14. Effects of an Opt-Out Protocol for Antibiotic De-escalation among Selected Patients with Suspected Sepsis: The DETOURS Trial

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The CDC Prevention Epicenters Program

Session: O-03. Building Your Toolkit for HAI Surveillance and Stewardship

Background. Sepsis guidelines recommend daily review to de-escalate or stop antibiotics in appropriate patients. We conducted a randomized controlled trial (NCT03571007) of an opt-out protocol to decrease unnecessary antibiotics in selected patients with suspected sepsis.

Methods. We evaluated non-ICU adults remaining on broad-spectrum antibiotics with negative blood cultures at 48-96 hours at ten U.S. hospitals during September 2018-May 2020. A 23-item safety check excluded patients with ongoing risks of infection, concerning or inadequate microbiologic data, or high-risk conditions (Figure 1). Eligible patients were randomized to the opt-out protocol vs. usual care. The primary outcome was 30-day post-enrollment antibacterial days of therapy (DOT). Clinicians caring for intervention patients were contacted by a pharmacist or physician to encourage antibiotic discontinuation or de-escalation using opt-out language, discuss rationale for continuing antibiotics, working diagnosis, and de-escalation and duration plans. Hurdle models separately compared odds ratios for exclusion were antibiotics given prior to blood culture (35%), positive culture (29%), and length of stay did not differ.

Results. Among 9606 screened, 767 (8%) were enrolled (Figure 2). Common reasons for exclusion were antibiotics given prior to blood culture (35%), positive culture (29%), and length of stay did not differ.

DETOURS Trial Flow Diagram

Flow of participants through the DETOURS Trial. Observed Days of Antibiotic Therapy Among Intervention and Control Subjects in the DETOURS Trial

Distribution of Observed Days of Therapy

Post-enrollment days of antibiotic therapy among 767 DETOURS Trial participants in 10 US acute care hospitals within 30 days after enrollment. Dark pink color indicates percent overlap between intervention (purple) and control (light pink) groups.

Conclusion. In this patient-level randomized trial of a stewardship intervention, the opt-out de-escalation protocol targeting selected patients with suspected sepsis resulted in more antibiotic discontinuations but did not affect safety events.
15. Real-World Changes in Clostridioides difficile infection (CDI) Treatment Utilization and Clinical Outcomes Associated with Updated 2017 IDSA Guidelines among Medicare Beneficiaries in the U.S.

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Session: O-04. Challenges in C. difficile

Background. The 2017 IDSA CDI guideline update phased out metronidazole (MTZ) and recommended vancomycin (VAN) or fidaxomicin (FDX) for first-line use. This study examined changes in CDI antibiotic use and clinical outcomes among Medicare beneficiaries with CDI pre- vs. post- the guideline update.

Methods. This retrospective claims analysis used 2016-2018 national Medicare claims data. The two study samples included continuously eligible fee-for-service Medicare beneficiaries aged 266 years with a new CDI diagnosis followed by an antibiotic fill in the pre-period (04/01/2017-09/30/2017) and post-period (04/01/2018-09/30/2018), respectively. Outcomes included type of CDI antibiotic received; sustained response and CDI recurrence. Multivariable regressions compared pre- vs. post-period outcomes while controlling for sociodemographic and clinical factors.

Results. The pre-period (N=7,389) and post-period (N=7,746) samples had similar characteristics (59% > 75 years, 32% male). Post-guideline update, absolute rates of MTZ use declined 27.2% (relative change [RC] -34.1%, p< 0.001) and VAN use increased 26.9% (RC +150.2%, p< 0.001) (Figure 1). While FDX use increased 0.8% (RC +87.8%, p< 0.001), overall use remained low (1.63%). Surprisingly, clinical outcomes did not improve between the pre- and post-period (Table 1). Even after adjustment, overall sustained response rates decreased (Odds Ratio [OR]: 0.93, p=0.0197) and overall CDI recurrence rates increased (OR: 1.13, p=0.0018) slightly in the post-versus pre-period. Additional analyses by type of antibiotic showed that VAN (55.0% and 35.1%) was similar in outcomes to MTZ (54.2% and 33.0%), whereas FDX (71.4% and 20.9%) had higher sustained response and lower CDI recurrence rates, respectively (Figure 2).

Figure 1. First-line use of CDI treatments, pre- vs. post- the guideline update, among Medicare beneficiaries with CDI

Table 1. Clinical outcomes, pre- vs. post- the guideline update, among Medicare beneficiaries with CDI

| Clinical outcomes | Pre-Guideline Update | Post-Guideline Update | p-value |
|-------------------|----------------------|-----------------------|---------|
| Sustained response (≥ 4 weeks) | N | 7389 | 7166 | 0.001 |
| N | 4205 | 656 | 548 | 0.01 |
| Sustained response (≥ 8 weeks) | N | 3997 | 3861 | 0.0002 |
| N | 2927 | 2381 | 409 | 100 |
| All patients with a clinical resolution | N | 3997 | 3861 | 0.0002 |
| N | 2927 | 2381 | 409 | 100 |
| CDI recurrence (4 weeks) | N | 1892 | 2168 | 0.001 |
| N | 135 | 328 | 33.8 | 0.001 |
| CDI recurrence (8 weeks) | N | 2190 | 2564 | 0.0001 |
| N | 95 | 235 | 31.6 | 0.0001 |

Figure 2. Clinical outcomes* by type of index CDI treatment among Medicare beneficiaries with CDI

Note. Pooled rates among patients on each index CDI treatment across the pre- and post-index periods.

Conclusion. The 2017 IDSA guideline update was associated with a substantial increase in VAN use and decrease in MTZ use. FDX use rates remained low (<2%). Overall CDI outcomes did not improve post guideline update despite the shift to guideline-indicated VAN. This may be because VAN was not associated with meaningfully improved outcomes relative to MTZ. However, improved outcomes seen with FDX relative to VAN and MTZ suggest potential benefits from its greater use in Medicare patients.

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16. Attributable Mortality, Healthcare Costs and Out-of-Pocket Costs of Clostridioides difficile Infection in US Medicare Advantage Enrollees

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Session: O-04. Challenges in C. difficile

Background. US attributable CDI mortality and cost data are primarily from Medicare fee-for-service populations. Little is known about Medicare Advantage Enrollees (MAEs), who comprise about 39% of the Medicare population.

Methods. Using 2017-2019 Optum's de-identified Clinformatics® Data Mart database, this retrospective cohort study identified first C difficile infection (CDI) episodes occurring in 2018 among eligible MAEs ≥66 y of age who were continuously enrolled for 12 mo before CDI diagnosis (baseline period). CDI was defined via ICD10 diagnosis codes or evidence of toxin testing with CDI antibiotic treatment. To assess all-cause mortality and CDI-associated healthcare and patient out-of-pocket (OOP) costs, CDI+ cases were matched 1:1 to CDI− controls using propensity scores (PS) and were followed through the earliest of death, disenrollment or end of the 12 mo followup. Additionally, outcome analyses were stratified by infection acquisition and hospitalization status.

Results. Among 3,450,354 eligible MAEs, 15,195 (0.4%) had a CDI episode in 2018. Using PS generated from >60 variables collected in the baseline period, 14,928 CDI+ cases were matched to CDI− controls. Over 12 mo of follow-up, the difference in 1-yr attributable mortality was 7.9% in the CDI+ (26.3%) vs CDI− (18.4%) cohort (Figure 1). CDI attributable mortality was higher among hospitalized CDI+ cases (18.4% for healthcare associated [HA]); 13.1% for community associated [CA]) vs nonhospitalized CDI+ cases (HA, 4.5%; CA, 1.0%). Similarly, healthcare costs were higher for CDI+ vs CDI− patients, with excess mean total cost of $13,363 at the 2-mo follow-up (Figure 2). Total excess mean healthcare costs were greater among hospitalized CDI+ patients (HA, $28,139; CA, $28,136)