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Risk of dementia and mild cognitive impairment among older adults in same-sex relationships

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Abstract

INTRODUCTION: Sexual minority discrimination might lead to a higher risk of mild cognitive impairment (MCI) and dementia. The aim of this study was to assess the risk of MCI and dementia between older adults in same-sex relationships (SSR) and opposite-sex relationships (OSR).

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METHODS: We analyzed longitudinal data from the National Alzheimer's Coordinating Center up to September 2017. Analyses included cognitively normal individuals 55+ at baseline who had a spouse, partner or companion as study partner at any assessment. Associations were calculated using survival analysis adjusting for demographics and APOE-E4 carrier status.

RESULTS: Hazard ratios of MCI and dementia did not differ statistically between SSR and OSR individuals in the total sample nor stratified by sex.

CONCLUSION: The lack of association between SSR and MCI and dementia warrants future research into their potential resilience mechanisms and the inclusion of sexual minority status questions in research and surveillance studies. The potential recruitment bias caused by non-probabilistic sampling of the cohort and the reporting and ascertainment bias caused by using SSR to infer sexual minority status may have influenced our findings.

Keywords

Dementia; Mild Cognitive Impairment; Sexual minorities; disparities

Background

There are reasons to believe that sexual minorities might experience a disproportionate burden of dementia.¹ According to the minority stress theory, sexual minorities experience greater lifetime exposure to stigma, discrimination, and victimization. These stressors may increase sexual minorities' risk for health problems and depression.²⁻⁶ There have been no published studies on cognitive impairment and dementia risk comparing sexual minorities to their heterosexual counterparts; however, in African American older adults, studies have shown a relationship between perceived discrimination and episodic memory⁷ and a link between depression and declines in global cognition, episodic memory, and visuospatial ability.^{8,9} Similarly, high levels of perceived stress were associated with a 30% greater risk of incident MCI in a diverse community-based sample of older adults (30% racial/ethnic minorities) after adjusting for demographics, depression and APOE.¹⁰ Given sexual minorities' potential greater exposure to lifelong stress, it is important to understand whether this group experiences differences in risk for cognitive impairment and dementia.

To our knowledge, only two studies have assessed the risk of dementia and cognitive impairment among sexual minorities. The national longitudinal study Aging With Pride found that 10%, 38% and 77% of their 50+ lesbian, gay, bisexual and transgender (LGBT) sample self-reported extreme, moderate or mild cognitive deficits, respectively, in at least one World Health Organization Disability Assessment Schedule II cognition domain.¹ The same study also found that under 1% of participants 80 and older reported a diagnosis of dementia, which was argued to potentially be related to selection and information bias. Another study found that about 25% of LGBT older adults reported subjective cognitive decline, which was particularly common among racial/ethnic minorities and those with depression and functional impairments.¹¹ No study has compared MCI or dementia risk between sexual minorities and their heterosexual counterparts using the same protocol for diagnosis. Moreover, the little existing research has relied on self-reports of cognitive impairment or dementia instead of clinical diagnosis evaluations. We address these gaps in

the literature by assessing the risk of MCI and dementia among sexual minority older adults by comparing the onset of clinical diagnosed MCI and dementia between individuals in same-sex relationships (SSR) and opposite-sex relationships (OSR) in the National Alzheimer's Coordinating Center Uniform Data Set (NACC UDS).^{12,13} We hypothesize that participants in SSR will have a higher risk of MCI and dementia than those in OSR. We also stratified results by sex to explore its potential moderating role in the associations between being in a SSR and risk of MCI and dementia.

Methods

Data source

We used data from the National Alzheimer's Coordinating Center (NACC).¹² NACC maintains the Uniform Data Set (UDS), which includes standardized clinical data reported by past and present NIA-funded Alzheimer's Disease Centers (ADCs) throughout the United States. Each ADC recruits participants according to its own protocols; subjects may come from clinician referral, self-referral by patients or family members, active recruitment through community organizations, and volunteers who wish to contribute to dementia research. Data were collected by clinicians or trained interviewers at each ADC. Participants were required to identify a study partner with whom they were in regular contact to answer questions about the participants' cognition and functioning. Assessments were conducted approximately yearly. Informed consent was obtained from all participants at the individual ADCs. Centers received approval to gather data at their institutional IRB. Research using the NACC database was approved by the University of Washington IRB.

Study sample

Figure 1 shows a flowchart of the analytic sample which consists of NACC UDS participants with data collected from UDS visits conducted between September 2005 and August 2017. Inclusion criteria for this analysis consisted of being 55 years and older and being clinically diagnosed with normal cognition at initial visit. Participants had to have at least 2 UDS visits and a spouse/partner/companion as a study partner at any one of their assessments. Statistical models only included participants with complete information for the main independent or dependent variable measures on at least two assessment points.

Measures

Independent variable—Being in a SSR or OSR: The NACC UDS includes information on the sex of the participant ("male" or "female"), their relationship to their study partners and their study partners' sex ("male" or "female") at all time points. In particular the relationship question in the current version of the UDS (version 3) states: "What is the co-participant's relationship to the subject" with six response options: "1) spouse, partner, or companion (include ex-spouse, ex-partner, fiancé(e), boyfriend, girlfriend); 2) child (by blood or through marriage or adoption); 3) Sibling (by blood or through marriage or adoption); 4) Other relative (by blood or through marriage or adoption); 5) friend, neighbor, or someone known through family, friends, work, or community (e.g. church); 6) paid caregiver, health care provider, or clinician." In the two previous versions of the NACC UDS, option 1 only included spouse or partner and specifications in brackets for the

remaining options were not provided. Participants whose study partners were their spouses, partners or companions and only reported these spouses, partners or companions to be of the opposite sex irrespective of the visit were considered as being in an OSR. Those with spouses, partners or companions of the same sex at any visit were considered as being in a SSR.

Dependent variable—MCI and dementia diagnoses were made by a clinician or a consensus team after the examination of all the available information. Clinicians were instructed to consult the Diagnostic and Statistical Manual of Mental Disorders for diagnostic purposes.¹⁴ In UDS version 3, all-cause dementia was determined when clinicians used the modified version of the McKhann criteria and in earlier versions, dementia was determined using the “standard criteria for dementia of the Alzheimer’s type, or other non-Alzheimer’s dementing disorders.”^{15,16} If a participant was not cognitively normal or demented, MCI in all versions was determined using an excerpted chart from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) manual based on Petersen’s criteria.¹⁷ We determined time to first clinical UDS dementia or MCI diagnosis using information on their onset. We determined time to first dementia or MCI by using clinical diagnosis information to estimate their onset. For participants who were cognitively normal and at their next visit had converted to dementia, the onset of MCI was estimated as the first quartile point between the last cognitively normal evaluation and the first evaluation with a dementia diagnosis. The onset of dementia was estimated as the midpoint between the last cognitively normal evaluation and the first evaluation with a dementia diagnosis, or the midpoint between last visit with MCI and first evaluation with a dementia diagnosis. Participants who did not develop dementia or MCI were censored at their last assessment.

Covariates and descriptive variables—We adjusted models by potential confounders including participants’ age in years at first visit, level of education, sex, living alone and the presence of at least one APOE-e4 allele.¹⁸ Age at first visit was assessed as a continuous variable. Education was categorized as high school or less (0–12 years); some college (13–15 years); graduated college (16 years); or graduate school (17+ years). We use the term sex acknowledging that any effect of this variable might be related to either genetic (sex) or social (gender) factors.¹⁹ Given the small number of ethnic minority groups, we did not include race/ethnicity as a covariate. We described ethnicity in the baseline characteristics, along with potential mediators or moderators of the association between sexual minorities and dementia or MCI including ADC region (South/Midwest US vs West/Northeast), Body Mass Index, smoking status, and self-reported diagnosis by a clinician of alcohol or other substance abuse, lifetime depression (active either within the past 2 years or previously), any psychiatric disorder other than depression, hypercholesterolemia, hypertension, diabetes, B12 deficiency, thyroid disease, cerebrovascular disease and cardiovascular disease.

Statistical Analyses

Sample characteristics of participants at their first visit were described and compared across main independent variable groups (SSR vs. OSR). Comparisons between participants included frequencies, percentages or means and standard deviations and the 95% p value of the χ^2 or t-test. Bivariate associations in risk of developing MCI or dementia according to

SSR or OSR were described using event incidence per 1000 person-years. Kaplan-Meier graphs were used to visualize differences in time to outcome. Multivariate associations used Cox models between SSR or OSR and the risk of developing MCI or dementia. Models included adjustment for clustering by ADC to account for potential correlations in assessment evaluations within centers, participants' age at baseline (continuous), sex (male vs female), education (categorically), living alone, and the presence of at least one APOE-e4 allele. Years since initial visit were used as the time scale, and the Efron method was used to handle ties in multiple observed event times.²⁰

To examine whether the association between SSR or OSR and risk of dementia or MCI varies based on sex or APOE e4 allele status, we repeated main analyses but included an interaction term for each potential effect modifier. We additionally ran a models for dementia and MCI risk stratified by sex to assess potential differences in this association. Proportional hazards assumptions were assessed analytically by testing Schoenfeld residuals and including covariates as time dependent and graphically by observing Schoenfeld residuals vs. time plots. Supremum tests were additionally used to graphically and numerically assess the null hypothesis that the proportional hazards assumption holds.²⁰ The level of statistical significance for all analyses was set at 0.05. Statistical analyses were performed using SAS 9.4 Software.²¹

Results

The final analytic sample consisted of 5,057 participants and included 307 (6%) participants in SSR. The number of incident cases was 1032 for MCI and 306 for dementia during follow-up. Table 1 summarizes the baseline characteristics for all participants, by relationship type and sex. Participants' mean age was 70.8 (SD=7.9) and 51% were women with a higher female representation among those in a SSR (12% higher; $p<0.01$). Most participants identified as non-Hispanic white (83%) and their average educational level was 16.1 years (SD=2.9). There were few differences in clinical variables between SSR and OSR groups. Those in OSR were more likely to be APOE e4 carriers (28% vs. 24%; $p=0.02$), 4% less lived alone ($p<0.01$), 7% more were never smokers ($p=0.05$), 2% fewer had abused other substances ($p<0.01$) and had marginally lower percentages of alcohol abuse (3% vs 5%, $p=0.06$), and lifetime depression (23% vs 28%, $p=0.08$). Men in SSR had a lower prevalence of diabetes than men in OSR, while women in SSR had a higher prevalence of living alone, lifetime smoking, cardiovascular disease and other substance abuse than women in OSR.

Table 2 shows the number of persons at risk for MCI or dementia, the average person-year of follow-up, the number of events and incidence rates of MCI and dementia. For the MCI analysis, individuals in SSR were followed up for 1505 persons-year and those in OSR for 20557. The incidence of MCI was 43.2 per 1,000 person-years (95%CI 32.7, 53.7) for participants in SSR and 47.0 (95%CI 44.0, 50.0) for those in OSR. For the dementia analysis, individuals in SSR were followed for 1640 person-years and 20,871 for those in OSR. Dementia incidence rates were 15.2 (95%CI 9.24, 21.2) for participants in SSR and 12.7 (95%CI 11.2, 14.2) for participants in OSR. Figure 2 shows Kaplan-Meier survival estimates for MCI and dementia by relationship status. In line with the incidence rates

reported earlier, those in SSR had a higher MCI but a lower dementia survival trends than those in OSR.

Table 3 shows the unadjusted and adjusted hazard ratios of being in a SSR on MCI/dementia. The risk of MCI was lower and dementia was higher among those in SSR but risks did not differ statistically from OSR. After adjusting for participants' age, sex, education, living alone and having at least one APOE-E4 alleles, hazard ratios continued to not be statistically significant, although the hazard ratio for MCI increased up to 1.05 and the dementia risk estimate for SSR increased slightly. Table 4 shows the unadjusted and adjusted hazard ratios of being in a SSR on MCI/dementia, separated by participants' sex. No association reached statistical significance, nor were there any significant interactions between SSR vs OSR and sex or APOE-E4 status. However, adjusted trends showed that risk of dementia was higher among men (1.14) and women in SSR (1.11) but the risk of MCI was only higher among women in SSR (1.23). In fact, the trend for MCI risk among men was lower than for their OSR counterparts.

To explore the influence of ADC region on our results, we conducted a sensitivity analysis stratifying the association by ADC region. SSR and risk of MCI/dementia were not significantly associated in this analysis (Supplementary Table 1). Additionally, we ran a model testing the association between MCI/dementia and sex, stratified by SSR or OSR. There was a significantly lower risk of MCI and dementia in OSR females vs males using unadjusted models. When models were adjusted for clustering by ADC, age at baseline, living alone and APOE e4 status, this association with dementia in OSR females disappeared (Supplementary Table 2).

Discussion

To our knowledge, this is the first study to compare the risk of MCI and dementia between older adults in SSR and OSR. We used a large cohort of older adults with clinical characterizations to explore the relationship between SSR and the onset of MCI and dementia. We hypothesized that participants in SSR would have a higher risk of dementia and MCI than those in OSR. Our hypothesis was based on known risk factors that disproportionately affect sexual minorities and other communities that face discrimination. Contrary to our hypothesis, we found that there is no difference in the risk of dementia or MCI between individuals in SSR and OSR. The potential recruitment bias caused by non-probabilistic sampling of the cohort and the reporting and ascertainment bias caused by using SSR to infer sexual minority status may have influenced our findings.

The risk of MCI and dementia did not differ between individuals in SSR and OSR in the present study. Our hypothesis was based on the Minority Stress Model by which sexual minority groups are more likely to experience a culturally rooted chronic stress in the shape of negative experiences and depreciation which increases health problems and depression which are risk dementia risk factors.²² One interpretation of the negative findings is that minority stress is not related to MCI and dementia. However, perceived discrimination and depression are associated with dementia risk factors and brain health cross-sectionally and longitudinally among other minorities.^{7-9,23} Potential biological pathways include vascular

disease, alterations in glucocorticoid steroid levels and hippocampal atrophy, increased deposition of amyloid- β plaques, inflammatory changes, and deficits of nerve growth factors.²⁴ Alternatively, given the study design, we might have selected a cohort of individuals in SSR with strong resilient factors that protect them from minority stress. In fact, sexual minority older adults are likely to have higher rates of dementia risk factors (i.e. depression, hypertension and diabetes) than their heterosexual peers.²⁵ However, SSR individuals in our cohort were not more likely to have depression and hypertension and men in SSR were less likely to have diabetes. Our sample included only individuals in relationships, which might have accounted for the lack of differences in MCI and dementia risk between SSR and OSR individuals. Being in a relationship, irrespective of whether it is a SSR or OSR, might have protected individuals from loneliness, which a dementia risk factor.^{26–30} Moreover, sexual minorities are more likely to be single and having a partner protects them from minority stress.^{31,32} Another potential resilience factor is educational level, which was particularly high in our sample and is known to be protective against MCI and dementia. Participants in this study were mostly volunteers who wanted to enroll in a research study or were referred to the ADC because of concerns with their health. It is likely that our sample has experienced fewer barriers to healthcare access, which is more common among sexual minorities and is associated with worsened health outcomes including risk factors for dementia.³³

The percentage of individuals in SSR in the study was relatively high ($\approx 6\%$). This estimate is higher than the 1% of same-sex couple households at the national level in the 2010 census.³⁴ This estimate is also somewhat higher than the percentage of LGB adults participating in national surveys and is closest to the 5% participating in the 2009 National Survey of Sexual Health and Behavior.³⁵ These findings may reflect a high concern on behalf of sexual minority older adults about their cognitive health. In fact, Aging With Pride found that 77% of their 50+ sexual minority sample self-reported mild cognitive deficits in at least one World Health Organization Disability Assessment Schedule II cognition domain.¹ This finding emphasizes the importance of studying MCI and dementia among sexual minority groups.

This study has limitations and therefore we cannot rule out there being MCI and dementia risk disparities among all sexual minority individuals. The sample size of individuals in SSR was relatively small, which might have affected statistical power to detect differences in MCI and dementia risks. The next limitations relate to selection bias. First, we operationalized individuals as belonging to a sexual minority if they attended at least one visit with a spouse, partner, or companion of the same sex. Previous studies have used a similar approach in population surveys.^{36,37} This approach may have failed to include respondents concealing a SSR who might have experienced more discrimination, had poorer coping mechanisms, and therefore have a higher MCI and dementia risk. Moreover, though we used this approach, the responses on the co-participant demographics form are proxies for being in a same-sex or opposite-sex relationship. The UDS does not assess sexual orientation, thus there is no way to validate these relationship categories. Second, this operationalization also ignores whether participants identify as transgender or belong to another sexual minority group. Third, the operationalization of SSR and OSR is an indicator of sexual behavior and fails to accurately capture whether participants have had sexual

relationships with same or opposite-sex partners. In addition, it does not capture whether they identify themselves with a sexual minority group or whether they feel attracted by people of the same or opposite-sex. Fourth, even though the NACC UDS is among the largest longitudinal datasets of dementia and cognitive aging characterization in the world, its sampling was non-probabilistic. Proof of this selection bias is the clear under-representation of ethnic minorities, who tend to have a higher dementia prevalence and where interactions between ethnicity and sexual minority status might exist, which could lead to an even higher MCI and dementia risk.^{38,39} In fact, incidence rates were lower in our study than a population study in Northern Manhattan.^{40,41} However, differences in incidence rates can also be related to our sample being younger and in a relationship.

This study has implications for research and public health policy. Further research should explore the factors associated MCI and dementia resilience among individuals in SSR including education, healthcare access, and social support. These studies should go beyond deficit-driven models as these can only explain poor health outcomes.⁴² Researchers may want to use our methodology in the NACC UDS to understand dementia-related aspects in a well-characterized sample of SSR individuals including behavioral and psychological symptoms of dementia, comorbidities or used of medications. ADCs, state and national public health agencies should assess sexual minority status in order to monitor health disparities that may inform policies and tailored interventions. Qualitative research shows that sexual minority questions are not considered offensive and national surveys show don't-know or non-response rates that are as low as 1% which is lower than income-related questions among older adults.⁴²⁻⁴⁴ In fact, the Health and Retirement Study started collecting information about sexual minority status in their 2016 wave, and, after several waves, the sample size will be big enough to explore research questions related to dementia risk among sexual minorities.

Conclusion

This study constitutes the first step to understanding MCI and dementia disparities among sexual minority older adults. We have found no differences in the risk of developing MCI and dementia among individuals in SSR and OSR using robust clinical diagnosis assessments and a design of longitudinal nature. Lines of future research should explore the role of resilience factors among sexual minorities including education, healthcare access and social support. Given the potential selection bias in this study, ADCs should consider assessing sexual minority status directly to better understand whether sexual minorities experience a higher MCI and dementia risk and to characterize well this population to inform effective prevention, treatment and caregiving interventions. Monitoring sexual minority disparities in MCI and dementia in state-wide and national surveys will also be important to inform health policies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

SSR	Same-sex relationships
OSR	Opposite-sex relationships
MCI	Mild cognitive impairment
ADC	Alzheimer's Disease Center
NACC UDS	National Alzheimer's Coordinating Center Uniform Data Set

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Key points:

- No studies have assessed dementia and mild cognitive impairment disparities among sexual minorities.
- Dementia and mild cognitive impairment risk did not differ between same and opposite-sex relationships.
- Further research is needed to understand the role of resilience mechanisms.

Figure 1.
Sample size flow chart.

Figure 2.
Kaplan-Meier Survival Estimates for risk of any MCI (left) and dementia (right) by relationship status

Table 1.

Participant characteristics at baseline visit

Characteristic	Same-sex relationships			Opposite-sex relationships			All participants		p-value		
	Total	Male	Female	Total	Male	Female	Total		Total	Male	Female
	n=307	n=118	n=189	n=4750	n=2377	n=2373	n=5057				
Age, yrs, mean (sd)	70.4 (8.1)	70.0 (8.2)	70.6 (8.1)	70.9 (7.9)	72.5 (8.0)	69.2 (7.3)	70.8 (7.9)		0.30	<0.01	0.03
Female, n (%)	189 (62)			2373 (50)			2562 (51)		<0.01	--	--
Race/ethnicity, n (%)									0.17	0.52	0.26
White	260 (85)	103 (87)	157 (83)	3918 (82)	1998 (84)	1920 (81)	4178 (83)				
Black	15 (5)	5 (4)	10 (5)	397 (8)	180 (8)	217 (9)	412 (8)				
Hispanic	13 (4)	3 (3)	10 (5)	202 (4)	88 (4)	114 (5)	215 (4)				
Other non-Hispanic	17 (6)	5 (4)	12 (6)	219 (5)	106 (5)	113 (5)	236 (5)				
Education, yrs, mean (sd)	16.1 (2.7)	16.7 (2.7)	15.7 (2.6)	16.1 (2.9)	16.5 (3.0)	15.7 (2.8)	16.1 (2.9)		0.80	0.60	0.95
Region									0.20	0.10	0.60
South/Midwest	153 (50)	52 (44)	101 (53)	2546 (54)	1231 (52)	1315 (55)	2699 (53)				
West/Northeast	154 (50)	66 (56)	88 (47)	2204 (46)	1146 (48)	1058 (45)	2358 (47)				
Living alone	27 (8.8)	4 (3.4)	23 (12.2)	184 (3.9)	89 (3.7)	95 (4.0)	211 (4.2)		<0.01	0.84	<0.01
APOE e4 carrier, n (%)	73 (24)	32 (27)	41 (22)	1353 (28)	681 (27.3)	745 (29)	1426 (28)		0.02	0.71	<0.01
Total GDS score, mean (sd)	1.3 (1.8)	1.3 (1.9)	1.3 (1.7)	1.1 (1.8)	1.2 (1.8)	1.1 (1.8)	1.1 (1.8)		0.20	0.55	0.20
BMI, mean (sd)	26.8 (4.8)	26.7 (4.5)	26.9 (5.0)	27.1 (4.8)	27.6 (4.2)	26.7 (5.3)	27.1 (4.8)		0.30	0.06	0.61
Smoking status, n (%)									0.05	0.33	0.04
Never	147 (48)	50 (42)	97 (51)	2544 (54)	1130 (48)	1414 (60)	2691 (53)				
Former	154 (50)	65 (55)	89 (47)	2042 (43)	1150 (48)	892 (38)	2196 (43)				
Current	5 (2)	2 (2)	3 (2)	122 (3)	68 (3)	54 (2)	127 (3)				
Hypercholesterolemia, n (%)	159 (52)	68 (57)	91 (48)	2439 (51)	1310 (55)	1129 (48)	2598 (51)		0.85	0.58	0.85
Hypertension, n (%)	138 (45)	58 (49)	80 (42)	2177 (46)	1185 (50)	992 (42)	2315 (46)		0.73	0.84	0.90
Diabetes, n (%)	26 (8)	8 (7)	18 (10)	501 (11)	320 (13)	181 (8)	527 (10)		0.24	0.04	0.36
Cerebrovascular disease, n (%)	11 (4)	5 (4)	6 (3)	266 (6)	168 (7)	98 (4)	277 (5)		0.13	0.24	0.52
Cardiovascular disease, n (%)	78 (25)	34 (29)	44 (23)	1156 (24)	763 (32)	393 (17)	1234 (24)		0.65	0.43	0.02
B-12 deficiency, n (%)	12 (4)	3 (3)	9 (5)	156 (3)	79 (3)	77 (3)	168 (3)		0.59	0.61	0.28

Characteristic	Same-sex relationships			Opposite-sex relationships			All participants		p-value	
	Total	Male	Female	Total	Male	Female	Total	Female	Male	Female
	n=307	n=118	n=189	n=4750	n=2377	n=2373	n=5057			
Thyroid disease, n (%)	57 (19)	6 (5)	51 (27)	848 (18)	238 (10)	610 (26)	905 (18)		0.08	0.73
Alcohol abuse, n (%)	15 (5)	10 (8)	5 (3)	141 (3)	110 (5)	31 (1)	156 (3)		0.06	0.13
Other substance abuse, n (%)	8 (3)	3 (3)	5 (3)	44 (1)	32 (1)	12 (1)	52 (1)		<0.01	<0.01
Lifetime depression, n (%)	85 (28)	22 (19)	63 (33)	1105 (23)	441 (19)	664 (28)	1190 (24)		0.08	0.11
Other psychiatric disorders, n (%)	20 (7)	6 (5)	14 (7)	244 (5)	114 (5)	130 (5)	264 (5)		0.29	0.10

Bold font means $p < 0.05$

Abbreviations: GDS, Geriatric Depression Scale; BMI, Body Mass Index

Table 2.

Same-sex vs opposite-sex relationships and events among UDS participants

	Persons at risk	Person-years of follow up	Events	Incidence rate per 1,000 person years (95% CI)
MCI				
Same-Sex - Overall	307	1505	65	43.2 (32.7, 53.7)
Opposite-Sex	4750	20557	967	47.0 (44.0, 50.0)
Dementia				
Same-Sex - Overall	307	1640	25	15.2 (9.24, 21.2)
Opposite-Sex	4750	22871	291	12.7 (11.2, 14.2)

Abbreviations: MCI, Mild Cognitive Impairment; UDS, Uniform Data Set

Table 3.
Association between risk of MCI or dementia and same-sex vs opposite-sex relationships

	Unadjusted model			Adjusted model**		
	Hazard ratio	(95% CI)	p-value	Hazard ratio	(95% CI)	p-value
MCI						
Same-Sex	0.92	(0.72–1.18)	0.51	1.05	(0.83–1.32)	0.70
Opposite-Sex	1.00	--	--	1.00	--	--
Dementia						
Same-Sex	1.14	(0.76–1.71)	0.54	1.21	(0.73–2.00)	0.46
Opposite-Sex	1.00	--	--	1.00	--	--

Abbreviations: MCI, Mild Cognitive Impairment; UDS, Uniform Data Set
** Adjusted for clustering by ADC, participant's age at baseline, sex, education, living alone and APOE e4

Table 4. Association between risk of MCI or dementia and same-sex vs opposite-sex relationships: stratified by sex

	Unadjusted model			Adjusted model**		
	Hazard ratio	(95% CI)	p-value	Hazard ratio	(95% CI)	p-value
MCI						
Males						
Same-Sex	0.72	(0.48–1.09)	0.12	0.84	(0.55–1.29)	0.43
Opposite-Sex	1.00	--	--	1.00	--	--
Females						
Same-Sex	1.26	(0.91–1.73)	0.17	1.23	(0.96–1.59)	0.11
Opposite-Sex	1.00	--	--	1.00	--	--
Dementia						
Males						
Same-Sex	0.94	(0.48–1.84)	0.86	1.14	(0.58–2.21)	0.70
Opposite-Sex	1.00	--	--	1.00	--	--
Females						
Same-Sex	1.43	(0.85–2.42)	0.18	1.11	(0.77–1.60)	0.57
Opposite-Sex	1.00	--	--	1.00	--	--

Abbreviations: MCI, Mild Cognitive Impairment; UDS, Uniform Data Set
** Adjusted for clustering by ADC, participant's age at baseline, sex, education, living alone and APOE e4