UC San Diego

UC San Diego Previously Published Works

Title

The Search for Contributors to Low Rates of Recognition of Paternal Alcohol Use Disorders in Offspring From the San Diego Prospective Study

Permalink

https://escholarship.org/uc/item/1xh2t213

Journal

Alcoholism Clinical and Experimental Research, 44(8)

ISSN

0145-6008

Authors

Schuckit, Marc A
Clarke, Dennis F
Smith, Tom L
et al.

Publication Date

2020-08-01

DOI

10.1111/acer.14401

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

Check for updates

ALCOHOLISM CLINICAL & EXPERIMENTAL RESEARCH

The Search for Contributors to Low Rates of Recognition of Paternal Alcohol Use Disorders in Offspring From the San Diego Prospective Study

Marc A. Schuckit, Dennis F. Clarke, Tom L. Smith, Lee Anne Mendoza, and Lara Schoen

Background: The most efficient approach for establishing family histories (FHs) asks informants about disorders in their relatives (a Family History Method [FHM]). However, FHMs underestimate family diagnoses. We evaluated if accuracies of young adult offspring report of their father's alcohol use disorders (AUDs) related to the age, sex, education, and/or substance-related patterns/problems of either the young adult informants or their AUD fathers.

Methods: Data from the San Diego Prospective Study (SDPS), a multigenerational 35-year investigation, compared father/offspring pairs where the proband father's alcohol problems were correctly (Group 1) or incorrectly (Group 2) noted by offspring. In the key analysis, Group 1 versus 2 results were entered into bootstrapped backward logistic regression analyses predicting Group 1 membership.

Results: Five proband and one offspring characteristic were associated with correct identification of their father's alcohol problems. None of these related to age, education, or sex. Characteristics associated with correct FHM diagnoses included the father's FH of AUDs, self-report of drinking despite social/interpersonal or physical/psychological alcohol-related problems, spending much time related to alcohol, and his having a religious preference. The single offspring item predicting correct identification of the father's problems was the number of DSM alcohol problems of the offspring.

Conclusions: In the SDPS, FHM sensitivity was most closely related to the father's drinking characteristics, not the offspring characteristics. While unique aspects of SDPS families potentially limit generalizability of results, the data demonstrate how the FHM can offer important initial steps in the search for genetically related AUD risks in a subset of families.

Key Words: Genetics, Alcoholism, Family History Method.

KNOWLEDGE ABOUT A person's family history (FH) of a disorder can be useful in both clinical and research settings (Rice et al., 1995; Vandeleur et al., 2015). For clinicians, knowing if relatives ever evidenced a Mendelian dominant or recessive genetic disorder (e.g., Huntington's disease or cystic fibrosis) can help identify early signs of the condition and might contribute to patients' decisions about having children. Knowledge of a familial complex genetically influenced disorder (e.g., high blood pressure or Type 2 diabetes) is also useful, but less informative because each relevant gene probably contributes to only a small proportion of the risk and environment is likely to play a major role (Schuckit, 2018). Directly relevant to the current report, knowledge of a subject's FH can also help researchers select individuals or families on which to focus efforts in order to control costs and maximize the usefulness of the data gathered (Rice et al., 1995; Schuckit et al., 2016a).

There is general agreement that the most accurate FH comes from the Family Study Method (FSM) that uses personal interviews with all available first- and second-degree relatives (Milne et al., 2009; Rice et al., 1995; Vandeleur et al., 2015; Waldron et al., 2012). But that approach has downsides including high cost, the time, and effort needed to gather the information from all available relatives, as well as the bias of nonrandom missing data resulting from lack of information on relatives who have died, those too ill to be interviewed, individuals who cannot be located, as well as those who refuse to participate.

In an alternate approach, the Family History Method (FHM), data can be gathered relatively quickly and at lower cost. Here, relatively simple instruments ask informants about demography and clinical conditions regarding multiple relatives (Hardt and Franke, 2007; Milne et al., 2009; Rice et al., 1995; Waldron et al., 2012; Walker et al., 1990). FHM downsides include inconsistencies in an individual's reports over time and disagreements among relatives regarding the familial problems (Boynton et al., 2011; Crews and Sher, 1992; Mojica-Perez et al., 2019). The most salient drawback is the relatively low sensitivity of FHMs (the proportion

From the Department of Psychiatry, University of California, San Diego, La Jolla, California.

Received for publication February 18, 2020; accepted June 15, 2020.

**Reprint requests: Marc A. Schuckit, MD, Department of Psychiatry, University of California, San Diego, 8950 Villa La Jolla Dr Suite B-218, La Jolla, CA 92037; Tel.: 858-822-0880; Fax: 858-822-1002; E-mail: mschuckit@ucsd.edu*

© 2020 by the Research Society on Alcoholism.

DOI: 10.1111/acer.14401

of subjects who had a condition who were correctly identified; e.g., Rice et al., 1995; Roy et al., 1994).

The specific disorder studied relates to FHM sensitivity where obvious medical conditions, (e.g., hip fractures) are likely to have high FHM sensitivities (Lix et al., 2017), but identifying relatives' psychiatric disorders have lower sensitivities (Milne et al., 2009; Thompson et al., 1982). Regarding substance use disorders (SUDs), more accurate FHM reports are seen for smoking tobacco (Pape et al., 2019) with less impressive sensitivities for misuse of alcohol and illicit drugs. Regardless of the condition studied, specificities (the proportions of subjects without a condition correctly identified as such by an informant) are often over 90%.

The average sensitivities of FHM studies of familial alcohol problems, including AUDs, usually range between 30 and >50% (Andreasen et al., 1986; Huen et al., 1996; Kendler et al., 1991, 2002; Milne et al., 2009; Vandeleur et al., 2008; Waldron et al., 2012). An example of more promising FHM results involved correlations of 0.70 between college students' alcohol problems of their parents and those parents self-report using variations of the Short Michigan Alcohol Screening Test (SMAST; Crews and Sher, 1992). However, offspring missed alcohol use disorder (AUD)-like problems in 17% of fathers and 50% of mothers. In addition, the parents' self-reports were not validated by repeated structured interviews over time, the analyses focused on problem patterns for the parents rather than AUDs, and no information was available regarding the performance of individual AUD criteria. Another study evaluated twin pair concordance regarding their father's alcohol problems (Slutske et al., 1996), but the paper focused on agreement among the offspring reports and did not include DSM AUD criteria.

In addition to the condition being studied, other characteristics are also associated with higher FHM sensitivities. These include more severe alcohol histories in the subjects (the relative being reported upon; Huen et al., 1996; Pape et al., 2019; Vandeleur et al., 2008; Waldron et al., 2012); informants with conditions that are similar to the subject's problems (Boynton et al., 2011; Chapman et al., 1994; Milne et al., 2009; Rice et al., 1995; Vandeleur et al., 2015); a subject for whom AUDs ran in their family (Boynton et al., 2011; Rice et al., 1995); a close genetic relationship between informant and subject (Rice et al., 1995); a focus on more observable criteria such as having ever been in treatment (Rhea et al., 1993; Sher and Descutner, 1986); the use of less demanding criteria for the subject's condition (e.g., alcohol problems rather than meeting full AUD criteria; Mann et al., 1985); and when multiple informants are used (Rice et al., 1995).

The relationships of informants' and subjects' demographic characteristics to the accuracy of the informant's reports vary across studies. Regarding *sex*, some investigations noted that female subjects with alcohol problems were more likely to be correctly identified than male subjects, although the *sex* of the informant might have less impact on the accuracy of the reports (Crews and Sher, 1992; Rice et al., 1995; Vandeleur et al., 2008). However, other studies noted that male offspring might more accurately report alcohol problems in their mothers and female offspring be more accurate in reporting alcohol problems in their fathers (Pape et al., 2019; Rhea et al., 1993). The importance to sensitivity of an informant's *education* is also not clear, with one study reporting a fivefold *lower* accuracy for an informant's report about a parent's smoking history for informants with a college education compared to those with less than high school completion (Pape et al., 2019). The informant's *age* was reported to have little relationship to the validity of their report in some studies (e.g., Vandeleur et al., 2008), but Pape and colleagues (2019) reported a twofold higher odds ratio for correct offspring reports for older informants.

The relationships of informants' and subjects' demographic characteristics to the accuracy of substance use histories using the FHM require additional study. If demography is closely related to FHM sensitivity, it could be easier to identify which informant is likely to give the most accurate FH. Our every 5-year evaluation over 35 years for members of 2 generations of the San Diego Prospective Study (SDPS; e.g., Schuckit et al., 2019a; Schuckit et al., 2019b) offers an opportunity to expand information regarding relationships of demography and other characteristics to the accuracy of reports of parental alcohol-related problems by offspring. The SDPS incorporates many of the better-established characteristics related to higher accuracy of informants' FHM reports. These include using standardized personal interviews with subjects and informants, relatively severe alcohol problems and high levels of alcohol intake in subjects, a first degree genetic relationship between informants and subjects, high rates of alcohol problems in both generations, and the focus on relatively broad alcohol problems for fathers that do not require that full AUD criteria be met for the informant's report to be considered valid.

The data reported here were used to evaluate 3 hypotheses. These included the following: (i) higher levels of education in the offspring with the potential greater understanding of human behavior and a greater awareness of problems in their environment will be associated with higher rates of recognition of paternal alcohol problems; (ii) for potential reasons similar to the impact of higher levels of education, older informants will more accurately report a father's alcohol problems; and (iii) female offspring will more accurately report their father's AUDs, as noted in some prior studies.

MATERIALS AND METHODS

Selection of SDPS Probands (Fathers of the Offspring)

Following approval from the University of California, San Diego (UCSD) Human Research Protections Committee, between 1978 and 1988 recruitment of original SDPS participants (probands/first-generation subjects) included drinking 18- to 25-year-old male UCSD respondents to randomly mailed questionnaires. Using the FHM and DSM-III AUD criteria (American Psychiatric Association, 1980), subjects with AUD fathers were selected if that student themselves never yet met criteria for AUDs or SUD on illicit drugs.

Note that the parents of the original probands were not interviewed. A FH-negative proband was then selected to match an FH-positive proband on age, sex, recent drinking history, smoking, and use of illicit drugs, but who reported no first degree relative with an AUD (Schuckit and Gold, 1988). Potential subjects with current bipolar or schizophrenic disorders were ineligible for participation. Reflecting the original hypothesis of the SDPS, each proband's level of response to alcohol (LR) was evaluated with oral alcohol challenges where peak BAC averaged 60 mg/dl at 60 minutes (e.g., Ehlers et al., 1999; Schuckit and Gold, 1988).

Follow-up of the First-Generation Probands and Selection of Their Second-Generation Offspring for the Current Analyses

After additional Human Subject's Protection Committee review, beginning in 1988 100% of the original 453 SDPS probands were located, 99% of whom agreed to participate in the follow-up protocol. Evaluations asked about their interval drinking status and problems, including each of what became the 11 DSM-IV AUD criteria (American Psychiatric Association, 1994) using questions derived from the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) instrument (validity, retest reliabilities, and cross-interviewer reliabilities of 0.7 to 0.8; Bucholz et al., 1994; Hesselbrock et al., 1999). Subsequently, over 90% of probands were evaluated every 5 years where data were gathered regarding their own drinking practices and problems, and where the probands and their spouses offered information regarding the proband's biological offspring. Note that the proband's AUD diagnoses used in the current analysis were based on personal interviews with that proband father.

For the current data, beginning at offspring age 18, an interview was carried out with these second-generation sons and daughters using a set of questions similar those asked during proband follow-ups. Offspring were also followed with personal interviews about every 5 years regarding changes in demography, substance use and problems, and development of major psychiatric disorders. Follow-up evaluations also included filling out the Impulsiveness Subscale of the Karolinska Scales of Personality and the Zuckerman Sensation Seeking Scale (Gustavsson et al., 2000; Zuckerman, 1978).

The offspring interviews contained items extracted from the Family History Assessment Module used in conjunction with the SSAGA in Collaborative Study of the Genetics of Alcoholism (COGA) research (Rice et al., 1995). As part of the FH section of their interview, offspring were asked: "Have any of your parents or siblings had any of the these [following] experiences because of their own drinking?". The items included the 11 DSM-IV AUD criteria plus a question about craving. In our offspring protocol, before exiting the FH section interviewers also asked about alcohol quantities and frequencies for each first degree relative along with a re-review of the alcohol problems. For these analyses, if the son or daughter endorsed 2 or more of the alcohol problem items for their father, the report was considered a positive indication of the proband's alcohol problem. This relatively liberal FH interpretation of alcohol problems was used considering the advice against invoking excessively restrictive criteria when identifying a FH of AUDs (Mann et al., 1985), as described in the Introduction.

At the time the current analyses were carried out, there were 447 probands' sons and daughters age 18+, of whom 352 (78.7%) had been interviewed. Of these 352, 135 were offspring (the second generation of directly interviewed participants) who were eligible for the analyses because they were drinking offspring of the 73 probands (first generation of directly interviewed participants) who had developed DSM-IV AUDs in the interval since entering the study. The major analyses focus on whether the offspring recognized the presence of their father's DSM-IV alcohol problems that had been identified from the father's own semi-structured interview. The proband's AUD FH listed in Table 1 was based on the proband's report of his mother's and father's alcohol problem history, but, using the FHM approach at study entry, the proband's parents were not directly interviewed. Among those AUD probands, 21 had only one relevant offspring, 44 had 2 offspring, and 8 reported 3 or more drinking offspring age 18+. The Design Effect related to the possible skew of results caused by the number of children per family ranged from 0.08 to 1.37 across the FH alcohol questions, where 2.0 or higher would indicate a potential meaningful effect of multiple offspring per family (Muthen and Satorra, 1995).

In addition to SSAGA interviews and personality questionnaires, all probands and drinking offspring also reported their usual intensity of response to alcohol using the retrospective Self-Report of the Effects of Alcohol (SRE) questionnaire (Schuckit, 2018; Schuckit et al., 2019a; Schuckit et al., 2016a; Schuckit et al., 2019b), which is the only LR to alcohol measure available in both generations. This 12-item instrument records the average number of standard drinks required for up to 4 effects during the approximate first 5 times of drinking (SRE-5), their period of heaviest alcohol intake, and the 3 most recent drinking months. The total SRE (SRE-T) score was the average drinks needed for effects across all 3 timeframes. The 4 possible effects included drinks required to: actually experience first alcohol effects, slurring speech, develop unsteadiness of walking, and unwanted falling asleep, with the greater the number of drinks for effects the lower the level of response, or sensitivity, per drink (Daeppen et al., 2000; Ray et al., 2010; Schuckit, 2018; Schuckit et al., 2019a; Schuckit et al., 2019b).

Data Analyses

The General Approach. Tables 1 (probands) and 2 (offspring) evaluate variables that *might* relate to an informant's correct identification of the proband's alcohol problems and describe sample characteristics. While the key results highlighted in the Discussion were generated in the regression analyses in Table 3, Tables 1 and 2 also allow the reader to understand the magnitude of the differences across groups for variables that significantly added to Table 3 regressions. Our emphasis is on all 135 AUD-proband/offspring pairs based on the data cited in the Introduction that different offspring (e.g., older vs. younger informants) might differ in the accuracy of their reports of a parent's problems. Group 1 versus 2 differences in Tables 1 and 2 were tested by ANOVA for continuous variables and chi-square for categorical data. To evaluate the possibility that the statistical tests in Tables 1 and 2 might themselves have value, an exact binomial test was run to determine the likelihood of obtaining the number of significant tests at alpha = 0.05 that emerged among the 60 items in those tables. An additional analysis using the Holm–Bonferroni sequential correction (Holm, 1979) was conducted to take into account multiple testing effects and to adjust for family-wise error.

The Bootstrapping Analyses. Table 3 presents the key results of this paper through a series of bootstrapped backward logistic regression analyses evaluating the combination of proband and offspring items that best related to the correct identification by offspring of their father's alcohol problems. An Elastic Net Regularization Model (Friedman et al., 2010) using 100 bootstraps in R identified the top 20% of the variables that had the strongest relationship to an offspring correctly identifying his or her father as having alcohol problems. Those selected variables were then used in the series of regression analyses. Subsequently, the analyses in Table 3 used R where each randomly selected proband was paired with his randomly selected offspring in relevant regression analyses, a process repeated through 1,000 bootstrapped iterations, thus minimizing the impact of possible cluster effects within families (R-Core Team, 2013).

For Table 3, proband–offspring subsets were selected using the sample_n function within the dplyr package in R (Wickham, et al.,

Table 1. *Probands* With Auds Described Overall and in Groups Based on Offspring's Recognition of Their Father's Aud

Variables proband	All Probands *N* 135 % or mean (SD)	Group 1 Offspring reports Correct *N* 30, 22.2% % or mean (SD)	Group 2 Offspring Reports Incorrect *N* 105, 77.8% % or mean (SD)	χ^2 or *F*-test
Demography				
Age	55.0 (4.10)	53.3 (4.46)	55.4 (3.99)	6.38[a]
European American %	98.5	100.0	98.1	0.58
Ever married %	99.3	100.0	99.0	0.29
Ever divorced %	25.2	26.7	24.8	0.45
Identify with a religion %	54.8	70.0	50.5	3.59·
Education (years)	17.7 (2.00)	17.6 (2.06)	17.8 (1.99)	0.17
Alcohol				
Parent AUD %	63.7	83.3	58.1	6.43[a]
Alcohol dependence %	60.7	83.3	54.3	8.26[b]
SRE-5	3.5 (1.37)	3.9 (1.50)	3.3 (1.31)	4.00[a]
SRE-T	4.9 (1.91)	5.7 (2.04)	4.7 (1.82)	6.39[a,x]
Maximum drinks	16.7 (5.21)	18.6 (6.08)	16.2 (4.83)	3.92[a,x]
DSM-IV criteria				
Number DSM items	5.5 (2.32)	7.07 (2.39)	5.07 (2.11)	8.75[b]
Tolerance	45.2	60.0	41.0	3.42
Withdrawal	28.1	36.7	25.7	1.38
Drink more/longer	87.4	90.0	86.7	0.24
Desire/unable decrease	60.0	53.3	61.9	0.47
Much time spent %	54.8	86.7	45.7	15.80[c]
↓ Activities to drink %	23.7	50.0	16.2	14.75[c]
Use despite physical or psychological problems %	28.9	53.3	21.9	11.22[c]
Missed obligations %	78.5	86.7	76.2	1.52
Hazardous use %	82.2	93.3	79.0	3.56
Legal problems %	20.7	30.0	18.1	2.01
Use despite social or interpersonal problems %	41.5	66.7	34.3	10.08[c]
Drugs				
Use tobacco %	53.3	56.7	52.4	0.17
Use CB %	93.3	100.0	91.4	2.76
Drugs other than CB %	72.6	18.5	54.1	2.24
SUD CB %	16.3	5.9	10.4	3.04
SUD other drugs %	20.7	33.3	17.1	3.72
Personality				
Karolinska impulsivity	20.2 (2.67)	20.8 (2.31)	20.0 (2.75)	2.50
Zuckerman sensation seeking	22.1 (4.69)	22.5 (5.49)	22.0 (4.56)	0.26

AUD, Alcohol Use Disorder; CB, cannabinol; SRE-5 and SRE-T, Self-Report of the Effects of Alcohol for first 5 times drink and for Total; DSM-IV, Fourth Diagnostic and Statistical Manual.

[a]$p < .05$; [b]$p < .01$; [c]$p < .001$; x = a variable that was not significant after Holm–Bonferroni testing; degrees of freedom: $F = 1,134$; $x^2 = 1$.

2018). All 1,000 bootstraps were included to calculate the mean adjusted pseudo R^2 using the psych package's fisherz and fisherz2r functions (Revelle, 2018) and the mean function within R. The odds ratios and mean *p*-values were calculated with the meanp function from the metap package (Dewey, 2019). As described elsewhere (Schuckit et al., 2019a), in the absence of generally accepted guidelines for the optimal number of bootstrapped regression analyses in which a variable must have entered significantly, we evaluated the clinical implications and internal consistency of results when a priori values of 100, 200, and 300 iterations marked the cutoff for inclusion of a variable in Table 3. Requiring inclusion in only 100 of the 1,000 iterations in Table 3 resulted in almost all variables from Tables 1 and 2 identified by the Elastic Net Regularization Model contributing significantly and requiring 300 iterations entered for Table 3 resulted in only 2 items entering. Thus, we required that variables needed to have added significantly to 200 iterations to be included in Table 3.

RESULTS

The data were based on personal interviews with 135 SDPS drinking offspring who were age 18 or older and whose fathers (the probands) developed DSM-IV alcohol abuse or dependence since entering the study as non-AUD drinkers at about age 20. To be included in analyses, the probands had to have at least one drinking biological offspring who was at least age 18 at the time of their most recent follow-up in 2018 or 2019 ($N = 135$). While not the focus of this report, additional data indicated that 97.2% of the offspring of non-AUD probands correctly identified their father's status (the specificity).

As shown in the first data column of Table 1, the average father in the proband–offspring pairs was 55 years old, European American, had ever been married, 25% ever divorced, and reported 18 years of education. Reflecting the criteria used to select the original SDPS probands, 64% had a parent with an AUD. During the 35 years of their follow-ups, 61% of these AUD probands met criteria for alcohol dependence and 39% for alcohol abuse. During the follow-up, these men reported a lifetime average maximum of 17 standard drinks per occasion and endorsed an average of 5.5

Table 2. *Offspring* of Probands With A-UDs Described Overall and in Groups Based on Offpring's Recognition of Their Father's AUD

Variables Offspring	All Offspring*N* 135 % or mean (SD)	Group 1 Offspring Reports Correct *N* 30, 22.2% % or mean (SD)	Group 2 Offspring Reports Incorrect *N* 105, 77.8% % or mean (SD)	χ^2 or *F*-test
Demography				
Female sex %	50.4	56.7	48.6	0.61
Age	25.0 (4.82)	25.3 (4.53)	24.9 (4.92)	0.12
European American %	97.0	100.0	96.2	1.18
Ever married %	18.5	20.0	18.1	0.06
Identify with a religion %	37.8	26.7	41.0	2.03
Education (years)	14.9 (2.43)	14.8 (2.19)	15.30 (2.46)	0.14
Alcohol				
Offspring AUD%	65.9	86.7	60.0	7.39[b]
Alcohol dependence %	40.7	60.0	35.2	5.93[a]
Alcohol abuse %	25.2	26.7	24.8	0.45
SRE-5	3.1 (1.27)	3.2 (1.15)	3.1 (1.30)	0.33
SRE-T	4.2 (1.66)	4.5 (1.39)	4.1 (1.73)	1.26
Maximum drinks	11.0 (5.50)	12.2 (5.18)	10.6 (5.56)	2.55
DSM-IV criteria				
Number DSM Items	3.0(2.60)	3.9(2.37)	2.7(2.61)	7.42[b]
Tolerance %	43.0	60.0	38.1	4.57[a,x]
Withdrawal %	3.0	6.7	1.9	1.84
Drank More/Longer %	60.0	76.7	55.2	4.46[a,x]
Desire/Unable decrease %	20.0	20.0	20.0	0.00
Much time spent %	60.0	83.3	53.3	8.75[b]
↓Activities to drink %	21.5	23.3	21.0	0.08
Use despite physical or psychological problems %	7.4	13.3	5.7	1.98
Missed obligations %	45.2	63.3	40.0	5.13[a,x]
Hazardous use %	20.7	20.0	21.0	0.01
Legal problems %	3.7	6.7	2.9	0.95
Use despite social or interpersonal problems %	15.6	3.7	11.9	0.04
Drugs				
Use tobacco %	31.9	36.7	30.5	0.41
Use CB %	71.1	83.3	67.6	2.80
Use drugs other than CB % %	34.1	36.7	33.3	0.12
SUD CB	14.1	20.0	12.4	1.12
SUD drugs other than CB %	5.9	1.5	4.4	0.04
Personality				
Karolinska impulsivity	21.4 (4.18)	21.8 (4.40)	21.2 (4.13)	0.48
Zuckerman sensation seeking	20.2 (8.59)	23.6 (6.15)	19.2 (8.97)	6.22[a,x]

AUD = Alcohol Use Disorder; SRE-5 and SRE-T = Self-Report of the Effects of Alcohol for first 5 times drink and for Total; DSM-IV = Fourth Diagnostic and Statistical Manual; CB = cannabis.
[a]$p < 0.05$; [b]$p < 0.01$; *x* = a variable that was not significant after Holm–Bonferroni testing; degrees of freedom $F = 1,134$ $x^2 = 1$.

of the 11 DSM-IV criterion items. The lifetime rate of endorsement for each AUD criterion ranged from 87% for often using alcohol in higher quantities or for longer periods than intended to 21% for recurrent alcohol-related legal problems. During the 35 years of follow-up, about half of these probands had used tobacco products, over 90% had used cannabis, 73% had used other illegal drugs, 16% ever met criteria for a cannabis use disorder, and 21% met criteria for a SUD on another illicit drug. Although the numbers for variables in Table 1 were generated by considering all 135 proband–offspring pairs, no values were significantly different from those in Table 1 if data were limited to the 73 individual AUD probands involved in these analyses.

Data columns 2 through 4 in Table 1 indicate 11 significant differences across the 22% of *probands* for whom at least 1 offspring reported knowing about their father's alcohol problems (Group 1) and the 78% of probands for whom no son or daughter recognized their father's condition (Group 2). Two of these 11 differences did not survive the Holm–Bonferroni procedure (SRE-T and maximum drinks). The 9 differences that did survive included a slight but significantly lower ages for Group 1 probands, but there were no other significant demographic differences, including similarities for the proportions who were divorced from the offspring's mothers. Group 1 also reported higher values for the proband having a parent (i.e., grandparent to the offspring—data supplied by the probands about their parents) with an AUD, a proband diagnosis of alcohol dependence, the need for more drinks for effects the first 5 times of drinking, and reporting a higher number of the 11 lifetime DSM-IV AUD items. The latter included noting higher proportions of probands who endorsed spending a great deal of time involved with alcohol, decreasing other important activities in order to drink, continuing to use alcohol despite medical or psychological problems caused by alcohol, and drinking despite social or interpersonal problems related to alcohol. Although

Table 3. Backward Logistic Regression Bootstrapping (1,000 Times) Predicting Whether the Offspring Recognized Their Father's Alcohol Problems

Variable	Times significantly contributed to a bootstrap out of 1,000	Average odds ratio	Average *p*-value
Proband: Much Time Spent Involved with Alcohol	729	9.46	0.01
Offspring: Total Number of DSM-IV Items Endorsed	592	3.58	0.03
Proband: Identify with a Religion	396	5.63	0.03
Proband: Use Despite Social/Interpersonal Problems	239	7.07	0.02
Proband: Use despite Physical/ Psychological Problems	237	6.62	0.02
Proband: Has an AUD Parent	224	5.56	0.04
McFadden pseudo $R^2 = 0.36$			

AUD = Alcohol Use Disorder; DSM-IV = Fourth Diagnostic and Statistical Manual.

not shown in Table 1, if the analyses were limited to counting each proband only once ($N = 73$) and selecting only the oldest son or daughter when data from multiple offspring were available, significant differences remained for criterion items of a great deal of time spent regarding alcohol, giving up important activities to drink, continuing to drink despite medical and psychological problems caused by alcohol and continuing despite interpersonal or social problems. In that smaller sample, group differences similar to those in Table 1 remained at a trend ($p < 0.10$) for a proband's AUD FH, his alcohol dependence diagnosis and for his maximum drinks.

Table 2 focuses on data from the 135 interviewed *offspring* of the probands who had developed an AUD during the 35 years of follow-up. Overall, these sons (50% of the sample) and daughters were 25 years old, European American, and had 15 years of education, with about 20% having ever been married and a third who identified with a religion. Two thirds of these offspring ever met criteria for an AUD (including 41% with dependence), their average lifetime maximum drinks per occasion was 11, and they reported experiencing an average of 3 of the 11 AUD criteria in their lives, ranging from 60% for spending a great deal of time involved with alcohol to 3% who ever fulfilled criteria for alcohol withdrawal. About 32% had used tobacco products, 71% had ever used cannabis (with 14% ever meeting criteria for a cannabis use disorder), and 6% ever met criteria for a SUD related to another illegal drug.

Among these 135 sons and daughters, 8 variables were significantly different across Group 1 offspring who correctly identified their proband father as having an alcohol problem and those who did not (Group 2). Four of these variables did not survive the Holm–Bonferroni procedure (tolerance, drinking more or longer than intended, missing obligations, and Zuckerman sensation seeking). Focusing on the 4 variables that survived the Bonferroni step, Group 1 offspring were more likely to have ever fulfilled criteria for an AUD, including higher rates than Group 2 for alcohol dependence. Overall, offspring in Group 1 reported experiencing a higher number of alcohol criterion items, including higher proportions who endorsed spending a great deal of time centered on alcohol. In Table 2, however, the 2 groups were similar on demography (e.g., sex, age, and years of education), use of tobacco products or illicit drugs, and had similar scores on impulsivity.

The major findings in this report relate to Table 3, and data from Tables 1 and 2 are offered to describe the populations overall and characterize how the group differences in Table 3 relate to the original data. Table 1 (probands) had 11 significant effects, and Table 2 (offspring) had 8, for a total of 19 such effects across the 2 tables. Using the Lowry VassarStats binomial program (website accessed 4-24-20), the exact binomial likelihood for 19 significant ($p \leq 0.05$) out of 60 tests is <0.0001, indicating that that number of significant findings would only occur by chance one in less than 10,000 times. Also, the Holm–Bonferroni sequential correction (Holm, 1979) was conducted to take into account multiple testing effects and adjusting for family-wise error in Tables 1 and 2, using the Gaetano (2013) EXCEL calculator. This yielded 13 variables that remained significant with adjusted *p*-values from 0.0143 to 0.044. These included 9 proband variables (4 DSM items: much time spent, decreased activities, use despite physical/psychological problems, and use despite social/interpersonal problems) as well as total number of DSM items, alcohol dependence, parent AUD, SRE-T, and age. Also included were 4 offspring items (DSM item much time spent, AUD diagnosis, total number of DSM items, and alcohol dependence). It is important to note that of the 6 variables that remained in the backward elimination logistic regression (see Table 3 below), 5 are among those that were still significant after correcting for multiple testing. Only the item "identify with religion" that remained in the final regression model was not on the list of those that were significant after the Holm–Bonferroni sequential correction.

The key step in these analyses, as shown in Table 3, simultaneously evaluated both fathers and offspring characteristics that related to Group 1 membership. Recognizing that many of the variables in Tables 1 and 2 were likely to correlate with each other, regression analyses were constructed to determine which characteristics remained robust when considered in the context of all other characteristics used in relevant analyses. To ensure that all father–offspring pairs were considered, the analyses used a bootstrap approach. In Table 3, all variables from Tables 1 and 2 were evaluated except for items that overlapped greatly with another variable (e.g., SRE-5 was used but SRE-T was not) or when the item (e.g., race/ethnicity) was endorsed similarly by the large majority of participants in both groups.

Table 3 presents the results from this bootstrapping approach for variables that added significantly to at least 200 iterations of the 1,000 bootstrap analyses. Here, for each relevant variable data column 1 presents the number of bootstrap regression analyses to which the variable added significantly, data column 2 presents the average odds ratio (OR) regarding correct identification that the AUD proband father had problems with alcohol, and the average significance level of that OR is presented in data column 3. With a mean McFadden pseudo R^2 of 0.36, 5 variables from the probands and one from the offspring significantly entered at least 200 bootstrap analyses. Significant items for probands that related to the offspring correctly indicating their father had alcohol problems included the father's self-report of spending a lot of time using alcohol or recovering from its effects, being more likely to identify with a religion (as opposed to stating he had no religious preference), the proband was more likely to report that he continued to drink despite social/interpersonal problems or despite physical/psychological problems and that the proband had a parent who met criteria for an AUD. The single offspring characteristic that contributed to a son or daughter correctly reporting alcohol problems for their AUD father was a higher number of the DSM-IV AUD criterion for themselves.

DISCUSSION

Our 3 original hypotheses focused on informant demographic characteristics that might be related to higher FHM sensitivities, but these predictions were not supported by the data. However, as shown in Table 3, the results indicated significant relationships to FHM sensitivity for several characteristics of the AUD father, including higher endorsement of 3 specific DSM-IV criterion items, that father's FH of AUDs and the father's identification with a religion. The current study is unique in evaluating FHM data from a longitudinal evaluation of members of 2 generations of the SDPS families using detailed validated and reliable semi-structured interviews with both probands and offspring regarding the roles of demography and other characteristics, including specific AUD criteria, in FHM sensitivity across generations.

Regarding demography, informant higher education was implicated regarding FHM sensitivities in some prior studies (e.g., Crews and Sher, 1992) but, like our negative findings, not in others (Pape et al., 2019). The older offspring were more accurate regarding a smoking FH in the Pape and colleagues (2019) large European study of diverse populations but Vandeleur et al.'s, 2008 study of the FH reports of AUDs, similar to ours, found little relationship of informant's age to FHM sensitivity. There is similar disagreement regarding the relationship of sex to FH accuracy (e.g., Crews and Sher, 1992; Rice et al., 1995), with our data revealing little evidence of a relationship. Thus, overall, there is little to indicate that easy to identify demographic characteristics of informants might give useful information about the likely sensitivity of offspring reports about parental alcohol use and problems. These negative findings might reflect differences in the samples studied (but the Crews and Sher, 1992 study was similar to the SDPS regarding sample education), or differences across the drugs evaluated, or the methods used (the SDPS data gathering using a validated broad polydiagnostic interview is fairly unique). Or the variation in results across studies could occur if the impact of demography only applies to a small subset of families or if demography has too small an effect size to be identified across studies. It is equally likely that both men and women, those with higher and lower education, as well as younger and older informants are all similar in the modest accuracy of their reports of positive AUD FHs. We favor the latter explanation.

While not originally hypothesized and with relatively few studies of this phenomenon in the literature, Table 3 regression analyses identified 5 characteristics of the AUD father but only one offspring variable that were associated with higher FHM sensitivity. The father's demography was not strongly related to FHM accuracy, but the probability of being correctly identified as having alcohol problems increased with the AUD father's severity of alcohol involvement. However, it is worth noting that many of the father's missed by the FHM had serious alcohol problems including an average of 16 maximum drinks per occasion, and an average endorsement of 5 of 11 DSM-IV criteria. The latter included 87% of Group 2 probands who drank more or longer than intended, 79% with hazardous use, 76% missing obligations, 62% with persistent problems decreasing alcohol use, and 46% spending much time involved with alcohol.

Significant proband variables in Table 3 predicting correct offspring reports included endorsement of AUD items of spending a great deal of time related to alcohol, continued use of alcohol despite social or interpersonal problems, and continued use despite physical or psychological problems. This supports the conclusion that the presence of problems more easily observed by the informant is related to higher sensitivities in FHM protocols (e.g., Rhea et al., 1993). The father's FH of AUDs was also highlighted in Table 3 perhaps because knowledge of alcohol problems in a grandparent might raise awareness of the risk for similar problems in an offspring's father (Rice et al., 1995). In addition, the regression analyses suggest that correct identification of the proband's problems related to his identification with a religion, which, if replicated, might relate to a family's emphasis on the need to recognize unacceptable problematic behaviors that might generalize to the recognition of alcohol problems.

The data in Table 1 suggest that several proband drug-related variables might contribute to offspring correctly identifying the father's alcohol problems, especially having a SUD for illicit drugs other than cannabis. While the lack of statistical significance could be a product of relatively low statistical power, none of the drug-related items in Table 1 were significantly different across Groups 1 and 2, the pattern of differences operated in different directions across different drug-related variables, and, most importantly, no drug-related item was significant in Table 3,.

Overall, the disappointing sensitivity of less than 30% in identifying a father's alcohol problems was found despite inclusion of many of the study characteristics reported to be associated with relatively higher sensitivities in the FHM approach (Mann et al., 1985; Rhea et al., 1993; Rice et al., 1995). This result is at the lower end of the studies of FHM sensitivity, and it is important to remember that Crews and Sher (1992) reported up to a 70% correlation for offspring and parent reports on the SMAST. The fact that 50% of the mothers with higher SMAST scores in that study would have been missed underscores the importance to recognizing the need to place FHM results into perspective. At the same time, the current results and the literature also indicate that even if sensitivities are relatively low, we know the direction of the bias is toward underreporting and that the families indicated as positive by offspring using the FHM are accurate over 90% of the time.

The current results also offer reminders of the potentially limited generalizability of FHM findings to other FH-positive families and that FHM-based FH-negative families, despite their high specificity, are likely to contain some FH-positive family units that have been mislabeled. The latter adds heterogeneity to the FH-negative group which might make it harder to establish significant differences in characteristics that might exist between FH-positive and FH-negative individuals. The limited sensitivity of the FHM indicates that the approach is not likely to be adequate in epidemiological studies or for public health planning.

However, despite the problems outlined above the FHM approach can be useful under some circumstances. Families identified as positive for a disorder can offer useful data regarding at least a subset of individuals with that condition. For example, in 1978 the SDPS used one offspring informant per family to identify FH-positive and FH-negative drinking but not yet alcoholic young adult participants. This relatively quick and inexpensive application of the FHM helped identify a subset of families with AUDs carrying the low response to alcohol as a familial potential risk factor for future heavy drinking in the young adult probands themselves (Schuckit and Gold, 1988) and a phenotype that turned out to be a good predictor of future alcohol problems (e.g., Schuckit et al., 2019a; Schuckit et al., 2019b). Establishing the validity of the original findings took decades of work that led to the development of a prevention approach that was successful in mitigating the impact of a low LR on heavy drinking and alcoholic blackouts in college students (Schuckit et al., 2016a, 2017). Thus, the FHM approach was a useful first step in identifying a risk factor for alcohol problems (Rice et al., 1995).

There are several important caveats to consider when interpreting results from the current report. First and foremost, longitudinal in-depth studies of several generations of families offer useful information, but results might not generalize widely to other populations. Recognizing the relatively high education and socioeconomic status and overwhelmingly European American background of the SDPS families, it is possible that our FHM findings might not apply equally to other FHM studies. A related consideration is that the SDPS originally recruited only male probands in order to maximize the heavier drinking outcome that might be expected of men. However, additional protocols from our laboratory have also studied female subjects (e.g., Eng et al., 2005; Schuckit et al., 2016b). A second major caveat is that although 135 AUD proband pairings are considered in Table 1 and that the data were also analyzed in R where pairings were evaluated in a regression analysis with 1,000 bootstraps, only 73 AUD probands contributed to the analyses. This approach of using bootstrapping to include multiple offspring from each family runs a risk that our results are impacted by nonindependence of some proband/offspring pairs, but results were similar when data were tested on only 73 generational pairs. Third, the modest statistical power reflecting a modest sized sample might underestimate the importance of some variables that were not significant in the current analyses. Fourth, the reasons behind the low sensitivity of the FHM in identifying an alcohol problem in the fathers of these offspring are not clear and are likely to reflect a combination of the offspring's ignorance of the problem and some offspring's hesitation to report what they actually know. Fifth, we have no information on additional potentially important explanations for the low sensitivity of the FHM such as poor communication between father and offspring. Another possibility is that these offspring did not view their fathers as having an alcohol problem because his behavior did not fit the usual (and probably inaccurate) public stereotype of what people with AUDs looks like.

In conclusion, this paper hypothesized that the sensitivity of the relatively quick and less expensive FHM approach to gathering a FH of alcohol problems could be improved by considering the demographic characteristics of the informants and/or the fathers on whom they were reporting. However, although none of the 3 demographic characteristics studied here consistently related to the sensitivity of the FHM regarding familial alcohol problems, multiple characteristics of the AUD fathers being reported upon were significantly related to FHM sensitivity, but for the offspring only their own higher number of alcohol problems related to the accuracy of their FH report. At the same time, the SDPS is an example of how the subset of correctly identified informants with a parental FH of an AUD can offer important preliminary information in the search for genetically related characteristics that increase the AUD risk in a subset of families.

ACKNOWLEDGMENTS

This work is supported by NIH/NIAAA grant number RO1 AA021162.

CONFLICTS OF INTEREST

No author of this paper has a conflict of interest with the material presented in the manuscript.

REFERENCES

American Psychiatric Association (1980) Diagnostic and Statistical Manual of Mental Disorders, 3rd ed. American Psychiatric Press, Washington DC.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Press, Washington DC.

Andreasen NC, Rice J, Endicott J, Reich T, Coryell W (1986) The family history approach to diagnosis. Arc Gen Psychiatry 43:421–429.

Boynton MH, Arkes J, Hoyle RH (2011) Brief report of a test of differential alcohol risk using sibling attributions of paternal alcoholism. J Stud Alcohol Drugs 72:1037–1040.

Bucholz KK, Cadoret R, Cloninger CR, Dinwiddie SH, Hesselbrock VM, Nurnberger JI Jr, Reich T, Schmidt I, Schuckit MA (1994) A new semi-structured psychiatric interview for use in genetic linkage studies: a report on the reliability of the SSAGA. J Stud Alcohol 55:149–158.

Chapman TF, Mannuzza S, Klein DF, Fyer AJ (1994) Effects of informant mental disorder on psychiatric family history data. Am J Psychiatry 151:574–579.

Crews TM, Sher KJ (1992) Using adapted short MASTs for assessing parental alcoholism: reliability and validity. Alcohol Clin Exp Res 16:576–584.

Daeppen JB, Landry U, Pecoud A, Decrey H, Yersin B (2000) A measure of the intensity of response to alcohol to screen for alcohol use disorders in primary care. Alcohol Alcohol 35:625–627.

Dewey M (2019) metap: Meta-analysis of Significance Valued. R package version 1.1

Ehlers CL, Garcia-Andrade C, Wall TL, Cloutier D, Phillips E (1999) Electroencephalographic responses to alcohol challenge in Native American Mission Indians. Biol Psychiatry 45:776–787.

Eng MY, Schuckit MA, Smith TL (2005) The level of response to alcohol in daughters of alcoholics and controls. Drug Alcohol Depend 79:83–93.

Friedman J, Hastie T, Tibshirani R (2010) Regularization paths for generalized linear models via coordinate descent. J Stat Softw 33:1–22.

Gaetano J (2013) Holm-Bonferroni sequential corrections: an EXCEL calculator-ver. 1.2 [accessed web site 4-24-20 at https://www.researchgate.net/publication/242331583_Holm-Bonferroni_Sequential_Correction_An_EXCEL_Calculator_-_Ver_12

Gustavsson JP, Berman H, Edman G, Ekselius L, von Knorring L, Linder J (2000) Swedish universities Scales of Personality (SSP) construction, internal consistency and normative data. Acta Psychiatr Scand 102:217–225.

Hardt J, Franke P (2007) Validity, reliability, and objectivity of the family history method in psychiatry: a meta-analysis. Euro Psychiatry 22:49–58.

Hesselbrock M, Easton C, Buchola KK, Schuckit M, Hesselbrock V (1999) A validity study of the SSAGA—a comparison with the SCAN. Addiction 94:1361–1370.

Holm S (1979) A simple sequentially rejective multiple test procedure. Scand J Stat 6:65–70.

Huen R, Hardt J, Burkart M, Maier W (1996) Validity of the family history method in relatives of gerontopsychiatric patients. Psychiatry Res 62:227–238.

Kendler KS, Prescott CA, Jacobson K, Myers J, Neale MC (2002) The joint analysis of personal interview and family history diagnoses: evidence for validity of diagnosis and increased heritability estimates. Psychol Med 32:829–842.

Kendler KS, Silberg JL, Neale M, Kessler RC, Heath AC, Eaves LJ (1991) The family history method: whose psychiatric history is measured? Am J Psychiatry 148:1501–1504.

Lix LM, Leslile WD, Yang S, Yan L, Walld R, Morin SN, Majumdar SR, Roos LL (2017) Accuracy of offspring-reported parental hip fractures: a novel population-based parent-offspring record linkage study. Am J Epidemiol 185:974–981.

Mann RE, Sobell LC, Sobell MB, Pavan D (1985) Reliability of a family tree questionnaire for assessing family history of alcohol problems. Drug Alcohol Depend 15:61–67.

Milne BJ, Caspi A, Crump R, Poulton R, Rutter M, Sears MR, Moffitt TE (2009) The validity of the family history screen for assessing family history of mental disorders. Am J Med Genet B Neuropsychiatr Genet 150B:41–49.

Mojica-Perez Y, Callinan S, Livingston M (2019) Time of year effects on self-reported estimates of post-year alcohol consumption. Alcohol Alcohol 54:540–544.

Muthen B, Satorra A (1995) Complex sample data in structural equation modeling. Sociol Methodol 25:267–316.

Pape K, Svanes C, Malinovschi A, Benediktsdottir B, Lodge C, Janson C, Moratalla J, Sanchez-Ramos JL, Braback L, Holm M, Jogi R, Bertelsen RJ, Sigsgaard T, Johannessen A, Schlunssen V (2019) Agreement of offspring-reported parental smoking status: the RHINESSA generation study. BMC Public Health 19:94–108.

R Core Team (2013) R: A Language and Environment of Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org/

Ray LA, MacKillop J, Monti PM (2010) Subjective responses to alcohol consumption as endophenotypes: advancing behavioral genetics in etiological and treatment models of alcoholism. Subst Use Misuse 45:1742–1765.

Revelle W (2018) psych: Procedures for Personality and Psychological Research. Northwestern University, Evanston, IL. https://CRAN.R-project.org/package = psych Version-1.8.12.

Rhea SA, Nagoshi CT, Wilson JR (1993) Reliability of sibling reports on parental drinking behaviors. J Stud Alcohol 54:80–84.

Rice JP, Reich T, Bucholz KK, Neuman RJ, Fishman R, Rochberg N, Hesselbrock VM, Nurnberger JI Jr, Schuckit MA, Begleiter H (1995) Comparison of direct interview and family history diagnoses of alcohol dependence. Alcohol Clin Exp Res 19:1018–1023.

Roy MA, Walsh D, Prescott CA, Kendler KS (1994) Biases in the diagnosis of alcoholism by the family history method. Alcohol Clin Exp Res 18:845–851.

Schuckit MA (2018) A critical review of methods and results in the search for genetic contributors to alcohol sensitivity. Alcohol Clin Exp Res 42:822–835.

Schuckit MA, Gold EO (1988) A simultaneous evaluation of multiple markers of ethanol/placebo challenges in sons of alcoholics and controls. Arch Gen Psychiatry 45:211–216.

Schuckit MA, Smith TL, Clarke D, Mendoza LA, Kawamura M, Schoen L (2019a) Predictors of increases in alcohol problems and alcohol use disorders in offspring in the San Diego prospective study. Alcohol Clin Exp Res 43:2232–2241.

Schuckit MA, Smith TL, Clausen P, Fromme K, Skidmore J, Shafir A, Kalmijn J (2016a) The low level of response to alcohol-based heavy drinking prevention program: one-year follow-up. J Stud Alcohol Drugs 77:25–37.

Schuckit MA, Smith TL, Paulus MP, Tapert SF, Simmons AN, Tolentino NJ, Shafir A (2016b) The ability of functional magnetic resonance imaging to predict heavy drinking and alcohol problems 5 years later. Alcohol Clin Exp Res 40:206–213.

Schuckit MA, Smith TL, Rana BK, Mendoza LA, Clarke D, Kawamura M (2019b) Performance of the self-report of the effects of alcohol questionnaire across sexes and generations. Alcohol Clin Exp Res 43:1384–1390.

Schuckit MA, Smith TL, Shafir A, Clausen P, Danko G, Goncalves PD, Anthenelli RM, Chan G, Kuperman S, Hesselbrock M, Hesselbrock V, Kramer J, Bucholz KK (2017) Predictors of patterns of alcohol-related blackouts over time in youth from the collaborative study of genetics of alcoholism: the roles of genetics and cannabis. J Stud Alcohol Drugs 78:39–48.

Sher KJ, Descutner C (1986) Reports of paternal alcoholism: reliability across siblings. Addict Behav 11:25–30.

Slutske WS, Heath AC, Madden PA, Bucholz KK, Dinwiddie SH, Dunne MP, Statham DJ, Martin NG (1996) Reliability and reporting biases for perceived parental history of alcohol-related problems: agreement between twins and differences between discordant pairs. J Stud Alcohol 57:387–395.

Thompson WD, Orvaschel H, Prusoff BA, Kidd KK (1982) An evaluation of the family history method for ascertaining psychiatric disorders. Arch Gen Psychiatry 39:53–58.

Vandeleur CL, Rothen S, Jeanpretre N, Lustenberger Y, Gamma F, Ayer E, Ferrero F, Fleischmann A, Besson J, Sisbane F, Preisig M (2008) Inter-informant agreement and prevalence estimates for substance use disorders:

direct interview versus family history method. Drug Alcohol Depend 92:9–19.

Vandeleur CL, Rothen S, Lustenberger Y, Glaus J, Castelao E, Preisig M (2015) Inter-informant agreement and prevalence estimates for mood syndromes: direct interview vs. family method. J Affect Dis 171:120–127.

Waldron M, Madden PA, Nelson EC, Knopik VS, Glowinski AL, Grant JD, Lynskey MT, Jacob T, Sher KJ, Bucholz KK, Heath AC (2012) The interpretability of family history reports of alcoholism in general community samples: findings in a Midwestern US twin birth cohort. Alcohol Clin Exp Res 36:1091–1098.

Walker HK, Hall WD, Hurst JW (1990) Clinical Methods, 3rd Edition, The History, Physical, and Laboratory Examinations. Butterworths, Boston.

Wickham H, Francois R, Henry L, Muller K (2018) dplyr: A grammar of data manipulation. R package version 0.7.8. https://CRAN.R-project.org/package-dplyr

Zuckerman M (1978) Sensation seeking and psychopathy, in *Psychopathic Behavior: Approaches to Research* (Hare RD, Schilling D eds), pp 165–186. Wiley, London, UK.