



ELSEVIER

Alcohol 35 (2005) 1–8

ALCOHOL

Treated and treatment-naive alcoholics come from different populations

George Fein*, Bennett Landman

Neurobehavioral Research, Inc., 201 Tamal Vista Boulevard, Corte Madera, CA 94925, USA

Received 3 June 2004; received in revised form 13 September 2004; accepted 19 October 2004

Abstract

In most research on alcoholism, convenience samples of individuals who have been in some type of treatment are used. Berkson's fallacy results when the associations found in studies of select samples are incorrectly presumed to apply to all alcoholics (i.e., including untreated alcoholics in the general population). In the current study, we examined whether treated and untreated alcoholics have similar early alcohol use histories by comparing abstinent alcoholics (treated and sober at least 6 months) with treatment-naive alcoholics (active drinkers). We studied 14 pairs of women and 25 pairs of men matched on the age at which they first met criteria for heavy alcohol use (women, 80 drinks per month; men, 100 drinks per month). The timeline follow-back interview method was used to gather retrospective alcohol use information. Alcohol dose and duration of use were subsequently computed for two intervals: (1) time between the person's first drink and date at which the person met criteria for heavy drinking and (2) period between when criteria for heavy drinking were met and current age of the treatment-naive person from each pair. During the period before the matching "heavy drinking" criteria were met, alcohol dose did not differ between groups. In the period after criteria for heavy alcohol use were met, in comparison with treatment-naive alcoholics, the treated alcoholics had higher average and peak alcohol doses. We rejected the hypothesis that the treatment-naive alcoholics and the treated alcoholics have similar alcohol use trajectories over time, with the treatment-naive sample simply being observed earlier in its alcohol use histories. Instead, we concluded that the two groups come from different populations with regard to alcohol use. In fact, the treated alcoholics had alcohol doses more than 50% higher than those of treatment-naive alcoholics in the years just after they began drinking heavily. This finding supports the suggestion that results from studies of alcoholics in treatment or after treatment (i.e., most studies of alcoholics) cannot be generalized to untreated individuals (who make up the majority of alcoholics). © 2005 Elsevier Inc. All rights reserved.

Keywords: Berkson's fallacy; Alcoholism; Treatment; Study design

1. Introduction

1.1. The potential bias in studying clinical samples: Berkson's fallacy

The first clues to the association between diseases and both their antecedents and their consequences often derive from the study of select samples of treated individuals, hospitalized patients, or autopsy cases. This is the case regarding our knowledge of the antecedents of alcoholism and of the effects of alcoholism on brain structure and function. Because not all alcoholics from the general population are equally likely to be in these study samples, bias may result when findings in these samples are presumed to apply to the population at large. This type of bias, known as Berkson's fallacy (after the person who first studied it in detail) (Berkson, 1946, 1955), occurs whenever the association be-

tween the independent variable (e.g., the diagnosis of alcohol dependence) and the dependent variable (e.g., the antecedents of alcoholism, severity of alcohol use, or the consequences of alcohol dependence) differs between the population from which the sample derives (hospitalized alcoholics or alcoholics in treatment or shortly after treatment) and (alcoholics in) the general population.

Fleiss (1981) presents examples of this bias, as well as the mathematics underlying it. A classic example of Berkson's fallacy occurred when Pearl (1929) found a negative association between the presence of cancer and tuberculosis in autopsy cases. Tuberculosis was less frequent in autopsy cases with cancer than in autopsy cases without cancer. Pearl inferred (erroneously) that the same negative association should apply to live patients and proposed treating patients with terminal cancer with tuberculin to arrest their cancer. He failed to understand that extrapolating an association found in autopsy cases to live patients is a fundamental error, unless all patients who die are equally likely to undergo autopsy.

Roberts et al. (1978) were the first to publish a study whose results empirically demonstrated Berkson's fallacy. Their

* Corresponding author. Tel.: +1-415-927-7676; fax: +1-415-924-2903.

E-mail address: george@nbresearch.com (G. Fein).

Accepting Editor: T.R. Jerrells

sample comprised 257 individuals (of a random sample of 2,784 individuals interviewed in the community) hospitalized during the prior 6 months. There was a very large positive association between the presence of respiratory disease and the presence of locomotor disease in the hospitalized individuals. However, Roberts et al. correctly ascertained that respiratory and locomotor diseases were essentially independent in the entire random sample. The spurious association between respiratory disease and locomotor disease arose because the hospitalization rate of people with both diseases (29%) was about three times the rate of people with only respiratory or locomotor disease or neither disease (7%–10%). As Fleiss (1981) succinctly stated, “unless something is known about differential hospitalization rates..., a good amount of skepticism should be applied to any generalization from associations found for hospitalized patients...to associations for people at large” (p. 13).

Parnas and Teasdale (1987) presented an example of Berkson’s fallacy in schizophrenia research with direct applicability to alcoholism research. In an American–Danish prospective study (Parnas & Teasdale, 1987) of children of schizophrenic mothers, individuals psychiatrically hospitalized or untreated for schizophrenia spectrum disorders were compared on a number of characteristics. Hospitalized and untreated individuals were similar on a number of measures. However, hospitalized individuals exhibited higher levels of substance abuse, affective symptoms, and psychopathic tendencies. Parnas and Teasdale suggest that “the clinical population may not be representative of the diagnostic category in question owing to [a greater] co-existence of confounding symptomatology (Berkson’s fallacy)” (p. 44).

Another instance of Berkson’s fallacy in the study of alcohol dependence could be created by drawing convenience samples from treated samples. Co-existing disorders (e.g., depression or bipolar affective disorder, antisocial personality disorder, attention deficit hyperactivity disorder, posttraumatic stress disorder, and other substance abuse disorders) may be greater in the treated samples than in alcoholics in the general population. However, these co-existing disorders may not be severe enough to result in clinical diagnoses that would exclude subjects from “alcoholism” research samples. Alternatively, the bias due to Berkson’s fallacy may result if the severity of alcoholism is greater in clinical versus general population samples. Once again (in either case), findings in clinical samples may not generalize to alcoholics in the general population.

1.2. How big is the potential bias in alcoholism research?

The magnitude of the potential bias consequent to Berkson’s fallacy depends on the proportion of alcoholics who are in the treated subpopulation. The most current study results available indicate that the number of alcoholics in treatment is a small proportion of alcoholics in the general

population. In the 1992 National Longitudinal Alcohol Epidemiologic Survey (Grant, 1997), it was estimated that more than 27 million Americans exhibit alcohol abuse or alcohol dependence. At about the same time, Harwood et al. (1994) estimated that there were approximately 1.8 million Americans who were receiving treatment for alcohol problems in non-Federal hospital and community-based treatment settings. Grant (1997) estimates that only one in 10 individuals who need treatment for alcohol abuse problems has actually sought treatment. These estimates derive from different methods and sampling plans. However, even if one assumes that three times the 1.8 million individuals from the Harwood study received some form of treatment for alcoholism, the treatment population is still less than a quarter of the number of people who exhibit alcohol problems. Therefore, it makes sense that estimates drawn from clinical samples represent at most only one quarter of individuals who exhibit alcohol abuse or dependence. Studies, in which alcoholics in treatment are compared with alcoholics who have not sought treatment, are needed to determine whether clinical samples differ from treatment-naïve samples in the antecedents, severity, and “consequences” (in the psychological, social, legal, and biologic arenas) of alcoholism.

1.3. The bias resulting from Berkson’s fallacy may differ between male and female alcoholics

The bias inherent in studying only treated alcoholics may be different for men and women, and this difference in bias may underlie the different results reported for male versus female clinical samples. The finding in the literature, showing that women, in comparison with men, suffer more cerebral consequences from long-term alcohol dependence, is based on studies of clinical samples (Bergman, 1987; Jacobson, 1986). However, this finding may be spurious if clinical samples of treated alcoholic women differ from treatment-naïve alcoholic women more than treated alcoholic men differ from samples of treatment-naïve alcoholic men. This is entirely possible, because it has been claimed that women (for a variety of reasons) are less likely than men to receive treatment for alcohol problems (The National Center on Addiction and Substance Abuse at Columbia University, 1996).

1.4. Examination of Berkson’s fallacy in alcoholism research

In our laboratory, we have two ongoing studies in which alcohol-dependent samples are being compared with age-comparable light drinking/nondrinking samples. In one study, we are examining alcoholics with 6 or more months of abstinence. All those individuals (between the ages of 35 and 55 years) underwent treatment (we include Alcoholics Anonymous as one form of treatment). In the other study, we examined alcohol-dependent individuals (between the ages of 20 and 50 years) who had never been in treatment. None of the latter subjects identified themselves as alcoholic, although all met DSM-IV [Diagnostic and Statistical

171 *Manual of Mental Disorders* (4th ed.); American Psychiatric
172 Association (1994)] criteria for alcohol dependence.

173 For the current study, we compared alcohol-dependent
174 subjects from the two ongoing studies in our laboratory as
175 to the subjects' alcohol use history, examining both quantity
176 and use trajectory. We tested the null hypothesis that the
177 treatment-naive alcoholics and the long-term abstinent alco-
178 holics have similar alcohol use trajectories over time (the
179 treatment-naive sample being observed earlier in their alco-
180 hol use histories). In addition, if their trajectories differed,
181 we tested the hypothesis that that difference is larger in
182 female subjects than it is in male subjects.

183 2. Materials and methods

184 2.1. Subjects

185 As noted above, subjects reported in this article came from
186 two different studies: one of abstinent alcoholics (age, 35–
187 55 years) and the other of treatment-naive alcoholics (age,
188 20–50 years). In both studies, alcohol-dependent and control
189 samples were recruited. For the analyses reported in this
190 article, only the alcohol-dependent samples were used. The
191 abstinent alcoholics needed to meet the lifetime criteria
192 for alcohol dependence and be abstinent for at least 6 months.
193 Treatment-naive alcoholics needed to meet lifetime criteria
194 for alcohol dependence and to have never been in treatment.
195 All participants for either study were informed of the study's
196 procedures and signed a written consent form before their
197 participation. There were a total of four sessions for each
198 study, each lasting between 1 and 2.5 h, involving clinical,
199 neuropsychologic, electrophysiologic, and neuroimaging as-
200 sessments. All subjects who participated in any session were
201 paid for their time and travel expenses. Subjects who com-
202 pleted all four aspects of either study received a completion
203 bonus. An independent review committee (the Institutional
204 Review Board, Independent Review Consulting, Corte
205 Madera, CA) approved all procedures before study, and all
206 procedures were carried out in compliance with the Helsinki
207 declaration of 1975, as revised in 1983.

208 Exclusion criteria for both studies were the following:
209 (1) history or presence of an axis I diagnosis on the Diagnos-
210 tic Interview Schedule [(DIS); Washington University, St.
211 Louis, MO; <http://epi.wustl.edu/dis/dishome.htm>]; (2) his-
212 tory of drug dependence other than caffeine or nicotine;
213 (3) significant history of head trauma or cranial surgery;
214 (4) history of diabetes, stroke, or hypertension that required
215 medical intervention, or of other significant neurologic dis-
216 ease; (5) clinical or laboratory evidence of active hepatic
217 disease; (6) clinical evidence of Wernicke–Korsakoff syn-
218 drome; or (7) current substance abuse other than alcohol
219 (aside from caffeine and nicotine). Table 1 shows reasons
220 for exclusion of subjects in both studies, as well as the total
221 number of participants who either were excluded or met

Table 1
Subject exclusion/inclusion data

| | Abstinent alcoholics (n) | Treatment-naive alcoholics (n) |
|---|-----------------------------|-----------------------------------|
| Reason for exclusion | | |
| Drug use | 26 | 123 |
| Did not meet alcohol use inclusion criteria ^a | 48 | 94 |
| Met medical exclusion criteria | 33 | 9 |
| Met psychiatric exclusion criteria | 32 | 7 |
| Other ^b | 21 | 30 |
| Total subjects | | |
| Excluded | 160 | 263 |
| Met all inclusion criteria and completed study | 47 | 70 |

^aFor abstinent alcoholics, either did not meet requirements for length of sobriety or did not meet requirements for alcohol dependence or alcohol use. For treatment-naive alcoholics, were either formerly treated for alcohol abuse or did not meet requirements for alcohol dependence or alcohol use.

^bFor example, did not want to commute, lost to follow-up, or refused continuation or participation.

inclusion criteria and completed the study. Table 2 presents
subject demographics.

2.2. Assessment

225 All subjects were assessed by using a computerized psy-
226 chiatric DIS. Subjects were also interviewed to assess their
227 drug and alcohol use by using the Lifetime Drinking History
228 (LDH) method (Skinner & Sheu, 1982; Sobell & Sobell,
229 1990; Sobell et al., 1988). In addition, medical histories were
230 reviewed, liver function tests were performed and evaluated,
231 and Family Drinking Questionnaires were administered on
232 the basis of the Family Tree Questionnaire by Mann et al.
233 (1985) [see also Stoltenberg et al. (1998)].

2.3. Subject matching and computation of dependent variables

236 The LDH assessment, which uses the timeline follow-
237 back interview method (in which subjects break their drink-
238 ing history into periods with consistent alcohol use) was used
239 to gather retrospective alcohol use information (Sobell &
240 Sobell, 1990, 1992; Sobell et al., 1988). We used data ob-
241 tained from the LDH to match abstinent alcoholic subjects
242 and treatment-naive alcoholic subjects on a one-to-one
243 basis. Subjects were matched on sex and age at the onset
244 of heavy drinking. Heavy drinking was defined as the age
245 when a female subject first reached a monthly dose of 80
246 drinks per month and a male subject first reached 100 drinks
247 per month. There were 47 abstinent alcoholic subjects, but
248 only 39 of these could be matched to a treatment-naive
249 subject. The remaining subjects first met the criteria for
250 heavy drinking relatively late in life (in their mid-30s), and
251 we did not have any same-sex treatment-naive subjects who
252 matched them on that variable. The average difference in
253 the age at which subjects met the criteria for heavy drinking

Table 2
Subject demographics

| Variables | Abstinent alcoholics | | Treatment-naive alcoholics | |
|--|------------------------|--------------------------|----------------------------|--------------------------|
| | Males (<i>n</i> = 25) | Females (<i>n</i> = 14) | Males (<i>n</i> = 25) | Females (<i>n</i> = 14) |
| Age, mean (\pm S.D.) | 45.6 (\pm 7.0) | 47.0 (\pm 6.3) | 32.2 (\pm 6.9) | 30.3 (\pm 6.7) |
| Years of education, mean (\pm S.D.) | 15.5 (\pm 2.0) | 15.0 (\pm 2.7) | 16.3 (\pm 1.7) | 15.9 (\pm 1.8) |
| Ethnicity ^a | 1 AA, 22 C, 1 H, 1M | 14 C | 2 A, 18 C, 4 H, 1M | 11 C, 3 M |

^aA = Asian; AA = African American; C = Caucasian; H = Hispanic; M = Multiracial.
S.D. = Standard deviation.

254 was 1.85 months [standard deviation (S.D.) = 15.4 months]
255 across the 14 female and 25 male matched-subject pairs. Once
256 the matches were completed, the alcohol use variables from
257 the LDH of the abstinent alcoholic subject from each pair
258 were computed as if that subject were the age of his or
259 her matched treatment-naive subject. For example, if an
260 abstinent alcoholic subject was 55 years of age, the matched
261 treatment-naive subject was 30 years of age, and both sub-
262 jects met the heavy drinking criteria at age 23 years, the
263 alcohol use variables for the abstinent alcoholic subject
264 were recomputed by using the drinking history up to the
265 point when that subject reached the age of 30 years. Alcohol
266 dose, duration of use, and duration of abstinence variables
267 were computed from the LDH for two intervals: the time
268 between the person's first drink and the date at which he or
269 she met criteria for heavy drinking, and the period between
270 that date and the current age of the treatment-naive
271 person from each pair. This procedure is illustrated in Fig. 1.

272 2.4. Analysis

273 The groups were compared on alcohol use variables by
274 using a repeated-measures analysis of variance (ANOVA)
275 within the Statistical Analysis System [(SAS), Release 8.02;
276 SAS Institute, Inc., Cary, NC]. The trajectories of alcohol
277 use were also examined visually. For that purpose, because
278 subject pairs first met the criteria for heavy use at very
279 different ages (range, 13 to 40 years), lifetime drinking his-
280 tories were normalized with the age of criteria for heavy
281 drinking being met set to zero. Each subject's use history was
282 subsequently plotted as a function of time. Data obtained
283 for subjects from the two groups were plotted by using
284 different colors to aid visualization of differences in drink-
285 ing trajectories between the two groups.

286 3. Results

287 Table 3 presents the drinking history data divided into
288 two intervals. The first interval is the period from an individ-
289 ual's first drink until the beginning of heavy drinking (as
290 defined above). The second interval is the period from the
291 beginning of heavy drinking to the age of the treatment-
292 naive subject in each subject pair. Thus, the duration of the
293 latter interval is the same for the two subjects in each absti-
294 nent alcoholic–treatment-naive alcoholic pair.

3.1. Interval from first drink to the beginning of heavy drinking

297 In the interval from first drink to first heavy use, there were
298 strong sex effects for all alcohol dose variables (average, peak,
299 and average in most recent 6 months), with male subjects
300 consistently having higher doses than were recorded for
301 female subjects. All effects were large, with sex accounting
302 for 14.9% of the variance of average dose, 22.1% of the
303 variance of peak dose, and 16.9% of the variance of the
304 dose in the most recent 6 months. The only group differ-
305 ence was on abstinence duration during this period, with
306 alcoholics who eventually were treated having some periods
307 of abstinence in this interval before they had even begun to
308 drink heavily. Treatment-naive alcoholics had no abstinence
309 periods during this interval. Of the 39 alcoholics who eventu-
310 ally were treated, five (four males and one female) had
311 periods of abstinence in this interval.

3.2. Interval from beginning of heavy drinking to end of matched period

314 In the interval from first heavy use to end of matched
315 period, there were strong sex effects for average dose and peak
316 dose, with sex accounting for 12.6% and 15.2% of the vari-
317 ance. There were also group effects that were larger than
318 sex effects, accounting for 27.8% of the variance of average
319 dose, 20.8% of the variance of peak dose, and 21.8% of
320 the variance of the dose in the most recent 6 months. For
321 all three variables, alcoholics who eventually were treated
322 had much higher alcohol doses. There were no significant
323 group by sex interaction effects. The effects for average
324 alcohol dose for this interval are illustrated in Fig. 2.
325 There were also significant group effects for duration of
326 alcohol use and duration of abstinence for this interval.
327 Alcoholics who eventually were treated had more abstinence
328 during this interval. Because the entire interval was the
329 same across groups, they had a smaller period of alcohol
330 use during this interval as a consequence of their greater
331 abstinence (Fig. 3).

332 Fig. 4 presents the alcohol use trajectories of all research
333 participants relative to the age at which the individual met
334 the criteria for heavy drinking. The figure shows that the
335 trajectories for treated and treatment-naive alcoholics over-
336 lap almost entirely in the period before subjects met the
337 criteria for heavy drinking, but that the treated alcoholics

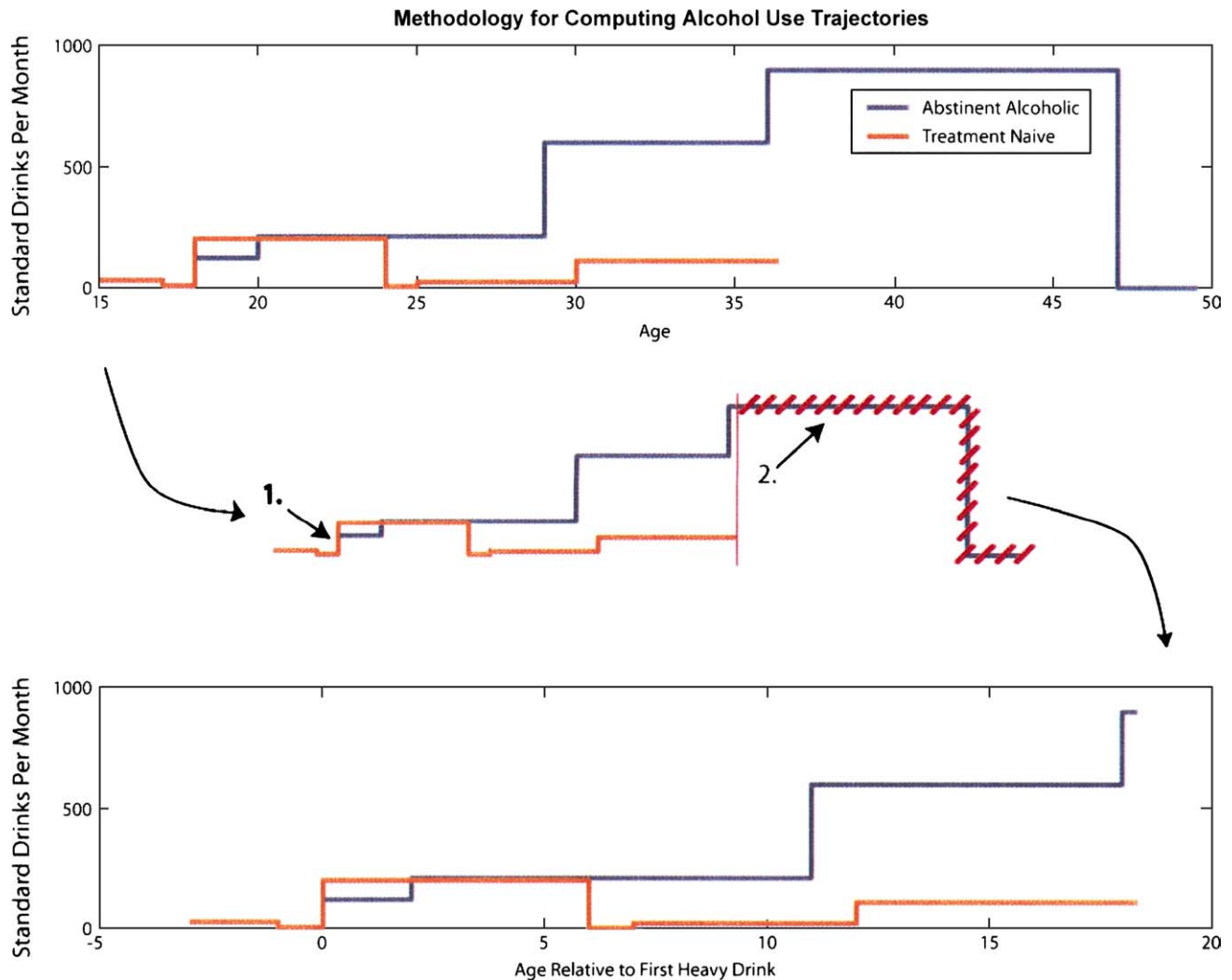


Fig. 1. Matching procedure. The top section of the figure presents the raw data for a matched pair of subjects [a 46-year-old male abstinent alcoholic (gray line) and a 34-year-old male treatment-naive alcoholic (orange line)], both of whom met criteria for heavy drinking at about 18 years of age. The middle section shows the two steps of the matching and alignment procedure. In the first step, the two subjects are aligned at their age of meeting the criteria for heavy drinking (this amounts to a shift of 4 months for the abstinent alcoholic subject), and that age is set to zero. In the second step, the data obtained for the abstinent alcoholic subject are truncated (red hash marks), so that they are followed for the same duration after criteria for heavy drinking were met as that for the treatment-naive subject. The bottom section shows the data after alignment and truncation.

338 have higher average doses in the period after criteria for
339 heavy drinking were met.

340 4. Discussion

341 The central finding of the current study is that treatment-
342 naive, alcohol-dependent individuals in the community come
343 from a population with much lower alcohol use than that of
344 treated alcoholics who have been successful in maintaining
345 abstinence. In other words, we rejected the null hypothesis
346 (that treatment-naive alcoholics have alcohol use trajec-
347 tories similar to those of treated alcoholics, but are just iden-
348 tified earlier in their drinking histories). This hypothesis was
349 tested with matched pairs of subjects consisting of a treatment-
350 naive alcoholic and a treated alcoholic of the same sex,

351 both of whom met criteria for heavy drinking at the same
352 age. The drinking pattern for both subjects in the pair was
353 subsequently examined for an identical period (after the
354 criteria for heavy drinking were met). During this period
355 (on average about 8 to 9 years in duration), the average
356 alcohol dose for the treated alcoholics was much higher than
357 that for the treatment-naive alcoholics (56% higher for males
358 and 68% higher for females).

359 Findings of the current study demonstrate Berkson's fal-
360 lacy with regard to the association of a diagnosis of alco-
361 hol dependence with the magnitude of alcohol use. This
362 association is markedly different in treated versus treatment-
363 naive samples (in the years immediately after criteria for
364 heavy drinking were met). We cannot generalize results from
365 clinical samples of alcoholics (those in treatment or after
366 treatment, as in most studies of alcoholics) to untreated

Table 3
Alcohol use measures by group and sex

| Alcohol use measures | Females (<i>n</i> = 14 pairs) | | Males (<i>n</i> = 25 pairs) | | Effect size (%) | | |
|--|--------------------------------|----------------------------|------------------------------|----------------------------|-----------------|--------|--------------|
| | Abstinent alcoholics | Treatment-naive alcoholics | Abstinent alcoholics | Treatment-naive alcoholics | Sex | Group | Group by sex |
| For period from first drink to first heavy use | | | | | | | |
| Duration of use (months) | 55.3 (± 38.0) | 59.1 (± 41.4) | 75.1 (± 57.1) | 71.5 (± 66.1) | 2.41 | 0.00 | 0.69 |
| Average dose (drinks/month) | 24.7 (± 16.6) | 25.4 (± 17.5) | 33.9 (± 18.0) | 41.2 (± 22.0) | 14.9* | 2.45 | 1.68 |
| Duration of peak use (months) | 23.6 (± 11.6) | 34.3 (± 27.0) | 29.3 (± 19.6) | 37.4 (± 40.6) | 0.97 | 6.27 | 0.11 |
| Peak dose (drinks/month) | 34.8 (± 25.5) | 31.2 (± 21.4) | 53.8 (± 27.6) | 56.2 (± 28.1) | 22.1** | 0.03 | 0.78 |
| Average dose in most recent 6 months | 33.6 (± 25.7) | 27.3 (± 20.4) | 50.8 (± 28.9) | 48.2 (± 30.7) | 16.9** | 1.45 | 0.25 |
| Duration of abstinence in period (months) | 13.7 (± 24.8) | 0.0 (± 0.0) | 3.6 (± 18.0) | 0.0 (± 0.0) | 5.49 | 13.9* | 4.73 |
| Level at first heavy use | | | | | | | |
| Dose (drinks/month) | 153 (± 67.6) | 112 (± 37.8) | 215 (± 138) | 149 (± 42.2) | 14.2* | 14.4* | 0.74 |
| For period from first heavy use to end of matched period | | | | | | | |
| Duration of use (months) | 97.2 (± 58.8) | 116 (± 64.5) | 104 (± 63.4) | 121 (± 59.2) | 0.27 | 23.6** | 0.04 |
| Average dose (drinks/month) | 165 (± 70.6) | 98.1 (± 30.1) | 210 (± 110) | 134 (± 56.8) | 12.6* | 27.8** | 0.14 |
| Duration of peak use (months) | 65.0 (± 50.5) | 45.4 (± 33.4) | 39.0 (± 29.4) | 45.9 (± 31.7) | 5.05 | 1.75 | 7.54 |
| Peak dose (drinks/month) | 190 (± 72.0) | 128 (± 46.5) | 297 (± 199) | 175 (± 67.3) | 15.2* | 20.8** | 2.25 |
| Average dose in most recent 6 months | 75 (± 87.4) | 108 (± 47.5) | 225 (± 170) | 120 (± 66.4) | 3.62 | 21.8** | 1.08 |
| Duration of abstinence in period (months) | 17.0 (± 45.5) | 6.00 (± 22.4) | 21.6 (± 32.2) | 0.48 (± 2.40) | 0.01 | 21.2** | 2.11 |

Matched pairs of an abstinent alcoholic and a treatment-naive alcoholic were analyzed as repeated measures. Sex is a between matched pairs effect. Group and group by sex are within matched pairs repeated-measures effects.

Measures are reported as mean (± standard deviation).

Effect is significance: * $P \leq .05$, ** $P \leq .01$.

367 individuals (who make up the majority of alcoholics) with
368 regard to measures of the severity of alcohol use. This means
369 that findings on any measures of the antecedents of alcohol
370 dependence that may be predictive of differences in alco-
371 hol use (e.g., preexisting co-morbid psychopathologic char-
372 aracteristics) or findings on measures of the consequences

of alcohol dependence that may be affected by differences in
alcohol use (alcohol use-associated morbid changes in
brain structure and function and exacerbation of co-morbid
psychopathologic characteristics) also are not likely to
extend from treated samples of alcoholics to alcoholics in
the general population. The difference in alcohol dose (both

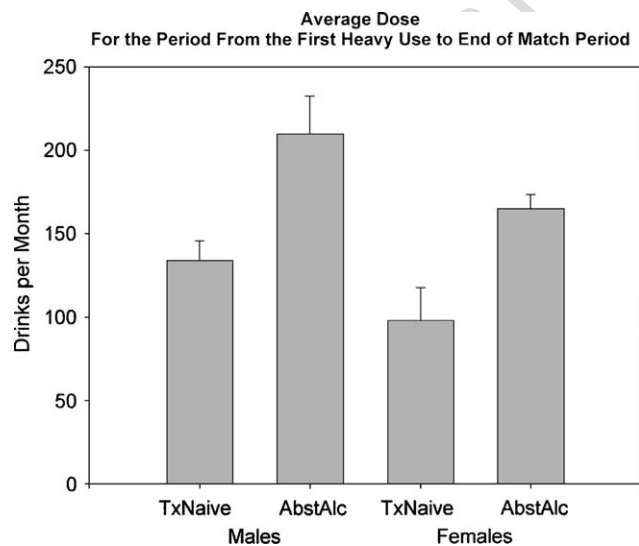


Fig. 2. Average dose for the period from the first heavy use to end of match period. In the matched period, the average alcohol dose was significantly lower in the treatment-naive subjects than in the treated subjects who eventually attained long-term abstinence ($P < .01$). In comparison with doses for male subjects, female subjects had lower doses ($P < .05$), but no group by sex interactions were observed. AbstAlc = Abstinent alcoholics; TxNaive = treatment-naive alcoholics.

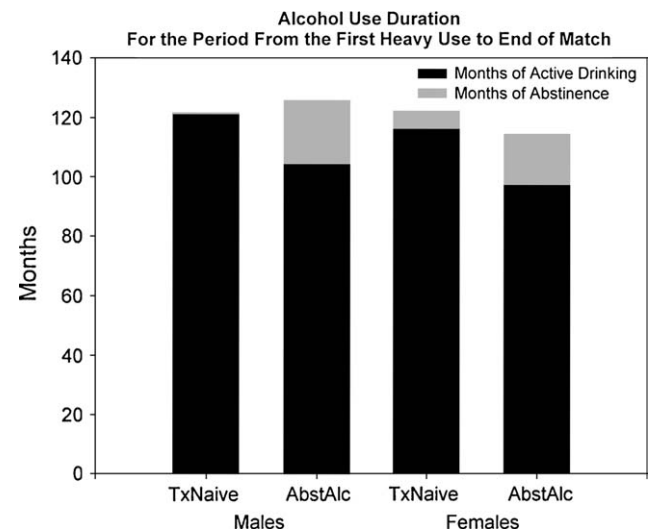


Fig. 3. Alcohol use duration for the period from the first heavy use to end of match period. In the matched period, the duration of alcohol use was lower for the abstinent alcoholics (AbstAlc) than for the treatment-naive alcoholics (TxNaive) ($P < .01$) owing to increased periods of abstinence in the treated subjects who eventually attained long-term abstinence. No sex or group by sex interactions were observed.

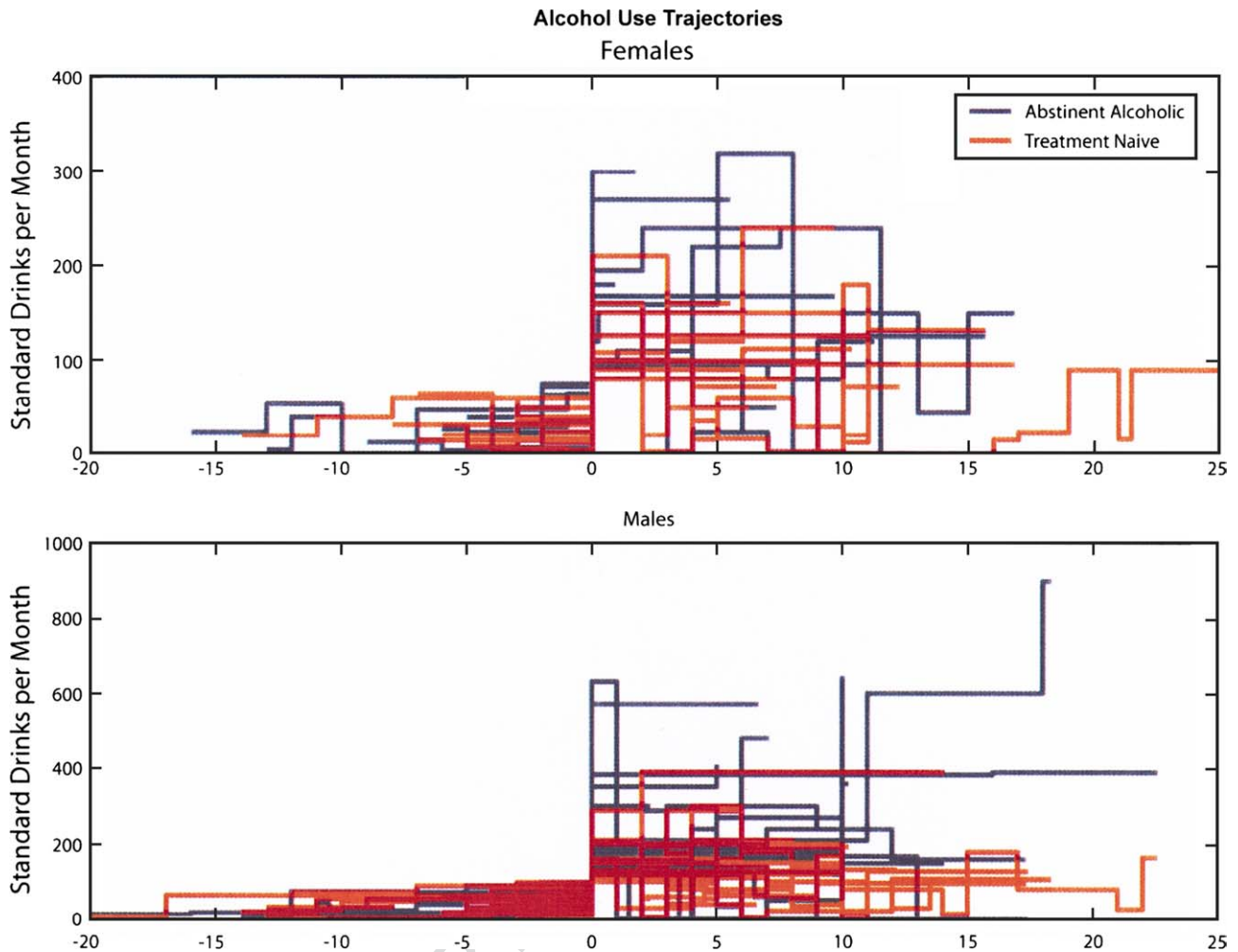


Fig. 4. Alcohol use trajectories. When the trajectories of an abstinent alcoholic and a treatment-naive alcoholic overlap, it is indicated in red. The trajectories for female subjects are lower than those for male subjects. (Note the difference in scale between the sections of the figure for female versus male subjects.) After criteria for heavy drinking were met, the trajectories for abstinent alcoholics (gray lines) are higher than the trajectories for treatment-naive alcoholics (orange lines).

379 average and peak) between treated alcoholics and treatment-
 380 naive alcoholics was similar for men and women. The com-
 381 parability of the differences between groups across sexes
 382 implies that treated samples of alcoholic women differ from
 383 treatment-naive alcoholic women comparably with treated
 384 versus treatment-naive samples of alcoholic men. This
 385 argues against the contention that women are less likely than
 386 men to receive treatment for alcohol problems ([The National](#)
 387 [Center on Addiction and Substance Abuse at Columbia Uni-](#)
 388 [versity, 1996](#)). It also supports the suggestion that the finding
 389 in the literature, showing that women, in comparison with
 390 men, suffer more cerebral consequences from long-term al-
 391cohol dependence ([Bergman, 1987](#); [Jacobson, 1986](#)), is true
 392 and not spurious owing to sampling bias.

393 Another interesting result is that the treated alcoholics
 394 had more episodes of (brief) abstinence after starting to
 395 drink heavily than did treatment-naive alcoholics. They even
 396 had more episodes of abstinence before they met the criteria
 397 for heavy drinking. (It is important to note here that all
 398 persons in both groups met criteria for alcohol dependence.)

Even though all individuals in both groups reported on inter-
 view that alcohol use had interfered with their lives, only
 people who eventually sought treatment and achieved absti-
 nence identified this early in their drinking history that their
 drinking was problematic. Attempts at abstinence this early
 in their drinking histories may not be characteristic of all
 alcoholics who go on to treatment. One must keep in mind
 that our treated sample consisted entirely of alcoholics who
 were eventually successful in achieving long-term absti-
 nence. It is possible that early attempts at abstinence are more
 characteristic of the subset of alcoholics who are eventually
 successful at achieving long-term abstinence. However, it
 is surely a commentary about the difficulty of achieving
 long-term abstinence that these male subjects continued
 drinking, on average, another 5.50 years and female subjects
 continued drinking, on average, another 10.24 years, after
 the observation period of the current analysis.

There are limitations to the current study. First, the primary
 data for analysis are each subject's recall of the duration of
 periods and dose of prior alcohol use, and the results may

419 reflect differences in recall, rather than differences in actual
 420 prior use. The treated sample was older than the treatment-
 421 naive sample and had long periods of abstinence before data
 422 were collected. It is possible that subjects exaggerated their
 423 use in comparison with the recollections of the treatment-
 424 naive subjects, who were recalling relatively recent experi-
 425 ence. We do not believe this is likely because the treated
 426 sample, in addition to recalling higher alcohol doses, re-
 427 called more episodes of abstinence. Therefore, if the data
 428 reflected primarily a recall error, that error would manifest
 429 as estimates of both less use (more abstinence) and more
 430 use (higher doses). It is difficult to imagine a recall error
 431 that would result in both these findings. The simplest hypoth-
 432 esis is that the recall data accurately reflect prior use.

433 A second limitation is that the study is focused on the
 434 subset of the treated population that eventually attains long-
 435 term abstinence. Observed differences in consumption pat-
 436 terns may be associated with the treated sample's ability
 437 eventually to achieve long-term abstinence. Different
 438 drinking histories may be present for treated samples that do
 439 not achieve long-term abstinence. However, it is also possi-
 440 ble that drinking histories are comparable across treated
 441 samples.

442 A third limitation is that the current study does not actu-
 443 ally measure antecedent factors (e.g., psychiatric and other
 444 co-morbidities) and consequences of alcohol abuse (e.g.,
 445 effects of chronic alcohol abuse on brain structure and func-
 446 tion). The main finding of this research is that treated alcohol-
 447 ics and treatment-naive alcoholics come from different
 448 populations with regard to alcohol use histories. This is a
 449 sobering finding for the field. It indicates that it is improper
 450 to generalize results and conclusions from convenience sam-
 451 ples to alcoholics in the general population. This is demon-
 452 strated in the current study for alcoholism severity, but it is
 453 also likely to be the case for antecedents and consequences of
 454 alcohol dependence (because such phenomena are associated
 455 with differences in alcohol dose). Findings of our study
 456 underline the importance of direct comparison between
 457 treated and treatment-naive alcohol-dependent samples on
 458 measures of the antecedents and consequences of alcohol
 459 dependence. To elucidate the public health implications of
 460 research findings, one must understand how to extrapolate
 461 such findings to alcohol-dependent individuals in the gen-
 462 eral population.

463 Acknowledgments

464 This work was supported by grants AA11311 (G.F.) and
 465 AA13659 (G.F.), both from the National Institute on Alcohol
 466 Abuse and Alcoholism. This study would not have been

possible without the dedicated recruitment team at NRI and
 our volunteer participants. 467
468

References 469

- American Psychiatric Association. (1994). *Diagnostic and Statistical* 470
Manual of Mental Disorders (4th ed.). Washington, DC: Author. 471
- Bergman, H. (1987). Brain dysfunction related to alcoholism: some results 472
 from the KARTAD project. In O. A. Parsons, N. Butters, & P. E. Nathan 473
 (Eds.), *Neuropsychology of Alcoholism: Implications for Diagnosis and* 474
Treatment (pp. 21–45). New York: Guilford Press. 475
- Berkson, J. (1946). Limitations of the application of fourfold table analysis 476
 to hospital data. *Biometrics Bulletin* 2, 47–53. 477
- Berkson, J. (1955). The statistical study of association between smoking 478
 and lung cancer. *Mayo Clin Proc* 30, 319–348. 479
- Fleiss, J. (1981). *Statistical Methods for Rates and Proportions*. New 480
 York: Wiley. 481
- Grant, B. F. (1997). The influence of comorbid major depression and 482
 substance use disorders on alcohol and drug treatment: results of a 483
 national survey. Paper presented at the National Institute on Drug Abuse 484
 Technical Review Meeting on Comorbid Mental and Addictive Disor- 485
 ders: Treatment and HIV-Related Issues, September 27–28, 1994. Avail- 486
 able at: [http://www.nida.nih.gov/pdf/monographs/monograph172/004-](http://www.nida.nih.gov/pdf/monographs/monograph172/004-015_Grant.pdf) 487
 015_Grant.pdf. Proceedings of meeting available: *NIDA Res Monogr* 488
172, 1–169; paper on pp. 4–15. 489
- Harwood, H. J., Thomson, M., & Nesmith, T. (1994). *Healthcare Reform* 490
and Substance Abuse Treatment: The Cost of Financing Under Alterna- 491
tive Approaches—A Final Report. Fairfax, VA: Lewin-VHI. 492
- Jacobson, R. (1986). The contributions of sex and drinking history to CT 493
 brain scan changes in alcoholics. *Psychol Med* 16, 547–559. 494
- Mann, R. E., Sobell, L. C., Sobell, M. B., & Pavan, D. (1985). Reliability 495
 of a family tree questionnaire for assessing family history of alcohol 496
 problems. *Drug Alcohol Depend* 15, 61–67. 497
- The National Center on Addiction and Substance Abuse at Columbia Uni- 498
 versity. (1996). *Substance Abuse and The American Woman*. New York: 499
 Author. Available at: [http://www.casacolumbia.org/pdshopprov/shop/](http://www.casacolumbia.org/pdshopprov/shop/item.asp?itemid=46) 500
 item.asp?itemid=46. 501
- Parnas, J., & Teasdale, T. (1987). A matched-paired comparison of treated 502
 versus untreated schizophrenia spectrum cases. A high-risk population 503
 study. *Acta Psychiatr Scand* 75, 44–50. 504
- Pearl, R. (1929). Cancer and tuberculosis. *Am J Hyg (now Am J Epidemiol)* 505
 9, 97–159. 506
- Roberts, R. S., Spitzer, W. O., Delmore, T., & Sackett, D. L. (1978). An 507
 empirical demonstration of Berkson's bias. *J Chronic Dis* 31, 119–128. 508
- Skinner, H. A., & Sheu, W. J. (1982). Reliability of alcohol use indices: the 509
 lifetime drinking history and the MAST. *J Stud Alcohol* 43, 1157–1170. 510
- Sobell, L. C., & Sobell, M. B. (1990). Self-report issues in alcohol abuse: 511
 state of the art and future directions. *Behav Assess* 12, 77–90. 512
- Sobell, L. C., & Sobell, M. B. (1992). Timeline follow-back: a technique 513
 for assessing self-reported alcohol consumption. In R. Z. Litten, & 514
 J. P. Allan (Eds.), *Measuring Alcohol Consumption: Psychosocial and* 515
Biochemical Methods (pp. 41–72). Totawa, NJ: Humana Press. 516
- Sobell, L. C., Sobell, M. B., Riley, D. M., Schuller, R., Pavan, D. S., 517
 Cancilla, A., Klajner, F., & Leo, G. I. (1988). The reliability of alcohol 518
 abusers' self-reports of drinking and life events that occurred in the 519
 distant past. *J Stud Alcohol* 49, 225–232. 520
- Stoltenberg, S. F., Mudd, S. A., Blow, F. C., & Hill, E. M. (1998). Evaluating 521
 measures of family history of alcoholism: density versus dichotomy. 522
Addiction 93, 1511–1520. 523