NACC Enrollment Factors and Incident Cognitive Impairment in non-Hispanic Black and White Participants

2023 Fall ADRC Meeting

Data Core Workshop

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A review of results, findings, and recommendations from…

"Association between enrollment factors and incident cognitive impairment in Blacks and Whites: Data from the Alzheimer's Disease Center"

- Carey E. Gleason, et. al.
- Alzheimers Dement. 2019 December ; 15(12): 1533–1545. doi:10.1016/j.jalz.2019.07.015

No disclosures to share

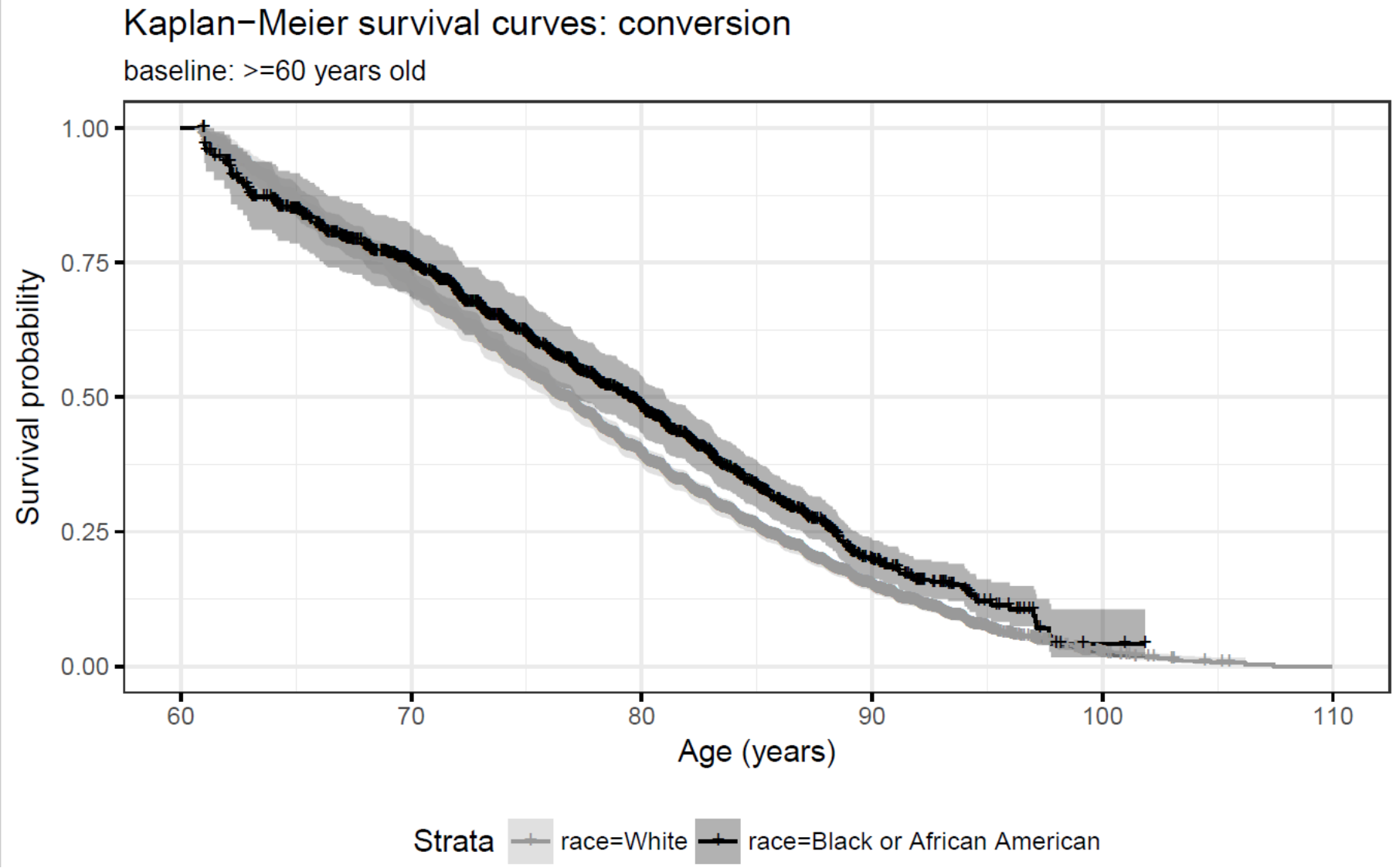
Project Genesis

- In separate research using the NACC data, it was noted that Black participants were associated with better / older age to incident cognitive impairment, compared to White subjects, in time-to-event analyses

- Incident cognitive impairment (i.e., “conversion”) defined as first diagnosis after baseline of a worse cognitive diagnosis (NACCUDSD):
  - Normal at baseline –> MCI or Dementia
  - MCI at baseline –> Dementia

- This contradict numerous prior reports of increased risk for incident cognitive impairment and dementia in Black compared to White participants

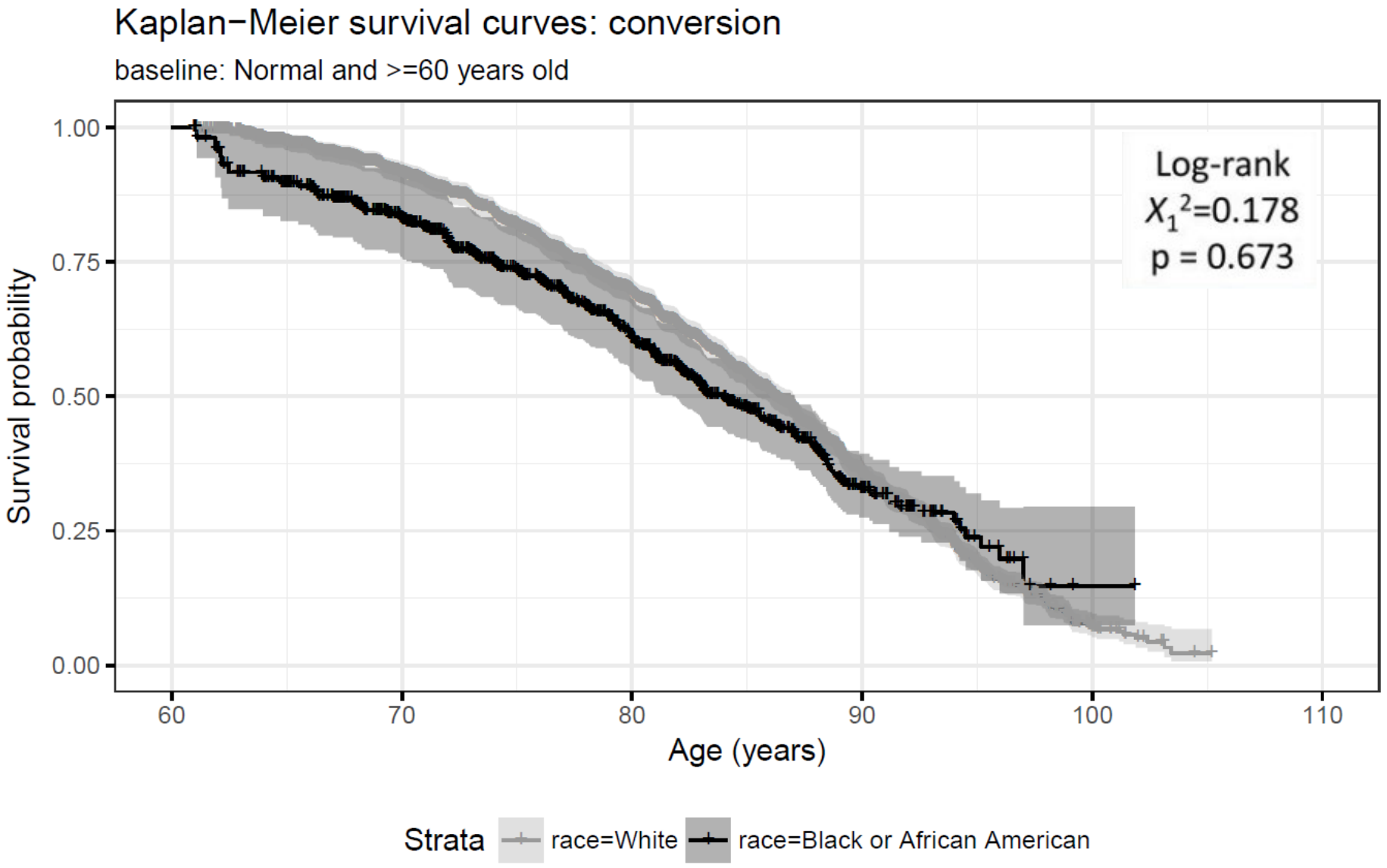
General NACC trend



- Exclusions: Hispanic ethnicity, baseline age <60, genetic mutations associated with dementia, FTD / FTLD MCI etiologies, no follow-up, not Normal or MCI at baseline

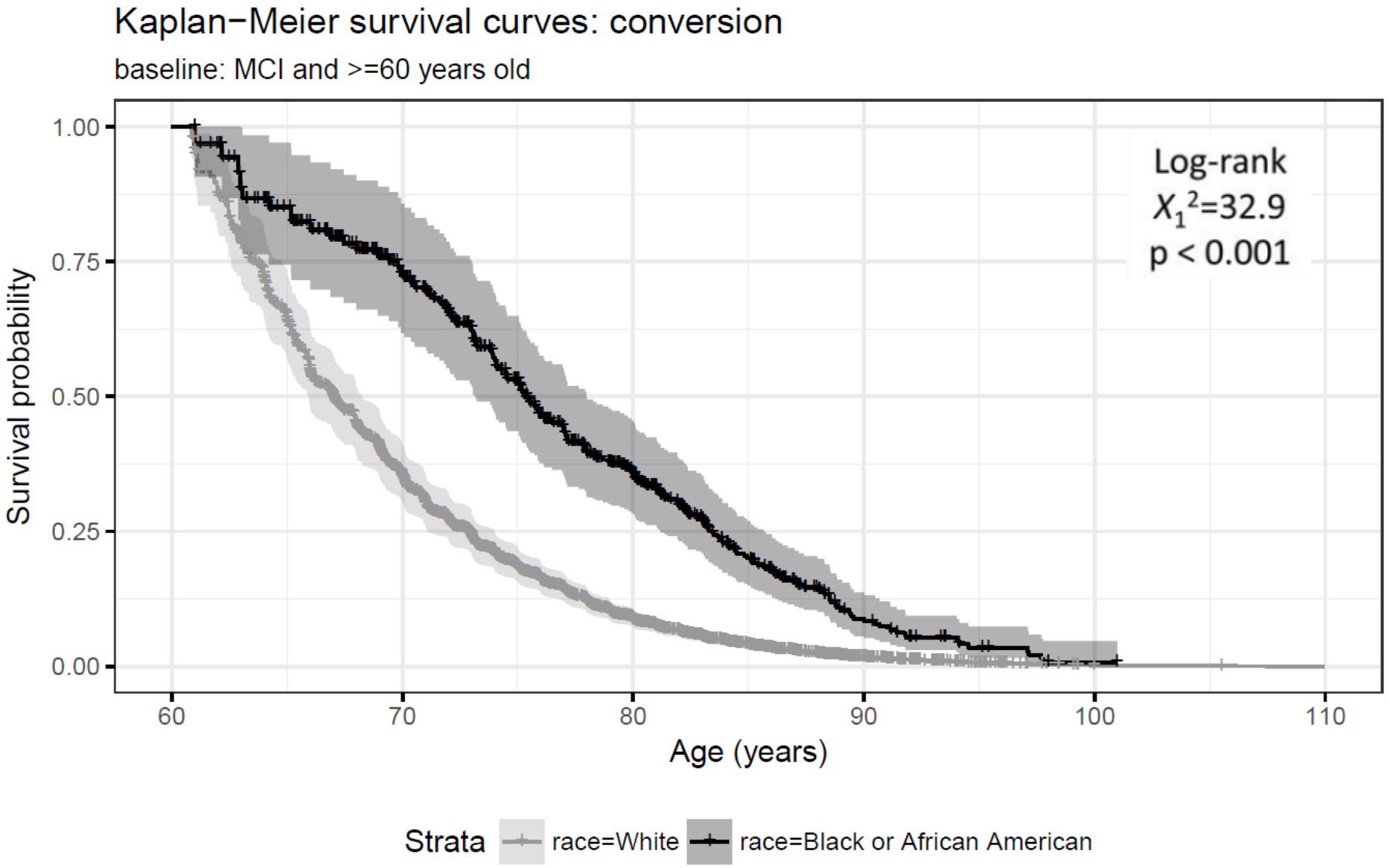
- Similar trends throughout noted for:
  - Death events only
  - Conversion or death

What about Normal cognition at baseline only?



- No statistical difference noted here…
- Though still not “statistically demonstrating” the expected higher risk for Black subjects...

What about MCI cognition at baseline only?



- <u>Substantial separation!</u>
- Black group has a much lower risk of incident cognitive impairment!

What might be causing this unexpected behavior?

	Normal baseline			MCI baseline		
	White	Black	p	White	Black	p
Incident impairment (N (%))	1559 (**22.6**)	267 (**20.7**)	**0.146**	1648 (**47.0**)	189 (**30.7**)	**<0.001**
Died (N (%))	971 (**14.1**)	120 (**9.3**)	**<0.001**	775 (**22.5**)	67 (**10.9**)	**<0.001**
Female (N (%))	4272 (**62.0**)	1014 (**78.7**)	**<0.001**	1559 (**44.4**)	423 (**68.7**)	**<0.001**
Entry age (mean (sd))	74.33 (8.16)	72.66 (7.08)	<0.001	75.18 (7.76)	73.58 (7.59)	<0.001
Years of followup (mean (sd))	4.92 (2.93)	4.77 (2.87)	0.158	3.86 (2.48)	3.79 (2.65)	0.109
Education (N (%))			**<0.001**			**<0.001**
under HS	116 (1.7)	124 (9.6)		114 (3.2)	92 (14.9)	
HS	896 (13.0)	282 (21.9)		577 (16.4)	172 (27.9)	
over HS	1229 (17.8)	341 (26.5)		612 (17.4)	145 (23.5)	
Bachelor	1738 (**25.2**)	186 (**14.4**)		905 (**25.8**)	82 (**13.3**)	
Master	2064 (**29.9**)	276 (**21.4**)		851 (**24.2**)	95 (**15.4**)	
Doctorate	822 (**11.9**)	76 (**5.9**)		443 (**12.6**)	30 (**4.9**)	
Unknown	29 (0.4)	3 (0.2)		8 (0.2)	0 (0.0)	

- Black participants have lower rates of death and incident impairment in both groups, especially in MCI
- Black participants slightly younger at entry, but have similar follow-up times
  - likely contributing, but not the main reason for the MCI separation
- Black participants are proportionally more female, but have lower proportions of college degrees

What about health conditions?

	Normal baseline			MCI baseline		
	White	Black	p	White	Black	p
Diabetes (N (%))						
absent	6307 (91.5)	956 (74.2)		3127 (89.1)	420 (68.2)	
recent/active	548 (**7.9**)	316 (**24.5**)	**<0.001**	351 (**10.0**)	184 (**29.9**)	**<0.001**
remote/inactive	27 (0.4)	6 (0.5)		23 (0.7)	8 (1.3)	
unknown	12 (0.2)	10 (0.8)		9 (0.3)	4 (0.6)	
Hyptertension (N (%))						
absent	3623 (52.6)	316 (24.5)		1704 (48.5)	132 (21.4)	
recent/active	3080 (**44.7**)	941 (**73.1**)	**<0.001**	1689 (**48.1**)	460 (**74.7**)	**<0.001**
remote/inactive	171 (2.5)	29 (2.3)		107 (3.0)	22 (3.6)	
unknown	20 (0.3)	2 (0.2)		10 (0.3)	2 (0.3)	
CHF, AFib, or heart attack (N (%))						
absent	5997 (87.0)	1143 (88.7)		2948 (84.0)	541 (87.8)	
recent/active	514 (**7.5**)	66 (**5.1**)	**0.009**	299 (**8.5**)	34 (**5.5**)	**0.027**
unknown	383 (5.6)	79 (6.1)		263 (7.5)	41 (6.7)	

- Black participants have substantially greater proportions of diabetes and hypertension
- Black participations, statistically, have lower proportions of cardiovascular events, but the percentage differences are small

What about how we are recruiting subjects, and what might motivate them to participate?

	Normal baseline			MCI baseline		
	White	Black	p	White	Black	p
Family History of dementia (N (%))			<0.001			<0.001
none 1st degree	2548 (37.0)	544 (42.2)		1202 (34.2)	262 (42.5)	
at least on 1st degree	3773 (**54.7**)	569 (**44.2**)		1999 (**57.0**)	283 (**45.9**)	
unknown	573 (8.3)	175 (13.6)		309 (8.8)	71 (11.5)	
Referral source (N (%))			<0.001			<0.001
self/relative/friend	2786 (40.4)	550 (42.7)		881 (25.1)	146 (23.7)	
health professional	1004 (**14.6**)	105 (**8.2**)		1550 (**44.2**)	154 (**25.0**)	
other	2846 (**41.3**)	593 (**46.0**)		966 (**27.5**)	288 (**46.8**)	
unknown	258 (3.7)	40 (3.1)		113 (3.2)	28 (4.5)	

- The Wisconsin ADRC, and other centers, have developed and used community-based recruitment strategies to aid in recruitment and retention of African American subjects!
- Especially in MCI, Black participations have much lower health professional / clinic recruitment compared to White subjects!

- Black subjects also have less known family history of dementia!
- What are the ramification of these items with respect to incident impairment?

Results from adjusted time-to-event analyses

	MCI at baseline			Normal at baseline		
	p value	HR	HR 95% CI	p value	HR	HR 95% CI
African American (ref.: White)	**<0.0001**	**0.71**	**0.61 — 0.84**	0.4864	1.05	0.91 — 1.21
Primary etiology ref: Alzheimer's disease						
Primary etiology: vascular disease	**0.0009**	**0.63**	**0.48 — 0.83**			
Primary etiology: Lewy Body	0.4079	1.10	0.88 — 1.38			
Primary etiology: other	**<0.0001**	**0.63**	**0.51 — 0.77**			
Primary etiology: missing/unknown	**<0.0001**	**0.63**	**0.57 — 0.70**			
Referral ref. category: self/relative/friend						
Referral: health professional	**<0.0001**	**1.46**	**1.29 — 1.64**	**<0.0001**	**1.39**	**1.21 — 1.6**
Referral: other	0.0574	0.88	0.77 — 1.00	**0.0005**	**1.2**	**1.08 — 1.33**
Referral: unknown	0.1225	0.80	0.61 — 1.06	**0.0282**	**1.29**	**1.03 — 1.62**
Family History ref. category: none on first degree						
Family History of Dementia: >= 1 first degree relative	**0.0256**	**1.12**	**1.01 — 1.25**	**0.0001**	**1.22**	**1.11 — 1.35**
Family History of Dementia: unknown	0.9727	1.00	0.83 — 1.21	0.1239	0.87	0.73 — 1.04

- Other covariates in models included:
  - Gender
  - Education category
  - Diabetes status
  - Hypertension status
  - Cardiac event status
- Gender, education, diabetes, and cardiac events were generally significant and in expected directions
- When referral source and family history are removed from models, results of other items are stable!

- Referral source and family history of dementia are significant in both the MCI and Normal cognition models!
- Primary etiology is important in the MCI models!
- However, these inclusions do not "eliminate" the lower hazard for the African American group.

In the NACC data…

- Differing recruitment efforts between Black and White participants is tantamount to different “sampling strategies”, and results in a different “type” of participant on average, and thus comparisons between data from different “sampling strategies” can be problematic, counter intuitive, and must be conducted with care!

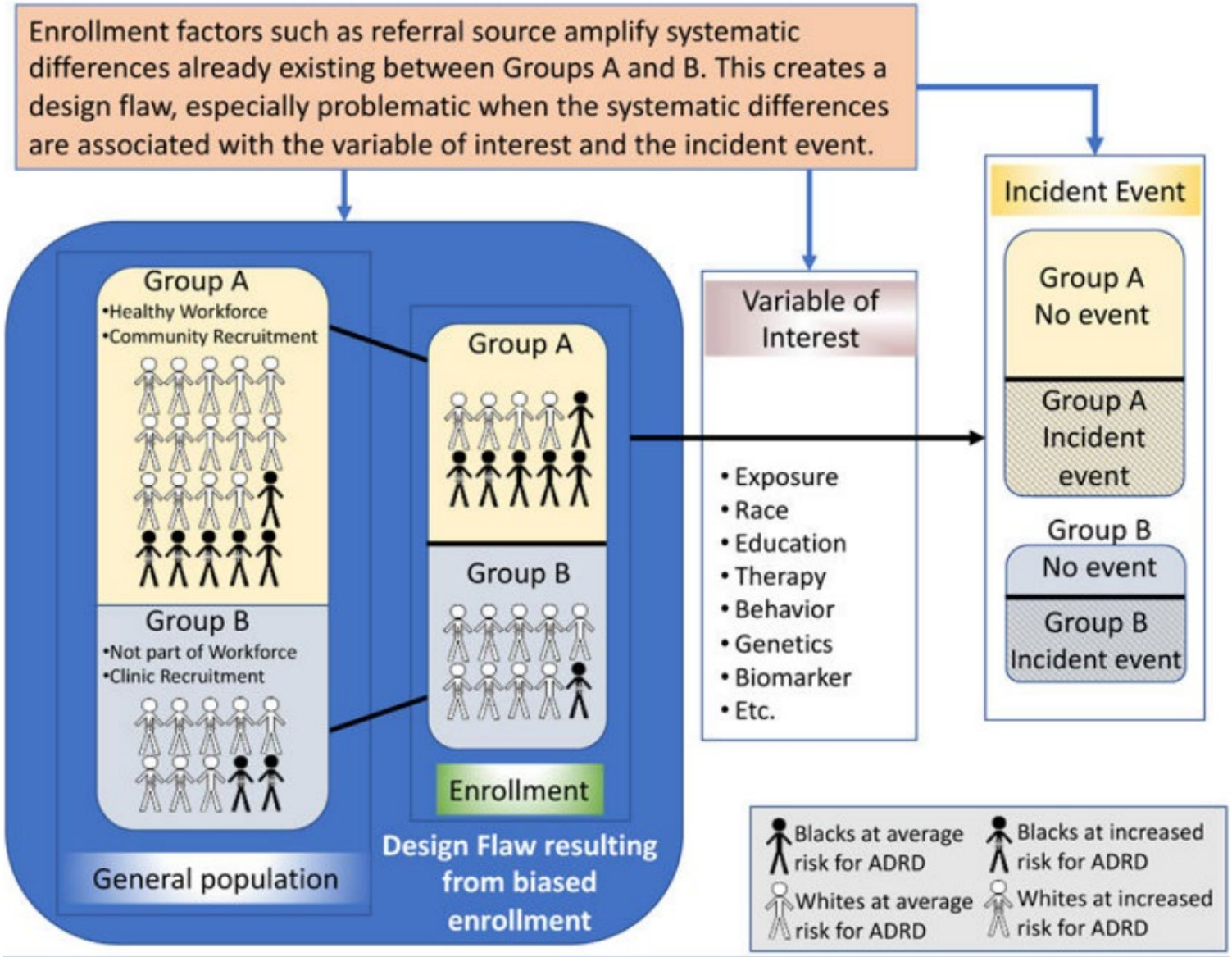
- Compared to White participants, Black participants tend to be recruited less from healthcare settings / health professionals, and have less known family history of dementia.

- Healthcare setting / professional recruitment is associated with younger age to incident cognitive impairment in our research!

- Known family history of dementia is associated with younger age to incident cognitive impairment in our research!

- These differences fundamentally introduce bias into Black vs. White comparisons in NACC, as well as any other items researchers would be interested in that correlate with differing recruitment efforts!

Recruitment factors can be thought of similar to Healthy Worker Bias (HWB)



- Participants recruited from the community (more likely for Black participants in NACC) can be thought of as the "healthy worker": they are at a lower risk for dementia and are less likely to seek out healthcare for dementia related issues
- Participants recruited from clinic (more likely for White participants in NACC) can be thought of as the "less healthy general population": they are experiencing dementia related issues and are more likely to seek out healthcare
- <u>Social Determinants of Health impact all components of these scenarios!</u>

Using Social Determinants of Health (SDoH) in your research!

- SDoH impacts health care access, knowledge, and families' past members to access that care and knowledge!
  - These factors are what necessitate varying recruitment strategies for different subgroups

- The SDoH form is now a part of NACC starting with UDS v4.0!
  - Has much greater depth and breath of information on these topics!
  - Will help researchers better understand and account for these important factors in their research :)
  - Will take time to gain this data to help in that understanding : (

- For past data without explicit SDoH information, consider:
  - Looking into and accounting for the referral source of subjects, as well as their known family history of dementia
  - Do not exclude "unknown" categories (for non-continuous data), as ones knowledge and access to it is affected by SDoH

Thank you for your time and attention!

Questions?

Comments?

Your own recommendations and experiences to share?