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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**Background.** The 2017 IDSA CDI guideline update phased out metronidazole (MTZ) and recommended vancomycin (VAN) or fidaxomycin (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 27.7% (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) in the post-vs. 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).

**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.

**Disclosures.** Erik R. Dubberke, MD, MSPH, Ferring (Grant/Research Support)Merck (Consultant)Pfizer (Consultant)Shire (Consultant)UpToDate (Consultant)Janssen, Inc. (Consultant)Janssen, Inc. (Consultant)Novartis (Consultant)AbbVie (Consultant)Arena Pharmaceuticals, Inc. (Consultant)COVIA Health Solutions (Employee)Engels N. Obi, PhD, Merck & Co. (Employee)ShareholderSachin Kamal-Bahi, PhD, AbbVie (Consultant)Arena Pharmaceuticals, Inc. (Consultant)AstraZeneca Pharmaceuticals (Shareholder)Janssen, Inc. (Consultant)Merck (Consultant)ShareholderNovartis (Consultant)Pfizer, Inc. (Consultant)ShareholderPhRMA (Consultant)Kaushal Desai, PhD, AstraZeneca Pharmaceuticals (Consultant)Bruce Stuart, PhD, COVIA Health Solutions (Consultant)Jalpa A. Doshi, PhD, Acadia (Consultant)Adler (Advisor or Review Panel member)Biogen (Grant/Research Support)Rechninger Ingelheim (Other Financial or Material Support)Scientific lecture Catalysis (Consultant)Humana (Grant/Research Support)Janssen, Inc. (Consultant)Grant/Research SupportMeiraGTx (Consultant)Merck (Grant/Research Support)Advisor or Review Panel member)Regeneron (Grant/Research Support)SAGE Therapeutics (Consultant)Sanofi (Grant/Research Support)Shire (Advisor or Review Panel member)The Medicines Company (Advisor or Review Panel member)

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

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**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 Clininformatics® Data Mart database, this retrospective cohort study identified first CDI episode 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)
than for nonhospitalized CDI+ patients (HA, $574; CA, $2503). CDI-associated excess mean OOP cost was $409 for CDI+ cases at the 2 mo followup. Total excess mean OOP cost was highest in CA hospitalized CDI+ cases, followed by HA hospitalized CDI+ cases, HA nonhospitalized CDI+ cases and finally CA nonhospitalized CDI+ cases ($964, $574, $231 and $197, respectively).

**Figure 1. Attributable all-cause mortality**

| Overall | Mortality by followup month |
|---------|-----------------------------|
|         | CDI+ (n=14,928) | CDI- (n=14,928) |
| 1 mo    | 4.4% | 16.4% |
| 2 mo    | 6.6% | 18.2% |
| 3 mo    | 8.8% | 18.2% |
| 6 mo    | 20.6% | 20.6% |
| 12 mo   | 20.6% | 20.6% |

**By CDI acquisition and hospitalization status (PS matched pairs)**

**Figure 2. Excess costs (2 months followup)**

| Healthcare associated (12 months postindex) | Community associated (12 months postindex) |
|--------------------------------------------|-------------------------------------------|
| Hospitalized | Nonhospitalized | Hospitalized | Nonhospitalized |
| CDI+ | CDI- | CDI+ | CDI- |
| $230 | $230 | $290 | $290 |

**Conclusion.** CDI is associated with major mortality and total healthcare and OOP costs. Preventing CDI in the elderly may improve outcomes and reduce costs for healthcare systems and patients.

**Disclosures.** Holly Yu, MSPH, Pfizer Inc (Employee, Shareholder); Jennifer L. Nguyen, ScD, MPH, Pfizer Inc (Employee); Tamuno Alfred, PhD, Pfizer Inc (Employee); Jingying Zhou, MA, Med, Pfizer Inc (Employee, Shareholder); Margaret A. Olsen, PhD, MPH, Pfizer (Consultant, Research Grant or Support).

17. **Comparative Assessment of a Machine Learning Model and Rectal Swab Surveillance to Predict Hospital Onset *Clostridioides difficile***

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**Background.** Hospital onset *Clostridioides difficile* infection (HO-CDI) is associated with significant morbidity and mortality. Screening individuals at risk could help limit transmission, however swab-based surveillance for HO-CDI is resource intensive. Applied to electronic health records (EHR) data, machine learning (ML) models present an efficient approach to assess patient risk. We compare the effectiveness of swab surveillance against daily risk estimates produced by a ML model in detecting patients who will develop HO-CDI.

**Methods.** Patients presenting to Michigan Medicine’s ICUs and oncology wards between June 6th and October 8th 2020 had rectal swabs collected on admission, weekly, and at discharge from the unit, as part of VRE surveillance. We performed an aerobic culture on the residual media followed by a custom, multiplex PCR on isolates to identify toxigenic *C. difficile*. Risk of HO-CDI was calculated daily for each patient using a previously validated EHR-based ML model. Swab results and model risk scores were aggregated for each admission and assessed as predictors of HO-CDI. Holding sensitivity equal, we evaluated both approaches in terms of accuracy, specificity, and positive predictive value (PPV).

**Results.** Of 2,044 admissions representing 1,859 patients, 39 (1.9%) developed HO-CDI. 23.1% (95% CI: 11.1–37.8%) of HO-CDI cases had at least one positive swab. At this sensitivity, model performance was significantly better than random but worse compared to swab surveillance—accuracy: 87.5% (86.8–88.9%) vs. 94.3% (93.3–95.3%), specificity: 88.7% (87.3–90.0%) vs. 95.7% (94.8–96.6%), PPV: 3.8% (1.6–6.4%) vs. 9.4% (4.3–16.1%). Combining swab AND model yielded lower sensitivity 2.6% (0.0–8.9%) compared to combining swab OR model at 43.6% (27.3–60.0%), and yielded PPV 7.1% (0.0–25.0%) vs. 43.6% (27.3–60.0%) respectively (Figure 1).

**Figure 1. Surveillance & risk score performance.**

Binary classification performance metrics of ML model (Model), toxigenic C. difficile rectal swab surveillance (Swab), and combination approaches (Model AND Swab and Model OR Swab), reported in terms of percentage points. Bold numbers highlight the best performing approach for a given performance metric. The combined approach of monitoring the Model AND Swab yielded the highest accuracy 97.5% (95% confidence interval: 96.8%, 98.1%), it also had the highest specificity 99.4% (99.0%, 99.7%), and yielded PPV 9.4% (4.3–16.1%) and F1 score 13.3% (6.2%, 21.8%). These results highlight the complementarity of the model and swab-based approaches.

**Conclusion.** Compared to swab surveillance using a ML model for predicting HO-CDI results in more false positives. The ML model provides daily risk scores and can be deployed using different thresholds. Thus, it can inform varied prevention strategies for different risk categories, without the need for resource intensive swabbing. Additionally, the approaches may be complimentary as the patients with HO-CDI identified by each approach differ.

**Disclosures.** Vincent B. Young, MD, PhD; American Society for Microbiology (Other Financial or Material Support, Senior Editor for mSphere); Vedanta Biosciences (Consultant); Krisha Rao, MD, MS; Bio-K+ International, Inc. (Consultant); Merck & Co., Inc. (Consultant, Research Support); Roche Molecular Systems, Inc. (Consultant); Seres Therapeutics (Consultant).

18. **Global Surveillance of *Clostridioides difficile* Demonstrates High Prevalence in Non-Healthcare Settings**

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