Identifying treatment responders using counterfactual modeling and potential outcomes

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Supplementary material

The percentage of simulation runs discarded because of convergence issues is presented for each scenario in Table S1.

The results on the mean estimated regression coefficients and standard errors, as well as coverage probabilities of 95% confidence intervals are presented for the simulations with 1, 4 and 10 covariates as a nested loop plots [1] (figures S1–S3).

The Figure S4 presents the distribution of calibration slopes of the predictions of the probability to be a responder in the setting with 4 covariates.

The Table S2 investigates the monotonicity assumption by contrasting the 10-year cumulative incidence of local recurrence for each subgroup of patients in the original (unweighted) sample and in the IPTW weighted sample.

Figures S5 and S6 present additional results of the analysis of the motivating example. On figure S5, an assessment of the monotinicty assumption is displayed, and on figure S6 the distributions of the predicted probabilities to be a responder are given according to patient and tumor characteristics.

References

[1] Rücker G and Schwarzer G. Presenting simulation results in a nested loop plot. *BMC Medical Research Methodology* 2014; 14(1): 129. DOI:10.1186/1471-2288-14-129.

Table S1: Percentage of simulations discarded due to convergence issues.

	$N = 1\,000$				$N = 2\,500$			
	Randomized		Non Randomized		Randomized		Non Randomized	
Number of variables	1:1	2:1	1:1	2:1	1:1	2:1	1:1	2:1
1 variable								
scenario 1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
scenario 2	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
scenario 3	0.1	0.1	0.0	0.1	0.0	0.0	0.0	0.0
scenario 4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
scenario 5	0.3	1.3	0.7	2.4	0.0	0.0	0.0	0.1
scenario 6	3.6	6.4	3.6	5.8	0.4	0.8	0.5	0.7
scenario 7	5.6	7.5	6.2	6.7	3.7	1.3	0.8	1.2
scenario 8	2.5	3.7	2.6	4.2	0.3	0.2	0.1	0.3
scenario 9	0.1	0.3	0.1	0.3	0.0	0.0	0.0	0.0
4 variables								
scenario 1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
scenario 2	0.1	0.3	0.4	1.4	0.0	0.0	0.0	0.0
scenario 3	0.2	0.5	0.3	0.9	0.0	0.0	0.0	0.0
scenario 4	0.1	0.1	0.0	0.1	0.0	0.0	0.0	0.0
scenario 5	3.3	6.1	10.1	19.8	0.1	0.1	0.5	2.4
scenario 6	20.9	29.0	32.7	41.6	3.6	7.6	10.1	17.0
scenario 7	24.5	28.2	29.1	34.8	5.4	8.2	6.9	11.4
scenario 8	20.8	20.4	19.4	24.2	3.7	3.8	2.7	5.8
scenario 9	3.0	2.6	2.5	4.7	0.0	0.0	0.0	0.2
10 variables								
scenario 1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
scenario 2	1.2	3.2	8.3	17.8	0.0	0.0	0.0	0.2
scenario 3	2.2	4.0	4.9	10.8	0.0	0.0	0.0	0.1
scenario 4	1.2	1.1	0.7	2.4	0.0	0.0	0.0	0.0
scenario 5	17.2	32.3	56.5	74.6	0.6	2.7	17.5	37.5
scenario 6	45.7	58.5	72.1	80.0	8.6	16.8	34.8	49.9
scenario 7	56.6	59.8	64.4	69.6	16.6	20.5	24.5	36.2
scenario 8	45.4	41.5	40.2	46.2	8.8	7.7	6.4	12.5
scenario 9	18.5	14.1	12.7	19.2	0.4	0.2	0.3	1.1

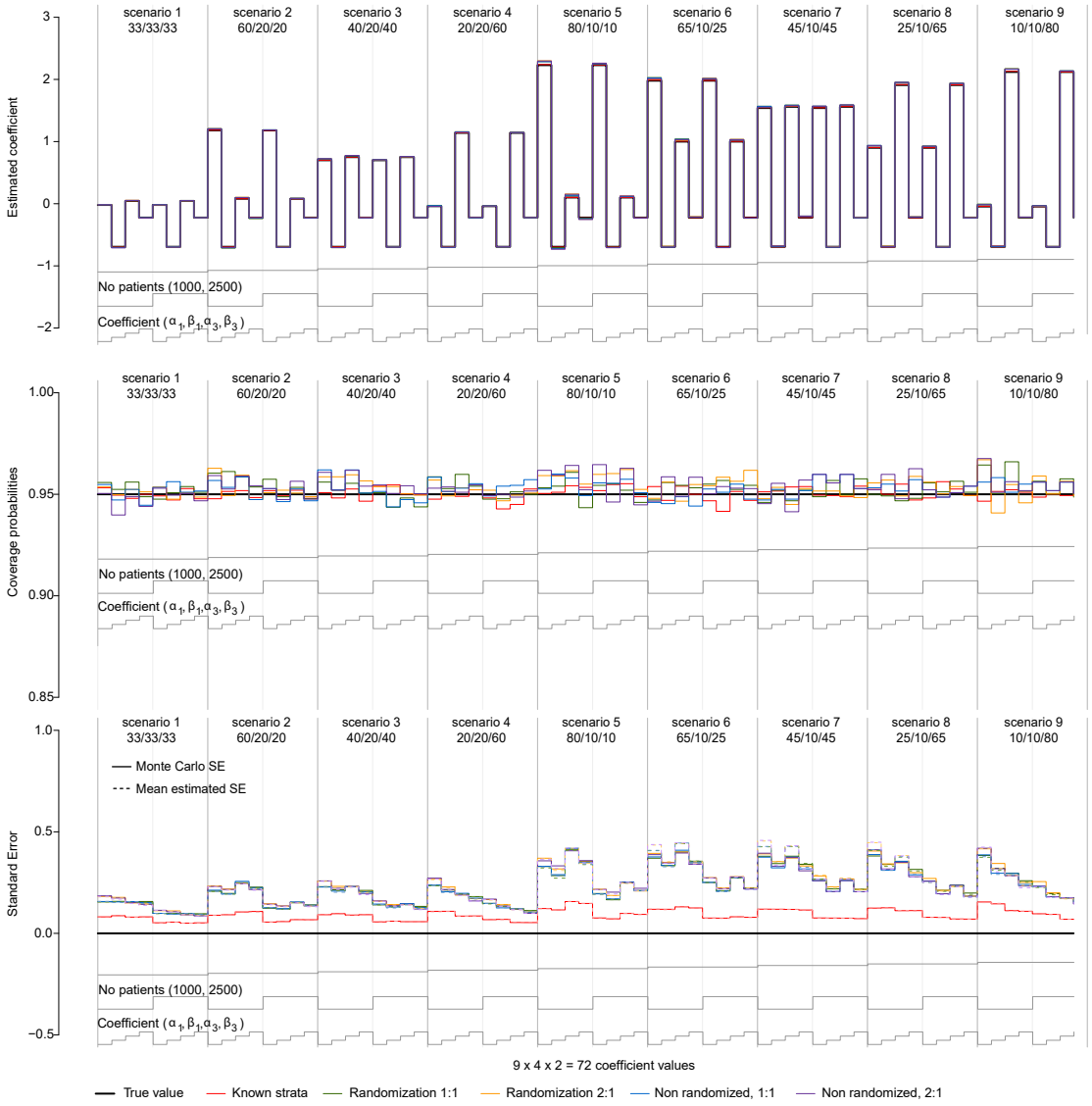

Figure S1: Simulation results for the estimation of model parameters from observed treatment and outcomes with one covariate.

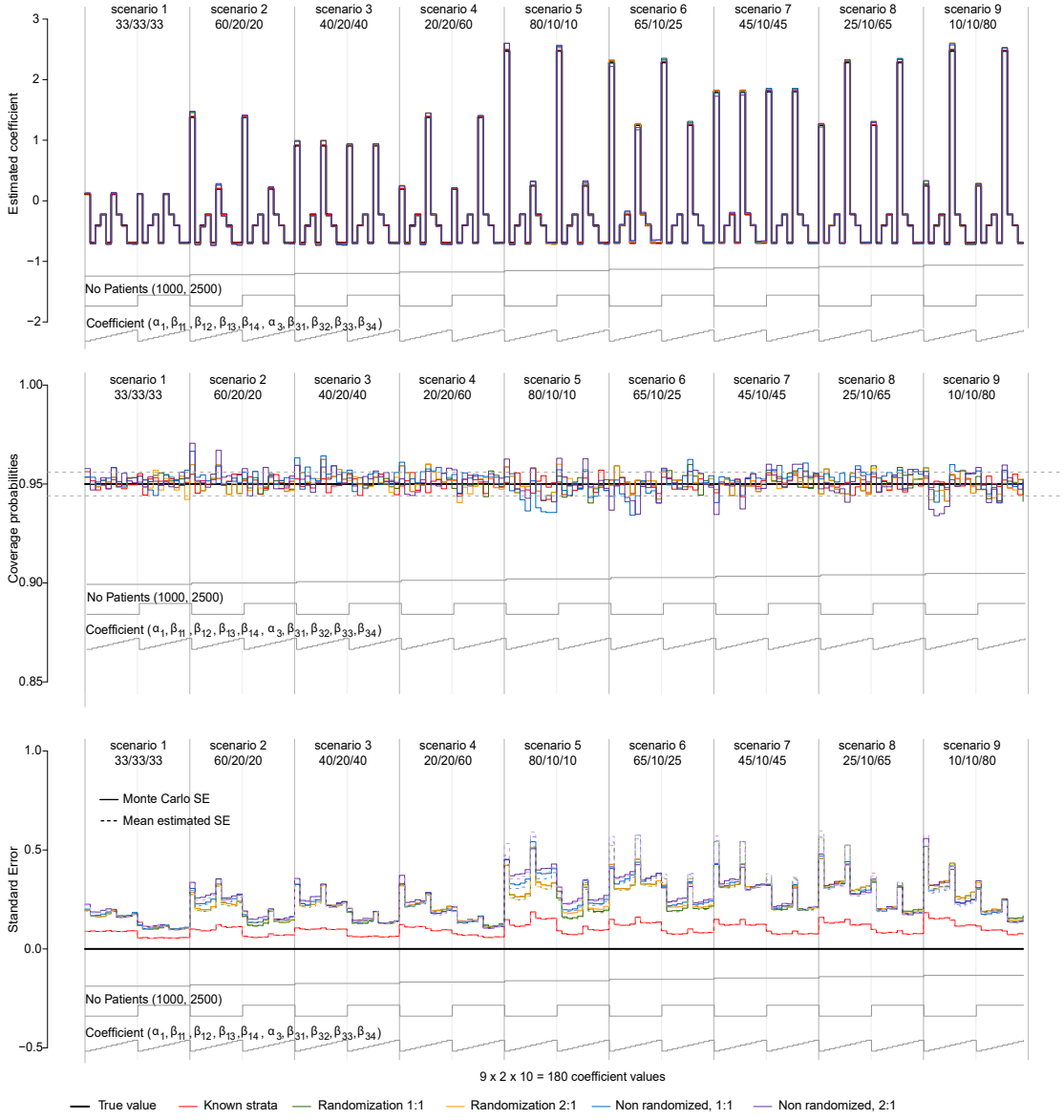

Figure S2: Simulation results for the estimation of model parameters from observed treatment and outcomes with four covariates.

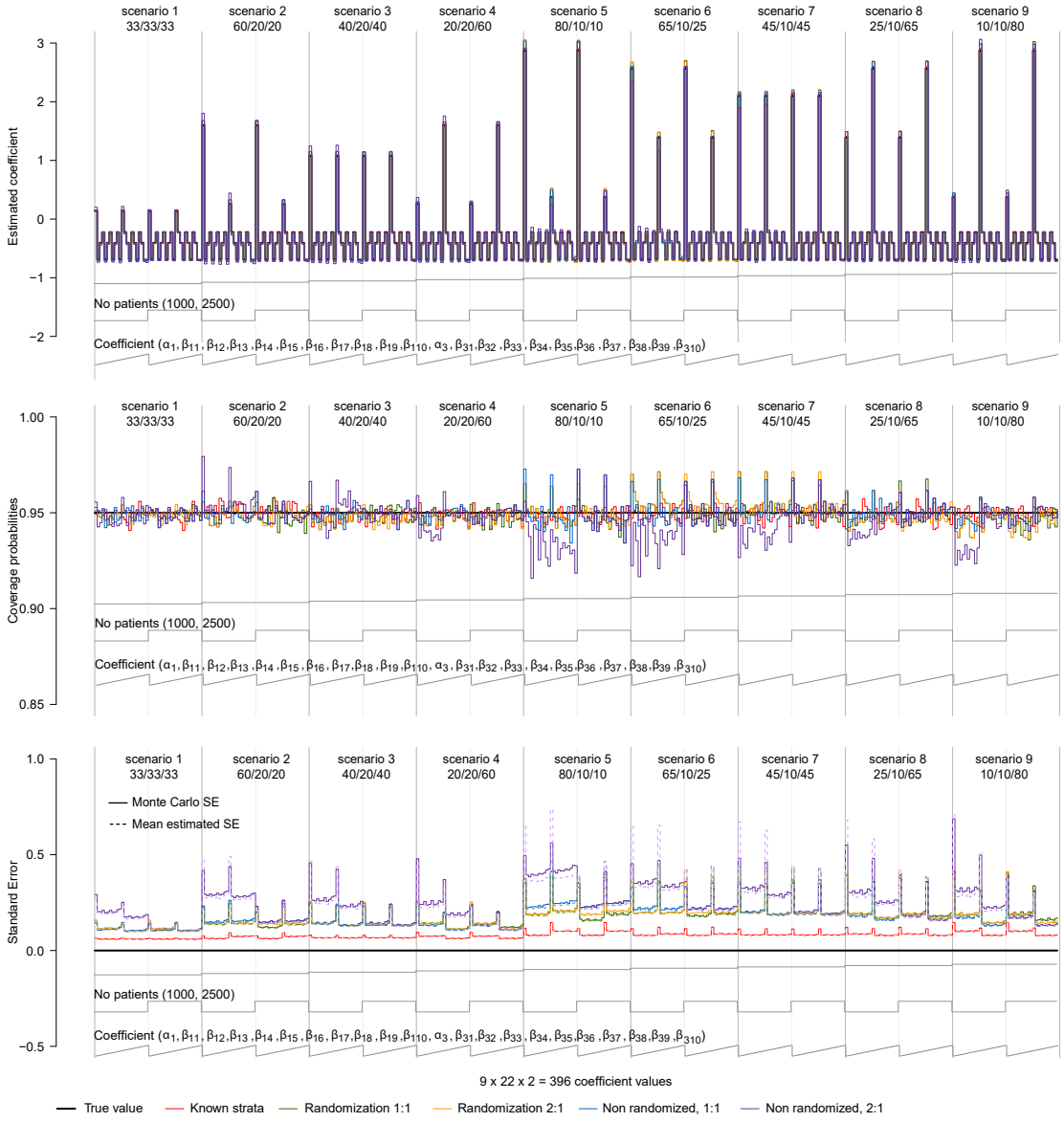

Figure S3: Simulation results for the estimation of model parameters from observed treatment and outcomes with ten covariates.

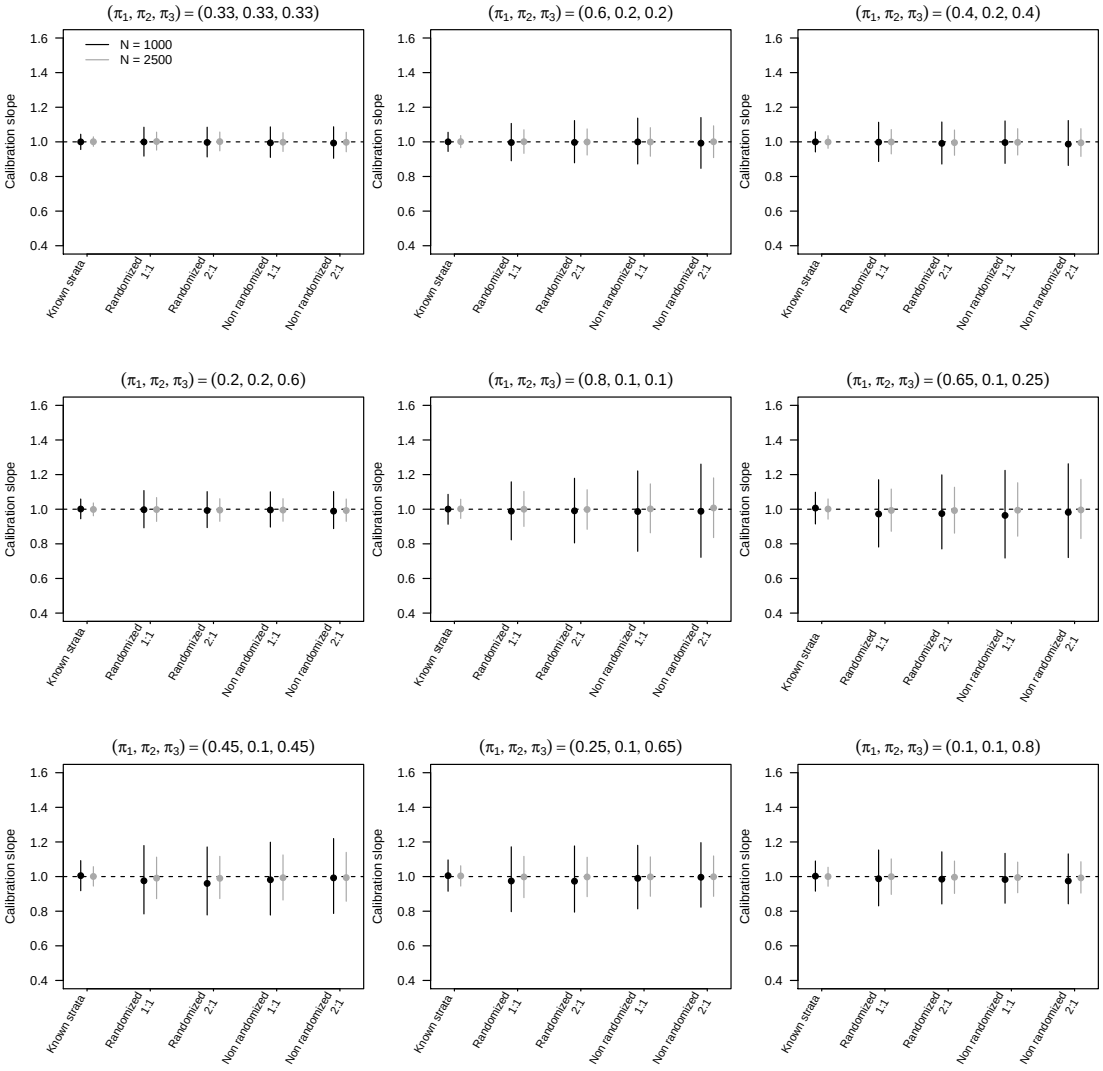

Figure S4: Calibration results for the estimation of model parameters from observed treatment and outcomes with four covariates.

Table S2: Evaluation of the monotonicty assumption. Cumulative incidence of local recurrence at 10 years (in percent) in the original (unweighted) and (IPTW) weighted samples.

	Unweighted		Weighted	
Characteristic	RT	No RT	RT	No RT
Age, ys				
[13,40]	9.3	5.0	8.5	7.7
(40,55]	5.8	15.5	4.5	12.4
(55,65]	6.9	8.5	7.0	4.9
(65,75]	7.3	22.4	6.6	31.4
(75,92]	8.9	30.7	8.0	16.5
Gender, no. (%)				
Female	9.2	13.5	8.5	14.2
Male	6.5	14.2	5.6	15.8
Tumor size, cm				
[0.5,3]	5.8	11.4	3.0	11.3
(3,5]	10.8	25.3	9.2	33.1
(5,8]	7.1	12.8	6.5	11.2
(8,12]	6.3	3.7	7.0	7.7
(12,40]	8.1	14.9	8.7	10.9
Tumour depth, no. (%)				
Superficial	4.5	13.1	3.4	12.2
Deep	8.6	15.7	8.7	16.6
Grade, no. (%)				
1	6.2	2.2	4.1	3.3
2	0.8	15.6	0.7	18.2
3	10.3	15.1	9.7	14.5
Site, no. (%)				
Lower extremity	8.0	12.3	6.9	12.8
Trunk	5.9	11.9	6.2	12.4
Upper extremity	7.5	21.3	6.8	22.2
Tumour, no. (%)				
Pleomorphic sarcoma	7.8	11.2	8.1	14.7
Leiomyosarcoma	7.7	20.2	5.5	17.0
Synovial sarcoma	4.5	6.7	3.8	10.5
MPNST	18.4	5.9	16.1	15.2
Liposarcoma	6.7	29.8	5.8	31.4
Fibrosarcoma	10.9	7.2	9.7	7.8
Solitary fibrous tumour	0.0	33.3	0.0	46.2
Angiosarcoma	0.0	35.1	0.0	25.7
Other STS	10.5	9.9	6.9	10.3

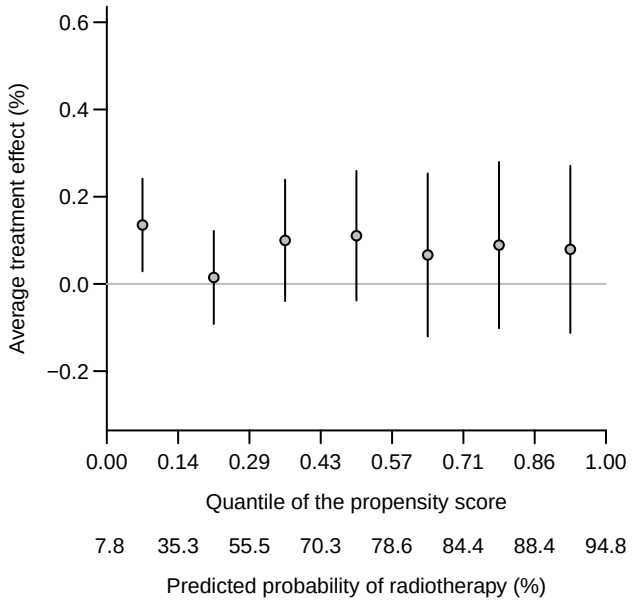

Figure S5: Assessment of the monotonicity assumption. The average treatment effect is dispalyed according to quantiles of the propensity score. The bars represent 95% confidence intervals.

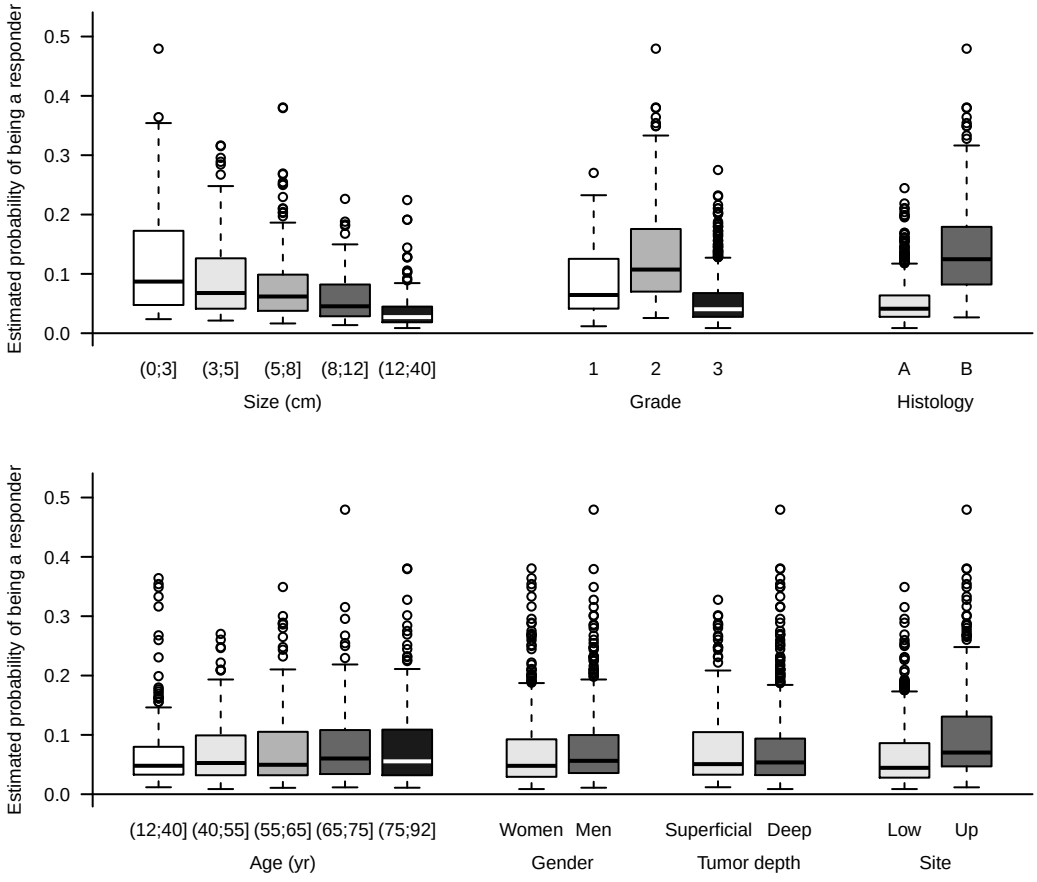

Figure S6: Distribution of the predicted probability of being a responder according to patient and tumor characteristics. Histology group B: leiomyosarcoma, MPNST, liposarcoma and angiosarcoma; group A: pleomorphic sarcoma, synovial sarcoma, fibrosarcoma, solitary fibrous tumor and other STS. Tumor location was grouped into "low" (lower limbs) and "up" (trunk and upper limbs).