

National Estimates of Antifungal Use among Inpatients Based on Administrative Data—United States, 2006–2012

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Background

- Antibiotic use in the United States has been well-characterized. In a previous study¹:
 - Fifty five percent of patients admitted to US hospitals during 2006–2012 received at least 1 dose of antibiotics during their hospital visit.
 - The overall national antibiotic days of therapy was 755 per 1000 patient-days.
- Antifungal use is less understood but is important to quantify to:
 - Understand practice patterns
 - Detect associations with antifungal resistance
 - Inform development of antifungal stewardship programs
- Primary objective:** Use administrative dataset from a large subset of US hospitals to estimate patterns of inpatient antifungal use during 2006–2012 and extrapolate findings to all US hospitals.

1. Baggs J et al, JAMA Int Med Sept 2016

Methods

- Adult and pediatric drug use data were obtained from the Truven Health MarketScan® Hospital Drug Database (HDD).
 - The HDD contains hospital discharge records for all patients discharged from participating US hospitals.
 - Includes discharge-specific diagnostic codes, demographic information, inpatient drug utilization data based on billing records, admission and discharge dates, and facility descriptors.
 - Included visits from January 1, 2006 through December 31, 2012.
 - For each discharge, we identified antifungal doses (oral, parental, and inhalation routes only) charged to the patient during the inpatient stay.
- Antifungal use calculated as days of therapy (DOT) / 1,000 patient days (PDs)
- Extrapolated national estimates of inpatient antifungal use using data submitted to the Centers for Medicare and Medicaid Services Healthcare Cost Report Information System (HCRIS).
- Assessed trends in antifungal use by year using a linear regression multivariable model (outcome distribution was approximately normal)
 - Used generalized estimating equations (GEE) to account for inter-hospital covariance.
 - Included as covariates facility characteristics such as case mix index (a marker of overall disease severity), average patient age, bed size category, teaching status, urban or rural location, proportion of surgical discharges, average co-morbidity score for the facility, and geographic region (by US Census division).

Results

- Data from >34 million discharges from 552 hospitals (~6–8% of all U.S. hospitals) representing 166 million PDs were included in the study.
- Overall, 2.7% of patients received ≥1 dose of an antifungal during their hospital stay.
- Among patients with at least 1 day in the ICU, 7.7% received an antifungal compared with 2.2% for patients without an intensive care stay.
- The overall antifungal DOT for all study years combined was 35.0 per 1,000 PDs.
- Usage of antifungals was >2-fold higher in ICUs compared to non-ICUs: (66.8 vs 29.9 DOT/1,000 PDs, p<0.0001).

Table 1: Demographic and clinical characteristics of inpatients who received and did not receive antifungals in the Truven MarketScan Hospital Drug Database, 2012

Characteristic	Frequency or Mean (SD)		% Antifungal	
	Did not receive antifungal	Received antifungal		
Age, Mean (SD)	50.0 (27.0)	59.0 (20.1)		
Length of stay, Mean (SD)	4.69 (14.0)	14.2 (18.5)		
Sex	Male	1848848	50264	2.7%
	Female	2420198	70070	2.8%
Age category (years)	0–17	589218	3736	0.6%
	18–44	1045119	22346	2.1%
	45–64	1109925	41725	3.6%
	65–84	1164919	42335	3.5%
	85+	359865	10192	2.8%
Critical care	Yes	383056	31907	7.7%
	No	3885990	88427	2.2%
Diagnostic related group type	Medical	3121318	84895	2.7%
	Surgical	1140908	35215	3.0%
Top 5 primary diagnosis codes	038.9 - Unspecified septicemia	75361	10508	12.2%
	486 - Pneumonia, organism unspecified	89082	4130	4.4%
	042 - Human immunodeficiency virus [HIV] disease	4097	3018	42.4%
	V58.11 - Encounter for antineoplastic chemotherapy	12771	2410	15.9%
	584.9 - Acute kidney failure, unspecified	53030	2063	3.7%

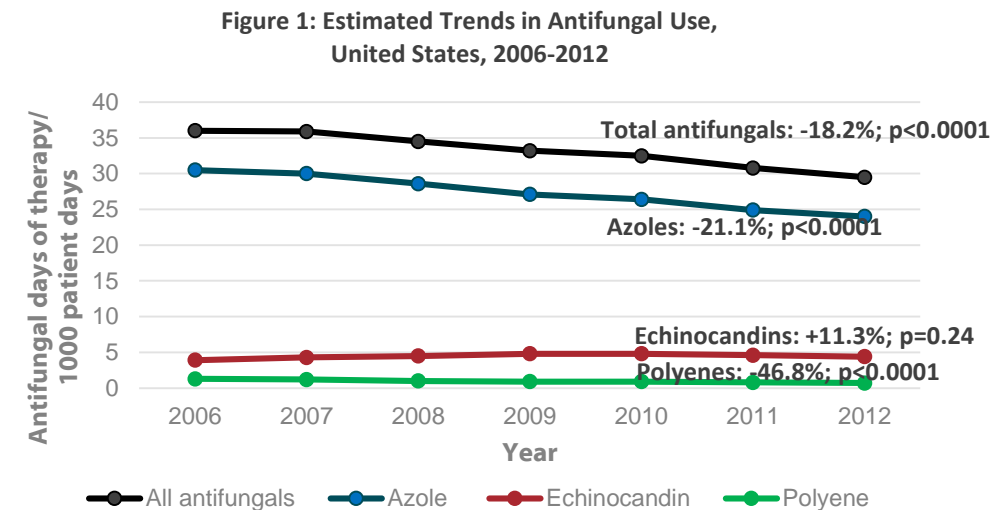


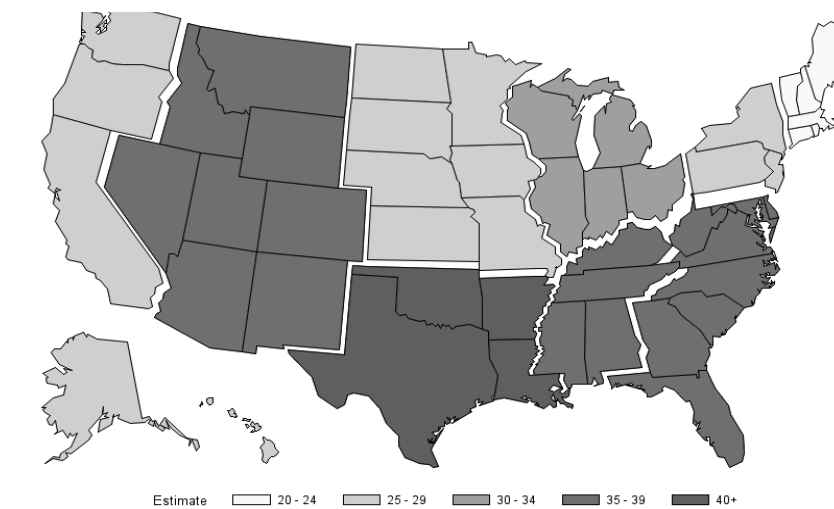
Table 2: Azole days of therapy /1000 patient days by year, United States, 2006–2012

Azole drug	2006	2007	2008	2009	2010	2011	2012	% change
Fluconazole	27.9	27.4	26	24.6	23.7	22.6	21.7	-22.40%
Posaconazole	0	0	0.1	0.1	0.2	0.2	0.2	>>100%
Voriconazole	2.0	2.0	1.9	1.8	1.8	1.6	1.6	-18.30%

Table 3: Proportion of inpatients receiving antifungals by year, United States, 2006–2012

Antifungal drug	2006	2007	2008	2009	2010	2011	2012	%change
All antifungals	2.66%	2.70%	2.74%	2.73%	2.75%	2.74%	2.67%	+0.38%
Azoles	2.51%	2.52%	2.54%	2.51%	2.52%	2.51%	2.44%	-2.9%
Echinocandins	0.22%	0.25%	0.29%	0.32%	0.33%	0.35%	0.33%	50.0%
Polyenes	0.09%	0.09%	0.08%	0.07%	0.07%	0.06%	0.06%	-33.3%

Figure 2: Mean Days of Antifungal Therapy per 1,000 Patient Days by US Census Division, Truven MarketScan Hospital Drug Database, 2006–2012



Discussion/Conclusion

- Although only a small proportion of all inpatients in the US receive antifungals (2.7%), a substantial proportion of ICU patients receive antifungals (7.7%).
- Overall antifungal days of therapy declined significantly during 2006–2012, but the proportion of patients receiving any antifungal drug did not change.
 - This may indicate that patients are receiving shorter treatment courses.
- Azoles accounted for the largest proportion of antifungals used, but there is a clear downward trend in the use of azoles in DOT.
 - Most of the decline was due to decreases in fluconazole and voriconazole use.
 - Posaconazole use increased, though overall DOT/PD were very small for posaconazole.
- Echinocandin use increased both by DOT and proportion of patients receiving echinocandins during the study period.
 - Increased use of echinocandins may reflect the changing epidemiology of *Candida* infections given the rise in the proportion of non-*albicans Candida* infections, which tend to be more resistant to fluconazole.
 - Trends in use of echinocandins should be closely monitored in light of 2016 IDSA guidelines recommending echinocandins as first-line therapy for all invasive candidiasis in adults.
- Septicemia was the most common underlying condition for which antifungals were administered.
 - Much of antifungal use in treatment of sepsis is empiric
 - Antifungal stewardship efforts could focus on stopping empiric antifungals among patients with sepsis when there is no evidence of a fungal infection after 48–72 hours.
- Regional variations in antifungal use mirror regional variations in antibiotic use.
- Including antifungal stewardship as part of antibiotic stewardship programs may help address overuse of antifungals.

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