

School of Pharmacy

THE PETER LAMY CENTER ON DRUG THERAPY AND AGING

Background

The challenge to improve effective and safe of antibiotics in post-acute and long-term care settings (PALTC) is a national focus of great importance. The goals of the national antibiotic stewardship initiative are to reduce the emergence of multi-drug resistant organisms, antibiotic adverse drug events (AADEs), and unnecessary cost.¹ The Centers for Disease Control and Prevention (CDC) suggest AADE monitoring as one of several appropriate resident outcome measures for antibiotic stewardship programs.² Processes for AADE identification, documentation, monitoring and reporting vary substantially among PALTC facilities.

Objectives

Our aim was to develop a standardized AADE clinical decision support tool to be embedded electronically into PALTC workflow.

- Educate clinicians about AADEs, their frequency, timing, manifestations and outcomes
- Provide an algorithmic approach for evaluation of possible AADEs
- Develop consistent workflow for evaluating if AADEs have occurred
- Accurately document and report AADEs and their outcome
- Ultimately, reduce antibiotic harm

Quality Improvement Methods

The Maryland Antimicrobial Stewardship Collaborative, funded by the CDC and the Maryland Department of Health:

- is led by The Peter Lamy Center on Drug Therapy and Aging;
- includes geriatricians, infectious diseases physicians and pharmacists, geriatrics nurses, geriatric pharmacotherapists, public health and CDC representatives as well as Think Research team members;
- met biweekly from March 2018 November 2018 to plan educational opportunities for LTC staff, then monthly thereafter through Jun 2018; and
- developed an AADE template and elicited interprofessional feedback during a live Antimicrobial Summit (Table 1); and

• interviewed key LTC stakeholders (Table 1) to further refine the AADE tool. Following integration of the feedback, the revised AADE template was transformed, by Think Research, into a prototype for integration into electronic health records (EHR). Interviews with participants revealed wide variability in access to laboratory integration, data sources, and workflows.

Table 1: Interprofessional Collaboration

Summit Participants	Number
Physicians	11
Nurses/Nurse Practitioners	40
Pharmacists	35
Infection Control/Epidemiologists	7
Quality Assurance Managers	4
Administrators	2
Other	11

Key Stakeholder Interviews	Number
Medical Directors	2
LTC Pharmacy Providers	3
Nursing Home Clinical 2 Managers/VPs	

Results

Common AADEs were characterized by signs and symptoms into gastrointestinal, renal, cardiovascular, hematologic, hepatic, skin, anaphylaxis, myositis/tendinitis, and neurologic AADEs.

In a recent publication a retrospective review of antibiotic therapy in 1,488 hospitalized adults (mean age 59 years, 51% female) provides insights regarding the prevalence and timing of antibiotic ADEs.³

Prevalence

Twenty percent of antibiotic-treated patients experienced at least one ADE. For every additional 10 antibiotic days of therapy an additional 3% increased risk of an ADE was conferred. The prevalence and timing of each ADE category is shown in Table 1.

Timing

The median time to development of an ADE was 5 days (range, 3 – 8 days). Most (73%) ADEs occurred during the hospital stay; 27% were identified after hospital discharge.

UNIVERSITY of MARYLAND Interprofessional Collaboration Improves Antibiotic Stewardship

Barbara Zarowitz¹, PharmD, Fatima Sheikh², MD, Fatima Naqvi, MD, Emily Heil¹, PharmD and Nicole Brandt¹, PharmD, MBA ¹University of Maryland School of Pharmacy, ²Division of Geriatrics & Gerontology, Department of Medicine, Johns Hopkins University School of Medicine and FutureCare Health, and ³Five Star Physician Services.

Table 2: Characterization of Antibiotic Adverse

Classification	Prevalence	Median	Time	Criteria
Classification	ricvarchee	Time	Interquartile	Criteria
		(days)	Range (days)	
Gastrointestinal	78 (42%)	5	2 - 9	Diarrhea: > 3 loose stools /day
				N/V: associated with antibiotic
Renal	45 (24%)	5	2 - 10	Increase Scr to > 1.5 x baseline
Hematologic (Blood)	28 (15%)	12	6 - 24	Anemia: Hgb < 10 g/dL
				Leukopenia: WBC < 4500 cells/µL
				Thrombocytopenia: platelets < 150 x 10 ³ /µL
Hepatobiliary (Liver)	13 (7%)	8	4 - 12	Total bilirubin > 3 mg/dL, ALT/AST > 3 x baseline
Neurologic	13 (7%)	3	2 - 4	Altered mental status, peripheral neuropathy,
				or seizures
Cardiac (Arrhythmia)	2 (1%)	11	4 - 18	QTc > 440 msec in females
				QTc > 460 msec in males
Myositis (Muscle)	2 (1%)	NA	NA	Increase in creatine phosphokinase > 5 x
				baseline
Dermatologic (Skin)	2 (1%)	minutes to	NA	Rash, hives, non-hive rashes, red man
		days		syndrome associated with non-vancomycin
				antibiotic
Anaphylaxis	1 (0.007%)	minutes	NA	Acute respiratory compromise, hypotension, or
				end-organ dysfunction within minutes of
				starting antibiotic

Where: ALT/AST=alanine aminotransferase/aspartate aminotransferase; Hgb=hemoglobin; N/V=nausea/vomiting; QTc=corrected QT interval; Scr=serum creatinine; WBC=white blood cell count

Figure 1: Algorithms, Characteristics, and Causes of Gastrointestinal (GI) and Renal AADEs

Antibiotic ADE: GI Event

- Diarrhea: > 3 loose stools per
- day; absence of laxatives Nausea and/or vomiting;
- nausea and vomiting
- associated with antibiotic; no other explanation
- Prevalence: 42%
- Median time to occurrence: 5 days (2 – 9)

amma PD, et al. Association of adverse events with antibiotic use in hospitalized ents. JAMA Int Med 2017:177:1308-15.

Assessment of possible anti-infective related adverse event observed (select all that apply):

□ Nausea □ Vomitin □ Distended abdomen □	-	 Abdominal tenderness/pain Infectious diarrhea (<i>C. difficile</i>)
Other 1. Possible Gastrointestina Provide details:	and se free	g staff observes and/or asks resident about the nce of any gastrointestinal signs and symptoms elects all that apply. Details can be provided in text (i.e., 3 bouts of loose stool/diarrhea and ea today). The date of observation should be
Date Observed	_	recorded.

ADE: Renal Event

- Increase in Scr to > 1.5 times baseline; absence of precipitating renal factors (i.e., sepsis, pre-renal azotemia, dehydration, other nephrotoxic drugs)
- Prevalence: 24%
- Median time to occurrence: 5 days (2 – 10)

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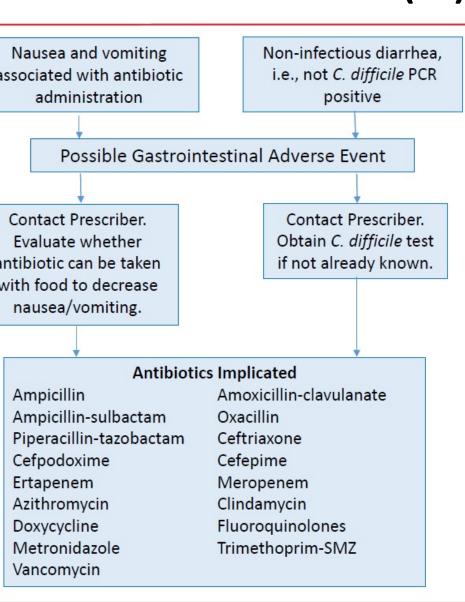
nt of possible anti-infective related adverse event observed (select all that apply)

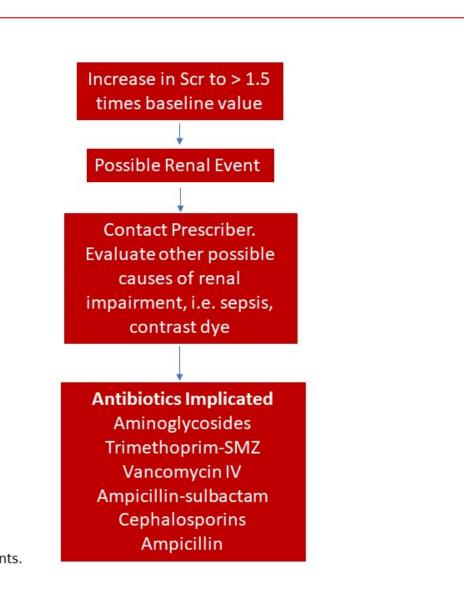
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Clinical algorithms identify antibiotics most commonly associated with signs and symptoms, median occurrence time post-antimicrobial initiation, and suggested laboratory monitoring. An exception-based logic was employed in the AADE template design to minimize required nursing documentation (Figure 3).

Results (continued)

e Drug Events ³	
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□ Blood in urine	□ Other
ne resident may not rep oms prior to a significar tinine value. For the an um creatinine should b kly while the resident re	nt increase in the serum tibiotics noted above, e monitored at least

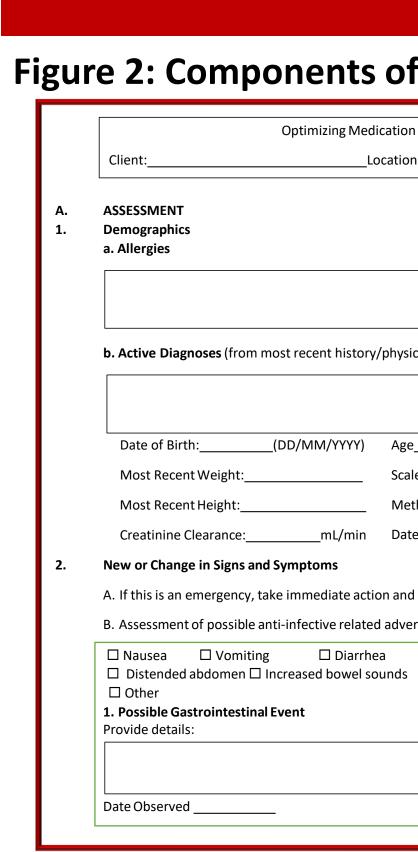


Figure 3: Proposed Antibiotic Adverse Drug Event Workflow

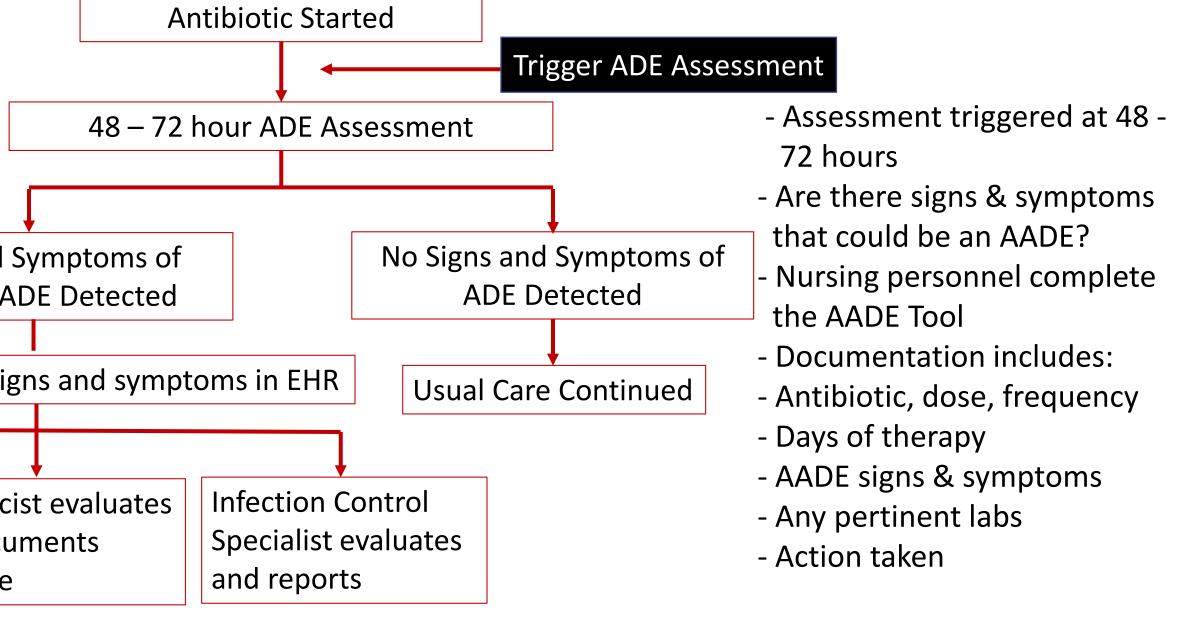
	Signs and S Possible A
	Nurse provides ADE sig
ar	D/NP evaluates Ind intervenes as Appropriate outcome
•	Through interprof integrated as a pr and trending of AA
•	Stakeholder mapp prescribing, monit
•	AADE drug, type stewardship metri
•	Alignment with cli
•	Further testing an
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Results (continued)		
the AADE Template		
Safety 4.0 Final 2018		
ı: <u></u>	Date ObservedSuspected Anti-infective	
	 3. Category of Possible Anti-infective Adverse Drug Event Allergy Anticipated/Expected/Dose-related Idiosyncratic/Unanticipated/Unpredictable 	
	 4. Event Outcome (Hartwig Severity Assessment Scale)¹ □ Level 1. Resolved, no residual harm. No change in treatment was needed. 	
cal)	Level 2. Resolved with suspected anti-infective held, discontinued or otherwise changed.	
	Level 3. Resolved with suspected anti-infective held, discontinued or otherwise changed AND/OR an antidote or other treatment was required.	
	Level 4. Any Level 3 ADE which causes hospitalization or increases length of stay by at least 1 day.	
e: Date:	Level 5. Any Level 4 ADE which requires intensive medical care.	
hod: Date:	□ Level 6. The ADE caused permanent harm to the resident.	
e of Creatinine:	Level 7. The ADE either directly or indirectly led to the death of the resident.	
notify PRESCRIBER . rse event observed (select all that apply):	Resulting Severity of the ADE □ A. Mild Event: Levels 1 and 2 □ B. Moderate Event: Levels 3 and 4 □ C. Severe Event: Levels 5, 6 and 7	
☐ Abdominal tenderness/pain ☐ Infectious diarrhea (<i>C. difficile</i>)	 3. EMR Documentation This adverse event should be documented in the resident's medical record to help avoid future exposure and adverse events. 1. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992; 49: 2229–2231. 	



Discussion

- ofessional collaboration an AADE tool was developed, refined, and rototype into PALTC EHRs to facilitate identification, documentation, ADEs
- ping is being conducted to identify accountabilities for antibiotic toring, and reporting
- number, and outcome can be trended with other antibiotic
- inical care is needed to support AADE⁴ reporting
- nd validation pilots are underway

References

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Disclosures