Incident dementia in non-Hispanic African Americans and Whites: Considering Effects of Enrollment factors

JUNE 22, 2023

RISK AND RESILIENCE TO ALZHEIMER'S DISEASE IN AFRICAN AMERICANS
RUTGERS UNIVERSITY

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Thank you to participants

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  (Gleason, Jacklin, Parker)

Learning Objectives

Review	Review core features of engagement efforts
Consider	How enrollment factors influence findings
Discuss	Discuss limitations of racial comparisons, especially those using data from the Alzheimer's disease Centers

Topics Covered

Among the avenues to address disparities - Inclusive research

Downside to community-based research – biased samples?

Concluding thoughts

Abbreviations:
AD: Alzheimer's Disease
ADRD: Alzheimer's disease and Related Dementias

Topics Covered

Among the avenues to address disparities - Inclusive research

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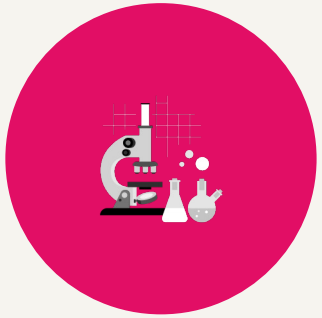
Models of Community Engaged Research

- **Green-Harris G**, Coley SL, Koscik RL, et al. Addressing Disparities in Alzheimer's Disease and African-American Participation in Research: An Asset-Based Community Development Approach. *Front Aging Neurosci*. 2019;11:125. doi:10.3389/fnagi.2019.00125
- **Gilmore-Bykovskyi A**, Croff R, Glover CM, et al. Traversing the Aging Research and Health Equity Divide: Toward Intersectional Frameworks of Research Justice and Participation. *Gerontologist*. Jul 29 2021;doi:10.1093/geront/gnab107
- **Glover CM**, Creel-Bulos C, Patel LM, et al. Facilitators of research registry enrollment and potential variation by race and gender. *J Clin Transl Sci*. Aug 2018;2(4):234-238. doi:10.1017/cts.2018.326
- **Denny A**, Streitz M, Stock K, et al. Perspective on the "African American participation in Alzheimer disease research: Effective strategies" workshop, 2018. *Alzheimers Dement*. Dec 2020;16(12):1734-1744. doi:10.1002/alz.12160

Acknowledge
more than mistrust and access

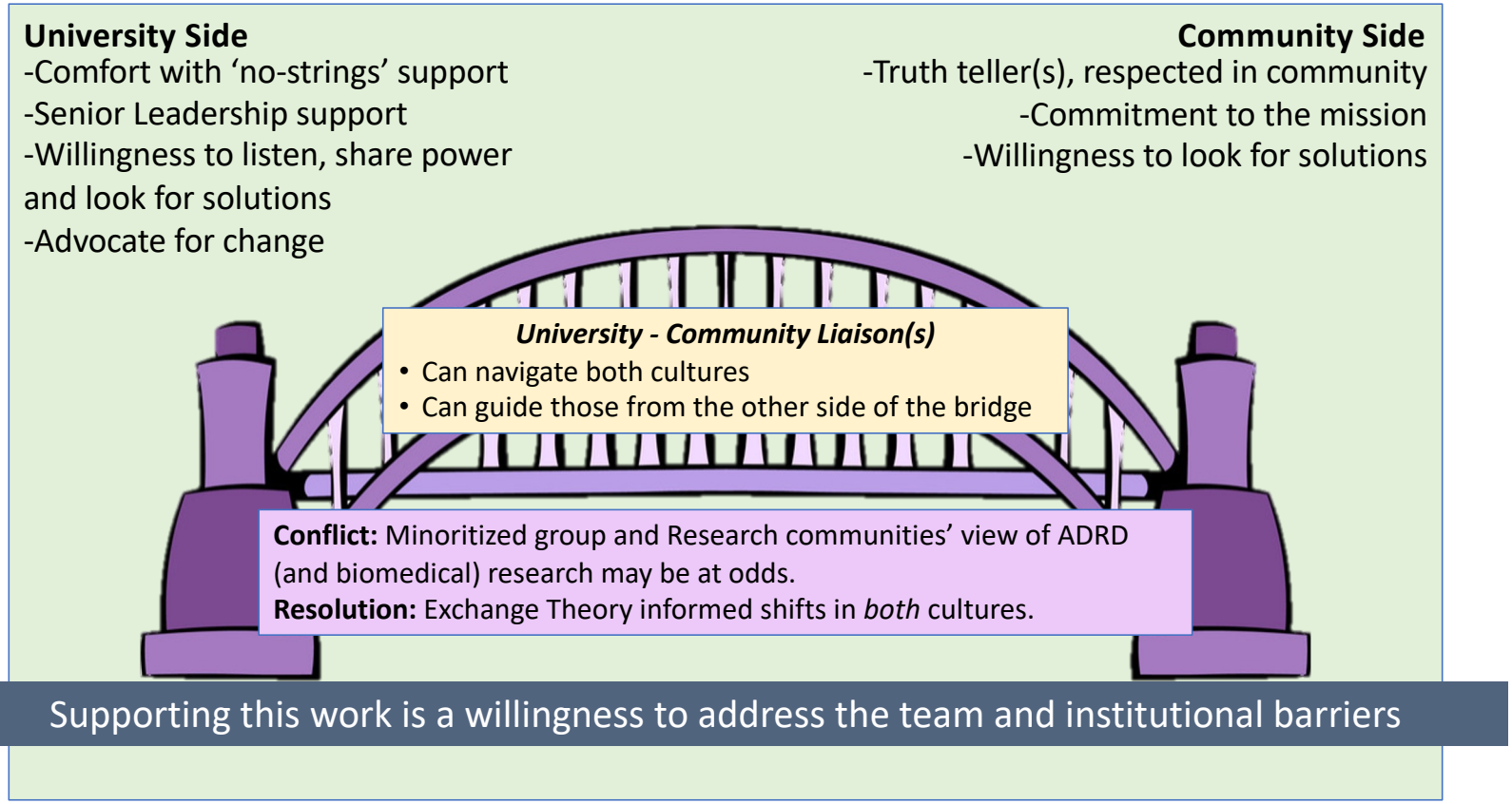
Acknowledge
Research culture



RECOGNIZE BARRIERS
CREATED BY THAT CULTURE

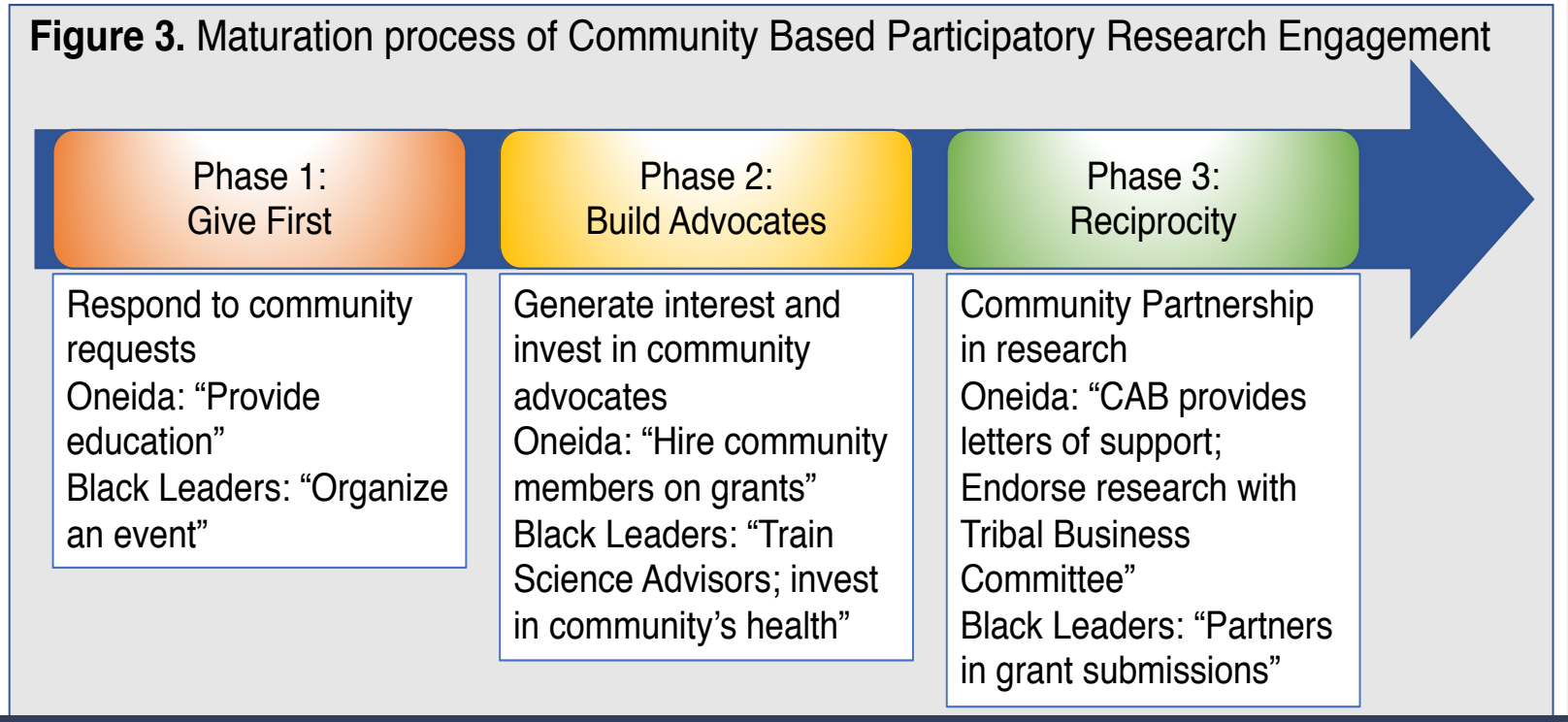
AND OUR POWER TO BE
PART OF THE SOLUTION

Intercultural Bridge Conceptual Model



Model adapted from Community Based Participatory Research framework: Wallerstein and Duran, AJPH (2011); Israel et al. ARPH (1998)

Timeline
Inclusion of Under-Represented Groups Core



Supporting this work is a willingness to address the team and institutional barriers

Re-Centering the "problem"

Re-defining "Recruitment"

- Successful recruitment starts with engagement
- Engagement should build relationships
- Relationships require investment and time

Research world/academia has a culture

- Acknowledge our cultural values and hegemony
- Encourage an inter-cultural approach

Personal Experiences with Tribal IRBs, Hidden Hegemony of Researchers, and the Need for an Inter-cultural Approach: Views from an American Indian Researcher

J. Neil Henderson

Introduction

Conducting research among American Indian tribes has not always involved IRB review. During much of the 20th century, most research projects started and ended at the will of investigators. By the 1970s, tribal councils were the primary gatekeepers for research requests. Beginning around 2000, many tribes added IRB expertise based on the *Belmont Report* by attending training sessions providing concepts and strategies for operating IRBs, in part in order to protect themselves as members of sovereign nations.

Cultural contradictions, however, may be seen when the *Belmont Report* is understood as a culture-specific document. American Indian tribes have cultural systems that can be very unlike the contemporary American majority population. Consequently, the basic tenets of the *Belmont Report* may not be universally applicable to American Indian life ways. For example, John Traphagan unmasks the American-specific cultural context of the *Belmont Report* by comparing American bioethics to that of Japan and finding significant differences, particularly related to the concept of autonomy, a value firmly embedded in the *Belmont Report*.[1] Autonomy is a very strong, foundational American value not shared as fully by all other societies. Simply put, "Bioethics — American style — are just that, American-style bioethics."[2] Still, Belmont remains the standard across American Indian tribes for IRB protocols.

I have conducted more than 30 years of research with American Indian populations on health, disease, and treatment. Over this time, I have observed numerous changes with regard to the ways in which to collaborate appropriately with tribal members. This paper is less a treatise on tribal IRBs and more a set

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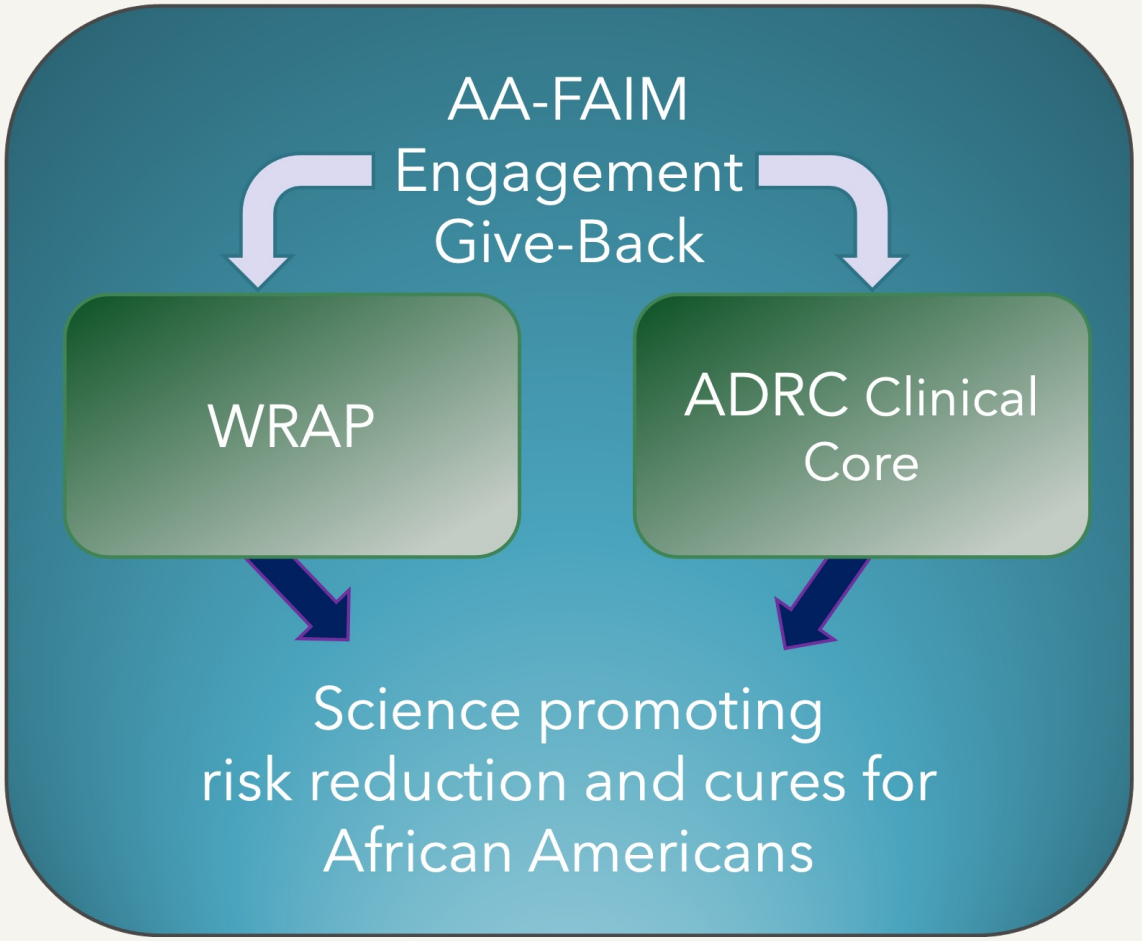
African Americans Fighting Alzheimer's in Midlife

Funded by NIH 2016 to 2022
Renewed through 2027



Engaged Research: Make Broad investments

- Prepared to answer the question, "How does this benefit the community?"

  Offer Brain Health programing
- Look at hiring practices, investments in Black/Indigenous business, and trainees.
- Trainees and staff from the communities being studied

What this approach as allowed us to accomplish

Where we started (2017) African American Enrollment:

AA – ADRC Clinical Core	Madison WRAP	Milwaukee WRAP
~110	~2	~125

Where we are now (June 2023):

Baseline cognitive assessments	**465**
MRI Scan	181
Amyloid PET	70
Tau PET	65
CSF collection	84

Most were recruited in Madison, WI 5.4% of Dane Co identifies as Black or AA

What this approach as allowed us to accomplish

Where we are now (June 2023) American Indian/Alaska Native Enrollment Between WRAP and ADRC:

Baseline cognitive assessments	**93**
MRI Scan	62
Amyloid PET	18
Tau PET	18
CSF collection	35

African Americans Fighting Alzheimer's in Midlife

3 Aims:

1) Test the amyloid hypothesis

2) Examine alignment of plasma & PET measurements of abeta

3) Science of recruitment Aim

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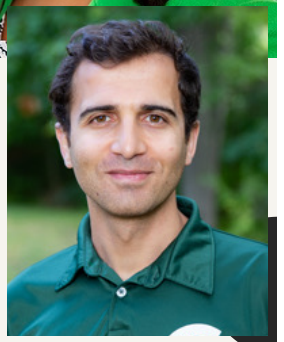


Emre Umucu

Topics Covered

Among the avenues to address disparities - Inclusive research

Downside to community-based research – biased samples?

Concluding thoughts

Abbreviations:
AD: Alzheimer's Disease
ADRD: Alzheimer's disease and Related Dementias

Began to wonder

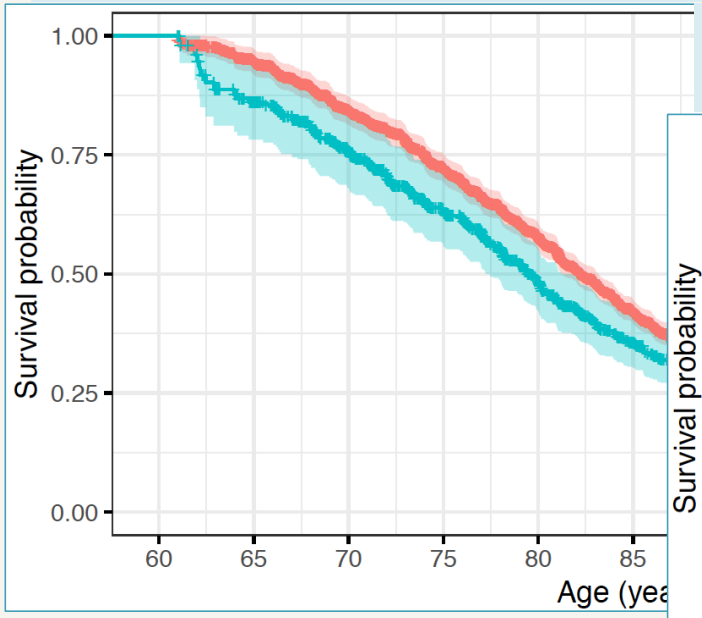
- Used NACC dataset, comparing non-Hispanic Whites and Blacks
- Looked at incident cognitive impairment
- Separate analyses based on baseline cognitive status

    Cognitively healthy at baseline

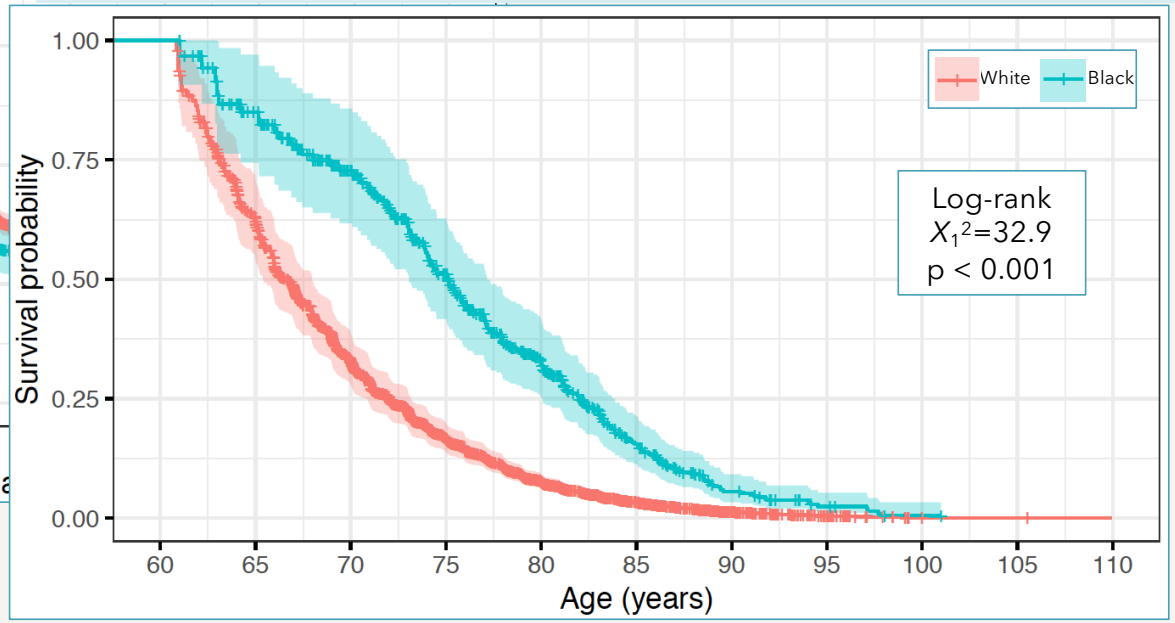
    Mild cognitive impairment

Surprised by findings

Kaplan-Meier Curves for non-Hispanic Whites and Blacks cognitively unimpaired at Baseline



Kaplan-Meier Curves for non-Hispanic Whites and Blacks diagnosed with MCI at Baseline



	Cognitively Normal at Baseline			MCI at Baseline		
	White	Black	p	White	Black	p
N	6894	1288		3444	616	
Converted, N(%)	1559 (22.6)	267 (20.7)	0.146	1598 (46.4)	189 (30.7)	<0.001
Entry age in yrs, mean(SD)	74.33 (8.16)	72.66 (7.08)	<0.001	75.27 (7.75)	73.58 (7.59)	<0.001
Female Sex, N(%)	4272 (62.0)	1014 (78.7)	<0.001	1526 (44.3)	423 (68.7)	<0.001
Died, N(%)	971 (14.1)	120 (9.3)	<0.001	775(22.5)	67 (10.9)	<0.001
Diabetes						
Absent, N(%)	6307 (91.5)	956 (74.2)		3066 (89.0)	420 (68.2)	
Recent/active, N(%)	548 (7.9)	316 (24.5)	<0.001	346 (10.0)	184 (29.9)	<0.001
Remote/inactive, N(%)	27 (0.4)	6 (0.5)		23 (0.7)	8 (1.3)	
unknown, (N%)	12 (0.2)	10 (0.8)		9 (0.3)	4 (0.6)	
Hypertension						
Absent, N(%)	3623 (52.6)	316 (24.5)		1672 (48.5)	132 (21.4)	
Recent/active, N(%)	3080 (44.7)	941 (73.1)	<0.001	1658 (48.1)	460 (74.7)	<0.001
Remote/inactive, N(%)	171 (2.5)	29 (2.3)		104 (3.0)	22 (3.6)	
Unknown, (N%)	20 (0.3)	2 (0.2)		10 (0.3)	2 (0.3)	
Cardiac event/Condition*						
Absent, N(%)	5997 (87.0)	1143 (88.7)		2887 (83.8)	541 (87.8)	
Recent/active, N(%)	514 (7.5)	66 (5.1)	0.009	295 (8.6)	34 (5.5)	0.022
Unknown, (N%)	383 (5.6)	79 (6.1)		262 (7.6)	41 (6.7)	

Other Explanations?

- Enrollment factors

Referral source

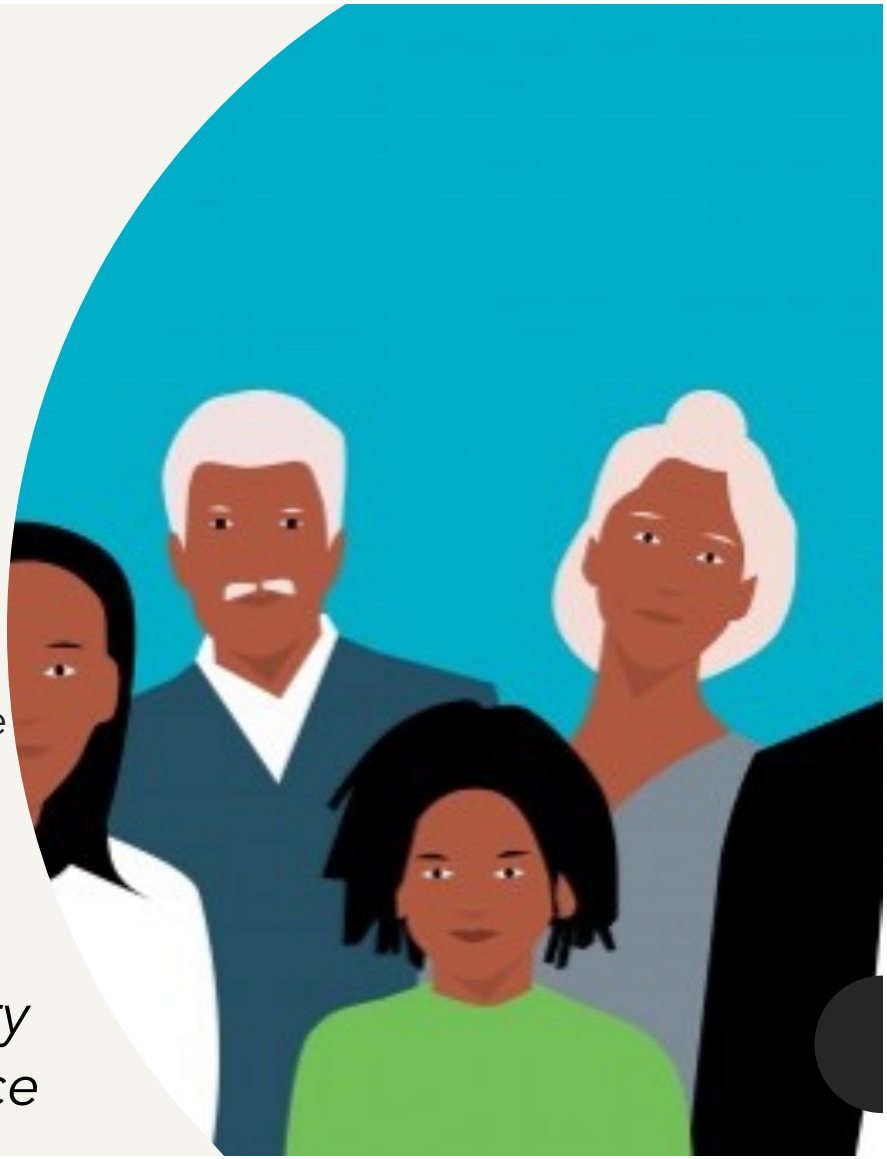
  - Health professional v. self/relative/friend

Family history of dementia

  - No 1st degree relative v. 1+ 1st degree relative

Propose that family history is more than genetic risk…

- *Knowledge of family history*
- *Access to diagnostic service*



Enrollment factors

- Referral source

  Self/relative/friend…

  Community Recruitment

  Health professional…

  Clinic Recruitment

  Other…

  Community Recruitment?

  Unknown…

  ????

- Family history

  No 1st degree relative…

  Why are they joining an ADRD study?

  ≥1 1st degree relative…

  Often recruit adult children during clinic appts

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Female Sex, N(%)	4272 (62.0)	1014 (78.7)	<0.001	1526 (44.3)	423 (68.7)	<0.001
Died, N(%)	971 (14.1)	120 (9.3)	<0.001	775(22.5)	67 (10.9)	<0.001
Referral Source						
Self/relative/friend, N(%)	2786 (40.4)	550 (42.7)		876 (25.4)	146 (23.7)	
Health professional, N(%)	1004 (14.6)	105 (8.2)	<0.001	1494 (43.4)	154 (25.0)	<0.001
Other, N(%)†	2846 (41.3)	593 (46.0)		961 (27.9)	288 (46.8)	
Unknown, N(%)	258 (3.7)	40 (3.1)		113 (3.3)	28 (4.5)	
Family History of dementia						
No 1st degree relative, N(%)	2548 (37.0)	544 (42.2)		1168 (33.9)	262 (42.5)	
≥ One 1st degree relative, N(%)	3773 (54.7)	569 (44.2)	<0.001	1976 (57.4)	283 (45.9)	<0.001
unknown, (N%)	573 (8.3)	175 (13.6)		300 (8.7)	71 (11.5)	

NESTED Regression Analyses

Separate models based on baseline cognitive status: Cognitively healthy and MCI

Predicting adjusted age to progression (either MCI/dementia or dementia)

MODEL 1 – Base model included: sex, education, race, diabetes, HTN, cardiac events, and for MCI group, etiology of syndrome

MODEL 2 included: Referral source and known family history

Individuals who are cognitively healthy at baseline

Coefficient	Model 1 HR	Model 1 HR 95% CI	Model 1 p value	Model 2 HR	Model 2 HR 95% CI	Model 2 p value
African American (reference: White)	0.99	0.86 — 1.14	0.8963	1.05	0.91 — 1.21	0.4864
Female (reference: Male)	**0.79**	**0.72 — 0.87**	**<0.0001**	**0.79**	**0.72 — 0.87**	**<0.0001**
Referral: (reference: referred by self/relative/friend)						
health professional				**1.39**	**1.21 — 1.60**	**<0.0001**
other				**1.20**	**1.08 — 1.33**	**0.0005**
unknown				**1.29**	**1.03 — 1.62**	**0.0282**
Family History of Dementia: (reference: no family hx)						
≥1 1st degree relative				**1.22**	**1.11 — 1.35**	**0.0001**
unknown				0.87	0.73 — 1.04	0.1239

Individuals who are cognitively healthy at baseline

health professional	**1.39**	**1.21 — 1.60**	**<0.0001**
other†	**1.20**	**1.08 — 1.33**	**0.0005**
unknown	**1.29**	**1.03 — 1.62**	**0.0282**
Family History of Dementia: (reference: no family history)			
≥1 1st degree relative	**1.22**	**1.11 — 1.35**	**0.0001**
unknown	0.87	0.73 — 1.04	0.1239

Highlights – Cognitively healthy

- Post-graduate education and female sex: 17-21% reduced hazard
- Diabetes was associated with 21% increased hazard over no diabetes
- Compared to those referred by family/friend,
  - Being referred by a health professional 39% increased hazard
- Compared to those reporting a family history of AD,
  - Known family history: 22% increased hazard

Individuals with mild cognitive impairment (MCI) at baseline

	Model 1			Model 2		
Coefficient	HR	HR 95% CI	p value	HR	HR 95% CI	p value
African American (reference: White)	**0.66**	**0.56 — 0.77**	**<0.0001**	**0.71**	**0.61 — 0.84**	**<0.0001**
Female (reference: Male)	1.01	0.91 — 1.11	0.8642	1.03	0.94 — 1.14	0.5172
Referral: (reference: referred by self/relative/friend)						
health professional				**1.46**	**1.29 — 1.64**	**<0.0001**
other†				0.88	0.77 — 1.00	0.0574
unknown				0.80	0.61 — 1.06	0.1225
Family History of Dementia: (reference: no family history)						
≥1 1st degree relative				**1.12**	**1.01 — 1.25**	**0.0256**
unknown				1.00	0.83 — 1.21	0.9727

Individuals with MCI at baseline

Vascular disease	0.60	0.46 — 0.79	0.0003	0.63	0.48 — 0.83	9.00E-04
missing/unknown	0.59	0.54 — 0.66	<0.0001	0.63	0.57 — 0.70	<0.0001
Referral: (reference: referred by self/relative/friend)						
health professional				**1.46**	**1.29 — 1.64**	**<0.0001**
other†				0.88	0.77 — 1.00	0.0574
unknown				0.80	0.61 — 1.06	0.1225
Family History of Dementia: (reference: no family history)						
≥1 1st degree relative				**1.12**	**1.01 — 1.25**	**0.0256**
unknown				1.00	0.83 — 1.21	0.9727

Highlights – MCI at baseline

Post-high school education and non-AD cause of MCI: 15-40% reduced hazard

Blacks demonstrated 34% lower hazard of age-adjusted progression compared to whites

Compared to those referred by family/friend,

Being referred by a health professional 46% increased hazard

Compared to those reporting a family history of AD,

Known family history: 12% increased hazard

Adding enrollment factors into model did not eliminate advantage for Blacks - but did attenuate (34% to 29% lower HR)

At the core

- ***"[When participants do not reflect the population at large]…such selection bias cannot be "adjusted for" and the remaining statistically significant results are spurious and likely due specifically or mostly to the character of the bias itself."***

Professor, Epidemiology
University of Washington
Director, NACC


Are those of us doing community engaged research part of the problem?

Outreach to Indigenous Participants

Started in 2015:

Oneida Nation Commission on Aging (ONCOA)

- *ONCOA: Asked for more information about Alzheimer's Disease in Indian Country*
- *Wisconsin ADRC: We don't know, because we have not conducted inclusive research*

2015-2017

- *Education events*
- *Memory Screenings*
- *Respond to requests from ONCOA*

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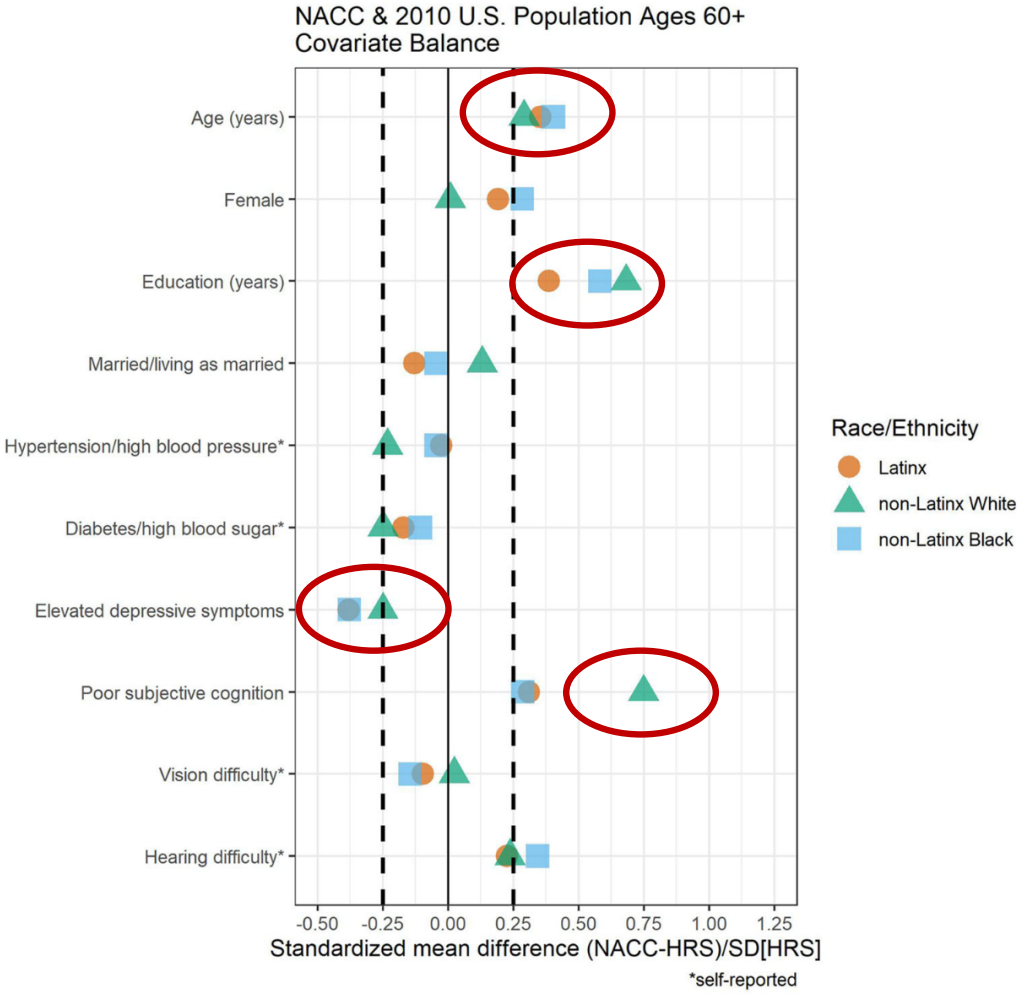
Alzheimer's & Dementia
Diagnosis, Assessment & Disease Monitoring

RESEARCH ARTICLE

Representativeness of samples enrolled in Alzheimer's disease research centers

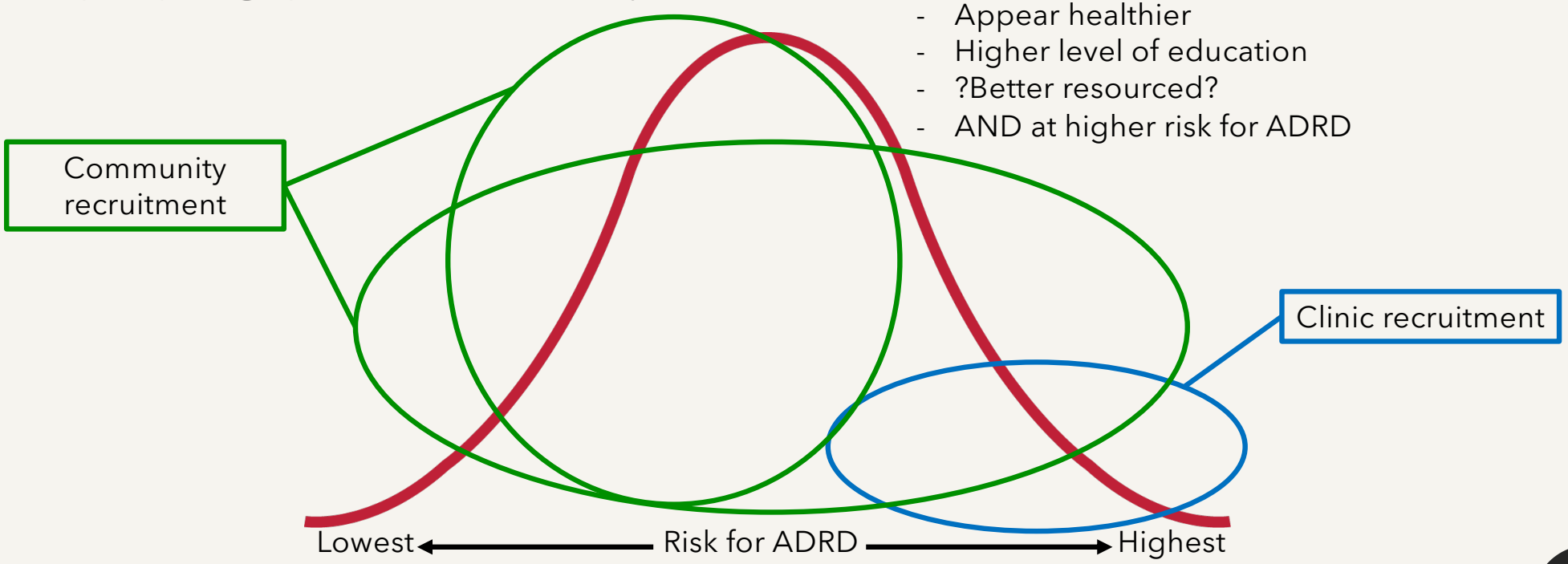
Miguel Arce Rentería[1] | Taylor M. Mobley[2] | Nicole D. Evangelista[3] | Luis D. Medina[4] | Kacie D. Deters[5] | Joshua T. Fox-Fuller[6] | Lex R. Minto[7] | Justina Avila-Rieger[1] | Brianne M. Bettcher[8]


NACC & 2010 U.S. Population Ages 60+
Covariate Balance
Age (years)
Female
Education (years)
Married/living as married
Hypertension/high blood pressure*
Diabetes/high blood sugar*
Elevated depressive symptoms
Poor subjective cognition
Vision difficulty*
Hearing difficulty*
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
1.25
Standardized mean difference (NACC-HRS)/SD[HRS]
*self-reported
Race/Ethnicity
Latinx
non-Latinx White
non-Latinx Black

Why does recruitment from clinic increase hazard?

Non-Hispanic white population in NACC/ADC samples, compared to general population:

- Appear healthier
- Higher level of education
- ?Better resourced?
- AND at higher risk for ADRD



Topics Covered

Among the avenues to address disparities - Inclusive research

Downside to community-based research – biased samples?

Concluding thoughts

Abbreviations:
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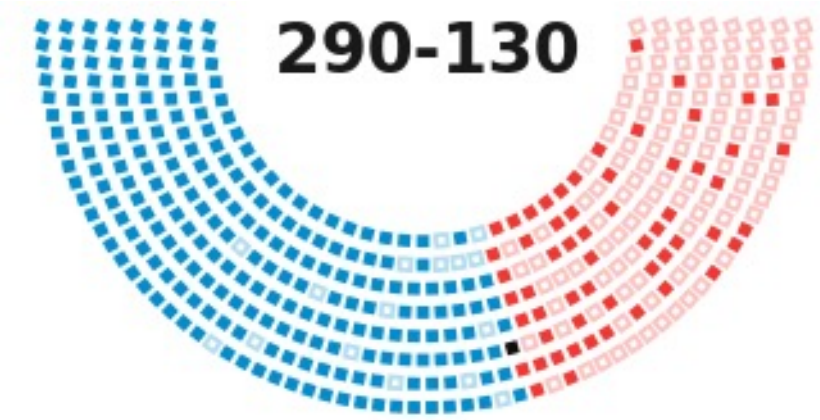
Address access to research

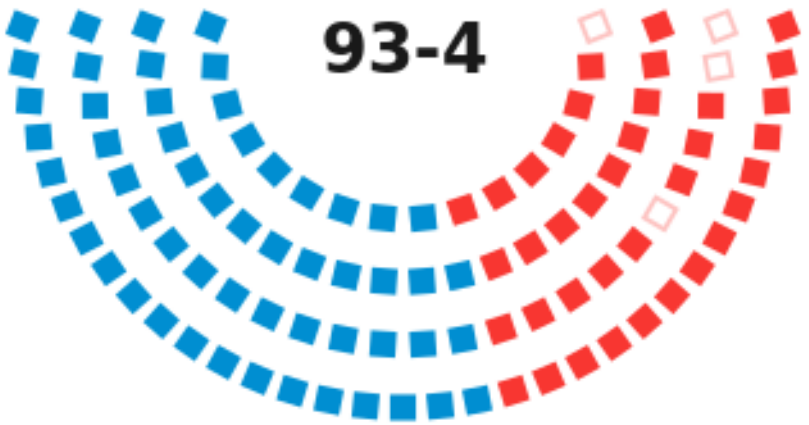
- Difficult diagnosis
- Intensive phenotyping procedures

Response - Equitable inclusion

1) Community based recruitment for all groups
2) Increase access to diagnostic clinics



House Vote



Senate Vote

Call to action

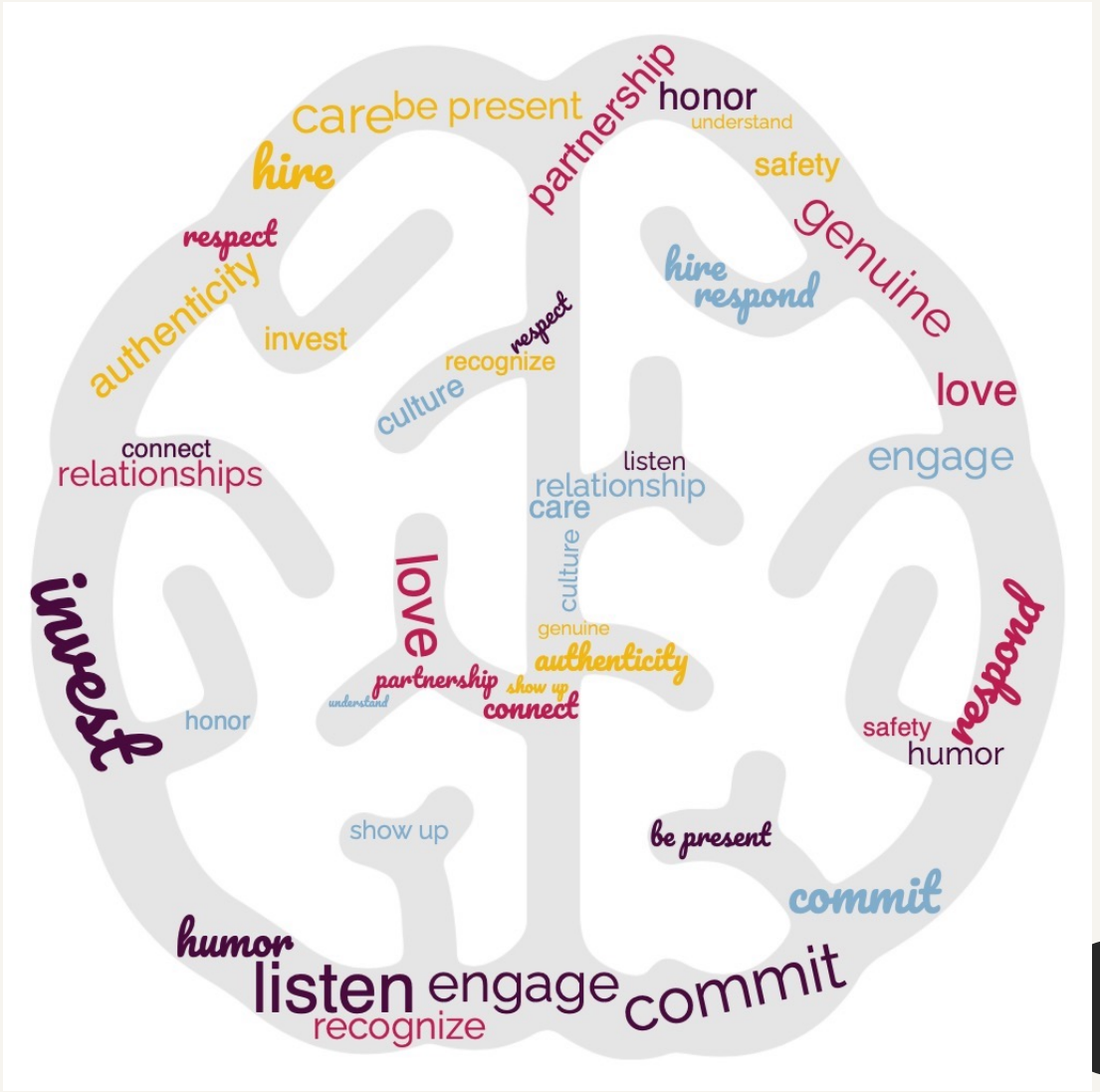
1993 NIH Revitalization Act

- Federal legislative mandate that NIH-funded research would allow for "valid analysis of whether the variables being studied in the trial affect…members of minority groups."
- NIH established policies
  - Women and minoritized individuals must be included in all NIH-funded clinical research
  - Must address the inclusion of groups in proposal

Summary - acknowledge our culture and its hidden hegemony

Re-defining “Recruitment”

- Successful recruitment starts with engagement
- Engagement should build relationships
- Relationships require investment and time



Conclusions

Must be able to trust that finding apply

Improving applicability depends on improving inclusion

Engage with groups outside the academic clinic

More work to be done to move the needle

Leadership - Faculty and Staff

Carey Gleason, PhD, MS
Inclusion of Under-Represented Groups
Core Leader

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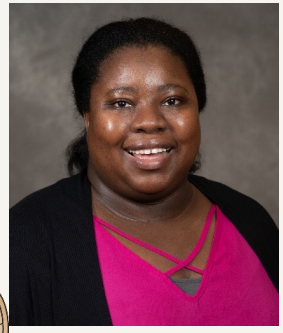

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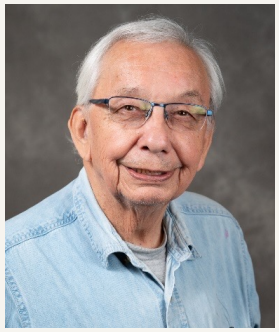

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Research Specialist

Margaret King
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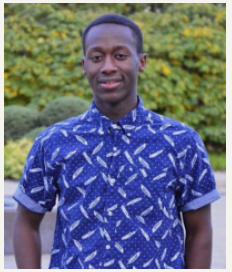

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Thank you for your time and attention
Thanks to the Outreach & Recruitment team
Thanks to our participants
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