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PESTICIDE USAGE AND SHORT-TERM MEMORY LOSS: 2011-2012 NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES)

BY

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Degree to be Awarded: M.P.H. (Applied Epidemiology)

Executive MPH

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M.P.H., Emory University, 2015
B.A Rutgers University, 2012
A.S. Camden County College, 2010

An abstract of
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Abstract

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In 2007, the United States alone is estimated to have spent over twelve billion dollars on herbicides, fungicides, and insecticides, and there are over 18,000 products licensed for use. Well over 1 billion pounds of pesticides were used that year, and while most of this was used in farms and agriculture and other commercial methods, approximately 20%, or around 173 million pounds, was used for household applications. Many studies have linked pesticides to health related concerns, and most frequently associated are neurological and learning issues. The purpose of this retrospective, cross-sectional study was to perform a statistical analysis of the NHANES survey data to determine prevalence of reported short-term memory loss among participants over age 60, prevalence of in-home pesticide usage, and to determine if there is any significant association with domestic pesticide usage and short term memory loss. 45% of study participants indicated that they had experienced some degree of short term memory loss within 7 days of the survey, while only 14% confirmed that they had used pesticides within the home within the same 7 day period. Interviewees who were aged 75 and over had 1.54 times the odds of reporting short-term memory loss as those 60-64 (95%

confidence interval=1.14-2.08), while those who had reported a history of stroke had 1.42 times the odds of reporting short-term memory loss as those who did not report stroke (95% CI=1.00-2.00). Females had 1.53 times the odds of males of experiencing memory loss over the 7 days prior to the interview (95% CI=1.26-1.85). While the study did not provide evidence for an association between in-home pesticide usage and short-term memory loss (OR=1.12, 95%CI=0.80-1.57), future studies are recommended which could employ a prospective, longitudinal design in order to delve into critical windows of exposure and non-acute effects, while also controlling for additional important confounders and reducing recall bias.

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BACKGROUND

In 2007, the United States alone is estimated to have spent over twelve billion dollars on herbicides, fungicides and insecticides, and there are over 18,000 products licensed for use (Grube & Donaldson, 2011). Well over 1 billion pounds of pesticides were used that year, and while most of this was used in farms and agriculture and other commercial methods, approximately 20%, or around 173 million pounds, was used for household applications. These enormous numbers encompass use in the household by a resident as well as over 500,000 private certified applicators and pest control firms operating within the United States.

While the overall volume of pesticides in use within the United States has been halved since the early 1980's, each household has an estimated 1.4 pesticide products within its cabinets (Bass, Ortega, Rosales, Peterson, & Philen, 2001) with insecticides making up 91%, thus indicating that the vast majority of households owns at least one insecticide. While most insecticides that were found were deemed "safe" for inside use when directions were followed, Bass et al. also noted that 14% were deemed to be a highly toxic class I pesticide. The U.S. Environmental Protection Agency (EPA) bestows the moniker of Class I Toxicity to a pesticide when rigorous testing determines that it is considered to be the most toxic, whereby, among other factors, oral ingestion of less than 5 grams of a substance can be fatal to an average human being (Code of Federal Regulations, 2015). Slightly more alarming was their finding that approximately 5% of the insecticides surveyed contained chemicals that had been altogether banned by the EPA.

The invention and use of pesticides has led to increased crop yield which has in turn led to more food, at lower prices, being produced for the Earth's ever-growing population. In fact, the EPA itself, on its' website, notes many direct benefits to society such as disease prevention, structure protection, disinfection, and treatment of recreational and drinking water. While it is true that insects can pose a significant risk to public health, there are also many risks associated with the use of, and exposure to, pesticides.

Up until recently, pesticides have historically been lauded for their contributions to public health. In one such case, the organochlorine class pesticide DDT was created in the late 1930's by chemist Paul Muller. It was inexpensive and thought to be safe at the time, so it was applied freely and was touted as somewhat of a miracle product since malarial outbreaks were mitigated, and in some instances eliminated, through vigorous mosquito spray programs. In fact, Dr. Muller would later win a Nobel Prize for his discovery. It was not until the 1960's when Rachel Carson questioned DDT's toxicity and its incredible persistence in the environment in her book *Silent Spring* (Carson, 1962) that we began to realize that there could be a very steep price to pay for pest control.

Many studies have linked pesticides to health related concerns, and most frequently associated are neurological and learning issues. Neurologic symptoms of acute and chronic pesticide exposure such as general malaise, memory impairment, headaches, and muscle weakness can mimic many other syndromes, and therefore, many researchers believe that "The difficulty in diagnosing the cause of a group of relatively nonspecific symptoms raises the question of whether chronic carbaryl neurotoxicity might be occurring more frequently than previously suspected" (Branch & Jacqz, 1986).

This case study begs the question: How many people could have pesticide-related chronic illness with an unknown or misidentified etiology?

Some of the strongest insecticides are now licensed only for use on crops or for other such commercial applications. However, in the early 1990's, a discovery that one such chemical, methyl parathion, was used illegally to control cockroaches within homes in multiple southern and Midwestern states led to a cohort study performed by researchers in 1999 which seemed to link exposure to short-term memory problems, attention deficits, and behavioral issues in children (Eubanks, 2004). There were some inconsistencies in associations within groups in different states, but this may have been because children in these states had been exposed at different times; when they were retested in 2000, outcomes were seemingly not as strongly linked within the groups.

A meta-analysis of 39 studies published from 1974 through 2003 was evaluated for the association of pesticide exposure and neurologic dysfunction (Kamel & Hoppin, 2004). All of the studies reviewed were based on occupational exposures in fields such as farm work and pesticide application. In addition, only one study had delved into cumulative exposure, with the majority of studies reviewing acute exposures and poisonings. Only seven studies included multiple chemical exposure while 27 chose to focus on organophosphate exposures only.

In 2012, an additional meta-review was conducted by a team of researchers in the United Kingdom (Mackenzie Ross, Mcmanus, Harrison, & Mason, 2012) and this study primarily focused on chronic exposure to pesticides. Inclusion criteria was strict: one of the exposures must have been an organophosphate, have included effects of long-term, low-level exposure, have been an observational group study, and have measurable

neurobehavioral outcomes with testing, not self-reporting. After screening, 17 studies from 1960 through February 2012 met the criteria and were included in the analysis. After the data were analyzed, the team found that the majority of the well-designed studies indicated a significant association with long-term organophosphate pesticide exposure and impaired neurobehavioral functions such as working memory, attention, and psychomotor speed, etc. It is also noteworthy to mention that the authors advised that potential significant bias in any meta-review is possible due to publication bias; researchers are less likely to publish articles that report non-significant findings.

Another, more recent, systemic review of the literature was performed in 2013 (Munoz MT, 2013). Munoz, et al., reviewed 27 peer reviewed studies that looked into the association between Organophosphate pesticide exposure in children and neurodevelopmental effects. They found that all studies, except for one, indicated some degree of negative effect on children's neurobehavioral development, as well a positive dose-response relationship between pesticide exposure and various negative neurodevelopmental outcomes.

Research continues to link pesticide exposures to a myriad of neurological impairments and diseases. A case-control study published in 2011 led credence to the long held belief that environmental pollutants, such as pesticides, were associated with Parkinson's disease (Tanner, et al., 2011). Using cases and controls taken from the Farming and Movement Evaluation (FAME) study which examines the health of 90,000 licensed pesticide applicators, researchers found that individuals that had used the pesticides rotenone or paraquat were 2.5 times more likely to develop Parkinson's than those that had not used either pesticide.

Likewise, researchers continue to try to find environmental triggers that lead some individuals to develop Alzheimer's. DTT metabolizes into DDE and even today remains pervasive in the environment well after its widespread use was halted in the 1970's. To determine possible association, a case control study was completed using participants of the Emory University Alzheimer's Disease Research Center and the University of Texas Southwestern Medical School's Alzheimer's Disease Center (Richardson, et al., 2014). Researchers determined that cases had 3.8 times the levels of DDE in their blood serum than their control counterparts and lower scores on the Mini-Mental State Examination. The team was also able to link a genetic component, the APOE ε4 allele, with effect modification; those carrying the allele who were also exposed scored significantly lower in the exam.

Although not a human subjects study, research has linked pesticides to spatial memory loss and dysfunction (Chen, et al., 2012). Chen, et al., found that deltamethrin (a common household insecticide) and carbofuran (a crop insecticide), when given to rats once a day for 28 days, induced spatial memory loss and learning deficits coupled with neuron degradation.

Perhaps somewhat alarming is the increasingly accepted notion that chronic pesticide exposure can cause such a myriad of symptoms that illnesses related to exposures could often go unnoticed or misdiagnosed by medical practitioners. Genuis notes that "…*demonstrating cause and effect between exposure and illness is difficult as slow bioaccumulation of chronic low-level exposures often leads to vague and insidious symptoms*" (Genuis, 2008).

Many studies completed up until this point have focused on occupational pesticide exposures, both acute and chronic, and/or organophosphate exposures. Much less information exists on possible risks of exposure within the home, where many of us spend an extended amount of time over our lifespans, or to non-organophosphate based pesticides, and/or multiple exposures. To an airline flight attendant, the enclosed space of the cabin can begin to feel like home; many spend 12 hour + shifts on the planes and can be assigned to duty for several days before they have a few days off. The World Health Organization had at one time recommended that airlines to spray their planes inside and out with pesticides when departing from countries with invasive insect vector populations such as islands in the Caribbean, Latin America and the Pacific in order to prevent the spread of disease. The United States called for an end to that procedure in 1994, however, some airlines continued. The pesticides that were most routinely being employed were pyrethoid based, which can have significant toxicity effects on humans. An environmental researcher on a flight noticed this process and decided that she would conduct research into the health effects of these chemicals using 33 exposed flight attendants, along with an unexposed control group of 202. In addition to other cognitive declines, she found that the exposed group reported short-term memory loss at a rate of almost 2:1 – with a risk ratio of 7.6 in the exposed group, and 3.5 in the control group. (Kilburn, 2004).

There are many conditions that can lead to, or contribute to, short term memory loss. Anecdotally, mothers commonly report alteration in cognitive functions. An Australian team completed a meta-analysis of 14 studies and determined that exposures during pregnancy significantly disrupted and impaired at least some measures of memory

(Henry & Rendell, 2007). Even a person's age can play a role in memory loss and dysfunction. A 10-year longitudinal study, dubbed the Whitehall II study, was conducted in Europe and included over 7,000 people. The study provided a range of cognitive tests to each person three times over the 10 year period. The researchers determined that there was a 3.6% decline in mental reasoning of individuals aged 45-49 and an average decline of around 8% in the 65-70 age group (Singh-Manoux, et al., 2012).

Alcohol is widely known to affect memory and impair brain function. Alcohol and other substances can affect people differently depending on how much and how often a person drinks, general health status, gender, genetic background, and history of alcoholism, but it is widely accepted that alcohol affects everyone's functioning in some manner (Alcohol's Damaging Effects on the Brain, 2004). Alcohol can have noticeable effects on cognitive functioning after ingestion of only a few drinks, and individuals that have been drinking over a long period of time can have more significant and lasting physiological changes within the brain which can lead to significant cognitive decline.

Other substances, in addition to alcohol, can have a negative effect on memory. A Northwestern study on the effects of smoking marijuana noted that teens that smoked heavily for three years, on average, were still having working memory problems and displayed visible brain abnormalities two years after they stopped smoking (Smith, et al., 2014).

Disorders and disease can also affect brain function and initiate problems with memory. John's Hopkins Medicine notes that benign and malignant brain tumors can affect the area of the brain responsible for memory which can lead to short-term memory loss. Researchers have also linked sleep disorders, such as sleep apnea, with physical

changes within the brain leading to issues with memory loss (Kumar, et al., 2008). The team out of UCLA found that the areas of the brain responsible for memory were 20% smaller than those of the comparison group.

The purpose of this study was to perform a statistical analysis of the 2011-2012 NHANES survey data to determine if there is any association with in home pesticide usage and short term memory loss. This study is important to the existing literature as there have been limited studies that have explored exposure associations within the home unit. This could be relevant as many individuals spend a lot of time within the home and thus may have a higher probability of continued and cumulative exposure to a myriad of types of pesticides.

METHODS

Data

The National Health and Nutrition Examination Surveys (NHANES) have been conducted by the Centers for Disease Control in some capacity since the 1960's, and on a continuous yearly basis since 1999 (Centers for Disease Control (CDC), n.d.). Participants are interviewed in their homes and then complete a physical examination and blood work in a mobile examination center (MEC) rather than private facilities. Employment of the MECs allow for more standardized data collection across the survey population.

NHANES employs a complex, multistage survey design for all civilian populations in all 50 states who are not institutionalized. In addition, in the 2011-2012 survey cycle, non-Hispanic Asians were oversampled in order to help increase precision of estimates within this racial group. Primary selection units were made within 30 counties or across a few contiguous counties. Clusters of households are then elected from within those units and then further whittled down by household member. In 2011-2012, 13,431 individuals were selected for participation, however, only 9,756 people (72.6% response rate) completed the interview portion of the survey while the number was further reduced to 9,338 (69.5% response rate) for the physical and blood panels.

As the in-home interview portion of the survey is the focus of this study, attention should be given to the way that it was performed. Interviewers were provided with translated materials, and were also subjected to cultural training. When necessary, local interpreters were employed. Each interviewer was provided with an electronic hand-held device which could be handed to the interviewee in order to help ascertain answers for

more personal or intrusive lines of questioning. Not all questions within the survey are posed to all participants; some questions are targeted to specific age groups or genders - for example, questions about pregnancy. Complete content detail, population targets, data sets, and tutorials can be found online at http://www.cdc.gov/nchs/nhanes.htm.

The data sets required for this study are considered public use and can be downloaded from the CDC's NHANES site along with the SAS coding to compile and format appropriately. The study includes an exposure, an outcome, and five covariates, all taken directly from the 2011-2012 NHANES survey questions. Details surrounding the interview questions are below:

Variable Name	NHANES Code	Question Wording	Available Answers	Targeted To:
Pesticide Usage	PUQ100	In the past 7 days, were any chemical products used in (your/his/her) home to control fleas, roaches, ants, or other insects?	Yes, no, refused, don't know, missing	Males and Females 6-150 years of age
Short-Term Memory Loss	MCQ380	During the past 7 days, how often have you had trouble remembering where you put things like your keys your wallet/ Would you say… (choice)	Never, about once, two or three times, nearly every day, several times a day, refused, don't know, missing	Males and Females 60-150 years of age
Gender	RIAGENDR	Male or Female?	Male, female, missing	Males and Females 0-150 years of age
Age at Time of Screening	RIDAGEYR	Age in years of the participant at the time of screening	0-80 whole integers, missing	Males and Females 0-150 years of age (80 and over are topcoded at 80)
Alcohol Use	ALQ101	In any one year, have you had at least 12 drinks of any alcoholic beverage?	Yes, no, refused, don't know, missing	Males and Females 18-150 years of age
History of Stroke	MCQ160f	Has a doctor or other health professional ever told you that you had a stroke?	Yes, no, refused, don't know, missing	Males and Females 20-150 years of age
History of Brain	MCQ230a,	Has a doctor or other	Multiple	Males and

Cancer	MCQ230b, MCQ230c	health professional ever told you that you have/had cancer? – What kind of cancer was it?	cancers to choose from (see survey data online)	Females 20-150 years of age
History of Sleep Disorder	SLQ060	Have you ever been told by a doctor or health professional that you had/have a sleep disorder?	Yes, no, refused, don't know, missing	Males and Females 16-150 years of age

Due to the limiting nature of the study question, the pool of participants had to be narrowed. Figure 1 details how the inclusion/exclusions were made. Originally, we planned to include some types of illicit drug usage and pregnancy status at time of interview as additional covariates; however, as the outcome question was limited to the age group of 60-80+ year olds, this was not necessary.

Providing definitions of the covariates is important to allow for replication of the study. All respondents with answer codes of "refused" and "don't know" were recoded to missing, short-term memory loss was defined as anyone that answered "about once, two or three times, nearly every day, several times a day", and history of brain cancer was defined as anyone reporting a prior diagnoses of brain cancer on any one of the three cancer questions (one question, can report up to three cancer diagnoses).

IRB Review

Prior to commencement of data retrieval and analysis, per HHS regulations (45 CFR 46) Emory University Human Subjects Review committee reviewed the IRB application for this study and subsequently exempted it from additional review as this study was deemed as de-identified, secondary data analysis.

Statistical Analysis

After the data were downloaded and compiled, data were analyzed using SAS v9.4 (SAS Institute Inc., Cary, NC, USA). Age was recategorized into four classes (60-64, 65-69, 70-74, and 75 and older). Weighted frequencies using proc Surveyfreq were run to check the distribution and skewedness and to review the data for any outliers. We reviewed the raw and adjusted estimated associations between short-term memory loss for pesticide use and other covariates and utilized the 10% rule to evaluate confounding. Backward regression techniques in Proc Surveylogistic were used to remove any interaction terms that did not have a Wald Chi-Square p-value of less than 0.05.

RESULTS

Study Population Characteristics as related to Outcome

Age was the only originally continuous variable in the study - the mean age was determined to be 69.8, with a standard deviation of 7.0 and was considered to be normally distributed after review of the probability plot and skewness (0.20) which indicted a small positive skewness in the data.

Frequency distributions by outcome were compared for exposure and potential confounders, while determining if there was a statistical difference in prevalence of short-term memory loss among the groups (Table 1). Analysis of the exposure variable indicated that of those that reported short term memory loss, 11% used pesticides in their home. Of those not experiencing memory loss 10.9% used pesticides. Of the 694 people who reported short term memory loss, 31.4% were aged 60-64, 20.8% were 65-69, 15.4% were 70-74, and 32.4% were 75 and older. Of those not reporting memory loss, approximately 34.6% were aged 60-64 at the time of the survey, 22.7% were 65-69, 20% were 70-74, and 22.7% were 75 and older.

Gender was also considered as a possible confounder – of those reporting short-term memory loss, 38.4% were males and 61.6% were female. Those not reporting memory loss were more evenly balanced between males and females; 50.2% were male and 49.8% females. 71.2% of those with memory loss also reported usage of alcohol compared to 28.8% that did not drink. Of those without a self-report of memory loss, 70.1% drank alcohol and 29.9% did not. 8.7% of those with memory loss reported that they had prior history of a stroke, while 91.3% reported that they did not. Of those with no memory loss, 5.8% had a stroke in the past while 94.2% did not. 12.4% of those with

memory loss had a sleep disorder. 11.5% of people without memory impairment reported a sleep disorder compared to 88.5% that did not. As only 2 people reported having a diagnoses of brain cancer, that covariate was removed from the final model.

A statistically significant difference in prevalence of short-term memory loss was discovered among the age groupings (p=0.04) as well as gender (p=0.004). This can be interpreted as evidence of a relationship between these categorical variables and the outcome status.

There were no significant interaction terms after backwards elimination regression procedures.

Study Population Characteristics as related to Exposure

Frequency distributions by exposure were compared for potential confounders, while determining if there was a statistical difference in prevalence of exposure among the groups (Table 1.2).

Of those interviewed and included in this study, 10.9% confirmed that they had used pesticides within their home over the past 7 days. Of those that reported pesticide usage, 30.1% were aged 60-64, 23.3% were aged 65-69, 12.3% were aged 70-74, and 34.2% were aged 75 and older. 52.5% were male, and 67.6% had history of alcohol use. Of those reporting pesticide use, 12.3% reported having a sleep disorder.

89.1% of those interviewed indicated that they had not used pesticides within the past 7 days. Of these interviewees, 31.4% were aged 60-64, 20.5% were 65-69, 18% were 70-74, and 30.1% were aged 75 and older at the time of the interview. 13.1% indicated that they had experienced short-term memory loss within the last 7 days prior to

the survey. 48.8% were male, 64.2% had a history of alcohol use, 8.3% reported a prior stroke diagnosis, and 11% reported a sleep disorder.

No statistically significant differences in exposure were observed among any of the covariate groups.

Unadjusted Analysis

Bivariate analysis was performed to access the crude associations between various participant's characteristics and the outcome (Table 2). Wald Chi-Square test p-values of 0.05 or less were used as the cut-off to determine any statistical association. After review, participants aged 75 and over, when compared to the reference group of those aged 60-64, at time of interview (OR 1.11, 95% CI 0.82-1.59), being female (OR 1.51, 95% CI 1.25-1.82), and having a history of stroke (OR 1.49, 95% CI 1.03-2.16) were found to have statistically significant associations with the outcome. The most significant association was seen between gender and short-term memory loss. In fact, females had 1.51 times the odds of reporting memory loss compared to males (95% CI 1.25-1.82).

Adjusted Analysis

A multivariable model was fitted with the variables that were found to be individually associated with the outcome (Table 3). After adjustment, age (OR 1.54 for age 75 and older vs. 60-64, 95% CI 1.14-2.08), female gender (OR 1.53, 95% CI 1.26-1.85), and history of stroke (OR 1.42, 95% CI 1.00-2.00) remained statistically significant predictors of short-term memory loss. Comparing crude to adjusted odds ratios, and utilizing the 10% difference rule, age and history of stroke were potential

confounders. Gender was not found to confound the pesticide use short-term memory loss association, however, as it was previously determined to be a significant predictor of the outcome, we retained it within the final model.

When adjusting for confounding, those that reported using pesticides within the home had 1.12 the odds of reporting short-term memory loss versus those that did not (OR. 1.12, 95% C.I 0.80-1.57). However, the odds ratio included the null value and results were not statistically significant at the 0.05 level (p-value=0.52).

DISCUSSION

Reported Prevalence of Short-Term Memory Loss

Within the study cohort, over 45% (n=694) of the participants age 60 and over reported short-term memory loss. This is a rather large prevalence, and indicates a real need for studies that delve further into this phenomena.

Reported Prevalence of Within Home Pesticide Usage

Only 14% of those included in the study stated that they had used pesticides within the home. This number seems quite low given the prior estimate provided which claimed that most households in the U.S. contained at least one pesticide product. Possible explanations, among others, include recall bias and group home living, as well as the question's wording in the survey since the language only asked about occurrences within the past seven (7) days. This study would therefore capture acute exposures, but does little to capture any effects from long-term exposure or exposure that was acute but may have occurred more than 7 days in the past.

Covariate Associations with Short-Term Memory Loss

We looked at the associations between the covariates and short term memory loss to determine how strongly the covariates were associated with the outcome. As expected, after adjusting for the other covariates, a significant association was found between the age group 75 and older ($p=0.005$), gender ($p=<0.001$) as well as having a history of stroke ($p=0.049$); Interviewees who were aged 75 and up had 1.54 times the odds of those in the age group 60-64 to have reported short-term memory loss, while those who had

reported a history of stoke had 1.42 times the odds of those of those that did not have a prior stroke to have reported short-term memory loss. Females had 1.53 times the odds of males to have experienced memory loss over the 7 days prior to the interview.

Association Between Pesticide Usage and Short Term Memory Loss

After adjusted analysis, we were did not observe an association between in-home pesticide usages and short-term memory loss (OR. 1.12, 95% C.I 0.80-1.57) based on the information that we had available to us. Therefore, we fail to reject the null hypothesis (H_0: $p_1=p_2$) at the 95% confidence level. However, as there are several study weaknesses, as presented below, this conclusion should not be construed as evidence that there is no type of association present.

Study Strengths and Weaknesses

The study has several strengths, including detailed information that was meticulously collected from each study participant in a standardized format. The population of the study was suitably large, and the participants were culled in a randomized fashion using cluster sampling techniques which helps to decrease information bias.

There were also some significant limitations to the study. For one, we were unable to collect data for all ages as not all questions were posed to all age groups. This was especially unfortunate when considering the drug use questions as it has been suggested that substance abuse in the elderly has been on the rise of late. In fact,

researchers from the National Institute on Drug Abuse estimate that as many as 112,000,000 people over the age of 50 will display some type of substance abuse by the year 2020 (Gfroerer, 2015). Data were also missing on specific prescription medication use that can contribute to memory loss, as well as neural diseases such as Dementia and Alzheimer's.

Another major limitation was the possibility of recall bias. As this was a study that relied on questionnaire data, it is possible that some participants did not fully understand the question, had failed to recall recent or prior pesticide usage, or even that they had experienced memory loss regarding applying pesticides. If this occurred, those truly experiencing short-term memory loss could have underreported using pesticides, which would contribute to an underestimate of the association between pesticides and memory loss. In addition, some participants may not have wished to disclose significant alcohol or drug use, regardless of the promised confidentiality.

The way that the exposure information was captured could also be a problem. Capturing only pesticide usage over the last 7 days may not accurately classify the exposure for several reasons. First, some critical windows of exposure may not be captured in these data (e.g., early childhood exposure → adult onset of disease) and use in the past 7 days may not be a good proxy of chronic exposure.

Recommendations and Potential for Additional Studies

To our knowledge, this is one of the only studies to dissect the association between domestic pesticide usage and the occurrence of short-term memory loss. While we were unable to observe that there is any statistically significant association between

in-home pesticide usage and short-term memory loss, future studies could seek to employ a more reliable study design such as a longitudinal, prospective format to rule out the possibility that memory loss affected the reporting of pesticide use, as well as negate some of the other previously mentioned study weaknesses. In addition, the gender category displayed the most statistically significant association ($p=<0.001$), and this would be a ripe topic for additional study opportunities. One possible explanation that deserves additional review is the theory that women typically have a higher percentage of body fat and some pesticides are known to be fat soluble. Therefore, women may have a greater build-up, and subsequent steady release, of these toxins within their bodies.

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FIGURES AND TABLES

Figure 1. Study Inclusion/Exclusion Flowchart

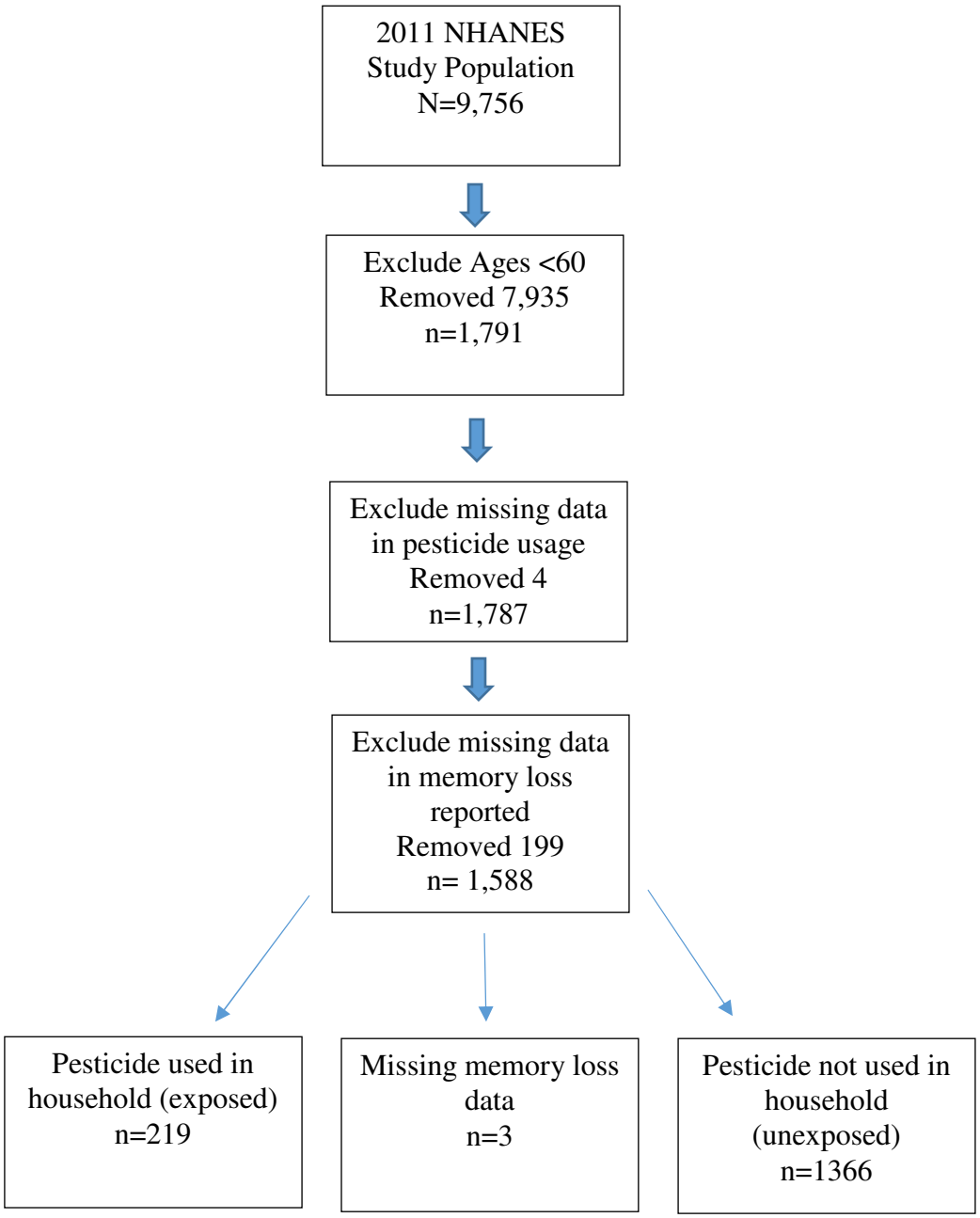

Table 1. Characteristics of Selected Interviewees from 2011-2012 NHANES Survey (Limited to respondents aged 60 and over who answered pesticide usage questions) N=1588

Short term memory loss reported^	Yes n=694	*45.4%*	No n=891	*54.6%*	X^2 (d.f.)*	*p-value*
Age at time of interview					3	*0.04*
60-64	200	*31.4%*	296	*34.6%*		
65-69	139	*20.8%*	192	*22.7%*		
70-74	103	*15.4%*	169	*20.0%*		
75 and over	252	*32.4%*	234	*22.7%*		
Pesticide use in household					1	0.99
Yes	102	*11.0%*	117	*10.9%*		
No	592	*89.0%*	774	*89.1%*		
Missing	3					
Gender						
Male	303	*38.4%*	480	*50.2%*	1	*0.004*
Female	391	*61.6%*	411	*49.8%*		
Missing	3					
History of alcohol use					1	0.7
Yes	455	*71.2%*	561	*70.1%*		
No	233	*28.8%*	323	*29.9%*		
Missing	16					
History of stroke					1	0.21
Yes	73	*8.7%*	65	*5.8%*		
No	620	*91.3%*	824	*94.2%*		
Missing	6					
History of brain cancer					*Not calculated due to 0 value cells*	
Yes	0	*0.0%*	0	*0.0%*		
No	0	*0.0%*	2	*100.0%*		
Missing	1586					
Sleep Disorder					1	*0.77*
Yes	86	*12.4%*	91	*11.5%*		
No	605	*87.6%*	800	*88.5%*		
missing	6					

^ Excludes missing data = 3

* Rao-Scott Chi-square d.f. = degrees of freedom

‡‡ Chi-square test excludes missing data

Table 1.2 Characteristics of Selected Interviewees from 2011-2012 NHANES Survey
(Limited to respondents aged 60 and over who answered pesticide usage questions) N=1588

In-Home Pesticide Usage^	Yes n=219	*10.9%*	No n=1369	*89.1%*	X^2 (d.f.)*	*p-value*
Age at time of interview					3	*0.1*
60-64	66	*30.1%*	430	*31.4%*		
65-69	51	*23.3%*	280	*20.5%*		
70-74	27	*12.3%*	246	*18.0%*		
75 and over	75	*34.2%*	413	*30.1%*		
Reported short-term memory loss					1	0.99
Yes	102	*14.7%*	117	*13.1%*		
No	592	*85.3%*	774	*89.9%*		
missing	3					
Gender					1	*0.78*
Male	115	*52.5%*	668	*48.8%*		
Female	104	*47.5%*	701	*51.2%*		
missing						
History of alcohol use					1	0.33
Yes	144	*67.6%*	874	*64.2%*		
No	69	*32.4%*	488	*35.8%*		
missing	13					
History of stroke					1	0.69
Yes	25	*11.4%*	113	*8.3%*		
No	194	*88.6%*	1253	*91.7%*		
missing	3					
History of brain cancer					*Not calculated due to 0 value cells*	
Yes	0	*0.0%*	0	*0.0%*		
No	0	*0.0%*	2	*100.0%*		
missing	1586					
Sleep Disorder					1	*0.62*
Yes	27	*12.3%*	150	*11.0%*		
No	192	*87.7%*	1216	*89.0%*		
missing	3					

* Rao-Scott Chi-square d.f. = degrees of freedom
‡‡ Chi-square test excludes missing data

Table 2. Unadjusted Associations of Characteristics and Short-Term Memory Loss in Interviewees aged 60 and over the NHANES 2011-2012

		Odds Ratio	*95% C.I.*[†]	p-value*
Pesticide use in household				
	Yes	1.14	(0.82,1.59)	
	No (reference)	1.00	---	0.44
Age at time of interview	60-64 (reference)	1.00	---	
	65-69	0.93	*(0.68,1.27)*	0.66
	70-74	1.11	*(0.84,1.46)*	0.46
	75 and over	0.63	(0.46,0.85)	0.003
Gender	Male (reference)	1.00	---	<0.001
	Female	1.51	*(1.25,1.82)*	
History of alcohol use	No (reference)	1.00	---	0.23
	Yes	1.12	*(0.93,1.36)*	
History of stroke	No (reference)	1.00	---	0.03
	Yes	1.49	*(1.03,2.16)*	
Sleep Disorder	No (reference)	1.00	---	
	Yes	1.25	*(0.85,1.84)*	0.26

[†] C.I. Confidence interval
* Wald Chi-Square p-value

Table 3. Adjusted Associations of Characteristics and Short-Term Memory Loss in Interviewees >60 Years of the NHANES 2011-2012

		Odds Ratio	*95% C.I.†*	p-value*
Pesticide use in household				
	Yes	1.12	(0.80,1.57)	0.52
	No (reference)	1.00	---	
Age at time of interview	60-64 (reference)	1.00	---	
	65-69	1.08	*(0.79,1.48)*	0.63
	70-74	0.90	*(0.68,1.19)*	0.44
	75 and over	1.54	(1.14,2.08)	0.005
Gender	Male (reference)	1.00	---	
	Female	1.53	*(1.26,1.85)*	<0.001
History of stroke	No (reference)	1.00	---	
	Yes	1.42	*(1.00,2.00)*	0.049

† C.I. Confidence interval
* Wald Chi-Square p-value
Note - all variables are adjusted for all other variables in the chart

APPENDIX

SAS CODE

```
*Set up data sets in directories;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\ALQ_G.xpt";
proc copy in=XP out=NH;
run;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\DEMO_G.xpt";
proc copy in=XP out=NH;
run;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\DUQ_G.xpt";
proc copy in=XP out=NH;
run;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\MCQ_G.xpt";
proc copy in=XP out=NH;
run;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\RHQ_G.xpt";
proc copy in=XP out=NH;
run;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\SLQ_G.xpt";
proc copy in=XP out=NH;
run;
libname NH "H:\THESIS\NHANES\DATA";
libname XP xport "H:\THESIS\NHANES\TEMP\PUQMEC_G.xpt";
proc copy in=XP out=NH;
run;

*Check contents of imported data;
libname NH "H:\THESIS\NHANES\DATA";
options ls=72;
proc contents data=NH.DEMO_G varnum;
proc contents data=NH.ALQ_G varnum;
proc contents data=NH.DUQ_G varnum;
proc contents data=NH.MCQ_G varnum;
proc contents data=NH.RHQ_G varnum;
proc contents data=NH.SLQ_G varnum;
proc contents data=NH.PUQMEC_G varnum;
run;

*Sort by SEQN and merge data into one dataset;
libname nh "H:\THESIS\NHANES\DATA";
options ls=72;

proc sort data=NH.DEMO_G;
      by SEQN;
proc sort data=NH.ALQ_G;
      by SEQN;
proc sort data=NH.DUQ_G;
      by SEQN;
```

```
proc sort data=NH.MCQ_G;
      by SEQN;
proc sort data=NH.RHQ_G;
      by SEQN;
proc sort data=NH.SLQ_G
      by SEQN;
run;
proc sort data=NH.PUQMEC_G
      by SEQN;
run;
data NHANES1;
      merge NH.DEMO_G
            NH.ALQ_G
            NH.DUQ_G
            NH.MCQ_G
            NH.RHQ_G
            NH.PUQMEC_G
            NH.SLQ_G;
      by SEQN;
run;
proc contents data=NHANES1 varnum;
proc means data=NHANES1 N Nmiss min max maxdec=2;
run;

*Save data set to permamnent library;
libname NH "H:\THESIS\NHANES\DATA";
data NH.NHANES1;
set NHANES1;
run;
proc contents data=nh.nhanes1 varnum;
run;

*check missing data;
libname NH "H:\THESIS\NHANES\DATA";
proc means data=nh.nhanes1 N nmiss min max;
var RIDAGEYR DUQ270Q DUQ220Q DUQ310Q DUQ350Q;
run;
proc freq data=nh.nhanes1;
table MCQ380 PUQ100 ALQ101 MCQ160f MCQ230a MCQ230b MCQ230c SLQ060
RHD143/list missing;
run;

*recode missing data;
libname NH "H:\THESIS\NHANES\DATA";
data nh.nhanes2;
set nh.nhanes1;
array _nhmiss
MCQ380 PUQ100 ALQ101 DUQ200 MCQ160f SLQ060 RHD143;
do over _nhmiss;
if _nhmiss in (7,9)
then _nhmiss=.;
end;
if DUQ270Q in (7777,9999)
then DUQ270=.;
if DUQ350Q in (7777,9999)
then DUQ350Q=.;
if DUQ310Q in (7777,9999)
```

```
then DUQ310Q=.;
run;
proc freq data=nh.nhanes2;
table MCQ380 PUQ100 ALQ101 MCQ160f MCQ230a MCQ230b MCQ230c SLQ060
RHD143/list missing;
run;


*recode age into catagorical variables age 60-80;
data nh.nhanes3;
set nh.nhanes2;
if (60<=ridageyr<=64)
then age=1;
if (65<=ridageyr<=69)
then age=2;
if (70<=ridageyr<=74)
then age=3;
if (75<=ridageyr<=80)
then age=4;
label age='Age 60-64=1, Age 65-69=2, Age 70-74=3, Age 75-80=4';
run;
proc freq data=nh.nhanes3;
table age;
run;
*add lables;
proc format;
value agef
1="Age 60-64"
2="Age 65-69"
3="Age 70-74"
4="Age 75-80";
run;
proc freq data=nh.nhanes3;
format age agef.;
tables age;
run;

*recode outcome variable to yes / no;
data nh.nhanes3;
set nh.nhanes3;
if MCQ380 = 1 then memory=1;
if MCQ380 = 2 then memory=1;
if MCQ380 = 3 then memory=1;
if MCQ380 = 4 then memory=1;
if MCQ380=0 then memory=0;
if MCQ380=. then memory=.;
label memory='Short-term memory loss over last week (0=no, 1=yes)';
end;
run;
proc freq data=nh.nhanes3;
tables ridageyr*memory;
where ridageyr >=60;
run;


*create category for brain cancer;
data nh.nhanes3;
```

```
set nh.nhanes3;
if (mcq230a=13) then brcanc=1;
if (1 <= mcq230a < 12) then brcanc=0;
if (14 <= mcq230a < 66) then brcanc=0;
if (mcq230a=.) then brcanc=.;
if (mcq230b=13) then brcanc=1;
if (1 <= mcq230b < 12) then brcanc=0;
if (14 <= mcq230b < 66) then brcanc=0;
if (mcq230b=.) then brcanc=.;
if (mcq230c=13) then brcanc=1;
if (1 <= mcq230c < 12) then brcanc=0;
if (14 <= mcq230c < 66) then brcanc=0;
if (mcq230c=.) then brcanc=.;
label brcanc='Brain Cancer (0=no, 1=yes)';
end;
run;

*Run descriptive statistics for table 1 demographics;
Proc surveyfreq data=nh.nhanes3;
cluster sdmvpsu;
tables age /CL (type=wilson) var DEFF;
run;

*keep only data for specified age groups 60-80 y/o and pesticide usage;
data nh.nhanes4;
set nh.nhanes3;
if age ^= .;
if puq100 ^=.;
run;
proc freq data=nh.nhanes4;
tables age/missing;
run;
proc freq data=nh.nhanes4;
tables puq100/missing;
run;

*recode sleep disorder to 0 and 1;
data nh.nhanes4;
set nh.nhanes4;
if slq060=2 then sleep=0;
if slq060=1 then sleep=1;
if slq060=. then sleep=.;
if slq060=7 then sleep=.;
if slq060=9 then sleep=.;
label sleep='Sleep Disorder (0=no, 1=yes)';
run;
proc freq data=nh.nhanes4;
tables sleep*memory;
run;

*check for outliers and distribution;
proc univariate data=nh.nhanes4 plot normal;
id seqn;
var ridageyr;
run;

*obtain data for table 1 descriptive statistics;
```

```
Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory /CHISQ CL(TYPE=WILSON);
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*PUQ100/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*age/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF) RISK1
OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*alq101/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*mcq160f/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*brcanc/CHISQ CL(TYPE=WILSON);
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*RIAGENDR/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF);
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
```

```
tables memory*SLQ060/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables memory*sleep/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF) RISK1
OR;
run;

*obtain data for table 1.2 descriptive statistics;
Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables puq100 /CHISQ CL(TYPE=WILSON);
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables PUQ100*memory/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables PUQ100*age/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF) RISK1
OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables PUQ100*alq101/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables puq100*mcq160f/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF)
RISK1 OR;
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables puq100*brcanc/CHISQ CL(TYPE=WILSON);
```

```
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables puq100*RIAGENDR/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF);
run;

Proc surveyfreq data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
Weight Wtint2yr;
tables PUQ100*sleep/NOCELLPERCENT CHISQ CL(TYPE=WILSON) ROW(DEFF) RISK1
OR;
run;


*calculate crude odds ratio;
proc surveylogistic data=nh.nhanes4;
class puq100 (ref='2')/param=ref;
stratum sdmvstra;
cluster sdmvpsu;
model memory (event='1') = puq100;
run;

*run automated regression to review and eliminate interaction terms if
non-significent;
proc logistic data=nh.nhanes4 descending;
class age (ref='1')/param=ref;
class sleep (ref='0')/param=ref;
class alq101 (ref='2')/param=ref;
class puq100 (ref='2')/param=ref;
class mcq160f (ref='2')/param=ref;
model memory=puq100 age sleep alq101 mcq160f riagendr puq100*age
puq100*alq101 puq100*mcq160f puq100*sleep puq100*riagendr /backward
include=6;
run;
*no significent interactions - will drop all from final model;


*check associations of covariates with outcome - bivariate - table 2;
proc surveylogistic data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
class age (ref='1')/ param=ref;
model memory = age/clparm vadjust=none;
run;

proc surveylogistic data=nh.nhanes4;
class alq101 (ref='2')/param=ref;
stratum sdmvstra;
cluster sdmvpsu;
model memory (event='1')= alq101 /clparm vadjust=none;;
run;

proc surveylogistic data=nh.nhanes4;
```

```
stratum sdmvstra;
cluster sdmvpsu;
model memory (event='1')= riagendr /clparm vadjust=none;;
run;

proc surveylogistic data=nh.nhanes4;
class mcq160f (ref='2')/param=ref;
stratum sdmvstra;
cluster sdmvpsu;
model memory (event='1')= mcq160f /clparm vadjust=none;
run;

proc surveylogistic data=nh.nhanes4;
class puq100 (ref='2')/param=ref;
class sleep (ref='0')/param=ref;
stratum sdmvstra;
cluster sdmvpsu;
model memory (event='1')= sleep/clparm vadjust=none;
run;

proc surveylogistic data=nh.nhanes4;
class puq100 (ref='2')/param=ref;
stratum sdmvstra;
cluster sdmvpsu;
model memory (event='1')= puq100/clparm vadjust=none;
run;

*check associations with outcome - multivariate - access confounding -
Table 3 - also final model;
proc surveylogistic data=nh.nhanes4;
stratum sdmvstra;
cluster sdmvpsu;
class puq100 (ref='2')/param=ref;
class age (ref='1')/ param=ref;
class mcq160f (ref='2')/param=ref;
model memory (event='1')= puq100 riagendr mcq160f age/clparm
vadjust=none;
run;
```