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Supplementary Material for **“Estimating the correlation between
semi-competing risk survival endpoints”**

By Lexy Sorrell, Yinghui Wei, Małgorzata Wojtyś and Peter Rowe

In the supplementary material we consider the Archimedean copulas and derive their derivatives for use in the likelihood function of equation (8) in the main text. We provide results from data analysis corresponding to Section 4 in the main text in Tables S1 to S4. Table S5 details the true values for the parameters used in the simulation studies involving the Exponential, Weibull and Gompertz survival distributions with the Normal, Clayton, Frank and Gumbel copulas. Simulation results for Section 5 of the main text investigating misspecification of the copula function in each of the three scenarios are provided in Tables S6 to S20. Finally, the contour plots from Section 4 of the main text are given in Figures S1 and S2.

1 Archimedean copulas

For a 2-dimensional random vector (U, V) , uniformly distributed on the unit cube $[0, 1]^2$ with observed values u and v , we consider the bivariate copula

$$C(u, v) = P(U \leq u, V \leq v).$$

Archimedean copulas can be written in the form,

$$C_\theta(u, v) = \psi^{-1}(\psi(u) + \psi(v)), \quad (1)$$

where θ is the association parameter and ψ is the generator function of the Archimedean copula that depends on θ , that is $\psi(u) = \psi(u; \theta)$.

Using known formula,

$$\frac{df^{-1}(y)}{dy} = \frac{1}{f'(x)|_{x=f^{-1}(y)}}, \quad (2)$$

we can use the generator functions of copulas to derive the first and second derivatives to use in the likelihood functions. First, we differentiate the copula function, equation (1), by u , using equation (2),

$$\frac{dC_\theta(u, v)}{du} = \frac{d}{du}(\psi^{-1}(\psi(u) + \psi(v))) = \frac{1}{\psi'(x)|_{x=\psi^{-1}(\psi(u) + \psi(v))}} \times \psi'(u) = \frac{\psi'(u)}{\psi'(C_\theta(u, v))}. \quad (3)$$

By symmetry, differentiating equation (1) by v ,

$$\frac{dC_\theta(u, v)}{dv} = \frac{\psi'(v)}{\psi'(C_\theta(u, v))}. \quad (4)$$

Finally, the second derivative of equation (1) is found by taking the derivative of equation (3) with respect to v ,

$$\begin{aligned} \frac{d^2 C_\theta(u, v)}{dudv} &= \frac{d}{dv} \frac{\psi'(u)}{\psi'(C_\theta(u, v))} = \psi'(u) \frac{d}{dv} \frac{1}{\psi'(C_\theta(u, v))} \\ &= \psi'(u) \frac{-1}{(\psi'(C_\theta(u, v)))^2} \frac{d}{dv} \psi'(C_\theta(u, v)) \\ &= \frac{-\psi'(u)}{(\psi'(C_\theta(u, v)))^2} \psi''(C_\theta(u, v)) \frac{d}{dv} C_\theta(u, v) \\ &= \frac{-\psi'(u)}{(\psi'(C_\theta(u, v)))^2} \psi''(C_\theta(u, v)) \frac{\psi'(v)}{\psi'(C_\theta(u, v))} \\ &= \frac{-\psi'(u)\psi'(v)\psi''(C_\theta(u, v))}{(\psi'(C_\theta(u, v)))^3}. \end{aligned} \quad (5)$$

Clayton Copula

The generator function for the Clayton copula is given by,

$$\psi(t) = \frac{t^{-\theta} - 1}{\theta}. \quad (6)$$

The first derivative of equation (6) is given by,

$$\psi'(t) = \frac{-\theta t^{-\theta-1}}{\theta} = -t^{-(\theta+1)}. \quad (7)$$

The second derivative of equation (6), by differentiating equation (7), is given by,

$$\psi''(t) = (\theta + 1)t^{-(\theta+2)}. \quad (8)$$

Substituting equations (6) and (7) into equations (3) and (4) we find the first derivatives of the Clayton copula function with respect to u and v to be,

$$\frac{\partial C_\theta(u, v)}{\partial u} = \frac{-u^{-(\theta+1)}}{-C_\theta(u, v)^{-(\theta+1)}} = \frac{C_\theta(u, v)^{\theta+1}}{u^{\theta+1}}, \quad (9)$$

$$\frac{\partial C_\theta(u, v)}{\partial v} = \frac{-v^{-(\theta+1)}}{-C_\theta(u, v)^{-(\theta+1)}} = \frac{C_\theta(u, v)^{\theta+1}}{v^{\theta+1}}. \quad (10)$$

Substituting equations (6), (7) and (8) into equation (5), we find the second derivative of the Clayton copula function to be,

$$\frac{\partial^2 C_\theta(u, v)}{\partial u \partial v} = \frac{u^{-(\theta+1)} v^{-(\theta+1)} (\theta+1) C_\theta(u, v)^{-(\theta+2)}}{C_\theta(u, v)^{-3(\theta+1)}} = \frac{(\theta+1) C_\theta(u, v)^{2\theta+1}}{u^{\theta+1} v^{\theta+1}}. \quad (11)$$

Frank copula

The generator function for the Frank copula is given by,

$$\psi(t) = -\log \left(\frac{e^{-\theta t} - 1}{e^{-\theta} - 1} \right). \quad (12)$$

Therefore, the first derivative of equation (12) is given by,

$$\psi'(t) = -\frac{-\theta e^{-\theta t}}{e^{-\theta} - 1} \frac{e^{-\theta} - 1}{e^{-\theta t} - 1} = \frac{\theta e^{-\theta t}}{e^{-\theta t} - 1} = \frac{\theta}{1 - e^{\theta t}}. \quad (13)$$

Using the quotient rule, the second derivative of equation (12), by differentiating equation (13), is given by,

$$\psi''(t) = \frac{0(1 - e^{\theta t}) - (-\theta^2 e^{\theta t})}{(1 - e^{\theta t})^2} = \frac{\theta^2 e^{\theta t}}{(1 - e^{\theta t})^2}. \quad (14)$$

Substituting equations (12) and (13) into equations (3) and (4) we find the first derivatives of the Frank copula function with respect to u and v to be,

$$\frac{\partial C_\theta(u, v)}{\partial u} = \frac{\theta}{1 - e^{\theta u}} \frac{1 - e^{\theta C_\theta(u, v)}}{\theta} = \frac{1 - e^{\theta C_\theta(u, v)}}{1 - e^{\theta u}}, \quad (15)$$

$$\frac{\partial C_\theta(u, v)}{\partial v} = \frac{\theta}{1 - e^{\theta v}} \frac{1 - e^{\theta C_\theta(u, v)}}{\theta} = \frac{1 - e^{\theta C_\theta(u, v)}}{1 - e^{\theta v}}. \quad (16)$$

Substituting equations (12), (13) and (14) into equation (5), we find the second derivative of the Frank copula function to be,

$$\begin{aligned} \frac{\partial^2 C_\theta(u, v)}{\partial u \partial v} &= \frac{-\theta^2}{(1 - e^{\theta u})(1 - e^{\theta v})} \frac{\theta^2 e^{\theta C_\theta(u, v)}}{(1 - e^{\theta C_\theta(u, v)})^2} \frac{(1 - e^{\theta C_\theta(u, v)})^3}{\theta^3} \\ &= \frac{-\theta^4 e^{\theta C_\theta(u, v)} (1 - e^{\theta C_\theta})}{\theta^3 (1 - e^{\theta u})(1 - e^{\theta v})} \\ &= \frac{\theta e^{\theta C_\theta(u, v)} (e^{\theta C_\theta(u, v)} - 1)}{(e^{\theta u} - 1)(e^{\theta v} - 1)}. \end{aligned} \quad (17)$$

Gumbel copula

The generator function for the Gumbel copula is given by the following,

$$\psi(t) = (-\log(t))^\theta. \quad (18)$$

The first derivative of equation (18) is given by,

$$\psi'(t) = \theta(-\log(t))^{\theta-1} \left(\frac{-1}{t} \right) = \frac{-\theta(-\log(t))^{\theta-1}}{t}. \quad (19)$$

The second derivative of equation (18) is given by,

$$\begin{aligned} \psi''(t) &= \frac{\theta(\theta-1)(-\log(t))^{\theta-2} - (-\theta(-\log(t))^{\theta-1})}{t^2} \\ &= \frac{\theta(-\log(t))^{\theta-2}((\theta-1) + (-\log(t)))}{t^2} \\ &= \frac{\theta(-\log(t))^{\theta-2}(\theta-1-\log(t))}{t^2}. \end{aligned} \quad (20)$$

Substituting equations (18) and (19) into equations (3) and (4) we find the first derivatives of the Gumbel copula with respect to u and v to be,

$$\frac{\partial C_\theta(u, v)}{\partial u} = \frac{\theta(-\log(u))^{\theta-1} C_\theta(u, v)}{\theta u (-\log(C_\theta(u, v)))^{\theta-1}} = \frac{C_\theta(u, v)(-\log(u))^{\theta-1}}{u(-\log(C_\theta(u, v)))^{\theta-1}}, \quad (21)$$

$$\frac{\partial C_\theta(u, v)}{\partial v} = \frac{\theta(-\log(v))^{\theta-1} C_\theta(u, v)}{\theta v (-\log(C_\theta(u, v)))^{\theta-1}} = \frac{C_\theta(u, v)(-\log(v))^{\theta-1}}{v(-\log(C_\theta(u, v)))^{\theta-1}}. \quad (22)$$

Substituting equations (18), (19) and (20) into equation (5) we find the second derivative of the Gumbel copula function to be,

$$\begin{aligned} \frac{\partial^2 C_\theta(u, v)}{\partial u \partial v} &= \frac{-\theta^2(-\log(u))^{\theta-1}(-\log(v))^{\theta-1} \theta(-\log(C_\theta(u, v)))^{\theta-2}(\theta-1-\log(C_\theta(u, v)))}{uv (C_\theta(u, v))^2} \\ &\quad \frac{(C_\theta(u, v))^3}{-\theta^3(-\log(C_\theta(u, v)))^{3\theta-3}} \\ &= \frac{C_\theta(-\log(u))^{\theta-1}(-\log(v))^{\theta-1}(\theta-1-\log(C_\theta(u, v)))}{uv(-\log(C_\theta(u, v)))^{2\theta-1}}. \end{aligned} \quad (23)$$

2 Tables and Figures

Table S1: Results from renal transplant data analysis, using the Weibull survival distribution and the Normal, Clayton, Frank and Gumbel copula functions to describe the association between graft failure and death. The shape and scale parameters, $\hat{\alpha}_1$ and $\hat{\beta}_1$ for the endpoint graft failure and $\hat{\alpha}_2$ and $\hat{\beta}_2$ for the endpoint death, respectively, are given alongside estimated Spearman's rank correlation coefficient, $\hat{\rho}$. The AIC is provided for each copula model.

Method	$\hat{\alpha}_1$ (95% CI)	$\hat{\beta}_1$ (95% CI)	$\hat{\alpha}_2$ (95% CI)	$\hat{\beta}_2$ (95% CI)	$\hat{\rho}$ (95% CI)	AIC
Normal	0.610 (0.539, 0.681)	0.063 (0.050, 0.075)	0.864 (0.776, 0.953)	0.039 (0.030, 0.049)	0.450 (0.348, 0.544)	4299.5
Clayton	0.633 (0.557, 0.709)	0.062 (0.049, 0.074)	0.864 (0.776, 0.953)	0.040 (0.031, 0.050)	0.678 (0.528, 0.766)	4309.4
Frank	0.630 (0.555, 0.704)	0.063 (0.050, 0.076)	0.863 (0.775, 0.952)	0.041 (0.031, 0.051)	0.540 (0.411, 0.640)	4300.5
Gumbel	0.600 (0.532, 0.668)	0.062 (0.050, 0.074)	0.841 (0.756, 0.926)	0.041 (0.032, 0.051)	0.301 (0.199, 0.382)	4322.6

Table S2: Results from the renal transplant data analysis, using the Gompertz survival distribution and the Normal, Clayton, Frank and Gumbel copula functions to describe the association between graft failure and death. The shape and rate parameters, $\hat{\gamma}_1$ and $\hat{\lambda}_1$ for the endpoint graft failure and $\hat{\gamma}_2$ and $\hat{\lambda}_2$ for the endpoint death, respectively, are given alongside estimated Spearman's rank correlation coefficient, $\hat{\rho}$. The AIC is provided for each copula model.

Method	$\hat{\gamma}_1$ (95% CI)	$\hat{\lambda}_1$ (95% CI)	$\hat{\gamma}_2$ (95% CI)	$\hat{\lambda}_2$ (95% CI)	$\hat{\rho}$ (95% CI)	AIC
Normal	-0.083 (-0.118, -0.047)	0.040 (0.032, 0.048)	-0.007 (-0.033, 0.019)	0.029 (0.024, 0.035)	0.388 (0.304, 0.473)	4364.5
Clayton	-0.063 (-0.099, -0.027)	0.039 (0.031, 0.047)	-0.010 (-0.036, 0.015)	0.032 (0.026, 0.038)	0.703 (0.573, 0.781)	4370.2
Frank	-0.069 (-0.104, -0.034)	0.040 (0.032, 0.048)	-0.010 (-0.036, 0.015)	0.032 (0.026, 0.038)	0.559 (0.441, 0.651)	4360.8
Gumbel	-0.091 (-0.126, -0.055)	0.039 (0.032, 0.047)	-0.004 (-0.029, 0.022)	0.028 (0.023, 0.034)	0.217 (0.137, 0.287)	4366.2

Table S3: Results from the Amsterdam Cohort Study data analysis, using the Weibull survival distribution and the Normal, Clayton, Frank and Gumbel copula functions to describe the association between virus phenotype switching from non-syncytium-inducing to syncytium-inducing (SI switch) and death from AIDS. The shape and scale parameters, $\hat{\alpha}_1$ and $\hat{\beta}_1$ for the endpoint SI switch and $\hat{\alpha}_2$ and $\hat{\beta}_2$ for the endpoint death from AIDS, respectively, are given alongside estimated Spearman's rank correlation coefficient, $\hat{\rho}$. The AIC is provided for each copula model.

Method	$\hat{\alpha}_1$ (95% CI)	$\hat{\beta}_1$ (95% CI)	$\hat{\alpha}_2$ (95% CI)	$\hat{\beta}_2$ (95% CI)	$\hat{\rho}$ (95% CI)	AIC
Normal	1.208 (1.032, 1.383)	0.043 (0.026, 0.059)	1.957 (1.751, 2.163)	0.009 (0.005, 0.013)	0.511 (0.399, 0.624)	2051.6
Clayton	1.125 (0.954, 1.296)	0.054 (0.033, 0.074)	1.952 (1.741, 2.164)	0.009 (0.005, 0.013)	0.639 (0.494, 0.730)	2051.6
Frank	1.061 (0.901, 1.221)	0.064 (0.040, 0.087)	1.903 (1.694, 2.112)	0.010 (0.005, 0.015)	0.674 (0.564, 0.752)	2048.2
Gumbel	0.914 (0.773, 1.055)	0.075 (0.051, 0.100)	1.933 (1.721, 2.146)	0.009 (0.005, 0.014)	0.414 (0.273, 0.518)	2070.4

Table S4: Results from the Amsterdam Cohort Study data analysis, using the Gompertz survival distribution and the Normal, Clayton, Frank and Gumbel copula functions to describe the association between SI switch and death from AIDS. The shape and rate parameters, $\hat{\gamma}_1$ and $\hat{\lambda}_1$ for the endpoint SI switch and $\hat{\gamma}_2$ and $\hat{\lambda}_2$ for the endpoint death from AIDS, respectively, are given alongside estimated Spearman's rank correlation coefficient, $\hat{\rho}$. The AIC is provided for each copula model.

Method	$\hat{\gamma}_1$ (95% CI)	$\hat{\lambda}_1$ (95% CI)	$\hat{\gamma}_2$ (95% CI)	$\hat{\lambda}_2$ (95% CI)	$\hat{\rho}$ (95% CI)	AIC
Normal	0.054 (-0.004, 0.112)	0.052 (0.036, 0.069)	0.228 (0.182, 0.274)	0.020 (0.013, 0.027)	0.567 (0.466, 0.670)	2053.4
Clayton	0.072 (0.013, 0.130)	0.050 (0.034, 0.066)	0.213 (0.167, 0.259)	0.022 (0.015, 0.030)	0.613 (0.458, 0.677)	2060.5
Frank	0.054 (-0.004, 0.111)	0.054 (0.037, 0.071)	0.218 (0.171, 0.264)	0.021 (0.014, 0.029)	0.583 (0.458, 0.677)	2053.1
Gumbel	0.030 (-0.027, 0.087)	0.056 (0.040, 0.073)	0.231 (0.185, 0.278)	0.019 (0.013, 0.026)	0.438 (0.314, 0.534)	2070.7

Table S5: True values used for simulating data from the Exponential, Weibull and Gompertz survival distributions used to mimic the Renal transplant and Amsterdam Cohort Study data sets for the simulations investigating the effects of misspecification. Presented are values of the hazard rates of the non-terminal and terminal events, λ_1 and λ_2 for the Exponential distribution. For the Weibull distribution the shape and scale parameters are given by, α_1 and β_1 for the non-terminal events, and α_2 and β_2 for the terminal events, respectively. For the Gompertz distribution, the shape and rate parameters are given by γ_1 and λ_1 for the non-terminal events, and γ_2 and λ_2 for the terminal events, respectively.

Data set	Underlying copula	Exponential			Weibull					Gompertz				
		λ_1	λ_2	ρ	α_1	β_1	α_2	β_2	ρ	γ_1	λ_1	γ_2	λ_2	ρ
Renal transplant	Normal	0.03	0.03	0.39	0.61	0.06	0.86	0.04	0.45	0.001	0.04	0.001	0.03	0.39
	Clayton	0.03	0.03	0.72	0.63	0.06	0.86	0.04	0.68	0.001	0.04	0.001	0.03	0.70
	Frank	0.03	0.03	0.58	0.63	0.06	0.86	0.04	0.54	0.001	0.04	0.001	0.03	0.56
	Gumbel	0.03	0.03	0.21	0.60	0.06	0.84	0.04	0.30	0.001	0.04	0.001	0.03	0.22
Amsterdam Cohort Study	Normal	0.07	0.07	0.63	1.21	0.04	1.96	0.01	0.51	0.05	0.05	0.23	0.02	0.64
	Clayton	0.07	0.07	0.75	1.13	0.05	1.95	0.01	0.64	0.07	0.05	0.21	0.02	0.61
	Frank	0.08	0.07	0.70	1.06	0.06	1.90	0.01	0.67	0.05	0.05	0.22	0.02	0.58
	Gumbel	0.07	0.07	0.50	0.91	0.08	1.93	0.01	0.41	0.03	0.06	0.23	0.02	0.44

2.1 Misspecification of the copula function simulation results with the renal transplant data

Table S6: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0$. The simulated data mimics the hazard rates for the endpoints of graft failure and death from the renal transplant data set. The data is generated from the Exponential survival distributions and the Independence copula function. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 1199 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution								
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary ¹
Independence	λ_1	0.001	95.9	0.001	95.5	0.001	95.9	0.001	95.9	
	λ_2	0.001	94.7	0.001	94.8	0.001	95.2	0.001	95.4	
	ρ	0.025	97.2	0.029	98.9	0.020	97.4	0.020	99.0	989

¹ Boundary refers to the number of times the lower confidence interval for θ is less than or equal to 1, the boundary for the Gumbel copula.

Table S7: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.25$. The simulated data mimics the hazard rates for the endpoints of graft failure and death from the renal transplant data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 1199 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution								
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Normal	λ_1	0.001	95.5	0.001	93.7	0.001	94.5	0.001	92.3	
	λ_2	0.001	95.2	0.001	95.0	0.001	94.3	0.001	94.7	
	ρ	0.039	95.0	0.050	94.1	0.040	94.0	0.074	60.0	34
Clayton	λ_1	0.001	92.6	0.001	93.4	0.001	94.0	0.001	88.5	
	λ_2	0.001	95.3	0.001	95.8	0.001	95.2	0.001	95.2	1
	ρ	0.066	77.1	0.047	94.6	0.060	80.6	0.140	12.4	392
Frank	λ_1	0.001	93.5	0.001	93.9	0.001	95.3	0.001	89.8	
	λ_2	0.001	93.4	0.001	94.9	0.001	95.5	0.001	94.7	
	ρ	0.041	93.6	0.058	89.2	0.039	95.1	0.088	47.5	68
Gumbel	λ_1	0.001	93.8	0.001	92.6	0.001	93.6	0.001	95.1	
	λ_2	0.001	94.2	0.001	95.5	0.001	94.2	0.001	94.2	
	ρ	0.063	76.8	0.056	91.8	0.046	91.4	0.035	93.8	

Table S8: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.5$. The simulated data mimics the hazard rates for the endpoints of graft failure and death from the renal transplant data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 1199 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution								
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Normal	λ_1	0.001	94.7	0.001	94.0	0.001	93.9	0.001	90.9	
	λ_2	0.001	95.0	0.001	94.3	0.001	94.4	0.001	92.5	
	ρ	0.032	95.1	0.054	84.3	0.034	95.0	0.105	14.8	
Clayton	λ_1	0.002	62.7	0.001	95.4	0.001	84.1	0.002	43.9	
	λ_2	0.001	91.2	0.001	96.0	0.001	84.3	0.001	79.2	
	ρ	0.141	0.0	0.017	95.0	0.070	9.9	0.257	0.0	
Frank	λ_1	0.001	94.8	0.001	94.7	0.001	94.2	0.001	91.2	
	λ_2	0.001	94.9	0.001	95.0	0.001	95.0	0.001	95.2	
	ρ	0.040	94.5	0.055	93.0	0.040	94.6	0.070	62.8	356
Gumbel	λ_1	0.001	93.6	0.001	93.0	0.001	91.1	0.001	95.5	
	λ_2	0.001	94.2	0.001	95.1	0.001	91.1	0.001	94.8	
	ρ	0.084	36.3	0.076	68.9	0.055	74.9	0.029	95.5	

Table S9: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.75$. The simulated data mimics the hazard rates for the endpoints of graft failure and death from the renal transplant data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 1199 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution							
		Normal		Clayton		Frank		Gumbel	
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage
Normal	λ_1	0.001	93.6	0.001	92.7	0.001	88.0	0.001	91.7
	λ_2	0.001	94.6	0.001	95.4	0.001	91.3	0.001	91.3
	ρ	0.018	95.0	0.046	59.4	0.019	96.2	0.102	0.9
Clayton	λ_1	0.001	71.2	0.001	96.4	0.001	87.9	0.002	57.6
	λ_2	0.001	90.6	0.001	96.0	0.001	89.1	0.001	84.1
	ρ	0.143	0.1	0.021	93.9	0.083	13.7	0.262	0.0
Frank	λ_1	0.001	79.4	0.001	92.2	0.001	93.8	0.002	65.4
	λ_2	0.001	93.0	0.001	95.0	0.001	95.2	0.001	85.7
	ρ	0.054	45.4	0.056	41.0	0.021	95.1	0.160	0.0
Gumbel	λ_1	0.001	94.3	0.001	89.5	0.002	77.6	0.001	93.0
	λ_2	0.001	94.0	0.001	93.7	0.002	76.5	0.001	93.6
	ρ	0.065	11.0	0.073	20.6	0.046	53.1	0.018	95.0

Table S10: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.9$. The simulated data mimics the hazard rates for the endpoints of graft failure and death from the renal transplant data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 1199 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution							
		Normal		Clayton		Frank		Gumbel	
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage
Normal	λ_1	0.001	94.8	0.001	85.9	0.001	77.8	0.001	93.0
	λ_2	0.001	94.6	0.001	94.4	0.001	87.3	0.001	92.2
	ρ	0.008	94.2	0.024	41.4	0.009	96.1	0.063	0.0
Clayton	λ_1	0.002	39.8	0.001	94.9	0.001	78.2	0.003	22.5
	λ_2	0.001	88.9	0.001	94.4	0.001	84.9	0.002	66.6
	ρ	0.128	0.0	0.009	95.7	0.047	6.9	0.232	0.0
Frank	λ_1	0.022	60.5	0.001	91.8	0.001	94.6	0.002	40.6
	λ_2	0.001	92.7	0.001	94.3	0.001	94.0	0.001	77.5
	ρ	0.060	1.2	0.029	25.2	0.009	94.6	0.148	0.0
Gumbel	λ_1	0.001	95.3	0.001	89.1	0.002	61.9	0.001	95.1
	λ_2	0.001	94.4	0.001	94.4	0.002	64.9	0.001	94.6
	ρ	0.032	4.7	0.038	7.7	0.025	33.9	0.001	93.9

2.2 Misspecification of the copula function simulation results with the Amsterdam Cohort Study data

Table S11: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0$. The simulated data mimics the hazard rates for the endpoints of SI switch and death from AIDS from the Amsterdam Cohort Study data set. The data is generated from the Exponential survival distributions and the Independence copula function. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 329 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution								
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Independence	λ_1	0.004	97.3	0.005	96.5	0.005	97.3	0.005	96.1	
	λ_2	0.004	95.8	0.004	95.4	0.004	96.1	0.004	95.1	
	ρ	0.039	97.6	0.042	98.8	0.036	97.6	0.031	99.7	997

Table S12: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.25$. The simulated data mimics the hazard rates for the endpoints of SI switch and death from AIDS from the Amsterdam Cohort Study data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 329 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula	Assumed copula distribution									
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Normal	λ_1	0.005	94.4	0.005	93.9	0.005	94.2	0.005	94.2	
	λ_2	0.004	94.3	0.004	94.3	0.004	94.6	0.004	95.4	
	ρ	0.072	93.8	0.078	91.2	0.070	96.3	0.081	86.0	508
Clayton	λ_1	0.005	93.4	0.005	94.8	0.004	95.3	0.005	92.7	
	λ_2	0.004	93.5	0.004	95.4	0.004	94.6	0.004	94.4	
	ρ	0.076	92.4	0.069	94.4	0.072	95.1	0.120	67.6	759
Frank	λ_1	0.005	94.3	0.005	93.8	0.005	94.1	0.005	93.4	
	λ_2	0.004	94.2	0.004	94.5	0.004	94.0	0.004	94.9	
	ρ	0.072	94.2	0.084	90.0	0.072	94.8	0.093	82.0	582
Gumbel	λ_1	0.005	94.2	0.005	90.9	0.005	94.9	0.005	95.0	
	λ_2	0.004	94.4	0.004	94.1	0.004	94.8	0.004	94.4	
	ρ	0.083	88.1	0.093	85.1	0.076	93.8	0.066	94.9	265

Table S13: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.5$. The simulated data mimics the hazard rates for the endpoints of SI switch and death from AIDS from the Amsterdam Cohort Study data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 329 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution								
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Normal	λ_1	0.005	94.8	0.005	93.3	0.005	94.6	0.004	94.1	
	λ_2	0.004	95.1	0.004	95.9	0.004	94.5	0.004	94.3	
	ρ	0.056	93.5	0.071	91.3	0.060	95.8	0.086	74.7	
Clayton	λ_1	0.008	66.6	0.004	95.9	0.005	80.8	0.001	61.3	
	λ_2	0.004	92.9	0.004	95.1	0.005	86.1	0.005	90.4	
	ρ	0.122	24.4	0.029	95.1	0.049	78.1	0.221	0.3	
Frank	λ_1	0.005	93.8	0.005	94.2	0.005	95.3	0.005	95.4	
	λ_2	0.004	95.4	0.004	95.2	0.004	94.9	0.004	95.6	
	ρ	0.072	96.8	0.074	96.9	0.069	97.3	0.081	91.3	815
Gumbel	λ_1	0.005	94.2	0.006	88.6	0.005	94.3	0.004	95.0	
	λ_2	0.004	94.5	0.004	94.9	0.004	95.2	0.004	94.3	
	ρ	0.074	81.4	0.091	83.5	0.066	92.9	0.057	94.2	

Table S14: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.75$. The simulated data mimics the hazard rates for the endpoints of SI switch and death from AIDS from the Amsterdam Cohort Study data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 329 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution							
		Normal		Clayton		Frank		Gumbel	
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage
Normal	λ_1	0.004	94.9	0.005	91.7	0.005	93.0	0.004	93.5
	λ_2	0.004	95.0	0.004	94.8	0.004	95.2	0.004	93.5
	ρ	0.033	94.2	0.043	92.9	0.037	95.5	0.076	58.1
Clayton	λ_1	0.007	74.8	0.004	94.1	0.005	85.6	0.007	67.7
	λ_2	0.004	93.9	0.004	94.8	0.005	89.7	0.005	87.8
	ρ	0.115	43.8	0.036	95.1	0.063	75.7	0.217	2.1
Frank	λ_1	0.005	85.8	0.005	93.6	0.004	95.1	0.006	83.2
	λ_2	0.004	96.2	0.004	94.5	0.004	95.0	0.004	92.1
	ρ	0.065	80.6	0.042	93.1	0.036	95.9	0.140	16.3
Gumbel	λ_1	0.004	94.3	0.006	88.2	0.005	91.9	0.004	94.3
	λ_2	0.004	95.2	0.004	95.9	0.005	91.4	0.004	95.1
	ρ	0.045	77.1	0.062	83.1	0.043	91.9	0.035	95.9

Table S15: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.9$. The simulated data mimics the hazard rates for the endpoints of SI switch and death from AIDS from the Amsterdam Cohort Study data set. The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 329 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution							
		Normal		Clayton		Frank		Gumbel	
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage
Normal	λ_1	0.004	95.0	0.005	89.9	0.005	89.0	0.004	95.6
	λ_2	0.004	94.6	0.004	94.6	0.004	94.9	0.004	93.0
	ρ	0.015	94.8	0.022	92.4	0.018	94.3	0.046	48.8
Clayton	λ_1	0.011	40.6	0.004	95.3	0.006	72.1	0.011	36.3
	λ_2	0.004	94.0	0.004	95.5	0.005	85.1	0.005	86.2
	ρ	0.127	3.8	0.017	95.8	0.039	66.3	0.217	0.1
Frank	λ_1	0.007	68.0	0.005	92.4	0.004	96.5	0.008	62.5
	λ_2	0.004	95.6	0.004	94.3	0.004	94.8	0.004	91.9
	ρ	0.069	39.0	0.022	91.9	0.019	94.1	0.143	1.2
Gumbel	λ_1	0.004	93.3	0.006	90.1	0.005	88.4	0.004	95.1
	λ_2	0.004	94.9	0.004	94.1	0.005	88.8	0.004	94.8
	ρ	0.021	78.7	0.042	76.2	0.024	90.0	0.019	94.4

2.3 Misspecification of the copula function with data mimicking the simulation study in Fu et al. (2013)

Table S16: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0$. The simulated data mimics the hazard rates from the simulation study in Fu et al. (2013). The data is generated from the Exponential survival distributions and the Independence copula function. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 100 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula	Assumed copula distribution									
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Independence	λ_1	0.015	95.6	0.014	96.4	0.014	95.2	0.014	95.7	
	λ_2	0.006	95.2	0.006	93.8	0.006	94.8	0.006	94.8	
	ρ	0.057	96.3	0.047	98.9	0.054	96.4	0.045	99.1	990

Table S17: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.25$. The simulated data mimics the hazard rates from the simulation study in Fu et al. (2013). The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 100 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula	Assumed copula distribution									
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Normal	λ_1	0.013	94.7	0.014	94.7	0.014	95.2	0.014	92.6	
	λ_2	0.006	94.8	0.006	95.2	0.006	94.7	0.006	94.4	
	ρ	0.099	94.5	0.103	91.1	0.094	97.3	0.102	91.4	748
Clayton	λ_1	0.014	95.4	0.013	95.5	0.014	92.4	0.014	92.6	
	λ_2	0.006	95.0	0.006	95.0	0.006	94.1	0.006	93.9	
	ρ	0.095	95.2	0.097	93.1	0.100	96.4	0.115	90.1	816
Frank	λ_1	0.013	95.6	0.014	94.5	0.013	96.1	0.014	94.2	
	λ_2	0.006	94.7	0.006	93.6	0.006	95.7	0.006	94.1	
	ρ	0.097	95.0	0.099	92.2	0.093	96.6	0.105	91.9	750
Gumbel	λ_1	0.014	95.6	0.014	95.4	0.014	95.7	0.014	94.7	
	λ_2	0.006	94.2	0.006	95.1	0.006	95.2	0.006	94.8	
	ρ	0.105	90.2	0.110	89.2	0.097	96.7	0.086	94.6	551

Table S18: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.5$. The simulated data mimics the hazard rates from the simulation study in Fu et al. (2013). The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 100 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution								
		Normal		Clayton		Frank		Gumbel		
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage	Boundary
Normal	λ_1	0.013	94.0	0.013	94.3	0.013	93.0	0.013	91.7	8
	λ_2	0.006	94.9	0.006	93.2	0.006	93.4	0.006	93.3	
	ρ	0.073	92.4	0.103	80.9	0.076	94.4	0.091	82.7	51
Clayton	λ_1	0.013	94.4	0.012	96.5	0.015	80.9	0.013	94.1	
	λ_2	0.006	94.2	0.006	95.4	0.007	79.0	0.006	95.0	
	ρ	0.049	83.9	0.032	96.0	0.035	92.8	0.125	22.4	
Frank	λ_1	0.013	95.4	0.014	95.1	0.015	93.8	0.013	94.4	
	λ_2	0.006	94.1	0.006	95.1	0.006	95.9	0.006	95.6	
	ρ	0.094	95.4	0.095	98.6	0.094	97.7	0.095	98.6	874
Gumbel	λ_1	0.013	95.2	0.014	95.2	0.013	94.3	0.012	96.5	
	λ_2	0.006	94.7	0.006	94.4	0.006	94.8	0.006	95.6	
	ρ	0.083	83.6	0.100	84.0	0.074	94.2	0.068	93.7	12

Table S19: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.75$. The simulated data mimics the hazard rates from the simulation study in Fu et al. (2013). The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 100 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution							
		Normal		Clayton		Frank		Gumbel	
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage
Normal	λ_1	0.012	95.2	0.012	94.4	0.012	93.8	0.012	95.3
	λ_2	0.006	95.3	0.006	94.7	0.006	92.5	0.005	95.0
	ρ	0.037	91.5	0.088	62.2	0.042	94.5	0.074	66.7
Clayton	λ_1	0.012	95.9	0.012	94.9	0.015	84.6	0.012	94.3
	λ_2	0.006	94.6	0.006	94.9	0.007	82.4	0.006	94.6
	ρ	0.054	89.1	0.041	94.4	0.048	92.6	0.134	34.0
Frank	λ_1	0.012	95.2	0.012	93.6	0.011	95.4	0.012	94.7
	λ_2	0.006	95.5	0.006	94.9	0.006	95.7	0.006	94.5
	ρ	0.046	92.0	0.093	57.5	0.041	94.8	0.100	48.5
Gumbel	λ_1	0.012	95.5	0.012	95.7	0.014	92.5	0.012	96.4
	λ_2	0.006	94.9	0.006	94.6	0.006	92.9	0.006	95.3
	ρ	0.048	73.6	0.089	59.4	0.042	93.4	0.035	95.1

Table S20: Simulation results investigating the effect of misspecification of the copula function with assumed Spearman's rank correlation coefficient, $\rho = 0.9$. The simulated data mimics the hazard rates from the simulation study in Fu et al. (2013). The data is generated from the Exponential survival distributions and the Normal, Clayton, Frank and Gumbel copula functions. The Exponential survival distribution along with the Normal, Clayton, Frank and Gumbel copula functions are used to compare the performance metrics of the hazard rates and correlation estimates under misspecification of the copula function. The number of simulated data sets is 1000 with 100 individuals in each. MAE refers to the mean absolute error and the coverage probability is given as a percentage.

Underlying copula		Assumed copula distribution							
		Normal		Clayton		Frank		Gumbel	
		MAE	Coverage	MAE	Coverage	MAE	Coverage	MAE	Coverage
Normal	λ_1	0.012	96.0	0.012	95.0	0.012	92.2	0.012	95.4
	λ_2	0.006	95.0	0.006	94.7	0.006	92.9	0.006	93.8
	ρ	0.014	93.6	0.056	43.6	0.017	94.1	0.040	49.5
Clayton	λ_1	0.014	93.5	0.012	94.7	0.018	72.0	0.013	92.8
	λ_2	0.006	94.7	0.005	95.3	0.009	69.1	0.006	92.0
	ρ	0.040	72.2	0.019	95.8	0.020	91.2	0.105	8.6
Frank	λ_1	0.013	94.8	0.012	94.5	0.011	95.2	0.012	95.5
	λ_2	0.006	95.8	0.006	94.0	0.005	94.6	0.006	94.8
	ρ	0.029	84.7	0.069	34.2	0.016	95.3	0.074	21.4
Gumbel	λ_1	0.012	94.8	0.012	95.4	0.015	89.5	0.011	95.7
	λ_2	0.054	94.9	0.006	95.1	0.007	89.5	0.005	95.4
	ρ	0.020	69.4	0.061	42.3	0.018	91.1	0.014	94.7

Figure S1: Normal, Clayton, Frank and Gumbel contour plots with their estimated association parameter from Table 3 of the main text, for the renal transplant data set.

Figure S2: Normal, Clayton, Frank and Gumbel contour plots with their estimated association parameter from Table 4 of the main text, for the Amsterdam Cohort Study data set.

References

- Fu, H., Wang, Y., Liu, J., Kulkarni, P., and Melemed, A. (2013). Joint modeling of progression-free survival and overall survival by a Bayesian normal induced copula estimation model. *Statistics Medicine*, 32:240–254.