

Supplementary Online Content

Goyal A, Schibler T, Alhanti B, et al. Assessment of North American clinical research site performance during the start-up of large cardiovascular clinical trials. *JAMA Netw Open*. 2021;4(7):e2117963. doi:10.1001/jamanetworkopen.2021.17963

eFigure 1. Regulatory Approval Time by Trial

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eTable 1. Milestone Pacing Site Activation

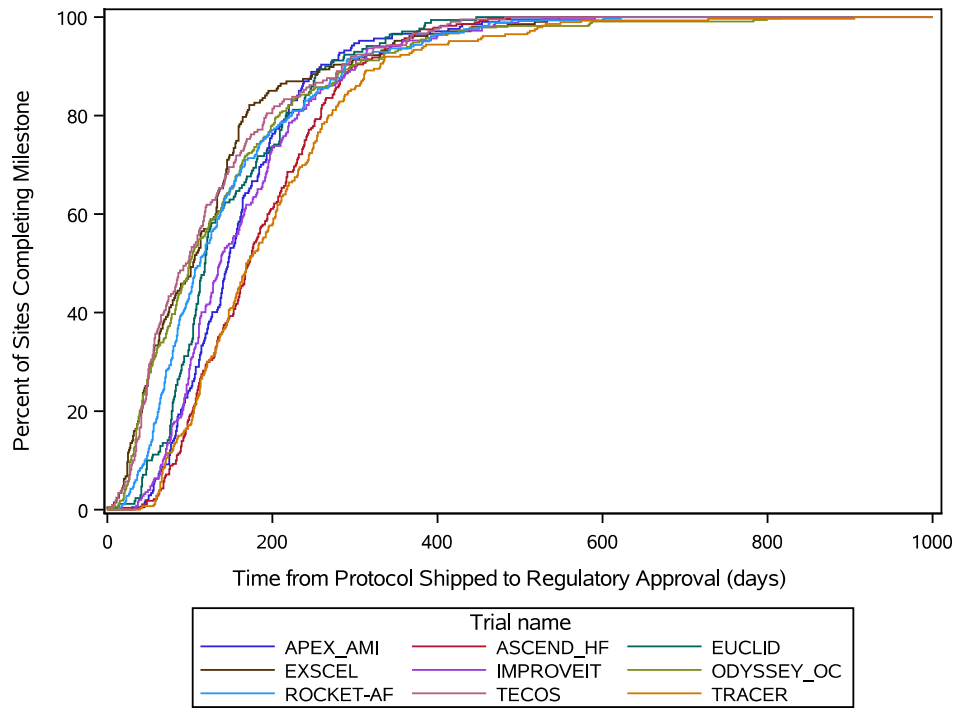
eTable 2. Milestone Pacing to Site Activation for Individual Trials

eTable 3. Time to Regulatory Approval for Individual Trials by IRB Type

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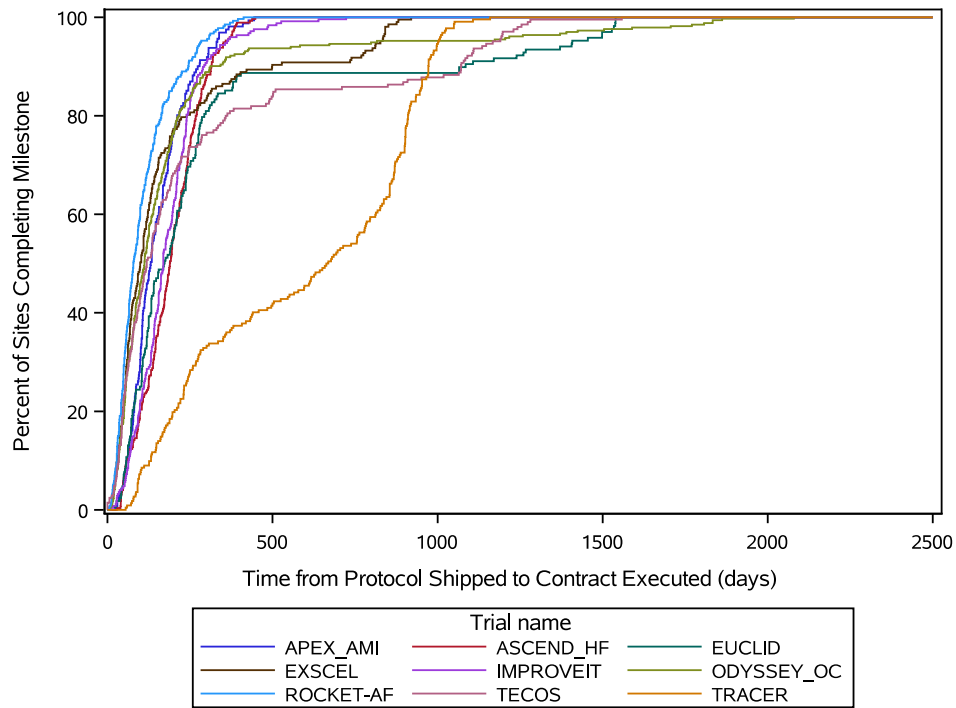
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Regulatory Approval Time by Trial



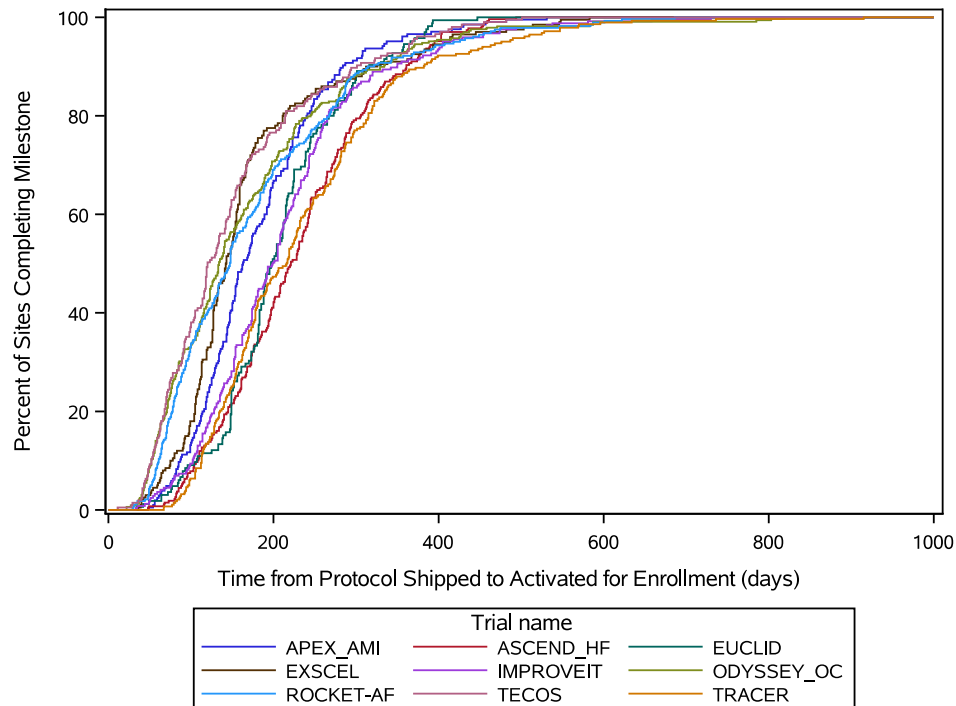
Caption: The time to regulatory approval for each trial represented by the percent of sites completing the milestone at a given time in days.

eFigure 2. Contract Execution Time by Trial



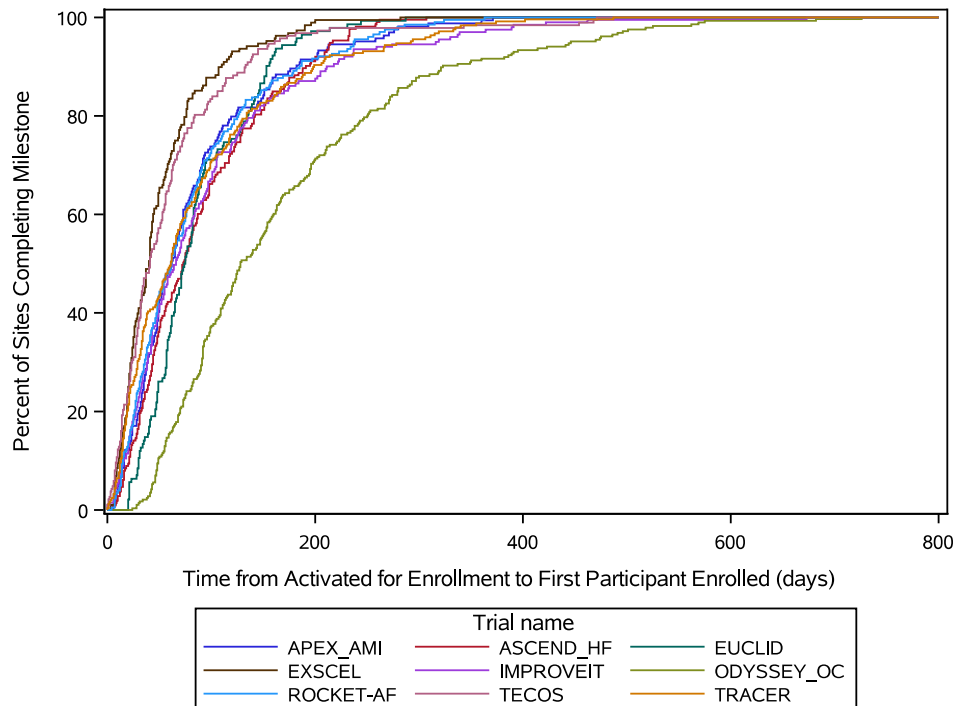
Caption: The time to contract execution for each trial represented by the percent of sites completing the milestone at a given time in days.

eFigure 3. Activation Time by Trial



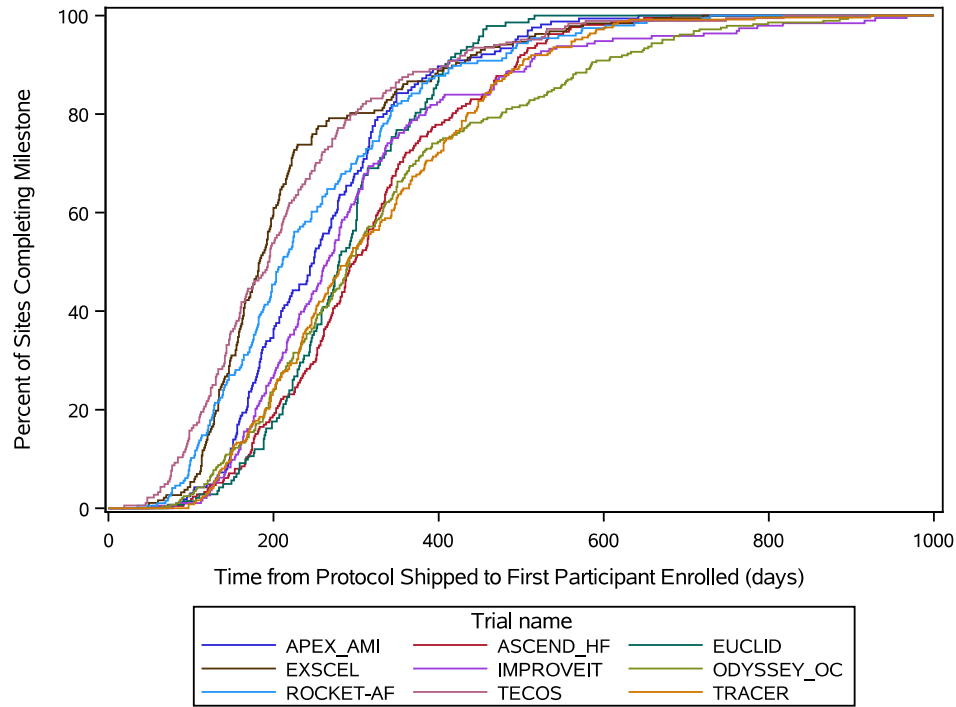
Caption: The activation time for each trial represented by the percent of sites completing the milestone at a given time in days.

eFigure 4. Enrollment of First Participant Time by Trial



Caption: The time to enrollment of the first participant for each trial represented by the percent of sites completing the milestone at a given time in days.

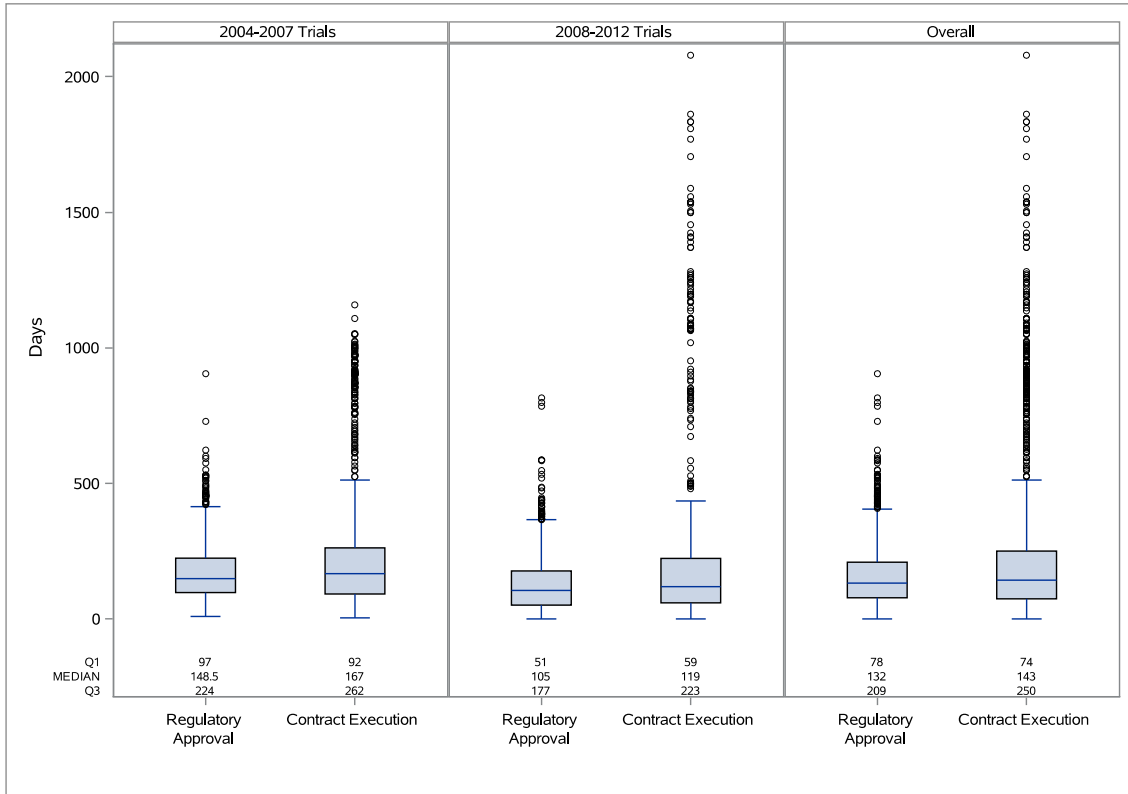
eFigure 5. Overall Start-Up Time by Trial



Caption: The overall start-up time for each trial represented by the percent of sites completing the milestone at a given time in days.

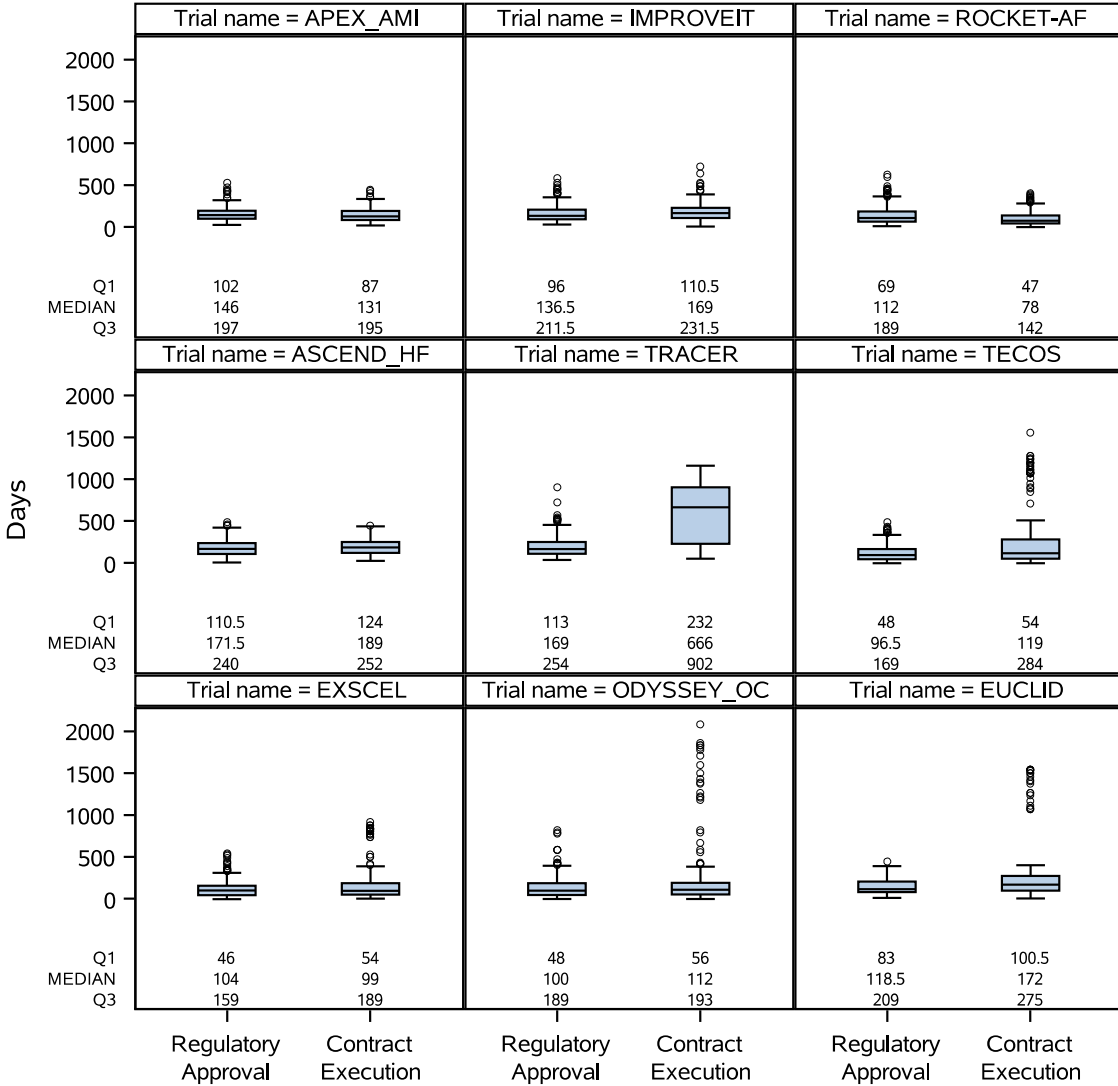
eFigure 6. Side-by-Side Boxplots of Regulatory Approval and Contract Execution by 2004-2007 vs 2008-2012 Trials

Regulatory Approval and Contract Execution by Trial Age



Caption: The boxplots show the days required to reach both regulatory approval and contract execution stratified by early trials from 2004-2007 (APEX-AMI, IMPROVE-IT, ROCKET-AF, ASCEND-AF, & TRACER) and contemporary trials from 2008-2012 (TECOS, EXSCEL, ODYSSEY, & EUCLID).

eFigure 7. Side-by-Side Boxplots of Regulatory Approval and Contract Execution by Trial



Caption: The boxplots show the days required to reach both regulatory approval and contract execution stratified by individual trial.

eTable 1. Milestone Pacing Site Activation

Milestone	All Trials	2004-2007* Trials	2008-2012† Trials	P-value‡
Contract Complete First, (% of sites)	49.6%	52.0%	46.6%	0.02
Regulatory Approval first; Subsequent Time to Contract Execution (days)	46 (13, 155)	60 (20, 210)	33 (8, 111)	<0.001
Contract Execution first; Subsequent Time to Regulatory Approval (days)	30 (12, 63)	33 (14, 63)	27 (8, 61)	0.03

Continuous variables are described using median (25th, 75th percentile). Categorical variables are described using frequency (%). *2004-2007 trials: APEX-AMI, IMPROVE-IT, ROCKET-AF, ASCEND-AF, & TRACER; †2008-2012 trials: TECOS, EXSCEL, ODYSSEY, & EUCLID; ‡P-value describes difference between 2004-2007 and 2008-2012 trials.

eTable 2. Milestone Pacing to Site Activation for Individual Trials

Trial	Contract Execution First, (% of sites)	Regulatory Approval First; Subsequent Time to Contract Execution (days)	Contract Execution First; Subsequent Time to Regulatory Approval (days)
APEX-AMI	55.6%	20 (6, 46)	26 (7, 47)
IMPROVE-IT	45.1%	51 (18, 83)	28 (12, 51)
ROCKET-AF	76.3%	29 (8, 63)	44 (20, 74)
ASCEND-HF	55.2%	48 (18, 100)	29 (13, 58)
TRACER	25.2%	642 (377, 758)	40 (15, 84)
TECOS	47.5%	35 (6, 777)	24 (8, 54)
EXSCEL	49.5%	34 (5, 99)	30 (9, 71)
ODYSSEY	48.0%	22 (7, 69)	29 (9, 57)
EUCLID	39.5%	54 (23, 150)	25 (8, 55)

Continuous variables are described using median (25th, 75th percentile). Categorical variables are described using frequency (%).

eTable 3. Time to Regulatory Approval for Individual Trials by IRB Type

Trial	IRB Type	Number of Sites, n	Time to Regulatory Approval, days
APEX-AMI	All sites	207	146 (102, 197)
	Local	207 (100%)	146 (102, 197)
IMPROVE-IT	All sites	252	137 (96, 212)
	Local	252 (100%)	137 (96, 212)
ROCKET-AF	All sites	283	112 (69, 189)
	Central	185 (65.4%)	84 (56, 130)
	Local	89 (31.4%)	194 (140, 286)
	Missing	9 (3.2%)	285 (156, 407)
ASCEND_HF	All sites	280	172 (111, 240)
	Central	15 (5.4%)	172 (109, 265)
	Local	90 (32.1%)	176 (127, 262)
	Missing	175 (62.5%)	167 (107, 236)
TRACER	All sites	286	169 (113, 254)
	Central	58 (20.3%)	134 (71, 216)
	Local	225 (78.6%)	183 (121, 258)
	Missing	3 (1.0%)	192 (90, 301)
TECOS	All sites	210	97 (48, 169)
	Central	97 (46.2%)	55 (41, 86)
	Local	94 (44.8%)	159 (100, 261)
	Missing	19 (9.0%)	102 (26, 193)
EXSCEL	All sites	207	104 (46, 159)
	Central	145 (70.0%)	65 (38, 117)
	Local	50 (24.2%)	194 (145, 332)
	Missing	12 (5.8%)	132 (62, 220)
ODYSSEY	All sites	330	100 (48, 189)
	Central	193 (58.5%)	58 (35, 102)
	Local	137 (41.5%)	190 (130, 276)
EUCLID	All sites	170	119 (83, 209)
	Central	105 (61.8%)	102 (76, 124)
	Local	65 (38.2%)	209 (121, 252)

Continuous variables are described using median (25th, 75th percentile). Categorical variables are described using frequency (%). IRB = institutional review board.

eTable 4. Time to Overall Start-Up for Individual Trials by IRB Type

Trial	IRB Type	Number of Sites, n	Time to Overall Start-up, days
APEX-AMI	All sites	165	249 (175, 316)
	Local	165 (100%)	249 (175, 316)
IMPROVE-IT	All sites	193	265 (194, 344)
	Local	193 (100%)	265 (194, 344)
ROCKET-AF	All sites	196	211 (142, 328)
	Central	141 (71.9%)	181 (125, 246)
	Local	54 (27.6%)	332 (253, 412)
	Missing	1 (0.5%)	602 (602, 602)
ASCEND_HF	All sites	212	298 (230, 378)
	Central	15 (7.1%)	324 (268, 351)
	Local	89 (42.0%)	308 (226, 386)
	Missing	108 (50.9%)	289 (230, 380)
TRACER	All sites	248	290 (203, 413)
	Central	52 (21.0%)	258 (197, 370)
	Local	196 (79.0%)	299 (207, 423)
TECOS	All sites	184	194 (128, 273)
	Central IRB	78 (42.4%)	145 (98, 196)
	Local IRB	92 (50.0%)	232 (168, 345)
	Missing IRB	14 (7.6%)	205 (115, 262)
EXSCEL	All sites	187	183 (137, 246)
	Central IRB	137 (73.3%)	162 (129, 200)
	Local IRB	47 (25.1%)	264 (207, 439)
	Missing IRB	3 (1.6%)	222 (215, 451)
ODYSSEY	All sites	285	292 (203, 405)
	Central IRB	169 (59.3%)	249 (179, 336)
	Local IRB	116 (40.7%)	359 (275, 508)
EUCLID	All sites	142	280 (223, 343)
	Central IRB	89 (62.7%)	252 (198, 301)
	Local IRB	53 (37.3%)	329 (278, 400)

Continuous variables are described using median (25th, 75th percentile). Categorical variables are described using frequency (%). IRB = institutional review board.