

**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

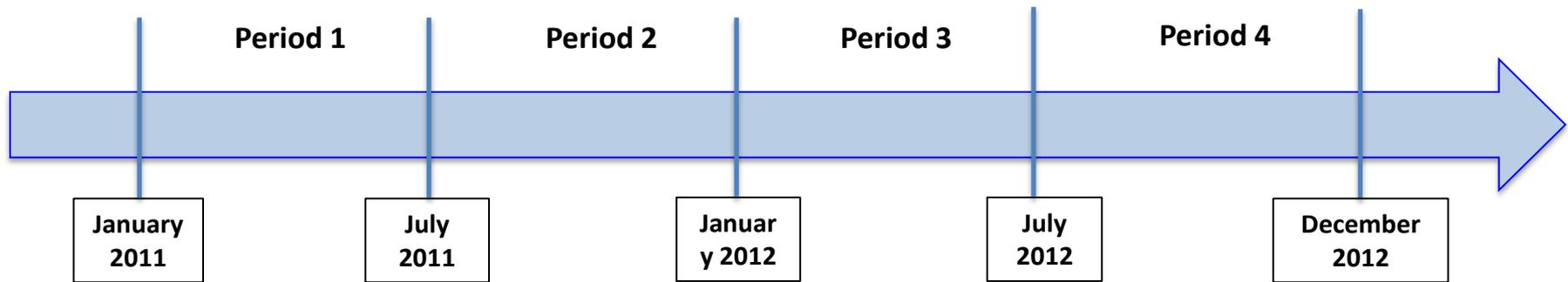
- The co-prescription of 2 or more diuretics
- The co-prescription of 4 or more antihypertensive drugs

# 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

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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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