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Authors have no conflicts of interest with industries related to studied products

## BACKGROUND

Nitrofurantoin is an oral antibiotic effective for the treatment of urinary tract infection and of particular activity against ESBL-producing E coli. Safety concerns include severe pulmonary and hepatic adverse reactions. Since March 2012, in France the use of nitrofurantoin has been restricted to the treatment of symptomatic cystitis for girls aged 6 years and older, adolescent girls and women under the conditions of a microbiological documentation and a lack of oral therapeutic alternatives, as specified in Dear Healthcare Professional Letters in 2012 and 2014. Nevertheless an empiric use may still be considered under certain conditions.

## OBJECTIVES

To assess the compliance with therapeutic indication and national guidelines in France.

## METHODS

A cohort of 7,660 subjects who initiated a nitrofurantoin treatment from March 1<sup>st</sup>, 2012 to February 28<sup>th</sup>, 2015 was identified using EGB database, a representative sample of the population protected by the French National Health Insurance.

Use of nitrofurantoin was considered as documented if a cytobacteriological examination of urine (CBEU) had been performed between 7 and 2 days before nitrofurantoin's dispensing. An empiric use was assumed if a CBEU had been performed within 2 days before nitrofurantoin's dispensing or prescribed the day of the dispensing and performed the day after nitrofurantoin's dispensing. Nitrofurantoin initiations in men or in the absence of CBEU in women were considered as non-compliant.

The frequencies of non-compliant, documented and empiric use of nitrofurantoin were assessed. In addition, characteristics associated with documented use of nitrofurantoin were identified using a logistic regression comparing women with a documented use versus those without CBEU.

## RESULTS

Overall, 15% of the users were men and 45% were women with no CBEU performed prior to nitrofurantoin initiation, resulting in an overall rate of non-compliant use of 60%. A documented use in women accounted for 26% of treatment courses and an empiric use for 14% of treatment courses.

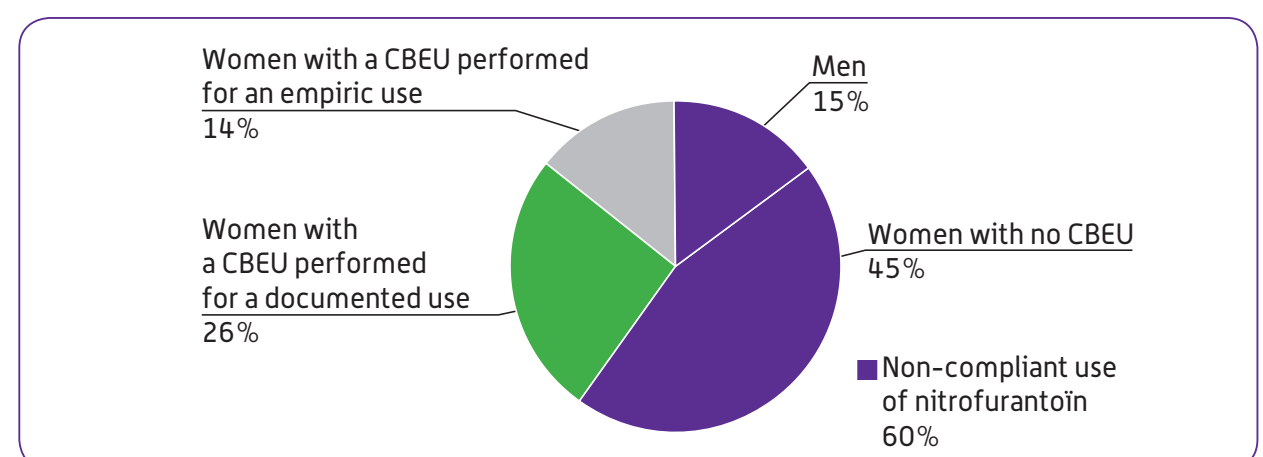
Documented use was significantly more frequent at treatment initiation compared to subsequent treatment courses (55.9% vs. 69.4%,  $p < 0.0001$ ). Age above 60 years, treatment duration of more than 7 days and prior antibiotics' courses were also significantly associated with an increased frequency of documented use of nitrofurantoin. Despite a slight decrease of nitrofurantoin's dispensing from March 2014, no sizeable modifications in the rates of documented use was found during the study period.

**Table 1: Patients', treatment courses' and prescribers' characteristics**

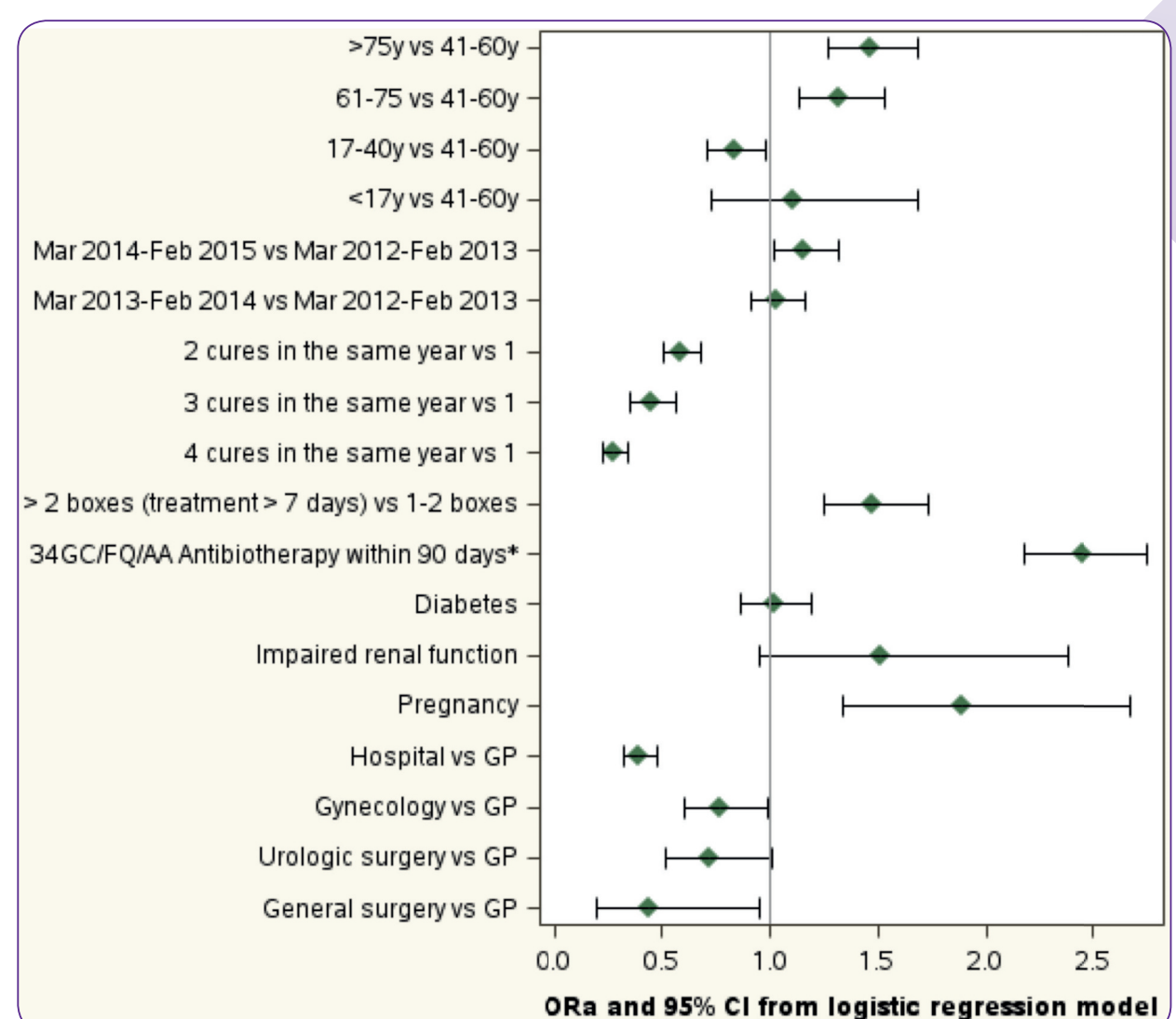
	Female N = 6,542	Male N = 1,118
Age, year (mean ± sd)	56.9 ± 22.4	66.6 ± 17.7
Diabetes	646 [9.9]	243 [21.7]
Impaired renal function	70 [1.1]	32 [2.86]
Pregnancy	202 [3.1]	-
Recurrent cystitis *	1,137 [17.4]	-
Treatment courses		
> 2 boxes (>7 days of treatment)	538 [8.2]	232 [20.8]
Mar 2012 - Feb 2013	2,166 [33.1]	381 [34.1]
Mar 2013 - Feb 2014	2,403 [36.7]	400 [35.8]
Mar 2014 - Feb 2015	1,973 [30.2]	337 [30.1]
Prescribers		
GP's	4,562 [69.7]	605 [54.1]
Hospital	665 [10.2]	118 [10.6]
Gynecology	304 [4.7]	-
Urologic surgery	119 [1.8]	123 [11.0]

\* more than 4 antibiotics among fosfomycin trometamol, amoxicillin-clavulanate, amoxicillin, pivmecillinam, fluoroquinolone, TMP-SMX, cefixime within 365 days.

**Figure 1: Compliance with therapeutic indication (N=10,390 courses)**



**Table 2: Characteristics associated with a documented use of nitrofurantoin**



\*34GC: 3<sup>rd</sup> 4<sup>th</sup> Gen. Cephalosporin, FQ: Fluoroquinolone, AA: amoxicillin-clavulanate

## CONCLUSIONS

This study shows a persistently low compliance with therapeutic indication and guidelines for nitrofurantoin use in France.