# 2023 Fall ADRC Meeting

## *Racial and Ethnic Differences in Neuropsychiatric Symptoms and Progression to Incident Cognitive Impairment*

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Washington University School of Medicine
UNIVERSITY OF JOHANNESBURG
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# Disclosures of Interest

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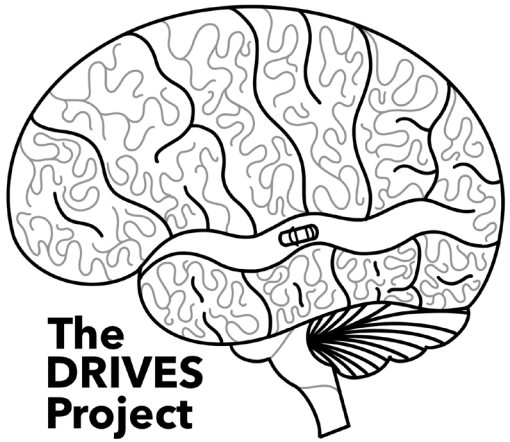




## Speakers Bureau

N/A

## Clinical Trials

N/A

## Consultant

N/A

I own no stocks or equity in any pharmaceutical company

# *NPS as a risk factor for ADRD*

Mild Behavioral Impairment as a Marker of Cognitive Decline in Cognitively Normal Older Adults

Byron Creese Ph.D. [a], Helen Brooker B.Sc. [a], Zahinoor Ismail M.D., B.Sc. [i], Keith A. Wesnes Ph.D. [a, b, c, d, e], Adam Hampshire Ph.D. [f], Zunera Khan Ph.D. [g], Maria Megalogeni M.Sc. [g], Anne Corbett Ph.D. [a], Dag Aarsland M.D. [g, h], Clive Ballard M.D. [a]

**Prevalence estimates of mild behavioral impairment in a population-based sample of pre-dementia states and cognitively healthy older adults**

Published online by Cambridge University Press: **21 September 2017**

Moyra E. Mortby, Zahinoor Ismail and Kaarin J. Anstey Show author details

**Neuropsychiatric Symptoms Mediated the Relationship Between Odor Identification and Cognition in Alzheimer's Disease Spectrum: A Structural Equation Model Analysis**

*Qiang Wang [1,2†], Ben Chen [1†], Xiaomei Zhong [1†], Huarong Zhou [3], Min Zhang [1], Naikeng Mai [3], Zhangying Wu [1], Xinru Chen [3], Mingfeng Yang [1], Si Zhang [1], Gaohong lin [1], Thomas Hummel [4] and Yuping Ning [1,5,6*]*

**Patterns of Neuropsychiatric Symptoms in Mild Cognitive Impairment and Risk of Dementia**

*Sarah N. Forrester, M.S., Joseph J. Gallo, M.D., Gwenn S. Smith, Ph.D., Jeannie-Marie S. Leoutsakos, Ph.D.*

Latent classes of neuropsychiatric symptoms in NACC controls and conversion to MCI or dementia

Jeannie-Marie S. Leoutsakos, PhD, MHS,[a,*] Sarah N. Forrester, MS,[a] Constantine G. Lyketsos, MD,[a] and Gwenn S. Smith, PhD[a]

The Course of Neuropsychiatric Symptoms in Dementia: A 3-Year Longitudinal Study

Henry Brodaty MD, BS, DSc [a, b], Michael H. Connors PhD [a, b], Jing Xu PhD [a, b], Michael Woodward MD, BS [c], David Ames MD, BS [d, e], PRIME study group

Cognitive & Behavioral Assessment

Time course of neuropsychiatric symptoms and cognitive diagnosis in National Alzheimer's Coordinating Centers volunteers

Elizabeth A. Wise, Paul B. Rosenberg, Constantine G. Lyketsos, Jeannie-Marie Leoutsakos*

**Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment**

Results From the Cardiovascular Health Study

Constantine G. Lyketsos, MD, MHS; Oscar Lopez, MD; Beverly Jones, MD; et al

The persistence of neuropsychiatric symptoms in dementia: the Cache County Study

Martin Steinberg, JoAnn T. Tschanz, Christopher Corcoran, David C. Steffens, Maria C. Norton, Constantine G. Lyketsos, John C.S. Breitner

**Affective and emotional dysregulation as pre-dementia risk markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria**

Published online by Cambridge University Press: **13 September 2017**

Zahinoor Ismail, Jennifer Gatchel, Daniel R. Bateman, Ricardo Barcelos-Ferreira, Marc Cantillon, Judith Jaeger, Nancy J. Donovan and Moyra E. Mortby Show author details

Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment

Zahinoor Ismail [a, b, c, d], Eric E. Smith [b, d], Yonas Geda [e, f], David Sultzer [g, h], Henry Brodaty [i], Gwenn Smith [j], Luis Agüera-Ortiz [k], Rob Sweet [l, m, n], David Miller [o], Constantine G. Lyketsos [p], ISTAART Neuropsychiatric Symptoms Professional Interest Area

Neuropsychiatric Symptoms as Risk Factors for Cognitive Decline in Clinically Normal Older Adults: The Cache County Study

Muhammad Haroon Burhanullah M.D. [a], JoAnn T. Tschanz Ph.D. [b], Matthew E. Peters M.D. [a], Jeannie-Marie Leoutsakos Ph.D. [a], Joshua Matyi B.A. [b], Constantine G. Lyketsos M.D., M.H.S. [a], Milap A. Nowrangi M.D. [a], Paul B. Rosenberg M.D. [a]

**Cortical β-amyloid burden, neuropsychiatric symptoms, and cognitive status: the Mayo Clinic Study of Aging**

Janina Krell-Roesch, Maria Vassilaki, Michelle M. Mielke, Walter K. Kremers, Val J. Lowe, Prashanthi Vemuri, Mary M. Machulda, Teresa J. Christianson, Jeremy A. Syrjanen, Gorazd B. Stokin, Lesley M. Butler, Martin Traber, Clifford R. Jack Jr., David S. Knopman, Rosebud O. Roberts, Ronald C. Petersen & Yonas E. Geda

**Neuropsychiatric Manifestations in Mild Cognitive Impairment: A Systematic Review of the Literature**

Liana G. Apostolova[a, b] Jeffrey L. Cummings[a, c]

The Mild Behavioral Impairment Checklist (MBI-C): A rating scale for neuropsychiatric symptoms in pre-dementia populations

Zahinoor Ismail, M.D.,[1,2] Luis Agüera-Ortiz, M.D., PhD,[3] Henry Brodaty, M.D.,[4] Alicja Cieslak, M.D.,[2] Jeffrey Cummings, M.D.,[5] Corinne E. Fischer, M.D.,[6] Serge Gauthier, M.D.,[7] Yonas E. Geda, M.D.,[8] Nathan Herrmann, M.D.,[9,10] Jamila Kanji, BSc,[2] Krista L. Lanctot, PhD,[10] David S. Miller, M.D.,[11] Moyra E. Mortby, PhD,[12] Chiadi U. Onyike, M.D.,[13] Paul B. Rosenberg, M.D.,[13] Eric E. Smith, M.D.,[2] Gwenn S. Smith, PhD,[15] David L. Sultzer, M.D.,[16] and Constantine Lyketsos, M.D.[17], for the NPS Professional Interest Area of the International Society of to Advance Alzheimer's Research and Treatment (NPS-PIA of ISTAART)

FEATURED ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

**Racial and ethnic differences in neuropsychiatric symptoms and progression to incident cognitive impairment among community-dwelling participants**

Ganesh M. Babulal[1,2,3,4] | Yiqi Zhu[5,6] | Jean-Francois Trani[2,4,6,7]

## Inclusion

- Age 50 and older
- CDR 0 @ baseline
- No impairment based on presumptive etiologic diagnosis of Alzheimer's disease
- NPIQ total score 0 @ baseline
- Baseline and at least 1 follow up
- Final n=6,980

## Methods

- Conversion: yes vs. no was 1:4
- Imbalance in N across racial groups
- PSM like nearest neighbor matching reduces sample size to ½ discarding data
- For CPHM - propensity score weighting
- Inverse probability of treatment weighting (IPTW) retains sample *(see Guo – Chapter 7)*.
- Participants were matched based on age, sex, education, and **race or ethnicity**
- Logistic regression estimated propensity score and weight was used in the survival models
- Optimal full match was used as a sensitivity check
- CPHM adjusted for NPS, race, sex, age education

Guo, S., & Fraser, M. W. (2014). *Propensity score analysis: Statistical methods and applications* (Vol. 11). SAGE publications.

# Unweighted models

| | | | Race/ethnicity (reference: nHW) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Black or AA | | Hispanic | | Asian | |
| NPS[a] | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| Delusions | 3.58*** | (2.99–4.28) | 0.92 | (0.79–1.07) | 1.59*** | (1.26–2.00) | 1.06 | (0.74–1.51) |
| Hallucinations | 2.97*** | (2.29–3.84) | 0.94 | (0.81–1.10) | 1.57*** | (1.25–1.99) | 1.06 | (0.74–1.51) |
| Agitation | 2.35*** | (2.10–2.64) | 0.97 | (0.83–1.13) | 1.70*** | (1.34–2.15) | 1.13 | (0.79–1.61) |
| Depression | 1.88*** | (1.69–2.09) | 1.06 | (0.90–1.23) | 1.58*** | (1.25–2.00) | 1.20 | (0.84–1.72) |
| Anxiety | 1.87*** | (1.68–2.09) | 1.02 | (0.87–1.19) | 1.63*** | (1.29–2.06) | 1.12 | (0.79–1.61) |
| Elation | 1.71*** | (1.24–2.36) | 0.94 | (0.80–1.09) | 1.60*** | (1.27–2.02) | 1.10 | (0.77–1.57) |
| Apathy | 2.86*** | (2.55–3.21) | 0.97 | (0.83–1.14) | 1.72*** | (1.37–2.17) | 1.14 | (0.80–1.63) |
| Disinhibition | 3.02*** | (2.61–3.49) | 0.98 | (0.84–1.14) | 1.65*** | (1.30–2.08) | 1.07 | (0.75–1.53) |
| Irritability | 3.02*** | (2.61–3.49) | 0.98 | (0.84–1.14) | 1.65*** | (1.30–2.08) | 1.07 | (0.75–1.53) |
| Motor disturbance | 3.30*** | (2.78–3.92) | 0.94 | (0.81–1.10) | 1.67*** | (1.32–2.11) | 1.11 | (0.77–1.58) |
| Nighttime behaviors | 1.79*** | (1.61–1.99) | 1.04 | (0.89–1.22) | 1.70*** | (1.35–2.15) | 1.16 | (0.81–1.66) |
| Appetite and eating | 1.83*** | (1.63–2.04) | 0.94 | (0.80–1.09) | 1.73*** | (1.37–2.19) | 1.09 | (0.76–1.56) |

Abbreviations: AA, African American; ICI, incident cognitive impairment; nHW non-Hispanic White; NPS, neuropsychiatric symptom.

[a]All survival analyses were adjusted for age, sex, and education.

***$p < 0.001$, **$p < 0.01$, *$p < 0.05$.

# Weighted models

| | | | Race/ethnicity (Reference: nHW) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Black or AA | | Hispanic | | Asian | |
| NPS[a] | HR | 95% CI | HR | 95% CI | HR | 95% CI | HR | 95% CI |
| Delusions | 2.07*** | (1.78–2.40) | 1.15* | (1.01–1.31) | 1.23 | (0.99–1.52) | 1.31 | (0.96–1.78) |
| Hallucinations | 2.05*** | (1.59–2.65) | 1.16* | (1.03–1.32) | 1.22 | (0.99–1.51) | 1.29 | (0.95–1.76) |
| Agitation | 1.66*** | (1.50–1.83) | 1.20** | (1.06–1.37) | 1.28* | (1.04–1.58) | 1.33 | (0.97–1.81) |
| Depression | 1.45*** | (1.33–1.59) | 1.23** | (1.08–1.40) | 1.22 | (0.98–1.51) | 1.40* | (1.02–1.92) |
| Anxiety | 1.53*** | (1.39–1.68) | 1.23** | (1.08–1.41) | 1.22 | (0.98–1.52) | 1.33 | (0.98–1.82) |
| Elation | 1.36* | (1.01–1.82) | 1.16* | (1.02–1.32) | 1.21 | (0.97–1.50) | 1.30 | (0.95–1.77) |
| Apathy | 1.95*** | (1.76–2.16) | 1.17* | (1.03–1.34) | 1.25 | (1.00–1.57) | 1.39* | (1.01–1.91) |
| Disinhibition | 1.91*** | (1.70–2.15) | 1.19** | (1.05–1.36) | 1.24* | (1.01–1.53) | 1.30 | (0.95–1.78) |
| Irritability | 1.91*** | (1.70–2.15) | 1.19** | (1.05–1.36) | 1.24* | (1.01–1.53) | 1.30 | (0.95–1.78) |
| Motor disturbance | 1.99*** | (1.71–2.33) | 1.16* | (1.01–1.32) | 1.26* | (1.02–1.56) | 1.32 | (0.97–1.80) |
| Nighttime behaviors | 1.36*** | (1.24–1.50) | 1.21** | (1.06–1.38) | 1.25* | (1.01–1.54) | 1.34 | (0.99–1.82) |
| Appetite and eating | 1.46*** | (1.33–1.60) | 1.15* | (1.01–1.31) | 1.27* | (1.02–1.58) | 1.31 | (0.96–1.79) |

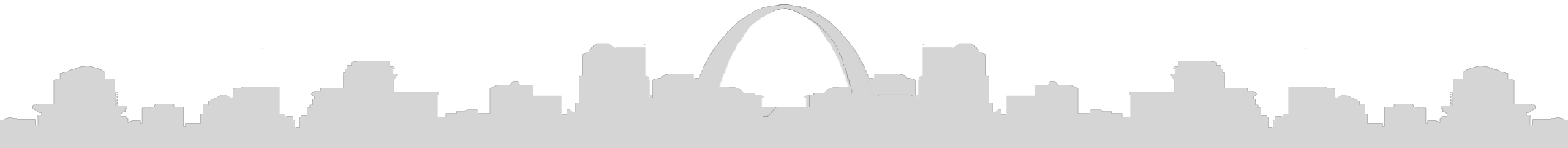
Abbreviations: AA, African American; ICI, incident cognitive impairment; nHW, non-Hispanic White; NPS, neuropsychiatric symptom.

[a]All survival analyses were adjusted for age, sex, and education.

***$p < 0.001$, **$p < 0.01$, *$p < 0.05$.

# Take away

- NPS, such as depression, anxiety, and agitation, increase AD risk for all, but there is a higher risk for African Americans and Hispanics
- Assess within-group differences first before comparing between groups
- Early recognition and delayed diagnosis of ADRD
- Under screening of cognitive symptoms
- Conflating NPS with disposition or personality for minoritized groups
- Addressing SR, stigma, trust in medicine, and awareness about ADRD is complex



# Thank you