

## REVISIÓN BIBLIOGRÁFICA JUNIO 2021:

## Selección de artículos

## **REVISTAS FARMACÉUTICAS**

## **European Journal of Hospital Pharmacy**

# Effect of a pharmacist-led educational intervention on clinical outcomes: a randomised controlled study in patients with hypertension, type 2 diabetes and hypercholesterolaemia

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#### Abstract

**Objectives** In recent years, hospital pharmacists have gained more importance in the clinical support of patients. However, most of the studies evaluating the impact of clinical pharmacy have only studied patients' adherence or satisfaction. The aim of this study was to evaluate the direct clinical outcomes of a pharmacist-led educational intervention in patients with chronic disease.

**Methods** We conducted a randomised, controlled, parallel, physician-blinded study in a day hospital and a consultation unit of a French teaching hospital over a 1-year period. Patients with hypertension, type 2 diabetes or hypercholesterolaemia who did not reach their therapeutic goals despite drug therapy were eligible. Patients in the intervention group received an intervention from a hospital pharmacist who provided patient education on pathology and drug management. The primary outcome was the proportion of patients reaching their therapeutic goals for blood pressure, glycated haemoglobin level or low-density lipoprotein cholesterol level at the 3-month follow-up consultation.

**Results** From January to December 2015, 89 patients were included and 73 completed the study. In the intervention group, 61.7% (21/34) of the patients reached their therapeutic goals compared with 33.3% (13/39) in the control group (p=0.015). The intervention was significantly more effective in polypharmacy patients (60.0% (12/20) vs 16.7% (4/24); p=0.005), in those aged >60 years (57.9% (11/19) vs 26.1% (6/23); p=0.037) and in patients with a high education level (68.8% (11/16) vs 29.4% (5/17); p=0.024).

**Conclusion** A single pharmacist-led educational intervention has a clinical impact, doubling the proportion of patients reaching their therapeutic goals at 3 months, especially in polypharmacy patients and those aged >60 years. This study confirms the value of clinical involvement of hospital pharmacists in patient care in a consultation unit and day hospital.

Disponible en: https://ejhp.bmj.com/content/early/2021/06/27/ejhpharm-2021-002787



#### Clinical frailty and polypharmacy in older emergency critical care patients: a single-centre retrospective case series

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Abstract

**Background and objectives** Admission of complex and frail patients to critical care units is common. Little is known about the relationship between clinical frailty and polypharmacy measures in critical care patients or how a critical care admission affects polypharmacy.

We sought to: (1) Describe the extent and relationship between clinical frailty and polypharmacy in a cohort of older emergency general critical care patients, and to (2) Describe the effect of the critical care pathway on patient polypharmacy measures.

**Methods** A retrospective evaluation was undertaken in all patients ≥70 years of age, admitted as emergencies to the general critical care units of a single large UK academic hospital, over a 2-year period (March 2016 to February 2018) (n=762). Patient Clinical Frailty Scale (CFS) and polypharmacy measures on admission were described and association was tested. Medication changes and documentation on care transitions were analysed in a randomly selected convenience cohort of critical care survivors (n=77).

**Results** On admission patients had a median of 9 (5;12) medicines, of which a median of 3 (2;5) were high-risk medicines. Polypharmacy (5–9 medicines) and hyperpolypharmacy ( $\geq$ 10 medicines) occurred in 80.7% (615/762) and 43.2% (329/762) of patients, respectively. A degree of frailty was the standard (median CFS 4 (3;5)) with 45.7% (348/762) CFS 4–5 and 20% (153/762) CFS  $\geq$ 6. The patient median CFS increased by 1 with polypharmacy classification increments (p<0.001). In the survivor cohort, a median of 6 (4;8) and 5 (4;8) medication changes occurred on critical care and hospital discharges, respectively. A minority of patients had detailed medication continuity plans on care transitions.

**Conclusions** Polypharmacy and frailty were very common in this UK single-centre cohort of older emergency critical care patients. There was a significant association between the degree of polypharmacy and frailty score. The critical care pathway created extensive changes in patient medication therapy. Medication changes on care transitions often lacked detailed documentation.

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## The Annals of Pharmacotherapy

## Major bleeding in users of direct oral anticoagulants in atrial fibrillation: a pooled analysis of results from multiple population-based cohort studies

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Abstract



#### Objective

To establish the risk of major bleeding in direct oral anticoagulant (DOAC) users (overall and by class) versus vitamin K antagonist (VKA) users, using healthcare databases from four European countries and six provinces in Canada.

#### Methods

A retrospective cohort study was performed according to a similar protocol. First-users of VKAs or DOACs with a diagnosis of non-valvular atrial fibrillation (NVAF) were included. The main outcome of interest was major bleeding and secondary outcomes included gastrointestinal (GI) bleeding and intracranial haemorrhage (ICH). Incidence rates of events per 1000 person years were calculated. Hazard ratios (HRs) and 95% confidence intervals (95% CI) were estimated using a Cox proportional hazard regression model. Exposure and confounders were measured and analysed in a time dependant way. Risk estimates were pooled using a random effect model.

#### Results

421 523 patients were included. The risk of major bleeding for the group of DOACs compared to VKAs showed a pooled HR of 0.94 (95% CI: 0.87–1.02). Rivaroxaban showed a modestly increased risk (HR 1.11, 95% CI 1.06–1.16). Apixaban and dabigatran showed a decreased risk of respectively HR 0.76 (95% CI 0.69–0.84) and HR 0.85 (95% CI 0.75–0.96).

#### Conclusions

This study confirms that the risk of major bleeding of DOACs compared to VKAs is not increased when combining all DOACs. However, we observed a modest higher risk of major bleeding for rivaroxaban, whereas for apixaban and dabigatran lower risks of major bleeding were observed compared to VKAs.

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## **REVISTAS GERIÁTRICAS**

## Archives of Gerontology and Geriatrics

#### **Cognitive impairment among patients with cardiovascular diseases:**

#### comparisons of sex, the elderly, and education

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#### Abstrac

#### Background

Evidence showed the relationship between cognitive impairment and cardiovascular diseases (CVD), but few studies used the Montreal Cognitive Assessment (MoCA) to assess cognitive impairment. MoCA was validated and designed to detect mild impairment with higher sensitivity.



#### Objective

This study aimed to determine the cognitive impairment and compare between sex, the elderly, and education level.

#### Methods

This cross-sectional study was conducted among patients with CVD at a teaching hospital in northern Thailand. Cognitive impairment was evaluated by interviewing patients using the MoCA as a tool, using cut-off score less than 25 out of 30 as cognitive impairment.

#### Results

Of 113 patients, 52% were male, and the mean age was  $63 \pm 14.9$  years. The mean total score of MoCA was  $20.16 \pm 5.14$ . The prevalence of cognitive impairment among CVD patients was 79% and did not differ between sex (male 84.8% vs female 72.2%, p-value 0.114) but differed between the elderly (age <65, 70.7% vs age  $\geq$ 65, 87.3 %, p-value 0.039), and education level (lower 86.2% vs higher 58.8 %, p-value 0.005).

#### Conclusion

Four-fifth of patients with CVD had cognitive impairment. The cognitive impairment did not differ between sex but differed between the elderly, and education level. Cognitive impairment should be routinely screened among patients with CVD. This study may guide the development of specific care for CVD patients with cognitive impairment.

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## **BMC Geriatrics**

## Older people's attitudes towards deprescribing cardiometabolic medication

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#### Abstract

#### Background

Overtreatment with cardiometabolic medication in older patients can lead to major adverse events. Timely deprescribing of these medications is therefore essential. Self-reported willingness to stop medication is usually high among older people, still overtreatment with cardiometabolic medication is common and deprescribing is rarely initiated. An important barrier for deprescribing reported by general practitioners is the patients' unwillingness to stop the medication. More insights are needed into the influence of patients' characteristics on their attitudes towards deprescribing and differences in these attitudes between cardiometabolic medication groups.

#### Methods

A survey in older people using cardiometabolic medication using the revised Patients' Attitudes Towards Deprescribing (rPATD) questionnaire was performed. Participants completed the general rPATD and an adapted version for four medication groups. Linear and ordinal logistic regression



were used to assess the influence of age, sex, therapeutic area and number of medications used on the patients' general attitudes towards deprescribing. Univariate analysis was used to compare differences in deprescribing attitudes towards sulfonylureas, insulins, antihypertensive medication and statins.

#### Results

Overall, 314 out of 1143 invited participants completed the survey (median age 76 years, 54% female). Most participants (80%) were satisfied with their medication and willing to stop medications if their doctor said it was possible (88%). Age, sex and therapeutic area had no influence on the general attitudes towards deprescribing. Taking more than ten medicines was significantly associated with a higher perceived medication burden. Antihypertensive medication and insulin were considered more appropriate than statins, and insulin was considered more appropriate than statins.

#### Conclusions

The majority of older people using cardiometabolic medication are willing to stop one of their medicines if their doctor said it was possible. Health care providers should take into account that patients perceive some of their medication as more appropriate than other medication when discussing deprescribing.

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## Association between frailty and ischemic heart disease: a systematic review and meta-analysis

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#### Abstract

#### Background

Frailty is increasingly reported among older adults with cardiovascular diseases and it has been demonstrated to increase negative health outcomes and mortality. To date, no systematic review of the evidence is available regarding the association between frailty and ischemic heart disease (IHD). We performed a systematic review of literature and a meta-analysis to assess the association between frailty and IHD.

#### Methods

We selected all the studies that provided information on the association between frailty and IHD, regardless of the study setting, study design, or definition of IHD and frailty. PubMed, Web of Science and Embase were searched for relevant papers. Studies that adopted the Fried definition for frailty were included in the meta-analyses. For each measure of interest (proportions and estimates of associations), a meta-analysis was performed if at least three studies used the same definition of frailty. Pooled estimates were obtained through random effect models and Mantel-Haenszel weighting.



#### Results

Thirty-seven studies were included. Of these, 22 adopted the Fried criteria to define frailty and provided estimates of prevalence and therefore they were included in meta-analyses. The pooled prevalence of IHD in frail individuals was 17% (95% Confidence Interval [95%CI] 11–23%) and the pooled prevalence of frailty in individuals with IHD was 19% (95% CI 15–24%). The prevalence of frailty among IHD patients ranged from 4 to 61%. Insufficient data were found to assess longitudinal association between frailty and IHD.

#### Conclusions

Frailty is quite common in older persons with IHD. The identification of frailty among older adults with IHD should be considered relevant to provide individualized strategies of cardiovascular prevention and care. Further research should specifically explore the association between frailty and IHD and investigate the potential common biological ground.

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## Frailty increases the risk for developing urinary tract infection among 79,887 patients with diabetic mellitus and chronic kidney disease

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#### Abstract

#### Background

Patients with diabetic mellitus (DM) and chronic kidney disease (CKD) are at an increased risk of urinary tract infection (UTI) due to their altered immunological integrity. These patients are similarly prone to developing frailty, a state of cumulative health deficits involving multiple domains and leading to adverse outcomes. Whether frailty predisposes affected individuals to UTI among patients with DM and CKD remains unclear.

#### Methods

A population-based cohort of patients with DM and CKD (n = 79,887) were assembled from the Longitudinal Cohort of Diabetes Patients, with their baseline frailty status measured by a modified FRAIL scale. We analyzed their risk of developing UTI depending on their severity of frailty, after accounting demographic profiles, lifestyle factors, comorbidities, concurrent medications, and major interventions. A secondary analysis focused on the risk of urosepsis related to frailty.

#### Results

Among all participants, 36.1 %, 50.3 %, 12.8 %, and 0.8 % did not have or had 1, 2, and  $\geq$  3 FRAIL items, respectively, at baseline. After 3.51 years, 11,175 UTI events occurred. Kaplan-Meier analysis showed that participants with DM, CKD and an increasing number of FRAIL items had successively higher incidence of UTI than those without any FRAIL items (log rank p < 0.001). Cox proportional hazard modeling revealed that after accounting for all confounders, those with more severe frailty exhibited a significantly higher risk of incident UTI (for groups of 1, 2, and  $\geq$  3 FRAIL items, hazard ratio 1.19, 1.24, and 1.43, respectively; all p < 0.001) than those without. An 11 % risk elevation for UTI could be observed for every FRAIL item increase. Participants with more severe frailty exhibited a trend of having higher risk of urosepsis as well.



#### Conclusions

Having frailty predicted a higher risk of developing UTI in the future in patients with DM and CKD. It would be prudent to screen for frailty in these patients and provide optimal frailty-directed management to attenuate their risk of UTI and improve their outcomes.

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## Drugs and Aging

#### Risk of Fractures in Older Adults with Chronic Non-cancer Pain Receiving Concurrent Benzodiazepines and Opioids: A Nested Case–Control Study

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#### Abstract

#### Objective

The aim of this study was to investigate the relationship between the concurrent use of benzodiazepines and opioids and the risk of fractures in older patients with chronic non-cancer pain.

#### Methods

Patients with osteoarthritis or low back pain ( $\geq$  65 years of age) included in the Korean National Health Insurance Service–National Sample Cohort database of Korea and with an incident diagnosis of hip, humeral, or forearm fracture between 2011 and 2015 were identified as cases. For each case, four controls were matched for age (within 5 years), sex, and year of cohort entry. We estimated the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for fractures associated with concurrent use of benzodiazepines and opioids using a conditional logistic regression analysis, adjusting for comorbidities and comedications.

#### Results

The aOR (95% CI) for the concurrent use of benzodiazepines and opioids was 1.45 (1.22–1.71), compared with those of non-use within 30 days before the index date. The aOR was 1.65 (1.22–2.23) in patients who were continuously receiving benzodiazepines and were newly initiated with concurrent opioids. The aORs for concurrent use were 1.95 (1.39–2.74) and 1.27 (1.03–1.56) in the case of hip fracture and forearm fracture, respectively.

#### Conclusion

The concurrent use of benzodiazepines and opioids was associated with an increased risk of fractures in older patients with chronic non-cancer pain. Therefore, patients continuously receiving benzodiazepines in whom opioids are newly initiated need careful monitoring, and such combined therapy should be limited to the shortest duration possible.

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#### Management of Metastatic Colorectal Carcinoma in Older Adults: Balancing Risks and Benefits of Novel Therapies

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#### Abstract

The prevalence of older patients with metastatic colorectal cancer (mCRC) will continue to increase with our aging population. Treatment of mCRC has changed significantly in the last few decades as we have learned how to personalize the treatment of mCRC to the biology of the tumor, utilizing new treatment approaches. With an ever-changing treatment paradigm, managing the population of older adults becomes paramount. This review highlights the pivotal clinical trials that defined the use of systemic therapy, immunotherapy and targeted therapies for mCRC, and how those are applied to the older patient population. In addition, we outline the tools for an in-depth assessment of an older adult in regards to treatment planning and management of therapy-related toxicities. A comprehensive geriatric assessment can assist in the selection of treatment for an older adult with mCRC. While frail older patients can frequently only tolerate single agents or modified regimens, fit older adults remain candidates for a wider range of treatment options. However, since all of these treatments are associated with possible toxicities, each patient's treatment must be personalized to the patient's goals and wishes through a shared decision-making process.

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### Journal of the American Geriatrics Society

#### **Predictors of short-term hospitalization and emergency department**

#### presentations in aged care

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#### Abstract

#### Objectives

To examine individual, medication, system, and healthcare related predictors of hospitalization and emergency department (ED) presentation within 90 days of entering the aged care sector, and to create risk-profiles associated with these outcomes.

#### **Design and setting**

Retrospective population-based cohort study using data from the Registry of Senior Australians.

#### Participants

Older people (aged 65 and older) with an aged care eligibility assessment in South Australia between January 1, 2013 and May 31, 2016 (N = 22,130).



#### Measurements

Primary outcomes were unplanned hospitalization and ED presentation within 90 days of assessment. Individual, medication, system, and healthcare related predictors of the outcomes at the time of assessment, within 90 days or 1-year prior. Fine–Gray models were used to calculate subdistribution hazard ratios (sHR) and 95% confidence intervals (CI). Harrell's C-index assessed predictive ability.

#### Results

Four thousand nine-hundred and six (22.2%) individuals were hospitalized and 5028 (22.7%) had an ED presentation within 90 days. Predictors of hospitalization included: being a man (hospitalization sHR = 1.33, 95% CI 1.26–1.42),  $\geq$ 3 urgent after-hours attendances (hospitalization sHR = 1.21, 95% CI 1.06–1.39), increasing frailty index score (hospitalization sHR = 1.19, 95% CI 1.11–1.28), individuals using glucocorticoids (hospitalization sHR = 1.11, 95% CI 1.02–1.20), sulfonamides (hospitalization sHR = 1.18, 95% CI 1.10–1.27), trimethoprim antibiotics (hospitalization sHR = 1.15, 95% CI 1.03–1.29), unplanned hospitalizations 30 days prior (hospitalization sHR = 1.13, 95% CI 1.04–1.23), and ED presentations 1 year prior (hospitalization sHR = 1.07, 95% CI 1.04–1.10). Similar predictors and hazard estimates were also observed for ED presentations. The hospitalization models out-of-sample predictive ability (C-index = 0.653, 95% CI 0.635–0.670) and ED presentations (C-index = 0.647, 95% CI 0.630–0.663) were moderate.

#### Conclusions

One in five individuals with aged care eligibility assessments had unplanned hospitalizations and/or ED presentation within 90 days with several predictors identified at the time of aged care eligibility assessment. This is an actionable period for targeting at-risk individuals to reduce hospitalizations.

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### International Journal of Geriatric Psychiatry

#### Risk of hospitalization and hip fracture associated with psychotropic

#### polypharmacy in patients with dementia: A nationwide register-based

#### study

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#### Abstract

#### Objective

To investigate the association of benzodiazepines and antidepressants on the risk of hospitalization and hip fracture in patients with dementia initiating antipsychotic drug treatment.

#### Methods

A register-based retrospective cohort study using data on all incident dementia cases (≥65 years) initiating antipsychotic treatment as monotherapy or in combination with benzodiazepines and/or antidepressants in Denmark from 2000 to 2015. The outcomes of interest were all-cause



hospitalization and hip fracture. Cox proportional hazards models with adjustment for multiple variables were used to investigate risk of hospitalization and hip fracture within 180 days.

#### Results

The risk of all-cause hospitalization during 180-days follow-up was significantly increased by 55% (adjusted HR: 1.55, 95% CI: 1.29–1.86, p < 0.0001), when antipsychotic use was combined with benzodiazepines, when compared to antipsychotic monotherapy. The association between the combination of antipsychotics and benzodiazepines with the risk of hip fracture did not reach statistical significance (adjusted HR: 1.50, 95% CI: 0.99–2.26, p = 0.0534).

#### Conclusions

The observed increased risk of all-cause hospitalization and hip fracture may indicate increased drug-related adverse events. Thus, careful and regular monitoring is needed to assess response to treatment and decrease the risk of adverse events, when antipsychotics are combined with BZDs, albeit confounding cannot be fully excluded within the current design.

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#### A 6-year prospective clinical cohort study on the bidirectional association

#### between frailty and depressive disorder

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#### Abstract

#### Introduction

Depressive disorder has been conceptualised as a condition of accelerated biological ageing. We operationalised a frailty index (FI) as marker for biological ageing aimed to explore the bidirectional, longitudinal association between frailty and either depressive symptoms or depressive disorder.

#### Methods

A cohort study with 6-year follow-up including 377 older ( $\geq$ 60 years) outpatients with a DSM-IVdefined depressive disorder and 132 never-depressed controls. Site visits at baseline, 2 and 6-year follow-up were conducted and included the CIDI 2.0 to assess depressive disorder and relevant covariates. Depressive symptom severity and mortality were assessed every 6 months by mail and telephone. A 41-item FI was operationalised and validated against the 6-year morality rate by Cox regression (HRFI = 1.04 [95% CI: 1.02–1.06]).

#### Results

Cox regression showed that a higher FI was associated with a lower chance of remission among depressed patients (HRFI = 0.98 [95% CI: 0.97–0.99]). Nonetheless, this latter effect disappeared after adjustment for baseline depressive symptom severity. Linear mixed models showed that the FI increased over time in the whole sample (B[SE] = 0.94 (0.12), p < .001) with a differential impact of depressive symptom severity and depressive disorder. Higher baseline depressive symptom



severity was associated with an attenuated and depressive disorder with an accelerated increase of the FI over time.

#### Conclusions

The sum score of depression rating scales is likely confounded by frailty. Depressive disorder, according to DSM-IV criteria, is associated with accelerated biological ageing. This argues for the development of multidisciplinary geriatric care models incorporating frailty to improve the overall outcome of late-life depression.

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## **REVISTAS MEDICINA GENERAL**

## JAMDA: Journal of the American Medical Directors

#### **Association**

#### Probable Delirium and Associated Patient Characteristics in Long-Term Care and Complex Continuing Care: A Population-Based Observational Study

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#### Abstract

#### Objectives

To estimate the prevalence of probable delirium in long-term care (LTC) and complex continuing care (CCC) settings and to describe the resident characteristics associated with probable delirium.

#### Design

Population-based cross-sectional study using routinely collected administrative health data.

#### **Setting and Participants**

All LTC and CCC residents in Ontario, Canada, assessed with the Resident Assessment Instrument– Minimum Dataset (RAI-MDS) assessment between July 1, 2016, and December 31, 2016 (LTC n=86,454, CCC n=10,217).

#### Methods

Probable delirium was identified via the delirium Clinical Assessment Protocol on the RAI-MDS assessment, which is triggered when individuals display at least 1 of 6 delirium symptoms that are of recent onset and different from their usual functioning. RAI-MDS assessments were linked to demographic and health services utilization databases to ascertain resident demographics and health status. Multivariable logistic regression was used to identify characteristics associated with probable delirium, with adjusted odds ratios (ORs) and 95% confidence intervals (CIs) reported.

#### Results

Delirium was probable in 3.6% of LTC residents and 16.5% of CCC patients. LTC patients displayed fewer delirium symptoms than CCC patients. The most common delirium symptom in LTC was periods of lethargy (44.6% of delirium cases); in CCC, it was mental function varying over the course of the day (63.5% of delirium cases). The odds of probable delirium varied across individual demographics and health characteristics, with increased health instability having the strongest association with the outcome in both care settings (LTC: OR 30.4, 95% CI 26.2-35.3; CCC: OR 21.0, 95% CI 16.7-26.5 for high vs low instability).



#### **Conclusions and Implications**

There were differences in the presentation and burden of delirium symptoms between LTC and CCC, potentially reflecting differences in delirium severity or symptom identification. Several risk factors for probable delirium in LTC and CCC were identified that may be amenable to interventions to prevent this highly distressing condition.

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