

# REVISIÓN BIBLIOGRÁFICA MARZO 2022: Selección de artículos

## **REVISTAS FARMACÉUTICAS**

### **British Journal of Clinical Pharmacology**

<u>Cost outcomes of potentially inappropriate prescribing in middle-aged</u> adults: A Delphi consensus and cross-sectional study

Ryan Jayesinghe, Frank Moriarty, Amandeep Khatter, Stevo Durbaba, Mark Ashworth, Patrick Redmond

#### **Abstract**

#### **Background**

Potentially inappropriate prescribing (PIP) is common in older adults and is associated with increased medication costs and costs of associated adverse drug events. PIP also affects almost 1/5 of middle-aged adults (45–64 y), as defined by the PRescribing Optimally in Middle-aged People's Treatments (PROMPT) criteria. However, there has been little research on PIP medication costs within this age group.

#### **Aims**

Calculate the medication costs of PIP for middle-aged adults according to the 22 PROMPT criteria and compare with the cost of consensus-validated, evidence-based (adequate) alternative prescribing scenarios.

#### Methods

Adequate alternatives to the 22 PROMPT criteria were created via literature review. A Delphi consensus panel of experts was recruited (n = 16), supported by a patient and public involvement group, to achieve consensus on the alternatives. A retrospective repeated cross-sectional study from 2014 to 2019 was then conducted utilising pseudonymised primary care data from Lambeth DataNet in South London (41 general practices,  $n = 1\ 185\ 335$ , using Lambeth DataNet May 2020 extract) to calculate the cost of PIP.

#### Results

The cross-sectional study included 55 880 patients. The total PIP cost was £2.79 million, with adequate alternative prescribing costing £2.74 million (cost savings of £51 278). Duplicate drug classes was the most costly criterion for both PIP and alternative prescribing.



#### Conclusion

This study calculated the medication costs of PIP and created alternative prescribing scenarios for the 22 PROMPT criteria. There is no substantial cost difference between adequate prescribing vs. PIP. Future studies should investigate the wider health economic costs of alternative prescribing, such as reducing hospital admissions.

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# 5-Alpha Reductase Inhibitors and the Risk of Anemia among Men with Benign Prostatic Hyperplasia: A Population-based Cohort Study

Henok Tadesse Ayele, Antonios Douros, Kristian B. Filion

#### **Background**

5-alpha reductase inhibitors ( $5\alpha RIs$ ) are effective for the treatment of benign prostatic hyperplasia (BPH). However,  $5\alpha RIs$  could lower levels of hemoglobin, increasing the risk of anemia.

#### Objective

To compare the rate of anemia between new users of  $5\alpha RIs$  and  $\alpha$ -blockers in the United Kingdom (UK).

#### **Methods**

We conducted a matched, active comparator, new-user cohort study using the Clinical Practice Research Datalink. The study population consisted of men aged 40+ years with incident BPH who initiated  $5\alpha RIs$  between 1998 and 2019 and were matched 1:1 on propensity score to new users of  $\alpha$ -blockers. Anemia was defined by a measured hemoglobin < 130 g/l. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for anemia.

#### **Results**

Our study cohort included 9,429 new users of  $5\alpha Rls$  and 9,429 matched new users of  $\alpha$ -blockers. Their median durations of follow-up were 136 days (interquartile range [IQR]: 54-336 days) and 77 days (IQR: 58-236), respectively. A total of 2,865  $5\alpha Rls$  users and 2,407  $\alpha$ -blocker users developed incident anemia, representing rates of 37.3 (95% CI: 33.6-41.3) and 42.0 (95% CI: 38.1-46.2) per 100 person-years, respectively. The use of  $5\alpha Rls$  was not associated with an increased risk of anemia compared to the use of  $\alpha$ -blockers (HR: 0.95, 95% CI: 0.90-1.00). Similarly, we did not observe an increased risk of mild, moderate, or severe anemia.

#### Conclusion

The use of  $5\alpha RIs$  was not associated with an increased risk of anemia compared to the use of  $\alpha$ -blockers among men with BPH.

Disponible: <u>https://doi.org/10.1111/bcp.15317</u>



## **Drug Safety**

## Intracranial Hemorrhage Following Anticoagulant Treatment in Denmark: Spontaneous Adverse Drug Reaction Reports Versus Real-World Data

Benedikte Irene von Osmanski, Astrid Blicher Schelde, Espen Jimenez-Solem, Martin Erik Nyeland & Henrik Horwitz

#### Introduction

In Denmark, physicians are legally obliged to report serious adverse drug reactions (ADRs), such as intracranial hemorrhage (ICH) following anticoagulant (AC) treatment, to the Danish Medicines Agency. We were therefore puzzled to discover a high number of reports concerning ICHs following treatment with the direct oral anticoagulants (DOACs) dabigatran, rivaroxaban, and apixaban compared with warfarin. This was surprising, as all DOACs have been found to be associated with a lower risk of ICH compared with warfarin in phase III randomized controlled trials.

#### **Objectives**

The primary aim of the study was to estimate the level of underreporting of ICH as an ADR following treatment with warfarin, dabigatran, rivaroxaban, and apixaban.

#### Methods

This observational study covered a 5-year period (2014–2018). Using nationwide registries held by the Danish Health Data Authority, the number of users, exposure time in person-years, and related ICH events for each of the study drugs were estimated. Data on ADR-ICH reports were extracted from the interactive ADR overviews held by the Danish Medicines Agency.

#### Results

From 2014 to 2018, 97.0% of the identified warfarin-related ICH events were not reported as ADRs. For the DOACs, the level of underreporting ranged from 88.8 to 90.8%.

#### Conclusion

We found a heavy and differentiated level of underreporting of ICH as an ADR following treatment with the four study drugs.

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### <u>Drug-Drug Interaction of the Sodium Glucose Co-Transporter 2 Inhibitors</u> <u>with Statins and Myopathy: A Disproportionality Analysis Using Adverse</u> <u>Events Reporting Data</u>

Wajd Alkabbani, Ryan Pelletier, Michael A. Beazely, Youssef Labib, Breanna Quan & John-Michael Gamble

#### Introduction

An increased risk of myopathy due to a potential interaction between sodium glucose cotransporter-2 inhibitors (SGLT-2i) and HMG-CoA reductase inhibitors (statins) has been suggested by case reports.

#### **Objective**

We aimed to assess if the reporting of myopathy is disproportionally higher among people using both SGLT-2i and statins compared to using either SGLT-2i or statins alone.

#### **Methods**

We conducted a disproportionality analysis using data from the US Food and Drug Administration Adverse Event Reporting System (FAERS). We included reports with at least one antihyperglycemic agent. We compared the proportion of myopathy cases to noncases between those not using SGLT-2i or statins, using SGLT-2i only, statins only, or both. We calculated the reporting odds ratio and 95% confidence interval. We further stratified by individual SGLT-2i and selected statins (rosuvastatin or atorvastatin).

#### Results

We included 688,388 reports with at least one antihyperglycemic agent recorded, of which 9.80% had at least one SGLT-2i agent. Among all included reports, there were a total of 2202 myopathy cases with the majority, 61.26%, occurring among those using statins alone and only 2.72% of myopathy cases were among those using both SGLT-2i and statins together. Reporting of myopathy was not disproportionally higher among those reporting the use of SGLT-2i with statins (reporting odds ratio 2.95, 95% confidence interval 2.27–3.85) compared to statins alone (reporting odds ratio 6.41, 95% confidence interval 5.86–7.02).

#### **Conclusions**

Reports of myopathy were not disproportionally higher among those using SGLT-2i with statins compared to SGLT-2i or statins alone at the class level. Further observational studies may be needed to better assess this interaction at the agent level.

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#### **β-Blockers and the Risk of Depression: A Matched Case–Control Study**

#### Delia Bornand, Daphne Reinau, Susan S. Jick & Christoph R. Meier

#### Introduction

Depression is a commonly cited adverse effect of  $\beta$ -blockers but the evidence for a causal relationship is limited.

#### Objective

We aimed to explore whether  $\beta$ -blockers are associated with an increased risk of new-onset depression.

#### **Methods**

We conducted a case–control study using the UK population-based Clinical Practice Research Datalink (CPRD) GOLD. We identified patients aged 18–80 years with an incident depression diagnosis between 2000 and 2016, and matched controls, and estimated the risk (odds ratio [OR]) of depression in association with use of  $\beta$ -blockers. We also conducted analyses of exposure, categorised by number and timing of prescriptions and by indication for  $\beta$ -blocker use.

#### **Results**

The study encompassed 118,705 patients with incident depression and the same number of matched controls. The odds of developing depression were increased for current short-term use of any  $\beta$ -blocker (adjusted OR [aOR] 1.91, 95% confidence interval [CI] 1.72–2.12), whereas current long-term use was not associated with the risk of depression compared with never use. The elevated risk of depression among short-term users was mostly confined to propranolol users with a neuropsychiatric disorder (aOR 6.33, 95% CI 5.16–7.76), while propranolol users with a cardiovascular indication were only at marginally increased risk of depression (aOR 1.44, 95% CI 1.14–1.82).

#### **Conclusions**

This study suggests that the association between use of  $\beta$ -blockers and depression may not be causal but rather a result of protopathic bias. Propranolol is often prescribed to treat neuropsychiatric symptoms, suggesting that the onset of depression may be related to the underlying indication rather than to an effect of a  $\beta$ -blocker therapy.

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### **European Journal of Clinical Pharmacology**

# <u>Plasma levels of direct oral anticoagulants in atrial fibrillation patients at the</u> time of embolic stroke: a pilot prospective multicenter study

Vladimír Nosál, Andrea Petrovičová, Ingrid Škorňová, Tomáš Bolek, Jana Dluhá, Lucia Stančiaková, Štefan Sivák, Lucia Babálová, Gabriel Hajaš, Ján Staško, Peter Kubisz, Egon Kurča, Matej Samoš & Marián Mokáň

#### **Background**

Patients with atrial fibrillation (AF) who are on long-term direct oral anticoagulants (DOAC) with low anti-Xa or anti-IIa levels may be at higher risk of recurrent stroke. However, no prospective post-marketing study has investigated these DOAC plasma levels at the time of embolic stroke. The aim of this study was to assess the anti-Xa (rivaroxaban, apixaban) and anti-IIa (dabigatran) plasma levels in DOAC-treated AF patients at the time of acute embolic stroke.

#### Patients and methods

We prospectively identified 43 patients with AF on long-term DOAC who experienced embolic strokes. We compared the DOAC plasma levels of these patients with a control sample of 57 patients who tolerated long-term therapeutic dose DOAC therapy without any adverse event. DOAC levels were assessed with drug-specific anti-Xa chromogenic analysis (rivaroxaban, apixaban) and with Hemoclot Thrombin Inhibitor assay (dabigatran).

#### **Results**

Dabigatran-treated patients with stroke had significantly lower anti-IIa levels when compared with the trough  $(40.7\pm36.9~vs.~85.4\pm57.2~ng/mL,~p<0.05)$  and peak samples of the controls  $(40.7\pm36.9~vs.~138.8\pm78.7~ng/mL,~p<0.001)$ . Similarly, there were significantly lower anti-Xa levels in apixaban-treated patients with stroke compared to the trough control samples  $(72.4\pm46.7~vs.~119.9\pm81.7~ng/mL,~p<0.05)$ , and in rivaroxaban-and apixaban-treated patients when compared to peak control samples (rivaroxaban:  $42.7\pm31.9~vs.~177.6\pm38.6~ng/mL,~p<0.001$ ; apixaban:  $72.4\pm46.7~vs.~210.9\pm88.7~ng/mL,~p<0.001$ ).

#### Conclusion

This observational study showed significantly lower anti-IIa and anti-Xa plasma levels in AF patients with embolic stroke compared to those who tolerated long-term therapeutic dose DOAC therapy.

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### Pharmacotherapy

# Effects of statin therapy and treatment duration on cardiovascular disease risk in patients with nephrotic syndrome: A nested case—control study

Xinliang Zou,Li Nie,Yi Liao,Zhihui Liu,Wanxiang Zheng,Xiaolong Qu,Xiang Xu,Haoran Qin,Haidong Wang,Jianping Liu,Guoxiang He,Tao Jing

#### **Abstract**

#### **Background**

Although statins are the cornerstone of lipid management, hardly any of the existing studies on statin treatment of dyslipidemia in nephrotic syndrome (NS) addressed patient-centered outcomes of cardiovascular events.

#### Objective

To evaluate whether statin treatment impacts the outcomes of cardiovascular events in patients with NS.

#### Design

A single-center, retrospective, nested case—control study analyzed data from the First Affiliated Hospital of Army Medical University.

#### **Patients**

Patients diagnosed with NS from January 1, 1999, to November 30, 2014, were selected and followed up for 5 years.

#### **Measurements and Main Results**

A total of 2706 patients with NS were enrolled in this study cohort. Among these, 115 patients diagnosed with cardiovascular disease (CVD) at the end of the observational period and 235 CVD-free controls enrolled by 1:2 matching with gender, age, and index time were included in the study. Propensity score matching was used to match (1:1) the baseline characteristics of the cases and controls. The chi-square test was performed based on whether the patient used a statin as an exposure factor, and binary logistic regression analysis of the association between cardiovascular events and statin therapy duration was conducted. Subgroup analyses for relevant variables were also performed. The chi-square test showed that statin therapy was significantly associated with a reduction in CVD risk in patients with NS (p = 0.002). Furthermore, the risk of cardiovascular events in patients with NS decreased as the length of statin treatment increased (OR = 0.82 [95% CI 0.73–0.89], p < 0.001).

#### **Conclusions**

For NS patients with dyslipidemia, statin therapy may be used to decrease CVD risk, and extended treatment was associated with more significant risk reduction.



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### Pharmacoepidemiology and Drug Safety

<u>PPIs may enhance the risk of citalopram- and escitalopram-associated</u> <u>sudden cardiac death among patients receiving hemodialysis</u>

Magdalene M. Assimon PharmD, PhD, Patrick H. Pun MD, MHS, Sana M. Al-Khatib MD, MHS, M. Alan Brookhart PhD, Bradley N. Gaynes MD, MPH

#### **Abstract**

#### **Purpose**

Polypharmacy is common in the hemodialysis population and increases the likelihood that patients will be exposed to clinically significant drug—drug interactions. Concurrent use of proton pump inhibitors (PPIs) with citalopram or escitalopram may potentiate the QT-prolonging effects of these selective serotonin reuptake inhibitors through pharmacodynamic and/or pharmacokinetic interactions.

#### **Methods**

We conducted a retrospective cohort study using data from the U.S. Renal Data System (2007–2017) and a new-user design to examine the differential risk of sudden cardiac death (SCD) associated with citalopram/escitalopram initiation vs. sertraline initiation in the presence and absence of PPI use among adults receiving hemodialysis. We studied 72 559 patients:14983 (21%) citalopram/escitalopram initiators using a PPI; 26 503 (36%) citalopram/escitalopram initiators not using a PPI;10 779 (15%) sertraline initiators using a PPI; and 20 294 (28%) sertraline initiators not using a PPI (referent). The outcome of interest was1-year SCD. We used inverse probability of treatment weighted survival models to estimate weighted hazard ratios (HRs) and 95% confidence intervals (CIs).

#### Results

Compared with sertraline initiators not using a PPI, citalopram/escitalopram initiators using a PPI had the numerically highest risk of SCD (HR [95% CI] =1.31 [1.11–1.54]), followed by citalopram/escitalopram initiators not using a PPI (HR [95% CI] =1.22 [1.06–1.41]). Sertraline initiators using a PPI had a similar risk of SCD compared with those not using a PPI (HR [95% CI] =1.03 [0.85–1.26]).

#### **Conclusions**

Existing PPI use may elevate the risk of SCD associated with citalopram or escitalopram initiation among hemodialysis patients.

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## Statin use and the risk of progression to vision threatening diabetic retinopathy

Elana Meer, J. Clay Bavinger, Yinxi Yu, Peiying Hua, Brendan McGeehan, Brian L. Vander Beek

#### **Abstract**

#### **Purpose**

This study aims to assess the effect of statins on progression from nonproliferative diabetic retinopathy (NPDR) to vision-threatening diabetic retinopathy (VTDR), proliferative diabetic retinopathy (PDR) or diabetic macular edema (DME).

#### **Methods**

Two cohort studies using a U.S. medical claims database from 2002 to 2019 including NPDR patients 18 years or older. A risk factor analysis performed a time-updating cox regression model assessing statin usage. A second new-user active comparator design analysis replicating a previously published study. Main outcomes included a new diagnosis of VTDR (composite of either PDR or DME) or DME and PDR individually for the risk factor study and included additional outcomes of new DR, NPDR, vitreous hemorrhage (VH) and tractional retinal detachment (TRD) for the new user study.

#### **Results**

Risk factor analysis included 66 617 statin users with NPDR at baseline and 83 365 nonstatin users. Of these, 27 325 (18.2%) progressed to VTDR, 4086 (2.71%) progressed to PDR, and 22 750 (15.1%) progressed to DME. After multivariable analysis, no protective effect of statin use was found for progression to VTDR, PDR, or DME (HR = 1.01–3, p > 0.33 for all comparisons). Replicated new user design analysis also showed no protective effect for statins on risk of development of DR (HR = 1.03, 95% CI: 0.99–1.07, p = 0.13), PDR (HR = 0.89, 95% CI: 0.79–1.02, p = 0.09), DME (HR = 0.94, 95% CI: 0.86–1.03, p = 0.21), VH (HR = 0.09, 95% CI: 0.86–0.09), and TRD (HR = 0.09).

#### Conclusion

Statin use was found not to be protective for progression of DR regardless of study methodology. These results suggest that the specifics of the population studied rather than differing study methodology are important in assessing the effect of statins on DR progression.

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### International Journal of Clinical Pharmacy

The standards of practice for delivery of polypharmacy and chronic disease medication reviews by general practice clinical pharmacists: a consensus study

<u>Katie Earle-Payne, Paul Forsyth, Chris F. Johnson, Heather Harrison, Susan</u> Robertson & Anita E. Weidmann

#### **Background**

General practice in the UK is experiencing a crisis. Greater multidisciplinary working is a potential solution. The new general practice contract in Scotland encourages this and includes a new pharmacotherapy service to be delivered by General Practice Clinical Pharmacists (GPCPs). Consensus is lacking for the standards of practice for delivery of pharmacotherapy medication reviews (which are polypharmacy and chronic medication reviews) as part of this service. Aim To identify and validate standards of practice for polypharmacy and chronic disease medication (pharmacotherapy level 3) reviews conducted by GPCPs.

#### Method

A two-phased mixed-methods consensus methodology was used. Phase 1: An expert group of GPCPs (n=4) and clinical pharmacist managers (n=2) responsible for delivering the pharmacotherapy service used a Modified Nominal Group Technique to generate potential standards. Phase 2: Two-round Delphi survey involving GPCPs with  $\geq 1$  year of experience of working in general practice (n=159).

#### **Results**

The expert group identified 44 potential standards of practice for polypharmacy and chronic disease reviews. Practicing GPCPs indicated during the Delphi phase that the 44 standards were applicable to practice. The standards of practice covered seven main categories: skills, environment, qualifications, qualities and behaviours, knowledge, process and experience.

#### Conclusion

Practicing GPCPs indicated that the standards identified by the expert group are acceptable and valid for current practice and the delivery of polypharmacy and chronic medication reviews. The application of these standards to practice may help GPCPs and general practices to ensure equitable delivery of patient care.

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## <u>Potential drug-drug interactions of immunosuppressants in kidney</u> <u>transplant recipients: comparison of drug interaction resources</u>

Aysel Pehlivanli, Rezzan Eren-Sadioglu, Merve Aktar, Sahin Eyupoglu, Sule Sengul, Kenan Keven, Sehsuvar Erturk, Bilgen Basgut & Arif Tanju Ozcelikay

#### **Background**

Drug-drug interactions are frequently observed in kidney transplant recipients due to polypharmacy and use of immunosuppressants. However, there is only one study evaluating clinically relevant potential drug-drug interactions of immunosuppressants specially in kidney transplant recipients by means of online databases and Stockleys Drug Interactions, as a gold standard.

#### Aim

This study aimed to compare four online databases used frequently to determined clinically relevant potential drug-drug interactions of immunosuppressants in kidney transplant recipients according to the Renal Drug Handbook.

#### Method

This was a descriptive cross-sectional study conducted between October 1, 2019, and March 18, 2020, in the nephrology ward of Ankara University School of the Medicine, Ibn-i Sina Hospital. In total, 52 adult patients' discharge prescriptions were retrieved from their medical records and analyzed retrospectively. Micromedex®, Lexicomp®, Medscape, and Drugs.com databases were used to evaluate drug interactions. The Renal Drug Handbook was used as a gold standard to do specificity and sensitivity analysis.

#### Results

A total of 127 potential drug-drug interactions between the immunosuppressants and comedications were detected by at least one online database. 32 (25.2%) of these were approved as clinically relevant potential drug-drug interactions by the Renal Drug Handbook. Lexicomp® and Drugs.com have exhibited the highest sensitivity (0.72 and 0.75) while Micromedex® has shown the highest specifity (0.83). Furthermore, the highest positive predictive value has been observed in Micromedex® (0.53). Micromedex® and Medscape had the highest negative predictive value (0.83 and 0.82). However, the kappa value of all was low. The values of inter-rater agreement (Kappa index) between online databases and the Renal Drug Handbook were weak (range 0.05–0.36). In addition, only 11 (8.7%) of potential drug-drug interactions were identified by all online databases.



#### Conclusion

This study showed that there was a weak compatibility between each database examined and the Renal Drug Handbook to detect clinically relevant potential drug-drug interactions for immunosuppressants in kidney transplant recipients. Therefore, we suggest that although databases might be practical to take a quick glance in detection of potential drug-drug interactions between immunosuppressants and co-medications, the data should be evaluated in detail and interpreted with caution in combination with a reference book like Renal Drug Handbook.

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Comparison of the prevalence and nature of potentially inappropriate medication use in geriatric outpatients between tertiary and community healthcare settings: a multicenter cross-sectional study

Yan Zeng, Yongpei Yu, Qingyang Liu,Su Su, Yang Lin, Hongyan Gu, Shicai Chen, PengmLi, Tong Xu, Naizhao Sun, Tao Lin, Qian Huang, Yujie Fan, Fengzhi Wang & Suying Yan

#### **Background**

Geriatric outpatients with polypharmacy have a high risk of potentially inappropriate medication (PIM) use.

#### Aim

To identify differences in both prevalence and patterns of PIMs and drug-related problems (DRPs) in older outpatients who visited the tertiary hospitals (THs) and community health centers (CHCs) and analyze associated factors.

#### Method

A prospective cross-sectional study was conducted in five THs and five CHCs from September 2018 to November 2019 in Beijing, China. Data were collected from outpatients aged ≥ 65 years with chronic diseases and polypharmacy. PIMs were evaluated using the 2015 and 2019 Beers Criteria and the Screening Tool of Older Persons' Prescriptions (STOPP) criteria. DRPs were classified using the Helper-Strand DRP Classification. The prevalence and types of PIMs and DRPs were compared, and relevant factors were analyzed.



The prevalence of PIMs based on the 2015 Beers Criteria was higher in patients from the THs, while PIMs based on the 2019 Beers Criteria did not show a significant difference. PIM prevalence based on STOPP Criteria and DRPs was higher in patients from CHCs.

Visiting CHCs was an independent factor of PIMs based on the 2015 Beers Criteria (OR 0.774, 95% CI 0.604–0.992) and the STOPP Criteria (OR 2.427, 95% CI 1.883–3.128), and DRPs (OR 3.612, 95% CI 2.682–4.865).

#### Conclusion

Differences in PIM and DRP might be due to the patients and settings. Specific measures to improve the appropriateness of medications in both settings should be used.

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## REVISTAS GERIÁTRICAS

### **BMC Geriatrics**

<u>Standards and quality of care for older persons in long term care facilities: a scoping review</u>

Kalideen, L., Govender, P. & van Wyk, J.M.

#### **Abstract**

Background

Caring for older persons has become a global necessity to ensure functional ability and healthy ageing. It is of paramount importance that standards of care are monitored, especially for older persons who live in long term care facilities (LTCF). We, therefore, scoped and summarised evidence relating to standards and the quality of care for older persons in LTCFs in gerontological literature globally.

#### **Methods**

We conducted a scoping review using Askey and O'Malley's framework, including Levac et al. recommendations. PubMed, CINAHL, Health Sources, Scopus, Cochrane Library, and Google Scholar were searched with no date limitation up to May 2020 using keywords, Boolean terms, and medical subject headings. We also consulted the World Health Organization website and the reference list of included articles for evidence sources. This review also included peer-reviewed publications and grey literature in English that focused on standards and quality of care for older residents in LTCFs. Two reviewers independently screened the title, abstract, and full-text of evidence sources screening stages and performed the data extraction. Thematic content analysis was used, and a summary of the findings are reported narratively.



Sixteen evidence sources published from 1989 to 2017 met this study's eligibility criteria out of 73,845 citations obtained from the broader search. The majority of the studies were conducted in the USA 56% (9/16), and others were from Canada, Hong Kong, Ireland, Norway, Israel, Japan, and France. The included studies presented evidence on the effectiveness of prompted voiding intervention for urinary incontinence in LTCFs (37.5%), the efficacy of professional support to LTCF staff (18.8%), and the prevention-effectiveness of a pressure ulcer programme in LTCFs (6.3%). Others presented evidence on regulation and quality of care (12.5%); nursing documentation and quality of care (6.3%); medical, nursing, and psychosocial standards on the quality of care (6.3%); medication safety using the Beer criteria (6.3%); and the quality of morning care provision (6.3%).

#### Conclusions

This study suggests most studies relating to standards and quality of care in LTCFs focus on effectiveness of interventions, few on people-centredness and safety, and are mainly conducted in European countries and the United States of America. Future studies on people-centerdness, safety, and geographical settings with limited or no evidence are recommended.

Disponible en:  $\underline{\text{https://bmcgeriatr.biomedcentral.com/track/pdf/}10.1186/s12877-022-02892-0.pdf}$ 

Low muscle mass is an independent risk factor for postoperative blood transfusion in total knee arthroplasty: a retrospective, propensity scorematched cohort study

Hwang, D., Han, HS., Lee, M.C.

#### Backround

Sarcopenia, an age-related loss of skeletal muscle mass and function, is correlated with adverse outcomes after some surgeries. This study examined the characteristics of sarcopenic patients undergoing primary total knee arthroplasty (TKA), and identified low muscle mass as an independent risk factor for postoperative TKA complications.

#### Methods

A retrospective cohort study examined 452 patients who underwent TKA. The skeletal muscle index (SMI) was obtained via bioelectrical impedance analysis (BIA), along with demographics, the Charlson Comorbidity Index, and medication, laboratory and operative data for 2018–2021. Patients were categorized into normal (n = 417) and sarcopenic (n = 35) groups using the SMI cut-off suggested by the Asian Working Group for Sarcopenia 2019 (males, < 7.0 kg/m2; females, < 5.7 kg/m2). Three postoperative complications were analysed: blood transfusion, delirium, and acute kidney injury (AKI). Baseline characteristics were propensity score-matched to address potential bias and confounding factors.



The proportion of sarcopenic patients in primary TKA was 7.7% (35/452). The sarcopenic group had a lower preoperative haemoglobin (12.18  $\pm$  1.20 vs. 13.04  $\pm$  1.73 g/dL, p = 0.004) and total protein (6.73  $\pm$  0.42 vs. 7.06  $\pm$  0.44 mg/dL, p = 0.001). Propensity scoring matching and logistic regression showed that more patients in the sarcopenic group received postoperative blood transfusions (OR = 6.60, 95% CI: 1.57–45.5, p = 0.021); there was no significant difference in AKI or delirium. Univariate receiver operating characteristic curve analysis of the propensity-matched group, to determine the predictive value of SMI for postoperative transfusion, gave an AUC of 0.797 (0.633–0.96) and SMI cut-off of 5.6 kg/m2.

#### Conclusion

Low muscle mass determined by BIA was an independent risk factor for postoperative transfusion in TKA. Multifrequency BIA can serve as a screening tool for sarcopenia that may influence the orthopaedic decision-making process or treatment planning in patients with sarcopenia undergoing primary TKA.

Disponible en: <a href="https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-022-02903-0.pdf">https://bmcgeriatr.biomedcentral.com/track/pdf/10.1186/s12877-022-02903-0.pdf</a>

### Drugs and aging

## **HOSPITAL Score and LACE Index to Predict Mortality in Multimorbid Older Patients**

#### Aubert, C.E., Rodondi, N., Terman, S.W

#### **Backround**

Estimating life expectancy of older adults informs whether to pursue future investigation and therapy. Several models to predict mortality have been developed but often require data not immediately available during routine clinical care. The HOSPITAL score and the LACE index were previously validated to predict 30-day readmissions but may also help to assess mortality risk. We assessed their performance to predict 1-year and 30-day mortality in hospitalized older multimorbid patients with polypharmacy.

#### **Methods**

We calculated the HOSPITAL score and LACE index in patients from the OPERAM (OPtimising thereof to prevent Avoidable hospital admissions in the Multimorbid elderly) trial (patients aged ≥ 70 years with multimorbidity and polypharmacy, admitted to hospital across four European countries in 2016–2018). Our primary and secondary outcomes were 1-year and 30-day mortality. We assessed the overall accuracy (scaled Brier score, the lower the better), calibration (predicted/observed proportions), and discrimination (C-statistic) of the models.



Within 1 year, 375/1879 (20.0%) patients had died, including 94 deaths within 30 days. The overall accuracy was good and similar for both models (scaled Brier score 0.01–0.08).

The C-statistics were identical for both models (0.69 for 1-year mortality, p = 0.81; 0.66 for 30-day mortality, p = 0.94). Calibration showed well-matching predicted/observed proportions.

#### **Conclusions**

The HOSPITAL score and LACE index showed similar performance to predict 1-year and 30-day mortality in older multimorbid patients with polypharmacy. Their overall accuracy was good, their discrimination low to moderate, and the calibration good. These simple tools may help predict older multimorbid patients' mortality after hospitalization, which may inform post-hospitalization intensity of care.

Disponible en: https://link.springer.com/content/pdf/10.1007/s40266-022-00927-0.pdf

### **Geriatrics and Gerontology International**

<u>Validation of the Spanish version of the Memory Failures of Everyday</u> questionnaire in older adults using Rasch analysis

<u>Carmen Rodríguez-Blázquez, Alba Ayala-García, Maria João Forjaz, Sara García-Herranz, César Venero, Raquel Rodríguez-Fernández, María del Carmen Díaz-Mardomingo</u>

#### Aim

The Memory Failures of Everyday (MFE) is a widely used instrument for assessing memory failure. The aim of the study was to analyze the MFE items using the Rasch model in a sample of cognitively older adults in Spain.

#### Methods

A cross-sectional validation study in a sample of 214 healthy people aged ≥60 years who used centers for older people in Madrid (Spain). The MFE for the assessment of memory complaints was used. The following properties of the Rasch model were assessed: data fit, reliability, unidimensionality, local dependence and lack of differential item functioning by gender, age and marital status.

#### **Results**

The MFE showed a good fit to the Rasch model ( $\chi 2(140) = 160.2$ ; P = 0.116) and high reliability (person separation index = 0.808). The questionnaire was unidimensional (6.54% t-test; IC binomial = 0.036–0.095). The items showed lack of local dependence between them and differential item functioning. The MFE scores were transformed into linear interval scores with a median of 44.31 and an observed range of 17.9–89.2 (theoretical range: 0–100).



#### **Conclusions**

The MFE is a unidimensional, reliable instrument to assess memory complaints in cognitively healthy older adults in Spain, with usefulness in clinical research and practice. The construct validity of the MFE linear score could not be fully confirmed and this deserves further investigation.

Disponible en: <a href="https://onlinelibrary.wiley.com/doi/epdf/10.1111/ggi.14364">https://onlinelibrary.wiley.com/doi/epdf/10.1111/ggi.14364</a>

## Occasions for laughter and dementia risk: Findings from a six-year cohort study

Yu Wang, Kokoro Shirai, Tetsuya Ohira, Mayumi Hirosaki, Naoki Kondo, Kenji Takeuchi, Chikae Yamaguchi, Yudai Tamada, Katsunori Kondo, Dorina Cadar, Hiroyasu Iso

#### Aim

Currently, there is little evidence on the relationship between laughter and the risk of dementia, and since laughter is mainly a social behavior, we aimed to examine the association between various occasions for laughter and the risk of dementia in Japanese older adults.

#### Methods

We draw upon 6-year follow-up data from the Japan Gerontological Evaluation Study, including 12 165 independent older adults aged 65 years or over. Occasions for laughter were assessed using a questionnaire, while dementia was diagnosed using the standardized dementia scale of the long-term care insurance system in Japan. Cox proportional hazards models were estimated, yielding hazard ratios and 95% confidence intervals (CIs).

#### Results

The multivariable hazard ratio of dementia incidence for all participants in the groups for high versus low variety of occasions for laughter was 0.84 (95% CI: 0.72–0.98, P for trend <0.001). A greater variety of occasions for laughter was associated with a lower risk of dementia 0.78 (95% CI: 0.63–0.96, P for trend <0.001) among women, but was less pronounced for men, with significant associations only for the medium group. Laughing during conversations with friends, communicating with children or grandchildren, and listening to the radio were primarily associated with decreased risk.

#### Conclusion

A greater variety of laughter occasions in individual and social settings was associated with a reduced risk of dementia.

Disponible en: <a href="https://onlinelibrary.wiley.com/doi/epdf/10.1111/ggi.14371">https://onlinelibrary.wiley.com/doi/epdf/10.1111/ggi.14371</a>



### Journal of Aging and Health

## <u>Loneliness, Social Isolation, and All-Cause Mortality in a Large Sample of Older Adults</u>

<u>Timothy L. Barnes, Manik Ahuja, Stephanie MacLeod, Rifky Tkatch, Laurie Albright, James A.</u> Schaeffer and Charlotte S.

#### **Objectives**

Using data from a large random sample of U.S. older adults (N = 7982), the effect of loneliness and social isolation on all-cause mortality was examined considering their separate and combined effects.

#### Methods

The UCLA-3 Loneliness Scale and the Social Network Index (SNI) were used to define loneliness and social isolation. Cox proportional hazards regression models were performed.

#### **Results**

Among study participants, there were 548 deaths. In separate, adjusted models, loneliness (severe and moderate) and social isolation (limited and moderate social network) were both associated with all-cause mortality. When modeled together, social isolation (limited and moderate social network) along with severe loneliness remained significantly associated with mortality.

#### Discussion

Results demonstrate that both loneliness and social isolation contribute to greater risk of mortality within our population of older adults. As the COVID-19 pandemic continues, loneliness and social isolation should be targeted safely in efforts to reduce mortality risk among older adults.

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### International Journal of Geriatric Psychiatry

## Pet ownership supports quality of life in home-dwelling people with Alzheimer's disease

<u>Tarja Välimäki, Anne Koivisto, Virve Kärkkäinen, Tuomas Selander, Kristiina Hongisto, Minna Rusanen</u>

#### **Objectives**

Human-animal interactions have beneficial psychosocial and psychophysiological effects on individuals in both the presence and absence of medical health conditions. No previous prospective studies with long follow-up have investigated the effects of domestic pets on individuals with Alzheimer's disease (AD) who live at home. We examined the effects of pets on quality of life (QoL) and general well-being during a 5-year follow-up of homedwelling persons with AD.

#### Methods

In a prospective study including 223 patients with very mild (Clinical Dementia Rating Scale [CDR] 0.5) or mild (CDR 1) AD at baseline who participated in the ALSOVA study, 40 (18%) had a pet. Self- and proxy-rated QoL in AD quality of life-AD (QoL-AD), 15D, and self-rated visual analogic scale (VAS) were assessed annually for 3 years and after 5 years. The Mini-Mental State Examination, Neuropsychiatric Inventory, and CDR sum of boxes (CDR sum of boxes) were measured at the same visits.

#### **Results**

A significant positive effect of pet ownership (p = 0.003, proxy-rated QoL-AD) on QoL was found over the entire follow-up. However, self-rated QoL-AD, 15D, and VAS did not significantly differ between pet owners and non-pet owners.

#### Conclusions

The findings suggest that having a pet may support QoL in home-dwelling persons with AD. Self-rated or general QoL or well-being measurements are not an accurate method for studying QoL in individuals with dementia over time due to a lack of insight. Adding proxyrated evaluations to this kind of study is recommended.

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## Coping strategies for memory problems in everyday life of people with cognitive impairment and older adults – a systematic review

Sabrina D. Ross, Lena M. Hofbauer, Francisca S. Rodriguez

#### **Objectives**

Dealing with memory loss is a major challenge for older people. Coping strategies for memory problems could enable cognitively impaired people to live independently for longer. We conducted a systematic review to summarize evidence on coping strategies for older people and people with cognitive impairment to stabilize everyday life functioning.

#### **Methods**

We systematically searched the databases PubMed, PsychInfo, Scopus and WebofScience using a well-defined search string. Studies were included if they were published between January 1990 and February 2021 and written in English, German, Spanish, French, or Swedish language. Two blind researchers independently checked the studies for inclusion and exclusion criteria and evaluated the quality of the studies using CASP - checklists. Evidence was summarized in a narrative synthesis.

#### **Results**

A total of 16 relevant studies with adequate quality were identified. These studies reported on three categories of strategies: external, internal, and behavioral coping strategies. External strategies included reminder systems and integrated features in the environment and were used by people with and without cognitive impairments. Internal strategies such as visualization, verbalization, active remembering, and systematic thinking were reported less often by people with cognitive impairment than those without cognitive impairment. Behavioral strategies such as reducing expectations and acceptance of support was most frequently reported by people with cognitive impairment.

#### **Conclusions**

The findings of our systematic review show a great number of coping strategies, which seem to depend on cognitive status. Appropriate training tools incorporating these strategies should be developed.

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## **REVISTAS MÉDICAS**

## JAMDA: Journal of the American Medical Directors Association

## <u>Surgical Hospitalization Is Not Associated With Cognitive Trajectory Over</u> <u>6 Years in Healthy Older Australians</u>

<u>Lucia Chinnappa-Quinn, Ben C.P. Lam, Lara Harvey, Nicole A. Kochan, Michael Bennett, John D. Crawford, Steve Robert Makkar, Henry Brodaty, MD, Perminder S. Sachdev</u>

#### Objective

The aim was to investigate the association of cognitive trajectories and overnight surgical hospitalization in older adults, while controlling for and comparing with the association with acute medical hospitalizations.

#### Design

This is a secondary analysis of data from a population-based, longitudinal cohort study of older Australians.

#### **Setting and Participants**

Cognition was assessed with 4 biennial waves of prospective neuropsychological data from 1026 Sydney Memory and Aging Study participants age 70 to 90 years at baseline. Hospitalization exposure was obtained from 10 years of electronically linked data from the New South Wales Admitted Patient Data Collection.

#### **Methods**

Latent growth curve modeling estimated global cognition *z* score baseline and slope over 6 years, and the effects of contemporaneous surgical and medical hospitalization predictors while controlling for potential demographic and comorbidity confounders.

#### Results

After controlling for confounding variables, this analysis showed that overnight surgical hospitalizations were not associated with worse baseline global cognition or accelerated cognitive decline over 6 years. This was despite this cohort having more surgeries and more complex surgeries compared with Australian data for overnight hospitalizations in over 70-year-olds. Conversely, recent medical hospitalizations were associated with accelerated cognitive decline.

#### **Conclusions and Implications**

This analysis finds that surgery and anesthesia are unlikely to be risk factors for medium to long-term global cognitive decline in healthy older adults, while controlling for contemporaneous medical hospitalizations. These findings are contrary to prior conclusions from several surgical studies that may have been impeded by insufficient comparison groups.



They are, however, consistent with recent population-based studies suggesting surgery has minimal association with cognitive decline in the medium to long-term. Future research needs to clarify the association of surgical hospitalization with the full spectrum of cognitive outcomes including subjective cognitive complaints and dementia, and importantly, how these cognitive outcomes correlate with clinically significant functional changes.

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