Supplementary Material: A copula-based approach for dynamic prediction of survival with a binary time-dependent covariate

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A Derivations

A.1 Dynamic prediction under copula formulation

Here, we present the derivation for the dynamic prediction for surviving the prediction window s given in Eq.(1) in our copula model notation (omitting the subscript for individual k and the covariate vector $\mathbf{X}$ for brevity). We use the notation $Z_\tau = Z(\tau)|T > \tau$ and $T_\tau = T|T > \tau$ to represent the cross-section marker data and conditional survival time distributions at prediction time τ. Then, the dynamic prediction in the copula formulation is given by

$$
\begin{aligned}
p(\tau, s|Z(\tau) = z) &= P(T \geq \tau + s|T > \tau, Z(\tau) = z) \\
&= \frac{P(T \geq \tau + s, Z(\tau) = z, T > \tau)}{P(T > \tau, Z(\tau) = z)} \\
&= \frac{P(T \geq \tau + s, Z(\tau) = z|T > \tau)P(T > \tau)}{P(Z(\tau) = z|T > \tau)P(T > \tau)} \\
&= \frac{P(T \geq \tau + s, Z(\tau) = z|T > \tau)}{P(Z(\tau) = z|T > \tau)} \\
&= \frac{P(T_\tau \geq \tau + s, Z_\tau = z)}{P(Z_\tau = z)}
\end{aligned}
$$

A.2 Dynamic prediction under latent variable formulation

Here, we present the derivation for Eqs.(2) and (3). We use the notation $F_{T_\tau}(x) = P(T \leq t|T > \tau)$, $F_{Z^*_\tau}(y) = P(Z^*(\tau) \leq y|T > \tau)$ and $F_{T_\tau, Z^*_\tau}(x, y) = P(T \leq x, Z^*(\tau) \leq y|T > \tau)$. Based on the latent variable formulation, $Z(\tau) = 0$ corresponds to $Z^*(\tau) < 0$, and $Z(\tau) = 1$ corresponds to $Z^*(\tau) \geq 0$. Thus,

$$
\begin{aligned}
P(T \geq \tau + s|T \geq \tau, Z(\tau) = 0) &= P(T \geq \tau + s|T > \tau, Z^*(\tau) < 0) \\
&= \frac{P(T \geq \tau + s, Z^*(\tau) < 0|T > \tau)}{P(Z^*(\tau) < 0|T > \tau)} \\
&= \frac{P(Z^*(\tau) < 0|T > \tau) - P(T < \tau + s, Z^*(\tau) < 0|T > \tau)}{P(Z^*(\tau) < 0|T > \tau)} \\
&= \frac{F_{Z^*_\tau}(0) - F_{T_\tau, Z^*_\tau}(\tau + s, 0)}{F_{Z^*_\tau}(0)}
\end{aligned}
$$

and the dynamic prediction for surviving the prediction window s conditional on $Z(\tau) = 1$ is given by

$$
\begin{aligned}
P(T \geq \tau + s|T > \tau, Z(\tau) = 1) &= P(T \geq \tau + s|T > \tau, Z^*(\tau) \geq 0) \\
&= \frac{P(T \geq \tau + s, Z^*(\tau) \geq 0|T > \tau)}{P(Z^*(\tau) \geq 0|T > \tau)} \\
&= \frac{P(Z^*(\tau) \geq 0|T > \tau) + P(T < \tau + s, Z^*(\tau) < 0|T > \tau) - P(T < \tau + s|T > \tau)}{1 - P(Z^*(\tau) < 0|T > \tau)} \\
&= \frac{[1 - F_{Z^*_\tau}(0)] - F_{T_\tau}(\tau + s) + F_{T_\tau, Z^*_\tau}(\tau + s, 0)}{1 - F_{Z^*_\tau}(0)}
\end{aligned}
$$

A.3 Binary marker distribution under illness-death model

We write out the distribution of the marker value at τ under the true illness-death model using the notation $\lambda_{ij}(t|\mathbf{X})$ to represent the hazard of transitioning from i to j (0: Healthy, 1:Ill, 2: Dead) as

$$\Pr(Z(\tau)=0|T>\tau,\mathbf{X}) = \frac{\Pr(Z(\tau)=0,T>\tau|\mathbf{X})}{\Pr(T>\tau|\mathbf{X})}$$
$$= \frac{e^{-\int_0^\tau \lambda_{01}(u|\mathbf{X})+\lambda_{02}(u|\mathbf{X})\,\mathrm{d}u}}{e^{-\int_0^\tau \lambda_{01}(u|\mathbf{X})+\lambda_{02}(u|\mathbf{X})\,\mathrm{d}u} + \int_0^\tau e^{-\int_0^v \lambda_{01}(u|\mathbf{X})+\lambda_{02}(u|\mathbf{X})\,\mathrm{d}u}\lambda_{01}(v|\mathbf{X})e^{-\int_v^\tau \lambda_{12}(u|\mathbf{X})\,\mathrm{d}u}\,\mathrm{d}v}$$
$$\Pr(Z(\tau)=1|T>\tau,\mathbf{X}) = 1-\Pr(Z(\tau)=0|T>\tau,\mathbf{X})$$

In the first equation, the numerator represents the probability that an individual remains in the healthy state from time 0 to time τ and does not transition to illness ($0 \to 1$) or death ($0 \to 2$) during this time. The denominator represents the probability that the individual does not transition to the death state by time τ, which is the sum of the first term, the probability that they don't transition to the death state from the health state during that period ($0 \to 2$), and the second term, the probability that they remain in the healthy state and at some time $0 < v < \tau$ they transition from the healthy state to the illness state ($0 \to 1$) and then remain there for time v to τ, i.e., don't transition to the death state ($1 \to 2$) during that time.

B Simulation Settings

B.1 Scenario 1: Markov, Single baseline covariate

B.1.1 Data Summary

Table B1: Proportion of patients ($n = 1000$) with particular number of inspection times within 15 years for binary marker Markov simulation setting with one baseline covariate.

No. insp times	1	2	3	4	5	6	7	8	9	10	11	12	13	≥14
Insp rate 0.5	26%	21%	15%	11%	10%	6%	4%	3%	2%	1%	1%	0%	0.1%	0.1%
Insp rate 1	14%	14%	11%	9%	9%	9%	5%	7%	5%	4%	3%	2%	2%	6%

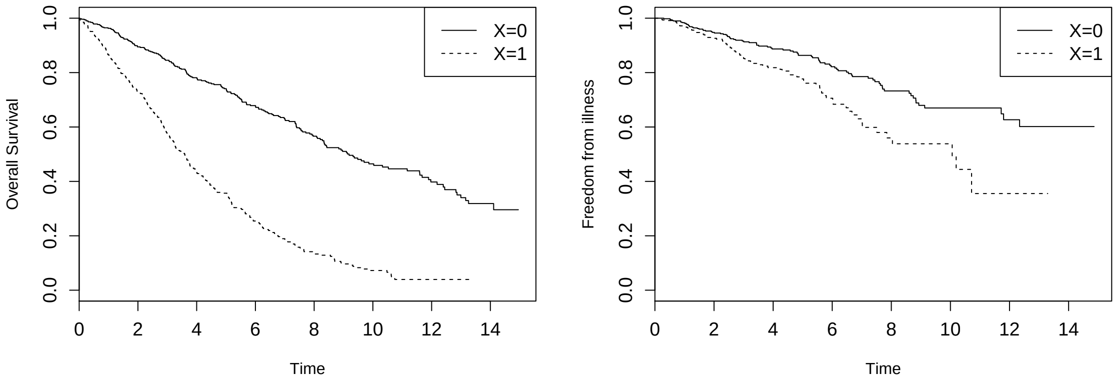
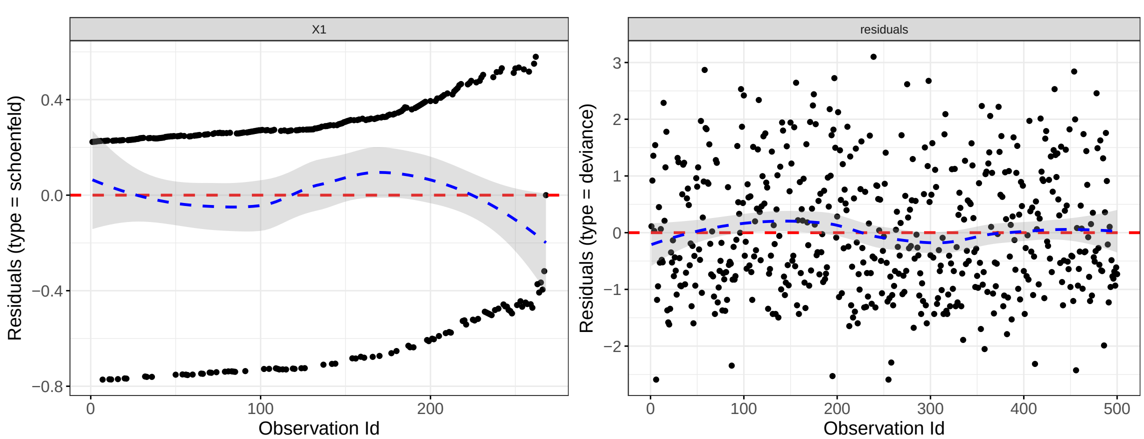


Figure B1: Overall survival (left) and Freedom from illness (right) curves by baseline covariate for binary marker Markov simulation setting with one baseline covariate.

B.1.2 Modeling Failure Time data

Testing proportional hazards assumption: We test the proportional hazards assumption using the Schoenfeld residuals and find that there is no significant evidence against the assumption (p=0.78) (Figure B2).

Checking influential observations: We check for outliers by examining the deviance residuals (normalized transform of martingale residuals) and find that they are symmetrically distributed about 0 (Figure B2).



Schoenfeld Residuals

Deviance Residuals

Figure B2: Cox model diagnostics for the binary marker Markov simulation setting with one baseline covariate.

B.1.3 Modeling Binary marker data

We examine the Pearson residuals from the probit model (BC1) fit to the marker data. We see that there is deviation from zero at later times (Figure B3).

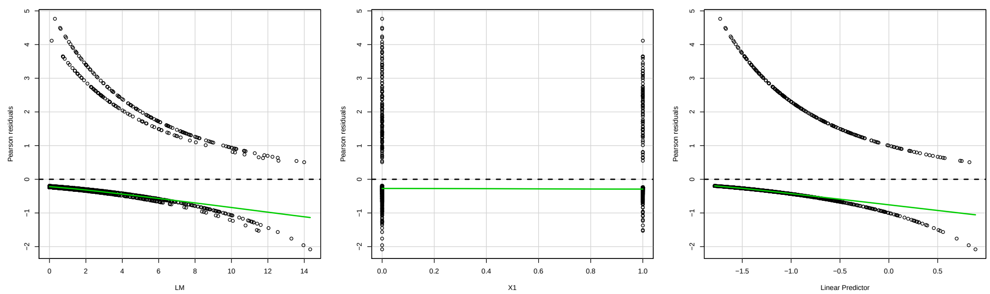


Figure B3: Pearson residuals for probit model (BC1) by measurement time (LM), baseline covariate X, and the linear predictor for the binary marker Markov simulation setting with one baseline covariate.

B.1.4 Evaluating predictions

We compare the predicted vs. actual probabilities for the joint, landmark, and copula models. The predictions for the MM, LMInt3, and BC1 models are similar. However, the predicted probabilities of the LM3 model (landmark model without the interaction) does not have a high enough prediction for those with $X = 1$ and $Z = 1$ (Figure B4).

B.2 Scenario 2: Semi-Markov, Single baseline covariate

B.2.1 Data summary

Table B2: Proportion of patients ($n = 1000$) with particular number of inspection times within 15 years for the binary marker semi-Markov simulation setting with one baseline covariate.

No. insp times	1	2	3	4	5	6	7	8	9	10	11	12	13	≥14
Insp rate 0.5	27%	20%	14%	13%	10%	6%	4%	2%	1%	1%	1%	1%	0.3%	0.4%
Insp rate 1	14%	14%	12%	10%	9%	6%	7%	6%	5%	4%	3%	3%	2%	7%

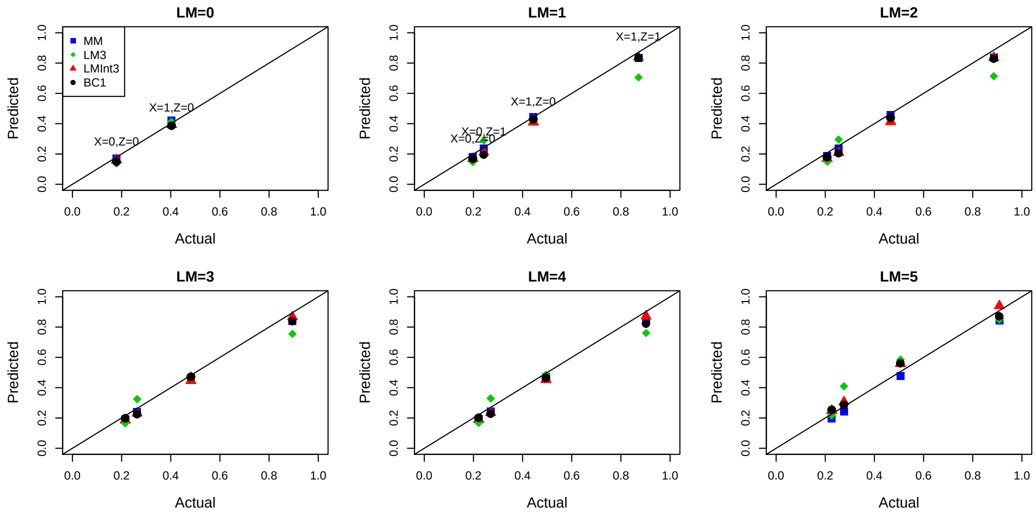


Figure B4: Predicted vs. actual probabilities by prediction time for the binary marker Markov simulation setting with one baseline covariate.

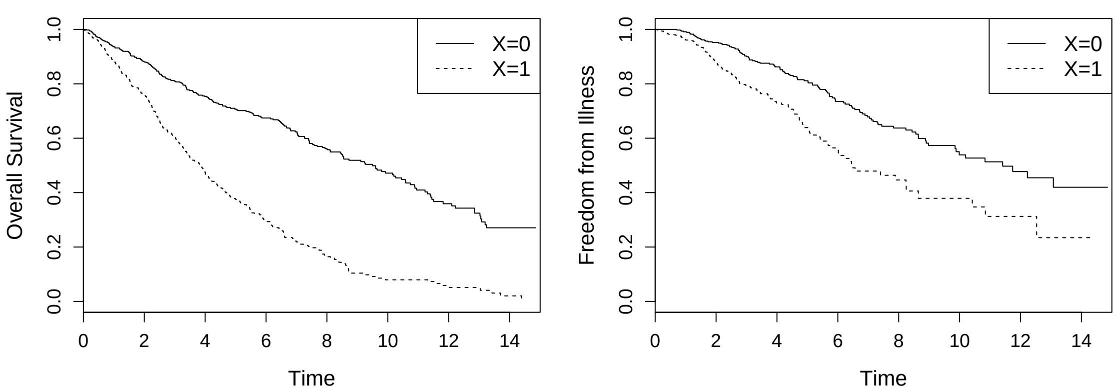
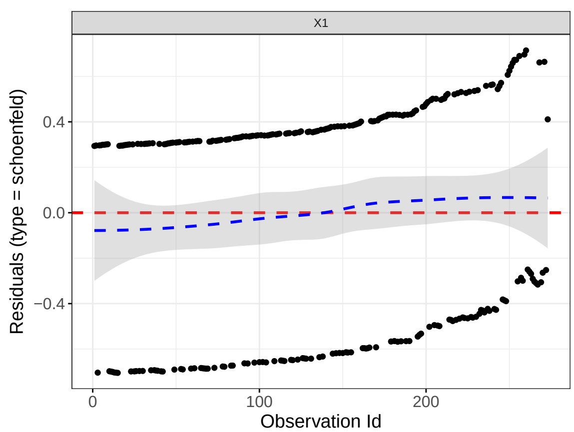


Figure B5: Overall survival (left) and Freedom from illness (right) curves by baseline covariate for the binary marker semi-Markov simulation setting with one baseline covariate.

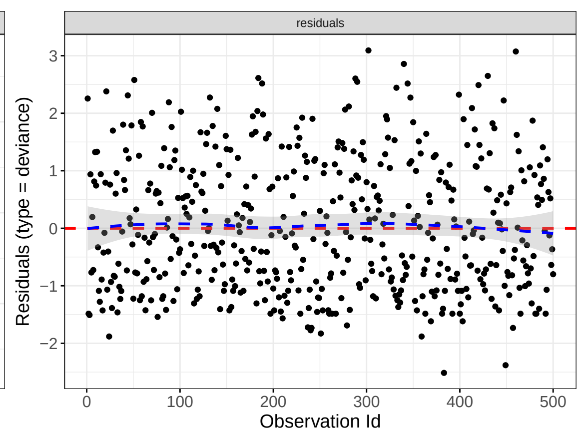
B.2.2 Modeling Failure Time data

Testing proportional hazards assumption: We test the proportional hazards assumption and find that there is possible evidence against the assumption for the baseline covariate X_1 (p=0.07). However, looking at the log(-log(Survival)) vs. log(time) we see that the curves are parallel and thus no evidence against the proportional hazards assumption (Figure B6).

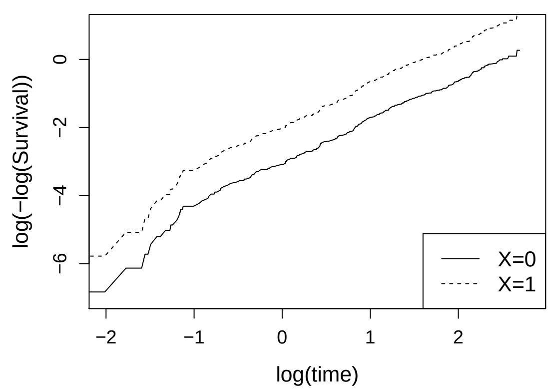
Checking influential observations: We check for outliers and find that they are symmetrically distributed about zero (Figure B6).



Schoenfeld Residuals



Deviance Residuals



Log(-Log(Survival)) vs. Log(Time)

Figure B6: Cox model diagnostics for the binary marker semi-Markov simulation setting with one baseline covariate.

B.2.3 Modeling Binary marker data

We examine the Pearson residuals from the probit model (BC1) and find that there is deviation from zero at later measurement times (Figure B7).

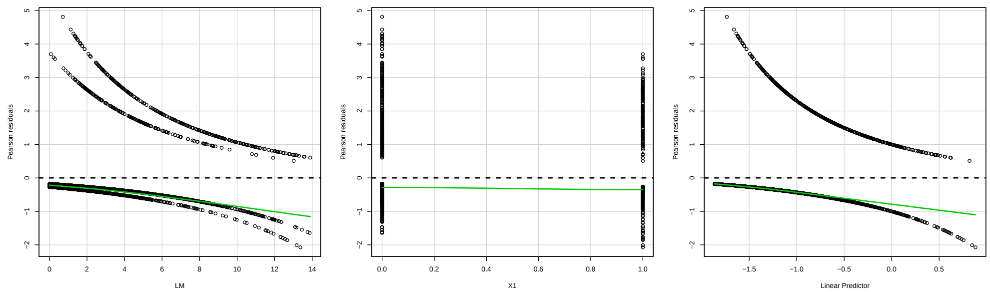


Figure B7: Pearson residuals for probit model (BC1) by measurement time (LM), baseline covariates X_1, X_2, and the linear predictor for the binary marker semi-Markov simulation setting with one baseline covariate.

B.2.4 Evaluating predictions

We compare the predicted vs. actual probabilities for the joint, landmark, and copula models. The predictions for the landmark model without an interaction (LM3) deviate from the true probabilities for those with $X_1 = 1$ and $Z = 1$ (Figure B8).

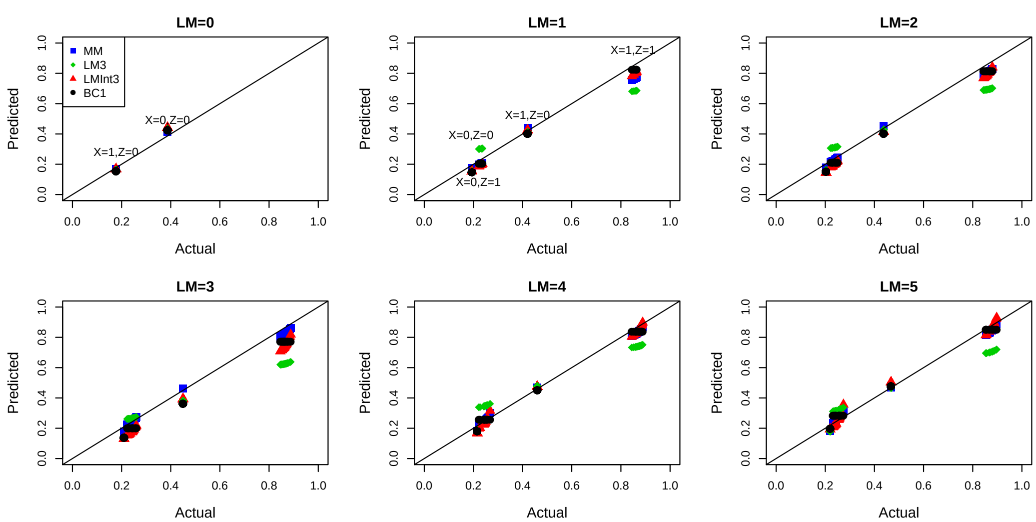


Figure B8: Predicted vs. actual probabilities by measurement time for the binary marker semi-Markov simulation setting with one baseline covariate.

B.3 Scenario 3: Markov, Two baseline covariates

B.3.1 Data summary

Table B3: Proportion of patients ($n = 1000$) with particular number of inspection times within 15 years for the binary marker Markov simulation setting with two baseline covariates.

No. insp times	1	2	3	4	5	6	7	8	9	10	11	12	13	≥14
Insp rate 0.5	27%	21%	17%	11%	8%	6%	4%	2%	1%	1%	0.5%	0.6%	0.1%	0%
Insp rate 1	15%	12%	12%	11%	11%	8%	6%	6%	4%	4%	3%	2%	1%	5%

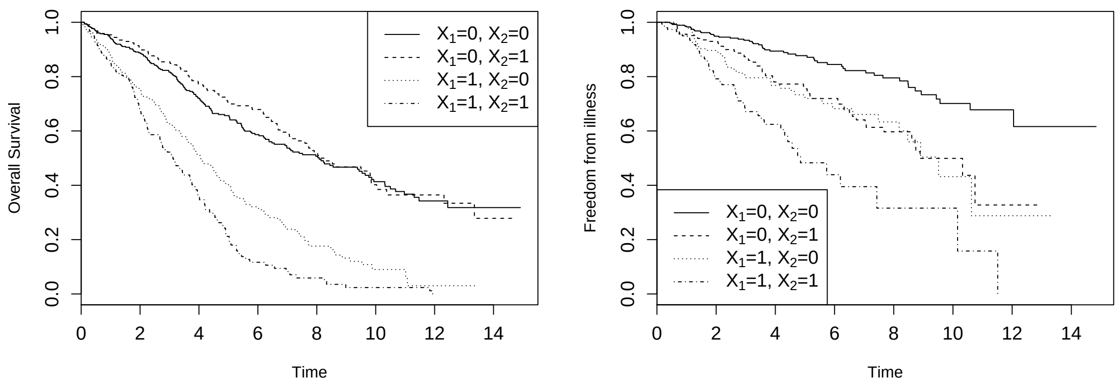


Figure B9: Overall survival (left) and Freedom from illness (right) curves by baseline covariates for the binary marker Markov simulation setting with two baseline covariates.

B.3.2 Modeling Failure Time data

Testing proportional hazards assumption: We test the proportional hazards assumption and find that there is no significant evidence against the assumption for the baseline covariates X_1 (p=0.33) and X_2 (p=0.15) (Figure B10).

Checking influential observations: We check for outliers and find that they are symmetrically distributed about zero (Figure B11).

B.3.3 Modeling Binary marker data

We examine the Pearson residuals from the probit model (BC1) and find that there is deviation from zero at later measurement times (Figure B12).

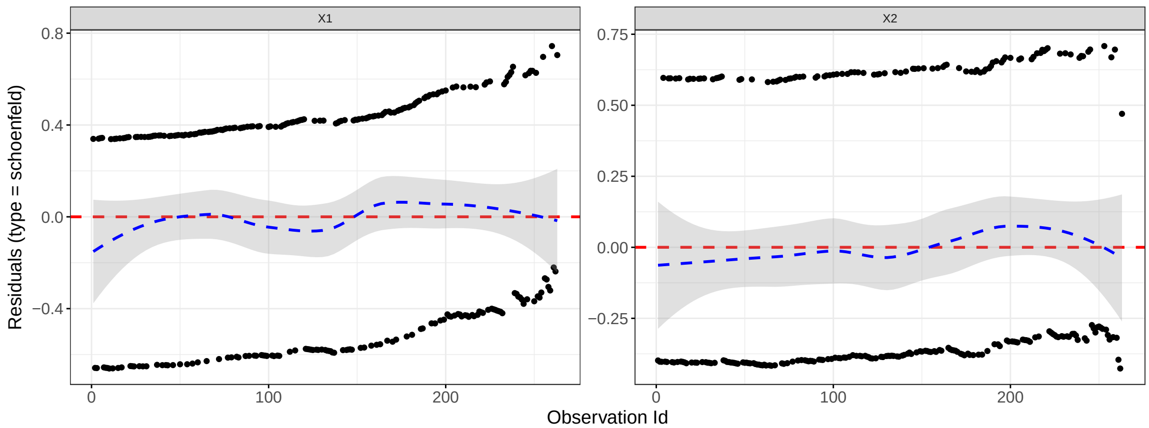


Figure B10: Cox model Schoenfeld residuals for the binary marker Markov simulation setting with two baseline covariates.

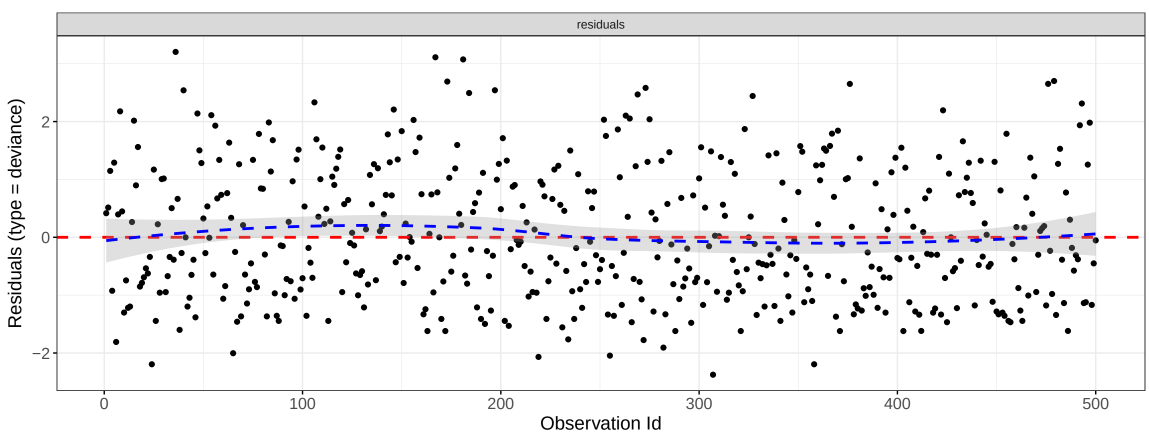


Figure B11: Cox model deviance residuals for the binary marker Markov simulation setting with two baseline covariates.

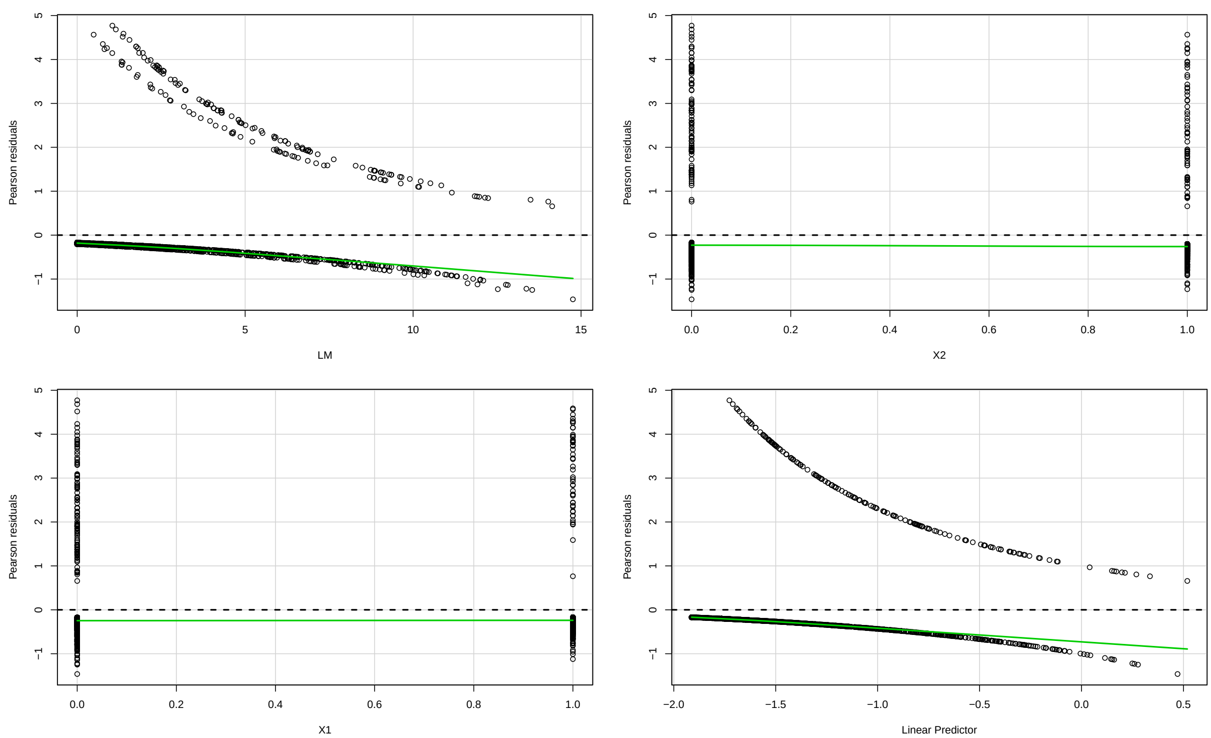


Figure B12: Pearson residuals for probit model (BC1) by measurement time (LM), baseline covariates X_1, X_2, and the linear predictor for the binary marker Markov simulation setting with two baseline covariates.

B.3.4 Evaluating predictions

We compare the predicted vs. actual probabilities for the joint, landmark, and copula models. The predictions for the landmark model without an interaction (LM3) deviate from the true probabilities for those with $X_1 = 1$ and the intermediate event ($Z = 1$) (Figure B8).

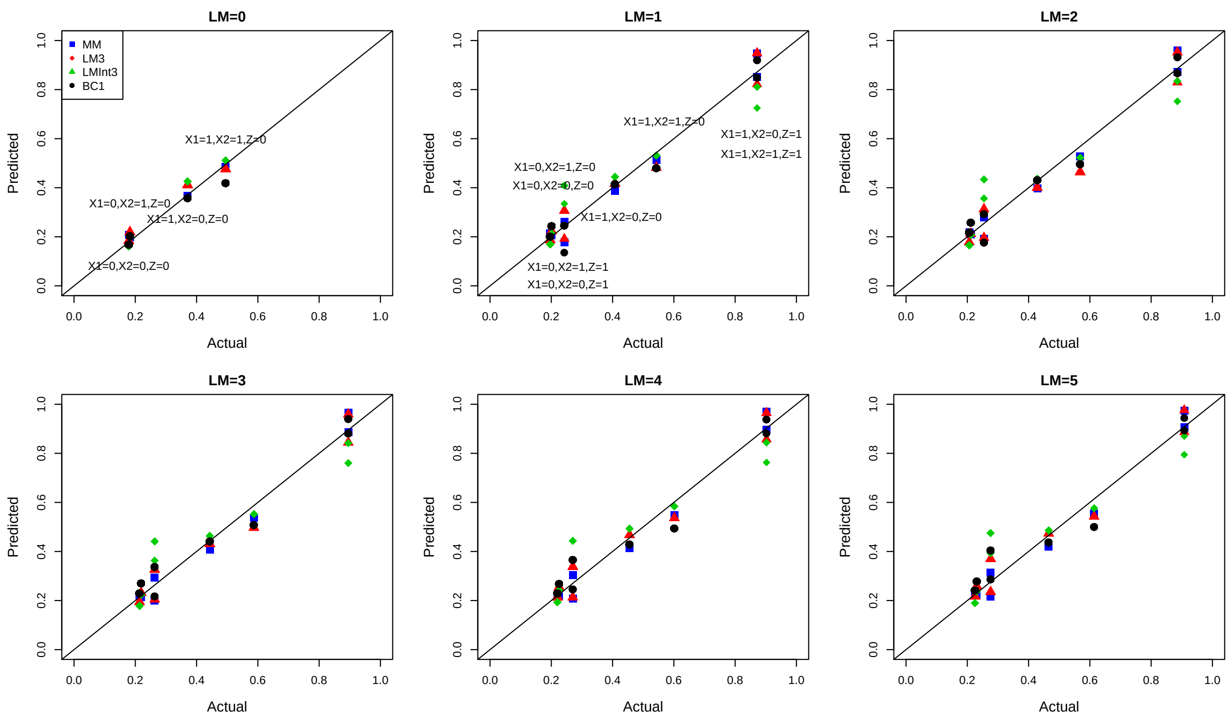


Figure B13: Predicted vs. actual probabilities by prediction time for the binary marker Markov simulation setting with two baseline covariates.

C Simulation Results

Table C1: Average computation time (seconds) for model estimation in the simulation study.

Model	Scenario 1a	Scenario 2a	Scenario 3a
MM	10.41	10.37	11.32
MMCox	0.017	0.016	0.011
MSM	-	975.1	-
MSMCox	-	0.017	-
SMM	-	527.7	-
LM3	1.620	1.550	1.139
LSM3	-	1.653	-
LMInt3	1.747	-	1.292
LM4	1.831	1.772	1.279
LSM4	-	1.829	-
LMInt4	1.928	-	1.404
BC1	0.916	0.911	1.260
BW1	0.916	0.911	1.268
BC2	0.918	0.912	1.261
BW2	0.918	0.912	1.266
BC3	1.868	1.849	3.236
BW3	1.926	1.897	3.245

C.1 Scenario 1a Results

- Markov model; Marker observed at random inspection times (rate=0.5); Single baseline covariate X

Table C2: Simulation results for binary marker Scenario 1a.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 1a.

	τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
	0	0.015 (0.011)	0.017 (0.012)	0.023 (0.016)	0.019 (0.014)	0.023 (0.016)	0.019 (0.014)	0.020 (0.013)	0.019 (0.013)	0.020 (0.013)	0.019 (0.013)	0.020 (0.013)	0.019 (0.013)
	1	0.016 (0.010)	0.020 (0.013)	0.027 (0.015)	0.024 (0.015)	0.032 (0.016)	0.025 (0.016)	0.020 (0.013)	0.017 (0.010)	0.020 (0.013)	0.017 (0.010)	0.021 (0.013)	0.017 (0.010)
	2	0.019 (0.011)	0.025 (0.015)	0.037 (0.016)	0.028 (0.017)	0.043 (0.017)	0.030 (0.018)	0.026 (0.016)	0.021 (0.012)	0.026 (0.016)	0.021 (0.012)	0.027 (0.016)	0.022 (0.012)
$X = 0$	3	0.022 (0.012)	0.030 (0.019)	0.047 (0.019)	0.034 (0.020)	0.052 (0.019)	0.035 (0.021)	0.033 (0.020)	0.026 (0.015)	0.033 (0.020)	0.026 (0.015)	0.033 (0.020)	0.026 (0.015)
	4	0.024 (0.014)	0.035 (0.020)	0.057 (0.022)	0.039 (0.022)	0.059 (0.023)	0.041 (0.023)	0.038 (0.022)	0.030 (0.017)	0.038 (0.022)	0.030 (0.017)	0.038 (0.022)	0.030 (0.017)
	5	0.026 (0.015)	0.040 (0.023)	0.066 (0.025)	0.044 (0.026)	0.063 (0.028)	0.047 (0.026)	0.041 (0.024)	0.034 (0.019)	0.041 (0.024)	0.034 (0.019)	0.041 (0.024)	0.035 (0.019)
	0	0.021 (0.017)	0.023 (0.018)	0.028 (0.021)	0.026 (0.020)	0.027 (0.021)	0.026 (0.019)	0.024 (0.019)	0.020 (0.016)	0.024 (0.019)	0.021 (0.016)	0.024 (0.018)	0.020 (0.016)
	1	0.021 (0.015)	0.036 (0.022)	0.043 (0.024)	0.035 (0.024)	0.039 (0.025)	0.037 (0.024)	0.030 (0.021)	0.023 (0.015)	0.030 (0.021)	0.024 (0.016)	0.030 (0.020)	0.024 (0.015)
	2	0.024 (0.016)	0.046 (0.025)	0.054 (0.028)	0.042 (0.028)	0.048 (0.029)	0.043 (0.028)	0.036 (0.023)	0.028 (0.017)	0.036 (0.023)	0.028 (0.018)	0.036 (0.023)	0.028 (0.017)
$X = 1$	3	0.027 (0.018)	0.054 (0.030)	0.061 (0.032)	0.046 (0.032)	0.056 (0.033)	0.047 (0.033)	0.041 (0.026)	0.031 (0.018)	0.041 (0.026)	0.031 (0.018)	0.041 (0.026)	0.031 (0.018)
	4	0.030 (0.020)	0.060 (0.035)	0.068 (0.034)	0.053 (0.034)	0.069 (0.035)	0.055 (0.035)	0.045 (0.029)	0.034 (0.019)	0.044 (0.029)	0.033 (0.019)	0.045 (0.029)	0.034 (0.019)
	5	0.033 (0.021)	0.063 (0.040)	0.076 (0.041)	0.061 (0.043)	0.082 (0.042)	0.064 (0.044)	0.054 (0.032)	0.038 (0.020)	0.054 (0.032)	0.038 (0.020)	0.054 (0.033)	0.039 (0.021)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 1a.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)
1	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)	0.664 (0.027)	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)	0.665 (0.027)
2	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)	0.680 (0.029)	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)	0.682 (0.029)
3	0.690 (0.035)	0.689 (0.035)	0.689 (0.035)	0.690 (0.035)	0.687 (0.036)	0.689 (0.035)	0.689 (0.035)	0.689 (0.035)	0.690 (0.035)	0.690 (0.035)	0.689 (0.035)	0.689 (0.035)
4	0.691 (0.038)	0.690 (0.038)	0.690 (0.039)	0.690 (0.038)	0.688 (0.040)	0.689 (0.038)	0.690 (0.038)	0.691 (0.038)	0.691 (0.038)	0.691 (0.038)	0.690 (0.038)	0.691 (0.038)
5	0.688 (0.045)	0.687 (0.045)	0.685 (0.047)	0.687 (0.045)	0.685 (0.047)	0.685 (0.045)	0.687 (0.046)	0.686 (0.046)	0.686 (0.045)	0.686 (0.045)	0.686 (0.045)	0.686 (0.045)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 1a.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)
1	0.203 (0.010)	0.203 (0.010)	0.204 (0.010)	0.204 (0.010)	0.204 (0.010)	0.204 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)
2	0.203 (0.010)	0.203 (0.010)	0.204 (0.011)	0.205 (0.011)	0.205 (0.011)	0.205 (0.011)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)
3	0.202 (0.013)	0.201 (0.012)	0.203 (0.013)	0.203 (0.013)	0.204 (0.013)	0.203 (0.013)	0.202 (0.012)	0.201 (0.012)	0.201 (0.012)	0.201 (0.012)	0.202 (0.012)	0.201 (0.012)
4	0.200 (0.014)	0.200 (0.014)	0.203 (0.015)	0.203 (0.015)	0.204 (0.015)	0.203 (0.015)	0.201 (0.013)	0.200 (0.013)	0.200 (0.013)	0.200 (0.013)	0.201 (0.013)	0.200 (0.013)
5	0.199 (0.016)	0.199 (0.016)	0.204 (0.017)	0.202 (0.017)	0.203 (0.017)	0.202 (0.017)	0.200 (0.015)	0.199 (0.015)	0.199 (0.015)	0.199 (0.015)	0.200 (0.015)	0.199 (0.015)

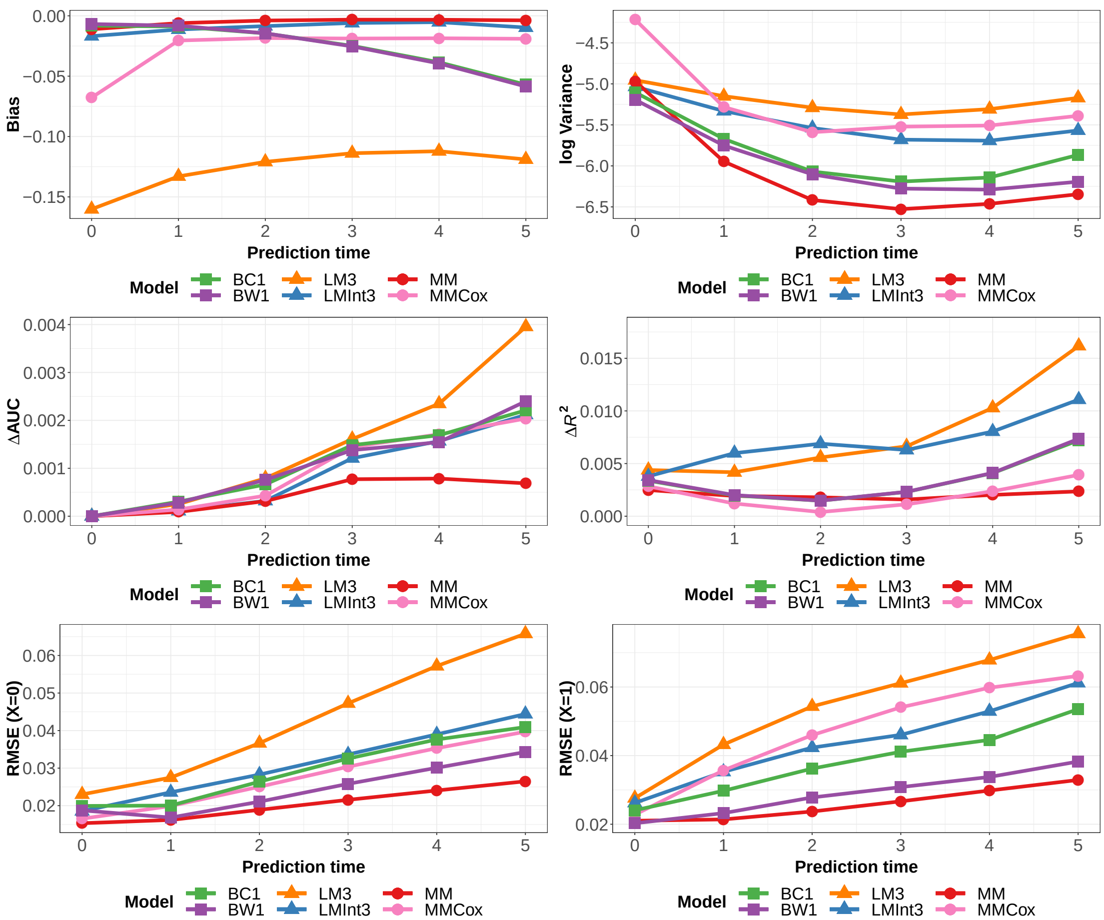


Figure C1: Simulation estimates for binary marker Scenario 1a for bias (upper-left) and variance (upper-right) for $Z(\tau) = 1, X = 1$, ΔAUC (middle-left), and ΔR^2 (middle-right), and RMSPE for $X = 0$ (bottom-left) and $X = 1$ (bottom-right) for predicted probability $P(T \leq \tau + 3|T > \tau, Z(\tau), X)$ from copula models (BC1), (BW1), joint models (MM), (MMCox), and landmark models (LM3), (LMInt3).

C.2 Scenario 1b Results

- Markov model; Marker observed at random inspection times (rate=1); Single baseline covariate X

Table C3: Simulation results for binary marker Scenario 1b.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 1b.

	τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
$X = 0$	0	0.015 (0.011)	0.016 (0.012)	0.024 (0.015)	0.018 (0.014)	0.024 (0.015)	0.018 (0.014)	0.020 (0.013)	0.019 (0.013)	0.020 (0.013)	0.019 (0.013)	0.020 (0.014)	0.019 (0.013)
	1	0.016 (0.010)	0.020 (0.013)	0.028 (0.014)	0.021 (0.014)	0.035 (0.015)	0.023 (0.014)	0.021 (0.013)	0.018 (0.010)	0.021 (0.013)	0.018 (0.010)	0.022 (0.013)	0.019 (0.010)
	2	0.019 (0.011)	0.025 (0.015)	0.039 (0.014)	0.026 (0.016)	0.048 (0.015)	0.028 (0.016)	0.027 (0.016)	0.022 (0.012)	0.027 (0.016)	0.022 (0.012)	0.028 (0.017)	0.023 (0.013)
	3	0.022 (0.012)	0.029 (0.017)	0.050 (0.017)	0.032 (0.018)	0.057 (0.018)	0.034 (0.019)	0.033 (0.020)	0.026 (0.015)	0.033 (0.020)	0.026 (0.015)	0.034 (0.020)	0.027 (0.016)
	4	0.024 (0.014)	0.035 (0.019)	0.060 (0.020)	0.037 (0.021)	0.062 (0.022)	0.039 (0.021)	0.038 (0.022)	0.030 (0.017)	0.038 (0.022)	0.030 (0.017)	0.038 (0.022)	0.031 (0.017)
	5	0.027 (0.015)	0.040 (0.021)	0.067 (0.023)	0.041 (0.023)	0.063 (0.026)	0.043 (0.024)	0.041 (0.024)	0.034 (0.019)	0.041 (0.024)	0.034 (0.019)	0.042 (0.024)	0.034 (0.019)
$X = 1$	0	0.021 (0.016)	0.023 (0.018)	0.029 (0.022)	0.026 (0.020)	0.029 (0.021)	0.026 (0.020)	0.025 (0.019)	0.021 (0.017)	0.026 (0.020)	0.022 (0.017)	0.025 (0.019)	0.021 (0.016)
	1	0.021 (0.014)	0.033 (0.022)	0.045 (0.021)	0.031 (0.021)	0.037 (0.023)	0.033 (0.022)	0.029 (0.020)	0.022 (0.015)	0.029 (0.020)	0.022 (0.015)	0.029 (0.019)	0.023 (0.014)
	2	0.023 (0.015)	0.040 (0.024)	0.055 (0.024)	0.037 (0.024)	0.046 (0.025)	0.038 (0.025)	0.034 (0.022)	0.026 (0.016)	0.034 (0.022)	0.026 (0.016)	0.035 (0.022)	0.027 (0.016)
	3	0.026 (0.017)	0.047 (0.027)	0.062 (0.026)	0.041 (0.027)	0.055 (0.028)	0.043 (0.028)	0.039 (0.025)	0.030 (0.017)	0.039 (0.025)	0.030 (0.017)	0.039 (0.025)	0.030 (0.017)
	4	0.029 (0.018)	0.052 (0.032)	0.067 (0.030)	0.047 (0.030)	0.066 (0.031)	0.049 (0.031)	0.044 (0.028)	0.034 (0.018)	0.044 (0.028)	0.033 (0.018)	0.044 (0.029)	0.034 (0.018)
	5	0.032 (0.020)	0.057 (0.037)	0.073 (0.033)	0.054 (0.034)	0.079 (0.036)	0.058 (0.035)	0.054 (0.032)	0.039 (0.020)	0.053 (0.031)	0.038 (0.019)	0.054 (0.033)	0.039 (0.020)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 1b.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)
1	0.668 (0.027)	0.668 (0.027)	0.668 (0.027)	0.667 (0.027)	0.666 (0.027)	0.668 (0.027)	0.667 (0.027)	0.667 (0.027)	0.667 (0.027)	0.667 (0.027)	0.667 (0.027)	0.667 (0.027)
2	0.687 (0.030)	0.687 (0.029)	0.687 (0.030)	0.687 (0.030)	0.685 (0.030)	0.687 (0.030)	0.687 (0.030)	0.687 (0.030)	0.687 (0.030)	0.687 (0.030)	0.687 (0.030)	0.687 (0.030)
3	0.695 (0.035)	0.695 (0.035)	0.695 (0.035)	0.695 (0.035)	0.693 (0.036)	0.695 (0.036)	0.695 (0.035)	0.695 (0.035)	0.695 (0.035)	0.695 (0.035)	0.694 (0.035)	0.695 (0.035)
4	0.696 (0.038)	0.695 (0.039)	0.695 (0.038)	0.695 (0.038)	0.694 (0.039)	0.695 (0.038)	0.695 (0.038)	0.695 (0.038)	0.695 (0.038)	0.695 (0.038)	0.695 (0.038)	0.695 (0.038)
5	0.691 (0.046)	0.691 (0.046)	0.690 (0.048)	0.691 (0.046)	0.690 (0.047)	0.690 (0.047)	0.691 (0.046)	0.691 (0.046)	0.691 (0.045)	0.691 (0.045)	0.691 (0.046)	0.691 (0.046)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 1b.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)
1	0.202 (0.010)	0.202 (0.010)	0.202 (0.010)	0.203 (0.010)	0.203 (0.010)	0.203 (0.010)	0.202 (0.010)	0.202 (0.010)	0.202 (0.010)	0.202 (0.010)	0.202 (0.010)	0.202 (0.010)
2	0.201 (0.011)	0.201 (0.011)	0.202 (0.011)	0.202 (0.011)	0.202 (0.011)	0.202 (0.011)	0.201 (0.011)	0.201 (0.011)	0.201 (0.011)	0.201 (0.011)	0.201 (0.011)	0.201 (0.011)
3	0.199 (0.013)	0.199 (0.012)	0.201 (0.013)	0.200 (0.013)	0.201 (0.013)	0.200 (0.013)	0.199 (0.012)	0.199 (0.012)	0.199 (0.012)	0.199 (0.012)	0.199 (0.012)	0.199 (0.012)
4	0.198 (0.014)	0.198 (0.014)	0.201 (0.014)	0.199 (0.014)	0.201 (0.014)	0.200 (0.014)	0.199 (0.013)	0.198 (0.013)	0.198 (0.013)	0.198 (0.013)	0.199 (0.013)	0.198 (0.013)
5	0.196 (0.016)	0.197 (0.016)	0.201 (0.017)	0.198 (0.017)	0.201 (0.017)	0.199 (0.017)	0.198 (0.015)	0.197 (0.015)	0.197 (0.015)	0.197 (0.015)	0.198 (0.015)	0.197 (0.015)

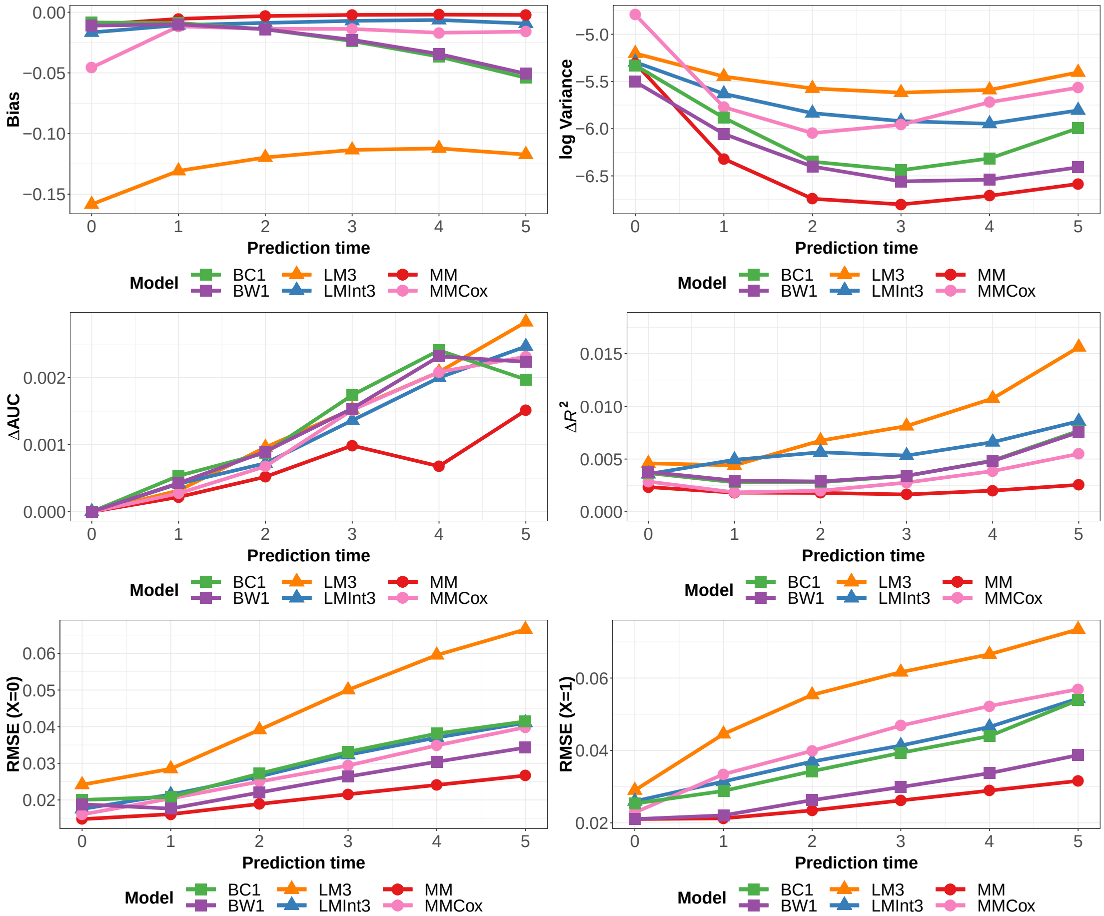


Figure C2: Simulation estimates for binary marker Scenario 1b for bias (upper-left) and variance (upper-right) for $Z(\tau) = 1, X = 1$, ΔAUC (middle-left), and ΔR^2 (middle-right), and RMSPE for $X = 0$ (bottom-left) and $X = 1$ (bottom-right) for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), X)$ from copula models (BC1), (BW1), joint models (MM), (MMCox), and landmark models (LM3), (LMInt3).

C.3 Scenario 1c Results

- Markov model; Marker observed continuously; Single baseline covariate X

Table C4: Simulation results for binary marker Scenario 1c.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 1c.

	τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
	0	0.015 (0.011)	0.016 (0.013)	0.023 (0.014)	0.016 (0.012)	0.023 (0.014)	0.016 (0.012)	0.020 (0.013)	0.019 (0.013)	0.020 (0.013)	0.018 (0.013)	0.020 (0.013)	0.019 (0.013)
	1	0.017 (0.010)	0.022 (0.013)	0.037 (0.011)	0.022 (0.013)	0.047 (0.015)	0.024 (0.014)	0.024 (0.013)	0.021 (0.011)	0.024 (0.013)	0.021 (0.011)	0.025 (0.014)	0.022 (0.012)
	2	0.020 (0.011)	0.026 (0.014)	0.049 (0.014)	0.026 (0.015)	0.058 (0.015)	0.028 (0.016)	0.029 (0.017)	0.024 (0.013)	0.029 (0.017)	0.024 (0.014)	0.030 (0.017)	0.025 (0.014)
$X = 0$	3	0.022 (0.012)	0.030 (0.017)	0.060 (0.018)	0.030 (0.018)	0.064 (0.019)	0.032 (0.018)	0.034 (0.021)	0.027 (0.016)	0.034 (0.021)	0.028 (0.016)	0.034 (0.021)	0.028 (0.016)
	4	0.024 (0.014)	0.035 (0.018)	0.069 (0.021)	0.035 (0.020)	0.067 (0.023)	0.037 (0.020)	0.038 (0.023)	0.031 (0.018)	0.038 (0.023)	0.031 (0.018)	0.039 (0.023)	0.031 (0.018)
	5	0.026 (0.015)	0.039 (0.022)	0.076 (0.024)	0.039 (0.022)	0.066 (0.027)	0.040 (0.022)	0.042 (0.024)	0.034 (0.019)	0.041 (0.024)	0.034 (0.020)	0.043 (0.024)	0.035 (0.020)
	0	0.020 (0.016)	0.023 (0.018)	0.027 (0.020)	0.023 (0.018)	0.027 (0.020)	0.024 (0.018)	0.025 (0.019)	0.020 (0.016)	0.025 (0.019)	0.021 (0.016)	0.024 (0.019)	0.020 (0.016)
	1	0.021 (0.014)	0.029 (0.018)	0.050 (0.018)	0.030 (0.018)	0.038 (0.021)	0.032 (0.019)	0.030 (0.019)	0.023 (0.014)	0.029 (0.019)	0.023 (0.014)	0.030 (0.019)	0.024 (0.014)
	2	0.023 (0.014)	0.031 (0.019)	0.056 (0.021)	0.033 (0.020)	0.046 (0.022)	0.033 (0.020)	0.033 (0.020)	0.026 (0.015)	0.033 (0.020)	0.026 (0.015)	0.033 (0.020)	0.026 (0.015)
$X = 1$	3	0.025 (0.015)	0.036 (0.022)	0.061 (0.023)	0.037 (0.022)	0.057 (0.025)	0.038 (0.023)	0.038 (0.023)	0.031 (0.016)	0.038 (0.023)	0.030 (0.016)	0.038 (0.023)	0.031 (0.016)
	4	0.027 (0.017)	0.042 (0.026)	0.064 (0.026)	0.041 (0.026)	0.069 (0.029)	0.043 (0.026)	0.046 (0.027)	0.039 (0.019)	0.044 (0.027)	0.037 (0.019)	0.046 (0.028)	0.039 (0.019)
	5	0.029 (0.018)	0.050 (0.031)	0.071 (0.029)	0.048 (0.030)	0.084 (0.033)	0.052 (0.030)	0.063 (0.036)	0.051 (0.024)	0.060 (0.035)	0.047 (0.024)	0.064 (0.036)	0.051 (0.025)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 1c.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)	0.638 (0.024)
1	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)	0.679 (0.028)	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)	0.681 (0.028)
2	0.702 (0.030)	0.701 (0.030)	0.701 (0.031)	0.701 (0.030)	0.699 (0.031)	0.701 (0.030)	0.701 (0.030)	0.701 (0.030)	0.701 (0.030)	0.701 (0.030)	0.701 (0.030)	0.701 (0.030)
3	0.707 (0.036)	0.707 (0.035)	0.706 (0.036)	0.706 (0.035)	0.705 (0.036)	0.706 (0.035)	0.707 (0.036)	0.707 (0.036)	0.707 (0.036)	0.707 (0.036)	0.706 (0.035)	0.707 (0.035)
4	0.705 (0.038)	0.705 (0.039)	0.705 (0.039)	0.704 (0.039)	0.705 (0.040)	0.704 (0.039)	0.704 (0.038)	0.705 (0.038)	0.705 (0.038)	0.705 (0.038)	0.704 (0.038)	0.704 (0.038)
5	0.700 (0.046)	0.700 (0.046)	0.698 (0.048)	0.699 (0.047)	0.700 (0.048)	0.699 (0.047)	0.700 (0.047)	0.700 (0.047)	0.700 (0.047)	0.700 (0.047)	0.699 (0.047)	0.699 (0.047)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 1c.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)	0.195 (0.009)
1	0.196 (0.010)	0.196 (0.010)	0.198 (0.010)	0.196 (0.010)	0.198 (0.011)	0.197 (0.010)	0.196 (0.010)	0.196 (0.010)	0.196 (0.010)	0.196 (0.010)	0.196 (0.010)	0.196 (0.010)
2	0.194 (0.011)	0.195 (0.011)	0.197 (0.011)	0.195 (0.011)	0.197 (0.011)	0.195 (0.011)	0.195 (0.011)	0.194 (0.011)	0.194 (0.011)	0.194 (0.011)	0.195 (0.011)	0.194 (0.011)
3	0.193 (0.013)	0.193 (0.013)	0.196 (0.013)	0.193 (0.013)	0.196 (0.013)	0.193 (0.013)	0.194 (0.012)	0.193 (0.012)	0.193 (0.012)	0.193 (0.012)	0.194 (0.012)	0.193 (0.012)
4	0.192 (0.014)	0.193 (0.015)	0.197 (0.014)	0.193 (0.015)	0.197 (0.014)	0.193 (0.015)	0.194 (0.014)	0.193 (0.014)	0.193 (0.014)	0.193 (0.014)	0.194 (0.014)	0.193 (0.014)
5	0.191 (0.017)	0.193 (0.017)	0.197 (0.017)	0.192 (0.017)	0.196 (0.016)	0.193 (0.017)	0.193 (0.016)	0.192 (0.015)	0.192 (0.015)	0.192 (0.015)	0.193 (0.016)	0.192 (0.015)

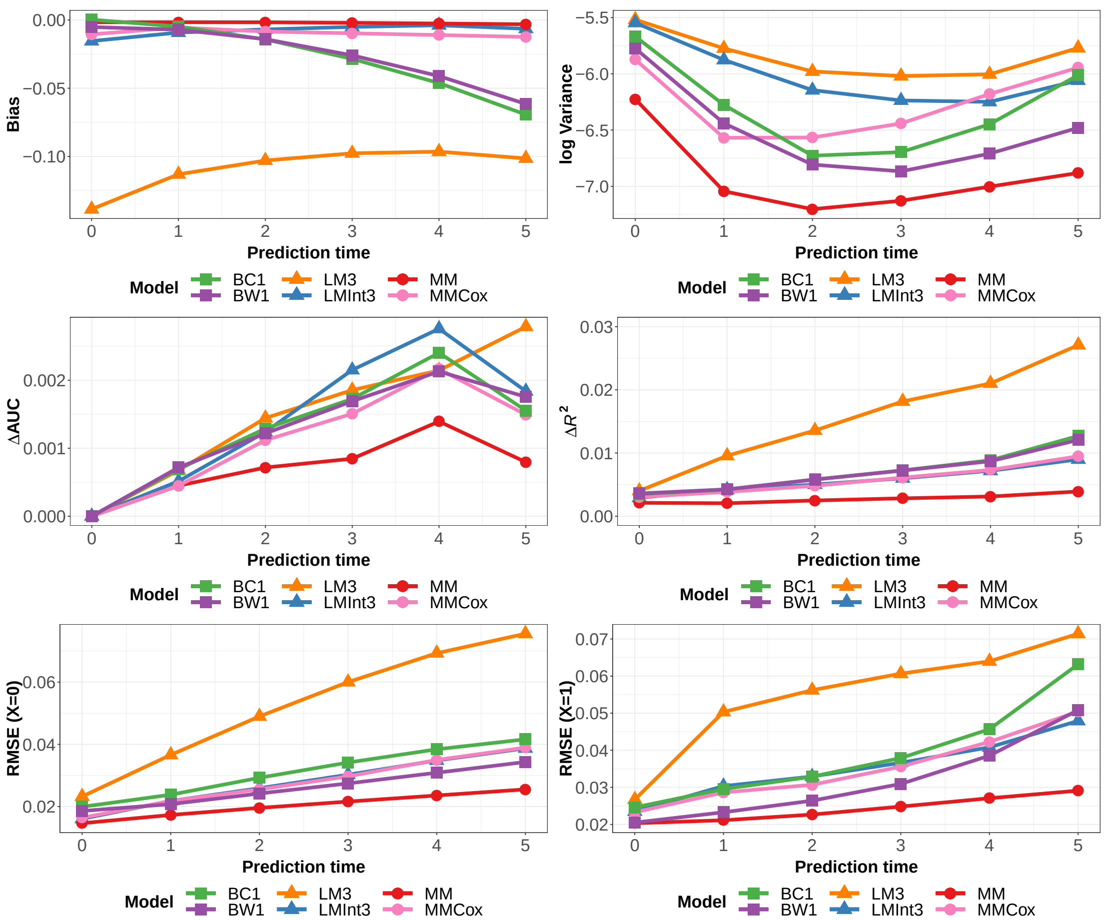


Figure C3: Simulation estimates for binary marker Scenario 1c for bias (upper-left) and variance (upper-right) for $Z(\tau) = 1, X = 1$, ΔAUC (middle-left), and ΔR^2 (middle-right), and RMSPE for $X = 0$ (bottom-left) and $X = 1$ (bottom-right) for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), X)$ from copula models (BC1), (BW1), joint models (MM), (MMCox), and landmark models (LM3), (LMInt3).

C.4 Scenario 2a Results

- Semi-Markov model; Marker observed at random inspection times (rate=0.5); Single baseline covariate X

Table C5: Simulation results for binary marker Scenario 2a.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 2a.

	τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
	0	0.013 (0.010)	0.016 (0.012)	0.014 (0.011)	0.023 (0.015)	0.022 (0.015)	0.021 (0.014)	0.020 (0.013)	0.021 (0.014)	0.020 (0.013)	0.021 (0.014)	0.020 (0.013)
	1	0.014 (0.009)	0.019 (0.012)	0.015 (0.010)	0.031 (0.016)	0.033 (0.016)	0.020 (0.012)	0.017 (0.010)	0.020 (0.012)	0.017 (0.010)	0.021 (0.012)	0.018 (0.010)
	2	0.016 (0.010)	0.025 (0.015)	0.018 (0.011)	0.043 (0.017)	0.046 (0.017)	0.026 (0.015)	0.021 (0.012)	0.026 (0.015)	0.021 (0.012)	0.027 (0.015)	0.022 (0.012)
$X = 0$	3	0.019 (0.011)	0.030 (0.017)	0.022 (0.012)	0.054 (0.020)	0.055 (0.020)	0.032 (0.018)	0.026 (0.014)	0.032 (0.018)	0.026 (0.014)	0.033 (0.018)	0.027 (0.014)
	4	0.021 (0.011)	0.037 (0.020)	0.025 (0.013)	0.064 (0.022)	0.062 (0.024)	0.038 (0.021)	0.031 (0.016)	0.038 (0.021)	0.031 (0.016)	0.038 (0.021)	0.031 (0.016)
	5	0.025 (0.013)	0.043 (0.024)	0.028 (0.014)	0.072 (0.026)	0.068 (0.029)	0.043 (0.026)	0.035 (0.018)	0.043 (0.026)	0.035 (0.018)	0.043 (0.026)	0.036 (0.018)
	0	0.021 (0.016)	0.022 (0.017)	0.021 (0.015)	0.027 (0.020)	0.027 (0.020)	0.023 (0.018)	0.021 (0.016)	0.023 (0.017)	0.021 (0.016)	0.023 (0.018)	0.021 (0.016)
	1	0.023 (0.015)	0.040 (0.026)	0.022 (0.015)	0.043 (0.025)	0.041 (0.024)	0.034 (0.023)	0.026 (0.017)	0.034 (0.024)	0.026 (0.018)	0.034 (0.023)	0.026 (0.017)
	2	0.026 (0.017)	0.052 (0.031)	0.026 (0.016)	0.052 (0.029)	0.048 (0.027)	0.041 (0.027)	0.032 (0.020)	0.041 (0.027)	0.032 (0.020)	0.041 (0.027)	0.031 (0.020)
$X = 1$	3	0.029 (0.018)	0.060 (0.032)	0.029 (0.017)	0.058 (0.030)	0.058 (0.030)	0.044 (0.027)	0.035 (0.021)	0.044 (0.027)	0.035 (0.021)	0.044 (0.027)	0.035 (0.021)
	4	0.032 (0.020)	0.067 (0.035)	0.032 (0.018)	0.068 (0.031)	0.073 (0.033)	0.046 (0.028)	0.038 (0.021)	0.046 (0.027)	0.038 (0.020)	0.047 (0.028)	0.038 (0.021)
	5	0.036 (0.021)	0.074 (0.041)	0.034 (0.019)	0.078 (0.036)	0.087 (0.039)	0.054 (0.031)	0.042 (0.020)	0.054 (0.031)	0.043 (0.020)	0.056 (0.031)	0.043 (0.021)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 2a.

τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)	0.629 (0.026)
1	0.657 (0.027)	0.657 (0.027)	0.657 (0.027)	0.656 (0.027)	0.656 (0.027)	0.657 (0.027)	0.657 (0.027)	0.657 (0.027)	0.657 (0.027)	0.657 (0.027)	0.657 (0.027)
2	0.677 (0.028)	0.677 (0.028)	0.677 (0.028)	0.676 (0.028)	0.675 (0.029)	0.677 (0.028)	0.677 (0.028)	0.677 (0.028)	0.677 (0.028)	0.677 (0.028)	0.677 (0.028)
3	0.690 (0.032)	0.690 (0.032)	0.690 (0.032)	0.687 (0.033)	0.687 (0.033)	0.690 (0.032)	0.690 (0.031)	0.690 (0.032)	0.690 (0.032)	0.690 (0.032)	0.690 (0.032)
4	0.694 (0.037)	0.693 (0.037)	0.693 (0.038)	0.690 (0.038)	0.690 (0.039)	0.693 (0.037)	0.693 (0.037)	0.693 (0.037)	0.693 (0.037)	0.693 (0.037)	0.693 (0.037)
5	0.691 (0.042)	0.690 (0.043)	0.691 (0.043)	0.687 (0.044)	0.687 (0.045)	0.691 (0.043)	0.691 (0.043)	0.691 (0.043)	0.691 (0.043)	0.691 (0.043)	0.691 (0.043)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 2a.

τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.192 (0.009)	0.192 (0.010)	0.192 (0.009)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)	0.192 (0.010)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)
1	0.201 (0.010)	0.201 (0.010)	0.201 (0.010)	0.202 (0.010)	0.202 (0.010)	0.201 (0.010)	0.201 (0.010)	0.201 (0.010)	0.201 (0.010)	0.201 (0.010)	0.201 (0.010)
2	0.201 (0.010)	0.201 (0.010)	0.202 (0.010)	0.203 (0.011)	0.203 (0.011)	0.202 (0.010)	0.201 (0.010)	0.202 (0.010)	0.202 (0.010)	0.202 (0.010)	0.201 (0.010)
3	0.200 (0.012)	0.199 (0.012)	0.200 (0.013)	0.202 (0.013)	0.202 (0.013)	0.200 (0.012)	0.199 (0.012)	0.200 (0.012)	0.200 (0.012)	0.200 (0.012)	0.199 (0.012)
4	0.198 (0.014)	0.198 (0.014)	0.198 (0.015)	0.201 (0.015)	0.201 (0.015)	0.199 (0.014)	0.198 (0.014)	0.199 (0.014)	0.199 (0.014)	0.199 (0.014)	0.198 (0.014)
5	0.196 (0.016)	0.196 (0.016)	0.196 (0.016)	0.200 (0.017)	0.201 (0.017)	0.198 (0.015)	0.196 (0.015)	0.198 (0.015)	0.198 (0.015)	0.198 (0.015)	0.196 (0.015)

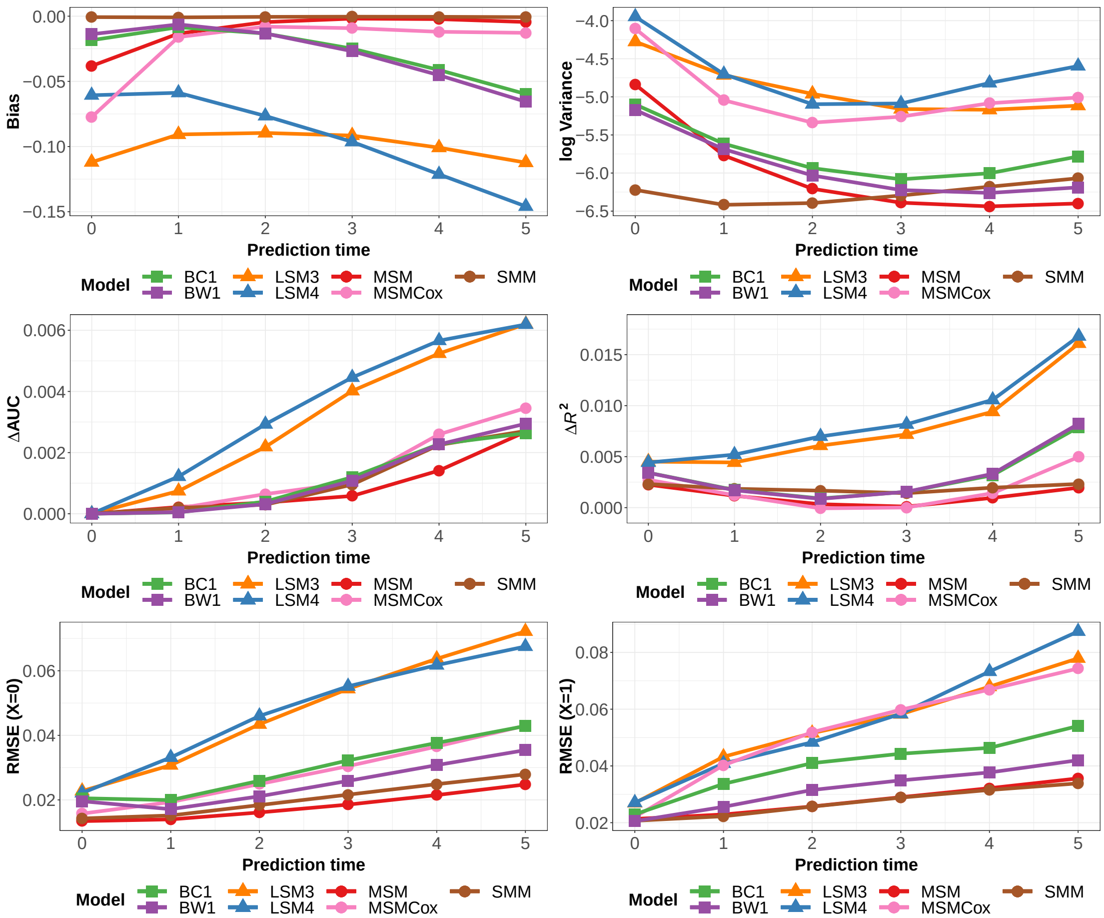


Figure C4: Simulation estimates for binary marker Scenario 2a for bias (upper-left) and variance (upper-right) for $Z(\tau) = 1, X = 1$, ΔAUC (middle-left), and ΔR^2 (middle-right), and RMSPE for $X = 0$ (bottom-left) and $X = 1$ (bottom-right) for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), X)$ from copula models (BC1), (BW1), joint models (MSM), (MSMCox), (SMM), and landmark models (LSM3), (LSM4).

C.5 Scenario 2b Results

- Semi-Markov model; Marker observed at random inspection times (rate=1); Single baseline covariate X

Table C6: Simulation results for binary marker Scenario 2b.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 2b.

	τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
	0	0.013 (0.011)	0.015 (0.012)	0.014 (0.011)	0.024 (0.016)	0.023 (0.016)	0.021 (0.014)	0.020 (0.013)	0.021 (0.014)	0.020 (0.013)	0.021 (0.014)	0.020 (0.014)
	1	0.014 (0.010)	0.020 (0.013)	0.016 (0.010)	0.034 (0.015)	0.038 (0.015)	0.021 (0.013)	0.018 (0.010)	0.021 (0.013)	0.018 (0.011)	0.022 (0.013)	0.019 (0.011)
	2	0.017 (0.010)	0.025 (0.015)	0.019 (0.011)	0.047 (0.016)	0.051 (0.016)	0.027 (0.016)	0.022 (0.012)	0.027 (0.016)	0.022 (0.012)	0.028 (0.016)	0.023 (0.013)
$X = 0$	3	0.019 (0.011)	0.030 (0.016)	0.022 (0.012)	0.058 (0.019)	0.060 (0.019)	0.033 (0.018)	0.026 (0.015)	0.033 (0.018)	0.027 (0.015)	0.033 (0.018)	0.027 (0.015)
	4	0.022 (0.012)	0.035 (0.020)	0.025 (0.013)	0.067 (0.023)	0.065 (0.024)	0.038 (0.021)	0.031 (0.017)	0.038 (0.021)	0.031 (0.017)	0.038 (0.021)	0.031 (0.017)
	5	0.025 (0.013)	0.041 (0.022)	0.028 (0.014)	0.075 (0.026)	0.069 (0.029)	0.042 (0.025)	0.035 (0.018)	0.042 (0.025)	0.035 (0.018)	0.043 (0.025)	0.036 (0.018)
	0	0.021 (0.016)	0.022 (0.016)	0.020 (0.015)	0.028 (0.020)	0.028 (0.020)	0.024 (0.018)	0.022 (0.017)	0.024 (0.018)	0.022 (0.017)	0.024 (0.018)	0.022 (0.016)
	1	0.023 (0.015)	0.037 (0.025)	0.022 (0.015)	0.044 (0.024)	0.039 (0.023)	0.032 (0.022)	0.024 (0.015)	0.032 (0.022)	0.024 (0.016)	0.032 (0.022)	0.024 (0.015)
	2	0.026 (0.016)	0.045 (0.028)	0.025 (0.016)	0.054 (0.026)	0.048 (0.024)	0.039 (0.024)	0.029 (0.017)	0.039 (0.025)	0.029 (0.017)	0.039 (0.025)	0.029 (0.017)
$X = 1$	3	0.028 (0.017)	0.051 (0.029)	0.029 (0.016)	0.061 (0.027)	0.060 (0.027)	0.042 (0.024)	0.033 (0.018)	0.042 (0.024)	0.033 (0.018)	0.042 (0.024)	0.032 (0.018)
	4	0.031 (0.018)	0.056 (0.032)	0.031 (0.017)	0.067 (0.029)	0.072 (0.031)	0.045 (0.027)	0.036 (0.019)	0.045 (0.026)	0.036 (0.018)	0.045 (0.027)	0.036 (0.019)
	5	0.033 (0.019)	0.063 (0.036)	0.033 (0.018)	0.078 (0.033)	0.087 (0.037)	0.053 (0.030)	0.041 (0.019)	0.053 (0.030)	0.041 (0.019)	0.054 (0.031)	0.042 (0.020)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 2b.

τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)	0.630 (0.026)
1	0.660 (0.027)	0.660 (0.027)	0.660 (0.027)	0.659 (0.027)	0.659 (0.027)	0.660 (0.027)	0.660 (0.027)	0.660 (0.027)	0.660 (0.027)	0.660 (0.027)	0.660 (0.027)
2	0.683 (0.028)	0.683 (0.029)	0.683 (0.029)	0.681 (0.028)	0.680 (0.029)	0.683 (0.028)	0.683 (0.029)	0.683 (0.028)	0.683 (0.028)	0.683 (0.028)	0.683 (0.028)
3	0.696 (0.031)	0.696 (0.032)	0.696 (0.031)	0.694 (0.033)	0.693 (0.033)	0.696 (0.032)	0.695 (0.032)	0.696 (0.032)	0.696 (0.032)	0.696 (0.032)	0.696 (0.032)
4	0.699 (0.038)	0.698 (0.037)	0.698 (0.038)	0.697 (0.039)	0.696 (0.040)	0.698 (0.038)	0.699 (0.038)	0.699 (0.038)	0.699 (0.038)	0.699 (0.038)	0.699 (0.038)
5	0.696 (0.045)	0.695 (0.044)	0.696 (0.045)	0.694 (0.043)	0.694 (0.043)	0.696 (0.045)	0.696 (0.045)	0.696 (0.045)	0.696 (0.045)	0.696 (0.045)	0.696 (0.045)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 2b.

τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.192 (0.009)	0.192 (0.009)	0.192 (0.009)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)	0.192 (0.010)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)	0.192 (0.010)
1	0.200 (0.010)	0.200 (0.010)	0.200 (0.010)	0.201 (0.010)	0.201 (0.010)	0.200 (0.010)	0.200 (0.010)	0.200 (0.010)	0.200 (0.010)	0.200 (0.010)	0.200 (0.010)
2	0.199 (0.011)	0.199 (0.010)	0.199 (0.011)	0.201 (0.011)	0.201 (0.011)	0.199 (0.010)	0.199 (0.010)	0.199 (0.010)	0.199 (0.010)	0.199 (0.010)	0.199 (0.010)
3	0.196 (0.012)	0.197 (0.012)	0.197 (0.012)	0.199 (0.012)	0.199 (0.012)	0.197 (0.012)	0.196 (0.012)	0.197 (0.012)	0.197 (0.012)	0.197 (0.012)	0.196 (0.012)
4	0.195 (0.015)	0.196 (0.014)	0.195 (0.015)	0.198 (0.015)	0.199 (0.015)	0.196 (0.014)	0.195 (0.014)	0.196 (0.014)	0.196 (0.014)	0.196 (0.014)	0.195 (0.014)
5	0.193 (0.017)	0.194 (0.017)	0.193 (0.017)	0.198 (0.016)	0.198 (0.016)	0.195 (0.016)	0.194 (0.016)	0.195 (0.016)	0.195 (0.016)	0.195 (0.016)	0.194 (0.016)

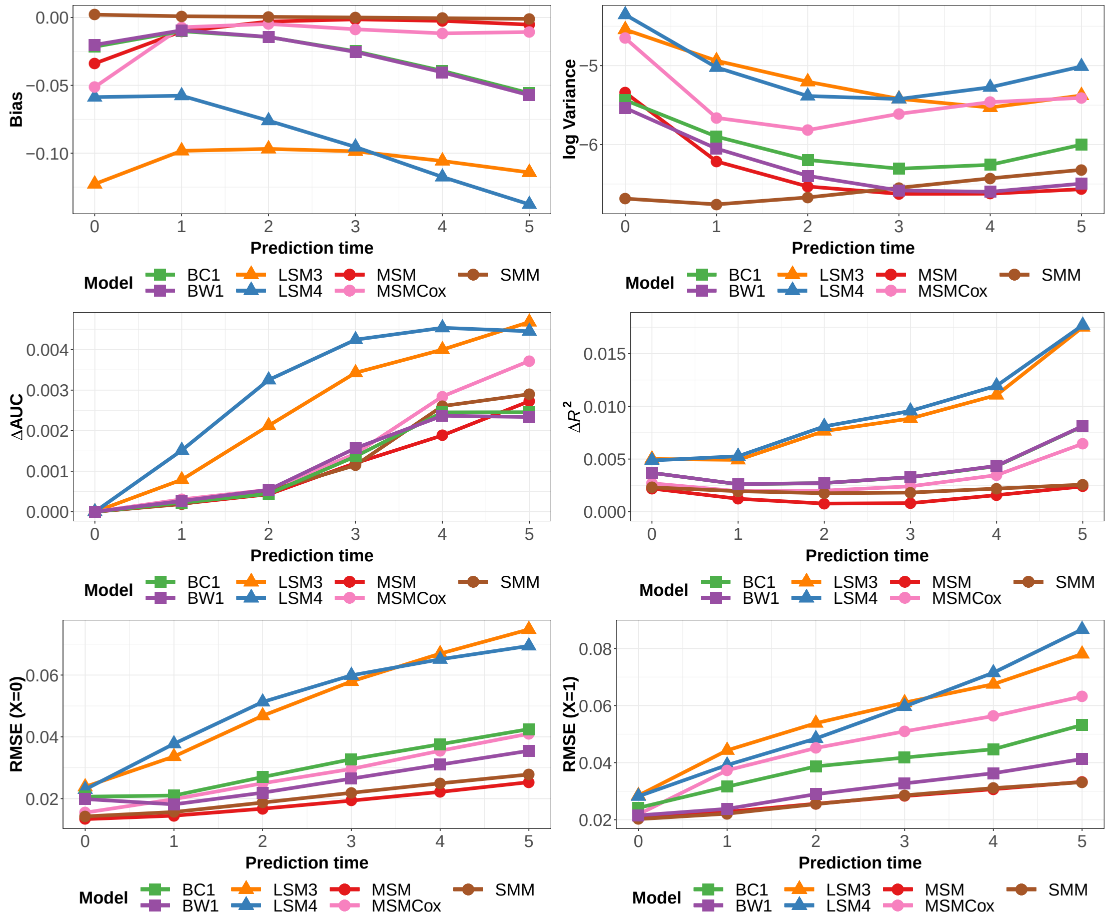


Figure C5: Simulation estimates for binary marker Scenario 2b for bias (upper-left) and variance (upper-right) for $Z(\tau) = 1, X = 1$, ΔAUC (middle-left), and ΔR^2 (middle-right), and RMSPE for $X = 0$ (bottom-left) and $X = 1$ (bottom-right) for predicted probability $P(T \leq \tau + 3|T > \tau, Z(\tau), X)$ from copula models (BC1), (BW1), joint models (MSM), (MSMCox), (SMM), and landmark models (LSM3), (LSM4).

C.6 Scenario 2c Results

- Semi-Markov model; Marker observed continuously; Single baseline covariate X

Table C7: Simulation results for binary marker Scenario 2c.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 2c.

	τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
	0	0.015 (0.011)	0.016 (0.013)	0.010 (0.008)	0.023 (0.014)	0.023 (0.014)	0.021 (0.013)	0.020 (0.013)	0.021 (0.014)	0.020 (0.013)	0.021 (0.013)	0.019 (0.013)
	1	0.017 (0.010)	0.022 (0.013)	0.012 (0.007)	0.041 (0.013)	0.048 (0.015)	0.025 (0.014)	0.022 (0.012)	0.025 (0.014)	0.022 (0.011)	0.026 (0.014)	0.023 (0.012)
	2	0.020 (0.011)	0.026 (0.014)	0.014 (0.007)	0.055 (0.016)	0.061 (0.015)	0.030 (0.017)	0.025 (0.014)	0.030 (0.017)	0.025 (0.014)	0.030 (0.018)	0.025 (0.015)
$X = 0$	3	0.023 (0.013)	0.031 (0.016)	0.016 (0.008)	0.066 (0.018)	0.068 (0.019)	0.035 (0.021)	0.028 (0.016)	0.035 (0.021)	0.028 (0.016)	0.035 (0.021)	0.028 (0.016)
	4	0.026 (0.015)	0.036 (0.018)	0.017 (0.009)	0.074 (0.021)	0.071 (0.023)	0.040 (0.022)	0.032 (0.018)	0.040 (0.022)	0.032 (0.018)	0.040 (0.022)	0.032 (0.018)
	5	0.029 (0.016)	0.042 (0.021)	0.019 (0.010)	0.080 (0.024)	0.072 (0.027)	0.043 (0.024)	0.036 (0.020)	0.043 (0.024)	0.036 (0.020)	0.045 (0.025)	0.038 (0.021)
	0	0.021 (0.016)	0.023 (0.018)	0.015 (0.012)	0.027 (0.020)	0.027 (0.020)	0.025 (0.019)	0.021 (0.016)	0.025 (0.019)	0.021 (0.016)	0.025 (0.019)	0.021 (0.016)
	1	0.024 (0.014)	0.030 (0.018)	0.016 (0.010)	0.048 (0.021)	0.040 (0.021)	0.031 (0.019)	0.024 (0.014)	0.031 (0.019)	0.025 (0.014)	0.033 (0.018)	0.026 (0.014)
	2	0.026 (0.015)	0.033 (0.019)	0.018 (0.010)	0.055 (0.022)	0.048 (0.021)	0.034 (0.020)	0.026 (0.015)	0.034 (0.020)	0.027 (0.015)	0.034 (0.020)	0.026 (0.015)
$X = 1$	3	0.029 (0.015)	0.038 (0.021)	0.019 (0.010)	0.062 (0.024)	0.061 (0.025)	0.037 (0.022)	0.029 (0.016)	0.037 (0.022)	0.029 (0.016)	0.036 (0.022)	0.029 (0.016)
	4	0.031 (0.017)	0.046 (0.026)	0.020 (0.011)	0.070 (0.027)	0.074 (0.030)	0.044 (0.026)	0.037 (0.019)	0.044 (0.026)	0.037 (0.019)	0.046 (0.026)	0.039 (0.019)
	5	0.034 (0.018)	0.053 (0.030)	0.021 (0.011)	0.082 (0.032)	0.090 (0.034)	0.063 (0.035)	0.051 (0.025)	0.062 (0.034)	0.050 (0.025)	0.067 (0.034)	0.055 (0.025)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 2c.

τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.630 (0.027)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)	0.631 (0.025)
1	0.676 (0.028)	0.676 (0.028)	0.677 (0.028)	0.675 (0.029)	0.673 (0.029)	0.676 (0.028)	0.676 (0.028)	0.676 (0.028)	0.675 (0.028)	0.675 (0.028)	0.675 (0.028)
2	0.698 (0.031)	0.698 (0.031)	0.699 (0.031)	0.696 (0.031)	0.694 (0.031)	0.698 (0.031)	0.698 (0.031)	0.698 (0.031)	0.697 (0.031)	0.697 (0.031)	0.697 (0.031)
3	0.705 (0.036)	0.705 (0.037)	0.707 (0.036)	0.703 (0.037)	0.702 (0.037)	0.705 (0.036)	0.705 (0.036)	0.705 (0.036)	0.704 (0.036)	0.704 (0.036)	0.704 (0.036)
4	0.707 (0.039)	0.705 (0.039)	0.709 (0.038)	0.704 (0.040)	0.704 (0.040)	0.705 (0.039)	0.705 (0.039)	0.705 (0.039)	0.705 (0.039)	0.705 (0.039)	0.705 (0.039)
5	0.702 (0.047)	0.701 (0.047)	0.706 (0.046)	0.699 (0.047)	0.700 (0.047)	0.700 (0.046)	0.701 (0.046)	0.700 (0.046)	0.701 (0.047)	0.701 (0.047)	0.701 (0.047)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 2c.

τ	MSM	MSMCox	SMM	LSM3	LSM4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.192 (0.009)	0.192 (0.009)	0.191 (0.009)	0.193 (0.009)	0.193 (0.009)	0.192 (0.010)	0.192 (0.010)	0.193 (0.010)	0.192 (0.010)	0.192 (0.010)	0.192 (0.010)
1	0.194 (0.010)	0.194 (0.010)	0.193 (0.010)	0.195 (0.011)	0.195 (0.011)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)
2	0.192 (0.011)	0.192 (0.011)	0.191 (0.011)	0.195 (0.011)	0.195 (0.011)	0.192 (0.011)	0.192 (0.011)	0.192 (0.011)	0.192 (0.011)	0.192 (0.011)	0.192 (0.011)
3	0.191 (0.013)	0.191 (0.014)	0.189 (0.013)	0.194 (0.013)	0.195 (0.013)	0.191 (0.013)	0.191 (0.013)	0.191 (0.013)	0.191 (0.013)	0.191 (0.013)	0.191 (0.013)
4	0.190 (0.015)	0.191 (0.015)	0.188 (0.015)	0.194 (0.015)	0.194 (0.014)	0.191 (0.014)	0.190 (0.014)	0.191 (0.014)	0.191 (0.014)	0.191 (0.014)	0.190 (0.014)
5	0.188 (0.017)	0.190 (0.018)	0.187 (0.017)	0.195 (0.017)	0.194 (0.017)	0.190 (0.017)	0.189 (0.016)	0.190 (0.017)	0.191 (0.017)	0.191 (0.017)	0.190 (0.016)

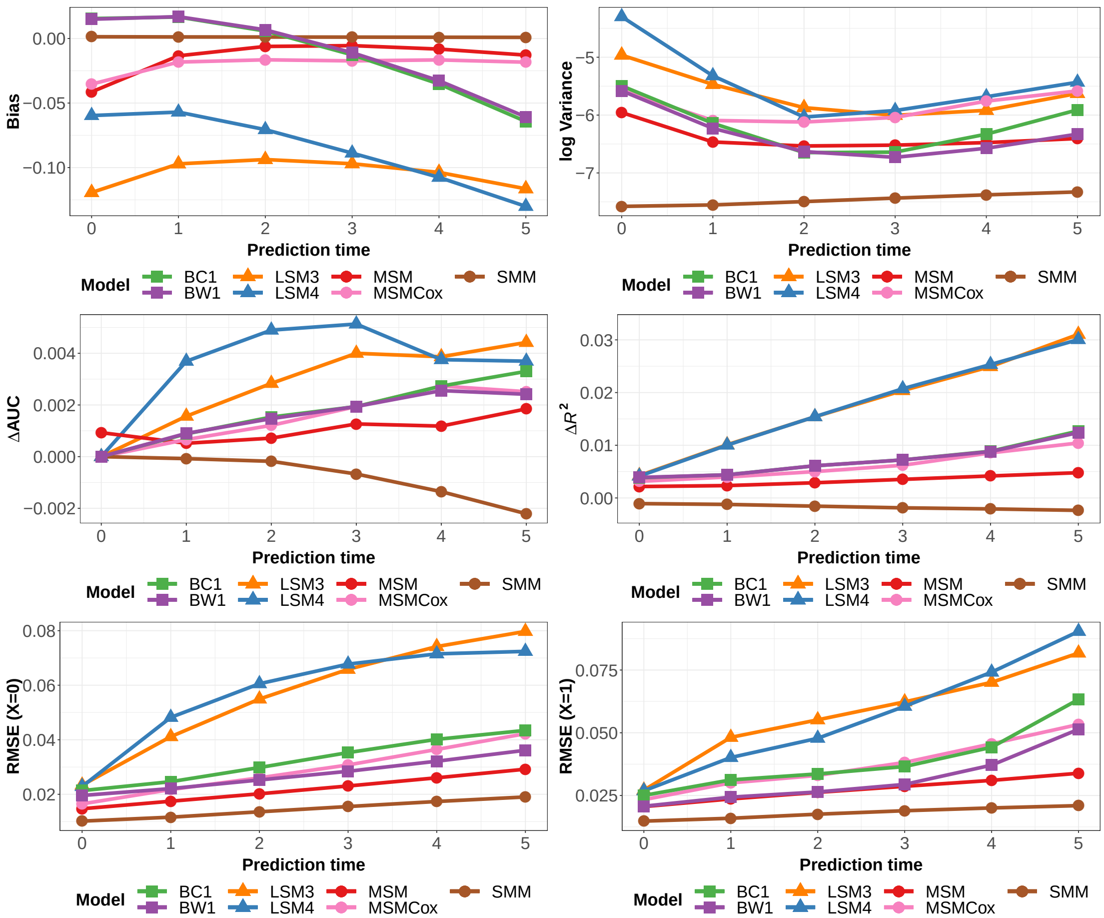


Figure C6: Simulation estimates for binary marker Scenario 2c for bias (upper-left) and variance (upper-right) for $Z(\tau) = 1, X = 1$, ΔAUC (middle-left), and ΔR^2 (middle-right), and RMSPE for $X = 0$ (bottom-left) and $X = 1$ (bottom-right) for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), X)$ from copula models (BC1), (BW1), joint models (MSM), (MSMCox), (SMM), and landmark models (LSM3), (LSM4).

C.7 Scenario 3a Results

- Markov model; Marker observed at random inspection times (rate=0.5); Two baseline covariates X_1, X_2

Table C8: Simulation results for binary marker Scenario 3a.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 3a.

	τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
$X_1 = 0$, $X_2 = 0$	0	0.018 (0.013)	0.022 (0.014)	0.027 (0.018)	0.022 (0.016)	0.027 (0.018)	0.022 (0.016)	0.028 (0.017)	0.029 (0.016)	0.029 (0.017)	0.029 (0.016)	0.029 (0.017)	0.029 (0.016)
	1	0.018 (0.012)	0.022 (0.014)	0.029 (0.017)	0.026 (0.017)	0.033 (0.018)	0.027 (0.017)	0.024 (0.015)	0.023 (0.014)	0.024 (0.015)	0.024 (0.014)	0.025 (0.015)	0.024 (0.014)
	2	0.021 (0.012)	0.025 (0.015)	0.034 (0.018)	0.031 (0.019)	0.039 (0.018)	0.032 (0.019)	0.027 (0.015)	0.024 (0.013)	0.027 (0.015)	0.024 (0.013)	0.028 (0.015)	0.025 (0.013)
	3	0.024 (0.013)	0.030 (0.016)	0.040 (0.019)	0.035 (0.021)	0.044 (0.020)	0.036 (0.021)	0.031 (0.017)	0.026 (0.014)	0.031 (0.017)	0.026 (0.014)	0.031 (0.017)	0.026 (0.014)
	4	0.026 (0.014)	0.032 (0.018)	0.046 (0.020)	0.040 (0.022)	0.047 (0.021)	0.041 (0.022)	0.033 (0.018)	0.028 (0.015)	0.033 (0.018)	0.028 (0.015)	0.033 (0.018)	0.028 (0.015)
	5	0.029 (0.016)	0.037 (0.020)	0.050 (0.022)	0.043 (0.024)	0.049 (0.024)	0.045 (0.025)	0.036 (0.019)	0.030 (0.016)	0.037 (0.019)	0.030 (0.016)	0.037 (0.019)	0.031 (0.017)
$X_1 = 1$, $X_2 = 0$	0	0.027 (0.020)	0.030 (0.024)	0.048 (0.034)	0.036 (0.027)	0.046 (0.034)	0.036 (0.027)	0.031 (0.024)	0.029 (0.023)	0.031 (0.024)	0.028 (0.022)	0.032 (0.024)	0.029 (0.023)
	1	0.028 (0.021)	0.045 (0.032)	0.062 (0.036)	0.040 (0.030)	0.055 (0.036)	0.041 (0.030)	0.046 (0.033)	0.039 (0.026)	0.044 (0.032)	0.037 (0.026)	0.047 (0.033)	0.040 (0.027)
	2	0.030 (0.021)	0.057 (0.034)	0.073 (0.035)	0.046 (0.031)	0.064 (0.035)	0.047 (0.031)	0.056 (0.034)	0.046 (0.029)	0.054 (0.034)	0.043 (0.028)	0.056 (0.035)	0.046 (0.029)
	3	0.033 (0.023)	0.063 (0.037)	0.078 (0.035)	0.051 (0.033)	0.072 (0.036)	0.051 (0.034)	0.058 (0.036)	0.048 (0.030)	0.055 (0.035)	0.046 (0.029)	0.058 (0.036)	0.048 (0.030)
	4	0.035 (0.024)	0.067 (0.041)	0.085 (0.037)	0.056 (0.038)	0.085 (0.038)	0.059 (0.039)	0.057 (0.036)	0.049 (0.030)	0.055 (0.036)	0.047 (0.029)	0.056 (0.037)	0.048 (0.030)
	5	0.037 (0.026)	0.068 (0.044)	0.085 (0.040)	0.058 (0.042)	0.092 (0.043)	0.062 (0.043)	0.056 (0.036)	0.048 (0.029)	0.055 (0.035)	0.047 (0.028)	0.057 (0.037)	0.048 (0.031)
$X_1 = 0$, $X_2 = 1$	0	0.021 (0.016)	0.022 (0.017)	0.021 (0.016)	0.028 (0.022)	0.021 (0.016)	0.028 (0.022)	0.020 (0.016)	0.019 (0.014)	0.020 (0.016)	0.019 (0.014)	0.020 (0.016)	0.019 (0.015)
	1	0.023 (0.016)	0.032 (0.021)	0.030 (0.018)	0.033 (0.024)	0.035 (0.019)	0.034 (0.024)	0.033 (0.022)	0.029 (0.018)	0.034 (0.022)	0.029 (0.018)	0.034 (0.022)	0.029 (0.019)
	2	0.027 (0.016)	0.039 (0.024)	0.044 (0.021)	0.039 (0.026)	0.052 (0.022)	0.041 (0.026)	0.045 (0.026)	0.039 (0.021)	0.046 (0.026)	0.040 (0.021)	0.046 (0.026)	0.039 (0.021)
	3	0.030 (0.017)	0.045 (0.024)	0.056 (0.024)	0.045 (0.026)	0.062 (0.025)	0.046 (0.026)	0.053 (0.028)	0.047 (0.023)	0.053 (0.028)	0.047 (0.023)	0.053 (0.028)	0.046 (0.023)
	4	0.032 (0.017)	0.050 (0.026)	0.066 (0.029)	0.051 (0.029)	0.069 (0.030)	0.052 (0.030)	0.058 (0.030)	0.053 (0.025)	0.058 (0.031)	0.052 (0.025)	0.058 (0.031)	0.053 (0.025)
	5	0.035 (0.019)	0.054 (0.029)	0.073 (0.032)	0.054 (0.031)	0.071 (0.035)	0.056 (0.033)	0.061 (0.033)	0.058 (0.027)	0.060 (0.033)	0.057 (0.028)	0.063 (0.034)	0.060 (0.029)
$X_1 = 1$, $X_2 = 1$	0	0.036 (0.027)	0.042 (0.029)	0.047 (0.034)	0.054 (0.038)	0.048 (0.034)	0.053 (0.038)	0.056 (0.037)	0.053 (0.038)	0.050 (0.035)	0.046 (0.031)	0.056 (0.037)	0.052 (0.033)
	1	0.036 (0.026)	0.041 (0.027)	0.059 (0.034)	0.066 (0.040)	0.060 (0.037)	0.067 (0.040)	0.053 (0.033)	0.067 (0.040)	0.049 (0.030)	0.047 (0.029)	0.053 (0.032)	0.052 (0.030)
	2	0.040 (0.028)	0.047 (0.029)	0.070 (0.039)	0.073 (0.044)	0.068 (0.042)	0.074 (0.044)	0.053 (0.036)	0.074 (0.044)	0.051 (0.034)	0.052 (0.031)	0.054 (0.035)	0.056 (0.032)
	3	0.044 (0.029)	0.053 (0.032)	0.079 (0.042)	0.079 (0.046)	0.078 (0.044)	0.079 (0.047)	0.063 (0.039)	0.079 (0.047)	0.062 (0.039)	0.064 (0.035)	0.063 (0.040)	0.064 (0.035)
	4	0.047 (0.031)	0.058 (0.035)	0.090 (0.051)	0.084 (0.052)	0.092 (0.052)	0.087 (0.053)	0.078 (0.047)	0.087 (0.053)	0.083 (0.049)	0.080 (0.041)	0.079 (0.049)	0.076 (0.040)
	5	0.050 (0.034)	0.065 (0.040)	0.101 (0.059)	0.089 (0.057)	0.106 (0.059)	0.093 (0.058)	0.102 (0.060)	0.093 (0.058)	0.116 (0.064)	0.104 (0.050)	0.106 (0.063)	0.094 (0.048)

(b) Mean (and standard deviation) of the AUC in 500 simulations simulations for binary marker Scenario 3a.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.655 (0.030)	0.656 (0.030)	0.653 (0.031)	0.654 (0.031)	0.653 (0.031)	0.654 (0.031)	0.655 (0.030)	0.655 (0.030)	0.656 (0.030)	0.656 (0.030)	0.655 (0.030)	0.655 (0.030)
1	0.679 (0.030)	0.681 (0.029)	0.678 (0.030)	0.679 (0.030)	0.678 (0.030)	0.679 (0.030)	0.679 (0.029)	0.679 (0.029)	0.680 (0.029)	0.680 (0.029)	0.679 (0.029)	0.679 (0.029)
2	0.690 (0.034)	0.691 (0.033)	0.689 (0.033)	0.690 (0.033)	0.689 (0.033)	0.690 (0.033)	0.689 (0.032)	0.689 (0.032)	0.690 (0.032)	0.690 (0.032)	0.689 (0.033)	0.690 (0.032)
3	0.689 (0.038)	0.689 (0.037)	0.690 (0.038)	0.689 (0.037)	0.688 (0.038)	0.689 (0.037)	0.689 (0.037)	0.688 (0.037)	0.689 (0.037)	0.689 (0.037)	0.688 (0.037)	0.688 (0.037)
4	0.678 (0.042)	0.676 (0.041)	0.679 (0.042)	0.677 (0.042)	0.678 (0.042)	0.677 (0.042)	0.676 (0.042)	0.677 (0.041)	0.676 (0.041)	0.676 (0.041)	0.676 (0.042)	0.676 (0.042)
5	0.662 (0.047)	0.660 (0.047)	0.664 (0.046)	0.661 (0.048)	0.664 (0.047)	0.661 (0.047)	0.661 (0.047)	0.662 (0.047)	0.661 (0.047)	0.661 (0.047)	0.660 (0.047)	0.661 (0.046)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations simulations for binary marker Scenario 3a.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)
1	0.193 (0.010)	0.193 (0.010)	0.195 (0.010)	0.195 (0.010)	0.195 (0.010)	0.195 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)
2	0.194 (0.011)	0.194 (0.011)	0.196 (0.011)	0.196 (0.011)	0.196 (0.011)	0.196 (0.011)	0.195 (0.011)	0.195 (0.011)	0.194 (0.011)	0.194 (0.011)	0.195 (0.011)	0.195 (0.011)
3	0.192 (0.013)	0.193 (0.013)	0.195 (0.013)	0.195 (0.013)	0.196 (0.013)	0.195 (0.013)	0.194 (0.012)	0.194 (0.012)	0.194 (0.012)	0.194 (0.012)	0.194 (0.012)	0.194 (0.012)
4	0.193 (0.014)	0.194 (0.013)	0.197 (0.014)	0.196 (0.014)	0.197 (0.014)	0.197 (0.014)	0.195 (0.013)	0.195 (0.013)	0.195 (0.013)	0.195 (0.013)	0.195 (0.013)	0.195 (0.013)
5	0.194 (0.017)	0.195 (0.017)	0.198 (0.018)	0.197 (0.018)	0.198 (0.018)	0.197 (0.018)	0.197 (0.016)	0.196 (0.016)	0.196 (0.016)	0.196 (0.016)	0.197 (0.017)	0.196 (0.016)

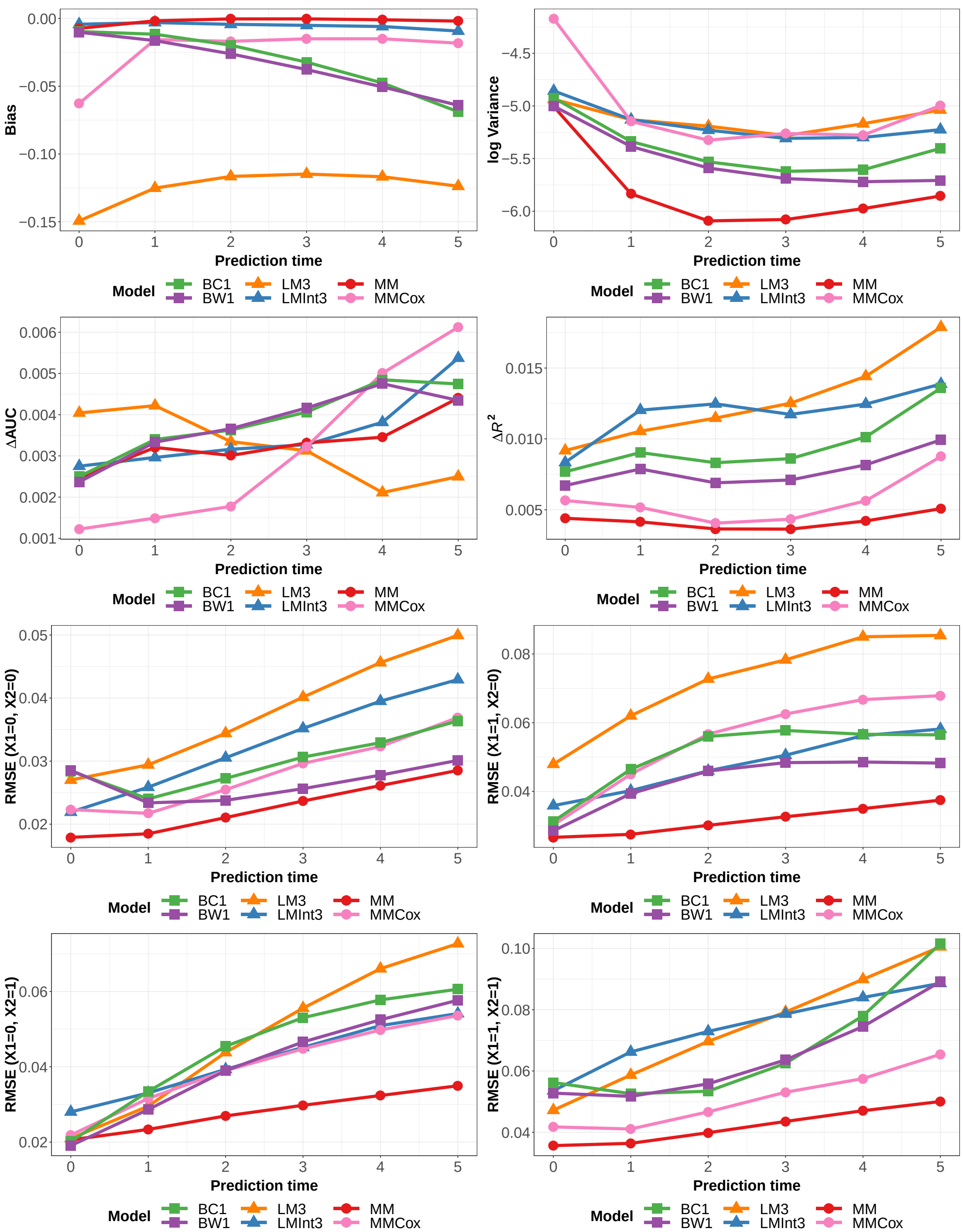


Figure C7: Simulation estimates for binary marker Scenario 3a for bias and variance for $Z(\tau) = 1, X_1 = 1, X_2 = 1$, ΔAUC, and ΔR^2, and RMSPE for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), \mathbf{X})$ from copula models (BC1), (BW1), joint models (MM), (MMCox) and landmark models (LM3), (LMInt3).

C.8 Scenario 3b Results

- Markov model; Marker observed at random inspection times (rate=1); Two baseline covariate X_1, X_2

Table C9: Simulation results for binary marker Scenario 3b.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 3b.

	τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
	0	0.017 (0.013)	0.020 (0.013)	0.027 (0.017)	0.021 (0.014)	0.027 (0.017)	0.021 (0.014)	0.029 (0.017)	0.029 (0.016)	0.029 (0.017)	0.029 (0.016)	0.029 (0.017)	0.029 (0.016)
	1	0.018 (0.012)	0.022 (0.014)	0.029 (0.016)	0.024 (0.015)	0.033 (0.016)	0.025 (0.016)	0.025 (0.014)	0.024 (0.014)	0.025 (0.015)	0.024 (0.014)	0.026 (0.015)	0.025 (0.014)
$X_1 = 0$	2	0.021 (0.012)	0.026 (0.015)	0.034 (0.016)	0.029 (0.016)	0.040 (0.016)	0.030 (0.017)	0.028 (0.015)	0.025 (0.013)	0.028 (0.015)	0.025 (0.013)	0.029 (0.015)	0.025 (0.013)
$X_2 = 0$	3	0.023 (0.012)	0.030 (0.016)	0.040 (0.017)	0.033 (0.017)	0.044 (0.017)	0.034 (0.018)	0.031 (0.017)	0.026 (0.014)	0.031 (0.017)	0.026 (0.014)	0.032 (0.017)	0.027 (0.014)
	4	0.026 (0.013)	0.033 (0.017)	0.044 (0.018)	0.036 (0.019)	0.045 (0.019)	0.037 (0.020)	0.033 (0.018)	0.028 (0.015)	0.033 (0.018)	0.028 (0.015)	0.033 (0.018)	0.028 (0.015)
	5	0.028 (0.014)	0.037 (0.019)	0.049 (0.020)	0.041 (0.022)	0.047 (0.022)	0.043 (0.022)	0.037 (0.019)	0.031 (0.016)	0.037 (0.020)	0.031 (0.017)	0.038 (0.020)	0.031 (0.017)
	0	0.026 (0.020)	0.030 (0.023)	0.051 (0.034)	0.035 (0.027)	0.049 (0.033)	0.035 (0.027)	0.031 (0.024)	0.027 (0.022)	0.030 (0.023)	0.027 (0.021)	0.031 (0.024)	0.028 (0.022)
	1	0.028 (0.020)	0.041 (0.029)	0.068 (0.033)	0.039 (0.028)	0.058 (0.033)	0.040 (0.028)	0.045 (0.031)	0.037 (0.025)	0.042 (0.030)	0.035 (0.024)	0.046 (0.031)	0.038 (0.025)
$X_1 = 1$	2	0.030 (0.020)	0.049 (0.030)	0.080 (0.032)	0.044 (0.029)	0.068 (0.031)	0.045 (0.029)	0.054 (0.033)	0.043 (0.027)	0.051 (0.032)	0.041 (0.026)	0.054 (0.033)	0.044 (0.027)
$X_2 = 0$	3	0.032 (0.021)	0.053 (0.033)	0.085 (0.032)	0.047 (0.029)	0.077 (0.032)	0.048 (0.029)	0.055 (0.034)	0.046 (0.028)	0.053 (0.034)	0.044 (0.027)	0.055 (0.034)	0.046 (0.028)
	4	0.034 (0.022)	0.057 (0.035)	0.089 (0.034)	0.051 (0.033)	0.088 (0.035)	0.053 (0.033)	0.055 (0.034)	0.047 (0.028)	0.054 (0.033)	0.046 (0.027)	0.055 (0.034)	0.047 (0.028)
	5	0.036 (0.023)	0.058 (0.038)	0.091 (0.036)	0.056 (0.037)	0.097 (0.040)	0.058 (0.038)	0.057 (0.034)	0.048 (0.027)	0.055 (0.034)	0.047 (0.027)	0.056 (0.035)	0.048 (0.028)
	0	0.020 (0.016)	0.021 (0.017)	0.021 (0.016)	0.028 (0.022)	0.021 (0.016)	0.028 (0.022)	0.020 (0.016)	0.019 (0.014)	0.020 (0.016)	0.019 (0.014)	0.020 (0.017)	0.019 (0.015)
	1	0.023 (0.015)	0.029 (0.020)	0.032 (0.016)	0.033 (0.024)	0.040 (0.018)	0.035 (0.024)	0.033 (0.022)	0.029 (0.018)	0.034 (0.022)	0.029 (0.018)	0.034 (0.021)	0.030 (0.018)
$X_1 = 0$	2	0.026 (0.016)	0.035 (0.021)	0.046 (0.020)	0.038 (0.024)	0.057 (0.021)	0.039 (0.024)	0.045 (0.025)	0.038 (0.021)	0.045 (0.025)	0.039 (0.021)	0.045 (0.025)	0.039 (0.021)
$X_2 = 1$	3	0.029 (0.016)	0.039 (0.022)	0.058 (0.024)	0.043 (0.025)	0.067 (0.024)	0.043 (0.025)	0.052 (0.028)	0.045 (0.023)	0.052 (0.028)	0.045 (0.023)	0.052 (0.028)	0.045 (0.023)
	4	0.032 (0.017)	0.044 (0.024)	0.068 (0.029)	0.047 (0.028)	0.071 (0.031)	0.048 (0.029)	0.056 (0.030)	0.051 (0.025)	0.056 (0.030)	0.050 (0.025)	0.057 (0.030)	0.051 (0.026)
	5	0.034 (0.019)	0.049 (0.027)	0.076 (0.034)	0.053 (0.030)	0.073 (0.037)	0.055 (0.031)	0.059 (0.033)	0.055 (0.027)	0.058 (0.033)	0.055 (0.027)	0.061 (0.034)	0.057 (0.028)
	0	0.035 (0.026)	0.043 (0.029)	0.046 (0.033)	0.055 (0.038)	0.047 (0.033)	0.055 (0.038)	0.063 (0.039)	0.055 (0.038)	0.056 (0.037)	0.052 (0.033)	0.062 (0.039)	0.058 (0.036)
	1	0.036 (0.026)	0.041 (0.027)	0.059 (0.031)	0.065 (0.038)	0.056 (0.033)	0.066 (0.037)	0.058 (0.034)	0.066 (0.037)	0.053 (0.032)	0.052 (0.031)	0.058 (0.034)	0.058 (0.032)
$X_1 = 1$	2	0.038 (0.026)	0.045 (0.028)	0.071 (0.036)	0.069 (0.041)	0.064 (0.037)	0.070 (0.041)	0.058 (0.036)	0.070 (0.041)	0.054 (0.035)	0.057 (0.032)	0.058 (0.036)	0.061 (0.033)
$X_2 = 1$	3	0.041 (0.027)	0.051 (0.031)	0.079 (0.040)	0.072 (0.043)	0.075 (0.041)	0.073 (0.043)	0.066 (0.040)	0.073 (0.043)	0.065 (0.040)	0.067 (0.035)	0.066 (0.041)	0.068 (0.036)
	4	0.044 (0.028)	0.055 (0.034)	0.086 (0.044)	0.076 (0.043)	0.088 (0.046)	0.078 (0.045)	0.080 (0.048)	0.078 (0.045)	0.083 (0.049)	0.081 (0.040)	0.081 (0.048)	0.079 (0.040)
	5	0.046 (0.030)	0.062 (0.039)	0.098 (0.055)	0.081 (0.050)	0.104 (0.056)	0.084 (0.051)	0.102 (0.059)	0.084 (0.051)	0.111 (0.061)	0.100 (0.048)	0.106 (0.059)	0.094 (0.046)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 3b.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.655 (0.030)	0.656 (0.030)	0.651 (0.031)	0.654 (0.031)	0.651 (0.031)	0.654 (0.031)	0.654 (0.030)	0.654 (0.030)	0.656 (0.030)	0.656 (0.030)	0.654 (0.030)	0.654 (0.030)
1	0.681 (0.030)	0.682 (0.030)	0.678 (0.030)	0.680 (0.030)	0.677 (0.030)	0.680 (0.030)	0.680 (0.029)	0.680 (0.029)	0.681 (0.030)	0.681 (0.030)	0.680 (0.029)	0.680 (0.029)
2	0.694 (0.034)	0.694 (0.033)	0.692 (0.033)	0.692 (0.033)	0.691 (0.033)	0.692 (0.033)	0.692 (0.033)	0.692 (0.033)	0.693 (0.032)	0.693 (0.032)	0.692 (0.033)	0.692 (0.033)
3	0.692 (0.038)	0.692 (0.037)	0.693 (0.037)	0.691 (0.037)	0.692 (0.038)	0.692 (0.037)	0.690 (0.037)	0.691 (0.037)	0.691 (0.037)	0.691 (0.037)	0.691 (0.037)	0.691 (0.037)
4	0.681 (0.042)	0.680 (0.042)	0.682 (0.043)	0.679 (0.042)	0.682 (0.043)	0.679 (0.043)	0.678 (0.042)	0.678 (0.043)	0.678 (0.042)	0.678 (0.042)	0.679 (0.043)	0.678 (0.042)
5	0.664 (0.049)	0.662 (0.047)	0.666 (0.048)	0.663 (0.048)	0.666 (0.048)	0.663 (0.048)	0.663 (0.047)	0.662 (0.047)	0.662 (0.047)	0.662 (0.047)	0.662 (0.048)	0.662 (0.048)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations for binary marker Scenario 3b.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.185 (0.010)	0.186 (0.010)	0.187 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)
1	0.192 (0.010)	0.192 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.194 (0.010)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)	0.193 (0.010)	0.194 (0.010)	0.193 (0.010)
2	0.192 (0.012)	0.192 (0.011)	0.194 (0.011)	0.194 (0.011)	0.194 (0.011)	0.194 (0.011)	0.193 (0.011)	0.193 (0.011)	0.193 (0.011)	0.193 (0.011)	0.193 (0.011)	0.193 (0.011)
3	0.191 (0.013)	0.191 (0.013)	0.193 (0.013)	0.192 (0.013)	0.194 (0.013)	0.193 (0.013)	0.192 (0.012)	0.192 (0.012)	0.192 (0.013)	0.192 (0.013)	0.192 (0.012)	0.192 (0.012)
4	0.191 (0.014)	0.192 (0.014)	0.195 (0.014)	0.193 (0.014)	0.195 (0.014)	0.193 (0.014)	0.193 (0.013)	0.193 (0.013)	0.193 (0.013)	0.193 (0.013)	0.193 (0.013)	0.193 (0.013)
5	0.192 (0.017)	0.194 (0.017)	0.197 (0.017)	0.195 (0.017)	0.197 (0.017)	0.195 (0.017)	0.195 (0.016)	0.194 (0.016)	0.194 (0.016)	0.194 (0.016)	0.195 (0.017)	0.194 (0.016)

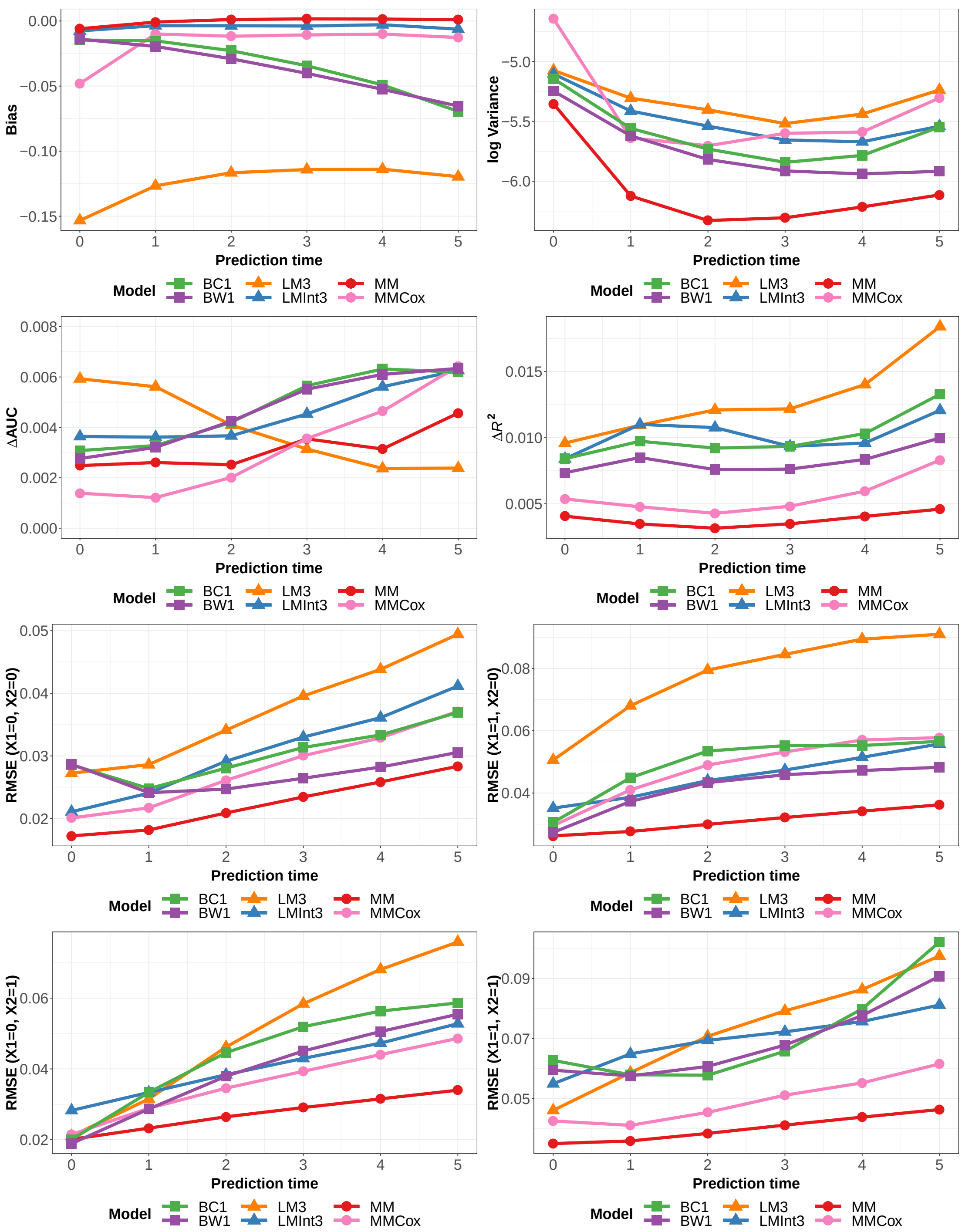


Figure C8: Simulation estimates for binary marker Scenario 3b for bias and variance for $Z(\tau) = 1, X_1 = 1, X_2 = 1$, ΔAUC, and ΔR^2, and RMSPE for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), \mathbf{X})$ from copula models (BC1), (BW1), joint models (MM), (MMCox) and landmark models (LM3), (LMInt3).

C.9 Scenario 3c Results

- Markov model; Marker observed continuously; Two baseline covariate X_1, X_2

Table C10: Simulation results for binary marker Scenario 3c.

(a) Mean (and standard deviation) of the root mean squared prediction error in 500 simulations for binary marker Scenario 3c.

	τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
$X_1 = 0$ $X_2 = 0$	0	0.016 (0.013)	0.018 (0.014)	0.027 (0.017)	0.020 (0.014)	0.027 (0.017)	0.020 (0.014)	0.028 (0.016)	0.028 (0.016)	0.029 (0.017)	0.029 (0.016)	0.028 (0.017)	0.028 (0.016)
	1	0.019 (0.011)	0.024 (0.015)	0.033 (0.014)	0.025 (0.014)	0.039 (0.014)	0.027 (0.014)	0.028 (0.015)	0.027 (0.014)	0.028 (0.015)	0.027 (0.014)	0.030 (0.014)	0.028 (0.014)
	2	0.021 (0.011)	0.028 (0.016)	0.039 (0.014)	0.029 (0.015)	0.045 (0.014)	0.030 (0.015)	0.030 (0.016)	0.027 (0.014)	0.030 (0.016)	0.027 (0.014)	0.032 (0.016)	0.028 (0.014)
	3	0.023 (0.012)	0.032 (0.018)	0.044 (0.016)	0.032 (0.017)	0.046 (0.016)	0.033 (0.018)	0.033 (0.018)	0.028 (0.015)	0.033 (0.018)	0.028 (0.015)	0.033 (0.018)	0.028 (0.015)
	4	0.025 (0.013)	0.035 (0.019)	0.048 (0.016)	0.034 (0.018)	0.046 (0.018)	0.036 (0.019)	0.034 (0.019)	0.029 (0.016)	0.034 (0.019)	0.029 (0.016)	0.034 (0.019)	0.030 (0.016)
	5	0.027 (0.014)	0.039 (0.021)	0.052 (0.017)	0.038 (0.020)	0.046 (0.019)	0.039 (0.021)	0.037 (0.020)	0.031 (0.017)	0.038 (0.020)	0.031 (0.017)	0.039 (0.020)	0.033 (0.018)
$X_1 = 1$ $X_2 = 0$	0	0.026 (0.020)	0.029 (0.022)	0.050 (0.032)	0.032 (0.025)	0.048 (0.032)	0.032 (0.025)	0.031 (0.024)	0.028 (0.022)	0.030 (0.023)	0.027 (0.021)	0.031 (0.024)	0.028 (0.022)
	1	0.027 (0.019)	0.035 (0.022)	0.075 (0.026)	0.038 (0.025)	0.062 (0.030)	0.040 (0.025)	0.046 (0.030)	0.038 (0.024)	0.043 (0.029)	0.036 (0.023)	0.047 (0.030)	0.040 (0.025)
	2	0.029 (0.019)	0.037 (0.024)	0.084 (0.026)	0.041 (0.025)	0.073 (0.026)	0.042 (0.025)	0.051 (0.031)	0.042 (0.025)	0.049 (0.030)	0.040 (0.025)	0.052 (0.031)	0.043 (0.026)
	3	0.030 (0.020)	0.040 (0.027)	0.087 (0.027)	0.043 (0.027)	0.083 (0.028)	0.044 (0.027)	0.051 (0.030)	0.043 (0.025)	0.050 (0.030)	0.041 (0.025)	0.051 (0.030)	0.043 (0.025)
	4	0.032 (0.021)	0.044 (0.028)	0.090 (0.028)	0.045 (0.028)	0.094 (0.032)	0.048 (0.029)	0.052 (0.029)	0.044 (0.024)	0.051 (0.030)	0.043 (0.025)	0.052 (0.029)	0.044 (0.025)
	5	0.033 (0.022)	0.050 (0.032)	0.091 (0.031)	0.048 (0.031)	0.104 (0.035)	0.051 (0.032)	0.061 (0.033)	0.049 (0.025)	0.057 (0.032)	0.047 (0.026)	0.061 (0.034)	0.050 (0.027)
$X_1 = 0$ $X_2 = 1$	0	0.018 (0.014)	0.019 (0.015)	0.019 (0.014)	0.027 (0.021)	0.019 (0.015)	0.027 (0.021)	0.020 (0.016)	0.018 (0.014)	0.020 (0.016)	0.019 (0.014)	0.020 (0.015)	0.018 (0.014)
	1	0.022 (0.013)	0.025 (0.015)	0.042 (0.016)	0.034 (0.021)	0.056 (0.020)	0.036 (0.021)	0.036 (0.021)	0.032 (0.018)	0.037 (0.021)	0.033 (0.018)	0.038 (0.022)	0.033 (0.019)
	2	0.025 (0.014)	0.030 (0.017)	0.059 (0.022)	0.038 (0.022)	0.070 (0.024)	0.039 (0.022)	0.046 (0.026)	0.040 (0.021)	0.047 (0.026)	0.040 (0.022)	0.047 (0.026)	0.040 (0.022)
	3	0.027 (0.016)	0.034 (0.019)	0.071 (0.027)	0.042 (0.023)	0.076 (0.029)	0.044 (0.024)	0.052 (0.028)	0.045 (0.024)	0.052 (0.028)	0.046 (0.023)	0.052 (0.028)	0.046 (0.024)
	4	0.029 (0.017)	0.038 (0.021)	0.080 (0.030)	0.045 (0.025)	0.077 (0.033)	0.047 (0.025)	0.055 (0.030)	0.050 (0.025)	0.055 (0.030)	0.049 (0.025)	0.056 (0.030)	0.051 (0.026)
	5	0.031 (0.019)	0.043 (0.024)	0.085 (0.033)	0.048 (0.028)	0.074 (0.035)	0.050 (0.029)	0.057 (0.033)	0.053 (0.027)	0.056 (0.032)	0.052 (0.027)	0.060 (0.034)	0.056 (0.029)
$X_1 = 1$ $X_2 = 1$	0	0.033 (0.025)	0.038 (0.027)	0.042 (0.031)	0.051 (0.035)	0.042 (0.031)	0.051 (0.036)	0.058 (0.037)	0.051 (0.036)	0.054 (0.036)	0.050 (0.032)	0.058 (0.037)	0.054 (0.033)
	1	0.034 (0.023)	0.041 (0.026)	0.065 (0.030)	0.060 (0.032)	0.056 (0.031)	0.062 (0.033)	0.056 (0.030)	0.062 (0.033)	0.053 (0.029)	0.052 (0.028)	0.058 (0.031)	0.057 (0.029)
	2	0.035 (0.023)	0.043 (0.028)	0.072 (0.036)	0.062 (0.034)	0.062 (0.035)	0.062 (0.034)	0.057 (0.033)	0.062 (0.034)	0.055 (0.032)	0.058 (0.030)	0.058 (0.033)	0.061 (0.031)
	3	0.036 (0.023)	0.047 (0.030)	0.077 (0.038)	0.063 (0.034)	0.075 (0.038)	0.065 (0.034)	0.069 (0.039)	0.065 (0.034)	0.069 (0.039)	0.072 (0.035)	0.069 (0.039)	0.072 (0.035)
	4	0.038 (0.024)	0.050 (0.030)	0.083 (0.041)	0.065 (0.035)	0.089 (0.043)	0.069 (0.036)	0.090 (0.048)	0.069 (0.036)	0.093 (0.049)	0.093 (0.041)	0.092 (0.048)	0.090 (0.040)
	5	0.040 (0.025)	0.058 (0.037)	0.093 (0.050)	0.069 (0.041)	0.107 (0.052)	0.074 (0.042)	0.121 (0.060)	0.074 (0.042)	0.129 (0.062)	0.119 (0.048)	0.125 (0.060)	0.114 (0.046)

(b) Mean (and standard deviation) of the AUC in 500 simulations for binary marker Scenario 3c.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.655 (0.030)	0.655 (0.030)	0.654 (0.031)	0.655 (0.031)	0.654 (0.031)	0.655 (0.031)	0.655 (0.030)	0.655 (0.030)	0.656 (0.030)	0.656 (0.030)	0.655 (0.030)	0.655 (0.030)
1	0.687 (0.030)	0.688 (0.030)	0.687 (0.030)	0.687 (0.030)	0.685 (0.030)	0.687 (0.030)	0.687 (0.029)	0.687 (0.029)	0.688 (0.030)	0.688 (0.030)	0.687 (0.030)	0.687 (0.029)
2	0.701 (0.034)	0.701 (0.034)	0.701 (0.033)	0.700 (0.032)	0.700 (0.033)	0.700 (0.032)	0.700 (0.032)	0.700 (0.033)	0.700 (0.033)	0.700 (0.033)	0.700 (0.033)	0.700 (0.033)
3	0.700 (0.038)	0.699 (0.038)	0.701 (0.037)	0.698 (0.037)	0.700 (0.037)	0.698 (0.037)	0.698 (0.037)	0.698 (0.037)	0.698 (0.037)	0.698 (0.037)	0.697 (0.037)	0.698 (0.037)
4	0.687 (0.041)	0.685 (0.042)	0.688 (0.041)	0.686 (0.042)	0.687 (0.041)	0.685 (0.042)	0.684 (0.041)	0.684 (0.041)	0.684 (0.041)	0.684 (0.041)	0.684 (0.041)	0.684 (0.042)
5	0.670 (0.049)	0.667 (0.049)	0.672 (0.047)	0.667 (0.047)	0.671 (0.047)	0.667 (0.047)	0.666 (0.047)	0.666 (0.047)	0.666 (0.047)	0.666 (0.047)	0.666 (0.048)	0.665 (0.048)

(c) Mean (and standard deviation) of the Brier Score in 500 simulations.

τ	MM	MMCox	LM3	LMInt3	LM4	LMInt4	BC1	BW1	BC2	BW2	BC3	BW3
0	0.185 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)	0.186 (0.010)
1	0.188 (0.010)	0.188 (0.010)	0.190 (0.010)	0.189 (0.010)	0.191 (0.010)	0.189 (0.010)	0.189 (0.010)	0.189 (0.010)	0.189 (0.010)	0.189 (0.010)	0.189 (0.010)	0.189 (0.010)
2	0.187 (0.012)	0.187 (0.012)	0.190 (0.011)	0.188 (0.012)	0.190 (0.012)	0.188 (0.012)	0.188 (0.011)	0.188 (0.011)	0.188 (0.011)	0.188 (0.011)	0.188 (0.011)	0.188 (0.011)
3	0.186 (0.013)	0.187 (0.013)	0.190 (0.013)	0.187 (0.013)	0.190 (0.013)	0.187 (0.013)	0.188 (0.012)	0.187 (0.012)	0.187 (0.012)	0.187 (0.012)	0.188 (0.012)	0.187 (0.012)
4	0.188 (0.014)	0.189 (0.014)	0.192 (0.014)	0.189 (0.014)	0.192 (0.013)	0.189 (0.014)	0.190 (0.013)	0.189 (0.013)	0.189 (0.013)	0.189 (0.013)	0.190 (0.013)	0.189 (0.013)
5	0.189 (0.017)	0.191 (0.018)	0.194 (0.017)	0.191 (0.018)	0.194 (0.017)	0.191 (0.018)	0.192 (0.017)	0.191 (0.016)	0.191 (0.016)	0.191 (0.016)	0.193 (0.017)	0.192 (0.016)

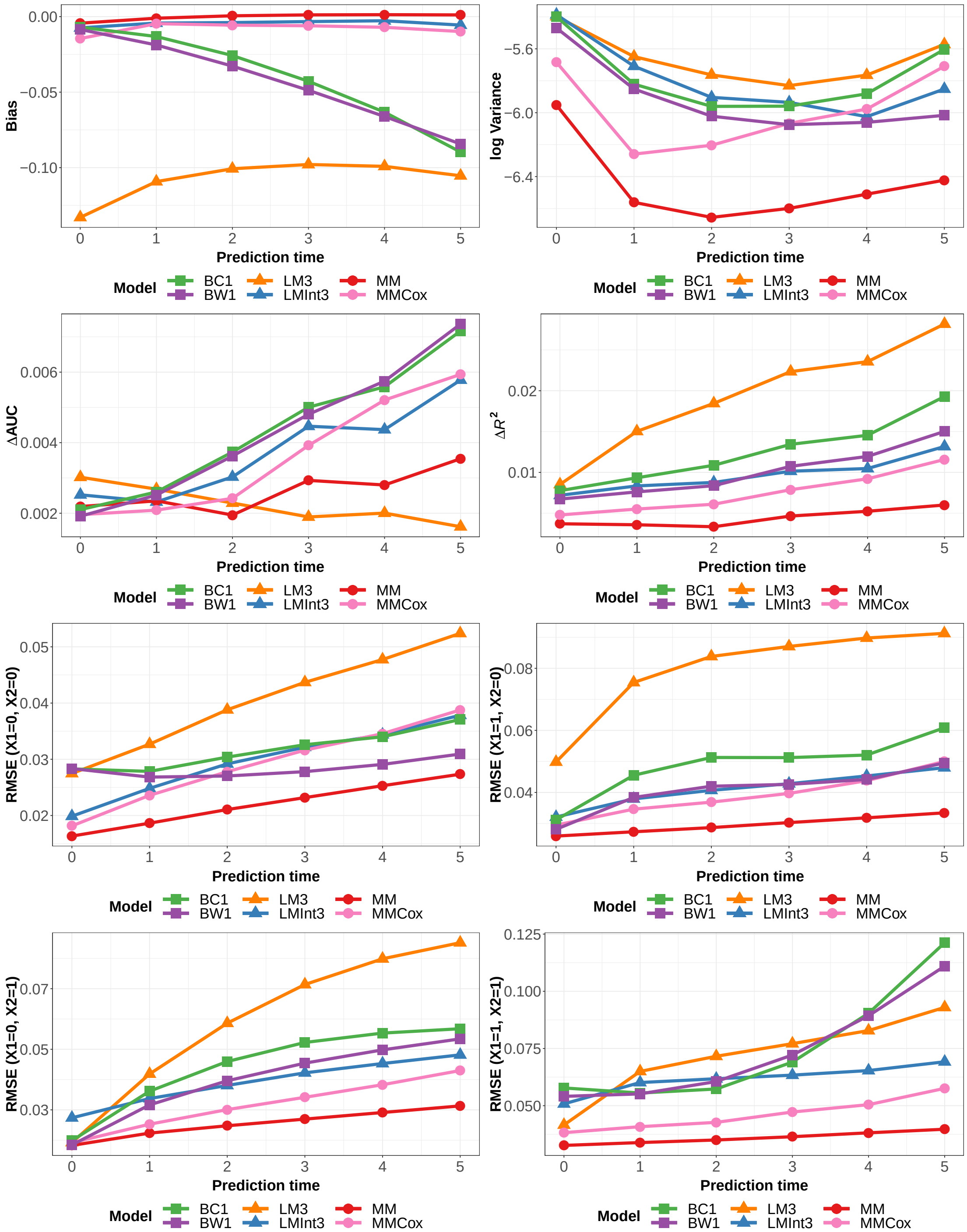


Figure C9: Simulation estimates for binary marker Scenario 3c for bias and variance for $Z(\tau) = 1, X_1 = 1, X_2 = 1$, ΔAUC, and ΔR^2, and RMSPE for predicted probability $P(T \leq \tau + 3 | T > \tau, Z(\tau), \mathbf{X})$ from copula models (BC1), (BW1), joint models (MM), (MMCox) and landmark models (LM3), (LMInt3).

D Prostate Cancer Study

D.1 Copula Model

For the proposed copula model, in Figures D1 and D2 we evaluate the fit of the Cox model to the failure time data. From the Schoenfeld residuals we find that there is no violation of the proportional hazards assumption for any of the baseline covariates. Since the deviance residuals are symmetrically distributed about zero there do not appear to be any influential observations in the data. To check the fit of the probit model to the binary marker data, we assess whether covariate transformation is required by examining the Pearson residuals in Figure D3 and find that there is no apparent deviation from zero. The model for the association parameter function was chosen to be a flexible function of landmark time (i.e., using splines) and baseline covariates.

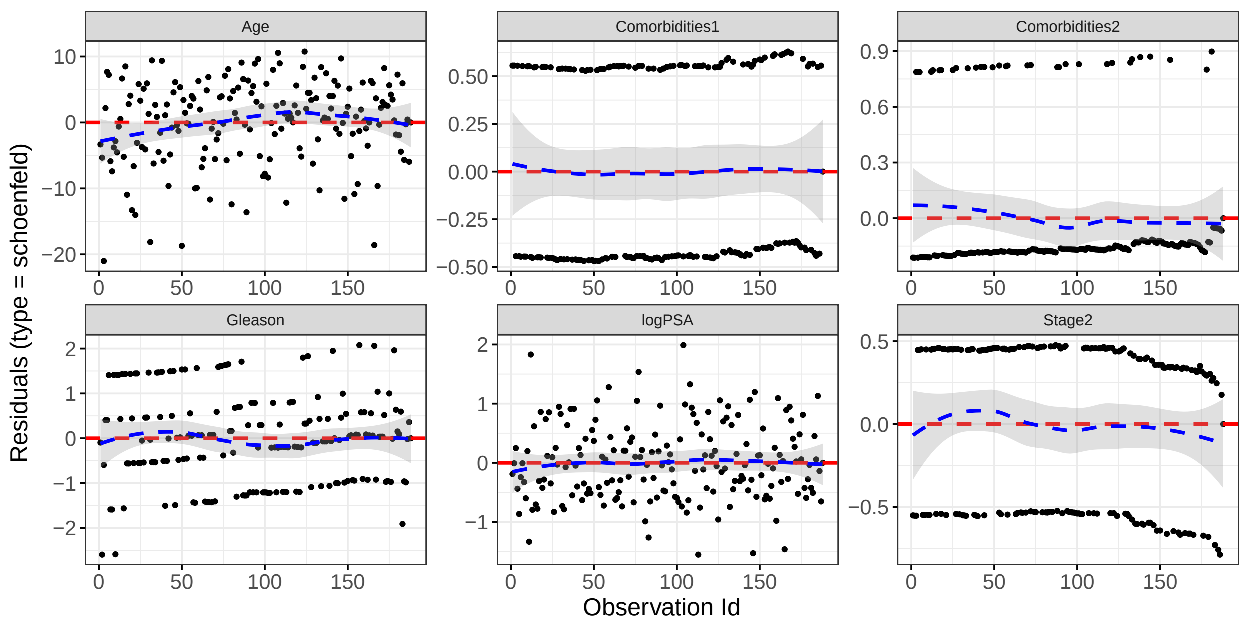


Figure D1: Schoenfeld residuals by baseline covariates for Cox model fit to prostate cancer failure time data. Dashed blue line is a smooth line of the local average for the residuals.

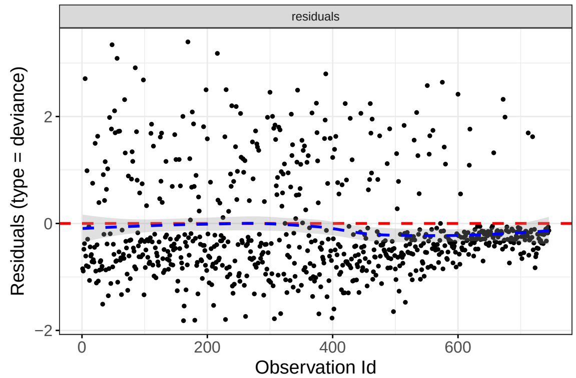


Figure D2: Deviance residuals for Cox model fit to prostate cancer failure time data. Dashed blue line is a smooth line of the local average for the residuals.

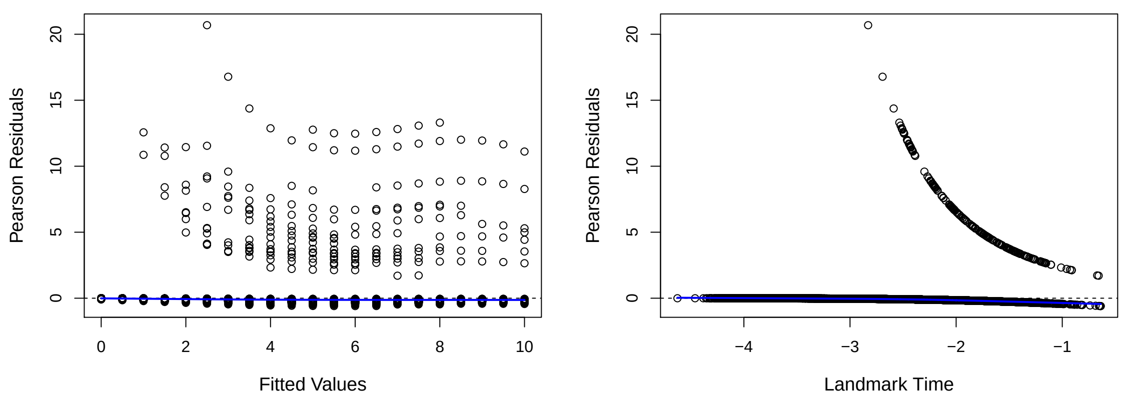


Figure D3: Pearson residuals for the probit model fit to the binary marker process by prediction time (left) and fitted values (right). Blue line is a lowess smoother for the Pearson residuals.

D.2 Joint Models

Table D1: Coefficient estimates for joint models applied to prostate cancer data.

		MM		**MMCox**	
Transition	Covariate	Coef.	SE	Coef.	SE
$0 \to 1$	Age	0.013	0.019	0.014	0.019
	$\log(\text{PSA} + 1)$	0.424	0.173	0.431	0.172
	Gleason score	0.740	0.156	0.753	0.159
	Stage T2-T3	0.798	0.349	0.767	0.349
	Comorbidities 1-2	0.053	0.302	0.061	0.302
	Comorbidities $\geq$3	0.263	0.497	0.271	0.497
$0 \to 2$	Age	0.077	0.013	0.080	0.013
	$\log(\text{PSA} + 1)$	0.204	0.126	0.193	0.127
	Gleason score	0.135	0.093	0.174	0.095
	Stage T2-T3	0.051	0.169	-0.03	0.172
	Comorbidities 1-2	0.678	0.181	0.700	0.182
	Comorbidities $\geq$3	1.426	0.236	1.491	0.238
$1 \to 2$	Age	0.049	0.024	0.043	0.025
	$\log(\text{PSA} + 1)$	-0.238	0.26	-0.183	0.319
	Gleason score	0.574	0.206	0.612	0.229
	Stage T2-T3	0.059	0.475	0.207	0.508
	Comorbidities 1-2	-0.927	0.421	-1.005	0.451
	Comorbidities $\geq$3	-0.507	0.646	-0.555	0.708
Log-likelihood			-966.4		-1182
AIC			1969		2399

D.3 Landmark Models

Table D2: Coefficient estimates for landmark models applied to prostate cancer data.

		LM4		**LMInt4**	
	Covariate	Coef.	SE	Coef.	SE
$\beta(\tau)$	CF	3.921	1.21	3.406	2.972
	CF$*\tau$	-0.46	0.409	-0.22	0.374
	CF$*\tau^2$	0.021	0.033	0.006	0.031
$\omega(\tau)$	CF$*(t-\tau)$	-0.562	0.175	-0.341	0.188
	CF$*(t-\tau)^2$	0.093	0.045	0.062	0.049
$\theta(\tau)$	τ	-0.069	0.023	-0.073	0.022
	τ^2	0.004	0.002	0.004	0.002
ζ	Age	0.08	0.012	0.082	0.013
	$\log(\text{PSA}+1)$	0.227	0.111	0.246	0.112
	Gleason score	0.289	0.091	0.269	0.094
	Stage T2-T3	0.042	0.167	0.057	0.171
	Comorbidities 1-2	0.42	0.17	0.474	0.174
	Comorbidities $\geq$3	1.214	0.247	1.23	0.252
$\zeta Z(\tau)$	CF*Age			-0.015	0.024
	CF*$\log(\text{PSA}+1)$			-0.577	0.366
	CF*Gleason score			0.336	0.252
	CF*Stage T2-T3			0.372	0.655
	CF*Comorbidities 1-2			-1.116	0.457
	CF*Comorbidities $\geq$3			-0.148	0.708
Log-likelihood			-11132		-11118
AIC			22289		22273