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

## REVISTAS FARMACÉUTICAS

## ANNALS OF PHARMACOTHERAPY

### Emergency Department Visits for Psychotropic-Related Adverse Drug Events in Older Adults With Alzheimer Disease, 2013-2014

Aryana Sepassi PharmD, Jonathan H. Watanabe, PharmD, MS, PhD

**Abstract**

**Background/objectives**

More than 1.3 million emergency department visits have been associated with adverse drug events (ADEs) in older adults. Increasing Alzheimer's disease (AD) prevalence in the geriatric population poses an additive risk of ADEs because of the array of psychotropic medications prescribed for AD patients. Scant research has been conducted at a nationwide level on psychotropic-related ADEs in this population. This study aimed to determine the incidence and economic burden of psychotropic ADEs in the geriatric AD population compared with the non-AD geriatric population.

**Methods**

A retrospective analysis was conducted of geriatric AD patients who visited the ED in 2013 with a psychotropic-related ADE to determine the incidence and resource utilization of these events. The relationship between presence of AD and an ADE was analyzed using multiple logistic regression.

**Results**

There were 427 969 Alzheimer's ED visits compared with 20 492 554 ED visits without. Of the AD cases, 1.04% were associated with at least 1 adverse event. AD cases more frequently were admitted as inpatients (64.90% vs 34.92%, $P < 0.01$). Common drug classes associated with AD-related ADEs were benzodiazepines, antipsychotics, and autonomic nervous system–affecting agents (adrenergic agonists, antimuscarinic agents, anticholinergic agents). There was a significantly higher likelihood for Alzheimer's cases to experience any psychotropic-related adverse event (OR = 1.66; 95% CI = 1.20, 1.82)

**Conclusions**

Alzheimer's patients more frequently experienced psychotropic-related adverse events and related adverse outcomes than older adults without Alzheimer's. Application of these findings should be implemented in protocol development to reduce future psychotropic-related adverse outcomes for this population.

Disponible en: https://journals.sagepub.com/doi/full/10.1177/1060028019866927

EUROPEAN JOURNAL OF CLINICAL PHARMACY

# Evaluation of use, efficacy and safety of sacubitril/valsartan

Canales Siguero D, Caro Teller JM, Martínez de la Torre F, Ferrari Piquero JM.

**Abstract**

**Background**

Sacubitril/valsartan is the only drug marketed as a neprilysin inhibitor to treat heart failure. The results of the clinical trial PARADIGM-HF led to its approval in Spain in 2015. The AEMPS issued a therapeutic positioning report that defined the criteria for use for a specific population. The objective is to analyze its efficacy and safety in the health and hospital area class 5 (cluster classification of hospitals) and to evaluate the suitability of the prescription to the therapeutic positioning report.

**Methods**

A retrospective observational study that included patients with heart failure treated with sacubitril/valsartan from its commercialization until March 2018.
It was recorded if the patients met the criteria of initiation according to therapeutic positioning report: functional class II-IV NYHA, left ventricular ejection fraction (LVEF)≤35%, previous treatment optimized with angiotensin-converting enzyme inhibitor or antagonist of the angiotensin II receptor, beta-blocker and aldosterone antagonist and plasma level of the amino-terminal fraction of the brain natriuretic peptide (NT-proBNP) elevated (≥600 pg/ml).
A follow-up was made through the electronic medical record. The variables collected were: age, sex, diagnosis, number of admissions, emergency visits and adverse events.

**Results**

We included 125 patients with 68.7±12.8 years. 100% of the prescriptions were made by Cardiology, adjusting in 38.4% to all the criteria of the therapeutic positioning report; 98.4% had heart failure II-IV NYHA, 81.6% had NT-proBNP levels>600 pg/ml, 69.6% had pre-treatment optimized and 65.6% of patients had LVEF≤35%. 26 patients (20.8%) presented hospital admissions and/or emergency visits due to decompensation of heart failure: there were 44 visits to the emergency and 23 hospital admissions (incidence of first hospitalization due to heart failure =13.6%). 88 patients (70.4%) presented adverse events that led to the suspension of treatment in 13 patients (10.2%). Most frequent adverse events: hypotension (40.8%), hyperkalemia (31.2%), and dizziness (28%) and impaired renal function (24.8%).

**Conclusion**

Less than 40% of the prescriptions were adapted to the therapeutic positioning report. The incidence of first hospitalization due to heart failure was slightly higher than that obtained from the clinical trial PARADIGM-HF. The most observed adverse effect was hypotension.

Disponible en: http://www.farmclin.com/seccion.asp?Id=8&articulo=1289

EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY

# Effectiveness of using STOPP/START criteria to identify potentially inappropriate medication in people aged ≥ 65 years with chronic kidney disease: a randomized clinical trial

Krystina Parker, Ingrid Bull-Engelstad, Jūratė Šaltytė Benth, Willy Aasebø, Nanna von der Lippe, Morten Reier-Nilsen, Ingrid Os, Knut Stavem

**Abstract**

**Background**

Polypharmacy and inappropriate prescribing are common in elderly with chronic kidney disease (CKD). This study identified potentially inappropriate prescriptions **(**PIPs) and potential prescribing omissions (PPOs) using the Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert doctors to the Right Treatment (START) criteria in elderly with advanced CKD and determined the effect of a medication review on medication adherence and health-related quality of life (HRQoL)

**Methods**

The intervention consisted of a medication review using STOPP/START criteria with a recommendation to a nephrologist or similar review without a recommendation. End points were prevalence of PIP and PPO, medication adherence, and HRQoL. Group differences in outcomes were assessed using a generalized linear mixed model.

**Results**

We randomized 180 patients with advanced CKD (mean age 77 years, 23% female). The prevalence of PIPs and PPOs in the intervention group was 54% and 50%, respectively. The odds of PPOs were lower in the intervention than the control group (OR 0.42, 95% CI 0.19–0.92, $p = 0.032$), while there was no intergroup difference in the number of PIPs (OR 0.57, CI 0.27–1.20, $p = 0.14$). There was no difference in changes in medication adherence or HRQoL from baseline to 6 months between the groups.

**Conclusion**

The intervention with the STOPP/START criteria identified a high prevalence of inappropriate medications in the elderly with advanced CKD and reduced the number of PPOs. However, there was no detectable impact of the intervention on medication adherence or HRQoL.

The trial was registered under www.clinicaltrial.gov (ID: NCT02424786).

Disponible en: https://link.springer.com/article/10.1007/s00228-019-02727-9

# Polypharmacy patterns in the last year of life in patients with dementia

Rachel Denholm, Richard Morris, Rupert Payne

**Abstract**

**Background Objective**

To describe prescribing of medicines in primary care in the last year of life in patients with dementia.

**Methods**

A retrospective cohort analysis in UK primary care using routinely collected data from the Clinical Practice Research Datalink. Number of medications and potentially inappropriate medication prescribed one year prior to, and including death, was ascertained.

**Results**

Dementia patients (*n* = 6923) aged 86.6 ± 7.3 years (mean ± SD) were prescribed 4.8 ± 4.0 drugs 1 year prior to death, increasing to 5.6 ± 4.0 2 months prior, before falling to 4.9 ± 4.1 at death. One year prior to death, 50% of patients were prescribed a potentially inappropriate medication, falling to 41% at death. Cardiovascular medications were the most common, with decreases in drug count only occurring in the last month prior to death. Prescriptions for gastrointestinal and central nervous system medication increased throughout the year, particularly laxatives/analgaesics, antidepressants and hypnotic/antipsychotics. Women (vs. men) and patients with Alzheimer's (vs. vascular dementia) were prescribed 4.7% (95% CI 2.3%–7%) and 14.6% (11.7–17.3%) fewer medications, respectively. Prescribing decreased with age and increased with additional comorbidities.

**Conclusions**

Dementia patients are prescribed high levels of medication, many potentially inappropriate, during their last year of life, with reductions occurring relatively late. Improvements to medication optimisation guidelines are needed to inform decision-making around deprescribing of long-term medications in patients with limited life-expectancy

Diponible en: https://link.springer.com/article/10.1007/s00228-019-02721-1

# THE SENIOR CARE PHARMACIST (AMERICAN SOCIETY OF CONSULTANT PHARMACISTS)

## Aspirin Use for Primary Prevention of Cardiovascular Disease in Older Patients: A Review of Clinical Guidelines and Updated Evidence

Lewis, Jelena; Bethishou, Laressa; Tsu, Laura V.

**Abstract**

**Background**

To provide an up-to-date review of current guidelines, previous trials, and new trials regarding aspirin use in primary prevention of cardiovascular (CV) disease in the elderly population.

The role of aspirin for primary prevention of CV disease in older adults is not well defined. As a result, the guideline recommendations for the use of aspirin in this setting are inconsistent. In 2018, the ARRIVE, ASCEND, and ASPREE studies were published. These studies tried to address some of the inconsistencies regarding the use of aspirin in primary prevention of CV disease. This article reviews the current recommendations along with previous and recent studies for aspirin use for primary prevention in older adults.

**Methods**

A PubMed search of articles published through April 2019 was performed using a combination of the following words: aspirin, bleeding, cardiovascular, elderly, hemorrhage, myocardial infarction, primary prevention, stroke. Relevant randomized controlled trials, meta-analyses, and guidelines were assessed for the use of aspirin in primary prevention of CV disease in older patients. References from the above literature were also evaluated. Articles were selected for inclusion based on relevance to the topic, detailed methods, and complete results.

**Results and conclusions**

The role of aspirin for primary prevention of CV disease in older adults should be individualized based on patient's risk factors, including risk of CV disease and likelihood of bleeding. Updated evidence provides more guidance regarding which patient populations will benefit from therapy.

Disponible en: https://www.ingentaconnect.com/contentone/ascp/tscp/2019/00000034/00000009/art00004

# REVISTAS GERIÁTRICAS

# BMC GERIATRICS

## Systematic review and meta-analysis of second-generation antidepressants for the treatment of older adults with depression: questionable benefit and considerations for frailty

Laurie Mallery, Tanya MacLeod, Michael Allen, Pamela McLean-Veysey, Natasha Rodney-Cail, Evan

**Abstract**

**Background**

Frail older adults are commonly prescribed antidepressants. Yet, there is little evidence to determine the efficacy and safety of antidepressants to treat depression with concomitant frailty. To better understand this issue, we examined the efficacy and safety of second-generation antidepressants for the treatment of older adults with depression and then considered implications for frailty.

**Methods**

Due to the absence of therapeutic studies of frail older adults with depression, we conducted a systematic review and meta-analysis of double-blind, randomized controlled trials that compared antidepressants versus placebo for adults with depression, age 65 years or older. We searched PubMed/MEDLINE, Cochrane Library, reference lists from meta-analyses/studies, hand searches of publication lists, and related articles on PubMed. Outcomes included rates of response, remission, and adverse events. After evaluating the data, we applied a frailty-informed framework to consider how the evidence could be applied to frailty.

**Results**

Nine trials were included in the meta-analysis (n = 2704). Subjects had moderate to severe depression. For older adults with depression, there was no statistically significant difference in response or remission to second-generation antidepressants compared to placebo. Response occurred in 45.3% of subjects receiving an antidepressant compared to 40.5% receiving placebo (RR 1.15, 95% CI: 0.96 – 1.37, p = 0.12, I2 = 71%). Remission occurred in 33.1% with antidepressant versus 31.3% with placebo (RR 1.10, 95% CI: 0.92 – 1.31, p = 0.30, I2 = 56%) (Figure 2 and 3). There were more withdrawals due to adverse events with antidepressants, 13% versus 5.8% (RR 2.30, 95% CI: 1.45–3.63; p < 0.001; I2 = 61%; NNH 14, 95% CI:10–28).

**Implications for frailty**

Subjects in the meta-analysis did not have obvious characteristics of frailty. Using framework questions to consider the implications of frailty, we hypothesize that, like older adults, frail individuals with depression may not respond to antidepressants. Further, observational studies suggest that those who are frail may be less responsive to antidepressants compared to the non-frail. Given the vulnerability of frailty, adverse events may be more burdensome.

**Conclusions**

Second-generation antidepressants have uncertain benefit for older adults with depression and cause more adverse events compared to placebo. Until further research clarifies benefit, careful consideration of antidepressant prescribing with frailty is warranted.

Disponible en: https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-019-1327-4

# REVISTAS DE MEDICINA GENERA

# ATENCIÓN PRIMARIA

## Riesgo de enfermedad neumocócica en pacientes ancianos con y sin vacunación previa

María Flores-Copetea, Ricardo Reolid-Martíneza, Mónica López-Garcíab, Pilar Alcantud-Lozanoc, Esther Mudarra-Terceroc, Milagros Azorín-Rasc, María del Campo-Giménezc, M. Candelaria Ayuso-Rayaa, Francisco Escobar-Rabadánc

**Resumen**

**Objetivos**

Conocer la cobertura vacunal antineumocócica en pacientes≥65 años, así como el riesgo de enfermedad neumocócica según hayan o no recibido dicha vacunación.

**Diseño** Estudio transversal, seguido de cohorte histórica.

**Emplazamiento** Ámbito urbano.

**Participantes**

Se seleccionaron por muestreo sistemático 2.805 personas≥65 años de la ciudad de Albacete.

**Mediciones principales**

Variable dependiente: diagnóstico de enfermedad neumocócica y fecha. Variables independientes: edad, sexo, enfermedades crónicas, medicación, vacunación antineumocócica y fecha. Se revisaron las historias clínicas informatizadas, de 1-1-2009 a octubre-diciembre de 2015. Se ha realizado un análisis descriptivo, se ha calculado el riesgo relativo de aparición de enfermedad neumocócica según la vacunación y se ha realizado un análisis de supervivencia con el programa estadístico SPSS 17.0.

**Resultados**

La mediana de edad era de 71 años; el 57,2% eran mujeres. Recibieron vacuna polisacárida el 46,0% (IC 95% 44,1-47,8). Solo 10 recibieron la conjugada. Fueron diagnosticadas de enfermedad neumocócica invasiva 22 personas, y de no invasiva, 153. El riesgo relativo de enfermedad neumocócica en vacunados frente a no vacunados, respectivamente para invasiva y no invasiva, era 1,59 (IC 95% 0,69-3,68) y 1,84 (IC 95% 1,33-2,54). Por regresión de Cox se demostró un mayor riesgo de enfermedad no invasiva para EPOC (1,95; IC 95% 1,32-2,89), tabaquismo (1,87; IC 95% 1,28-2,73), corticoterapia (1,73; IC 95% 1,08-2,79), vacunación polisacárida (141,41; IC 95% 5,92-3.378,49) y edad (1,11; IC 95% 1,08-1,14), con interacción entre estas 2 (0,94; IC 95% 0,91-0,98).

**Conclusiones**

Existe un mayor riesgo de presentar enfermedad neumocócica en pacientes≥65 años vacunados con la polisacárida, si bien habría que considerar un efecto protector en los vacunados de mayor edad.

Disponible en: https://www.elsevier.es/es-revista-atencion-primaria-27-pdf-S0212656718302348

REVISTA CLINICA ESPAÑOLA

# Simplificación de la escala de Barthel para el cribado de fragilidad y dependencia severa en pacientes pluripatológicos

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**Resumen**

**Objetivos**
Analizar la sensibilidad (S), la especificidad (E) y los valores predictivos positivo (VPP) y negativo (VPN) de cada dimensión del índice de Barthel (IB) con respecto al cuestionario completo en pacientes pluripatológicos (PPP).

**Métodos**
Estudio transversal multicéntrico. Se consideraron dos puntos de corte del IB (≥90 puntos para el cribado de fragilidad y <60 puntos para el diagnóstico de dependencia severa). Para cada dimensión y combinaciones de dos dimensiones se calcularon la S, la E, el VPP y el VPN con respecto al IB completo.

**Resultados**
El IB medio de los 1.632 PPP incluidos (edad media de 77,9±9,8años, 53% varones) fue 69±31 (<90 en el 58,7% y <60 en el 31,4% de pacientes). La dimensión «alimentación» obtuvo los mayores VPN para tener un IB≥60 y ≥90 puntos (87% y 99,6%, respectivamente). Las dimensiones «deambular» y «subir y bajar escaleras» obtuvieron el mayor VPP para tener un IB≥60 y ≥90 (99,2/99,5% y 81/92%, respectivamente; la combinación de ambas preguntas aumentó el VPP al 95 y al 99,6%, respectivamente.

**Conclusiones**
Los PPP de ámbito hospitalario presentan con elevada frecuencia deterioro funcional. La dimensión referente a alimentarse obtuvo el mayor VPN, por lo que se puede utilizar para el diagnóstico de dependencia severa, mientras que la combinación de deambular y subir y bajar escaleras obtuvo el mayor VPP, pudiendo utilizarse para plantear el cribado de fragilidad de los PPP.

Disponible en: https://www.revclinesp.es/es-simplificacion-escala-barthel-el-cribado-articulo-S0014256519301110

JAMA INTERNAL MEDICINE

# Association Between Drug Treatments for Patients With Osteoporosis and Overall Mortality Rates. A Meta-analysis

Steven R. Cummings, Li-Yung Lui, Richard Eastell, et al

**Abstract**

**Importance** Previous studies have reported that drug treatments, particularly treatment with bisphosphonates, is associated with reduced overall mortality rates in addition to decreased fracture risk. If so, drug treatments should be recommended for this reason alone, regardless of a patient's risk of fracture.

**Objective** To assess whether randomized clinical trials demonstrate that treatment with bisphosphonates, particularly zoledronate, is associated with reduced mortality rates.

**Data Sources** Science Direct, MEDLINE, Embase, and the Cochrane Library were searched for randomized placebo-controlled clinical trials of drug treatments for osteoporosis published after 2009 and published or in press before April 19, 2019. Conference abstracts from annual osteoporosis society meetings were also included in the search.

**Study Selection** Included studies were clinical trials that (1) were randomized and placebo-controlled; (2) studied drug treatments with proven antifracture efficacy; (3) used agents at the approved dose for treatment of osteoporosis; and (4) had a duration of 1 year or more. Abstracts from the literature searches were reviewed for inclusion and exclusion criteria, and mortality rate data were abstracted from the article by 1 researcher and validated by a second. A total of 2045 records were screened; 38 (1.8%) were included in the meta-analyses.

**Data Extraction and Synthesis** The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist was followed for abstracting data and assessing data quality and validity. Data were pooled using random-effects models, and between-study variability was assessed using the $I^2$ index. The risk of bias for each study was assessed, and funnel plots and Egger and Begg statistics were used to evaluate publication bias.

**Main Outcomes and Measures** Associations of all drug treatments, particularly bisphosphonate and zoledronate treatments, with overall mortality.

**Results** Of 38 clinical trials that included 101 642 unique participants, 38 were included in the meta-analyses of all drug treatments (45 594 participants randomized to placebo; 56 048 to treatment); 21 clinical trials, of bisphosphonate treatments (20 244 participants randomized to placebo; 22 623 to treatment); and 6 clinical trials, of zoledronate treatments (6944 participants randomized to placebo; 6926 to treatment). No significant association was found between all drug treatments for osteoporosis and overall mortality rate (risk ratio [RR], 0.98; 95% CI, 0.91-1.05; $I^2$ = 0%). Clinical trials of bisphosphonate treatment (RR, 0.95; 95% CI, 0.86-1.04) showed no significant association with overall mortality. Also, clinical trials of zoledronate treatment (RR, 0.88; 95% CI, 0.68-1.13) showed no association with overall mortality rate; however, evidence existed for heterogeneity of the results ($I^2$ = 48.2%).

**Conclusions and Relevance** Results of this meta-analysis suggest that bisphosphonate treatment may not be associated with reduced overall mortality rates in addition to decreased fracture risk and should only be recommended to reduce fracture risk. Additional trials are needed to clarify whether treatment with zoledronate reduces mortality rates.

Disponible en: https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2747869

# Clinical Outcomes After Intensifying Antihypertensive Medication Regimens Among Older Adults at Hospital Discharge

Timothy S. Anderson, Bocheng Jing, Andrew Auerbach, et al

**Abstract**

**Importance** Transient elevations of blood pressure (BP) are common in hospitalized older adults and frequently lead practitioners to prescribe more intensive antihypertensive regimens at hospital discharge than the patients were using before hospitalization.

**Objective** To investigate the association between intensification of antihypertensive regimens at hospital discharge and clinical outcomes after discharge.

**Design, Setting, and Participants** In this retrospective cohort study, patients 65 years and older with hypertension who were hospitalized in Veterans Health Administration national health system facilities from January 1, 2011, to December 31, 2013, for common noncardiac conditions were studied. Data analysis was performed from October 1, 2018, to March 10, 2019.

**Exposures** Discharge with antihypertensive intensification, defined as receiving a prescription at hospital discharge for a new or higher-dose antihypertensive than was being used before hospitalization. Propensity scores were used to construct a matched-pairs cohort of patients who did and did not receive antihypertensive intensifications at hospital discharge.

**Main Outcomes and Measures** The primary outcomes of hospital readmission, serious adverse events, and cardiovascular events were assessed by competing risk analysis. The secondary outcome was the change in systolic BP within 1 year of hospital discharge.

**Results** The propensity-matched cohort included 4056 hospitalized older adults with hypertension (mean [SD] age, 77 [8] years; 3961 men [97.7%]), equally split between those who did vs did not receive antihypertensive intensifications at hospital discharge. Groups were well matched on all baseline covariates (all standardized mean differences <0.1). Within 30 days, patients receiving intensifications had a higher risk of readmission (hazard ratio [HR], 1.23; 95% CI, 1.07-1.42; number needed to harm [NNH], 27; 95% CI, 16-76) and serious adverse events (HR, 1.41; 95% CI, 1.06-1.88; NNH, 63; 95% CI, 34-370). At 1 year, no differences were found in cardiovascular events (HR, 1.18; 95% CI, 0.99-1.40) or change in systolic BP among those who did vs did not receive intensifications (mean BP, 134.7 vs 134.4; difference-in-differences estimate, 0.6 mm Hg; 95% CI, −2.4 to 3.7 mm Hg).

**Conclusions and Relevance** Among older adults hospitalized for noncardiac conditions, prescription of intensified antihypertensives at discharge was not associated with reduced cardiac events or improved BP control within 1 year but was associated with an increased risk of readmission and serious adverse events within 30 days.

Disponible en: https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2747871