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Alcohol effects on Cognitive Change in Middle-Aged and Older Adults

#### Abstract

13 **Objectives:** This study examines cognitive outcomes for alcohol drinking status over time, 14 across cognitive ability and age groups. Methods: Data (1998-2005) from N=571 Seattle 15 Longitudinal Study participants age 45+years (middle-aged: 45-64, young-old: 65-75, old-old: 16 (75+) were analyzed to examine the alcohol drinking status effect (e.g. abstinent, moderate (<717 drinks/week), at-risk (>8 drinks/week)) on cognitive ability (e.g., Memory, Reasoning, Spatial, Verbal Number, Speed abilities). **Results**: Findings indicated that alcohol drinking status was 18 19 associated with change in verbal ability, spatial ability, and perceptual speed. Decline in verbal 20 ability was seen among alcohol abstainers and moderate alcohol consumers, but at-risk drinkers 21 displayed relative stability. At-risk old-old adults and middle-aged adults (regardless of drinking 22 status), displayed relative stability in spatial ability. Decline in spatial ability was however 23 present among young-old adults across drinking status, and among abstaining and moderate 24 drinking old-old adults. At-risk drinkers showed the most positive spatial ability trajectory. A 25 gender effect in perceptual speed was detected, with women who abstained from drinking 26 displaying the most decline in perceptual speed compared with women that regularly consumed 27 alcohol, and men displaying decline in perceptual speed across drinking status. **Discussion**: In 28 this study, consuming alcohol is indicative of cognitive stability. This conclusion should be 29 considered cautiously, due to study bias created from survivor effects, analyzing two time points, 30 health/medication change status, and overrepresentation of higher socioeconomic status and 31 white populations in this study. Future research needs to design studies that can make concrete 32 recommendations about the relationship between drinking status and cognition.

**33 Key words**: alcohol, cognition, aging

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#### Alcohol effects on Cognitive Change in Middle-Aged and Older Adults

#### **36 INTRODUCTION**

Adults are recommended to reduce alcohol consumption as they age. This 37 38 recommendation stems from a decrease in endogenous water levels in which to dilute alcohol, 39 leading to a higher blood alcohol concentration in older adults compared to younger adults after 40 consuming the same amount of alcohol (Dufour, Archer, & Gordis, 1992). For both men and 41 women it has been suggested that individuals aged 65 and over should, on average, consume no 42 more than one drink a day (Blow, 2004; National Institute on Aging, 2012; National Institute on 43 Alcohol Abuse and Alcoholism, 1992). In addition, compared to younger adults, older adults can 44 unknowingly become more impaired when consuming similar doses of alcohol (Gilbertson, Ceballos, Prather, & Nixon, 2009). 45 46 Interestingly, there is evidence for alcohol having a positive effect on multiple health 47 outcomes (Sun et al., 2011). Specifically, multiple studies have shown that moderate alcohol 48 consumption (approximately 1 drink/day) protects cognition in aging adults, compared to 49 abstinent or excessive alcohol usage (Ganguli, Vanderbilt, Saxton, Shen, & Dodge, 50 2005;Rodgers, et al, 2005). Moderate alcohol use also appears to reduce the risk of late life 51 dementia and cognitive impairment (Chan, Chiu, & Chu, 2010; Solfrizzi et al., 2007; Weyerer et 52 al., 2011).

Alcohol consumption has been speculated to affect cognition through its association with
higher levels of high-density lipoprotein (HDL), increased sensitivity to insulin over time
(Kiechl et al., 1998), increased cerebral blood flow (CBF; Sano et al., 1993), and evidence for an
anti-inflammatory function (Albert, Glynn, & Ridker, 2003; Imhof et al., 2004). Collectively,
these factors affect the risk of atherosclerosis, which is linked to progressive neurodegeneration

(Yi et al., 2009). Additionally, the anti-inflammatory function of alcohol can decrease chronic
cerebral inflammation (McGeer & McGeer, 1999). Together, increased cerebral blood flow and
decreased inflammation reduces cognitive decline through reducing the risk of vascular
pathology and neurodegeneration (Panza et al., 2008).

62 Contrary to findings indicating beneficial effects of moderate alcohol consumption in 63 older adults, excessive drinking can be very dangerous. Consuming too much alcohol can lead to 64 accelerated neurodegeneration (Cairney, Clough, Jaragba, & Maruff, 2007; Chan et al., 2010). Excessive alcohol consumption can also have negative interactions with medications commonly 65 66 used by older adults and is a major risk factor for prescription drug misuse (Culberson & Ziska, 67 2008; McCabe, Cranford, & Boyd, 2006; Onder et al, 2002; Simoni-Wastila & Strickler, 2004). 68 Older adults are actually hospitalized for alcohol-related complications as often as for 69 myocardial infarctions and medication overdoses in older adults are commonly associated with 70 alcohol (Dukes, Robinson, Thomson, & Robinson, 1992; Finkle, McCloskey, Kiplinger, & 71 Bennett, 1976; Ødegård & Rossow, 2004). Excessive alcohol and prescription drugs can: a) 72 undermine the treatment of existing disorders, b) lead to unintentional injuries and consequences 73 (i.e. falls, cognitive impairment, medical complexities), c) lead to fatal alcohol-drug interactions; 74 and d) and increase morbidity and mortality, and health costs in older adults (Barry, Gallagher, & 75 Ryan, 2008; Finlayson, 1995; Larson, Kukull, Buchner, & Reifler, 1987; Philips, Barker, & Eguchi, 2008). 76

Another wrinkle that needs to be considered is that there is an association between
gender, cognition, and alcohol consumption indicating that consuming moderate amounts of
alcohol is potentially beneficial for women (Dufouil, Ducimetiere, & Alperovitch, 1997; Elias et
al., 1999; Forette et al., 1998; Onland-Moret et al., 2005; Wise et al., 2001). While not fully

understood, gender differences in alcohol associations may be attributed to differences in
hormone levels. Women who consume alcohol have elevated levels of estrogen (Gavaler &
Love, 1992; Onland-Moret, Peeters, van der Schouw, Grobbee , & van Gils, 2005); estrogen has
been controversially associated with cognition in women (Wise, Dubal, Wilson, Rau, & Liu,
2001), but more recent hormone replacement trials have indicated an increased risk for dementia
(Coker, et al., 2010). Accordingly there is a need to better understand how alcohol consumption
differently affects cognition across gender.

Unfortunately, clear-cut alcohol consumption recommendations pertaining to cognitive 88 89 outcomes cannot be made due to research being limited by several factors, such as cross-90 sectional designs (Cooper et al., 2009), inclusion of men only (Gross et al., 2011), inclusion of 91 women only (Espeland et al., 2006; Stampfer et al., 2005), gender variance (findings not 92 consistent across gender) (McGuire, Ajani, & Ford, 2007; Stott et al., 2008), global cognitive 93 measurements (Bond et al., 2005; Galanis et al., 2000), and mixed or unsupportive findings 94 (Panza et al, 2009; Townsend, Devore, Kang, & Grodstein, 2009). Clear evidence for alcohol 95 and cognition guidelines should ideally be consistent across gender, across cognitive 96 measurement, and be longitudinally based. Despite the evidence supporting moderate alcohol 97 consumption as a means to prevent cognitive decline and dementia, relatively little is known 98 about the effects of alcohol on specific cognitive domains (Gross et al., 2011). Given the benefits 99 of moderate alcohol consumption and the risks of excessive drinking, the interplay among 100 alcohol use, cognition, and aging requires further study to formulate a more crystallized 101 understanding of the effect alcohol consumption has on cognitive health outcomes (Chiu, 2008; 102 Panza et al, 2009; Peters, Peters, Warner, Beckett, & Bulpitt, 2008).

103 This study will advance current knowledge by considering the developmental aging 104 perspective and examining the effects of alcohol consumption on cognition over time 105 (longitudinally) and across age groups (Anstey, 2008; Schaie, 2009). Cognitive level differences 106 that exist between middle age (45-65 years of age) and late life need to be better understood as 107 indicated by age-based associations with cognition (Cherbuin et al., 2009; Järvenpää, Rinne, 108 Koskenvuo, Räihä, & Kaprio, 2005; Lang, Wallace, Hupper, & Melzer, 2007;). Furthermore, this 109 study will examine effects across cognitive abilities, considering that distinct cognitive domains 110 do not change unilaterally with aging (Schaie, 2005). For example, perceptual speed is one of the 111 first cognitive abilities to decline, while verbal ability remains steadfast until much later in life, 112 at which very modest declines occur. Finally, alcohol and cognition associations with gender will 113 also be considered due to speculation about a gender-based relationship between alcohol and 114 cognition (Dufouil et al, 1997; Elias et al., 1999; Forette et al., 1998; Onland-Moret et al., 2005; 115 Wise et al., 2001). Accordingly, the objective of this study is to evaluate the relationship between 116 cognitive change and alcohol consumption across abilities and age: middle-aged adults (46-64 117 years old), young-old adults (65-74 years old), and old-old adults (75+ years of age) and gender, 118 using a longitudinal design. Differences in cognitive change will be examined among a) alcohol 119 abstainers, b) moderate alcohol consumers (<7 drinks/week), and c) at-risk alcohol consumers 120  $(\geq 8 \text{ drinks/week})$ , considering the effects of age and gender.

#### 121 METHODS

The study sample (N = 571) contained adults age 45+ years participating in the 1998 and 2005
waves of the Seattle Longitudinal Study (SLS). The 1998 and 2005 waves were selected because

124 alcohol consumption patterns and cognitive data were collected simultaneously. The SLS

125 database consists of psychological assessments conducted during seven major testing cycles

126 (1956, 1963, 1970, 1977, 1984, 1991, 1998, and 2005). Written consent was acquired during 127 each wave with the understanding that all research data would remain unidentified. 128 Approximately 6000 people have now participated at some time in this study. Of the original 129 participants, 26 people remain who have now been in the study for 50 years. Current participants 130 range in age from 22 to 101 years. Throughout its course, SLS has lost participants to attrition, 131 resulting in the overrepresentation of people with better cognitive performance and good health. 132 No statistical methodology was implemented to account for attrition/missing data. All 133 participants were members of the Group Health Cooperative health maintenance organization of 134 Puget Sound in Washington State at the time they entered into the study. At each interval, all 135 persons who had previously participated were asked to participate in subsequent waves. Potential 136 participant were randomly selected using a sampling-with-replacement methodology within the 137 420,000 member organization. The research interviews took place in an in-person group setting 138 for cognitive assessments (using a classroom testing approach), with a mail-in homework 139 component for supplement surveys. A more detailed description of the SLS is available in a 140 previous publication (Schaie, 2005).

#### 141 Measurement Variables

Participants assessed in 1998 (Time 1) and 2005 (Time 2) were given an extensive assessment
test battery from which alcohol consumption, cognitive ability, and demographic measurements
were extracted.

Alcohol Consumption: Alcohol consumption was calculated from the sum of three open-ended
questions assessed in the SLS Health Behavior Questionnaire: 1) How many GLASSES OF
WINE did you drink last week?; 2) How many BOTTLES OR CANS OF BEER did you drink
last week?; and 3) How many drinks containing HARD LIQUOR did you drink last week?

149 Having three individual alcohol questions can reduce the common practice of underreporting 150 alcohol consumption (Ekholm, Strandberg-Larsen, & Grønbæk, 2011). Furthermore, a one-week 151 recall period is a valid and reliable time frame for alcohol recall (Dawson, 2003). Accordingly, 152 the number of total drinks was categorized into drinking status categories: 1) Alcohol abstainer: 153 no alcohol consumed, 2) Moderate alcohol consumer: no more than 7 drinks/week, and 3) At-154 risk alcohol consumers: more than 7 drinks/week (Blow, 2004; National Institute on Aging, 155 2012; National Institute on Alcohol Abuse and Alcoholism, 1992). Alcohol consumption 156 classifications were equivalent across gender and age. 157 Cognitive Ability: Twenty-nine cognitive ability scores were transformed into six standardized 158 cognitive domain scores; mean score = 50, standard deviation = 10. The cognitive domains were 159 based on Thurstone Primary Mental Abilities (Thurstone, 1962; Thurstone & Thurstone, 1949). 160 The cognitive battery was then expanded and transformed using structural equational modeling 161 to represent latent variables for memory, reasoning, spatial, verbal, numeric, and perceptual 162 speed abilities using well-validated instruments (Schaie, 2005). Transitioning from an observed 163 to a latent variable was done to create more stabilized cognitive constructs. Details on the 164 structural analysis and individual instruments are available in Schaie, 2005. Briefly described, 165 the targeted cognitive domains are: 166 Memory Ability - memorization and recall of meaningful language units. (Measured by: Immediate Recall (Zelinski, Gilewski, & Schaie, 1993), Delayed Recall (Zelinski, Gilewski, & 167 168 Schaie, 1993), and Primary Mental Abilities (PMA) Word Fluency (Thurstone & Thurstone, 169 1949)) 170 *Reasoning Ability* - recognize and understand novel concepts or relationships; solve logical

171 problems, and foresee and plan. (Measured by: PMA Reasoning (Thurstone & Thurstone, 1949),

- 172 Adult Development and Enrichment Project (ADEPT) Letter Series (Blieszner, Willis, & Baltes,
- 173 1981), Word Series (Schaie, 1985), and Number Series (Thurstone, 1962))
- 174 *Spatial Ability* visualize and mentally manipulate spatial configurations in two or three
- dimensions, maintain orientation with respect to spatial objects, and perceive relationships
- among objects in space. (Measured by: PMA Space (Thurstone & Thurstone, 1949), Object
- 177 Rotation (Quayhagen, 1979; Schaie, 1985), Alphanumeric Rotation (Willis & Schaie, 1983), and
- 178 Cube Comparison (Ekstrom et al., 1976))
- 179 Verbal ability understand ideas expressed in words. (Measured by: PMA Verbal Meaning
- 180 (Thurstone & Thurstone, 1949), Educational Testing Service (ETS) Vocabulary V-2 (Ekstrom et
- 181 al., 1976), and ETS Vocabulary V-4 (Ekstrom et al., 1976))
- 182 *Numeric ability* understand numerical relationships, work with figures, and solve simple
- 183 quantitative problems rapidly and accurately. (Measured by: PMA Number (Thurstone &
- 184 Thurstone, 1949), Addition (Ekstrom et al., 1976), and Subtraction & Multiplication (Ekstrom et al., 1976))
- 186 *Perceptual speed* find figures, make comparisons, and carry out simple tasks involving visual
- 187 perception with speed and accuracy. (Measured by: Identical Pictures (Ekstrom et al., 1976),
- 188 Findings As (Ekstrom et al., 1976), and Number Comparison (Ekstrom et al., 1976))
- 189 *Demographics*: Age, gender, education, and income were obtained from the 1998 self-report
- 190 SLS: Life Complexity Inventory Questionnaire, and smoking status from the SLS: Health
- 191 Behavior Questionnaire.

#### **Data analysis**

- 193 Twelve linear mixed models were analyzed in SAS 9.1 (Time x Drinking Status x Age and Time
- 194 x Drinking Status x Gender) for each cognitive domain: memory, reasoning, spatial, verbal,

195 numeric, and speed). The models included Time (2 levels: 1998, 2005), Drinking Status (3 196 levels: abstinent, moderate, at-risk), and Age-group (3 levels: middle-aged, young-old, old-old) 197 or Gender (2 levels: male, female) as independent variables. Age was treated as a categorical 198 variable to make distinctions and detect patterns across age group instead of creating 199 implications for 50 age categories (Nagin, 1999), as indicated by the age range of study 200 participants. Existing literature has determined education, income and smoking have significant 201 effects on drinking status (Dufouil et al, 1997; Gavaler et al., 1992; Hellwig, 2011; Kawas et al., 202 1997; Onland-Moret et al., 2005; Schmidt et al., 1996; Wise et al., 2001). Therefore, analyses 203 controlled for these factors in addition to gender and age group and baseline drinking levels 204 (beer, wine, and liquor) to account for within drinking category variation in alcohol consumed. 205 To assess the gender effect for drinking status, linear mixed models were conducted with time, 206 drinking status, and gender serving as independent variables (while still controlling for age-207 group, education, income, and drinking levels), and smoking status. In all analyses, the cognitive 208 domains served as the dependent variables.

#### 209 **RESULTS**

210 <u>Sample characteristics</u>:

The 1998 sample (N=839) consisted of 371 males (44%), with a mean age of 67.44 years (range 45-94). Forty-two percent were middle-aged adults (46-64 years of age), 25% young-old adults (65-74 years of age), and 33% old-old adults (75+ years of age). Between 1998 and 2005, 68% (N=571) of the 1998 sample returned for the 2005 follow-up. Sample differences indicated that the returning sample was less likely to never drink (41% vs. 53%; p=.0055) and reported higher consumption of wine (1.1 vs. 1.8 glasses of wine/week; p=.0023) and proportion of wine consumed, compared to total alcohol consumption (0.21 vs. 0.31; p=.0008) in 1998. The returning sample was also younger (73.8 vs. 64.7 years of age; p=.0001), with more education
(15 vs. 16 years; p=.0001) and income (\$39,199 vs. \$48,749; p=.0001), and higher cognitive
abilities across all domains (p<.0001).</li>

221 Table 1 depicts 1998 demographic characteristics across drinking status for the study 222 sample. There were significant differences (p < .05) for all variables across drinking status, with 223 the exception of smoking status. Abstainers were older and reported less income and education, 224 and there were fewer female at-risk alcohol consumers. As expected, amount of alcohol 225 consumed was significantly greater for the at-risk group across drinking variables. For the 226 moderate drinking group (N=252), the median level of drinking was 3 drinks, the mode was 1 227 drink, with 25% quartile reporting 1 drink and 75% quartile reporting 5 drinks. For the at-risk 228 drinking group (N=82), the median level of drinking was 12.5 drinks, the mode was 8 drinks, 229 with 25% quartile reporting 9 drinks and 75% quartile reporting 17 drinks. Cognition levels were 230 significantly ( $p \le .05$ ) different across drinking categories, with the exception of Time 2 memory 231 ability, with abstainers generally reporting lower cognitive performance (Table 2).

#### 232 <u>Cognitive Effects</u>:

The linear mixed models (Table 3) indicated that there is a significant Time x Drinking status effect for verbal ability ( $F_{(2, \text{ within groups df})} = 3.10$ ; p = .0459), Time x Age group x Drinking status effect for spatial ability ( $F_{(4, \text{ within groups df})} = 2.92$ ; p = .0208), and Time x Gender x Drinking status effect on perceptual speed ( $F_{(2, \text{ within groups df})} = 4.84$ ; p = .0083). No other significant effects were identified.

Time x Drinking status interaction indicated the greatest degree of decline in verbal
ability was seen among alcohol abstainers (Differences of Least Squares Means estimate (est.) =
1.5421; SE = 0.2299; df= 539; p < .0001), followed by moderate alcohol consumers ((est.=</li>

241 1.1830; SE = 0.2407; df = 539; p < .0001) see Figure 1). At-risk drinkers showed relative stability 242 in verbal ability (est. = 0.3350; SE = 0.4306; df= 539; p = .4370). Ad-hoc analyses identified 243 significant differences in change over time between alcohol abstainers and at-risk drinkers ( $F_{(1)}$ 244 within groups df = 6.16; p = .0136), with abstainers showing more decline. 245 Time x Age group x Drinking status effects on spatial ability (see Figure 2) indicated 246 relative stability in spatial ability in middle-aged adults, across drinking status (abstainers: est. = 247 -0.6239; SE = 0.4847; df= 539; p = .1986; moderate drinkers: est. = 0.5144; SE = 0.4258; df= 248 539; p = .2275; at-risk drinkers: est. = 0.9236; SE = 0.7402; df= 539; p = .2126). There was 249 spatial ability decline in young-old adults across drinking status (abstainers: est. = 3.4527; SE = 250 0.6174; df= 539; p <.0001; moderate drinkers: est. = 1.7330; SE = 0.6628; df= 539; p = .0092; 251 at-risk drinkers: est. = 3.4151; SE = 1.1651; df= 539; p = .0035). In old-old adults, there was 252 decline among abstainers (est. = 3.4972; SE = 0.6446; df= 539; p < .0001) and moderate drinkers 253 (est. = 4.5655; SE = 0.7157; df= 539; p < .0001), but no detectable change among at-risk drinkers 254 for spatial ability (est. = 1.6224; SE = 1.3064; df = 539; p = .2148). Ad-hoc analyses identified 255 significant differences in change over time between young-old alcohol abstainers and moderate drinkers ( $F_{(1, \text{ within groups df})} = 3.86$ ; p = .0517), with abstainers showing more decline in spatial 256 257 ability. In addition, ad-hoc analyses identified significant differences in change over time 258 between old-old moderate and at-risk drinkers ( $F_{(1, \text{ within groups df})} = 4.46$ ; p = .0390), with 259 moderate drinkers showing more decline in spatial ability. 260 Time x Gender x Drinking status effect on perceptual speed (Figure 3) indicated 261 perceptual speed remained stable for women with at-risk drinking status, but declined for the

263 drinkers: est. = 2.1230; SE = 0.3871; df=542; p < .0001; at-risk drinkers: est. = 0.5580; SE =

other drinking categories (abstainers: est. = -3.2427; SE = 0.3744; df = 542; p < .0001; moderate

0.9150; df= 542; p = .5422). On the other hand, men's cognitive ability declined across drinking status (abstainers: est. = 1.9079; SE = 0.4887; df= 542; p =.0001; moderate drinkers: est. = 2.5570; SE = 0.4409; df= 542; p < .0001; at-risk drinkers: est. = 2.8811; SE = 0.6168; df= 542; p < .0001). Ad-hoc analyses identified significant differences in change over time between female alcohol abstainers showing more decline in perceptual speed compared with both moderate drinkers ( $F_{(1, within groups df)} = 4.36$ ; p = .0378) and at-risk drinkers ( $F_{(1, within groups df)} = 9.06$ ; p = .0030).

271 **DISCUSSION** 

272 In the current study alcohol consumption was linearly associated with decline in verbal 273 ability over time such that abstainers showed the greatest decline, moderate drinkers showed less 274 decline, and at-risk drinkers showed relative stability. A similar pattern for alcohol consumption 275 was found for spatial ability, with middle-aged adults remaining stable, regardless of drinking 276 status, while young-old adults' spatial ability declined across drinking status, and old-old adults 277 spatial ability was relatively stable among at-risk drinkers. In addition, while previous studies 278 have reported a greater protective effect of alcohol consumption on cognition among women in 279 cross-sectional (Dufouil et al., 1997; Elias et al., 1999; Forette et al., 1998; Onland-Moret et al., 280 2005) and longitudinal studies (McGuire et al., 2007; Stott et al, 2008), in the current study there 281 was only evidence that alcohol consumption was connected with less decline in perceptual speed 282 among at-risk drinking women, an effect not previously seen in the literature. Surprisingly, 283 across models there was no significant alcohol effect for memory, reasoning, and number 284 abilities.

Based on the results from the current study, the consumption of over 7 alcohol
drinks/week is positively related to verbal and spatial ability performance in older adults. Also

287 alcohol consumption appears to be positively related to perceptual speed in women. Findings 288 indicate a stronger relationship between alcohol consumption and cognition exists in older 289 adults, compared to their younger counterparts. These findings cannot be extended to memory, 290 reasoning, and number abilities. The mix in effects on various cognitive domains may be due to 291 the structural and functional heterogeneity (Tisserand et al., 2002) of the frontal lobe. Verbal 292 ability (Frey et al., 2008), spatial ability (Ganis et al., 2004), perception (Roca et al., 2009), 293 reasoning (Greene and Haidt, 2002), and numeric ability (Pesenti, Thioux, Seron & De Volder, 294 2000) are each performed in highly localized regions of the frontal lobe (Duncan & Owen, 295 2000). This localization may explain why certain functions are affected by alcohol while others 296 remain unaffected (Moselhy et al., 2001). The current study also did not find evidence that 297 alcohol consumption is related to memory. This finding may be due to the Time 2 cohort being 298 significantly younger than the Time 1 cohort (73.8 vs 64.7 years of age; p=0.0001), considering 299 that significant changes in memory do not typically manifest until 70 years of age or older 300 (Aartsen et al., 2002).

301 These results must be interpreted with some of the caveats that accompany studies 302 examining alcohol consumption effects on cognitive functioning over time among older adults. 303 For example, preserved spatial ability for at-risk drinkers, compared to moderate drinkers or 304 abstainers in old-old adults seen in the current study may indicate a survivor effect. Individuals with poorer spatial ability who engaged in at-risk drinking behaviors may have dropped out of 305 306 the study due to complications associated with their greater alcohol consumption (De Labry et 307 al., 1992). Such differential dropout would leave only the healthiest (both physically and 308 cognitively) old-old at-risk drinkers, because the drinkers with poor cognitive trajectories may be 309 deceased or too disabled to participate. Another limitation to this study that needs to be

considered is that only two data collection points (1998 and 2005) assessed alcohol consumption
patterns and cognition simultaneously. It is difficult to make definitive conclusions based on the
analysis of two time points (Singer & Wilett, 2003). Also any relationship between alcohol and
cognitive benefits is curvilinear, with cognition worse among chronic alcoholics over time
(Cairney, et al., 2007; Chan et al., 2010).

315 Along with the challenge of differentiating a survivor effect from a true consequence of 316 alcohol consumption, other explanations should be considered. One such explanation for the 317 alcohol-cognition effect can be a positive neuro-physiological response on cognition due to 318 alcohol consumption reducing vascular risk factors (Albert et al, 2003;Imhof et al., 2004; Kiechl 319 et al., 1998; McGeer et al, 1999; Panza et al., 2008; Sano et al., 1993; Yi et al., 2009). Another 320 explanation to consider for the alcohol-cognition effect is the positive correlation between 321 alcohol consumption and social activity (Menon et al., 2010). Older adults with higher cognitive 322 function are likely to remain engaged in social activities (Murphy et al., 2007) which may 323 involve alcohol consumption, leading such individuals to drink more than those with declining 324 cognition that withdraw from social activities (James et al., 2011). Evidence has indicated that 325 social drinkers (i.e., persons that consume alcohol while in the presence of others; Spijkerman et 326 al., 2010) are at a decreased risk for cognitive decline (Leroi et al., 2002) and many types of 327 dementias (for a review, see Neafsey & Collins, 2011). Alternatively, the positive cognitive 328 effect could be an artifact of older adults with better cognition simply having a tendency to 329 consume more alcohol than older adults with poorer cognition (Cooper et al., 2009). These 330 plausible explanations require future controlled studies in both laboratory and community 331 settings to determine the exact mechanism for the alcohol-cognition relationship.

332 Despite the contribution this study makes to the science of alcohol on cognitive function, 333 it is limited by several factors. The majority of participants were White and had high levels of income and education, representing the upper 75<sup>th</sup> tier of income in the US (Schaie, 2005). 334 335 Accordingly, it is unclear how the current study's findings would translate to sample populations 336 with lower income, less education, and/or different races. Additionally, because the average 337 annual income of participants was well above the poverty line (Federal Register, 1998), it is 338 likely that results were attenuated by the shielding effect of affluence on mental and physical 339 health (Kitagawa & Hauser, 1973). Future research should assess the interplay among aging, 340 alcohol drinking status, and cognition among populations with greater educational, economic, 341 and racial diversity.

342 Finally it is important to consider the reliability of the self-reporting of alcohol. While 343 most research points to the fact the self-reported alcohol consumption is a reliable method for 344 detecting drinking patterns (Chu, et al., 2010; Dawson, 2003; Ekholm, et al., 2011), research also 345 indicates that past-week alcohol recall as measured in this study is not as reliable for sporadic 346 drinkers (Gmel & Daeppen, 2007). For example, asking about drinks a week does not 347 differentiate between drinkers that consume 1 drink a day compared to individuals that consume 348 the same quantity over 1-2 days or even those that did not have a drink during the last week 349 because they drink certain weeks of a month (e.g. pay weeks) or the year (e.g. weddings). Future 350 studies should incorporate methodologies for tracking sporadic, irregular, or binge alcohol 351 consumers to elucidate the alcohol and cognition relationship and associated health outcomes. It 352 is also important to consider the limitations of the snapshot of alcohol measurement approach utilized in the current study does not account for change in lifetime drinking patters caused by 353 354 life events such as health incidents and medications (Molander, Yonker, & Krahn, 2010).

Research indicates that for the most part drinking patterns remain consistent, with heavy drinkers more likely to decline their drinking levels, with abstinent and moderate drinkers remaining abstinent and moderate respectively throughout their lifespan (Molander, Yonker, & Krahn, 2010). In the current study, lifetime drinking patterns and health/medication was not considered. Accordingly future studies should incorporate the measurement of lifetime drinking patters, including accounting for changes in health status and medications to achieve a more accurate understanding of individual drinking level status.

362 Furthermore, the at-risk criteria (consuming more than 7 drinks/week) used in this study 363 is quite conservative and can classify a range of individuals (Moore, et al., 2011). For example, 364 the at-risk criteria in this study places individuals that report drinking 8 drinks in the last week 365 and those that report consuming 33 drinks in the last week in the same category. Typically 366 someone that consumes 8 drinks a week compared to someone that consumes 33 drinks can be 367 quite different, but not so much difference between someone that reports consuming 7 drinks 368 compared to 8 drinks in the last week. However in the current study, drinking levels were 369 significantly different (p<.05) across groups with mean drinking levels for moderate drinkers 370 being 3 drinks in the last week (s.d. = 2; range 1-7) and for at-risk drinkers being 14 drinks in the 371 last week (s.d. = 6; range 8-33). Further, analysis in this study controlled for within drinking 372 category ranges, by accounting for number of drinks. Future studies should examine variations in 373 at-risk drinking levels on cognitive outcomes; however a sufficient sample size of at-risk 374 drinkers will need to be recruited to examine the relationship.

Even with acknowledging the inherent challenges, this study contributes significantly to a growing body of research examining alcohol and cognition. In this study, there was evidence of cognitive stability in certain domains, among older adults that consumed alcohol. This study is

378 one of very few longitudinal studies assessing the effects of alcohol consumption in several 379 cognitive ability domains across age groups and gender. Longitudinal studies such as this study 380 can enlighten findings that may be missed or wrongly identified in cross-sectional research. For 381 instance, cross-sectional studies can only provide evidence for group differences, whereas 382 longitudinal work provides insights about actual change, and the factors that can affect change 383 across groups. The strength of the current study rests in the large sample of community-dwelling, 384 middle aged and older adults who have been followed over time to assess changes in behavioral 385 patterns and cognitive performance. Given the expenses and complications associated with 386 longitudinal research (Ruspini, 2002; Schaie, 2005), such well-characterized samples are limited. 387 Also, breaking down and investigating cognition by domain was extremely important. In this 388 study interestingly there was evidence that alcohol consumption is related to verbal, spatial, and 389 perceptual speed, but not memory, reasoning, and number abilities.

Given the inconsistent nature of the evidence for a protective effect of alcohol
consumption on older adults' cognition, firm recommendations for alcohol consumption among
older adults cannot be determined with the current evidence. Recommendation cannot be made
due to the inherent difficulty in detecting a causal relationship, due to bias created from survivor
effects, analyzing two time points, not considering health/medication status, and
overrepresentation of higher socioeconomic status and white populations in this study. Based on
the results in the current study, having more than 7 alcoholic drinks a week may be connected to

397 decreasing cognitive decline in old-old adults. However, further longitudinal and experimental

investigation is required to support this finding prior to making public health recommendations.

399

#### **400 Total Word Count**: 4700

402 **References** 

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404 Adams, W., Yuan, Z., Barborial, J.J., & Rimm, A.A. (1993). Alcohol-related hospitalizations of
405 elderly people. *Journal of the American Medical Association*, 270, 1222-1225.

406 Albert, M.A., Glynn, R.J., & Ridker, P.M. (2003). Alcohol consumption and plasma

407 concentration of C-reactive protein. *Circulation*, *107*(3), 443-447.

- 408 Alzheimer's Association (2010). 2010 Alzheimer's disease facts and figures. *Alzheimer's*
- 409 *Dementia*, 6(2), 158-194.
- 410 Anstey, K.J. (2008). Alcohol exposure and cognitive development: an example of why we need a
- 411 contextualized, dynamic life course approach to cognitive ageing--a mini-review.
- 412 *Gerontology*, *54*(5), 283-291.
- Barry, P.J., Gallagher, P., & Ryan, C. (2008). Inappropriate prescribing in geriatric patients. *Current Psychiatry Reports*, *10*(1), 37-43.
- 415 Biessels, G.J., Deary, I.J., & Ryan, C.M. (2008). Cognition and diabetes: a lifespan perspective.
  416 *Lancet Neurology*, 7, 184-190.
- 417 Blieszner, R., Willis, S.L., & Baltes, P.B. (1981). Training research in aging on the fluid ability
- 418 of inductive reasoning. *Journal of Applied Development Psychology*, 2, 247-265.
- Blow, F.C. (2004). Substance Abuse among older adults: Treatment Improvement Protocol (TIP)
  series. U.S. Department of Health and Human Services.
- 421 Blow, F.C., Walton, M.A., Chermack, S.T., Mudd, S.A., & Brower, K.J. (2000). Older adult
- 422 treatment outcome following elder-specific inpatient alcoholism treatment. *Journal of*
- 423 *Substance Abuse Treatment, 19, 67-75.*

- 424 Bond, G.E., Burr, R., McCurry, S.M., Rice, M.M., Borenstein, A.R., & Larson, E.B. (2005).
- Alcohol and cognitive performance: a longitudinal study of older Japanese Americans:
  The Kame Project. *International Psychogeriatrics*, *17*, 653-668.
- 427 Cagney, K.A., & Lauderdale, D.S. (2002). Education, wealth, and cognitive function in later life.

428 *Journal of Gerontology B Psychological Science and Social Sciences*, 57(2), P163-P172.

- Cairney, S., Clough, A., Jaragba, M., & Maruff, P. (2007). Cognitive impairment in Aboriginal
  people with heavy episodic patterns of alcohol use. *Addiction*, *102*(6), 909-915.
- 431 Chan, K.K., Chiu, K.C., & Chu, L.W. (2010). Association between alcohol consumption and
- 432 cognitive impairment in Southern Chinese older adults. *International Journal of*
- 433 *Geriatric Psychiatry*, 25(12), 1272-1279.
- 434 Cherbuin, N., Reglade-Meslin, C., Kumar, R., Jacomb, P., Easteal, S., Christensen, H., ...
- Anstey, K.J. (2009). Risk factors of transition from normal cognition to mild cognitive
  disorder: the PATH through Life Study. *Dementia and Geriatric Cognitive Disorders*,
  28(1), 47-55.
- 438 Chiu, E. (2008). Alcohol for the older person--friend or foe? *Age and Ageing*, *37*(5), 505-512.
- 439 Chu, A.Y., Meoni, L.A., Wang, N.Y., Liang, K.Y., Ford, D.E., & Klag, M.J. (2010). Reliability
- 440 of alcohol recall after 15 years and 23 years of follow-up in the Johns Hopkins Precursors
  441 Study. *Journal of Studies in Alcohol and Drugs*, *71*(1), 143-149.
- 442 Coker, L.H., Espeland, M.A., Rapp, S.R., Legault, C., Resnick, S.M., Hogan, P., ... Shumaker,
- 443 S.A. (2010). Postmenopausal hormone therapy and cognitive outcomes: the Women's
- 444 Health Initiative Memory Study (WHIMS). Journal of Steroid Biochemistry and
- 445 *Molecular Biology*, *118*(4-5), 304-310.

446	Cooper, C., Bebbington, P., Meltze, H., Jenkins, R., Brugha, T., Lindesay, J.E., & Livingston, G.
447	(2009). Alcohol in moderation, premorbid intelligence and cognition in older adults:
448	Results from the Psychiatric Morbidity Survey. Journal of Neurology, Neurosurgery and
449	Psychiatry, 80(11), 1236-1239.
450	Culberson, J.W., & Ziska, M. (2008). Prescription drug misuse/abuse in the elderly. Geriatrics,
451	63(9), 22-31
452	Dawson, D.A. (2003) Methodological issues in measuring alcohol use. Alcohol Research and
453	Health, 27(1), 18-29.
454	De Labry, L.O., Glynn, R.J., Levenson, M.R., Hermos, J.A., LoCastro, J.S., & Vokonas, P.S.
455	(1992). Alcohol consumption and mortality in an American male population: Recovering
456	the u-shaped curveFindings from the Normative Aging Study. Journal of Studies on
457	Alcohol and Drugs, 53(1), 25-32.
458	Dufouil, C., Ducimetiere, P., & Alperovitch, A. (1997). Sex differences in the association
459	between alcohol consumption and cognitive performance. American Journal of
460	Epidemiology, 146, 405-412.
461	Dufour, M.C., Archer, L., & Gordis, E. (1992). Alcohol and the elderly. Clinics in Geriatric
462	Medicine, 8, 127-141.
463	Dukes, P.D., Robinson, G.M., Thomson, K.J., & Robinson, B.J. (1992). Wellington coroner
464	autopsy cases 1970-89: Acute deaths due to drugs, alcohol and poisons. New Zealand
465	Medical Journal, 105(927), 25-27.
466	Educational Testing Service (1977). Basic Skills Assessment Test-Reading. Princeton, NJ:
467	Educational Testing Service.

468	Ekholm, O., Strandberg-Larsen, K., & Grønbæk, M. (2011). Influence of the recall period on a
469	beverage-specific weekly drinking measure for alcohol intake. European Journal of
470	<i>Clinical Nutrition</i> , 65(4), 520-525.
471	Elias, P.K., Elias, M.F., D'Agostino, R.B., Silbershatz, H., & Wolf, P.A. (1999). Alcohol
472	consumption and cognitive performance in the Framingham Heart Study. American
473	Journal of Epidemiology, 150(6), 580-589.
474	Ekstrom, R.B., French, J.W., Harman, H., & Derman, D. (1976). Kit of factor-referenced
475	cognitive tests (rev. ed.). Princeton, NJ: Educational Testing Service.
476	Espeland, M.A., Coker, L.H., Wallace, R., Rapp, S.R., Resnick, S.M., Limacher, M.,
477	Messina, C.R. (2006). Women's Health Initiative Study of Cognitive Aging. Association
478	between alcohol intake and domain-specific cognitive function in older women.
479	Neuroepidemiology, 27(1), 1-12.
480	Federal Register (1998). Department of Health and Human Services, 63(36), 9235-9238.
481	Finkle, B.S., McCloskey, K.L., Kiplinger, G.F., & Bennett, I.F. (1976). A national assessment of
482	propoxyphene in postmortem medicolegal investigation, 1972-1975. Journal of Forensic
483	Sciences, 21(4), 706-741.
484	Finlayson, R.E. (1995). Misuse of prescription drugs. International Journal of Addiction, 30(13-
485	14), 1871-1901.
486	Forette, F., Seux, M.L., Thijs, L., Le Divenah, A., Pérol, M.B., Rigaud, A.S., Staessen, J.A.
487	(1989). Detection of cerebral aging, an absolute need: Predictive value and cognitive
488	status. European Neurology, 39(suppl 1), 2-6.

489	Galanis, D.J., Joseph, C., Masaki, K.H., Petrovich, H., Ross, G.W., & White, L. (2000). A
490	longitudinal study of drinking and cognitive performance in elderly Japanese American
491	men: the Honolulu-Asia aging study. American Journal of Public Health, 90, 1254-1259.
492	Ganguli, M., Vanderbilt, J., Saxton, J.A., Shen, C., & Dodge, H.H. (2005). Alcohol consumption
493	and cognitive function in late life: a longitudinal community study. Neurology, 65(8),
494	1210-1217.
495	Gavaler, J.S., & Love, K. (1992). Detection of the relationship between moderate alcohol
496	beverage consumption and serum levels of estradiol in normal postmenopausal women:
497	Effects of alcohol consumption quantitation methods and sample size adequacy. Journal
498	of Studies on Alcohol and Drugs, 53, 389-394.
499	Gilbertson, R., Ceballos, N.A., Prather, R., & Nixon, S.J. (2009). Effects of acute alcohol
500	consumption in older and younger adults: perceived impairment versus psychomotor
501	performance. Journal of Studies on Alcohol and Drugs, 70(2), 242-252.
502	Gmel, G., & Daeppen, J.B. (2007). Recall bias for seven-day recall measurement of alcohol
503	consumption among emergency department patients: implications for case-crossover
504	designs. Journal of Studies on Alcohol Drugs, 68(2), 303-310.
505	Gross, A.L., Rebok, G.W., Ford, D.E., Chu, A.Y., Gallo, J.J., Liang, K.Y., Klag, M.J. (2011).
506	Alcohol consumption and domain-specific cognitive function in older adults: longitudinal
507	data from the Johns Hopkins Precursors Study. Journals of Gerontology B: Psychological
508	Sciences/ Social Sciences, 66(1), 39-47.
509	Hellwig, J.P. (2011). Smoking and cognitive function: Midlife smoking may double dementia

510 risk. Nursing and Women's Health, 15(1), 19-25.

- 511 Imhof, A., Woodward, M., Doering, A., Helbecque, N., Loewel, H., Amouyel, P., ... Koenig, W.
- 512 (2004). Overall alcohol intake, beer, wine, and systemic markers of inflammation in
- 513 Western Europe: results from three MONICA samples (Augsburg, Glasgow, Lille).
- 514 *European Heart Journal*, 25(23), 2092-2100.
- Järvenpää, T., Rinne, J.O., Koskenvuo, M., Räihä, I., & Kaprio, J. (2005). Binge drinking in
  midlife and dementia risk. *Epidemiology*, *16*(6), 766-771.
- 517 Kawas, C., Resnick, S., Morrison, A., Brookmeyer, R., Corrada, M., Zonderman, A., ... Metter,
- 518 E. (1997). A prospective study of estrogen replacement therapy and the risk of
- 519developing Alzheimer's disease: The Baltimore Longitudinal Study of Aging. Neurology,10(1)1515
- **52048(6)**, 1517-1521.
- Kiechl, S., Willeit, J., Rungger, G., Egger, G., Oberhollenzer, F., & Bonora, E. (1998). Alcohol
  consumption and atherosclerosis: what is the relation? Prospective results from the
  Bruneck Study. *Stroke*, *29*(5), 900-907.
- Kitagawa, E.M., & Hauser, P.M. (1973). *Differential Mortality in the United States: A Study of Socioeconomic Epidemiology*. Cambridge, MA: Harvard University Press.
- 526 Kivipelto, M., Helkala, E.L., Laakso, M.P., Hänninen, T., Hallikainen, M., Alhainen, K., ...
- 527 Nissinen, A. (2001). Midlife vascular risk factors and Alzheimer's disease in later life:
  528 longitudinal, population based study. *British Medical Journal, 322*, 1447-1451.
- 529 Lang, I, Wallace, R.B., Huppert, F.A., & Melzer, D. (2007). Moderate alcohol consumption in
- older adults is associated with better cognition and well-being than abstinence. *Age and*
- 531 *Ageing*, *36*, 256-261

532	Larson, E.B., Kukull, W.A., Buchner, D., & Reifler, B.V. (1987). Adverse drug reactions
533	associated with global cognitive impairment in elderly persons. Annals of Internal
534	Medicine, 107(2), 169-173.

- 535 Luchsinger, J.A., Reitz, C., Honig, L.S., Tang, M.X., Shea, S., & Mayeux, R. (2005).
- Aggregation of vascular risk factors and risk of incident Alzheimer disease. *Neurology*,
  65(4), 545–551.
- Luchsinger, J.A., Tang, M.X., Stern, Y., Shea, S., & Mayeux, R. (2001). Diabetes mellitus and
  risk of Alzheimer's disease and dementia with stroke in a multiethnic cohort. *American Journal of Epidemiology*, *154*, 635–641.
- McCabe, S.E., Cranford, J.A., & Boyd, C.J. (2006). The relationship between past-year drinking
  behaviors and nonmedical use of prescription drugs: prevalence of co-occurrence in a
  national sample. *Drug Alcohol Dependence*, *84*(3), 281-288.
- McGeer, E.G., & McGeer, P.L. (1999). Brain inflammation in Alzheimer disease and the
  therapeutic implications. *Current Pharmaceutical Design*, *5*, 821-836.
- McGuire, L.C., Ajani, U.A., & Ford, E.S. (2007). Cognitive functioning in late life: the impact of
  moderate alcohol consumption. *Annals of Epidemiology*, *17*(2), 93-99.
- Meyer, J.S., Rogers, R.L., Judd, B.W., Mortel, K.F., & Sims, P. (1988). Cognition and cerebral
  blood flow fluctuate together in multi-infarct dementia. *Stroke*, *19*(2), 163–169.
- 550 Molander, R.C., Yonker, J.A., & Krahn, D.D. (2010). Age-related changes in drinking patterns
- from mid- to older age: results from the Wisconsin longitudinal study. Alcohol Clinical
- and Experimental Research, 34(7), 1182-1192.

- 553 Moore, A.A., Blow, F.C., Hoffing, M., Welgreen, S., Davis, J.W., Lin, J.C., ... Barry, K.L.
- 554 (2011). Primary care-based intervention to reduce at-risk drinking in older adults: a
  555 randomized controlled trial. *Addiction*, *106*(1), 111-120.
- Nagin, D.S. (1999). Analyzing developmental trajectories: A semiparametric, group-based
  approach. *Psychological Methods*, 4(2), 139-157.
- National Institute on Aging (2012). AgePage: Alcohol use in older people. National Institutes of
  Health: NIH...Turning Discovery into Health. U.S. Department of Health and Human
  Services.
- 561 National Institute on Alcohol Abuse and Alcoholism (1992). No. 16 PH 315.
- 562 Neafsey E.J. & Collins, M.A. (2011). Moderate alcohol consumption and cognitive risk.
   563 *Neuropsychiatric Disorder Treatment*, 7, 465-484.
- 564 Notkola, I.L., Sulkava, R., Pekkanen, J., Erkinjuntti, T., Ehnholm, C., Kivinen, P., ... Nissinen,
- 565 A. (1998). Serum total cholesterol, apolipoprotein E epsilon 4 allele, and Alzheimer's
  566 disease. *Neuroepidemiology*, *17*(1), 14-20.
- 567 Ødegård, E., & Rossow, I. (2004). Alcohol and non-fatal drug overdoses. *European Addiction*568 *Research*, 10(4), 168-172.
- Onder, G., Landi, F., Vedova, C.D., ... Gambassi, G. (2002). Moderate alcohol consumption and
  adverse drug reactions among older adults. *Pharmaepidemiology and Drug Safety*, *11*,
  385-392.
- 572 Onland-Moret, N.C., Peeters, P.H., van der Schouw, Y.V., Grobbee, D. E., & van Gils, C.H.
- 573 (2005). Alcohol and endogenous sex steroid levels in postmenopausal women: A cross-
- 574 sectional study. *The Journal of Clinical Endocrinology & Metabolism*, 90(3), 1414-1419.

5/5 Panza, F., Capurso, C., D'Introno, A., Colacicco, A.M., Frisardi, V., Lorusso	). M	Solfrizzi.	٧.
---	------	------------	----

- 576 (2009). Alcohol drinking, cognitive functions in older age, predementia, and dementia
  577 syndromes. *Journal of Alzheimer's Disease*, *17*(1), 7-31.
- 578 Panza, F., Capurso, C., D'Introno, A., Colacicco, A.M., Frisardi, V., Santamato, A., ... Solfrizzi
- 579 V. (2008). Vascular risk factors, alcohol intake, and cognitive decline. *Journal of*580 *Nutrition Health & Aging*, *12*(6), 376-381.
- Peters, R., Peters, J., Warner, J., Beckett, N., & Bulpitt, C. (2008). Alcohol, dementia and
  cognitive decline in the elderly: a systematic review. *Age and Ageing*, *37*(5), 505-512.
- 583 Phillips, D.P., Barker, G.E., & Eguchi, M.M. (2008). A steep increase in domestic fatal
- 584 medication errors with use of alcohol and/or street drugs. *Archives of Internal Medicine*,
  585 *168(14)*, 1561-1566.
- Quayhagen, M. (1979). *Training spatial rotation in elderly women*. Unpublished docural
  dissertation, University of California, Los Angeles.
- 588 Reitz, C., Tang, M.X., Luchsinger, J., & Mayeux, R. (2004). Relation of plasma lipids to
- 589 Alzheimer disease and vascular dementia. *Archives of Neurology*, *61*(5), 705-714.
- 590 Ridker, P.M., Vaughan, D.E., Stampfer, M.J., Glynn, R.J., & Hennekens, C.H. (1994).
- Association of moderate alcohol consumption and plasma concentration of endogenous
  tissue-type plasminogen activator. *Journal of the American Medical Association*, 272,
  929-933.
- 594 Rodgers, B., Windsor, T.D., Anstey, K.J., Dear, K.B., F Jorm, A., & Christensen, H. (2005).
- 595 Non-linear relationships between cognitive function and alcohol consumption in young,
- 596 middle-aged and older adults: the PATH Through Life Project. Addiction, 100(9), 1280-
- **597** 90.

- 598 Ruspini, E. (2002). *Introduction to Longitudinal Research*. New York, NY: Routledge.
- Sano, M., Wendt, P.E., Wirsén, A., Stenberg, G., Risberg, J., & Ingvar, D.H. (1993). Acute
- 600 effects of alcohol on regional cerebral blood flow in man. *Journal of the Study of*601 *Alcohol*, *54*, 369–376.
- 602 Schaie, K.W. (1985). *Manual for the Schiae-Thurstone Adult Mental Abilities Test (STAMAT)*.
  603 Pal Alto, CA: Consulting Psychological Press.
- 604 Schaie, K.W. (2005). *Developmental Influences on Adult Intelligence: The Seattle Longitudinal*605 *Study*. Oxford: Oxford University Press.
- 606 Schaie, K.W. (2009). "When does age-related cognitive decline begin?" Salthouse again reifies
- 607 the "cross-sectional fallacy". *Neurobiology of Aging*, *30*(4), 528-529; discussion 530-533.
- Schaie, K. W., Maitland, S. B., Willis, S. L., & Intrieri, R. C. (1998). Longitudinal invariance of
  adult psychometric ability factor structures across seven years. *Psychology and Aging*,
- 610 *13*, 8-20.
- 611 Schmidt, R., Fazekas, F., Reinhart, B., Kapeller, P., Fazekas, G., Offenbacher, H., ... Freidi W
- 612 (1996). Estrogen replacement therapy in older women: a neuropsychological and brain
- 613 MRI study. *Journal of the American Geriatric Society*, 44(11), 1307-1313.
- 614 Simoni-Wastila, L.,& Strickler, G. (2004). Risk factors associated with problem use of
  615 prescription drugs. *American Journal of Public Health*, 94(2), 266-268.
- 616 Singer, J.D., & Wilett, J.B. (2003). *Applied Longitudinal Data Analysis: Modeling Change and*617 *Event Occurrence*. Oxford, NY: Oxford University Press.
- 618 Solfrizzi, V., D'Introno, A., Colacicco, A.M., Capurso, C., Del Parigi, A., Baldasarre, G., ...
- 619 Panza, F. (2007). Italian Longitudinal Study on Aging Working Group. Alcohol

620 consumption, mild cognitive impairment, and progression to dementia. *Neurology*,

**621** *68*(21), 1790-1799.

- 622 Stampfer, M.J., Kang, J.H., Chen, J., Cherry, R., & Grodstein, F. (2005). Effects of moderate
- alcohol consumption on cognitive function in women. *New England Journal of Medicine*,
  352, 245–253.
- Stott, D.J., Falconer, A., Kerr, G.D., Murray, H.M., Trompet, S., Westendorp, R.G., ... Ford, I.
  (2008). Does low to moderate alcohol intake protect against cognitive decline in older
  people? *Journal of the American Geriatric Society*, *56*(12), 2217-2224.
- 628 Sun, Q., Townsend, M.K., Okereke, O.I., Rimm, E.B., Hu, F.B., Stampfer, M.J., & Grodstein, F.
- 629 (2011). Alcohol consumption at midlife and successful ageing in women: a prospective
  630 cohort analysis in the nurses' health study. *PLoS Medicine*, 8(9), e1001090. Epub 2011.
- 631 Teunissen, C.E., van Boxtel, M.P, Bosma H, Bosmans, E., Delanghe, J., De Bruijn, C., ... de
  632 Vente J. (2003). Inflammation markers in relation to cognition in a healthy aging

633 population. *Journal of Neuroimmunology*, *134*(1-2), 142-150.

- 634 Thurstone, T.G. (1962). Primary mental abilities for Grades 9-12. Chicago, IL: Science
- 635 Research Associates.
- 636 Thurstone, L.L, & Thurstone, T.G. (1949). *Examiner manual for the SRA Primary Mental*637 *Abilities Test (Form 10-14)*. Chicago, IL: Science Research Associates.
- 638Townsend, M.K., Devore, E., Kang, J.H., & Grodstein F. (2009). The relation between moderate
- alcohol consumption and cognitive function in older women with type 2 diabetes.
- 640 *Diabetes Research and Clinical Practice*, 85(3), 322-327.
- 641 Weyerer, S., Schäufele, M., Wiese, B., Maier, W., Tebarth, F., van den Bussche, H., Pentzek, M.,
- 642 ... Riedel-Heller, S.G. (2011). German AgeCoDe Study group (German Study on

643	Ageing, Cognition and Dementia in Primary Care Patients). Current alcohol consumption
644	and its relationship to incident dementia: results from a 3-year follow-up study among
645	primary care attenders aged 75 years and older. Age and Ageing, 40(4), 456-463.
646	Wise, P.M., Dubal, D.B., Wilson, M.E., Rau, S.W., & Liu, Y. (2001). Estrogens: Trophic and
647	protective factors in the adult brain. Frontiers in Neuroendocrinology, 22(1), 33-66.
648	Yaffe, K., Lindquist, K., Penninx, B.W., Simonsick, E.M., Pahor, M., Kritchevsky, S., Harris,
649	T. (2003). Inflammatory markers and cognition in well-functioning African-American
650	and white elders. <i>Neurology</i> , 61(1), 76-80.
651	Yi, J., Horky, L.L., Friedlich, A.L., Shi, Y., Rogers, J.T., & Huang, X. (2009). L-arginine and
652	Alzheimer's disease. International Journal of Clinical and Experimental Pathology, 2(3),
653	211-238.
654	Zelinski, E.M., Gilewski, M.J., & Schaie K.W. (1993). Individual differences in cross-sectional
655	and 3-year longitudinal memory performance across the adult life span. Psychology of
656	Aging, 8(2), 176-186.
657 658	

		Drinking Status	
	Abstainers	Moderate	At-risk
	(n=237, 42%)	(n=252, 44%)	(n=82, 14%)
Age (mean(SD) range)	65.8 (11.1)	63.6 (11.7)	62.6 (11.0)
	Range=45-93	Range=45-90	Range=45-84
Gender (% female)	63%	57%	29%
Income (median range)	\$40,000-\$34,999	9 \$50,000-\$54,999	9 \$55,000-59,999
Education years (mean (SD))	15.0 (2.6)	16.2 (2.5)	16.1 (2.9)
	Range=8-20	Range=10-20	Range=7-20
Smoking (% smokers)	3%	5%	7%
Mean Total Alcohol Drinks/ Week (mean (SD))	0	3.3 (2.1)	14.1 (6.1)
		Range = 1-7	Range = 8-33
Mean Beer Drinks/Week (mean (SD))	0	0.7 (1.2)	3.5(6.1)
		Range = 0-7	Range = 0-30
<b>Beer Proportion/ Total Alcohol Drinks</b>	0	.24	.23
Mean Wine Drinks/Week (mean (SD))	0	1.8 (1.9)	6.8 (5.0)
		Range = 0-7	Range = 0-20
Wine Proportion/ Total Alcohol Drinks	0	.54	.52
Mean Liquor Drinks/Week (mean (SD))	0	0.8 (1.5)	3.8 (6.0)
		Range = 0-7	Range = 0-30
Liquor Proportion/ Total Alcohol Drinks	0	.24	.25

659 Table 1. Baseline (1998) Sample Demographics (N=571)

660 Note. Significant differences ( $p \le .05$ ) across drinking status for all variables, with the exception

661 of smoking status.

			Drinki	ng Statu	IS	
	Abst	ainers	Mod	lerate	At-	risk
	(n=23'	7, 42%)	(n=252	2, 44%)	(n=82	, 14%)
	Time1	Time2	Time 1	Time 2	Time 1	Time 2
Memory (mean (SD))	48.6	46.9	50.8	48.8	51.1	49.3
	(9.5)	(10.3)	(9.0)	(10.6)	(9.2)	(9.4)
Reasoning (mean (SD))	50.1	47.8	52.4	50.1	52.7	50.8
	(8.0)	(8.9)	(7.9)	(9.4)	(7.1)	(8.4)
Spatial (mean (SD))	49.2	47.3	51.3	49.6	52.1	50.6
	(8.5)	(9.6)	(8.2)	(9.3)	(8.0)	(8.3)
Verbal (mean (SD))	50.4	49.2	53.8	53.1	52.8	52.8
	(8.4)	(8.6)	(6.5)	(7.1)	(6.6)	(6.6)
Number (mean (SD))	48.8	45.2	50.4	46.9	51.8	49.2
	(8.8)	(9.4)	(8.3)	(9.1)	(7.9)	(8.3)
Speed (mean (SD))	49.3	46.4	50.8	48.3	50.9	48.8
	(7.1)	(8.8)	(6.6)	(8.9)	(5.6)	(7.5)

### 662 Table 2. Cognitive Levels Across Time (N=571)

663 $\overline{Note}$ . Significant differences (p < .05) across drinking status for all variables, with the exception</th>664of Time 2 memory ability.

	Memory	Reasoning	Spatial	Verbal	Number	Speed
Age Group Models						
Time	35.22***	210.93***	63.12***	31.61***	363.44***	187.96***
Time x Age Group	6.14*	35.26***	16.01***	18.56***	42.52***	32.84***
Time x Drinking Status	1.14	1.66	0.10	3.10*	2.08	0.53
Time x Age x Drinking	2.05	0.90	2.92*	1.26	1.22	1.42
<u>Status</u>						
<u>Gender Models</u>						
Time	21.75 ***	113.85***	29.38***	10.69**	207.28***	90.34***
Time x Gender	0.76	0.01	1.14	0.01	0.58	1.04
Time x Drinking Status	0.72	0.51	0.10	2.98	1.49	0.92
Time x Gender x	1.51	0.74	1.64	0.89	0.92	4.84**
Drinking Status						
	din CACO	1 using Dro	c Mixed .cc	ntrolling f	or Income	Education

# 666 667 Table 3. Drinking Effects on Cognitive Change (1998-2005) by Age Group (f-values)

670 Age Group in Gender models.

- 671 Time indicated two points: Time 1 = 1998 and Time 2 = 2005.
- Bolding indicates significant (p <.05) differences;  $*=p \le .05$ ;  $**=p \le .01$ ;  $***=p \le .001$ .

673



## 675 Figure 1. Changes in Verbal Ability



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