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Appendix for *"A state transition framework for patient-level modeling of engagement and retention in HIV care using longitudinal cohort data"*

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This material contains supplementary figure and table for the model assessment described in the main text.

As described in Section 5.4 of the main text, we assessed potential lack of fit using plots of observed and predicted proportion in each state (i.e., predicted marginal state membership probability) for each interval. Predicted proportion in each state at each interval was calculated as follows: We used the multistate model with covariates to generate predicted state membership probabilities at each t_j. Hence each person has 6 predicted probabilities at each t_j, one corresponding to each state. Then we added up the probabilities at each t_j and divided it by the total sample size (92,215) to obtain the predicted proportion in each state at each t_j. We calculated standard error of the predicted proportion in each state using 1,000 bootstrap samples. The observed proportion was obtained based only on those who have state information observed at t_j. The Figure 1 shows observed and predicted marginal state probabilities over the study follow-up period, along with 95% confidence intervals for the predicted proportions.

Figure 1 shows that with small exceptions, predicted state probabilities show good agreement with observed probabilities. Our model may lack of fit early disengagement (short disengagement at day 200 and 400 since enrollment) and transfer-out. This may imply violation of the first order Markov assumption and evidence of higher order dependence in transition rates. Ninety-five percent confidence intervals for predicted state probabilities were very small for most of cases.

To assess the effects of potential violations of the first order Markov assumption, we re-fit the regression model in Section 5.3 of the main text by adding information about the second order state membership S_{j-2} as a categorical covariate. We examined the second order dependence for the engagement model only, because disengagement state at t_j is always determined by S_{j-2}. More specifically, for a patient whose state at t_j is 2 (disengaged in the short-term), his/her state membership at t_{j-2} should be state 2 as well. Similarly, for a patient whose state at t_j is 3 (moderate-term disengagement) or 4 (long-term disengagement), his/her state membership at t_{j-2} should be engaged in care or disengaged in the short-term, respectively.

Our model diagnostic results shown in Table 1 indicate that there is the second order dependence in transition from engaged to other states. The results imply that those who engaged in two consecutive intervals are more likely to disengage from care, transfer-out, but less likely to die, compared to those who missed visits and return to engage in care. However, it did not change the substance of our findings and the estimated effect of covariates on transition rates are very robust between two multistate models with (Table 1) and without adjusting for S_{j-2} (Table 4 in the main text).

Using the second order dependence model, we re-generated the plots of observed and predicted state probabilities. Figure 2 shows that the model fit for early disengagement (day 200 in short disengagement) and transfer-out is slightly better compared to those in Figure 2.

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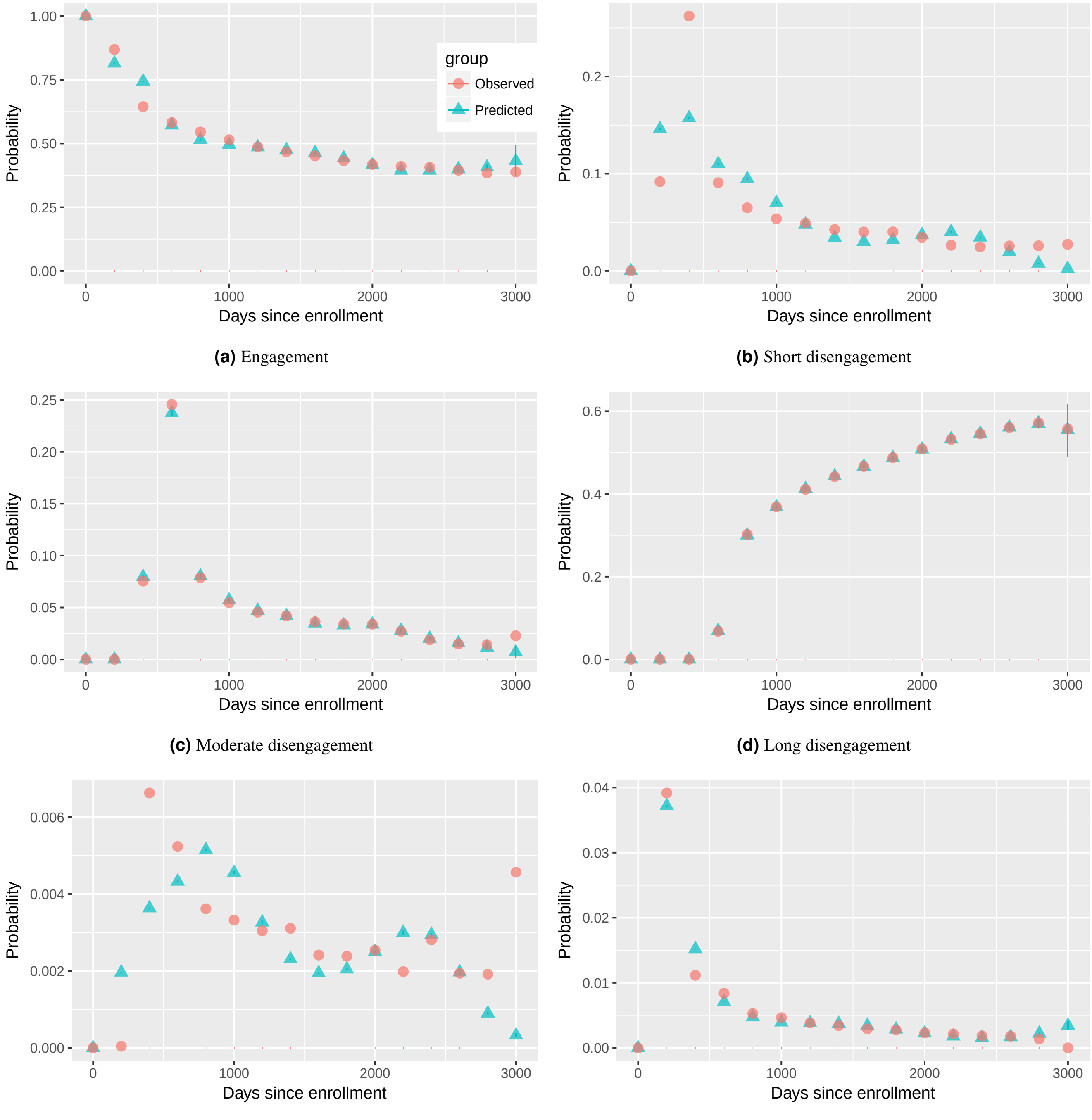


(a) Engagement

(b) Short disengagement

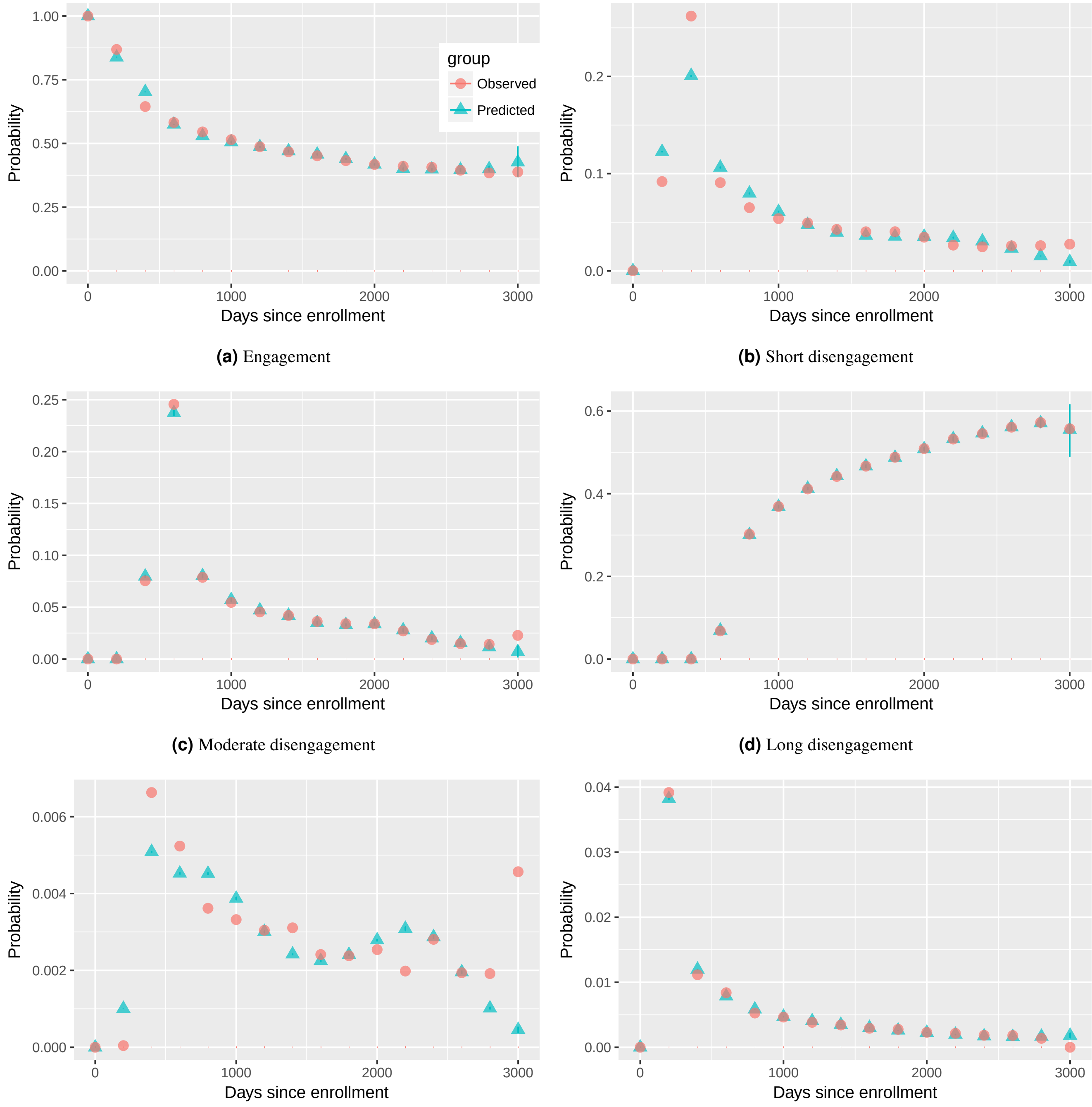
(c) Moderate disengagement

(d) Long disengagement

(e) Transfer-out

(f) Death

Figure 1. Observed vs predicted marginal state probabilities



(a) Engagement

(b) Short disengagement

(c) Moderate disengagement

(d) Long disengagement

(e) Transfer-out

(f) Death

Figure 2. Observed vs predicted marginal state probabilities after adjusting for S_{j-2} in the multistate model

Table 1. Relative risk ratios (RRR) and 95% bootstrapped confidence intervals for effect of covariates on transitions from engaged in care ($S_{j-1} = 1$) to disengaged ($S_j = 2$), transfer-out ($S_j = 5$) or death ($S_j = 6$), relative to remaining engaged in care ($S_j = 1$) when the multistate model ***includes*** the second order state membership S_{j-2}.

State at t_{j-1}		Engaged	
State at t_j	Disengaged	Transfer	Death
Age≥35	.64	.58	1.03
	(.62, .66)	(.52, .65)	(.92,1.15)
Male	1.09	.86	1.56
	(1.06, 1.12)	(.76, .98)	(1.40, 1.73)
CD4 < 350, ARV$^-$		Reference	
CD4<350, ARV$^+$	.15	.26	.70
	(.15, .16)	(.21, .33)	(.56, .86)
CD4≥350, ARV$^-$	.28	.22	.19
	(.27, .30)	(.17, .29)	(.14, .26)
CD4≥350, ARV$^+$	.11	.17	.23
	(.11, .12)	(.13, .22)	(.18, .29)
No CD4, ARV$^-$	1.77	1.54	1.24
	(1.61, 1.94)	(1.07, 2.22)	(.82, 1.88)
No CD4, ARV$^+$	.28	.45	.78
	(.26, .30)	(.33, .59)	(.58, 1.05)
Disengaged at t_{j-2}		Reference	
Engaged at t_{j-2}	.25	.52	.46
	(.24, .27)	(.40, .68)	(.35, .59)