Title

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Journal

Alcoholism Clinical and Experimental Research, 43(8)

ISSN

0145-6008

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Publication Date

2019-08-01

DOI

10.1111/acer.14116

Peer reviewed

A Pilot Follow-Up Study of Older Alcohol-Dependent COGA Adults

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Background: Alcohol consumption and problems are increasing among older adults, who are at elevated risk for alcohol-related accidents and medical problems. This paper describes a pilot follow-up of older adults with a history of alcohol dependence that was designed to determine the feasibility of conducting a more extensive investigation.

Methods: The sample consisted of previously assessed subjects in the Collaborative Studies on the Genetics of Alcoholism who: (i) were age 50+; (ii) had lifetime DSM-IV AD; and (iii) had DNA available. Individuals were located through family contacts, Internet searches, and death registries. A brief telephone interview assessed demographics, health, and alcohol involvement.

Results: Of the total sample (N = 2,174), 36% were contacted, 24% were deceased, and 40% were not yet located. Most (89%) contacted subjects were interviewed, and 99% of them agreed to future evaluation. Thirty percent of interviewed subjects reported abstinence for 10+ years, 56% reported drinking within the past year, and 14% last drank between >1 and 10 years ago. There were no age-related past-year differences in weekly consumption (overall sample mean: 16 drinks), number of drinking weeks (30.8), maximum number of drinks in 24 hours (8.1), or prevalence of weekly risky drinking (19%). Among those who drank within the past 5 years, the 3 most common alcohol-related problems were spending excessive time drinking or recovering (49%), drinking more/longer than intended (35%), and driving while intoxicated (35%); and about a third (32%) received some form of treatment.

Conclusions: Over a 1-year period, we located 60% of individuals last seen an average of 23 years ago. The majority of contacted individuals were interviewed and willing to be evaluated again. Although the proportion of individuals currently drinking diminished with age, subjects exhibited troublesome levels of alcohol consumption and problems. Our findings suggest the importance and feasibility of a more comprehensive follow-up.

Key Words: Follow-Up, Older Adults, Alcohol Dependence, COGA.

RESEARCH ON ALCOHOL use and disorders (AUDs) has largely targeted individuals in late adolescence through the mid-20s. This is a logical focus, because that timeframe represents a period of peak consumption for most people and an age during which AUDs first manifest themselves in significant numbers (Williams et al., 2018). In addition, this developmental period is ideal for identifying early antecedents of alcohol-related problems.

Although considerably less research has spotlighted alcohol misuse in later life, there are compelling reasons to do so. Older individuals constitute an increasing proportion of the American population (Vespa et al., 2018). In 2014, the majority of adults between 60 and 64 (65%) and 65 or more (56%) reported current drinking (Center for Behavioral Health Statistics and Quality, 2015), and national data collected over the past 2 decades indicate that such consumption has been on the rise. Among individuals aged 60 or greater, findings from the National Health Interview Surveys collected consecutively between 1997 and 2014 (Breslow et al., 2017) document increases in men's and women's current drinking from 54.0 to 59.9% and from 37.8 to 47.5%, respectively. Although the prevalence of binge drinking did not change significantly among men across this period (about 20%), it rose significantly in females (from 4.9 to 7.5%; Breslow et al., 2017). Similarly, data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) collected at 2 time points (2001 to 2002 and 2012 to 2013) revealed increases among individuals aged at least 65 in current drinking (from 45.1 to 55.2%), high-risk drinking (from 2.3 to 3.8%), and AUD prevalence (from 1.5 to 3.1%; Grant et al., 2017).

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Received for publication September 7, 2018; accepted May 20, 2019.

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DOI: 10.1111/acer.14116

Although American epidemiological surveys indicate that fewer older individuals than their younger counterparts are current or heavy drinkers (Breslow et al., 2017; Grant et al., 2017), AUDs from earlier periods may persist or reemerge. In addition, misuse of alcohol can have an especially ominous impact among older adults. There is a tendency for alcohol to produce higher blood alcohol levels as people advance in years (Bjork et al., 2008), increasing their vulnerability to alcohol-related accidents and falls. In addition, over 3-quarters of current drinkers aged 65 + take medications that may interact adversely with alcohol (Breslow et al., 2015), and age-related changes can lead to greater toxicity and/or reduced effectiveness of medication (Moore et al., 2007). A greater understanding of alcohol use and problems at this stage of life is clearly warranted.

A number of long-term follow-up investigations have examined the precursors of older age alcohol involvement (see Schuckit et al., 2018, for a detailed review). In these studies, samples range considerably both in size and in type, including registry-based population samples (Kendler et al., 2016), former students (Gonçalves et al., 2017; Vaillant, 2003), community residents (Moos et al., 2010; Vaillant, 2003), civil servants (Knott et al., 2018), and clinic outpatients (Holahan et al., 2017). A variety of alcohol-related topics has been addressed, including mortality (Haver et al., 2009; Holahan et al., 2017; Kendler et al., 2016; Lundin et al., 2015); the interplay between social resources and high-risk consumption (Moos et al., 2010); trajectories/stability of consumption, abuse, and dependence (Jacob et al., 2009; Knott et al., 2018; Vaillant, 2003); and the association between drinking level, drinking pattern, and number of alcohol problems in later years (Holahan et al., 2017).

These studies have contributed a considerable body of knowledge, establishing or confirming, among other findings, that alcohol abuse, as defined in the Fourth Diagnostic and Statistical Manual (DSM-IV; American Psychiatric Association, 2000), can persist for many years without necessarily progressing to dependence (Vaillant, 2003) and that a considerable number of individuals transition from alcohol dependence to a less severe status over time (Jacob et al., 2009; Knott et al., 2018; Vaillant, 2003). Nevertheless, much remains to be learned about the antecedents and effects of later life drinking. The Collaborative Study on the Genetics of Alcoholism (COGA) has interviewed a large number of subjects from both high-risk and comparison families (Begleiter et al., 1995; Edenberg and Foroud, 2006). A follow-up of older adults from this project has the potential to contribute knowledge in several ways, by: (i) incorporating a sample of subjects from high-risk families, which are not well represented in existing longitudinal investigations; (ii) targeting not only alcohol consumption, symptoms, and treatment, but a variety of other alcohol-relevant outcomes, such as depression and impaired cognitive functioning; and (iii) identifying young adult predictors of later life drinking that encompass environmental, behavioral, psychiatric, genetic, neurophysiological (EEG/ERP), and neuropsychological information, thereby allowing predictive models to incorporate a broad spectrum of explanatory variables.

In 1990, 6 COGA sites began recruitment of treated alcohol-dependent subjects, as well as their first-degree and extended family members, a number of whom were also alcohol-dependent. Community-ascertained comparison families were also included. Both samples were administered the same broad assessment protocol, which included: (i) a comprehensive interview (the Semi-Structured Assessment for the Genetics of Alcohol, SSAGA; Bucholz et al., 1994, 2006) that measures major psychiatric diagnoses, including drinking and substance use disorders, as well as key environmental domains such as childhood upbringing and peer substance use; and (ii) questionnaires that address a wide range of personal and environmental characteristics related to drinking (e.g., sensation seeking). In addition, participating families that were most genetically informative were genotyped and administered EEG/ERP protocols and neuropsychological tasks that tap addiction-relevant constructs (e.g., executive functioning, reward sensitivity; Begleiter et al., 1995). In 2005, COGA initiated an ongoing prospective study of adolescents and young adults (Bucholz et al., 2017). To date, over 17,000 subjects have participated in one or more phases of COGA. About half (53%) are female, and most ethnicities are represented (67% European ancestry, 23% African ancestry, 7% Hispanic, 1% Asian, and 2% Other).

Recognizing COGA's potential contribution to understanding older drinking, in 2016 to 2017, the funded a pilot study to briefly reevaluate selected COGA participants who, if still living, would be at least 50 years of age. These individuals were last seen between 1991 and 2004 (at ages 25 to 80), a mean (SD) of 21.6 (3.4) years prior. The pilot study had 3 objectives: (i) to determine the feasibility of locating, recruiting, and evaluating older COGA participants; (ii) to assess key aspects of living subjects' current demography, health, and alcohol involvement using a brief telephone interview; and (iii) to determine the rates and causes of mortality among deceased subjects.

In this paper, our first aim was to describe this completed pilot study's logistics, compare subjects whose whereabouts remained uncertain (after 12 months of effort) against located individuals (either contacted or confirmed deceased), and gauge likely participation in a subsequent follow-up study. Our second aim was to descriptively characterize interviewed subjects' current living circumstances; mental and physical health; alcohol consumption, problems, and treatment, by age-group. In particular, 3 hypotheses are examined:

(1) Older subjects who are relatives of current younger COGA participants will be easier to locate than older individuals who lack such a family connection.

(2) The majority of located living subjects will express willingness to take part in a subsequent follow-up study.

(3) Fewer subjects in the older age-groups will be current drinkers than subjects in the younger age-groups, and, among older current drinkers, fewer will exhibit problematic alcohol use than their younger counterparts (Breslow et al.,

2017; Grant et al., 2017; Knott et al., 2018; Vaillant, 2003; Vestal et al., 1977).

MATERIALS AND METHODS

Subjects

Follow-up search and interviewing took place between November 2016 and November 2017. Pilot study subjects were drawn from 6 COGA sites (SUNY Brooklyn, University of Connecticut, Indiana University, Washington University in St. Louis, University of Iowa, and University of California, San Diego); all living participants provided informed consent in compliance with their local IRBs. Due to limited time and resources, we restricted our sample to COGA subjects who: (i) would be at least 50 years of age in 2016 if still alive (born in 1966 or earlier); (ii) were assessed in 1991 to 2004 as adults with the SSAGA interview (median follow-up interval = 23 years); (iii) met criteria for lifetime DSM-IV alcohol dependence at the baseline interview; (iv) had provided a DNA sample; and (v) had not refused future participation when last evaluated in COGA (fewer than 1% of COGA participants). These criteria yielded a sample of 2,174 candidates from 1,528 nuclear families, of which 74% were single-participant families. Living participants' contact details were in many cases determined through family members and Internet searches. Death information was initially obtained from relatives, state death registries, newspapers, and online obituaries (e.g., obituaries.com, legacy.com, findgraves.com, Social Security Death Index). In addition, the National Death Index (NDI; https://www.cdc.gov/nchs/ndi/index.htm), a comprehensive database that compiles death certificate information from all states, was used to establish or validate dates and causes of death for deceased individuals and those of uncertain status.

COGA Follow-Up Telephone Interview (Complete Interview is in Appendix S1)

In order to maximize subject participation, we designed a telephone-administered, computerized interview (Fig. 1) that typically lasted 10 to 20 minutes and collected information about current:

Marital status
Living arrangements
Education
Employment
Physical health (overall rating and specific disorders)
Mental health (overall rating and rating of memory compared to same-aged peers)
Alcohol involvement

Subjects were administered questions on the basis of their most recent drink.

Individuals who drank *within the past year* were asked about the previous week's consumption, typical weekly consumption during the year, and heavy drinking (bingeing, maximum drinks in 24 hours), as well as alcohol-related problems (AUD symptoms, physical complications), and treatment (emergency room, inpatient, outpatient, self-help) within the past 5 years. Subjects who drank *more than 1 but 5 or fewer years ago* were only asked about heavy drinking, problems, and treatment during the past 5 years. Subjects who last drank *more than 5 but 10 or fewer years ago* were only asked about problems and treatment, but not consumption. Individuals who last drank *more than 10 years ago* were not asked any alcohol questions.

Willingness to participate again:

In order to gauge the feasibility of an additional follow-up in the future, all subjects were asked, at the end of the interview, "We are hoping to contact you again in a year or so to see how you are doing. Is that okay with you?"

The interview was created on the University of Iowa's local Research Electronic Data Capture platform (REDCap; Harris et al., 2009), which provides an interface for computer-based assessment, as well as data storage and descriptive statistics.

Analyses

To address the first aim of this paper and evaluate Hypotheses 1 (ability to locate selected follow-up subjects) and 2 (estimation of future participation rate among located living subjects), data collected at 2 time points [baseline SSAGA and current status] were used. Subjects were categorized into 3 groups: Contacted, Deceased, and To Be Located (at the end of the 12-month study period). In

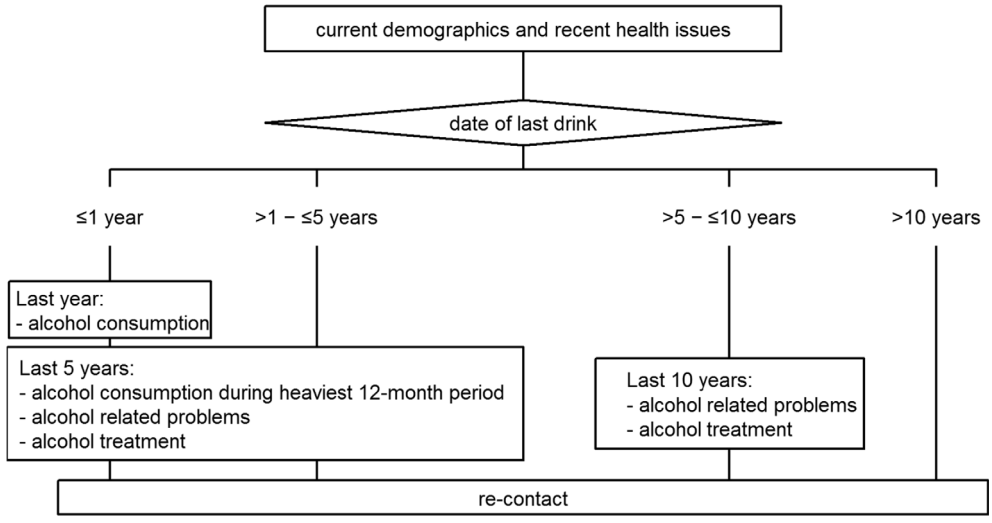

Fig. 1. Schematic overview of the COGA follow-up telephone interview: branching logic based on date of last drink.

addition to determining the membership and size of each group, we compared them on a range of baseline characteristics, including: demographics; self-reported health; alcohol use, consequences, and treatment; history of other substance dependence; and history of externalizing (antisocial personality disorder, ASPD) and internalizing diagnoses (major depressive episode, social phobia, agoraphobia, panic attacks, obsessive-compulsive disorder, and/or posttraumatic stress disorder). In order to identify baseline characteristics associated with the likelihood of determining subject status at this pilot follow-up, 3 sets of comparisons were conducted: (i) between "Contacted," "Deceased," and "To Be Located"; (ii) between "To Be Located" and "Located" (Contacted or Deceased); and (iii) between "Interviewed" and "Not-Interviewed" located living subjects. Next, the proportion of located living subjects who were willing to participate in a subsequent follow-up study was determined.

To address the second aim and evaluate Hypothesis 3 (alcohol involvement at follow-up by age), subjects who completed the interview were divided into 4 age-groups (50 to 54, 55 to 59, 60 to 64, and 65+). These age divisions were imposed in order to obtain a more fine-grained (primarily 5-year) characterization of outcome, because the total age span of this sample encompasses different life stages and circumstances (e.g., employment vs. retirement and children in the home vs. out of the home).

Group descriptive statistics and generalized linear mixed model (GLMM) were used to characterize and compare baseline and follow-up measures. Familial clustering was taken into account in all GLMMs. Furthermore, baseline age was treated as a covariate when comparing baseline characteristics in a sensitivity analysis. Effect sizes (either odds ratio or proportion estimate and corresponding 95% confidence interval) were used to assess the degree that the 3 hypotheses were supported by the data. To correct for multiple comparisons, only variables with false discovery rate (FDR)-adjusted p-values <0.05 were considered statistically significant (Benjamini and Yekutieli, 2001). SAS 9.4 was used for all analyses.

RESULTS

Prevalence of Contacted, Deceased, and To Be Located

Of the total sample (N = 2,174), we were able to determine the vital status of 1,313 (60%) individuals: 789 (36%) were alive and contacted, and 524 (24%) were confirmed deceased. Most of the remaining 861 (40%) subjects were likely to be alive (since relatives, Internet websites, and a comprehensive NDI search failed to identify any of them as deceased), but had not yet been contacted by the end of the one-year active study period (Fig. 2).

Baseline Characteristics of To Be Located Subjects Compared With Contacted and Deceased Subjects

Initial comparisons between Contacted, Deceased, and To Be Located subjects revealed significant (FDR-adjusted $p \leq 0.001$) differences with respect to demographics, self-rated general health, alcohol involvement, psychiatric comorbidity, and whether they were a relative of current prospective study participants (Table 1). Comparing subjects whose whereabouts were still unknown versus located individuals (i.e., confirmed alive or deceased) revealed that the To Be Located subjects were younger and were less likely to be a relative of prospective participant, to be of European ancestry, or to have ever been married (all with FDR-adjusted $p < 0.001$) at baseline. In addition, To Be Located subjects had an earlier onset of DSM-IV alcohol dependence, a greater number of other substance use disorders (in particular, marijuana and cocaine), and a higher lifetime prevalence of ASPD at baseline (all with FDR-adjusted $p < 0.001$; Table 1). After controlling for baseline age, the differences in marital status, age of onset of DSM-IV alcohol dependence, marijuana dependence, number of nonalcohol substance dependence disorders, and ASPD were no longer significant. As anticipated (Hypothesis 1), having a relative in the current prospective study increased the chances of an older subject being located (odds ratio and 95% confidence interval = 1.81 [1.47, 2.23]).

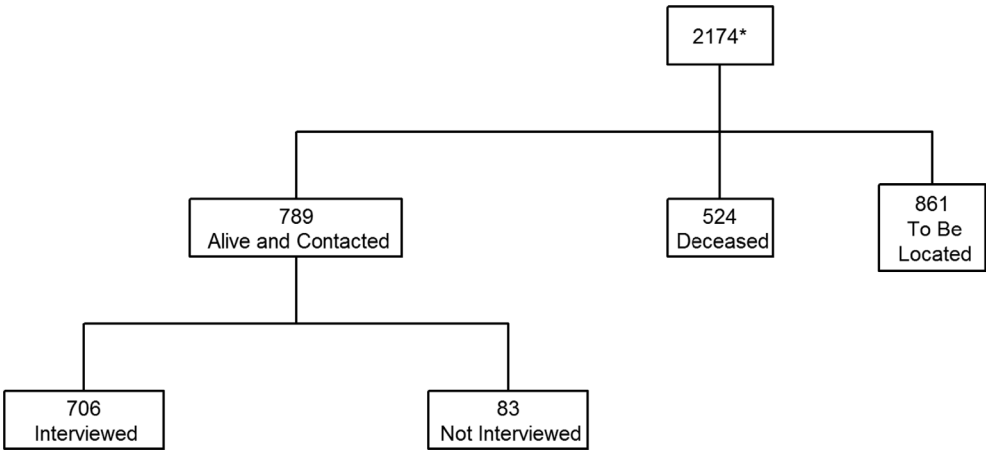

Fig. 2. Flowchart of the COGA older alcohol-dependent pilot study. *2174 COGA participants were assessed and met criteria for lifetime DSM-IV alcohol dependence in 1991 to 2004, were born before 1967, and had contributed DNA.

Table 1. Baseline Characteristics of Three Groups (n = 2,174): % for Categorical Variables and Mean (SD) for Continuous Variables

Baseline characteristics *n*	Contacted 789, 36%	Deceased 524, 24%	To be Located 861, 40%
Gender[a]: Male (%)	58	77	66
Race[b] (%)			
European ancestry	79	78	69
African ancestry	18	20	27
Other	3	2	4
Ethnicity			
Hispanic (%)	6	4	7
Age[b]	39.4 (8.3)	47.7 (11.8)	38.2 (7.8)
Marital status[b] (%)			
Married	44	43	38
Widowed	1	3	1
Separated	10	8	9
Divorced	23	26	22
Never married	22	20	30
Education (%)			
Less than High School	23	30	30
High School	30	30	29
Beyond High School	47	40	42
Employment[a] (%)			
Unemployed	36	56	43
Part-time	11	7	7
Full-time	53	37	51
Relative of current COGA participant[b,c]	77	69	61
General Health[a] (%)			
Excellent/Good	86	72	84
Fair/Poor	14	28	16
Age of onset of DSM-IV alcohol dependence[b,d]	24.6 (7.6)	28.6 (10.5)	24.0 (7.0)
Number of DSM-IV alcohol dependence symptoms[a,d]	5.3 (1.5)	5.6 (1.4)	5.4 (1.5)
Lifetime maximum drinks in a 24-hour period[a]	27.2 (15.5)	31.2 (17.5)	29.5 (16.5)
Received treatment for alcohol problems[a] (%)	62	74	67
Marijuana dependence[b,d] (%)	38	27	44
Cocaine dependence[b,d] (%)	37	25	49
Opiate dependence[d] (%)	11	13	14
Stimulant dependence[d] (%)	21	18	17
Sedative dependence[d] (%)	10	12	13
Number of nonalcohol substance dependence disorders[b,d] (%)			
0	42	55	33
1	24	18	26
2+	34	26	40
ASPD[b,d,e] (%)			
Positive	16	16	23
Alcohol/drug-related only[f]	4	3	5
Anxiety dx[d,e] (%)			
Positive	13	9	14
Alcohol/drug-related only[f]	1	2	1
Mood dx[d,e] (%)			
Positive	18	14	17
Alcohol/drug-related only[f]	31	36	34

[a]Significantly different across 3 groups: Contacted versus Deceased versus To Be Located, false discovery rate (FDR)-adjusted $p < 0.05$, but not significant between 2 groups: Located (Contacted or Deceased) versus To Be Located.

[b]Significantly different across 3 groups: Contacted versus Deceased versus To Be Located, FDR-adjusted $p < 0.05$, and also significantly different between 2 groups: Located (Contacted or Deceased) versus To Be Located, FDR-adjusted $p < 0.05$.

[c]Older subject was from the same extended family as currently evaluated younger participant in COGA prospective study.

[d]Alcohol dependence was always diagnosed in accordance with DSM-IV criteria. All other disorders listed were diagnosed by either DSM-IV or DSM-III-R criteria, depending on the prevailing diagnostic system at the time of the baseline interview.

[e]ASPD = antisocial personality disorder; Anxiety dx = at least one diagnosis of social phobia, panic disorder, posttraumatic stress disorder, agoraphobia, obsessive-compulsive disorder, and/or panic disorder; Mood dx = major depressive episode.

[f]Occurred only in the context of alcohol or other substance use.

Baseline Characteristics of Interviewed and Not-Interviewed Subjects

The majority (706, 89%) of the 789 contacted living subjects was interviewed (Fig. 2). Noninterviewed subjects included those who refused (N = 55) and those who were unavailable for assessment due to cognitive or physical frailty or inaccessibility (e.g., institutionalization; N = 28). Baseline characteristics of these 83 -noninterviewed individuals were not statistically different from those of the 706 interviewed subjects (all with FDR-adjusted $p \geq 0.05$), with or without controlling for baseline age.

Willingness to be Recontacted

Nearly all (699 of 706, i.e., 99%) interviewees agreed to be contacted for an additional follow-up evaluation. As anticipated (Hypothesis 2), the likely participation rate among located living subjects was high (proportion and 95% confidence interval = 0.89 [0.86, 0.91]) for a subsequent follow-up study.

Interviewed Subjects' Demographic and Health Status

Table 2 provides descriptive statistics of the current interview findings, by age category. Although gender differences across the age-groups were not statistically significant (FDR-adjusted $p = 0.11$), the proportion of males increased from about half of the youngest age-group to about two-thirds of the oldest age-group. There were no significant differences in educational achievement between the 4 groups, with 30% holding a high school diploma and an additional 61% reporting at least 1 year of education beyond that point. Interestingly, although the number of specific medical conditions experienced rose significantly from an average of 1 to 1.8 between the youngest and oldest age categories (FDR-adjusted $p < 0.001$), self-ratings of overall physical health did not differ significantly, with 62% of the sample reporting good or excellent health (FDR-adjusted $p > 0.99$). In particular, endorsements of high blood pressure, cancer, and heart disease increased with age (all with FDR-adjusted $p < 0.01$). There were also no age-related differences in their self-reported global mental health or memory compared with same-aged peers (FDR-adjusted $p > 0.05$). Over 70% endorsed "excellent/good" mental health, and over 80% considered their memory to be as good as or better than that of their peers (Table 2).

Table 2. Current Demographics, Health Outcomes, and Recency of Drinking Across 4 Age Groups of Interviewed Participants (n = 706): % for Categorical Variables and Mean (SD) for Continuous Variables

Follow-up characteristics n	50 to 54 180, 26%	55 to 59 199, 28%	60 to 64 167, 24%	65+ 160, 23%
Gender: Male (%)	49	52	58	66
Race (%)				
White	76	78	77	89
Black	19	18	20	9
Other	5	3	3	2
Hispanic	6	8	7	3
Marital status[a] (%)				
Married	49	45	46	53
Widowed	2	9	7	19
Separated	6	4	4	1
Divorced	23	30	33	20
Never married	20	13	11	7
Living arrangement (%)				
Alone	19	25	23	25
With spouse	52	48	49	54
With family	27	25	25	18
Assisted living	1	1	2	3
No fixed home	1	1	1	1
Education (%)				
Less than High School	8	10	8	9
High School	28	34	33	25
Beyond High School	64	56	59	66
Employment[a]	66	62	46	18
Physical health (%)				
Excellent	13	12	13	12
Good	53	47	46	52
Fair	27	32	25	29
Poor	7	9	16	7
Mental health (%)				
Excellent	28	23	25	31
Good	44	54	57	57
Fair	24	17	14	10
Poor	3	6	4	1
Memory (compared to same-aged peers) (%)				
Better	20	26	23	35
The Same	61	56	57	56
Worse	19	18	20	9
Self-reported medical issues (%)				
High blood pressure[a]	42	48	59	65
Diabetes	11	21	25	24
Chronic obstructive pulmonary disease (COPD)	11	14	22	21
Cancer[a]	7	8	13	28
Heart Disease[a]	5	7	14	24
Brain Injury or Concussion	8	7	11	3
Hepatitis C	3	9	7	4
Stroke	3	3	5	6
Liver Disease	3	2	5	4
Epilepsy	2	4	4	2
Number of Medical Issues[a]	1.0 (1.0)	1.2 (1.2)	1.6 (1.4)	1.8 (1.2)
Last drink [a] (%)				
≤1 year	68	54	53	46
>1 to ≤5 years	7	11	8	6
>5 to ≤10 years	4	9	7	3
>10 years	21	26	32	45

[a]FDR-adjusted $p < 0.05$.

Table 3. Past 12 Months of Alcohol Consumption Across Four Age Groups (n = 392 Who Drank During That Period): % for Categorical Variables and Mean (SD) for Continuous Variables

n	50 to 54 122, 31%	55 to 59 108, 28%	60 to 64 88, 22%	65+ 74, 19%
Typical number of drinks in a week during drinking weeks	18.0 (27.4)	18.5 (24.9)	13.4 (19.6)	12.5 (17.0)
Number of drinking weeks	30.9 (20.3)	30.6 (20.2)	28.4 (20.0)	33.5 (19.0)
Maximum drinks in 24-hours	9.0 (8.8)	8.7 (8.1)	7.7 (7.5)	6.1 (6.3)
Weekly risky drinking[a]	21%	20%	10%	23%

[a]Weekly risky drinking = male/female drinkers who drank every week and typically drank more than 14/7 drinks a week.

Table 4. Past 5 Years of Alcohol-Related Problems and Treatment Across Four Age-Groups (n = 450 Who Drank During That Period): % for Categorical Variables and Mean (SD) for Continuous Variables

Last 5 years of problems/treatment n	50 to 54 135, 30%	55 to 59 129, 29%	60 to 64 102, 23%	65+ 84, 19%
Spent 4 or more hours a day drinking or recovering from drinking (%)	56	52	45	38
Drank more than intended or longer than intended (%)	40	33	40	25
Drunk driving (%)	35	40	38	23
Problems with getting things done or getting along with people (%)	39	33	39	15
Tried but failed to cut down (%)	37	30	30	15
Blackout 3 or more times (%)	27	25	27	14
Withdrawal: sweat (%)	22	20	17	7
Withdrawal: shakes (%)	16	14	16	5
Withdrawal: heart palpitations (%)	20	14	9	2
Withdrawal: nausea or vomit (%)	17	11	13	4
Withdrawal: seizure or fit (%)	2	2	0	1
Impaired memory (%)	21	17	15	5
Tingling or numbing feet (%)	10	7	6	4
Liver disease or jaundice (%)	1	2	3	2
Vomited blood (%)	2	2	4	0
Pancreatitis (%)	3	2	2	0
Any treatment (%)	35	36	34	19
Counseling (%)	31	27	25	15
Outpatient alcohol program (%)	10	11	9	4
Inpatient alcohol program (%)	13	8	6	5
AA or other self-help meetings (%)	24	27	21	10

Interviewed Subjects' Alcohol Consumption, Alcohol-Associated Problems, and Treatment

Fifty-six percent of interviewed subjects reported alcohol consumption within the past 12 months, and 30% reported abstinence for at least the past 10 years. Eight percent indicated no drinking within the past year but drank within the past 5 years, and 6% indicated no drinking within the past 5 years, but drank within the past 10 years. Time since the last alcoholic drink increased with age (FDR-adjusted $p \leq 0.001$; Table 2); over two-thirds of participants aged 50 to 54 reported drinking within the past year, compared with fewer than half of subjects aged 65+. In particular, relative to the youngest (aged 50 to 54) interviewees, odds ratios [and 95% confidence intervals] of being a current drinker (defined as drank within the last 12 months) for 55 to 59, 60 to 64,

and 65+ were 1.02 [0.67, 1.57], 1.34 [0.87, 2.06], and 0.55 [0.36, 0.85], respectively.

Table 3 furnishes additional information about recent alcohol consumption among the 392 interviewees who consumed any alcohol in the 12 months prior to the interview (Fig. 1). There were no significant age-related differences in typical weekly consumption, number of drinking weeks, maximum number of drinks in a 24-hour period, or weekly risky drinking (all FDR-adjusted $p > 0.67$). Weekly risky drinking was defined as typically drinking more than 7 (for females)/14 (for males) drinks every week in the past year (NIAAA, Rethinking Drinking). Specifically, relative to the 50- to 54-year-old subjects, odds ratios [and 95% confidence intervals] of weekly risky drinking for 55 to 59, 60 to 64, and 65+ were 2.26 [0.94, 5.38], 0.86 [0.41, 1.84], and 0.95 [0.49, 1.87], respectively.

Table 4 details alcohol problems and treatment among the 450 interviewees who drank at any point within the past 5 years (Fig. 1). Overall, 63% endorsed at least 1 alcohol dependence symptom/blackout, 23% endorsed at least 1 alcohol withdrawal symptom, and 19% endorsed at least 1 alcohol-related medical condition. Endorsement rates of alcohol-related problems did not significantly differ by age-group (FDR-adjusted $p > 0.38$). Relative to the 50- to 54-year-old interviewees, odds ratios [and 95% confidence intervals] of experiencing any alcohol-related problems for 55 to 59, 60 to 64, and 65+ were 0.88 [0.49, 1.58], 0.44 [0.24, 0.79], and 1.06 [0.61, 1.83], respectively. The proportions of subjects who reported specific alcohol-related medical conditions were too small to obtain statistically meaningful results, except for memory impairment, which was nonsignificant for age-group (FDR-adjusted $p = 0.46$). Finally, only 32% received any treatment for alcohol problems within the previous 5 years, with no differences observed for age-group (FDR-adjusted $p > 0.58$). Relative to the 50- to 54-year-old subjects, odds ratios [and 95% confidence intervals] of being treated for alcohol problems for 55 to 59, 60 to 64, and 65 + were 0.38 [0.12, 1.17], 0.65 [0.18, 2.38], and 0.65 [0.20, 2.09], respectively.

DISCUSSION

The first aim of this paper was to address the logistics and feasibility of locating, recruiting, and evaluating older COGA participants with a lifetime history of DSM-IV alcohol dependence. Although this sample is not epidemiological in nature, the long-term outcome of subjects from high-risk families has not been well studied prospectively, and for this reason, we considered this investigation to critical to help fill this gap. Within a short period of 12 months, we were able to locate 60% of targeted individuals who had not been contacted for an average of 23 years. We anticipate that another 15 to 25% of this pilot sample will be located with additional time and resources as part of the more comprehensive follow-up study. Individuals with younger relatives currently participating in the prospective study were easier to locate and to confirm as living or deceased, consistent with Hypothesis 1. These family connections, which are an integral part of COGA's design, helped counterbalance the constraints imposed by the short time frame of the pilot study, as well as the challenges associated with following subjects with a history of alcohol dependence. As suggested by others (Faden et al., 2004; Farabee et al., 2016; Stouthamer-Loeber et al., 1992), investigators conducting follow-up studies with long latencies may benefit from utilizing a multipronged approach that includes family connections, when available. Two of the baseline factors that were negatively associated with locating subjects—a prior history of other substance use disorders and ASPD—are consistent with other studies (c.f., Koloski et al., 2013). However, sensitivity analyses indicated that these 2 factors, associated with a more severe course of illness, were no longer significant after controlling for baseline age. Our intention was to provide an initial descriptive look at living subjects by age-group at follow-up rather than conduct analyses that adjust for other baseline characteristics, which we acknowledge is an important step in later analyses with more complete samples. Readers should view the current findings as provisional, given that they are based on a subset of this sample. Our outcomes may also have been biased in the direction of less severity from deceased subjects, because they included some of the most affected individuals. Selective attrition due to death is inherent in many follow-up studies of chronic disease, and a limitation of this study is that we did not statistically take this into account. The numerical increase in the proportion of males interviewed across the age-groups was not anticipated and might reflect, in part, cohort increases in alcohol dependence among younger women. Of the 789 located living subjects, 89% expressed a willingness to be evaluated again in the future, supporting Hypothesis 2.

Our second aim was to describe key aspects of older alcohol-dependent subjects' long-term demographic, health, and alcohol-related outcomes by age-group. While it was not surprising that the overall number of reported medical disorders increased with age, as well as the specific types found to be significant (e.g., cancer), we did not expect that self-ratings of overall physical health would be similar for each age-group. Such global ratings are subjective and therefore may be prone to biases of social desirability (e.g., a disinclination to complain). A separate paper, in preparation, will examine in detail the ages, causes, and baseline predictors of mortality in this sample. In contrast to physical health, the increase in positive mental health ratings with age is consistent with some prior research (Garrido et al., 2009).

Alcohol consumption questions revealed that proportionally fewer older than younger subjects were currently drinking, in line with other studies (Vaillant, 2003) and supportive of the first part of Hypothesis 3. The prevalence of current drinking among COGA subjects aged 65+ (46%) was

somewhat lower than that reported by same-aged population-sample subjects in NESARC-III (55.2%; Grant et al., 2017), CBHSC (56%; Center for Behavioral Health Statistics and Quality, 2015), and the National Health Interview Surveys (approximately 57%; Breslow et al., 2017). These differences may be due to several factors. First, a number of our historically alcohol-dependent subjects may have adhered to the widespread treatment goal of total abstinence, which leads to a more stable recovery pattern than moderate drinking (Vaillant, 2003). Second, almost 1-quarter of our target sample had died since their baseline interview, thereby selectively removing some of the most severely alcohol-dependent individuals. Finally, 40% yet to be located subjects had a relatively severe addiction history, further contributing to the underrepresentation of highly affected individuals. Although fewer COGA subjects reported current drinking, a dramatically higher proportion of those aged 65+ reported high-risk drinking in the past 12 months (23%) than did their peers in the NESARC sample (3.8%). The main source of this discrepancy probably lies with the alcohol-dependence-based COGA sample versus the epidemiologically based NESARC sample, which contained substantially fewer alcohol-dependent subjects. In sum, relative to the general population, a smaller percentage of interviewed older COGA subjects were currently drinking, but those who did exhibited far greater levels of high-risk consumption. Schuckit and colleagues (2018) provide additional details about the characteristics and predictors of these older COGA pilot subjects' alcohol involvement, classifying them into subgroups arrayed along a continuum of severity.

Among the COGA sample, the prevalence of current drinking was negatively associated with age, as the literature suggested and the first part of Hypothesis 3 predicted. However, among current drinkers, problematic alcohol involvement, as indexed by weekly risky drinking, alcohol-related symptoms, and treatment, failed to exhibit a clear relationship with follow-up age, contrary to the second part of Hypothesis 3. When additional subjects are included in the future COGA follow-up, this issue will need to be reexamined, as it runs counter to much of the literature. One possible source of discrepancy may lie with the historically alcohol-dependent COGA sample, which contrasts with the epidemiological samples presented in Breslow and colleagues (2017), Vestal and colleagues (1977), and Grant and colleagues (2017); the British civil servants examined in Knott and colleagues (2018); and the Harvard undergraduates and socially disadvantaged adolescents reported by Vaillant (2003).

It is worth noting that only a relatively small proportion (19%) of the oldest participants received any treatment for their alcohol problems within the past 5 years, whether formal or self-help in nature. This suggests a public health need that is not being sufficiently addressed (Kelly et al., 2018), particularly in light of the high risk for medical problems and early death associated with heavy drinking among older adults (Breslow et al., 2015; Vestal et al., 1977).

This pilot study helps to set the stage for a more extensive follow-up that incorporates a broader sample and a wider range of outcome and predictor measures. Adding older individuals who lack a history of alcohol dependence at baseline would furnish a critical comparison group for the present affected sample. These affected–nonaffected comparisons would be especially informative for individuals from the same families, due to their overlapping environmental and genetic backgrounds. It is anticipated that, as a group, historically unaffected subjects may be easier to locate (Koloski et al., 2013) and that a greater percentage of them may be alive (Whitfield et al., 2017). In addition, the array of outcome measures can be expanded to include: (i) other substance use disorders (e.g., marijuana and opioids); (ii) psychiatric conditions (e.g., depression); and (iii) cognitive status, with an emphasis on mild impairment and dementia. Lastly, we would like to utilize a broader range of baseline predictors, including environmental variables (e.g., socioeconomic status, traumatic experiences), neuropsychological test performance, endophenotypic measures (e.g., neurophysiological [EEG and ERP]), and genetic data. In sum, COGA's extensive assessment of these domains provides a rare opportunity to search comprehensively for the long-term harbingers of alcohol use and consequences among its oldest members.

ACKNOWLEDGMENTS

We continue to be inspired by our memories of Henri Begleiter and Theodore Reich, founding PI and Co-PI of COGA, and also owe a debt of gratitude to other past organizers of COGA, including Ting-Kai Li, P. Michael Conneally, Raymond Crowe, and Wendy Reich, for their critical contributions. This national collaborative study is supported by NIH Grant U10AA008401 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA).

CONFLICT OF INTEREST

None.

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APPENDIX

COGA: The Collaborative Study on the Genetics of Alcoholism (COGA), principal investigators B. Porjesz, V. Hesselbrock, H. Edenberg, L. Bierut, includes 11 different centers: University of Connecticut (V. Hesselbrock); Indiana University (H.J. Edenberg, J. Nurnberger Jr., T. Foroud; Y. Liu); University of Iowa (S. Kuperman, J. Kramer); SUNY Downstate (B. Porjesz); Washington University in St. Louis (L. Bierut, J. Rice, K. Bucholz, A. Agrawal); University of California at San Diego (M. Schuckit); Rutgers University (J. Tischfield, A. Brooks); Department of Biomedical and Health Informatics, The Children's Hospital of Philadelphia; Department of Genetics, Perelman School of Medicine, University of Pennsylvania, Philadelphia PA (L. Almasy); Virginia Commonwealth University (D. Dick); Icahn School of Medicine at Mount Sinai (A. Goate); and Howard University (R. Taylor). Other COGA collaborators include the following: L. Bauer (University of Connecticut); J. McClintick, L. Wetherill, X. Xuei, D. Lai, S. O'Connor, M. Plawecki, S. Lourens (Indiana University); G. Chan (University of Iowa; University of Connecticut); J. Meyers, D.

Chorlian, C. Kamarajan, A. Pandey, J. Zhang (SUNY Downstate); J.-C. Wang, M. Kapoor, S. Bertelsen (Icahn School of Medicine at Mount Sinai); A. Anokhin, V. McCutcheon, S. Saccone (Washington University); J. Salvatore, F. Aliev, B. Cho (Virginia Commonwealth University); and Mark Kos (University of Texas Rio Grande Valley). A. Parsian and H. Chen are the NIAAA Staff Collaborators.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1. BETHANY – Older Subjects follow-up interview updated 12/20/16