Building an Evidence-Base for Exercise Medicine in Targeted Populations Through Rigorous Clinical Trials

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46th ANNUAL MEETING

May 18-21, 2025

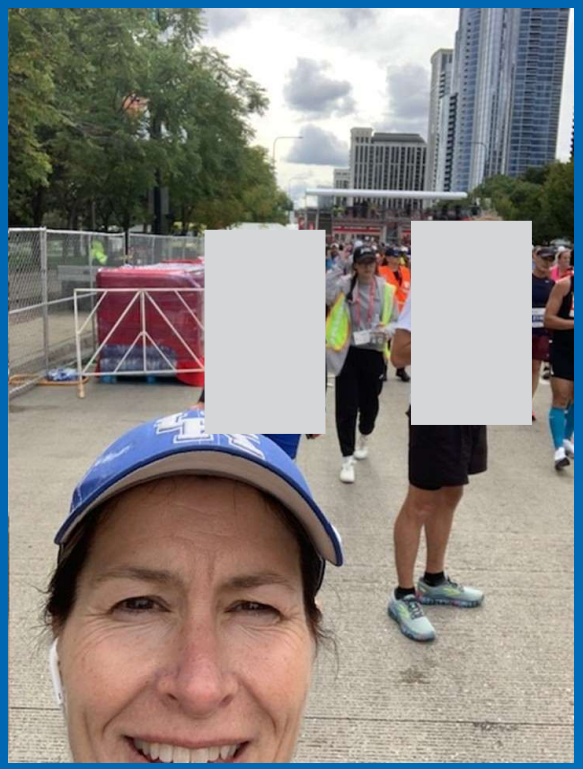
VANCOUVER
CANADA

SCT
SOCIETY FOR CLINICAL TRIALS

Disclosures

- No relevant disclosures


BANK OF AMERICA
CHICAGO MARATHON
CHICAGO 2023
TOGETHER FOR THE RUN

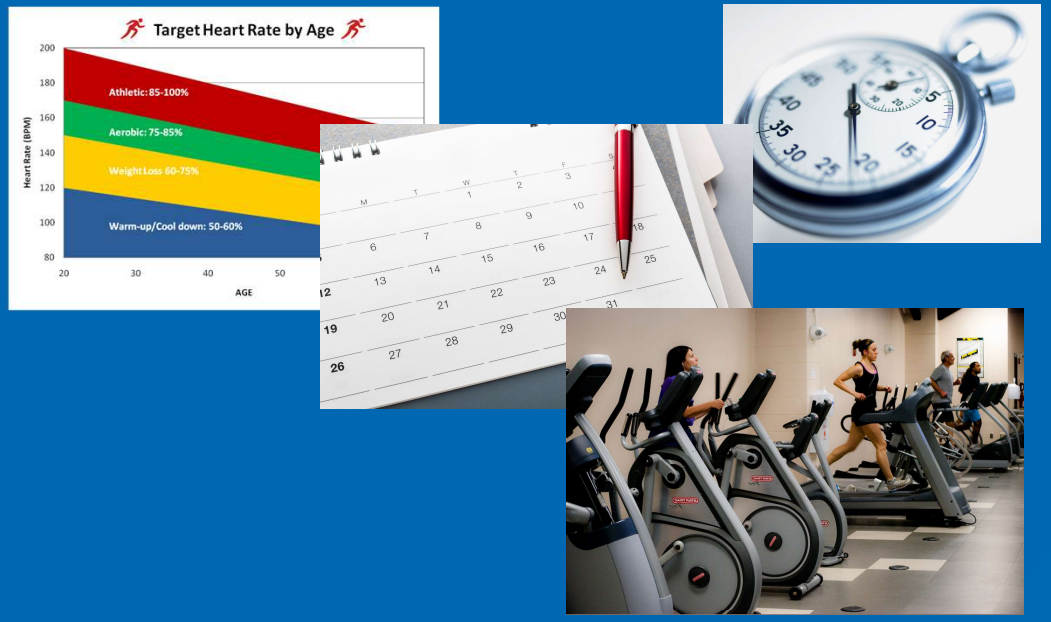


My Journey into Exercise Studies: Parkinson Disease

Courtesy Judy Cameron, University of Pittsburgh, ~2010

Exercise and Parkinson Disease

- Dosing!
  - Intensity
  - Frequency
  - Duration
  - Modality



- Original 2 x 2 Factorial Design
  - $14 M trial

Exercise and PD

"It's only exercise."

"We do not fund small, underpowered, efficacy trials."

"Do you even know if you can exercise people at high intensity?"

Is a control group needed? At the time, no "natural" cohort.

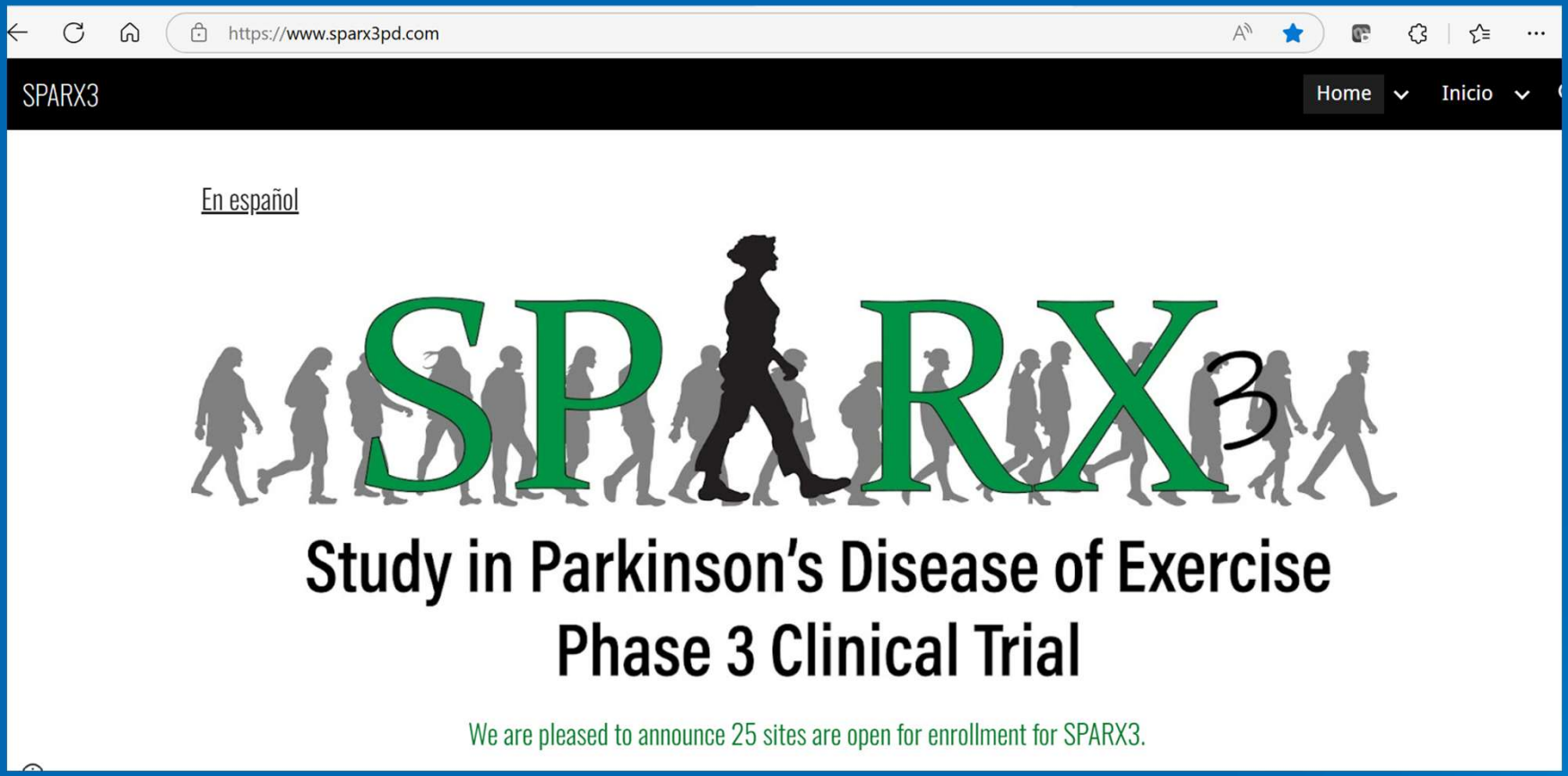
It's only exercise-make it like a drug study

- Study of Exercise in Parkinson Disease
  - (Phase II futility, multicenter N=126)

3 sites

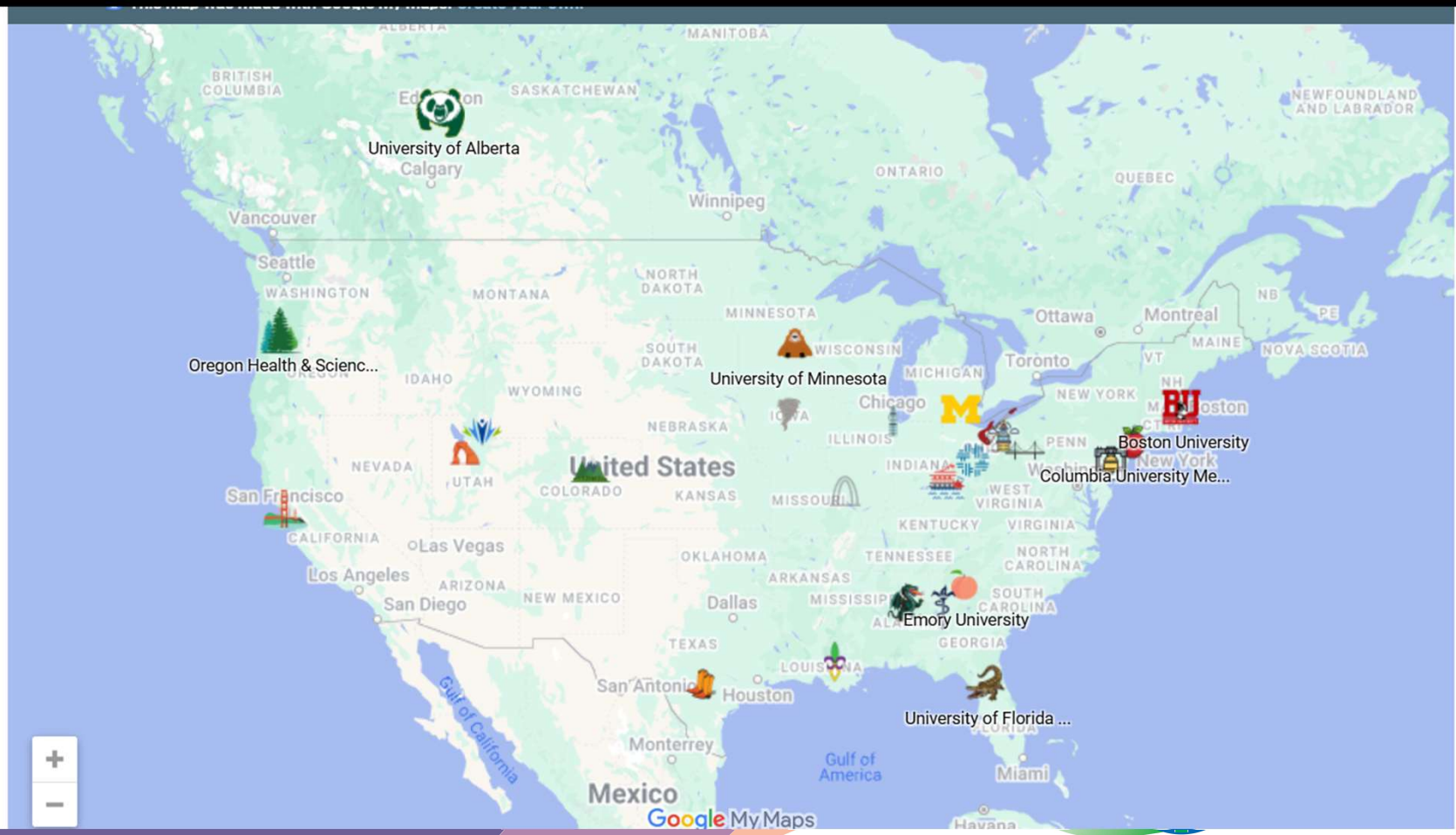
NCT01506479
R01NS074343

Can do high and moderate intensities!
Safe!
High intensity warrants further investigation!


https://www.sparx3pd.com
SPARX3
Home
Inicio
En español
SPARX3
Study in Parkinson's Disease of Exercise
Phase 3 Clinical Trial
We are pleased to announce 25 sites are open for enrollment for SPARX3.

SPARX3

Home Inicio



SOCIETY FOR CLINICAL TRIALS

Your speakers for today

Daniel M. Corcos, PhD
Professor
Department of Physical Therapy and Human Movement Sciences
Northwestern University

Katie Schmitz, PhD
Professor
Department of Medicine, Division of Hematology and Oncology
University of Pittsburgh

Eduardo Bustamante, PhD
Associate Professor
Department of Kinesiology and Nutrition
University of Illinois Chicago

David X. Marquez, PhD
Professor and Department Head
Department of Kinesiology and Nutrition
University of Illinois Chicago

SCT | 46TH ANNUAL MEETING

Summary

- Design matches intent
  - Population
  - Outcomes
  - Stage of research question

- Opportunities are endless!
- Challenges – behavior change is hard.

Adverse Events and DSM

Table 3. Adverse Events and Serious Adverse Events[a]

Event	Participants With Event, No. (%)		
	High-Intensity Exercise (n = 43)	Moderate-Intensity Exercise (n = 45)	Usual Care (n = 40)
Adverse events			
Adverse events related to exercise	13 (30.2)	8 (17.8)	0
Adverse events related to exercise, severity greater than mild	9 (20.9)	4 (8.9)	0
Events >10% in a single arm			
Fall	6 (14.0)	5 (11.1)	9 (22.5)
Fall with severity greater than mild	1 (2.3)	1 (2.2)	0
Pain in extremity	8 (18.6)	3 (6.7)	1 (2.5)
Pain with severity greater than mild	4 (9.3)	3 (6.7)	1 (2.5)
Organ system >10% in a single group			
Musculoskeletal and connective-tissue disorders	15 (34.9)	6 (13.3)	2 (5.0)
Musculoskeletal and connective-tissue disorders with severity greater than mild	10 (23.2)	4 (8.9)	2 (5.0)
Injury, poisoning, and procedural complications[b]	7 (16.3)	8 (17.8)	9 (22.5)
Injury, poisoning, and procedural complications with severity greater than mild	2 (4.6)	3 (6.7)	0 (0.0)
Infections and infestations	6 (14.0)	3 (6.7)	2 (5.0)
Infections and infestations with severity greater than mild	5 (11.6)	3 (6.7)	2 (5.0)
Serious adverse events			
Gastrointestinal tract disorders	0	1 (2.3)	0
Renal and urinary tract disorders	0	1 (2.3)	0

- Use CTCAE or PRO CTCAE
- SMCs and DSMBs
- SIVs and for-cause IV's

JAMA Neurology 2018; 75(2):219-226

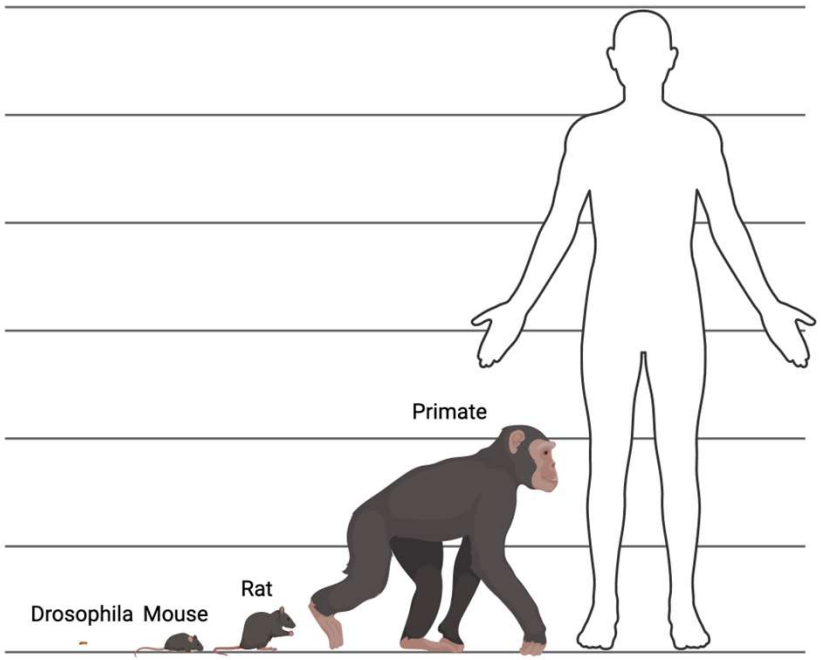
Can We Delay the Progression of Parkinson's Disease? The Dose-Response SPARX3 Trial

Daniel M. Corcos, PhD

Department of Physical Therapy & Human Movement Sciences
Northwestern University

Why Are Clinical Trials Failing in Parkinson's Disease?

- Wrong patients (heterogeneity)
- Wrong doses
- Wrong time/stage
- Wrong molecules (BBB penetration, specificity, PK/PD, tox)
- Wrong targets



Wrong models?

Adapted from and courtesy of Tiago Outeiro

WHY SPARX3 NEEDS TO BE DONE

Disease-modifying trials in PD: the 4-plus decade consequence of one-size-fits-all

Completed Phase 2/3 or 3 trials

- **Vitamin E** — Antioxidant
- **GPI-1485** — Neuroimmunophilin
- **Riluzole** — Glutamate antagonist
- **TCH346** — Propargylamine
- **Ambroxol** — Increases lysosomal f…
- **CEP-1347** — Anti-apoptotic
- **GDNF** — Intraputaminal neurotrophic factor
- **Co Q10** — Mitochondrial enhancer
- **Mitoquinone** — Mitochondrial enhancer
- **Cinpanemab** — Anti-synuclein antibody
- **Pramipexole** — Dopamine agonist
- **Cogane** — Modulates GDNF & BDNF (PYM50028)
- **Creatine** — Mitochondrial modulator
- **Pioglitazone** — PPAR γ agonist; anti-inflammatory
- **Nilotinib** — C-Abl inhibitor
- **Rasagiline** — MAO-B inhibitor
- **Glutathione** — Antioxidant
- **Isradipine** — Calcium-channel blocker
- **Inosine** — Urate-enhancing drug
- **Deferiprone** — Iron trapping
- **Venglustat** — Lowers α-synuclein

…in the pipeline

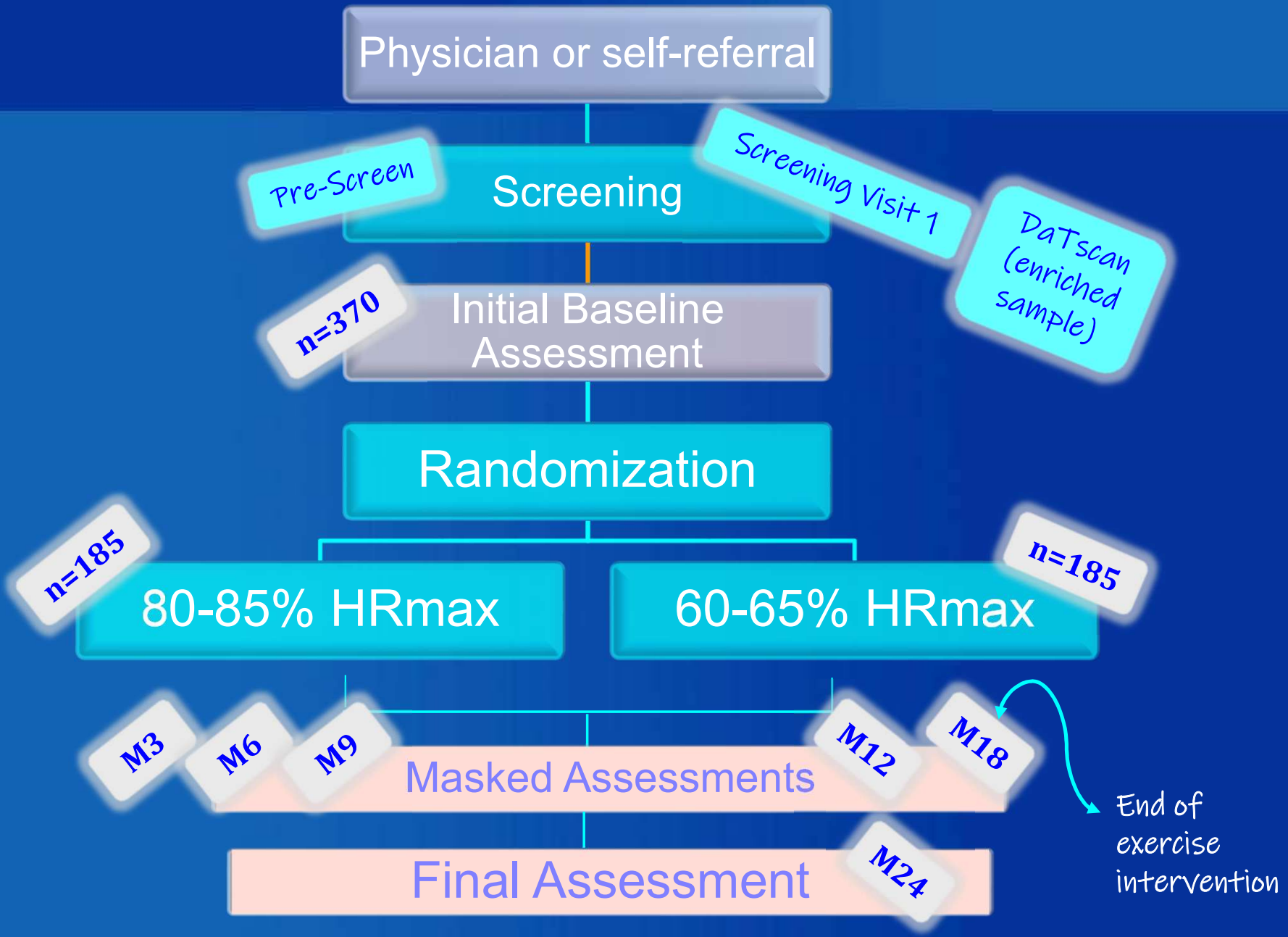
Phase 3

- **Exenatide / Lixisenatide** — GLP1 agonists
- **Memantine** — NMDA antagonist
- **Buntanetap** — mRNA inhibitor
- **SPARX3** — Polypharmacy

Phase 2 (a sample)

- **Idebenone** — CoQ10 analog
- **Minzasolmin** — α-Syn misfolding inhibitor
- **Semaglutide** — GLP1 agonist
- **Carvedilol** — Beta-blocker
- **IKT148009, K0706, radotinib** — cAbl inhibitors
- **BIIB122 / BIIB094** — LRRK2 inhibitor & ASO
- **BIA 28-6156** — GCase activator
- **Terazosin** — α1-adrenergic blocker
- **Ceftriaxone** — Anti-glutamatergic

SPARX3 Trial Design



Intervention

Week 1
4 sessions
Supervised as needed.

Week 2
4 sessions
Supervised as needed.

Week 3
4 unsupervised sessions, as appropriate

Week 4
4 unsupervised sessions

Weeks 5-78
1 in person contact every month

18 months
4 days per week
40 minutes per session
Treadmill only

Group 1: 60-65% HRmax

Group 2: 80-85% HRmax

5 minute warm up
30min at target HR
5 minute cool down

HRmax is the highest HR achieved during the baseline VO_2peak test

Primary Outcome

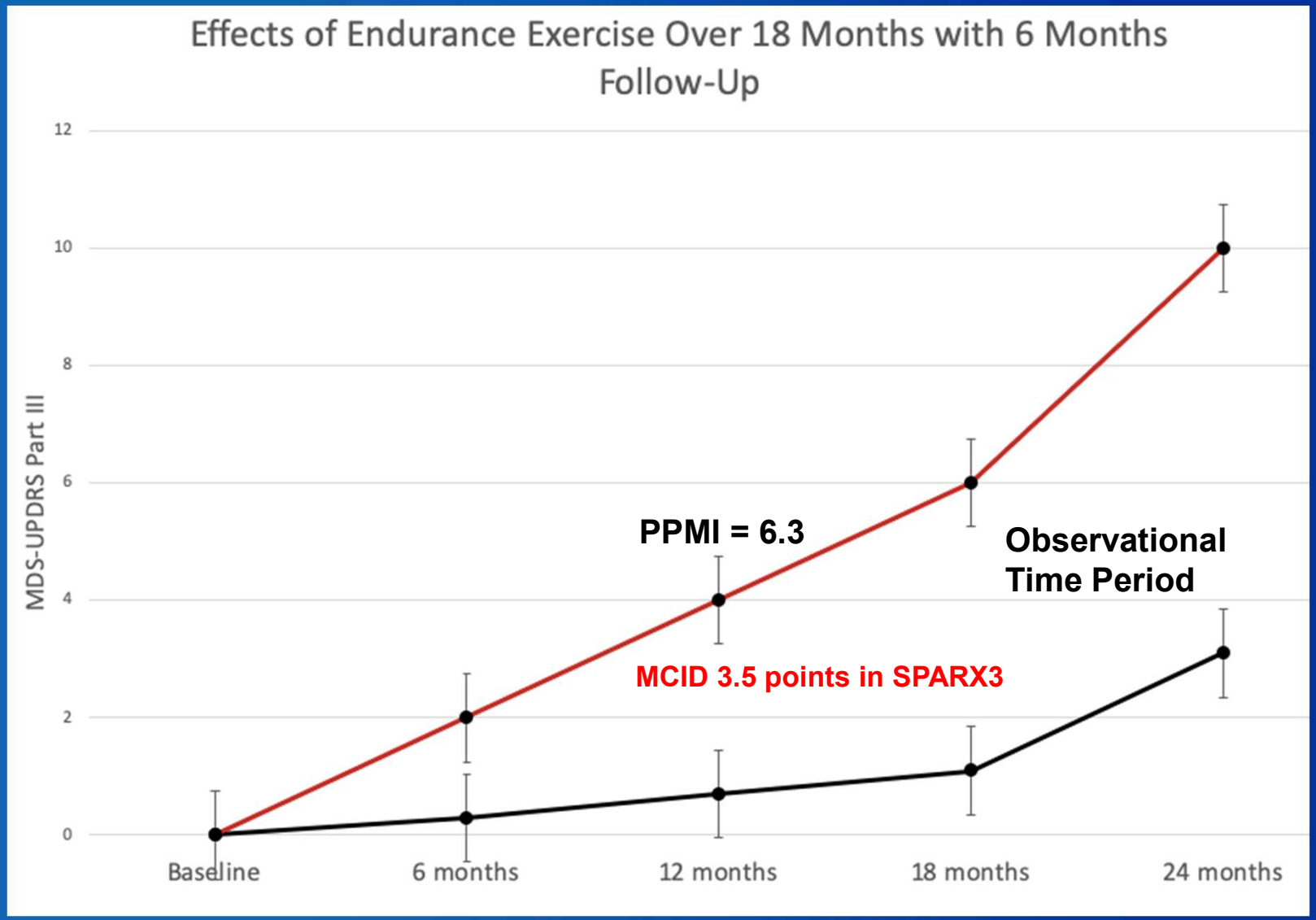
- **MDS-UPDRS**
  - **Part I (non-motor experiences of daily living)**
  - **Part II (motor experiences of daily living)**
  - **Part III (motor examination) off meds**
  - **Part IV (motor complications)**

Note these are non-medicated participants.

Secondary & Tertiary & Additional Outcomes

- Secondary outcomes
  - Quantified DaTscan SPECT – brain biology
  - Vo2peak – cardiovascular biology
  - 6 min walk distance
  - Blood biomarkers (CRP and BDNF)
  - Cognitive function (MoCA)
  - Self report quality of life
  - Daily steps (ActivPal activity monitor)
  - Time to initiate dopaminergic medication
- Tertiary outcomes
  - Change in stride length (OPALS)
  - Change in turning velocity (OPALS)
- Additional Outcomes
  - Exploratory biomarkers (diagnosis, progression, prediction and explanation).
  - Neuroendocrine, neurotrophic and inflammatory panel of biomarkers.

Possible SPARX3 Outcomes



Increased Dopamine Transporter

Fig. 1: Dopamine Transporter Levels Pre- and Post-Exercise.

From: Intense exercise increases dopamine transporter and neuromelanin concentrations in the substantia nigra in Parkinson's disease

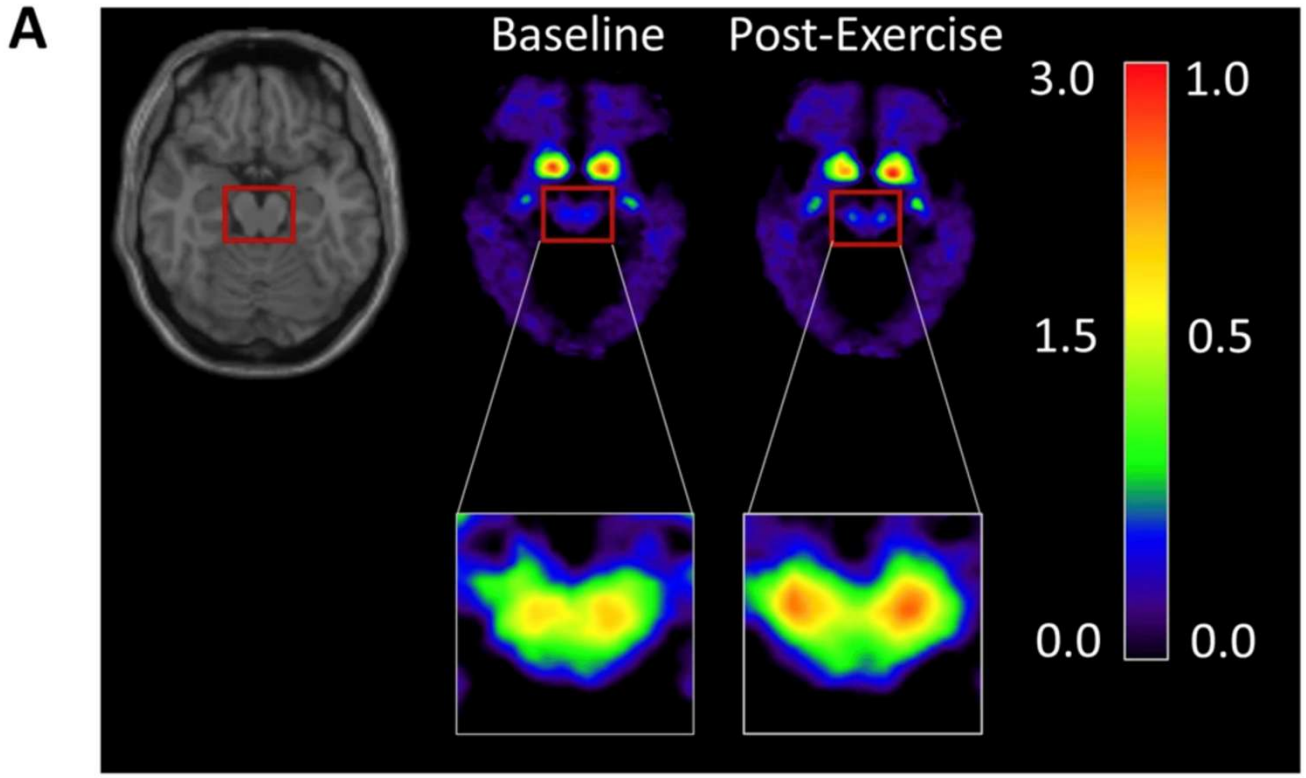
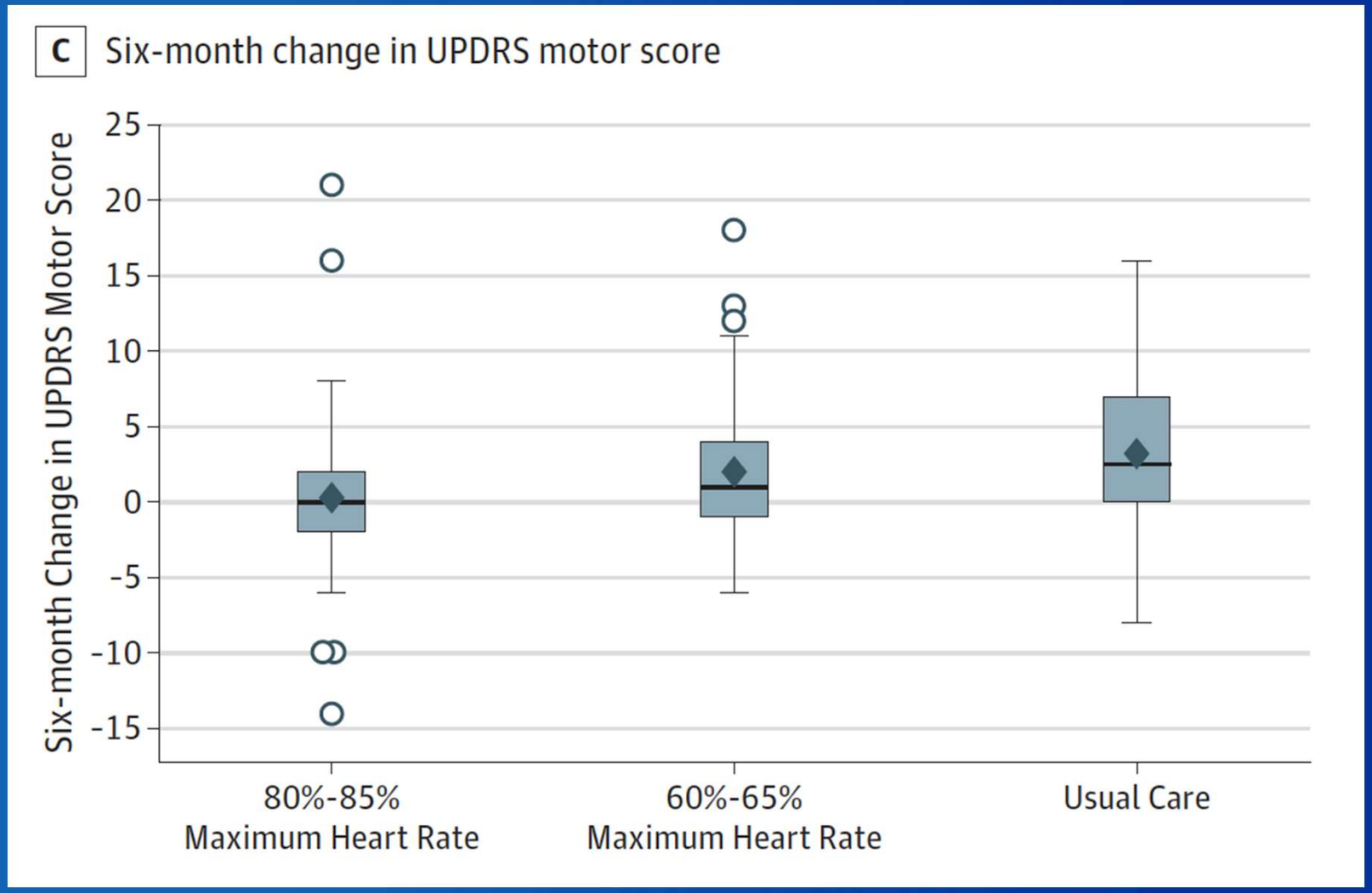


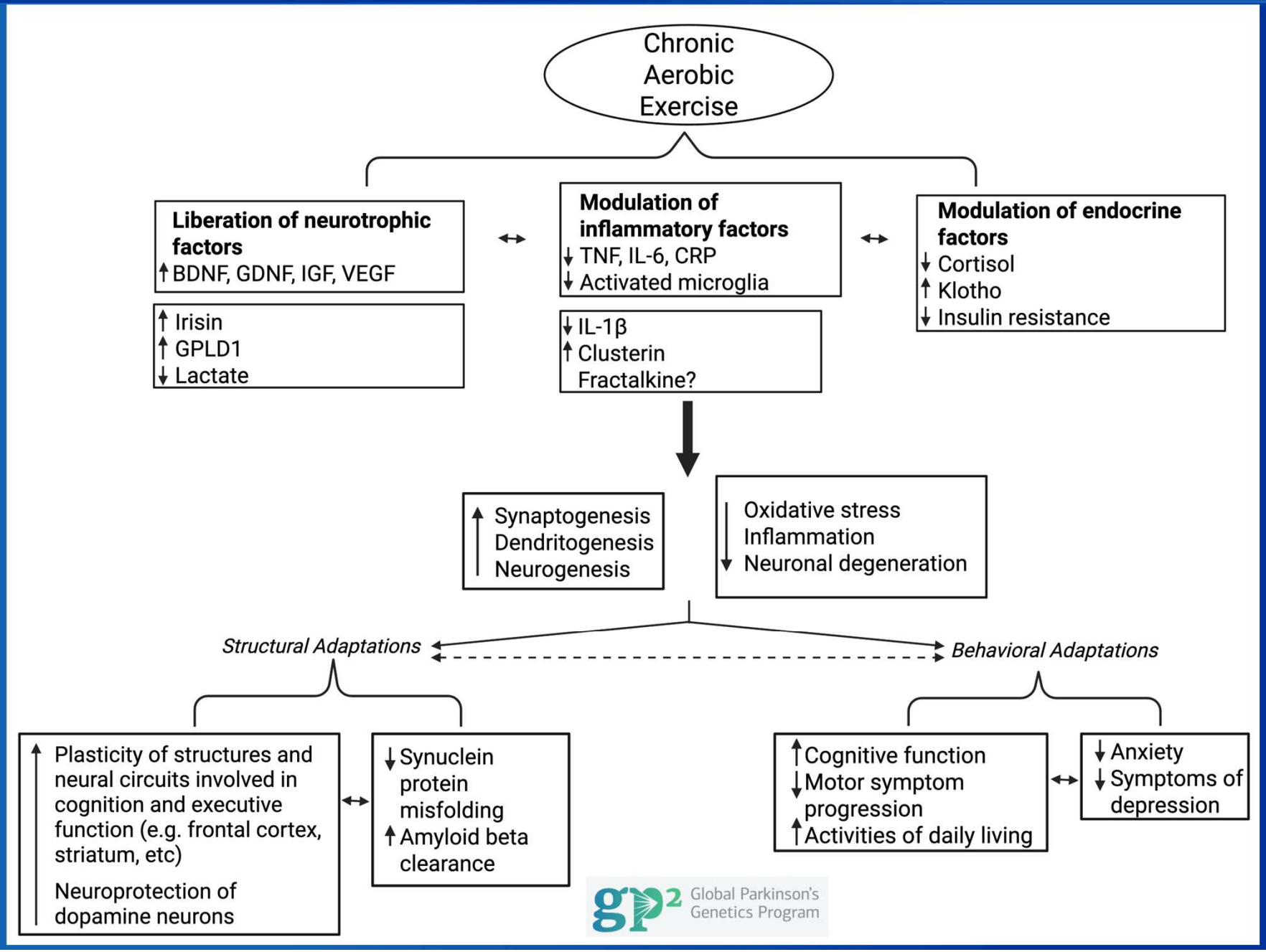
Fig. 1 Dopamine Transporter Levels Pre- and Post-Exercise.
A Average 18F-FE-PE2I DAT BPND images before and after six months of exercise. The red box including the midbrain and SN is enlarged.
Note: The left side of the color bar (0.0–3.0) corresponds to the DAT BPND in the striatum and the right side (0.0–1.0) to the DAT BPND in the SN shown in the inset images. BPND is unitless. Orientation is axial.

Differential Levels of Response



Schenkman et al. JAMA Neurol. 2018;75(2):219-226.

Factors Mediating Exercise

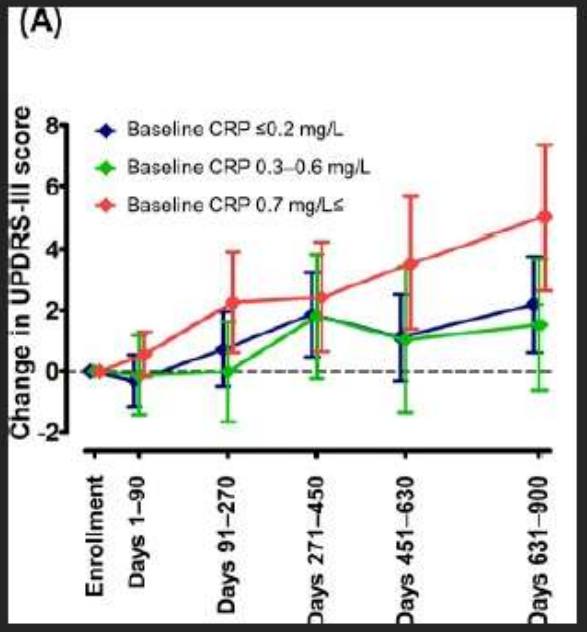


Inflammation

CRP predicts motor prognosis in PD, maybe…

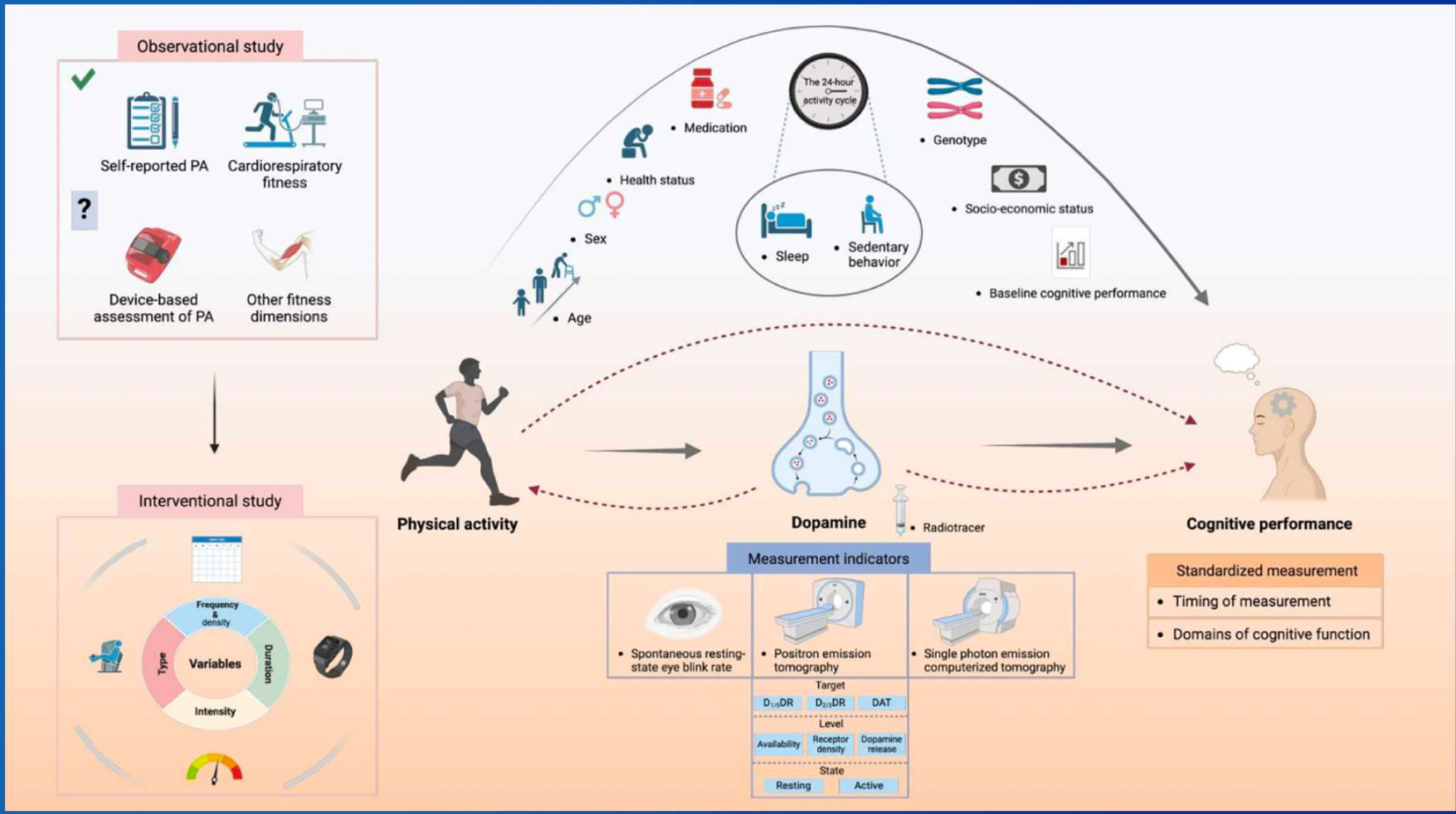
Baseline Plasma C-Reactive Protein Concentrations and Motor Prognosis in Parkinson Disease

Change in UPDRS-III scores was significantly greater in PD patients with CRP concentrations ≥0.7 mg/L than in those with CRP concentrations <0.7 mg/L.
Baseline plasma CRP levels were associated with motor deterioration and predicted motor prognosis in patients with PD. These associations were independent of sex, age, PD severity, dementia, and anti-Parkinsonian agents, suggesting that subclinical systemic inflammations could accelerate neurodegeneration in PD.

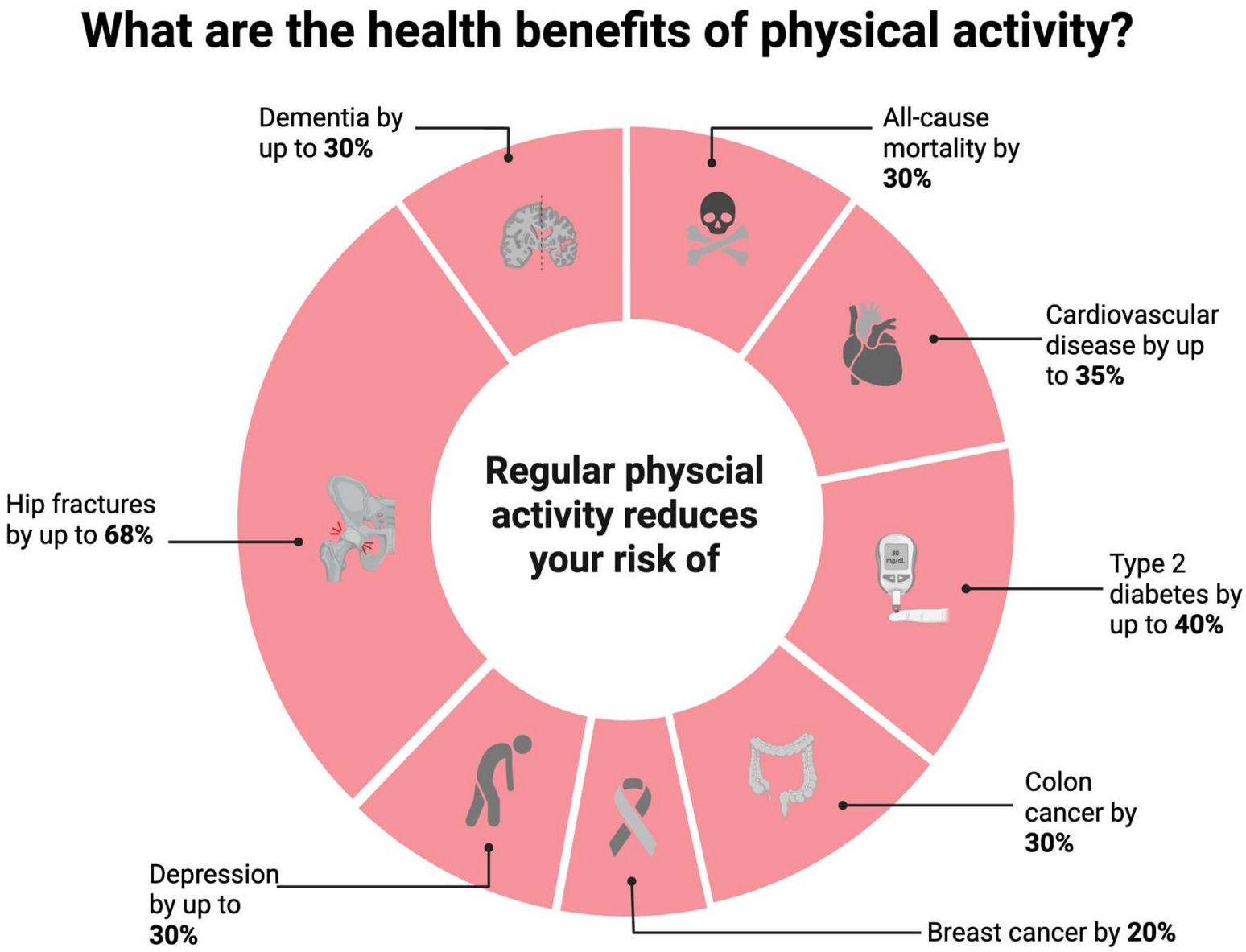


PLoS One. 2015; 10(7): e0134118.

Physical Activity: Dopamine



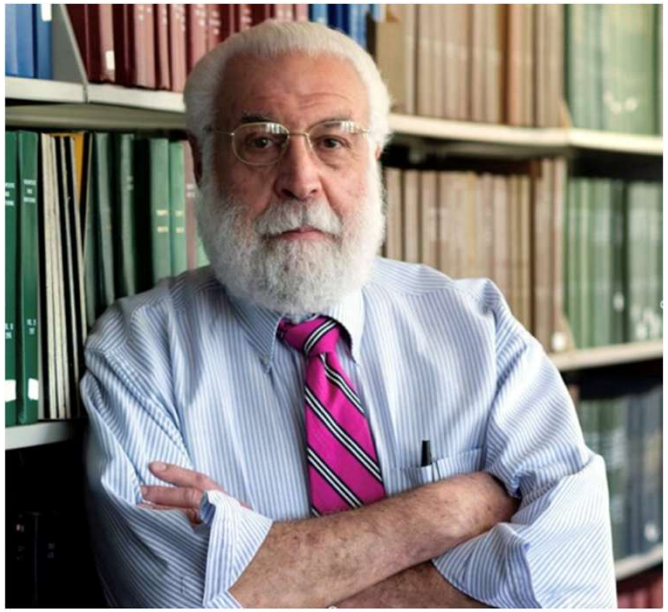
Physical Activity:
The Universal Pluripotent Pill



Thank You

Research in Progress: The ENICTO Consortium and the THRIVE-65 Study

Schmitz (Contact PI), Ligibel (MPI), Berger (MPI)



In memory of our colleague and THRIVE-65 MPI
Dr. Nate Berger

Exercise and Nutrition Interventions to Improve Cancer Treatment-Related Outcomes

Primary goal: evaluate the impact of diet and exercise interventions during treatment on received dose intensity (RDI) and treatment toxicity

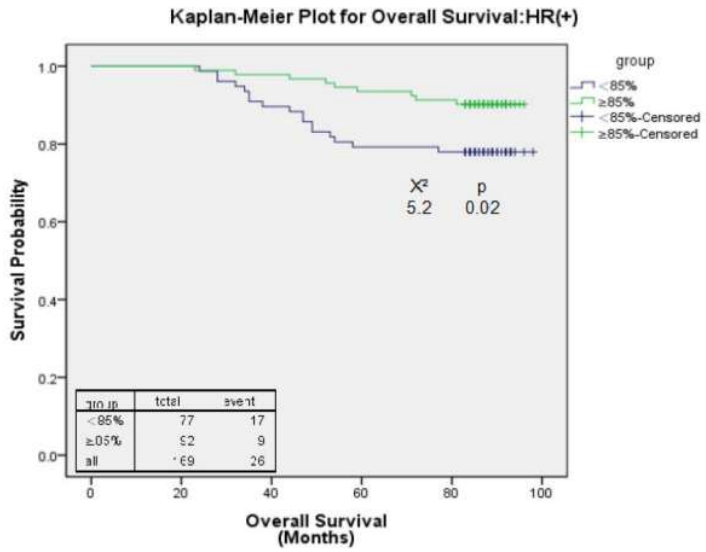
https://enicto.bsc.gwu.edu/web/enicto/home

What is Received Dose Intensity (RDI)?

$$\frac{\textbf{Delivered Dose Intensity (DDI)}}{\textbf{Standard Dose Intensity (SDI)}} \times 100$$

RDI expresses how much of a planned chemotherapy regimen a patient received and how closely the patient received it according to the planned schedule

RDI is associated with breast cancer recurrence and survival



Qi et al. Sci Reports 2020

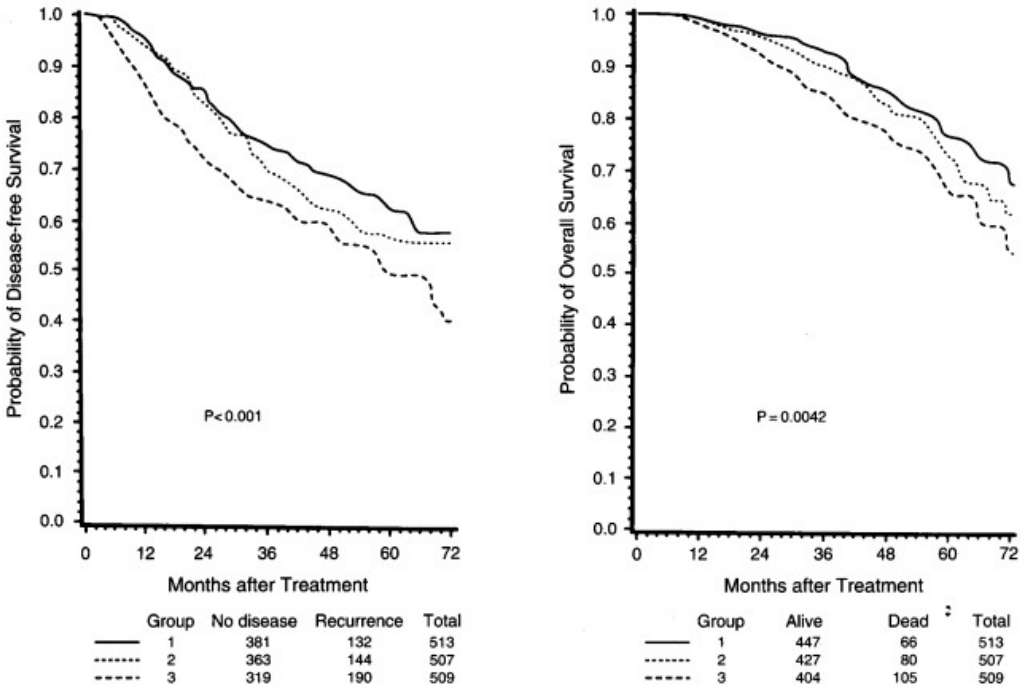


Figure 1. Actuarial Disease-free and Overall Survival According to Dose Intensity of Chemotherapy in Women with Stage II Breast Cancer.

Wood et al. NEJM 1994

Age >65 significantly predicts chemotherapy dose reductions and delays

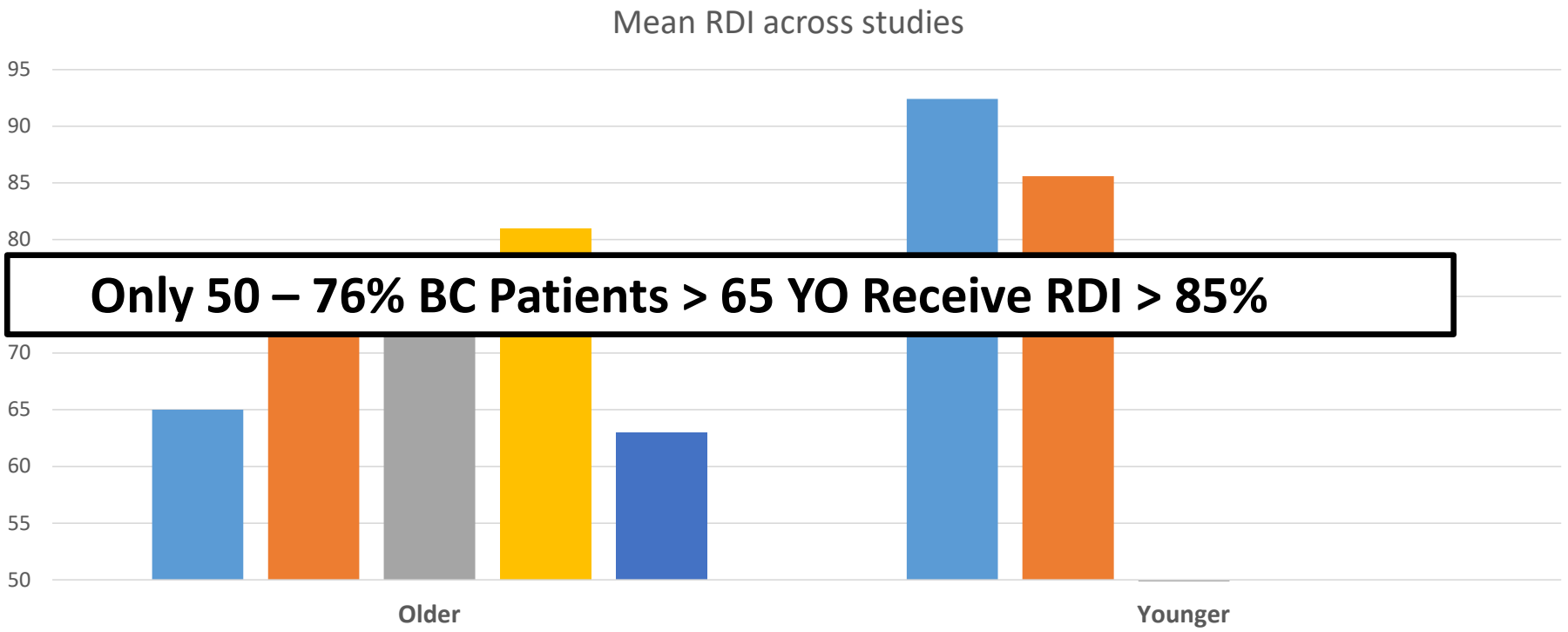
Table 3 Predictive factors significant on multivariate analysis

Outcome	Predictive factors	Adjusted odds ratio	95% CI	*P*-value
Overall RDI reduction	BMI	1.05	1.00–1.09	0.032
	Age ≥65	8.36	2.40–29.08	0.001
RDI < 50%	Age ≥65	7.37	1.71–31.78	0.007
Cessation	Age ≥65	2.96	1.13–7.71	0.027
Initial dose reduction	Obesity†	55.91	7.44–419.95	0.000
	BMI†	1.281	1.18–1.39	0.000
Dose reduction (unplanned)	G-CSF use	3.48	1.58–7.67	0.002
Dose reduction >15%	G-CSF use	3.72	1.41–9.81	0.008
Dose delay >7days	Age ≥65	3.26	1.10–9.65	0.033
	Dose dense	6.65	1.49–29.62	0.013

†Separate models were used to assess the effect of BMI and obesity on initial dose reduction. BMI, body mass index; G-CSF, granulocyte colony-stimulating factor; RDI, relative dose intensity.

Sandy 2013

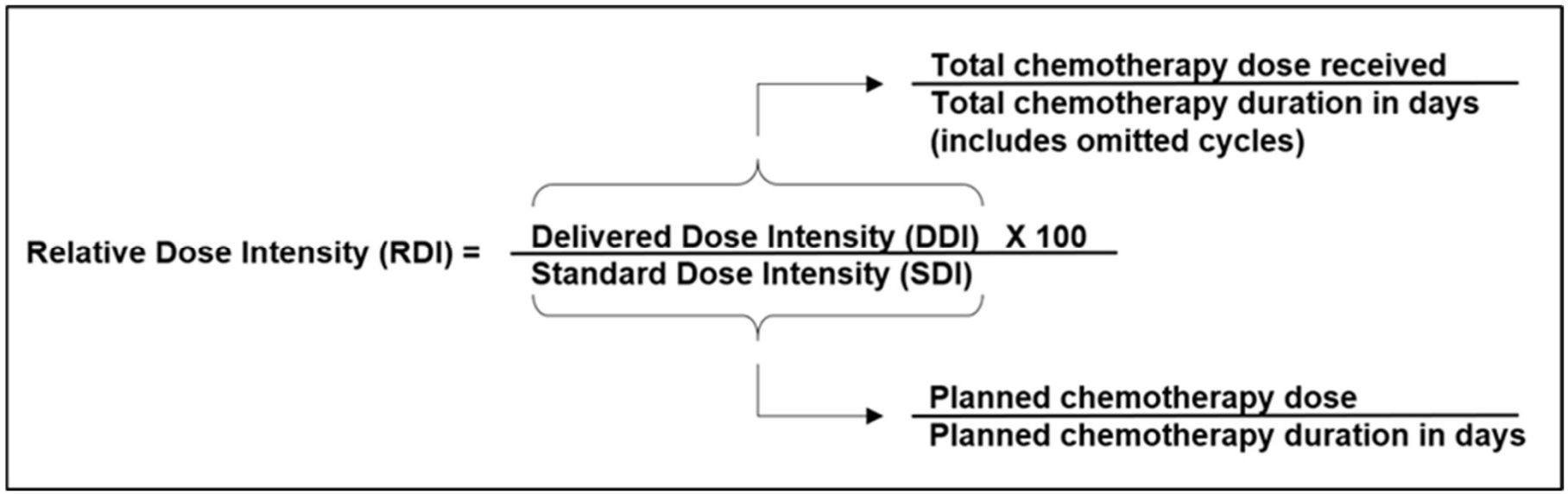
Relative Dose Intensity is lower in older women with breast cancer



Only 50 – 76% BC Patients > 65 YO Receive RDI > 85%

Oladipo 2009; Ngamphaiboon 2012; Wildiers 2012; Raza 2013, Ladwa 2018; Sandy 2013; Raza 2009

Calculating RDI…. Deceptively simple

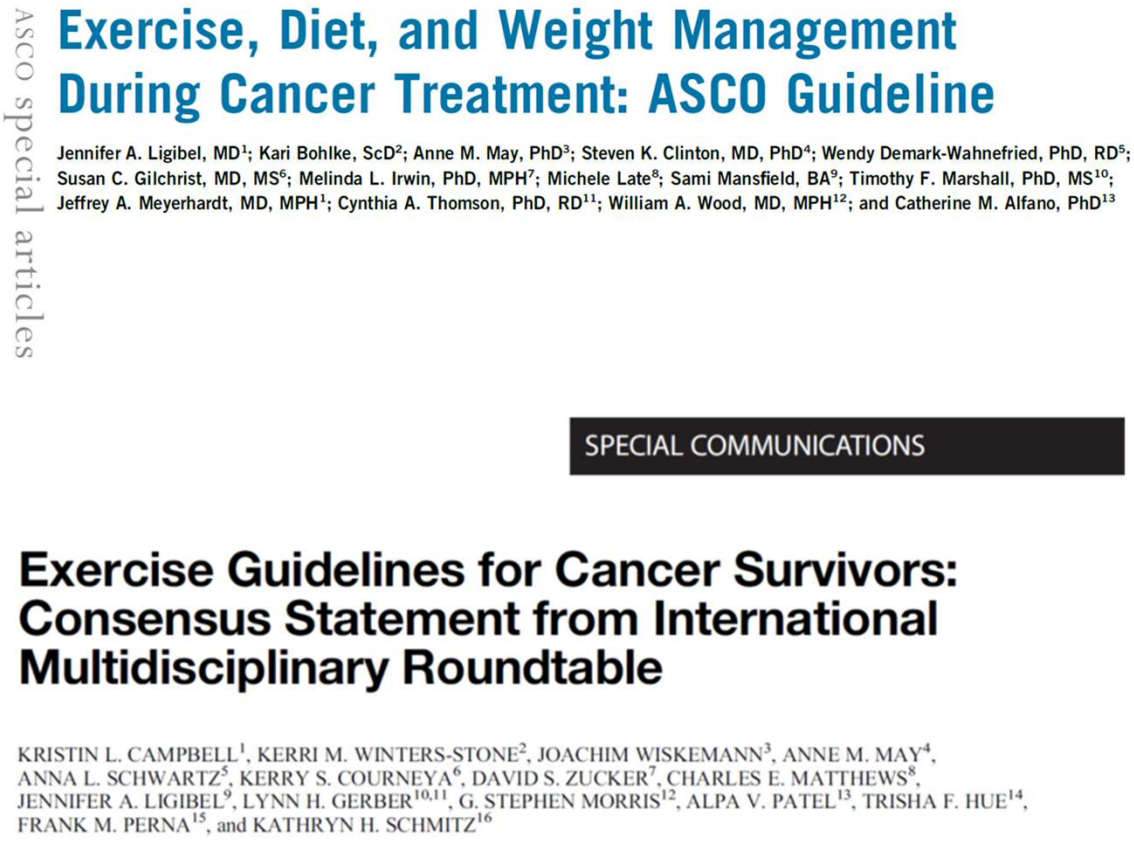


RDI Calculations: Devil in the details

#	Drug Regimen	Days Planned		Days Actual		SDI		DDI		Drug RDI		Regimen RDI	
		Hand	Machine	Hand	Machine	Hand	Machine	Hand	Machine	Hand	Machine	Hand	Machine
1	Docetaxel	84	85	84	85	3.57	3.53	3.57	3.53	100	100	100	100
	Cyclophosphamide	84	85	84	85	28.57	28.24	28.57	28.24	100	100		
2	Doxorubicin	112	57	119	64	2.14	4.21	2.02	3.75	94.12	89.07	93.86	92.137
	Cyclophosphamide	112	57	119	64	21.43	42.11	20.17	37.5	94.12	89.05		
	Paclitaxel	112	57	120	58	6.25	12.28	5.83	12.07	93.33	98.29		
3	Docetaxel	84	85	87	88	3.57	3.53	3.45	3.41	96.55	96.6	96.55	96.585
	Cyclophosphamide	84	85	87	88	28.57	28.24	27.59	27.27	96.55	96.57		
4	Docetaxel	84	85	84	85	3.57	3.53	2.98	2.94	83.33	83.29	83.33	83.305
	Cyclophosphamide	84	85	84	85	28.57	28.24	23.81	23.53	83.33	83.32		
5	Paclitaxel	84	120	84	120	11.43	8	11.43	8	100	100	92.59	92.707
	Doxorubicin	56	57	63	64	4.29	4.21	3.81	3.75	88.89	89.07		
	Cyclophosphamide	56	57	63	64	42.86	42.11	38.1	37.5	88.89	89.05		

Exercise has been shown to impact several factors that predict lower RDI

- Functional Status
- Depression
- Falls
- Sarcopenia



ASCO special articles

Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline

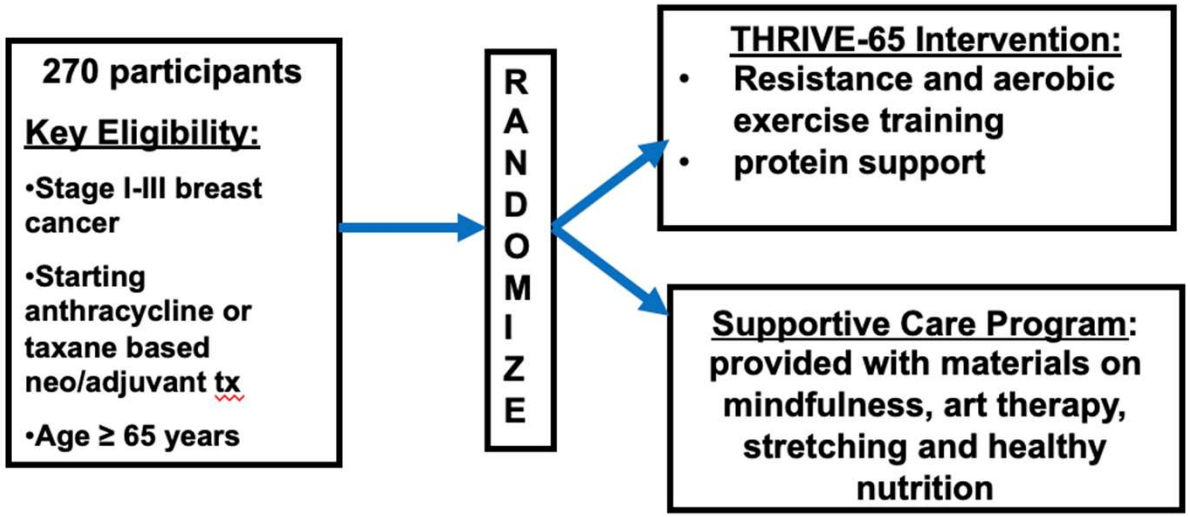
Jennifer A. Ligibel, MD[1]; Kari Bohlke, ScD[2]; Anne M. May, PhD[3]; Steven K. Clinton, MD, PhD[4]; Wendy Demark-Wahnefried, PhD, RD[5]; Susan C. Gilchrist, MD, MS[6]; Melinda L. Irwin, PhD, MPH[7]; Michele Late[8]; Sami Mansfield, BA[9]; Timothy F. Marshall, PhD, MS[10]; Jeffrey A. Meyerhardt, MD, MPH[1]; Cynthia A. Thomson, PhD, RD[11]; William A. Wood, MD, MPH[12]; and Catherine M. Alfano, PhD[13]

SPECIAL COMMUNICATIONS

Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable

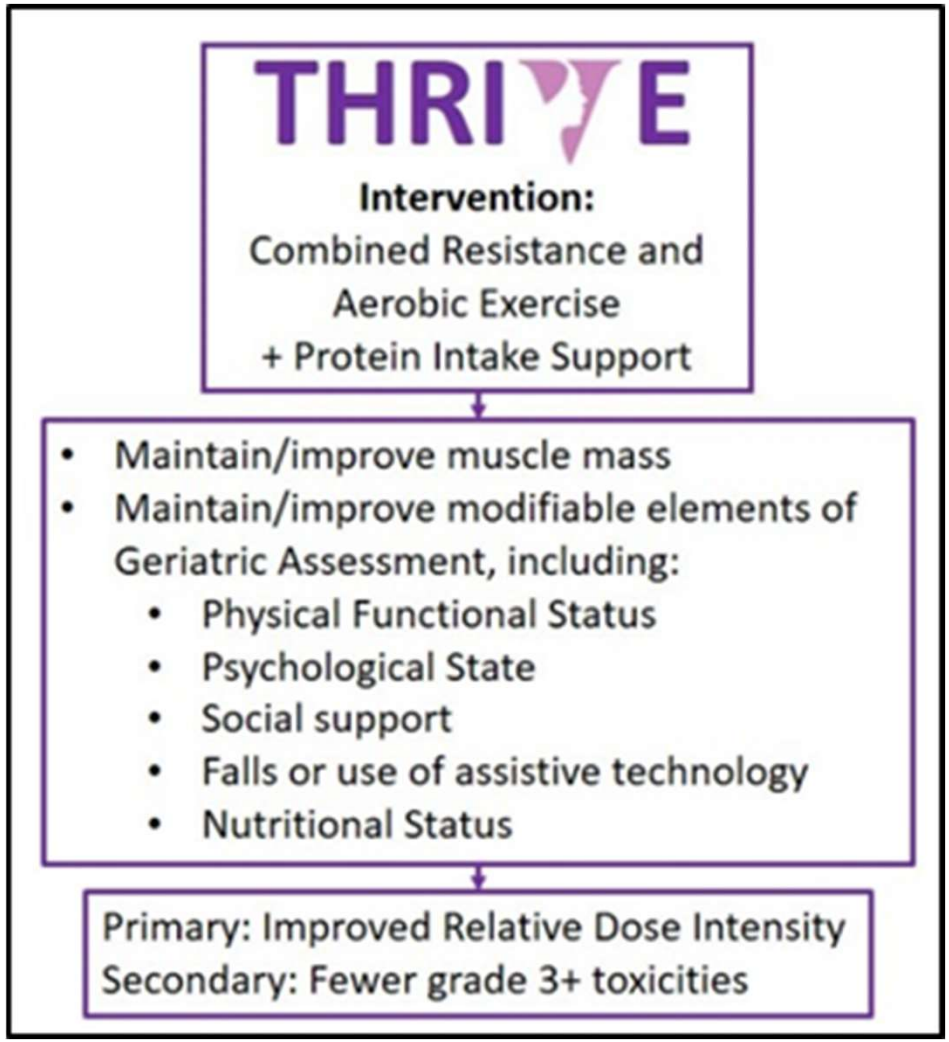
KRISTIN L. CAMPBELL[1], KERRI M. WINTERS-STONE[2], JOACHIM WISKEMANN[3], ANNE M. MAY[4], ANNA L. SCHWARTZ[5], KERRY S. COURNEYA[6], DAVID S. ZUCKER[7], CHARLES E. MATTHEWS[8], JENNIFER A. LIGIBEL[9], LYNN H. GERBER[10,11], G. STEPHEN MORRIS[12], ALPA V. PATEL[13], TRISHA F. HUE[14], FRANK M. PERNA[15], and KATHRYN H. SCHMITZ[16]

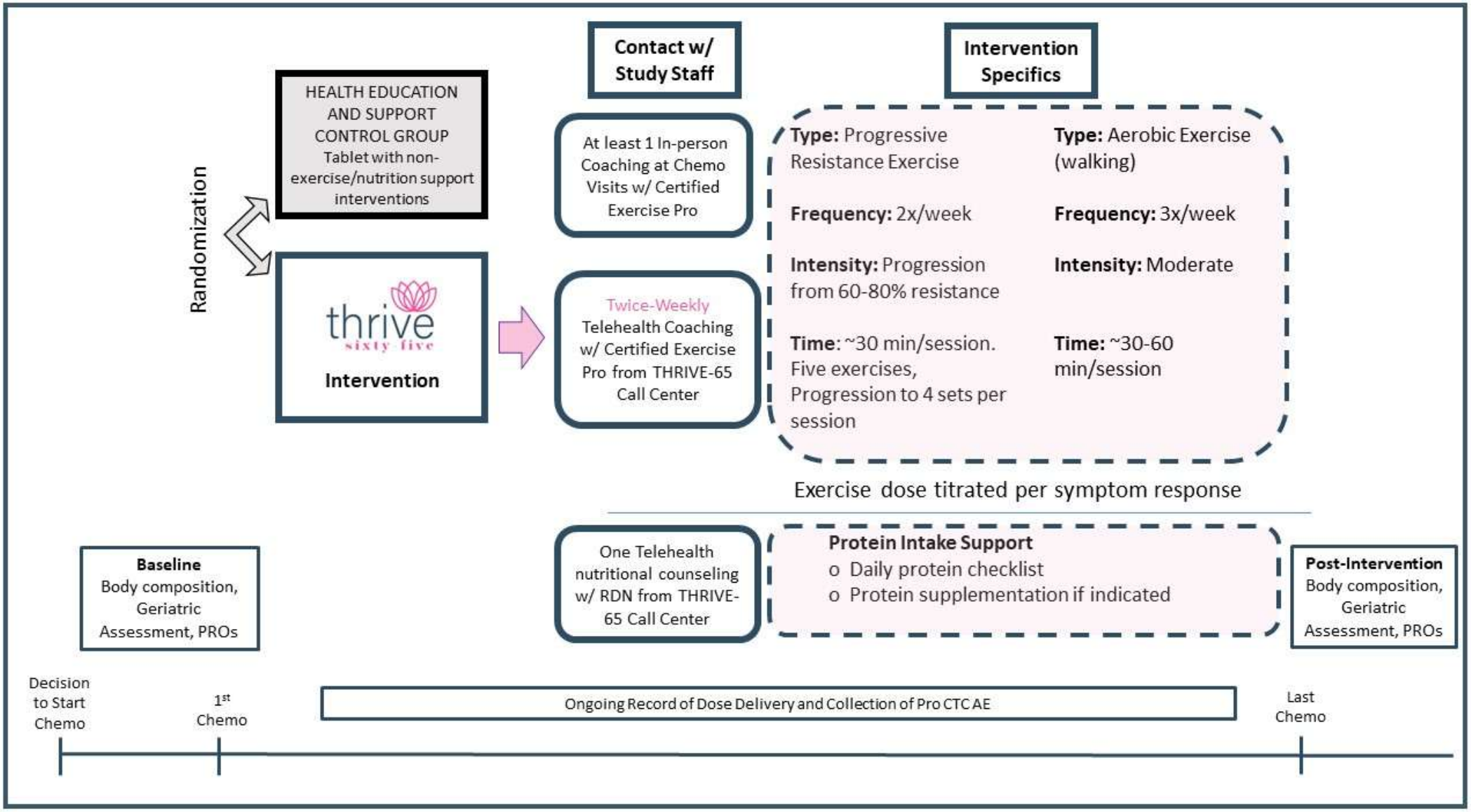
TeleHealth Resistance exercise Intervention to preserve dose intensity and Vitality in Elder Breast Cancer Patients



U01-CA271277
Kathryn Schmitz, Contact PI
Jennifer Ligibel, MPI

THRIVE-65 Objectives:




Randomization
HEALTH EDUCATION AND SUPPORT CONTROL GROUP
Tablet with non-exercise/nutrition support interventions
thrive
sixty five
Intervention
Contact w/ Study Staff
Intervention Specifics
At least 1 In-person Coaching at Chemo Visits w/ Certified Exercise Pro
Twice-Weekly Telehealth Coaching w/ Certified Exercise Pro from THRIVE-65 Call Center
Type: Progressive Resistance Exercise
Frequency: 2x/week
Intensity: Progression from 60-80% resistance
Time: ~30 min/session. Five exercises, Progression to 4 sets per session
Type: Aerobic Exercise (walking)
Frequency: 3x/week
Intensity: Moderate
Time: ~30-60 min/session
Exercise dose titrated per symptom response
One Telehealth nutritional counseling w/ RDN from THRIVE-65 Call Center
Protein Intake Support
o Daily protein checklist
o Protein supplementation if indicated
Baseline
Body composition, Geriatric Assessment, PROs
Post-Intervention
Body composition, Geriatric Assessment, PROs
Decision to Start Chemo
1st Chemo
Ongoing Record of Dose Delivery and Collection of Pro CTC AE
Last Chemo

Recruitment Highlights

	CWRU/UH	DFCI	PITT/UPMC	Total
Screened	110	234	188	532
Consented	20	54	58	132
Withdrawn After consent/before randomization	5	6	8	19
Randomized	15	46	39	100
Active	5	8	6	19
Completed Study	9	36	30	75
Withdrawn After randomization	1	2	2	5
Became Ineligible After randomization	0	1	3	4

THRIVE-65 Team

Dana Farber Cancer Institute
MPI: Jennifer Ligibel
Anna Tanasijevik
Kaedryn Diguglielmo
Jay Oppenheim
Wendy Kemp
Truong Nguyen
Samantha Anderson

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William Evans
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Shawna Doerksen
Sara Garrett
Jenna Binder
Mohamed Ahmed
Michele Sobolewski

University of Arizona
Cyndi Thomson
Angela Yung

MD Anderson
Karen Basen-Engquist

Conducting physical activity trials in diverse populations (with a focus on Latinos)

David X. Marquez, PhD

Professor

Department Head

Department of Kinesiology and Nutrition

University of Illinois Chicago

Rush Alzheimer's Disease Center, Rush University

UIC UNIVERSITY OF ILLINOIS AT CHICAGO

Disclaimer

- No relevant disclosures

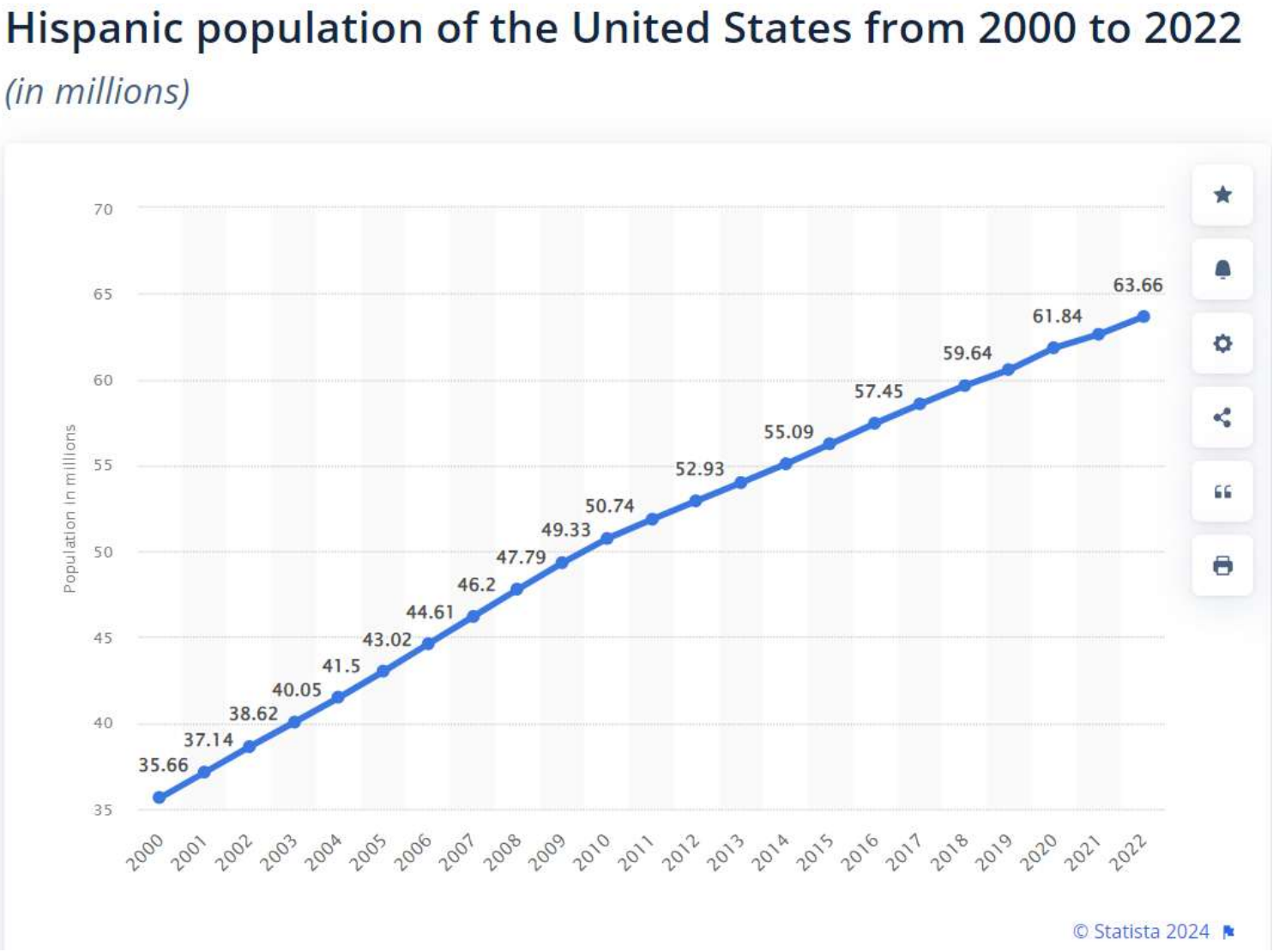
Overview

- Background info about Latinos
- Dance research
- Recruitment and Retention

UIC UNIVERSITY OF ILLINOIS AT CHICAGO

Demographics

- Largest ethnic minority group in the US



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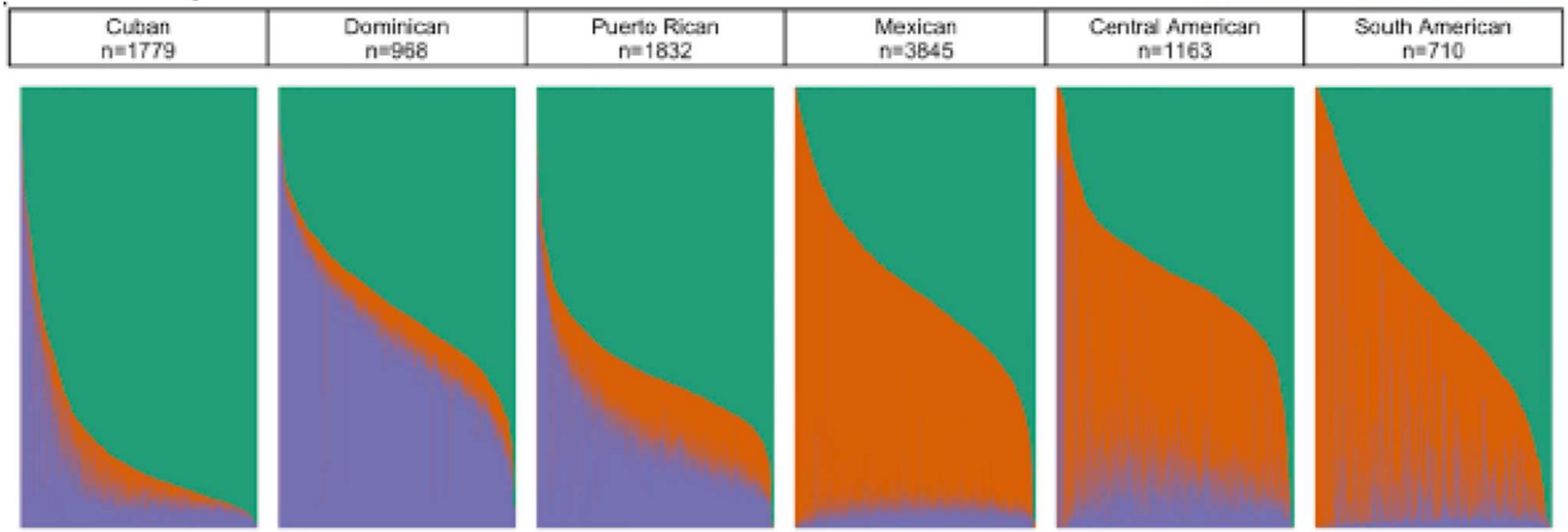
Genetic Ancestry of Latinos

Latino genetic continental ancestries diversity

- African
- Amerindian
- European



Conomos et al, HCHS/SOL, *Am J Human Genetics* 2016
NPR

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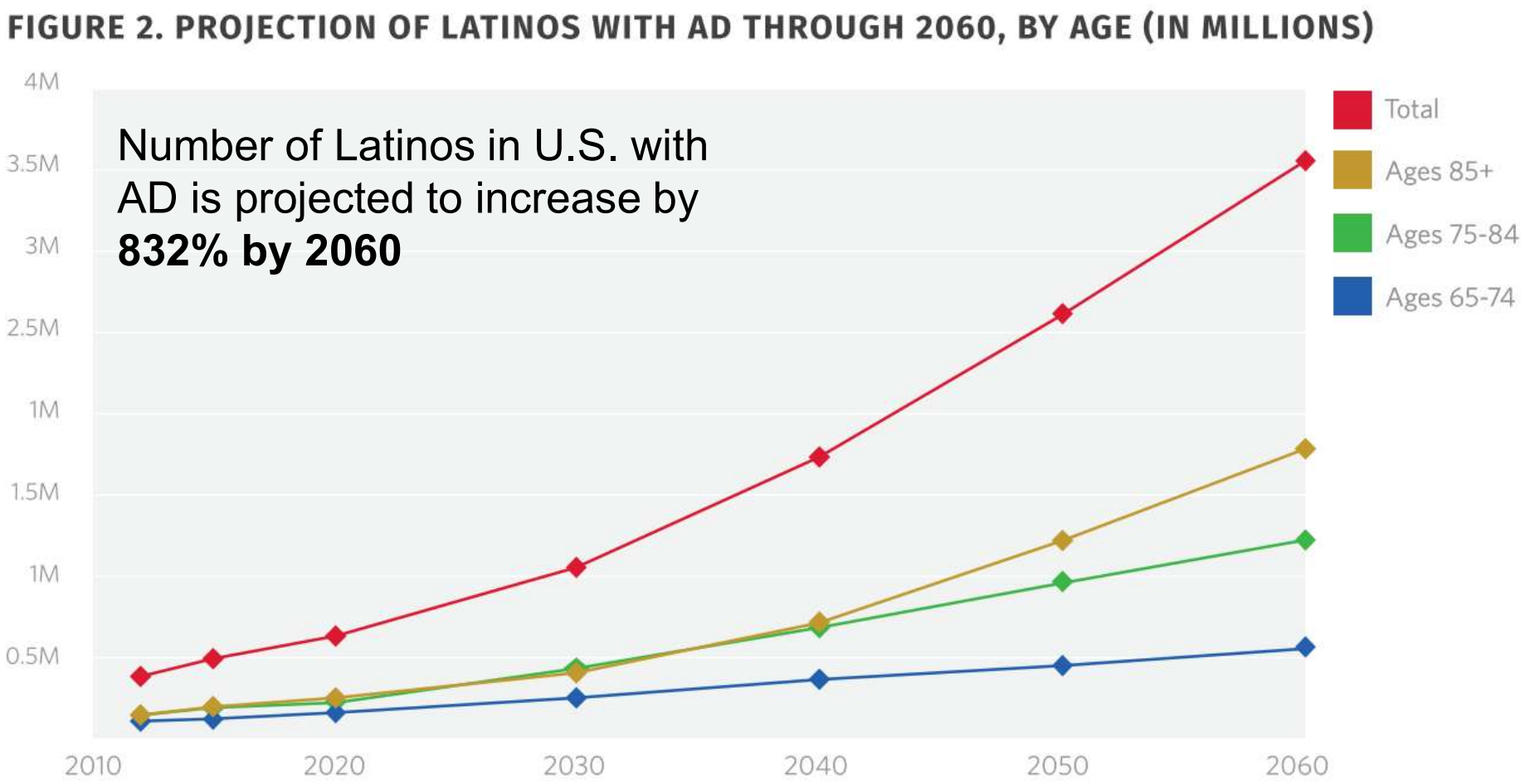
Slide courtesy of Hector Gonzalez, PhD

Older Latinos in the US

- Older non-Latino Whites
  - From 2000 to 2009
  - 65+: 10% increase
- Older Latinos
  - From 2000 to 2009
  - 65+: **59%** increase (up to 2.7 million)
- In 2017, Latinos were 8% of older adults
- 2060, projection is 21% of older adults
- The people are there; it is on us to create welcoming environments

Alzheimer's Disease in Latinos



(Wu, Vega, Resendez, Jin, & Scholar, 2016)

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Dance as Physical Activity

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HOLD UP, WAIT A MINUTE!

WHO IS GOING TO TRUST:

-AN OUTSIDER OF THE NEIGHBORHOOD

-APPARENT WHITE-LOOKING

-NON-DANCER

Challenge

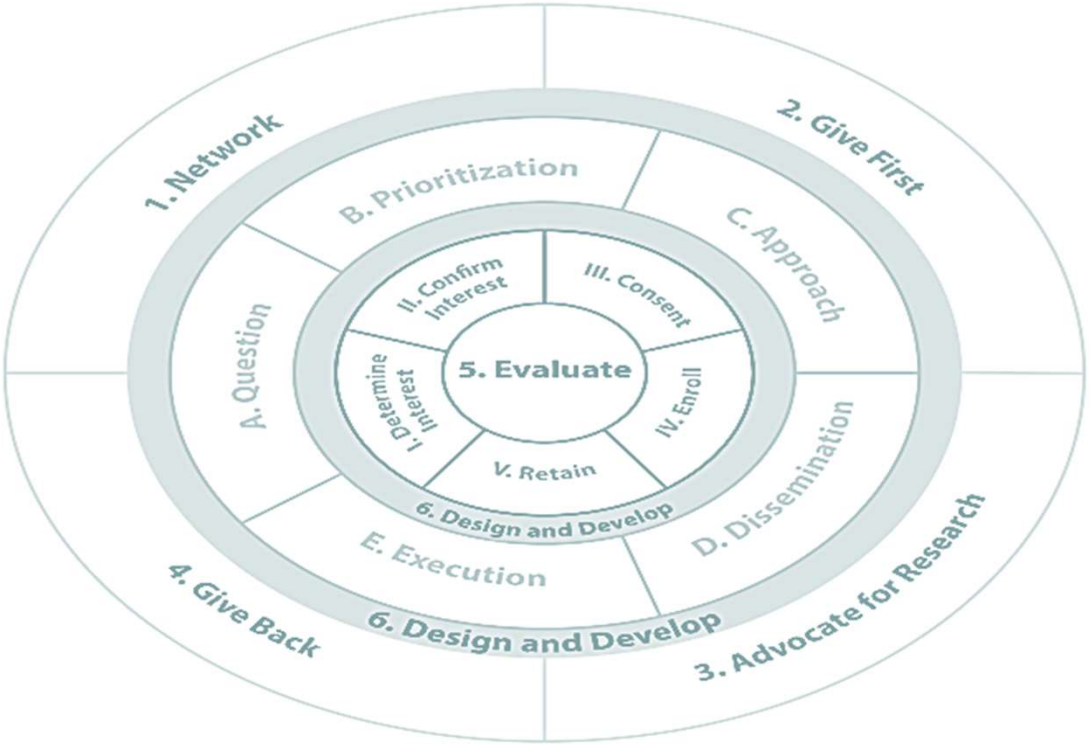
- Distrust
  - Older Latinos are skeptical of the research process, especially undocumented: I feel like a guinea pig
  - Current social climate
    - Fear of providing information

- Need to make it/keep it personal

NGAGEDD Model

The NGAGEDD Model

Network
Give First
Advocate for Research
Give Back
Evaluate
Design
Develop



Outer circle represents community activities, middle circle represents participant input on research, and inner circle represents individual study activities.

Glover, Shah, et al. Under Review

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BAILAMOS™ dance program

(Balance & Activity In Latinos, Addressing Mobility in Older adultS)

- Enjoyable
- Not hard, boring, & tedious

Marquez, D. X., Bustamante, E. E., Aguiñaga, S., & Hernandez, R. (2015). BAILAMOS©: Development, pilot testing, and future directions of a Latin dance program for older Latinos. Health Education & Behavior, 42(5), 604-610. doi: 10.1177/1090198114543006

- Age-appropriate PA for older Latinos
- Challenge physically ***and*** cognitively

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Recruitment

- Presentations at Herencia Latina (Latino Club) at the senior center
- Hospitals/clinics
- Flyers in mailboxes of senior housing facilities
- Announcements at Spanish masses at Roman Catholic churches
  - Flyers in weekly bulletins
  - Stand by exits with flyers and sign-up sheets
- Word of mouth

BAILA: Being Active, Increasing older Latinos healthy Aging

- **David X. Marquez, PhD**
  - Department of Kinesiology and Nutrition (UIC)
- **Michael Berbaum, PhD**
  - Institute for Health Research and Policy (UIC)
- **David Buchner, MD, MPH**
  - Department of Kinesiology and Community Health (UIUC)
- **Susan Hughes, PhD**
  - School of Public Health (UIC)
- **Kyriakos Markides, PhD**
  - University of Texas Medical Branch, Galveston
- **Edward McAuley, PhD**
  - Department of Kinesiology and Community Health (UIUC)
- **JoEllen Wilbur, PhD**
  - Rush College of Nursing
- **Robert Wilson, PhD**
  - Rush Alzheimer's Disease Center

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Marquez, D.X., Wilbur, J., Hughes, S., Berbaum, M.L., Wilson, R., Buchner, D. M., & McAuley, E. (2014). B.A.I.L.A. - A Latin dance randomized controlled trial for older Spanish-speaking Latinos: Rationale, design, and methods. Contemporary Clinical Trials, 38(2), 397-408. doi: 10.1016/j.cct.2014.06.012

Attendance

- Non-scientific factor analysis of reasons people miss classes (in no particular order)
  - Caregiving
  - Out of country/state
  - Work status change
  - Health issues
  - Transportation
  - Lost interest – but don't say that

Marquez et al., (2020). TBM;10:1566–1572; doi: 10.1093/tbm/ibz127

Recruitment challenge	Recruitment solution/strategy
Lack of trust of the researchers and the research process	Promotora/CHW to assist with recruit, identify and screen potential participants, schedule appointments, and support data collection
	Bilingual, bicultural staff working on the program
	Use established community connections to disseminate study materials (e.g., churches to invite congregations)
	Do not ask for social security numbers
Lack of insurance	Do not use lack of insurance as an exclusion criteria
	Use the EASY tool, so that only participants who have new or uncontrolled conditions need to get medical clearance
Working late into life	Conduct data collection in the community
	Flexible testing times and class times (e.g., early evenings and weekends as possibilities)
Acute and chronic illnesses	Flexible testing times (e.g., to make up missed classes due to appointments)
Reliable phone contact	Get the name and phone number of three other people who could be contacted
Low literacy makes consent and data collection a lengthy process	Adapt consent forms to a lower reading level (e.g., sixth grade level) and have a data collector administer questionnaires interview style
	Break up data collection appointments to avoid overwhelming participants in one sitting
Lack of safety (e.g., potential participants who would rely on walking to the intervention site)	Advise participants to walk with someone (e.g., another participant)
	Use phone app to share real-time location with others/research staff

Marquez et al., (2020). TBM;10:1566–1572; doi: 10.1093/tbm/ibz127

Retention challenge	Retention solution/strategy
Travel to home country (e.g., Mexico)	Flexible class times (e.g., to make up missed classes)
Work responsibilities (e.g., changes in work schedules for participants during the study)	Flexible class times, including early evening (e.g., to make up missed classes)
Caring for family members (e.g., child care)	Involve family members in classes
Acute and chronic illnesses	Flexible class times (e.g., to make up missed classes due to appointments)
Transportation problems (e.g., car trouble, too expensive, rely on another participant who can no longer attend)	Reimburse travel expenses; provide bus passes
	Create a carpool among participants
Religious holidays (e.g., Day of the Virgin of Guadalupe, Christmas days in December)	Flexible class times (e.g., to make up missed classes)
	Add classes to the end of the program
Lack of safety (e.g., potential participants who would rely on walking to the intervention site)	Advise participants to walk with someone (e.g., another participant)
	Use phone app to share real-time location with others/research staff
Spanish speakers and bilinguals in the same class	Have a bilingual instructor and maintain a comfortable emotional climate for all to feel received
	Have classes in Spanish only
Weather	Host PA interventions during warmer months
Caregiving	Offer childcare during PA interventions
	Create intergenerational PA interventions

Marquez et al., (2020). TBM;10:1566–1572; doi: 10.1093/tbm/ibz127

Summary

- Latinos are a large portion of the (older) adult population
- Many Latinos have poor health profiles
- Challenges to recruit and retain Latinos in research are present; but can be addressed

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- National Institute of Aging of NIH under Award Number 3P30AG010161-25S1
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Thank You

Physical Activity and Mental Health: The Promise of Context

Eduardo Esteban Bustamante, PhD, FACSM
Assistant Professor of Kinesiology and Nutrition
Director, UIC Healthy Kids Lab
University of Illinois Chicago
Society for Clinical Trials Annual Meeting
May 2025

AGENDA

I. Physical Activity & Mental Health Clinical Trial Evidence

II. The Confounding Role of Context

III. The Promise of Context to Promote Mental Health

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I. Physical Activity & Mental Health Clinical Trial Evidence

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DEFINITIONS

- **Mental Health:** A state of well-being that enables people to cope with the stresses of life, realize their abilities, learn well and work well and contribute to their community. Mental health is more than the absence of mental disorders.
- **Intrinsic effects:** Benefits arising innately from features of physical activity dose (frequency, intensity, duration, mode) and type (yoga, swimming, running, weightlifting).
- **Acute effects**: transient changes in brain function, cognition, and mood following single bouts.
- **Chronic effects**: durable changes in brain structure, brain function, mental health over weeks, months, or years.

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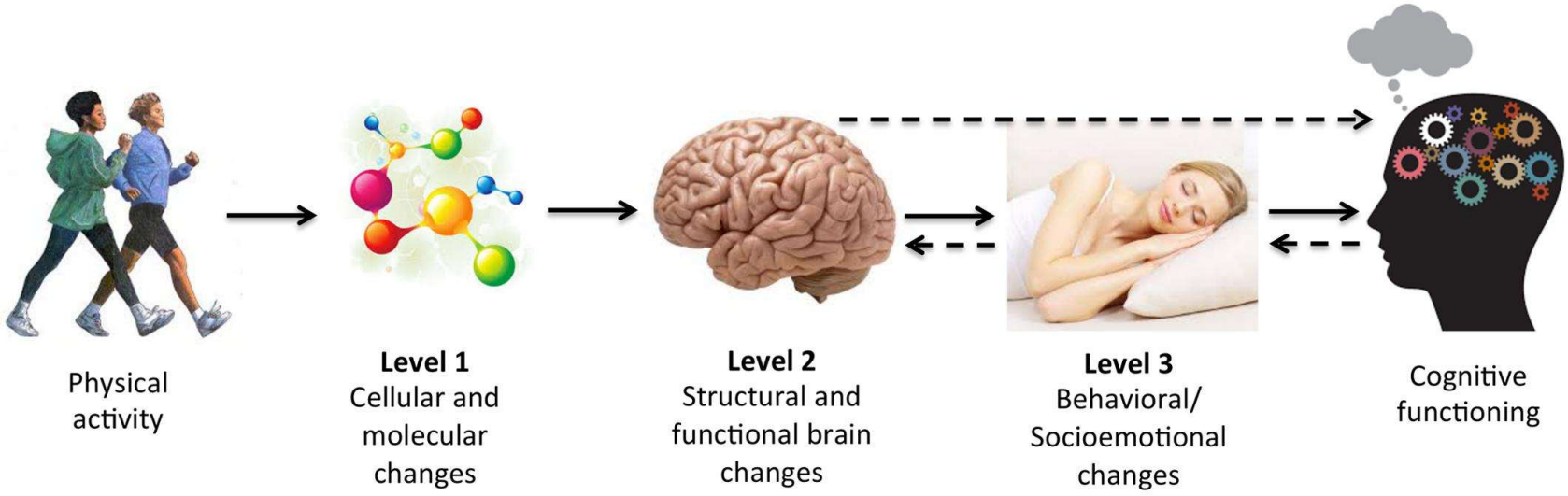
Umbrella Review on PA, Depression, Anxiety, and Psychological Distress

- 97 meta-analyses
- 1,039 unique trials
- **<u>128,119 unique participants over 40 years</u>**
- Depression median SMD = -0.43 (IQR = -0.66 to -0.27)
- Anxiety median SMD = −0.42 (IQR = −0.66 to –0.26)
- Distress SMD = -0.60 (95% CI = -0.78 to -0.42)



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Singh et al. (2023), *British Journal of Sports Medicine; Stillman et al. (2020), Frontiers in Human Neuroscience*

PA-Mental Health Clinical Trial Limitations

- **Short Durations**
  - >80% of trials are shorter than 6-months
  - Phase 2 FDA guideline suggest up to 2-years
- **Spontaneous Remission**
  - 33% of depression cases spontaneously remit by 6-months vs <1% of untreated hypertension cases remit
- **Small Samples**
  - ~70% of trials include fewer than 100 participants
  - Phase 2 FDA guidelines suggest 100-300 participants
- **Impossible to Blind Participants**
  - Placebo and expectancy effects depending on comparison group

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Bustamante et al. (2025) *Medicine & Science in Sports & Exercise*

PA-Mental Health Clinical Trial Limitations

- **Publication Bias**
  - Power in typical exercise trials estimated at 45%, yet >80% of publications report significant findings
  - Many trials before modern reporting standards
- **Small Effect Sizes on Well-Being**
  - One meta-analysis of 23 RCTs reports SMD = 0.05 in clinical samples and SMD = 0.21 in non-clinical samples.
- **White Affluent Samples**
  - Do results generalize?
- **Context Matters for Mental Health**
  - Relationships don't matter for blood sugar, but they do matter for moods and emotions

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Bustamante et al. (2025) *Medicine & Science in Sports & Exercise;*
Mesquida et al. (2023) *Journal of Sport Science*

II. The Confounding Role of Context

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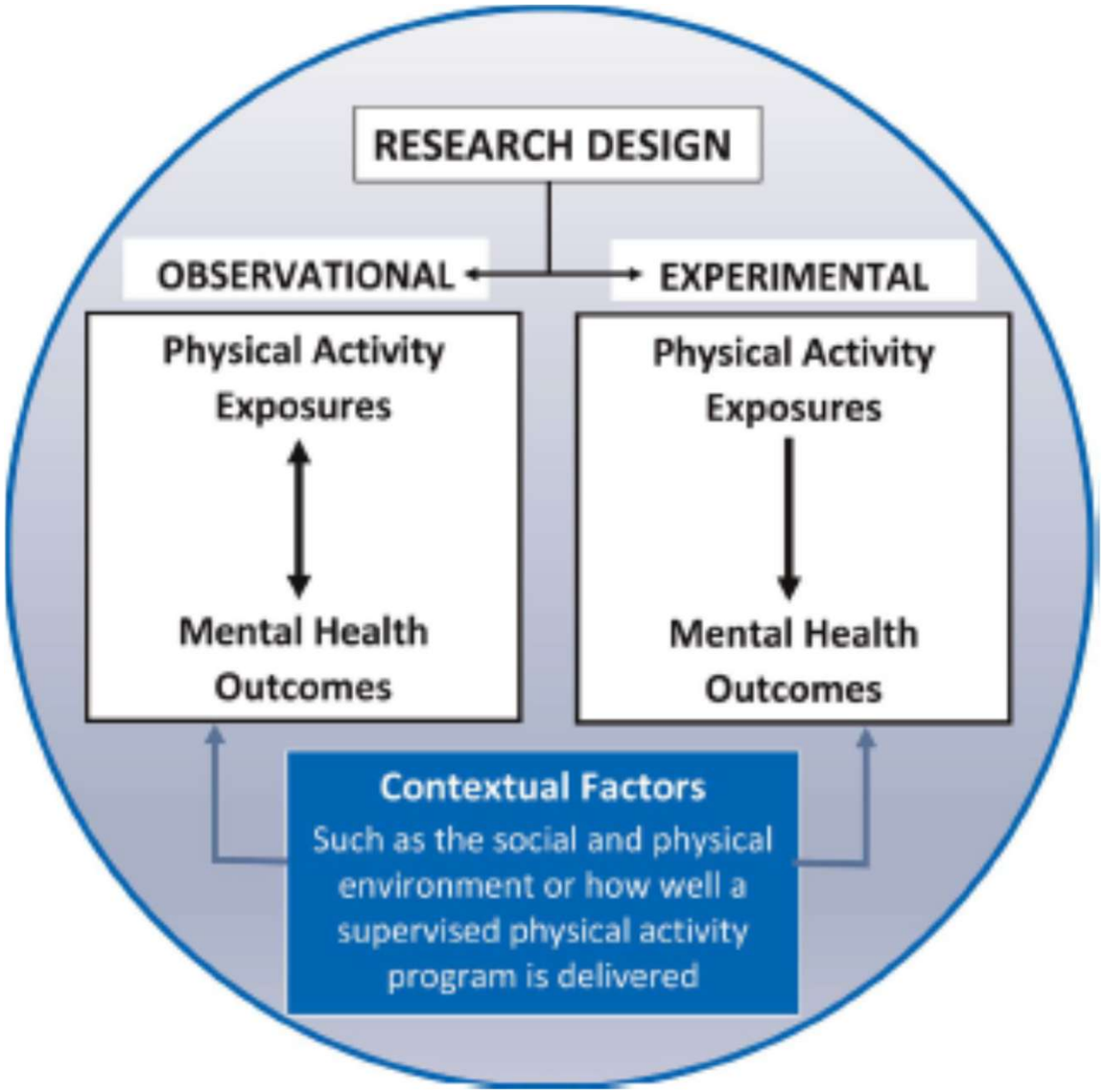
DEFINITIONS

Contextual effects:
Benefits arising from surrounding contextual features that can be intentionally and systematically manipulated to achieve an outcome that is not already fully realized innately by the PA itself. It includes rules, routines, relationships, and reinforcements.



Contextual Effects #1: Project Play

- Is the Benefit of Physical Activity Programs on ADHD Attributable to Physical Activity Itself, or Other Program Features?
- Pilot Randomized Controlled Trial
- N= 42 African American students with Elevated Symptoms of ADHD and DBD, 14 TD siblings
- 10-week physical activity program vs. 10-week comparable but sedentary attention control program

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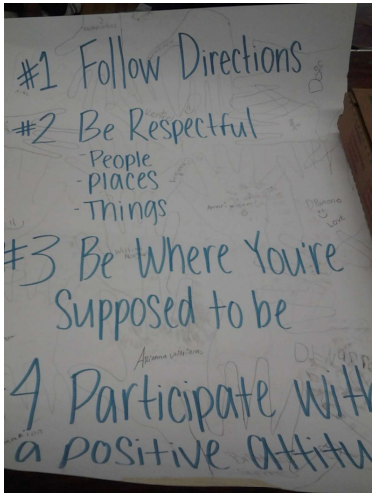
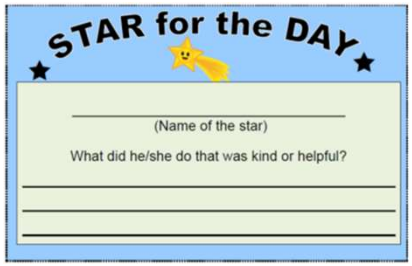
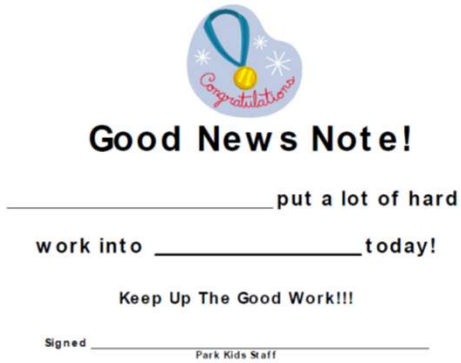
Bustamante et al. (2016) *Medicine & Science in Sports & Exercise*; Ramer et al. (2020) *Pediatric Exercise Science;* Santiago-Rodriguez et al. (2022) *International Journal of Psychological Studies*

CONTEXTUAL EFFECTS #1: PROJECT PLAY







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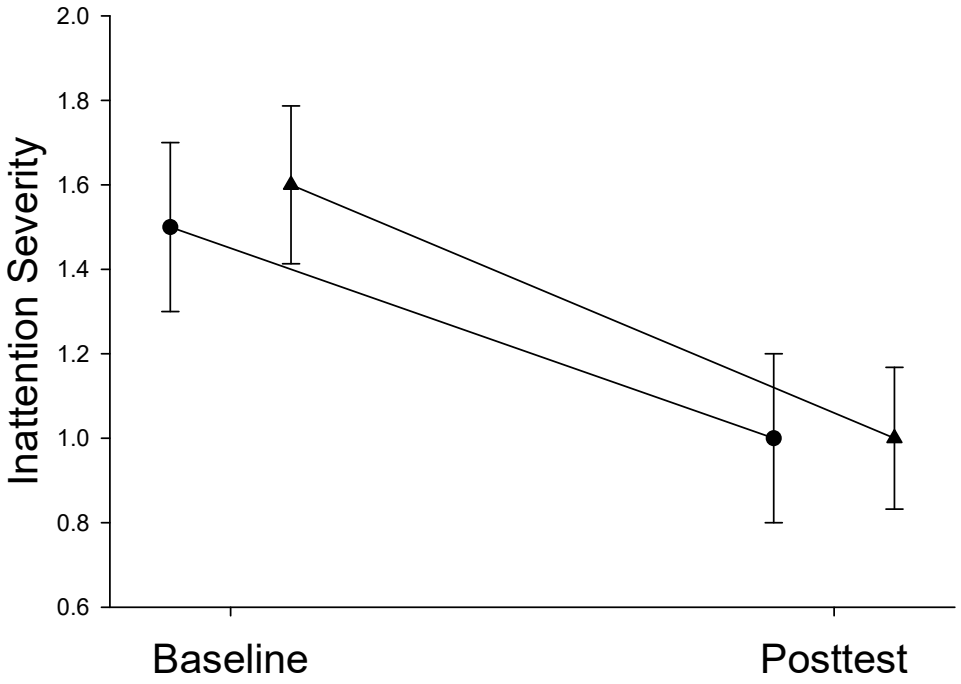
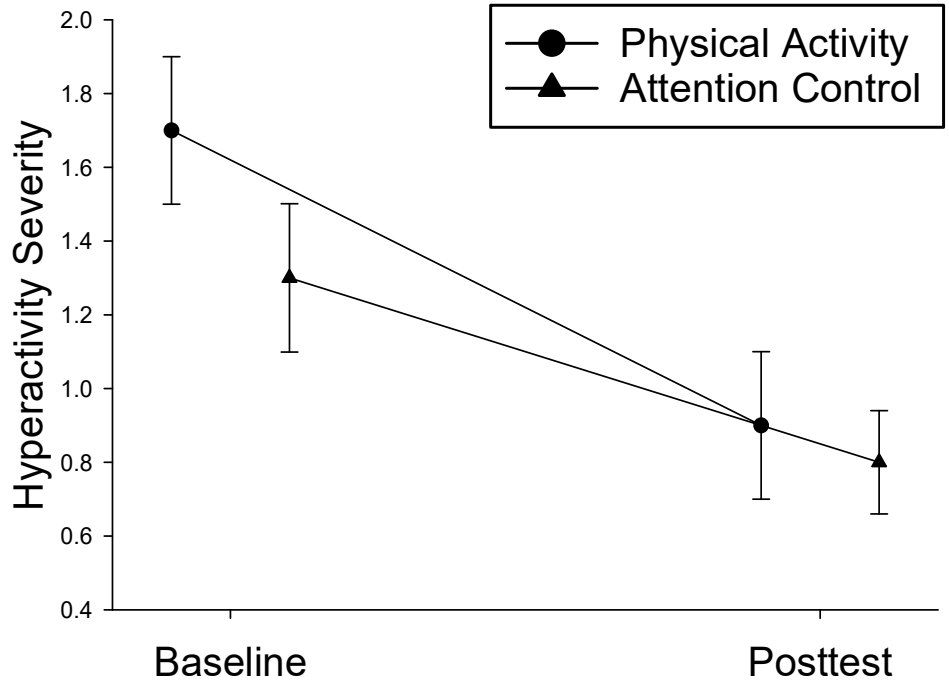
Bustamante et al. (2016) *Medicine & Science in Sports & Exercise*; Ramer et al. (2020) *Pediatric Exercise Science;* Santiago-Rodriguez et al. (2022) *International Journal of Psychological Studies*

Contextual Effects #1: Project Play

- 10-week intervention, n = 42 children
- Physical activity vs. sedentary attention control



PA ES: *d* = 0.83**;** AC ES: *d* = 0.92; BG: *d* = -0.16

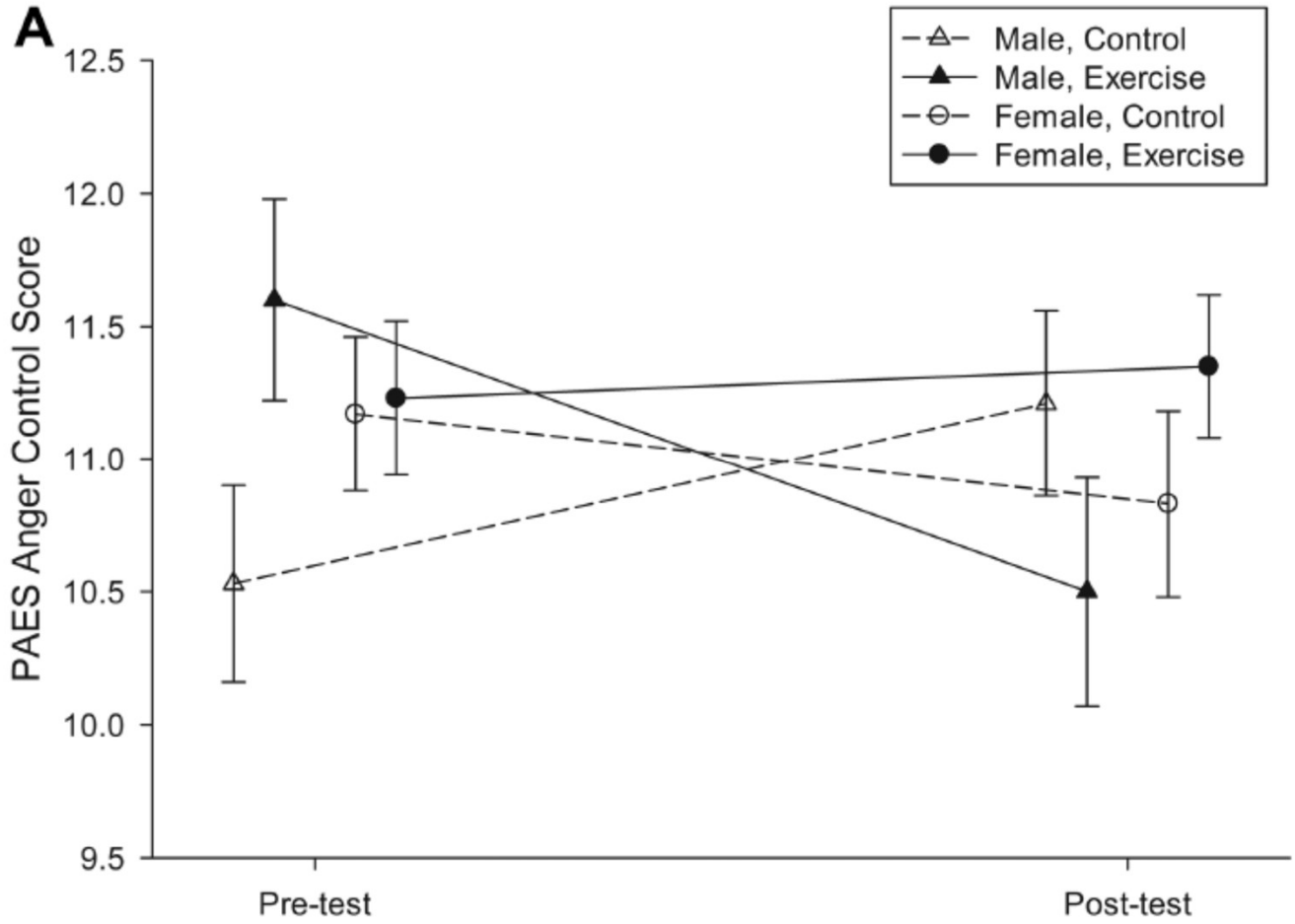


PA ES: *d* = 1.23**;** AC ES: *d* = 0.83; BG: ***d* = 0.48**

Bustamante et al. (2016) *Medicine & Science in Sports & Exercise*

Contextual Effects #2: The SMART Trial

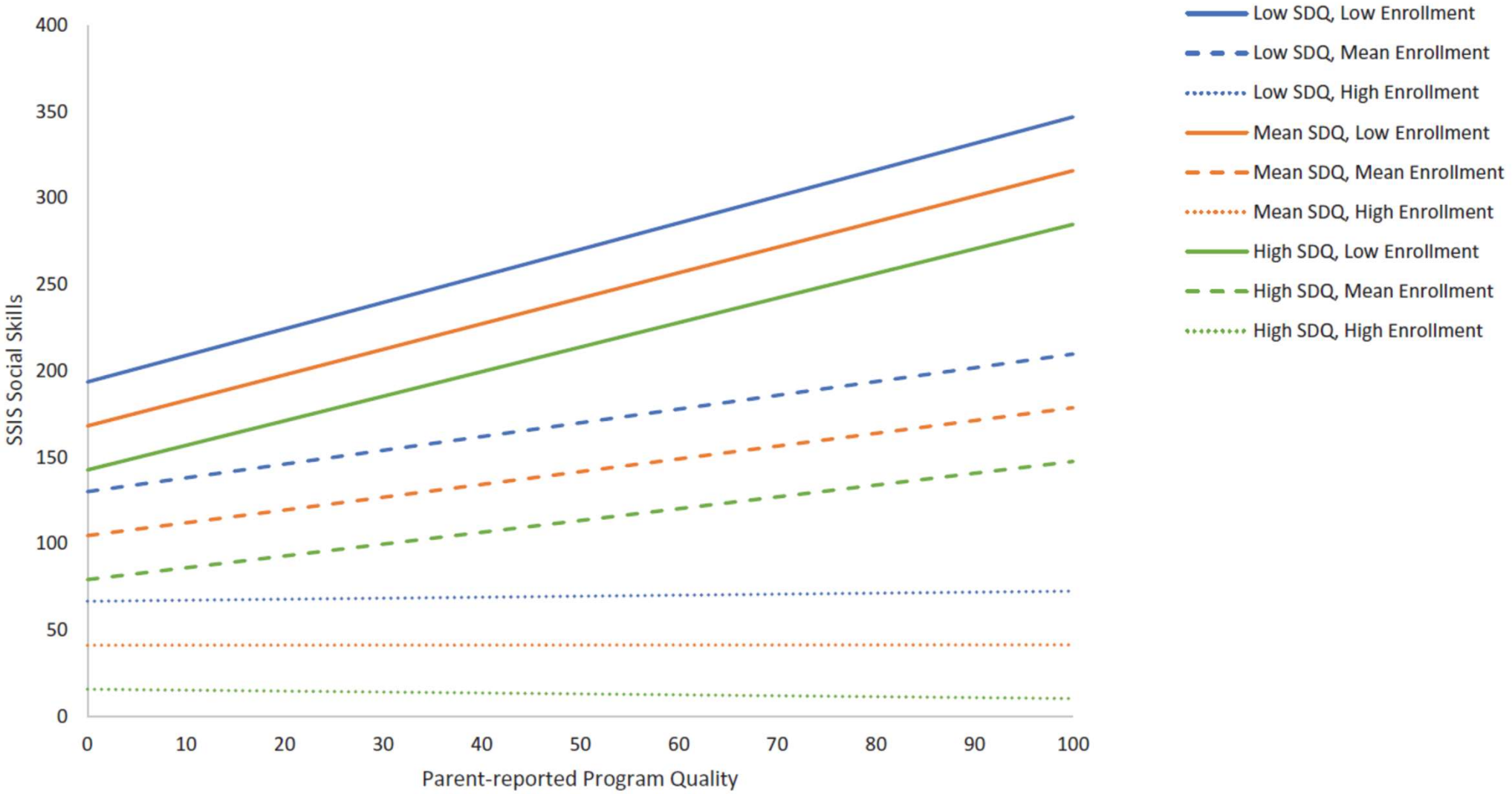
- **9-month intervention, n = 175 Overweight Children**
- **Physical activity vs. attention control**



Williams et al. (2018) *Translational Behavioral Medicine*

CONTEXTUAL EFFECTS #3: PROJECT NAFASI

- Cross-sectional study (32 parks, N=141 staff, N=593 children)



Frazier et al. (2020) *Journal of Clinical Child & Adolescent Psychology*

Contextual Effects #4: PA & ADHD Meta-Analysis

- 14 RCT and 2 QED Studies (N=815)
- 9 studies (N = 397) utilized passive comparisons
- 8 studies (N = 476) utilized active comparison groups

Physical Activity

Yoga
Walking
Running
Jog
Obstacle Course
Exergame
Cybercycling
Aerobic Games
Sports Therapy
Equestrian Therapy
Sports
Table Tennis

Comparison Groups

Mastery / Basketball Shooting
Standard Physical Education
Arts & Crafts / Board Games
Education for Behavior Control
Neurofeedback
~~**Methylphenidate**~~
Parent Education & Support

Bustamante et al. (2022) *Psychology of Sport & Exercise*

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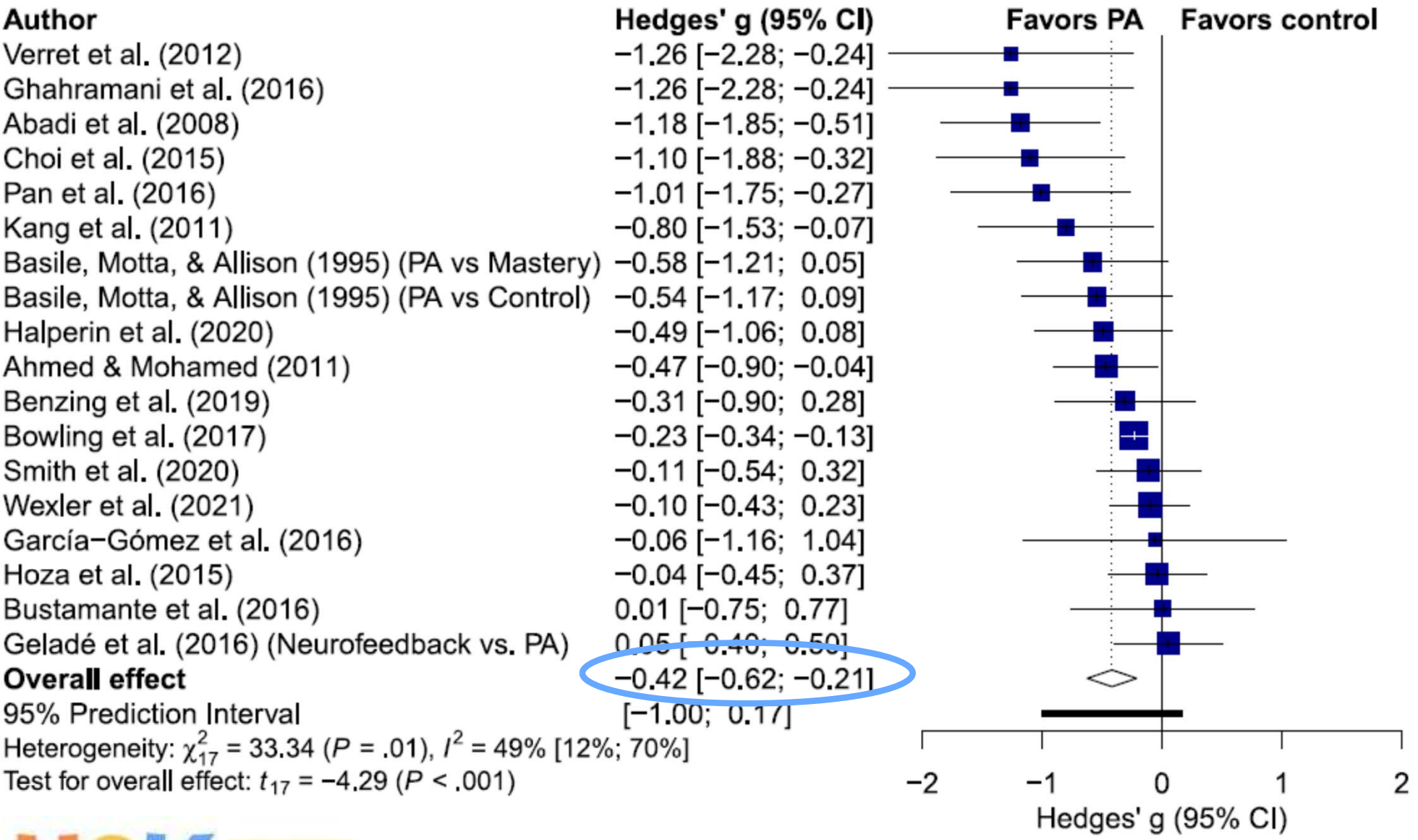
Contextual Effects #4: PA & ADHD Meta-Analysis



Heterogeneity: $\chi^2_{17} = 33.34$ ($P = .01$), $I^2 = 49\%$ [12%; 70%]

Test for overall effect: $t_{17} = -4.29$ ($P < .001$)

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Bustamante et al. (2022) *Psychology of Sport & Exercise*

Contextual Effects #4: Systematic PA & ADHD Meta-Analysis

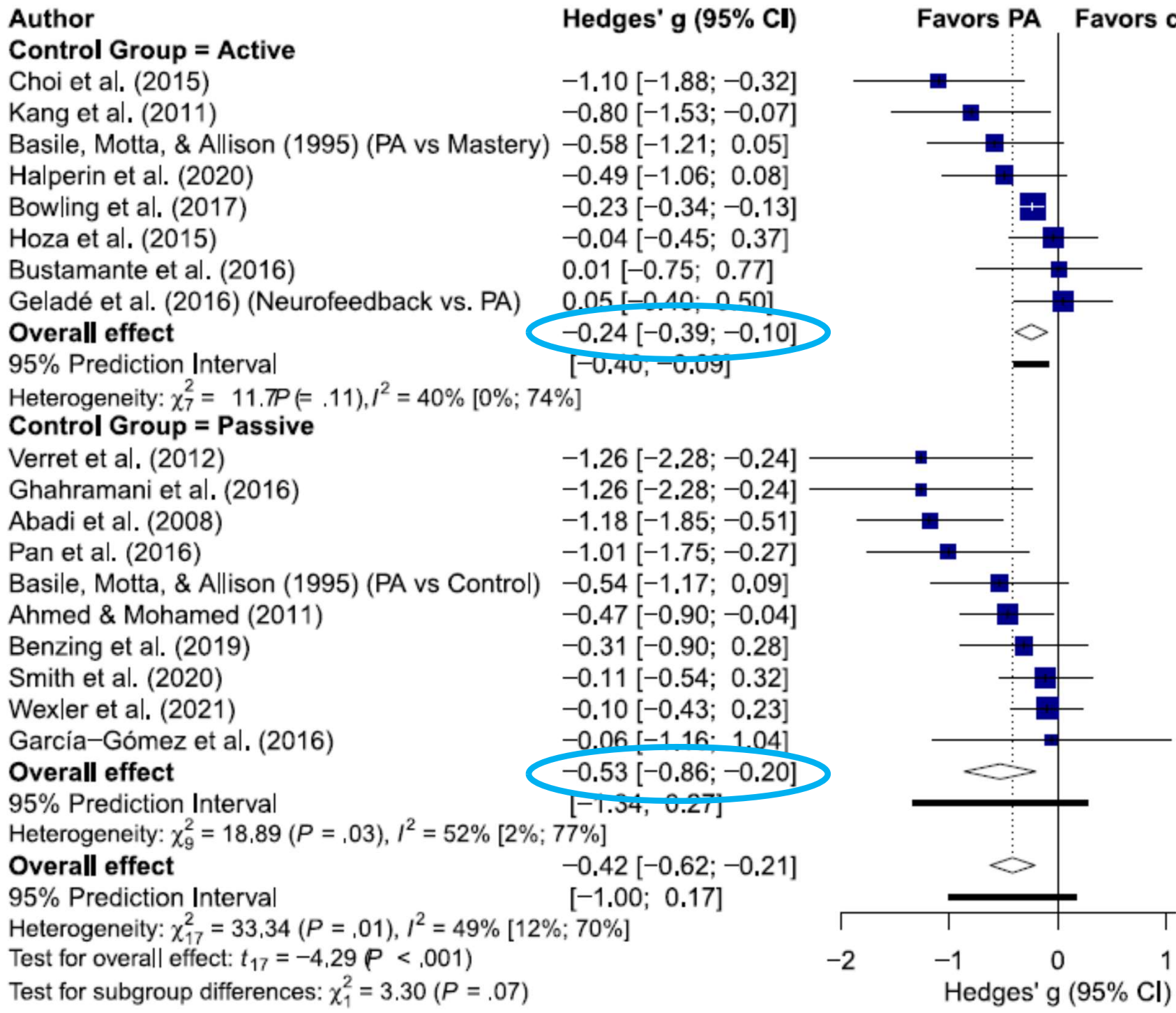
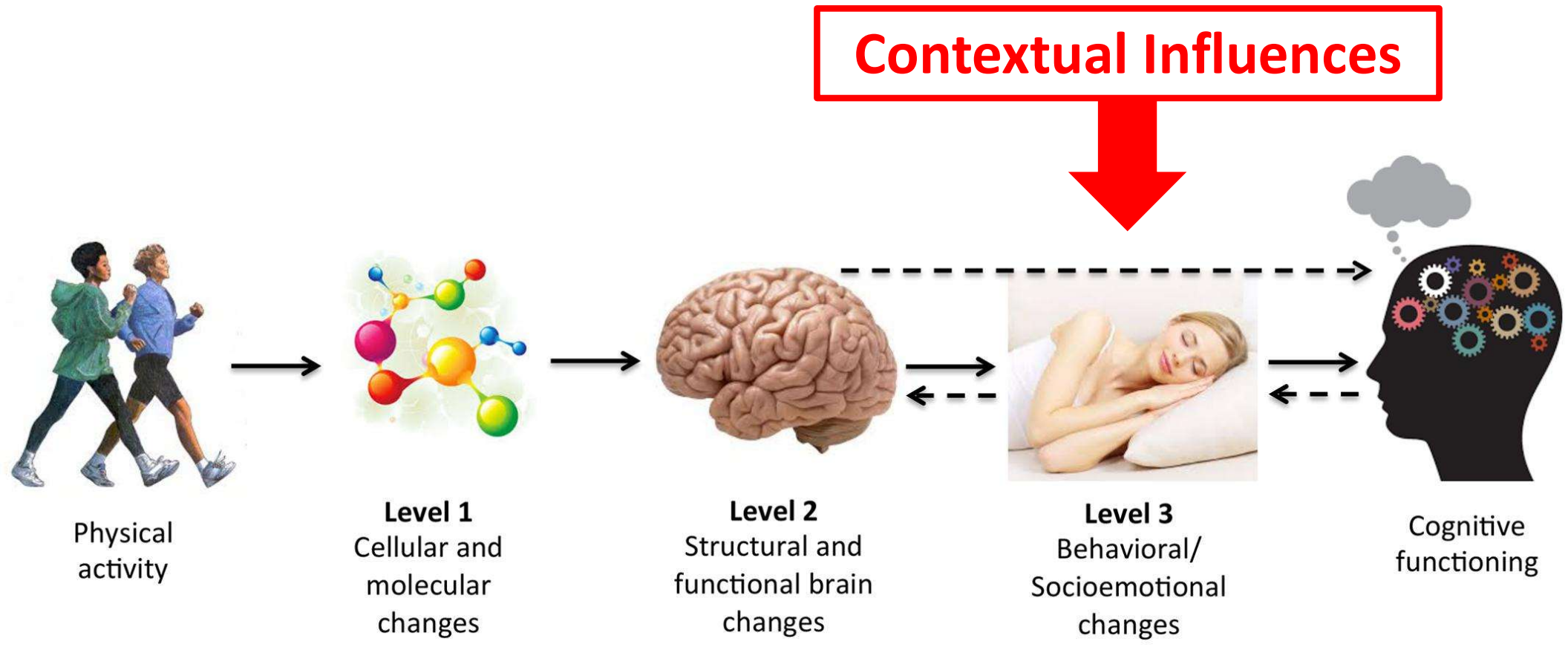


Figure 6. Subgroup analysis by comparison group category (active vs. passive) on omnibus ADHD

Intrinsic Effects on Neurocognitive & Mental Health: Multiple Level Mediators



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Stillman et al. (2016) *Frontiers in Human Neuroscience*

II. Embracing Context to Promote Mental Health

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Harnessing Context for Early Job Skills: Leaders @ Play

Leaders @ Play is designed to intentionally and systematically harness opportunities inherent within sports and recreation to instill early job skills among at-risk youth (i.e., communication, problem solving, emotion reg.)

Teaching Early Job Skills through Physical Activity

Skill	Description	Sample Activity
EMOTION REGULATION	Affect identification; relationship between feelings and physiology; relaxation; cognitive restructuring	**Bad Ref**: Make strategic calls to generate pressure and frustration
EFFECTIVE COMMUNICATION	Introduction to verbal and non-verbal communication; strategies for avoiding misunderstandings	**Rule Change Sports**: Teams must effectively communicate in order to overcome shifting rules.
PROBLEM SOLVING	Define the problem; generate potential solutions; evaluate the feasibility and likely outcome for each alternative; select, implement, and evaluate success	**Amazing Race**: Adolescents are in teams and must coordinate to complete specific fitness task faster than others

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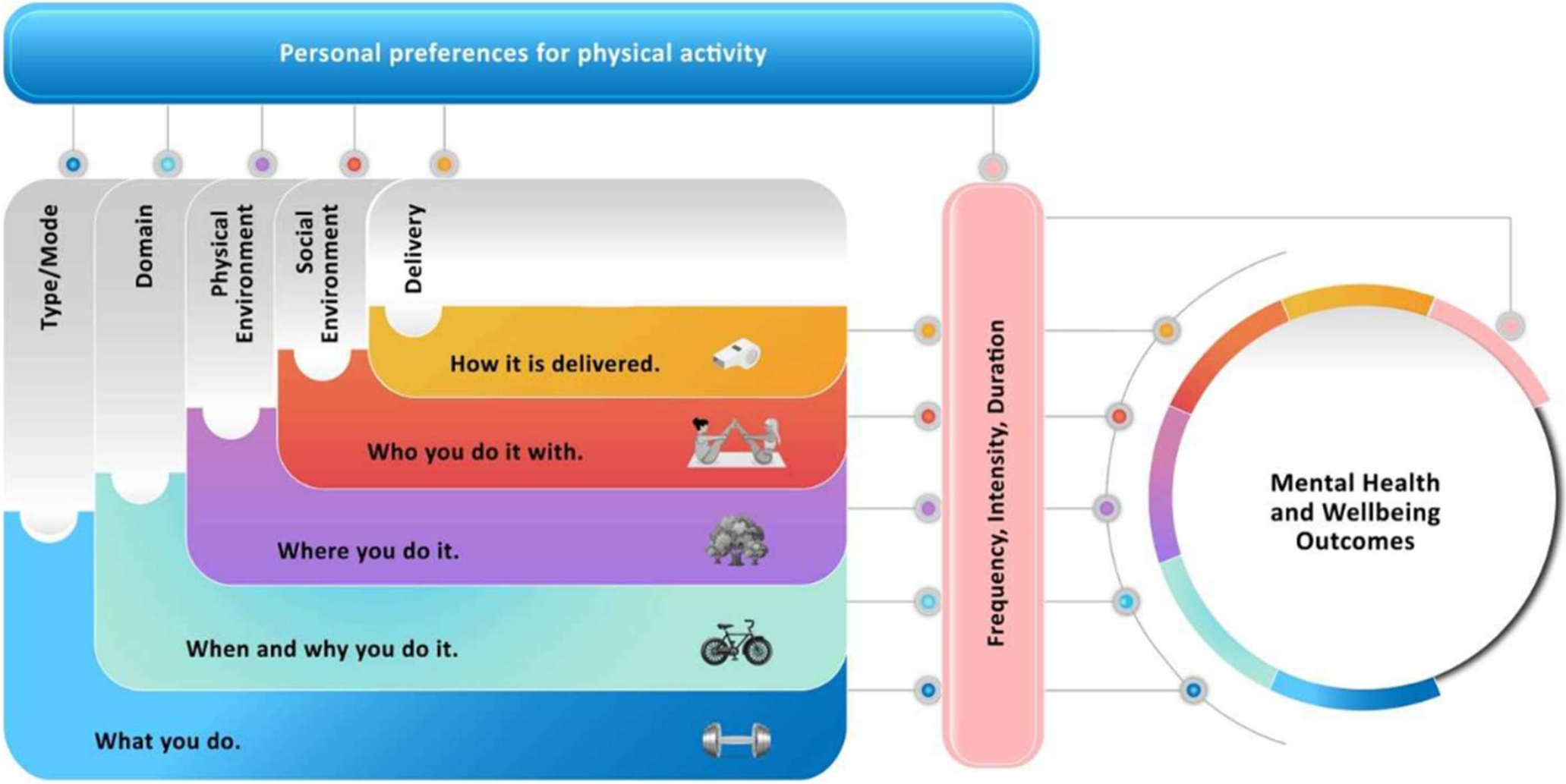
Frazier et al. (2015); Bustamante et al. (2018, 2019)

Be Unstoppable In Life Together (BUILT)
Family Lifestyle Program

- **<u>Physical activity, nutrition, and sleep combine to provide a structured home routine for children.</u>**
- 6-week family lifestyle program co-facilitated by UIC students and CPD staff
- Pilot utilized single-group pre-post design with N=44 children and N=30 parents
- Sumer camp iteration enrolled N=281 children
- Health behaviors, cognition, home environment, and mental health pre-post

BUILT
Scan
Me

A Model of PA Context & Mental Health



Vella et al. (2023) *Mental Health and Physical Activity*

How We Have Been Asking Research Questions for 40 Years

Does physical activity of type A, in dose B, improve mental health of form C, in population D, compared with intervention E?

How We Need To Ask Research Questions Moving Forwards

Does physical activity of type A, in dose B, in physical environment C, social context D, and delivery modality E, improve mental health of form F, in population G, compared with intervention H?

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  - Urban Initiatives
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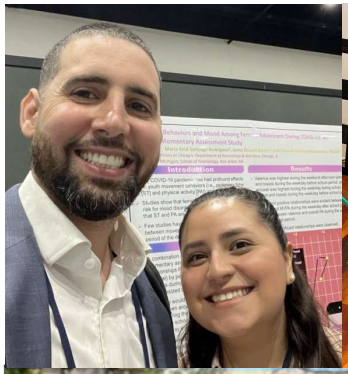

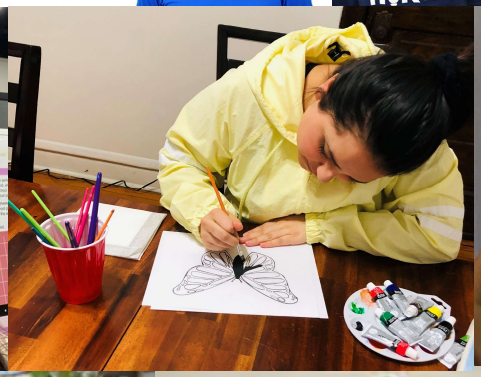

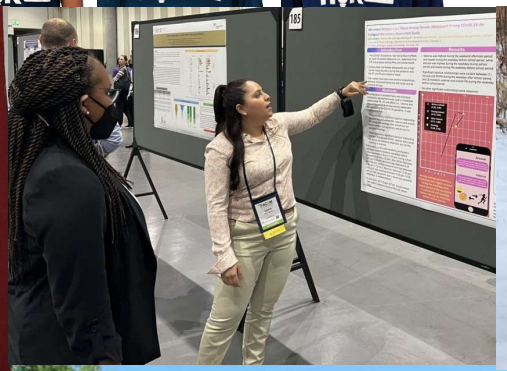

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