# REVISIÓN BIBLIOGRÁFICA ENERO 2021: Selección de artículos

## REVISTAS GERIÁTRICAS

## Age and Ageing

### The burden of psychotropic and anticholinergic medicines use in care homes: population-based analysis in 147 care homes

Paula Grill, Charis Marwick, Nicosha De Souza, Jennifer Kirsty Burton, Carmel Hughes, Bruce Guthrie

**Background**

older people living in care-homes are particularly vulnerable to adverse effects of psychotropic and anticholinergic drugs.

**Methods**

anonymised dispensed prescription data from all 4,478 residents aged ≥ 60 years in 147 care-homes in two Scottish health boards were analysed. Psychotropic medicines examined were antipsychotics, antidepressants, hypnotic/anxiolytics, opioids and gabapentinoids. Anticholinergic burden was measured using the modified anticholinergic risk scale (mARS). Variation between care-homes and associations with individual and care-home characteristics were examined using multilevel logistic regression.

**Results**

63.5% of residents were prescribed at least one psychotropic drug, and 27.0% two or more, most commonly antidepressants (41.6%), opioids (20.3%), hypnotic/anxiolytics (16.9%) and antipsychotics (16.7%). 48.1% were prescribed an anticholinergic drug, and 12.1% had high anticholinergic burden (mARS ≥ 3). Variation between care-homes was high for antipsychotics (intra-cluster correlation coefficient [ICC] 8.2%) and hypnotics/anxiolytics (ICC = 7.3%), and moderate for antidepressants (ICC = 4.7%) and anticholinergics (ICC = 2.8%). Prescribing of all drugs was lower in the oldest old. People with dementia were more likely to be prescribed antipsychotics (adjusted OR = 1.45, 95%CI 1.23–1.71) but less likely to be prescribed anticholinergics (aOR = 0.61, 95%CI 0.51–0.74). Prescribing of antipsychotics was higher in Tayside (aOR = 1.52, 95%CI 1.20–1.92), whereas prescribing of antidepressants (particularly tricyclic-related) was lower (aOR = 0.66, 95%CI 0.56–0.79). There was no association with care-home regulator quality scores.

**Conclusion**

care-home residents have high psychotropic and anticholinergic burden, with considerable variation between care-homes that is not related to existing measures of quality of care. Research to better understand variation between care-homes and the interaction with local prescribing cultures is needed.

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# Archives of Gerontology and Geriatrics

## Utilization and Spending on Potentially Inappropriate Medications by US Older Adults with Multiple Chronic Conditions using Multiple Medications

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**Background**:
The utilization of potentially inappropriate medications (PIMs) in older adults can lead to adverse events and increased healthcare costs. Polypharmacy, the concurrent utilization of multiple medications, is common in older adults with multiple chronic conditions.

**Objective**:

To investigate the utilization and costs of PIMs in multimorbid older adults with polypharmacy over time.

**Methods:**

This retrospective cross-sectional study used linked Medicare claims and electronic health records from seven hospitals/medical centers in Massachusetts (2007-2014). Participants were ≥65 years old, had ≥2 chronic conditions (to define multimorbidity), and used drugs from ≥5 pharmaceutical classes for ≥90 days (to define polypharmacy). Chronic conditions were defined using the Chronic Conditions Indicator from the Agency for Health Research and Quality. PIMs were defined using the American Geriatrics Society 2019 version of the Beers criteria. We calculated the percentage of patients with ≥1 PIMs and the percentages of patients using different types of PIMs. We used logistic regression analyses to test the odds of taking ≥1 PIMs. We calculated mean costs spent on PIMs by dividing the costs spent on PIMs by the total medication cost.

**Results**:

≥69% of patients used ≥1 PIM. After adjusting for healthcare utilization, chronic conditions, medication intake, and demographic factors, female sex (2014: Odds ratio (OR)=1.20, 95%CI: 1.17-1.22), age (2014: OR=0.92, 95%CI: 1.25-1.30), and Hispanic ethnicity (2014: OR=1.41, 95%CI: 1.27-1.56) were associated with PIM use. Gastrointestinal drugs and central nervous system drugs were the most commonly-used PIMs. In patients using ≥1 PIM, >10% of medication costs were spent on PIMs.

**Conclusion**:

The utilization of PIMs in US older adults with multimorbidity and polypharmacy is high.

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# Drugs and Aging

## Differential Diagnoses and Clinical Implications of Medication Nonadherence in Older Patients with Chronic Kidney Disease: A Review

Montgomery T. Owsiany, Chelsea E. Hawley & Julie M. Paik

**Abstract**

Older adults with chronic kidney disease (CKD) often have many comorbidities, which requires them to take multiple medications. As the number of daily medications prescribed increases, the risk for polypharmacy increases. Understanding and improving medication adherence in this patient population is vital to avoiding the drug-related adverse events of polypharmacy. The primary objective of this review is to summarize the existing literature and to understand the factors leading to medication nonadherence in older patients with CKD. In this review, we discuss the prevalence of polypharmacy, the current lack of consensus on the incidence of medication nonadherence, the heterogeneity of assessing medication adherence, and the most common differential diagnoses for medication nonadherence in this population. Specifically, the most common differential diagnoses for medication nonadherence in older adults with CKD are (1) medication complexity; (2) cognitive impairment; (3) low health literacy; and (4) systems-based barriers. We provide tailored strategies to address these differential diagnoses and subsequently improve medication adherence. The clinical implications include deprescribing to decrease medication complexity and polypharmacy, utilizing a team-based approach to identify and support patients with cognitive impairment, enriching communication between health providers and patients with low health literacy, and improving health care access to address systems-based barriers. Further research is needed to determine the effects of addressing these differential diagnoses and medication adherence in older adults with CKD.

Disponible en: https://doi.org/10.1007/s40266-020-00804-8

## Pharmacist Identification of Medication Therapy Problems Involving Cognition Among Older Adults Followed by a Home-Based Care Team

Allison M. P. Levine, Erin E. Emonds, Marie A. Smith, Nathaniel M. Rickles, George A. Kuchel, David C. Steffens, Alis Ohlheiser & Richard H. Fortinsky.

**Abstract**

**Background**

Dementia, depression, and delirium alone or in combination (3Ds) can threaten independence among older adults, and polypharmacy may further accelerate decline. Clinical pharmacists can play an important role on multidisciplinary home-based care teams by identifying medication therapy problems (MTPs) involving cognition. Within a larger ongoing clinical trial, this paper describes cognition-related MTPs and pharmacist recommendations among older adults with 3Ds followed by a home-based care team.

**Methods**

We conducted a retrospective analysis of medication data among Medicare Advantage members aged ≥ 65 years living at home in Connecticut with International Statistical Classification of Diseases and Related Health Problems, 10th Revision codes related to 3Ds; analyses include the first 105 subjects randomized to the home-based care team from March 2017 to January 2019.

Advanced practice registered nurses conducted in-home medication reconciliations along with medical and cognitive assessments. Clinical pharmacists then conducted medication reviews centered on agents treating or exacerbating 3Ds. After review by the study advanced practice registered nurse, geriatrician, and psychiatrist, salient recommendations were forwarded to primary care providers for consideration. Medication therapy problems related to cognition were retrospectively abstracted and classified as: (1) indication: underuse or overuse; (2) effectiveness: ineffective agent or low dose (mainly for antidepressants); and (3) safety: undesirable effect (e.g., impaired cognition, dementia treatment side effects), unsafe medication (e.g., potentially inappropriate medications that can harm cognition), drug interaction, or high dose.

**Results**

Pharmacists identified 166 cognitive MTPs, with a mean (standard deviation) of 1.58 (1.35) [range 0–6] MTPs per subject. Indication MTPs represented 34% of total MTPs, of which 79% involved underuse and 21% overuse; effectiveness represented 13% of total MTPs; and safety represented over half (52%) of all MTPs, with benzodiazepines and anticholinergics frequently implicated. Recommendations commonly included medication reduction (discontinuation 23% and dose reduction 19%). We found MTPs involving cognition among most (79%) patients.

**Conclusions**

Our study findings support the role of pharmacists on multidisciplinary teams to identify cognitively harmful medications, dementia treatment side effects, and untreated cognitive conditions.

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# Geriatrics and Gerontology International

## Association of drugs with special caution in the guidelines with falls: A case–control and case–crossover study in Japan

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**Abstract**

**Aim**

To determine the relationship between multiple medications and falls.

**Methods**

This case–control and case–crossover study was carried out at Kudanzaka Hospital in Chiyoda, Tokyo, Japan. A total of 325 patients who experienced their first falls when hospitalized between January 2016 and November 2018, and 1285 controls matched by sex, age and clinical departments were included in this study. Hospitalization duration and fall risk score were adjusted for in the analyses.

**Results**

In the case–control study, multivariable logistic regression showed that increasing the intake of oral medications was not significantly associated with the incidence of falls (odds ratio 1.02, 95% confidence interval 0.998–1.049). In contrast, drugs prescribed with special caution in accordance with the Elderly Oral Medication Guidelines were significantly associated with falls (odds ratio 1.17, 95% confidence interval 1.09–1.26). A similar pattern was observed in the case–crossover analysis. Among the drugs to be prescribed with special caution according to the guidelines, atypical antipsychotics, non-benzodiazepine hypnotics and magnesium oxide were significantly associated with the risk of falls.

**Conclusion**

The drugs to be prescribed with special caution according to the guidelines were associated with an increased fall risk. The risk of falls in hospitalized older people due to multiple medications varies among medications

Disponible en: **https://doi.org/10.1111/ggi.14127**

# Journal of Geriatric Oncology

## Efficacy and safety of Nivolumab in older patients with pretreated lung cancer: A subgroup analysis of the Galician lung cancer group

David Arias Ron, Maria Carmen Areses Manrique, Joaquín Mosquera Martínez, Jorge García González, Francisco Javier Afonso Afonso, Martín Lázaro Quintela, Natalia Fernández Núñez, et al

**Abstract**

**Background**

Nivolumab is an anti PD1 immunotherapy drug approved for advanced Non-Small Cell Lung Cancer (NSCLC) patients who previously received at least one prior line of treatment. Older patients are often not represented in clinical trials and drugs with acceptable safety profiles are necessary. We aim to report the efficacy and safety profile of Nivolumab in the real-world older subgroup of the Galician lung cancer group study.

**Patients and Methods**

We retrospectively reviewed 188 advanced NSCLC patients treated with at least one prior therapy. We collected data from patients who were ≥70 years old treated with Nivolumab in second or subsequent lines. Patient characteristics, treatment efficacy (overall survival, progression-free survival, and response rate), and safety profile were reported.

**Results**

Thirty-eight patients aged ≥70 years were included in the subgroup analysis. The median age was 74.5 years, a high percentage of patients were males (95%), most had a Performance Status of 1 (79%) and only 13% were non-smokers. The predominant histology was adenocarcinoma (53%), and 18% of patients received 2 or more lines. The median Progression-Free Survival was 7.53 months (CI 4.3–17.3, $p = 0.15$) and the median Overall Survival was 14.85 months (CI 10.5–20.7, $p = 0.44$). The objective response rate was 42%. No new adverse events were reported in comparison to a global population.

**Conclusions**

The efficacy and safety profile of Nivolumab in advanced NSCLC patients treated with at least one prior therapy and age ≥70 years old can be overlapped to a global population. Further prospective trials are needed to define and confirm these results.

Disponible en: DOI:https://doi.org/10.1016/j.jgo.2020.11.010

# International Journal of Geriatric Psychiatry

## Benzodiazepines and antidepressants: Effects on cognitive and functional decline in Alzheimer's disease and Lewy body dementia

Miguel Germán Borda, Alberto Jaramillo-Jimenez, Ragnhild Oesterhus, Jose Manuel Santacruz, Diego Alejandro Tovar-Rios, Hogne Soennesyn, Carlos Alberto Cano-Gutierrez

**Abstract**

**Objectives**

We aim to study the effects of the prescription of benzodiazepines and antidepressants on cognitive and functional decline in older adults living with Alzheimer's disease (AD) and Lewy body dementia (LBD) over a 5-year follow-up.

**Methods**

This is a longitudinal analysis of a Norwegian cohort study entitled "The Dementia Study of Western Norway" (DemVest). We included 196 patients newly diagnosed with AD (n = 111) and LBD (n = 85), followed annually for 5 years. Three prescription groups were defined: only benzodiazepines (BZD), only antidepressants (ADep), and the combination of benzodiazepines and antidepressants (BZD-ADep). Linear mixed-effects models were conducted to analyze the effect of the defined groups on the outcomes. The outcomes were functional decline, measured by the Rapid Disability Rating Scale—2, and cognition measured with the Mini-Mental State Examination.

**Results**

Prescription of the combination of benzodiazepines and antidepressants in LBD was associated with faster functional decline. In AD, the prescription of BZD and BZD-ADep was associated with greater functional deterioration. ADep alone did not show positive or negative significant associations with the studied outcomes.

**Conclusions**

BZD and especially the combination of BZD and ADep are associated with functional decline in AD and LBD and should be used cautiously.

Disponible en: **https://doi.org/10.1002/gps.5494**

# REVISTAS FARMACÉUTICAS

# European Journal of Clinical Pharmacology

## Benzodiazepine withdrawal in older people: what is the prevalence, what are the signs, and which patients?

Alexandra Jobert, Edouard-Jules Laforgue, Marie Grall-Bronnec, Morgane Rousselet, Morgane Péré, Pascale Jolliet, FAN-Network, Fanny Feuillet & Caroline Victorri-Vigneau

**Abstract**

**Purpose**

Benzodiazepines (BZDs) and related drugs (Z-drugs) are mainly taken chronically, and older people are much more likely to take them on a chronic basis despite recommendations. Withdrawal symptoms could be an obstacle to stopping BZD/Z-drug administration. The main objective of this study is to estimate the prevalence of withdrawal symptoms in patients aged 65 years and older who have experience a stop of BZD/Z-drug. The secondary objectives are to describe the withdrawal symptoms and identify factors associated.

**Method**

This ancillary study was based on a national observational study in patients with chronic BZD/Z-drug consumption. Patients who made at least one BZD/Z-drug stop experience were selected. Withdrawal symptoms are described, and a logistic regression was carried out to identify the variables most associated with withdrawal symptoms.

**Results**

In total, 697 patients were selected: 78% experienced at least one withdrawal symptom after a stop administering BZDs or Z-drugs; most of the withdrawal symptoms were psychological disorders.

**Conclusion**

Our study identifies a specific population experiencing withdrawal symptoms and who cannot stop administering BZD/Z-drug. We assume that withdrawal symptoms in patients with chronic use play an essential role in the nonstop use of BZD/Z-drugs.

Disponible en: https://doi.org/10.1007/s00228-020-03007-7

# The Annals of Pharmacotherapy

## The Role of Sodium-Glucose Cotransporter-2 Inhibitors in Patients With Heart Failure, Regardless of Diabetes Status: Focus on Cardiovascular Disease

Filipe Ferrari, BSc, MSc, Vítor M. Martins, MD, PhD, Rafael S. Scheffel, MD, PhD,

**Abstract**

**Objective:**

To provide clinical guidance and an overview of the available data on the use of sodium-glucose cotransporter-2 (SGLT2) inhibitors in patients with heart failure with reduced ejection fraction (HFrEF), regardless of the presence of type 2 diabetes mellitus (T2DM).

**Data Sources:**

We searched the MEDLINE database via PubMed (from January 2015 to November 2020) for the following key terms: SGLT2 inhibitors, sodium-glucose co-transporter-2 inhibitors, SGLT2i, heart failure, and heart failure with reduced ejection fraction.

**Study Selection and Data Extraction:**

To be included in the review, the articles needed to assess the effects of SGLT2 inhibitors in the heart failure (HF) scenario.

**Data Synthesis:**

There is consistent evidence that SGLT2 inhibitors reduce the risk of major adverse cardiovascular (CV) events and hospitalization in patients with HFrEF, even in the absence of T2DM. On May 5, 2020, the U.S. Food and Drug Administration approved dapagliflozin for adults with HFrEF, regardless of the presence of T2DM, even in those patients on standard therapy, including an angiotensin receptor/neprilysin inhibitor.

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

The SGLT2 inhibitors are well tolerated, and their once-daily dosing without the need for adjustments is convenient. These drugs can be considered a major breakthrough in pharmacotherapy for HF, providing physicians with a new treatment approach to reduce major clinical outcomes.

**Conclusions:**

SGLT2 inhibitor therapy reduces CV death and hospitalizations in HFrEF patients regardless of T2DM. The decision to prescribe this class of drugs should not be determined by glycemic status.

Disponible en: https://doi.org/10.1177/1060028020985111

# Journal of Clinical Pharmacy and Therapeutics

## Potentially inappropriate medications and potentially prescribing omissions in Chinese older patients: Comparison of two versions of STOPP/START

Zhuo Ma MS Yalan Tong MS Caixia Zhang BSc Lihong Liu PhD

**Abstract**

**What is known and objective**

The aim of this study was to compare the prevalence of potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs) in elderly Chinese patients identified by the Screening Tool of Older Persons' Prescriptions/Screening Tool to Alert to Right Treatment (STOPP/START) version 2 (v2) and version 1 (v1). The secondary objective was to analyse the risk factors associated with the PIMs/PPOs.

**Methods**

This was a retrospective cross-sectional study, and all patients were aged ≥65 years and discharged from internal medical wards of Beijing Chaoyang Hospital in December 2018. STOPP/START v2 and STOPP/START v1 were used to detect PIMs/PPOs. The concordance between the two versions was calculated using kappa tests. A logistic regression analysis was carried out to determine variables independently associated with PIM/PPO use.

**Results and discussion**

In the 662 patients included, the median age was 73 years and 361 were male (54.53%). PIMs were present in 36.1% and 47.7% of participants according to the STOPP v1 and STOPP v2, respectively. The prevalence of PPOs was 42.0% and 64.2% according to the START v1 and START v2, respectively. Drug prescribed without indication was the most common item in PIMs, whereas ACEIs were the drugs most frequently involved with PPOs according to the STOPP/START v2. Two versions of the STOPP criteria indicated a moderate coherence, whereas two versions of the START criteria showed poor accordance. Age (OR 1.029, 1.004-1.054), gender (OR 1.536, 1.103-2.138) and the number of prescribed medications (<5: OR 1; 5-9: OR 2.503, 1.173-5.342; ≥10: OR 4.324, 2.204-9.235) were associated factors with PIMs identified by the STOPP v2, whereas PPOs identified by the START v2 were independently associated with age (OR 1.039, 1.012-1.066), activities of daily living (ADL) score (OR 2.713, 1.818-4.048), the number of prescribed medications (<5: OR 1; 5-9: OR 2.704, 1.524-4.795; ≥10: OR 3.075, 1.704-5.549) and Charlson Comorbidity Index (OR 1.302, 1.110-1.529).

**What is new and conclusion**

This study showed a high prevalence of PIMs/PPOs in aged internal medical ward inpatients in China, which was associated with various correlates. The STOPP/START v2 had a higher detection rate than v1.

Disponible en: **https://doi.org/10.1111/jcpt.13237**

# REVISTAS DE MEDICINA GENERAL

# JAMDA: Journal of the American Medical Directors Association

## Antihypertensive Medication Classes and the Risk of Dementia: A Systematic Review and Network Meta-analysis

Melina G.H.E. den Brok, MD , Jan Willem van Dalen, PhD, Hanna Abdulrahman, MD, Willem A. van Gool, MD, Eric P. Moll van Charante, MD, PhD, Edo Richard, MD, PhD

**Abstract**

**Objectives**

To systematically review and synthesize the evidence on differential associations between antihypertensive medication (AHM) classes and the risk of incident dementia.

**Design**

Systematic review and random effects frequentist network meta-analysis. Embase, MEDLINE, and the Cochrane library were searched from origin to December 2019.

Setting and participants

Randomized controlled trials (RCTs) and prospective cohort studies that compared associations of different AHM classes with incident all-cause dementia and/or Alzheimer's disease over at least 1 year of follow-up.

**Measures**

All cause dementia and/or Alzheimer's disease.

**Results**

Fifteen observational studies and 7 RCTs were included. Data on AHM classes were available for 649,790 participants and dementia occurred in 19,600 (3.02%). Network meta-analysis showed that in observational studies, treatment with either calcium channel blockers (CCBs) or angiotensin II receptor blockers (ARBs) was associated with lower dementia risks than treatment with other antihypertensives: CCBs vs angiotensin converting enzyme inhibitors (ACE inhibitors) (HR=0.84, 95% CI 0.74-0.95), beta blockers (HR=0.83, 95% CI 0.73-0.95) and diuretics (HR=0.89, 95% CI 0.78-1.01) and ARBs vs ACE inhibitors (HR=0.88, 95% CI 0.81-0.97), beta blockers (HR=0.87, 95% CI 0.77-0.99), and diuretics (HR=0.93, 95% CI 0.83-1.05). There were insufficient RCTs to create a robust network based on randomized data alone.

**Conclusions and Implications**

Recommending CCBs or ARBs as preferred first-line antihypertensive treatment may significantly reduce the risk of dementia. If corroborated in a randomized setting, these findings reflect a low-cost and scalable opportunity to reduce dementia incidence worldwide.

Disponible en: DOI:https://doi.org/10.1016/j.jamda.2020.12.019

# European Journal of Internal Medicine

## Pharmacist-driven medication recognition/ reconciliation in older medical patients

Maria Teresa Chiarelli, Stefania Antoniazzi, Laura Cortesi, Alessandro Nobili

**Abstract**

**Background**

In older medical patients polypharmacy is often associated with poor prescription appropriateness and harmful drug-drug interactions. An effort that jointly involved hospital pharmacists and clinicians attending multimorbid older patients acutely admitted to medical wards was implemented for medication recognition and reconciliation aided by the use of a computerized support system.

**Methods**

Six internal medicine wards enrolled consecutively 90 acutely admitted multimorbid patients aged 75 years or more taking 5 or more different drugs. Two hospital pharmacists carried out the recognition of medications taken at hospital ward admission, and interacted with the clinicians in a process of drug reconciliation, using also the computerized support system to evaluate drug related problems, prescription inappropriateness or drug-drug interactions. The process was repeated at hospital discharge.

**Results**

Among a total number of 911 drugs prescribed to 90 older medical patients at ward admission, the pharmacists identified during their recognition/reconciliation 455 drug-related problems, mainly due to prescription of medications inappropriate for older multimorbid patients and clinically harmful drug-drug interactions. When these drug-related problems were identified by the pharmacist, the attending clinicians accepted and implemented the suggestions for changes for approximately two thirds of the discrepancies, thereby leading to deprescribing the implicated drugs or at least to their closer monitoring.

**Conclusions**

This interventional prospective study based upon the integrated expertise of hospital pharmacists and clinicians confirms that drug-related problems are frequent in multimorbid older patients acutely admitted to hospital medical wards, and demonstrates afresh the feasibility and mutual acceptance of a trajectory of recognition/reconciliation based upon an integrated collaboration between hospital pharmacists and ward clinicians in the process of medication optimization.

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