

AWARD NUMBER: W81XWH-22-1-0961

TITLE: Military Risk Factors and Dementia in Veterans: The Impact of Race and Social Determinants of Health

PRINCIPAL INVESTIGATOR: Kristine Yaffe, MD

CONTRACTING ORGANIZATION: Northern California Institute for Research and Education
San Francisco, CA

REPORT DATE: October 2023

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

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REPORT DOCUMENTATION PAGE

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OMB No. 0704-0188

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|---|--------------------|---------------------------------|-----------------------------------|---|---|
| 1. REPORT DATE October 2023 | | 2. REPORT TYPE Annual | | 3. DATES COVERED 01Sep2022-31Aug2023 | |
| 4. TITLE AND SUBTITLE Military Risk Factors and Dementia in Veterans: The Impact of Race and Social Determinants of Health | | | | 5a. CONTRACT NUMBER | |
| | | | | 5b. GRANT NUMBER W81XWH-22-1-0961 | |
| | | | | 5c. PROGRAM ELEMENT NUMBER | |
| 6. AUTHOR(S) Kristine Yaffe, MD E-Mail: Kristine.yaffe@ucsf.edu | | | | 5d. PROJECT NUMBER | |
| | | | | 5e. TASK NUMBER | |
| | | | | 5f. WORK UNIT NUMBER | |
| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Northern California Institute for Research and Education 4150 Clement Street (151 NC) San Francisco, CA 94121-1545 | | | | 8. PERFORMING ORGANIZATION REPORT NUMBER | |
| 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012 | | | | 10. SPONSOR/MONITOR'S ACRONYM(S) | |
| | | | | 11. SPONSOR/MONITOR'S REPORT NUMBER(S) | |
| 12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited | | | | | |
| 13. SUPPLEMENTARY NOTES | | | | | |
| 14. ABSTRACT There are significant racial and ethnic differences in risk of developing Alzheimer's disease and related dementias (ADRD) that require immediate attention and understanding, especially for Veterans. Social determinants of health and ADRD may offer an important inroad to reduce health disparities. Investigating regional differences in dementia incidence may offer clues for understanding disparities and focusing dementia prevention efforts. This project aims to investigate the effects of military risk factors, social determinants of health, and how they interact with race/ethnicity on the risk of dementia. We propose to leverage the strength of a large and diverse, recently obtained dataset of older Veterans who get care at VA health centers across the entire U.S. We are addressing our Specific Aims using our recently assembled 5% random sample of all older Veterans receiving care at the Veterans Health Administration (VHA). In the first year of our grant, we published a manuscript examining dementia risk and disadvantaged neighborhoods (Aim 2). In the sample of 1,637,484 VHA patients, during a mean follow-up of 11.0 years, 12.8% of veterans developed dementia; those in greater disadvantage groups had an increased risk of dementia in models adjusted for demographic characteristics and comorbid conditions, and those residing within the most disadvantaged neighborhood quintile demonstrated the greatest risk. Findings suggest that within a representative national cohort of older veterans who received care, significant differences in dementia incidence existed based on neighborhood deprivation. | | | | | |
| 15. SUBJECT TERMS Alzheimer's disease and related dementia (ADRD), aging, Veterans, social determinants of health, health disparities, risk factors | | | | | |
| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON USAMRDC |
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | 19b. TELEPHONE NUMBER (include area code) |
| Unclassified | Unclassified | Unclassified | Unclassified | 9 | |

TABLE OF CONTENTS

| | <u>Page</u> |
|---|-------------|
| 1. Introduction | 4 |
| 2. Keywords | 4 |
| 3. Accomplishments | 4 |
| 4. Impact | 6 |
| 5. Changes/Problems | 6 |
| 6. Products | 6 |
| 7. Participants & Other Collaborating Organizations | 7 |
| 8. Special Reporting Requirements | 9 |
| 9. Appendices | 9 |

- **INTRODUCTION:** While racial differences in dementia incidence and risk are well established, more work is needed to understand the factors which contribute to these disparities especially among Veterans. Veterans are most likely at an increased risk for dementia because they incur military-related risk exposures as part of their time in the service. Moreover, Veterans' risk of dementia is highly likely to be impacted by social determinants of health. Both types of risk factors, military-related exposures and social determinants of health, may also contribute to race/ethnic disparities, yet little research has examined the intersection of military-related risk factors, social determinants of health, and race/ethnicity and dementia risk. Careful investigation of these interrelationships will identify both risk and resilience factors for dementia in diverse groups of older adults. Given the tremendous economic and healthcare burden that is associated with dementia and ADRD, identification of disease modifying risk factors and their contributions to regional differences in dementia incidence also have the potential for informing interventions to reduce health disparities among Veterans. There are significant racial and ethnic differences in risk of developing Alzheimer's disease and related dementias (ADRD) that require immediate attention and understanding, especially for Veterans. Social determinants of health and ADRD may offer an important inroad to reduce health disparities. Investigating regional differences in dementia incidence may offer clues for understanding disparities and focusing dementia prevention efforts. This project aims to investigate the effects of military risk factors, social determinants of health, and how they interact with race/ethnicity on the risk of dementia. We propose to leverage the strength of a large and diverse, recently obtained dataset of older Veterans who get care at VA health centers across the entire U.S. We are addressing our Specific Aims using our recently assembled 5% random sample of all older Veterans receiving care at the Veterans Health Administration (VHA).
- **KEYWORDS:** Alzheimer's disease and related dementia (ADRD), aging, Veterans, social determinants of health, health disparities, risk factors
- **ACCOMPLISHMENTS:**
 - **What were the major goals of the project?**
 - Task 1: Planning and Regulatory Review (Months 1-4)
 - Task 2: Aim 1 - To evaluate the relationship between race/ethnicity, social determinants of health, and military risk factors among older Veterans by determining: a) If and how military risk factor prevalence differs by race/ethnicity; b) The association between social determinants of health (including Area Deprivation Index (ADI), education, income) and military risk factor prevalence. (Months 4-18)
 - Task 3: Aim 2 - To determine if social determinants of health are associated with dementia incidence in older Veterans. (Months 12-26)
 - Task 4: Aim 3 - To investigate if the observed health disparities in dementia incidence among older Veterans may be partially explained by differences in military risk factors and social determinants of health. (Months 14-26)
 - Task 5: Aim 4 - To evaluate the US regional differences in dementia incidence according to military risk factors and social determinants of health. (Months 22-36)
 - **What was accomplished under these goals?**

In the first year of this grant, we made excellent progress, completing Aim 2 and beginning Aim 1. We began regular project meetings to discuss ongoing analyses, timelines, and plan future projects/manuscripts. We presented one abstract at the 2023 Alzheimer's Association International Conference (AAIC) in Amsterdam, and we published a manuscript in *JAMA Neurology*. We also began analyses on a second project.

Task 1: Completed planning and regulatory review as scheduled.

Task 3 (Aim 2): In the first year of the project we completed the analysis and published a manuscript on the association between dementia risk and neighborhood advantage. Residence in a disadvantaged neighborhood may be associated with an increased risk for cognitive impairment and dementia but is understudied in nationally representative populations. The object was to investigate the association between the Area Deprivation Index (ADI) and dementia. The study was a retrospective cohort study within the US Veterans Health Administration from October 1, 1999, to September 30, 2021, with a national cohort of older veterans receiving care in the largest integrated

health care system in the United States. For each fiscal year, a 5% random sample was selected from all patients (n = 2 398 659). Patients with missing ADI information (n = 492 721) or missing sex information (n = 6) and prevalent dementia cases (n = 25 379) were excluded. Participants had to have at least 1 follow-up visit (n = 1 662 863). The final analytic sample was 1 637 484. Neighborhoods were characterized with the ADI, which combines several sociodemographic indicators (eg, income, education, employment, and housing) into a census block group-level index of disadvantage. Participants were categorized into ADI rank quintiles by their census block group of residence (higher ADI rank quintile corresponds with more deprivation).

Time to dementia diagnosis (using International Classification of Diseases, Ninth Revision and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision codes) was estimated with Cox proportional hazards models with age as the time scale, and the sensitivity of the findings was evaluated with Fine-Gray proportional hazards models, accounting for competing risk of death. Among the 1 637 484 Veterans Health Administration patients, the mean (SD) age was 68.6 (7.7) years, and 1 604 677 (98.0%) were men. A total of 7318 patients were Asian (0.4%), 151 818 (9.3%) were Black, 10 591 were Hispanic (0.6%), 1 422 713 (86.9%) were White, and 45 044 (2.8%) were of other or unknown race and ethnicity. During a mean (SD) follow-up of 11.0 (4.8) years, 12.8% of veterans developed dementia. Compared with veterans in the least disadvantaged neighborhood quintile, those in greater disadvantage groups had an increased risk of dementia in models adjusted for sex, race and ethnicity, and psychiatric and medical comorbid conditions (first quintile = reference; second quintile adjusted hazard ratio [HR], 1.09 [95%CI, 1.07-1.10]; third quintile adjusted HR, 1.14 [95%CI, 1.12-1.15]; fourth quintile adjusted HR, 1.16 [95%CI, 1.14-1.18]; and fifth quintile adjusted HR, 1.22 [95%CI, 1.21-1.24]) (see Figure). Repeating the main analysis using competing risk for mortality led to similar results.

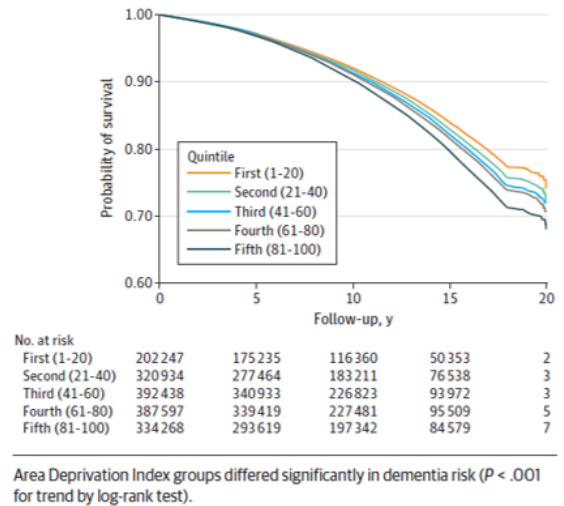


Figure 1: Kaplan Meier Dementia-Free Survival by ADI Quintile Groups

Results of this study suggest that residence within more disadvantaged neighborhoods was associated with higher risk of dementia among older veterans integrated in a national health care system.

Task 2 (Aim 1): We recently began an analysis examining factors (cardiovascular risk, social determinants of health, and military risk factors) that may explain the differences in dementia incidence based on race/ethnicity.

- **What opportunities for training and professional development has the project provided?**
 - On this project, Dr. Christina Dintica, a postdoctoral student at UCSF, mentored by Dr. Yaffe, has been conducting the analyses examining the association between dementia risk and area deprivation. She presented her results at an international conference and published the manuscript in a high-profile journal. In the coming year, she will begin another analysis looking at regional differences in dementia incidence. During this project she collaborated with this group's experienced team of researchers, gaining knowledge about the area deprivation index (ADI), Veteran's health, and working with large administrative datasets.
- **How were the results disseminated to communities of interest?**
 - For this project we have selected national and international meetings to disseminate our work through poster and oral presentations in which a broad range of multidisciplinary researchers and clinicians invested in reducing the effects of traumatic brain injury on cognitive aging and improving Veterans' health would be present. We submit our manuscripts to journals that also target multidisciplinary researchers and clinicians who are invested in improving TBI outcomes and Veterans' health.

- **What do you plan to do during the next reporting period to accomplish the goals?**
 - In the next year, we will complete the analysis for the Aim 1 project examining factors (cardiovascular risk, social determinants of health, and military risk factors) that may explain the differences in dementia incidence based on race/ethnicity. Once the analysis is complete, we will write up the results for publication. We will begin analyses for Aims 3 and 4, looking at social determinants of health, dementia incidence, and regional difference in dementia incidence. Throughout the year we will continue regular meetings to discuss ongoing analyses and future projects.

- **IMPACT:**

- **What was the impact on the development of the principal discipline(s) of the project?**
 - Nothing to report
- **What was the impact on other disciplines?**
 - Nothing to report
- **What was the impact on technology transfer?**
 - Nothing to report
- **What was the impact on society beyond science and technology?**
 - Nothing to report

- **CHANGES/PROBLEMS:**

- **Changes in approach and reasons for change**
 - Nothing to report
- **Actual or anticipated problems or delays and actions or plans to resolve them**
 - Nothing to report
- **Changes that had a significant impact on expenditures**
 - Nothing to report
- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
 - N/A

- **PRODUCTS:**

- **Publications, conference papers, and presentations**
 - **Journal publications.**
Dintica CS, Bahorik A, Xia F, Kind A, Yaffe K. Dementia Risk and Disadvantaged Neighborhoods. *JAMA Neurology*, 223; 80(9):903-909.
 - **Books or other non-periodical, one-time publications.**
Nothing to report

- **Other publications, conference papers, and presentations.**

Dintica CS, Bahorik A, Xia F, Kind A, Yaffe K. The association between the area deprivation index and dementia in a Veteran Population. 2023 Alzheimer’s Association International Conference.

- **Website(s) or other Internet site(s)**

Nothing to report

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

- Nothing to report

- **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

- **What individuals have worked on the project?**

| | |
|--|---|
| Name: | Kristine Yaffe |
| Project Role: | Principal Investigator |
| Researcher Identifier (e.g. ORCID ID): | KYAFFE |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Yaffe provides scientific leadership and input on the analyses and interpretation of results. |
| Funding Support: | n/a |

| | |
|--|--|
| Name: | Carrie Peltz |
| Project Role: | Project Coordinator |
| Researcher Identifier (e.g. ORCID ID): | n/a |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Peltz coordinates the project and assists with data analysis, reporting, and publications. |
| Funding Support: | n/a |

| | |
|--|-----------------|
| Name: | Beth Cohen |
| Project Role: | Co-Investigator |
| Researcher Identifier (e.g. ORCID ID): | COHENBETH |

| | |
|------------------------------|---|
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Cohen advises on analysis and interpretation related to military risk factors and assists on manuscripts and abstracts. |
| Funding Support: | n/a |

| | |
|--|--|
| Name: | Michelle Albert |
| Project Role: | Co-Investigator |
| Researcher Identifier (e.g. ORCID ID): | MAALBERT |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Albert advises on analysis and interpretation related to social determinants of health and race and ethnic difference. She assists on manuscripts and abstracts. |
| Funding Support: | n/a |

| | |
|--|---|
| Name: | John Boscardin |
| Project Role: | Co-Investigator |
| Researcher Identifier (e.g. ORCID ID): | BOSCARDIN2 |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Boscardin will work closely with the study team on data analysis and interpretation of results, and will assist on manuscripts and abstracts. |
| Funding Support: | n/a |

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Summary: Dr. Yaffe had one grant begin and four grants end since the grant submission.

Title: Health & Aging Brain Study – Health Disparities (HABS-HD)

(Yaffe--Multiple PI)

Time Commitment: 1% (0.12 calendar months)

Supporting Agency: NIH/NIA

Performance period: 07/21-06/26

Level of funding:

Title: Health Disparities in Alzheimer’s Disease and Mild Cognitive Impairment among Mexican Americans (HABLE)

(Yaffe--Multiple PI)

Time Commitment: 1% (0.12 calendar months)

Supporting Agency: NIH/NIA

Performance period: 09/2017-05/2022

Level of funding:

Title: Healthy Heart, Healthy Brain? A Pooled Life-course Cohort for Dementia Risk Assessment (HARMONY)
(Yaffe--Multiple PI)
Time Commitment: 2% (0.24 calendar months)
Supporting Agency: NIH/NIA
Performance period: 05/2017-04/2022 NCE
Level of funding:

Title: An Alzheimer's Blood Test for Primary Care
(Yaffe--Multiple PI)
Time Commitment: 1% (0.12 calendar months)
Supporting Agency: NIH/NIA
Performance period: 06/2018-05/2022 NCE
Level of funding:

- **What other organizations were involved as partners?**
 - Nothing to report

- **SPECIAL REPORTING REQUIREMENTS**

- Not Applicable

- **APPENDICES:** Nothing to report