Supplementary material to “Regularized win ratio regression for variable selection and risk prediction, with an application to a cardiovascular trial”

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Abstract

This supplementary file contains additional numerical results referenced in the main text.

Keywords: Concordance index, Hierarchical composite endpoints, Elastic net, Lasso, Proportional win-fractions

S1 Additional simulation studies

S1.1 $\alpha = 0.5$

The same set of simulations in the main text were repeated for mixture parameter $\alpha = 0.5$. The sensitivity and specificity data are summarized in Table S1, with the distributions of test C-indices plotted in Fig. S1. The results are similar to those under $\alpha = 1$.

S1.2 Higher death rates

Under the joint model specified in the simulations section of the main text, we instead set $\lambda_D = 0.4$ and $\lambda_H = 2$. The other settings were kept as is. This leads to a death rate of about 52% and a nonfatal event rate of about 80%.

The sensitivity and specificity data are summarized in Table S2, with the distributions of test C-indices plotted in Fig. S2. For $n = 200$, the sensitivity of the win ratio model for variables that have a direct effect on the nonfatal event is decreased, likely due to the increased emphasis on death as a result of the higher death rates. On the other hand, win ratio's advantage over the Cox model in predictive performance as measured by the C-index notably widens. This is not surprising given that now accurate prediction of death plays an even more important role in the overall concordance measure.

S1.3 Higher-dimensional z

Instead of fixing $p = 20$, we set $p = n/2 = 100, 250$ and 500 for $n = 200$, 500, and 1000. The results are summarized in Table and Fig. S3. Because the presence of many covariates makes it less likely that any given one will be selected, specificity tends to be universally high. For the same reason, sensitivity becomes the distinguishing metric for evaluation.

Unlike in previous settings, sensitivity of the Cox model for the first five covariates remains low ($< 50\%$) even for sample size as large as 500. For the C-index, the two models perform similarly for $n = 200$, a sample size still too small to differentiate the methods. However, the differences become clear when $n = 500$ and 1000, with the win ratio outperforming the Cox model by considerable margins.

Table S1 Sensitivity and specificity of variable selection by regularized win ratio (Cox) regression models ($\alpha = 0.5$) in different scenarios.

	$n = 200$		$n = 500$		$n = 1000$		$n = 2000$	
	S1	S2	S1	S2	S1	S2	S1	S2
Sensitivity								
$z_{\cdot 1}$	1 (1)	1 (0.58)	1 (1)	1 (0.80)	1 (1)	1 (0.96)	1 (1)	1 (1)
$z_{\cdot 2}$	1 (1)	0.99 (0.62)	1 (1)	1 (0.81)	1 (1)	1 (0.97)	1 (1)	1 (1)
$z_{\cdot 3}$	1 (1)	0.99 (0.60)	1 (1)	1 (0.82)	1 (1)	1 (0.96)	1 (1)	1 (1)
$z_{\cdot 4}$	1 (1)	1 (0.63)	1 (1)	1 (0.83)	1 (1)	1 (0.96)	1 (1)	1 (1)
$z_{\cdot 5}$	1 (1)	1 (0.66)	1 (1)	1 (0.82)	1 (1)	1 (0.96)	1 (1)	1 (1)
$z_{\cdot 6}$	1 (1)	0.98 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 7}$	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 8}$	1 (1)	0.98 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 9}$	1 (1)	0.98 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 10}$	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
Specificity								
$z_{\cdot 11}$	0.56 (0.47)	0.49 (0.61)	0.62 (0.63)	0.53 (0.56)	0.61 (0.67)	0.59 (0.53)	0.74 (0.74)	0.70 (0.48)
$z_{\cdot 12}$	0.53 (0.46)	0.48 (0.62)	0.55 (0.61)	0.52 (0.59)	0.7 (0.69)	0.59 (0.51)	0.72 (0.74)	0.67 (0.51)
$z_{\cdot 13}$	0.51 (0.47)	0.49 (0.62)	0.62 (0.62)	0.52 (0.58)	0.65 (0.68)	0.56 (0.5)	0.73 (0.72)	0.67 (0.48)
$z_{\cdot 14}$	0.48 (0.42)	0.47 (0.63)	0.58 (0.61)	0.52 (0.63)	0.65 (0.68)	0.61 (0.56)	0.73 (0.75)	0.7 (0.53)
$z_{\cdot 15}$	0.5 (0.41)	0.5 (0.61)	0.56 (0.6)	0.53 (0.56)	0.67 (0.71)	0.56 (0.51)	0.74 (0.73)	0.62 (0.48)
$z_{\cdot 16}$	0.50 (0.47)	0.49 (0.57)	0.56 (0.62)	0.52 (0.57)	0.66 (0.69)	0.62 (0.56)	0.69 (0.72)	0.67 (0.49)
$z_{\cdot 17}$	0.53 (0.45)	0.48 (0.59)	0.58 (0.6)	0.51 (0.57)	0.69 (0.70)	0.61 (0.54)	0.69 (0.73)	0.68 (0.54)
$z_{\cdot 18}$	0.5 (0.44)	0.50 (0.62)	0.60 (0.58)	0.51 (0.59)	0.65 (0.69)	0.56 (0.53)	0.72 (0.73)	0.65 (0.50)
$z_{\cdot 19}$	0.55 (0.45)	0.51 (0.62)	0.59 (0.62)	0.52 (0.57)	0.67 (0.69)	0.61 (0.56)	0.72 (0.74)	0.65 (0.52)
$z_{\cdot 20}$	0.51 (0.47)	0.51 (0.63)	0.57 (0.59)	0.51 (0.59)	0.65 (0.71)	0.59 (0.54)	0.71 (0.73)	0.69 (0.47)

S1, S2: Scenarios 1 and 2. Each entry is based on $N = 1000$ replicates.

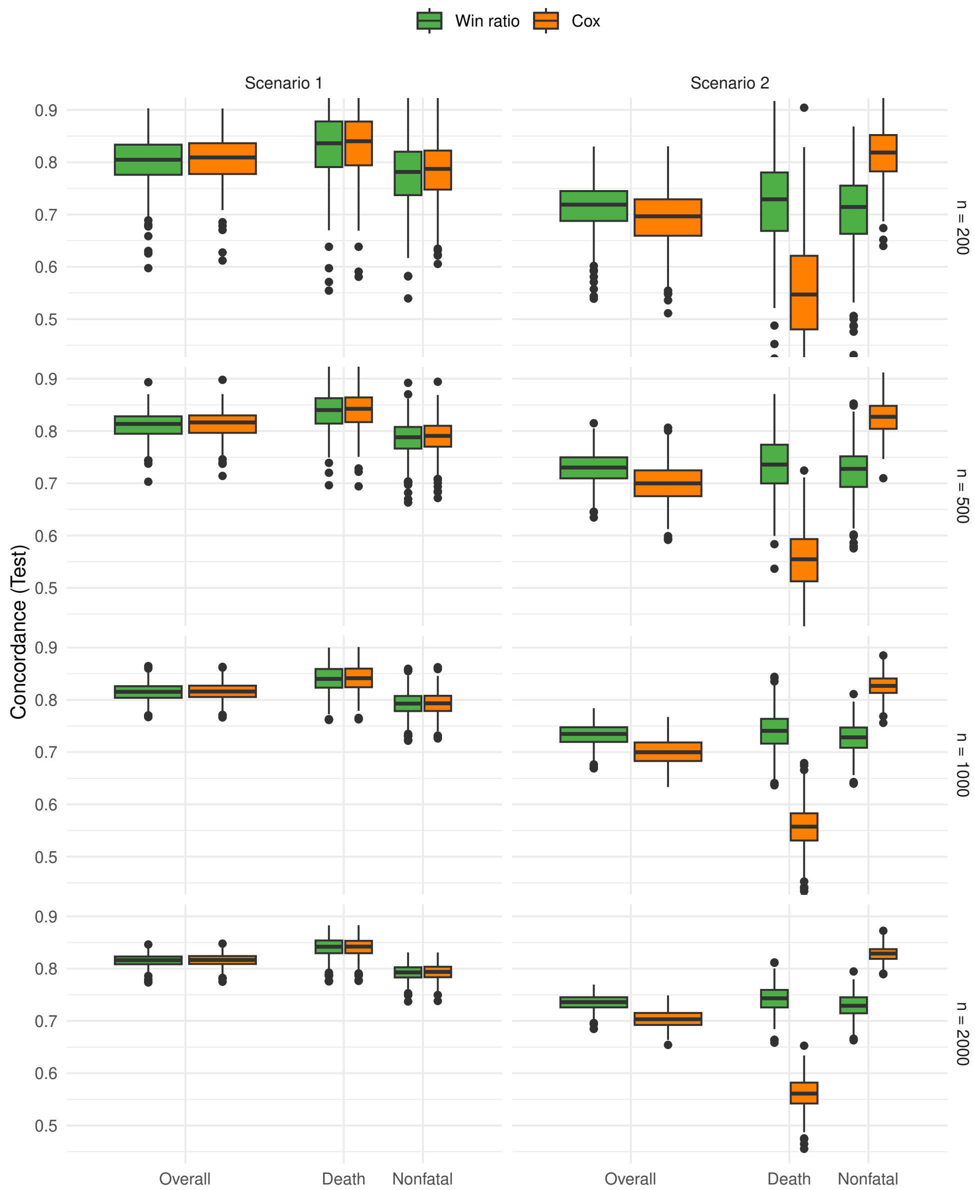

Fig. S1 Regularized win ratio (`wrnet`) and Cox models trained on 80% of data at $\alpha = 0.5$ (half-lasso and half-ridge) and tested on remaining 20%.

Table S2 Sensitivity and specificity of variable selection by regularized win ratio (Cox) regression models ($\alpha = 1$) in different scenarios under higher death rates ($> 50\%$).

	$n = 200$		$n = 500$		$n = 1000$		$n = 2000$	
	S1	S2	S1	S2	S1	S2	S1	S2
Sensitivity								
$z_{\cdot 1}$	1 (1)	0.99 (0.80)	1 (1)	1 (0.97)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 2}$	1 (1)	1 (0.83)	1 (1)	1 (0.99)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 3}$	1 (1)	1 (0.80)	1 (1)	1 (0.97)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 4}$	1 (1)	1 (0.80)	1 (1)	1 (0.98)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 5}$	1 (1)	1 (0.85)	1 (1)	1 (0.97)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 6}$	1 (1)	0.87 (1)	1 (1)	0.97 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 7}$	1 (1)	0.85 (1)	1 (1)	0.95 (1)	1 (1)	0.99 (1)	1 (1)	1 (1)
$z_{\cdot 8}$	1 (1)	0.84 (1)	1 (1)	0.96 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 9}$	1 (1)	0.86 (1)	1 (1)	0.97 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 10}$	1 (1)	0.85 (1)	1 (1)	0.94 (1)	1 (1)	1 (1)	1 (1)	1 (1)
Specificity								
$z_{\cdot 11}$	0.55 (0.48)	0.60 (0.53)	0.67 (0.65)	0.53 (0.44)	0.75 (0.72)	0.61 (0.49)	0.75 (0.74)	0.73 (0.52)
$z_{\cdot 12}$	0.56 (0.48)	0.62 (0.52)	0.69 (0.63)	0.57 (0.50)	0.72 (0.70)	0.64 (0.52)	0.77 (0.75)	0.74 (0.51)
$z_{\cdot 13}$	0.54 (0.48)	0.63 (0.52)	0.65 (0.66)	0.6 (0.52)	0.72 (0.72)	0.65 (0.49)	0.77 (0.77)	0.72 (0.5)
$z_{\cdot 14}$	0.56 (0.51)	0.60 (0.52)	0.68 (0.66)	0.58 (0.50)	0.72 (0.72)	0.62 (0.49)	0.76 (0.77)	0.70 (0.48)
$z_{\cdot 15}$	0.55 (0.53)	0.62 (0.53)	0.66 (0.61)	0.60 (0.51)	0.73 (0.73)	0.64 (0.50)	0.76 (0.79)	0.70 (0.47)
$z_{\cdot 16}$	0.56 (0.50)	0.59 (0.52)	0.64 (0.63)	0.58 (0.49)	0.73 (0.72)	0.64 (0.49)	0.75 (0.73)	0.7 (0.46)
$z_{\cdot 17}$	0.58 (0.51)	0.64 (0.55)	0.64 (0.67)	0.56 (0.49)	0.72 (0.70)	0.62 (0.50)	0.75 (0.73)	0.71 (0.53)
$z_{\cdot 18}$	0.55 (0.51)	0.61 (0.51)	0.69 (0.62)	0.61 (0.49)	0.72 (0.71)	0.62 (0.51)	0.76 (0.72)	0.68 (0.49)
$z_{\cdot 19}$	0.56 (0.54)	0.61 (0.48)	0.64 (0.65)	0.60 (0.50)	0.70 (0.72)	0.59 (0.52)	0.78 (0.74)	0.71 (0.48)
$z_{\cdot 20}$	0.61 (0.52)	0.64 (0.54)	0.68 (0.64)	0.56 (0.51)	0.73 (0.71)	0.64 (0.48)	0.79 (0.75)	0.73 (0.51)

S1, S2: Scenarios 1 and 2. Each entry is based on $N = 1000$ replicates.

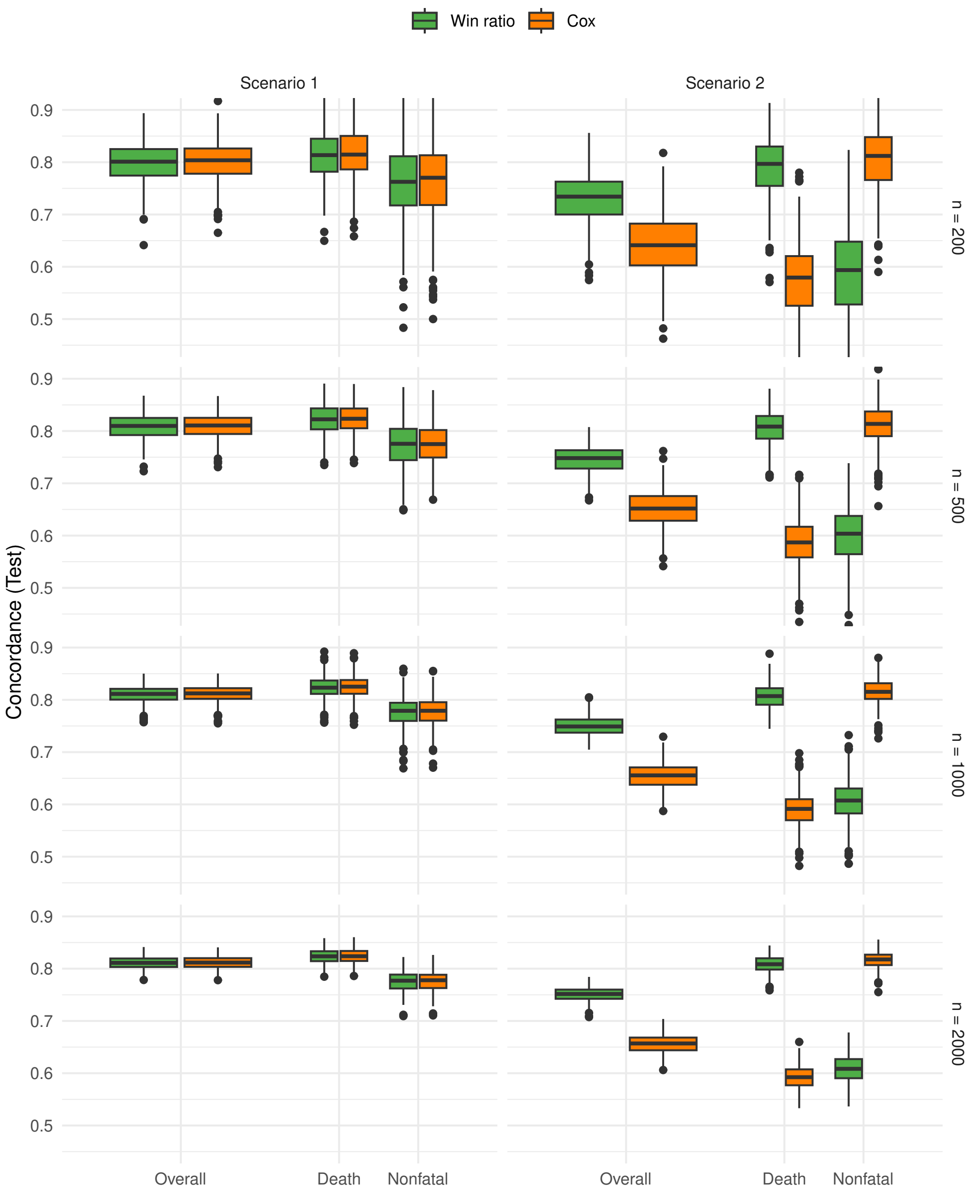

Fig. S2 Regularized win ratio (`wrnet`) and Cox models trained on 80% of data at $\alpha = 1$ (lasso) and tested on remaining 20% under higher death rates ($> 50\%$).

Table S3 Sensitivity and specificity of variable selection by regularized win ratio (Cox) regression models ($\alpha = 1$) in different scenarios with $p = n/2$.

	$n = 200$		$n = 500$		$n = 1000$	
	S1	S2	S1	S2	S1	S2
Sensitivity						
$z_{\cdot 1}$	0.98 (1)	0.89 (0.30)	1 (1)	1 (0.40)	1 (1)	1 (0.60)
$z_{\cdot 2}$	0.98 (0.98)	0.89 (0.33)	1 (1)	1 (0.41)	1 (1)	1 (0.72)
$z_{\cdot 3}$	1 (1)	0.89 (0.37)	1 (1)	1 (0.44)	1 (1)	1 (0.68)
$z_{\cdot 4}$	0.98 (1)	0.86 (0.34)	1 (1)	0.99 (0.42)	1 (1)	1 (0.69)
$z_{\cdot 5}$	0.99 (0.98)	0.83 (0.32)	1 (1)	0.98 (0.47)	1 (1)	1 (0.69)
$z_{\cdot 6}$	1 (0.99)	0.96 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 7}$	0.98 (0.99)	0.95 (0.99)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 8}$	0.98 (1)	0.93 (1)	1 (1)	1 (1)	1 (1)	1 (1)
$z_{\cdot 9}$	0.98 (0.98)	0.95 (1)	1 (1)	0.99 (1)	1 (1)	1 (1)
$z_{\cdot 10}$	0.96 (0.98)	0.95 (0.99)	1 (1)	0.98 (1)	1 (1)	1 (1)
Specificity						
V11	0.82 (0.79)	0.74 (0.86)	0.97 (0.98)	0.94 (0.96)	0.99 (0.98)	0.98 (0.97)
V12	0.8 (0.86)	0.75 (0.87)	0.96 (0.96)	0.95 (0.96)	0.99 (0.99)	0.98 (0.96)
V13	0.83 (0.83)	0.81 (0.89)	0.96 (0.96)	0.96 (0.99)	0.98 (0.98)	0.99 (0.97)
V14	0.8 (0.81)	0.79 (0.87)	0.94 (0.92)	0.94 (0.97)	1 (0.98)	0.99 (0.98)
V15	0.84 (0.86)	0.77 (0.86)	0.98 (0.96)	0.94 (0.96)	0.98 (0.98)	0.98 (0.96)
V16	0.86 (0.79)	0.81 (0.88)	0.96 (0.96)	0.95 (0.96)	0.98 (0.99)	0.98 (0.98)
V17	0.83 (0.86)	0.76 (0.89)	0.96 (0.93)	0.95 (0.96)	0.97 (0.98)	0.97 (0.96)
V18	0.82 (0.83)	0.79 (0.85)	0.98 (0.97)	0.94 (0.95)	1 (0.98)	0.98 (0.95)
V19	0.84 (0.85)	0.79 (0.87)	0.95 (0.94)	0.94 (0.98)	1 (0.98)	0.99 (0.98)
V20	0.85 (0.86)	0.78 (0.91)	0.98 (0.96)	0.96 (0.98)	0.99 (1)	0.98 (0.98)

S1, S2: Scenarios 1 and 2. Each entry is based on $N = 1000$ replicates.

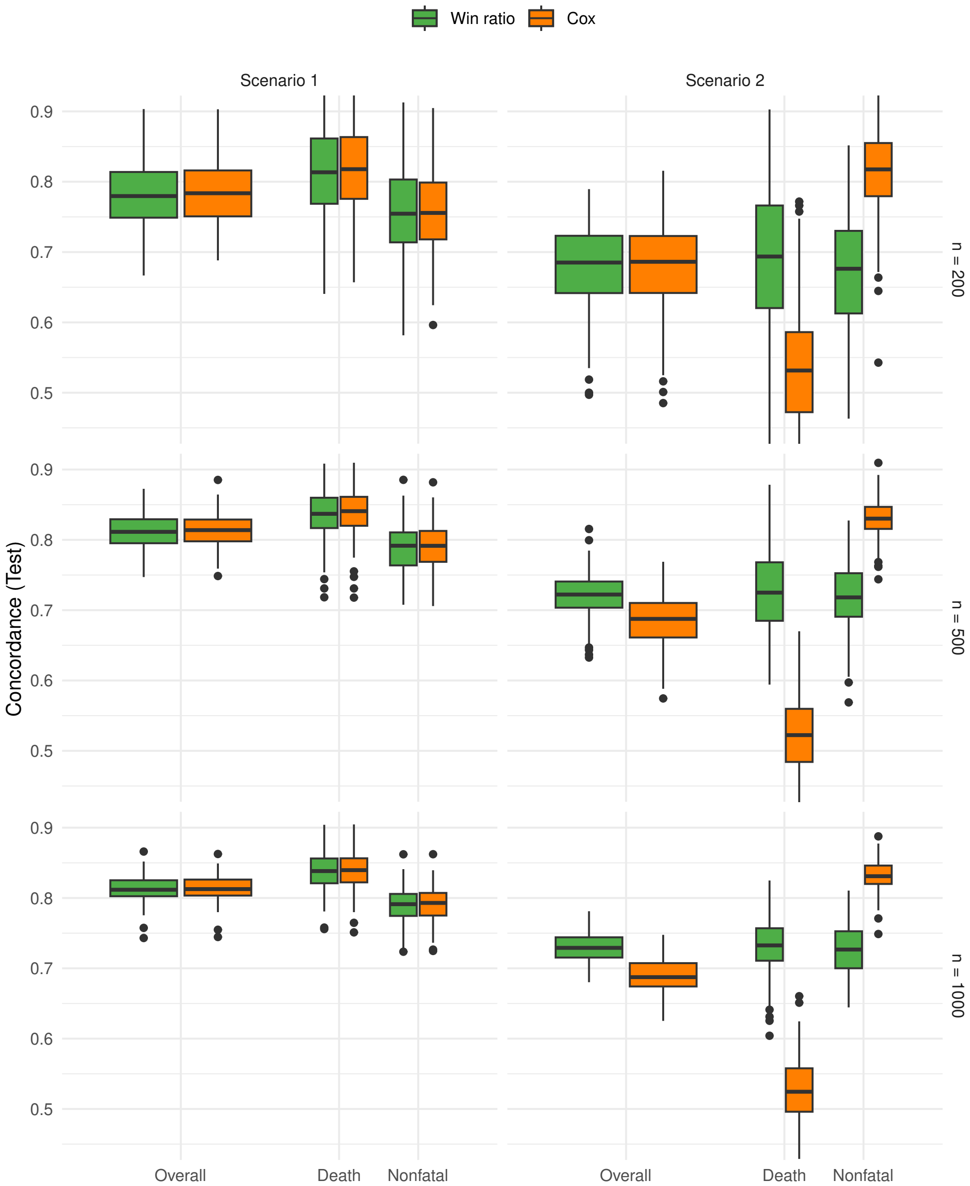

Fig. S3 Regularized win ratio (`wrnet`) and Cox models trained on 80% of data at $\alpha = 1$ (lasso) and tested on remaining 20% with $p = n/2$.