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Overtraining through a new lens: Characterization of overreach in recreationally active adults and the hormetic implications

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Acknowledgements


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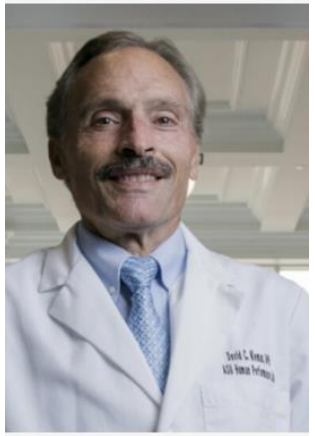
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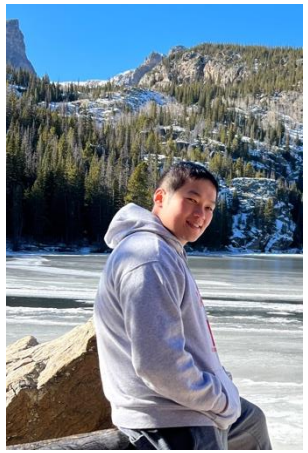
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Agenda

- Acknowledgements
- **Background**
  - Physical Activity Dose-Response
  - Introduction to Overtraining
    - Previous Theories
    - Gaps in Literature
- **Original Research**
- **Discussion**
  - Hormesis Theory and Overtraining

Background

Exercise is Medicine ®

-American College of Sports Medicine

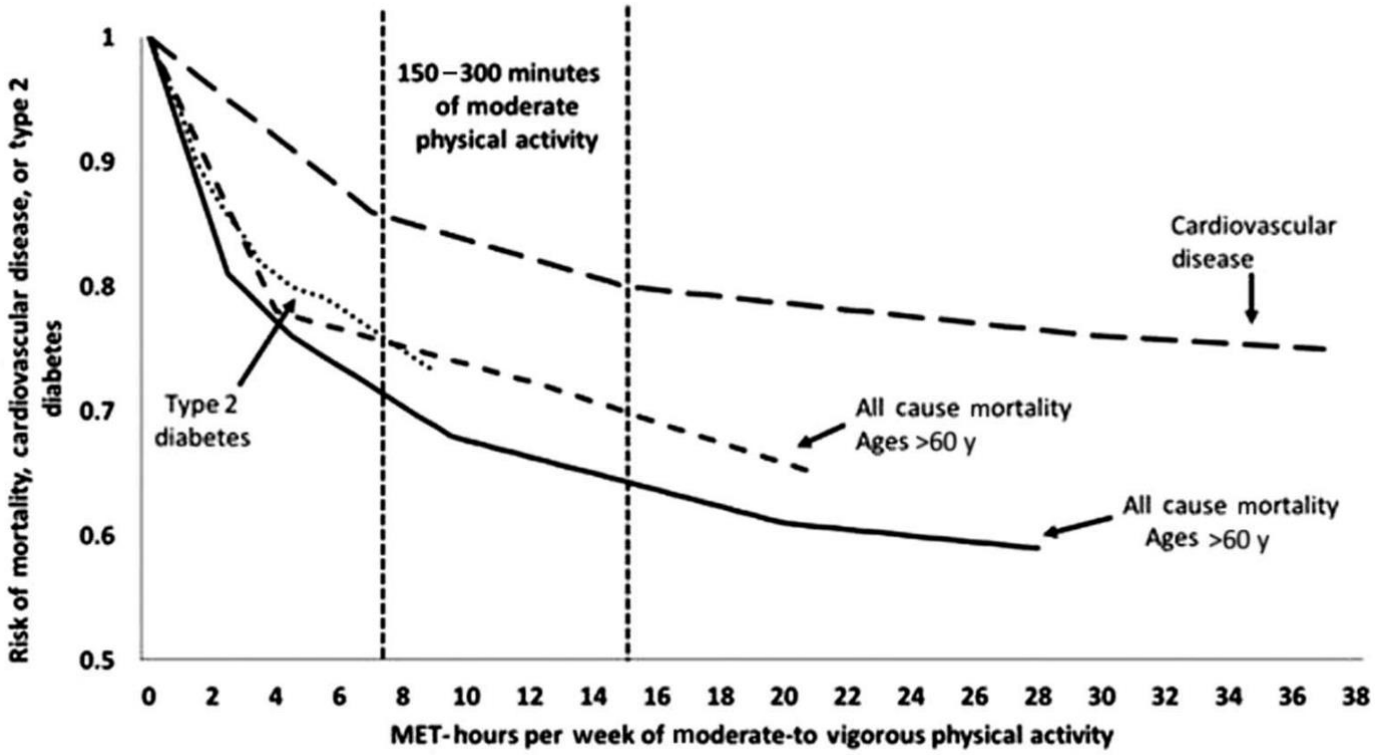
Dosis sola facit venenum

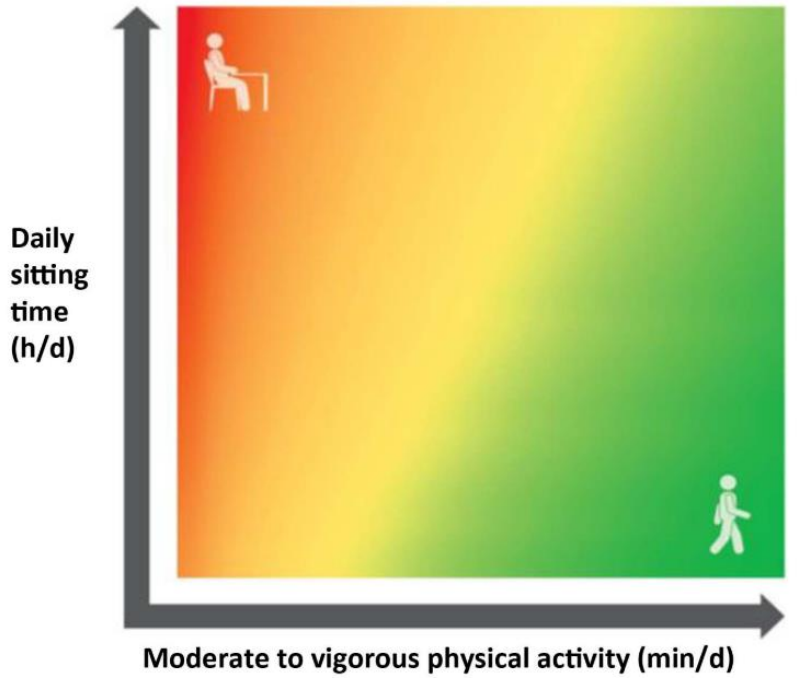
(The dose makes the poison)

-Paracelsus

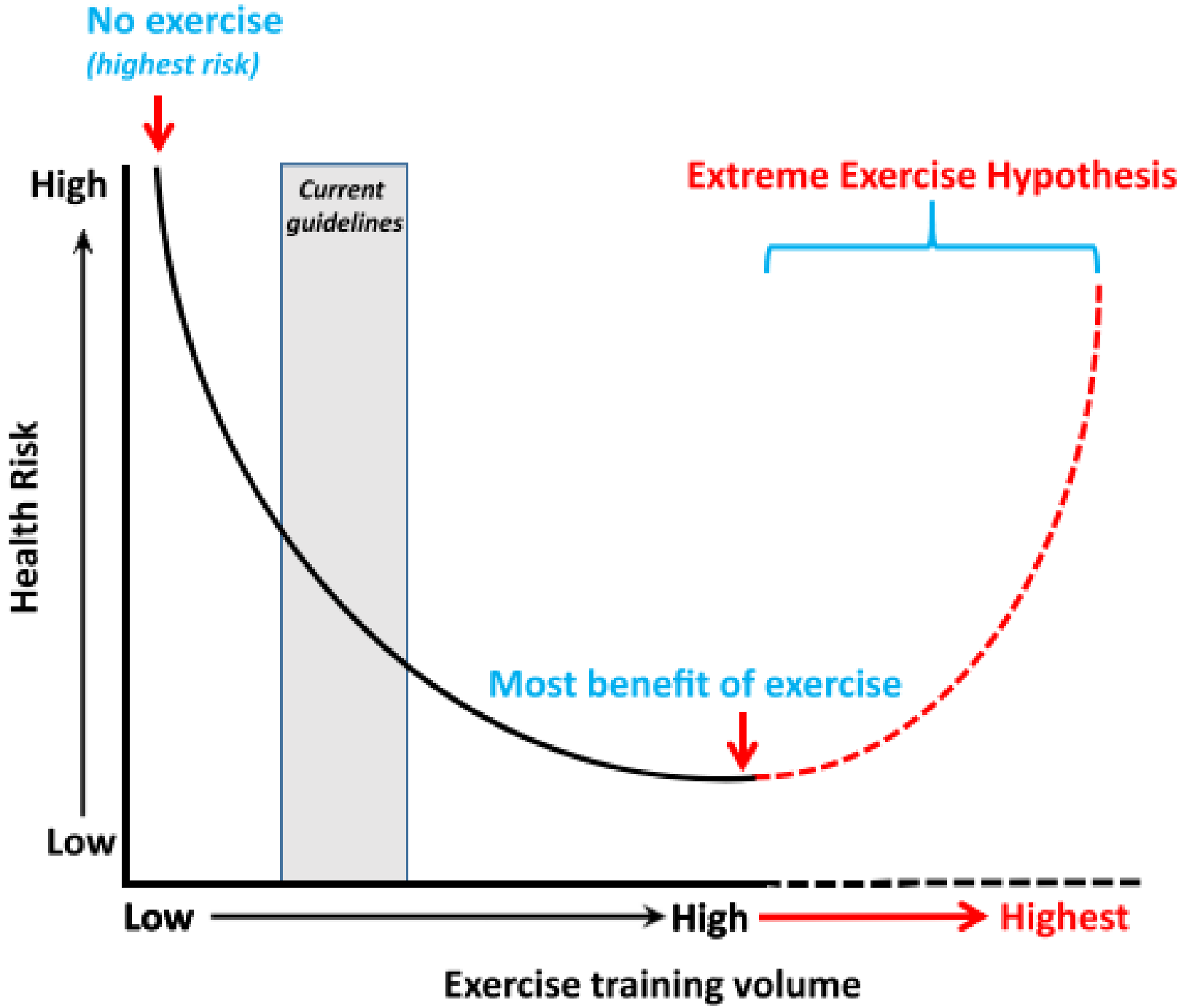
Physical Activity Guidelines

- 150 to 300 minutes of moderate-to-vigorous aerobic activity per week.
- ≥2 days muscle-strengthening activities per week.

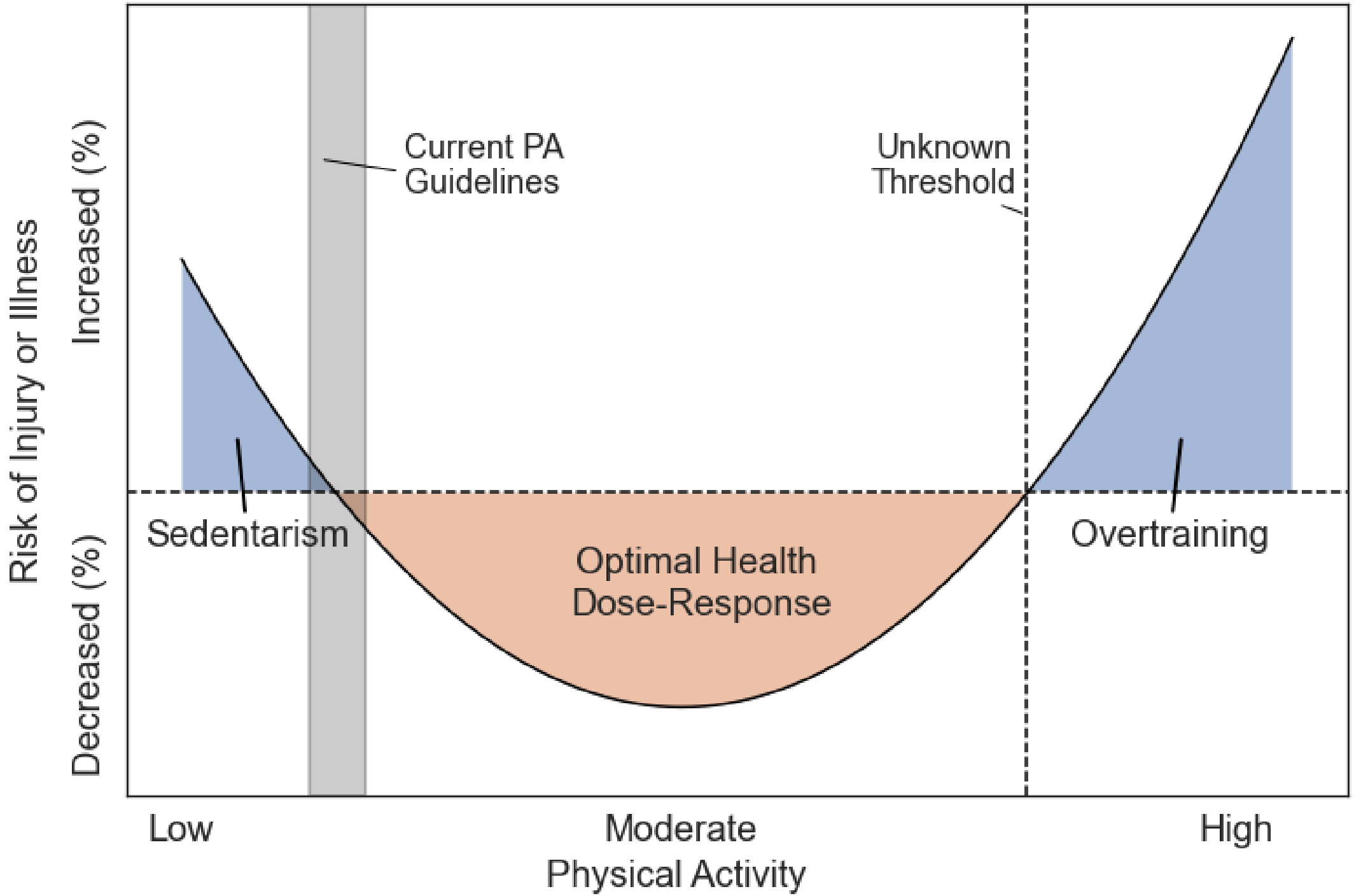




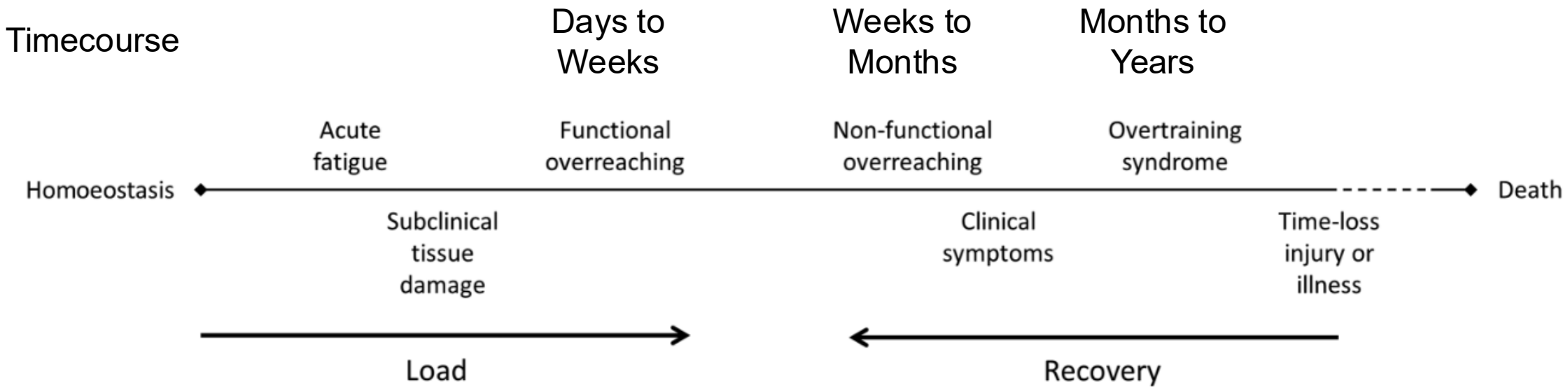
Powell et al. 2018



Eijsvogels 2018



Overtraining Syndrome



Schwellnus et al. 2016

Hypotheses of OTS

Glycogen depletion

Central Fatigue

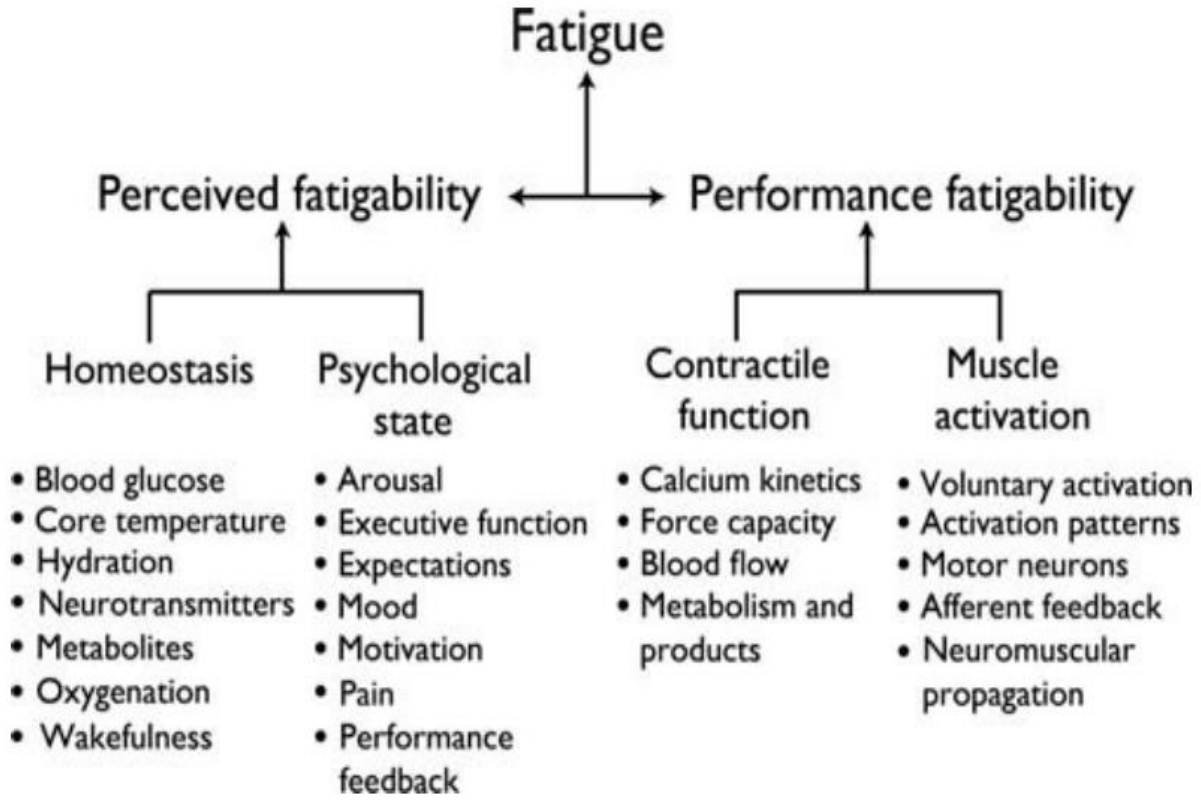
Glutamine deficiency

Excessive oxidative stress

Autonomic Nervous System imbalance

Cytokine Storm

Hypothalamic Dysfunction (HPA-axis)



Enoka & Duchateau (2016)

Gaps in Overtraining Research

Previous pathophysiological theories cannot explain all symptomology of overtraining

- No validated diagnostic criteria
- Interindividual symptoms associated with OTS
  - Inconsistent, conflicting results in previous research
- Overtraining substates are ill-defined

Overtraining research has focused on high-level, predominately male athletes

- Limited sample sizes
- Females (athletes) historically marginalized in research
- Limited applicability of findings to broader populations
- Older studies lacked clear performance measures.

Overtraining remains a diagnosis of exclusion (unexplained underperformance syndrome)

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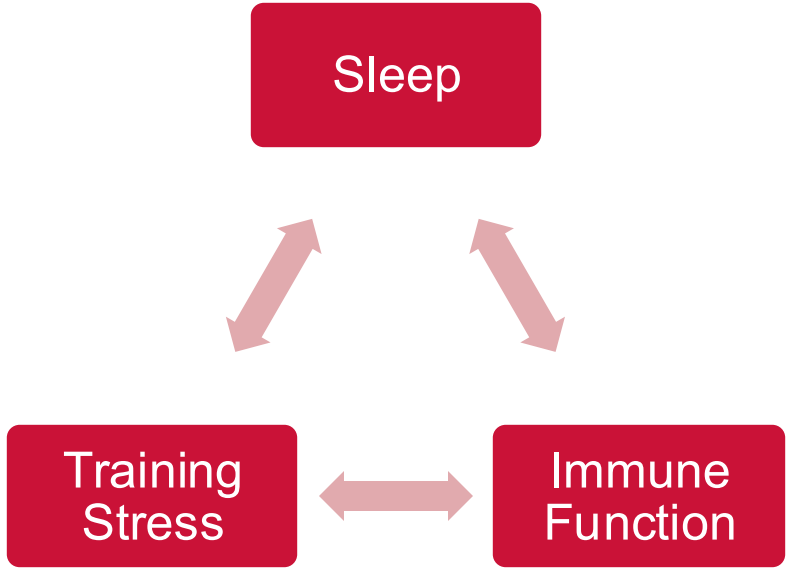
Questions to Address

1. Can individuals besides elite-level (male) athletes experience overtraining?

2. What marker(s) can be used to identify the overtraining response?
    a) What markers might be used to distinguish FOR from NFOR/OTS?

3. What is the impact of intensified training on sleep and *vice versa*?

4. What is the immune response associated with overtraining?



Central Hypothesis and Aims

The Central Hypothesis is that overtraining is not exclusive to high-level athletes and can occur in recreationally active male and females

Specific Aim 1: Characterize the physiological responses to a 3-week high-intensity training protocol in recreationally active adults

Specific Aim 2: Identify subjective and objective variables associated with overtraining during a 3-week high intensity training protocol and subsequent recovery

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Study Design

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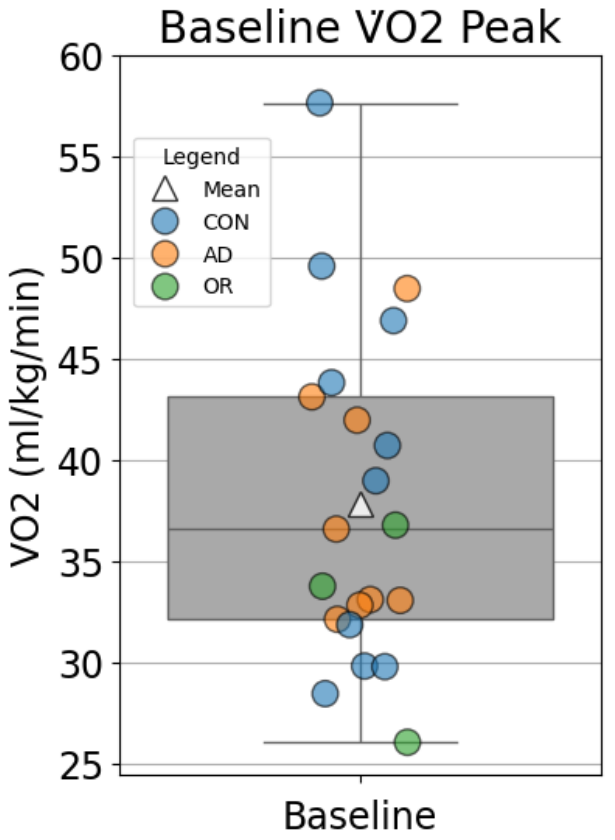
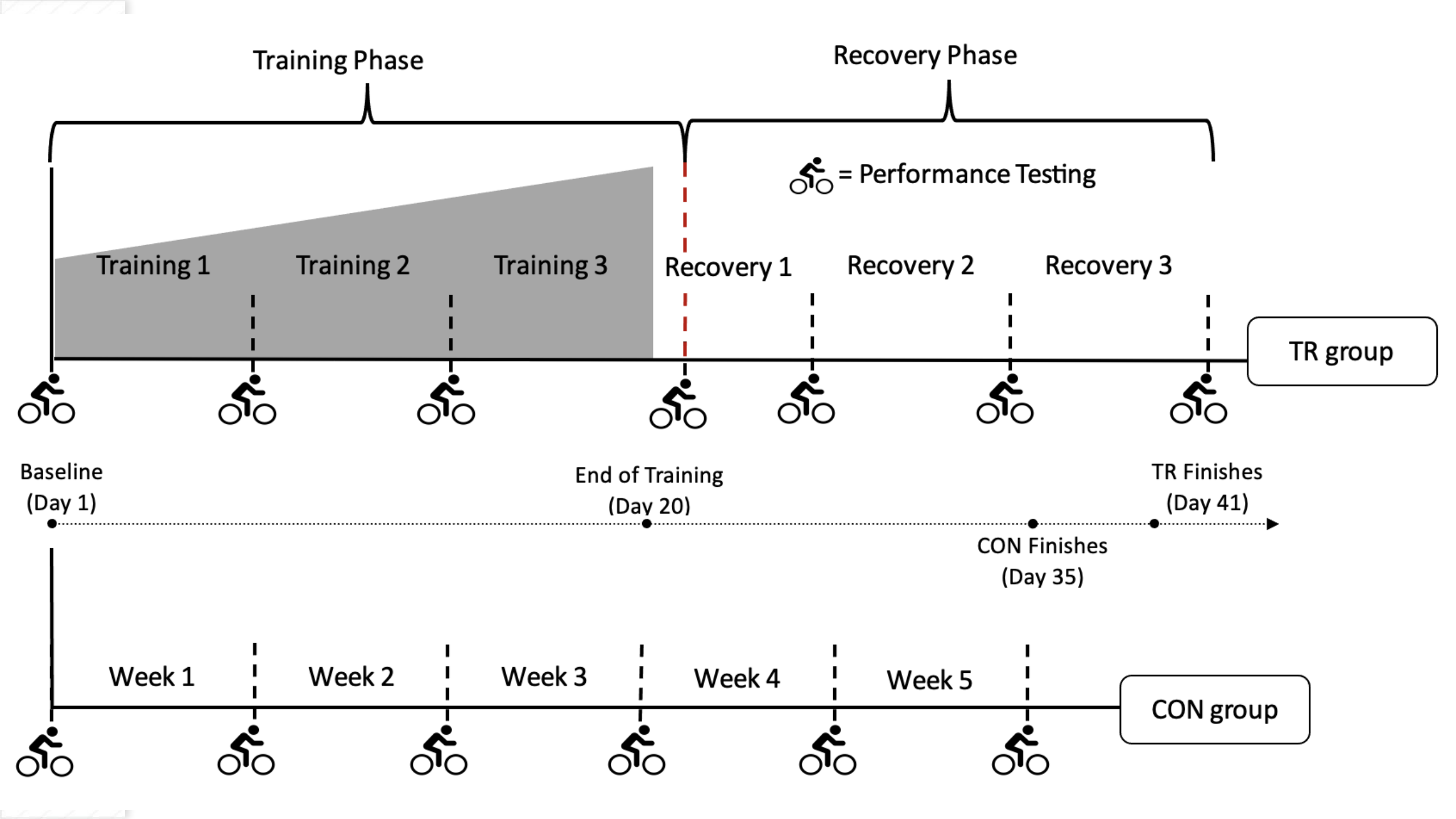
Participants

- Healthy recreationally active males and females
  - 18 to 50 years of age
  - No known disease or illness that would affect outcome measures
  - Have been fully vaccinated against COVID-19
  - Lung function >80% predicted values

- Exclusionary criteria
  - Known pulmonary, metabolic, renal, or autoimmune disease
  - Use of prescription medications that may confound important variables
  - Woman who are pregnant
  - Habitual cigarette use
  - Habitual smoking or vaping

- Withdrawal criteria:
  - <85% participation adherence
  - Consecutive POMS-SF scores >100
  - Failure of subject to comply with dietary & exercise habit requirements




Training Phase
Recovery Phase
= Performance Testing
Training 1
Training 2
Training 3
Recovery 1
Recovery 2
Recovery 3
TR group
Baseline
(Day 1)
End of Training
(Day 20)
TR Finishes
(Day 41)
CON Finishes
(Day 35)
Week 1
Week 2
Week 3
Week 4
Week 5
CON group

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Actigraphy and Surveys

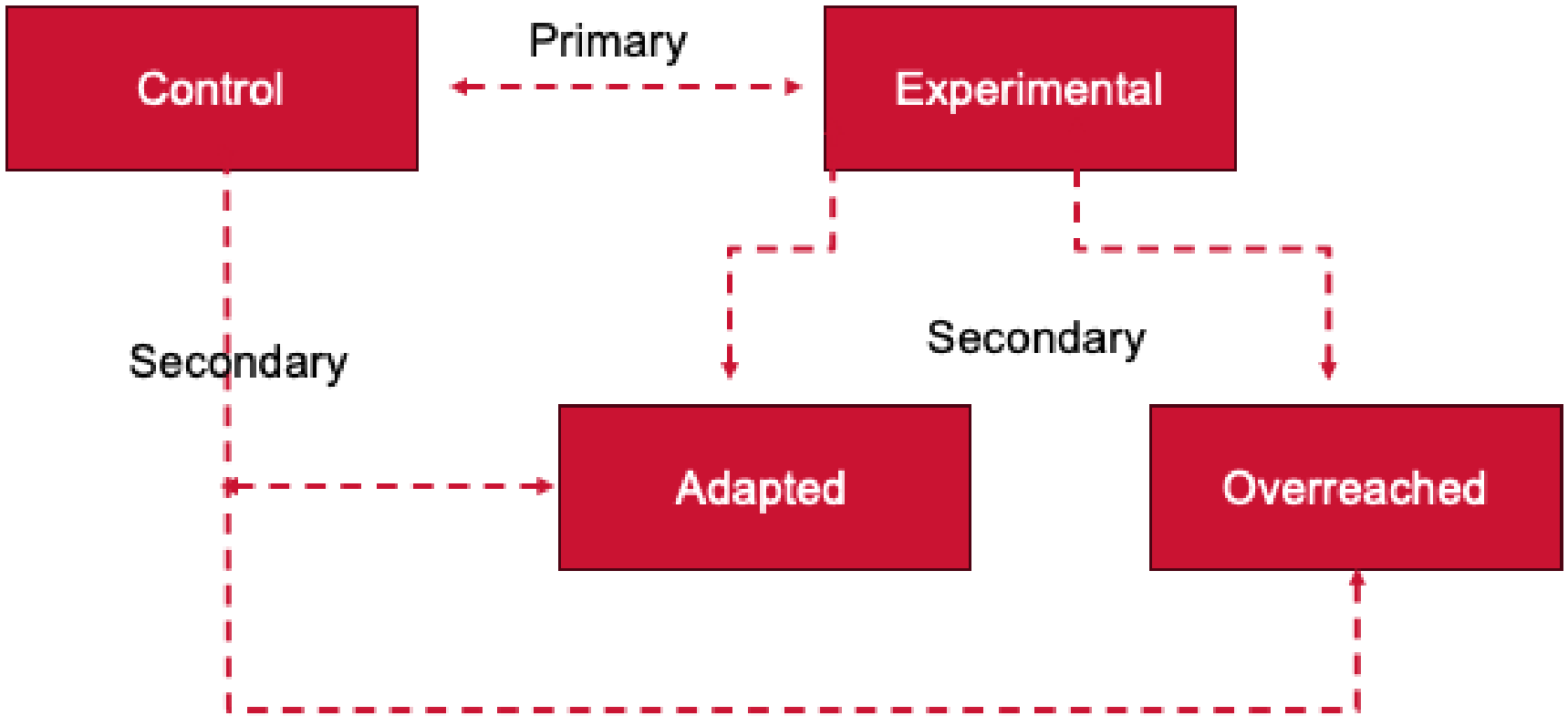
Actigraphy: Wrist-worn actigraph to objectively monitor sleep

Profile of Mood States-short form (POMS): Tracks mood states: tension, anger, vigor, depression, confusion, fatigue

Wisconsin Upper Respiratory Symptom Survey (WURSS-11): Assess upper respiratory illness symptoms

Sleep Survey: Bed/Wake times, subjective sleepiness, fatigue, and quality of sleep

Analysis Plan



Flow of Analysis

Descriptive Statistics

- Missing Data
  - MICE

Separate Groups

- OR threshold
  - CON
  - AD
  - OR

Test for Data Normality

- Levene's
- Shapiro-Wilk
- Visual Inspection
  - QQ plots
  - Residual plots

Mixed-Effect Models

- CON vs. TR
- CON, AD, OR

Post-hoc Testing

- Games-Howell
  - Group*Time
  - Group*Phase

Heirarchical Models

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Lab-based Measures

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Chapter One

Aim: To investigate whether a symptoms of overtraining could be induced in recreationally active adults using a lab-controlled training protocol.

- Performance (PWL)
- Aerobic Capacity ($\dot{V}O_{2Peak}$)
- Lactate (LA_{Peak})
- Maximum Heart Rate (MHR)
- Heart Rate Recovery (HRR)
- Body composition (BodPod)

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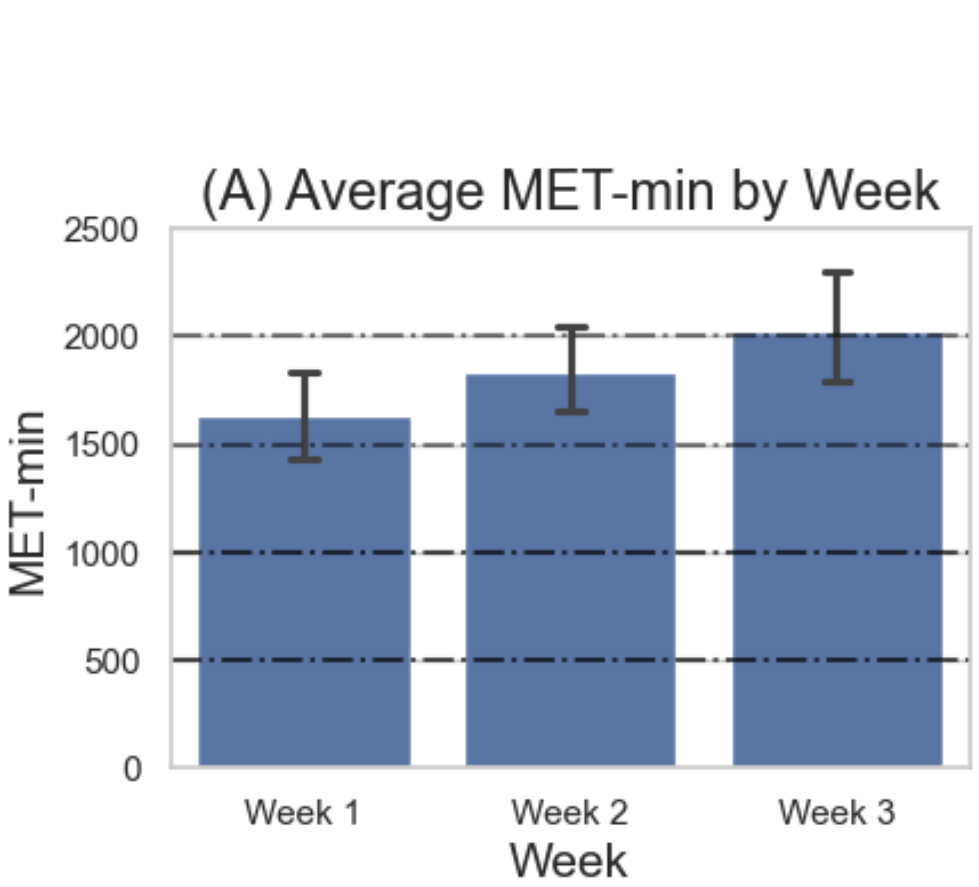
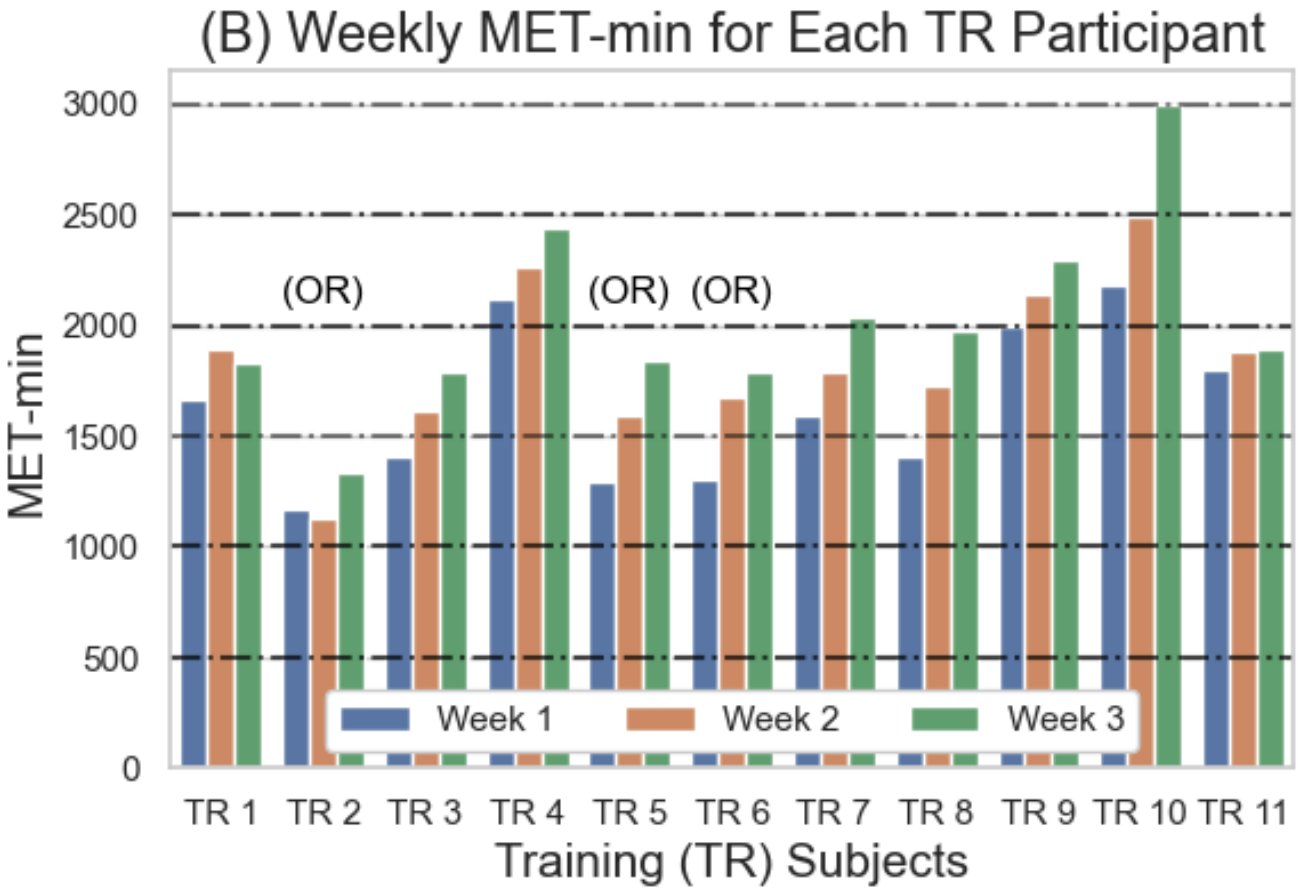
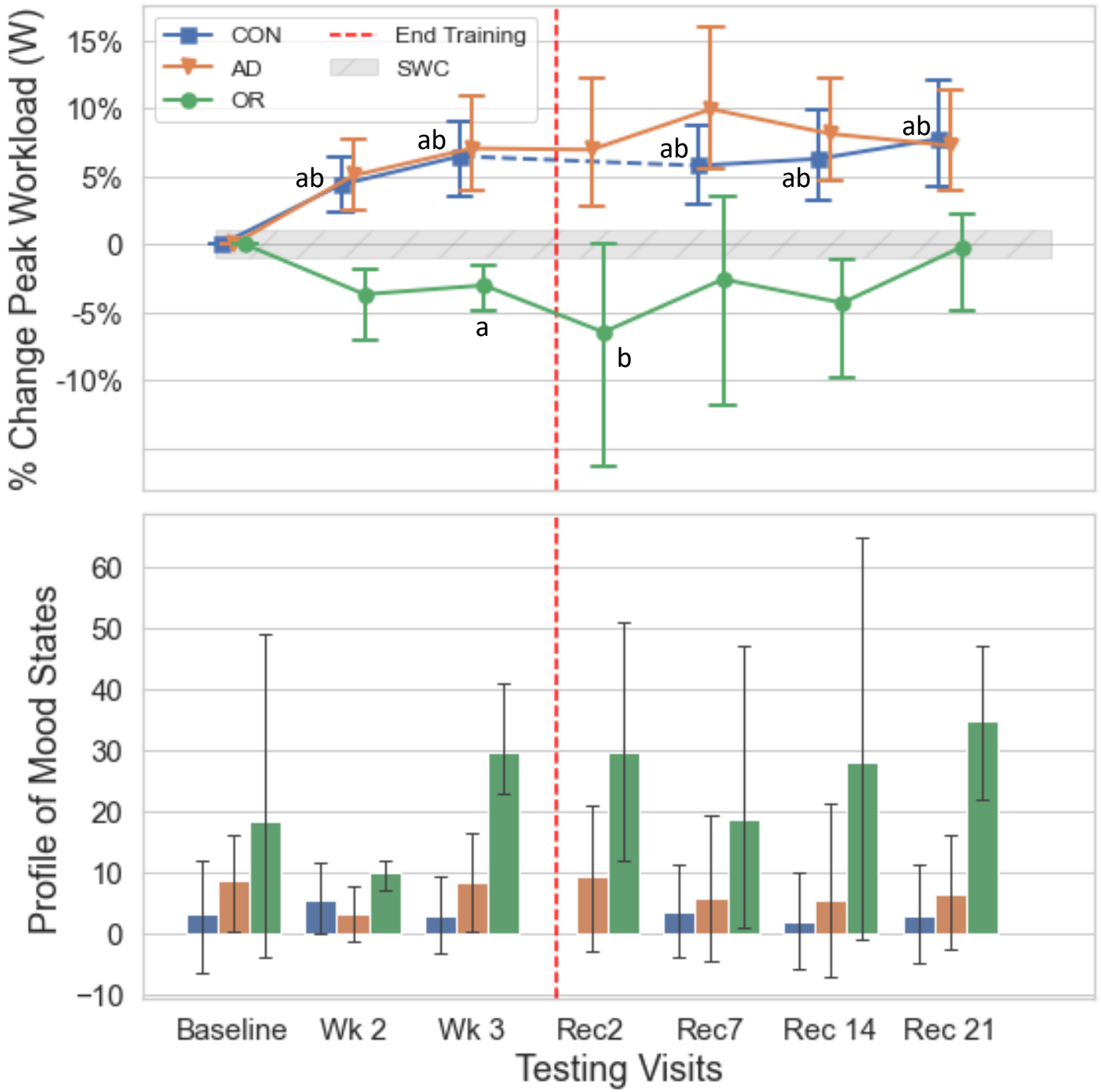
Baseline Characteristics

Group	N (sex)	Age (years)	Height (cm)	Weight (kg)	VO_{2Peak} (ml/kg/min)	VO_{2Peak} (% Predicted)
CON	**10 (6f)**	**28.8 ± 8.7**	**168 ± 11.1**	**68.9 ± 12.9**	**39.7 ± 9.8**	**97% ± 22.9%**
TR	**11 (10f)**	**28.4 ± 8.1**	**168.8 ± 8.4**	**72.8 ± 17.3**	**36.2 ± 6.2**	**105.3% ± 29.3%**
AD	8 (7f)	29.4 ± 9.1	170 ± 8.0	76.6 ± 18.7	37.7 ± 6.1	113.4% ± 29.6%
OR	3 (3f)	25.7 ± 5.0	166 ± 10.2	62.8 ± 7.6	32.2 ± 5.5	83.6% ± 15.9%

MET-min per Week







OR Threshold:

Smallest Worthwhile Change

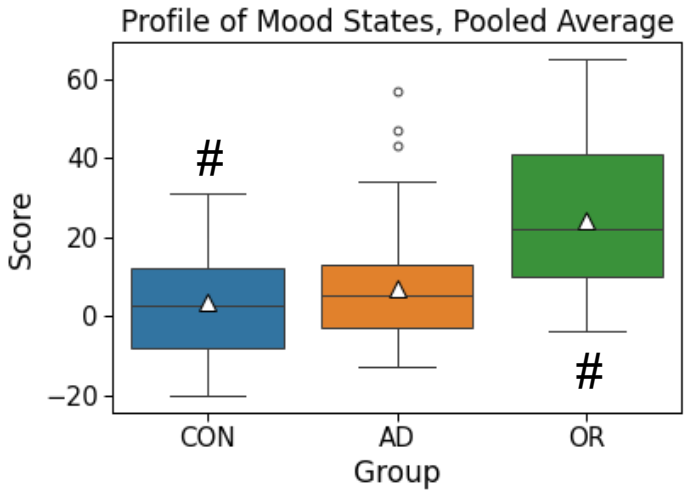
$$coefficient\ of\ variation\ (CV) \times 0.3$$

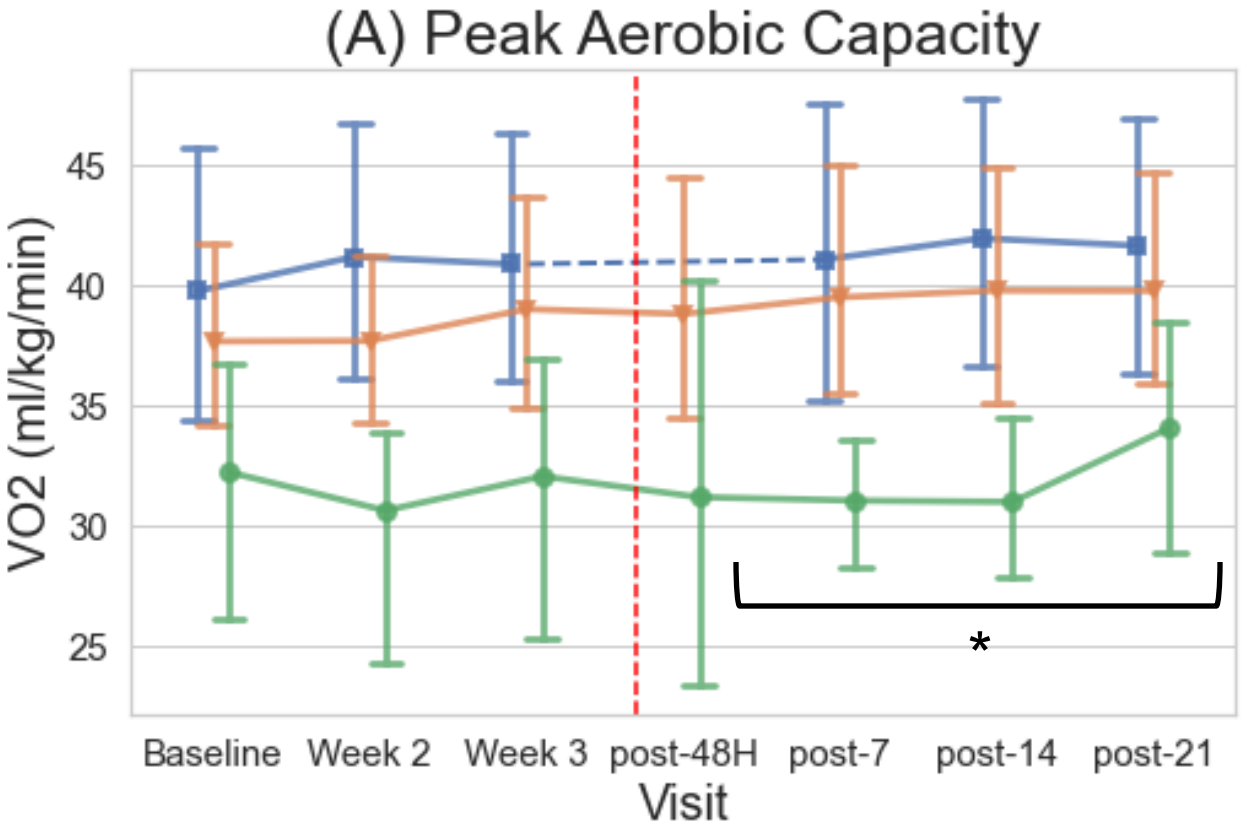
$$CV = (SD \div Mean) \times 0.3) \times 100\ (\%)$$

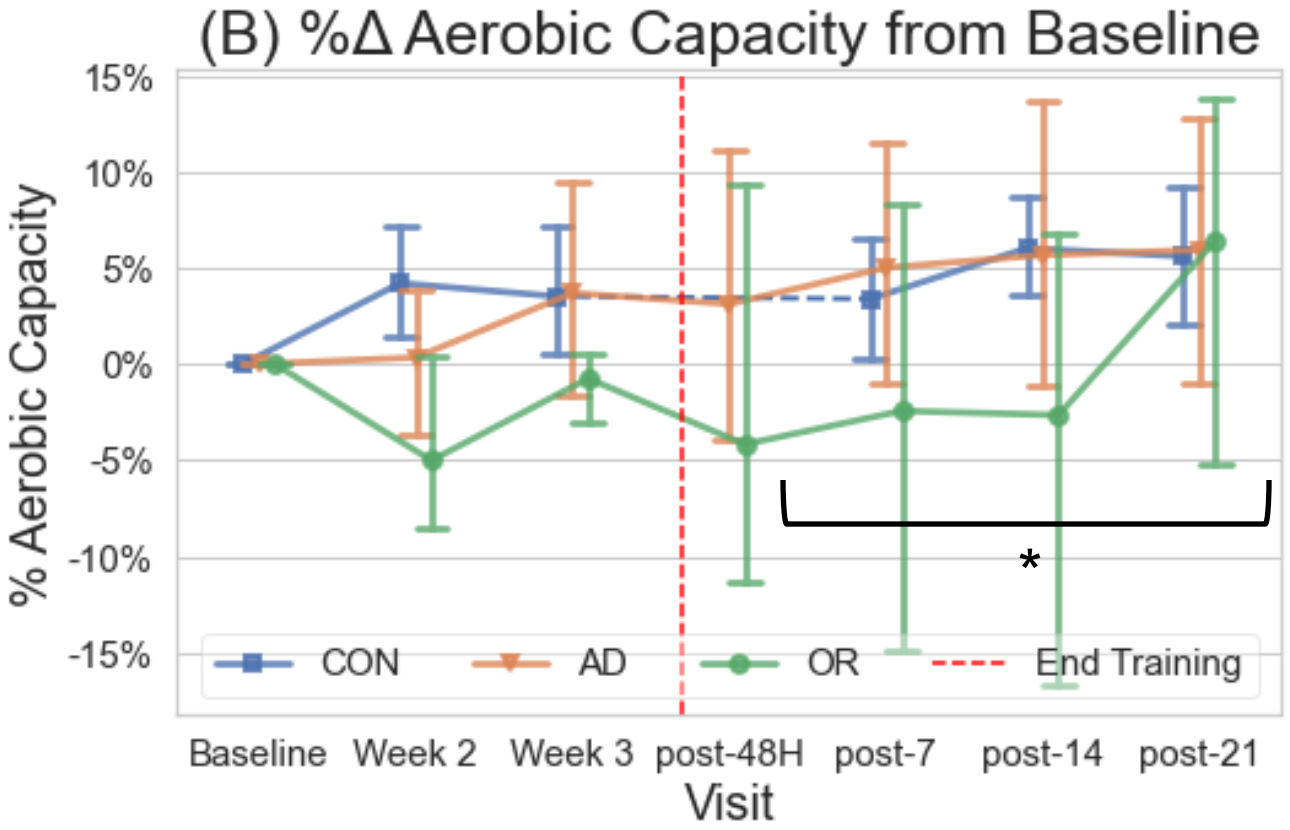
OR Threshold:

- $CV = ((7.44 \div 222.13) \times 0.3) \times 100$
- 1.00% from baseline Performance

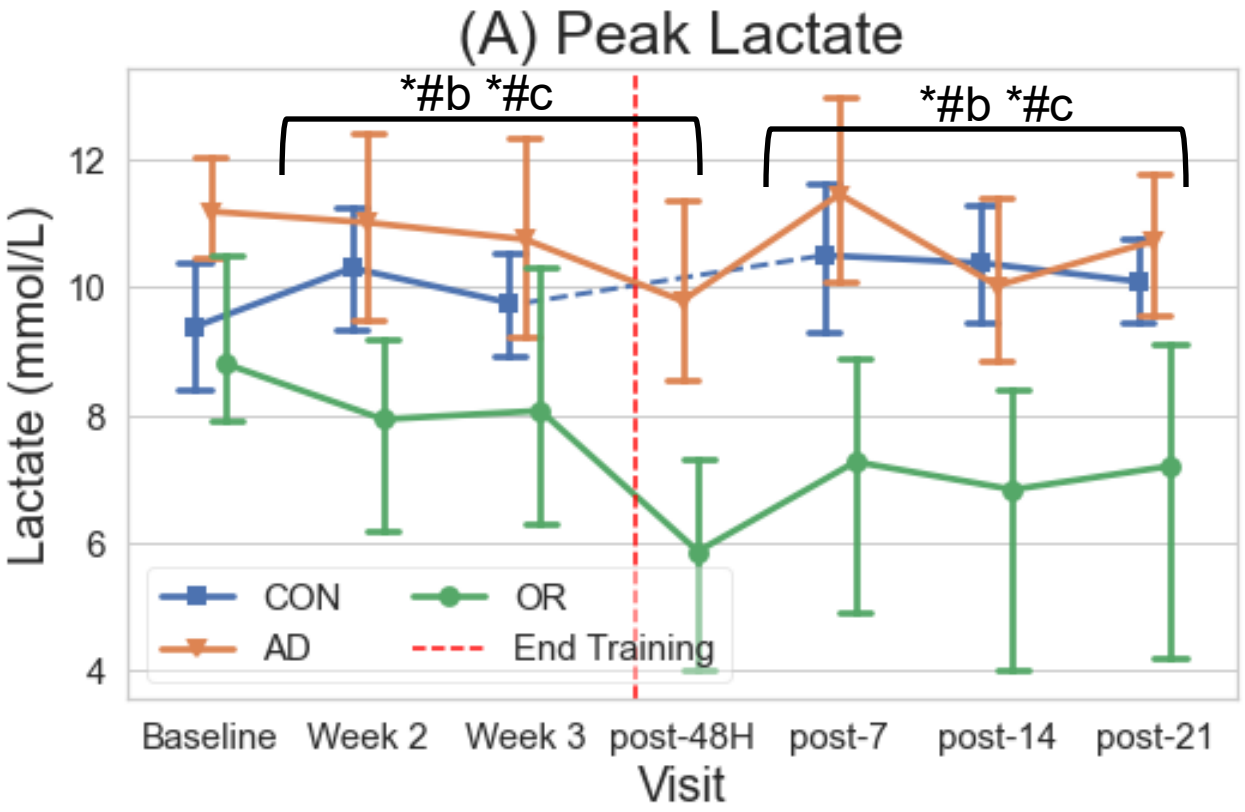
- **OR nadir performance**:
  -10.3% ± 5.4%

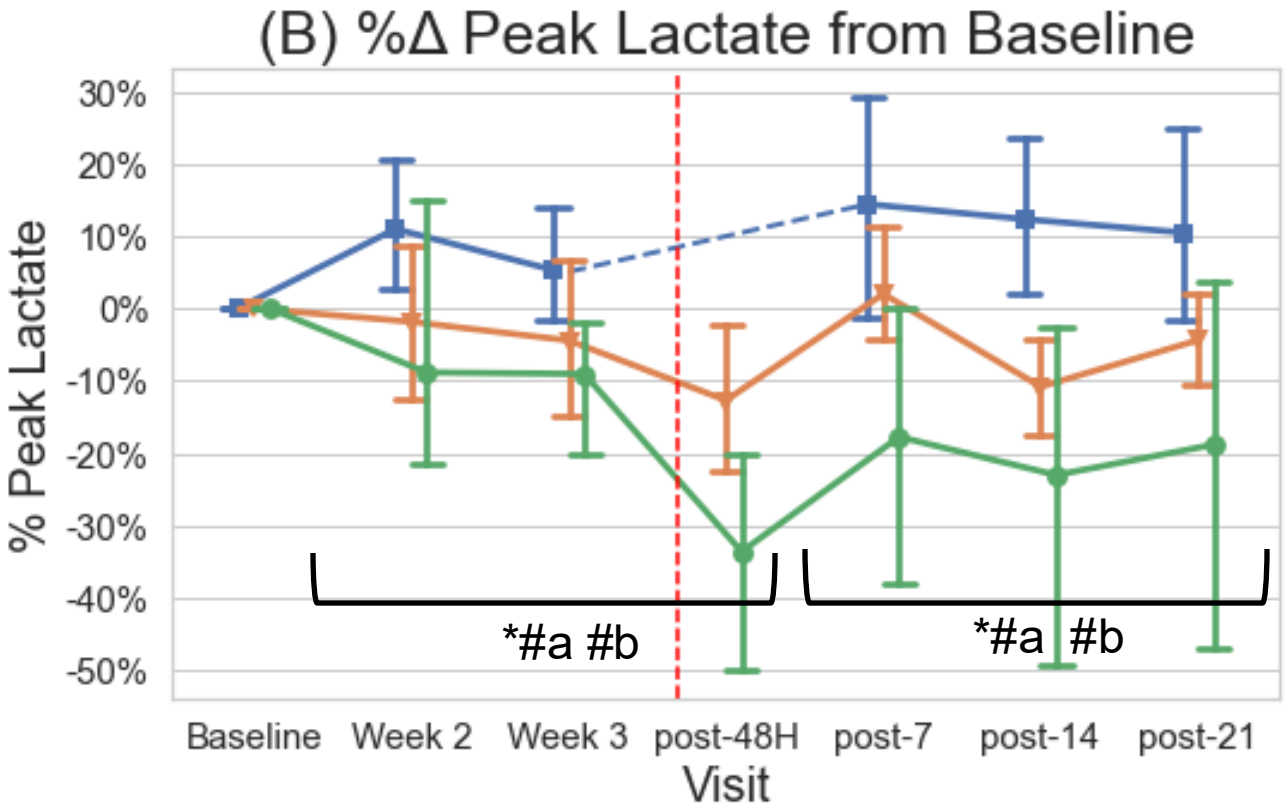




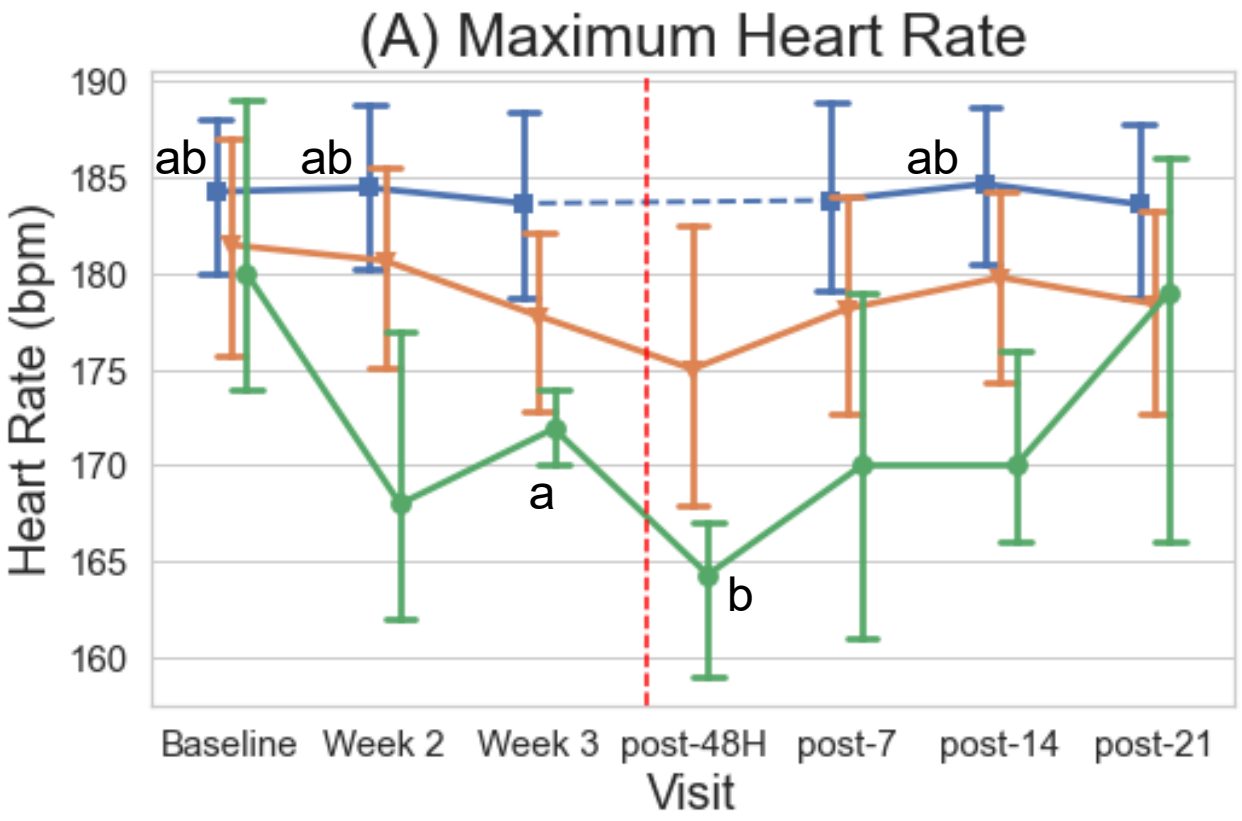


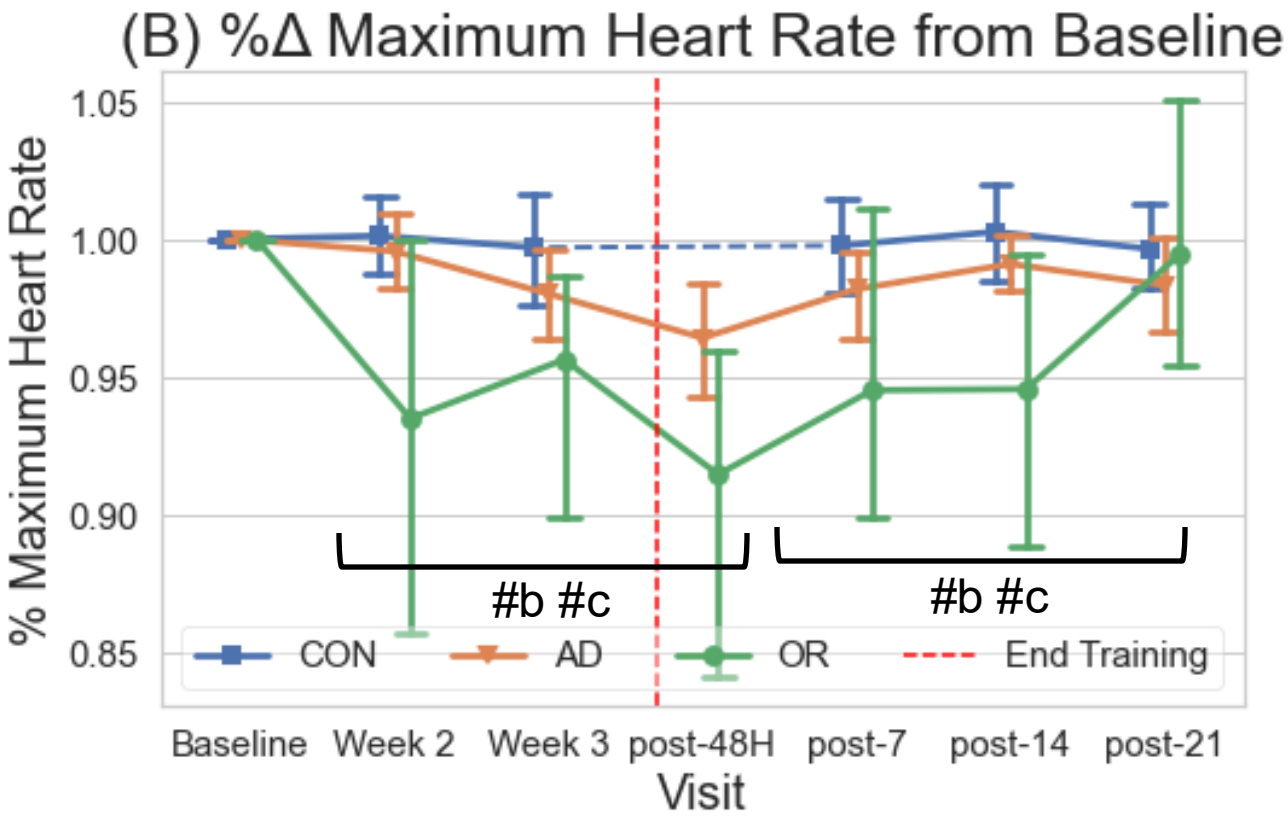
*P<0.05 Main effect time





*P< 0.05 with bracket, significant main effect (phase) from baseline in all groups.
Lowercase letter with brackets, P< 0.05 group-time(phase) interaction (a=CON, AD; b= CON, OR, c= AD, OR).
*with letter, group differences occur during same phase;
#with letter, group differences occur between different phases.





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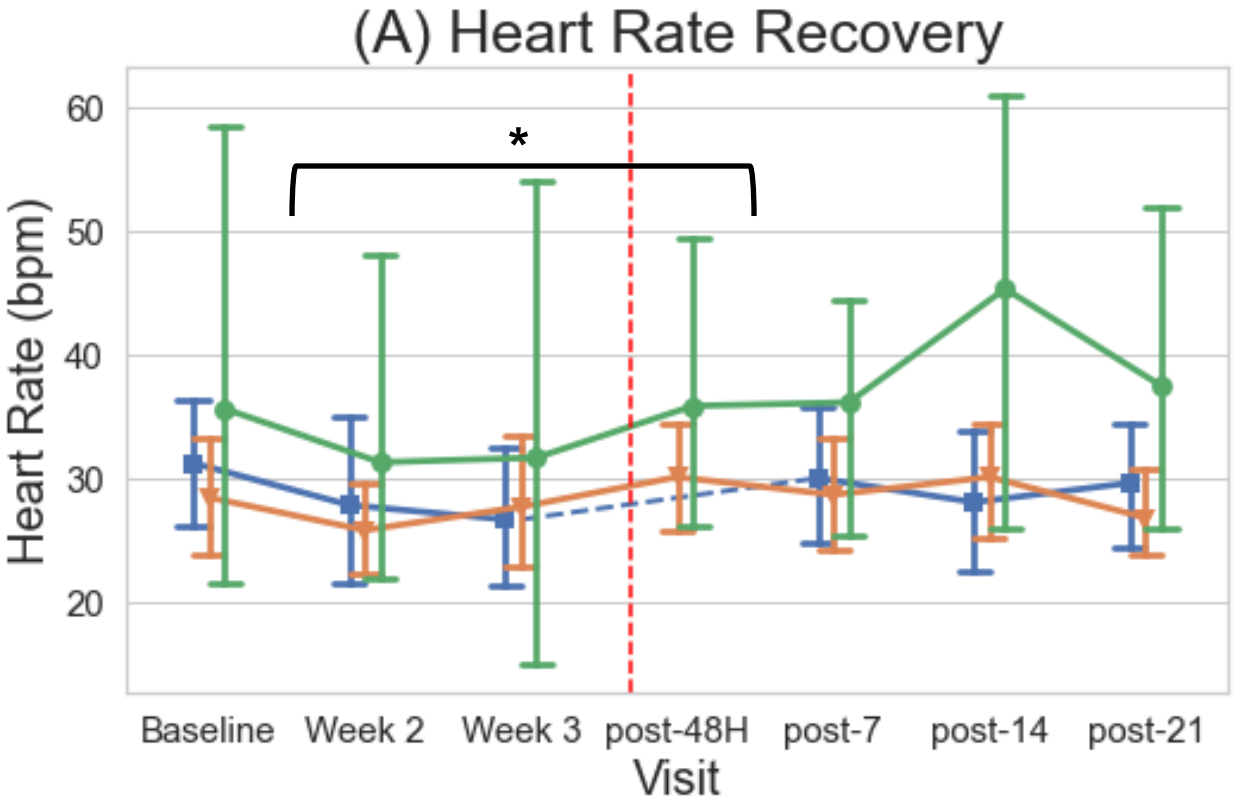

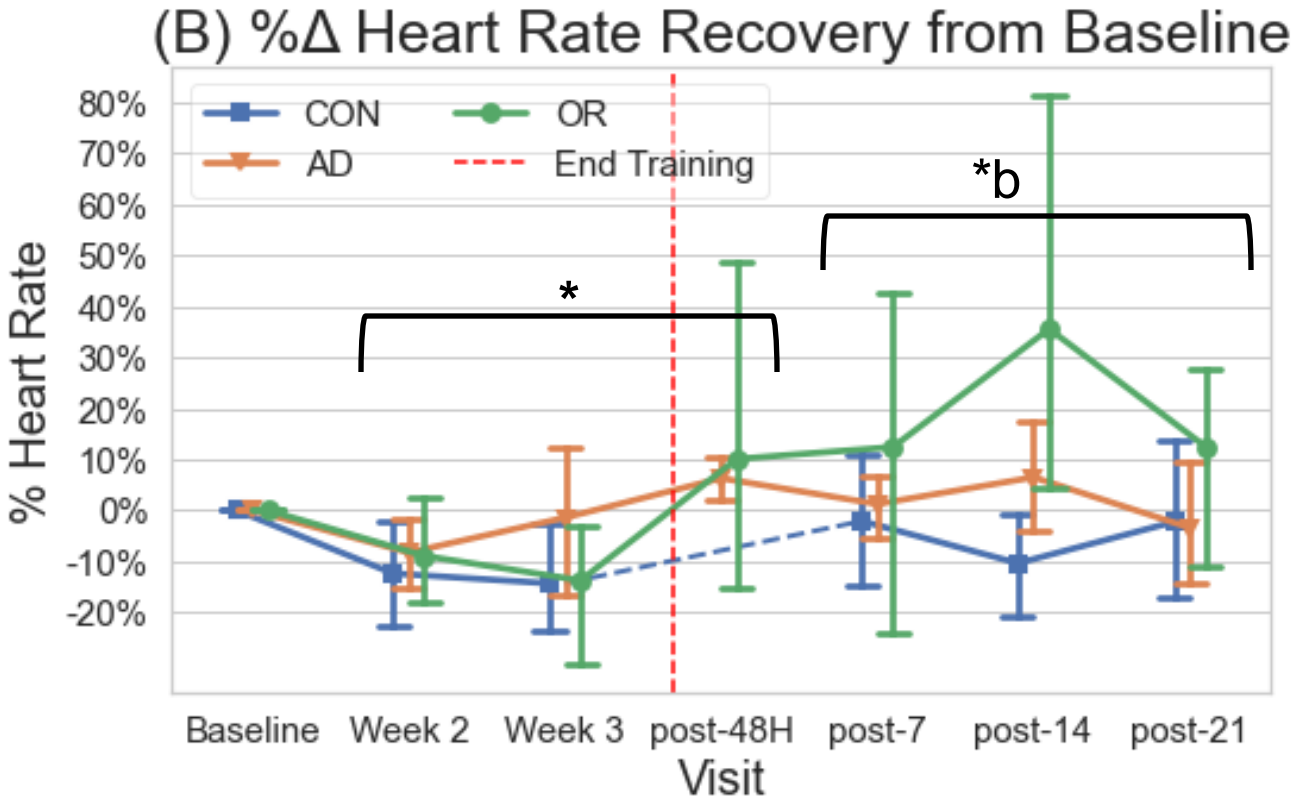

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Sleep

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Chapter Two

Aim: To investigate the influence that high-intensity training has on sleep; to determine if there are differences in sleep parameters between AD, OR, and CON participants.

- Sleep Duration (duration of attempted sleep in 24-h period)
- Total Sleep Time (actual time spent asleep)
- Cumulative Sleep Debt (cumulative difference in TST and recommended 7 hours per night)
- Sleep Efficiency (TST ÷ SD)
- Sleep Quality
- Subjective Sleepiness (Karolinska sleepiness scale)
- Fatigue (Samn-Perelli fatigue scale)
- Upper Respiratory Illness Symptoms (WURSS-11)

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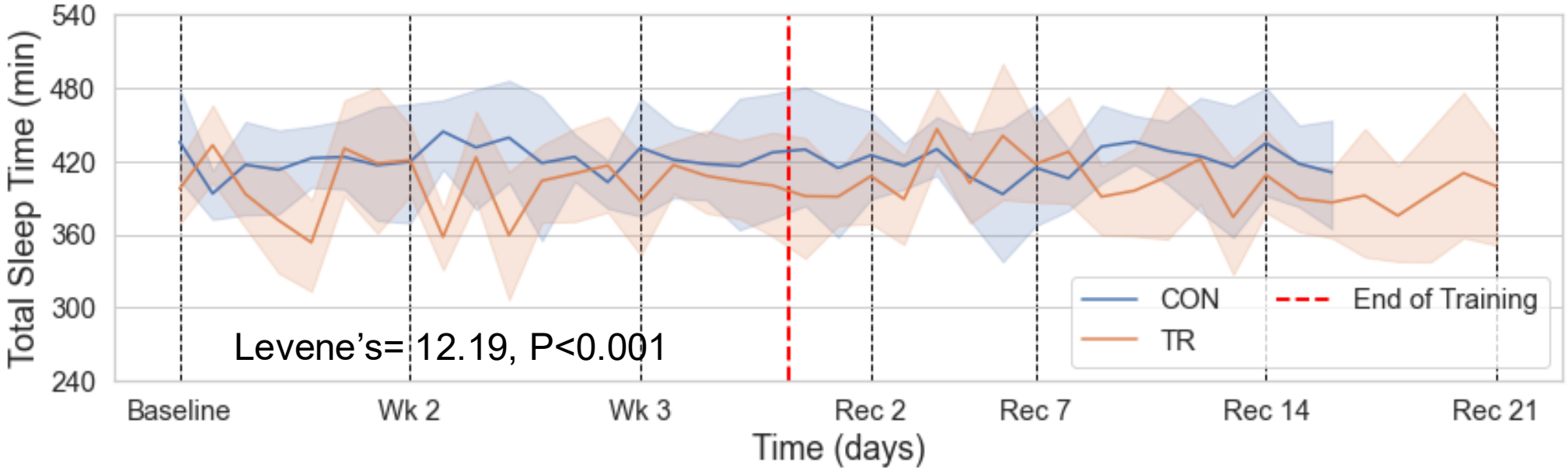
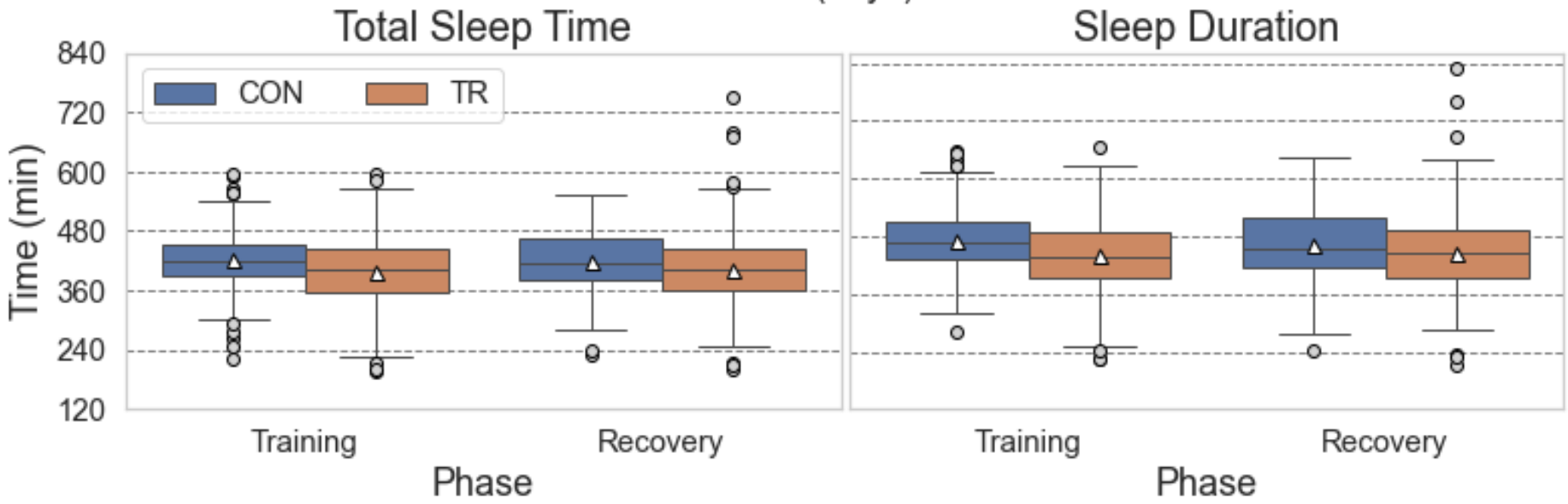
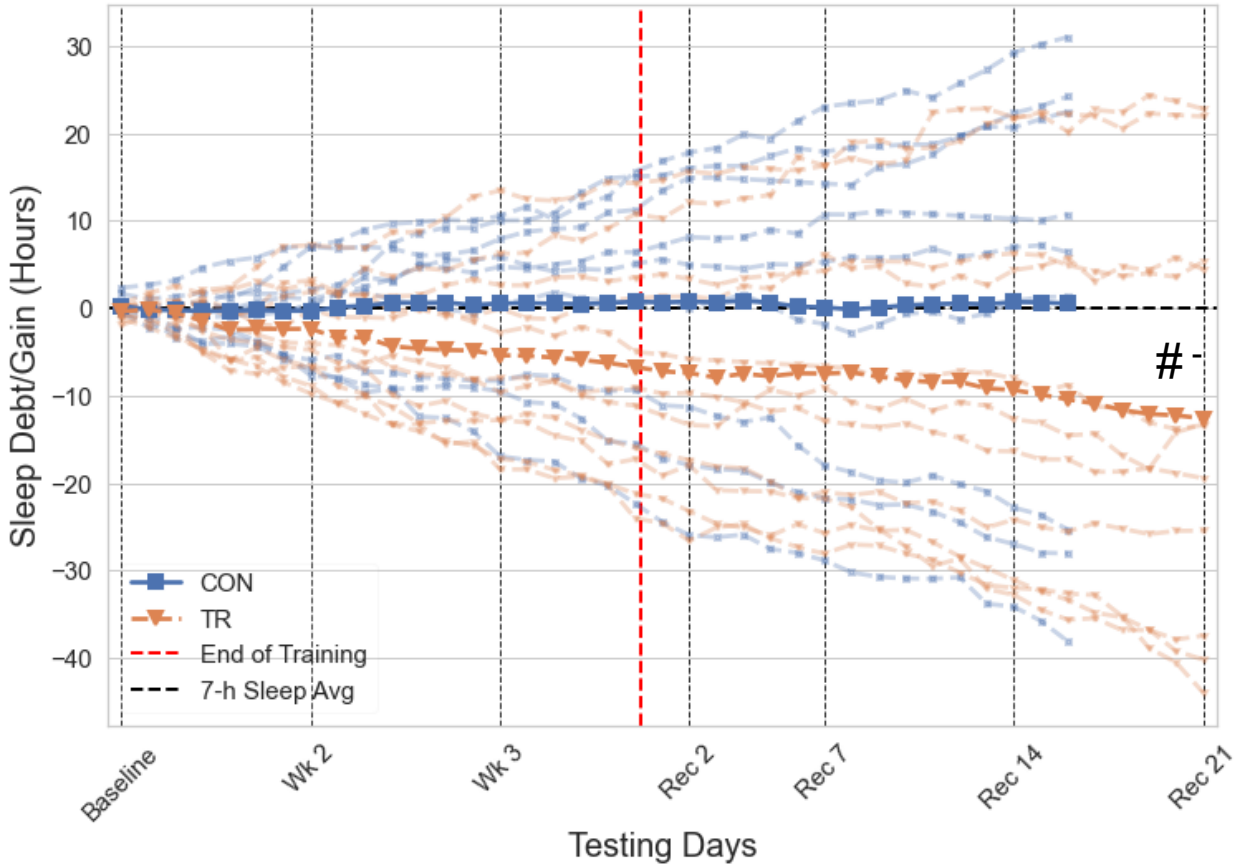
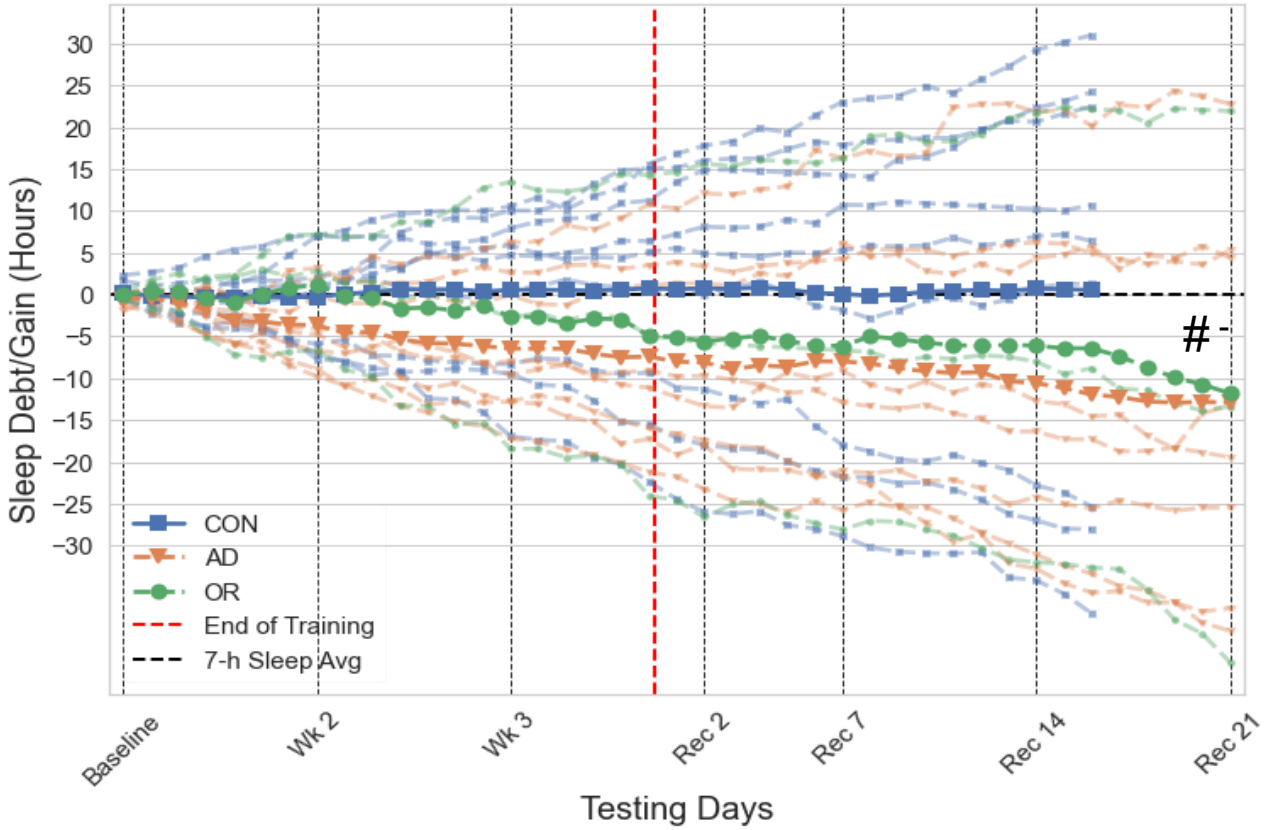
Total Sleep Time



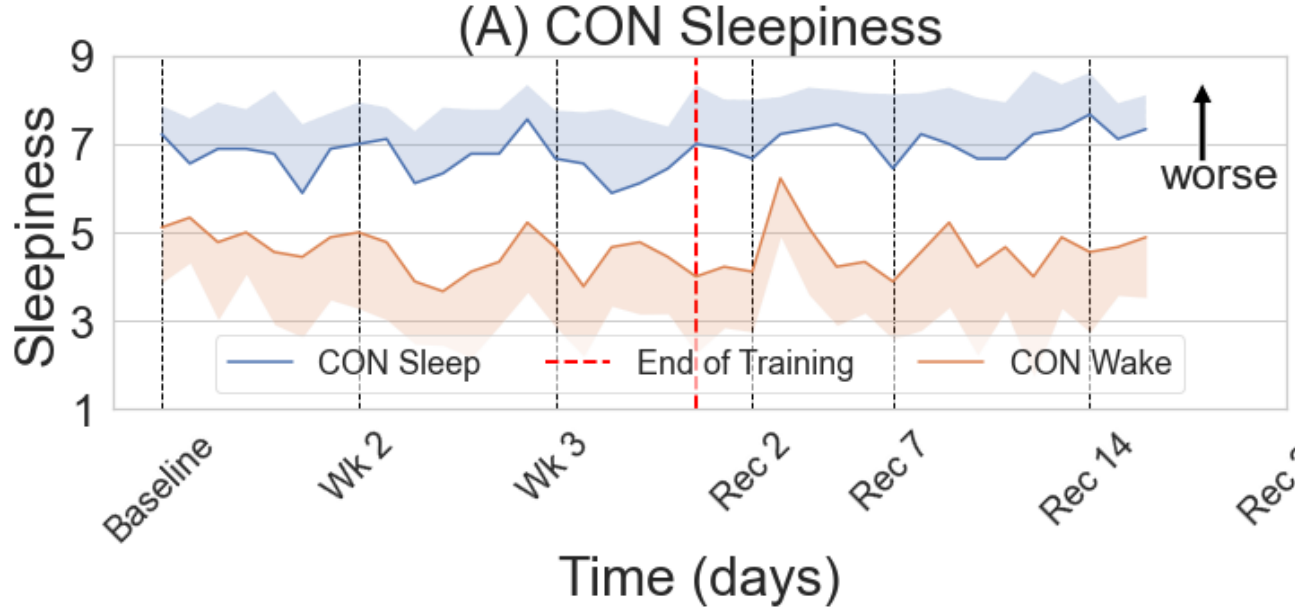


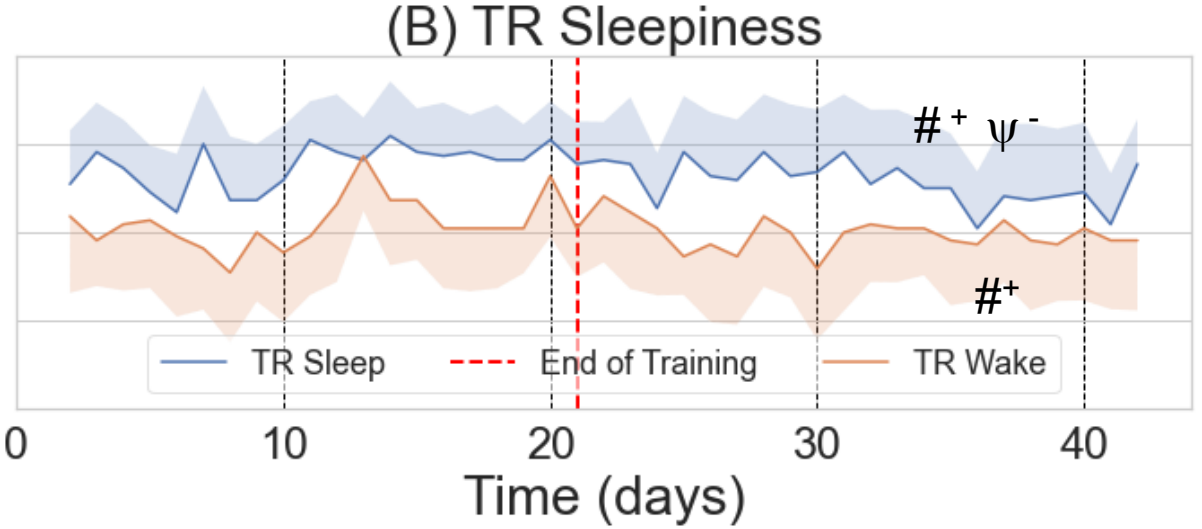
Cumulative Sleep Debt

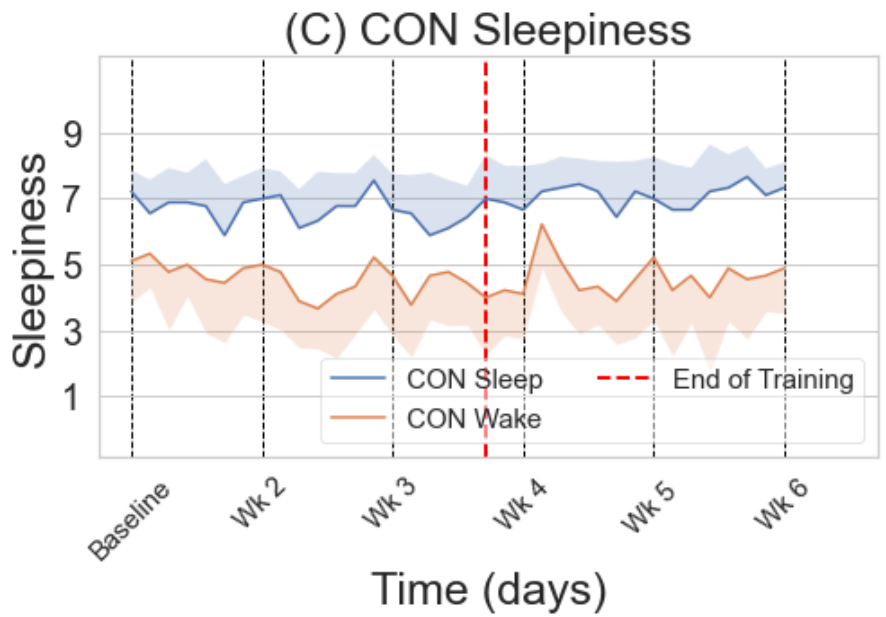


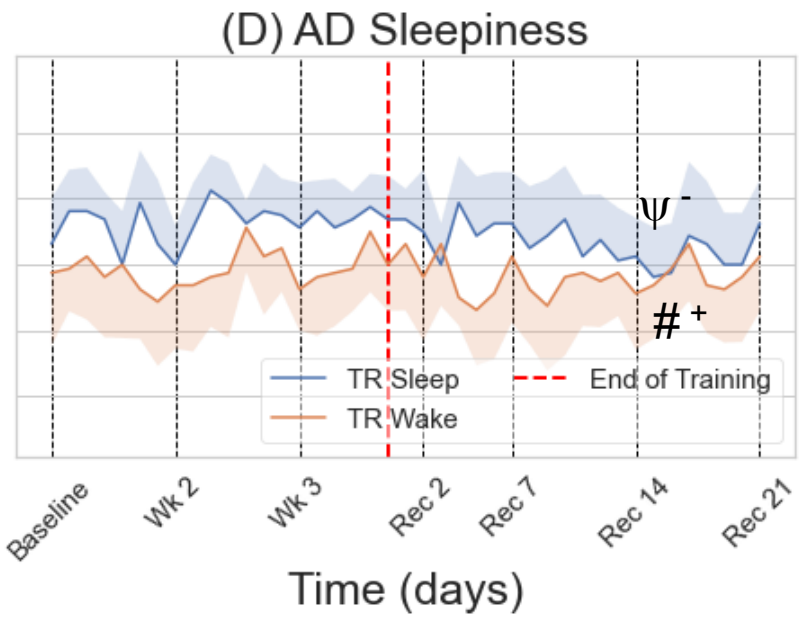


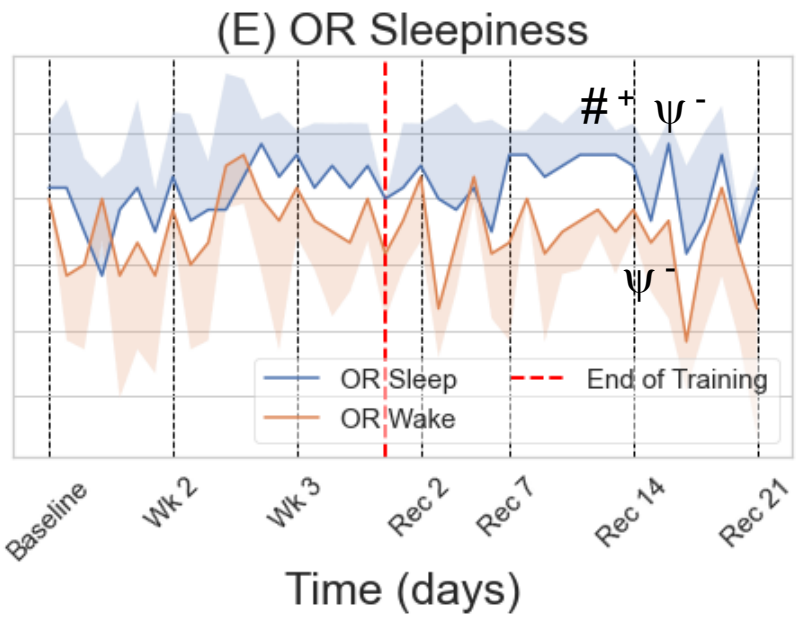
 # AD,CON







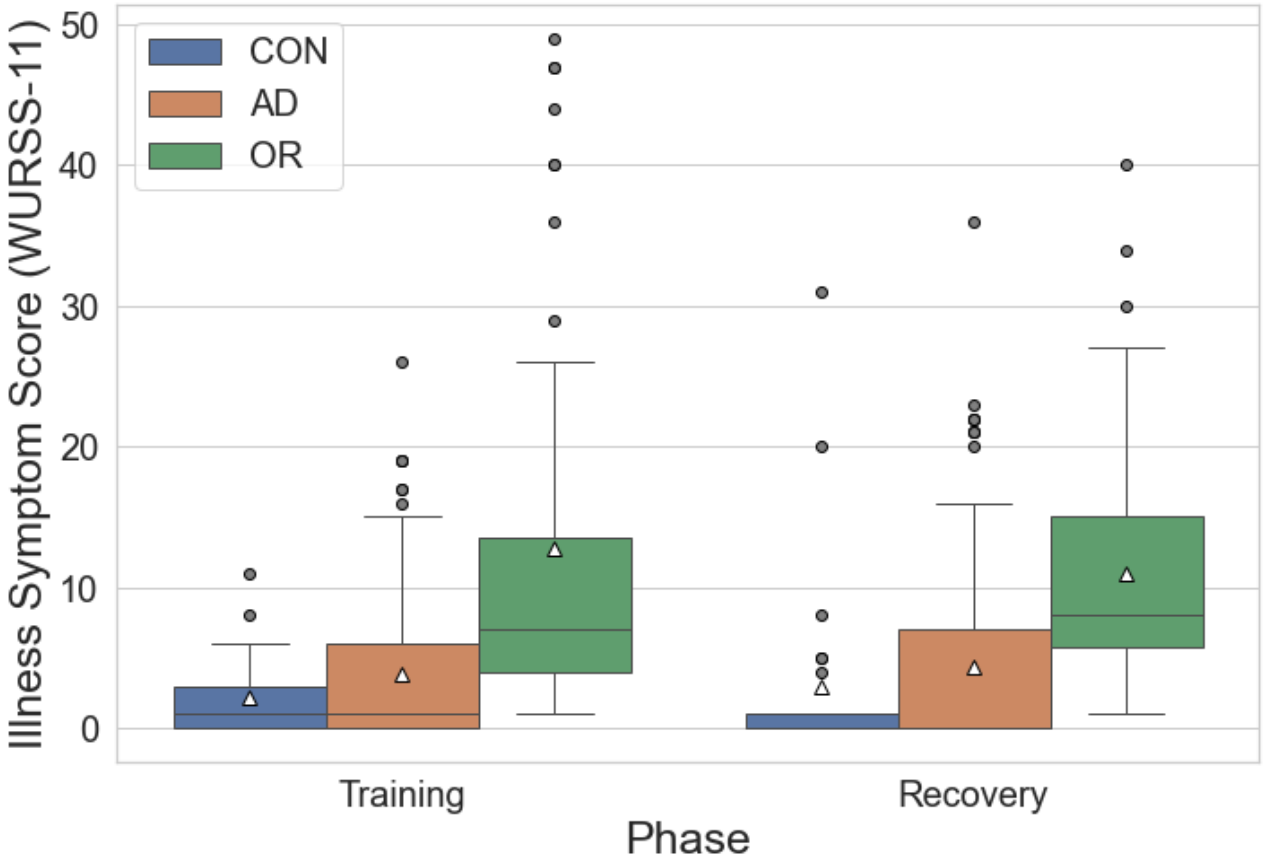


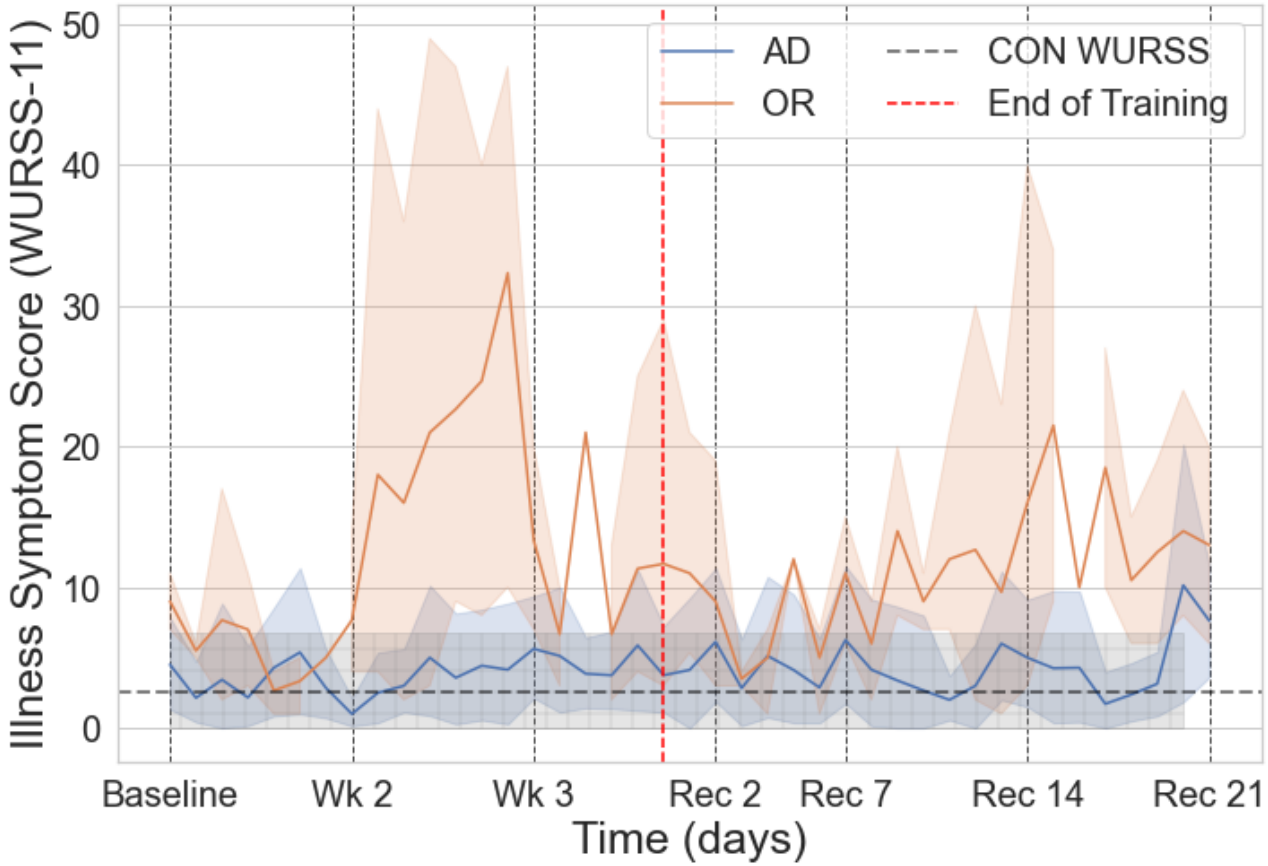


group-time P<0.05

ψ group-time-phase P<0.05

Upper Respiratory Symptoms





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Proteomics

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Chapter Three

Aim: Investigate the proteomic response to high-intensity exercise in recreationally active males and females during a three-week lab-controlled training protocol.

- Proteomic analysis in subset of TR participants (n=7)
- STRING (Search Tool for Retrieval of Interacting Genes/Proteins) v12.0

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Collect Blood Samples

Extract Proteins (processing)

Proteomic Analysis (HPLC-MS/MS)

Log2 Transform relative protein abundance

Friedman Test and Wilcoxon Signed Rank Tests

STRING → Reactome Pathways

380 unique Proteins Identified

- 206 proteins identified in all samples
- 209 BL and MID
- 219 BL and END

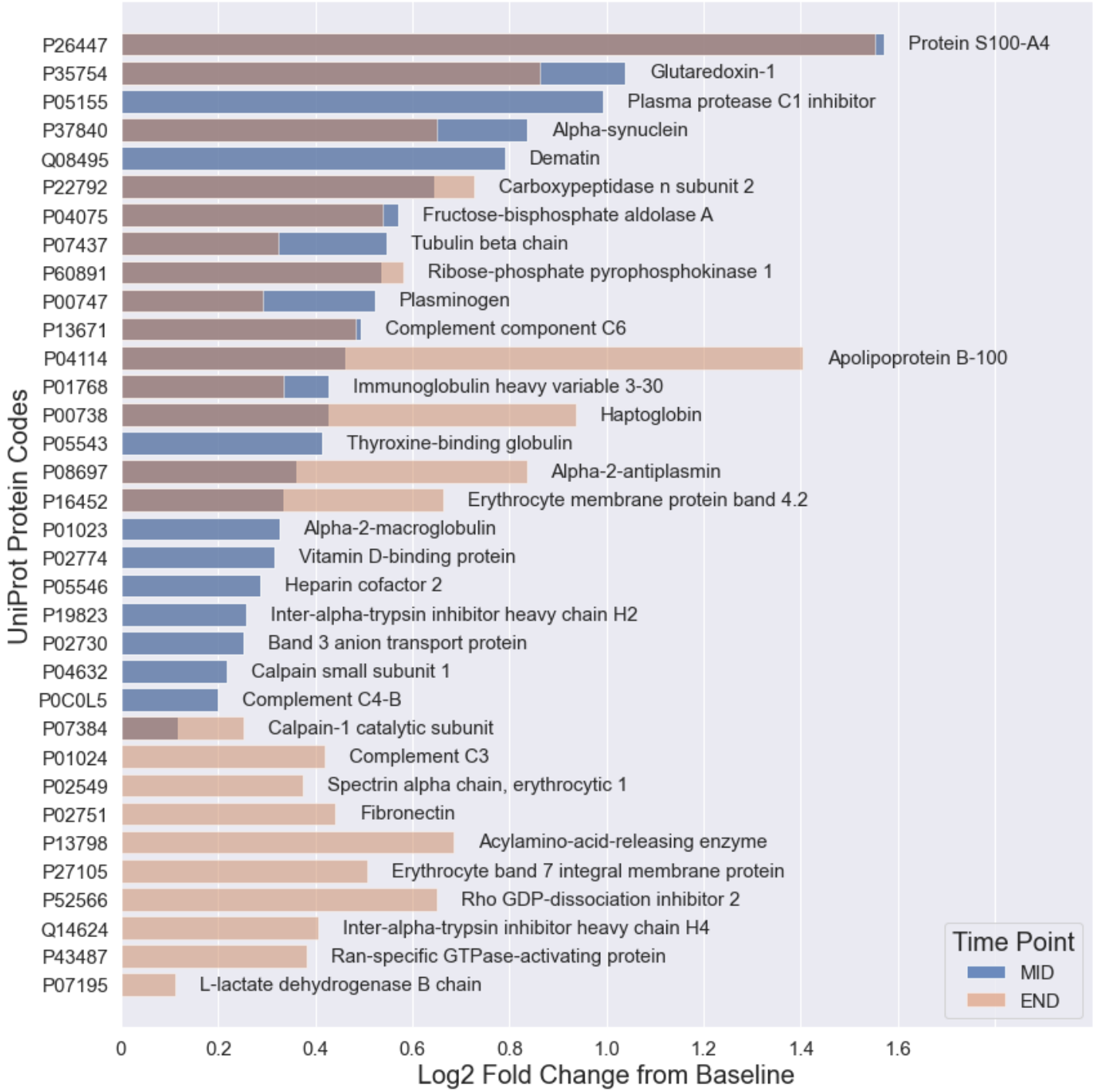
Statistical Analysis

- 35 proteins upregulated at MID or END ($P<0.1$)
- 6 proteins downregulated at MID or END ($P<0.1$)

STRING

Reactome Pathways

- 19 immune-related proteins



Upregulated Proteins at MID or END

- Upregulated proteins n=35 (P<0.1)
  - Protein-protein interaction network (PPI) in STRING
- Downregulated proteins (n=6)
  - Insufficient for PPI network

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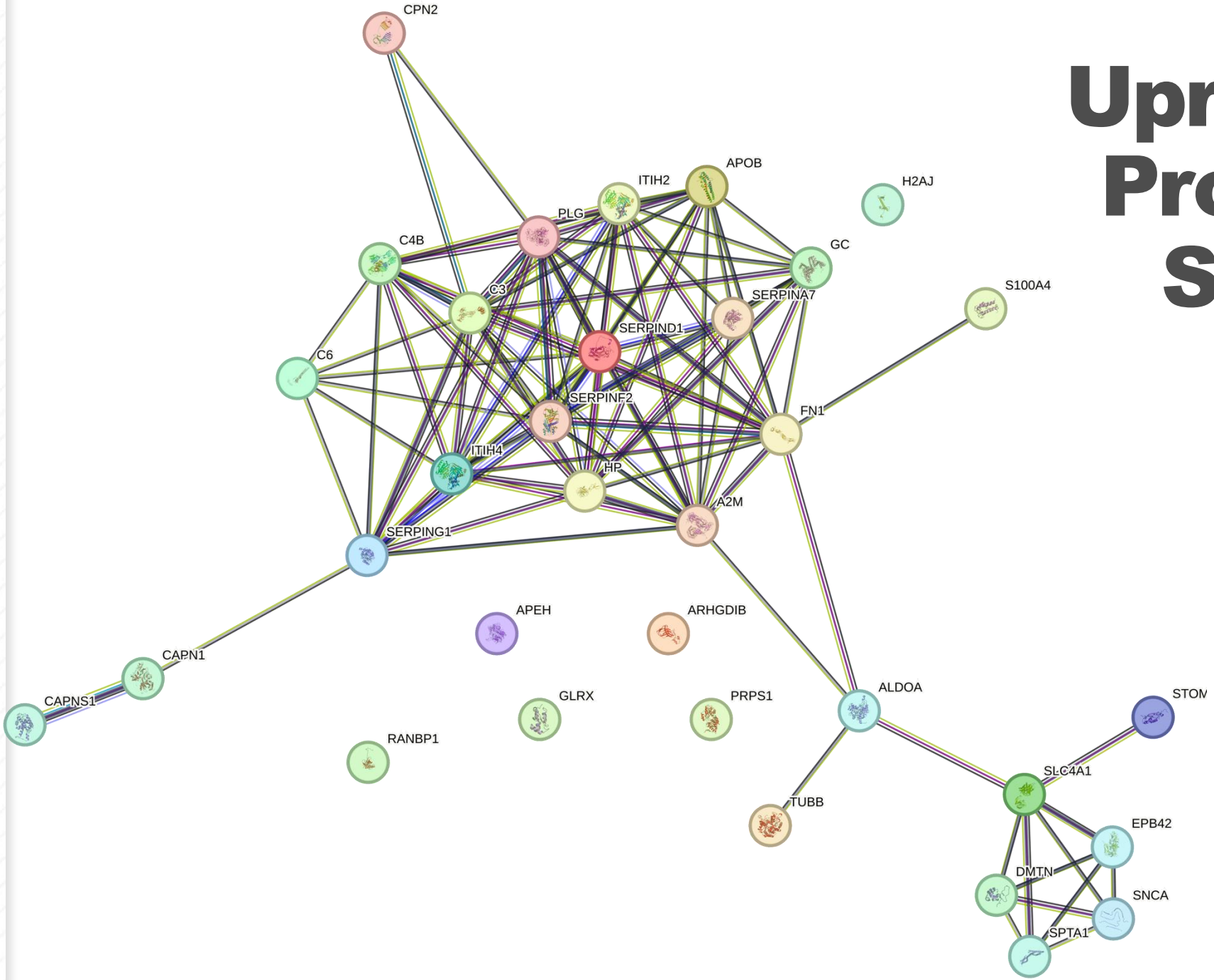
Upregulated Proteins in STRING



Local cluster coefficient
0.706 (P<0.001)

STRING

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KEGG Pathways

pathway	description	count in network	strength	false discovery rate
hsa04610	Complement and coagulation cascades	8 of 82	1.77	5.79e-10
hsa05322	Systemic lupus erythematosus	4 of 94	1.4	0.0035
hsa05133	Pertussis	3 of 73	1.39	0.0309
hsa05150	Staphylococcus aureus infection	3 of 86	1.32	0.0369

Reactome Pathways

pathway	description	count in network	strength	false discovery rate
HSA-174577	Activation of C3 and C5	2 of 7	2.23	0.0148
HSA-75205	Dissolution of Fibrin Clot	2 of 13	1.96	0.0370
HSA-140837	Intrinsic Pathway of Fibrin Clot Formation	3 of 23	1.89	0.0021
HSA-977606	Regulation of Complement cascade	5 of 49	1.78	2.16e-05
HSA-114608	Platelet degranulation	7 of 126	1.52	4.54e-06
HSA-381426	Regulation of Insulin-like Growth Factor (IGF) transport and ...	6 of 124	1.46	3.58e-05
HSA-8957275	Post-translational protein phosphorylation	5 of 107	1.45	0.00029
HSA-9645723	Diseases of programmed cell death	3 of 73	1.39	0.0370
HSA-1474228	Degradation of the extracellular matrix	5 of 140	1.33	0.00092
HSA-109582	Hemostasis	9 of 607	0.95	0.00015
HSA-6798695	Neutrophil degranulation	7 of 476	0.94	0.0022
HSA-168249	Innate Immune System	12 of 1041	0.84	3.58e-05
HSA-168256	Immune System	13 of 1979	0.59	0.0019

(less ...)

Not pictured: IGHV3-30 (immunoglobulin)

Summary of Findings

Chapter One: Exercise Performance Response

- $\dot{V}O_{2Peak}$ increased ~6% in all three groups (CON, AD, OR) by end of recovery
  - Despite three weeks of training at ~3 to 4 times recommended PA levels

- OR subjects exhibited progressive decreases to MHR and LA^{-}_{Peak} (baseline to post-48h)
  - MHR: -8.5% ± 6.4%, 180 ± 7.9 bpm to 164 ± 4.6 bpm
  - HRR: +35.6% ± 40.6%; 35.7 ± 20.0 to 45.3 ± 17.8; (BL to post-14)
  - LA^{-}_{Peak}: -33.6% ± 15.1%, 8.80 ± 1.47 to 5.86 ± 1.69 mmol/L

- AD also demonstrated similar changes to LA_{Peak}
  - LA^{-}_{Peak}: -12.7% ± 16.1%, 11.19 ± 1.26 to 9.79 ± 2.22 mmol/L

Implications:

- Results support autonomic dysfunction theory of overtraining.
- Supportive evidence that overreaching/overtraining may attenuate aerobic capacity improvements

Summary of Findings Cont.

Chapter Two: Sleep

- Compared to CON subjects, TR subjects:
  - Slept less on average (7.02 $\pm$ 1.02 vs. 6.68 $\pm$ 1.20 hours per night)
  - More variable sleep patterns (Levene's= 12.19, $P<0.05$)
  - More likely to accumulate sleep debt
  - More persistent subjective sleepiness (bedtime/wake)

- OR subjects consistently reported higher URTI symptoms ($P<0.05$).

Implications:

- Heavy or excessive training may impair ability to obtain sufficient sleep
  - May impact consistency of sleep patterns
- Higher URTI symptoms in OR group may support immune dysfunction associated with overtraining response, independent of sleep disturbance.

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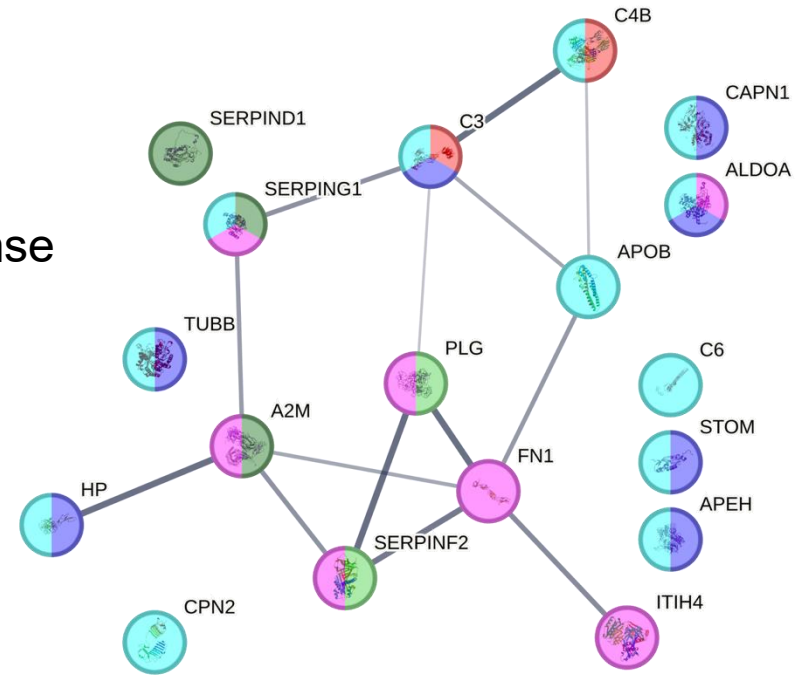
Summary of Findings Cont.

Chapter Three: Proteomics

- Proteomics analysis identified 38 proteins upregulated at MID or END (P<0.1)
  - 19 related to several aspects of innate immune system.

Implications:

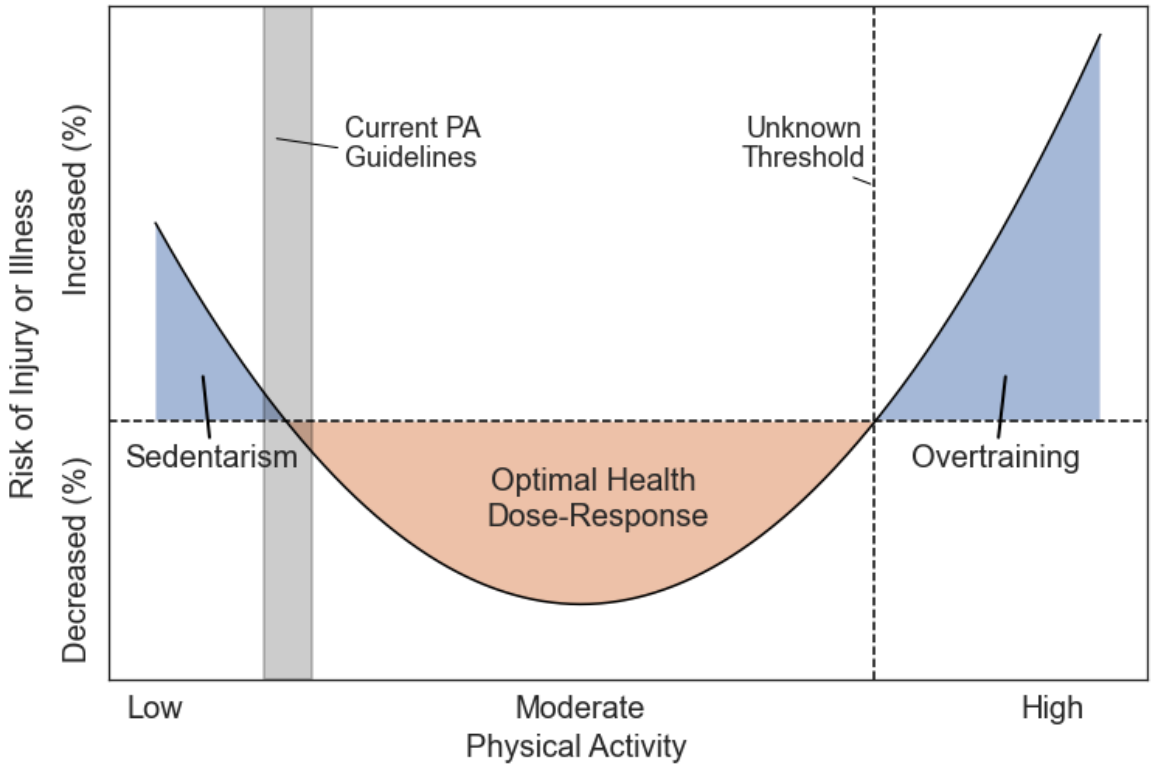
- Possible implications of chronic acute-phase immune response following high-intensity training.

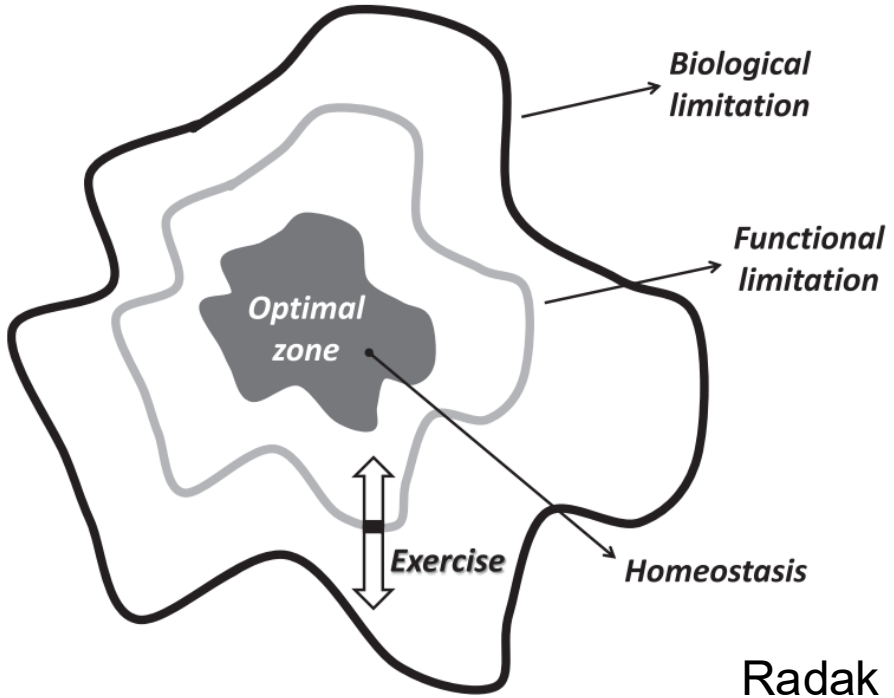


Exercise Hormesis Theory

A a chain is no stronger than its weakest link

-Thomas Reid, *Essays on the Intellectual Powers of Man*





Radak et al. (2017)

Strengths and Limitations

Strengths

- Timecourse of intervention (temporality)
- Sample Size (*versus* previous studies)
- Frequency of outcome measures
- Novel population to study OT response
  - Female participants
- Lab-based study design
  - Control of training parameters
- Biological Plausibility among different CRF populations

Limitations

- Small sample size (power level)
  - Distribution of sex
  - Selection Bias?
- No reference period for sleep measures
- Small OR threshold for performance (SWC)
- Proteomics analysis
  - Unadjusted P<0.1– Type I error risk
  - Cost
  - Sensitivity of measures
  - ‘Coverage’ of Proteome

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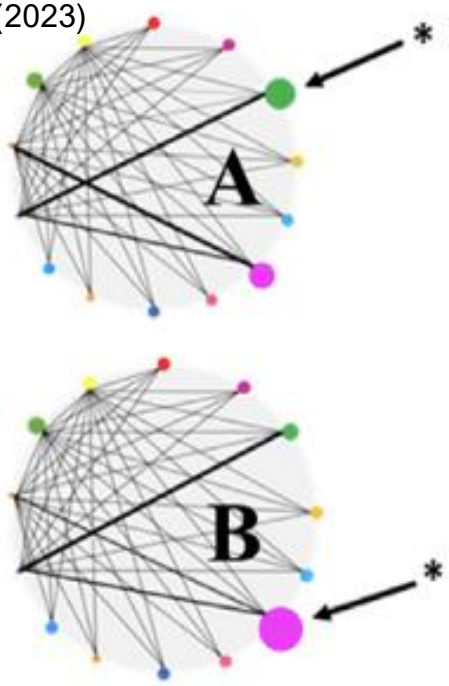
Conclusions

Armstrong et al. (2023)



1) OT is not exclusive to elite-level athletes
   - ***Anyone* can experience OT**
     - Weekend warriors, first-time marathoners, military personnel,
     - Exercise responder vs. Non-responder debate

2) Maladaptive overtraining response to ***excessive* exercise is interindividual**
   - Example:
     - Athlete A presents symptoms of overtraining via autonomic dysfunction;
     - Athlete B presents symptoms of overtraining via immune dysfunction

3) Exercise-induced Hormesis may be 'unifying theory' of OT pathophysiology
   - Allows **multiple pathophysiological mechanisms of OT** to coexist
     - Complex Systems Phenomenon (Armstrong et al. 2023)
     - Interindividual symptoms via interindividual pathophysiological mechanisms

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Future Research

- Build off exercise-induced hormesis theory
  - Re-examine existing overtraining literature with hormesis framework
- Larger sample sizes
  - Observe OT response across the fitness spectrum
- Sleep
  - Sleep Pattern Variability
  - Longer duration sleep studies (in athletes, among others)
  - Objective sleep measures
- Incorporate modern methods of data collection/analysis
  - Wearable Fitness Technology (24-h continuous monitoring)
  - Multiomics
  - Artificial Intelligence / Machine Learning
- Precision exercise (medicine) prescription

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Thank you!

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Questions?

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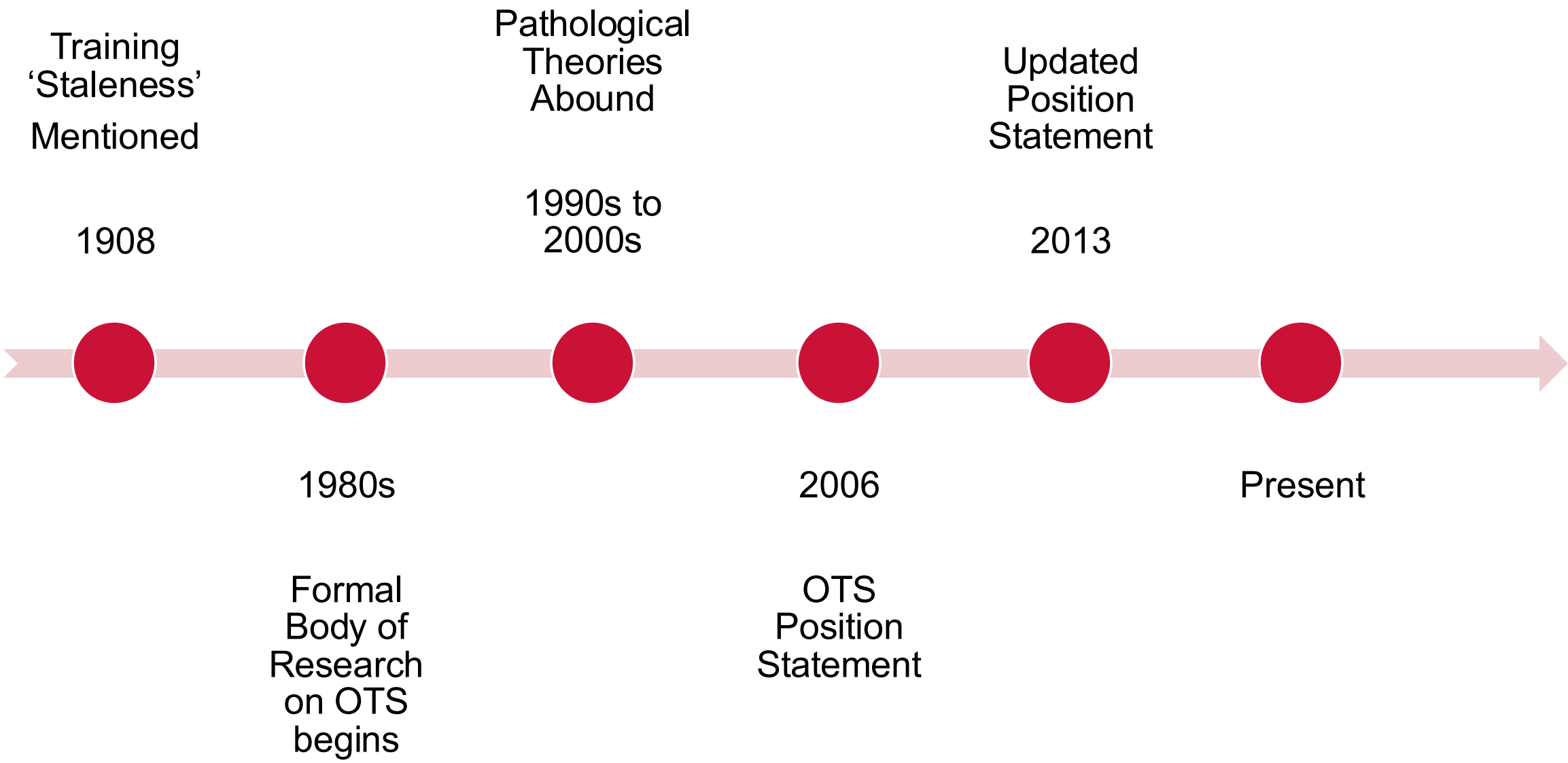
Additional Slides



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Week 1	Week 2	Week 3
Performance testing Day Grip strength, Vert. Jump, 2-bout GXT	Performance testing Day Grip strength, Vert. Jump, 2-bout GXT	Performance testing Day Grip strength, Vert. Jump, 2-bout GXT
50-min ride @60% PWL	50-min ride @65% PWL	50-min ride @ 70% PWL
5x5min @75% PWL 3-min active recovery	5x5:15min @75% PWL 3-min active recovery	5x5:31min @75% PWL 3-min active recovery
2x20min @65% PWL 5-min active recovery	2x25min @65% PWL 5-min active recovery	2x30min @65% PWL 5-min active recovery
12x45s @130% PWL 2-min active recovery	12x50s @130% PWL 2-min active recovery	12x55s @130% PWL 2-min active recovery
50-min Lactate Ride 3mmol*L^{-1}	55-min Lactate Ride 3mmol*L^{-1}	60-min Lactate Ride 3mmol*L^{-1}
Rest day	Rest day	Rest day

PWL	CON_1	CON_2	CON_3	CON_4	CON_5	CON_6	CON_7	CON_8	CON_9	CON_10
V2	287.00	238.75	199.50	180.00	184.00	193.38	126.25	208.25	281.00	218.75
V8	290.75	257.13	198.75	195.00	191.25	209.13	137.00	209.75	288.63	225.00
V14	291.25	271.11	201.00	197.25	187.00	212.50	138.50	213.00	311.13	230.00
rec48										
rec7	293.50	271.13	202.50	203.25	200.00	213.25	129.75	207.00	284.13	230.50
rec14	290.00	283.38	206.00	202.50	185.50	214.00	131.25	216.75	292.38	227.00
rec21	293.50	281.88	211.25	203.50	188.75	229.38	137.00	215.25	284.13	227.25
Average	291.00	267.23	203.17	196.92	189.42	211.94	133.29	211.67	290.23	226.42
Intra Subject STD DEV	2.43	16.84	4.72	9.00	5.77	11.51	4.92	3.94	10.99	4.27

CON AVG
222.13
AVG Intra STD DEV
7.44

Coeficcient of Variation	
(STDEV/mean)	0.033
times .3	0.010
times .5	0.017
converted to %	
.3 CV (%) --> SWC	1.00%
.5 CV (%) --> SWC	1.67%
2*CV	0.0669831

	TR_1	TR_2	TR_3	TR_4	TR_5	TR_6	TR_7	TR_8	TR_9	TR_10	TR_11
V2	209.50	117.25	215.50	246.25	201.75	167.50	261.25	226.00	180.75	164.50	203.00
V8	213.50	114.75	229.25	257.00	198.00	155.75	261.25	254.00	191.50	177.25	206.25
V14	215.00	115.50	227.25	260.25	192.00	163.00	263.25	254.00	194.00	193.25	212.50
rec48	210.00	113.75	234.75	259.00	168.75	167.50	263.00	228.25	197.75	201.25	219.00
rec7	216.00	118.00	232.00	265.75	208.75	147.75	265.75	245.50	197.00	212.25	228.25
rec14	222.75	115.00	233.50	257.25	199.50	151.00	259.75	252.75	198.75	197.25	212.50
rec21	218.25	119.75	228.00	257.25	206.25	159.25	260.00	245.50	192.00	198.00	221.00
	215.00	116.29	228.61	257.54	196.43	158.82	262.04	243.71	193.11	191.96	214.64

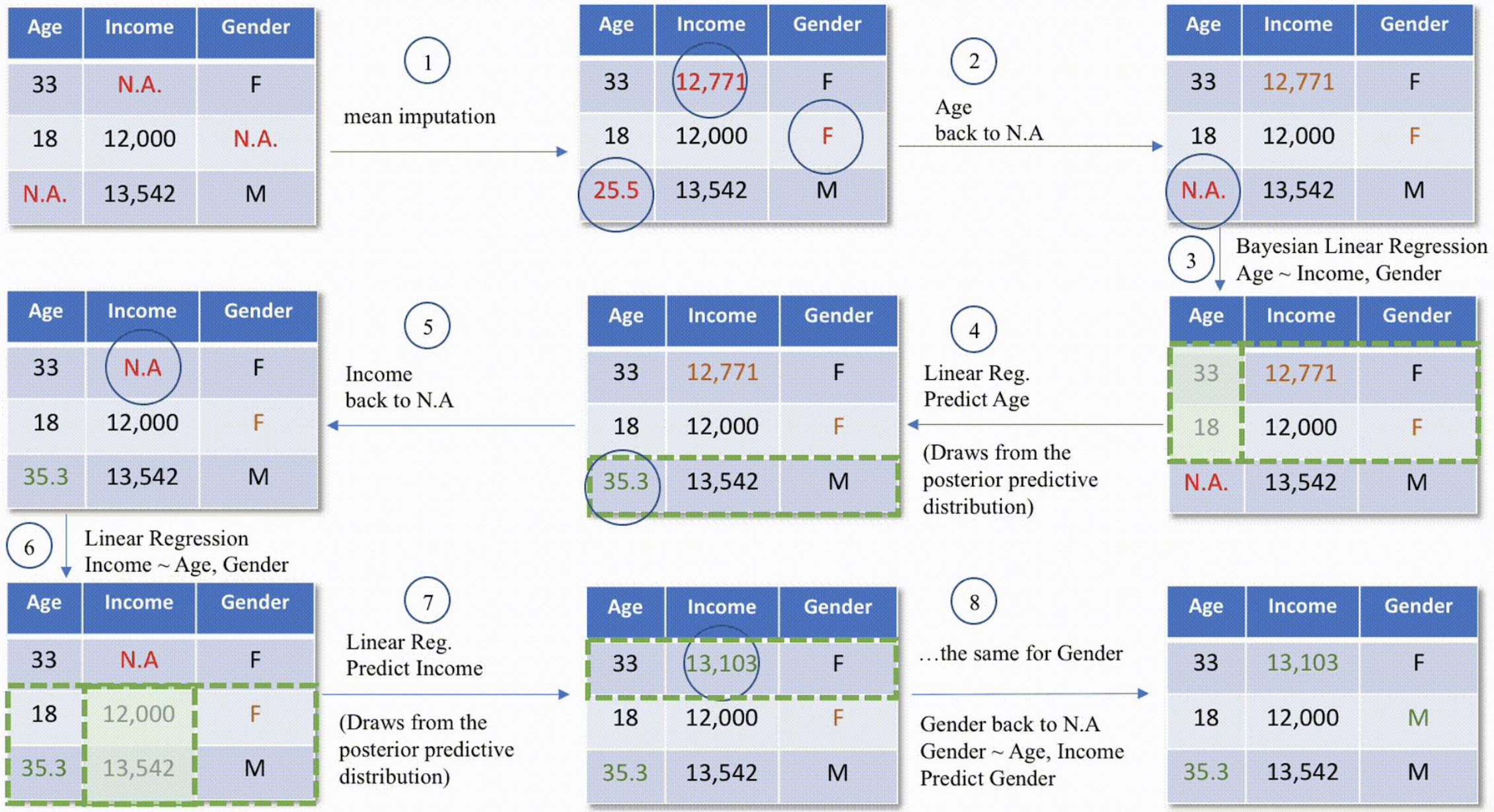
"OR" thresholds for Exp Subjects

TR_1	TR_2	TR_3	TR_4	TR_5	TR_6	TR_7	TR_8	TR_9	TR_10	TR_11
207.39506	116.07193	213.33477	243.77581	199.72292	165.81705	258.6251	223.72927	178.93392	162.84719	200.96036

Indicates OR Threshold

	TR_1	TR_2	TR_3	TR_4	TR_5	TR_6	TR_7	TR_8	TR_9	TR_10	TR_11
V2	209.50	117.25	215.50	246.25	201.75	167.50	261.25	226.00	180.75	164.50	203.00
V8	213.50	114.75	229.25	257.00	198.00	155.75	261.25	254.00	191.50	177.25	206.25
V14	215.00	115.50	227.25	260.25	192.00	163.00	263.25	254.00	194.00	193.25	212.50
rec48	210.00	113.75	234.75	259.00	168.75	167.50	263.00	228.25	197.75	201.25	219.00
rec7	216.00	118.00	232.00	265.75	208.75	147.75	265.75	245.50	197.00	212.25	228.25
rec14	222.75	115.00	233.50	257.25	199.50	151.00	259.75	252.75	198.75	197.25	212.50
rec21	218.25	119.75	228.00	257.25	206.25	159.25	260.00	245.50	192.00	198.00	221.00

Multiple Imputation by Chained Equations (MICE) – Single Iteration



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Mixed Effect Models: Power Analysis

frontiers in PSYCHOLOGY

METHODS ARTICLE
published: 17 April 2012
doi: 10.3389/fpsyg.2012.00111

A practical guide to calculating Cohen's f^2, a measure of local effect size, from PROC MIXED

Arielle S. Selya[1], Jennifer S. Rose[1], Lisa C. Dierker[1], Donald Hedeker[2] and Robin J. Mermelstein[2]*

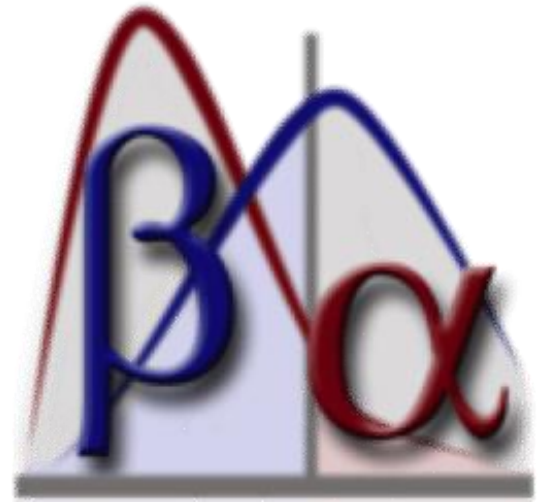
[1] *Psychology Department, Wesleyan University, Middletown, CT, USA*
[2] *Institute for Health Research and Policy, University of Illinois at Chicago, Chicago, IL, USA*

PeerJ

A brief introduction to mixed effects modelling and multi-model inference in ecology

Xavier A. Harrison[1], Lynda Donaldson[2,3], Maria Eugenia Correa-Cano[2], Julian Evans[4,5], David N. Fisher[4,6], Cecily E.D. Goodwin[2], Beth S. Robinson[2,7], David J. Hodgson[4] and Richard Inger[2,4]

G* Power



1) Cohen's $f^2 = {}^{R^2}/_{1-R^2}$

2) Cohen's $f^2 = (R^2_{AB} \_ R^2_A) / (1 - R^2_{AB})$

3) $R^2 = (V_{null} - V_{full}) / V_{null}$

Effect Sizes

Mixed Effects

.02 = Small

.15= Medium

.35= Large

- R^2_{AB} = residual variance of full model containing A and B together
- R^2_A = residual variance of model (without B) for each B
- V_{null} = residual model of variance without regressors (fixed effects)
- V_{Full} = residual model of variance with regressors (fixed effects)
- B= Dependent Variable
- A= set of all other variables (i.e., regressors)

Thus,

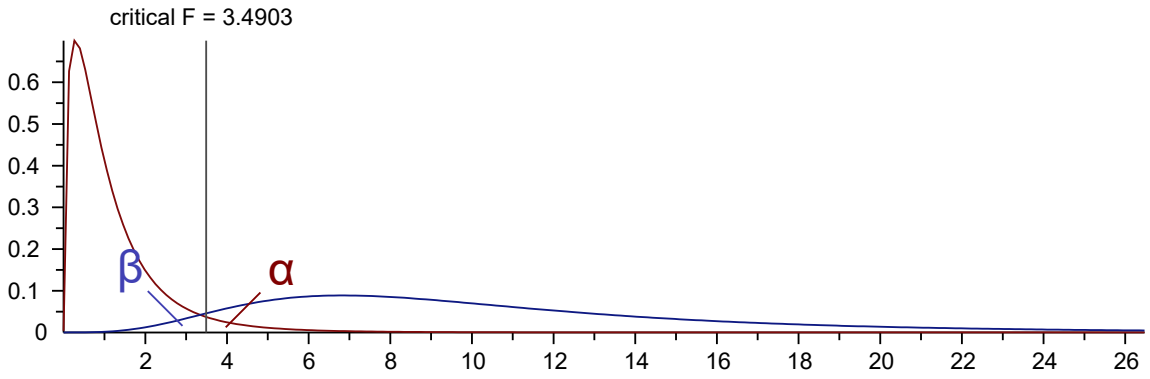
- $R^2_{AB} = (V_{null} - V_{full}) / V_{null}$
- $R^2_A = (V_{null} - V_A) / V_{null}$

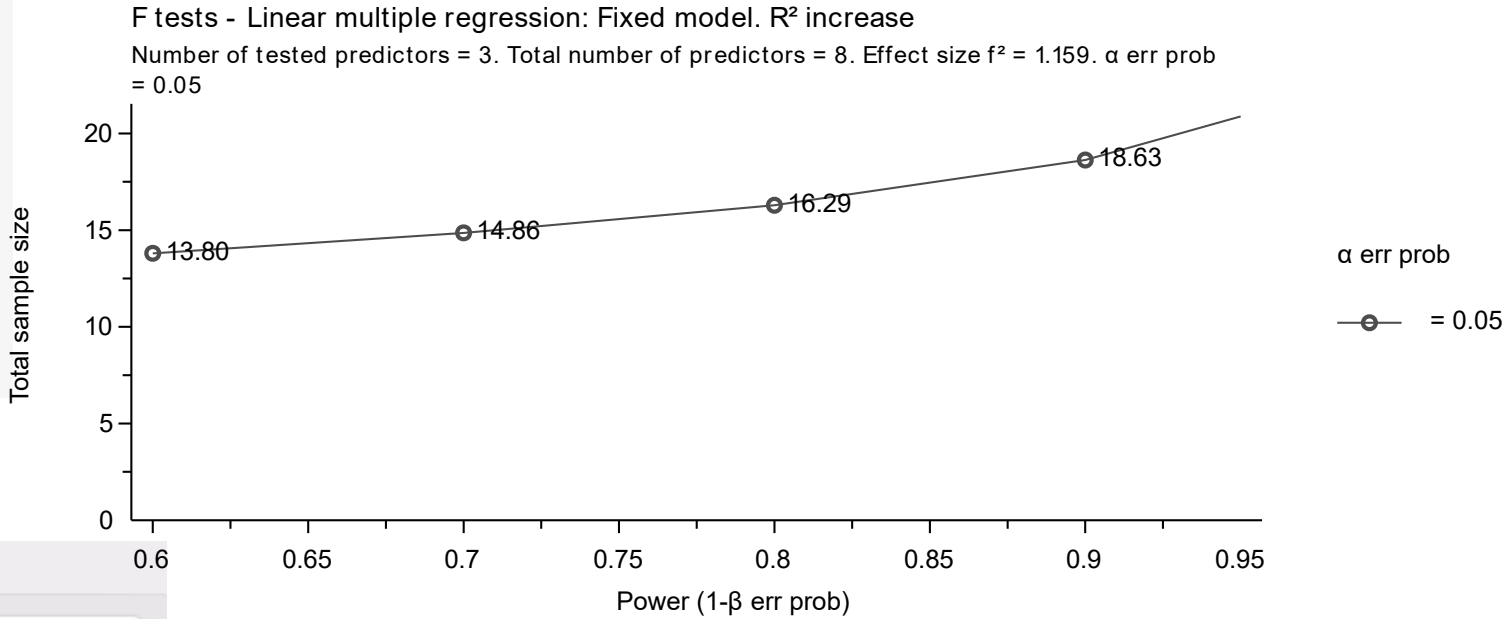
DV Fixed effects Random effects

Example: (Pcn_MHR ~ training status * phase) | (subject)

```python
import statsmodels.formula.api as smf

# Fit the mixed model
md = smf.mixedlm("pwl ~ ot_status * phase", data=df_LMM, groups=df_LMM['subject'])
mdf = md.fit()
print(mdf.summary())

# Extract the variance components
var_random = mdf.cov_re.iloc[0, 0]  # Random effect variance
var_residual = mdf.scale  # Residual variance

# Calculate the fitted values using the fixed effects
y_fitted = mdf.fittedvalues

# Calculate the variance of the fixed effects
var_fixed = y_fitted.var()

# Calculate Marginal R-squared (R2_m)
R2_m = var_fixed / (var_fixed + var_random + var_residual)

# Calculate Conditional R-squared (R2_c)
R2_c = (var_fixed + var_random) / (var_fixed + var_random + var_residual)

print(f"Marginal R-squared: {R2_m}")
print(f"Conditional R-squared: {R2_c}")

# Calculate Cohen's f^2 for the fixed effects
f2_fixed = R2_m / (1 - R2_m)

print(f"Cohen's f^2 (f2_fixed): {f2_fixed}")
# Calculate ICC
ICC = var_random / (var_random + var_residual)

print(f"Intraclass Correlation Coefficient (ICC): {ICC}")
```

```
Marginal R-squared: 0.536835067020343
Conditional R-squared: 0.986043536364831
Cohen's f²: 1.159058099599094
```





Type of power analysis

Post hoc: Compute achieved power - given α, sample size, and effect size

Input parameters

Determine

Effect size f²	1.159
α err prob	0.05
Total sample size	21
Number of tested predictors	3
Total number of predictors	8

Output parameters

Noncentrality parameter λ	24.3390000
Critical F	3.4902948
Numerator df	3
Denominator df	12
Power (1-β err prob)	0.9518218

Parameters

Plot (on y axis) Total sample size ☑ with markers ☑ displaying the values in the plot showing 2 digit(s)

as a function of Power (1-β err prob) from 0.6 in steps of .1 through to 0.95

Plot 1 graph(s) interpolating points

with α err prob at 0.05

and Effect size f² at 1.159

Draw plot

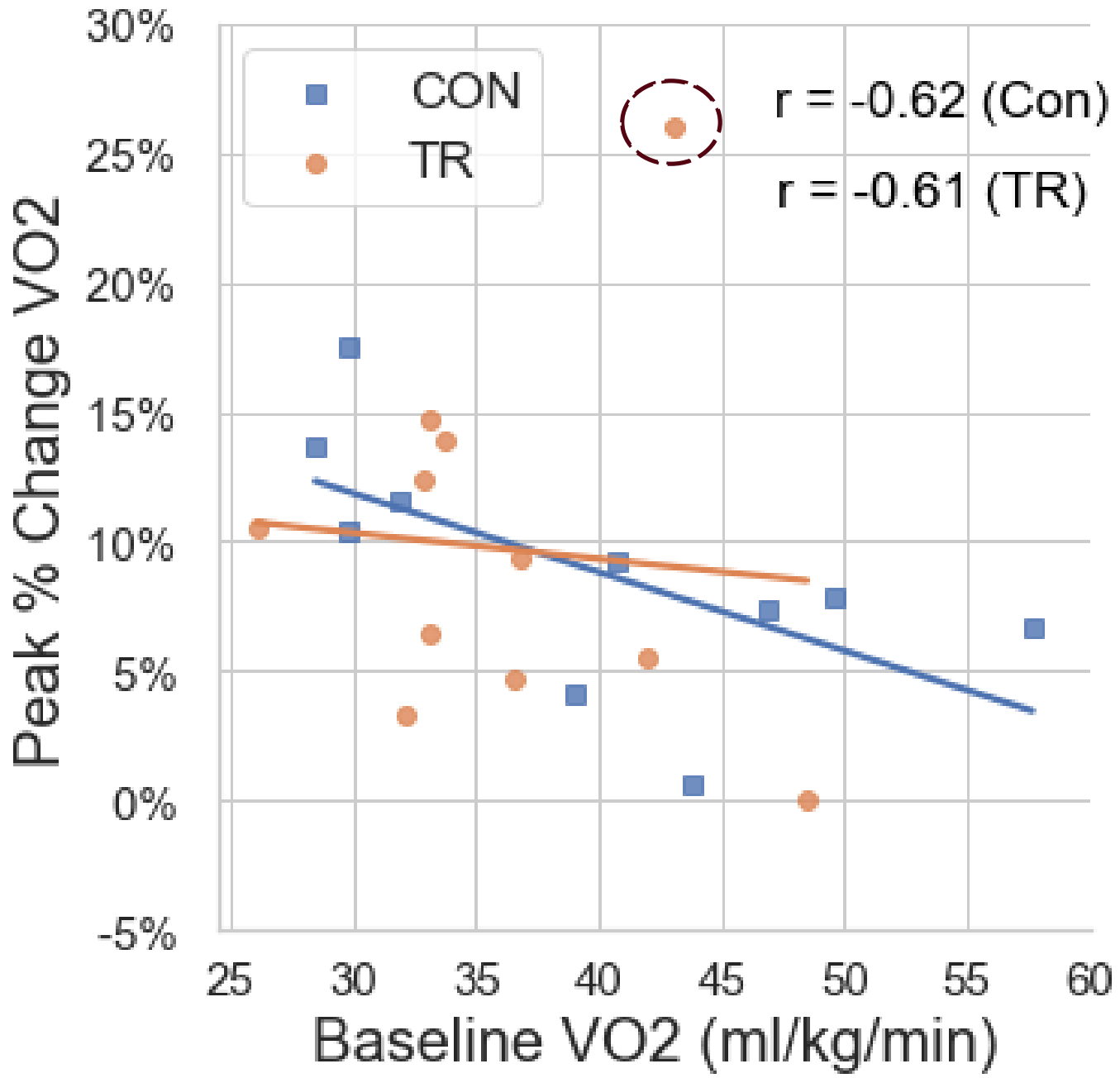
Power Calculations	Marginal R^2	Conditional R^2	ICC	N	Tested Predictors	Total Predictors	Effect Size F^2	Post-hoc B	Estimated Total n for B=0.8
Peak Workload*	**0.537**	**0.986**	**0.970**	**21**	**3**	**8**	**1.159**	**0.950**	**16**
% Δ Peak Workload*	**0.491**	**0.761**	**0.529**	**21**	**3**	**8**	**0.966**	**0.907**	**18**
Relative VO2*	**0.482**	**0.970**	**0.942**	**21**	**3**	**8**	**0.931**	**0.896**	**18**
% Δ Relative VO2	0.329	0.649	0.477	21	3	8	0.491	0.621	28
Maximum Heart Rate*	**0.484**	**0.872**	**0.751**	**21**	**3**	**8**	**0.938**	**0.898**	**18**
% Δ Maximum Heart Rate	0.409	0.704	0.499	21	3	8	0.693	0.782	22
Heart Rate Recovery*	**0.432**	**0.880**	**0.789**	**19**	**3**	**8**	**0.761**	**0.822**	**20**
% Δ Heart Rate Recovery	0.241	0.423	0.239	19	3	8	0.318	0.430	39
Peak Lactate*	**0.450**	**0.755**	**0.554**	**21**	**3**	**8**	**0.818**	**0.851**	**19**
% Δ Peak Lactate	0.384	0.617	0.379	21	3	8	0.623	0.733	24

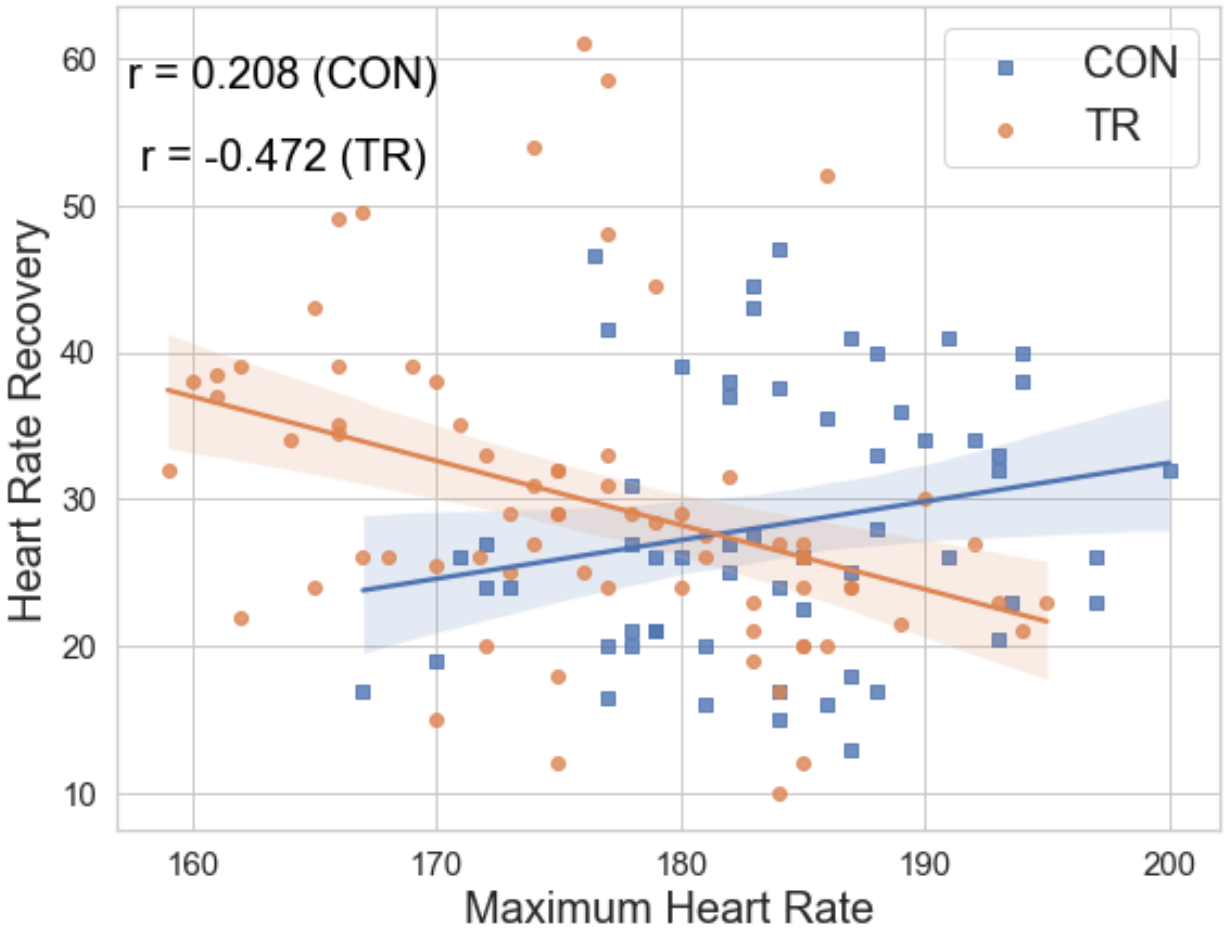
Effect Sizes

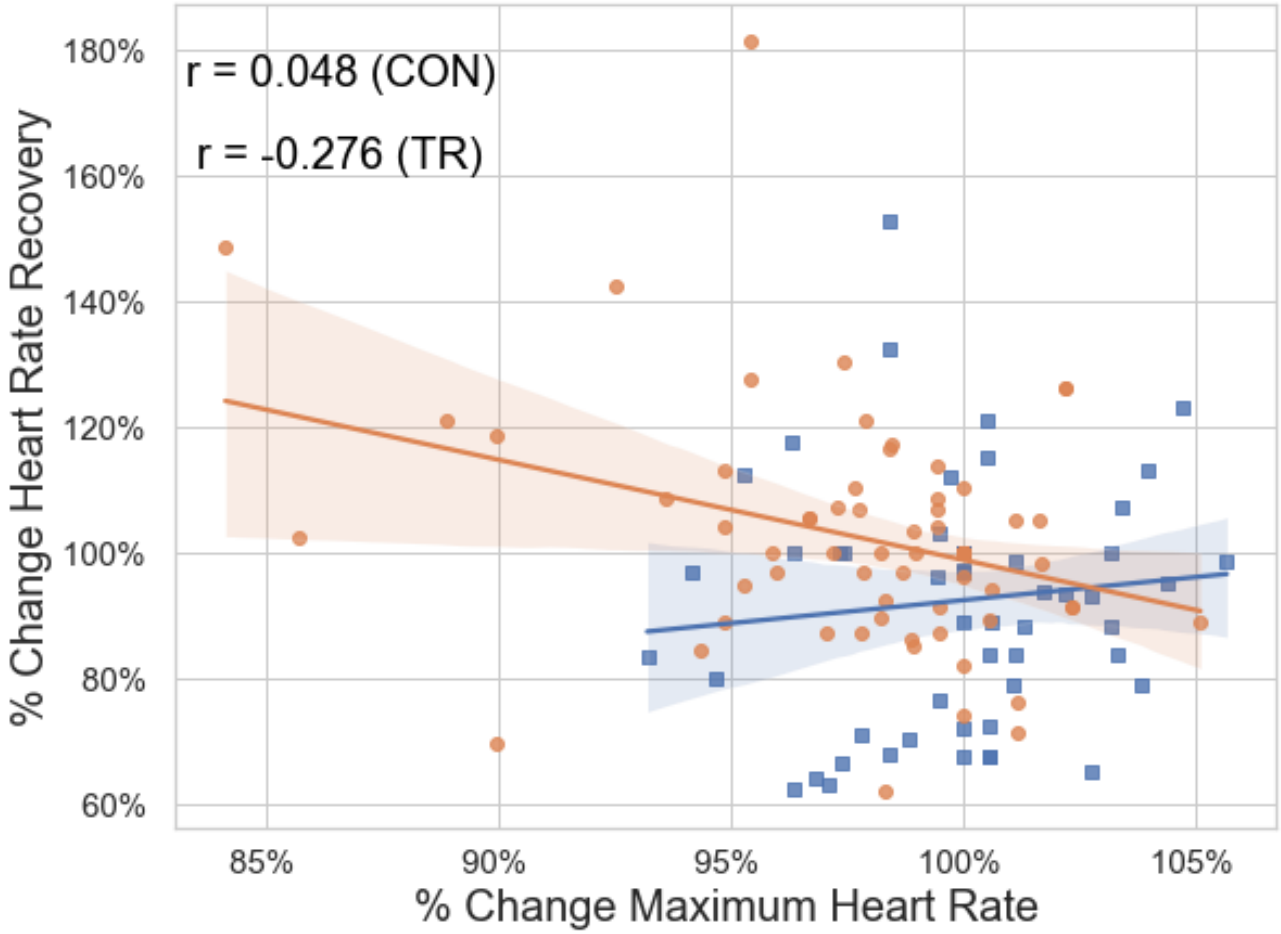
.02 = Small .15= Medium .35= Large

Sleep Variables (CON, TR)	Marginal R^2	Conditional R^2	ICC	N	Tested Predictors	Total Predictors	Effect Size F^2	Post-hoc B	Estimated Total n for B=0.8
Sleep Duration	0.213	0.435	0.283	20	7	7	0.270	0.210	61
Total Sleep Time	0.208	0.435	0.287	20	7	7	0.263	0.205	62
Cumulative Sleep Debt	0.435	0.866	0.763	20	7	7	0.770	0.570	27
WASO	0.253	0.517	0.354	20	7	7	0.339	0.260	50
Sleep Efficiency	0.259	0.542	0.382	20	7	7	0.349	0.267	49
Sleep Quality	0.201	0.417	0.271	20	7	7	0.252	0.197	65
Bedtime Sleepiness	0.204	0.392	0.236	20	7	7	0.256	0.200	80
Waking Sleepiness	0.229	0.473	0.316	20	7	7	0.297	0.230	70
Bedtime Fatigue	0.249	0.529	0.372	20	7	7	0.332	0.253	52
Waking Fatigue	0.222	0.443	0.284	20	7	7	0.285	0.221	58

Sleep Variables (CON, AD, OR)	Marginal R^2	Conditional R^2	ICC	N	Tested Predictors	Total Predictors	Effect Size F^2	Post-hoc B	Estimated Total n for B=0.8
Sleep Duration	0.219	0.452	0.298	20	7	11	0.281	0.183	60
Total Sleep Time	0.213	0.450	0.301	20	7	11	0.271	0.177	61
Cumulative Sleep Debt	0.426	0.869	0.771	20	7	11	0.742	0.452	29
WASO	0.256	0.528	0.366	20	7	11	0.343	0.218	50
Sleep Efficiency	0.258	0.550	0.394	20	7	11	0.348	0.220	50
Sleep Quality	0.202	0.424	0.278	20	7	11	0.254	0.168	65
Bedtime Sleepiness	0.223	0.371	0.190	20	7	11	0.288	0.186	58
Waking Sleepiness	0.236	0.462	0.296	20	7	11	0.309	0.198	55
Bedtime Fatigue	0.259	0.515	0.345	20	7	11	0.350	0.222	50
Waking Fatigue	0.229	0.434	0.267	20	7	11	0.296	0.191	57




r = 0.208 (CON)
r = -0.472 (TR)
CON
TR
Heart Rate Recovery
Maximum Heart Rate
60
50
40
30
20
10
160
170
180
190
200


r = 0.048 (CON)
r = -0.276 (TR)
% Change Heart Rate Recovery
% Change Maximum Heart Rate
180%
160%
140%
120%
100%
80%
60%
85%
90%
95%
100%
105%

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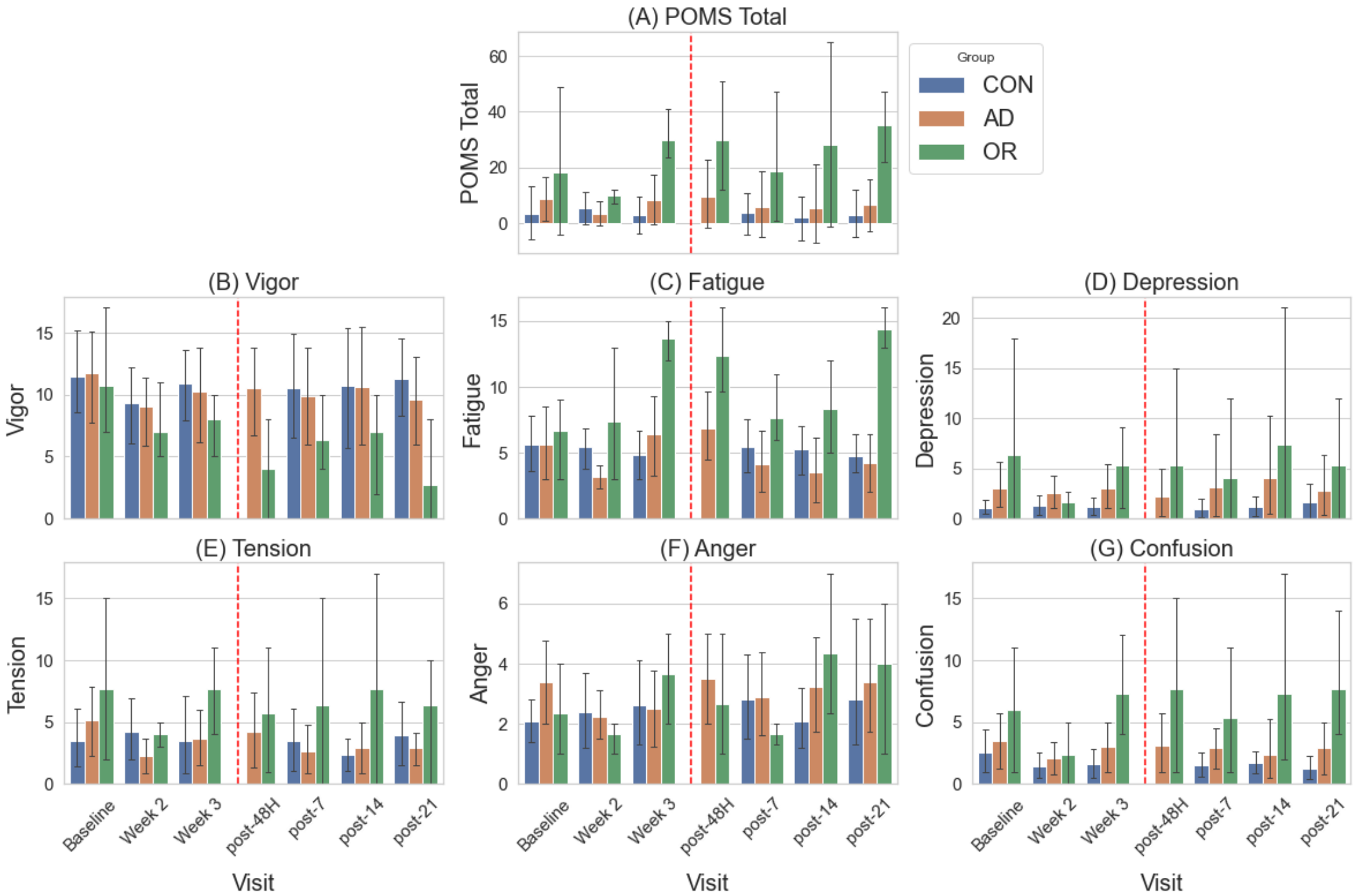

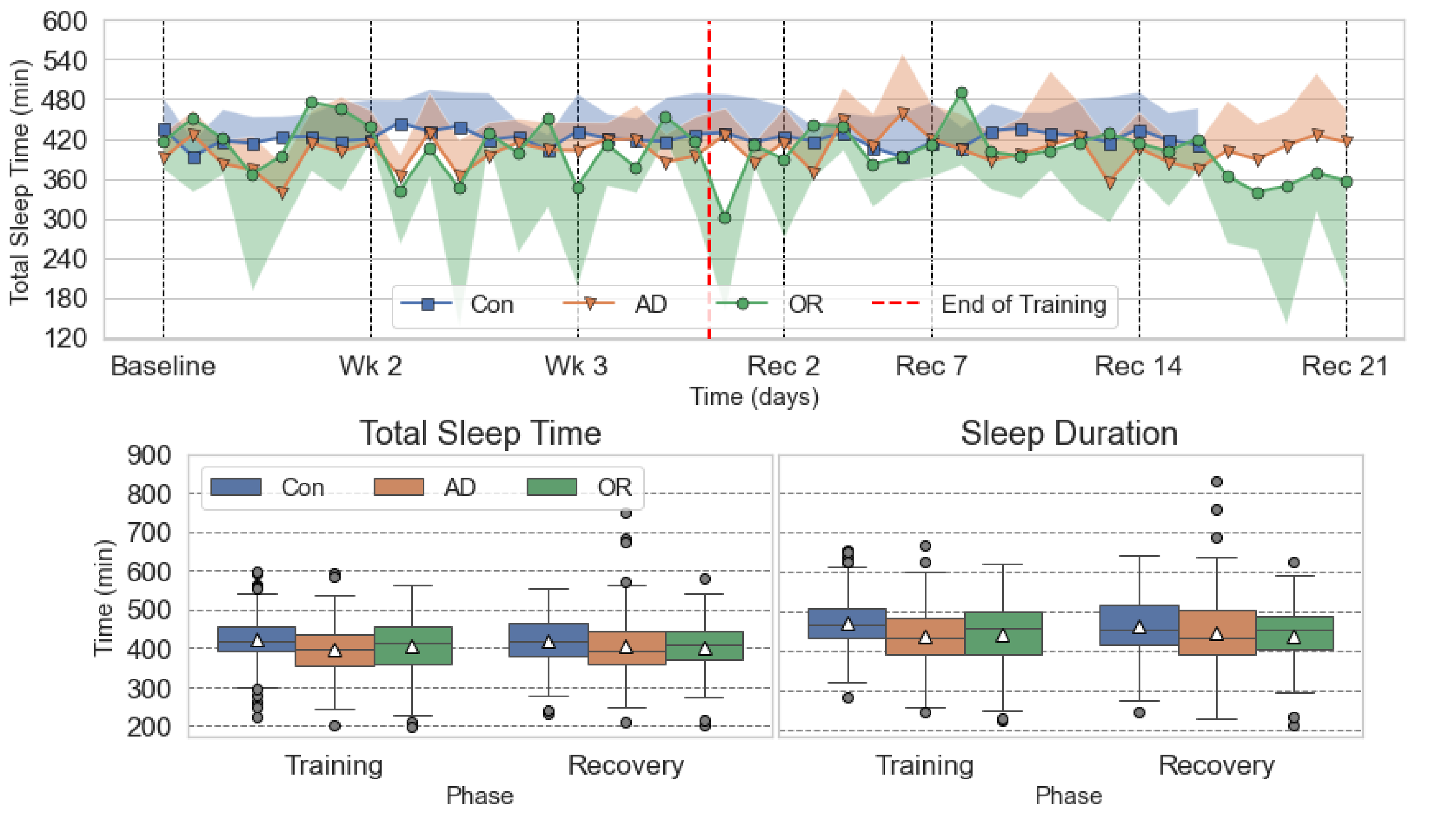
Total Sleep Time (min)
600
540
480
420
360
300
240
180
120
Con
AD
OR
End of Training
Baseline
Wk 2
Wk 3
Rec 2
Rec 7
Rec 14
Rec 21
Time (days)
Total Sleep Time
Sleep Duration
Time (min)
900
800
700
600
500
400
300
200
Con
AD
OR
Training
Recovery
Phase
Training
Recovery
Phase

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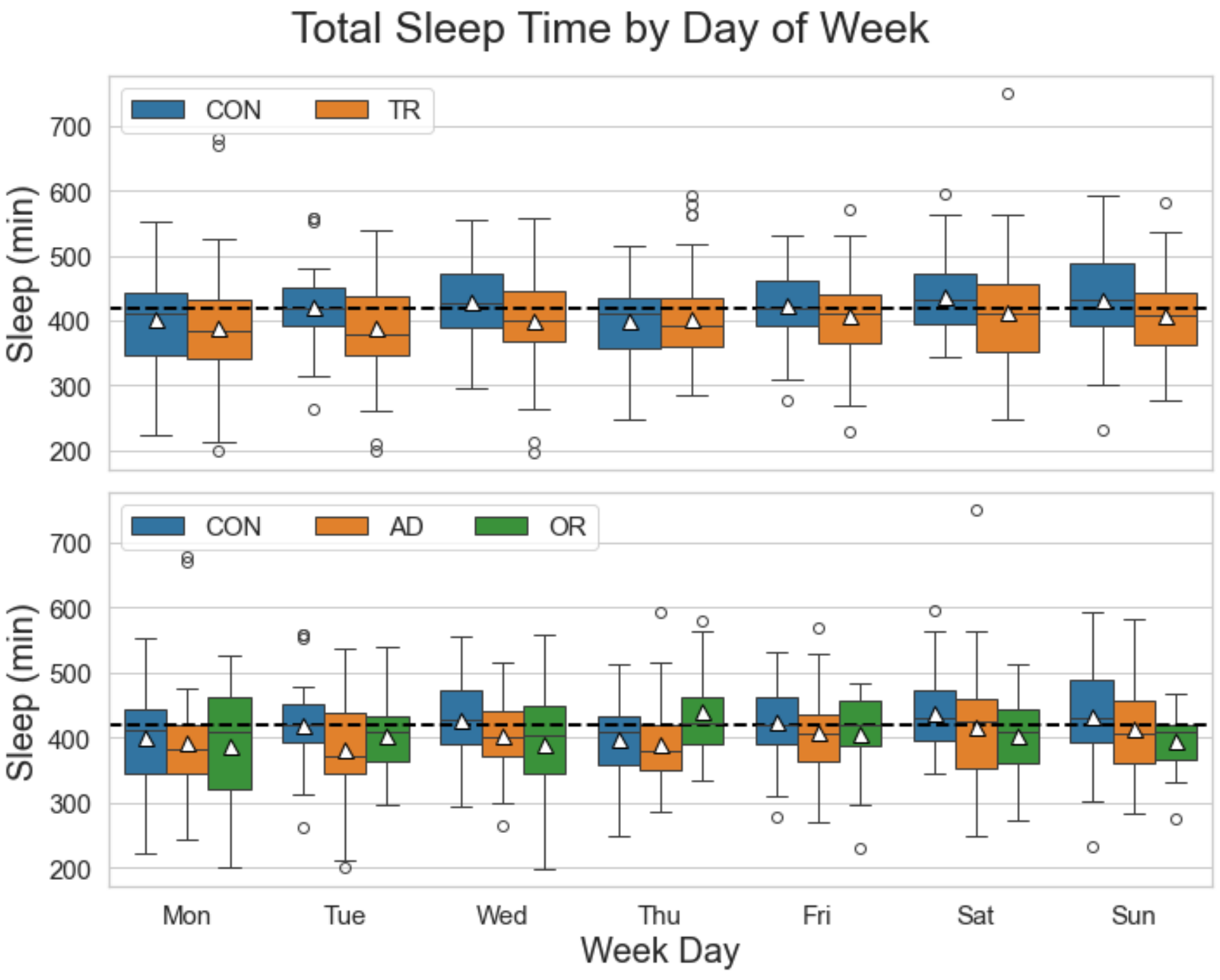
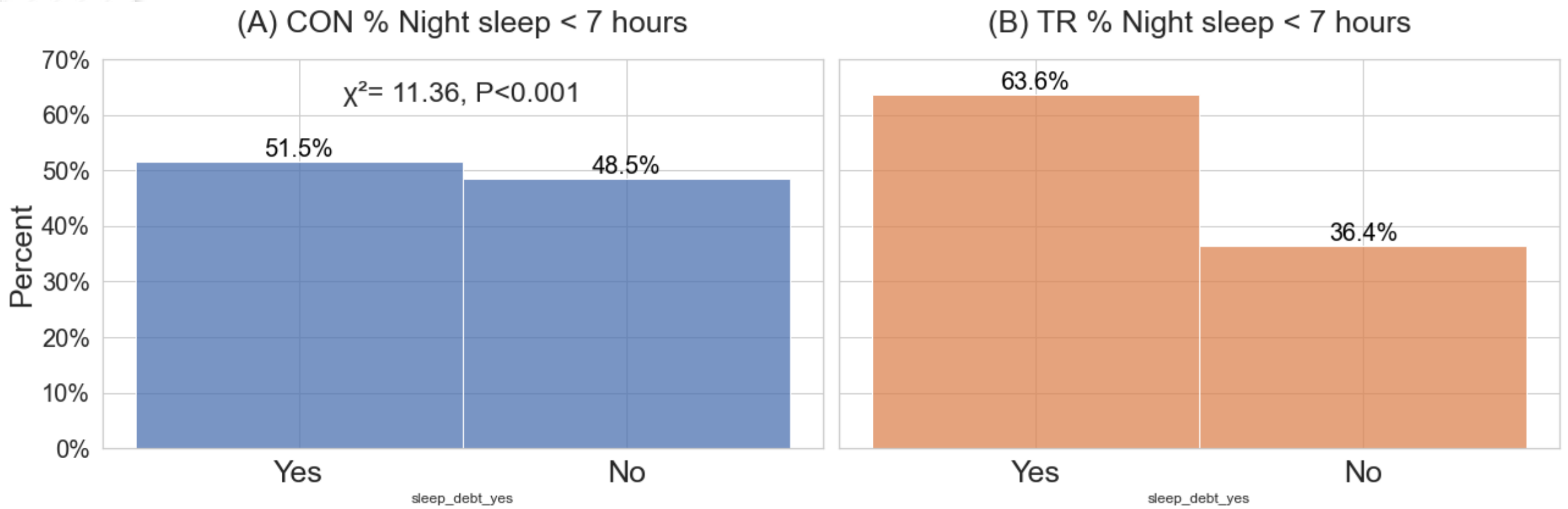
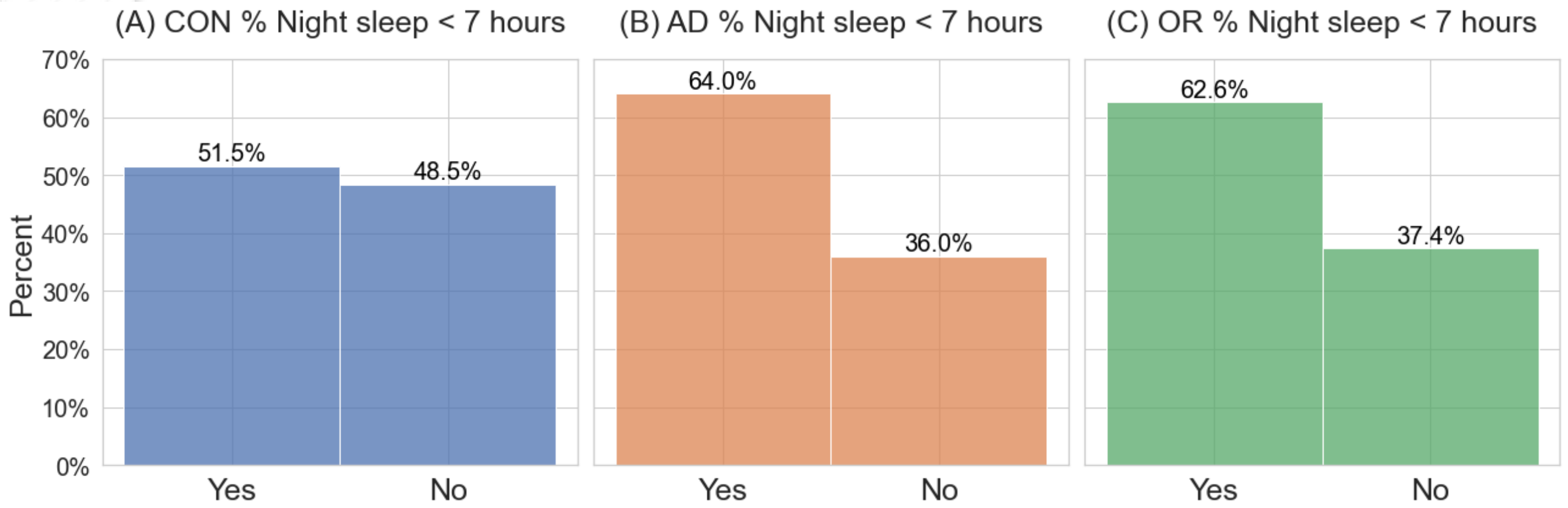



(A) CON % Night sleep < 7 hours
(B) TR % Night sleep < 7 hours
Percent
70%
60%
50%
40%
30%
20%
10%
0%
χ²= 11.36, P<0.001
51.5%
48.5%
63.6%
36.4%
Yes
No
sleep_debt_yes


(A) CON % Night sleep < 7 hours
(B) AD % Night sleep < 7 hours
(C) OR % Night sleep < 7 hours
Percent
70%
60%
50%
40%
30%
20%
10%
0%
51.5%
48.5%
64.0%
36.0%
62.6%
37.4%
Yes
No
Yes
No
Yes
No

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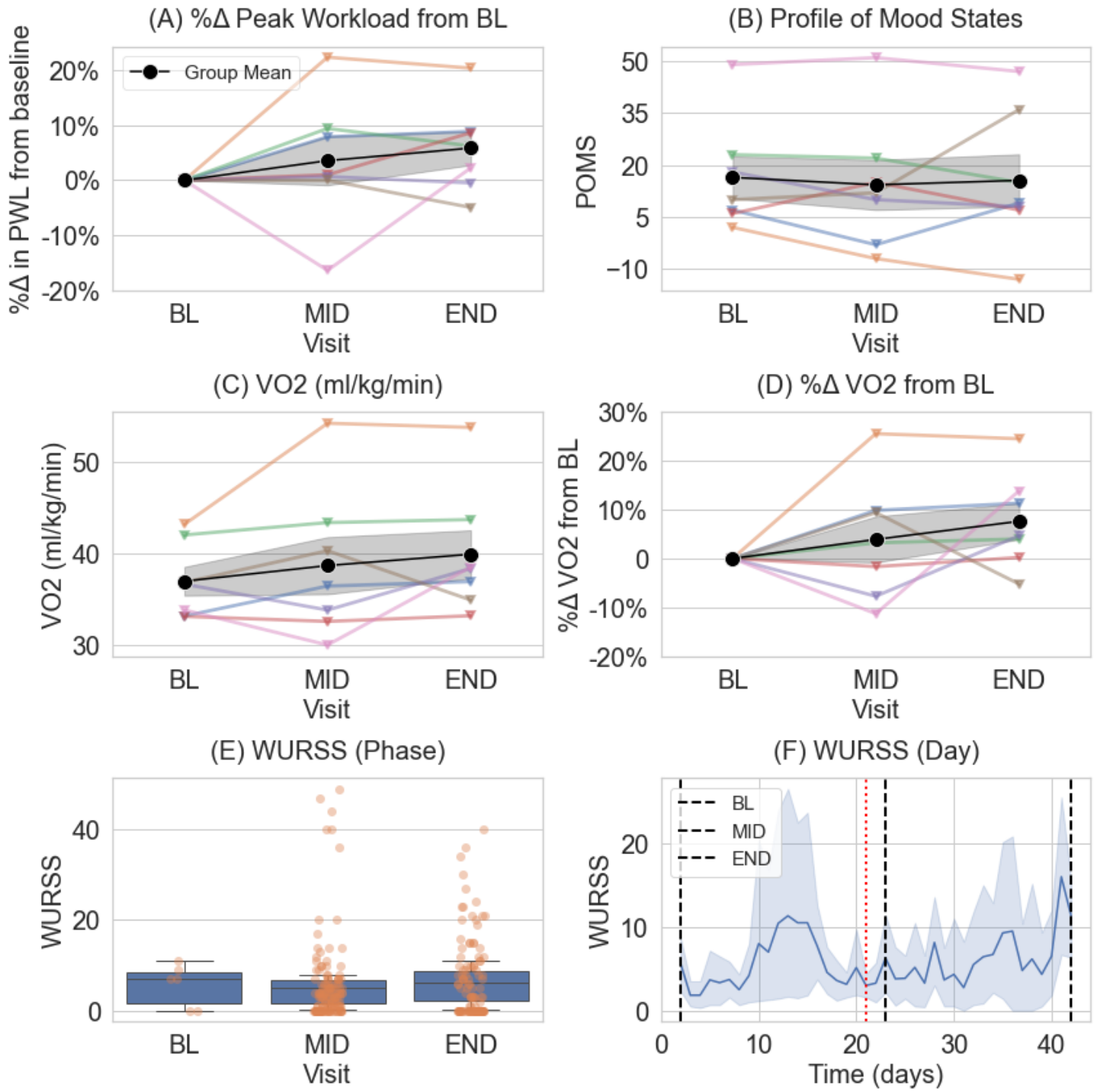
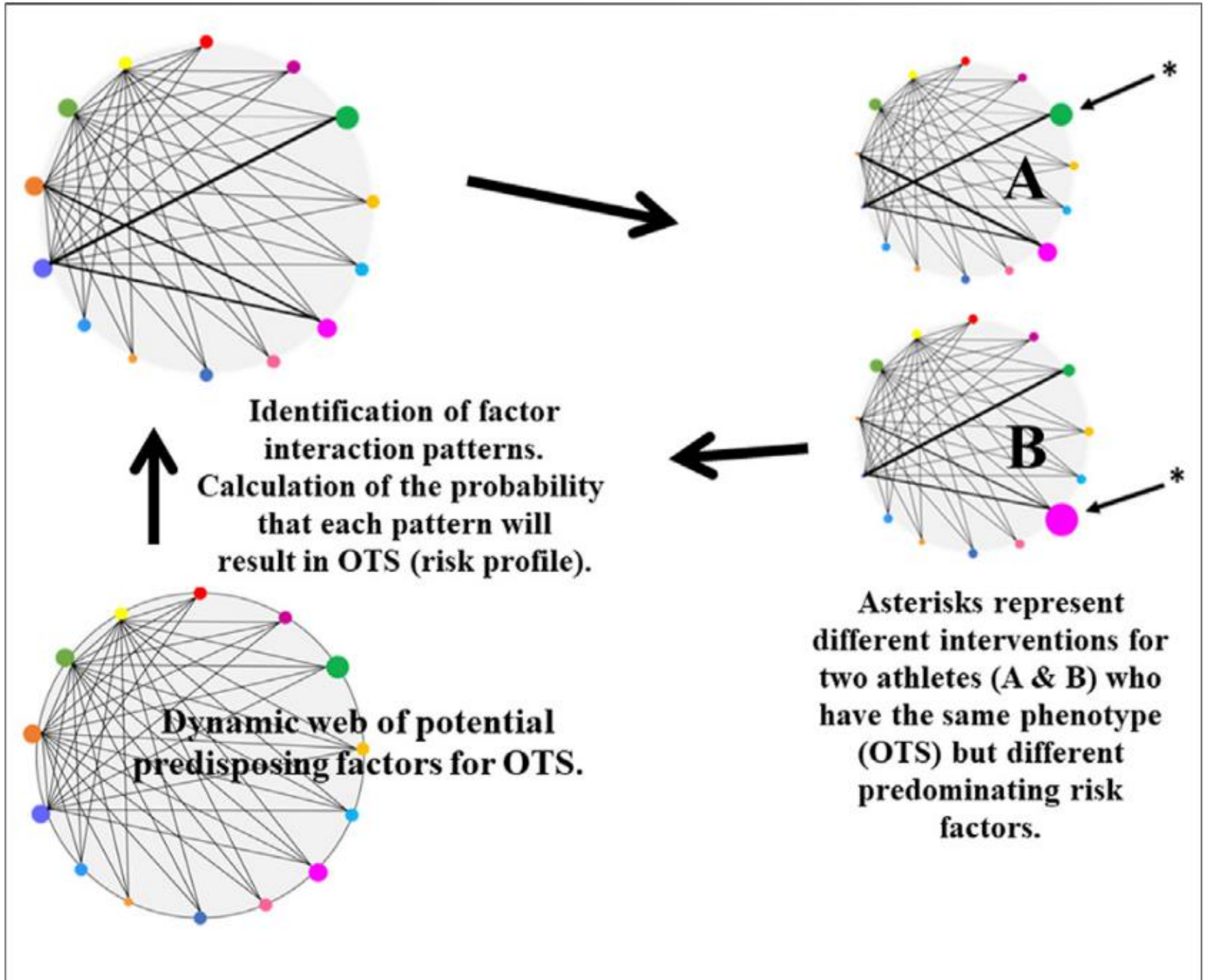


Overtraining as a Complex System Phenomenon



Armstrong et al. (2022)

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Chapter Aims

Central Hypothesis: Overreach/Overtraining is not exclusive to elite-level athletes.

Introduction: Set the stage for the dissertation. Introduce the chapters involved in the dissertation; provide a narrative on how these chapters relate to one another.

Chapter I: Characterize the physiological responses to a 3-week high-intensity training protocol in recreationally active adults. Identify subjective and objective variables that correlate with exercise performance capacity during a 3-week high-intensity training protocol and subsequent recovery

Chapter II: Characterize the sleep patterns of recreationally active adults during and after a three-week lab-controlled overreaching protocol. Determine whether differences exist between sleep parameters observed in experimental subjects *versus* control subjects.

Chapter III: Characterize the proteome's response to chronic high-intensity exercise in recreationally active adults before, during, and after a three-week lab-controlled training protocol.

Discussion/Closing: Reiterate introduction section, tie chapters back to introduction. Close

Related concepts in hormesis and exercise literature.

Hormetic Term/Concept	Basic Definition	Related Exercise Science Concept	Example in Exercise
Hormesis 'J'-shaped dose-response	Low doses of a stressful stimuli generate an adaptive, protective response; high (toxic) doses of a stimuli can inhibit or harm an organism's homeostatic mechanisms.	Relationship between Physical Activity and associated health outcomes appear to follow a J-shaped dose-response.[35,139]	Low levels of physical activity are linked to chronic illness;[4] moderate levels of physical activity have shown to promote health and longevity; excessive exercise can lead to overtraining.[37]
Pre-conditioning (adaptive response)	A titrated exposure to a stressor at an appropriate dose will generate an adaptive response to protect against similar doses of the stressor in the future.	FITT Principle (Frequency, Intensity, Type, Time); SAID principle (Specific Adaptations to Imposed Demands); Progressive Overload; [28] General Adaptation Syndrome.[111]	Engaging in a running training program to train for a marathon. Increasing mileage and pace overtime will result in better tolerance to running distances and speeds; Aerobic training over time can improve aerobic capacity.[140]
Post-conditioning	Exposure to stressor following damaging event will lead to future protective adaptive response.	Exercise is used as a therapeutic modality following injury or surgery.	Physical therapy rehabilitation after tearing an ACL to regain quadriceps function.
Remote conditioning	Hormetic signals emanating from a tissue under stress can communicate to distant tissues.	Physiological response to exercise is systemic.	Interleukin-6 and Lactate generated from muscles during exercise will perfuse through the body, acting as signaling molecules to various tissues beyond muscle. [141,142]
Early- and late-phase hormetic responses	Some adaptive responses to hormesis are observed acutely following exposure to stressor, whereas other adaptations appear delayed	There are both acute and chronic physiological responses to exercise, which may provide a protective mechanism	An acute exercise bout can immediately improve cognitive function.[143] "Repeat-bout effect" in which a single bout of eccentric exercise confers a protective effect against future bouts of exercise-induced muscle