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TITLE: Effects of Alzheimer's Disease in the Prediagnosis Period on Financial Outcomes

PRINCIPAL INVESTIGATOR: Carole Roan Gresenz

CONTRACTING ORGANIZATION: RAND Corporation
Seattle, WA 98095

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E-Mail: gresenz@rand.org

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1776 Main St
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14. ABSTRACT

The goal of this research is to understand how Alzheimer's Disease (AD)—before it is diagnosable using currently availability tools—affects the financial well-being of the individuals and families of those it afflicts. We are conducting analyses of the Health and Retirement Study (HRS) data linked to Medicare claims data. The HRS includes longitudinal information on financial outcomes for a large panel of U.S. adults over age 50. Linking the HRS to Medicare claims data enables us to identify individuals who were diagnosed with AD by a physician and their date of diagnosis, so that we can look backward over time at the vulnerable period prior to diagnosis. In Year 1 of our project, we constructed the merged data; derived key dependent and independent variables and calculated descriptive statistics. In Year 2, we performed analyses of the effect of AD on financial outcomes and drafted our first paper. In Year 3, we will complete our analyses and disseminate our results.

15. SUBJECT TERMS
Alzheimer's Disease, dementia, assets, savings, wealth, debt, financial outcomes

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1. INTRODUCTION

Alzheimer's Disease (AD) affects an estimated 5.3 million people in the U.S. and tens of millions of people worldwide, exacting substantial human and monetary costs. Existing tools for diagnosing AD lead to diagnoses that typically occur after the onset of severe symptoms. However, significant limitations and rapid declines in financial capacity occur among patients with mild and early stage AD, years before the disease is diagnosable. Some argue that financial decision-making deficits are among the first functional changes in people with AD. But, burgeoning limitations in financial capacity are unlikely to be fully appreciated or recognized by individuals and their families prior to diagnosis, and may therefore result in consequential effects on household financial outcomes such as spending, debt, and susceptibility to financial exploitation. Thus, the time period before AD is diagnosable represents a uniquely vulnerable period for individuals and households. The extent to which AD in its early stages contributes to adverse financial outcomes among those afflicted is unknown. We hypothesize that AD, during the period before it is diagnosable, negatively affects a wide range of household financial outcomes. We further hypothesize that the effects of AD during the period before it is diagnosable on household financial outcomes are more consequential when the financial head of household is afflicted as opposed to a spouse or partner of the financial household head. The goal of this research is to understand how AD—before it is diagnosable using currently availability tools—affects the financial well-being of the individuals and families of those it afflicts. We are conducting analyses of the Health and Retirement Study (HRS) data linked to Medicare claims data. The HRS includes rich, longitudinal information on financial outcomes for a large panel of U.S. adults over age 50. Linking the HRS to Medicare claims data enables us to identify individuals who were diagnosed with AD by a physician and their date of diagnosis, so that we can look backward over time at the vulnerable period prior to diagnosis.

2. KEYWORDS

Alzheimer's Disease, dementia, assets, savings, wealth, debt, financial outcomes

3. ACCOMPLISHMENTS

- **Major Goals**

Our specific aims are to (1) estimate the effects of AD during the period before it is diagnosable on household financial outcomes and (2) determine how the effects of AD during the period before it is diagnosable on financial outcomes differ depending on whether the financial head of household is afflicted or the spouse or partner of the financial head of household is afflicted.

Major Task 1: Submit data applications, including IRB application as well as application to HRS/CMS for restricted use data. *Anticipated Timeframe: Month 1. Completion: 100 percent*

Major Task 2: Identify individuals with relevant conditions from linked HRS/Medicare claims data and construct observation periods. *Anticipated Timeframe: Months 1-5. Completion: 100 percent.*

- **Milestone 1**: Apply algorithms to identify individuals with specific health conditions from the Medicare claims data. Identify date of diagnosis for individuals with AD and dementia. *(Completed)*
- **Milestone 2:** Construct the asymptomatic pre-diagnosis period (T1) and the symptomatic pre-diagnosis period (T2) for individuals diagnosed with AD. *(Completed)*

Major Task 3: Construct variables and perform analyses. *Anticipated Timeline: Months 5-16 Completion: 80 percent.*

- **Milestone 3:** Construct variables for the empirical models, including indicator for financial head of household. *(Completed)*
- **Milestone 4:** Conduct descriptive analyses. *(Completed)*
- **Milestone 5:** Estimate difference-in-differences models; conduct sensitivity analyses. *(Partially completed)*

Major Task 4: Assess potential selection bias using treatment effects model. *Anticipated timeline: Months 15-20. Completion: 85 percent*

- **Milestone 6:** Apply algorithm to identify individuals with probable dementia. *(Completed)*
- **Milestone 7:** Estimate treatment effects model to ascertain if there is any bias associated with using a sample of persons with diagnosed AD in our main analyses; conduct sensitivity analyses. (*Partially completed)*

Major Task 5: Manuscript preparation and dissemination. *Anticipated timeline: Months 12-24. Completion: 50 percent*

- **Milestone 8:** Prepare manuscripts based on the findings. (*In progress)*
- **Milestone 9:** Disseminate our findings including presentation at the DoD PRARP in-Progress Review Meeting (*Not asked to participate last year*)

- **Accomplishments by Goal**

In Year 1, we completed Major Tasks 1 and 2, worked on Major Task 3, and created descriptive tables for eventual use in our report of findings (Major Task 5). In Year 2, we made significant progress on Major Tasks 3, 4 and 5.

In Year 2, we worked in earnest on all aspects of our analyses and sensitivity analyses (Major Tasks 3 and 4). We obtained the predicted probabilities of normal cognitive status, cognitive impairment but not demented (CIND), and demented from the Hurd et al (2013) imputation algorithm for every respondent age 65 and over for every wave except for the first three waves of the HRS data (Major Task 4). We merged the three predicted probabilities to each person in each wave. Although we originally intended to use these probabilities just for Task 4, we realized that they could be valuable in helping us in our main analyses (Major Task 3). We use the predicted probabilities to determine the probable cognitive state of each person in each wave in order to determine the length of time the person may have been vulnerable (cognitively impaired to some degree) prior to diagnosis. We analyze not only the variable-length window determined by the imputed probabilities but also standard-length windows as originally proposed. We also use the imputed probabilities to define our comparison group of cognitively healthy individuals.

We used two approaches to estimating our main models (Task 3): a fixed-effect approach and a propensity-score matched difference-in-differences approach. The results were robust to these approaches and reviewers to date have favored the fixed-effect approach. Consequently, the most recent version of our draft emphasizes these results. We analyze variables using the continuous values of our outcome variables (liquid assets, net wealth) using inverse hyperbolic sine (IHS) transformation models to account for negative values and masses at zero. We also analyze dichotomous indicators of large adverse changes in net wealth or liquid assets. We use the 75th percentile and 90th percentile values of the distribution of percentage point changes in these outcomes to define a "large" change. We conducted multiple several sensitivity analyses. We examine an AD indicator based solely on the diagnosis code of 331.0 and an AD and related disorder indicator based on a larger set of diagnosis codes. In addition, we used both a standard-length and variable-length windows to capture early stage AD. Finally, we used the imputed probable dementia variable to examine the sensitivity of our results to using only the sample of individuals who have diagnosed dementia (Major Task 4). Our first draft does not contain the results of this sensitivity analysis because the paper was already very complex, but we plan to include these in a subsequent paper. We finalized our analyses and then prepared descriptive and results tables and wrote the background, methods, results and discussion sections of our draft paper. We completed a draft of our first paper, shared it with colleagues for feedback, and submitted the paper to a journal for review (Major Task 5). We also presented our work in a seminar series at Georgetown (Major Task 5).

- **Training and professional development opportunities**
  - Nothing to report

- **Dissemination of Results to Communities of Interest**
  - We presented our work at the Georgetown University Population Health and Health Services Research Seminar Series on September 19, 2018.
  - We are scheduled to present our work as part of the RAND Health seminar series on November 6, 2018.

- **Plans for Next Reporting Period**
  - We have requested a no cost extension because of the long delay we experienced receiving the linked Medicare HRS data. In the next reporting period (year 3 of our project), our focus will be on conducting remaining analyses, including conducting revisions in response to reviewer comments, and disseminating our findings.

4. IMPACT

- **Impact on the Development of the Principal Discipline**
  - This work will have impact in several important ways. First, this work makes an important contribution to cost-of-illness studies. In the context of dementia, cost-of-illness studies have focused on economic costs associated with health care for the condition or home care/caregiving required for individuals afflicted by dementia. This work provides a broader lens through which to think about cost-of-illness, and

will contribute to a more comprehensive understanding of the true costs of dementia. Second, this work will make an important contribution to how we think about valuing screening tools for conditions, especially those for which treatment options are either non-existent or limited. Sources of value are less obvious compared to conditions for which early treatment improves health outcomes; but, in the case of dementia, the signaling value of diagnosis may be very important for avoiding adverse financial outcomes. This work advances the field by quantifying the potential value of that signal. In addition, this work has led us to think more about the relationship between health and wealth more generally—a long-standing issue of concern for health and labor economists—and what other novel data might be combined to address key questions such as the one this research addresses. This work has also helped catalyze ideas around the potential of new data sources—including Medicare claims data combined with a longitudinal consumer credit data—to further examine the nexus between health and wealth generally, as well as between Alzheimer's disease and financial outcomes specifically. Drs. Mitchell and Gresenz were recently award a one-year R56 grant from NIH to conduct the linkage of these two data sources and evaluate the quality of the data match.

- **Impact on Other Disciplines**
  - Nothing to Report

- **Impact on Technology Transfer**
  - Nothing to report

- **Impact on Society beyond Science and Technology**
  - As described above, the research will be important at a societal level for providing increased visibility regarding the true costs of dementia and, at the household-level, for helping families recognize the potential vulnerability of their spouses and parents even when cognitive symptoms may be limited. Furthermore, the research will provide information about the types of vulnerabilities that are most likely to affect individuals with dementia before it can be diagnosed with currently available tools. Knowing the adverse outcomes to which individuals with AD are most susceptible is crucial for designing and targeting interventions to help prevent them. This is another dimension of the long-term value of the research—the possibility of developing indicators based on financial data for identifying people who should receive additional screening for AD.

5. CHANGES/PROBLEMS

- **Changes in Approach and Reasons for Change**
  - We modified some details of analytic aspects of the approach we described in the proposal based on our work with and assessment of the actual data once we had it. We expanded our control group to include individuals who were cognitively healthy, regardless of whether they had another (non-cognitive) chronic condition, in order to increase our sample size. We had planned to study foreclosure as an outcome, but the

prevalence of foreclosures in the data is very limited and the variation is insufficient for studying foreclosures as a separate outcome. We also tried a summary variable that combined foreclosure with other infrequent but significant outcomes, but variation in this summary outcome was still insufficient for analysis. Additionally, in looking at the diagnosis codes in the claims data, we had large number of claims coded as dementia, not otherwise specified (NOS)/classified. Moreover, there has been increased recognition that AD often co-occurs with other forms of dementia, including Lewy body dementia and frontotemporal lobe dementia. To ameliorate concern that many of these NOS dementia cases may in fact be AD and in consultation with our collaborator, Dr. Federoff, our analyses include, separately, the subset of individuals with AD as well as all individuals with dementia. In addition, in our sensitivity analyses of individuals with all dementia vs diagnosed dementia, we compare our main results to those from a single-stage analysis of all individuals with probable dementia to ensure the conceptual similarity of the windows of observation prior to onset of dementia. In our main analyses, we anticipated that our primary approach would be a difference-in-differences model and we estimated this type of model using propensity score matching, but our models using fixed effects were more highly regarded by reviewers and the results largely robust across the two approaches, so our most recent version of the paper focuses on the fixed-effect models.

- **Actual or Anticipated Problems or Delays and Actions or Plans to Resolve Them**
    - The approval/arrival of our data in Year 1 took longer than we anticipated. While we waited for the data, we made significant progress using the public use HRS data. However, we require a no cost extension in order to complete our work, including submission of our findings for review and revisions in response to reviewers.

- **Changes That Had a Significant Impact on Expenditures**
    - The delay in data slowed down our spending in Year 1. We have made steady and consistent progress in Year 2, but we have not expended all of our funds as of the end of Year 2 because of the initial delay.

- **Significant Changes in Use or Care of Human Subjects, Vertebrate Animals, Biohazards, and/or Select Agents**
    - No significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period.
    - Institutional Review Board approval dates:
        - Human Resources Protection Office (HRPO) Protocol [HRPO Assigned Number]: A-19817; Title: Effects of Alzheimer's Disease in the Pre-diagnosis Period on Financial Outcomes; HRPO contact: Karen Eaton, Human Subjects Protection Scientist
        - Initial IRB review approved by RAND IRB (Human Subjects Protection Committee) for period from 5/31/16-5/30/2017 (HSPC ID 2016-0395). IRB memorandum received June 2, 2016.

- Continuing review approved by RAND IRB (HSPC) on May 1, 2017, expired 30 May 2018. HRPO continuing review acknowledgement memorandum, received May 31 2017.
- Continuing review approved by RAND IRB (HSPC) on April 20, 2018, expires 19 April 2019. HRPO continuing review acknowledgement memorandum, received 4 June 2018**.**

6. PRODUCTS

- **Publications, conference papers, and presentations**
  - **Journal publications.** We have a draft article that is undergoing review.
  - **Books or other non-periodical, one-time publications:** Nothing to report
  - **Other publications, conference papers, and presentations:** We presented our work at the Georgetown University Population Health and Health Services Research Seminar Series on September 19, 2018.
- **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

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

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

Name:	Carole Roan Gresenz
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	0000-0002-7381-7914
Nearest person month worked:	2
Contribution to Project:	Dr. Gresenz has overarching responsibility for the project. Together with Dr. Mitchell, she directs the work of Dr. Marrone. In the last year, Dr. Gresenz has led the work of the team through specification of analyses, interpretation of results, writing/editing of the first paper, and dissemination of findings. She coordinates the work of the team by leading regular team meetings and takes primary responsibility for reporting tasks.
Funding Support:	In addition to this award, Dr. Gresenz receives support from AHRQ for a study of how physician practice structure and compensation characteristics affect prostate cancer treatment outcomes. Dr. Gresenz also has funding from Georgetown University for work to explore how social media data can inform gun policy. Dr. Gresenz is PI of a new R56 grant (beginning September 2018) from NIH to merge a credit data with Medicare claims data, with the hope of using this new data

	source to further explore questions related to financial outcomes associated with early stage dementia.

Name:	Jean Mitchell
Project Role:	Co-investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-2765-4624
Nearest person month worked:	1
Contribution to Project:	Dr. Mitchell, together with Dr. Gresenz, directs the work of Dr. Marrone. Dr. Mitchell contributes to all aspects of the research project, including design of analyses, interpretation of results, writing and editing draft papers, and participating in other forms of dissemination. She participates in regular team meetings and has primary responsibility for overseeing the RA's work, which has included regular updates of the literature.
Funding Support:	In addition to this award, Dr. Mitchell serves as principal investigator for a grant funded by AHRQ to examine the influence of physician practice structure and compensation characteristics affect prostate cancer treatment outcomes among men with low-risk prostate cancer. Dr. Mitchell also serves a principal investigator for a grant funded by the National Cancer Institute to evaluate treatment patterns and health outcomes among women with newly diagnosed ductal carcinoma. Dr. Mitchell has institutional support from Georgetown University to link cancer registry records with Census data for cancer survivors. Lastly, Dr. Mitchell is a co-investigator on a new NIH R56 grant (beginning September 2018) to merge credit data with Medicare claims data, with the hope of using this new data source to further explore questions related to financial outcomes associated with early stage dementia.

Name:	James Marrone
Project Role:	Co-investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-8125-6598
Nearest person month worked:	2
Contribution to Project:	Dr. Marrone implements the analyses of the merged HRS-Medicare data and contributes to analytic decisions regarding their design and specification. He contributed to the writing of the first draft paper and to interpretation of results.
Funding Support:	Dr. Marrone also serves as principal investigator for a grant from OSD to study attrition among first-term service members across all branches of the military. He has funding from the NBER's DRC to study the impact of interstate migration on disability insurance applications. He is also a researcher on projects supported by State Department, conducting international CVE program evaluations; FEMA,

	analyzing disaster recovery efforts; and U.S. Army, examining the impact of senior enlisted soldiers on junior enlisted attrition.

Name:	Caitlin Chamberlain
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Chamberlain conducts regular reviews of the relevant literature and reviews of particular areas/topics as requested, under Dr. Mitchell's direction. Her responsibilities also include assisting with the development of presentations and briefings.
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?**
    - Dr. Gresenz
        - The following are changes between our last reporting period (covering the time period through 9/30/17) and present day.
        - *Previously active projects now completed*
            - None to report
        - *Pending support now active*
            - None to report
        - *New active support*
            - NIH funded a new R56 grant, "Assessing the Early Vulnerability of Individuals with Alzheimer's Disease to Adverse Financial Outcomes" (beginning September 2018) to merge a credit data with Medicare claims data. The data should provide a resource for additional exploration of questions related to financial outcomes associated with early stage dementia. Dr. Gresenz is PI with 35 percent time.
            - Dr. Gresenz is PI of a grant from Georgetown University to study the use of social media data to inform gun policy (10 percent time).

    - Dr. Mitchell
        - *Previously active projects now completed*
            - Dr. Mitchell completed her project funded through institutional support from Georgetown University to identify factors associated with the increased use of contralateral prophylactic mastectomy among women diagnosed with non-metastatic unilateral breast cancer.
        - *Pending support now active*
            - None to report
        - *New active support*

- NIH funded a new R56 grant, "Assessing the Early Vulnerability of Individuals with Alzheimer's Disease to Adverse Financial Outcomes" (beginning September 2018) to merge a credit data with Medicare claims data. The data should provide a resource for additional exploration of questions related to financial outcomes associated with early stage dementia. Dr. Mitchell is a co-investigator with 12 percent time.
- Dr. Mitchell is a PI for an Georgetown University-funded project, "Linking Cancer Registry Records with Census Data for Cancer Survivors." She has less than 2 percent effort on this project.

- **What other organizations were involved as partners?**

We partnered with Georgetown University and the University of California-Irvine (UCI). One of the project's co-investigators (Dr. Mitchell) is affiliated with GU and our research assistant is also at GU. We also have collaborated with Dr. Howard Federoff of UC Irvine.

  - Organization Name: Georgetown University (academic institution)
  - Location of Organization: Washington, DC
  - Partner's contribution to the project
    - *Facilities*
      - Dr. Mitchell's affiliation is with Georgetown University. She uses GU facilities to conduct her work, including her office and computing equipment. The research assistant, Caitlin Chamberlain, also is associated with GU and conducts her work using computing technology from the University.
    - *Collaboration*
      - Dr. Mitchell is a co-investigator on the award. She collaborates with Dr. Gresenz on all aspects of the project and additionally oversees a research assistant, also from GU, who also contributes to the project.

  - Organization Name: University of California-Irvine (academic institution)
  - Location of Organization: Irvine, CA
  - Partner's contribution to the project
    - *Facilities*
      - Dr. Federoff's affiliation is UCI. He uses UCI facilities to conduct his work, including her office and computing equipment.
    - *Collaboration*
      - Dr. Federoff has provided expert consultation on clinical aspects of dementia and AD that affect our work.

8. SPECIAL REPORTING REQUIREMENTS

- **QUAD CHART**
  - Attached.

9. APPENDICES

None.

Effects of Alzheimer's Disease in the Prediagnosis Period on Financial Outcomes

AZ150099

W81XWH-16-1-0746

PI: Carole Roan Gresenz **Org:** RAND Corporation **Award Amount:** $757,578

Study/Product Aims

- Estimate the effects of AD during the period before it is diagnosable on household financial outcomes.

- Determine how the effects of AD during the period before it is diagnosable on financial outcomes differ depending on whether the financial head of household is afflicted or the spouse or partner of the financial head of household is afflicted.

Approach

We analyze Health and Retirement Study (HRS) data linked to Medicare claims data. The HRS includes rich, longitudinal information on financial outcomes for a large panel of U.S. adults over age 50. Linking the HRS to Medicare claims data enables us to identify individuals who were diagnosed with AD by a physician and their date of diagnosis, so that we can look backward over time at the vulnerable period *prior* to diagnosis. We use a difference-in-differences approach to evaluate the effect of AD during the period before the disease is diagnosable on financial outcomes.

Accomplishments (Q8): Revised and improved draft first paper, continued additional sensitivity analyses, prepared and conducted scholarly presentation at Georgetown.

Timeline and Cost

Activities	Q1-Q2	Q3-Q4	Q5-Q6	Q7-Q8
Apply for and obtain restricted use data (IRB, HRS, CMS applications)				
Identify analytic sample using merged data; construct observation periods				
Construct variables and perform analyses				
Manuscript prep and dissemination				
Estimated Budget ($K)	**$381,662**		**$375,916**	

Goals/Milestones Not begun Begun, not complete Complete

Year 1 Goals/Milestones

Milestone 1/2: Identify treatment and controls from merged data and construct observation periods

Milestone 3/4: Construct variables and conduct descriptive analyses.

Goals/Milestones Spanning Years 1-2

Milestone 5: Estimate difference-in-differences models; conduct sensitivity analyses.

Year 2 Goals/Milestones

Milestone 6/7: Apply algorithm to identify individuals with probable dementia and test sensitivity to selection on AD diagnosis

Milestone 8/9: Prepare manuscripts and disseminate results

Comments/Challenges/Issues/Concerns

- Received merged data in mid May. Behind original timeline in terms of analyses, manuscript prep and dissemination. .

Budget Expenditure to Date

Projected Expenditure: Straight line expenditures over project life

Actual Expenditure: **$539,269** (lower than projected due to data delay)

Updated: 30 Sep 2018