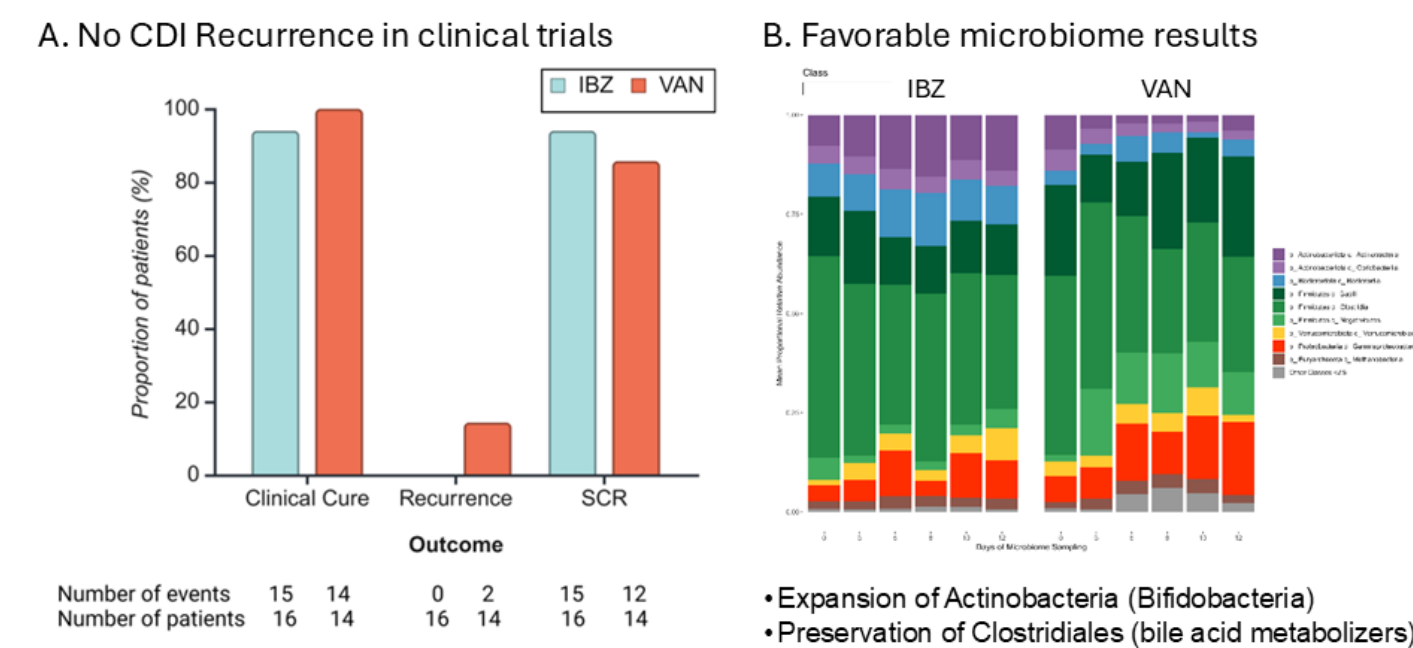


BACKGROUND

- Ibezapolstat (IBZ) is a Gram-positive selective spectrum (GPSS®) oral antibiotic that inhibits the bacterial DNA polymerase III α currently in clinical trial development for the treatment of *C. difficile* infection (CDI) in adults
- During phase 2 trials in CDI patients with ≤ 1 CDI recurrence, no CDI recurrence was observed most likely due to favorable effects on the human gut microbiome



- Clinical trials of IBZ focused on patients with multiple recurrent CDI are planned
- How patients with multiple recurrent CDI episodes will respond to IBZ vs. comparators is unknown

OBJECTIVES

The objective of this study was to assess the use of IBZ in patients with multiple recurrent CDI

- **Aim 1 (epidemiology):** Determine whether beneficial microbes identified in the phase 2 studies on initial and 1st recurrent CDI are still be present in patients with multiple (≥ 2) recurrent CDI
- **Aim 2 (laboratory):** Assess killing effects of IBZ vs. comparators in planktonic and biofilm mono- and duo-culture studies; specifically, measure killing of VRE by VAN, FDX, and IBZ in planktonic and biofilm cultures

FUNDING

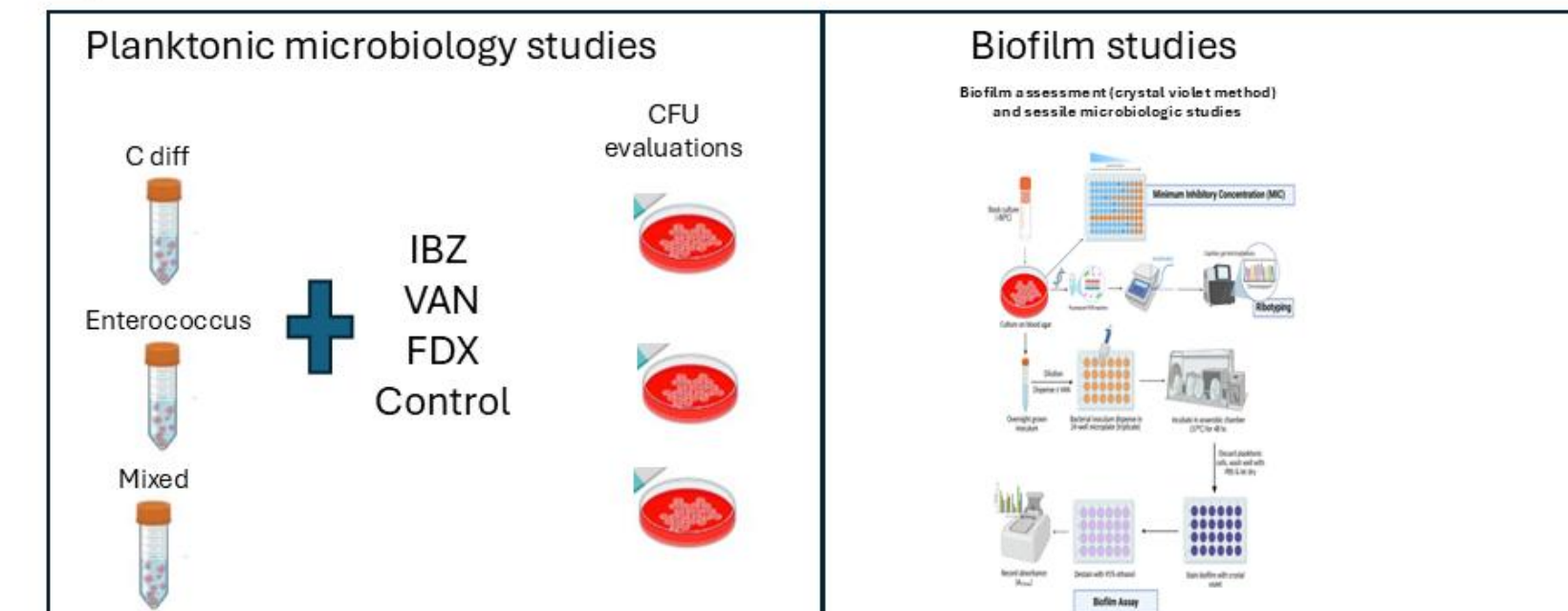
This study was funded by
Acurx Pharmaceuticals

METHODS

Specific aim 1. Epidemiology and microbiome studies of multiply recurrent CDI



Specific aim 2. Co-culture *C. difficile* and *Enterococcus* in vitro studies

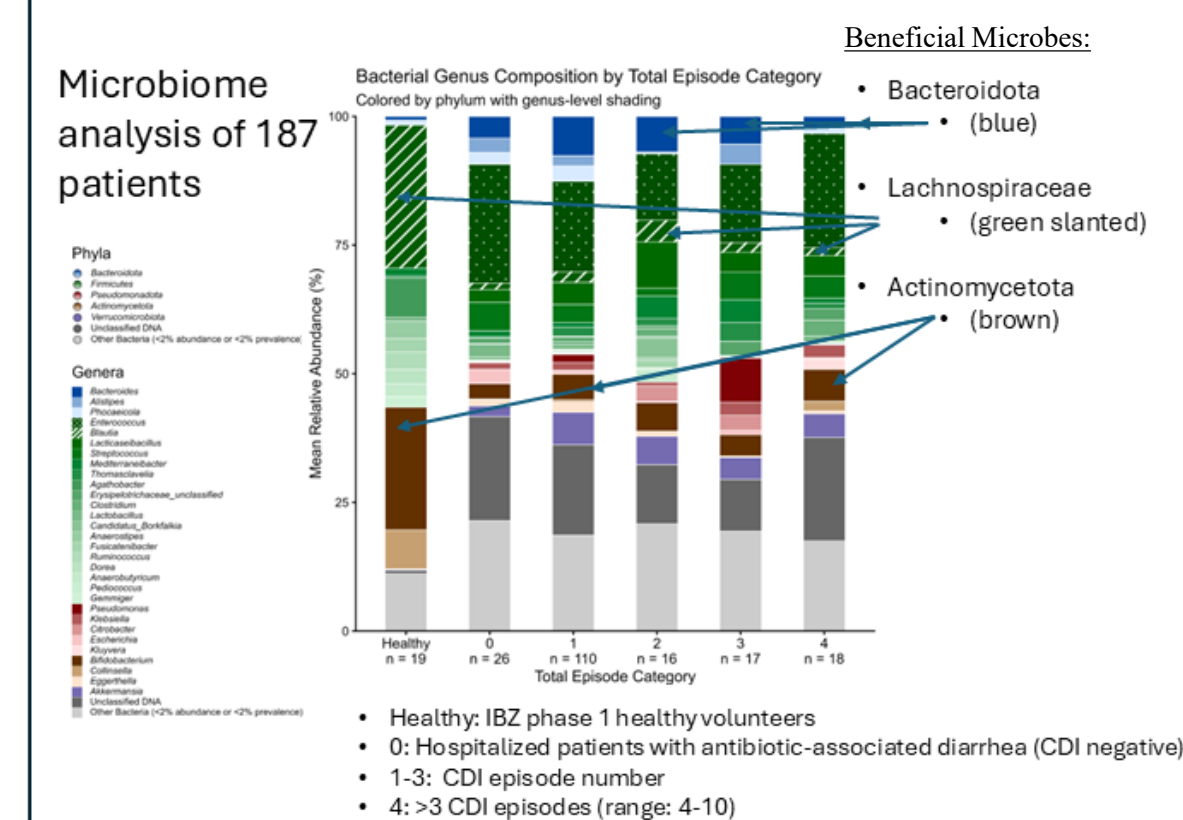


IBZ: ibezapolstat
FDX: fidaxomicin
VAN: vancomycin

RESULTS

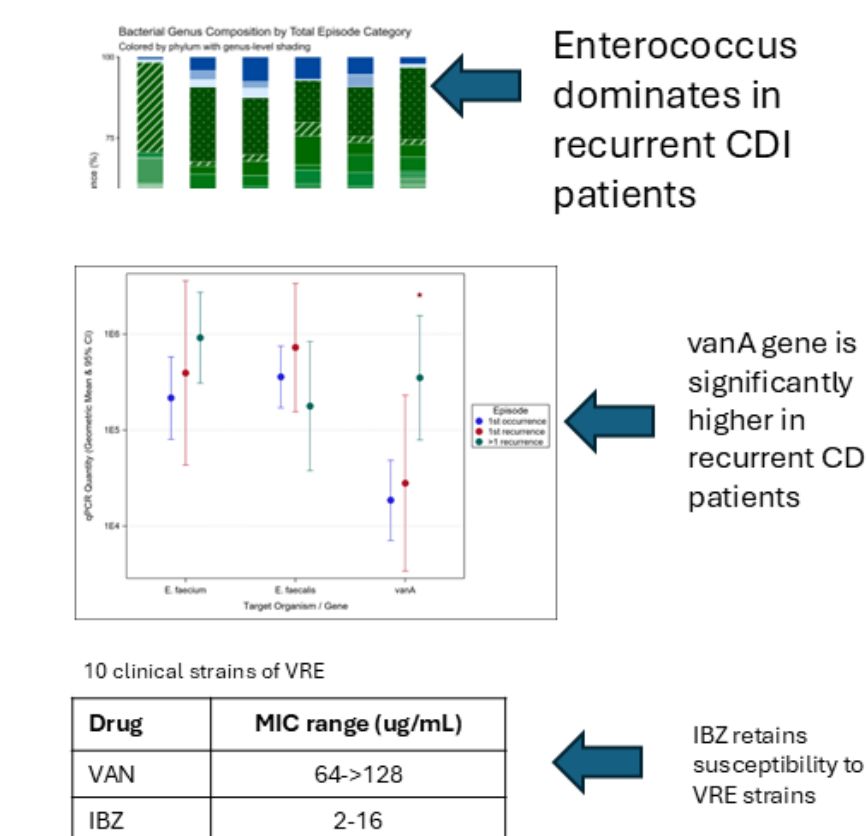
Microbiome analyses in patients with multiple recurrent CDI episodes

Research question: what beneficial microbes are still present in the microbiome of recurrent CDI patients?



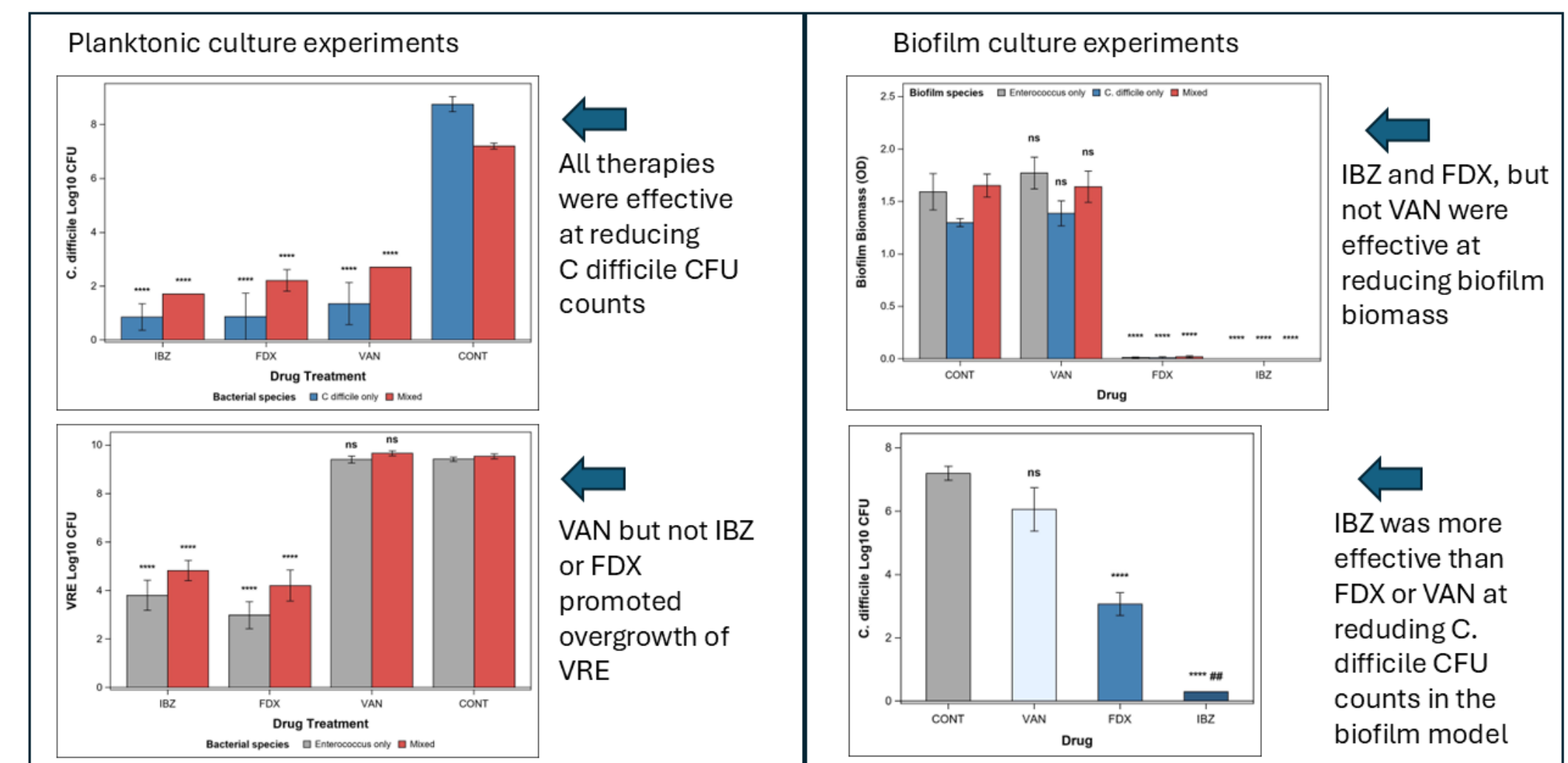
Conclusion: beneficial microbes that can regrow in the presence of IBZ are present in the microbiome of recurrent CDI patients

Research question: what non-beneficial microbes are present in the microbiome of recurrent CDI patients?



Conclusion: IBZ may be superior to VAN to prevent the overgrowth of VRE in recurrent CDI patients

***In vitro* C. difficile & Enterococcus co-cultures**



CONCLUSIONS

- 1. Epidemiology aim:** Beneficial microbes continued to be present in the microbiome of multiple recurrent CDI patients although at lower proportions. There is an increase in vancomycin-resistant Enterococcus (VRE) in multiple recurrent CDI patients. IBZ levels in CDI patients are sufficient for killing VRE.
- 2. Laboratory aim:** VRE overgrowth was observed in vancomycin experiments. IBZ and FDX were superior in biofilm models. IBZ was significantly more effective at *C. difficile* killing than VAN and FDX in the biofilm models.