BIOSTAT 629 001
Final presentation

Longitudinal study of impact of exercise on PROMIS-based cognitive outcomes

Introduction

The **Michigan Predictive Activity and Clinical Trajectories (MIPACT) Study** represents a unique opportunity for researchers to garner insights from

1. **Electronic health records:** demographic information, medical history and dietary habit.

2. **Genomic information:** ancestry information.

3. **Wearable device-based data:** physical activity and mental health monitoring.

Overview of project

Investigate the association between **self-reported PROMIS® cognitive functioning scores** and **time spent exercising** in the MIPACT participant cohort.

Hypothesis: exercise can help ease mental health disorders such as anxiety and depression

1. Meta-analysis of fifty eight randomised trials examining the effects of exercise on depression revealed that participants in the exercise treatment arm had significantly lower depression scores than those receiving the control treatment (Rethorst et al., 2009).

2. Longitudinal studies on association between self-reported physical activity and anxiety and depression symptom severity for patients with Type 2 Diabetes (Ivanova et al., 2017) and long-term physical disabilities (Battalio et al., 2020) predicted that symptoms of anxiety or depression would intensify over time as a consequence of lower exercise frequency.

Phenotype: PROMIS® Cognitive Scores

PROMIS® is a publicly available short self-report form used to assess an individual's perception of their cognitive status.

1. **Cognitive abilities:** positively worded questions.

2. **Cognitive concerns:** negatively worded.

Answers form an ordinal scale (1 - 5).

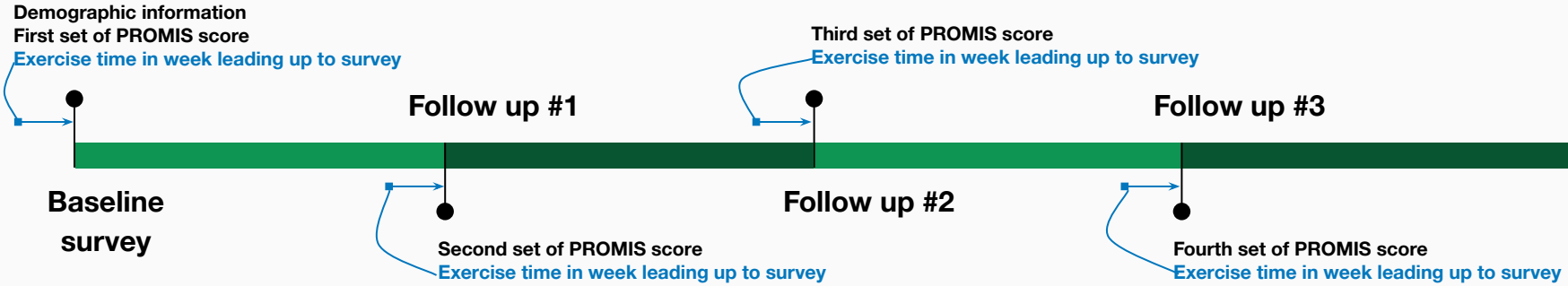
Cognitive concerns:

In the past seven days

(a) I have had trouble shifting back and forth between different activities that require thinking.
(b) I have had to work harder than usual to keep track of what I was doing.
(c) My thinking has been slow.
(d) It has seemed like my brain was not working as well as usual.

Items are summed to create a total score for each subscale (4 - 20).

Covariates: EHR and HealthKit data



Phenotype: PROMIS score
Covariate of interest: Apple Exercise Time (in minutes)
Demographic covariates we adjust for:

1. Age of participant at time of enrolment (18-30, 30-45, 45-60 and 60+)
2. Sex (female or male)
3. Race (African American, Asian, Caucasian or other)
4. Marital status (married or unmarried)

Descriptive statistics and figures

Covariate	PROMIS® scores		
	Mean (SD)	Median [Min, Max]	Missing (%)
Overall (N = 6555)	6.83 (3.37)	6.00 [4.00, 20.00]	22 (0.3%)
Age group (in years)			
18 – 30 (N = 1445)	6.68 (3.32)	5 [4, 20]	5 (0.3%)
30 – 45 (N = 1510)	6.89 (3.55)	6 [4, 20]	4 (0.3%)
45 – 60 (N = 1878)	6.81 (3.41)	6 [4, 20]	9 (0.5%)
60 + (N = 1709)	6.87 (3.21)	6 [4, 20]	4 (0.2%)
Race			
African American (N = 1115)	7.06 (3.54)	6 [4, 20]	11 (1.0%)
Asian (N = 1040)	6.38 (2.92)	5 [4, 20]	3 (0.3%)
Caucasian (N = 3640)	6.89 (3.41)	6 [4, 20]	7 (0.2%)
Other (N = 760)	6.85 (3.48)	6 [4, 20]	1 (0.1%)
Sex			
Female (N = 3521)	7.11 (3.51)	6 [4, 20]	10 (0.3%)
Male (N = 3034)	6.48 (3.15)	5 [4, 20]	12 (0.4%)
Marital Status			
Married (N = 3629)	6.70 (3.25)	6 [4, 20]	13 (0.4%)
Unmarried (N = 2367)	7.00 (3.55)	6 [4, 20]	9 (0.4%)

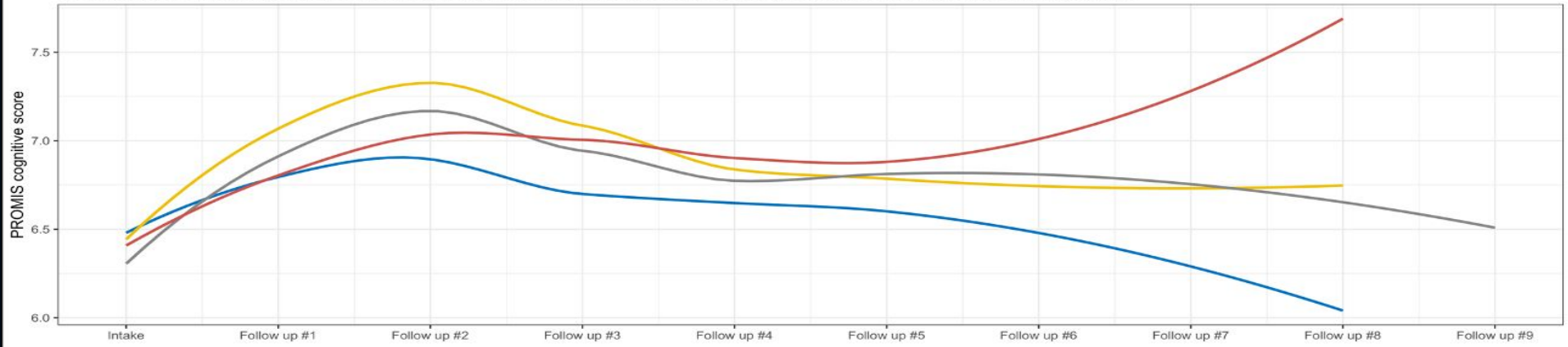
Table 1: *Descriptive summary of PROMIS® scores when stratified by age, sex, race and marital status.*

Descriptive statistics are calculated by stratifying the dataset by

1. Age groups (18-30, 30-45, 45-60 and 60+)
2. Race (African American, Asian, Caucasian or other)
3. Sex (male or female)
4. Marital status (unmarried or married)

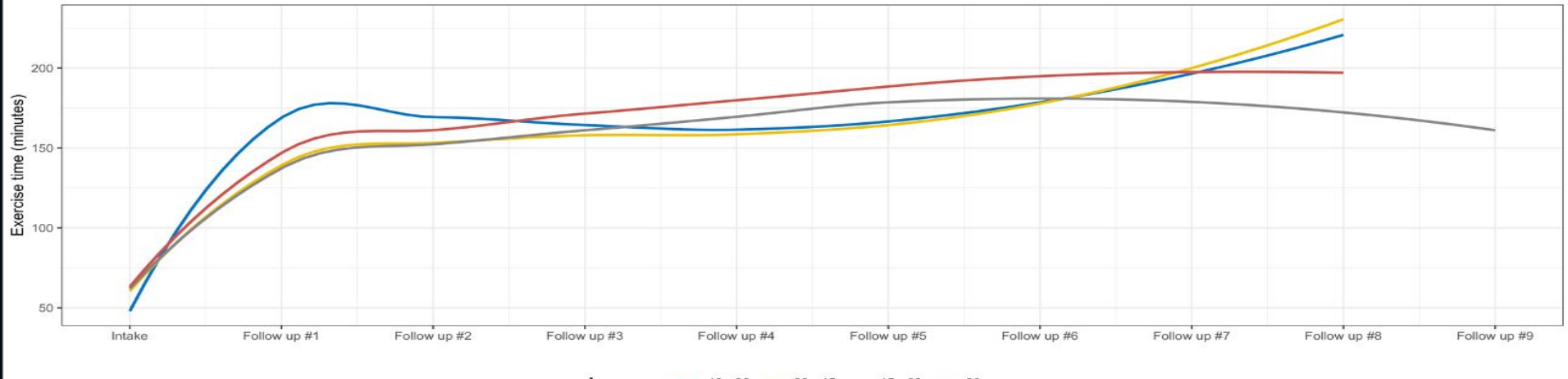
GAM-smoothed curve of self-reported PROMIS scores in MIPACT study patients (stratified by age group)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey.
We examine the smoothed trajectories of self-reported PROMIS scores over the course of multiple surveys for patients, stratified by age group.



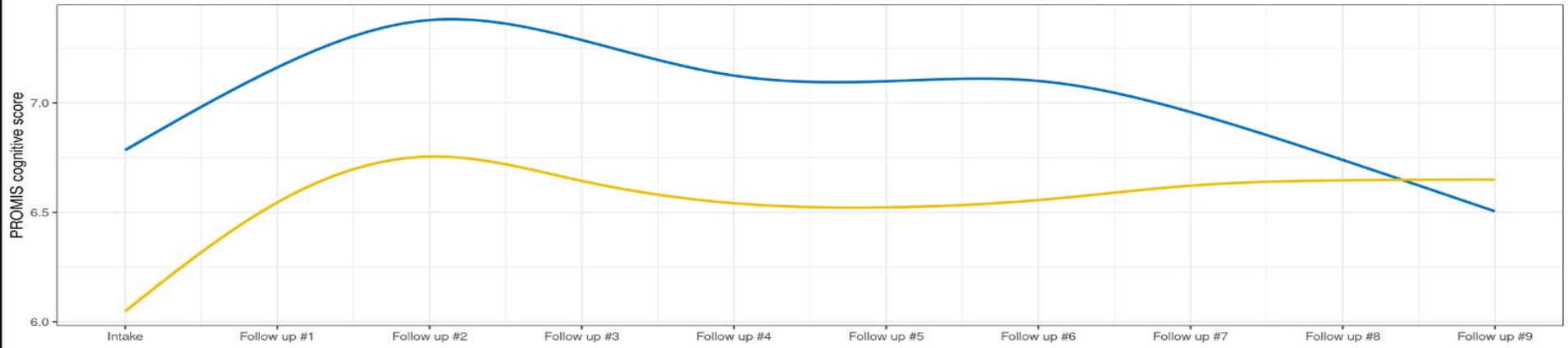
GAM-smoothed curve of HealthKit© Exercise Time (stratified by age group)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey.
We examine the smoothed trajectories of time spent exercising (collected through Apple HealthKit©) in the week leading up to each survey, over the course of multiple surveys, stratified by age group.



GAM-smoothed curve of self-reported PROMIS scores in MIPACT study patients (stratified by gender)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey.
We examine the smoothed trajectories of self-reported PROMIS scores over the course of multiple surveys for patients, stratified by gender.



GAM-smoothed curve of HealthKit© Exercise Time (stratified by gender)

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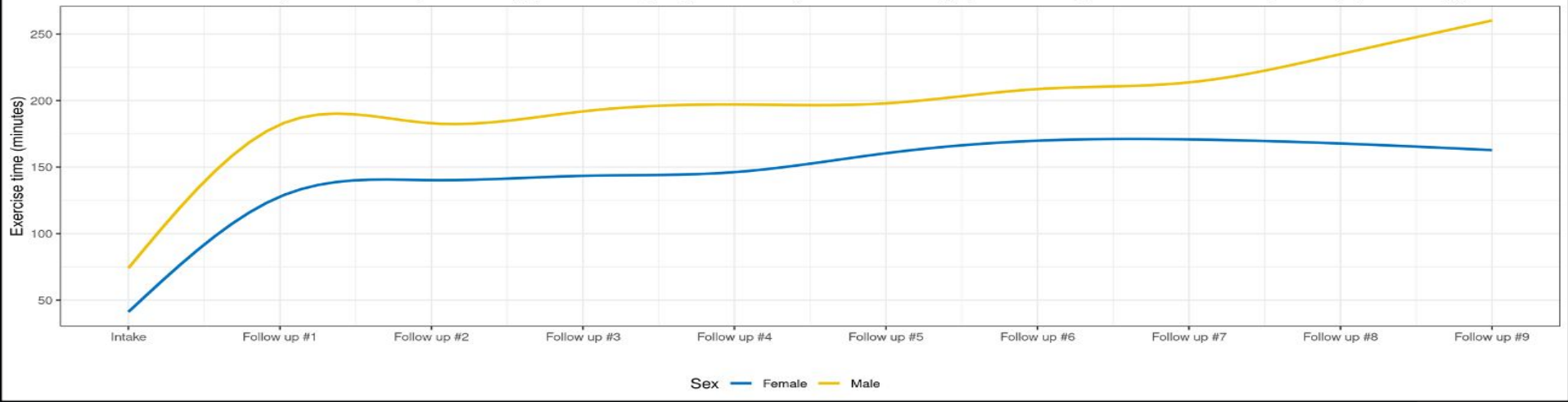
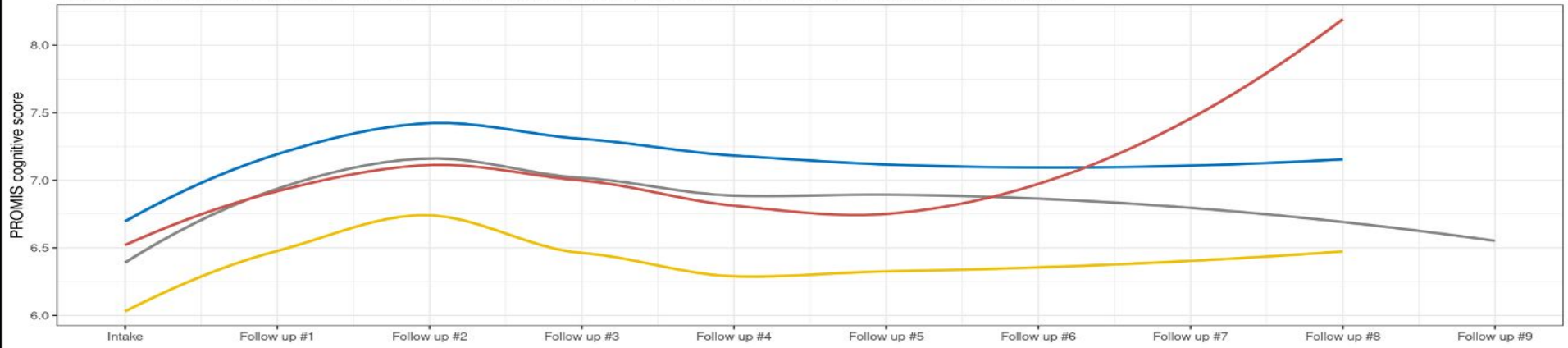


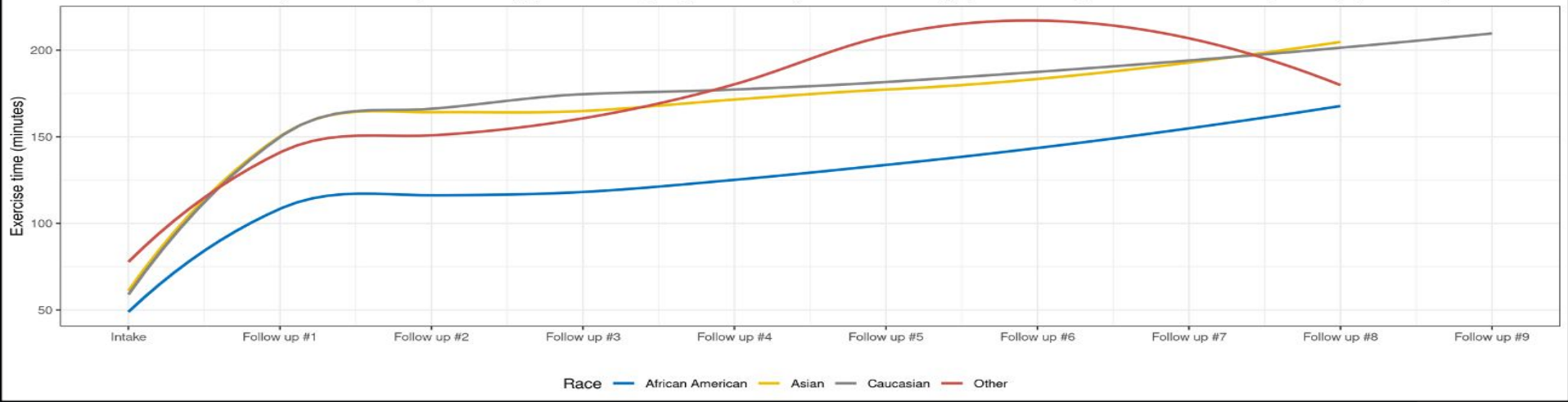
GAM-smoothed curve of self-reported PROMIS scores in MIPACT study patients (stratified by race)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey. We examine the smoothed trajectories of self-reported PROMIS scores over the course of multiple surveys for patients, stratified by race.



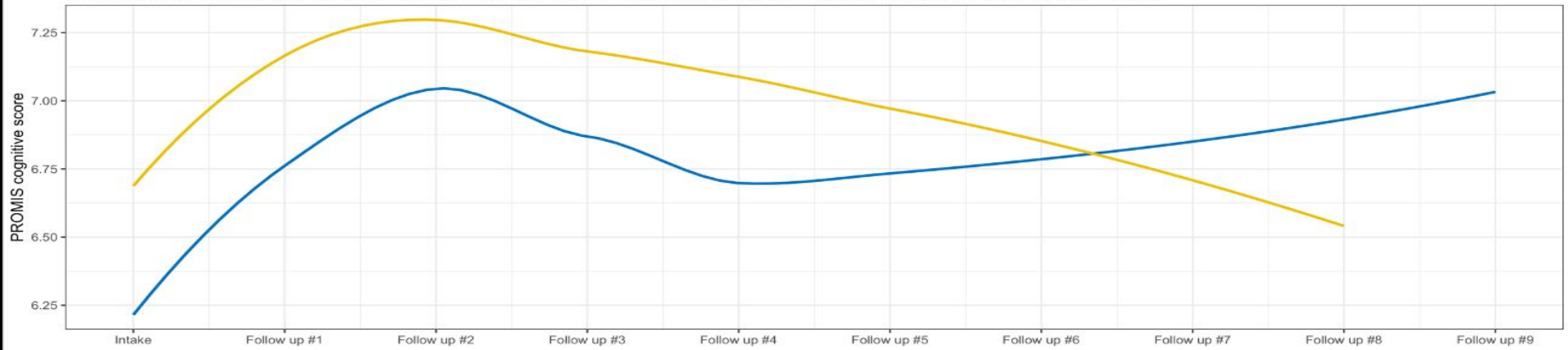
GAM-smoothed curve of HealthKit© Exercise Time (stratified by race)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey. We examine the smoothed trajectories of time spent exercising (collected through Apple HealthKit©) in the week leading up to each survey, over the course of multiple surveys, stratified by race.



GAM-smoothed curve of self-reported PROMIS scores in MIPACT study patients (stratified by marital status)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey.
We examine the smoothed trajectories of self-reported PROMIS scores over the course of multiple surveys for patients, stratified by marital status.



GAM-smoothed curve of HealthKit© Exercise Time (stratified by marital status)

During each survey (intake and subsequent quarterly follow-up) patients were asked to report PROMIS cognition scores based on their mental health during the week leading up to the survey.
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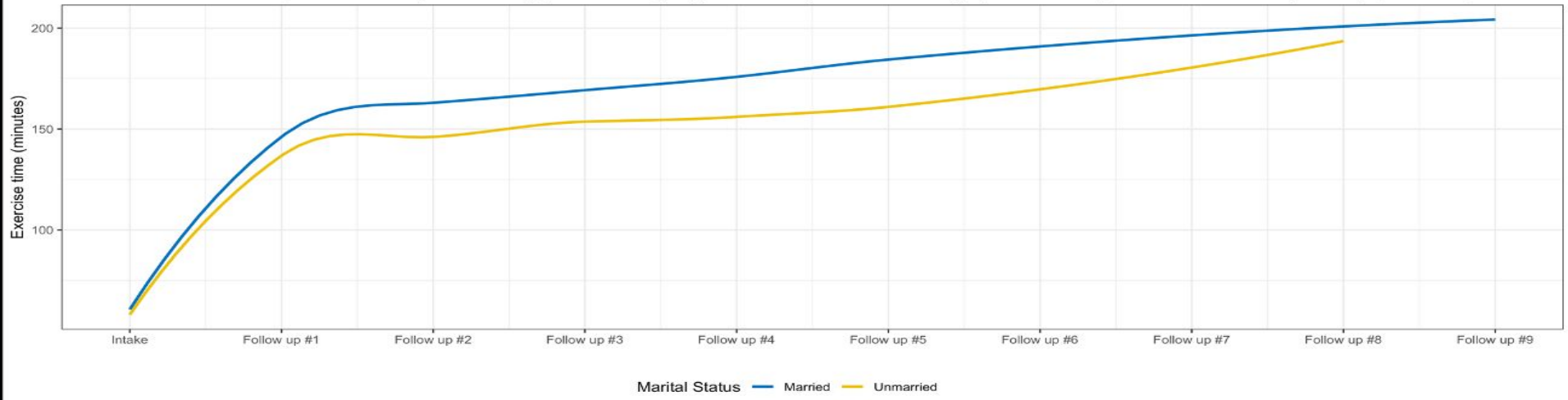

Statistical modeling with LMM

$$Y_{ij} = \beta_0 + b_i + \beta_1 AET_{ij} + \beta_2 I(S_i = Male) +$$

$$\beta_3 A_i + \beta_6 I(R_i = \text{Asian}) + \beta_7 I(R_i = \text{Caucasian}) +$$

$$\beta_8 I(MS_i = \text{Unmarried}) + \sum_{k=1}^{10} \beta_{8+k} I(Time_{ij} = k) + \epsilon_{ij}$$

Response of the i^{th} participant during the j^{th} survey

Apple Exercise Time (measures every full minute of movement that equals or exceeds the intensity of a brisk walk) for the i^{th} person in the week leading up to the j^{th} survey

Sex of the i^{th} participant

Race of the i^{th} participant

Age at enrolment of the i^{th} participant

Marital status of the i^{th} participant

Terms circled in red are random components.

LMM summary table

Fixed effects			
Predictors	**Estimate**	**Std. Error**	**t-value**
Intercept	*6.615*	*0.185*	*35.794**
Time (Baseline = Intake)	-	-	-
Quarterly follow-up 1	*0.535*	*0.040*	*13.271**
Quarterly follow-up 2	*0.839*	*0.042*	*20.054**
Quarterly follow-up 3	*0.679*	*0.043*	*15.692**
Quarterly follow-up 4	*0.586*	*0.045*	*12.953**
Quarterly follow-up 5	*0.663*	*0.050*	*13.237**
Quarterly follow-up 6	*0.874*	*0.060*	*14.533**
Quarterly follow-up 7	*0.798*	*0.092*	*8.654**
Quarterly follow-up 8	*0.773*	*0.192*	*4.025**
Quarterly follow-up 9	1.589	1.429	1.112
Age	0.111×10^{-2}	0.275×10^{-2}	0.405
Sex (Baseline = Female)	-	-	-
Male	*-0.589*	*0.078*	*-7.537**
Marital Status (Baseline: Married)	-	-	-
Unmarried	*0.367*	*0.091*	*4.052**
Race (Baseline: African American)	-	-	-
Asian	*-0.515*	*0.139*	*-3.702**
Caucasian	-0.083	0.112	-0.745
Other	-0.041	0.155	-0.267
Apple Exercise Time	-0.021×10^{-2}	0.007×10^{-2}	*-2.885**

Random effects			
Groups	**Name**	**Variance**	**Std. Dev.**
Patient ID	Random intercept	7.562	2.750
Residual	White noise	3.693	1.922

Effect size of -0.589 (p- value: < 0.001) on PROMIS scores for male participants as compare to (otherwise identical) female counterparts in the study.

Asian participants report significantly better cognitive functioning as compared to the baseline group of African Americans in the study, with an effect size of -0.515 (p-value: < 0.001).

Unmarried participants report significantly higher PROMIS scores, indicating poorer cognitive functioning as compared to (otherwise identical) married participants, with an estimated effect size of 0.367 (p-value < 0.001)

Significant association between time spent exercising and self- reported PROMIS® scores with an effect size of −0.00021 (p-value: 0.004).

Conclusion

In this report we investigate the association between self-reported PROMIS cognitive functioning scores and time spent exercising in the MIPACT participant cohort.

Using LM-model, while controlling for variability due to age, sex, race and marital status, we report a significant negative effect of Exercise Time (in minutes) on self-reported PROMIS scores – this finding agrees with previous studies which noted improved cognitive functioning with increased physical activity (Hötting & Röder, 2013; Mandolesi et al., 2018).

Although the response is a count-type variable, we still use a linear model to investigate the presence of any significant association between the response and covariate of interest. Consider a GLM-based analysis?

Evidence to support association between basal body temperature and BMI and perception of cognitive functioning - scarcity of HealthKit data as of now.

More granularity in covariate: talk about which physical activity has most impact - running, swimming, cycling, downhill sports?


"That's all Folks!"