Zolpidem prescribing practices before and after FDA required product labeling changes

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BACKGROUND

- Zolpidem IR (Ambien®), zolpidem CR (Ambien CR®), and sublingual zolpidem (Intermezzo ®) were FDA approved in 1992, 2005, and 2011, respectively
- Intermezzo® was labeled with different recommended doses for men and women from the time of approval, due to data that showed men and women had different serum drug concentrations the morning after taking a dose
- Intermezzo® studies showed patients had significant driving impairment at a zolpidem serum concentration ≥ 50 ng/mL
- Intermezzo® studies prompted the FDA to review PK data from zolpidem IR and zolpidem CR studies
- PK data showed more women had serum drug concentrations ≥ 50 ng/mL than men 8- to 9- hours after taking zolpidem IR 10 mg (15% vs. 3%, respectively) and zolpidem CR 12.5 mg (33% vs. 25%, respectively)
- The product labeling was changed on 4/19/2013 to recommend women are *initially* prescribed zolpidem IR 5 mg or zolpidem CR 6.25 mg
- The product labeling was changed on 5/7/2008 to recommend elderly patients (≥65) take a maximum of zolpidem IR 5 mg or zolpidem CR 6.25 mg

DEFINITIONS

- "Low-Dose" zolpidem = zolpidem IR ≤ 5 mg or zolpidem CR ≤ 6.25 mg
- Elderly = patients ≥ 65 years old

OBJECTIVES

Primary Objective
- Determine the proportion of patients prescribed low-dose zolpidem before and after the label change

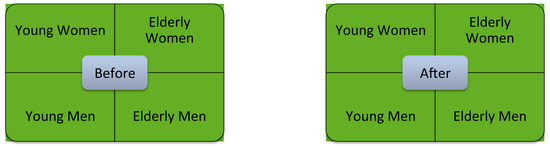
Secondary Objectives
- Determine the proportion of young men, young women, elderly men, and elderly women prescribed low-dose zolpidem before and after the label change
- Compare the number of adverse effects potentially due to zolpidem before and after the label change

REFERENCES

1. Ambien [package insert]. Sanofi. 1992. 2. Ambien CR [package insert]. Sanofi. 2005.3. Intermezzo [package insert]. Sanofi. 2011.
4. Farkas R. FDA Clinical review: dosing for zolpidem products. Reference ID 3137324
5. FDA Drug Safety Communication: http://www.fda.gov/Drugs/DrugSafety/ucm334033.htm

METHODS

- Retrospective, pre/post chart review
- List generated from EPIC was stratified into 8 groups with 50 patients in each group



Inclusion Criteria
- Patients who received care at a UCH ambulatory clinic since April 1, 2011
- Initiation of zolpidem IR or CR between 4/1/2011–4/1/2013 or 6/1/2013–6/1/2015

Exclusion Criteria
- Patients prescribed zolpidem prior to the index prescription date

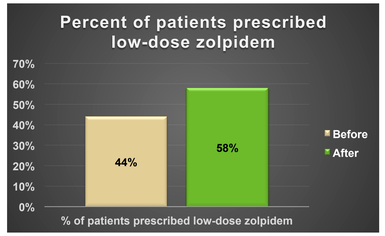
Data Collection
- Included 11 patient factors related to patient demographic data, zolpidem prescribing information, and adverse effects

Data Analysis
- Descriptive statistics were completed using Microsoft Excel
- Logistic regression analyses were completed using R statistical software

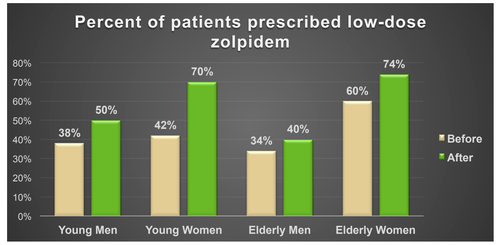
BASELINE DEMOGRAPHICS

Characteristic	Before (n=200)	After (n=200)	p-value
Age (years)	56.8	57.5	0.71
Ethnicity (n, %)			0.50
Non-Hispanic	168 (84%)	174 (87%)	
Hispanic	15 (7.5%)	15 (7.5%)	
Unknown	17 (8.5%)	11 (5.5%)	
Race (n, %)			0.62
White	154 (77.0%)	159 (79.5%)	
Black	12 (6.0%)	13 (6.5%)	
Other	20 (10.0%)	20 (10.0%)	
Unknown	14 (7.0%)	8 (4.0%)	

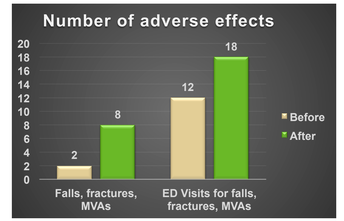
RESULTS



Primary Objective
- The percent of patients prescribed low-dose zolpidem increased after the zolpidem labeling change in 2011 (p=0.020)



Secondary Objective – Subgroup Analysis
- The proportion of patients prescribed low-dose zolpidem increased in all subgroups including young men (p=0.23), young women (p=0.0045), elderly men (p=0.53), and elderly women (p=0.14)
- The effect of the labeling change was not significantly different between the 4 subgroups (young men, young women, elderly men, elderly women) [p=0.46]



Secondary Objective – Adverse Effects
- Patients experienced more adverse effects after the label change
- 55% (n=22) of the adverse effects occurred in patients prescribed low-dose zolpidem

CONCLUSIONS

- The FDA labeling change effectively increased the proportion of patients prescribed low-dose zolpidem
- The proportion of patients prescribed low-dose zolpidem increased in all sub-groups following the label change
- The magnitude of change was similar between subgroups, but was greatest in young women
- The lack of a significant prescribing change in elderly patients is likely due to previous labeling changes affecting older adults
- There were more adverse effects after the label change