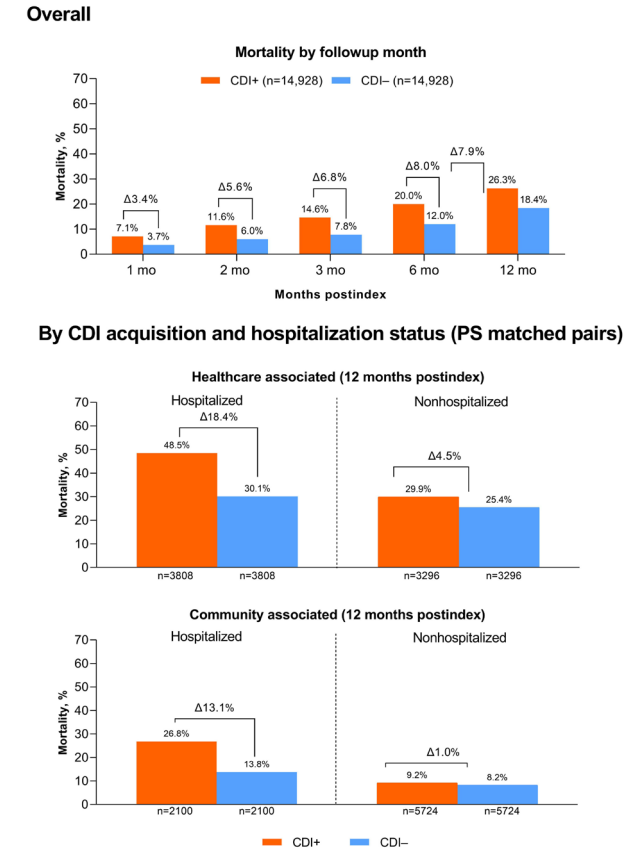
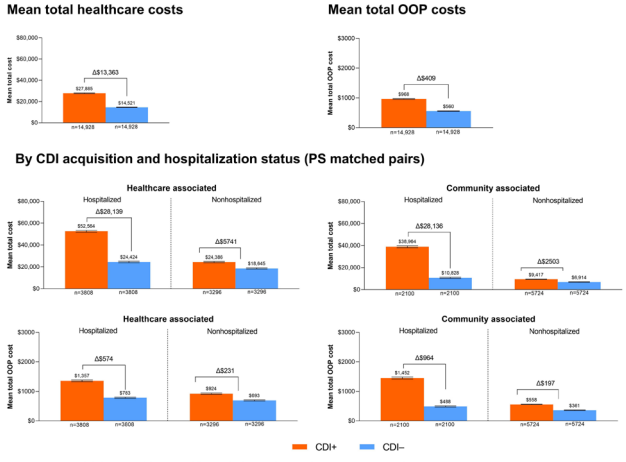
than for nonhospitalized CDI+ patients (HA, $5741; CA, $2503). CDI-associated excess mean OOP cost was $409 for CDI+ cases at the 2 mo followup. Total excess mean OOP cost was highest in CA hospitalized CDI+ cases, followed by HA hospitalized CDI+ cases, HA nonhospitalized CDI+ cases and finally CA nonhospitalized CDI+ cases ($964, $574, $231 and $197, respectively).

Figure 1. Attributable all-cause mortality



CDI+=*C difficile* infection positive case; CDI–=*C difficile* infection negative control; PS=propensity score.

Figure 2. Excess costs (2 months followup)



CDI+=*C difficile* infection positive case; CDI–=*C difficile* infection negative control; OOP=out of pocket; PS=propensity score.
Error bars are the standard error.

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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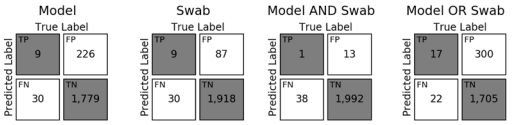
Session: O-04. Challenges in C. difficile

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 anaerobic 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% (86.0–88.9%) 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.



	Model	Swab	Model AND Swab	Model OR Swab
Accuracy	87.5	94.3	**97.5**	84.2
Sensitivity	23.1	23.1	2.6	**43.6**
Specificity	88.7	95.7	**99.4**	85.0
PPV	3.8	**9.4**	7.1	5.4
NPV	98.3	98.5	98.1	**98.7**
F1	6.6	**13.3**	3.8	9.6

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%). The combined approach of monitoring the Model OR Swab yielded the highest sensitivity 43.6% (27.3%, 60.0%) and negative predictive value (NPV) 98.7% (98.2, 99.2%). Using the Swab alone yielded the highest 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) **Krishna Rao, MD, MS**, **Bio-K+ International, Inc.** (Consultant)**Merck & Co., Inc.** (Grant/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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Session: O-04. Challenges in C. difficile

Background. *Clostridioides difficile* is a Gram-positive, spore-forming, toxin-producing organism that is the leading cause of healthcare-associated infections. However, past studies have isolated *C. difficile* spores from the community, suggesting an environmental reservoir that may play a role in transmission. This study aimed to examine the prevalence and strain types of *C. difficile* isolated from the United States (US) and internationally.

Methods. From 2014 to 2017, environmental swabs were collected from public areas, healthcare settings, and shoe soles. Samples were considered positive for *C. difficile* following growth on CCFA plates and confirmatory PCR testing for toxin genes and fluorescent PCR ribotyping (RT). The rate of *C. difficile* positivity and associated RT distribution were compared between settings, including shoe soles which were investigated for their potential role in environmental transmission.

Results. A total of 11,986 unique isolates were obtained primarily from the US (n=11,002; 92%) in addition to 11 other countries including Taiwan (n=200) and India (n=187). Samples were categorized as being from outdoor environments (n=2,992), private residences (n=2,772), shoe soles (n=1,420), public buildings (n=1,104) or acute care settings (n=3,698). Worldwide *C. difficile* sample positivity was 26% and was similar between US and non-US sampling sites. In the US, private residences (26.2%) and outdoor environments (24.1%) had the highest positivity rate compared to public buildings (17.2%). In a Texas sub-analysis (n=8,571), positivity rates were highest from outdoor samples (27%) and were similar between private residences (24%) and healthcare buildings (24%). The most prevalent RTs overall were F014-020 (16.4%), F106 (14.9%), and FP310 (11%). Shoe soles had the highest positivity rate (45%) with similar RT distribution between shoe soles and environmental samples.

Conclusion. Using a worldwide sample, 26% of environmental samples tested positive for toxigenic *C. difficile* strains from healthcare and non-healthcare sites. Community stewardship efforts will be needed to reduce the risk of CDI in vulnerable patients. Shoe sole sampling may be an ideal surveillance tool to test for emerging epidemic strains.

Disclosures. **Kevin W. Garey, Pharm.D., M.S., FASHP**, **Summit Therapeutics** (Research Grant or Support)

19. The Impact of Investigational Purified Microbiome Therapeutic SER-109 on Health-Related Quality of Life (HRQoL) of Patients with Recurrent *Clostridioides difficile* Infection (rCDI) in ECOSPOR III, a Placebo-Controlled Clinical Trial

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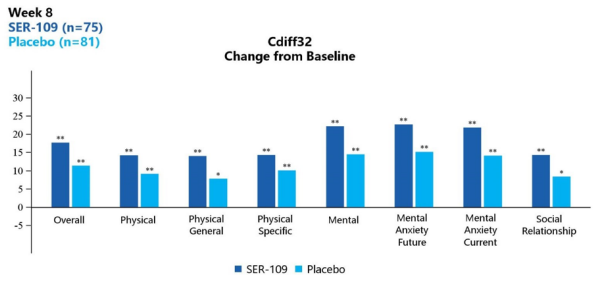
Session: O-04. Challenges in C. difficile

Background. Following standard of care antibiotics, investigational microbiome therapeutic, SER-109, achieved superiority vs placebo (PBO) at 8 weeks in reducing rCDI in patients with ≥3 prior episodes (12.4% vs 39.8%, respectively; p< 0.001). We evaluated the impact of SER-109 vs PBO on HRQoL with general (EQ-5D-5L) and disease-specific (Cdiff32) measures [Garey 2016].

Methods. EQ-5D-5L measures outcomes in 5 domains (mobility, self-care, activities, pain/discomfort, and anxiety/depression) while Cdiff32 measures outcomes in 3 domains (physical, mental, and social) including 5 associated subdomains. Patients completed EQ-5D-5L and Cdiff32 measures at baseline (BL), Wk 8, and at recurrence/early termination. Changes from BL were assessed between SER-109 vs PBO and by clinical outcome (recurrence versus nonrecurrence) in the ITT population and within each treatment arm. The between treatment group comparison analysis controlled for age, gender, prior antibiotics, and number of prior CDI episodes.

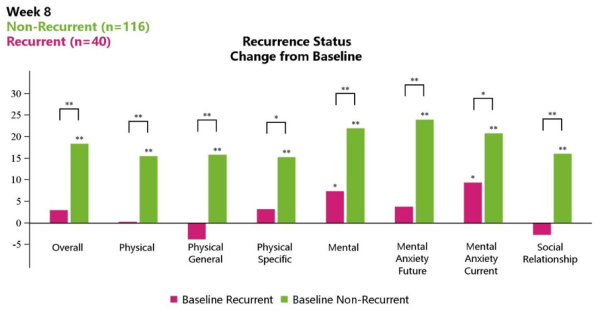
Results. Mean EQ-5D-5L and Cdiff32 scores were comparable between SER-109 and PBO at BL. EQ-5D-5L did not detect differences at Wk 8 from BL between SER-109 and PBO or by clinical outcome. In contrast, Cdiff32 detected significant improvements at Wk 8 from BL within both SER-109 subjects and PBO subjects (Fig1) and by recurrence status (Fig2). Subjects achieved significant improvement in all domains at Wk 8 from BL regardless of treatment group. When examining recurrence status within treatment arms, all PBO subjects with non-recurrence showed improvement in all health domains, while PBO subjects with recurrence had declines in several subdomains (Fig3B). Similarly, SER-109 subjects with non-recurrence showed improvement in all domains compared to BL. However, overall and mental domain/subdomains scores also improved in SER-109 subjects with recurrence (Fig3A).

Figure 1: Change from Baseline at Week 8 in Cdiff32 HRQoL Questionnaire by Treatment Group, ITT Population



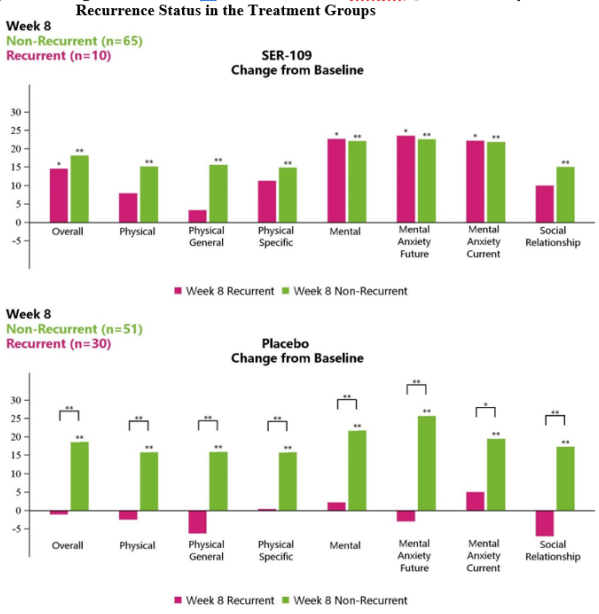
* *P*<0.05; ** *P*<0.001; ⊓ Between group comparison

Figure 2: Change from Baseline in Cdiff32 HRQoL Questionnaire by Recurrence Status at Weeks 8, ITT Population



* *P*<0.05; ** *P*<0.001; ⊓ Between group comparison

Figure 3: Change from Baseline At Week 8 in Cdiff32 HRQoL Questionnaire by Recurrence Status in the Treatment Groups



* *P*<0.05; ** *P*<0.001; ⊓ Between group comparison

Conclusion. Significant HRQoL improvements were associated with CDI nonrecurrence, which highlights the negative impact of this debilitating infection. SER-109 was associated with improved overall and mental scores, regardless of clinical outcome. Further investigation is warranted on the impact of SER-109 on mental health even among those with CDI recurrence.

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20. Risk Factors for Breakthrough Cytomegalovirus (CMV) Infection and *De Novo* Resistance in Hematopoietic Cell Transplantation (HCT) Recipients Receiving Letermovir Prophylaxis

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