Emerging Research on Alcohol Use Disorders: Trends and Treatments

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Introduction

Alcohol-related problems remain among the most significant public health issues in the United States. Alcohol use is a leading cause of preventable death in the U.S. Each year more than 88,000 Americans die from chronic and acute alcohol-related causes, the most common chronic cause being alcoholic liver disease and the most common acute cause being motor vehicle crashes. For at least a decade, numbers and rates of deaths due to alcohol-induced causes have been on the rise. In 2017, approximately 14.5 million Americans had an alcohol use disorder (AUD), and more than 10% of American children lived with a parent with alcohol problems. In 2015, nearly one in five adults in the U.S., an estimated 53 million Americans, experienced at least one harm attributable to someone else’s drinking, with the risk of physical aggression due to someone else’s drinking being particularly elevated among heavy drinking women. Altogether, alcohol misuse is estimated to cost the U.S. about $249 billion per year.

Given the tremendous financial and personal costs of alcohol-related problems, researchers have continued to investigate ways to address alcohol use disorders and their treatment. This research brief gives an overview of alcohol use-disorder-related research that has taken place over the last year (2018-2019). To prepare the brief, the top general medical and alcohol-related journals were searched for articles published since January 2018 that were directly relevant to the treatment of AUD. A content analysis allowed the articles to be grouped according to major themes, which are identified below along with summaries of recently published research.

Key Findings

- Alcohol use disorders have been linked to abnormal GABA signaling in the central amygdala.
- The search is ongoing for medications to treat AUD. Meanwhile, expanding use of existing medications could improve outcomes.
- Mindfulness-based interventions have gained additional research support.
- Technologies are being developed and adapted to enhance existing interventions.
- Recovery supports provide important benefits, especially to homeless persons with AUD.
- “Recovery” is not necessarily a linear process, and this term does not resonate with a notable subset of persons with alcohol problems.
State-of-the-Art of Medications to Treat AUD

In a review article published in *JAMA* in August 2018, Kranzler and Soyka⁹ reviewed the state-of-the-art in the pharmacologic treatment of AUD, including medications approved by the US Food and Drug Administration (FDA) for AUD treatment and those used off label. Currently, four medications are FDA-approved for AUD treatment: acamprosate (Campral), disulfiram (Antabuse), oral naltrexone (Revia), and long-acting injectable naltrexone (Vivitrol). Acamprosate is believed to improve alcohol-related outcomes through its modulation of glutamatergic neurotransmission.⁹ However, the pharmacodynamics of acamprosate are complex, and it is believed also to act as a positive allosteric modulator of GABA-A receptors.¹⁰ Disulfiram is known to work by inhibiting an enzyme that neutralizes a toxic byproduct of alcohol metabolism, called acetaldehyde. When taking disulfiram, drinking alcohol causes a buildup of acetaldehyde that results in nausea, flushing, vomiting, sweating, hypotension, and palpitations. Naltrexone is understood to reduce the rewarding effects of alcohol modulated by interactions between the opioid and dopamine systems in the brain. While the general consensus is that none of these medications represents a so-called silver bullet for AUD, they all have the potential to improve the likelihood of recovery and remain underutilized.⁹,¹¹

In addition to the four medications approved by the FDA specifically for AUD treatment, Kranzler and Soyka⁹ noted three FDA-approved medications are used off label for AUD: baclofen, topiramate, and gabapentin.⁹ Baclofen is a GABA-B receptor agonist approved to reduce spasticity associated with neurologic disorders. On the basis of evidence showing improvement in abstinence-related outcomes, baclofen has been given a temporary recommendation in France for treating AUD. A recent study indicated that baclofen treatment was more likely to be effective in patients with high levels of baseline drinking¹² and a recent review supported the safety and efficacy of baclofen with liver cirrhosis.¹³ Topiramate acts as a positive allostatic modulator of GABA-A receptors.¹⁴ A recent review found that topiramate reduced harmful drinking patterns in AUD and raised the possibility that patients likely to respond to topiramate could be identified through genetic testing, an approach called “precision medicine.”¹⁴ However, a recent review of the pharmacogenetics of AUD treatments concluded that a precision medicine approach is not yet ready for widespread clinical implementation with respect to AUD.¹⁵ Gabapentin is chemically similar to GABA but does not affect GABA receptors.¹⁶ Some evidence suggests that gabapentin is associated with higher abstinence and lower binge drinking rates compared to placebo.¹⁷ However, gabapentin has some abuse lability.⁹ Beyond these FDA-approved medications, Kranzler and Soyka⁹ noted that a promising non-FDA-approved drug, nalmeffene, an opioid-receptor antagonist and partial agonist, has been approved in the European Union to reduce alcohol consumption in patients with alcohol dependence.

A review of pharmacotherapy for AUD by Ray et al.¹¹ additionally reported beneficial findings for varenicline, a nicotinic acetylcholine receptor partial agonist, which is FDA-approved to treat nicotine dependence. The investigators noted that varenicline is well tolerated.
and has been found to reduce weekly percent heavy drinking days, drinks per day, drinks per drinking day, and alcohol craving, particularly in smokers. They published a figure that illustrates the strength of the evidence for various pharmacological treatments by stage of AUD.

**Treatment guidelines** addressing the four FDA-approved drugs as well as topiramate and gabapentin for the treatment of AUD have been published by both the Department of Veterans Affairs/Department of Defense in 2015 and the American Psychiatric Association (APA) in 2018. In particular, APA recommends that naltrexone or acamprosate be offered to patients with moderate to severe AUD who have a goal of reducing alcohol consumption or achieving abstinence and prefer pharmacotherapy or have not responded to nonpharmacological treatments alone; disulfiram be offered to patients with moderate to severe AUD who have a goal of achieving abstinence, prefer disulfiram or are intolerant to or have not responded to naltrexone and acamprosate, and are capable of understanding the risks of alcohol consumption while taking disulfiram; and topiramate or gabapentin be offered to patients with moderate to severe AUD who have a goal of reducing alcohol consumption or achieving abstinence, prefer topiramate or gabapentin or are intolerant to or have not responded to naltrexone and acamprosate.

A systematic review and meta-analysis conducted by Palpacuer et al. examined pharmacologically controlled drinking in the treatment of AUD using naltrexone, acamprosate, baclofen, topiramate, and nalmefene. The primary outcome was total alcohol consumption; secondary outcomes included other measures of alcohol consumption and health. Similar trends were observed for primary and secondary outcomes. While nalmefene, baclofen, and topiramate were superior to placebo, naltrexone or acamprosate showed no efficacy. Notably, no treatment was judged to have high-grade evidence for pharmacologically controlled drinking in AUD.

**Studies of Candidate Medications**

A landmark study published in *Science* in June 2018 by Augier at al. presented evidence that impaired GABA clearance within the amygdala contributes to alcohol addiction. Seeking to validate their findings in rodents and translate the findings to humans, the investigators conducted RNA sequencing of postmortem tissue samples from deceased persons with and without alcohol dependence. They found that, compared to controls, patients with confirmed alcohol dependence showed down-regulation of the GABA transporter, GAT-3, in the central amygdala but not in other brain regions. These findings suggest that alcohol addiction is associated with neuroadaptations affecting GABA signaling in the amygdala and that preexisting differences in GABAergic gene expression in the amygdala may influence susceptibility to developing alcohol addiction. These findings may also help to illustrate how medications that modulate GABA transmission (e.g., acamprosate, baclofen, topiramate) exert their observed effects in AUD treatment.

Noting the promise of GABAergic agents in the treatment of AUD and concerns about the safety profile of existing medications (particularly baclofen), Maccioni and Colombo reviewed the findings from preclinical studies of positive allosteric modulators (PAMs) of the GABA-B receptor, which have a more favorable toxicological profile. Their findings indicated that all GABA-B PAMs tested to date have been reported to reduce, or even suppress, excessive alcohol drinking, and relapse- and binge-like drinking, among other alcohol-related outcomes in rodents, which showed a lack of tolerance to these effects. The authors noted that at least two GABA-B PAMs are entering the initial phases of clinical testing, which will begin to demonstrate whether the promising findings in rodents translate to humans with AUD.

Research is ongoing regarding potential mechanisms beyond the GABA system. Prazosin is an α-1 adrenoceptor antagonist that reduces brain α-1 adrenoceptor–mediated signaling. It is FDA-approved to treat hypertension but is also used to treat sleep disturbance in post-traumatic stress disorder (PTSD). Because the noradrenergic system plays an important role in AUD, prazosin has garnered interest as a candidate AUD treatment medication. Two research groups published papers on prazosin for AUD in 2018. Wilcox et al. conducted a randomized controlled trial (RCT) in which 36 individuals with AUD were randomized to receive either prazosin or
placebo for 6 weeks. Compared with placebo, prazosin did not significantly affect alcohol use outcomes in the intent-to-treat sample, but the authors noted that poor adherence and tolerability may have contributed to null effects. However, prazosin was superior to placebo in individuals with high but not low diastolic blood pressure. Thus, while the findings did not support the clinical utility of prazosin for all persons with AUD, the investigators suggested it might have some efficacy in individuals who can tolerate it, and particularly those with high blood pressure. In another RCT, conducted in Seattle, Simpson et al.24 randomized 92 participants with AUD but not PTSD to receive either prazosin or placebo for 12 weeks. Compared to placebo, prazosin was associated with a greater decrease over time in rate of drinking and the probability of heavy drinking. However, those in the prazosin condition experienced more side effects and tended to be less likely to complete medication titration.

**Samidorphan** is an experimental drug that functions as a µ-opioid antagonist and has more favorable pharmacokinetics and pharmacodynamics compared to naltrexone.27 O'Malley et al.27 conducted a 12-week double-blind RCT of samidorphan in adults with AUD. There was no statistical difference between samidorphan and placebo in the primary outcome of percentage of subjects with no heavy drinking days during weeks 5 to 12. However, there were improvements observed in other alcohol-related outcomes, including risk levels of drinking, alcohol craving, and patient global assessment of response to therapy.

**Mecamylamine** is a nicotinic acetylcholine receptor antagonist that has been shown to reduce alcohol consumption in preclinical studies and to reduce the stimulant effects of alcohol and alcohol craving in humans.28 Petrakis et al.28 conducted an RCT in which 136 individuals with AUD were randomized to receive mecamylamine or placebo for 13 weeks and assessed at 3-months post-treatment. Mecamylamine showed no significant effect on alcohol consumption; both groups comparably reduced their number of their heavy drinking days, drinking days, drinks per drinking day, and alcohol craving relative to their baseline severity.

**Citicoline** is a widely available over-the-counter supplement with few side effects that has shown some benefit in the treatment of cocaine use and cognitive disorders. It acts through cholinergic pathways and phospholipid metabolism and appears to affect dopamine systems in the brain.29,30 Brown et al.29 examined the effect of citicoline on alcohol-related outcomes in individuals with alcohol use disorder in a 12-week, randomized, double-blind, parallel-group, placebo-controlled, pilot study. Although citicoline was well tolerated, compared to placebo, it was not associated with a reduction in alcohol use.

In summary, the search continues for more effective and efficacious medications to treat AUD. While there have been tantalizing findings with respect to GABA-ergic medications, other types of medications continue to hold promise in the treatment of AUD.

**State-of-the-Art Psychosocial Treatments for AUD**

Ray et al.11 reviewed the evidence for psychosocial treatments for AUD, noting that treatments vary in the degree to which they have received empirical support. In their review, published online in October 2018, they found the strongest evidence for **cognitive-behavioral therapy (CBT)** for moderate to severe AUD. **Motivational interviewing and motivational enhancement therapy**
were also well supported for less-than-severe AUD. **Contingency management, community reinforcement, and twelve step facilitation** were also judged to have good evidence for moderate to severe AUD. **Brief interventions** were considered to be well supported for non-dependent AUD. At the time of publication, the evidence for mindfulness-based therapy, behavioral couples therapy and cue exposure therapy was judged to be less strong.

Chisholm et al.31 remarked that evidence on the comparative cost-effectiveness of alcohol control strategies—including both psychosocial interventions and structural interventions, such as policy-making—is highly important to public policy and resource allocation. Thus, more than a decade after an initial global analysis, the researchers re-examined the comparative cost-effectiveness of a range of alcohol control strategies using global evidence on alcohol use exposures and risk relations and on intervention costs and impacts with a new modeling tool, called OneHealth. They estimated population-level effects of interventions to reduce the harmful use of alcohol, including not only brief psychosocial interventions, but also excise taxes and the enactment and enforcement of restrictions and laws related to alcohol marketing, alcohol availability, and drunk-driving. Costs were estimated for 16 countries in international dollars (I$) for the year 2010 and effects were expressed in healthy life years gained. Results indicated that brief psychosocial treatments had favorable ratios of costs to effects (<I$150 and <I$1,500 in low- and high-income settings, respectively). With regard to policymaking, increasing excise taxes had a highly favorable ratio of costs to effects (<I$100 per healthy life year gained in both low- and high-income settings). Availability and marketing restrictions were also deemed highly cost effective (<I$100 in low-income settings and <I$500 in high-income settings). Enforcement of drunk-driving laws and blood alcohol concentration limits via sobriety checkpoints had cost-effectiveness ratios in the range of $1,500-3,000. The researchers concluded that pricing policies and restrictions to alcohol availability and marketing continue to represent a highly cost-effective use of resources.

Also highly relevant to policymaking, Boit et al.32 examined whether there was a significant difference between those who received **voluntary versus involuntary AUD treatment** in regard to length of sobriety. Using a quasi-experimental design, the researchers compared veterans with AUD who were admitted to residential treatment under recommendation by court order (n = 60) to veterans with AUD who were admitted to residential treatment without recommendation of court order (n = 60), matched by age, gender, and ethnicity. Characteristics of the residential treatment were not described. Findings revealed no significant differences between groups. The average number of days of sobriety post-treatment were 100 in the voluntary group and 117 in the involuntary group. The researchers concluded that whether a person is admitted to a residential program for AUD on a voluntary basis versus strong recommendation of the court may have less of an impact on treatment results than the person's motivation or stage of change.

**Mindfulness-Based Interventions**

Byrne et al. conducted a systematic review of mindfulness-based therapies for AUDs in adults. They identified 11 studies where mindfulness was used for treating AUDs and 6 where Acceptance and Commitment Therapy in particular was used for AUDs, including RCTs, non-randomized controlled studies, and uncontrolled studies. They found some evidence that mindfulness-based therapies provide a viable alternative to existing treatments, but noted that few studies directly compared mindfulness-based therapies to first line treatments.

Meyer et al.33 reported findings from an uncontrolled pilot study of **Acceptance and Commitment Therapy (ACT)** for co-occurring AUD and PTSD in which 29 veterans completed at least 10/12 outpatient individual therapy sessions. At post-treatment and 3-month follow-up, ACT treatment was associated with improvements in symptoms of AUD, PTSD, and depression; functional impairment; and quality of life. Further improvements in total drinking, heavy drinking days, and functional disability were noted between post-treatment and follow-up. The researchers concluded that ACT is feasible and promising for promoting recovery in people with both AUD and PTSD.
Gryczynski et al.\textsuperscript{34} investigated the potential benefit of integrating \textit{transcendental meditation (TM)} into standard AUD treatment. Sixty adults with AUD who were inexperienced with meditation and newly admitted to inpatient treatment were recruited in sequential cohorts. The first 30 participants received treatment as usual (TAU) while the second 30 received TAU with additional training in TM. TAU consisted of about 3-4 weeks of residential treatment, including medically managed withdrawal, structured activities, and group and individual counseling for AUD and mental health using cognitive-behavioral and 12-step approaches. TM training was delivered in group and individual sessions, and participants were advised to practice TM twice per day for 20 minutes. Outcomes were examined 3-months post-discharge. Most participants in the TM condition demonstrated high adherence and reported that they were still meditating at the 3-month follow-up. Findings showed that TM training did not improve outcomes related to stress, craving, psychological distress, or alcohol consumption. Both cohorts improved significantly from baseline in similar ways. However, in the TM cohort, better adherence to recommended TM practice was significantly correlated with better outcomes across a range of measures.

Zgierska et al.\textsuperscript{35} assessed the effects of \textit{mindfulness-based relapse prevention (MBRP)} for alcohol dependence on drinking and related consequences in a RCT with 123 alcohol-dependent adults in early recovery. Participants were randomly assigned to receive 8 weeks of either usual care plus MBRP or usual-care-alone. Outcomes were assessed at baseline, 8 weeks and 26 weeks. Findings revealed that, as an adjunct to usual-care, MBRP did not improve outcomes, as both groups demonstrated comparable improvements. A recent paper by Greenfield et al.\textsuperscript{36} found that race and ethnicity moderate the effectiveness of mindfulness-based SUD treatment such that MBRP appears to be more effective than RP in preventing heavy drinking relapse among Whites while MBRP appears to more effective than RP in preventing drug use relapse among racial and ethnic minorities.

Noting cultural differences between the U.S. and Europe, Von Hammerstein et al.\textsuperscript{37} examined feasibility, acceptability, and preliminary efficacy of an 8-week MBRP intervention for AUD in an uncontrolled study in France. Fifty-two participants attended a baseline appointment, 35 were assessed at 3 months, and 38 were assessed at a 6 month follow-up. Results showed that most participants introduced mindfulness meditation into their daily lives and used mindfulness techniques in high-risk situations. Participants reported significant reductions in craving, days of alcohol use, depression and anxiety and increases in mindfulness and psychological flexibility at 6 months. The investigators concluded that MBRP is feasible, acceptable, and promising with French participants.

Naturally, mindfulness-based therapies were not the only psychosocial treatments examined in 2018-2019. A number of other studies looked to improve existing treatments or to expand their evidence base.

**Expanding the Evidence Base for Existing Psychosocial Treatments**

Murphy et al.\textsuperscript{38} conducted an RCT to examine the efficacy of a 4-session brief alcohol intervention in the context of community-based treatment for partner violence. Partner-violent men with hazardous or problem drinking (N=228) were recruited at three Intimate Partner Violence (IPV) treatment agencies and randomly assigned to receive either Motivational Enhancement Therapy or Alcohol Education before standard agency counseling services for IPV. After 4-sessions of MET, participants displayed greater acknowledgment of problems with alcohol compared to 4 sessions of AE participants. Both groups exhibited significant changes from baseline in days of alcohol abstinence, heavy drinking, illicit drug use, and IPV. The investigators concluded that although the results did not provide evidence of a unique benefit of MET in reducing alcohol use in partner violent men, continued use of brief alcohol interventions in community IPV services were warranted.

Noting that women with AUD have a distinct clinical and risk factor profile, Epstein et al.\textsuperscript{39} compared \textit{woman-specific individual versus group CBT} for AUD. Adult women with AUD (N=155) were randomly assigned to receive 12 sessions of an efficacious woman-specific individual treatment in the existing individual format or in a new group format. Groups consisted of 3-7 women. Outcomes were assessed at 3 months, 9 months, and 12
months. Both conditions exhibited comparable improvements in alcohol consumption that were maintained throughout the follow-up period. Comparable improvements were also observed in non-drinking outcomes. The investigators noted that such results are consistent with existing literature showing generally equivalent outcomes for group and individual therapies for AUD. Using the same dataset, Olmstead et al.\textsuperscript{40} sought to determine the relative cost-effectiveness of the group vs. individual format woman-specific CBT for AUD. Cost-related data, including indicators of service utilization, were collected prospectively during the trial. While cost-effectiveness depends on the value that providers place on an additional unit of effect (i.e., one fewer drinking day, one fewer day of heavy drinking), the investigators concluded that, compared to individual CBT, group CBT holds promise as a cost-effective approach for improving drinking outcomes of women with AUD in both the short run and the long run.

**Improving Upon Existing Psychosocial Treatments**

Koffarnus et al.\textsuperscript{41} noted that technological barriers to remote verification of alcohol abstinence and delivery of incentives have limited the dissemination of contingency management (CM). To evaluate feasibility of potential solutions to these barriers, the investigators conducted an RCT in which they employed a breathalyzer that allows remote, user-verified collection of a breath alcohol sample, text messaging, and reloadable debit cards for remote delivery of incentives in the context of CM treatment of AUD, seeking to create a version of CM that can be delivered with no in-person contact. Treatment-seeking participants with AUD ($n = 40$) were randomly assigned to either a contingent- or a non-contingent-reinforcement group ($n = 20$ each). The contingent group received nearly immediate monetary incentives each day they remotely provided negative breathalyzer samples. The non-contingent group received matched monetary incentives each day they successfully provided samples, regardless of alcohol content. The primary outcome was percent days abstinent as measured by the remote breathalyzer samples. Abstinence rates were significantly higher in the contingent group (85%) compared to the non-contingent group (38%). Participant ratings of acceptability were high, and breathalyzer collection adherence rates exceeded 95%. The investigators concluded that their results supported the efficacy, acceptability, and feasibility of remotely deliverable abstinence reinforcement in adults with AUD, which they believe has potential for broad dissemination, given low provider and participant burden.

Noting that results for cue-exposure therapy (CET) have been inconsistent, Ghita et al.\textsuperscript{42} reviewed the literature to consider whether virtual reality (VR) could enhance effectiveness of cue-exposure techniques, with particular attention to alcohol craving as it is highly relevant to CET. The investigators identified 13 studies on alcohol craving that implemented VR as an assessment or treatment tool. They found that studies that used an avatar to exert social pressure in healthy individuals showed greater craving was triggered by social pressure than by alcohol cues. On the other hand, regardless of social pressure, individuals with AUD experienced greater craving when exposed to alcohol-related virtual situations than when exposed to neutral situations. Despite finding no clinical trials on the efficacy of VR as a treatment tool, no studies of the generalization of craving responses in the real world, and no studies of the long-term effects of VR treatment, the investigators concluded that VR holds promise in eliciting and reducing alcohol craving.

Agyapong et al.\textsuperscript{43} evaluated the effectiveness of supportive text messaging to improve treatment outcomes for those with AUD. In a randomized, controlled design, 59 patients who had completed a residential AUD treatment program were randomly assigned to either usual aftercare or usual aftercare plus supportive text messages for three months following discharge. The primary outcome of cumulative abstinence duration was assessed at 3-months. Secondary outcomes included drinks per drinking day and latency (days) to first drink. Findings revealed small to moderate effects for cumulative abstinence duration and drinks per drinking day. A large though non-significant effect was found for days to first drink; latency in the experimental group was over twice that of the control group (60 vs. 26 days, respectively). The results suggested that text messaging is a promising addition to aftercare for patients discharged from residential AUD treatment.

Moody et al.\textsuperscript{44} examined a pilot treatment using implementation intentions assessed with remote
assessments and treatment prompts. The implementation intention intervention linked high-risk situations with alternative responses while the control intervention selected situations and responses but did not link them. Treatment-seeking adults with AUD (N=35) were quasi-randomly assigned to complete two-weeks of either active or control implementation intention interventions. Daily ecological momentary interventions of participant-tailored implementation intentions were delivered via text message. Alcohol consumption was assessed daily with self-reported ecological momentary assessments of drinks consumed the previous day and remotely-submitted breathalyzer samples to assess reliability of self-reports. Findings showed that, during the two-week intervention period, compared to the control condition, the active implementation intentions group reduced alcohol consumption on drinking days (80% of days). The active implementation intention intervention was associated with a 1.09 drink per day decrease in alcohol consumption on drinking days compared to a decrease of 0.29 drinks per day in the control condition. However, the between-group difference was not observed at one-month follow-up. The investigators concluded that remote assessment of implementation intentions could be combined with other treatments to help individuals to reduce alcohol consumption.

Deane et al. noted that following up with participants once they have left residential AUD treatment presents major logistical and financial challenges for organizations but is an important component of service provision and indicator of treatment quality. The investigators assessed the impact and effectiveness of an early follow-up contact (at 2 weeks post-discharge) and brief interview on subsequent 3-month follow-up success. Participants were 800 clients who had attended residential AUD treatment and/or other substance use disorder (SUD) treatment provided by The Salvation Army. Participants were randomly assigned to usual 3-month follow-up or early follow-up plus 3-month follow-up. Primary outcomes were the proportions of participants who were followed-up and successfully surveyed at 3 months. Findings showed significantly higher 3-month follow-up rates for those in the early contact group (55.6%) compared those in the usual contact group (46.1%); however, rates of successful survey completion did not differ between groups. The researchers concluded that the modest increase in follow-up rates may not fully justify the additional costs associated with early contact.

**SBIRT and Treatment in Primary Care**

Another major emphasis of research in 2018-2019 was the provision of AUD treatment in primary care, primarily brief interventions, with continuing investigation of the utility of screening, brief intervention, and referral to treatment (SBIRT).

Importantly, the U.S. Preventive Services Task Force (USPSTF) released an updated recommendation statement regarding screening and behavioral counseling interventions to reduce unhealthy alcohol use in adolescents and adults. In particular, the USPSTF recommends screening for unhealthy alcohol use in primary care settings in adults 18 years or older, including pregnant women, and providing persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce unhealthy alcohol use. The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening and brief behavioral counseling interventions for alcohol use in primary care settings in adolescents aged 12 to 17 years.

Beyer et al. conducted an updated Cochrane systematic review to assess the effectiveness of SBIRT to reduce hazardous or harmful alcohol consumption in general practice or emergency care settings. The authors searched multiple resources for RCTs of brief interventions to reduce hazardous or harmful alcohol consumption in people attending general practice, emergency care or other primary care settings for reasons other than alcohol treatment. Brief intervention was defined as a conversation comprising five or fewer sessions of brief advice or brief lifestyle counseling and a total duration of less than 60 min. The primary outcome was alcohol consumption in grams per week. Altogether, 69 studies were included, of which 42 were newly incorporated into the updated review. Results of the meta-analysis provided moderate-quality evidence that brief intervention reduced consumption compared to control after one year (mean difference -20 g/week).
Subgroup analysis showed a similar effect for men and women. The authors concluded that short, advice-based interventions may be as effective as extended, counseling-based interventions for patients with harmful alcohol use and reduce harmful and hazardous alcohol consumption in men and women.

Wamsley et al. reviewed current literature regarding SBIRT effectiveness, training, and implementation by physicians, nurses, psychologists, and social workers, noting that “professional ownership” of SBIRT skills remains open, and the optimal clinical flow for team-based SBIRT delivery has not been established. They pointed out that SBIRT can be a valuable approach to screening and treatment for SUDs when delivered by a range of healthcare professionals, as each profession perceives, experiences, learns, and delivers SBIRT differently, with varying strengths and weaknesses. They suggested that inter-professional models of SBIRT delivery that maximize the strengths of each profession could be developed to promote truly collaborative, team-based care and effectively transform SUD treatment across the healthcare system.

Bandara et al. examined the association between screening and brief intervention with receipt of treatment, i.e., SBIRT. The investigators used data from the National Survey on Drug Use and Health to identify adults reporting prior year symptoms of AUD and calculated survey-weight adjusted prevalence of prior year receipt of alcohol screening in an ambulatory care medical setting, alcohol-oriented brief intervention in a medical setting, and AUD treatment in any setting. Despite high use of ambulatory care (74.4%), prevalence of screening (52.5%), brief intervention (13.5%), and AUD treatment (6.8%) were low. Screening and intervention were associated with increased odds of AUD treatment in general, particularly treatment in medical and specialty behavioral health settings. Receipt of screening and intervention were low in adults with AUD but strongly associated with use of alcohol treatment in this group. The investigators concluded that their findings suggest missed opportunities to encourage a high-risk population to access treatment services. They suggested that future research should examine SBIRT prospectively to assess whether entry into treatment settings may be mediated by screening and intervention in ambulatory care settings or if brief intervention is occurring at the time of treatment.

Johnson et al. examined the effect of electronic brief intervention on the uptake of specialty treatment by hospital outpatients with likely AUD using a randomized controlled design. One hundred twenty-three outpatients at an Australian hospital screened positive for AUD with the AUDIT-C and were randomly assigned to receive either an electronic referral to specialty care alone or both an electronic brief intervention and referral to specialty care. Delivered via iPad without human interaction, the brief intervention took 5-10 minutes. It involved completing the full Alcohol Use Disorders Identification Test (AUDIT), the Leeds Dependence Questionnaire, and questions to enable estimation of their peak blood alcohol concentration and money spent on alcohol during recent drinking episodes. Personalized feedback was provided with relevant normative referents. Three additional pages provided information about alcohol, tips for reducing the risk of harm, and sources of support for drinking problems. Primary outcomes were the proportions of patients who accepted and attended a drug and alcohol outpatient clinic. Results revealed that uptake of specialty treatment was low regardless of whether they received the brief intervention; only ten patients (five per group) accepted an appointment, and only one patient (from the control condition) attended. The researchers concluded that a large randomized trial does not appear to be feasible.

Wallhed Finn et al. noted that treatment of AUD in primary care may be a way to broaden the base of treatment for alcohol dependence, reducing the current treatment gap. Thus, the investigators examined whether AUD treatment in primary care is as effective as AUD treatment in specialty settings. General practitioners at 12 primary care centers received 1-day manualized training in treatment for AUD. Using a randomized controlled design, 288 adults meeting criteria for alcohol dependence were assigned to treatment in either primary care or specialty setting. The primary outcome was change in weekly alcohol consumption at 6-months follow-up, as measured with the timeline follow back method. Secondary outcomes included heavy drinking days, severity of dependence, consequences of drinking, psychological health, quality of life, satisfaction with treatment and biomarkers. Findings showed that treatment in specialty settings was not generally superior to treatment in primary care. Sub-analysis suggested that specialty care was superior to primary care only for
patients with high severity of dependence. The investigators concluded that treatment for AUD in primary care is a promising approach for individuals with low to moderate dependence.

Nadkarni et al.\textsuperscript{56} conducted a study to examine the feasibility, acceptability and preliminary cost-effectiveness of a \textit{psychosocial treatment for AUD in men in a primary care setting}. Sixty-six men scoring > 19 on the Alcohol Use Disorders Identification Test were randomly assigned to either usual care or usual care plus a psychosocial intervention. Delivered by a lay counselor over four 30- to 45-minute weekly or biweekly sessions, the manualized intervention involved detailed assessment followed by personalized feedback, cognitive-behavioral skills-training, and relapse prevention. Outcomes included mean daily alcohol consumed, percentage of days abstinent (PDA) and percentage of days of heavy drinking (PDHD), measured at 3 and 12 months post-randomization. Findings revealed a significant effect on PDHD but not mean daily alcohol consumption or PDA, providing mixed support for the intervention.

\textbf{Recovery Supports}

Recovery supports emerged as another major theme in AUD treatment research in 2018-2019. Kelly et al.\textsuperscript{57} noted that the \textit{concept of recovery} has become an organizing paradigm in the addiction field globally, but little is known regarding the prevalence and correlates of adopting an identity of being “in recovery.” They identified individuals resolving a significant alcohol or other drug (AOD) problem (n=1,995) in a nationally representative cross-sectional survey (N=39,809). Participants were asked whether they currently or ever considered themselves to be in recovery. Those who indicated they were never in recovery were asked, “You indicated that you once had a problem with alcohol/drugs but you no longer do, and you have never considered yourself to be ‘in recovery.’ What is the main reason why you have never considered yourself to be ‘in recovery’?” Those who indicated they were no longer in recovery were asked, “You indicated that you once considered yourself to be in recovery but no longer do. Why is that?” Additional questions assessed substance use, mental health diagnoses, history of drug court involvement, use of recovery support services, and psychological well-being and functioning. The proportion of individuals currently identifying as being in recovery was 45.1%, never in recovery 39.5%, and no longer in recovery 15.4%. Predictors of identifying as being in recovery included formal treatment and mutual-help participation and history of being diagnosed with AOD or other psychiatric disorders. Reasons for no current or past recovery identity related to low AOD problem severity, viewing the problem as resolved, or having little difficulty of stopping. The authors concluded that, despite increasing use of the recovery label and concept, many resolving AOD problems do not identify as being “in recovery.” They suggested that AOD public health communication efforts may need to consider additional concepts and terminology beyond “recovery” in order to attract, engage, and accommodate a larger number of individuals with AOD-related problems.

Barnett et al.\textsuperscript{58} noted that \textit{addiction treatment providers’ views about the disease model of addiction} (DMA) in general and the brain disease model of addiction (BDMA) in particular are an understudied area. Thus, they systematically reviewed literature related to treatment providers' attitudes about the DMA/BDMA. Identifying 34 pertinent studies, the researchers found that treatment providers tended to support the disease concept and moral, free-will or social models simultaneously. Support for the DMA was positively associated with treatment providers' age, year of qualification, certification status, religious beliefs, being in recovery, and Alcoholics Anonymous attendance and negatively associated with education level. The researchers suggested that treatment providers may endorse disease and other models while strategically deploying the DMA for presumed therapeutic benefits and that future policy development may benefit from considering how treatment providers adopt disease concepts in practice.

To gain a better understanding of specific \textit{recovery support services in relation to homelessness} in the context of alcohol problems, Asana et al.\textsuperscript{59} analyzed 2-year prospective longitudinal data from 255 homeless individuals recruited from shelters and street locations. The investigators examined relationships between AUD, alcohol use, housing status, and service use over time using data collected in 3 annual assessments. Findings revealed that lifetime AUD was positively associated with substance and medical service use. In support of
Housing First policy, stable housing was negatively associated with psychiatric and substance service use. Alcohol problems did not hinder attainment of stable housing, and placement in housing did not necessarily increase risk for alcohol use. Obtaining housing may have ameliorative effects on mental health, diminishing perceived need for psychiatric services. The investigators noted that services may be more accessible during homelessness. Substance services provided a gateway to psychiatric services, which in turn provided a gateway to medical services.

Collins et al. reported findings from a RCT of harm-reduction treatment for alcohol (HaRT-A), conducted in Seattle. HaRT-A is a compassionate and pragmatic approach that aims to help people reduce alcohol-related harm and improve quality of life without requiring abstinence or even reduction in alcohol use. Persons with co-occurring homelessness and AUD (N=168) were recruited in community-based clinical and social services settings and randomly assigned to receive either HaRT-A or services-as-usual (SAU). HaRT-A components include collaborative tracking of participant-preferred alcohol-related metrics, elicitation of participants' own harm-reduction and/or quality of life goals as the primary treatment focus, and discussion of safer-drinking strategies. Outcomes were assessed at enrollment, weeks 1-3, month 1, and month 3. Outcome variables were chosen to assess the efficacy of HaRT-A with respect to alcohol harm reduction and improvement in quality of life. Findings revealed that HaRT-A increased confidence for engaging in alcohol harm reduction and improved alcohol outcomes (even on biological measures) but did not improve quality of life. The researchers concluded that HaRT-A has short-term efficacy for improving alcohol outcomes in people experiencing homelessness and AUD.

**Ongoing Findings from Project MATCH and Project COMBINE**

During 2018-2019, multiple studies were new findings emerged from Project MATCH (Matching Alcoholism Treatment to Client) and the Combined Pharmacotherapies and Behavioral Interventions (COMBINE) Study.

Maisto et al. sought to understand alcohol behavior change as a process over time by identifying patterns of relapse and remission after outpatient treatment and evaluating how these patterns predict longer-term clinical outcomes. They conducted latent profile analyses using data from the outpatient arm in Project MATCH. Relapse and remission episodes were defined by the number of consecutive 14-day periods that included any heavy drinking days and no heavy drinking days. The researchers identified 6 profiles: 1) "remission," 2) "transition to remission", 3) "few long transitions," 4) "many short transitions," 5) "transition to relapse," and 6) "relapse." Profile 1, the "remission" profile, had the best long-term outcomes. Long-term outcomes were not uniform in individuals with profiles 2 through 6, i.e., those with at least some heavy drinking (75% of the sample). Individuals who transitioned back to and sustained periods of remission (profiles 2-4) had better long-term outcomes than those who failed to transition out of relapse (profiles 5-6) following treatment. The researchers concluded that post-treatment change in alcohol use is a process in which individuals transition in and out of "relapse" and "remission" statuses in diverse ways, noting that any heavy drinking following treatment is not necessarily a sign of treatment failure. They asserted these findings point to the value of a more nuanced look at the process of AUD change by considering whether individuals are able to transition to and sustain periods of remission.

In related work, Witkiewitz et al. examined low risk drinking outcomes during treatment and outcomes 3 years after treatment using data from the outpatient arm in Project MATCH (n = 877). Drinking outcomes were defined by repeated measures latent class analysis of weekly abstinence, low risk drinking days (<4/5 drinks for women/men), and heavy drinking days (4/5 drinks for women/men) during 12 weeks of treatment. Mixture modeling was used to examine the association between drinking classes and outcomes, including psychosocial functioning, alcohol use, and alcohol-related consequences. The researchers identified 7 classes based on drinking during treatment: persistent heavy drinking, abstinence to heavy drinking, abstinence and heavy drinking, heavy drinking to mostly abstinent, low risk and heavy drinking, abstinence and low risk drinking, and abstinence. As compared with heavier drinkers, individuals who achieved mostly abstinence or low risk drinking, even with some heavy drinking episodes during treatment, had significant improvements in alcohol use, alcohol-related consequences, and psychosocial functioning 3 years after treatment. Those who were mostly abstinent
or engaged in low risk drinking during treatment did not differ on any outcomes at 3 years after treatment. The researchers concluded that **low risk drinking is achievable for some individuals** during treatment and that improvement in functioning among low risk drinkers can be observed at 3 years after treatment.

Using data from the COMBINE Study, Subbaraman et al.\(^6\) examined the relationship between the frequency of cannabis use during AUD treatment and post-treatment alcohol-related consequences. Longitudinal drinking data were compared between 206 cannabis users and 999 cannabis abstainers during COMBINE treatment. Outcomes were alcohol-related problems at the end of treatment and one-year post-treatment as measured by the Drinker Inventory Consequences. Results indicated that, compared to cannabis abstinence, the most frequent level of use during treatment (using cannabis 12x/month or more) was related to 1.44 times as many physical consequences one-year post-treatment. However, cannabis use was not related to physical consequences immediately after treatment, or to intrapersonal, interpersonal, social responsibility or impulse control problems at either post-treatment time point. The investigators concluded that **individuals in treatment for AUD who also use cannabis might benefit from reducing or stopping cannabis use** to avoid alcohol-related physical problems.

**Conclusions**

In summary, alcohol treatment-related research covered a wide range of themes in 2018-2019. While there were no major breakthroughs in medication-assisted treatment for AUD, some tantalizing findings increase hope that more effective treatment medications are on the horizon. At the same time, the evidence base for psychosocial treatments was expanded, including new evidence for cost effectiveness and promising treatment enhancements using technology-based approaches. As AUD treatment increasingly moves into primary care settings, research has been ongoing as to the indications for and effectiveness of SBIRT. Conducting brief interventions in primary care appears to be feasible and beneficial, though not wildly successful. Research underscored the importance of recovery supports, particularly among homeless persons with AUD and pointed to alternative conceptualizations of treatment success.

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