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ALCOHOLISM CLINICAL & EXPERIMENTAL RESEARCH

Can Alcohol Use Disorder Recovery Include Some Heavy Drinking? A Replication and Extension up to 9 Years Following Treatment

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Background: Recent research indicates some individuals who engage in heavy drinking following treatment for alcohol use disorder fare as well as those who abstain with respect to psychosocial functioning, employment, life satisfaction, and mental health. The current study evaluated whether these findings replicated in an independent sample and examined associations between recovery profiles and functioning up to 6 years later.

Methods: Data were from the 3-year and 7- to 9-year follow-ups of subsamples initially recruited for the COMBINE study (3-year follow-up: n = 694; 30.1% female, 21.0% non-White; 7- to 9-year follow-up: n = 127; 38.9% female, 27.8% non-White). Recovery at 3 years was defined by latent profile analyses including measures of health functioning, quality of life, employment, alcohol consumption, and cannabis and other drug use. Functioning at the 7- to 9-year follow-up was assessed using single items of self-rated general health, hospitalizations, and alcohol consumption.

Results: We identified 4 profiles at the 3-year follow-up: (i) low-functioning frequent heavy drinkers (13.9%), (ii) low-functioning infrequent heavy drinkers (15.8%), (iii) high-functioning heavy drinkers (19.4%), and (iv) high-functioning infrequent drinkers (50.9%). At the 7- to 9-year follow-up, the 2 high-functioning profiles had the best self-rated health, and the high-functioning heavy drinking profile had significantly fewer hospitalizations than the low-functioning frequent heavy drinking profile.

Conclusions: Previous findings showing heterogeneity in recovery outcomes were replicated. Most treatment recipients functioned well for years after treatment, and a subset who achieved stable recovery engaged in heavy drinking and reported good health outcomes up to 9 years after treatment. Results question the long-standing emphasis on drinking practices as a primary outcome, as well as abstinence as a recovery criterion in epidemiologic and treatment outcome research and among stakeholder groups and funding/regulatory agencies. Findings support an expanded recovery research agenda that considers drinking patterns, health, life satisfaction, and functioning.

Key Words: Alcohol Use Disorder, Alcohol Treatment, Recovery, Mixture Models, COMBINE.

ABSTINENCE FROM ALCOHOL remains the primary treatment target in most specialty treatment programs for alcohol use disorder (AUD; Davis and Rosenberg, 2013; Davis et al., 2017; Rosenberg and Davis, 1994) and is embedded in the program philosophies of many mutual-help organizations (e.g., Alcoholics Anonymous). The U.S. Food and Drug Administration (FDA) recommends either abstinence or no heavy drinking days as primary clinical endpoints in alcohol medication development (FDA, 2015), and many definitions of AUD recovery focus on abstinence as a defining feature of recovery (Betty Ford Institute Consensus Panel, 2007; SAMHSA, 2011).

Historical precedence notwithstanding, a growing body of conceptual and empirical work supports a broader conceptualization of AUD recovery that is not limited to alcohol-related outcomes but also includes other domains of psychosocial functioning (Ashford et al., 2019; Best et al., 2016; Kaskutas et al., 2014; Kelly et al., 2018b; Neale et al., 2016; Witbrodt et al., 2015; Witkiewitz and Tucker, 2020). Recent definitions of recovery advanced by key stakeholder

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Received for publication April 24, 2020; accepted July 7, 2020.

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DOI: 10.1111/acer.14413

groups include this expanded set of criteria. For example, SAMHSA (2011) defines recovery as "a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential," although the definition also focuses on abstinence from substances as a means to improve health. The Recovery Science Research Collaborative defines recovery as "an individualized, intentional, dynamic, and relational process involving sustained efforts to improve wellness" (p. 5; Ashford et al., 2019) and does not require or mention abstinence as a means to achieve recovery. Mixed-methods research examining the experience of recovery has identified multiple non-drinking-related areas of functioning as important to individuals, including self-care, processes of growth and development, relationships, improved outlook on life, coping with negative feelings and thoughts, and changing one's relationship to substances (Kaskutas et al., 2014; Neale et al., 2016; Witbrodt et al., 2015). Thus, both recent stakeholder and patient perspectives on defining recovery have advocated for a greater focus on well-being and functional improvements than on abstinence as a defining feature of recovery. This expanded perspective is similar to definitions of recovery from other psychiatric disorders in emphasizing improved functioning rather than the absence of symptoms, including recovery from depression (Furukawa et al., 2008), schizophrenia (Leucht and Lasser, 2006) and attention-deficit/hyperactivity disorder (Rostain et al., 2015).

Similarly, recent empirical work using a data-driven approach to define recovery has yielded findings that support an expanded definition that includes improved well-being and functioning. In a secondary analysis of individuals in the outpatient arm of Project MATCH (Project MATCH Research Group, 1997), Witkiewitz and colleagues (2019) found 4 profiles (i.e., subgroups) of individuals defined by measures of alcohol use, alcohol-related consequences, life satisfaction, and psychosocial functioning 3 years following treatment. These subgroups included: (i) low-functioning frequent heavy drinkers (15.8%), (ii) low-functioning infrequent heavy drinkers (16.1%), (iii) high-functioning heavy drinkers (16.9%), and (iv) high-functioning infrequent nonheavy drinkers (51.2%). Numerous covariates were examined to probe differences among these 4 groups. Overall, there were few differences between the high-functioning infrequent nonheavy drinkers and the high-functioning heavy drinkers. Notably, individuals who were high-functioning heavy drinkers had lower baseline severity of alcohol dependence relative to the high-functioning infrequent nonheavy drinkers, and they also reported fewer alcohol-related consequences and greater purpose in life compared to patients in the 2 lower functioning profiles. The high-functioning heavy drinkers also had a low probability of endorsing unemployment, other drug use, psychiatric symptoms, and life dissatisfaction, and were more likely to be non-Hispanic Whites.

In order to determine the generalizability of these results, we used an independent sample to replicate and extend the Witkiewitz et al.'s (2019) findings by examining alcohol-related outcomes and psychosocial functioning among individuals who completed a 3-year follow-up (Zarkin et al., 2008) following participation in the multisite trial of the Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence (COMBINE) study (Anton et al., 2006). We hypothesized that a 4-profile model would be replicated in the COMBINE study data, such that individuals would be classified as low-functioning frequent heavy drinkers, low-functioning infrequent heavy drinkers, high-functioning heavy drinkers, and high-functioning infrequent nonheavy drinkers at the 3-year follow-up. In addition, we examined whether recovery profiles at 3 years were associated with long-term functioning among a subset of participants who completed a brief questionnaire approximately 4 to 6 years after the 3-year follow-up. We hypothesized that those in the high-functioning recovery profiles would report better health, less frequent and intense drinking, and fewer hospitalizations at the 7- to 9-year follow-up.

MATERIALS AND METHODS

Participants and Procedures

The participants recruited for the COMBINE study (N = 1,383; Anton et al., 2006) met criteria for alcohol dependence based on the Diagnostic and Statistical Manual for Mental Disorders, fourth edition (American Psychiatric Association, 1994), and were recruited from the community across 11 research sites. Exclusion criteria included current drug use disorder (other than nicotine or cannabis), a psychiatric disorder requiring medication, or an unstable medical condition. After an intake assessment, participants were randomized to receive 16 weeks of treatment with (i) active naltrexone (100 mg/d) or placebo naltrexone, (ii) active acamprosate (3,000 mg/d) or placebo acamprosate, and (iii) medication management (MM) or combined behavioral intervention (CBI) with MM. One additional condition received CBI only and no pills.

Among participants recruited into the COMBINE trial, 874 participants from 9 sites (n = 1,144; 76.4%) consented to a 3-year follow-up, called the COMBINE Economic Study (Zarkin et al., 2008, 2010), and 694 participants (79% of COMBINE participants who consented to the 3-year follow-up) provided data at the 3-year assessment. The COMBINE Economic Study was continued for a longer-term follow-up at 7 to 9 years following randomization, and assessments for these follow-ups were completed by phone. The wide range for the longer-term follow-up (i.e., 7 to 9 years postrandomization) was due to these assessments being conducted over a span of several months, while recruitment and randomization for the COMBINE study spanned several years. Overall, 198 individuals from 4 of the 9 sites that participated in the COMBINE Economic Study (n = 369; 53.7%) agreed to enroll in a longer-term follow-up. Of these 198 individuals, 133 (67%) completed that longer-term follow-up, and 127 had both 3-year and 7- to 9-year follow-up data (64%).

Measures

Substance Use and Employment at 3-Year Follow-Up. Alcohol and other drug use were assessed using the Form 90 (Miller, 1996), a calendar-based, self-report method to measure daily alcohol and other drug use over the past 90 days, and employment status was assessed using the Economic Form 90 (Bray et al., 2007; Zarkin et al., 2005). Using data from the Form 90, we calculated summary measures of alcohol consumption, defined by drinking intensity (drinks per drinking day, DDD), drinking frequency (percent

drinking days, PDD), and percent heavy drinking days (PHDD, defined as the percent of days with consumption of at least 4/5 drinks for women/men). We also calculated binary measures of any cannabis use, any other drug use, and employment.

Functioning at 3-Year Follow-Up. The 12-Item Short-Form Health Survey (SF-12; Ware et al., 1996) was used to assess physical and mental health at 6 of the 9 sites that agreed to participate in the COMBINE Economic Study. The SF-12 physical health and mental health composite scores assess how physical health (e.g., pain) and affective symptoms (e.g., feeling depressed or anxious) have influenced functioning in daily life, respectively. The SF-12 has been shown to have good internal consistency (e.g., Huo et al., 2018), and in COMBINE, the SF-12 had an internal consistency reliability of $\alpha = 0.91$. The World Health Organization Quality-of-Life Scale-BREF (WHOQOL-BREF; WHOQOL Group, 1998) was used to assess participants' perceived quality of life in the past 4 weeks in physical health, psychological, social, and environmental (e.g., home environment, finances, safe/security) domains of functioning. This questionnaire consists of 26 items with varying 5-point scales (1 = very poor; very dissatisfied; not at all to 5 = very good; very satisfied; an extreme amount, depending on the question). In COMBINE, the WHOQOL-BREF had an internal consistency reliability of $\alpha = 0.91$.

Functioning at the Longer-Term Follow-Up. A self-report questionnaire was administered to participating individuals from October 2009 to January 2010, approximately 7 to 9 years following randomization in the COMBINE study. In the current analyses, we used single-item questions of general health ("In general, how you would rate your current health?" with response options on a 4-point scale from 1 = excellent; 2 = good; 3 = fair; to 4 = poor that were dichotomized for analysis into 0 = poor or fair and 1 = good or excellent) and hospitalizations ("During the last 12 months did you spend the night in a hospital in order to receive care for yourself?" with response options of 0 = No or 1 = Yes). Single-item questions to assess average DDD ("On those days when you (drink/drank) wine, beer, or hard liquor, how many drinks (did/do) you usually have per day?") and PHDD ("During the last 30 days, how many times did you have five or more [Women: 'four or more'] drinks of any alcoholic beverages in one day?") were also included in the analyses.

Covariates. Consistent with our prior work, covariate predictors of profile membership were included based on prior studies of AUD treatment outcomes (Connors et al., 2001; Dawson et al., 2005; Maisto et al., 2006; Moos and Moos, 2005; Tonigan et al., 2013; Witkiewitz et al., 2017) and the availability of measures in the COMBINE dataset. Pretreatment covariates included: (i) demographic variables (age, sex, race, marital status), (ii) COMBINE treatment condition, (iii) baseline alcohol dependence severity assessed by the Alcohol Dependence Scale (Skinner and Horn, 1984), (iv) percent heavy drinkers in the social network assessed by the Important People and Activities Instrument (Clifford and Longabaugh, 1991), and (v) baseline self-efficacy as measured by the Alcohol Abstinence Self-Efficacy Scale (DiClemente et al., 1994).

Statistical Analysis Plan

We conducted latent profile analysis (LPA) in M*plus* 8.4 (Muthén and Muthén, 2019) of the 3-year follow-up data. LPA is a type of finite mixture model in which individuals' pattern of responses based on each indicator variable (e.g., drinking outcomes, WHOQOL-BREF) is used to identify profiles that classify subsets of participants with similar response patterns (Witkiewitz et al., 2010). We used a maximum likelihood estimator with robust standard errors and 2,000 random initial starting values and 1,000 random starting values during the final-stage optimization. All models included PDD, PHDD, and DDD as indicators of alcohol use, 4 continuous WHOQOL-BREF quality-of-life subscales (physical, psychological, social, and environmental), 2 continuous subscales of the SF-12 (physical and mental health), and 3 binary variables (employment status, marijuana use, and other drug use). Missing data in the indicators were accommodated via the maximum likelihood estimator, and a small number of individuals ($n = 8$; 1.2% of the sample) with missing data on baseline covariates were not included in the final analyses ($n = 686$). Sensitivity analyses using multiple imputation of baseline covariates did not reveal substantively different findings. Thus, models estimated with maximum likelihood are presented, and data were assumed to be missing at random (Hallgren and Witkiewitz, 2013).

Models were estimated with (i.e., adjusted) and without (i.e., unadjusted) baseline covariates as predictors of profile membership, and profile solutions were compared across models to determine whether covariates influenced class solutions. All models were estimated with adjustment for research site using a sandwich estimator (Yuan and Bentler, 2010). We started with a 4-profile solution in order to test for replication of Witkiewitz and colleagues (2019). We examined the Bayesian information criterion (BIC) and sample size–adjusted BIC (aBIC) to assess whether the 4-profile model provided a reasonable fit to the data, as compared to 3- and 5-profile models. Lower BIC and aBIC indicate a better fitting model. The Lo–Mendell–Rubin likelihood ratio test and bootstrapped likelihood ratio test, which are commonly employed to determine the number of classes (Nylund et al., 2007), have not been developed for complex sampling designs (Muthén, 2016) and thus were not used to select classes in the current analyses given clustering by site.

Associations between baseline characteristics and the latent profiles were examined using model-based multinomial logistic regression with patient characteristics predicting odds of membership (odds ratios with 95% confidence intervals [CIs]) in each of the latent profiles. In these models, all covariates were included as predictors of latent profile membership with 1 profile serving as the reference profile.

Once the final latent profile solution was selected, we used distal outcome analysis via the manual 3-step Bolck, Croon, and Hagenaars (Bolck et al., 2004) approach to examine profile differences in longer-term follow-up outcomes (Nylund-Gibson et al., 2019), assessed at 7 to 9 years posttreatment, controlling for site and covariate effects. Distal outcome analysis provided an estimate of the mean differences in long-term follow-up outcomes across profiles based on a Wald chi-square test.

A priori power analyses, using a Monte Carlo simulation based on effect size estimates from our prior work (Witkiewitz et al., 2019), indicated we would have power greater than 0.94 to estimate a 4-profile model at the 3-year follow-up in the COMBINE dataset with excellent profile separation (i.e., high entropy) and power greater than 0.80 to detect small-to-medium effects of covariates in predicting profile membership. Power to detect distal effects of profile membership on 7- to 9-year outcomes was limited, with power greater than 0.63 to detect medium effect sizes and power greater than 0.97 to detect large effect sizes.

RESULTS

Descriptive Analyses

Participants who provided 3-year follow-up data ($n = 694$) were 30.1% female, 21.2% non-White, and had a mean age of 44.97 (SD = 10.3) at the initiation of treatment in COMBINE. The means (standard deviations) for

Table 1. Frequencies and Means (*M*; Standard Deviation, SD) for Demographic and Risk Covariates by Latent Profiles Based on Highest Probability of Profile Membership (Analysis *N* = 686)

Three-year indicators (total *N*)	Total sample *M* (SD)	Profile 1: Low-functioning frequent heavy drinking (*n* = 95) *M* (SD)	Profile 2: Low-functioning infrequent heavy drinking (*n* = 105) *M* (SD)	Profile 3: High-functioning heavy drinking (*n* = 136) *M* (SD)	Profile 4: High-functioning infrequent drinking (*n* = 350) *M* (SD)
Percent drinking days (*n* = 694)	30.82 (37.38)	91.85 (12.00)	14.22 (16.84)	67.33 (24.41)	4.99 (9.95)
Percent heavy drinking days (*n* = 694)	20.10 (31.32)	87.68 (14.17)	9.88 (13.58)	27.51 (19.04)	1.89 (5.17)
Drinks per drinking day (*n* = 694)	5.18 (6.70)	10.96 (7.08)	7.77 (9.43)	6.70 (5.06)	2.25 (4.22)
SF-12 physical T score (*n* = 497)	50.35 (9.13)	49.74 (9.89)	42.85 (11.35)	52.50 (6.99)	52.83 (6.32)
SF-12 mental T score (*n* = 497)	47.42 (10.83)	43.49 (10.98)	37.24 (11.47)	48.06 (9.81)	52.55 (6.42)
WHOQOL physical (*n* = 638)	28.34 (4.65)	26.97 (4.16)	22.16 (4.70)	29.21 (3.00)	30.50 (2.92)
WHOQOL psychological (*n* = 638)	22.79 (4.06)	21.33 (3.72)	17.78 (3.40)	22.87 (3.19)	24.93 (2.61)
WHOQOL social (*n* = 637)	10.90 (2.57)	10.03 (2.75)	8.50 (2.48)	11.07 (2.22)	11.87 (2.01)
WHOQOL environmental (*n* = 638)	31.38 (5.29)	30.47 (5.33)	24.89 (5.10)	32.64 (3.94)	33.37 (3.71)

	Total sample *N* (%)	Profile 1 *N* (%)	Profile 2 *N* (%)	Profile 3 *N* (%)	Profile 4 *N* (%)
Unemployed (*n* = 667)	142 (21.3%)	15 (16.9%)	42 (40.8%)	27 (20.5%)	56 (17.2%)
Cannabis use (*n* = 666)	85 (12.8%)	18 (20.2%)	19 (18.4%)	11 (8.3%)	34 (10.3%)
Other drug use (*n* = 666)	13 (2.0%)	2 (2.2%)	6 (5.8%)	3 (2.3%)	2 (0.6%)
Baseline covariates	**Total sample *N* (%)**	**Profile 1 *N* (%)**	**Profile 2 *N* (%)**	**Profile 3 *N* (%)**	**Profile 4 *N* (%)**
Sex %, male (*n* = 694)	485 (69.9%)	67 (70.5%)	80 (76.2%)	79 (58.1%)	253 (72.3%)
Marital status %, married (*n* = 694)	305 (43.9%)	49 (51.6%)	27 (25.7%)	63 (46.3%)	165 (47.1%)
Race %, White (*n* = 694)	548 (79.0%)	77 (81.1%)	74 (70.5%)	124 (91.2%)	271 (77.4%)
	Total sample *M* (SD)	**Profile 1 *M* (SD)**	**Profile 2 *M* (SD)**	**Profile 3 *M* (SD)**	**Profile 4 *M* (SD)**
Age	44.94 (10.33)	45.24 (9.33)	43.42 (10.06)	48.63 (11.44)	44.00 (9.92)
Social network drinking (IPA, *n* = 688)	0.11 (0.16)	0.12 (0.15)	0.11 (0.16)	0.12 (0.18)	0.10 (0.15)
Alcohol dependence (ADS, *n* = 693)	17.17 (7.49)	15.74 (6.75)	20.84 (7.90)	15.10 (7.90)	17.30 (6.97)
Self-efficacy (AASE, *n* = 689)	2.59 (.733)	2.58 (0.78)	2.55 (0.72)	2.52 (0.67)	2.65 (0.75)

AASE, Alcohol Abstinence Self-Efficacy Scale; ADS, Alcohol Dependence Scale; IPA, Important People and Activities; SF-12, 12-Item Short-Form Health Survey; WHOQOL, World Health Organization Quality-of-Life Scale. All covariates listed were included in the models. Sample size (*n*) for each profile is based on most likely class membership.

continuous outcomes and number (%) endorsing binary outcomes at 3 years following treatment are presented in Table 1.

The subset of participants who provided data at both the 3- and the 7- to 9-year follow-ups ($n = 127$) were 39.4% female, 28.3% non-White, and had a mean age of 46.56 (SD = 10.4) at the initiation of treatment. Those who completed the 7- to 9-year follow-up were significantly more likely to be female ($\chi^2(1) = 6.70$, $p = 0.01$) and non-White ($\chi^2(1) = 4.01$, $p = 0.045$), but were not significantly different ($p > 0.10$) on other baseline characteristics (including alcohol dependence severity, self-efficacy, age) or with respect to drinking or functioning at 3 years.

Latent Profiles of 3-Year Outcomes

Latent profile models with 3, 4, and 5 profiles were estimated and the BIC and aBIC continued to decrease with each additional profile. The substantive interpretation of the 4-profile solution replicated our prior results, and the fifth profile in the 5-profile model appeared to be a split of the high-functioning heavy drinking group (profile 3 of the 4-profile model) into a lower functioning occasional heavy drinking profile and a higher functioning occasional heavy drinking profile (see Fig. S1 and a similar 5-profile solution replicated in the Project MATCH data, as shown in Fig. S2). Given our prior work examining the 4-profile model in

Table 2. Model Fit and Class Solutions for 3- Through 5-Profile Models With and Without Covariate Adjustment

	Unadjusted	Adjusted by covariates
3-Profile model		
BIC	39,517.499	38,812.915
aBIC	39,368.265	38,600.181
Entropy	0.888	0.903
Profile 1 "Low functioning, frequent heavy drinking"	18.7%	18.4%
Profile 2 "Low functioning infrequent heavy drinking"	18.7%	16.6%
Profile 3 "High functioning infrequent heavy drinking"	62.6%	65.0%
4-Profile model		
BIC	39,056.863	38,402.675
aBIC	38,866.352	38,116.691
Entropy	0.927	0.920
Profile 1 "Low functioning, frequent heavy drinking"	13.1%	13.9%
Profile 2 "Low functioning, infrequent heavy drinking"	15.5%	15.8%
Profile 3 "High functioning, heavy drinking"	17.5%	19.4%
Profile 4 "High functioning, infrequent drinking"	54.0%	50.9%
5-Profile model		
BIC	38,627.596	37,997.984
aBIC	38,395.808	37,639.193
Entropy	0.939	0.942
Profile 1 "Low functioning, frequent heavy drinking"	13.8%	14.0%
Profile 2 "Low functioning, infrequent heavy drinking"	13.3%	13.7%
Profile 3 "Lower functioning, occasional heavy drinking"	13.7%	14.0%
Profile 4 "High functioning, infrequent drinking"	49.2%	48.3%
Profile 5 "High functioning, infrequent heavy drinking"	10.0%	10.0%

Bayesian information criterion (BIC) and sample size–adjusted BIC (aBIC).

Project MATCH (Witkiewitz et al., 2019), as well as concerns in the field about overextraction of latent classes in mixture models (Bauer and Curran, 2003), we selected the 4-profile model as our final model. Model BIC, aBIC, class solutions, and model entropy for 3- through 5-profile models are provided in Table 2.

The classification precision of the 4-profile model was excellent (entropy = 0.92). Model results were substantively unchanged when controlling for site and with adjustment for baseline covariates. Results of the adjusted models, controlling for site and covariates, are reported below. For descriptive purposes, Table 1 provides the means and standard deviations for continuous outcomes and frequency of endorsing binary distal outcomes for the 4 latent profiles using the highest probability of profile membership.

Figure 1 presents standardized scores across the 4 profiles with a mean = 0 and standard deviation = 1. The profiles replicated Witkiewitz and colleagues (2019) and were substantively meaningful. Profile 1 (13.9% of the total sample), the "low functioning frequent heavy drinking" profile, reported frequent heavy drinking (PDD = 92%, PHDD = 88%) with approximately 11 DDD, below-average physical and mental health on the SF-12, and below-average quality of life on the WHOQOL-BREF. Compared to other profiles, participants with expected classification in profile 1 also reported low levels of unemployment (17%), moderate cannabis use (20%), and low levels of other drug use (2%). None of the individuals with expected classification in profile 1 were abstinent from alcohol at the 3-year follow-up.

Profile 2 (15.8% of the total sample), the "low functioning infrequent heavy drinking" profile, reported infrequent heavy drinking (PDD = 14%, PHDD = 10%) and approximately 8 DDD, below-average physical and mental health on the SF-12, and below-average quality of life on the WHOQOL-BREF. Profile 2 had the highest level of unemployment (41%), moderate cannabis use (18%), and highest level of other drug use (6%) compared to all other profiles. Among those with expected classification in profile 2, 32.7% were abstinent at the 3-year follow-up.

Profile 3 (19.4% of the total sample), the "high functioning heavy drinking" profile, reported frequent drinking and occasional heavy drinking (PDD = 67%; PHDD = 28%) and approximately 7 DDD. Compared to other profiles, profile 3 had above-average physical health and average mental health on the SF-12, average to above-average quality of life on the WHOQOL-BREF, low unemployment (21%), and low cannabis (8%) and other drug (2%) use. None of the individuals with expected classification in profile 3 were abstinent from alcohol at the 3-year follow-up.

Finally, profile 4, the largest of the sample (50.9%), was the "high functioning infrequent non-heavy drinking" profile, who reported infrequent drinking (PDD = 5%; PHDD = 2%) and approximately 2 DDD. Compared to other profiles, profile 4 had above-average physical health and average mental health on the SF-12, average to above-average quality of life on the WHOQOL-BREF, low unemployment (17%), and low cannabis (10%) and other drug (0.6%) use. Among those with expected classification in profile 4, 61.4% were abstinent at the 3-year follow-up.

Covariate Predictors of Latent Profiles

As shown in Table 3, sex, age, race, marital status, and receipt of acamprosate were significantly associated with profile membership. Males had greater odds of expected membership in profile 2 ("low functioning infrequent heavy drinking") and profile 4 ("high functioning infrequent non-heavy drinking"), as compared to profile 3 ("high functioning heavy drinking"). Older individuals had greater odds of expected membership in profile 3, as compared to profile 4. Individuals who were non-Hispanic White had greater odds of membership in profile 3, as compared to all other profiles. Marriage predicted a greater probability of membership in profile 4, as compared to profile 2. Those who received acamprosate versus placebo had greater odds of expected membership in profile 3, as compared to profile 1 ("low functioning frequent heavy drinking"). With respect to baseline clinical

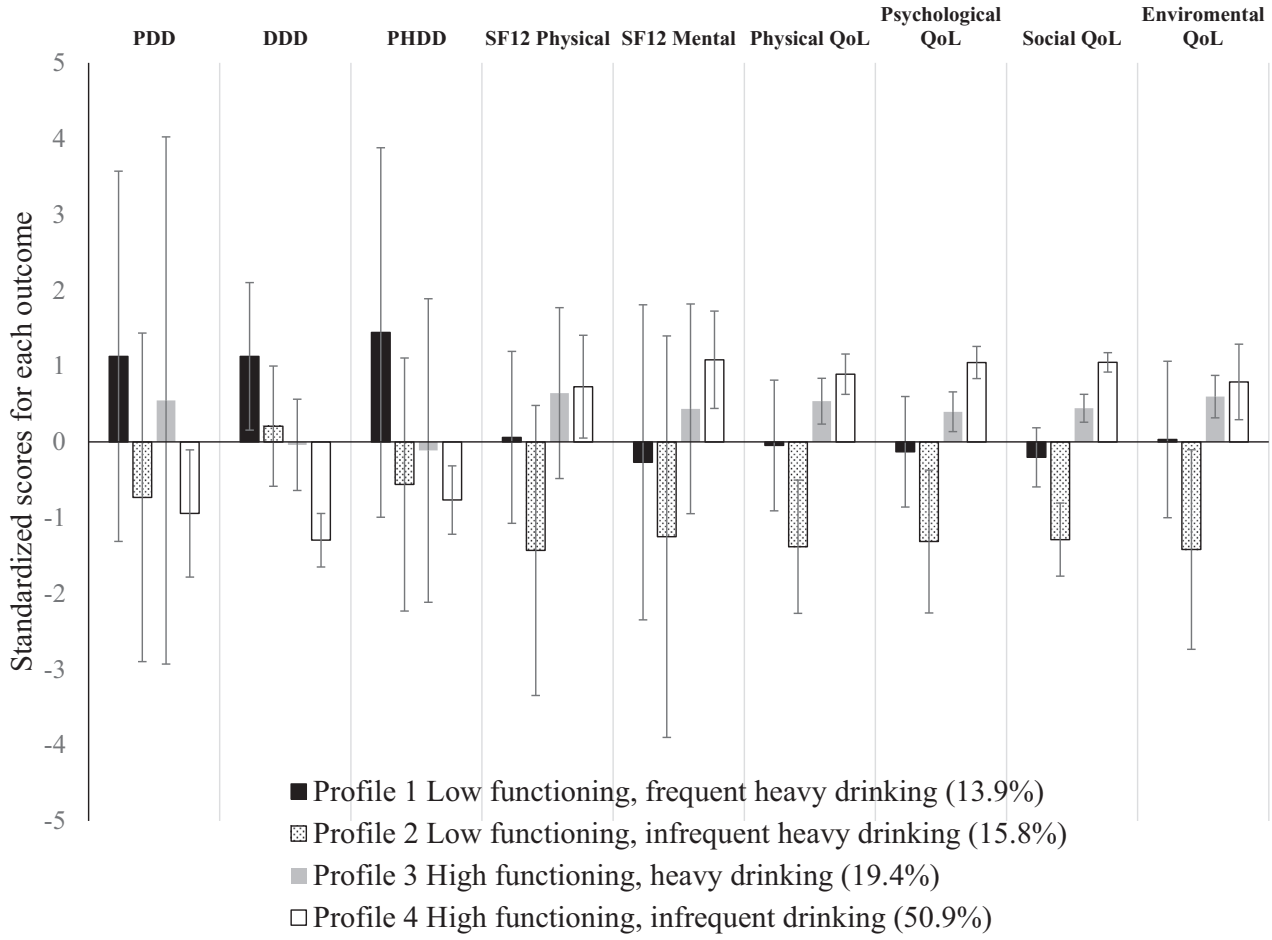

Fig. 1. Standardized mean scores (sample mean = 0 and standard deviation = 1) on each of the continuous outcome indicators by latent profiles with error bars representing standard error of mean estimates. DDD, drinks per drinking day; QoL, quality of life; PDD, percentage drinking days; PHDD, percentage heavy drinking days.

covariates, patients with a greater percentage of heavy drinkers in their social networks had greater odds of expected membership in profile 3, as compared to profile 4. Individuals with greater alcohol dependence severity had greater odds of membership in profile 2, as compared to all other profiles.

Distal Outcomes at Long-Term Follow-Up

Significant differences in drinking frequency, intensity, and hospital stays were found between profiles at the longer-term follow-up. For descriptive purposes, Table 4 presents the means and standard deviations for continuous outcomes and frequency of endorsing binary distal outcomes at 7 to 9 years postrandomization by the 4 latent profiles using the highest probability of profile membership. Self-reported health was greatest among profiles 3 and 4 (high-functioning profiles), although the differences in self-rated health between profiles were not statistically significant in the distal outcome analyses ($ps = 0.05$). Profiles 2 and 4 had significantly fewer heavy drinking days than profiles 1 and 3 ($ps < 0.01$). Profile 1 had significantly greater frequency of drinking days than all other profiles ($ps < 0.001$). Profile 3 had significantly fewer hospital stays than profile 1 ($p = 0.015$).

DISCUSSION

Using COMBINE study data, the current research replicated and extended recent research that examined recovery from AUD using an expanded definition of recovery that included indicators of life-health functioning and allowed for some heavy drinking (Witkiewitz et al., 2019). When recovery was defined by being classified within high-functioning profiles, the majority of COMBINE participants (70.3% of the current sample, profiles 3 and 4) were in recovery from AUD up to 3 years following treatment, and a subset of participants (19.4% of the current sample, profile 3) engaged in occasional heavy drinking and reported improved functioning that was similar to those who were mostly abstinent/non-heavy drinkers (profile 4). As found previously using Project MATCH data (Witkiewitz et al., 2019), those in profile 3 were engaging in limited heavy drinking on less than 30% of days (about 2 d/wk), consuming an average of about 6 to 7

Table 3. Odds Ratios (95% Confidence Intervals) for Covariate Effects in Multinomial Logistic Regressions With Patient Characteristics predicting Odds of Membership in Each Profile (Rows) Versus the Reference Group (Columns)

Baseline covariate	Profile 1: Low-functioning frequent heavy drinking (reference)	Profile 2: Low-functioning infrequent heavy drinking (reference)	Profile 3: High-functioning heavy drinking (reference)	Profile 4: High-functioning infrequent drinking (reference)
Sex, male = 1				
Versus Profile 1	–	0.80 (0.33, 1.93)	1.78 (0.88, 3.61)	0.97 (0.59, 1.59)
Versus Profile 2	1.25 (0.52, 3.01)	–	2.23 (1.26, 3.93)**	1.21 (0.61, 2.41)
Versus Profile 3	0.56 (0.28, 1.14)	0.45 (0.25, 0.879**	–	0.54 (0.33, 0.91)*
Versus Profile 4	1.03 (0.63, 1.70)	0.83 (0.42, 1.65)	1.84 (1.10, 3.07)*	–
Age				
Versus Profile 1	–	0.99 (0.96, 1.02)	0.97 (0.94, 1.01)	1.01 (0.99, 1.03)
Versus Profile 2	1.01 (0.98, 1.04)	–	0.98 (0.95, 1.02)	1.02 (0.98, 1.06)
Versus Profile 3	1.03 (0.99, 1.07)	1.02 (0.98, 1.06)	–	1.04 (1.01, 1.07)*
Versus Profile 4	0.99 (0.97, 1.01)	0.98 (0.94, 1.02)	0.96 (0.94, 0.99)*	–
Race, non-Hispanic White = 1				
Versus Profile 1	–	1.77 (0.74, 4.26)	0.47 (0.30, 0.75)**	1.20 (0.76, 1.90)
Versus Profile 2	0.57 (0.24, 1.36)	–	0.27 (0.11, 0.64)**	0.68 (0.30, 1.52)
Versus Profile 3	2.13 (1.34, 3.38)**	3.77 (1.57, 9.07)**	–	2.56 (1.38, 4.74)**
Versus Profile 4	0.83 (0.53, 1.32)	1.47 (0.66, 3.30)	0.39 (0.21, 0.72)**	–
Marital status, married = 1				
Versus Profile 1	–	2.20 (0.99, 4.89)	1.64 (0.91, 2.96)	1.13 (0.65, 1.96)
Versus Profile 2	0.45 (0.20, 1.01)	–	0.74 (0.38, 1.45)	0.51 (0.33, 0.79)**
Versus Profile 3	0.61 (0.34, 1.10)	1.35 (0.69, 2.62)	–	0.69 (0.37, 1.26)
Versus Profile 4	0.89 (0.51, 1.55)	1.96 (1.26, 3.05)**	1.46 (0.79, 2.68)	–
Treatment contrast, acamprosate = 1				
Versus Profile 1	–	0.98 (0.55, 1.72)	0.60 (0.45, 0.78)***	0.78 (0.55, 1.08)
Versus Profile 2	1.02 (0.58, 1.80)	–	0.61 (0.34, 1.10)	0.79 (0.48, 1.31)
Versus Profile 3	1.68 (1.28, 2.20)***	1.64 (0.91, 2.96)	–	1.30 (0.93, 1.83)
Versus Profile 4	1.29 (0.92, 1.80)	1.26 (0.76, 2.09)	0.77 (0.55, 1.08)	–
Treatment contrast, naltrexone = 1				
Versus Profile 1	–	0.70 (0.41, 1.22)	1.21 (0.72, 2.03)	1.09 (0.74, 1.60)
Versus Profile 2	1.42 (0.82, 2.47)	–	1.72 (0.84, 3.52)	1.55 (0.98, 2.43)
Versus Profile 3	0.83 (0.49, 1.40)	0.58 (0.28, 1.19)	–	0.90 (0.50, 1.61)
Versus Profile 4	0.92 (0.62, 1.36)	0.65 (0.41, 1.02)	1.11 (0.62, 2.00)	–
Treatment contrast, CBI = 1				
Versus Profile 1	–	1.33 (0.55, 3.21)	0.77 (0.38, 1.54)	1.23 (0.69, 2.19)
Versus Profile 2	0.75 (0.31, 1.82)	–	0.58 (0.31, 1.09)	0.93 (0.48, 1.79)
Versus Profile 3	1.30 (0.65, 2.61)	1.72 (0.92, 3.24)	–	1.60 (0.77, 3.31)
Versus Profile 4	0.81 (0.46, 1.45)	1.08 (0.56, 2.09)	0.63 (0.30, 1.29)	–
Heavy drinkers in network (IPA)				

Continued.

Table Table 3. (Continued)

Baseline covariate	Profile 1: Low-functioning frequent heavy drinking (reference)	Profile 2: Low-functioning infrequent heavy drinking (reference)	Profile 3: High-functioning heavy drinking (reference)	Profile 4: High-functioning infrequent drinking (reference)
Versus Profile 1	–	1.81 (0.27, 11.32)	0.80 (0.16, 3.94)	2.68 (0.56, 12.80)
Versus Profile 2	0.55 (0.09, 3.46)	–	0.44 (0.10, 2.03)	1.48 (0.52, 4.20)
Versus Profile 3	1.26 (0.25, 6.21)	2.27 (0.49, 10.46)	–	3.36 (1.29, 8.77)*
Versus Profile 4	0.37 (0.08, 1.79)	0.68 (0.24, 1.92)	0.30 (0.11, 0.78)*	–
Alcohol dependence severity (ADS)				
Versus Profile 1	–	0.92 (0.87, 0.97)**	1.01 (0.95, 1.07)	0.97 (0.94, 1.01)
Versus Profile 2	1.09 (1.03, 1.15)**	–	1.10 (1.05, 1.15)***	1.06 (1.03, 1.09)***
Versus Profile 3	0.99 (0.94, 1.05)	0.91 (0.87, 0.95)***	–	0.96 (0.92, 1.01)
Versus Profile 4	1.03 (0.99, 1.07)	0.95 (0.92, 0.97)***	1.04 (1.00, 1.08)	–
Self-efficacy (AASE)				
Versus Profile 1	–	1.00 (0.56, 1.78)	1.02 (0.66, 1.60)	0.84 (0.55, 1.30)
Versus Profile 2	1.00 (0.56, 1.78)	–	1.02 (0.74, 1.42)	0.84 (0.65, 1.09)
Versus Profile 3	0.98 (0.63, 1.53)	0.98 (0.71, 1.31)	–	0.82 (0.66, 1.02)
Versus Profile 4	1.19 (0.77, 1.83)	1.19 (0.92, 1.54)	1.22 (0.98, 1.51)	–

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. All covariates listed in Table 1 were included in the models. ADS, Alcohol Dependence Scale; AASE, Alcohol Abstinence Self-Efficacy Scale; CBI, combined behavioral intervention; IPA, Important People and Activities.

Table 4. Frequencies and Means (Standard Deviation) for Distal Outcomes at 7- to 9-Year Follow-Up by Latent Profiles ($n = 127$)

Distal outcomes	Profile 1: Low-functioning frequent heavy drinking ($n = 18$)	Profile 2: Low-functioning infrequent heavy drinking ($n = 20$)	Profile 3: High-functioning heavy drinking ($n = 27$)	Profile 4: High-functioning infrequent drinking ($n = 62$)
Health rated "Good" to "Excellent," *N* (%)	14 (77.8%)	11 (55.0%)	24 (88.9%)	54 (87.1%)
Any hospital stays, *N* (%)	3 (16.7%) $_{3}$	2 (10.0%)	2 (7.4%) $_{1}$	9 (14.5%)
% drinking days, mean (SD)	72.4% (36.4%)$_{2,3,4}$	33.2% (29.0%) $_{1, 3}$	65.5% (35.8%) $_{1,2,4}$	27.8% (31.8%) $_{1, 3}$
% heavy drinking days, mean (SD)	39.4% (42.3%)$_{2,4}$	6.0% (12.2%)$_{1, 3}$	30.4% (32.0%) $_{2, 4}$	14.8% (26.4) $_{1, 3}$
Drinks per drinking day, mean (SD)	6.0 (4.3)	7.8 (16.4)	5.7 (6.3)	4.3 (7.0)

Subscripts indicate significant differences ($p < 0.05$) between profiles, based on the profile number indicated by the subscript. All covariates listed in Table 1 were included in the models. Sample size (*n*) for each profile is based on most likely class membership; however, distal outcome models were estimated using a model-based approach.

DDD. Importantly, this level of alcohol consumption far exceeds national guidelines for moderate alcohol consumption and is likely not without physical health consequences and the potential for alcohol toxicity and accidental injury (Rehm et al., 2017). In addition, prior epidemiological work has identified that recurrence of some AUD symptoms is linearly associated with level of drinking, and heavier drinking was associated with more symptoms of AUD 3 years later (Dawson et al., 2007). The vast majority of individuals in the current high-functioning profiles were those who engaged in infrequent heavy drinking (profile 4). Thus, encouraging drinking reductions, even short of total abstinence, is clearly recommended in clinical practice.

Also consistent with our prior findings (Witkiewitz et al., 2019), those who engaged in infrequent drinking or achieved abstinence did not necessarily have better functional outcomes than those in profile 2. One explanation for the poor recovery outcomes captured by profile 2 may have more to

do with their very low scores in the WHOQOL-BREF Environmental domain, which assesses financial resources, freedom, physical safety and security, home environment, pollution, noise, traffic and climate, accessibility and quality of health care, transport, opportunities for acquiring new information and skills, and opportunities for recreation or leisure. The present study and our prior findings (Witkiewitz et al., 2019) indicate that 3-year recovery outcomes among those most likely classified in profile 2 lag behind the majority of the sample, despite large reductions in alcohol consumption. Individuals in profile 2 were also more likely to be non-White in the current sample. Other baseline risk and protective factors that predicted recovery outcomes were similar in both the current study and our prior analyses of the Project MATCH sample.

In addition, although the sample size was small (n = 127) and power was limited, outcomes at 7 to 9 years postrandomization in COMBINE supported the long-term stability of the 4 latent profiles identified at the 3-year follow-up. Individuals with expected classification in the 2 high-functioning recovery profiles (profiles 3 and 4) reported the highest self-rated health, and those in the high-functioning heavy drinking profile (profile 3) reported significantly fewer hospital stays. Among those most likely classified in profile 3, average levels of drinking at the 7- to 9-year follow-up were similar to levels of drinking at the 3-year follow-up. These longitudinal findings support the notion that long-term recovery from AUD is achievable among those with AUD who continue to engage in some drinking.

Taken together, the results provide further evidence that definitions of recovery should be extended to focus on functioning and allow for the possibility that recovery from AUD may include some heavy drinking occasions. As discussed elsewhere (Witkiewitz, 2013; Witkiewitz and Tucker, 2020), consumption-based thresholds, such as the 4/5 heavy drinking definition, have not been well-validated (Pearson et al., 2016), and they lack sensitivity and specificity for predicting problems related to alcohol use, health, and functioning (Pearson et al., 2017; Wilson et al., 2016), as we found here. Similar research on natural recovery from AUD without treatment found that a composite quantity–frequency index of prerecovery drinking did not predict 1-year postrecovery outcomes, whereas functional indicators of problem severity did (e.g., alcohol-related negative consequences, behavioral economic index of alcohol reward value; Cheong et al., 2020; Tucker et al., 2020). Other recent research among Veterans has found those with some heavy drinking occasions do not have worse outcomes with respect to brain health and cognitive functioning as compared to complete abstainers (Meyerhoff and Durazzo, 2020). This is an important finding that requires replication.

Our findings using Project MATCH and COMBINE data support a broader conceptualization of AUD recovery that is not limited to alcohol-related outcomes but also includes domains of health, well-being, and functioning that are often adversely affected by harmful drinking. Most definitions of recovery advanced by diverse stakeholders, ranging from AA to the Recovery Science Research Collaborative to diagnostic systems like the DSM-5 (American Psychiatric Association, 2013), do not include consumption-based criteria and instead focus on improved well-being and functioning. As noted earlier, definitions of recovery from other psychiatric disorders are similar and emphasize improved functioning, rather than the absence of symptoms. In a similar vein, patient-centered mixed-methods research (e.g., Neale et al., 2014, 2016) has established that functional improvements are central to patient needs, values, and perspectives on recovery, such as improvements in physical health, engaging in meaningful activities, increased social functioning, and housing stability. Further conceptual and empirical work to develop useful measures of functioning, well-being, and associated life contexts that are meaningful and influential in AUD recovery deserves high priority in future research.

Limitations and Future Directions

Some differences in the current sample and profile solutions, as compared to our prior Project MATCH analyses (Witkiewitz et al., 2019), warrant mention as study qualifications. First, we did not have exactly the same measures of functioning in both samples. Second, rates of other drug use were higher in the Project MATCH sample and, in the current sample, there was almost twice as much cannabis use in the low- compared to the high-functioning profiles. The extent to which cannabis use may have influenced functional outcomes is unclear (Curran et al., 2016). Additional limitations include the reduced sample sizes collected at the 3-year and especially the 7- to 9-year follow-ups compared to the originally enrolled COMBINE sample (Zarkin et al., 2008). The samples recruited at the 3-year and the 7- to 9-year follow-up were not randomly selected or purposively sampled for participation, and the extent of possible bias in the retained sample is unknown. The power to detect effects at the longer-term follow-up was particularly limited. Also, the COMBINE study excluded individuals with cooccurring substance use disorders, psychiatric comorbidities, and unstable medical conditions (Anton et al., 2006). Whether the current findings generalize to the broader heterogeneous population of persons who receive AUD treatment is an empirical question that should be explored in future work. Finally, the reliance on self-report measures and lack of collateral informants or objective measures of health, functioning, and well-being are also limitations.

With respect to future directions, examining whether the present findings replicate when objective or verifiable measures of health, well-being, and functioning are included is indicated. A related issue is investigating the extent to which patient perspectives on recovery converge with quantitative and objective measures (Neale et al., 2014, 2016). For example, our work supports an empirical definition of long-term

"recovery" that can include some heavy drinking, but it is unclear whether patients in Project MATCH or COMBINE self-identified as being in recovery and the extent to which their recovery definitions may include other domains, such as stable housing, employment, meaningful relationships, and meeting personal goals. The same issues apply to their families and other social network members. Kelly and colleagues (2018a) conducted critically important mixed-methods work on self-identification as "being in recovery" in a nationally representative sample and found in quantitative analyses that those who identified as being in recovery were more likely to engage in mutual help, use recovery support, receive formal treatment, and be diagnosed with a substance use disorder. Qualitative analyses revealed that those with lower problem severity and those who perceived less difficulty in resolving an alcohol or drug problem were less likely to identify with being "in recovery" and there was greater focus on problem "resolution." For some, the "recovery" label was viewed as negative. The potential effects of labeling and defining recovery from AUD (vs. using the terms "remission" or "problem resolution") are an important topic that requires future work (Vilsaint et al., 2019). Whichever term is used, the emphasis of most extant recovery definitions, including those from the recovery community, on well-being and functional improvements rather than drinking per se suggests that the degree of convergence between these multiple data sources may be quite good.

Finally, more research is required to examine the relationships between premorbid functioning, functional outcomes, and recovery. For example, the poor physical and mental health, low levels of alcohol consumption, and high unemployment captured by profile 2 could be reflective of "sick-quitters" (Sarich et al., 2019), with health problems that are severe enough to drive drastic reductions in alcohol consumption, and perhaps in this case, corollary challenges to sustained employment. Profile 2, however, was also the youngest subgroup in the Project MATCH and COMBINE samples, with a mean age of 37 and 43 years, respectively. Although age, in and of itself, does not disqualify the sick-quitter hypothesis, it does raise questions. Profile 2 also had the highest unemployment and the worst functioning in both samples, was more likely to be non-White in the COMBINE sample, and had greater depression and anxiety in the Project MATCH sample (Witkiewitz et al., 2019). It may be the case that individuals in profile 2 are adversely affected by lower socioeconomic status and opportunity (Best and Lubman, 2012; Lancaster, 2017), such that even if these individuals do the hard work of recovery (McKay, 2017), including dramatic reductions in alcohol consumption, the functional outcomes are not as good for these individuals given preexisting social disadvantage, inequities, systemic racism, and/or comorbid mental health symptoms. Some recent work has begun to investigate the links between socioeconomic status, behavioral economic indicators, and recovery (Mericle et al., 2018; Tucker et al., 2020), and this is an area that demands further inquiry.

Implications of an Expanded Definition of "Recovery"

The current study and other recent work support an expanded definition of recovery to focus on a process of change characterized by improvements in well-being, quality of life, and functioning (Witkiewitz et al., 2020). The push to extend beyond abstinence as a necessary condition for AUD recovery is based on quantitative data among diverse samples of treatment seekers and those who achieve natural recovery (Cheong et al., 2020; Kelly et al., 2018b; Meyerhoff and Durazzo, 2020; Wilson et al., 2016; Witkiewitz et al., 2019), qualitative data from individuals with AUD (Kaskutas et al., 2014; Kelly et al., 2018a; Neale et al., 2016), as well as by definitions provided by stakeholder groups (Ashford et al., 2019; SAMHSA, 2011).

Resistance to this recommendation is likely given that abstinence has long been considered the "gold standard" outcome for AUD clinical trials and is deeply embedded in the philosophy and program recommendations of AA and other mutual-help organizations that have existed for nearly a century. Nevertheless, progress has been made in developing measures of functioning and contextual factors surrounding recovery and relating them to outcomes of change attempts that are essential to advance a broadened definition of recovery. For example, several efficacious treatments guided by behavioral principles explicitly aim to reduce substance use by increasing engagement in rewarding alternatives to use in domains of life-health functioning adversely affected by use. This is a key component of the community reinforcement approach (Meyers et al., 2002) and the substance-free activity session used in conjunction with a brief motivational intervention (Murphy et al., 2019). This research has produced reliable and valid measures of rewarding alternatives to alcohol and drug use that have utility to predict outcomes (Acuff et al., 2019). Recovery from AUD coincides with and appears to be promoted by increased access to rewarding nondrug activities and commodities in both untreated and treated samples (Moos and Moos, 2007; Tucker et al., 2020), and such enriched life contexts likely motivate and reinforce recovery processes and outcomes. Access to rewarding social opportunities also likely contributes to the appeal and effectiveness of mutual-help groups (Kelly et al., 2012) and to findings showing that prevention programs led by peers tend to have better outcomes than educational approaches (Dobbie et al., 2019). Thus, the groundwork has been laid to support and expand research and practice that rest on a broadened definition of recovery and the life contexts that support it.

CONCLUSION

The present findings replicated our Project MATCH findings (Witkiewitz et al., 2019) in a new sample and provided support for definitions of recovery that consider patient functioning and quality of life (Ashford et al., 2019; Neale et al., 2016; Witkiewitz and Tucker, 2020). The results also call into

question definitions of AUD recovery that rely strictly on abstinence or not exceeding a particular level of alcohol consumption (e.g., no heavy drinking days) as the defining feature (Betty Ford Institute Consensus Panel, 2007). A broader definition of recovery may help to engage more individuals in pursuing positive change, including but not limited to drinking reductions, which could reduce the stigma of AUD and reduce the burden of disease from alcohol (Morris et al., 2020; Probst et al., 2015; Vilsaint et al., 2019; Wallhed Finn et al., 2014).

ACKNOWLEDGMENTS

The preparation of this manuscript was supported in part by grants from the National Institute on Alcohol Abuse and Alcoholism (R01 AA022328, K05 AA016928, K01 AA024796, K01 AA023233, F31 AA026773, and T32 AA018108).

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

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

Fig. S1. Standardized mean scores (sample mean = 0 and standard deviation = 1) on each of the continuous outcome indicators by latent profiles in the five profile model in COMBINE.

Fig. S2. Standardized mean scores (sample mean = 0 and standard deviation = 1) on each of the continuous outcome indicators by latent profiles in the five-profile model in Project MATCH (from Witkiewitz et al., 2019).