

**Association between psychotropic and cardiovascular iatrogenic alerts and risk of hospitalizations in elderly people treated for dementia:**  
*a self-controlled case series study based on the matching of two French health insurance databases*

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# CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report

# Background

- Between **5% and 20%** of all hospital admissions are known to be related to **adverse drug events (ADE)** in people aged  $\geq 65$  years, and **40% to 70%** of these admissions could be preventable
- This has prompted the **development of criterion-based tools**, based on explicit measures, to **assess and correct inappropriate prescription** in elderly people
- However, the evidence that **inappropriate prescription**, as defined by the explicit measures, **is associated with adverse patient outcomes**, and notably hospitalizations, **is mixed and contradictory**

Budnitz, NEJM, 2011  
Gurwitz, JAMA, 2003  
Budnitz, JAMA, 2006  
Pirmohamed, BMJ, 2004  
Hanlon, Ann Pharmacother, 2010

# Background

- In **2011**, the **French National Authority for Health** commissioned a panel of French health professionals to determine the **most important criteria for cardiovascular and psychotropic drugs** known to be involved in ADE-related admissions
- **Five iatrogenic alerts (IAs)** were identified which **were easy to assess and clinically relevant** for the prevention of serious ADE in the elderly, based on a literature search and the panel members' clinical experience

## 3 PSYCHOTROPIC IAs

- The prescription of a long-half benzodiazepine
- The prescription of antipsychotic drug in Alzheimer patients
- The co-prescription of 3 or more psychotropic drugs

## 2 CARDIOVASCULAR IAs

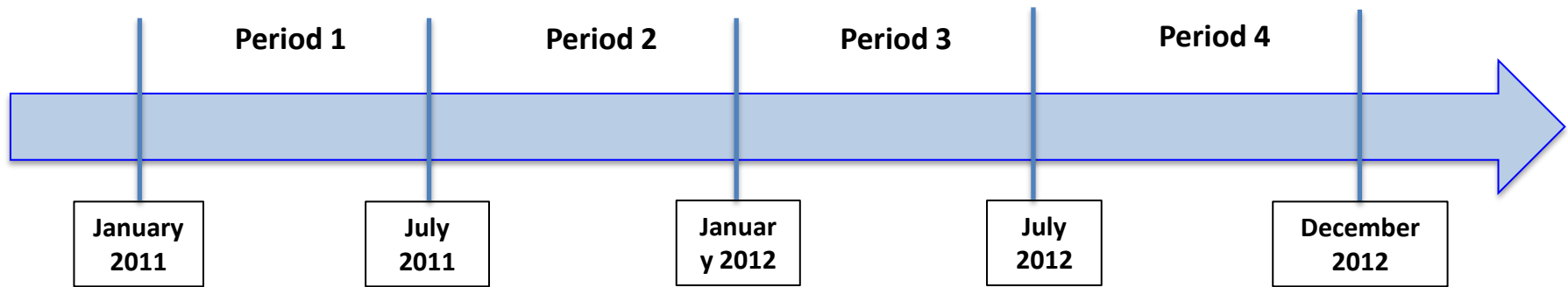
- The co-prescription of 2 or more diuretics
- The co-prescription of 4 or more antihypertensive drugs

# Objectives

- The aim of our study was to **validate this new screening tool** for inappropriate prescriptions in elderly people, by measuring the **association between these IAs and the risk of all-cause hospitalizations**
- We focused on patients treated for **Alzheimer disease** because they are at high risk of hospitalizations and because one of the IAs was specific for this population

# Design

- Between **January 1, 2011** and **December 31, 2012** a longitudinal, national database study based on the “**self-controlled case series**” methodology was performed



- **Epidemiologic study design in which individuals act as their own controls:**  
comparing each patient to themselves in a different period

**« RSI » database: Social security scheme for self-employed individuals**

- Ambulatory drug delivery and Hospitalization (private hospitals)
- 1/01/2011- 31/12/2012
- Patients > 75 years old
- **N = 308 588**

**« SNIIRAM » database: French National Health Insurance Information System**

- Hospitalization (public hospitals)

**Patients treated for dementia**  
 (ICD 10 code Alzheimer's disease: F00- F03 AND drug code ATC: NO6D)  
**N = 12196**

- No dementia: **N = 280 024**
- Untreated dementia : **N = 16368**

- Database matching unsuccessful **N = 1408**  
 Patients with repeat planned admissions **N = 34**
- Chemotherapy
  - Dialysis
  - Reeducation session

**Patients aged > 75 years receiving treatment for Alzheimer's disease and available data on drug prescriptions, hospitalizations in public and private hospitals**  
**N = 10754**

# Results

**N = 10754**

	Population totale
<b>Age</b> (years, mean +/- SD)	85 +/- 5
<b>Sex</b> (% female)	61.1%
<b>Comorbidities</b>	
- Cardiovascular diseases	29%
- Neuropsychiatric diseases	10 %
- Cancer	12%
<b>Charlson Comorbidity Index</b>	5.5 +/- 1.0
<b>Polypharmacy</b> (% per 6-month period)	90%
<b>Death</b> (% per year)	10%



# Results

	Population
<b>IA long-half benzodiazepine</b>	9.7%
<b>IA one antipsychotic drug</b>	16.5%
<b>IA co-prescription of 3 or more psychotropic drugs</b>	15.5%
<b>IA 3 or more diuretics</b>	5.9%
<b>IA co-prescription of 4 or more antihypertensive drugs</b>	5.4%

(% per 6-month period)

# Results: all-cause hospitalizations and IAs

	Proportional Fold Change	Attributable risk
<b>At least one IA (per 6-month period)</b>	1.95 [1.8, 2.1]	22%
<b>Long-half benzodiazepine</b>	1.65 [1.5, 1.8]	5%
<b>One antipsychotic drug</b>	1.79 [1.7, 1.9]	9%
<b>≥ 3 psychotropic drugs</b>	2.04 [1.9, 2.2]	12%
<b>≥ 2 diuretics</b>	1.73 [1.5, 2.0]	3%
<b>≥ 4 antihypertensive drugs</b>	2.08 [1.8, 2.3]	5%

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**All-cause hospitalizations rate doubled in a 6-month period when at least one IA was prescribed**

# Discussion

## Strengths of the study

- **First study** to analyze the potential association between these IAs and hospitalizations in a selected population known to be at risk for repeated admissions: elderly people treated for dementia
- **Approach similar to the self-controlled case series**
  - To reduce the bias of confusion
  - Lot of data are not available in these databases because their primary purpose is not medical but either administrative or for reimbursement
  - Self comparison automatically takes into account variables associated with hospitalization among the elderly: marital status, education, autonomy, place of living...

# Discussion

## Limits of the study

- We included only patients **treated for Alzheimer disease**
  - This could lead to an overestimation of the hospitalization rates and an overestimation of the prevalence of IAs
- There was no code for **ADE-related hospitalizations**
  - Second analysis based on the major diagnosis category (MDC)
  - We adopted a minimalist approach, considering only poisoning and trauma as potentially ADE-related hospitalizations
- With the sequential analysis, it was not possible to know whether the **IA occurred before, during, or after the hospitalization** within the same period

# Conclusion

- **The risk of hospitalization nearly doubled in elderly patients being treatment for Alzheimer disease when they were exposed to psychotropic and/or cardiovascular IAs**
- **Interventional studies are now needed** to assess if the reduction of theses IAs could be associated with better clinical outcomes, particularly with reduction of hospital admissions

JAMDA 18 (2017) 549.e1–549.e13



Original Study

Association Between Psychotropic and Cardiovascular Iatrogenic Alerts and Risk of Hospitalizations in Elderly People Treated for Dementia: A Self-Controlled Case Series Study Based on the Matching of 2 French Health Insurance Databases



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