Implications of *C. difficile* Treatment on Environmental Contamination: A Randomized Controlled Trial with Microbiologic, Environmental and Molecular Outcomes

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with

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Disclosures

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The original trial was funded by Merck. Merck did not have a role in the design or conduct of the trial.

Outline

I. **Background**
II. Design
III. Outcomes
IV. Implications

Environmental Contamination… is everywhere

Computer keyboard 20%

Sink 25%

Bedrail 78%

Chair arm 64%

Bathroom assist bar 43%

Bathroom floor 90%

Toilet seat 57%

Bedside table 67%

Linen bin 20%

Door handle 60%

Floor 86%

Ali et al *J Clin Micro* 2015

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Environmental *C. difficile* Increases Risk

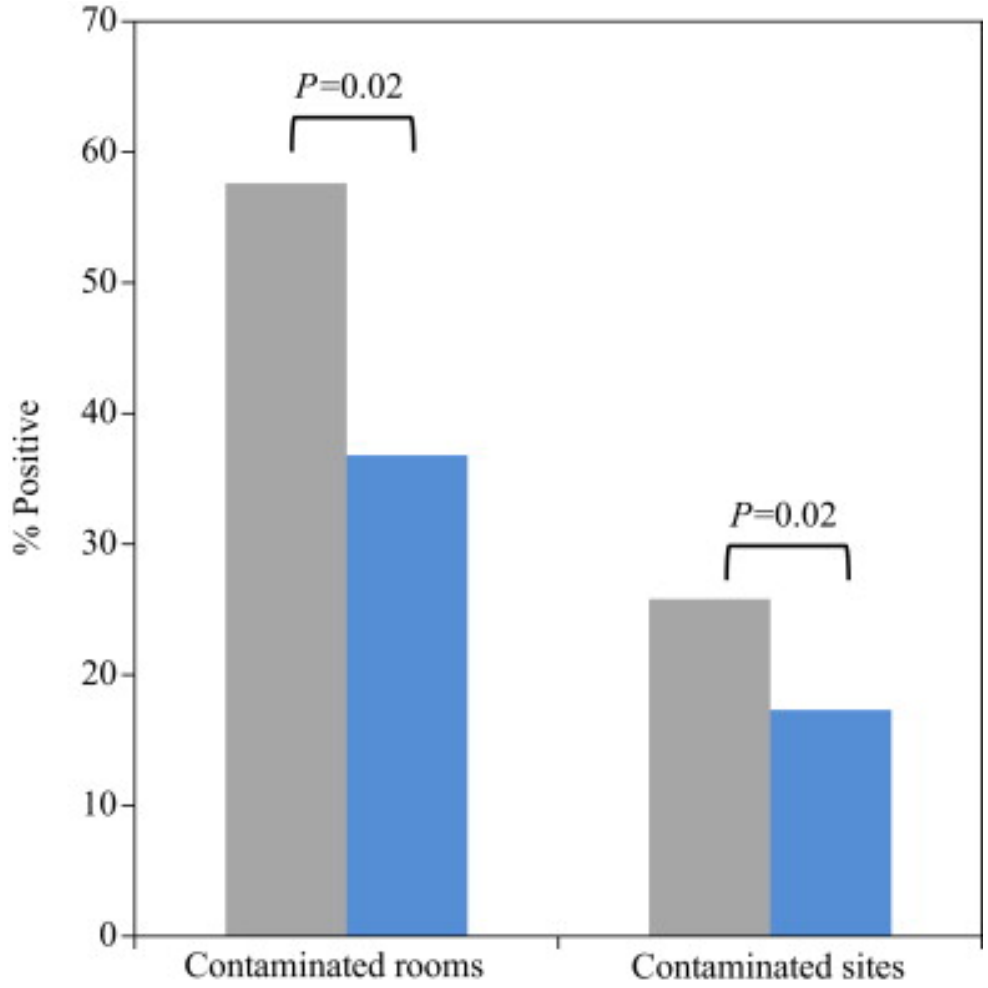
Table 3.

Multivariate Analysis of Risk Factors for Acquisition of *Clostridium difficile* Infection (CDI)

Risk factor	HR (95% CI)	*P*
Prior room occupant with CDI	2.35 (1.21–4.54)	.01
Greater age	1.00 (0.99–1.01)	.71
Higher APACHE III score	1.00 (1.00–1.01)	.06
Proton pump inhibitor use	1.11 (0.44–2.78)	.83

Shaughnessy et al *ICHE* 2011

Treatment choice may reduce shedding



Vancomycin or metronidazole

Fidaxomicin

Biswas *J Hosp Inf* 2015

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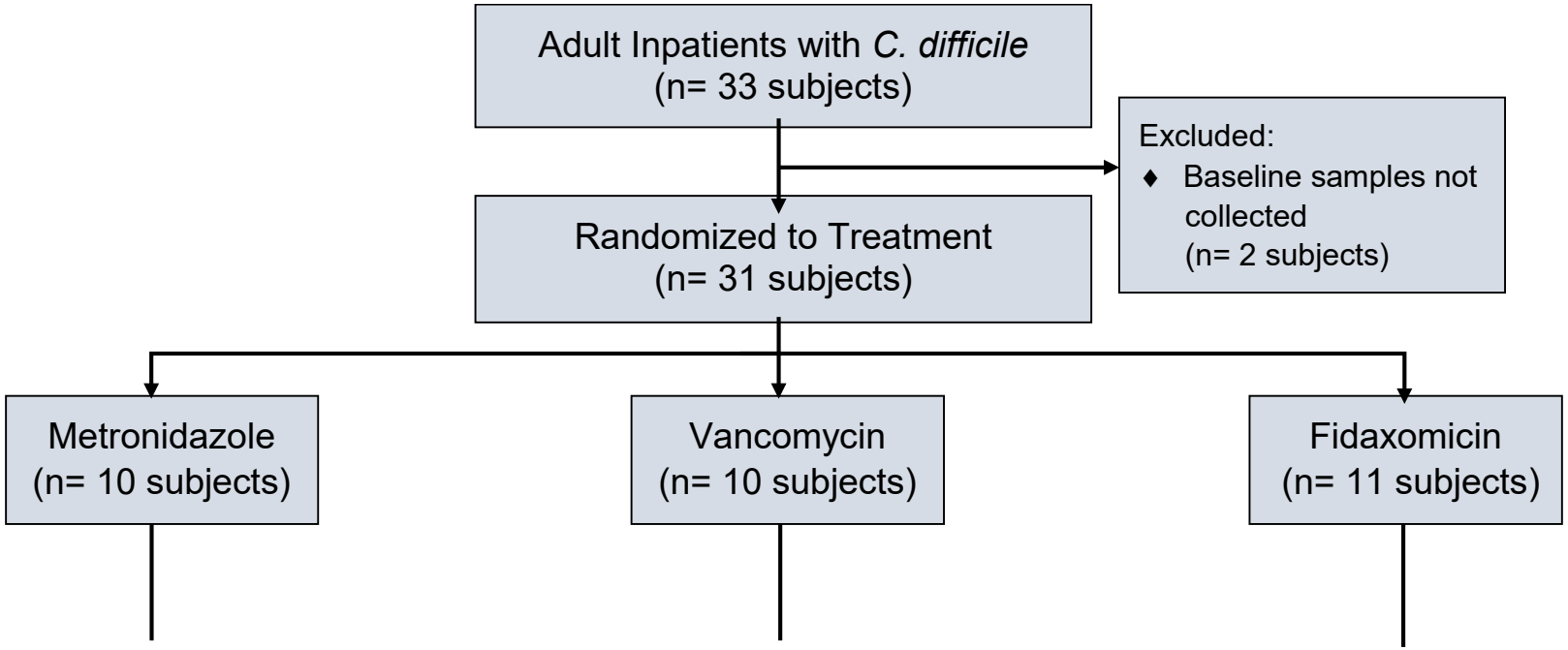
Study Design



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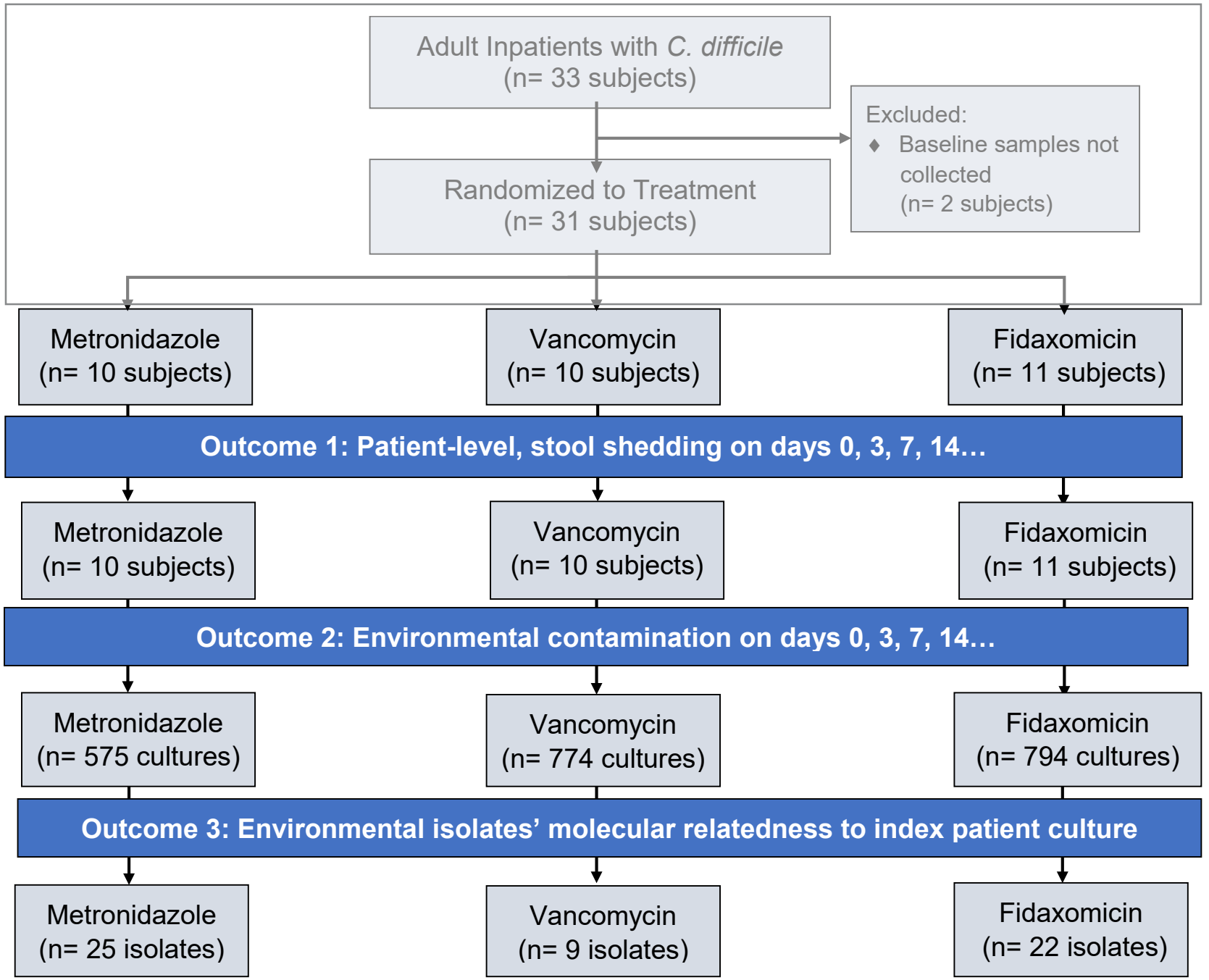

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Environmental Sampling

RODAC plates applied to 5 sites per room:

1) Bedrail
2) Over-bed table
3) Sink
4) Toilet
5) Floor

(x5 replicates for each site)

Photo courtesy of Bobby Warren

Participants

*Severe CDI based on presence of either WBC >15, <4 or Cr >1.5x change from baseline at any point

**Complicated CDI based on presence of hypotension, shock, or ileus at any point

	Metronidazole N=10 (%)	Vancomycin N=10 (%)	Fidaxomicin N=11 (%)
Age [median, IQR]	65 [57-68]	61 [56-71]	59 [45-68]
Gender, male	4 (40.0)	5 (50.0)	7 (63.6)
Race, white	5 (50.0)	6 (60.0)	6 (54.5)
Severe CDI*	1 (10.0)	4 (40.0)	1 (9.1)
Complicated CDI**	0 (0)	1 (10.0)	0 (0)
Cancer	8 (80.0)	4 (40.0)	4 (36.4)
Diabetes	4 (40.0)	6 (60.0)	6 (54.5)
CHF	4 (40.0)	4 (40.0)	5 (45.5)
CKD	2 (20.0)	3 (30.0)	4 (36.4)
CTD	2 (20.0)	2 (20.0)	2 (18.2)
CVA	1 (10.0)	5 (50.0)	2 (18.2)
Liver	0 (0)	1 (10.0)	0 (0)
Pulmonary	2 (20.0)	1 (10.0)	3 (27.3)
HIV	0 (0)	0 (0)	0 (0)
Charlson Index [median, IQR]	5.2 [3.7-9.4]	7.2 [2.7-11.0]	4.2 [3.2-9.4]
WBC [median, IQR]	10.1 [5.0-11.2]	12.5 [9.8-20.4]	9.2 [4.5-12.2]
Cr [median, IQR]	1.4 [0.9-1.7]	0.9 [0.7-1.2]	0.8 [0.7-1.0]

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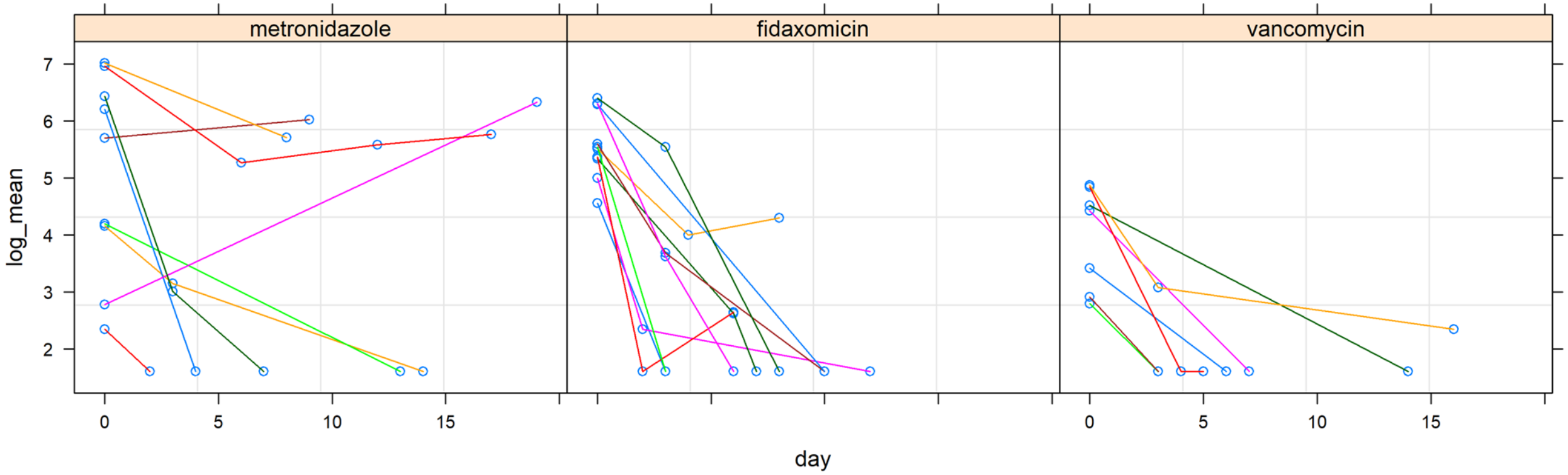
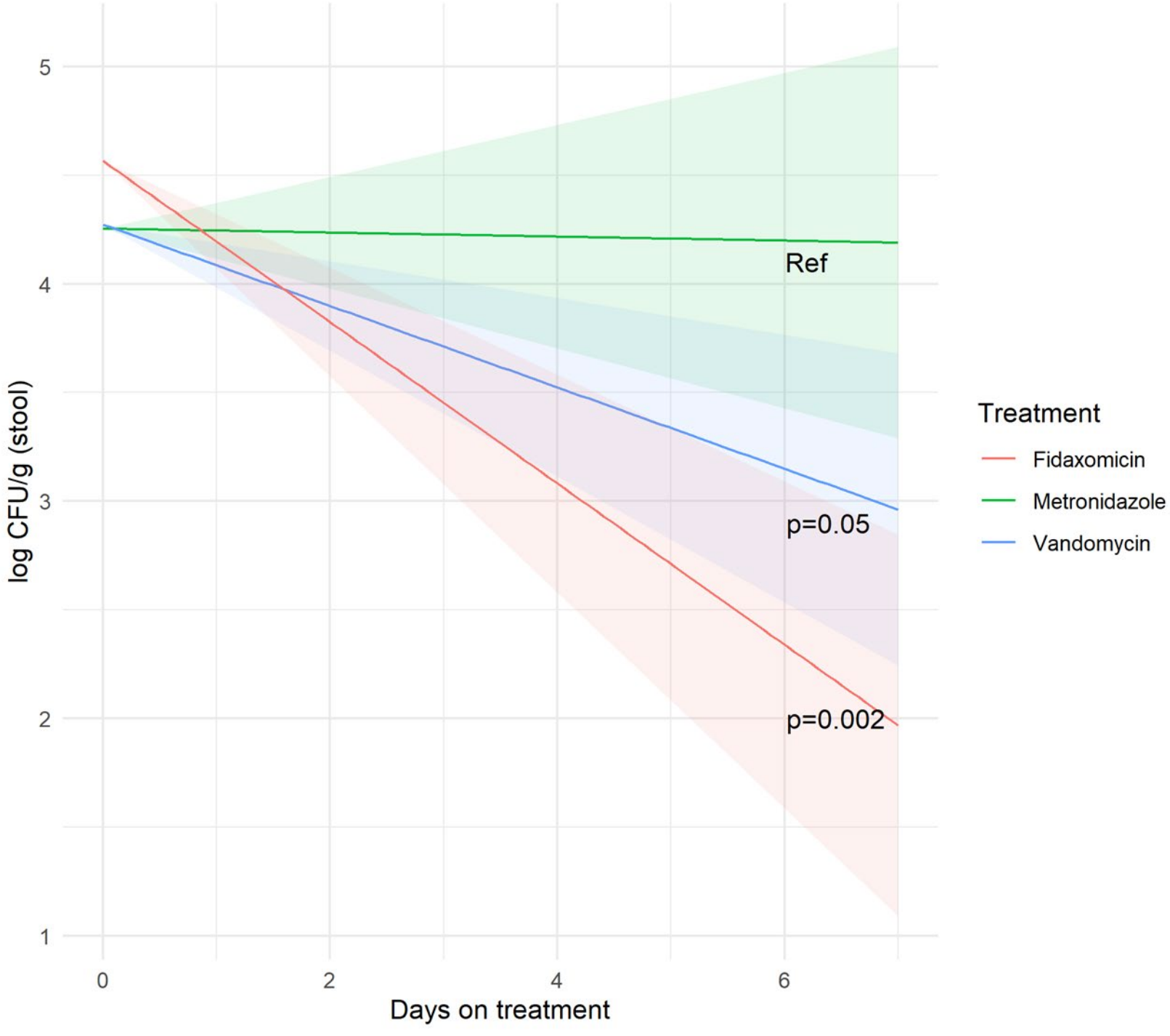
Raw Longitudinal Data



Effect on *C. difficile* Shedding

Mixed effects model



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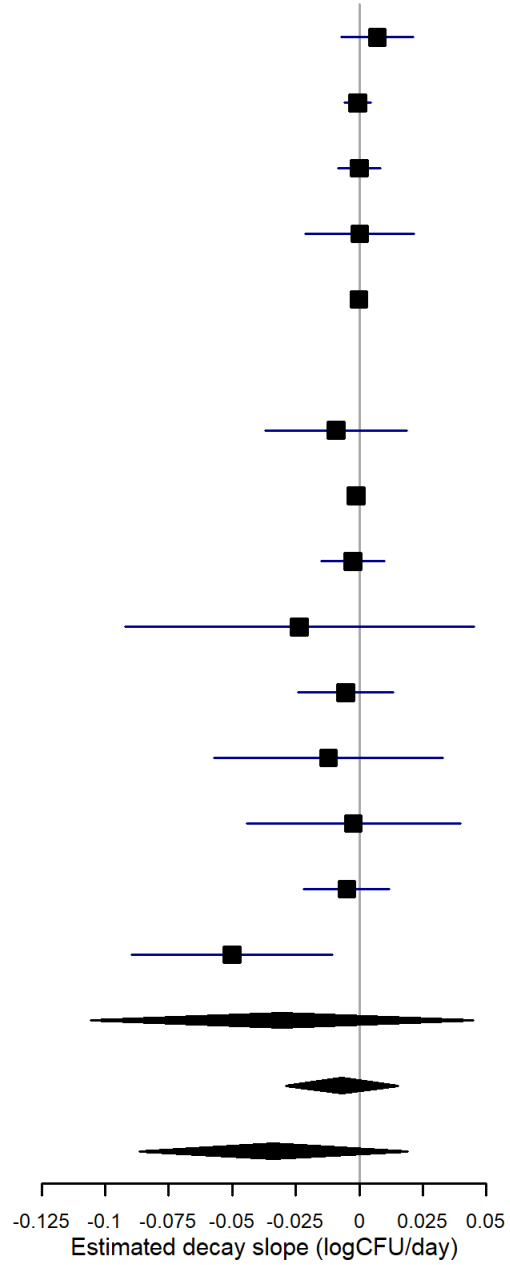
Effect on *C. difficile* Environmental Contamination

Mixed effects model

Site	Treatment	p-value
Bedrail	Metronidazole	Ref
	Vancomycin	0.38
	Fidaxomicin	0.13
Overbed	Metronidazole	Ref
	Vancomycin	0.23
	Fidaxomicin	*
Sink	Metronidazole	Ref
	Vancomycin	0.22
	Fidaxomicin	0.53
Toilet	Metronidazole	Ref
	Vancomycin	0.13
	Fidaxomicin	0.44
Floor	Metronidazole	Ref
	Vancomycin	0.96
	Fidaxomicin	0.61
Total CFUs	**Metronidazole**	**Ref**
	Vancomycin	**0.25**
	Fidaxomicin	**0.69**



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Effect on *C. difficile* Environmental Contamination

Proportional t-tests

Site	Treatment	Positive cultures (%)	p-value*
Bedrail	Metronidazole	12/115 (10.4)	Ref
	Vancomycin	15/154 (9.7)	0.99
	Fidaxomicin	5/155 (3.2)	0.03
Overbed	Metronidazole	8/115 (7.0)	Ref
	Vancomycin	3/155 (1.9)	0.08
	Fidaxomicin	3/160 (1.9)	0.07
Sink	Metronidazole	16/115 (13.9)	Ref
	Vancomycin	6/155 (3.9)	0.006
	Fidaxomicin	12/160 (7.5)	0.13
Toilet	Metronidazole	33/115 (28.7)	Ref
	Vancomycin	13/155 (8.4)	<0.001
	Fidaxomicin	30/160 (18.8)	0.07
Floor	Metronidazole	38/115 (33.0)	Ref
	Vancomycin	22/155 (14.2)	<0.001
	Fidaxomicin	56/159 (35.3)	0.81
Total	Metronidazole	107/575 (18.6)	Ref
	Vancomycin	59/774 (7.6)	<0.001
	Fidaxomicin	106/794 (13.3)	0.01

*2-sample proportional t-test with continuity correction

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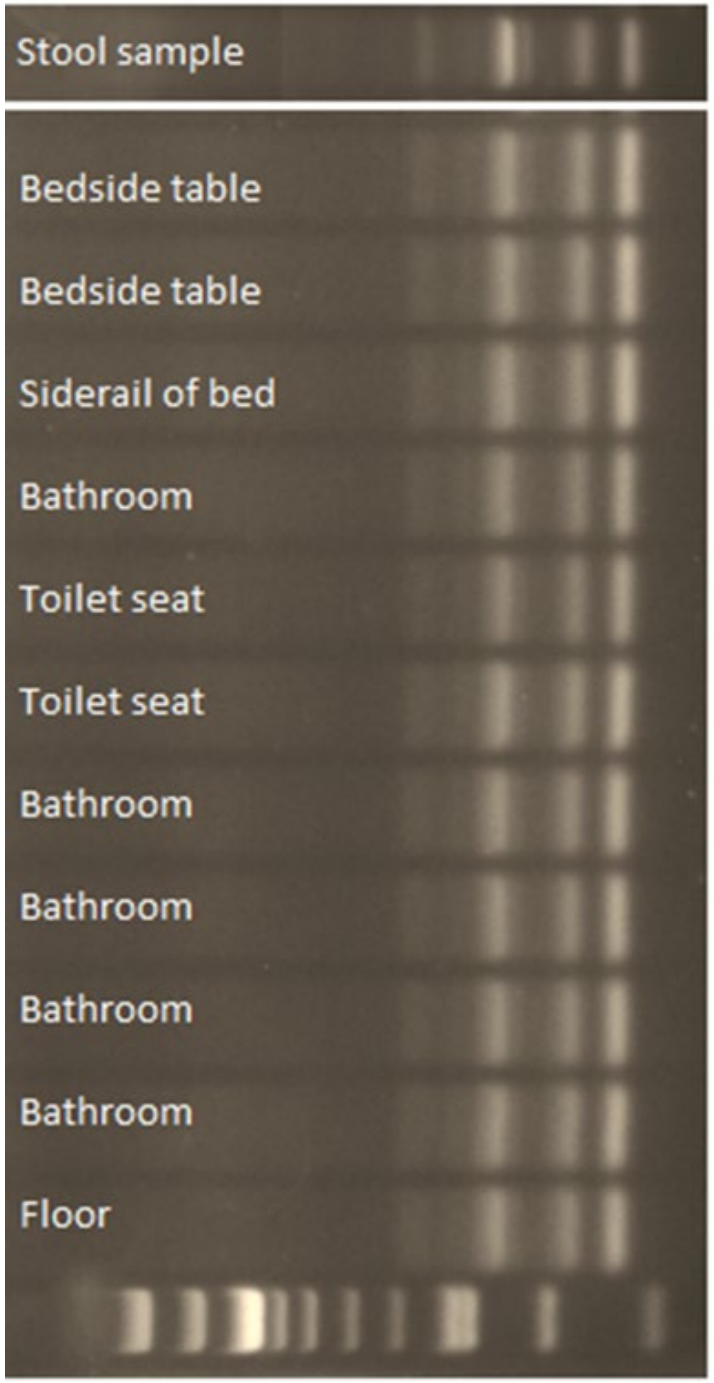
Patient: Room Isolate Matching

Pilot cohort



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Patient: Room Isolate Matching

Pilot cohort

Treatment	% Matching	p-value
Metronidazole [reference]	20/25 (80%)	--
Vancomycin	7/9 (78%)	0.99
Fidaxomicin	15/22 (68%)	0.52

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Limitations

1) Environmental sampling has a high degree of inter-sample variability
2) Low power

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Conclusions

1) Fidaxomicin and vancomycin **reduced *C. difficile* shedding more rapidly** than metronidazole
2) While total environmental CFUs were not significantly different, fidaxomicin and vancomycin were associated with **lower proportions of positive environmental cultures**
3) Environmental strains mostly (but don't always) match patient isolates

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