1000 bootstrap replications, decision curve analysis (DCA), and calibration curve.

##### Results:

One thousand eighty-four eligible patients got included and 7 preoperative variables were identified to be independently associated with early infections, including heart disease (odds ratio (OR): 2.17; P: 0.026), cerebrovascular disease (OR: 2.25; P: 0.019), liver disease (OR: 8.99; P: < 0.001), time to surgery (OR: 1.10; P: 0.012), hematocrit (44.52; OR: 2.73; P: 0.047), and high-sensitivity C-reactive protein (HCRP; > 78.64mg/L; OR: 3.71; P: < 0.001). For the nomogram model, AUC was 0.807 (95% confidence interval (CI): 0.742– 0.873), the Hosmer-Lemeshow test demonstrated no overfitting (P = 0.522), and C-index was 0.807 (95% CI: 0.742– 0.872) with corrected value of 0.784 after 1000 bootstrapping validations. Moreover, the calibration curve and DCA exhibited the tools' good prediction consistency and clinical practicability.

##### Conclusion:

Heart disease, cerebrovascular disease, liver disease, time to surgery, hematocrit, PMR, and HCRP were significant preoperative predictors for early infections following primary arthroplasty in elderly hip fracture patients, and the converted nomogram model had strong discriminatory ability and translatability to clinical application.

**Disponible en:** <https://doi.org/10.2147/CIA.S392393>

## Comparison of Perioperative Outcomes in Patients Undergoing Short-Level Lumbar Fusion Surgery After Implementing Enhanced Recovery After Surgery: A Propensity Score Matching Analysis Focusing on Young-Old and Old-Old

Cui P, Wang P, Hu X, Kong C, Lu S

### **Abstract**

#### Background:

There were exponentially increased studies focused on revealing the satisfactory outcomes after implementing enhanced recovery after surgery (ERAS) in patients undergoing lumbar fusion surgery. However, little attention has been paid to the impact of chronologic age alone on perioperative outcomes.

#### Methods:

In the present study, patients were dichotomized into two groups: young-old (65– 79 years), and old-old (80 years and older). Given the heterogeneity and age-related comorbidities in this population and the need to compare similar groups, we performed propensity score matching for gender, body mass index (BMI), operation time, American Society of Anesthesiologists (ASA) grade, Charlson Comorbidity Index (CCI), fusion levels and frail status. Perioperative outcomes were compared between two groups.

#### Results:

In our study, we found there were significant discrepancies in length of stay (LOS) ( $7.17 \pm 2.81$  vs  $8.11 \pm 3.57$  days,  $p = 0.031$ ) and postoperative nausea and vomiting (3.7% vs 11.0%,  $p = 0.038$ ); however, there were no significant differences in C-reactive protein ( $21.50 \pm 26.52$  vs  $19.22 \pm 22.04$  mg/L,  $p = 0.490$ ), overall complication rates (24.8% vs 33.0%,  $p = 0.179$ ), ambulation time ( $2.89 \pm 1.34$  vs  $2.55 \pm 1.49$  days,  $p = 0.078$ ) or removal of urinary catheter time ( $2.47 \pm 1.44$  vs  $2.32 \pm 1.40$  days,  $p = 0.446$ ).

#### Conclusion:

There were few differences in perioperative outcomes between young-old and old-old groups. Despite similar postoperative complication rates, the old-old group might experience longer LOS when complications occur. More importantly, current outcomes suggested that chronologic age alone does not appear to have the capacity to reflect the tolerance of elderly patients to surgery.

**Disponible en:** <https://doi.org/10.2147/CIA.S389927>

## **Prediction of Prognosis in Geriatric Palliative Care Patients with Diagnosed Malnutrition: A Comparison of Nutritional Assessment Parameters**

Deligöz Ö , Ekinçi O

### **Abstract**

#### **Objective:**

Malnutrition is very commonly encountered in palliative care centers (PCC), especially in geriatric patients. It is known that development of malnutrition increases morbidity and mortality. In this study, we aimed to investigate the effectiveness of commonly used nutritional assessment parameters in predicting prognosis in geriatric patients diagnosed in PCC with malnutrition.

#### **Methods:**

Our study included 1451 patients aged  $\geq 65$  years, who were diagnosed with malnutrition in PCC between 2016– 2020 and did not yet start receiving nutritional support. Demographic data, comorbidities, The Nutritional Risk Screening 2002 (NRS-2002), body mass index (BMI), albumin, prealbumin and C-reactive protein (CRP) values of the patients were recorded. Prognostic course was evaluated by dividing the patients into 3 groups, namely mortal patients during PCC follow-up, patients transferred from PCC to Intensive Care (ICU) and patients discharged to home from PCC.

#### **Results:**

Logistic Regression analysis showed that low albumin levels affected transfer to ICU ( $P < 0.05$ ). Elevated NRS-2002 and low albumin and prealbumin levels were found to be factors affecting mortality ( $P < 0.05$ ). Areas under the ROC Curve were calculated to attain patients' differential diagnosis. The area under the ROC Curve of low albumin in patients transferred to ICU was found to be significant ( $P < 0.05$ ). In the differential diagnosis of patients with mortal course, the area under the ROC Curve of low albumin and prealbumin and high CRP was found to be significant ( $P < 0.05$ ).

#### **Conclusion:**

We found that BMI had no prognostic predictive effects in geriatric PCC patients with malnutrition. We concluded that NRS-2002 and high CRP and low albumin and prealbumin can be used to predict mortality. In addition, we found that low albumin indicates a poor prognosis and predicts patients to be transferred to ICU.

**Disponible en:** <https://doi.org/10.2147/CIA.S38053>

## Geriatrics and Gerontology International

### Association between subjective cognitive complaints, balance impairment and disability among middle-aged and older adults: Evidence from a population-based cohort study

Raoping Tu, Suhang Wang, Huihui He, Jiali Ding, Qingping Zeng, Lu Guo, Yueping Li, Tianwei Xu, Guangyu Lu

#### **Abstract**

##### Aim

To quantify the association between subjective cognitive complaints and balance impairment in relation to the occurrence of disability.

##### Methods

In total, 6885 adults aged  $\geq 45$  who participated in the China Health and Retirement Longitudinal Study (CHARLS) were followed for 7 years. Subjective cognitive complaints were evaluated by self-reported memory problems. Balance impairment was tested by side-by-side stand, semi-tandem stand and full tandem stand. Disability was measured by activities of daily living (ADL) and instrumental activities of daily living (IADL). Multivariate logistic regression models were applied to test the joint effect between baseline subjective cognitive complaints and balance impairment on disability. The multiplicative interaction was examined.

##### Results

A joint effect of experiencing both subjective cognitive complaints and balance impairment was identified, showing a 1.63-fold higher risk of ADL and IADL disability than those experienced by neither of the two (odds ratio = 1.63, 95% confidence interval: 1.36–1.95). There was evidence of multiplicative interaction ( $P = 0.004$ ).

##### Conclusions

Among middle-aged and older people, the coexistence of subjective cognitive complaints and balance impairment may lead to a higher disability risk, which is much higher than the simple sum of the two individual effects. Future interventions are required to target these symptoms simultaneously to reduce the risks of disability.

**Disponible en:** <https://doi.org/10.1111/ggi.14501>

## International Journal of Geriatric Psychiatry

### Effect of vitamin D supplementation on depression in older Australian adults

Sabbir T. Rahman, Mary Waterhouse, Briony Duarte Romero, Catherine Baxter, Dallas R. English, Osvaldo P. Almeida, Michael Berk, Peter R. Ebeling, Bruce K. Armstrong

#### **Abstract**

##### Objectives

To investigate whether vitamin D supplementation reduces depressive symptoms and incidence of antidepressant use.

##### Methods

We used data from the D-Health Trial (N = 21,315), a randomized double-blind placebo-controlled trial of monthly vitamin D3 for the prevention of all-cause mortality. Participants were Australians aged 60–84 years. Participants completed the Patient Health Questionnaire (PHQ–9) at 1, 2 and 5 years after randomization to measure depressive symptoms; national prescribing records were used to capture antidepressant use. We used mixed models and survival models.

##### Results

Analyses of PHQ-9 scores included 20,487 participants (mean age 69.3 years, 46% women); the mean difference (MD) in PHQ-9 score (vitamin D vs. placebo) was 0.02 (95% CI –0.06, 0.11). There was negligible difference in the prevalence of clinically relevant depression (PHQ-9 score  $\geq 10$ ) (odds ratio 0.99; 95% CI 0.90, 1.08). We included 16,670 participants in the analyses of incident antidepressant use (mean age 69.4 years, 43% women). Incidence of antidepressant use was similar between the groups (hazard ratio [HR] 1.04; 95% CI 0.96, 1.12). In subgroup analyses, vitamin D improved PHQ-9 scores in those taking antidepressants at baseline (MD –0.25; 95% CI –0.49, –0.01; p-interaction = 0.02). It decreased risk of antidepressant use in participants with predicted 25(OH)D concentration  $< 50$  nmol/L (HR 0.88; 95% CI 0.75, 1.02; p-interaction = 0.01) and increased risk in those with predicted 25(OH)D  $\geq 50$  nmol/L (HR 1.10; 95% CI 1.01, 1.20).

##### Conclusion

Monthly supplementation with high-dose vitamin D3 was not of benefit for measures of depression overall, but there was some evidence of benefit in subgroup analyses.

**Disponible en:** <https://doi.org/10.1002/gps.5847>



## **Are neuropsychiatric symptoms a marker of small vessel disease progression in older adults? Evidence from the Lothian Birth Cohort 1936**

Una Clancy, Ratko Radakovic, Fergus Doubal, Maria del C. Valdés Hernández, Susana Muñoz Maniega, Adele M. Taylor, Janie Corley, Francesca M. Chappell, Tom C. Russ, Simon R. Cox

### **Abstract**

#### **Background**

Neuropsychiatric symptoms could form part of an early cerebral small vessel disease prodrome that is detectable before stroke or dementia onset. We aimed to identify whether apathy, depression, anxiety, and subjective memory complaints associate with longitudinal white matter hyperintensity (WMH) progression.

#### **Methods**

Community-dwelling older adults from the observational Lothian Birth Cohort 1936 attended three visits at mean ages 73, 76, and 79 years, repeating MRI, Mini-Mental State Examination, neuropsychiatric (Dimensional Apathy Scale, Hospital Anxiety and Depression Scale), and subjective memory symptoms. We ran regression and mixed-effects models for symptoms and normalised WMH volumes (cube root of WMH:  $ICV \times 10$ ).

#### **Results**

At age 73, 76, and 79,  $m = 672$ ,  $n = 476$ , and  $n = 382$  participants attended MRI respectively. Worse apathy at age 79 was associated with WMH volume increase ( $\beta = 0.27$ ,  $p = 0.04$ ) in the preceding 6 years. A 1SD increase in apathy score at age 79 associated with a 0.17 increase in WMH ( $\beta = 0.17$  normalised WMH percent ICV,  $p = 0.009$ ). In apathy subscales, executive ( $\beta = 0.13$ ,  $p = 0.05$ ) and emotional ( $\beta = 0.13$ ,  $p = 0.04$ ) scores associated with increasing WMH more than initiation scores ( $\beta = 0.11$ ,  $p = 0.08$ ). Increasing WMH also associated with age ( $\beta = 0.40$ ,  $p = 0.002$ ) but not higher depression ( $\beta = -0.01$ ,  $p = 0.78$ ), anxiety ( $\beta = 0.05$ ,  $p = 0.13$ ) scores, or subjective memory complaints ( $\beta = 1.12$ ,  $p = 0.75$ ).

#### **Conclusions**

Apathy independently associates with preceding longitudinal WMH progression, while depression, anxiety, and subjective memory complaints do not. Patients with apathy should be considered for enrolment to small vessel disease trials.

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## **Use of benzodiazepine and Z-drugs and mortality in older adults after myocardial infarction**

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### **Abstract**

#### **Background**

The adverse cardiovascular effects of benzodiazepines and Z-drugs (jointly referred as BZDRs) have been of concern. Yet, little is known about the use of BZDRs in relation to mortality risk among older adults with myocardial infarction history (post-MI).

#### **Methods**

This study is a secondary analysis of the Alpha Omega Cohort study, comprising post-MI patients aged 40–60 years. Self-reported information on the use of BZDRs, including types and dose, was collected at baseline. Four categories of mortality were examined, namely all-cause mortality, cardiovascular (CVD) mortality, cancer mortality, and non-CVD/non-cancer mortality. Associations between BZDRs use, by types and doses, and mortality were estimated with Cox regression models, adjusted for demographic and classic cardiovascular risk factors.

#### **Results**

A total of 433 (8.9%) out of 4837 (21.8% females) patients reported BZDRs use at baseline. During a median follow-up of 12.4 years, 2287 deaths were documented, of which 825 (36.1%) were due to CVD. BZDRs use was related to a statistically significantly higher risk of all-cause and CVD mortality; adjusted hazard ratios [95% CI] were (1.31 [1.41, 1.52]) and (1.43 [1.14, 1.81]), respectively. These relationships were dose-dependent—patients using BZDRs on an as-needed basis had similar risks compared to the non-uses, whereas patients with a daily use schedule and increasing doses had higher risks (p-value for trend: <0.001).

#### **Conclusion**

BZDRs use was independently associated with a higher risk of all-cause and cardiovascular mortality in older post-MI patients, and there was evidence for a dose-dependent relationship.

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