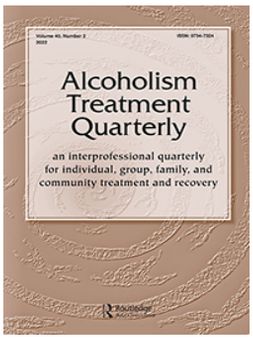

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ABSTRACT

Despite existing interventions that have shown some promise for people with alcohol use disorder (AUD), there is a sizable number of patients that fail to respond to or complete treatment. In the current study, we analyzed data from the Treatment Episode Data Set (TEDS) to create profiles that indicate who may be more likely to resist treatment-as-usual. For the analysis, chi-square and logistic regression were used to associate personal characteristics with being at high and low risk of treatment resistance. Characteristics that put someone at higher risk of resisting treatment-as-usual include being unemployed, homelessness (or a dependent living arrangement), using daily, being male, and co-occurring mental and substance abuse disorders. The results suggest that general demographic information at patients' admission can be used to identify population groups where conventional strategies for standard AUD treatment may be insufficient. As such, the findings can help to inform, shape, and personalize treatment, leading to successful outcomes for the subgroup of individuals who will not benefit from typical AUD interventions.

KEYWORDS

Alcohol use disorder; treatment recycling; recidivism; treatment resistance; risk factors; treatment-as-usual

Introduction

Alcohol use disorder (AUD) is both deeply pervasive and harmful, associated with myriad disabilities, illnesses, injuries, and other conditions. According to data from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the prevalence of AUD (based on DSM-IV criteria) was 8.5% and 30.3% for 12-months and lifetime, respectively (Grant et al., 2015); strikingly, the 2012–2013 NESCARC-III prevalence increased to 12.7% and 43.6% for 12-months and lifetime (Grant et al., 2015). In fact, the World Health Organization (2018) reports that 63.3 million people (15 years or older) in the region of the Americas alone had an alcohol use disorder in 2016. Such a growth in prevalence is considerable, particularly given AUD's relationship to psychiatric and physical illnesses, such as cancer and depression, as well as other intentional and accidental injuries (Kranzler & Soyka, 2018; Rehm, 2011). Overall, AUD is a highly consequential disease with an array of social, physical, psychological, mental, financial, and communal implications.

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Supplemental data for this article can be accessed on the publisher's website

Alcohol use disorder (AUD)

Even in the wealthiest countries worldwide, AUD is ranked as the third-most disabling disease category, making up 3.9 million years of life lost to disability (5.7% of all years of life lost to disability; Rehm, 2011). Indeed, Rehm et al. (2014) found that heavy drinking has a causal relationship with 200 diseases and injures from the International Classification of Diseases-10. Of those 200, 30 have alcohol in their name or description; that is, alcohol is the fundamental component leading to these diseases, which includes alcohol use disorder (Rehm, 2011). Among the many illnesses and injuries fomented by AUD, there are cardiovascular disease, infectious disease, pancreatic cancer, pancreatitis, liver cirrhosis, diabetes, and stroke (Grant et al., 2015; Kranzler & Soyka, 2018). There is a substantive degree of co-morbidity, too, in regard to mental illness and disorder, such as tobacco use, depression, bipolar disorder, phobias, and borderline personality disorder (Kranzler & Soyka, 2018; Rehm et al., 2014). The interplay of AUD and comorbidities has negative consequences on behavior due to impairment, thereby possibly contributing to acts of violence or driving while intoxicated (Grant et al., 2017). Moreover, neuroscientists have consistently found evidence to support the assertion that addiction is a brain disorder, including AUD (Naqvi & Morgenstern, 2015; Volkow, Koob, & McLellan, 2016). The way in which the brain reacts to and adjusts to alcohol makes its management and regulation all the more challenging for those with AUD.

Current treatment

Treatment for AUD consists of pharmacological and psychosocial interventions and has typically been oriented toward abstinence, though harm-reduction models have been recently receiving greater attention, as well (Laramée et al., 2015). The United States Food and Drug Administration has approved three medications for treating AUD: disulfiram, naltrexone, and acamprosate (Kranzler & Soyka, 2018). Despite potential benefits, 9% or less of people with AUD are prescribed medications as part of treatment. Questions over the efficacy of such pharmacological treatments factor into their limited use (Kranzler & Soyka, 2018; Maisel, Blodgett, Wilbourne, Humphreys, & Finney, 2013).

More often, AUD treatment-as-usual consists of psychosocial intervention. These treatments include, but are not limited to, social skills training, relapse prevention therapy, brief interventions, couples or family therapy, Twelve-Step programs, psychotherapy, case management, and general counseling (Martin & Rehm, 2012). Motivational interviewing, cognitive-behavioral therapy, and other interventions related to behavior change have been shown to be among the most useful of psychosocial treatments (Miller & Wilbourne, 2002). Moreover, the therapist plays a key role, regardless of the evidence-base for particular interventions; that is, how well a practitioner can deliver the treatment can be a boon or obstacle in treatment (Martin & Rehm, 2012). Still, across prescription and therapeutic treatments, the evidence-base suggests modest effectiveness. Several studies have found that treatment-as-usual outcomes can have a wide range of success (Naqvi & Morgenstern, 2015), with some studies showing very few patients successfully completing treatment (Patterson Silver Wolf, BlackDeer, Beeler-Stinn, Zheng, & Stazrad, 2021; Patterson Silver Wolf, Dulmus, Maguin, Linn, & Hales, 2019). In all, the general public suffering with AUD does not seem to achieve sustained, positive outcomes from existing treatment-as-usual options.

Gaps in knowledge

Although pharmacological and psychosocial interventions have shown some promise for people with AUD, there are a sizable number of patients who fail to respond to or complete treatment (Lappan, Brown, & Hendricks, 2019). Like other brain disorders, AUD treatment should be targeted at the individual's particular circumstances, biology, and general needs; failure to take a more personalized approach may perpetuate treatment recidivism (Benyamin et al., 2008; Dean et al., 2006; Dematteis et al., 2017; McLellan, Arndt, Metzger, Woody, & O'Brlen, 1993). Factors such as housing-status and race are key barriers to treatment. For instance, Black and Hispanic people and those experiencing homelessness are more likely to be disproportionately impacted by the negative effects of alcohol use (Collins, 2016). Moreover, other factors also play into treatment failure and relapse. Patients may have negative side-effects related to medications. Others may prefer to keep drinking – but treatments may be oriented to abstinence only (Laramée et al., 2015). Despite long-standing and prevailing treatments for people with AUD, the disease is clearly branded as being a chronically relapsing illness (Witkiewitz & Marlatt, 2007). Although treatment recidivism is high, there continue to be gaps in knowledge as to why this is the case. When people relapse and reenter treatment, they likely are given the same treatment options as before so the revolving door of treatment continues (Naqvi & Morgenstern, 2015; Patterson Silver Wolf et al., 2021). Such unremitting entrances and exits of treatment are not meeting the needs of patients or the goals of clinicians.

Treatment resistant alcohol use disorder

Similar to other treatment-resistant disorders, relapsing following treatment completion and/or failure to complete treatment for people with AUD needs to be seen as a characteristic of the disease. Extant literature points to treatment-resistant depression and opioid use disorder, illuminating how failure to complete treatment has to do with the disease's nature (Conway, George, & Sackeim, 2017; McIntyre et al., 2014; Patterson Silver Wolf & Gold, 2020). However, AUD treatment resistance, the process of relapsing and reentering treatment repeatedly, has historically been seen as failure of the patient, rather than relying on a more multifaceted framework of alcohol use disorder that explains its chronicity (Conway et al., 2017; Naqvi & Morgenstern, 2015). On the contrary, the persistent relapse among a substantial sub-population of people with AUD points to the existence of treatment resistance. For treatment-resistant depression, Conway et al. (2017) and McIntyre et al. (2014) identified successful treatments, showing promise for successfully intervening in chronic AUD, as well. There is a need to identify the environmental and biopsychosocial factors that instigate resistance in order to mirror such successes. As such, this exploratory study uses secondary data analysis to examine such factors associated with people that persistently fail AUD treatment.

Hypothesis

For the current study, we hypothesize that by analyzing available data collected from patients admitted to SUD treatment, we will be able to identify profiles that indicate who may be more likely to resist treatment-as-usual. This has direct practical implications.

When new patients enter SUD treatment, the intake process includes a self-report of various factors, such as life circumstances, habits and behaviors, and other biopsychosocial conditions. These factors can then inform choices for precision medication and treatment plans. This project can begin to inform, shape, and personalize treatment and lead to successful treatment outcomes for the subgroup of individuals who will not benefit from AUD treatment-as-usual.

Methods

Data from the Treatment Episode Data Set (TEDS), specifically the TEDS-A-2017 dataset, were downloaded from the Substance Abuse & Mental Health Data Archive. This dataset includes over 2 million records of individuals who have received care from a substance abuse treatment facility. 64.5% of patients in this dataset are male, while 35.5% are female. Patients who identified their race as White make up the majority of this dataset's population at 65.1%. The remaining population consists of 17.7% Black/African American patients, 2.1% American Indian, with each other identified race being of a very small percentage. Individuals who have at most completed high school or received their GED account for 69.9% of this population, whereas those who have completed 13–15 years of education represent 17.2% and those with 16+ years of education consist of 5.8% of the population. Those who are unemployed constitute a majority of this dataset's population with 69.2% unemployed, 15.8% working full-time and 6.8% working part-time. Just over half or 60% of the population lives independently while 14.9% are homeless and 17.6% are in a dependent living arrangement. The vast majority reported alcohol or heroin to be their primary substance of use at admission. These two types together account for 56.05% of the population, followed by marijuana (12.5%), methamphetamine (11.4%), other opioids and synthetics (7.24%), and cocaine/crack (5.11%). All remaining types generate a very small percentage. Close to 70% of this population began using between 12 and 24 years of age. Our focus for this study is on those individuals who reported alcohol as their primary substance at admission.

The intention of this study is to discover what factors may contribute to the likelihood an individual will undergo five or more treatments. Our subset of TEDS data was therefore categorized into two groups: one for those who have received one to four treatments and one for those who received five or more treatments. We call these two groups the "low treatment" and "high treatment" groups, respectively.

Ten variables were chosen to study their associations with low and high treatment groups in those who reported alcohol as their primary substance use at admission.

The variables of interest were collapsed into fewer, more aggregated categories for analysis (see Supplementary Table). Education was recoded to create two groups: low and high education. The low education category includes those with 8–12 years or a GED (codes 1, 2, 3) and high education includes those with 13–16+ years (codes 4 and 5). Employment was also collapsed into two groups: employed and not employed. Employed includes those who work full-time or part-time (codes 1 and 2) and not employed includes those with no employment (codes 3 and 4). Two groups were created for living arrangement: homeless/dependent (codes 1 and 2) and independent (code 3). The frequency in which the patient uses was recoded as daily (code 3) and not daily (code 1, 2). Age at first use was categorized as 20 years and under (codes 1, 2, 3, 4) and over 20 years of age (codes 5, 6, 7). Whether the

patient had co-occurring mental and substance use disorders was left unchanged: yes (code 1) and no (code 2). Age at admission was categorized into the following groups: 12–29 years (codes 1, 2, 3, 4, 5), 30–49 years (codes 6, 7, 8, 9), 50–64 years (codes 10, 11), and 65+ years (code 12). Gender was left unchanged: male (code 1) and female (code 2). Marital status was recoded to create three categories: married (code 2), never married (code 1), and separated/divorced (code 3 and 4). Race was categorized into 4 categories: American Indian (code 2), White (code 5), Black/African American (code 4), and other (code 1, 3, 6, 7, 8, 9). Number of days waiting was left unchanged: 0 days (code 0), 1–7 days (code 1), 8–14 days (code 2), 15–30 days (code 3), and 31 plus days (code 4). All missing data were removed to create a final dataset with 208,435 records used for analysis. Population and outcome characteristics were compared between the final records used for analysis and those that were not used due to missing data. We observed the missing data had a slightly lower rate in the high treatment group (16% in missing data versus 17.5% for data used in the analysis). More detail of this regrouping process can be found in the supplementary material.

For univariate analysis, chi-squared tests were carried out to determine the association between individual factors and the low and high treatment groups. For multivariate analysis, logistic regression was used to investigate the effect of variables of interest simultaneously, which allows a better understanding of which variables increase a patient's chance of unsuccessful treatment attempts jointly. We also calculated the probability of being in the high treatment group using the logistic regression with the parameter estimates for the covariates. We chose the covariate values of the high-risk group based on the ones that produced the highest odds ratios.

Results

Patients who reported alcohol as their primary substance use at admission who received five or more treatments were chosen to represent the high treatment category based on frequency results generated from TEDS data. Figure 1 shows the results of patient responses to number of prior treatments. The majority of patients were entering treatment for the first time. Frequency of prior treatments decreases until the 5 or more option where responses increase to 82,939, representing 16.35% percent of the AUD population. It should be noted that this frequency analysis was completed prior to removing missing data and therefore the sample size is larger than that for the subsequent analyses.

Table 1 shows how the alcohol population is distributed within variables of interest. Results suggest, for example, that those with high education vs a low education had a slight increase in the high treatment group. Similarly, individuals who had an increased distribution in the high treatment group include those who were unemployed, homeless, use daily, started using under 20 years of age, suffer from co-occurring mental and substance use disorders, were between the ages of 30 and 64 at the time of admission, were male, never married or separated/divorced/widowed, and were of American Indian or White race category. It should be noted that all results were statistically significant.

Odds ratio results (displayed in Table 2) produced from multivariate logistic regression show being homeless or in a dependent living arrangement had a significant effect on increased treatment attempts as compared to those who live independently. This is also true for those who drink alcohol daily as opposed to not daily. When adjusted with other factors, the high education group seems to be more vulnerable to high treatment compared to the

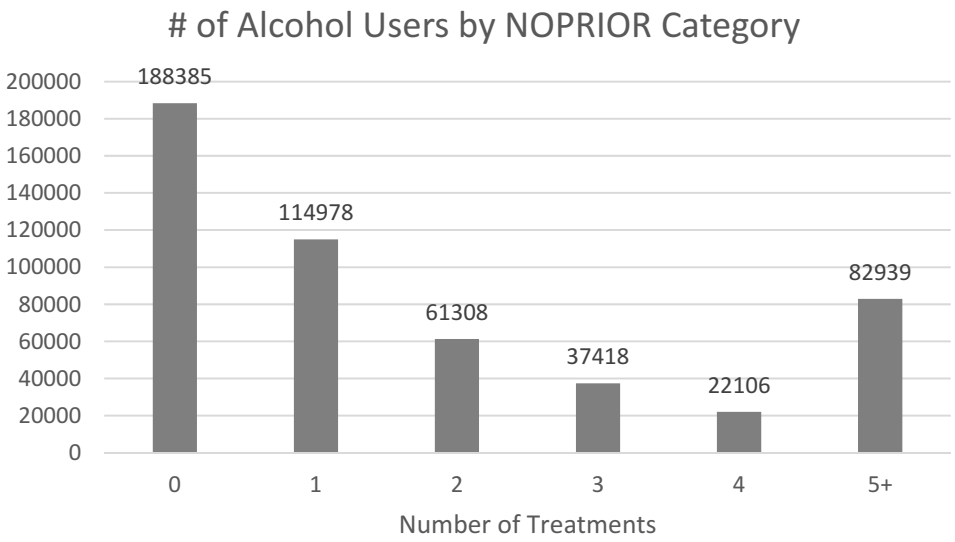

Figure 1. Frequency of the alcohol population and number of prior treatments.

low education group. This result differs from univariate analysis where we saw only a slight difference between low and high education. Individuals between 50 and 64 years have a higher risk of being in the high treatment group, while, adjusted with other factors, those 30–49 years show a similar risk to those 65+ years of being in high treatment group. The lowest risk was shown among ages 12 and 29 years.

Odds ratio results were also used to create high-risk and low-risk groups, described below:

- High Risk: High education, not employed, homeless/dependent living arrangement, use daily, started using at age 20 and under, co-occurring mental and substance use disorders, age 50–64 years at admission, male, never married, American Indian race category.
- Low Risk: Low education, employed, independent living arrangement, does not use daily, started using over age 20, no co-occurring mental and substance use disorders, age 12–29 years at admission, female, married, Black or African American.

Patients who meet all high-risk categories have an overall probability of 66.3% of being in the high treatment group. Patients who meet all low-risk categories have an overall probability of 0.6% of being in the high treatment group.

It was also observed that number of prior treatments did not have a significant effect on number of days waiting for treatment (Figure 2). Ordinal logistic regression yielded a *p*-value of 0.1719.

Discussion

The literature indicates that chronic relapse and low completion rates are highly characteristic of alcohol use disorder (AUD), though gaps exist in understanding the reasons for such high recidivism (Patterson Silver Wolf et al., 2019; Witkiewitz & Marlatt, 2007). Our study

Table 1. Distribution (%) of the alcohol population into high and low treatment groups.

Variable	High treatment	Low treatment	P-Value
	N (%)	N (%)	
Education			
Low	24,874 (68.37)	118,805 (69.05)	0.0101
High	11,510 (31.63)	53,246 (30.95)	
Employment			
Employed	5,950 (16.35)	63,597 (36.96)	<.0001
Not employed	30,434 (83.65)	108,454 (63.04)	
Living arrangement			
Homeless/dependent	17,758 (48.81)	49,658 (28.86)	<.0001
Independent	18,626 (51.19)	122,393 (71.14)	
Frequency of use			
Daily	20,726 (56.96)	62,952 (36.59)	<.0001
Not daily	15,658 (43.04)	109,099 (63.41)	
First use age			
≤ 20 years	33,537 (92.18)	149,792 (87.06)	<.0001
Over 20 years	2,847 (7.82)	22,259 (12.94)	
Co-occurring mental and substance use disorders			
No	16,911 (46.48)	96,873 (56.30)	<.0001
Yes	19,473 (53.52)	75,178 (43.70)	
Age at admission			
12–29 years	3,632 (9.98)	42,462 (24.68)	<.0001
30–49 years	18,338 (50.40)	85,840 (49.89)	
50–64 years	13,759 (37.82)	40,631 (23.62)	
65+ years	655 (1.80)	3,118 (1.81)	
Gender			
Female	8,790 (24.16)	51,964 (30.20)	<.0001
Male	27,594 (75.84)	120,087 (69.80)	
Marital status			
Married	3,197 (8.79)	27,714 (16.11)	<.0001
Never married	21,196 (58.25)	98,940 (57.50)	
Separated/divorced/widowed	11,991 (32.96)	45,397 (26.39)	
Race			
American Indian	2,439 (6.70)	6,871 (3.99)	<.0001
White	26,390 (72.53)	120,599 (70.09)	
Black or African American	4,535 (12.47)	29,307 (17.03)	
Other	3,020 (8.30)	15,274 (8.89)	

Note. N = 208,435 (High Treatment = 36,384 and Low Treatment = 172,051).

Table 2. Odds ratio results displaying effect of alcohol population on the high treatment group.

Effect	Point estimate	95% Wald Confidence Limits	
Education: high vs low	1.161	1.131	1.192
Employment: employed vs. not employed	0.510	0.494	0.527
Living arrangement: homeless/dependent vs independent	1.749	1.705	1.793
Frequency of use: daily vs not daily	1.770	1.727	1.813
First use age: ≤ 20 years vs over 20 years	1.628	1.561	1.699
Co-occurring mental and substance use disorders: no vs yes	0.772	0.753	0.791
Age at admission: 12–29 years vs 65+ years	0.401	0.365	0.442
Age at admission: 30–49 years vs 65+ years	0.970	0.887	1.061
Age at admission: 50–64 years vs 65+ years	1.427	1.305	1.561
Gender: female vs male	0.776	0.755	0.798
Marital Status: married vs separated/divorced/widowed	0.628	0.601	0.656
Marital Status: never married vs separated/divorced/widowed	1.169	1.136	1.202
Race: American Indian vs White	1.556	1.478	1.638
Race: Black or African American vs White	0.571	0.551	0.592
Race: Other vs White	0.769	0.736	0.803

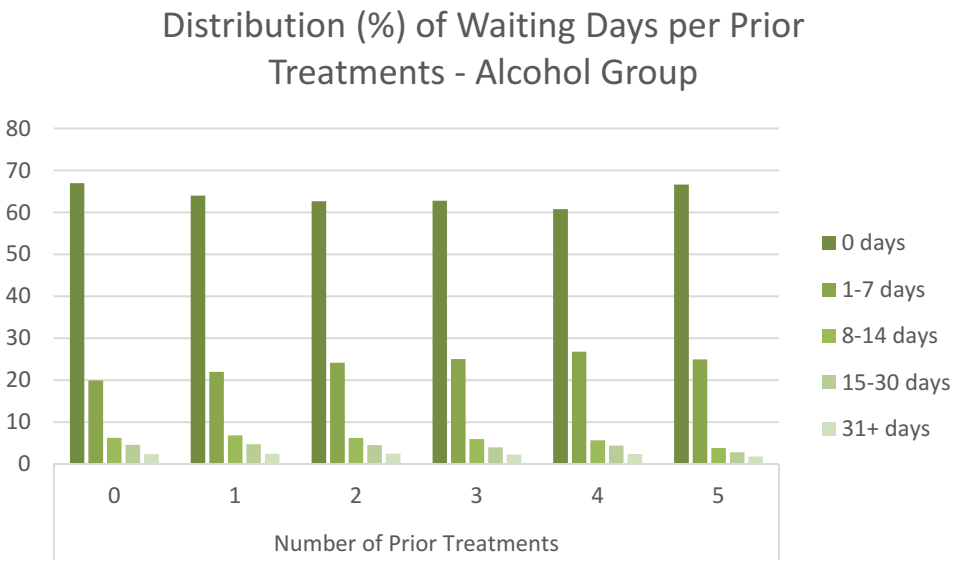

Figure 2. Distribution of number days waiting into number of prior treatment groups.

shows that general demographic information at patients' admission may have some prognostic capacity for treatment of alcohol use disorder (AUD), and thus it can be used to identify population groups where conventional strategies for addiction treatment may be insufficient. The analysis described above has shown significant relationships between patient characteristics and alcohol treatment resistance. Odds ratio results suggest that if a patient is homeless or in a dependent living arrangement, they are almost twice as likely as someone who lives independently to be resistant to treatment-as-usual. Similarly, a patient who drinks alcohol on a daily basis as opposed to not daily is also almost twice as likely to resist treatment. In addition, it was observed that individuals between 50 and 64 years have a higher risk of being in the treatment resistant group as well as those in the American Indian population. The chance a patient who meets all high-risk categories will end up resisting treatment is over 60%. Patients who meet all low-risk categories are unlikely to be resistant to usual treatment. Treatment must target the particular demographic and psychosocial factors of the individual; discounting such characteristics can obstruct treatment effectiveness (Benyamin et al., 2008; Dean et al., 2006; Dematteis et al., 2017; McLellan et al., 1993). Consequently, the results of this study highlight particular characteristics that may put a patient at increased risk of failing treatment and, in turn, indicate the need for approaches beyond treatment-as-usual. Interventions that address modifiable characteristics may help reduce the risk of treatment resistant AUD.

For America's substance use disorder (SUD) treatment and research industries to adapt to treatment resistance, as proposed here, it will likely require a major belief alteration that can be furthered by continued research and evidence-based literature. Presently in our national treatment services infrastructure, as well as our scientific research systems, whenever the term resistance is proposed, it is based on the patient's beliefs, attitudes and behaviors that are resisting treatment (Bien, Miller, & Tonigan, 1993; DiClemente, Bellino, & Neavins, 1999; Miller & Rollnick, 1991; Zweben & Zuckoff, 2002). Rather than

understanding resistance as the "disease" being resistant to the treatment as it is understood when treating a virus or infection, throughout the SUD industry, we target the "choices" of the patient.

It would be medical negligence if the attending physician blamed the patient for their infection not responding to antibiotic treatment (Pandit & Pandit, 2009). Further, that malpractice would continue and be made potentially worse and possibly more resistant, by offering the same recycled treatment that has proven to be inadequate (Patterson Silver Wolf & Gold, 2020). Treatment-as-usual services must disregard the accepted belief system that it takes several treatment attempts before patients fully recover (Kelly, Greene, Bergman, White, & Hoeppner, 2019; Mcquaid et al., 2017). This belief is especially troubling given that treatment yielding higher abstinence rates does not seem to be available to everyone at equal rates. For example, physicians suffering from SUDs are offered treatment that results in about an 80% total abstinent success rate 5 years post treatment (McLellan, Skipper, Campbell, & DuPont, 2008). Further, when physicians experience a relapse, the treatment plan is adjusted rather than recycling the physician back through the same treatment proven to be ineffective (DuPont, McLellan, Carr, Gendel, & Skipper, 2009).

Given the paucity of literature on treatment-resistant AUD, scientific research efforts should follow the path of those investigating treatment-resistant depression (Conway et al., 2017; Yoon, Ravindran, & Ravindran, 2018). Similar to treatment-resistant depression, biological research must establish the defining criteria for treatment-resistant alcohol use disorder (Conway et al., 2017, 2018). The primary research questions that must be answered are as follows: what causes resistance to AUD treatment and what current, proven treatments are best deployed to appropriately address this condition? Indeed, this study opens the doors to future clinical research that can identify said causes, appropriate treatments, and altogether suggest personalized interventions to effectively treat AUD.

Limitations

In addition to the valuable results and implications of this study, there are limitations, as well. Due to the cross-sectional nature of the data, the prognosis of the low treatment group in the long term is unknown. There is a chance that some low treatment cases may progress to the high treatment group. Moreover, it is possible that people that have moved through, for instance, four treatments, are en route to additional treatments, but are just earlier in the overall intervention trajectory for AUD. Still, the nature of this study makes it impossible to rigorously determine the likelihood of that. Additional qualitative research will be a beneficial way to develop a richer, detailed understanding of patients' backgrounds and identities that may be linked with receiving repeated AUD treatments.

Conclusion

The high and low-risk groups in the study draw attention to characteristics that clinicians must be attentive to when admitting new patients. When a patient fits, for instance, factors in the high-risk group, their likelihood for successfully completing typical treatment is slim. Consequently, assessing for these personal factors, up front, tells a clinician when a tailored treatment plan may be necessary to achieve more desirable outcomes. In other words, personalizing the intervention will curtail potential treatment failure. Additionally,

resources and future research can be channeled toward the populations most susceptible to recidivism. Both cross-sectional and longitudinal research will shed light on effective, tailored therapies for people at highest risk of cycling through treatment.

Alcohol use disorder treatment recycling cannot be reduced to being the responsibility of the individual, but rather, it suggests gaps and insufficiencies in treatment. In order to increase treatment uptake and achieve recovery for more patients, it is imperative to examine how treatments can be altered, shifted, and personalized. For patients returning again and again to treatment, the problem is not seeded in the patient, but the acts of providing the same intervention(s) that have proved repeatedly to be ineffective.

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