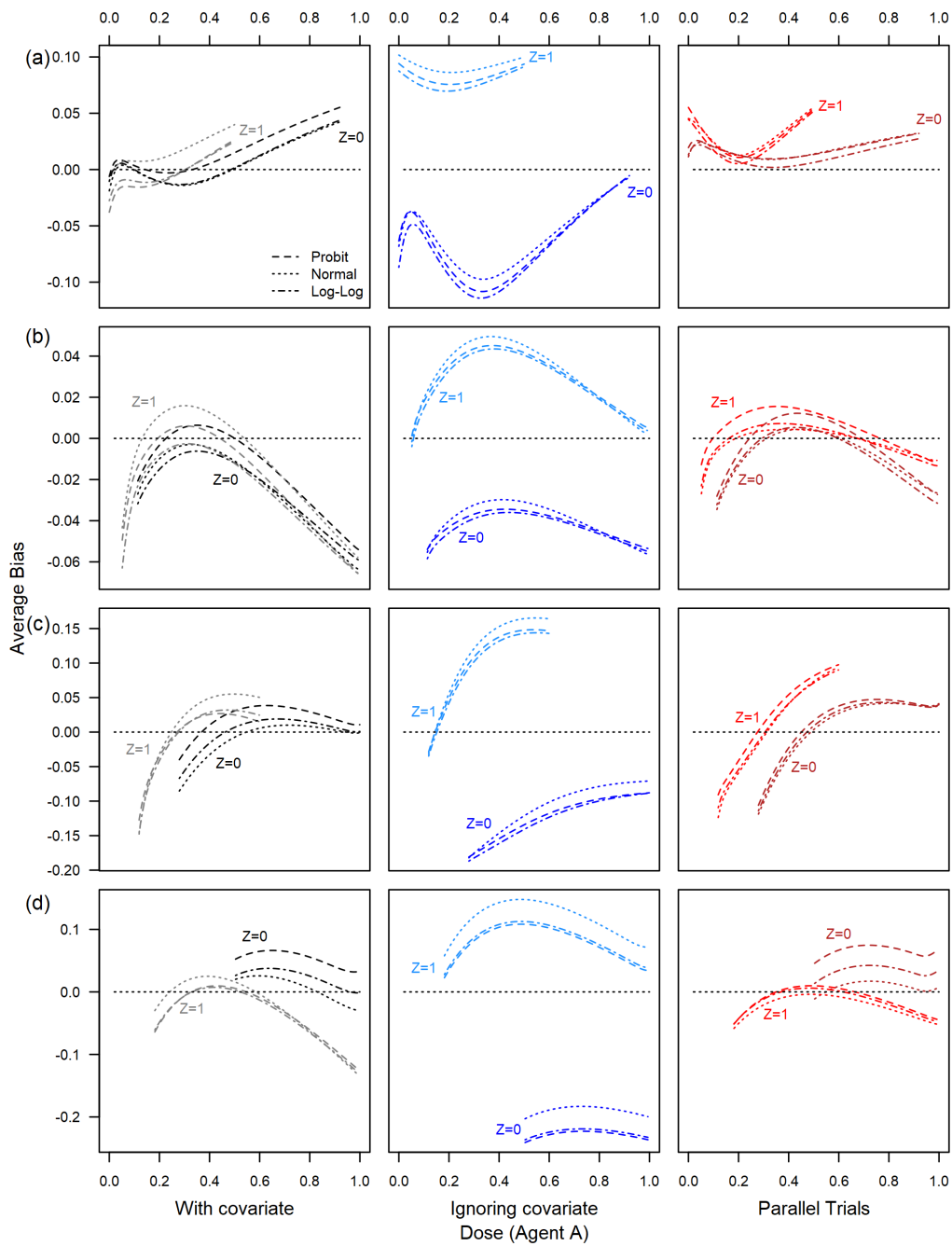


## 6. Supplementary Material

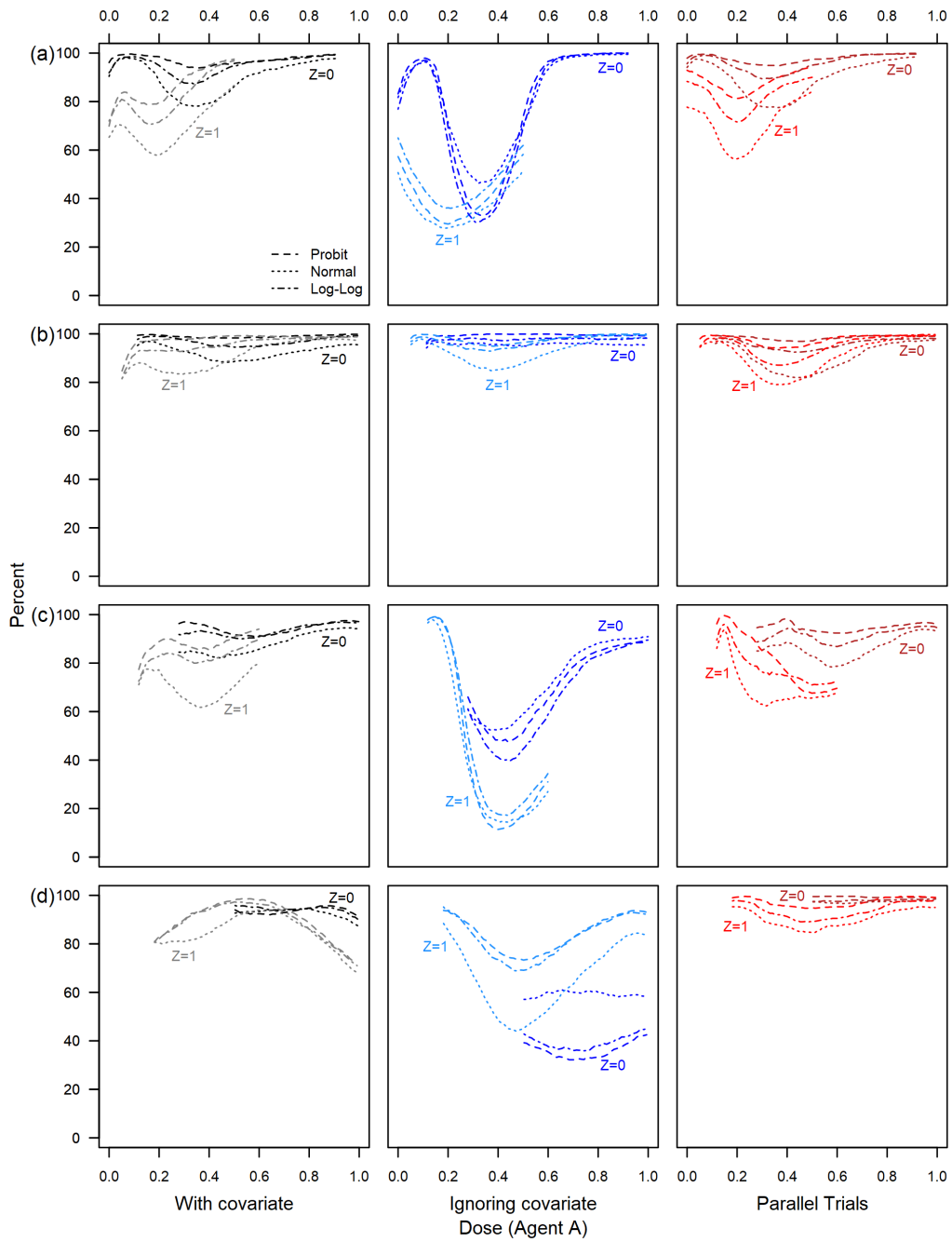
**Table S1:** Operating characteristics summarizing trial safety for designs using a covariate (WC), ignoring the covariate (IC), and parallel trials (PT) considering continuous dose combinations,  $\theta = 0.33$

Scenario	True model	Design	Average % DLTs (% Trials: DLT rate $< \theta - 0.1$ ; DLT rate $> \theta + 0.1$ )		
			Overall	Z = 0	Z = 1
(a)	Probit	WC	30.61 (5.0 ; 0.2)	20.62 (64.3 ; 0.0)	40.59 (0.0 ; 37.6)
		IC	30.65 (6.7 ; 0.4)	7.63 (98.3 ; 0.0)	53.67 (0.0 ; 90.8)
		PT	-	22.59 (50.8 ; 0.0)	30.28 (6.2 ; 1.3)
	Normal	WC	30.17 (8.0 ; 0.1)	22.10 (54.2 ; 0.2)	38.24 (0.7 ; 27.4)
		IC	29.67 (9.7 ; 0.4)	16.66 (79.1 ; 0.1)	42.68 (0.4 ; 50.4)
		PT	-	21.40 (59.9 ; 0.0)	29.45 (10.9 ; 1.8)
	CLog-log	WC	30.47 (5.1 ; 0.2)	21.52 (58.7 ; 0.2)	39.42 (0.1 ; 31.5)
		IC	30.29 (7.6 ; 0.2)	11.75 (94.4 ; 0.0)	48.84 (0.1 ; 76.3)
		PT	-	22.13 (54.7 ; 0.0)	29.97 (9.0 ; 1.4)
(b)	Probit	WC	24.79 (39.8 ; 0.0)	19.61 (73.4 ; 0.0)	29.97 (8.3 ; 1.5)
		IC	26.15 (26.6 ; 0.0)	15.99 (80.8 ; 0.0)	36.31 (3.7 ; 21.6)
		PT	-	17.54 (90 ; 0.0)	20.03 (70.6 ; 0.0)
	Normal	WC	23.90 (51.0 ; 0.0)	19.44 (71.2 ; 0.0)	28.37 (18.1 ; 1.9)
		IC	25.11 (40.7 ; 0.0)	19.19 (66.5 ; 0.2)	31.02 (15.5 ; 9.7)
		PT	-	16.58 (90.5 ; 0.0)	19.11 (78.0 ; 0.0)
	CLog-log	WC	24.42 (46.0 ; 0.0)	19.29 (74.2 ; 0.0)	29.55 (11.0 ; 2.1)
		IC	25.62 (34.8 ; 0.0)	17.83 (75.5 ; 0.0)	33.41 (9.1 ; 13.9)
		PT	-	16.96 (91.6 ; 0.0)	19.66 (73.5 ; 0.0)
(c)	Probit	WC	24.17 (46.4 ; 0.0)	12.30 (97.8 ; 0.0)	36.05 (0.3 ; 14.5)
		IC	26.35 (30.6 ; 0.0)	3.69 (100 ; 0.0)	49.01 (0.0 ; 78.0)
		PT	-	15.21 (97.8 ; 0.0)	23.13 (48.3 ; 0.0)
	Normal	WC	24.25 (47.7 ; 0.0)	14.63 (90.8 ; 0.0)	33.87 (4.2 ; 10.9)
		IC	24.88 (43.0 ; 0.0)	10.37 (95.1 ; 0.0)	39.39 (2.0 ; 35.2)
		PT	-	14.49 (96.6 ; 0.0)	22.13 (55.0 ; 0.0)
	CLog-log	WC	24.16 (46.8 ; 0.0)	13.53 (95.2 ; 0.0)	34.80 (1.7 ; 11.6)
		IC	25.84 (33.1 ; 0.0)	7.23 (99.5 ; 0.0)	44.46 (0.2 ; 59.7)
		PT	-	14.96 (96.3 ; 0.0)	22.95 (48.2 ; 0.0)
(d)	Probit	WC	16.55 (99.7 ; 0.0)	4.12 (100.0 ; 0.0)	28.98 (7.0 ; 0.1)
		IC	22.90 (60.0 ; 0.0)	0.60 (100.0 ; 0.0)	45.20 (0.0 ; 62.3)
		PT	-	7.27 (100.0 ; 0.0)	15.44 (95.2 ; 0.0)
	Normal	WC	17.24 (97.0 ; 0.0)	6.04 (100.0 ; 0.0)	28.44 (14.2 ; 1.0)
		IC	21.24 (74.8 ; 0.0)	3.44 (100.0 ; 0.0)	39.05 (0.3 ; 30.5)
		PT	-	6.44 (100.0 ; 0.0)	14.84 (95.6 ; 0.0)
	CLog-log	WC	16.60 (99.3 ; 0.0)	4.86 (100.0 ; 0.0)	28.34 (11.7 ; 0.2)
		IC	22.36 (65.5 ; 0.0)	1.78 (100.0 ; 0.0)	42.94 (0.3 ; 51.6)
		PT	-	7.08 (100.0 ; 0.0)	14.62 (97.2 ; 0.0)

*Abbreviation:* CLog-log, complementary log-log. Scenario  $(\rho_{000}, \rho_{100}, \rho_{101}, \rho_{010}, \eta)$ : (a) (0.01, 0.4, 0.8, 0.4, 10), (b) (0.005, 0.1, 0.2, 0.1, 10), (c) (0.005, 0.2, 0.7, 0.01, 10), (d)  $(10^{-4}, 10^{-3}, 0.05, 10^{-3}, 10)$ .



**Figure S1:** Pointwise average relative minimum distance from the true MTD curve to the estimated MTD curve with designs using a covariate (WC), ignoring the covariate (IC), and parallel trials (PT) under scenarios (a)-(d)



**Figure S2:** Pointwise percent of MTD recommendation for  $p = 0.2$  with designs using a covariate (WC), ignoring the covariate (IC), and parallel trials (PT) under scenarios (a)-(d)