# Assessment of Potential Antimicrobial-Related Harms in Hospitalized Adults with Common Infections

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## Introduction

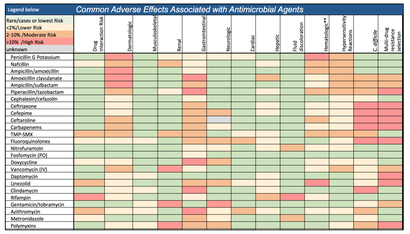
- 30-50% of antibiotics prescribed in hospitals are inappropriate
- 1 in 5 inpatients receiving antimicrobials develop antibiotic-related harms (Tamma)
- Antimicrobial-related harms are likely under-quantified by to the multifactorial exposures in hospitalized patients
- Targeted and shorter courses of antibiotics reduce the risk of medication-related harm

## Methods

### Study Design and Objectives

This was a retrospective cohort conducted at Henry Ford Hospital, Detroit, MI. The departments of family medicine and pharmacy sought to:

1. Describe inpatient antimicrobial-related harms/ adverse drug events (ADE)
2. Predict outcomes and ADEs in patients treated for common infections



Institutional tool for antibiotic-ADE monitoring

### Subjects

- Adults receiving antimicrobials and providers prescribing antimicrobials on the family medicine ward Jan-March of 2017/2018 with the following: respiratory tract, uncomplicated skin/skin structure, or urinary tract infection

### Statistical Analyses

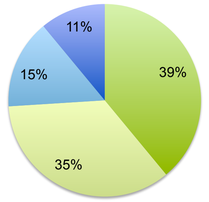
- Descriptive: median, (interquartile range) n, (%) for continuous/categorical variables
- Comparisons: Chi-squared/Fisher's Exact test, or Mann-Whitney U, as appropriate
- Prediction of poor outcomes and ADEs were assessed with multiple logistic regression

| Definitions | |
|---|---|
| ADE | Temporally associated with antibiotic exposure and measured by Naranjo score |
| Mild/moderate ADE | Rash, transaminitis, altered mental status, diarrhea, N/V, prolonged QTc without event, acute renal risk, electrolyte abnormality without cardiac/neurologic event |
| Serious ADE | *Clostridium difficile*, development of 90-day MDRO, anaphylaxis, rhabdomyosis, acute renal injury/failure, seizure, drug-induced thrombocytopenia/neutropenia/anemia, SJS/TEN |
| Nephrotoxicity | As defined by Δ serum creatinine following initiation of antimicrobial therapy, classified by AKIN criteria |
| MDRO | Multi-drug resistant organism isolation without prior colonization including: methicillin-resistant *S. aureus*, *Pseudomonas, Acinetobacter,* vancomycin-resistant *Enterococci*, ceftriaxone/carbapenem-resistant Enterobacteriaceae |

## Results

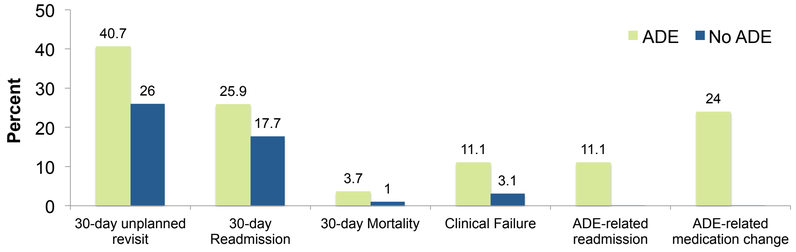
| Baseline Demographics | N=150 |
|---|---|
| Age, years (IQR) | 62 (50—72) |
| Sex, male (%) | 64 (42.7) |
| Length of stay, days (IQR) | 3 (2—4) |
| Antibiotic duration, days (IQR) | 7 (5—10) |
| Total antibiotic days, median (IQR) | 8 (6—14) |
| Beta-lactam allergy, n (%) | 27 (18) |
| Charlson score, median (IQR) | 2 (1—4) |
| 30-day readmission, n (%) | 31 (20.7) |
| 30-day ED/unexpected office visit | 41 (27.3) |
| **Event rate: 3.33 ADEs per 100 antibiotic days** | |
| Days of antibiotic prescribed | 1499 |
| Unique patients with potential ADEs<br>• Total potential ADEs | 36 (24.0)<br>50 |

**Infection Type**

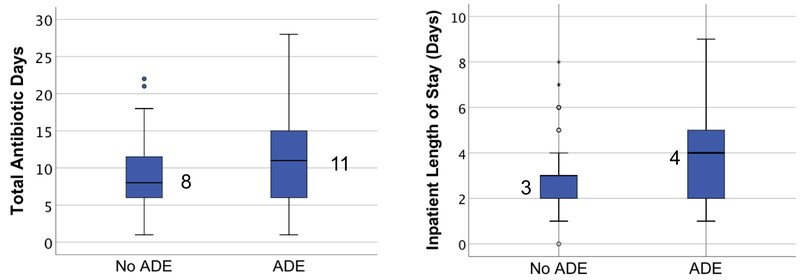



UTI: urinary tract infection; ABSSSI: acute bacterial skin/skin structure infection; AECOPD: acute exacerbation of chronic obstructive pulmonary disease

**Outcomes Associated with ADE**




**Process Measures Associated with ADE** (p <0.05)




| Possible Antibiotic-Related Harms | N=150 | Contributing Medications | Naranjo score (range) |
|---|---|---|---|
| Patients experiencing mild/moderate ADE, n (%) | 41 (27.3) | | 3 (1—7) |
| • Any diarrhea | 24 (16) | 18 (75) | 3 (1—7) |
| • Diarrhea without concurrent laxative | 6 (4) | 0 (0) | 4 (3—7) |
| • Nausea/vomiting | 7 (4.7) | 3 (42.8) | 3 (1—5) |
| • QTc prolongation without event | 8 (5.3) | 3 (37.5) | 4 (3—4) |
| • Acute renal risk | 9 (6) | 7 (77.8) | 3 (2—5) |
| • Transaminitis | 2 (1.3) | 0 (0) | 4 (2—6) |
| • Altered mentation | 3 (2) | 0 (0) | 4 (3—5) |
| Patients experiencing severe ADE, n (%) | 13 (8.7) | | 4 (3—7) |
| • Hematologic | 5 (3.3) | 0 (0) | 4 (3—6) |
| • Renal injury/failure* | 4 (2.7) | 3 (75) | 4.5 (3—6) |
| • *C. difficile* diarrhea | 1 (0.7) | 0 (0) | 7 |
| • Neurotoxicity | 2 (1.3) | 2 (100) | 4 |
| • Anaphylaxis/hives | 1 (0.7) | 0 (0) | 4 |
| • Cardiac event | 2 (1.3) | 2 (100) | 4 (2—6) |
| Subsequent isolation of MDRO, n (%) | 7 (4.7) | -- | -- |

**Logistic Regression ADE Prediction Model**

| Covariate | No ADE (n= 96) | ADE (n= 54) | p | Adjusted OR |
|---|---|---|---|---|
| Prior admission (90 days) | 18.8% | 33.3% | 0.045 | **2.52 (1.09—5.84)** |
| Dementia | 4.2% | 16.7% | 0.014 | -- |
| Beta-lactam allergy | 19.8% | 14.8% | 0.446 | -- |
| Definitive quinolone | 21.9% | 35.2% | 0.086 | 2.07 (0.92—4.66) |
| Age, years (IQR) | 63 (50—70) | 61 (49—75) | 0.956 | -- |
| Charlson score | 2 (1—4) | 2.5 (1—4) | 0.647 | -- |
| Length of stay | 3 (2—3) | 4 (2—5) | <0.001 | **1.51 (1.21—1.89)** |
| Total antibiotic days | 8 (6—12) | 11 (6—15) | 0.036 | **1.05 (0.99—1.13)** |

## Discussion

- 1 in 4 hospitalized ward patients receiving antimicrobials for common infections experienced at least one potential ADE
- ADE was associated with more readmission and unplanned healthcare visits.
- Patients with ADEs received more antibiotic days compared to those without
- Antibiotic duration of therapy and definitive quinolone therapy may represent modifiable risks for ADE.

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