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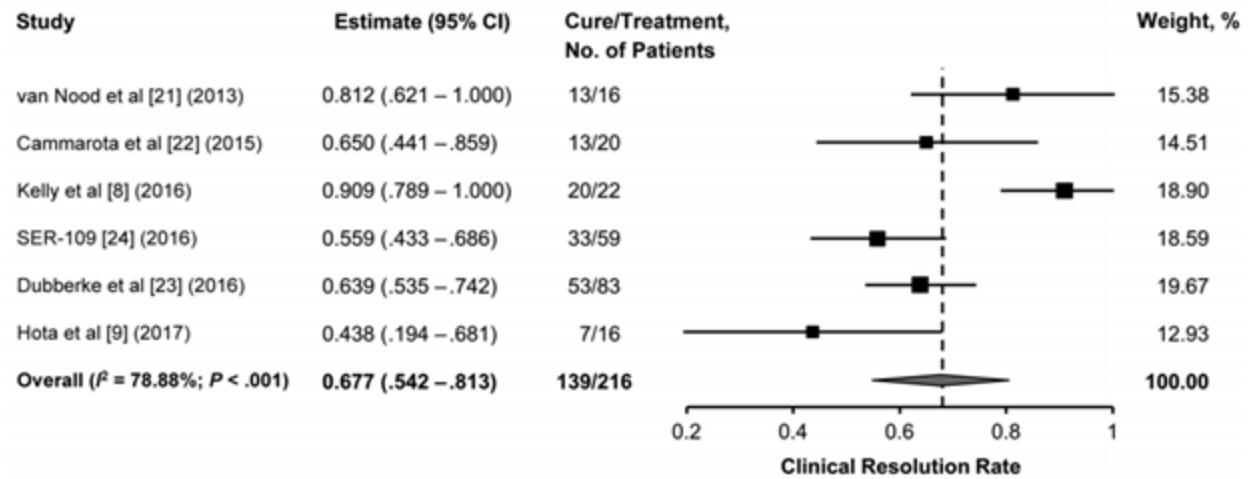
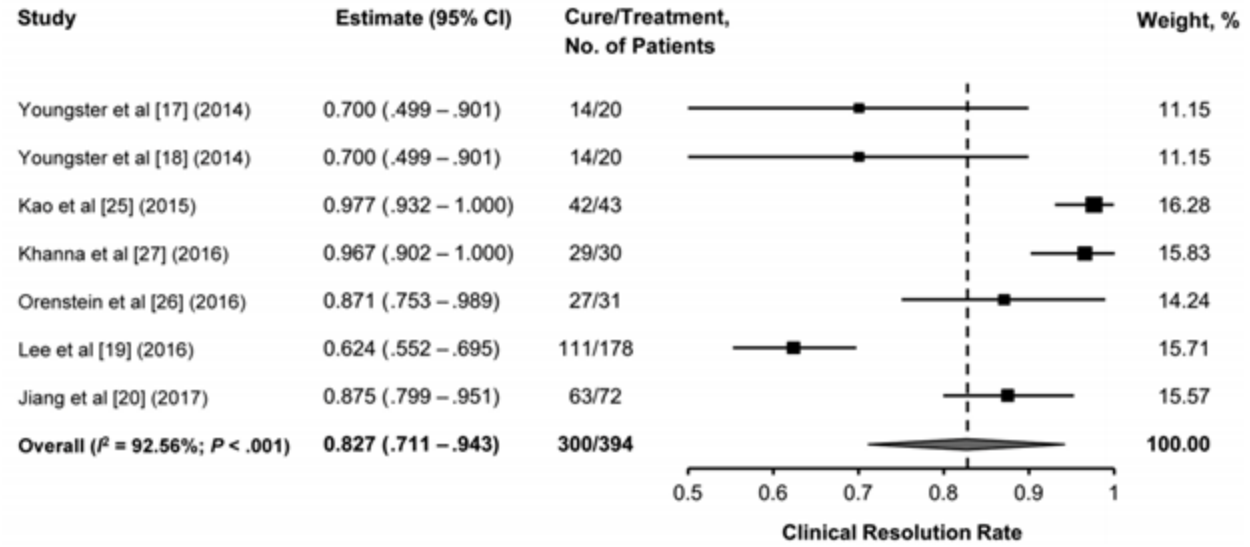
Low Cure Rates in Controlled Trials of FMT

Trials with a non-FMT comparator group
Cure rate: 67.7%



Open-label trials
Cure rate: 82.7%



Tariq et al., 2019

29 Stool Pathogens Tested for in Every Donation

Donation Testing

29 Stool pathogens testing every donation

1. C. difficile A/B
2. Enteroaggregative E. coli (EAEC)
3. Enterotoxigenic E coli (ETEC)
4. Entamoeba histolytica
5. Astrovirus
6. Sapovirus (Genogroups I, II, IV, V, V)
7. Listeria culture
8. Cryptosporidium
9. Cyclospora
10. Cystoisospora
11. Ova & Parasite Exam
12. Aeromonas
13. Plesiomonas shigelloides
14. Campylobacter species
15. Salmonella species
16. Vibrio species/ cholerae
17. Yersinia enterocolitica
18. Enteropathogenic *E. coli* (EPEC)
19. Shiga-like-toxin-prod *E. coli* (STEC)
20. Shigella/Enteroinvasive *E. coli* (EIEC)
21. Enteroaggregative *E.coli* (EAEC)
22. Giardia lamblia
23. Norovirus GI/GII
24. Rotavirus A
25. Adenovirus F40/41

<u>Multi-drug resistant organisms:</u>

26. ESBL (extended spectrum beta-lactamase)
27. VRE (Vancomycin-resistant Enterococci)
28. CRE (carbapenem-resistant Enterobacterales)
29. MRSA (Methicillin-resistant Staphylococcus aureus)

Safety In Patients with IBD

2019-01: Safety Overview in Patients with and without IBD

	RBX2660 N = 483	
	With IBD N=54	Without IBD N=429
AEs	57%	63%
Severity*		
Mild	13%	17%
Moderate	26%	30%
Severe	19%	13%
Potentially Life-threatening	0%	3%
SAEs	6 (11%)	45 (10%)
AEs Leading to Discontinuation**	0%	5 (1%)
AEs Leading to Death	0%	3 (0.7%)

* Severity as assessed by investigator using CTCAE criteria

** AEs leading to discontinuation were only collected in Studies 2017-01 and 2019-01, which also includes deaths in these studies.

Immunosuppressed Patients in 2019-01

Ongoing Open-label Study

n (%)	Total N = 483
Patients Identified as Immunosuppressed*	91 (19%)
Reason for Immunocompromised	
SMQ of med hx "malignant tumors"	24 (5%)
Other medical history	
End Stage Renal Disease	6 (1%)
Immunodeficiency syndromes	5 (1%)
HIV	2 (0.4%)
Haemoglobinopathies congenital	1 (0.2%)
Concomitant Medications	
Corticosteroid Use	13 (3%)
Systemic Immunosuppressive medications	61 (13%)

*Patients may be in more than one of categories below, % of patients in 2019-01 as of data cut-off

Safety in Immunocompromised Patients

Ongoing Open-label Study 2019-01

	RBX2660 N = 483	
	Immunocompromised N=91	Non-Immunocompromised N=392
AEs	65%	62%
Severity*		
Mild	15%	17%
Moderate	27%	30%
Severe	20%	12%
Potentially Life-Threatening	2%	3%
SAEs, n (%)	18 (20%)	33 (8%)
AEs Leading to Discontinuation, n (%)**	1 (1%)	4 (1%)
AEs Leading to Death, n (%)**	1 (1%)	2 (0.5%)

* Severity as assessed by investigator using CTCAE criteria
** AEs leading to discontinuation also includes deaths

Study 2014-01 Safety Overview (8-Week Double-Blind Period)

Failures Censored at Time of CDI Recurrence

	Blinded RBX2660 x 2 N = 42	Blinded RBX2660 → Placebo N = 42	Blinded Placebo x 2 N = 44
AE	**26 (62%)**	**29 (69%)**	**25 (57%)**
Severity*			
Mild	8 (19%)	13 (31%)	17 (39%)
Moderate	9 (21%)	12 (29%)	7 (16%)
Severe	7 (17%)	4 (10%)	1 (2%)
Potentially life-threatening	2 (5%)	0	0
SAE	**8 (19%)**	**5 (12%)**	**1 (2%)**
AE leading to death	**2 (5%)**	**0**	**0**

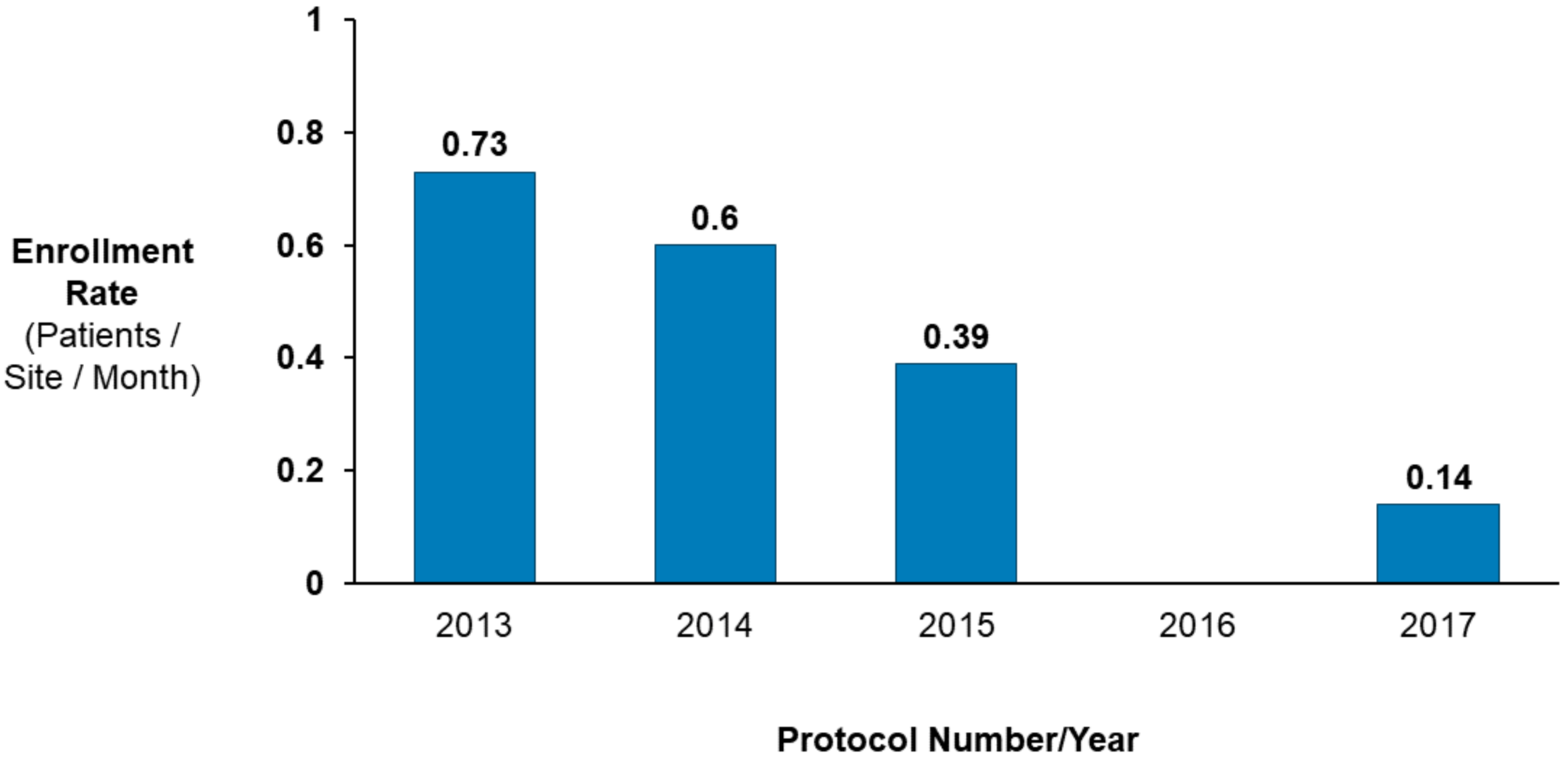
- **AEs reported by maximum severity as assessed by investigator using CTCAE criteria**

Safety Overview – SAEs

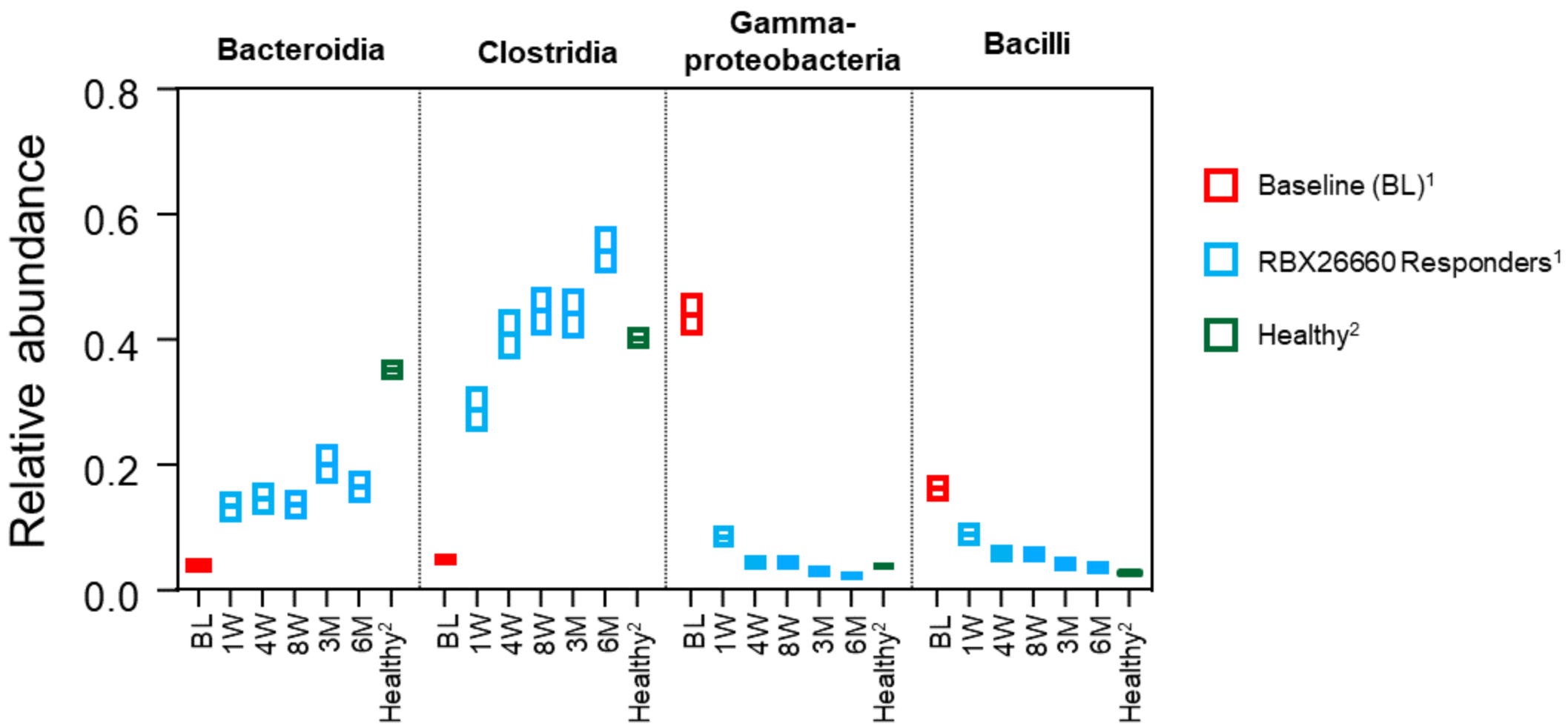
Study 2014-01 Double-Blind Period (First 8 weeks) Censored at CDI recurrence

	RBX2660 (2 doses) N = 42	**RBX2660** (1 dose) N = 42	**Placebo** N = 44
Any SAE	**8 (19%)**	**5 (12%)**	**1 (2%)**
Anaemia	**0%**	**1 (2%)**	**0%**
Leukocytosis	**1 (2%)**	**0%**	**0%**
Abdominal pain	**1 (2%)**	**0%**	**0%**
Abdominal pain upper	**0%**	**1 (2%)**	**0%**
Constipation	**1 (2%)**	**0%**	**0%**
Intestinal ischemia	**1 (2%)**	**0%**	**0%**
Intestinal obstruction	**0%**	**1 (2%)**	**0%**
Osteomyelitis chronic	**0%**	**1 (2%)**	**0%**
Urinary tract infection	**1 (2%)**	**0%**	**0%**
Back pain	**1 (2%)**	**0%**	**0%**
Diabetic neuropathy	**0%**	**1 (2%)**	**0%**
Nephrolithiasis	**1 (2%)**	**0%**	**1 (2%)**
Renal impairment	**1 (2%)**	**0%**	**0%**
Ureteric stenosis	**1 (2%)**	**0%**	**0%**
Acute respiratory failure	**1 (2%)**	**0%**	**0%**

Declining Enrollment Rates Observed Over Course of the Development Program



Study 2017-01: Restoration of Microbiome Composition Among RBX2660 Treatment Responders



[1]OFID 2021, 8: S624 [2]Pooled data from two large healthy cohorts; Nature 2012, 486: 207; Gut 2020, 69:1076.

Make an Accurate Diagnosis in Practice

Assess risk factors for CDI

Assess for presence of symptoms

- Diarrhea, abdominal pain, dehydration, fever

A positive test for *C difficile* infection

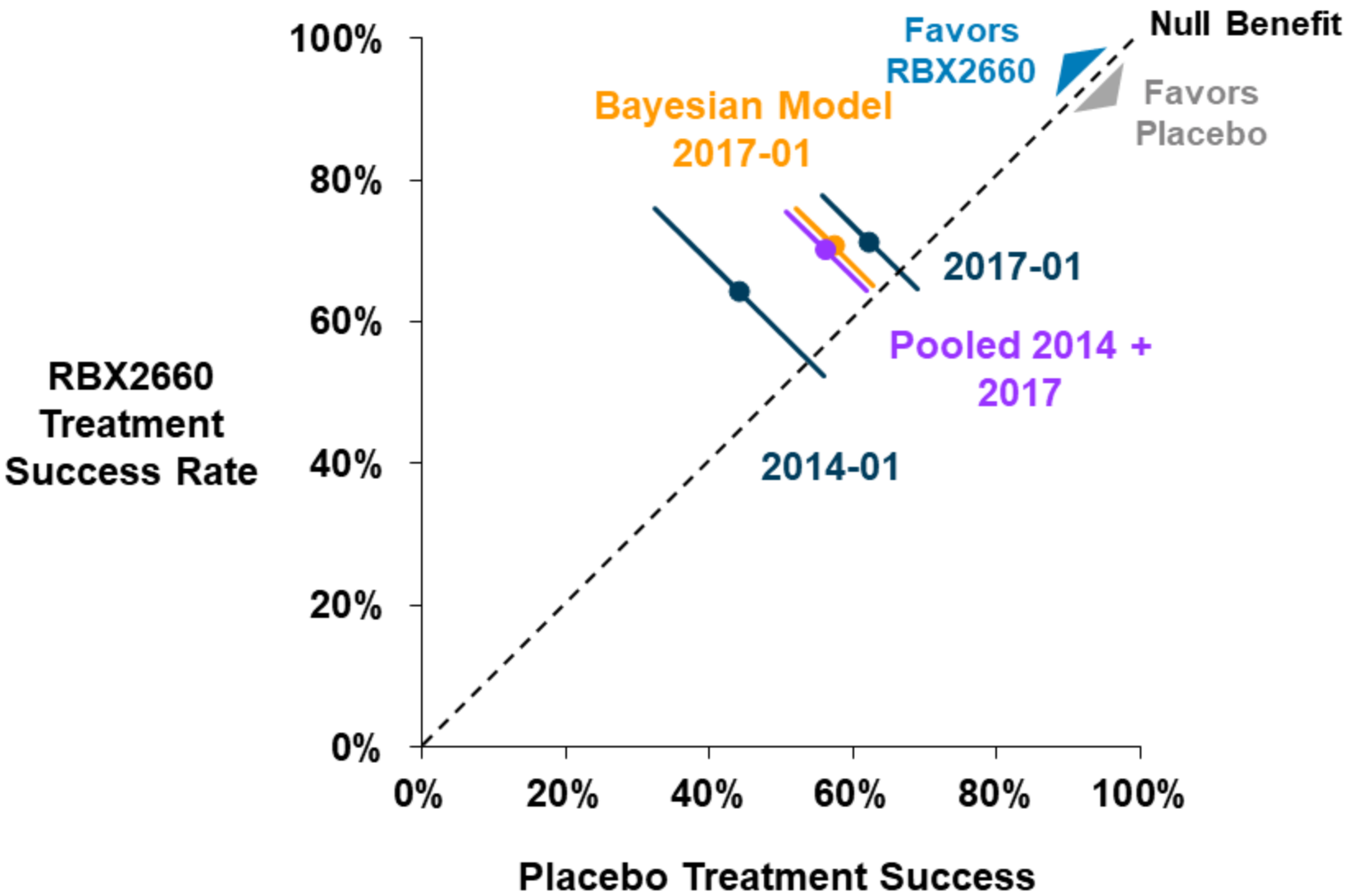
- PCR or toxin-based assay

Assess response to treatment

- Non-response to vancomycin / fidaxomicin is rare and suggests alternate diagnoses

Khanna and Pardi 2020

Bayesian Hierarchical Model Results



Number of patients borrowed

- SD for placebo arm estimated by primary analysis = 0.0481
- SD for placebo arm raw estimate = 0.0526
- Ratio of variances = 1.196
- ~ 16.6 patients borrowed
- SD for treatment effect estimated by primary analysis = 0.0552
- SD for treatment effect raw estimate = 0.0626
- Ratio of variances = 1.286
- ~ 74.9 patients borrowed

Study 2014-01 and 2017-01 Key Demographics Comparable Across Studies

	2014-01			2017-01	
	RBX2660 (2 doses) N = 45	**RBX2660** (1 dose) N = 44	**Placebo** N = 44	**RBX2660** N = 177	**Placebo** N = 85
Age (years), mean (SD) Min, max	**63.6** (19.2) (24 – 89)	**61.0** (19.7) (18 – 88)	**58.8** (19.2) (19 – 92)	**61.3** (16.8) (19, 93)	**57.5** (15.9) (26, 86)
Female	**58%**	**57%**	**68%**	**69%**	**69%**
White	**98%**	**96%**	**98%**	**93%**	**89%**
Duration of CDI (days), mean (SD)	**19** (13)	**17** (11)	**20** (18)	**26.3** (14.8)	**25.3** (11.4)
Previous episodes of CDI*, mean	**4.3**	**4.1**	**3.8**	**3**	**3**
Hospitalization					
Due to CDI episode	**58%**	**43%**	**57%**	**13%**	**12%**
Duration (days), median (IQR)	**9.5** (15.0)	**7.0** (6.0)	**5.0** (3.5)	**5.0** (4.0)	**5.0** (4.0)
Vancomycin during screening	**91%**	**86%**	**91%**	**87%**	**89%**