

## Supplementary Document

### 1. Results

#### *1.1 Variance and MSE*

The variance of the treatment parameter ( $\beta_1$ ) decreased as the pair proportion decreased for all five survival models. At 90% pairing the nested MPL frailty model resulted in the highest variance of 0.007. The PWP model and the HKC model had the lowest variance of 0.004. At 50% pairing the nested MPL frailty model continued to have the highest variance of 0.009. Similar to the treatment variable, the nested MPL frailty model resulted in the highest variance, and the HKC model had the lowest variance for the ear ( $\beta_2$ ) and interaction ( $\beta_3$ ) variables. The interaction variable consistently had the highest variance of the three parameters, where the dynamic treatment effect and the static ear parameter had similar variances. All survival models had an increase in variance as pair proportion decreased from 90% to 10% (Figure 1-3). All results were comparable for the null simulations (Table 8 -11).

#### *1.2 Type-1 Error*

All models for the treatment ( $\beta_1$ ), ear ( $\beta_2$ ), and interaction ( $\beta_3$ ) parameters across the different pair proportions had type-1 error rates between 1.2% to 6.8% across all scenarios (Table 8 - 11). Though consistently near 5%, the type-1 error rates did fluctuate up and down at each change in pair proportion as seen in the type-1 error plot of Figure 5, which may be attributable to the variation across simulated trials, where more consistent estimates may be achieved with a larger number of simulated trials. For the parameter of ear ( $\beta_2$ ) and the interaction ( $\beta_3$ ) the logistic regression model resulted in the lowest type-1 error rate starting around 1% at 90% pairs and increasing to 4% by 10% pairs.

Table IV. Bias, Variance, MSE and Power results across all scenarios for the treatment parameter

<b><math>\beta_1 = \text{Treatment} = 0.3</math></b>					
Pair %	Model	Bias (95% CI)	Variance	MSE	Power
<b>90</b>	Logistic				34.1%
	PWP	-0.082 (-0.210, 0.046)	0.004	0.011	92.6%
	GF	-0.008 (-0.170, 0.154)	0.005	0.005	94.8%
	NF MPL <sup>a</sup>	0.003 (-0.161, 0.168)	0.007	0.007	95.6%
	NF PPL	-0.018 (-0.171, 0.135)	0.006	0.006	95.5%
	HKC	-0.082 (-0.210, 0.045)	0.004	0.011	92.6%
<b>80</b>	Logistic				33.3%
	PWP	-0.074 (-0.204, 0.056)	0.005	0.010	91.2%
	GF	-0.002 (-0.167, 0.163)	0.005	0.005	94.7%
	NF MPL <sup>a</sup>	0.010 (-0.155, 0.175)	0.007	0.007	96.1%
	NF PPL	-0.011 (-0.167, 0.144)	0.006	0.007	94.9%
	HKC	-0.075 (-0.204, 0.055)	0.005	0.010	91.1%
<b>70</b>	Logistic				34.7%
	PWP	-0.073 (-0.203, 0.057)	0.005	0.010	91.6%
	GF	0.001 (-0.164, 0.164)	0.006	0.006	94.1%
	NF MPL <sup>a</sup>	0.012 (-0.155, 0.178)	0.008	0.008	95.3%
	NF PPL	-0.010 (-0.165, 0.145)	0.007	0.007	94.1%
	HKC	-0.074 (-0.204, 0.056)	0.005	0.010	91.7%
<b>60</b>	Logistic				30.4%
	PWP	-0.076 (-0.215, 0.062)	0.005	0.011	88.0%
	GF	-0.004 (-0.182, 0.174)	0.006	0.006	91.4%
	NF MPL <sup>a</sup>	0.007 (-0.176, 0.190)	0.008	0.008	92.6%

	NF PPL	-0.014 (-0.181, 0.154)	0.007	0.007	91.9%
	HKC	-0.077 (-0.216, 0.062)	0.005	0.011	88.1%
<b>50</b>	Logistic				28.7%
	PWP	-0.075 (-0.224, 0.074)	0.006	0.011	86.1%
	GF	-0.004 (-0.187, 0.180)	0.007	0.007	90.0%
	NF MPL <sup>a</sup>	0.009 (-0.176, 0.194)	0.009	0.009	91.6%
	NF PPL	-0.013 (-0.188, 0.163)	0.008	0.008	90.8%
	HKC	-0.076 (-0.225, 0.073)	0.005	0.011	85.6%
<b>10</b>	Logistic				23.2%
	PWP	-0.078 (-0.246, 0.090)	0.008	0.014	72.5%
	GF	-0.007 (-0.217, 0.203)	0.009	0.009	78.3%
	NF MPL <sup>a</sup>	0.007 (-0.208, 0.222)	0.012	0.012	81.4%
	NF PPL	-0.016 (-0.218, 0.185)	0.011	0.011	77.2%
	HKC	-0.078 (-0.246, 0.089)	0.007	0.014	72.4%

<sup>a</sup>NF MPL convergence: 90%: 959 simulations, 80%: 959 simulations, 70%: 940 simulations, 60%: 941 simulations, 50%: 937 simulations, 10%: 907 simulations. GF = Gamma frailty, NF = nested frailty, MPL = maximum penalized likelihood estimation, PPL = penalized partial likelihood estimation, HKC = hierarchical Kendall copula

Table 5. Bias, Variance, MSE and Power results across all scenarios for the ear parameter

<b><math>\beta_2 = \text{Ear} = 0.4</math></b>					
Pair %	Model	Bias (95% CI)	Variance	MSE	Power
<b>90</b>	Logistic				53.4%
	PWP	-0.110 (-0.226, 0.006)	0.004	0.016	99.8%
	GF	-0.010 (-0.164, 0.144)	0.005	0.005	99.9%
	NF MPL <sup>a</sup>	0.003 (-0.153, 0.159)	0.008	0.008	99.9%
	NF PPL	-0.023 (-0.169, 0.124)	0.006	0.006	100%
	HKC	-0.110 (-0.225, 0.006)	0.004	0.016	100 %
<b>80</b>	Logistic				53.5%
	PWP	-0.103 (-0.222, 0.017)	0.005	0.015	99.7%
	GF	-0.001 (-0.162, 0.160)	0.005	0.005	100%
	NF MPL <sup>a</sup>	0.013 (-0.151, 0.177)	0.008	0.008	100%
	NF PPL	-0.014 (-0.165, 0.137)	0.006	0.006	100%
	HKC	-0.103 (-0.222, 0.016)	0.004	0.014	100%
<b>70</b>	Logistic				49.8%
	PWP	-0.105 (-0.230, 0.019)	0.005	0.016	99.1%
	GF	-0.004 (-0.168, 0.159)	0.006	0.006	99.7%
	NF MPL <sup>a</sup>	0.010 (-0.156 0.176)	0.009	0.009	99.7%
	NF PPL	-0.019 (-0.174, 0.137)	0.006	0.007	99.7%
	HKC	-0.105 (-0.229, 0.019)	0.004	0.015	99.5%
<b>60</b>	Logistic				47.9%
	PWP	-0.105 (-0.237, 0.027)	0.005	0.016	98.6%
	GF	-0.004 (-0.182, 0.174)	0.006	0.006	98.8%
	NF MPL <sup>a</sup>	0.009 (-0.173, 0.191)	0.009	0.009	99.1%
	NF PPL	-0.017 (-0.183, 0.149)	0.007	0.007	99.4%
	HKC	-0.105	0.005	0.015	99.5%

		(-0.236, 0.027)			
<b>50</b>	Logistic				45.1%
	PWP	-0.102	0.006	0.016	97.2%
		(-0.244, 0.041)			
	GF	-0.001	0.006	0.006	98.3%
		(-0.189, 0.187)			
	NF MPL <sup>a</sup>	0.013	0.010	0.010	98.8%
<b>10</b>		(-0.177, 0.203)			
	NF PPL	-0.015	0.007	0.008	99.0%
		(-0.191, 0.162)			
	HKC	-0.102	0.005	0.015	98.4%
		(-0.244, 0.040)			
	Logistic				34.4%
<b>10</b>	PWP	-0.101	0.008	0.018	91.9%
		(-0.272, 0.071)			
	GF	0.002	0.009	0.009	93.5%
		(-0.221, 0.225)			
	NF MPL <sup>a</sup>	0.018	0.014	0.014	94.8%
		(-0.207, 0.243)			
<b>10</b>	NF PPL	-0.013	0.012	0.012	94.9%
		(-0.225, 0.198)			
	HKC	-0.100	0.008	0.018	92.1%
		(-0.272, 0.071)			

<sup>a</sup>NF MPL convergence: 90%: 959 simulations, 80%: 959 simulations, 70%: 940 simulations, 60%: 941 simulations, 50%: 937 simulations, 10%: 907 simulations. GF = Gamma frailty, NF = nested frailty, MPL = maximum penalized likelihood estimation, PPL = penalized partial likelihood estimation, HKC = hierarchical Kendall copula

Table 6. Bias, Variance, MSE and Power results across all scenarios for the interaction parameter

$\beta_3 = \text{Interaction} = -0.25$					
Pair %	Model	Bias	Variance	MSE	Power
<b>90</b>	Logistic				10.7%
	PWP	0.071 (-0.088, 0.229)	0.009	0.014	46.8%
	GF	0.009 (-0.193, 0.212)	0.010	0.010	55.1%
	NF MPL <sup>a</sup>	0.001 (-0.206, 0.204)	0.013	0.013	59.1%
	NF PPL	0.018 (-0.177, 0.213)	0.011	0.011	60.2%
	HKC	0.071 (-0.087, 0.229)	0.007	0.012	56.2%
<b>80</b>	Logistic				11.0%
	PWP	0.058 (-0.110, 0.226)	0.009	0.012	52.0%
	GF	-0.003 (-0.220, 0.213)	0.011	0.011	59.0%
	NF MPL <sup>a</sup>	-0.015 (-0.235, 0.205)	0.014	0.014	61.9%
	NF PPL	0.005 (-0.202, 0.211)	0.011	0.012	63.4%
	HKC	0.059 (-0.109, 0.226)	0.008	0.011	59.5%
<b>70</b>	Logistic				13.7%
	PWP	0.060 (-0.112, 0.233)	0.010	0.013	49.6%
	GF	0.001 (-0.220, 0.221)	0.011	0.011	55.4%
	NF MPL <sup>a</sup>	-0.011 (-0.235, 0.214)	0.015	0.015	58.3%
	NF PPL	0.009 (-0.201, 0.219)	0.012	0.012	60.1%
	HKC	0.061 (-0.111, 0.233)	0.008	0.012	56.9%
<b>60</b>	Logistic				11.5%
	PWP	0.065 (-0.113, 0.243)	0.010	0.014	43.9%
	GF	0.003 (-0.23, 0.237)	0.012	0.012	51.2%
	NF MPL <sup>a</sup>	-0.007 (-0.245, 0.232)	0.016	0.016	53.2%
	NF PPL	0.012 (-0.207, 0.230)	0.013	0.013	54.7%
	HKC	0.065	0.009	0.013	49.9%

(-0.113, 0.0243)					
<b>50</b>	Logistic				11.5%
	PWP	0.063 (-0.133, 0.260)	0.011	0.015	43.5%
	GF	0.004 (-0.241, 0.249)	0.013	0.013	49.2%
	NF MPL <sup>a</sup>	-0.008 (-0.255, 0.240)	0.017	0.017	51.7%
	NF PPL	0.012 (-0.223, 0.248)	0.014	0.014	53.1%
	HKC	0.064 (-0.132, 0.260)	0.010	0.014	49.3%
<b>10</b>	Logistic				11.1%
	PWP	0.059 (-0.171, 0.290)	0.015	0.018	35.1%
	GF	-0.003 (-0.290, 0.283)	0.017	0.017	38.8%
	NF MPL <sup>a</sup>	-0.016 (-0.307, 0.275)	0.023	0.023	41.6%
	NF PPL	0.006 (-0.268, 0.279)	0.021	0.021	38.8%
	HKC	0.060 (-0.170, 0.290)	0.014	0.018	36.5%

<sup>a</sup>NF MPL convergence: 90%: 959 simulations, 80%: 959 simulations, 70%: 940 simulations, 60%: 941 simulations, 50%: 937 simulations, 10%: 907 simulations. GF = Gamma frailty, NF = nested frailty, MPL = maximum penalized likelihood estimation, PPL = penalized partial likelihood estimation, HKC = hierarchical Kendall copula

Table 7. Bias, Variance, MSE and Power results across all scenarios for the cluster parameters

Pair %	Model	$\rho = 0.30$	$\eta = 0.15$
		Bias (95% CI)	Bias (95% CI)
<b>90</b>	Logistic	-	-
	PWP	-	-
	GF	0.101	-
		(-0.048, 0.250)	-
	NF MPL	-0.293	0.280
		(-0.293, -0.293)	(0.136, 0.424)
	NF PPL	0.019	-0.044
		(-0.087, 0.125)	(-0.158, 0.070)
<b>80</b>	HKC	-0.005	0.231
		(-0.108, 0.099)	(0.111, 0.352)
	Logistic		
	PWP		
	GF	0.098	-
		(-0.049, 0.245)	-
	NF MPL	-0.293	0.276
		(-0.293, -0.293)	(0.135, 0.418)
<b>70</b>	NF PPL	0.019	-0.047
		(-0.089, 0.127)	(-0.158, 0.065)
	HKC	-0.005	0.229
		(-0.110, 0.101)	(0.109, 0.349)
	Logistic	-	-
	PWP	-	-
	GF	0.101	-
		(-0.043, 0.246)	-
<b>60</b>	NF MPL	-0.293	0.281
		(-0.293, -0.293)	(0.138, 0.424)
	NF PPL	0.023	-0.049
		(-0.091, 0.137)	(-0.168, 0.069)
	HKC	0.001	0.231
		(-0.117, 0.117)	(0.110, 0.352)
	Logistic	-	-
	PWP	-	-
<b>50</b>	GF	0.098	-
		(-0.056, 0.252)	-
	NF MPL	-0.293	0.279
		(-0.293, -0.293)	(0.127, 0.431)
	NF PPL	0.022	-0.051
		(-0.100, 0.144)	(-0.175, 0.074)
	HKC	0.001	0.23
		(-0.125, 0.128)	(0.106, 0.354)
<b>50</b>	Logistic	-	-
	PWP	-	-
	GF	0.097	-



		(-0.060, 0.254)	
	NF MPL	-0.293	0.276
		(-0.293, -0.293)	(0.116, 0.436)
	NF PPL	0.016	-0.047
		(-0.117, 0.148)	(-0.181, 0.087)
	HKC	-0.006	0.228
		(-0.140, 0.128)	(0.097, 0.358)
<b>10</b>	Logistic	-	-
	PWP	-	-
	GF	0.093	
		(-0.088, 0.274)	-
	NF MPL	-0.293	0.272
		(-0.293, -0.293)	(0.079, 0.465)
	NF PPL	0.007	-0.040
		(-0.251, 0.264)	(-0.283, 0.203)
	HKC	0.018	0.228
		(-0.300, 0.335)	(0.074, 0.381)

GF = Gamma frailty, NF = nested frailty, MPL = maximum penalized likelihood estimation, PPL = penalized partial likelihood estimation, HKC = hierarchical Kendall copula

Table 8. Bias, Variance, MSE and Power results across all null scenarios for the treatment parameter

$\beta_1 = \text{Treatment} = 0$					
Pair %	Model	Bias (95% CI)	Variance	MSE	Type I Error
<b>90</b>	Logistic				5.6%
	PWP	-0.008 (-0.140, 0.124)	0.005	0.005	5.2%
	GF	-0.007 (-0.017, 0.156)	0.005	0.005	5.2%
	NF MPL <sup>a</sup>	0.001 (-0.164, 0.166)	0.007	0.007	5.6%
	NF PPL	-0.007 (-0.162, 0.148)	0.006	0.006	4.9%
	HKC	-0.008 (-0.140, 0.124)	0.005	0.005	5.2%
<b>80</b>	Logistic				5.2%
	PWP	0.001 (-0.134, 0.134)	0.005	0.005	4.1%
	GF	0.001 (-0.165, 0.165)	0.006	0.006	4.9%
	NF MPL <sup>a</sup>	-0.007 (-0.160, 0.157)	0.007	0.007	5.7%
	NF PPL	0.001 (-0.156, 0.157)	0.007	0.007	4.3%
	HKC	0.001 (-0.134, 0.134)	0.005	0.005	4.5%
<b>70</b>	Logistic				4.1%
	PWP	0.001 (-0.132, 0.134)	0.005	0.005	4.2%
	GF	0.002 (-0.163, 0.166)	0.006	0.006	3.8%
	NF MPL <sup>a</sup>	0.009 (-0.158, 0.176)	0.008	0.008	4.1%
	NF PPL	0.002 (-0.155, 0.159)	0.007	0.007	3.9%
	HKC	0.001 (-0.132, 0.134)	0.005	0.005	3.7%
<b>60</b>	Logistic				4.3%
	PWP	-0.002 (-0.145, 0.141)	0.005	0.005	4.8%
	GF	-0.002 (-0.180, 0.176)	0.006	0.006	5.3%
	NF MPL <sup>a</sup>	0.007 (-0.176, 0.189)	0.008	0.008	6.0%
	NF PPL	-0.001 (-0.170, 0.167)	0.007	0.007	4.6%

	HKC	-0.002 (-0.144, 0.140)	0.005	0.005	5.0%
<b>50</b>	Logistic				5.5%
	PWP	-0.002 (-0.152, 0.149)	0.006	0.006	5.7%
	GF	-0.001 (-0.184, 0.181)	0.007	0.007	5.3%
	NF MPL <sup>a</sup>	0.007 (-0.177, 0.192)	0.009	0.009	5.4%
	NF PPL	-0.001 (-0.176, 0.174)	0.008	0.008	5.1%
	HKC	-0.002 (-0.151, 0.148)	0.006	0.006	5.7%
<b>10</b>	Logistic				4.4%
	PWP	-0.004 (-0.172, 0.166)	0.008	0.008	4.6%
	GF	-0.005 (-0.214, 0.205)	0.009	0.009	4.9%
	NF MPL <sup>a</sup>	0.006 (-0.207, 0.219)	0.012	0.012	5.5%
	NF PPL	-0.004 (-0.205, 0.197)	0.011	0.011	4.6%
	HKC	-0.004 (-0.172, 0.166)	0.008	0.008	4.5%

<sup>a</sup>NF MPL convergence: 90%: 989 simulations, 80%: 990 simulations, 70%: 990 simulations, 60%: 980 simulations, 50%: 974 simulations, 10%: 952 simulations. GF = Gamma frailty, NF = nested frailty, MPL = maximum penalized likelihood estimation, PPL = penalized partial likelihood estimation, HKC = hierarchical Kendall copula

Table 9. Bias, Variance, MSE and Power results across all null scenarios for the ear parameter

$\beta_2 = \text{Ear} = 0$					
Pair %	Model	Bias (95% CI)	Variance	MSE	Type I Error
<b>90</b>	Logistic				1.2%
	PWP	-0.006 (-0.124, 0.112)	0.005	0.005	2.1%
	GF	-0.007 (-0.159, 0.146)	0.005	0.005	2.6%
	NF MPL <sup>a</sup>	0.001 (-0.154 0.157)	0.008	0.008	2.9%
	NF PPL	-0.006 (-0.153, 0.140)	0.006	0.006	4.8%
	HKC	-0.006 (-0.124, 0.112)	0.004	0.004	5.5%
<b>80</b>	Logistic				1.3%
	PWP	0.002 (-0.121, 0.125)	0.005	0.005	1.8%
	GF	0.003 (-0.158, 0.163)	0.005	0.005	3.6%
	NF MPL <sup>a</sup>	0.010 (-0.152, 0.173)	0.008	0.009	3.7%
	NF PPL	0.003 (-0.149, 0.155)	0.006	0.006	4.6%
	HKC	0.002 (-0.121, 0.124)	0.004	0.004	4.4%
<b>70</b>	Logistic				1.4%
	PWP	-0.002 (-0.129, 0.125)	0.005	0.005	2.6%
	GF	-0.003 (-0.166, 0.161)	0.006	0.006	3.3%
	NF MPL <sup>a</sup>	0.006 (-0.160, 0.172)	0.009	0.009	3.6%
	NF PPL	-0.003 (-0.159, 0.153)	0.006	0.006	5.4%
	HKC	-0.002 (-0.129, 0.125)	0.004	0.004	4.9%
<b>60</b>	Logistic				1.8%
	PWP	-0.001 (-0.137, 0.134)	0.005	0.005	3.0%
	GF	-0.001 (-0.178, 0.175)	0.006	0.006	2.8%
	NF MPL <sup>a</sup>	0.008 (-0.171, 0.187)	0.009	0.010	3.5%
	NF PPL	-0.001 (-0.166, 0.164)	0.007	0.007	5.2%
	HKC	-0.001	0.005	0.005	4.6%

		(-0.136, 0.134)			
<b>50</b>	Logistic				2.5%
	PWP	0.002	0.006	0.006	4.3%
		(-0.143, 0.146)			
	GF	0.002	0.007	0.007	5.3%
		(-0.185, 0.190)			
	NF MPL <sup>a</sup>	0.011	0.010	0.010	4.9%
		(-0.181, 0.204)			
<b>10</b>	NF PPL	0.003	0.008	0.008	6.4%
		(-0.174, 0.179)			
	HKC	0.002	0.005	0.005	6.8%
		(-0.143, 0.146)			
	Logistic				4.0%
	PWP	0.004	0.008	0.008	4.2%
		(-0.172, 0.180)			
<b>5</b>	GF	0.007	0.009	0.009	4.1%
		(-0.217, 0.230)			
	NF MPL <sup>a</sup>	0.019	0.014	0.014	5.0%
		(-0.207, 0.245)			
	NF PPL	0.006	0.012	0.012	4.6%
		(-0.207, 0.219)			
	HKC	0.004	0.008	0.008	4.7%
		(-0.172, 0.180)			

<sup>a</sup>NF MPL convergence: 90%: 989 simulations, 80%: 990 simulations, 70%: 990 simulations, 60%: 980 simulations, 50%: 974 simulations, 10%: 952 simulations.

Table 10. Bias, Variance, MSE and Power results across all null scenarios for the interaction parameter

<b><math>\beta_3 = \text{Interaction} = 0</math></b>					
<b>Pair %</b>	<b>Model</b>	<b>Bias (95% CI)</b>	<b>Variance</b>	<b>MSE</b>	<b>Type I Error</b>
<b>90</b>	Logistic				2.0%
	PWP	0.008 (-0.156, 0.172)	0.009	0.009	2.7 %
	GF	0.007 (-0.200, 0.214)	0.011	0.011	3.2%
	NF MPL <sup>a</sup>	0.001 (-0.210, 0.211)	0.014	0.014	4.0%
	NF PPL	0.008 (-0.192, 0.207)	0.011	0.011	4.8%
	HKC	0.008 (-0.156, 0.172)	0.007	0.008	4.3%
<b>80</b>	Logistic				2.2%
	PWP	-0.004 (-0.177, 0.170)	0.010	0.010	2.8%
	GF	-0.004 (-0.224, 0.215)	0.011	0.011	3.7%
	NF MPL <sup>a</sup>	-0.011 (-0.233, 0.211)	0.015	0.015	3.7%
	NF PPL	-0.005 (-0.215, 0.205)	0.012	0.012	5.6%
	HKC	-0.003 (-0.176, 0.169)	0.008	0.008	4.5%
<b>70</b>	Logistic				2.8%
	PWP	0.001 (-0.177, 0.176)	0.010	0.010	3.2%
	GF	0.001 (-0.223, 0.225)	0.012	0.012	3.7 %
	NF MPL <sup>a</sup>	-0.006 (0.233, 0.221)	0.016	0.016	3.7%
	NF PPL	0.001 (-0.211, 0.213)	0.013	0.013	4.6%
	HKC	0.001 (-0.176, 0.176)	0.009	0.009	4.7%
<b>60</b>	Logistic				2.2%
	PWP	0.003 (-0.182, 0.187)	0.011	0.011	3.2%
	GF	0.002 (-0.234, 0.238)	0.012	0.012	3.4%
	NF MPL <sup>a</sup>	-0.006 (-0.247, 0.234)	0.016	0.017	4.4%
	NF PPL	0.002 (-0.220, 0.223)	0.013	0.013	4.4%

	HKC	0.002 (-0.180, 0.185)	0.009	0.009	4.4%
<b>50</b>	Logistic				3.3%
	PWP	0.002 (-0.198, 0.203)	0.012	0.012	3.4%
	GF	0.003 (-0.245, 0.251)	0.013	0.01	3.5%
	NF MPL <sup>a</sup>	-0.005 (-0.259, 0.250)	0.018	0.018	4.0%
	NF PPL	0.002 (-0.236, 0.241)	0.015	0.015	4.7%
	HKC	0.003 (-0.197, 0.202)	0.010	0.010	4.7%
<b>10</b>	Logistic				4.3%
	PWP	-0.004 (-0.238, 0.230)	0.016	0.016	4.0%
	GF	-0.007 (-0.297, 0.283)	0.018	0.018	4.4%
	NF MPL <sup>a</sup>	-0.016 (-0.313, 0.280)	0.024	0.024	5.0%
	NF PPL	-0.007 (-0.284, 0.271)	0.022	0.022	3.7%
	HKC	-0.004 (-0.238, 0.230)	0.015	0.015	4.4%

<sup>a</sup>NF MPL convergence: 90%: 989 simulations, 80%: 990 simulations, 70%: 990 simulations, 60%: 980 simulations, 50%: 974 simulations, 10%: 952 simulations.

Table 11. Bias, Variance, MSE and Power results across all null scenarios for the cluster parameters

Pair %	Model	$\rho = 0.3$	$\eta = 0.15$
		Bias (95% CI)	Bias (95% CI)
<b>90</b>	Logistic	-	-
	PWP	-	-
	GF	0.105 (-0.054, 0.264)	-
	NF MPL <sup>a</sup>	-0.292 (-0.302, -0.283)	0.283 (0.122, 0.445)
	NF PPL	0.014 (-0.094, 0.121)	-0.050 (-0.168, 0.068)
	HKC	-0.023 (-0.122, 0.076)	0.230 (0.100, 0.359)
<b>80</b>	Logistic	-	-
	PWP	-	-
	GF	0.102 (-0.058, 0.261)	-
	NF MPL <sup>a</sup>	-0.293 (-0.293, -0.293)	0.281 (0.125, 0.438)
	NF PPL	0.012 (-0.097, 0.122)	-0.052 (-0.167, 0.063)
	HKC	-0.024 (-0.125, 0.077)	0.228 (0.100, 0.355)
<b>70</b>	Logistic	-	-
	PWP	-	-
	GF	0.105 (-0.051, 0.261)	-
	NF MPL <sup>a</sup>	-0.292 (-0.305, -0.279)	0.285 (0.125, 0.445)
	NF PPL	0.017 (-0.099, 0.133)	-0.054 (-0.175, 0.067)
	HKC	-0.020 (-0.132, 0.092)	0.230 (0.102, 0.358)
<b>60</b>	Logistic	-	-
	PWP	-	-
	GF	0.103 (-0.061, 0.267)	-
	NF MPL <sup>a</sup>	-0.293 (-0.293, -0.293)	0.283 (0.119, 0.447)
	NF PPL	0.016 (-0.108, 0.139)	-0.056 (-0.182, 0.071)
	HKC	-0.018 (-0.139, 0.102)	0.228 (0.095, 0.362)
<b>50</b>	Logistic	-	-
	PWP	-	-



	GF	0.101 (-0.068, 0.270)	-
	NF MPL <sup>a</sup>	-0.292 (-0.315, -0.269)	0.279 (0.104, 0.455)
	NF PPL	0.010 (-0.122, 0.142)	-0.052 (-0.186, 0.082)
	HKC	-0.025 (-0.153, 0.104)	0.226 (0.083, 0.370)
<b>10</b>	Logistic	-	-
	PWP	-	-
	GF	0.094 (-0.104, 0.292)	-
	NF MPL <sup>a</sup>	-0.292 (-0.312, -0.272)	0.276 (0.063, 0.488)
	NF PPL	0.001 (-0.257, 0.257)	-0.045 (-0.282, 0.192)
	HKC	0.001 (-0.308, 0.308)	0.225 (0.061, 0.390)

<sup>a</sup>NF MPL convergence: 90%: 989 simulations, 80%: 990 simulations, 70%: 990 simulations, 60%: 980 simulations, 50%: 974 simulations, 10%: 952 simulations.

Table 12. Bias, Variance, MSE and Power results when no Sub-cluster variance for 90% pairs

Parameter	Model	Bias	Variance	MSE	Power
$\beta_1$ Treatment = 0.3					
	Logistic				31.3%
	PWP	-0.065	0.004	0.009	94.9%
	GF	-0.007	0.005	0.005	96.6%
	NF MPL	0.004	0.006	0.006	97.4%
	NF PPL	-0.008	0.006	0.006	97.1%
	HKC	-0.064	0.004	0.008	96.1%
$\beta_2$ Ear = 0.4					
	Logistic				50.9%
	PWP	-0.086	0.004	0.012	99.9%
	GF	-0.004	0.005	0.005	100%
	NF MPL	0.011	0.007	0.007	100%
	NF PPL	-0.006	0.005	0.005	100%
	HKC	-0.087	0.003	0.011	100%
$\beta_3$ Interaction = -0.25					
	Logistic				10.1%
	PWP	0.053	0.008	0.011	58.9%
	GF	0.004	0.009	0.009	63.9%
	NF MPL	-0.007	0.012	0.012	67.7%
	NF PPL	0.006	0.010	0.010	71.1%
	HKC	0.056	0.007	0.010	67.6%
$\rho$ Cluster = 0.15					
	GF	-0.019			
	NF MPL	-0.293			
	NF PPL	0.023			
	HKC	0.085			
$\eta$ Sub-Cluster = 0					
	NF MPL	0.309			
	NF PPL	0.008			
	HKC	0.280			

Table 13. Bias, Variance, MSE and Power results when large Sub-cluster variance for 90% pairs

Parameter	Model	Bias	Variance	MSE	Power
$\beta_1$ Treatment = 0.3					
	Logistic				35.2%
	PWP	-0.118	0.005	0.019	74.0%
	GF	0.001	0.007	0.007	84.6%
	NF MPL	0.011	0.010	0.010	86.9%
	NF PPL	-0.032	0.010	0.011	78.2 %
	HKC	-0.119	0.005	0.019	74.1%
$\beta_2$ Ear = 0.4					
	Logistic				52.6%
	PWP	-0.174	0.005	0.035	88.2%
	GF	-0.002	0.007	0.007	94.3%
	NF MPL	0.007	0.013	0.013	95.5%
	NF PPL	-0.058	0.011	0.015	89.3 %
	HKC	-0.173	0.005	0.035	89.1%
$\beta_3$ Interaction = -0.25					
	Logistic				14.8%
	PWP	0.097	0.010	0.019	34.0%
	GF	-0.004	0.015	0.015	44.3%
	NF MPL	-0.013	0.019	0.019	46.8%
	NF PPL	0.029	0.018	0.019	35.8%
	HKC	0.100	0.009	0.019	36.4%
$\rho$ Cluster = 0.15					
	GF	0.807			
	NF MPL	-0.293			
	NF PPL	-0.017			
	HKC	-0.185			
$\eta$ Sub-Cluster = 1.15					
	NF MPL	-0.001			
	NF PPL	-0.100			
	HKC	-0.233			

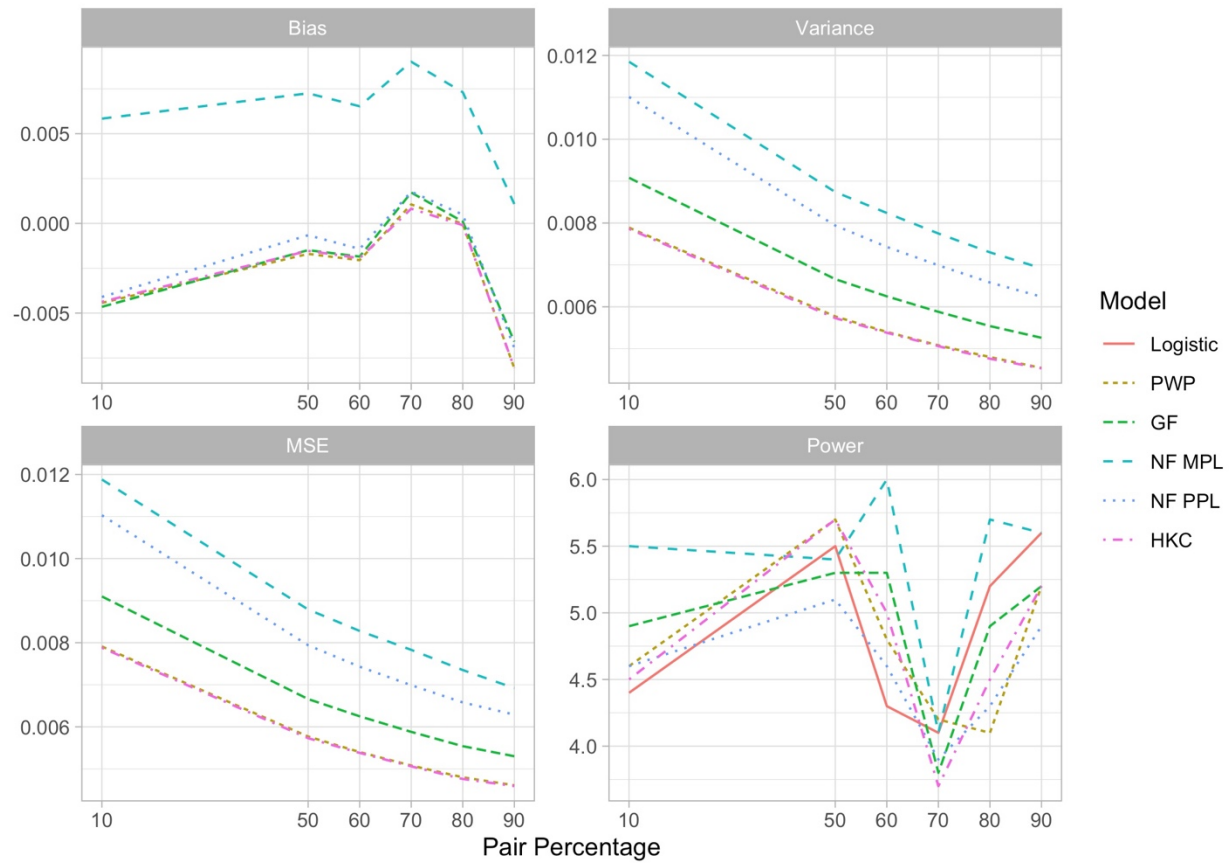
Table 14. Bias, Variance, MSE and Power results when no Sub-cluster or cluster variance for 90% pairs

Parameter	Model	Bias	Variance	MSE	Power
$\beta_1$ Treatment = 0.3					
	Logistic				31.4%
	PWP	0.004	0.004	0.004	99.7%
	GF	0.004	0.004	0.004	99.7%
	NF MPL	0.005	0.002	0.002	100%
	NF PPL	0.008	0.004	0.004	100%
	HKC	-0.002	0.004	0.004	99.2%
$\beta_2$ Ear = 0.4					
	Logistic				44.3%
	PWP	-0.002	0.004	0.004	100%
	GF	-0.002	0.004	0.004	100%
	NF MPL	-0.006	0.002	0.002	100%
	NF PPL	0.006	0.004	0.004	100%
	HKC	-0.015	0.004	0.004	100%
$\beta_3$ Interaction = -0.25					
	Logistic				13.3%
	PWP	-0.001	0.008	0.008	79.1%
	GF	-0.001	0.008	0.008	79.6%
	NF MPL	-0.001	0.005	0.005	88.6%
	NF PPL	-0.006	0.008	0.008	80.1%
	HKC	0.005	0.008	0.008	78.9%
$\rho$ Cluster = 0					
	GF	0.001			
	NF MPL	0.007			
	NF PPL	0.006			
	HKC	0.000			
$\eta$ Sub-Cluster = 0					
	NF MPL	0.013			
	NF PPL	0.011			
	HKC	-0.004			

Table 15. Average AIC of results for all scenarios

Model	Pair %					
	90%	80%	70%	60%	50%	10%
Logistic	-	-	-	-	-	-
PWP	22576.31	21202.32	19829.63	18468.57	17122.20	11888.87
GF	24937.37	23441.34	21941.95	20457.37	18986.52	13255.24
NF MPL	-	-	-	-	-	-
NF PPL	24893.55	23402.48	21908.34	20428.80	18965.31	13254.86
HKC	25153.65	23644.34	22135.47	20638.06	19155.18	13378.80

Figure 5. Line graphs for the bias, variance, MSE and power from all null simulations across pair percentages for the treatment effect.



PWP - Prentice-Williams-Peterson, GF - Gamma frailty, NF - nested frailty, HKC - hierarchical Kendall copula

Figure 6. Line graphs for the bias, variance, MSE and power from all null simulations across pair percentages for the ear effect.

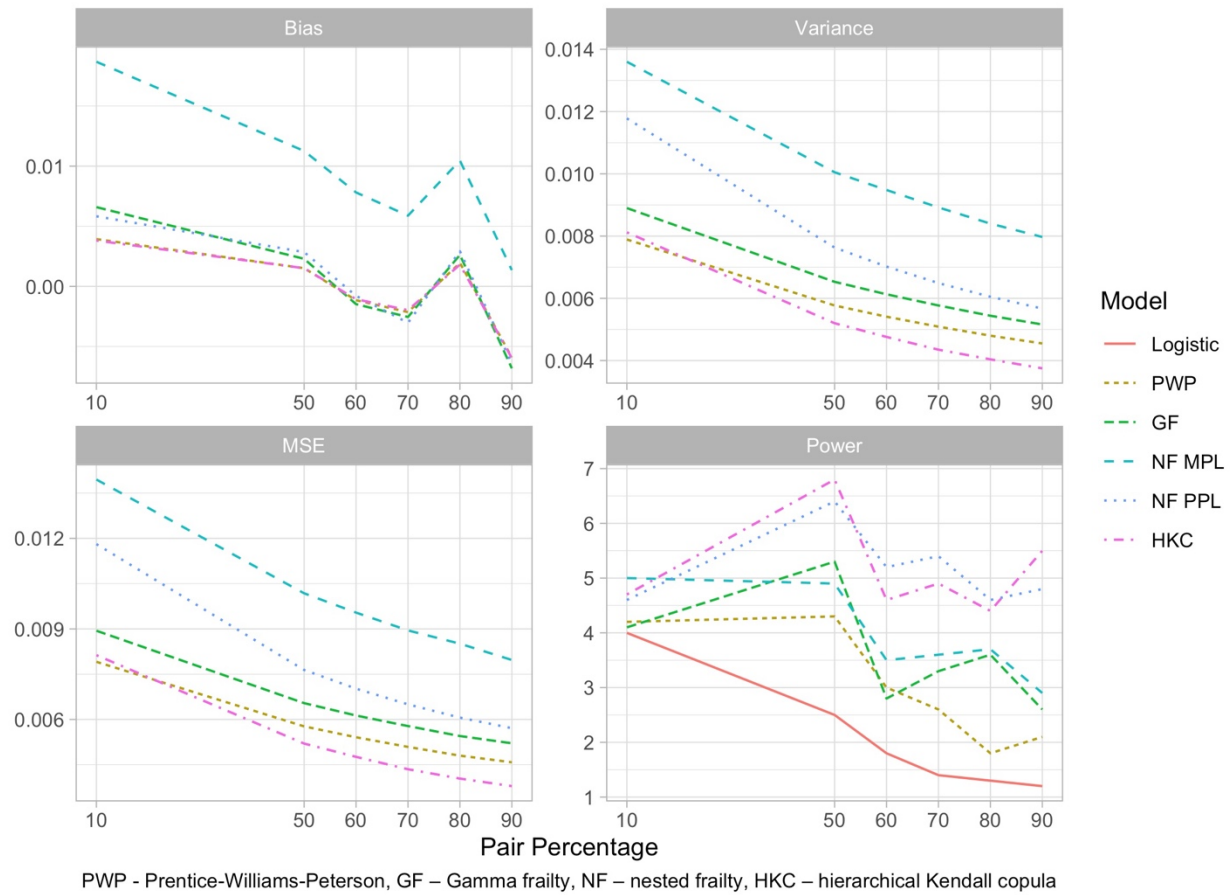


Figure 7. Line graphs for the bias, variance, MSE and power from all null simulations across pair percentages for the interaction effect.

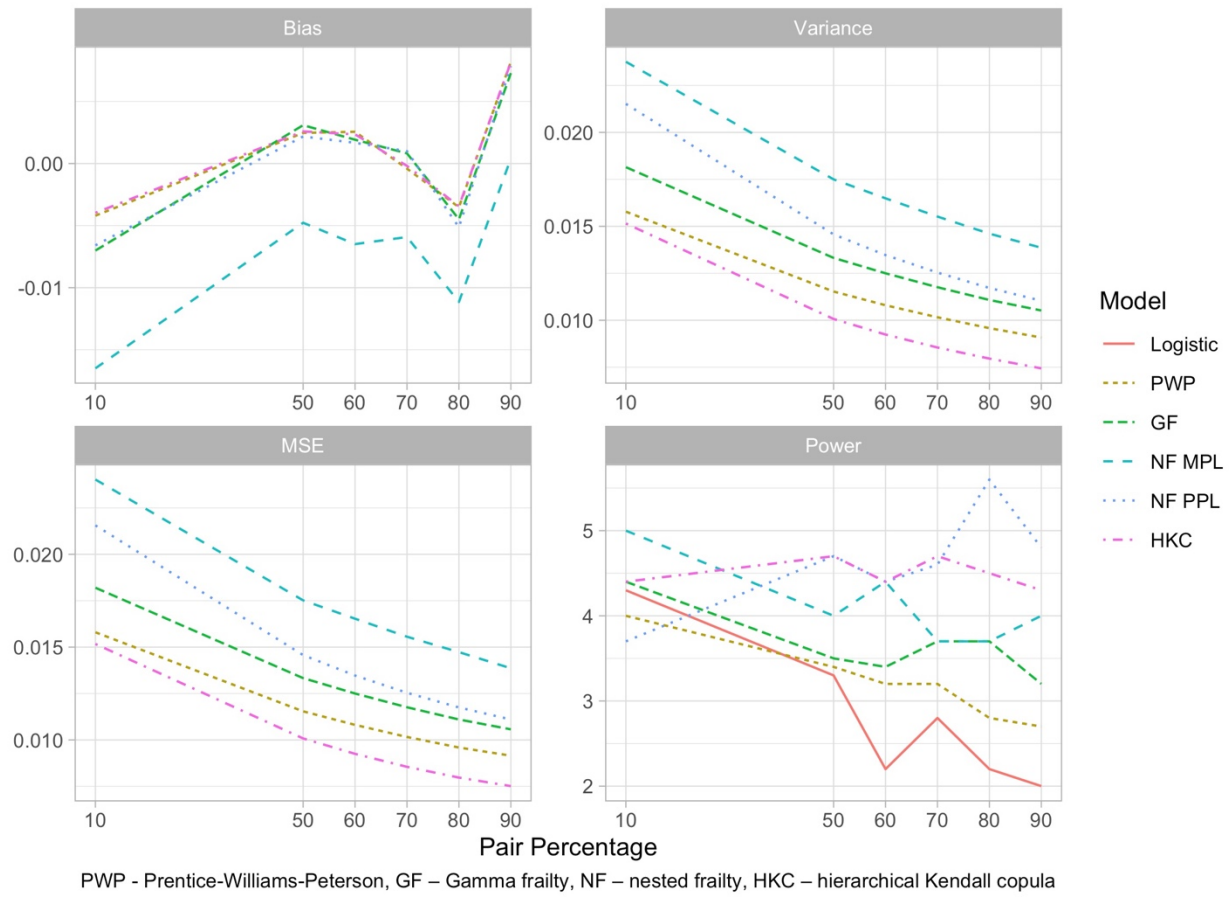




Figure 8. Line graphs for the bias from all null simulations across pair percentages for the random effect.

