Take Care of Me: Findings from a Randomized Controlled Trial Testing a Novel Online

Integrated Intervention for Young Adults with Alcohol Misuse-Emotion Comorbidities

by

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Abstract

It is currently estimated that nearly 40% of young adults who struggle with alcohol misuse also experience emotional difficulties, such as depression or anxiety. Despite calls for integrated treatment, there is a paucity of accessible interventions for this population. As such, the primary aim of this dissertation was to develop a novel, online, integrated treatment for young adults struggling with comorbid alcohol misuse and emotional problems. Study 1 ($N =$ 222) was a two-arm RCT examining the efficacy of *Take Care of Me*, an 8-week, minimally guided program using principles of cognitive behaviour therapy and motivational interviewing. Participants were randomized to either the integrated treatment or a psychoeducational control condition. Assessment data was collected at baseline, at the end of treatment (8 weeks), and at follow-up (24 weeks). Results supported larger reductions in depression, hazardous drinking, as well as increases in psychological quality of life and confidence in the treatment group relative to the control group at the end of treatment. Effects on hazardous drinking and psychological quality of life were maintained at follow-up. However, effects were not observed for the primary outcome, total weekly alcohol use. Therefore, the goal of Study 2 was to explore heterogeneity in treatment outcomes based on pre-treatment factors. First, latent-class analyses were used to identify subgroups within the sample based on pre-treatment factors that have been shown to be relevant for substance use treatment, namely background factors (i.e., gender, previous mental health diagnosis and treatment, family history of alcohol use), symptom severity (i.e., depression, anxiety, alcohol-related problems, cannabis use), executive function, and motivation. Results revealed evidence for three distinct classes: a low severity group ($n =$ 123), a moderate severity group ($n =$ 57), who were highly likely to endorse a previous mental health diagnosis and treatment and higher symptom severity than the low group, and a high severity group ($n =$ 42), who endorsed a family history of alcoholism, the highest baseline symptom severity, and the lowest executive functioning skills. Furthermore, individuals showed differential responses to the treatment based on their class membership. Results of moderated regression analyses revealed that high severity individuals in the treatment condition had higher levels of alcohol consumption and hazardous drinking, and lower quality of life at follow-up relative to the low severity group. Moderate severity individuals in the treatment condition had lower levels of alcohol consumption at follow-up and lower hazardous drinking at the end of treatment relative to the low severity group. Overall, this dissertation provided auspicious initial evidence for the *Take Care of Me*

program, as well as provided insight into key pre-treatment factors (e.g., symptom severity, cognitive capacity) that may improve treatment outcomes for future iterations of the intervention.

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CONTRIBUTIONS OF AUTHORS

Study 1

      In collaboration with my supervisor Dr. Matthew Keough, I designed the research question, obtained ethics approval from the University of Manitoba, translated, adapted, and created the treatment content, recruited participants, conducted data cleaning and statistical analyses, and wrote and submitted the manuscript for publication. I secured funding from the Canadian Institutes of Health Research and Dr. Keough independently secured funding from Research Manitoba. Co-authors Ms. Rapinda and Drs. Schaub, Wenger, Baumgartner, Johnson, O'Connor, Vincent, Blankers, Ebert, Hadjistavropoulos, Mackenzie, Wardell, Augsburger, Goldberg, and Keough provided extensive feedback on the manuscript, and contributed to study conceptualization. Drs. Schaub and Wenger contributed to the software of the program. The final manuscript represents a substantial combined effort from all authors.

Study 2

      In collaboration with my supervisor Dr. Matthew Keough, I designed the research question, obtained ethics approval from the University of Manitoba, translated, adapted, and created the treatment content, recruited participants, conducted data cleaning and statistical analyses, and wrote and submitted the manuscript for publication. I secured funding from the Canadian Institutes of Health Research and Dr. Keough independently secured funding from Research Manitoba. Co-authors Ms. Rapinda and Drs. Schaub, Wenger, Baumgartner, Johnson, Blankers, Ebert, Hadjistavropoulos, Mackenzie, Wardell, Edgerton, and Keough provided extensive feedback on the manuscript. The final manuscript represents a substantial combined effort from all authors.

TABLE OF CONTENTS

LIST OF FIGURES

CHAPTER 1
GENERAL INTRODUCTION

Scope

It is currently estimated that nearly 20% of Canadians over the age of 15 exceed Canada's Low-Risk Drinking Guidelines (Government of Canada, 2020), with the highest rates of risky use observed among individuals ages 18 to 24 (Canadian Centre on Substance Use and Addiction [CCSA], 2019). This peak in alcohol use is often considered normative at this developmental stage, and many age out of problematic use as they enter adulthood (Patrick et al., 2016). However, some young people do not mature out of risky drinking, putting them at the greatest risk of alcohol use disorders (AUD) relative to any other age group (Adlaf et al., 2005). This finding is particularly concerning given previous results of the Canadian Campus Wellbeing Survey revealed that 30-40% of young adults in Canada drink at harmful levels (Adlaf et al., 2005; Faulkner et al., 2019). Unfortunately, alcohol misuse rarely occurs in isolation from other mental health concerns. Indeed, current reports suggest that nearly half of individuals with AUDs also suffer from comorbid emotional problems (i.e., depression and anxiety; Boschloo et al., 2012; Lai et al., 2015), making them one of the most frequent comorbidities among all mental health concerns (Castillo-Carniglia et al., 2019; Conway et al., 2006).

The impact of comorbid alcohol use and emotional disorders is greater relative to just one disorder alone. In fact, the literature shows that having an alcohol-emotional disorder comorbidity often leads to disproportionate impairments in social, physical, and occupational functioning, as well as poorer overall well-being (Beidel et al., 2014; Grant et al., 2015). For example, these individuals often experience relationship problems, have difficulty maintaining employment, are overrepresented in the justice system, are at a greater risk of developing diseases associated with frequent alcohol consumption (e.g., liver disease, cancer), have elevated suicidality, and early death (Beidel et al., 2014; Government of Canada, 2015; Whiteford et al., 2013). Furthermore, relative to those with only a single problem, individuals who suffer from both disorders experience greater clinical severity of each disorder (Baker et al., 2007, Lai et al., 2015), higher rates of relapse, greater functional impairment, and have poorer responses to treatment (Baker et al., 2007; Lubman et al., 2007; Lai et al., 2015). In addition to individual challenges, the consequences of comorbid alcohol misuse and emotional problems often place a burden on the healthcare system due to complex treatment requirements, frequent use of

healthcare resources, compensation for disability, and involvement with the law (Whiteford et al., 2013; World Health Organization, 2014). The annual governmental cost of alcohol-related harm in Canada is estimated to exceed 14 billion dollars (CCSA, 2019), and individuals with co-occurring mental health issues report higher rates of service uptake relative to individuals with single disorders (Smetanin et al., 2011).

Multiple theories have been used to explain the alcohol misuse-emotional comorbidly. At present, literature supports the reciprocal associations model, where bi-directional associations exist between alcohol use and emotional problems (Stewart et al., 2016). This provides further context for why difficulties with alcohol use are highly prevalent among those with mood and/or anxiety disorders, and vice versa. Following from theory, it is important that mental health interventions consider both alcohol misuse and emotional challenges simultaneously given their complex interconnected nature. At present, research would suggest that integrated treatments are likely to yield the best outcomes (DeVido & Weiss, 2012; McKee, 2017; Mueser et al., 2003). Recently, promising research has emerged for the efficacy of integrated treatments for substance use and co-occurring disorders, such as mood and anxiety-related disorders (Morley et al., 2016; Riper et al., 2014), with evidence likewise mounting for the efficacy of said programs when offered in an online format (Deady et al., 2016; Schouten et al., 2021). At present, however, there is a lack of accessible, integrated treatments, designed specifically to address the unique and prevalent co-occurring mental health concerns experienced by young adults. It is important to understand the best way to intervene with problematic alcohol use while individuals are in a vulnerable and critical juncture with regard to mental health, where problems would either persist and worsen, or improve by the time they enter further into adulthood. For the purpose of the current dissertation, young adulthood will be conceptualized as synonymous with emerging adulthood (Arnett, 2000, 2005).

The overall goal of this dissertation was to develop and examine the efficacy of a novel, online, integrated treatment for comorbid alcohol misuse, depression, and anxiety. Integrated programs designed to address alcohol misuse and the full range of emotional problems that highly co-occur are limited, particularly for young adults. This is a problem, as young adults represent a vulnerable population in critical need of support due to high prevalence rates of mental health issues, and relatively low service utilization (Eisenberg & Chung, 2012; Werlen et al., 2020), putting them at risk for severe mental health disorders in the future Thus, the goal was

to address this gap in the treatment literature. As will be presented in this dissertation, the current studies provide evidence for an integrated, minimally guided, online intervention designed to target alcohol misuse, depression, and anxiety concurrently, as well as provides insight into factors that influenced treatment response among our sample.

Young Adulthood

Young adulthood, defined as "Emerging Adulthood" by Arnett (2000, 2005) is a unique developmental period used to describe the stage of life between childhood and adulthood. While this time is typically comprised of individuals between the ages of 18-25, it is often also defined by the *experiences* of individuals within this developmental stage. This period is often characterized by new and exciting opportunities, identity exploration, and increased independence. Despite potential positive opportunities in this stage of life (e.g., career exploration and development, new relationships, education), it is also a transitional time that can be difficult for some to navigate successfully (Matud et al., 2020). For example, it is during this time where individuals may be coping with several substantial life changes for the first time, such as moving away from their childhood home, gaining financial and personal independence, creating new social connections, and beginning post-secondary education or full-time employment (Wendlandt & Rochlen, 2008). For many, this vulnerable period often leads to high levels of stress, instability, feeling overwhelmed, and identity confusion. It is therefore not surprising that this stage of life is also associated with a greater prevalence and increase in mental health challenges relative to other age groups (Johnston et al., 2015). Indeed, epidemiological data have revealed that prevalence rates for mental health concerns are highest in this age group relative to any other group (e.g., adolescents, adults, older adults). In North America, more than 40% of young adults report serious mental health issues (Arnett et al., 2014; Carver et al., 2015; Gustavson et al., 2018; Kwan et al., 2013).

Among the mental health concerns reported during this developmental stage, prevalence rates are particularly high for substance misuse, mood disorders, and anxiety disorders (Arnett et al., 2014; Ibrahim et al., 2013). For example, from adolescence to young adulthood, rates of binge drinking increase from 10.7% to 41.9%, and rates of heavy alcohol use increase from 2.6% to 14.9% (Wood et al., 2017). Young adulthood is associated with the highest prevalence of AUDs and a greater severity of alcohol-related problems relative to any other age group (Johnston et al., 2007). Likewise, nearly 30% of young adults endorse clinically elevated levels

of depression and anxiety (Ibrahim et al., 2013; Schry & White, 2013). Overall, young adults experience the highest rates of comorbid alcohol misuse and emotional difficulties (i.e., mood and anxiety symptoms) relative to any other age group (Grothues et al., 2008).

Given the disproportionately high rates of alcohol misuse, depression, and anxiety observed during young adulthood, it is critical for researchers and practitioners to understand the optimal way to support individuals during this vulnerable stage of life. Intervention is particularly important to consider among young adults given that service utilization remains low among this population relative to other age groups despite the high need for it (Gustavson et al., 2018). Literature has revealed several barriers that impede treatment for this age group, including high cost, lack of accessible options, and attitudinal barriers such as stigma, desire for anonymity, and a preference for managing their difficulties independently (Elbert et al., 2019; Jung et al., 2017). Even though young adults are still early on in the risk-pathway, untreated mental health issues during this time increase one's risk of developing severe and persistent mental health issues later in adulthood (Carver et al., 2015; Lai et al., 2015), making effective and preventative interventions critical during this stage.

Theoretical Background

In order to make evidence-based decisions regarding treatment, it is critical for researchers to understand the relations between alcohol use and emotional challenges theoretically. Indeed, various theories have been developed to understand the relationship between alcohol use and co-occurring emotional difficulties. In the context of psychological research and practice, three main models have been explored in regard to the causal or temporal associations between alcohol and emotional disorders (i.e., depression and anxiety).

Vulnerability Model

Vulnerability models view emotional distress as a precursor to difficulties with alcohol use (Cappell & Greeley, 1987; Mushquash et al., 2013; Sher & Grekin, 2007). The self-medication hypothesis (Khantzian, 1997) posits that individuals use alcohol to numb depressive symptoms. Over time, however, individuals become more reliant on the self-medicating effects of alcohol, whereby alcohol becomes the main coping mechanism for depressed mood. While this self-medication often provides short-term benefits (i.e., numbing painful emotions, increasing mood), these individuals are exacerbating their problems in the long run by becoming reliant on alcohol. Mushquash and colleagues (2013) conducted a four-wave longitudinal study

over four consecutive weeks among a general sample of undergraduate women ($N = 200$). They used cross-lagged panel models to test bi-directional relationships between depressive symptoms and heavy drinking frequency across the four time points. Results revealed that depressive symptoms significantly predicted heavy drinking one week later, whereas paths from heavy drinking to depressive symptoms one week later were not significant within the same model (Mushquash et al., 2013). Overall, findings provided support for the vulnerability model, and authors postulated that the young adults in their sample may have increased their drinking due to elevated depressive symptoms. Relatedly, tension reduction theory states that individuals use alcohol to reduce anxiety (Hussong et al., 2011; Kalodner et al., 1989). This is supported by research that found generalized anxiety disorders and social anxiety disorders at baseline (i.e., high school) to predict AUDs 4 years later in young adulthood, but baseline AUDs did not predict anxiety disorders at follow-up (Smith & Book, 2010; Wolitzky-Taylor et al., 2012).

Overall, drinking to cope with negative affect, be it depression or anxiety, often leads to an increase in alcohol-related problems and maladaptive patterns of alcohol use in the future (e.g., increased quantity; Blevins et al., 2016; Cooper, 1994; Stewart et al., 2011). Research has demonstrated that it is common for young adults to drink to cope with depressive symptoms (Grant et al., 2009; Robinson et al., 2009), as well as with the challenges associated with this developmental period (Keough & O'Connor, 2016). In fact, coping motives for drinking are more common among young adults than any other reason for drinking (Grant et al., 2009), such as for social reasons, or to conform to the behaviour of others (Kuntsche et al., 2005), and many will regulate their emotions by using substances rather than engaging in more adaptive coping strategies (e.g., exercise, meditation; Chandley et al., 2014). Despite the empirical support for vulnerability models, emotional distress as a precursor to alcohol misuse continues to be debated in the literature (Anker & Kushner, 2019). For example, a recent systematic review of prospective longitudinal studies examined early life mental health (grouped into childhood, early adolescence, and adolescence) as a precursor to alcohol use in adulthood. Authors found that only 14% of the 49 eligible studies reported a positive association between internalizing symptoms (i.e., depression, anxiety-related disorders) and alcohol use behaviours, and over half reported no significant association (Ning et al., 2020).

Scar/Complication Model

In contrast to vulnerability models, the scar/complication model suggests that frequent or problematic alcohol use precedes difficulties with depression, whether short-term (i.e., complication) or permanent (i.e., scar; Schuckit, 2006; Stewart et al., 1999). This model posits that this occurs by causing changes to one's personality or behaviour that makes them more susceptible to emotional problems. For example, an individual who misuses alcohol may experience physical sensations that mimic symptoms of anxiety. The individual may eventually come to fear the symptoms, resulting in anxiety surrounding physical sensations more generally (Bartel et al., 2018). Heavy alcohol use may also result in feelings commonly associated with depression, such as low self-worth, hopelessness, or guilt due to the functional impairment or consequences of drinking (Davidson & Ritson, 1993; Ramsey et al., 2005). Relatedly, Ferugsson and colleagues (2009) examined the causal links between alcohol abuse or dependence (AAD) and major depression in a longitudinal cohort study of individuals at ages 18, 21, and 25. Using fixed-effect regressions and structural equation modelling, authors reported that AAD increased the risk of developing major depression over the time period studied (OR = 1.59, p = .02). Results of the reciprocal effects model revealed that the data best fit a model from AAD to increased depression, but the reverse effect from depression to AAD was not supported (Ferugsson et al, 2019).

Reciprocal Relations

Reciprocal relations theory suggests that the relationship between emotional problems (i.e., depression, anxiety) and alcohol misuse is bidirectional (Stewart et al., 2016). More specifically, a feedback loop exists between the two, whereby emotional disorders lead to risk for alcohol use while alcohol misuse simultaneously increases one's risk for depression or anxiety. Indeed, previous research has demonstrated reciprocal associations between alcohol use and emotions (i.e., depression, anxiety).

An early prospective study by Kushner and colleagues (1999) examined the relationship between anxiety disorders and AUD over a span of seven years. They found that those with an anxiety disorder diagnosis at years 1 or 4 had a 3.5 to 5 times higher likelihood of developing alcohol dependence at 7 years. Moreover, those with alcohol dependence at years 1 or 4 were 4 times more likely to develop an anxiety disorder at the 7-year assessment (Kushner et al., 1999). Bidirectional patterns between AUD and anxiety disorders were also found in follow-up path

models. An additional study examined the reciprocal relationship between depression and alcohol problems among a national sample of individuals from early adolescence to early adulthood across three waves (i.e., baseline, M_{age} = 15.66, 1-year, M_{age} = 16.22, and 6-years, M_{age} = 21.96; Marmorstein, 2009). Authors used multilevel modelling to examine the trajectories and relationships between depression and alcohol problems over time, including gender as a predictor. Results supported reciprocal relations between variables, whereby high initial levels of alcohol problems were associated with increased depression over time and vice versa, particularly among females. Furthermore, males with higher baseline depressive symptoms experienced faster growth in alcohol-related problems than their female or low initial depression counterparts. Colder and colleagues (2019) likewise found support for reciprocal relations using a subset of longitudinal data from a community sample of adolescents and young adults ages 17-20 (N = 387) who completed measures annually for nine years, with waves 7 through 9 utilized in the current study. Using latent curve modelling, authors tested reciprocal relations between emotional symptoms (i.e., depression, social anxiety), and substance use (i.e., alcohol, cannabis), and also included motives for drinking (i.e., coping, social/enhancement) within each model. In the depression-alcohol use model, authors reported reciprocal relationships between depressive symptoms and coping motives, whereby depression at wave 7 predicted alcohol coping motives at wave 8, which subsequently predicted depression at wave 9. This was the case at both the between- and within-individual level. Reciprocal relations were not statistically significant in the social anxiety-alcohol use model, as elevated social anxiety at wave 7 was associated with higher coping motives at wave 8, but this did not subsequently predict greater social anxiety at wave 9. Interestingly, alcohol quantity and problems did not predict depression or anxiety at any wave, nor vice versa. However, coping motivated drinking was associated with alcohol problems cross-sectionally. The recent study by Colder and colleagues (2019) suggests that this reciprocal process may be driven by coping motives among young adults who over time become increasingly reliant on the anxiolytic effects of alcohol. Support for reciprocal associations also has implications for evidence-based clinical practice (Stewart et al., 2016), as theory suggests that targeting both alcohol misuse and emotional difficulties concurrently is likely to yield the best outcomes given the effects each one has on the other. Furthermore, given the interconnectedness of alcohol use and emotional challenges, failing to concurrently address both in treatment increases the risk of relapse (CCSA, 2009).

Overall, existing research supports reciprocal associations between alcohol use and emotional symptoms, which likewise fits with the clinical experience of individuals struggling with comorbid alcohol misuse and emotional challenges (Marel et al., 2016). This evidence is not without limitations and would benefit from additional robust research designed to clarify and strengthen existing claims regarding the relationship between emotional symptomology and alcohol use. More specifically, in order to demonstrate evidence of reciprocal causation, tightly controlled experimental designs and longitudinal studies with multiple waves over time (i.e., early before problems begin into later adulthood) are needed. While additional evidence is warranted to establish temporal precedence among constructs, previous research supports bidirectional *associations* (Stewart et al., 2016), which has implications for practice.

Treatment Approaches

Given the importance of evidence-based practice, the reciprocal associations that exist between alcohol misuse and emotional difficulties from a theoretical standpoint support the use of integrated treatment in clinical practice. Existing treatments typically utilize parallel or sequential interventions. In sequential treatment, the disorder perceived as more severe is commonly treated first, which in many cases is alcohol use. In this case, co-occurring emotional symptoms are typically not addressed until the individual has achieved some level of abstinence from drinking. While sequential methods may, in fact, be more useful in severe situations (e.g., acute suicidality resulting from depression, medically dangerous levels of alcohol use), attaining abstinence may not be feasible for individuals with extremely low mood or anxiety (DeVido & Weiss, 2012). This may be especially true given that many are maintaining high levels of alcohol use as a coping mechanism for their emotional distress (Grant et al., 2009). In parallel or simultaneous treatment, alcohol use and emotional challenges are treated concurrently but in different settings or by separate professionals who have differing expertise in each area. While clients may benefit from receiving targeted treatment for each of their symptoms, they may also receive conflicting treatment recommendations from each source, and struggle to integrate the distinct treatment plans independently (DeVido & Weiss, 2012). For example, a family physician or psychiatrist may emphasize pharmacological treatment, whereas a mental health professional would emphasize behavioural recommendations (e.g., coping skills development to reduce drinking). Thus, in the parallel model, providers proceed with their treatment separately, as there is rarely any formal coordination of care (DeVido & Weiss, 2012).

While sequential and parallel methods are commonly used in clinical practice, they are limited approaches to treating comorbid addiction and emotional issues that lack a comprehensive treatment framework derived from theory. Neither parallel nor sequential methods of treatment take into consideration the interconnectedness of these highly comorbid disorders (Conway et al., 2006). In line with the reciprocal relations model, a person who suffers from depression would find it difficult to reduce drinking if their depressive symptoms (i.e., a common trigger for drinking) were not addressed in treatment. In turn, these depressive symptoms would likely worsen as a result of repeated unsuccessful attempts to control their drinking. In this case, it would be challenging for the individual to make progress for either area or in either treatment setting. Furthermore, communication between professionals is often limited in parallel methods, who may differ on their conceptualization, diagnostic considerations, and treatment recommendations for their client. As a result, the individual may receive conflicting recommendations from each professional, making it difficult to integrate this diverging information (DeVido & Weiss, 2012). This may be especially challenging given that many individuals struggling with alcohol misuse experience cognitive impairment (e.g., executive dysfunction; Mueser et al., 2003; Stacy & Wiers, 2010), making the integration of diverging information from different providers particularly difficult.

Integrated Treatment

Given the complex etiology of the co-occurring conditions and the support for reciprocal associations (Stewart et al., 2016), it is not surprising that solely treating alcohol misuse or an emotional difficulty (e.g., depression, anxiety) does not have a substantial effect on the other (Anker & Kushner, 2019). Theory would suggest that integrated psychological treatments are needed in order to yield the best outcomes. A recent report by the Canadian Psychological Association (CPA) released best practices for the treatment of individuals with substance use disorders and concurrent mental health issues (McKee, 2017). Perhaps not surprisingly, the use of integrated treatment for both substance use and mental health issues concurrently and systematically is considered best practice (McKee, 2017; Yule & Kelly, 2019). Furthermore, prominent institutions such as the Centre for Addiction and Mental Health (CAMH) and Substance Abuse and Mental Health Services Administration (SAMHSA) are beginning to follow suit with these recommendations. Most recently, the CPA highlighted the critical need for integrated care, noting that psychologists are particularly well-positioned to bridge the current

gaps in mental health care of comorbid conditions (Corace et al., 2021). In practice, integrated treatment can take on many forms. For example, some models target both alcohol misuse and emotional challenges simultaneously by the same professionals in the same setting or treatment program, with each problem given equal weight (Mueser et al., 2003). This could involve an individual seeking support from a mental health professional where strategies for both reducing alcohol-use and managing anxiety are discussed. Other models utilize coordinated or multidisciplinary care, whereby treatment teams consisting of various professionals (e.g., physicians, psychiatrists, psychologists, social workers) work together to provide a well-rounded approach to treatment under one comprehensive framework (SAMHSA, 2009). However, the integrated approach to treating concurrent alcohol misuse and emotional challenges remains relatively new, and additional research is needed regarding if, how, and why integrated approaches may be superior to traditional parallel or sequential models. Furthermore, the operational definition of integrated treatment within mental health settings is nuanced (e.g., primary care, residential, community), with various approaches to integrating care for comorbid alcohol misuse and emotional challenges. For the current research, integrated treatment involved targeting both alcohol misuse and emotional challenges (i.e., depression and anxiety), within the same online program.

Consistent with the limitations of both parallel and sequential approaches, studies have demonstrated that integrated treatments may be superior to parallel or sequential methods for substance use and concurrent disorders (Drake et al., 2008; Otasowie, 2021). In one study comparing the efficacy of parallel versus integrated treatment for individuals with severe substance use and mental health issues, authors found that individuals in the integrated treatment condition had a greater reduction in both hospitalization incidence, and total number of days in a psychiatric hospital relative to the parallel treatment condition who showed an increase in both (Mangrum et al., 2006). A recent study also demonstrated that integrated cognitive behavioural therapy (CBT) and motivational interviewing (MI) resulted in a greater increase in motivation for treatment during a 12-month trial among individuals with substance use disorder and depression and/or anxiety relative to a treatment-as-usual control group (Wüsthoff et al., 2014). Additional research has examined the efficacy of integrated treatments that include services from other disciplines (e.g., integrated pharmacological and psychological treatment), where strong evidence has demonstrated the superiority of integrated treatments versus focusing solely on one

disorder (Otasowie, 2021). For instance, Kelly and colleagues (2012) conducted a systematic review of the literature on the treatment of substance use and comorbid psychiatric disorders, and found that integrated treatment (i.e., psychotherapy, behavioural, and pharmacological) was more effective for dually diagnosed individuals than any treatment in isolation. Furthermore, Hobbs and colleagues (2011) conducted a meta-analysis examining the results of randomized controlled trials (RCTs) that augmented AUD treatment with either behavioural or pharmacological treatment for depression or anxiety. Results revealed that the addition of CBT had a significant effect on alcohol outcomes and both emotional symptoms (i.e., depression and anxiety; Cohen's $d = 0.66$), and this effect was larger than the pooled effect size of integrated medication treatment ($d = 0.24$). Overall, the authors concluded that researchers and clinicians can expect a moderate but significant benefit from augmenting the addition of depression and anxiety-based treatment to interventions for alcohol misuse. Despite being a relatively new area of study in the treatment of comorbid disorders, the currently available literature is promising. However, additional research is needed in order to optimize integrated care (e.g., content, modality, theoretical approach, length, setting, provider) for this population (Stewart et al., 2016).

Evidence for Integrated Treatment

The use of integrated treatment to target alcohol misuse and emotional symptoms simultaneous has gained momentum over the past decade (e.g., Deady et al., 2016; Riper et al., 2014). Two of the most cited frameworks used in integrated care for alcohol use and emotional comorbidities are CBT and MI. Within a CBT framework, individuals are encouraged to modify maladaptive behaviours and cognitions in order to manage and improve emotional symptoms (e.g., depression, anxiety) and undesirable behaviour (Hofmann et al., 2012). The goal of MI is to work collaboratively with the client to identify meaningful goals and increase motivation and reduce ambivalence for change (Miller & Rollinck, 2002, 2013). Integrating principles of CBT and MI is recommended for alcohol use-emotional comorbidities in order to help the individual clarify their goals and engage with treatment as well as work towards meaningful behaviour change (e.g., adaptive coping skills to replace drinking, emotion regulation, behavioural activation, balanced thinking, setting boundaries; Iarussi, 2019; Yule & Kelly, 2019).

Riper and colleagues (2014) conducted a meta-analysis of studies using a combination of in-person CBT and MI to treat both clinical and sub-clinical AUDs and major depression among

adults. Authors included both randomized and non-randomized controlled trials where combined CBT and MI was compared to treatment-as-usual (TAU), or to an alternative psychological treatment (e.g., pharmacological therapy, 12-step facilitation therapy). Overall, 12 studies (15 comparisons) met inclusion criteria ($N = 1721$), 9 of which were RCTs. Quality was assessed based on four validity indicators: adequate generation of participant assignment, blinding of the assignment to the different conditions, blinding of assessors, and handling of incomplete outcome data. Nine of the 12 studies were RCTs, 7 utilized independent parties to assign participants to conditions, 8 were blinded, and 8 utilized intention-to-treat analyses (ITT) to handle missing data. Six studies met all four quality criteria, and dropout rates ranged from 3-40%. Overall, they found small but significant effects for depression at the end of treatment ($g = 0.27$, 95% CI = 0.13–0.41) and at follow up between 6- and 12-months post treatment ($g = 0.26$, 95% CI = −0.01 to 0.54). They also observed small but significant effects on alcohol consumption at the end of treatment ($g = 0.17$, 95% CI = 0.07–0.28) and follow up between 6- and 12-months post-treatment ($g = 0.31$, 95% CI = 0.16–0.47), and this relationship was strengthened over time.

Gaps in Treatment Literature

While there are demonstrable benefits of targeting alcohol misuse and depression concurrently, there is a paucity of research examining the effects of integrated treatment for symptoms of anxiety as well. This is a shortcoming of current clinical research, as there are likely benefits to considering emotional disturbances more broadly in treatment. As previously discussed, depression and anxiety are highly comorbid, with current worldwide estimates suggesting that over half of individuals with 12-month major depression will also report a lifetime anxiety disorder (Kessler et al., 2015). This comorbidity is particularly prevalent among young adults, with this age group experiencing the highest levels of depression as well as anxiety relative to other age groups (Gustavson et al., 2018; Carver et al., 2015). Furthermore, much like the literature on the alcohol use-emotional comorbidity, it is often difficult to establish temporal precedence in the depression-anxiety relationships (Kessler et al., 2015). Targeting symptoms of both simultaneously alleviates the necessity to establish the symptoms driving the majority of impairment and stands to improve the overall well-being of the individual. Furthermore, CBT addresses symptoms of both anxiety and depression by focusing on transdiagnostic skills such as challenging thoughts and building adaptive coping. In the context of alcohol use, both depression

and anxiety play a large role in alcohol misuse comorbidities (SAMHSA, 2020; Stewart et al., 2016), providing further relevance for the inclusion of both emotional symptoms within integrated treatment. Researchers in the field have called on the importance of targeting anxiety-related disorders in integrated treatments for alcohol misuse (Stewart et al., 2016), and there is a notable gap in early interventions designed specifically for the vulnerable population of young adults who are struggling with all three challenges at concerning rates.

The Online Treatment Modality

It is perhaps not surprising that interventions delivered online (via computers, tablets, or smartphones) have become more prominent within addiction and mental spaces given the prevalence of technology in all aspects of everyday life (Cunningham et al., 2020; Deady et al., 2016; Etzelmueller et al., 2020; Garrido et al., 2019). This can take many forms in practice, including individual and group intervention with a mental health professional via videoconference (e.g., CBT, MI), text-based therapy (e.g., coaching, accountability), internet-based psychoeducational programs, completely self-guided treatment programs, or therapist-assisted programs (i.e., components of both automated and therapist-contact). What follows will include a general overview of the broader online intervention literature to date, followed by a specific focus on mainly self-guided and therapist-assisted interventions delivered online.

A growing body of literature has emerged demonstrating the efficacy of online self-help or minimal guidance programs for alcohol use (Hadjistavropoulos et al., 2020), and depression and anxiety (Christ et al., 2020; Garrido et al., 2019; Karyotaki et al., 2021) among young adults. However, online interventions integrating CBT and MI specifically for alcohol-misuse-emotional comorbidities remain relatively novel. Recently, Schouten and colleagues (2021) conducted a systematic review and meta-analysis of online interventions targeting comorbid alcohol use and depression. Only six studies met inclusion criteria, of which only two targeted young adults specifically. Four studies were completely self-guided, one included nine videoconference sessions with a therapist, and one was primarily self-guided with one videoconference session. Authors reported small but significant pooled effects sizes for short-term depression (i.e., 3 months; $g = 0.34$) and longer-term alcohol use (i.e., 6 months, $g = 0.14$; Schouten et al., 2021). Overall, the findings highlight a need for additional online interventions that include content for emotional distress defined more broadly (i.e., the inclusion of anxiety in addition to depression),

as well as a need to optimize early integrated care specifically for young adults with these comorbidities.

Efficacy of Online vs. Face-to-Face Treatment

As previously mentioned, online interventions can take many forms in practice, and thus in clinical research as well. Many meta-analyses comparing the efficacy of face-to-face (i.e., in-person) to online interventions have included multiple formats within a single study, rather than isolating a specific form of online intervention for comparison, such as videoconference with a therapist, or a completely automated program. This can make the direct comparison of face-to-face vs. specific forms of online intervention challenging. Despite the variability in format, previous research has demonstrated similar effect sizes between online therapist-assisted and face-to-face CBT for depression, anxiety, and alcohol use among adult populations (Andersson et al., 2019; Carlbring et al., 2018). Luo and colleagues (2020) conducted a recent systematic review and meta-analysis of 17 RCTs comparing electronically delivered to in-person CBT for depression among adults. Electronically delivered CBT was defined as CBT delivered via the internet with the option of utilizing therapist support, which ranged from text-based support to videoconferencing sessions. Quality of the evidence was variable, with 11 out of 17 studies being not blinded and five not utilizing randomization procedures. Authors reported that among 14 eligible studies ($N = 1136$), online CBT resulted in a larger pooled effect size (mean difference of $d = -1.73$, 95% CI = 2.72 to 0.74) than face-to-face CBT for reducing depression severity. However, they did note that heterogeneity was high. They also reported no significant differences between the two formats on patient satisfaction. Based on their findings, they suggested that internet-delivered CBT is a cost-effective, accessible, and flexible option for the treatment of depressive symptoms among adults. An additional systematic review and meta-analysis of 24 RCTs compared the efficacy of internet-based CBT for depression and anxiety among young people ages 12-25 to active (e.g., face-to-face CBT, treatment as usual) or waitlist controls (Christ et al., 2020). Of the 24 studies, 14 were therapist-guided (e.g., phone calls, texts), which included support, progress, monitoring, and in nine of the studies, personalized feedback. The remaining 10 studies were self-guided. The overall quality of the evidence was deemed low to moderate due to high risk of bias from self-report measures, high proportions of missing data, and overall heterogeneity, although these are common limitations of RCTs. Results revealed that effect sizes were similar between online CBT and active treatment for symptoms of

anxiety (g = 0.04, 95% CI −0.23-0.31). Findings for depressive symptoms alone revealed that effect sizes favoured active treatment (g = −0.70, 95% CI −1.51-0.11), but internet-based CBT still had a significant effect on symptom reduction at long-term follow-up relative to passive controls (g = 0.27, 95% CI = 0.09-0.45), and authors again noted that heterogeneity was high. This is supported by the findings from a systematic review and meta-analysis comparing therapist guided internet-based and traditional face-to-face CBT for single disorder treatment of various psychiatric and somatic disorders (e.g., social anxiety, depression, panic, body dissatisfaction; Andersson et al., 2014). Results revealed that the pooled post-treatment effects for the 13 included studies were equivalent between internet and face-to-face CBT (g = -.01, 95% CI = -.13 to .12). This was also the case when authors examined pooled effects for just social anxiety and depression studies. The currently available research would suggest that the efficacy of treatment is not compromised for adults using an online format for single disorder programs relative to in-person approaches, and this is also the case for young adults in particular. No studies to date have compared online vs. face-to-face approaches for integrated or single disorder treatment among young adults specifically. However, given the efficacy of online CBT for single disorder (i.e., depression, anxiety, alcohol misuse) interventions among young adults and the growing body of research using online integrated treatments, it follows that similar interventions designed for a younger population are likely to yield similar results.

Integrated Online Treatment

To date, only two integrated, internet-based treatments for adults struggling with comorbid alcohol use and depression have been examined, with additional trials underway (Kaal et al., 2020; Schaub et al., 2018). A recent three-arm RCT by Baumgartner and colleagues (2021) was conducted among a sample of adults (N = 689, M_{age} = 42.8) from Switzerland, Germany, and Austria. The authors developed and examined the efficacy of a self-guided, internet-based integrated treatment for depression and alcohol use compared to alcohol use only treatment and internet as usual (IAU) at 3- and 6- month follow-ups. The integrated treatment condition included eight modules of CBT and MI in addition to automated feedback for accountability. Authors reported that individuals in both the integrated treatment and alcohol only conditions experienced significant reductions in alcohol use at 3- (d = .11, d = .24, respectively) and 6-month (d = .10, d = .20, respectively) follow ups relative to the control group. They also reported significant improvements in alcohol use disorder severity and depression symptoms in

both the integrated treatment and alcohol only conditions at 3- and 6-month follow-ups relative to the control group, with larger effect sizes observed than for alcohol use. Authors conducted equivalence testing and reported non-inferiority between the integrated and alcohol-only conditions. Augsburger and colleagues (2021) conducted a similar trial among adults ($N = 589$, $M_{age} = 37.86$) in Estonia. They examined the efficacy of integrated (i.e., CBT and MI) online self-help treatment for alcohol misuse relative to a control group (i.e., personalized normative feedback and an information booklet). The authors accounted for missing data (i.e., 35% at 6-month follow-up) using both baseline observation carried forward (BOCF) and multiple imputation. Authors found that those in the integrated treatment group had significantly lower scores on an alcohol-related problems measure at follow-up relative to those in the control group, with small effect sizes. In general, they reported larger effect sizes using multiple imputation relative to BOCF ($d = .46$, 95% CI $= 0.30$-$.63$, $d = .21$, 95% CI $= 0.04$-0.37, respectively).

Only one study to date has examined the efficacy of online integrated treatment for anxiety and alcohol use among young adults specifically (Stapinski et al., 2021). Participants ($N = 123$, $M_{age} = 21.6$) were a community sample in Australia struggling with moderate or higher levels of anxiety and alcohol problems. Participants were randomly assigned to either the treatment condition consisting of five CBT modules (e.g., negative thoughts, drinking goals, avoidance, social support, relapse prevention), or a psychoeducational control group, and were assessed at baseline, 2-, and 6-months post-treatment. Results revealed that individuals in both groups significantly reduced their alcohol consumption at 2-months, but individuals in the treatment group had larger reductions at 6-months than those in the control group ($d = 0.24$). Regarding symptoms of anxiety, individuals in the treatment group had larger reductions at 2-months relative to control group ($d = 0.88$), however no between group differences were observed at 6-months, as individuals in the control group had a reduction in symptoms at comparable levels to participants in the treatment group. Individuals in the treatment group also experienced significantly larger reductions in hazardous drinking at 2- and 6-month follow-ups ($d = 0.35$, $d = 0.38$, respectively) relative to the control group. While the findings from recent trials are promising, similar online integrated programs designed specifically for young adults struggling with alcohol misuse and depression and/or anxiety are still needed.

Treatment Modality Preferences Among Young Adults

Research suggests that young adults may even prefer an online format for treatment. As previously discussed, this age group needs mental health services (Johnston et al., 2015). This is problematic, however, given young adults with comorbid alcohol use, depression, and anxiety often do not readily access face-to-face treatment (Capron et al., 2017). A recent study demonstrated that only 24.6% of 13,984 sampled college students reported that they would seek support in person for emotional difficulties (Ebert et al., 2019), and engagement with in-person therapies are generally low among this population (Salaheddin & Mason, 2016). Therefore, the opportunity to seek support online may be far more appealing and engaging for young people. This is supported by several recent findings. Among a cross-sectional general sample of first year college students, most participants self-reported a preference for online support compared to face-to-face services (Lungu & Sun, 2016). A similar community-based study among adults in Australia revealed that younger age (i.e., 18-25) predicted a higher preference for online mental health programs and a lower preference for face-to-face programs (Batterham & Calear, 2017). Secondary qualitative data from a meta-analysis (i.e., thematic analysis and narrative synthesis of 41 studies examining the efficacy of online CBT for depression and anxiety in young people) revealed that a large reason young participants were drawn to online formats in the first place was *because* they were offered online (Garrido et al., 2019). Furthermore, stigma has consistently been cited as a considerable barrier to treatment among young adults (Priester et al., 2016; Whiteford et al., 2013), making the privacy and anonymity of online treatment particularly important and desirable for this population (Boydell et al., 2014; Chan et al., 2016). Young adults have also reported a preference to handle their problems independently due to feelings of embarrassment, which is also more feasible using online formats (Ebert et al., 2019). Finally, online interventions are typically less costly than in-person services (Yates, 2020), and a recent study identified cost as a less important albeit still notable barrier to treatment endorsed by young adults (Ebert et al., 2019). Given the preference for online modalities among young adults, internet-based treatments are particularly well-suited to this population. Incorporating young adults' preferences when designing online interventions may improve both engagement with and benefits of such treatments. However, there currently remains a need to integrate content for both depression and anxiety simultaneously into internet-based treatments for comorbid alcohol

misuse and emotional problems (Corace et al., 2021), as well as a need to target such treatment specifically for young adults.

Current Research

An examination of previous literature revealed several key directions for the current research program. Young adults with comorbid alcohol misuse and emotional challenges are less likely to mature out of risky drinking relative to those without said challenges (Keough & O'Connor, 2016). Therefore, young adults with comorbid challenges are particularly vulnerable to the development of emotional challenges and alcohol-related problems over time. This alerts researchers and practitioners to a time period where early intervention is critical for those less likely to mature out. Second, intervention research examining the efficacy of treatment for alcohol misuse and emotional problems concurrently is growing (e.g., Deady et al., 2016; Schouten et al., 2021), and recent comorbidity literature would suggest that integrated treatments are likely to yield promising outcomes by targeting all symptomology simultaneously (Iarussi, 2019; Riper et al., 2014; Yule & Kelly, 2019). Third, online interventions stand to mitigate many of the barriers associated with low treatment uptake for this population, (Garrido et al., 2019; Salaheddin & Mason, 2016). Young adults may even prefer this format over other interventions (Lungu & Sun, 2016), which may motivate them to seek treatment when they otherwise would have chosen not to. Furthermore, individuals who suffer from both alcohol misuse and comorbid depression and anxiety often place a burden on the healthcare system due to their complex treatment requirements (Whiteford et al., 2013). Thus, online treatments provide a cost-effective treatment option without sacrificing the benefits of in-person treatment (Luo et al., 2020; Yates, 2020). Unfortunately, few studies to date have targeted alcohol-emotional comorbidities for this population in an integrated way using the accessible and desirable online format. Furthermore, the few studies that have examined the efficacy of online, integrated treatments for this population (Augsburger et al., 2021, Baumgartner et al., 2021) were limited in their focus only on depression or anxiety (Stapinski et al., 2021), rather than treating the broader spectrum of emotional issues.

Goals of Study 1

Despite promising recent advances in this field of research, there remains a paucity of accessible, online, integrated interventions designed to address comorbid alcohol misuse and common emotional problems among young adults. There is currently a need for this type of

intervention in Canada given the high rates of these mental health concerns observed among this population across the country. In light of these gaps, the overarching goal of this dissertation was to develop and examine the efficacy of an online, minimally guided, integrated intervention designed specifically to address mental health treatment gaps for this population. The main goal of study 1 was to adapt a previous iteration of the intervention conducted by Baumgartner and colleagues (2021) for use in English and expand it to include symptoms of anxiety. Study 1 examined the overall efficacy of the program, *Take Care of Me*, on primary (i.e., alcohol consumption), and secondary mental health and well-being outcomes (i.e., hazardous drinking, depressive and anxious symptoms, quality of life, motivation). It is important to note that data was collected between September 2018 and September 2019, with final follow-up data received in early March of 2020, immediately prior to the onset of the COVID-19 pandemic. Therefore, it is not expected that the pandemic impacted results of the intervention.

Goals of Study 2

The goal of study 1 was to determine the overall efficacy of the *Take Care of Me* program. While this is the pivotal first step in understanding clinical trials, Kraemer (2016) discusses how simply determining whether or not a treatment yields significant effects on outcomes of interest does not provide clinicians with sufficiently meaningful information. Rather, it is duly important for researchers and clinicians to conduct follow-up moderation analyses in order to glean important clinical information on treatment outcomes. Examining moderation is important for researchers and clinicians alike for a number of reasons. First, it helps to understand for whom treatment works for, under what conditions it works best, and why it does not work for some (Kraemer et al., 2016). Second, it can help delineate appropriate inclusion and exclusion criteria for future versions of the same or similar trials. Finally, gleaning information about differing treatment effects based on individual difference factors can then be used to adapt future versions of programs and ensure that those individuals are optimally supported for their unique needs. Gaining insight of this nature was particularly relevant in the current study given the highly inclusive recruitment efforts, in that individuals endorsing moderate or higher symptoms on hazardous drinking, depression, or anxiety were eligible to participate. Therefore, an important extension of study 1 was to conduct secondary analyses of the main trial findings and capture potential heterogeneity in responses to the intervention based on individual difference factors.

Moderation. Conducting moderation analyses is an important step in delineating clinically meaningful findings of treatment studies (Kraemer et al., 2016). Traditional approaches have involved regression-based moderation analyses where factors are examined in isolation (e.g., Castro et al., 2017). While this is a common and informative method for understanding interactions between treatment variables, it fails to account for the interaction of multiple moderating variables simultaneously. This is a noteworthy limitation to traditional moderation approaches given the often-complex interrelation among clinical variables, as is the case with mental health comorbidities. Alternative to traditional approaches, researchers in the field have discussed the valuable information that can be garnered from conducting secondary subgrouping analyses of clinical samples when there is empirical reason to suspect underlying subgroups within their sample based on shared characteristics (Lanza & Rhoades, 2013). Latent class analysis (LCA) is a method where one is able to identify meaningful subgroups within samples based on shared characteristics, as well as consider the interaction of multiple characteristics simultaneously. Furthermore, LCA can identify varying levels of risk within clinical samples (Müller et al., 2020). Comorbid alcohol misuse and emotional difficulties do not occur in a vacuum, in that there is high variability in the etiology, presentation, and experience of these challenges. LCA is a relatively new, albeit clinically meaningful, way of conducting follow-up moderation analyses in clinical trials. Furthermore, identifying subgroups of individuals within samples that may share clinical presentations or responses to treatment could have implications for both diagnosis and treatment of said individuals. In order to capture multiple individual characteristics simultaneously, LCA was utilized in study 2 to identify potentially meaningful subgroups within the sample (Lanza & Rhoades, 2013) based on pre-treatment individual characteristics (i.e., background factors, symptom severity, cognitive capacity, motivation). Next, moderated regression analyses were conducted to determine whether differential responses to treatment existed based on membership in a particular group.

Pre-Treatment Factors. To date, there is no body of literature outlining key baseline characteristics to consider as moderators of treatment outcomes specifically within online, integrated treatments for comorbid alcohol misuse and emotional challenges. Given the novelty of interventions of this kind, it was somewhat challenging to find literature for the current integrated program specifically. While there is ample research on predictors of success for single disorder online treatments, much less exists for populations struggling with comorbid

difficulties, as internet-based integrated treatment remains rather novel. Relevant pre-treatment factors to include in the subtyping analyses were selected by expanding the literature to variables that might be relevant to the current intervention. In some cases, this meant inferring information for a novel integrated intervention based on slightly different treatments for similar populations, such as single disorder (versus integrated) online treatment, in-person treatment, or general adult populations.

Background Factors. It is perhaps not surprising that the majority of studies that have examined predictors of treatment response include sociodemographic data (e.g., Amati et al., 2018; Haug & Schaub, 2016; Müller et al., 2020). While the specific factors included vary among addiction and mental health trials, this often includes variables such as gender, age, education level, and socioeconomic status. There is variability in the impact of said factors on treatment response and they are often included in order to better explain the sample within a particular treatment. The impact of gender as a predictor of treatment response remains inconclusive (Haug & Schaub, 2016; Polak et al., 2015). Some studies have found that females are more likely to have poorer response to substance use treatment (Greenfield et al., 2010), others have found that identifying as female positively predicts treatment outcomes (Amati et al., 2018), and others still have yielded no meaningful differences (Vîslă et al., 2021). Additional background factors that are often included as potential moderators of treatment include mental health history (e.g., previous diagnosis and treatment, family history; Amati et al., 2018; Haug & Schaub, 2016; Müller et al., 2020). The literature from single-disorder studies is mixed for the impact of having a previous mental health diagnosis on outcomes, while success in previous treatment has been shown to be a predictor of success in subsequent treatment (Amati et al., 2018). Alternatively, an LCA of perceived barriers to alcohol use treatment conducted by Schuler and colleagues (2015) found that a family history of alcohol problems was predictive of membership in the high treatment barriers class (i.e., attitudinal, financial, stigma, readiness-for-change).

Symptom Severity. It is well-established in the extant literature that baseline symptom severity is likely to influence treatment outcomes of addiction and mental treatment (Bahorik et al., 2018; Cochran et al., 2016; Reins et al., 2021; Witkiewitz et al., 2017). Amati and colleagues (2018) conducted a systematic review of variables that predicted recovery among individuals receiving community-based psychological therapy for common mental health disorders (e.g.,

depression, anxiety-related disorders), and observed that more severe mental health symptoms at baseline predicted poorer responses to treatment. Similarly, baseline depression, anxiety, low life satisfaction, alcohol use, and cannabis use have all been shown to predict negative outcomes in treatment for alcohol misuse (Bahorik et al., 2018; Cochran et al., 2016; Haug & Schaub, 2016; Witkiewitz et al., 2017).

Cognitive Capacity. The nature of minimally guided online treatment for alcohol misuse and emotional difficulties requires strong executive function (EF) skills (e.g., planning ahead, organizing, sustaining attention, engaging in treatment). In such treatment, individuals are required to manage multiple treatment components, including self-paced work through modules, completing homework, formulating and working towards goals, and monitoring mood and behaviour, all tasks that individuals low in EF may find challenging. As such, researchers have examined the moderating impact of EF on addiction treatment outcomes (e.g., Hunt et al., 2009). This is particularly relevant in the context of comorbid alcohol misuse and emotional difficulties, where lower EF skills have been shown to be associated with both alcohol use (Stacy & Wiers, 2010) and emotional difficulties (Castaneda et al., 2008). Therefore, EF is a logical baseline factor to include when considering potential moderators of treatment outcomes (Domínguez-Salas et al., 2016). Indeed, one study found that higher EF skills predicted success in CBT treatment for comorbid hazardous alcohol use and depression (Hunt et al., 2009).

Motivation. Recent research suggests that baseline motivation predicts success in substance use treatment (Martínez-González et al., 2020), and motivation barriers to treatment (i.e., attitudinal, financial, stigma, and readiness-for-change) have been shown to be associated with alcohol dependence, and lifetime mood disorder and anxiety disorders (Schuler et al., 2015). One study examining the impact of motivation on alcohol use treatment found being "in action" at the end of alcohol use treatment was associated with abstinence and non-problem drinking at follow-up (Cook et al., 2015). Motivation is a particularly relevant construct to consider in the treatment of alcohol misuse, given that MI is commonly used as either the primary treatment approach (Miller & Rollinck, 2013), or integrated with other modalities (e.g., CBT; Schouten et al., 2021), as was the case in the current study.

Outcomes. Overall, it was important to conduct follow-up treatment analyses to gain a more nuanced understanding of the program outcomes based on the aforementioned pre-treatment factors. Therefore, it was vital to include outcomes in the regression analyses that

would provide meaningful information about the program response while also ensuring that there was not overlap with the other study variables. It was expected that differential outcomes on said variables would be observed based on group membership. Outcome variables included overall alcohol consumption, hazardous drinking, coping motives for drinking, and quality of life. Both alcohol consumption and hazardous drinking were outcomes included in the primary trial given the goal of targeting alcohol misuse, and thus were deemed relevant outcomes to consider with regard to treatment response. Furthermore, quality of life has been shown to be an important indicator of success in substance use treatment (Kirouac et al., 2017). Finally, coping motives are widely accepted as maladaptive reasons for using alcohol relative to different reasons (e.g., social, enhancement, conformity; Stewart et al., 2011), and are associated with severe alcohol-related problems. It followed logically that individuals in the program may have differed on likelihood of endorsing coping motives for drinking at the end of treatment, with lower endorsement being an indicator of success.

CHAPTER 2
STUDY 1

Efficacy of a Minimally Guided Internet Treatment for Alcohol Misuse and Emotional Problems in Young Adults: Results of a Randomized Controlled Trial

Chapter 2 is reprinted as it appears in:

Abstract

Objective: Many young adults struggle with comorbid alcohol misuse and emotional problems (i.e., depression and anxiety). However, there is currently a paucity of evidence-based, integrated, accessible treatment options for individuals with these comorbidities. The main goal of this study was to examine efficacy of a novel online, minimally guided, integrated program for comorbid alcohol misuse and emotional problems in young adults. Method: The study was an open-label two-arm RCT. Participants ($N = 222$, $M_{age} = 24.6$, 67.6% female) were randomized to one of two conditions: the Take Care of Me program (an 8-week, online integrated treatment condition consisting of 12 modules), or an online psychoeducational control condition. Intervention modules incorporated content based on principles of cognitive behavioral therapy and motivational interviewing. Participants completed assessment data at baseline, at the end of treatment (i.e., 8 weeks), and at follow-up (i.e., 24 weeks). Data were analyzed using generalized linear mixed models. Results: We observed that participants in the treatment condition showed larger reductions in depression, hazardous drinking, as well as increases in psychological quality of life and confidence at the end of treatment. We did not find group differences on total alcohol use at follow-up, but participants in the treatment group reduced their hazardous drinking and improved their quality of life at 24-week follow-up. Conclusions: Our study provides promising initial evidence for the first iteration of the comorbid alcohol misuse and emotional problems online program.

Keywords: alcohol misuse; depression; anxiety; cognitive behavioural therapy; motivational interviewing; integrated treatment; online; minimally guided; emerging adulthood

Introduction

Alcohol misuse and emotional problems represent one of the most common mental health comorbidities in the general population (Castillo-Carniglia et al., 2019; Lai et al., 2015), with 50–60% of individuals with an alcohol use disorder also meeting criteria for depression and/or anxiety (Davis et al., 2008). Young adulthood, defined as ages 18–29 (Arnett et al., 2014), is a critical time to consider the co-occurrence of alcohol misuse and emotional problems. Individuals in this age group report the highest rates of hazardous drinking (e.g., misuse, alcohol-related problems; Whiteford et al., 2013) and emotional problems such as depression and anxiety (Ibrahim et al., 2013; Schry & White, 2013). Not surprisingly given the high comorbidity rates, these emotional challenges are likewise related to drinking problems among young adults (Grothues et al., 2008). The impact of both disorders leads to disproportionately greater impairment than either disorder alone, including poor health and treatment outcomes, higher rates of relapse, increased suicidality, relationship difficulties, increased risk of injury or accidents, and early mortality (Beidel et al., 2014; Grant et al., 2015; Lai et al., 2015; Prior et al., 2017). Furthermore, people with comorbid alcohol misuse and emotional problems place a burden on the healthcare system due to the complex treatment needs, frequent use of healthcare resources, compensation for disability, and involvement with the law (Whiteford et al., 2013; World Health Organization, 2014).

Treatment Approaches

Many theories have been used in the addictions literature to explain the high co-occurrence of alcohol and emotional problems. In general, the literature supports reciprocal associations between emotional problems and alcohol misuse (Stewart et al., 2016), suggesting that these two mental health issues are interconnected. Despite this high comorbidity, limited studies have examined the effects of integrated treatment for both problems within a single intervention.

Most existing treatments for comorbid alcohol misuse and emotional problems utilize either sequential or parallel approaches (DeVido & Weiss 2012; Mueser et al., 2003). Sequential methods involve treating the disorder deemed more severe first, whereas in parallel treatment methods, individuals are treated for both alcohol misuse and emotional problems concurrently, but in different settings or by distinct professionals. Although parallel or sequential approaches to treatment may be suitable in certain situations (e.g., crisis situations, limited availability of

28

services in a given area), both methods fail to acknowledge the complex interconnected nature of these issues. Unfortunately, without addressing both disorders concurrently, people often cannot experience marked improvements in either problem (Drake et al., 2007). Compared to traditional approaches, the goal of integrated treatment is to target symptoms of both alcohol misuse and emotional problems simultaneously within the same program and setting (Mueser et al., 2003), thus addressing limitations within sequential and parallel frameworks.

The existing literature would suggest that integrating cognitive behavioural therapy (CBT; Hofmann et al., 2012) and motivational interviewing (MI; Vasilaki et al., 2006) concurrently within a single intervention would be beneficial for addressing difficulties with both alcohol use and emotional symptomology (Riper et al., 2014; Morley et al., 2016; Westra et al., 2016). The goal of CBT is to help clients address maladaptive thinking patterns and behaviours that maintain feelings of depression and anxiety, as well as build helpful coping skills for managing stressors and triggers. CBT is a highly efficacious, recommended treatment for mood and anxiety disorders (Etzelmueller et al., 2020; Hofmann et al., 2012). MI is a collaborative treatment approach designed to reduce ambivalence or resistance and elicit motivation for change and is widely accepted and supported as treatment for alcohol use (Miller & Rollinck, 2013), resulting in moderate-to-large effect sizes compared to no treatment (Vasilaki et al., 2006). Previous research has demonstrated CBT may also be effective for treating substance use (Baker et al., 2012), and MI can reduce symptoms of depression and anxiety (Arkowitz & Burke, 2008), albeit with smaller effect sizes for each.

In light of the call for integrated treatment options, previous studies have demonstrated CBT and MI may be promising approaches when combined to address both alcohol misuse and emotional symptomology simultaneously (Riper et al., 2014). CBT requires engagement from the client (e.g., homework, environmental changes, activities, confronting stressors). Given that resistance to treatment is a common barrier among individuals struggling with substance use (Priester et al., 2016), MI stands to increase readiness for change (e.g., reducing or eliminating alcohol use), as well as improve treatment engagement with CBT-specific content. Furthermore, MI helps clients act in ways that are more closely aligned with their goals and values, which may likewise increase motivation for behavioural change. It follows logically that implementing both CBT and MI would yield promising results, as the two complement each other theoretically, and thus therapeutically (Iarussi, 2019).

Research examining the efficacy of integrated CBT and MI treatment for comorbid alcohol misuse and emotional has only emerged over the past several years. For example, a meta-analysis by Riper and colleagues (2014) found that integrated CBT and MI was effective at reducing symptoms of alcohol use and depression with small effect sizes compared to alternate treatments, and similar effect sizes were observed for subclinical populations. While these findings are promising, few studies to date have examined the efficacy of integrated CBT and MI for comorbid alcohol misuse and anxiety. Given the considerable overlap between anxious and depressive symptoms, it follows that interventions designed to manage emotional distress defined more broadly are both feasible and likely to yield beneficial results comparable to treatments that target alcohol use and depression exclusively.

Internet-Based Treatment

Considerable effort and research are being placed into the development of new online interventions for addiction and mental health issues (Cunningham et al., 2020; Deady et al., 2016; Garrido et al., 2019). Previous research has demonstrated the efficacy of online treatment for depression (Buntrock et al., 2015; Karyotaki et al., 2017, 2021), anxiety (Andersson et al., 2019), and alcohol use (Hadjistavropoulos et al., 2020; Riper et al., 2018) in isolation. However, internet-based interventions that have integrated CBT and MI content designed to target all symptoms simultaneously have only emerged recently. A recent systematic review and meta-analysis of the literature examined the effects of online interventions for comorbid alcohol use and depression (Schouten et al., 2021). Of the six studies that met inclusion criteria, they found small significant pooled effects for depression at 3-months ($g = 0.34$) but not at the 6-month follow up, and small significant effects for alcohol at 6-month follow-up ($g = 0.14$) but not 3-months. This review highlights the emergence of an important line of treatment for addiction and mental health that may be more cost-effective than in-person treatments (Yates, 2020). However, programs of this nature are still relatively new, and additional trials are needed. Furthermore, additional programs designed specifically for young adults and that target anxiety explicitly are still needed.

Unfortunately, despite the billions of dollars expended annually on healthcare for this population (Government of Canada, 2015), most people with alcohol problems who also suffer from an emotional disorder do not receive the appropriate treatment required for their complicated needs (Boschloo et al., 2011; Hasin et al., 2007). This is due to numerous existing

barriers, including stigma, limited resources, and cost (Priester et al., 2016). At present, existing treatment options for these comorbid problems are not sufficient, and it is therefore critical to develop evidence-based interventions that address the disparity in mental health care for this population.

Aims and Objectives

In light of existing treatment limitations for comorbid alcohol misuse and emotional problems in young adults, the goal of the current study was to examine the efficacy of a novel integrated intervention using online service delivery. We were able to integrate treatment for alcohol use and emotional problems within a single intervention by combining key principles of CBT and MI (Hofmann et al., 2012; Vasilaki et al., 2006), given the empirical support for both approaches in treating alcohol misuse and emotional symptoms. The utilization of an online modality provides many strengths over traditional approaches. First, online formats are often more accessible both physically and financially than in-person formats (Canadian Medical Association and Canadian Psychiatric Association, 2016; Priester et al., 2016), where there are known barriers to accessing in-person treatment. Second, young adults are often reluctant to seek traditional in person psychological treatment due to the pervasive stigma in doing so (Livingston et al., 2012). As such, young adults may be more inclined to participate in an online treatment format due to increased privacy and anonymity. Third, intervening while young adults are experiencing moderate levels of alcohol misuse and emotional problems (i.e., early in the risk pathway) may prevent their symptoms from developing into severe clinical disorders in the future (Deady et al., 2016). Finally, given the billions of dollars being expended on health care, online treatments have potential to reduce the burden on the health care system. Thus, the goal of our program was to improve both efficacy and accessibility of services for young adults struggling with alcohol use, depression, and anxiety.

We took the *Take Care of You* program that targets depression and alcohol misuse simultaneously (Schaub et al., 2016) and is currently being evaluated in German, and adapted it for use in English. The current program, entitled *Take Care of Me*, included additional content to also target anxiety symptomology. We conducted a randomized controlled trial (RCT) with treatment and psychoeducational control groups and obtained outcome data at both short- (8 weeks, T1) and long-term (24 weeks, T2) follow-ups.

The hypotheses were as follows:

1. **Hypothesis 1**: Participants in the integrated treatment condition would show larger reductions in weekly alcohol use (primary outcome) relative to participants in the psychoeducational control group over the course of the 8-week program.

2. **Hypothesis 2**: Participants in the integrated treatment condition were expected to show larger reductions in hazardous drinking, alcohol problems, depression, anxiety, as well as increases in quality of life over the 8-week program relative to controls (secondary outcomes).

3. **Hypothesis 3**: Improvements for the treatment group were expected to be maintained at a 24-week follow-up.

Method

Design

The research was designed in accordance with the ethical principles of the Declaration of Helsinki and reported in accordance with the CONSORT guidelines for internet-based interventions (Eysenbach, 2011), and was granted procedural ethics approval from the Psychology/Sociology Research Ethics Board at the University of Manitoba, P2017:128. The intervention was pre-registered on clinicaltrials.gov for traceability (ID: NCT03406039) and was updated at each stage of the research process. The procedure was conducted in accordance with the published protocol (Frohlich et al., 2018).

The study was an open-label two-arm RCT. Participants were randomly assigned by the web server to either the integrated treatment condition ($n = 114$), or to the psychoeducational control condition ($n = 108$). Assessment data were collected at three distinct time points: baseline (i.e., T0), end of treatment (i.e., T1, 8 weeks), and follow-up (i.e., T2, 24 weeks). Participants received a $10 CAD Amazon gift card for each assessment period they completed, making the total compensation $30 CAD. Researchers and participants were not blinded to group assignment.

Procedure

Participants

A total of 275 people were initially screened for participation, but 52 did not meet the eligibility criteria and were not included. This resulted in a final sample of 222 participants ($M_{age} = 24.6$, $SD_{age} = 4.37$, 67.6% female) in the trial. Of this sample, individuals identified as: 59.5% White, 10.8% Indigenous, 8.6% Black, 10.8% East/Southeast Asian or Pacific Islander, 2.7% Hispanic or Latino, 2.3% Middle Eastern, North African, or Central Asian, 3.6% South Asian,

and 1.8% Other. Participants were recruited from September 2018 to September 2019 using various strategies, including online (e.g., Google Ads, Facebook, emails to university students), and community-based (e.g., posters at doctor's offices and organizations) methods. Eligibility was expanded to the age of 35 in order to provide help more broadly while still remaining within the early life stage (Arnett et al., 2014). The program was compatible for use on all electronic devices (i.e., computers, tablets, and smartphones).

Eligibility for the program included: 1) being between 18 and 35 years old, 2) self-reporting a score of >3 for females and >4 for males on the Alcohol Use Disorders Identification Test – Consumption screener (AUDIT-C; Saunders et al., 1993), 3) self-reporting at least moderate depression and/or anxiety symptoms (i.e., scoring >16 on the Center for Epidemiological Studies Depression Scale [CES-D, Radloff et al., 1997], and/or a score of >10 on the Generalized Anxiety Disorder Scale [GAD-7, Spitzer et al., 2006], 4) being fluent in English, and 5) having access to the internet. Participants were excluded if: 1) they self-reported engaging in either psychological or pharmacological treatments for alcohol misuse and/or depression/anxiety, 2) scored greater than "minimal risk" on the P4 suicidality screener (Dube et al., 2010), or 3) reported current symptoms of psychosis or mania. Informed consent for participation was provided electronically on the study website prior to registering for an account.

Program Overview

Treatment Condition. Once registered, participants in the treatment condition were able to access the program dashboard, which included their mood and drinking diary, 12 treatment modules, a page of mental health and crisis support lines across major Canadian cities, and their user information. Participants were given 8 weeks to complete the treatment modules. While they were given access to all 12 modules at the outset of the program, they were encouraged to work through them in sequential order by completing 1-2 modules per week. Participants were able to return to all modules as many times as desired within the 8 weeks. They were also able to keep track of their progress throughout the program via a status bar at the bottom of each module. Modules were translated and adapted to English from the Swiss version of the intervention (Schaub et al., 2016), with additional content added to target symptoms of anxiety in addition to depression. The 12 modules combined principles of CBT and MI to help participants target goals related to both alcohol consumption and emotional improvement. This included strategies such as realistic goal setting (e.g., reducing the number of overall drinks consumed), coping with craving, learning

to decline social invitations to drink, identifying triggers, preventing relapse, challenging negative thinking, relaxation (e.g., deep breathing, muscle relaxation), behavioral activation for improving mood, and self-care (e.g., exercise, sleep hygiene). Modules ranged in length from 3-13 pages (M = 9.4), which included both educational text and self-directed activities. Extensive information, including module content is included in the previously published protocol (Frohlich et al., 2018).

Individuals also received ongoing feedback from an intervention support person throughout the 8-week program in order to increase treatment adherence. This involved automated feedback about module progress sent via email, automated reminders for timely completion of remaining modules and assessment time points, and automated motivational content. For example, all participants in the intervention condition received a message after the first week congratulating them on completing the week with the message of "at this time, we would also like to encourage you to start another module if you haven't yet done so" and wishing them well in the week ahead. Participants could also troubleshoot any difficulties that arose throughout the program by corresponding with the intervention support person via e-mail. The intervention support person was a research assistant and not a therapist due to the minimally guided nature of the program. Although participants could initiate contact via email, the majority did not, and those that did were primarily seeking administrative support with the program. Participants were also encouraged to track mood and alcohol use using a daily diary calendar on the website.

Control Condition. Participants assigned to the control group were directed to psychoeducational material for alcohol use (www.niaaa.nih.gov/publications/brochures-andfact-sheets) and mental illness (e.g., www.healthymindscanada.ca/resources/) that are readily available to the public. This is common practice for online addiction and mental health RCTs (Garrido et al., 2019; Riper et al., 2014). They did not have access to the treatment modules at the outset but were provided with full access to the intervention upon completion of the 24 weeks.

Measures

All measures were administered at all three time points (i.e., T0 to T2) with the exception of the suicidality screener (Dube et al., 2010) and the demographic questionnaire which were completed at T0 only.

Primary Outcome

The primary outcome was total weekly alcohol consumption using the Timeline Follow-Back (TLFB; Sobell & Sobell, 1992). Participants were asked to report the number of standard

drinks (i.e., 12oz can or bottle of beer, a 5oz glass of wine, or a 1.5oz shot of hard liquor) consumed each day for the past week. This value was then summed to calculate the number of standard drinks in the past week for each assessment time point. The TLFB is widely used in addictions research and is considered a reliable and valid representation of alcohol consumption (Mohr et al., 2011; Pedersen et al., 2012).

Secondary Outcomes

Depression. Depression was assessed using the CES-D (Radloff, 1977), which has excellent reliability and validity evidence in treatment research (González et al., 2017). Sum scores were calculated and the CES-D internal consistency at baseline was good ($\alpha = .86$).

Anxiety. The GAD-7 (Spitzer et al., 2006) was used to assess anxiety. Sum scores were calculated and the GAD-7 internal consistency was good at baseline ($\alpha = .80$).

Alcohol Problems. In addition to quantity of drinking using the TLFB, participants completed the 10-item AUDIT (Saunders et al., 1993), a self-report screener for alcohol-related problems. The AUDIT has demonstrable reliability and validity evidence in addictions research (Saunders et al., 1993), and yielded good internal consistency at baseline within the present sample ($\alpha = .86$). We looked at both the AUDIT-C (i.e., hazardous drinking) and the full AUDIT as outcome variables. Given that the AUDIT-C was a main inclusion criterion, it was important to examine whether change was observed for this variable.

Combined Reduction of Alcohol Use and Emotional Problems. Given the interconnectedness between alcohol use and emotional difficulties, a combined outcome was also examined. This was done by calculating a dichotomous variable for each participant based on cut-off scores from the CES-D (i.e., scoring below 16), GAD-7 (i.e., scoring below 5), and the first three items of the AUDIT (i.e., the AUDIT-C; scoring below 3 for females and 4 for males), all of which would suggest that participants were no longer experiencing clinical levels of emotional distress or problematic drinking. Participants no longer exceeding cut-offs for both alcohol misuse and emotional problems were coded as 0, whereas those exceeding cut-offs on the AUDIT and at least one emotion measure were coded as 1.

Quality of Life. An additional secondary outcome was participants' overall quality of life, which was measured using the World Health Organization Quality of Life Assessment (WHOQOL-BREF, WHOQOL Group, 1998). The questionnaire includes 26 self-report items that assess quality of life in four distinct domains. The reliability of each subscale was

acceptable, physical health (α = .71), psychological (α = .70), social relationships (α = .61), and environment (α = .76), with the exception of the social subscale which fell in the questionable range.

Drug Use. In order to assess potential reductions in other drug use, participants reported their levels of use over the past three months using the National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement Screening Test (NIDA ASSIST; NIDA, 2009). The NIDA ASSIST is a widely utilized tool within addictions research and treatment studies, with strong reliability and validity (Humeniuk et al., 2008).

Motivation. Given the fact that motivational content was deliberately included in the treatment program, participants also reported their readiness to improve their emotional well-being and alcohol use issues, how important it was to make said changes, and how confident they were in their ability to make changes at the time. Single items were created to assess participants' level of motivation from 0 *(Not Important/Confident/Ready)* to 10 *(Very Important/Confident/Ready)*.

Demographics. Demographic information was collected from participants at T0 to describe the sample and determine eligibility. This included age, biological sex, gender, ethnicity, history and treatment for any physical or mental conditions, and family history of alcoholism. A family history density of alcoholism score was also calculated for each participant by calculating the unique contribution of risk from first (i.e., 0.5)- and second-degree (i.e., 0.25) relatives (Stoltenberg et al., 1998).

Statistical Analysis

Power

Based on the results of similar interventions utilizing CBT and MI for alcohol use and depressive symptoms (Schouten et al., 2021), we anticipated small effect sizes of $g = .25$ for both drinking measures and emotional symptoms following the intervention. We used G*Power to calculate the optimal sample size to detect a small (i.e., 0.2) effect with 80% power, α = .05, and a correlation of .50 between repeated measures using a mixed between (treatment versus control) within (time) design. This resulted in a total sample of $N = 164$. However, we also considered previous online trials for alcohol use and depression as a benchmark for estimating attrition rates, which was expected to be approximately 30% lost at follow-up (Deady et al.,

2016). Thus, we aimed to recruit a sample of at least 214 participants in order to mitigate the risk of attrition.

Data Analytic Plan

Data was analyzed using SPSS version 25.0. First, we ran preliminary analyses on the dataset (i.e., descriptives, missing data analyses) to observe trends within the sample and identify any systematic missingness, which allowed us to include relevant covariates in the main analyses. We also calculated the proportion of participants who fell below clinical cut-offs on the AUDIT, CES-D and GAD-7 at the end of treatment. Initial analyses revealed that the retention rate at T1, though lower than anticipated and suboptimal, was similar to previous interventions (Hadjistavropoulos et al., 2020) at 55% ($n = 122$), with an equal 50% in each group (i.e., $n = 61$ in the treatment group, $n = 61$ in the control group). However, despite efforts to mitigate attrition in study procedures (e.g., accountability checks, automatic reminders, and compensation), we experienced far higher rates of attrition at 24 weeks (i.e., T2) than anticipated. We predicted that attrition rates at 24 weeks would be approximately 30%, whereas only 75 out of 222 participants were retained (i.e., 66% drop-out rate). Furthermore, attrition at the 24-week follow-up was very biased, as only 18 of the remaining participants were from the control condition (i.e., ~ 8% of the entire sample).

Next, in accordance with the previously published protocol (Frohlich et al., 2018), we used Generalized Linear Mixed Models (GLMM) with an intent-to-treat (ITT) framework to examine immediate treatment effects at T1, thus testing Hypotheses 1 (primary outcome) and 2 (secondary outcomes). GLMM was also used to examine longer-term treatment effects at follow-up (i.e., T2), thus testing Hypothesis 3. However, it is important to note that the systematic and substantial attrition experienced at 24 weeks is a notable limitation and may have negatively impacted our power to detect an interaction effect at the longer-term follow-up (Groenwold et al., 2014). For all main analyses, we used separate mixed models to examine the effects of time (within-subjects), intervention (between-subjects), and intervention by time interaction on the primary and second outcomes. The trend for time was linear, random intercepts (but not random slopes) were specified, and all outcomes were treated as continuous with the exception of the dichotomous combined reduction outcome. Relevant covariates were also included in the models (i.e., sex, age, family history of alcoholism, baseline AUD symptomology) based on the missing data analysis, with the goal of reducing potential biases associated with systematic data loss (Preacher et al., 2010).

Results

Descriptive Statistics and Missing Data Analysis

See Figure 2.1 for the CONSORT trial flow chart. Demographic information for each condition is presented in Table 2.1. Some participants reported having a mental health diagnosis (i.e., 32.4%) and seeking either pharmacological or psychological treatment in the past (i.e., 33.3%). The mean number of modules completed by those in the treatment group was 5.72 ($SD =$ 5.00) with only 28% completing all 12 modules. Missing data analyses were conducted using independent samples t-test and hierarchical linear regressions. Results of the t-tests revealed that individuals with missing data at the end of treatment differed significantly from those with complete data on baseline TLFB ($t(220) = 2.20$, $p = .029$, Cohen's $d = 0.29$) and AUDIT ($t(218)$ $= 2.98$, $p = .003$, $d = 0.40$) scores. The groups did not differ significantly on baseline depression ($t(220) = 0.79$, $p = .43$, Cohen's $d = 0.11$) or anxiety ($t(220) = 1.81$, $p = .07$, Cohen's $d = 0.25$) scores. Next, regressions were used to examine relevant auxiliary variables that accounted for missingness in baseline TLFB and AUDIT scores. The dichotomous missingness variable was included in Step 1, and relevant covariates (i.e., sex, age, family history of alcoholism, and baseline AUDIT, depression, and anxiety) were included in Step 2. In both the TLFB and AUDIT models, the missing data variable emerged as a statistically significant predictor of baseline scores in Step 1, but the effects became non-statistically significant in Step 2 ($p = .95$ and .058, respectively). Identifying the sources of systematic missingness and being able to control for them in the linear models allowed us to consider the data sufficiently MAR, permitting us to use GLMM with full information maximum likelihood estimation.

Preliminary Analyses

While descriptive in nature, it was also valuable to report the proportion of individuals still above at-risk cut-off levels for each main variable at the end of treatment (i.e., T1). The percentage of individuals exceeding cut-offs on the AUDIT-C (collapsed across gender) was 70% for the treatment group and 88% for the control group. For depressive symptoms, 69% of individuals in the treatment group and 85% in the control group still exceeded cut-offs at T1. Finally, 79% of individuals in the treatment group and 90% in the control group remained above cut-offs for at least moderate anxiety at T1. This suggests that despite immediate improvements on these variables, most people continued to struggle with emotional symptoms at the end of treatment.

Main Trial Analyses

Separate mixed effect models were run for each outcome. Non-statistically significant model results are presented in the supplementary file.

Hypothesis 1: Immediate Effects on the Primary Outcome

Contrary to our predictions, there was no statistically significant interaction effect on participants' weekly alcohol use as measured by the TLFB ($p = .219$); thus, Hypothesis 1 was not supported. Results of the analysis are presented in the supplementary file.

Hypothesis 2: Immediate Effects on the Secondary Outcomes

Hazardous Drinking. Separate mixed effects models were run for each secondary outcome in order to test Hypothesis 2. The AUDIT covariate added to the models was the full AUDIT score minus the AUDIT-C items. Inconsistent with our hypotheses, there were no statistically significant immediate interaction effects on AUDIT scores using the full measure (see supplementary file). Interestingly, however, the time by condition interaction was statistically significant ($p = .024$) for the AUDIT-C. While we observed statistically significant reductions in both groups over the 8 weeks of treatment ($B = -1.57$, $SE = 0.23$, $p < .001$ for the treatment group, $B = -0.91$, $SE = 0.26$, $p = .001$ for the control group), the interaction term suggests that participants in the treatment condition showed larger reductions in hazardous drinking during the intervention period compared to those in the control condition.

Emotional Outcomes. The results of the mixed model analyses for emotional outcomes at 8 weeks are presented in Table 2.2 and partially supported our hypotheses. With regard to depression, there was a statistically significant time by condition interaction ($p = .036$). Furthermore, while both groups were changing over time, participants in the treatment group showed larger reductions in depressive symptoms compared to those in the control condition ($B = -7.96$, $SE = 1.34$, $p < .001$, $B = -3.84$, SE = 1.52, $p = .012$, respectively, see Figure 2.2). For anxiety, the time by condition interaction was not supported. There were no statistically significant changes in combined alcohol use and emotional difficulties (see supplementary file).

Quality of Life. The only immediate effect on quality of life was in the psychological domain, where the time by condition interaction was statistically significant ($p = .015$; see Table 2.3). Participants in the treatment group experienced a statistically significant improvement in scores over the 8 weeks ($B = 1.38$, $SE = 0.29$, p < .001) while those in the control group did not

($B = 0.22$, $SE = 0.40$, $p = .577$; see Figure 2.2). No statistically significant effects were observed for the remaining quality of life domains.

Drug Use. Likewise, there was no statistically significant immediate effects on participants' self-reported levels of drug use other than alcohol using the NIDA (see supplementary file), which is inconsistent with our hypothesis.

Motivation. The final set of variables examined were the motivational outcomes (see Table 2.3). The time by condition interaction was statistically significant for treatment readiness (B = -1.20, $p = .004$). Participants in the control group experienced a statistically significant reduction in treatment readiness over the intervention period ($B = -1.11$, $SE = 0.34$, $p = .001$), whereas this effect was not statistically significant in the treatment group ($B = .04$, $SE = 0.28$, $p = .88$; see Figure 2.2). There was no statistically significant interaction on confidence. However, participants in the treatment group reported statistically significant increases in their confidence over 8 weeks ($B = 0.89$, $SE = 0.25$, $p = .001$), while those in the control group did not ($B = 0.27$, $SE = 0.32$, $p = .402$).

Hypothesis 3: Follow-up Effects

Overall, we did not observe the expected follow-up treatment effects on our primary outcome of interest (i.e., weekly alcohol use using the TLFB), nor on the majority of the secondary outcomes at 24 weeks (see supplementary file). However, the time by condition interaction was statistically significant for hazardous drinking (i.e., the AUDIT-C; $p = .026$). Furthermore, individuals in the treatment group experienced larger reductions in hazardous drinking than those in the control group ($B = -1.34$, $SE = .171$, $p = <.001$, $B = -0.67$, $SE = .242$, $p = .006$, respectively, see Table 2.4). Graphical representations of interaction effects are presented in Figure 2.3.

While we did not observe any other statistically significant treatment effects on mental health outcomes when we included the 24-week follow-up data, we did observe statistically significant interaction effects on three of the four quality of life domains, despite one being marginally significant. The treatment group significantly improved over time for the psychological ($B = 0.89$, $SE = .22$, $p < .001$), social ($B = 0.84$, $SE = .32$, $p = .01$), and environmental ($B = 0.47$, $SE = .22$, $p = .039$) domains, whereas the control group did not (see Table 2.4).

Discussion

The overarching goal of the current study was to develop and examine the efficacy of an online, minimally guided, integrated treatment for young adults struggling with comorbid alcohol misuse and emotional problems. Given the high comorbidity between the disorders, it is important that accessible, efficacious, and economical treatment options exist for these individuals, particularly those who are early on in the risk pathway for more severe disorders later in life. Our program was the first online integrated treatment for use in English designed to address this comorbidity in young adults, and the first intervention of its kind to integrate treatment for both alcohol use and the full range of emotional symptomology (i.e., depression *and* anxiety).

Overall, we did not observe significant effects on the primary outcome (i.e., total weekly alcohol use) at the end of treatment. However, we did observe meaningful effects on several secondary outcomes. At the end of treatment, we observed immediate reductions in hazardous drinking (i.e., AUDIT-C) and depression, as well as increases in psychological quality of life and readiness for change. As discussed, we experienced challenges with differential and high attrition at the longer-term follow-up. While we did observe some indication that the program led to longer-term decreases in hazardous drinking (i.e., the AUDIT-C) and multiple domains of quality of life, we did not see expected effects on our primary measure of alcohol consumption or measures of depression and anxiety being maintained over time. Overall, these results should be interpreted with caution given the substantial and differential attrition we experienced at follow-up, which poses a threat to the validity of the data. We therefore cannot conclude whether Hypothesis was 3 was supported or not. Although we need to remain cautious about the trial findings, our results reflect some preliminary support for *Take Care of Me* in the short-term.

Principal Results and Comparison with Prior Work

The results of our study revealed that at the end of the 8-week program, individuals in the treatment group did not experience a significant reduction in overall alcohol consumption using the TLFB, but they did experience significant improvements on hazardous drinking (i.e., AUDIT-C). This is inconsistent with previous research and our first hypothesis, which demonstrated that combined CBT and MI resulted in small but significant reductions in alcohol consumption using internet formats (Deady et al., 2016), and this effect was maintained at follow-up (Schouten et al., 2021). At present, we are left to speculate why the program did not significantly reduce overall alcohol consumption (i.e., TLFB). One possibility is the distinction between overall alcohol use

and hazardous drinking, whereby one does not necessarily equal the other (e.g., a total of seven drinks in one day vs. spread over one week). The module content in the current program was designed to reduce the risk of short- and long-term consequences of heavy drinking. Therefore, it is possible that participants were reducing their overall level of risk, but the quantity of drinks they consumed in a given week did not significantly decrease. This might have happened, for example, if participants had two drinks on four occasions in a week, rather than eight drinks on one occasion. The AUDIT-C is also a well-established measure of hazardous drinking within addictions literature, including for use among young adults (Verhoog et al., 2020), and was the measure we used to determine eligibility during enrolment. It plausible that we observed immediate treatment benefits on the AUDIT-C and not the TLFB because it is more sensitive to changes in hazardous drinking than simply quantity of consumption.

With regard to secondary emotion outcomes, our second hypothesis for immediate treatment effects was partially supported. Consistent with previous treatment of this nature (Etzelmueller et al., 2020; Hofmann et al., 2012), individuals in the program experienced a significant reduction in depressive symptoms over the course of the 8 weeks. This supports the notion that integrated treatment works, as individuals can change both their drinking and emotions simultaneously. Similar to the aforementioned findings with risky drinking, we are unable to conclude whether the benefits on emotional symptoms were lost at follow-up, or whether we were simply underpowered to detect such an effect long-term.

We also observed immediate effects on psychological quality of life, and the effect on many facets of quality of life were observed at the longer-term follow-up. This suggests that in addition to reductions on secondary clinical outcomes, the 8-week program also had a positive impact on individuals' psychological, social, and environmental well-being. Although not always included in clinical research studies, quality of life has been deemed an important indicator of success in mental health treatment (Oliveira et al., 2016), including treatment for substance use (Kirouac et al., 2017). This suggests that in addition to the clinical outcomes, these findings are meaningful for participants and a further indicator of preliminary support for the program. We also observed significant improvements on one facet of motivation (i.e., treatment readiness) at the end of treatment. Given that motivation, namely treatment readiness, significantly increased in the treatment group but not the control group, it is possible that these individuals would now be ready to engage in further treatment to reduce alcohol consumption in the future.

We also predicted that the benefits of the program would be maintained at the 24-week follow-up. While we observed significant effects on hazardous drinking and quality of life at follow-up, systematic and high attrition may have threatened our power to detect long-term impacts. Thus, we cannot conclude whether our non-significant results at follow-up are due to reduced power or a genuine lack of treatment effects. A main focal point in future iterations of the program should be to improve retention and recruit a large sample in order to clarify the impacts of the program. It is important to note that a recent review of internet-delivered CBT by Hadjistavropoulos and colleagues (2020) found that 2 out of the 11 included studies saw attrition rates greater than 60% at follow-up, and an additional 8 saw attrition rates between 30-50%. While our attrition rates at follow-up were also biased against the control group, our findings taken in the context of overall internet-based programs suggest that this is an ongoing challenge for addictions researchers in the field.

Implications

Overall, our results offer preliminary evidence that 8 weeks of minimally guided online CBT and MI can have positive effects on hazardous drinking, depression, motivation, and quality of life. From a research perspective, this adds to the body of literature demonstrating synergistic benefits of CBT and MI in integrated treatment programs (Riper et al., 2014; Westra et al., 2016). This suggests that theoretically, programs of this nature can in fact target the emotional symptoms commonly experienced by young adults who are also struggling with alcohol use.

The current program is an important addition to addictions literature with regard to internet interventions. Online support is becoming increasingly popular in this field (Cunningham et al., 2020; Schouten et al., 2021), and is especially timely amidst an ongoing global pandemic where lack of accessibility for in-person activities and the potential for increases in mental health concerns persist (Wardell et al., 2020). While preliminary in nature, our findings suggest that integrated CBT and MI can yield benefits for both depression and anxiety in addition to alcohol misuse. While the program itself needs to be more widely tested in the future, its format offers advantages for low cost and accessible public health style interventions.

It is also important to note many individuals were still meeting cut-offs for risky drinking and emotional problems at the end of treatment. This is not entirely surprising given that we included individuals with a wide spectrum of problems, including those with severe alcohol problems. This was done in order to collect preliminary data on the efficacy of the program overall.

However, the literature shows that people with severe problems (i.e., AUDIT > 20) may require residential treatment to address their needs, and low intensity brief interventions are more commonly indicated for less severe problems, as has been shown using the Screening, Brief Intervention and Referral to Treatment (SBIRT) initiative (Del Boca et al., 2017).

Limitations and Future Directions

Despite the strengths of the current study, there are important limitations. First and foremost, we experienced substantial biased attrition at the 24-week follow-up, despite our attempts at mitigating data loss (i.e., social presence, engaging activities, automated reminders, monetary incentives). This may have been in part due to the use of a waitlist control group, which may have increased the risk for biased attrition (Ainsworth et al., 2010). This prevents us from drawing any concrete inferences about the longer-term impacts of the program on the primary outcome measures as intended. Participant retention is consistently reported as a challenge in internet-based treatment programs, particularly individuals with mood (Gill et al., 2014), or substance-use difficulties (Hadjistavropoulos et al., 2020). Future iterations of the program should prioritize retention strategies beyond those employed in the current trial in order to prevent systematic attrition. For example, Scott (2004) has highlighted the potential benefits of proactively following a standardized protocol for reducing attrition, entitled the Engagement, Verification, Maintenance and Confirmation (EVMC) Protocol. The EVMC protocol could be adapted for use within internet-based programs in order to reduce high rates of attrition. Future iterations could also aim to keep more intensive contact with study participants in order to prevent study non-response at all time points.

Additionally, empirical support for the use of therapist assistance within internet-based interventions is growing. Indeed, online interventions for alcohol misuse that incorporate therapist assistance have been found to yield larger effect sizes than minimal or self-guided programs, and some studies have found that attrition is lower, and engagement is higher with an explicit accountability component (e.g., therapist assistance; Hadjistavropoulos et al., 2020). This may be particularly important for individuals with clinically elevated depression, who are likely to experience greater benefits with therapist assistance than completing a self-directed program (Karyotaki et al., 2021). Future research will reveal the optimal format by which to provide said assistance (Sundström et al., 2020), but therapist assistance presents a promising future avenue.

A second limitation, which is likely related to overall the attrition, was that engagement with the program content itself was low, as evidenced by the fairly low module completion rate. The goal of the program was to integrate treatment content using a minimally guided framework, which had not previously been done. It is possible that many of the individuals struggling with comorbid alcohol misuse and emotional problems are experiencing difficulties with motivation and energy as well. Although the program was effective for some of the participants, engaging in treatment that is largely self-guided may have been too challenging for all individuals involved, such as those with more severe symptoms.

Finally, aiming to recruit an increasingly diverse sample would help with the generalizability of the findings to different groups. This could include subclinical populations, individuals living in remote areas, and a more ethnically representative sample as nearly 60% of the sample identified as White. Furthermore, the results may not generalize to all individuals of all ages (e.g., older adults), although the module content relied on core principles of CBT and MI that we would expect to yield benefits across the lifespan. An important next step of this research will be to examine relevant moderators and mediators of treatment effects with this data sample, which we intend to do after publishing these primary and planned findings. This may provide insight into the lack of significant effects on alcohol consumption, the fact that both the treatment and control group seemed to benefit from the program at the end of treatment, and the potential impact of baseline symptom severity (e.g., AUDIT scores) on treatment effectiveness.

Conclusion

Take Care of Me adds to the emerging body of work designed to target alcohol use and emotional problems in one treatment. By adapting and designing an integrated, internet-based, minimally guided treatment program, we found preliminary evidence that at the end of treatment, young adults experienced a reduction in hazardous drinking, emotional symptoms and an improvement in quality of life. Overall, this is promising initial evidence for the first iteration of the program. Taking into consideration the above limitations, the program could be readily adapted and has the potential for far reaching benefits at both the individual (e.g., symptom reduction, improved quality of life, preventing the escalation of severe clinical disorders) and societal (e.g., reduce disease burden) level.

Table 2.1

Descriptive Statistics of Study Variables by Group at Baseline

Variable	Intervention	
	Treatment (*n* = 114)	Control (*n* = 108)
Age, *M* (SD)	24.83(4.44)	24.30 (4.30)
Sex, % (*n*)		
Female	69.3 (79)	65.7 (71)
Male	30.7 (35)	33.3 (36)
Ethnicity, % (*n*)		
Indigenous	8.8 (10)	13.0 (14)
Black	7.9 (9)	9.3 (10)
White	57.0 (65)	62.0 (67)
East Asian/South-East Asian/Pacific Islander	14.0 (16)	7.4 (8)
Hispanic	4.4 (5)	0.9 (1)
Middle Eastern/North African/Central Asian	2.6 (3)	1.9 (2)
South Asian	4.4 (5)	2.8 (3)
Other	0.9 (1)	2.8 (3)
Family History Density, *M* (SD)	0.75 (0.67)	0.84 (0.58)
TLFB, *M* (SD)	18.3 (16.97)	19.77 (17.09)
CES-D, *M* (SD)	32.55 (9.59)	33.63 (9.78)
GAD-7, *M* (SD)	11.98 (4.32)	13.02 (4.56)
AUDIT, *M* (SD)	16.05 (7.84)	17.56 (8.07)
NIDA-Cannabis, *M* (SD)	1.99 (2.05)	2.14 (1.98)
QOL-Physical, *M* (SD)	13.47 (2.65)	13.16 (2.41)
QOL-Psychological, *M* (SD)	10.16 (2.40)	10.36 (2.58)
QOL-Social, *M* (SD)	11.07 (5.60)	10.96 (3.62)
QOL-Environmental, *M* (SD)	13.42 (2.67)	13.40 (2.77)
Importance, *M* (SD)	7.88 (1.99)	7.72 (2.23)
Confidence, *M* (SD)	6.63 (2.18)	6.29 (1.84)
Readiness, *M* (SD)	7.85 (1.92)	7.31 (2.15)

Note. TLFB = Timeline Follow-Back, CES-D = Center for Epidemiological Studies Depression Scale, GAD-7 = Generalized Anxiety Disorder Scale, AUDIT = Alcohol Use Disorders Identification Test, NIDA = National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement Screening Test, QOL = World Health Organization Quality of Life Assessment.

Table 2.2

Hypothesis 2 – End of Treatment Model for Secondary Outcomes (Drinking and Depression)

Parameter	B	Std. Error	t	Sig.
Hazardous Drinking				
Intercept	5.24	0.50	10.57	< .001
Group	-0.52	0.46	-1.13	0.261
Time	-1.58	0.22	-7.23	< .001
AUDIT – Cov *(AUDIT-C items excluded)*	0.22	0.01	15.09	< .001
CES – Cov	-0.02	0.01	-1.23	0.22
GAD – Cov	0.01	0.03	0.20	0.842
Sex	0.02	0.01	1.33	0.186
Age – Cov	-0.00	0.00	-0.20	0.839
Time x Intervention	**0.71**	**0.31**	**2.27**	**0.024**
Family History – Cov	-0.01	0.17	-0.06	0.956
Depression				
Intercept	25.10	2.65	9.48	< .001
Time	-7.10	1.34	-5.94	< .001
AUDIT- Cov	0.04	0.08	0.50	0.62
GAD – Cov	1.18	0.13	9.08	< .001
Sex	0.04	0.08	0.54	0.588
Age	0.01	0.02	0.59	0.556
Family History – Cov	0.56	0.96	0.58	0.562
Group	-3.88	2.81	-1.38	0.168
Time x Intervention	**4.08**	**1.93**	**2.11**	**0.036**
Intercept	25.10	2.65	9.48	< .001

Note. Secondary drinking outcome for hazardous drinking was the AUDIT-C and for depression was the CES-D at the end of treatment (i.e., T1). "Cov" denotes the inclusion of a relevant covariate. Significant interaction is bolded.

Table 2.3

Hypothesis 2 – End of Treatment Model for Secondary Outcomes (Quality and Motivation)

Parameter	*B*	Std. Error	t	Sig.
Psychological				
Intercept	14.41	0.69	20.98	< .001
Time	1.38	0.29	4.70	< .001
AUDIT – Cov	-0.02	0.02	-0.91	0.364
Sex	-0.02	0.02	-0.87	0.386
Age	-0.00	0.00	-0.09	0.927
Family History – Cov	-0.05	0.24	-0.22	0.822
CESD – Cov	-0.12	0.02	-6.93	< .001
GAD – Cov	-0.11	0.04	-2.79	0.006
Group	1.49	0.62	2.38	0.018
Time x Intervention	**-1.04**	**0.42**	**-2.47**	**0.015**
Confidence				
Intercept	6.62	0.62	10.73	< .001
Time	0.90	0.26	3.49	0.001
Sex	-0.02	0.02	-1.11	0.268
Age	0.00	0.00	0.27	0.787
Family History – Cov	0.30	0.22	1.35	0.178
CESD – Cov	-0.01	0.02	-0.75	0.454
GAD – Cov	0.00	0.04	0.03	0.979
Group	0.35	0.55	0.64	0.523
Time x Intervention	-0.64	0.37	-1.72	0.088
AUDIT – Cov	-0.05	0.02	-2.59	0.01
Readiness				
Intercept	7.28	0.65	11.18	< .001
Time	0.04	0.29	0.14	0.884
Sex	-0.00	0.02	-0.03	0.977
Age	-0.00	0.00	-0.89	0.374
Family History – Cov	0.64	0.22	2.83	0.005
CESD – Cov	-0.01	0.02	-0.50	0.62
GAD – Cov	0.01	0.04	0.32	0.747
AUDIT – Cov	0.02	0.02	0.89	0.376
Group	0.59	0.60	0.99	0.325
Time x Intervention	**-1.20**	**0.41**	**-2.93**	**0.004**

Note. Outcome variable for quality of life was the psychological subscale of the WHOQOL-

BREF and motivation outcomes were single items assessed at the end of treatment (i.e., T1).

"Cov" denotes the inclusion of a relevant covariate. Significant interaction is bolded.

Table 2.4

Hypothesis 3 – Follow-up Model for Secondary Outcomes (Drinking and Quality of Life)

Parameter	*B*	Std. Error	t	Sig.
Hazardous Drinking				
Intercept	7.87	0.36	22.17	< .001
Sex	0.31	0.23	1.35	0.176
Intervention	-0.38	0.53	-0.71	0.476
Time	-1.34	0.18	-7.59	< .001
Time x Intervention	**0.67**	**0.30**	**2.23**	**0.026**
Age – Cov	0.06	0.03	2.19	0.029
Family History – Cov	-0.06	0.21	-0.29	0.766
CESD – Cov	-0.02	0.01	-1.61	0.113
GAD – Cov	0.03	0.03	1.13	0.26
AUDIT – Cov *(AUDIT-C items excluded)*	0.19	0.02	10.27	< .001
Psychological				
Intercept	9.30	0.45	20.84	< .001
Sex	-0.01	0.30	-0.05	0.96
Intervention	1.32	0.67	1.97	0.049
Time	0.89	0.22	4.01	< .001
Time x Intervention	**-1.01**	**0.38**	**-2.66**	**0.008**
Age – Cov	0.03	0.03	.095	0.352
Family History – Cov	0.03	0.26	0.12	0.906
AUDIT – Cov	-0.02	0.02	-1.27	0.212
CES-D – Cov	-0.10	0.02	-5.52	< .001
GAD-7 – Cov	-0.14	0.04	-3.68	< .001
Environmental				
Intercept	12.91	0.45	28.52	< .001
Sex	-0.09	0.30	-0.29	0.773
Intervention	1.20	0.68	1.77	0.077
Time	0.47	0.23	2.07	0.039
Time x Intervention	**-0.92**	**0.38**	**-2.40**	**0.016**
Age – Cov	0.01	0.03	0.34	0.744
Fam History – Cov	-0.18	0.27	-0.66	0.506
AUDIT – Cov	-0.01	0.02	-0.52	0.59
CES-D – Cov	-0.08	0.02	-4.46	< .001
GAD-7 – Cov	-0.20	0.04	-5.12	< .001

Note. Outcome variable for hazardous drinking was the AUDIT-C, and for quality of life were two subscales of the WHOQOL-BREF at follow-up (i.e., T2). "Cov" denotes the inclusion of a relevant covariate. Significant interaction is bolded.
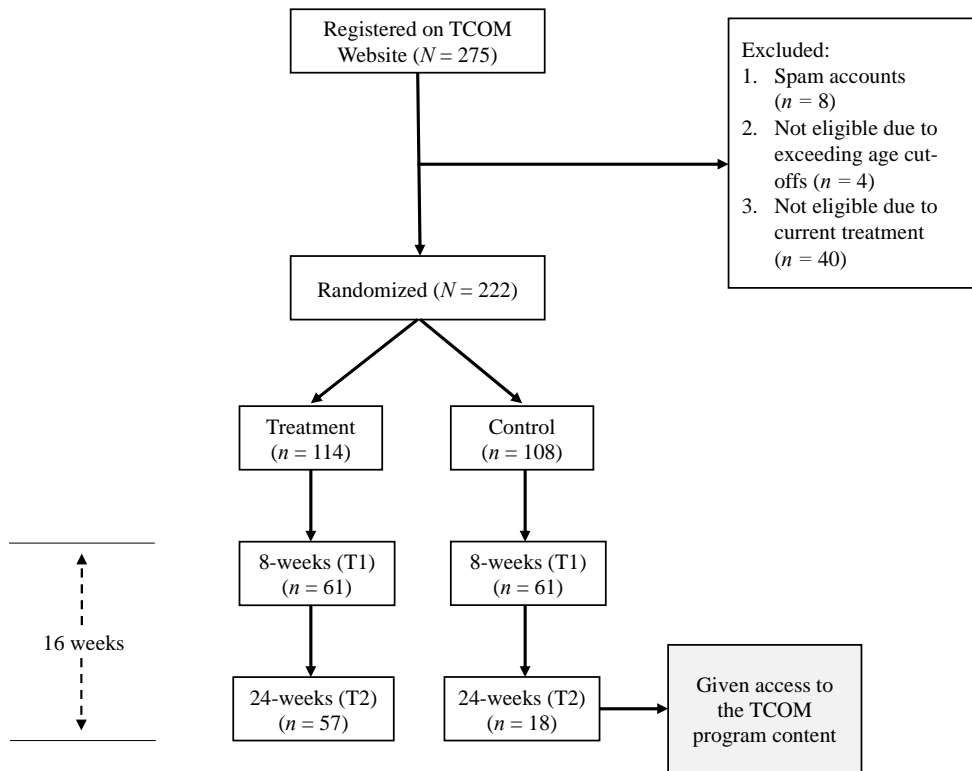
Figure 2.1. CONSORT trial flow chart.

AUDIT-C Scores

Depression Symptom Scores

Psychological Quality of Life

Confidence
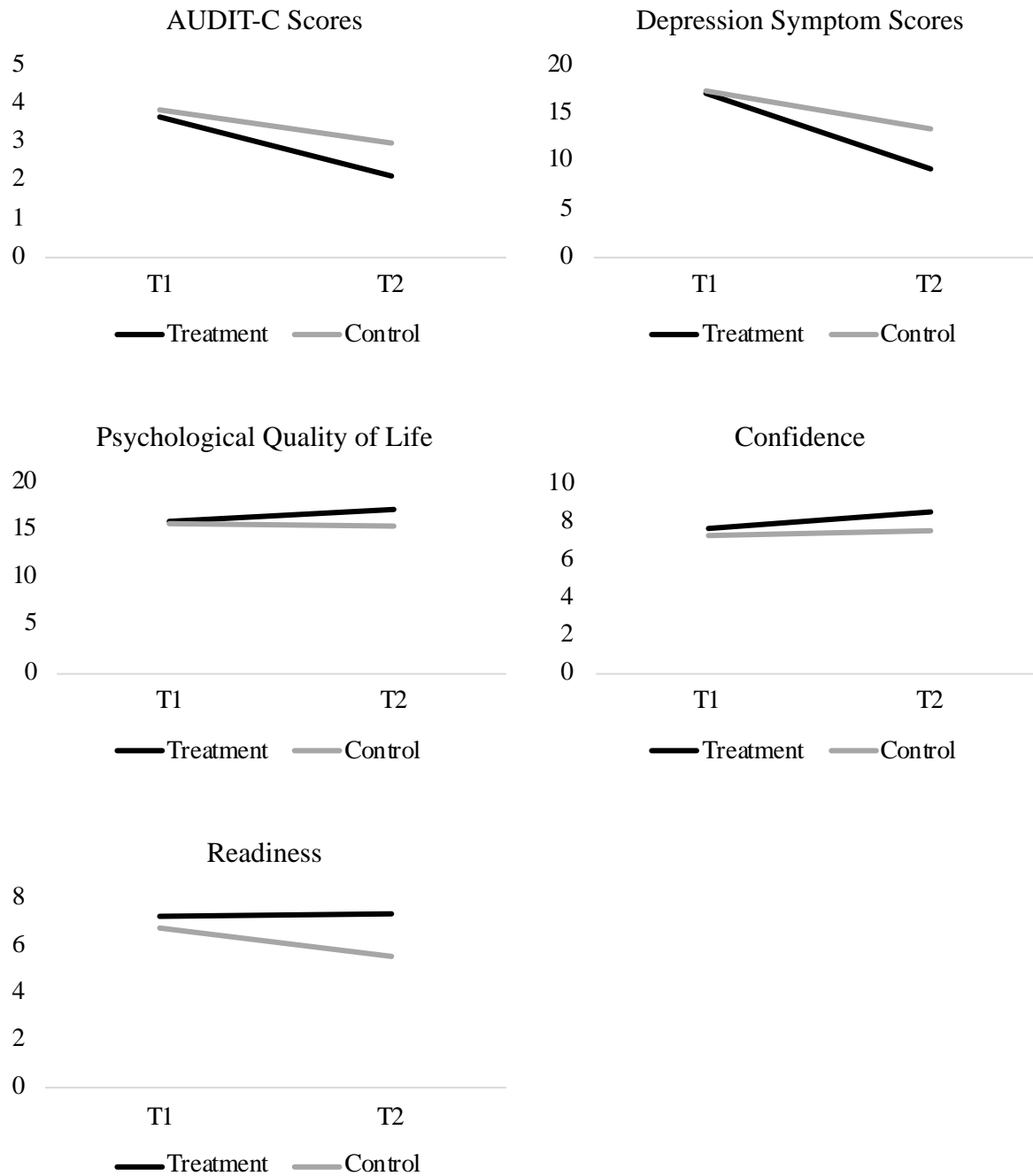
Readiness

Figure 2.2. Changes in hazardous drinking, depression, and motivation from pre- to post-treatment. *Note*: Time x Condition interactions were significant for AUDIT-C (p = .024), depression (p = .036), psychological quality of life (p = .015) and readiness (p = .004).

AUDIT-C

Psychological Quality of Life

Social Quality of Life

Environmental Quality of Life
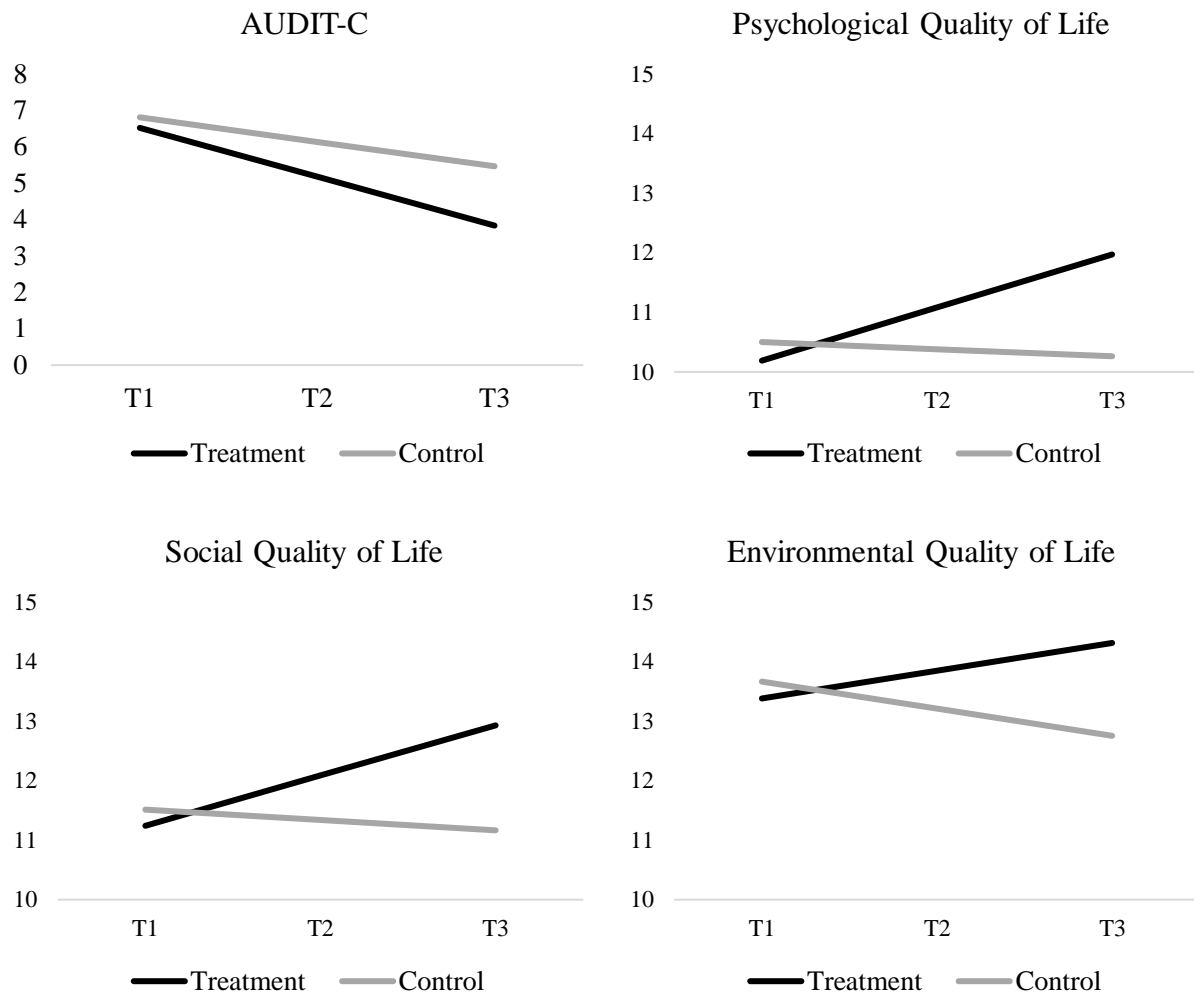
Figure 2.3. Changes in hazardous drinking and quality of life over time from pre-treatment to follow-up. *Note:* Time x Condition interactions were significant for the AUDIT-C ($p = .026$), psychological ($p = .008$) and environmental domains ($p = .016$).

SUPPLEMENTARY TABLES

Table 2.5

Hypothesis 1 – End of Treatment Model for Primary Outcome (Drinking)

Parameter	B	Std. Error	df	t	Sig.
Intercept	8.41	3.72	317.17	2.26	0.024
Time	-10.13	1.58	128.45	-6.39	$< .001$
AUDIT – Cov	1.14	0.10	178.98	10.74	$< .001$
Sex	0.07	0.11	129.38	0.70	0.486
Age – Cov	0.01	0.03	182.41	0.48	0.635
Family History – Cov	1.29	1.30	175.21	0.99	0.325
CESD – Cov	0.05	0.10	171.94	0.49	0.624
GAD – Cov	-0.08	0.21	164.21	-0.37	0.714
Group	-3.12	3.36	176.48	-0.93	0.354
Time x Intervention	2.80	2.27	126.20	1.24	0.219

Note. Primary drinking outcome variable was the TLFB at the end of treatment (i.e., T1). "Cov" denotes the inclusion of a relevant covariate.

Table 2.6

Hypothesis 2 – End of Treatment Model for Secondary Outcomes (Problems, Anxiety, Drug Use)

Parameter	*B*	Std. Error	df	t	Sig.
Alcohol Problems					
Intercept	9.40	1.70	298.54	5.54	< .001
Time	-2.84	0.61	139.19	-4.62	< .001
Sex	-0.07	0.06	176.87	-1.23	0.218
Age	-0.00	0.01	211.60	-0.03	0.976
Family History – Cov	2.12	0.65	209.07	3.27	0.001
CESD – Cov	0.03	0.05	207.39	0.60	0.553
GAD – Cov	0.19	0.11	202.23	1.78	0.077
Group	-0.41	1.38	236.79	-0.3	0.765
Time x Intervention	1.21	0.88	138.06	1.37	0.172
AUDIT – Cov	0.26	0.02	214.64	10.79	< .001
Anxiety					
Intercept	7.48	1.27	323.82	5.91	< .001
Time	-3.46	0.57	180.03	-6.12	< .001
AUDIT – Cov	0.02	0.04	225.42	0.44	0.659
Sex	0.06	0.04	173.51	1.74	0.083
Age	-0.01	0.01	227.15	-0.86	0.39
Family History – Cov	0.18	0.44	219.30	0.42	0.676
Group	-0.75	1.19	217.58	-0.63	0.531
Time x Intervention	1.37	0.81	177.74	1.69	0.093
CESD – Cov	0.24	0.03	232.37	8.55	< .001
Drug Use					
Intercept	1.94	0.57	271.72	3.42	0.001
Group	-0.29	0.42	253.99	-0.70	0.483
Time	-0.04	0.18	122.70	-0.25	0.801
AUDIT – Cov	0.01	0.02	199.22	0.40	0.69
CES – Cov	-0.04	0.02	198.80	-2.70	0.008
GAD – Cov	0.09	0.04	195.28	2.61	0.01
Sex	-0.03	0.02	174.52	-1.69	0.092
Age – Cov	-0.00	0.00	201.25	-0.91	0.364
Time x Intervention	0.22	0.25	122.53	0.87	0.386
Family History – Cov	0.53	0.22	198.54	2.41	0.017

Note. Outcome variable for alcohol problems was the full AUDIT, for anxiety was the GAD-7, and for drug use was the NIDA ASSIST at the end of treatment (i.e., T1). "Cov" denotes the inclusion of a relevant covariate.

Table 2.7

Hypothesis 2 – End of Treatment Model for Secondary Outcomes (Quality of Life)

Parameter	*B*	Std. Error	t	Sig
Physical Health				
Intercept	17.53	0.72	24.18	< .001
Family History – Cov	-0.06	0.22	-0.26	0.794
Time	0.74	0.37	2.01	0.044
AUDIT – Cov	-0.00	0.02	-0.22	0.836
GAD – Cov	-0.13	0.04	-3.63	< .001
Sex	0.03	0.02	1.50	0.129
Age	-0.01	0.00	-1.36	0.176
CESD – Cov	-0.09	0.02	-5.73	< .001
Time x Intervention	-0.74	0.53	-1.40	0.163
Group	0.72	0.77	0.94	0.349
Social				
Intercept	13.65	1.11	12.29	< .001
Family History – Cov	0.36	0.34	1.06	0.285
Time	1.33	0.57	2.35	0.019
AUDIT – Cov	-0.05	0.03	-1.92	0.054
GAD – Cov	-0.03	0.05	-0.50	0.624
Sex	-0.02	0.03	-0.73	0.462
Age	-0.00	0.01	0.30	0.712
CESD – Cov	-0.09	0.03	-3.63	< .001
Time x Intervention	-1.49	0.81	-1.83	0.068
Group	1.68	1.17	1.44	0.15
Environmental				
Intercept	17.44	0.80	21.8	< .001
Family History – Cov	-0.35	0.24	-1.45	0.148
Time	0.40	0.41	0.97	0.332
AUDIT – Cov	0.01	0.02	0.30	0.75
GAD – Cov	-0.15	0.04	-3.78	< .001
Sex	0.03	0.02	1.55	0.115
Age	0.00	0.00	0.41	0.661
CESD – Cov	-0.08	0.02	-4.36	< .001
Time x Intervention	-0.79	0.59	-1.34	0.179
Group	1.15	0.84	1.36	0.174

Note. Outcome variables were subscales of the WHOQOL-BREF assessed at the end of

treatment (i.e., T1). "Cov" denotes the inclusion of a relevant covariate.

Table 2.8

Hypothesis 2 – End of Treatment Model for Secondary Outcome (Importance)

Parameter	B	Std. Error	df	t	Sig.
Intercept	6.00	0.64	318.31	9.39	< .001
Time	-0.44	0.29	173.91	-1.54	0.126
AUDIT – Cov	0.08	0.02	216.28	4.47	< .001
GAD – Cov	-0.02	0.03	197.57	-0.54	0.588
Sex	0.00	0.02	159.12	0.27	0.789
Age	-0.00	0.00	215.16	-0.30	0.766
Family History – Cov	0.42	0.22	213.70	1.91	0.058
Group	0.04	0.61	205.90	0.07	0.945
Time x Intervention	-0.39	0.41	170.59	-0.95	0.344
Intercept	6.01	0.64	318.31	9.39	< .001

Note. Outcome variable was a single item assessed at the end of treatment (i.e., T1). "Cov" denotes the inclusion of a relevant covariate.

Table 2.9

Hypothesis 3 – Follow-up Model for Primary Outcome (Drinking)

Parameter	*B*	Std. Error	t	Sig.
Intercept	22.94	2.09	10.96	< .001
Sex	1.85	1.38	1.34	0.179
Intervention	0.70	3.12	0.22	0.823
Time	-5.63	1.03	-5.47	< .001
Time x Intervention	0.25	1.75	0.14	0.885
Age – Cov	0.52	0.15	3.43	0.001
Family History – Cov	0.67	1.23	0.55	0.583
CESD – Cov	0.08	0.08	0.97	0.333
GAD – Cov	-0.10	0.18	-0.55	0.585
AUDIT – Cov	0.90	0.09	10.13	< .001

Note. Outcome variable was the TLFB at follow-up (i.e., T2). "Cov" denotes the inclusion of a relevant covariate.

Table 2.10

Hypothesis 3 – Follow-up Model for Alcohol Problems

Parameter	*B*	Std. Error	t	Sig.
Intercept	18.74	1.09	17.21	$< .001$
Sex	-0.19	0.73	-0.27	0.791
Intervention	0.82	1.63	0.51	0.612
Time	-2.57	0.54	-4.73	$< .001$
Time x Intervention	0.44	0.92	0.47	0.636
Age – Cov	0.08	0.07	1.05	0.292
Family History – Cov	1.62	0.64	2.54	0.011
CESD – Cov	0.04	0.04	1.00	0.314
GAD – Cov	0.20	0.09	2.15	0.031
TLFB – Cov	0.24	0.02	10.90	$< .001$

Note. Outcome variable was the full version of the AUDIT at follow-up (i.e., T2). "Cov" denotes the inclusion of a relevant covariate.

Table 2.11

Hypothesis 3 – Follow-up Model for Secondary Outcomes (Emotions)

Parameter	*B*	Std. Error	t	Sig.
Depression				
Intercept	37.54	1.82	20.68	< .001
Sex	-0.35	1.19	-0.30	0.768
Intervention	0.11	2.72	0.04	0.967
Time	-4.53	0.91	-4.99	< .001
Time x Intervention	0.60	1.54	0.39	0.695
Age – Cov	-0.25	0.13	-1.98	0.048
Family History – Cov	0.67	1.07	0.63	0.53
GAD – Cov	1.12	0.13	8.62	< .001
AUDIT – Cov	0.07	0.08	0.88	0.345
Anxiety				
Intercept	12.70	0.82	15.43	< .001
Sex	0.24	0.54	0.43	0.664
Intervention	1.19	1.23	0.96	0.335
Time	-1.56	0.41	-3.78	< .001
Time x Intervention	-0.04	0.70	-0.06	0.955
Age – Cov	0.07	0.06	1.13	0.259
Family History – Cov	0.31	0.49	0.64	0.521
AUDIT – Cov	-0.02	0.04	-0.48	0.625
CES-D – Cov	0.19	0.03	6.98	< .001

Note. Outcome variable for depression was the CES-D and for anxiety was the GAD-7 at follow-up (i.e., T2). "Cov" denotes the inclusion of a relevant covariate.

Table 2.12

Hypothesis 3 – Follow-up Model for Secondary Outcomes (Quality of Life)

Parameter	*B*	Std. Error	t	Sig.
Social				
Intercept	10.40	0.66	15.77	< .001
Sex	-0.45	0.43	-1.04	0.299
Intervention	1.29	0.99	1.30	0.193
Time	0.84	0.33	2.57	0.01
Time x Intervention	-1.02	0.56	-1.82	0.069
Age – Cov	0.02	0.05	0.50	0.644
Fam History – Cov	0.13	0.39	0.32	0.75
AUDIT – Cov	-0.06	0.03	-2.00	0.046
CES-D – Cov	-0.11	0.03	-4.16	< .001
GAD-7 – Cov	0	0.06	0.00	0.997
Physical Health				
Intercept	13.05	0.42	31.40	< .001
Sex	-0.10	0.27	-0.38	0.703
Intervention	0.41	0.63	0.66	0.508
Time	0.36	0.21	1.73	0.083
Time x Intervention	-0.47	0.35	-1.33	0.182
Age – Cov	0.02	0.03	0.61	0.54
Family History – Cov	-0.07	0.25	-0.30	0.768
AUDIT – Cov	-0.02	0.02	-0.90	0.362
CES-D – Cov	-0.08	0.02	-5.00	< .001
GAD-7 – Cov	-0.19	0.03	-5.42	< .001

Note. Outcome variables were subscales from the WHOQOL-BREF at follow-up (i.e., T2).

"Cov" denotes the inclusion of a relevant covariate.

Table 2.13

Hypothesis 3 – Follow-up Model for Secondary Outcome (Drug Use)

Parameter	*B*	Std. Error	t	Sig.
Intercept	4.63	1.09	4.24	< .001
Sex	-0.14	0.72	-0.19	0.848
Intervention	0.93	1.61	0.58	0.563
Time	-0.64	0.55	-1.16	0.244
Time x Intervention	0.19	0.90	0.21	0.833
Age – Cov	-0.06	0.07	-0.83	0.401
Family History – Cov	-0.21	0.67	-0.31	0.754
AUDIT – Cov	0.12	0.05	2.53	0.011
CES-D – Cov	-0.06	0.04	-1.42	0.15
GAD-7 – Cov	0.07	0.09	0.74	0.461

Note. Outcome variable was the NIDA ASSIST at follow-up (i.e., T2). "Cov" denotes the inclusion of a relevant covariate.

Table 2.14

Hypothesis 3 – Follow-up Model for Secondary Outcomes (Motivation)

Parameter	*B*	Std. Error	t	Sig.
Importance				
Intercept	8.03	0.40	20.21	8.81
Sex	-0.06	0.26	-0.4	0.45
Intervention	0.31	0.60	0.52	1.48
Time	-0.21	0.20	-1.07	0.18
Time x Intervention	-0.49	0.34	-1.44	0.17
Age – Cov	0.05	0.03	1.72	0.12
Family History – Cov	0.26	0.24	1.07	0.73
AUDIT – Cov	0.06	0.02	3.55	0.09
CES-D – Cov	0.05	0.02	3.07	0.08
GAD-7 – Cov	-0.03	0.03	-0.86	0.04
Confidence				
Intercept	6.13	0.36	16.84	6.84
Sex	-0.29	0.24	-1.22	0.18
Intervention	0.25	0.55	0.46	1.32
Time	0.59	0.18	3.24	0.94
Time x Intervention	-0.46	0.31	-1.49	0.14
Age – Cov	0.05	0.03	1.77	0.20
Family History – Cov	0.21	0.22	0.95	0.63
AUDIT – Cov	-0.07	0.02	-4.67	-0.04
CES-D – Cov	0.01	0.01	1.00	0.03
GAD-7 – Cov	-0.01	0.03	-0.49	0.05
Readiness				
Intercept	8.11	0.39	20.56	8.88
Sex	0.11	0.26	0.43	0.62
Intervention	-0.29	0.59	-0.49	0.87
Time	-0.14	0.20	-0.72	0.24
Time x Intervention	-0.60	0.33	-1.80	0.05
Age – Cov	0.02	0.03	0.54	0.07
Family History – Cov	0.74	0.23	3.16	1.20
AUDIT – Cov	0.00	0.02	0.06	0.03
CES-D – Cov	0.02	0.02	1.18	0.05
GAD-7 – Cov	-0.02	0.03	-0.48	0.05

Note. Outcome variables for motivation were single items assessed at follow-up (i.e., T2). "Cov" denotes the inclusion of a relevant covariate.

Table 2.15

Hypothesis 2 – End of Treatment Model for Secondary Outcome (Combined)

Parameter	B	Std. Error	t	Sig.
Intercept	-2.17	1.01	-2.15	0.032
Sex	-0.05	0.02	-2.76	0.006
Intervention	0.14	1.40	0.10	0.922
Time	2.97	0.51	5.81	< .001
Time x Intervention	-0.65	0.80	-0.81	0.416
Age – Cov	0.00	0.01	0.50	0.633
Family History – Cov	0.39	0.32	1.24	0.216
CESD – Cov	-0.01	0.02	-0.58	0.551
GAD – Cov	-0.22	0.05	-4.01	< .001
AUDIT – Cov	-0.08	0.03	-2.79	0.005

Note. Outcome variable was the combined alcohol use and emotional difficulties outcome at the end of treatment (i.e., T1). "Cov" denotes the inclusion of a relevant covariate.

CHAPTER 3
TRANSITION TO STUDY 2

Current addiction treatment literature has pointed to the need for online, integrated treatments for young adults that specifically targets the highly prevalent comorbidity between alcohol misuse and symptomology, that includes content for both depression *and* anxiety. The main purpose of study 1 was to adapt and translate previous versions of the intervention (Augsburger et al., 2021; Baumgartner et al., 2021) for use in English, and include content for the full range of emotional symptomology that young adults experience alongside alcohol misuse. Using a two-arm RCT, it was posited that individuals assigned to the treatment condition, consisting of 12 CBT and MI modules, would experience larger reductions in both primary (i.e., total alcohol use) and secondary (i.e., hazardous drinking, depression, anxiety, motivation, drug use, quality of life) outcomes relative to those in the psychoeducational control condition. Contrary to what was hypothesized, results revealed no significant effects of the intervention on overall alcohol consumption. Significant intervention effects were observed for hazardous drinking, depression, psychological quality of life, and treatment readiness, where individuals in the treatment condition had greater improvements on all measures relative to the control condition, partially supporting hypotheses. Results also revealed significant reductions on hazardous drinking and improvements on psychological quality of life were maintained at follow-up.

Overall, the results of study 1 offered preliminary yet promising support for the first version of the *Take Care of Me* program, suggesting that online, minimal guidance, integrated interventions may indeed be suitable and beneficial for young adults. This adds to the extant literature that has been accumulating for trials of this nature. However, the results also left open a need for further inquiry into the efficacy of the program, given the null results on the primary outcome of interest (i.e., total alcohol consumption). Furthermore, the recruitment strategies utilized were highly inclusive, in that all individuals endorsing moderate or greater symptomology were included. This yielded a sample with a wide range of clinical severity (i.e., moderate to severe), who may not have responded to the treatment in the same way. Indeed, previous research has highlighted the importance of conducting follow-up analyses of clinical trials in order to glean evidence on who treatment works or does not work for, and under what condition it is beneficial (Kraemer et al., 2016). Given the unanswered questions from study 1, it

was important to conduct secondary analyses on the data. Results from study 2 help clarify the efficacy of the intervention (i.e., study 1) in greater detail, determine differential responses to the treatment, and overall provide clinical insight into the sample that can be used to guide future versions of the program.

CHAPTER 4
STUDY 2

Examining Differential Responses to the *Take Care of Me* Trial:
A Latent Class and Moderation Analysis

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Abstract

Objective: Given prevalent alcohol misuse-emotional comorbidities among young adults, we developed an internet-based integrated treatment called *Take Care of Me*. Although the treatment had an impact on several secondary outcomes, effects were not observed for the primary outcome. Therefore, the goal of the current study was to examine heterogeneity in treatment responses. *Method*: The initial study was an open-label two-arm RCT. Participants were randomized to either a treatment or a psychoeducational control condition. We conducted an exploratory latent class analysis to distinguish individuals based on pre-treatment risk and then used moderated regressions to examine differential treatment responses based on class membership. *Results*: We found evidence for three distinct groups. Most participants fell in the "low severity" group ($n = 123$), followed by the "moderate severity" group ($n = 57$) who had a higher likelihood of endorsing a previous mental health diagnosis and treatment and higher symptom severity than the low group. The "high severity" group ($n = 42$) was less prevalent and endorsed a family history of alcoholism, the highest symptom severity, and the lowest executive functioning. Moderated regressions revealed significant class differences in treatment responses. In the treatment condition, high severity (relative to low severity) participants reported higher alcohol consumption and hazardous drinking and lower quality of life at follow-up, whereas moderate severity (relative to low severity) individuals had lower alcohol consumption at follow-up, and lower hazardous drinking at end-of-treatment. No class differences were found for participants in the control group. *Conclusions*: Higher risk individuals in the treatment condition had poorer responses to the program. Tailoring interventions based on severity may be important to examine in future research.

Keywords: online treatment; alcohol use; emotional problems; latent class analysis; moderation

Introduction

Emotional disorders (e.g., depression and anxiety) and alcohol misuse are highly comorbid and impairing among young adults (Deeken et al., 2020). Early intervention for emotional-alcohol use comorbidities in young adulthood may prevent severe, lifelong problems (Pedrelli et al., 2016), and there have been recent calls to develop more effective, accessible, integrated treatments for this population (Schouten et al., 2021). Given the need for integrated interventions, we adapted and translated the *Take Care of You* program, a successful integrated treatment for alcohol misuse and depression in German (Baumgartner et al., 2021) for use in English with content added for symptoms of anxiety. We then conducted a randomized controlled trial (RCT) to evaluate the efficacy of the intervention for alcohol misuse and emotional problems relative to a psychoeducational control. Surprisingly, we did not observe significant reductions during the intervention on our primary outcome, total weekly alcohol use. Participants in the treatment condition did, however, show larger post-treatment reductions in depressive symptoms, hazardous drinking, as well as increases in psychological quality of life and readiness for change at the end of treatment compared to the control condition (Frohlich et al., 2021). Effects on hazardous drinking and psychological quality of life were maintained at the 24-week follow-up. It is important to note that we were inclusive in our recruitment, in that we included all individuals with moderate-to-severe comorbid problems. While the program yielded some positive effects, we were left with unanswered questions, and it was important to clarify whether differential responses to treatment existed.

There is a need to examine variability in treatment responses (e.g., who treatment works or does not work for and under what conditions it works best) based on individual characteristics (Kraemer et al., 2016). Traditionally, researchers have explored this using moderation analyses, which often involves testing (one at a time) how characteristics influence treatment response (e.g., Castro et al., 2017). In contrast, as argued by Lanza and Rhoades (2013), latent class analysis (LCA) is a better way to examine treatment response heterogeneity because it considers the interaction of multiple characteristics simultaneously. This allows for the identification of meaningful treatment responder subgroups. Given the complex etiology and presentation of comorbid alcohol use and emotional problems, LCA provides a comprehensive way of examining varying levels of risk within clinical samples (Müller et al., 2020).

Predictors of Substance Use Treatment Response

At present, specific pre-treatment factors for online integrated treatments remain unknown. However, looking at the broader literature on moderation within brief, outpatient, substance use and mental health treatments orients us to groups of factors that are likely to be relevant for our novel integrated treatment. Most studies examining predictors of treatment response have included pre-treatment background factors such as sociodemographic information, previous treatment, prior mental health diagnoses, and family history (Amati et al., 2018; Haug & Schaub, 2016). The results remain inconclusive for whether a previous mental health diagnosis predicts positive treatment outcomes, however previous successful treatment has been shown to be beneficial for recovery among people with comorbid anxiety and depression (Amati et al., 2018). A family history of alcohol problems tends to be associated with greater symptom severity and low treatment engagement among people with alcohol use disorders (Schuler et al., 2015). The impact of gender on addiction treatment response remains inconclusive (Amati et al., 2018).

Several studies have examined the moderating impact of baseline symptom severity on responses to substance use and mental health treatment (Reins et al., 2021; Witkiewitz et al., 2017) on various clinical outcomes. A recent systematic review by Amati and colleagues (2018) examined factors that impacted recovery among individuals receiving in person psychological therapy for common mental health disorders (e.g., depression and anxiety disorders). They found that greater severity of mental health symptoms at baseline negatively impacted treatment outcomes. Similar findings have been observed for alcohol misuse interventions, where baseline emotional severity (e.g., depression, anxiety, low life satisfaction; Haug & Schaub, 2016; Witkiewitz et al., 2017), alcohol use (Cochran et al., 2016; Witkiewitz et al., 2017), and cannabis use (Bahorik et al., 2018) predicted poorer treatment outcomes (e.g., retention, problem drinking).

In addition to participant background and symptom severity, it is also important to consider pre-treatment cognitive factors that may impact individuals' engagement with treatment content. The link between poorer executive functioning (EF) skills and alcohol use is well-established (Stacy & Wiers, 2010), and EF difficulties are also common among individuals struggling with depression and anxiety (Castaneda et al., 2008). This is particularly relevant in treatments like cognitive behavioural therapy (CBT) and motivational interviewing (MI). While engaging in these treatments, clients are required to formulate goals, monitor their mood and behaviour, and complete consistent homework - all tasks that require strong EF skills. Thus, people with low EF

skills may find CBT/MI particularly challenging. Indeed, Hunt and colleagues (2009) found that people with comorbid problem drinking and depression who were higher in EF had better CBT treatment responses. It follows that EF may differentially predict treatment outcomes and engagement among people with alcohol-emotional comorbidities (Domínguez-Salas et al., 2016).

Participant motivation has also been identified as an important predictor of success in substance use treatment (Martínez-González et al., 2020). For example, Cook and colleagues (2015) found post-treatment motivation to change (i.e., being in action) had a strong association with abstinence and non-problem drinking at a 9-month follow-up. An additional study found that attitudinal barriers and readiness for change were barriers to treatment uptake (Schuler et al., 2015). It follows that motivational barriers may have adversely impacted treatment efficacy for some participants in our *Take Care of Me* program for comorbid alcohol and emotional problems.

Aims and Objectives

The overarching goal of the current study was to conduct a secondary analysis of the data from the published *Take Care of Me* RCT (Frohlich et al., 2021) in order to understand heterogeneity in treatment responses. We used LCA to examine subgroups based on pre-treatment characteristics known to impact treatment response, namely *background factors* (i.e., gender, previous mental health diagnosis and treatment, family history of alcohol use), *symptom severity* (i.e., depression, anxiety, alcohol-related problems, cannabis use), *cognitive capacity* (i.e., EF), and *motivation*. It is unknown, however, what profiles of characteristics are most optimal for responding to a novel, integrated, online treatment, thus this analysis was exploratory in nature. We then used moderated regressions to explore differential program responses by subgroup for overall alcohol use, hazardous drinking, coping motives for drinking, and quality of life. The two drinking outcomes were included given the overarching goal of the intervention. Coping motives was selected as an additional outcome, given that it is a malleable cognitive factor that has been shown to be linked with severe alcohol problems (Stewart et al., 2016). Quality of life was selected as the fourth outcome because it has been shown to be an important indicator of success in mental health treatments (Kirouac et al., 2017). Overall, we expected to identify subgroups that showed differential responses to our treatment in terms of the four outcomes.

71

Method

Design

The main *Take Care of Me* study was a two-arm RCT where participants were randomly assigned to one of two conditions: the treatment condition ($n = 114$), or a psychoeducational control condition ($n = 108$). Participants in the treatment condition were provided access to 12 self-directed modules of CBT and MI to help with alcohol misuse and emotional difficulties (e.g., coping with cravings, and challenging negative thinking). Data was collected at baseline, at the end of treatment (i.e., 8 weeks), and at follow-up (i.e., 24 weeks). Participants received a $10 CAD Amazon gift card for each time point completed, for a total compensation of $30 CAD. Ethics approval was granted from the first author's institution and followed the previously published protocol (Frohlich et al., 2018). The trial was registered on clinicaltrials.gov (ID: NCT03406039). Participants ($N = 222$, $M_{age} = 24.6$, $SD_{age} = 4.37$, 67.6% female, 59.5% White) included all individuals who took part in the program. All participants reported at least moderate alcohol and emotional problems (see Frohlich et al., 2018 for detailed description of the study procedure, including full eligibility criteria). Participants were recruited using online ads, mass emails to university students, and posters in the community (e.g., addiction services, doctors' offices). Primary trial results have been recently published (Frohlich et al., 2021).

Measures

Latent Class Indicators.

Gender. Participants indicated (at baseline) whether they identify as a man, woman, transgender, non-binary, or other. Only one participant did not identify as either a man or woman, thus gender was coded as missing for this participant.

Psychiatric History. Participants were asked to report (at baseline) whether they had ever been diagnosed with a mental disorder, and if they had received psychological treatment in the past. If they answered "yes," which was coded as 1, they were asked to specify the diagnosis and form of treatment. Responses of "no" were coded as 0.

Family History of Alcoholism. Participants were also asked to report (at baseline) whether they believed their parent(s), sibling(s), grandparent(s), aunt(s), uncle(s), or biological cousins were problem drinkers. A binary variable was used (1 = any family history; 0 = no family history).

Cannabis Use. Participants' pre-treatment cannabis use was assessed using the cannabis item from the National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement

Screening Test (NIDA, 2009). Participants indicated how often in the past three months they used cannabis on a scale ranging from 0 *(Never)* to 4 *(Daily or Almost Daily).* Given low endorsement of use, we created a binary use variable (1 = any use; 0 = no use).

Executive Functioning. Pre-treatment EF was assessed at baseline using the 6-item WebExec (Buchanan et al., 2010). Responses ranged from 1 *(No Problems Experienced)* to 4 *(A Great Many Problems Experienced).* Higher scores mean greater subjective problems with EF. Good internal consistency was observed in our sample ($\alpha = 0.86$).

Motivation. Participants reported their levels of *readiness* and *confidence*, as well as the *importance* to make changes to improve their emotional and alcohol use issues. Responses ranged from 0 *(Not Important/Confident/Ready)* to 10 *(Very Important/Confident/Ready)*. Consistent with previous work, mean scores were created across the three items as a proxy variable for level of motivation at the outset of treatment (McNeish & Wolf, 2020).

Depression. Pre-treatment depression was assessed using the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977). Sum scores were calculated and the internal consistency at baseline was good in our sample ($\alpha = .86$).

Anxiety. The Generalized Anxiety Disorder Scale (GAD-7; Spitzer et al., 2006) was used to assess pre-treatment anxiety. Sum scores were used, and the internal consistency was good at baseline in our sample ($\alpha = .80$).

Alcohol Problems. Pre-treatment alcohol problems were assessed using the Alcohol Use Disorder Identification Test (AUDIT; Saunders et al., 1993), a 10-item self-report screener for past-year alcohol problems. The internal consistency at baseline was good in our sample ($\alpha = .86$).

Treatment Outcomes.

Weekly Alcohol Use. Alcohol use was assessed using the Timeline Follow-Back (TLFB; Sobell & Sobell, 1992) at all three timepoints. Participants reported the number of standard drinks consumed each day for the past week (prior to each assessment survey), and a sum score was then created (reflecting total weekly alcohol use). The TLFB is widely used and is considered a reliable and valid representation of alcohol use (Pedersen et al., 2012).

Hazardous Drinking. Hazardous drinking was captured using the sum of the first three items of the AUDIT (i.e., AUDIT-C) at all three timepoints. The AUDIT-C is a widely used measure of hazardous drinking within the addictions literature (Verhoog et al., 2020).

Coping Motives. Coping motives for drinking were measured using the three-item coping subscale from the Drinking Motives Questionnaire Revised – Short Form (Kuntsche & Kuntsche, 2009) at all three timepoints. Participants respond to questions based on how often they use alcohol for coping reasons (1 *[Never]* to 3 *[Almost Always]*). The internal consistency for this sample was good (α = .81-.84) across time points.

Quality of Life. Participants' quality of life was measured using the widely validated 26-item World Health Organization Quality of Life Assessment (WHOQOL Group, 1998) at all three timepoints. An overall sum score was created used and the internal consistency for this sample was good (α = .87-.93) across time points.

Data Analysis Plan

Data were analyzed in Mplus (Muthén & Muthén, 2012). Primary results are reported in the main trial publication (Frohlich et al., 2021). The 8-week retention rate was 55% (*n* = 122), with an equal number of participants in each condition. Attrition at 24-weeks was high, with only 75 out of 222 participants remaining. In the primary trial, we speculated that high attrition may have been due to the self-guided nature of the program, which may have subsequently resulted in lower engagement and accountability with the program content and follow-up assessments. Missing data was handled using full information maximum likelihood. Regarding the main analyses, we first used LCA (Jung & Wickrama, 2007) to determine unobserved subgroups of individuals based on our selected pre-treatment factors. A total of one-through-six latent class models were tested. The fit of each class was compared against a set of indices to determine the number of distinct groups that best fit the data, namely the Bayesian information criterion (BIC; Schwartz, 1978), entropy, and the parametric bootstrapped Lo (2001) likelihood ratio test (LRT; Jung & Wickrama, 2007). Lower BIC values are indicative of a better-fitting model (Raftery, 1995). Entropy is a classification statistic ranging from 0 to 1, with values closer to 1 suggesting a more accurate classification of participants within the model. The LRT examined whether adding an additional class resulted in a significantly better model fit, whereby non-significant values suggest that the model with one fewer class should be retained. Finally, it is recommended that class sizes comprised of less than 5% of the total sample should not be retained. In addition to examining the fit statistics to determine model fit, it was also important to consider the theoretical interpretability within the data (Yang, 2006), such that the patterns observed among each class are clinically meaningful based on previous research.

Next, moderated regressions were used to explore the intervention by class interactions predicting immediate and longer-term follow-up outcomes. Dummy coded variables were used to represent the class variable and were used to create interaction terms with treatment condition. Class mean differences on all outcomes were examined first by conditioning models on the treatment condition, followed by re-conditioning on the control condition. Baseline levels of each outcome were included in the regression models as a covariate.

Results

Descriptive Statistics and Preliminary Analyses

Participants in the treatment group completed an average of 5.72 (SD = 5.00) modules, and only 28% completed all 12 modules. We used independent t-tests (continuous variables) and chi-square tests of independence (dichotomous variables) to examine whether individuals who completed vs. did not complete assessments differed on baseline characteristics. We observed significant differences between individuals with missing vs. complete data on the TLFB ($t(220)$ = 2.10, p = .037), full AUDIT ($t(218)$ = 2.94, p = .004), AUDIT-C ($t(218)$ = 2.69, p = .008), EF ($t(217)$ = 2.16, p = .032), and family history of alcoholism $\chi^2(1, N = 222)$ = 9.95, p = .002).

Determining the Number of Latent Classes

See Table 4.1 for the fit statistics for models with one-through-six classes. LRT values were significant for each class solution, suggesting that it was important to examine the remaining fit indices. BIC values decreased from one-to-five class solutions. Class three had the highest entropy value and classification probabilities for each class exceeded 0.93, suggesting that it had the best classification accuracy. The model with four classes had subpar entropy, and models with five and six classes had some very small class sizes (<5% of the total sample). To aid in our decision making, we also considered the interpretability of the data by plotting the four-class solution. Inspection of the plots revealed minimal and less clinically meaningful differences between the three- and four-class solutions, including two groups with small sample sizes and considerable overlap on many variables. Alternatively, the three-class solution supported three distinct groups with clinically meaningful patterns on the grouping variables. Taking into consideration both fit statistics and interpretability, we had sufficient support to retain a 3-class solution to the data.

Class Characteristics

Class characteristics and group differences for pre-treatment factors are in Table 4.2 and Figures 4.1 and 4.2. The largest group was labelled the *low severity* class (55.4% of the sample) which had the lowest endorsement of previous mental health diagnoses and treatment, and the lowest levels of baseline alcohol problems, depression, anxiety, and executive dysfunction. The second largest group was labelled the *moderate severity* class (25.7% of the sample). All people in this group endorsed a previous mental health diagnosis and mental health treatment. This group was also characterized by moderate baseline levels of alcohol problems, depression, anxiety, and executive dysfunction. The remainder of participants were classified into the *high severity* class (18.9% of the sample). These people had the highest endorsement of a family history of alcoholism, as well as the highest levels of alcohol problems, depression, anxiety, and executive dysfunction. There were no significant differences between classes for gender, cannabis use, and motivation.

Regression Analyses

Separate moderated regression analyses were run for each outcome variable at both the end of treatment and at follow-up. The latent classes were summarized by two dummy codes in the models, with the low severity group as the reference class. Thus, we compared interactions between class membership and treatment condition for the high severity class versus the low severity class, and the moderate severity class versus the low severity class. Class mean differences were examined first by conditioning the model on the treatment condition, followed by re-conditioning the model to get class mean differences in the control group. We expected class differences to emerge in the treatment (and not in the control) group. Given the relatively low engagement, we also conducted an exploratory analysis on whether subgroups differed on module completion. There was no significant effect of group membership on number of modules completed [$F(2,111) = .374$, $p = .689$].

Total Weekly Alcohol Use

There were no significant class by intervention interactions at the end of treatment on the TLFB (see Table 4.3). However, at follow-up, the class by condition interactions were statistically significant. In the treatment group, individuals in the high severity group consumed more alcohol at follow-up than the low severity group and participants in the moderate severity group consumed less alcohol than the low severity group. We did not observe mean differences between classes

when the model was reconditioned on the control group (High vs. Low Class, $B = 0.41$, $SE = 3.34$, $p = .903$; Moderate vs. Low Class, $B = -1.42$, $SE = 1.68$, $p = .339$).

Hazardous Drinking

There was a significant class by intervention interaction for predicting hazardous drinking at the end of treatment (see Table 4.4). In the treatment condition, individuals in the moderate severity group had lower AUDIT-C scores at the end of treatment compared to those in the low severity group. At follow-up, a significant class by intervention interaction effect suggested that, in the treatment condition, people in the high severity group had higher AUDIT-C scores than the low severity group. In the control condition, we did not observe mean differences between classes at the end of treatment (High vs. Low Class, $B = 0.16$, $SE = 0.75$, $p = .835$; Moderate vs. Low Class, $B = 0.35$, $SE = 0.53$, $p = 0.505$) or at follow-up (High vs. Low Class, $B = -0.43$, $SE = 0.82$, $p = .606$; Moderate vs. Low Class, $B = -0.77$, $SE = 0.57$, $p = .176$).

Coping Motives

There were no statistically significant class by intervention interactive effects on coping motives at the end of treatment or at follow-up (see Table 4.5).

Quality of Life

There were no significant class by intervention interaction effects on quality of life at the end of treatment (see Table 4.6). However, at follow up, a significant class by intervention interaction effect suggested that, in the treatment group, participants in the high severity group had lower quality of life scores than the low severity group. We did not observe mean differences between classes when the model was reconditioned on the control group (High vs. Low Class, $B = 2.59$, $SE = 3.12$, $p = .408$; Moderate vs. Low Class, $B = 1.66$, $SE = 2.78$, $p = .550$).

Discussion

Given the need for accessible, integrated treatments for young adults struggling with comorbid alcohol misuse and emotional problems, we developed and examined the efficacy of the *Take Care of Me* program. We found promising evidence for 8-weeks of minimally guided, internet-based, integrated treatment for depression, hazardous drinking, psychological quality of life, and treatment readiness (Frohlich et al., 2021). However, we did not observe significant reductions on our primary outcome of interest (i.e., total alcohol use), and were left to speculate why this may have been the case. Given our inclusive recruitment strategies (i.e., moderate or

greater difficulties with alcohol use, depression, and/or anxiety), it was important to conduct secondary analyses of the trial findings to clarify potential differential responses to the treatment.

Using subtyping analyses, we were able to distinguish individuals based on shared patterns of pre-treatment characteristics, with evidence for low-, moderate-, and high-severity groups. This is one of the first studies of its kind to use LCA as a secondary analysis for an integrated treatment with the goal of capturing distinct participant profiles and heterogeneity in treatment responses (Lanza & Rhoades, 2013). While exploratory in nature, the emergence of three distinct groups is consistent with previous studies that observed varying patterns of risk for alcohol use and co-occurring emotional difficulties (e.g., Müller et al., 2020). Furthermore, participants had differential responses to treatment depending on their group membership. Individuals in the high severity group had higher levels of alcohol consumption and hazardous drinking, and lower quality of life at follow-up relative to the low severity group. This is consistent with previous research that found pre-treatment family history of alcohol problems, baseline symptom severity, and EF deficits predicted poorer responses to alcohol use treatment (Domínguez-Salas et al., 2016; Haug & Schaub, 2016; Schuler et al., 2015). Interestingly, participants in the moderate group had significantly lower alcohol consumption at follow-up, and lower hazardous drinking at end-of-treatment relative to the low severity group, suggesting that they responded best to the program. It is possible that individuals in the high severity group were less engaged with the program and thus benefited less from treatment, whereas those in the moderate group may have had more to gain than the low group while also being more engaged with the treatment.

Given the novelty and integrated nature of the *Take Care of Me* program, we were inclusive in our recruitment efforts, and were hopeful that higher-severity individuals would benefit from the program. Unfortunately, this was not the case. However, the results are consistent with previous research that found higher baseline symptom severity resulted in greater perceived barriers to treatment and poorer clinical outcomes for alcohol misuse treatment (Schuler et al., 2015; Haug & Schaub, 2016). Again, we were speculating that similar moderators would be relevant for online and self-guided treatments based on literature from relevant addiction treatment (e.g., outpatient CBT and MI), which appears to be the case. This is important from a clinical standpoint, as young adults with moderate symptomology may be an optimal group to target for early intervention using efforts such as minimally guided, internet-based treatment, whereas those with higher severity may require additional or more intensive treatment.

This secondary analysis shares limitations with the main manuscript, such as substantial and biased attrition at follow-up, and relatively low engagement, which were discussed in detail previously (see Frohlich et al., 2021). As such, results of both the primary trial and those in the current manuscript should be considered preliminary in nature. First, while we were sufficiently powered to run the desired analyses, our sample size was still relatively small, and this may have prevented us from finding additional meaningful subgroups. Second, due to our modest sample size, we opted to use a classify and analyze approach to examining subgroup differences on treatment outcomes rather than using the preferred three-step approach (i.e., where the LCA and regression model for class differences on distal outcomes is done within the same model). While we had very high classification accuracy (which offsets the main concern about classify and analyze approaches), future studies using the *Take Care of Me* program should recruit sufficiently larger sample sizes to use the three-step approach and, ideally, evaluate class differences on all outcomes simultaneously. Third, we only looked at short-term follow-up effects (i.e., 24-weeks), whereas helpful information about program efficacy and differential responses could be gleaned from longer-term assessments. Future versions of the program should prioritize strategies designed to improve engagement, increase sample size, and mitigate attrition. Finally, our measures of EF, family and mental health history, and cannabis use were brief and were selected to reduce participant burden. However, it is important for future work to expand on these broad measures to get a more nuanced understanding of the impact of pre-treatment factors on treatment response.

The initial results of the *Take Care of Me* trial were promising. However, given our inclusive recruitment efforts, it was important to conduct secondary analyses to gain insight into differential treatment responses. We found evidence for three distinct subgroups varying in severity based on pre-treatment factors. Individuals in the moderate severity group experienced the greatest benefits from the program relative to the high- and low-severity groups. Future programs should consider important pre-treatment factors (e.g., symptoms severity, EF) and tailor interventions accordingly to maximize treatment effectiveness.

Table 4.1

Fit Indices for One to Six Latent Class Growth Models

Number of Classes	Fit Statistics			Smallest Group (%)
	SSBIC	Entropy	LRT	
1-Class	7959.544	n/a	n/a	100%
2-Class	7827.195	0.775	<.001	34%
3-Class	**7759.011**	**0.842**	**<.001**	**18.91%**
4-Class	7742.947	0.773	<.001	5%
5-Class	7729.312	0.816	<.001	3%
6-Class	7718.877	0.802	0.013	2.20%

Note. BIC = Sample-Size Adjusted Bayesian Information Criterion; LRT = Likelihood Ratio

Test. Bold print indicates the retained class model.

Table 4.2

Class Characteristics and Statistical Tests of Group Differences from LCA

	Class			
	1 *Moderate* (*n* = 57)	2 *High* (*n* = 42)	3 *Low* (*n* = 123)	
Continuous Variables				
		M (SD)		ANOVA
Executive Functioning	16.84 (3.91)	20.2 (3.32)	14.07 (3.70)	$F(2,216) = 46.12, p < .001$ $\eta^2 = .299$
Motivation	7.20 (1.49)	7.33 (1.52)	7.30 (1.62)	$F(2,219) = .11, p = .897$ $\eta^2 = .001$
Depression	35.56 (8.27)	44.50 (6.66)	28.02 (7.05)	$F(2,219) = 83.89, p < .001$ $\eta^2 = .434$
Anxiety	13.46 (4.19)	17.02 (2.82)	10.49 (3.70)	$F(2,219) = 46.12, p < .001$ $\eta^2 = .299$
Alcohol Problems	17.56 (7.43)	20.00 (9.04)	15.33 (7.50)	$F(2,217) = 6.00, p = .003$ $\eta^2 = .052$
Dichotomous Variables				
		n (%)		Chi-Square
Gender				
Male	15 (26.8)	11 (26.2)	45 (36.9)	$X^2(2) = 2.67, p = .263,$
Female	41 (73.2)	31 (73.8)	77 (63.1)	Cramer's V = .11
MH Diagnosis				
No	0 (0)	38 (90.5)	111 (90.2)	$X^2(2) = 155.22, p < .001$
Yes	56 (100)	4 (9.5)	12 (9.8)	Cramer's V = .84
MH Treatment				
No	0 (0)	35 (83.3)	112 (91.8)	$X^2(2) = 153.59, p < .001,$
Yes	57 (100)	7 (16.7)	10 (8.2)	Cramer's V = .83
Family Hx				
No	17 (29.8)	4 (9.5)	26 (21.1)	$X^2(2) = 5.97, p = .050,$
Yes	40 (70.2)	38 (90.5)	97 (78.9)	Cramer's V = .16
Cannabis Use				
No	21 (36.8)	20 (47.6)	47 (38.2)	$X^2(2) = 1.41, p = .494,$
Yes	36 (63.2)	22 (52.4)	76 (61.8)	Cramer's V = .08

Note. MH = Mental Health. Family Hx = A family history of alcoholism. ANOVAs were conducted for all continuous variables, and chi-square tests were conducted for all dichotomous variables.

Table 4.3

Moderated Regression Analysis for Alcohol Consumption at T1 and T2

Parameter	Estimate	Std. Error	*B*	t	Sig.
T1 (End of Treatment)					
Baseline TLFB	0.42	0.12	0.66	3.63	< .001
Intervention	-3.52	2.18	-0.16	-1.62	0.11
Class 2 vs. Class 3	-0.84	2.84	-0.03	-0.30	0.77
Class 1 vs. Class 3	-2.65	2.82	-0.10	-0.94	0.35
Intervention by Class 2 vs. Class 3	-1.64	3.65	-0.04	-0.49	0.65
Intervention by Class 1 vs. Class 3	1.45	3.42	0.04	0.41	0.68
R-square	0.47	0.13	--	3.61	< .001
T2 (Follow-up)					
Baseline TLFB	0.12	0.06	0.20	2.13	0.03
Intervention	2.64	2.95	-0.12	-0.89	0.37
Class 2 vs. Class 3	22.57	3.27	0.82	6.89	< .001
Class 1 vs. Class 3	-8.18	2.99	-0.33	-2.74	0.01
Intervention by Class 2 vs. Class 3	**-22.16**	**4.17**	**-0.59**	**-5.32**	**< .001**
Intervention by Class 1 vs. Class 3	**6.76**	**3.35**	**0.22**	**2.02**	**0.04**
R-square	0.59	0.07	--	8.41	< .001

Note. For the interaction term, treatment group is the reference group. Significant interactions are

bolded. TLFB = Timeline Follow-Back.

Table 4.4

Moderated Regression Analysis for Hazardous Drinking at T1 and T2

Parameter	Estimate	Std. Error	*B*	t	Sig.
T1 (End of Treatment)					
Baseline AUDIT-C	0.68	0.10	0.64	7.96	< .001
Intervention	-1.50	0.36	-0.32	-4.22	< .001
Class 2 vs. Class 3	-1.48	0.63	-0.25	-2.33	0.020
Class 1 vs. Class 3	-1.27	0.47	-0.23	-2.68	0.007
Intervention by Class 2 vs. Class 3	1.63	0.99	0.20	1.65	0.100
Intervention by Class 1 vs. Class 3	**1.62**	**0.72**	**0.24**	**2.26**	**0.024**
R-square	0.49	0.08	--	6.43	< .001
T2 (Follow-up)					
Baseline AUDIT-C	0.47	0.11	0.39	4.30	< .001
Intervention	-0.99	0.60	-0.19	-1.66	0.10
Class 2 vs. Class 3	3.77	0.72	0.55	5.22	< .001
Class 1 vs. Class 3	-2.10	0.84	-0.34	-2.52	0.01
Intervention by Class 2 vs. Class 3	**-4.19**	**1.02**	**-0.45**	**-4.12**	**< .001**
Intervention by Class 1 vs. Class 3	1.33	1.01	0.17	1.32	0.19
R-square	0.54	0.06	--	9.91	< .001

Note. For the interaction term, treatment group is the reference group. Significant interactions are bolded. AUDIT-C = Brief version of the Alcohol Use Disorder Identification Test.

Table 4.5

Moderated Regression Analysis for Coping Motives at T1 and T2

Parameter	Estimate	Std. Error	*B*	t	Sig.
T1 (End of Treatment)					
Baseline DMQR-SF (Cop)	0.61	0.07	0.62	8.45	$< .001$
Intervention	-0.35	0.18	-0.17	-1.20	0.05
Class 2 vs. Class 3	0.31	0.31	0.11	0.98	0.33
Class 1 vs. Class 3	0.03	0.22	0.01	0.12	0.91
Intervention by Class 2 vs. Class 3	0.14	0.40	0.04	0.36	0.72
Intervention by Class 1 vs. Class 3	0.55	0.32	0.19	1.74	0.08
R-square	0.49	0.06	--	7.89	$< .001$
T2 (Follow-up)					
Age	0.00	0.03	-0.01	-0.07	0.94
Baseline DMQR-SF (Cop)	0.43	0.10	0.43	4.31	$< .001$
Intervention	-0.07	0.21	-0.04	-0.24	0.81
Class 2 vs. Class 3	-0.37	0.28	-0.14	-1.30	0.20
Class 1 vs. Class 3	0.18	0.44	0.07	0.30	0.69
Intervention by Class 2 vs. Class 3	1.10	0.61	0.30	1.80	0.07
Intervention by Class 1 vs. Class 3	0.27	53	0.10	0.50	0.62
R-square	0.25	0.08	--	2.97	0.003

Note. For the interaction term, treatment group is the reference group. Significant interactions are bolded. DMQR-SF (Cop) = Drinking Motives Questionnaire Revised – Short Form, coping subscale.

Table 4.6

Moderated Regression Analysis for Overall Quality of Life at T1 and T2

Parameter	Estimate	Std. Error	*B*	t	Sig.
T1 (End of Treatment)					
Baseline QOL	0.80	0.09	0.63	8.97	$< .001$
Intervention	1.65	1.95	0.08	0.84	0.40
Class 2 vs. Class 3	-3.49	2.57	-0.13	-1.36	0.17
Class 1 vs. Class 3	-0.99	2.33	-0.04	-0.43	0.67
Intervention by Class 2 vs. Class 3	1.88	3.75	0.05	0.50	0.62
Intervention by Class 1 vs. Class 3	2.05	3.61	0.07	0.57	0.57
R-square	0.46	0.08	--	6.07	$< .001$
T2 (Follow-up)					
Baseline QOL	0.59	0.14	0.46	4.33	$< .001$
Intervention	2.17	2.52	0.10	0.86	0.30
Class 2 vs. Class 3	-12.57	2.15	-0.45	-5.85	$< .001$
Class 1 vs. Class 3	4.43	6.49	0.18	0.68	0.49
Intervention by Class 2 vs. Class 3	**15.15**	**3.90**	**0.39**	**3.88**	**$< .001$**
Intervention by Class 1 vs. Class 3	-2.77	6.96	-0.10	-0.40	0.69
R-square	0.44	0.09	--	4.86	$< .001$

Note. For the interaction term, treatment group is the reference group. Significant interactions are bolded. QOL = World Health Organization Quality of Life Assessment.
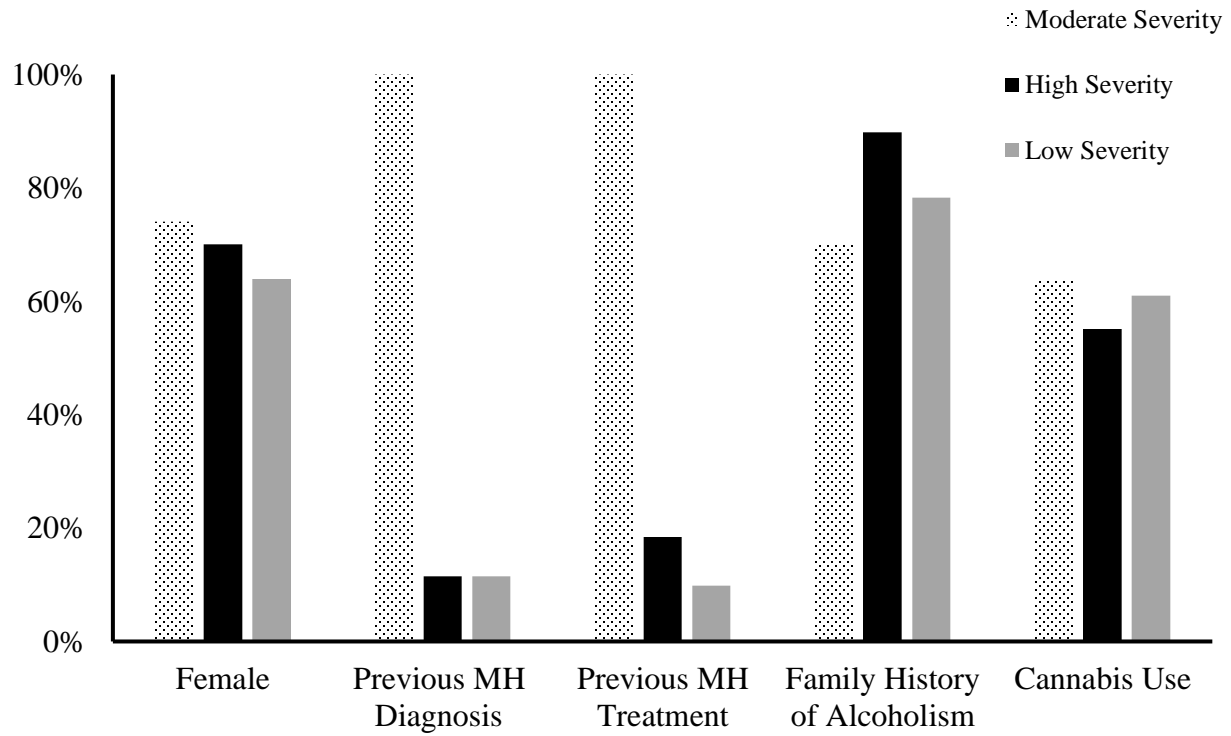
Figure 4.1. Class differences on binary indicators. *Note.* Percentages indicate the proportion of individuals in each group that endorsed the variable.
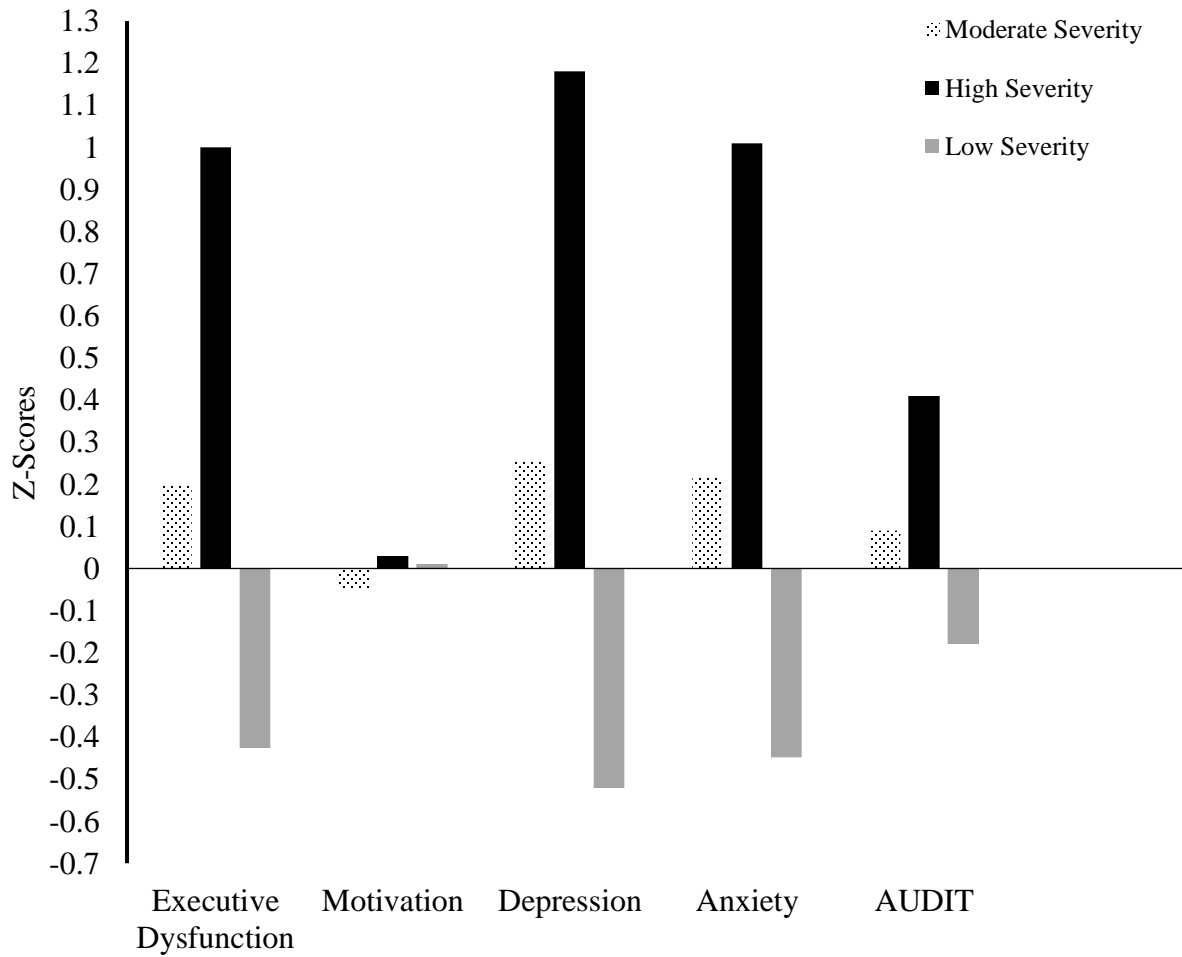
Figure 4.2. Standardized class differences on continuous indicators.

CHAPTER 5

GENERAL DISCUSSION

Summary of Findings

A review of clinical research within the addiction domain revealed a lack of accessible, online, integrated treatments for comorbid alcohol misuse and emotional difficulties (i.e., depression and anxiety) among young adults. This was striking as young adults are struggling with higher rates of comorbid alcohol misuse and emotional problems than any other age group (Gustavson et al., 2018), yet few access the support they need due to barriers such as stigma, cost, and desire for anonymity (Capron et al., 2017; Ebert et al., 2019). Therefore, the overarching goal of this dissertation was to gain initial evidence for an adapted online, integrated, minimally guided treatment for young adults endorsing moderate or greater difficulties with comorbid alcohol misuse and emotional difficulties (i.e., depression and/or anxiety). The results of this dissertation offer preliminary support for the efficacy of *Take Care of Me*, in terms of improving hazardous drinking, mood, and quality of life among young adults. This dissertation also provides insight into moderating factors that help explain differential responses to the treatment program. Overall, the results add to the growing body of literature examining online, integrated interventions for treating common mental health concerns, and have implications for improving the well-being of young adults in the population.

Study 1

The main objective of study 1 was to examine the efficacy of an 8-week, minimally guided intervention developed for young adults struggling with comorbid alcohol misuse and emotional difficulties (i.e., depression and anxiety) using principles of CBT and MI. This was inspired by the *Take Care of You* program, an online intervention offered in German, that integrated treatment for alcohol misuse and depression (Baumgartner et al., 2021; Schaub et al., 2016), as well as the recent trial conducted in Estonia (Augsburger et al., 2021). We adapted this program for use in English and added content for anxiety to address the broader spectrum of emotional problems experienced by young adults. Unexpectedly, significant reductions on the primary outcome of interest, total alcohol consumption, were not observed at the end treatment or at follow-up relative to the psychoeducational control group. While this finding was inconsistent with hypotheses, it is possible that some individuals who participated in the program reduced the overall risk of their drinking patterns without reducing the quantity of alcohol

consumed in a given week, as overall consumption is only one aspect of problematic alcohol use. For example, an individual who initially engaged in one heavy drinking episode per week (e.g., consuming seven drinks on a Saturday) may have changed their drinking habits to having one drink per night on each day of the week. In this case, the overall quantity of alcohol that they consumed would be unchanged, but hazardous drinking behaviour (i.e., drinking a large amount in one sitting) would be reduced. This is supported by the finding that significant secondary effects were observed for hazardous drinking (i.e., risky patterns of consumption) at the end of treatment. While the TLFB is commonly used as a primary outcome within addictions research, in retrospect it may not have most accurately captured the benefits of the integrated program. Future iterations of the trial should utilize a more appropriate outcome (e.g., AUDIT-C), as obtaining a measure of overall alcohol consumption may not sufficiently portray benefits of the intervention from an overall risk perspective. Indeed, a recent study found that the AUDIT was more sensitive at detecting AUDs among young people aged 15-24 than the TLFB (Kuteesa et al., 2019), and recent alcohol use interventions have utilized the AUDIT-C as a primary outcome measure (e.g., Tait et al., 2019). Furthermore, the AUDIT-C has been found to be a reliable predictor of need for integrated care among individuals struggling with alcohol misuse (Naps et al., 2018). Taken together with the results of the current study, the AUDIT-C may be both a meaningful and sensitive measure to include as a primary outcome in integrated alcohol use and emotional interventions.

Consistent with the second hypothesis, significant improvements were also observed for depression, psychological quality of life, and readiness to change at the end of treatment. These findings add strength to the short-term benefits of the program on these outcomes and are consistent with findings from similar trials that observed significant reductions in depression (Deady et al., 2016; Baumgartner et al., 2021) and quality of life (Kirouac et al., 2017) at the end of treatment. We did not observe significant reductions in symptoms of anxiety. One possible explanation for this null result is the difference in pre-treatment severity of the two emotional challenges. More specifically, baseline symptoms of anxiety were in the moderate range at baseline for both the treatment and control groups, whereas baseline depression fell in the severe range for both the treatment and control groups. Given that mood symptoms were more severe than anxiety symptoms in the sample at the outset, it is possible that individuals had more

substantial changes to make in this area, and thus significant reductions were observed for depressive but not anxious symptoms.

Due to the substantial attrition experienced at follow-up that was biased towards the treatment condition, the study was not sufficiently powered to make any formal conclusions about long-term effects of the program. However, among those that remained in the program, effects on hazardous drinking were maintained, and individuals reported significant improvements in their psychological and environmental quality of life. While this cannot be taken as robust evidence of the long-term efficacy of the program, it is promising that outcomes were in the expected direction. Additional trials of the program that mitigate substantial attrition will determine whether benefits on several alcohol use and mental health outcomes are in fact observed at follow-up.

The results of study 1 are consistent with previous interventions that have yielded small but significant improvements using integrated CBT and MI for alcohol-emotional comorbidity treatment (e.g., Deady et al., 2016; Schouten et al., 2021). Findings from the current study are partially consistent with the original trial conducted by Baumgartner and colleagues (2021). Contrary to the current study, they did observe significant reductions on overall alcohol use at both 3- and 6-month follow-ups. However, results of the current program are consistent with the observed significant reductions on both hazardous drinking and depressive symptoms at both follow-ups. The current results are also consistent with the results from the Estonia trial (Augsberger et al., 2021), where small but significant reductions in alcohol-related problems were observed at follow-up. Taken together, the results of these three versions of the trial provide promising initial evidence for the *Take Care of Me* program.

The substantial and biased attrition experienced at follow-up is also not unique to the current study and has been noted as a consistent challenge within addiction research and for online interventions (Hadjistavropoulos et al., 2020). It is possible that despite the strategies utilized in order to mitigate potential attrition (e.g., automated feedback and reminders, engaging content within modules such as activities and videos, a personal companion), this was not sufficient to prevent a large proportion of the sample from being lost at follow-up. Despite some of the challenges experienced with the trial, those that remained did experience some notable improvements (e.g., depression, quality of life). Additional trials of *Take Care of Me* will support the adaptation and implementation of programs of this nature on a larger scale.

Study 2

        Participants endorsing moderate or greater alcohol misuse-emotional difficulties were included in the program, with the goal of supporting as many individuals as possible. Given the inclusive nature of the program regarding symptomology and the surprising lack of effects on alcohol consumption, the purpose of study 2 was conduct a secondary analysis of the dataset to capture heterogeneity in responses to treatment. Results revealed three distinct groups of participants within the *Take Care of Me* trial, who differed in pre-treatment severity based on background risk factors, symptom severity, and cognitive capacity. Those in the higher-risk group who received treatment did not experience the same benefits as those in the low-risk group, while moderate severity individuals seemed to respond best to the program overall. More specifically, relative to the low severity group, high severity individuals in the treatment condition reported higher alcohol consumption and hazardous drinking and lower quality of life at follow-up, whereas moderate severity individuals in the treatment condition had lower alcohol consumption at follow-up, and lower hazardous drinking at end-of-treatment.

        Overall, the results of study 2 are consistent with previous subtyping studies that have differentiated individuals with comorbid alcohol misuse and emotional difficulties based on level of severity (Müller et al., 2020; Orui et al., 2020), as well as the findings that suggest not all individuals will respond to treatment the same way given individual difference factors. It follows logically that distinct classes of severity emerged in the current sample given the inclusivity in recruitment. As discussed, limited trials of this nature existed in the broader literature prior to the current study, much less secondary analyses delineating relevant pre-treatment factors to include in moderation analyses. Therefore, the results of study 2 shed light on pre-treatment factors that are likely to be relevant in secondary analyses of integrated, online trials for comorbid alcohol use and emotional difficulties.

        Consistent with previous research that outlined the importance of examining background factors (e.g., sociodemographic information, family history, mental health history) as moderators of treatment response (Amati et al., 2018; Haug & Schaub, 2016), individuals in the current sample were distinguished based on previous mental health diagnosis and treatment, as well as a family history of addiction. While previous treatment was examined more generally (rather than success in said treatment), results suggest that this along with mental health and family history were relevant to the current intervention. This also adds to the inconclusive literature on mental

health diagnosis being important to consider (Amati et al., 2018). While gender was included as a grouping variable, there were no significant differences between classes based on identifying as male or female. This could be due to the fact that a large proportion (i.e., 67.6%) of the sample identified as female. However, this is consistent with findings that have not found gender to be associated with intervention outcomes within general psychotherapy research (Constantino et al., 2021; Vîslă et al., 2021). Furthermore, future research will need to consider meaningful ways to examine gender in studies of this nature that do not reduce the construct to a binary system (i.e., male-female), as this fails to consider the disproportionately high mental health concerns faced by individuals who do not conform to this system (e.g., transgender, non-binary; Stanton et al., 2021; Valentine & Shipherd, 2018). Given that only one participant in the sample identified as non-binary, analyses of this nature could not be conducted in the current study.

Regarding baseline symptom severity, results of subtyping analyses are consistent with previous research that has found baseline symptom severity (i.e., depression, anxiety, alcohol-related problems) to predict poorer response to alcohol-use and mental health interventions (Amati et al., 2018; Reins et al., 2021; Witkiewitz et al., 2017). These findings also add strength to the notion that determining an individual's level of symptomology at baseline may be an important predictor of their subsequent response to treatment, which could have implications for the intensity, modality, and duration of treatment offered in the future. As predicted, EF also differentiated the severity of individuals and predicted poorer responses to treatment. This is consistent with previous research (Domínguez-Salas et al., 2016; Hunt et al., 2009), and suggests that these individuals may have had lower cognitive capacity (e.g., planning, organization, self-control) to engage in a minimally guided treatment, and thus did not experience the same benefits as those in lower severity groups. Interestingly, motivation did not distinguish individuals within the sample. This is inconsistent with previous research that found motivation (e.g., being in action) and attitude towards treatment to be significant predictors of treatment response (Cook et al., 2015; Schuler et al., 2015). This may have been due to the fact that a proxy item was created to reflect overall motivation based on three single items (i.e., importance, confidence, readiness). While there was both operational and methodological support to do so (McNeish & Wolf, 2020), it is possible that variability in motivation may have been more accurately captured using a full self-reported measure of motivation rather than just the three distinct facets (e.g., the Readiness to Change Scale; Rollnick et al., 1992). The selection of three

single items was done in order to reduce participant burden given the inclusion of many clinical variables at each time point. Furthermore, for those who have not previously engaged in treatment, it may have been that many young adults did not have a realistic understanding of their readiness to do the work of therapy and thus may have overestimated readiness. Future studies could measure treatment readiness again partway into the program once they better understand what it is required of them.

The observed differences in treatment response based on group membership is also consistent with previous research that found individuals with higher symptom severity at baseline did not experience the same benefits of online mental health and addiction treatment relative to individuals with lower pre-treatment severity (Reins et al., 2021; Haug & Schaub, 2016). It is possible that higher risk individuals may not be as well-suited for minimally guided interventions given the level of motivation and mental capacity required to navigate treatment independently (Babor et al., 2017). Alternatively, moderate severity individuals may reflect an optimal group for minimally guided, online treatment, who can both engage with and experience benefits from this format. Taken together, valuable information was gleaned regarding program efficacy and future iterations of the program by conducting follow-up analyses in that not all participants responded to *Take Care of Me* in the same way.

Implications

Theory and Research

The current intervention was designed with the reciprocal associations model in mind (Stewart et al., 2016). While it is outside the scope of the current research program to comment on directional correlations between alcohol misuse and emotional symptomology during the trial, initial efficacy evidence supports the notion that targeting alcohol misuse is important for reducing emotional distress, and strategies for emotional difficulties likewise may reduce the risk of hazardous drinking. If evidence continues to mount for the use of integrated treatments for comorbid alcohol misuse and emotional problems, determining the directionality of change will add support to the reciprocal relations theory in practice. Recent research in the field has highlighted important considerations when examining bidirectional associations between variables within addiction research (Littlefield et al., 2021). Most commonly, directional relations are examined using cross-lagged panel models (CLPM). However, authors of a current study discuss how CLPM can be problematic as it does not sufficiently distinguish between- and

within-person variability (Littlefield et al., 2021). The results of study 2 add strength to the notion that individual differences are paramount to consider within complex dynamic relationships between variables (i.e., emotional symptoms and drinking behaviours). Indeed, Littlefield and colleagues (2021) provided recommendations for alternative methods for gathering temporal evidence between constructs that better account for trait like stability among individuals, such as random-intercept CLPM, or latent-curve modelling with structured residuals (Littlefield et al., 2021). Furthermore, the selection of models should be driven by theory, empirical assumptions, and practicality. Overall, considering the optimal way to conduct temporal analyses and thus gather empirical evidence for reciprocal relations theory will be important in future versions of similar integrated treatment trials for co-occurring alcohol and emotional problems.

The methods utilized (i.e., LCA and moderated regressions) in study 2 also provide support for using subtyping analyses as a clinically meaningful way to capture distinct groups and examine moderation in clinical trials, particularly when underlying subgroups are expected, as is the often case with samples consisting of complex mental health concerns (Lanza & Rhoades, 2013). This is still a relatively novel, albeit meaningful way of conducting follow-up analyses in clinical research, relative to examining each potential moderating factor separately (Castro et al., 2017). The presence of distinct profiles based on shared characteristics is common in addiction and clinical research (Cochran et al., 2016; Orui et al., 2020), and LCA allowed for the consideration of multiple characteristic interactions simultaneously. This is important for researchers in the field, who may opt to use LCA as a way of examining risk patterns within their sample in a more fulsome way going forward (Müller et al., 2020).

Clinical

There are clinical implications of the current research. First, the results of the main trial findings suggest that the *Take Care of* Me program, the first of its kind available in English, is a promising initial iteration of the intervention. If efficacy evidence for future trials of the program continues to mount, it could be readily adapted for use in different settings and implemented widely across organizations and institutions (e.g., schools, universities, workplaces, hospitals, community organizations). Widespread implementation of the program could result in at least moderate benefits for both individuals (e.g., reduction in hazardous drinking, improved mood and quality of life) and society at large (e.g., reduced disease burden). While the program may

require adapting (e.g., increased engagement, larger samples recruited and retained) and replication studies are needed, the overall format is promising as an accessible and cost-effective mental health program. Furthermore, the results suggests that minimally guided, online, integrated programs may provide a promising initial step for individuals who may otherwise not have accessed services due to barriers (e.g., stigma, accessibility, cost, desire for anonymity). For individuals experiencing less severe symptoms, the program may reduce the likelihood of developing severe disorder by promoting more adaptive coping with mental health challenges. Alternatively, for individuals experience greater symptom severity, participating in such programs may be foundational for subsequent interventions that are more intensive (e.g., in-person, hospital-based programs, residential care).

The results also have implications for mental health treatment of young adults more generally. Young adults are vulnerable to the effects of alcohol misuse and emotional difficulties that may have lifelong consequences if they remain unaddressed. The evidence is promising for a brief, integrated intervention that may prevent the development of severe mental health issues among young adults if implemented. While mental health service utilization among young adults remains low, this may be slowly shifting. Indeed, a recent report revealed that college students' willingness to utilize mental health services increased as the years they were surveyed went on (Oswalt et al., 2020). This is particularly relevant in the context of a global pandemic, where the digital era of healthcare has been exacerbated. Hawke and colleagues (2021) examined the perspectives of youth between the ages of 14 and 28 on virtual mental health and substance use services during the pandemic. They found that many individuals with internalizing disorders (e.g., depression, anxiety, trauma) and substance use disorders reported a willingness to engage in individual virtual services (72.1% and 78.9%, respectively). Qualitative data also revealed that youth identified convenience, accessibility, low cost, privacy, and anonymity as components of virtual services that they valued. This insight is important, as brief, online, integrated programs can satisfy the preferences of young adults, and take advantage of a shift where this age group may be more open to utilizing online mental health supports. Furthermore, programs of this nature could be incorporated into service delivery models for young adults, where accessible and youth-friendly formats are paramount (Settipani et al., 2019). Taking into consideration the shifting attitudes of young people for seeking services, especially online, now is an opportune time for researchers and practitioners alike to develop effective interventions for this population.

It was important to be as inclusive as possible with recruitment for *Take Care of Me* to ensure that all those who may have benefited from the program had access to it, including higher-severity individuals. Unfortunately, high severity individuals did not respond as well to the treatment relative to those in the lower-severity groups. These results suggest that the current program may be relevant to the Screening, Brief Intervention and Referral to Treatment (SBIRT) literature (Babor et al., 2017; Del Boca et al., 2017), where individuals are pre-screened for substance use problems, and subsequent treatment recommendations are made based on symptom severity. For example, pre-screened individuals with moderate problems are recommended brief, minimally guided treatment, similar to the current intervention, while those meeting criteria for a probable substance-use disorder are referred for more intensive treatment (e.g., face-to-face, hospital-based, residential programs). It is possible that in the current study, individuals in the high severity group struggled to engage with the minimally guided treatment as it was not matched to their needs. While this group did not complete significantly fewer modules than the other groups, they may have experienced greater difficulty applying content to their lives and making changes independently. On the other hand, the program offers preliminary evidence that individuals with moderate difficulties seem to be responding best in terms of drinking behaviours. Taken together, intervening while young adults are still early in the risk pathway in terms of both age and symptom severity is likely to be efficacious in preventing severe substance use and mood disorders in the future. As such, young adults with moderate symptomology may be an optimal group to target for early intervention using efforts such as minimally guided, internet-based treatment, while those with higher severity may require additional or more intensive treatment.

Future Directions

The results of both studies within this dissertation open the door to many potential avenues for future research. Overall, there is a need for a larger RCT of *Take Care of Me* with some notable improvements. More specifically, the trial warrants a structured plan to mitigate attrition and improve engagement. There are many ways that this could be achieved in future studies.

First, the program warrants a more robust plan to mitigate attrition that is built into the study procedure. This could be done using the Engagement, Verification, Maintenance, Confirmation (EVMC; Scott, 2004) protocol, which was developed as a standardized procedure

for improving follow-up in programs and studies among individuals struggling with addiction. Important components of the EVMC protocol include educating and motivating participants, obtaining informed consent about contact, systematic scheduling, timely location verification, frequent reminders (e.g., follow-ups, engagement, updates in location), and direct contact with participants at follow-up points (i.e., telephone). Studies that do not have contact with participants often yield attrition rates up to 50% (Scott, 2004). There is also a higher risk of bias among studies with a retention rate of 70% or lower. Studies that have incorporated the EVMC have demonstrated retention rates of 90% and higher among various populations (e.g., adolescents, adults, alcohol, cocaine, opioids, cannabis). As noted, attrition in the current study at follow-up was both substantial (i.e., 66%) and biased towards the treatment condition, which prevented any formal conclusions about the long-term efficacy of the program from being drawn. This is a problem, yet a common challenge endorsed by addiction researchers, particularly those conducting large-scale clinical trials (Hadjistavropoulos et al., 2020). Future versions of *Take Care of Me* would benefit from collecting minimally sufficient information about participants to retain a larger sample that yields less biased results and more generalizable findings. While this makes the program not completely anonymous, there are telling signs of being willing to engage with interventions using personal information (e.g., accountability, reminders; Scott et al., 2004). Relatedly, given the short follow-up of the program, there is a need to look at the effects of the program longer term (e.g., 1- and 2-years post-treatment), and determine how *Take Care of Me* has impacted longer term mental health outcomes in the future.

Second, therapist assistance has been shown to improve engagement with online treatment relative to completely self-guided programs (Hadjistavropoulos et al., 2020). For a program like *Take Care of Me,* this could involve weekly check-in sessions with a mental health professional to discuss goals, progress, motivation, and problem solving, reminders about upcoming assessment points, and overall accountability. While the current program attempted to include a small social presence (e.g., videos, automated reminders, personal companion), evidently this was not sufficient to promote engagement. Therapist assistance may be particularly important for individuals with co-occurring mood or anxiety challenges (Karyotaki et al., 2021), where making progress completely independently may be too large a feat, and the additional accountability and problem-solving support may mitigate some of the mental health barriers. Therapist-assisted online interventions have also been shown to have lower attrition

rates than completely self-guided online interventions (Hadjistavropoulos et al., 2020). Therefore, incorporating support of this nature would also increase the power of future versions of the program by way of larger samples, which is important for determining long-term effects, reducing the possibility of bias, and conducting more complex secondary analyses. Relatedly, in-person treatment outcomes are improved in the context of a strong therapeutic alliance (Flückiger et al., 2018). This would require both a conceptualization of what constitutes therapeutic alliance within therapist-guided or self-guided online interventions, as well as optimal ways to measure said alliance. For many, engagement may be higher and retention lower if they felt connected to the treatment (or an individual associated with the treatment) in some capacity. Based on this research, it is conceivable that optimizing the therapeutic alliance within future online interventions would benefit both retention and treatment outcomes.

Third, there may be a need to optimize treatment components after the first trial. For example, recent research suggests that young adults find treatment content that includes video games more engaging rather than solely reading text (Garrido et al., 2019). While the current intervention did utilize some videos, additional lessons and activities could be incorporated in a more engaging and interactive way, while still maintaining the minimally guided nature of the intervention. Using a video-game style to present elements of the treatment for the population of young adults may also stand to improve engagement with program content and ideally translate to better treatment outcomes than what was observed in the current study.

Fourth, future trials should incorporate measures of treatment attitudes and perceived stigma, and subsequently examine the potential impact on treatment uptake and response. Depending on the attitudes of young adults at the outset of treatment, these could be additional pre-treatment factors that are worthy of consideration when examining treatment outcomes. Researchers, clinicians, and program developers could also incorporate young adults' perspectives into the development of said interventions, as this may result in more positive outcomes (Hadjistavropoulos et al., 2021). For example, it may be beneficial to conduct focus groups with emerging adults struggling with comorbid alcohol misuse and emotional difficulties who would opt to participate in an online, mainly self-guided intervention, and incorporate their feedback into programs (e.g., the development of video-game style treatment content, length, format).

Fifth, there is a need to look at the specific mechanisms by which the intervention works. This would provide insight into what changes allow people to be in a better position to change their emotional and alcohol use health. For example, cognitive capacity, particularly EF, has been shown to predict treatment response among individuals seeking support for alcohol misuse (Hunt et al., 2009), and was a relevant pre-treatment factor in the current research. Future studies could therefore examine whether changes in EF help explain improvements in alcohol misuse and overall mental health. Similar studies could also be conducted for additional mechanisms, such as motivation for change, attitudes towards treatment, motives for drinking (e.g., coping or enhancement), expectancies of success in treatment (Cook et al., 2015; Martínez-González et al., 2020; Stewart et al., 2016), or therapeutic alliance (Henson et al., 2019). For example, a recent subgrouping study of undergraduate students found that individuals in the high depression and alcohol misuse class were more likely to endorse coping motives for drinking relative to the lower-risk class of individuals with low depression and alcohol misuse (Orui et al., 2020). Enhancement motives for drinking (i.e., to increase positive affect) have likewise been shown to be associated with alcohol problems among adolescents and young adults through higher levels of drinking (Cooper et al., 1994; Merrill et al., 2014). While the current study did not observe differing treatment outcomes for coping motives, previous research suggests that coping and enhancement motives may be important mechanisms of change in treatment for these comorbid disorders.

Last, the results of the follow-up analyses raise the question of whether programs like *Take Care of Me* are more appropriate for individuals with problems of low- to moderate-severity. Previous research would suggest that those in the high-severity group may have struggled to engage with the program independently due to the severity of their symptoms (Del Boca et al., 2017). Building on the results of study 2 could also lay the foundation for future treatment studies. More specifically, future research could clarify whether substance use treatments should be tailored to meet the needs of young adults based on relevant pre-treatment level of risk according to the factors included in the current program (i.e., background risk factors, symptom severity, EF). Taking this a step further, researchers could then examine whether matched interventions result in more positive outcomes overall, similar to the SBIRT protocol. Overall, studies of this nature would clarify the optimal population to target using programs like *Take Care of Me.* This research would also support inclusive recruitment strategies

(i.e., endorsing moderate or greater difficulties with alcohol misuse and emotional challenges), so long as appropriate interventions are available as recommendations for the full spectrum of severity.

Conclusion

In sum, it is evident that many young adults struggle with their mental health, yet most do not access the support that they need. This dissertation filled a gap in clinical research by developing and testing the efficacy of an online, integrated treatment for some of the most common mental health concerns endorsed by this population, namely, alcohol misuse, depression, and anxiety. The current research provides preliminary support for the *Take Care of Me* program on hazardous drinking, emotional symptoms, and quality of life, but not for overall alcohol consumption, and not all participants responded the same way. Individuals with higher pre-treatment severity in the treatment condition experienced less benefits relative to low-risk individuals, while moderate-severity individuals experienced greater benefits of the program. Overall, this research adds promising initial evidence to the emerging body of work targeting alcohol use and emotional problems (i.e., depression and anxiety) in young adults using online integrated treatments. Future research is needed to improve engagement and retention within minimally guided treatments for this population, and to clarify whether tailoring alcohol misuse and emotional interventions based on pre-treatment risk is warranted.

References

Adlaf, E.M., Begin, P., & Sawka, E. (2005). *Canadian Addiction Survey (CAS): A national survey of Canadians' use of alcohol and other drugs: Prevalence of use and related harms. Detailed report.* Ottawa, ON: Canadian Centre on Substance Abuse. Retrieved from https://www.ccsa.ca/sites/default/files/2019-05/ccsa-004028-2005.pdf

Ainsworth, H. R., Torgerson, D. J., & Kang 'Ombe, A. R. (2010). Conceptual, design, and statistical complications associated with participant preference. *The Annals of the American Academy of Political and Social Science, 628*(1), 176–188. https://doi.org/10.1177/0002716209351524.

Amati, F., Banks, C., Greenfield, G., & Green, J. (2018). Predictors of outcomes for patients with common mental health disorders receiving psychological therapies in community settings: A systematic review. *Journal of Public Health, 40*(3), e375–e387. https://doi.org/10.1093/pubmed/fdx168

Andersson, G., Carlbring, P., Titov, N., & Lindefors, N. (2019). Internet interventions for adults with anxiety and mood disorders: A narrative umbrella review of recent meta-analyses. *The Canadian Journal of Psychiatry*, *64*(7) 465-470. https://doi.org/10.1177/0706743719839381

Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., & Hedman, E. (2014). Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: A systematic review and meta-analysis. *World Psychiatry, 13*(3), 288–295. https://doi.org/10.1002/wps.20151

Anker, J. J., & Kushner, M. G. (2019). Co-Occurring alcohol use disorder and anxiety: Bridging psychiatric, psychological, and neurobiological perspectives. *Alcohol Research: Current Reviews, 40*(1), e1-8. https://doi.org/10.35946/arcr.v40.1.03

Arkowitz, H., & Burke, B. L. (2008). Motivational interviewing as an integrative framework for the treatment of depression. In H. Arkowitz, H. A. Westra, W. R. Miller, & S. Rollnick (Eds.), *Motivational interviewing in the treatment of psychological problems* (pp. 145-272). The Guildford Press.

Arnett, J. J. (2000). Emerging adulthood: Theory of development from the late teens through the twenties. *American Psychologist, 55*(5), 469-480. https://doi.org/10.1037/0003-066X.55.5.469

Arnett, J. J. (2005). The developmental context of substance use in emerging adulthood. *Journal of Drug Issues, 35*(2), 235-253. https://doi.org/10.1177/002204260503500202

Arnett, J. J. (2014). *Emerging adulthood: The winding road from the late teens through the twenties*. New York: Oxford University Press.

Augsburger, M., Kaal, E., Ülesoo, T., Wenger, A., Blankers, M., Haug, S., Ebert, D. D., Riper, H., Keough, M., Noormets, H., Schaub, M. P., & Kilp, K. (2021). Effects of a minimal-guided on-line intervention for alcohol misuse in Estonia: A randomized controlled trial. *Addiction, 117*(1), 108–117. https://doi.org/10.1111/add.15633

Babor, T. F., Del Boca, F., & Bray, J. W. (2017). Screening, brief intervention and referral to treatment: Implications of SAMHSA's SBIRT initiative for substance abuse policy and practice. *Addiction, 112*, 110–117. https://doi.org/10.1111/add.13675

Bahorik, A. L., Campbell, C. I., Sterling, S. A., Leibowitz, A., Travis, A., Weisner, C. M., & Satre, D. D. (2018). Adverse impact of marijuana use on clinical outcomes among psychiatry patients with depression and alcohol use disorder. *Psychiatry Research, 259*, 316–322. https://doi.org/10.1016/j.psychres.2017.10.026

Baker, A., Thornton, L., Hiles, S., Hides, L., & Lubman, D. (2012). Psychological interventions for alcohol misuse among people with co-occurring depression or anxiety disorders: A systematic review. *Journal of Affective Disorders, 139*(3), 217–229. https://doi.org/10.1016/j.jad.2011.08.004

Bartel, S. J., Sherry, S. B., Smith, M. M., Vidovic, V. V., & Stewart, S. H. (2018). Is anxiety sensitivity a risk factor for, or complication of, alcohol misuse? A meta-analysis. *Personality and Individual Differences, 135*, 258–263. https://doi.org/10.1016/j.paid.2018.07.031

Batterham, P. J., & Calear, A. L. (2017). Preferences for internet-based mental health interventions in an adult online sample: Findings from an online community survey. *JMIR Mental Health, 4*(2), e26. https://doi.org/10.2196/mental.7722

Baumgartner, C., Schaub, M. P., Wenger, A., Malischnig, D., Augsburger, M., Lehr, D., Blankers, M., Ebert, D. D., & Haug, S. (2021). "Take Care of You" - Efficacy of integrated, minimal-guidance, internet-based self-help for reducing co-occurring alcohol misuse and depression symptoms in adults: Results of a three-arm randomized controlled

trial. *Drug and Alcohol Dependence, 225*, 108806.
https://doi.org/10.1016/j.drugalcdep.2021.108806

Beidel, D.C., Frueh, B.C., & Hersen, M. (2014). *Adult psychopathology and diagnosis (7th Edition).* Wiley.

Blevins, C., Abrantes, A., & Stephens, R. (2016). Motivational pathways from antecedents of alcohol use to consequences: A structural model of using alcohol to cope with negative affect. *The American Journal of Drug and Alcohol Abuse, 42*(4), 395-403. https://doi.org/10.3109/00952990.2016.1141915

Boschloo, L., Vogelzangs, N., Smit, J. H., Van den Brin, W., Veltman, J. H., Beekman, A. T. F., & Penninx, B. W. J. H. (2011). Comorbidity and risk indicators for alcohol use disorders among persons with anxiety and/or depressive disorders: Findings from the Netherlands Study of Depression and Anxiety (NESDA). *Journal of Affective Disorders, 131,* 233-242. https://doi.org/10.1016/j.jad.2010.12.014

Boydell, K. M., Hodgins, M., Pignatiello, A., Teshima, J., Edwards, H., & Willis, D. (2014). Using technology to deliver mental health services to children and youth: A scoping review. *Journal of the Canadian Academy of Child and Adolescent Psychiatry, 23*(2), 87–99.

Buchanan, T., Heffernan, T. M., Parrott, A.C., Ling, J., Rodgers, J., & Scholey, A. B. (2010). A short self-report measure of problems with executive function suitable for administration via the Internet. *Behavior Research Methods*, *42*(3), 709-714. https://doi.org/10.3758/BRM.42.3.709

Buntrock, C., Ebert, D., Lehr, D., Riper, H., Smit, F., Cuijpers, P., & Berking, M. (2015). Effectiveness of a web-based cognitive behavioural intervention for subthreshold depression: Pragmatic randomised controlled trial. *Psychotherapy and Psychosomatics, 84*(6), 348–358. https://doi.org/10.1159/000438673

Canadian Centre on Substance Use and Addiction. (2009). *Substance abuse in Canada: Concurrent disorders*. Retrieved from https://www.ccsa.ca/sites/default/files/2019-04/ccsa-011811-2010.pdf

Canadian Centre on Substance Use and Addiction. (2019). *Canadian drug summary.* Retrieved from https://www.ccsa.ca/sites/default/files/2019-09/CCSA-Canadian-Drug-Summary-Alcohol-2019-en.pdf

Canadian Medical Association and Canadian Psychiatric Association. (2016). *Joint statement on access to mental health care from the Canadian Medical Association and Canadian Psychiatric Association.* Ottawa, ON: Canadian Medical Association. Retrieved from https://policybase.cma.ca/documents/policypdf/PD16-04.pdf

Cappell, H., & Greeley, J. (1987). Alcohol and tension reduction: An update on research and theory. In H. T. Blane & K. E. Leonard (Eds.), *Psychological theories of drinking and alcoholism* (pp. 15–54). Guilford Press.

Capron, D. W., Bauer, B. W., Madson, M. B., & Schmidt, N. B. (2017). Treatment seeking among college students with comorbid hazardous drinking and elevated mood/anxiety symptoms. *Substance Use & Misuse, 53*(6), 1041–1050. https://doi.org/10.1080/10826084.2017.1392982

Carlbring, P., Andersson, G., Cuijpers, P., Riper, H., & Hedman-Lagerlöf, E. (2018). Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: An updated systematic review and meta-analysis. *Cognitive Behaviour Therapy, 47*(1), 1–18. https://doi.org/10.1080/16506073.2017.1401115

Carver J., Cappelli, M., Davidson, S., Caldwell, W., Belair, M.-A., & Vloet, M. (2015). *Taking the next step forward: Building a responsive mental health and addictions system for emerging adults*. Retrieved from https://www.mentalhealthcommission.ca/wp-content/uploads/drupal/Taking%252520the%252520Next%252520Step%252520Forward_0.pdf

Castaneda, A. E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lönnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. *Journal of Affective Disorders, 106*(1-2), 1–27. https://doi.org/10.1016/j.jad.2007.06.006

Castillo-Carniglia, A., Keyes, K. M., Hasin, D. S., & Cerdá, M. (2019). Psychiatric comorbidities in alcohol use disorder. *The Lancet Psychiatry, 6*(12), 1068–1080. https://doi.org/10.1016/s2215-0366(19)30222-6

Castro, R. P., Haug, S., Kowatsch, T., Filler, A., & Schaub, M. P. (2017). Moderators of outcome in a technology-based intervention to prevent and reduce problem drinking among adolescents. *Addictive Behaviors, 72*, 64–71. https://doi.org/10.1016/j.addbeh.2017.03.013

Chan, J. K., Farrer, L. M., Gulliver, A., Bennett, K., & Griffiths, K. M. (2016). University students' views on the perceived benefits and drawbacks of seeking help for mental health problems on the internet: A qualitative study. *Journal of Medical Internet Research: Human Factors, 3*(1), e3. https://doi.org/10.2196/humanfactors.4765

Chandley, R. B., Luebbe, A. M., Messman-Moore, T. L., & Ward, R. M. (2014). Anxiety sensitivity, coping motives, emotion dysregulation, and alcohol-related outcomes in college women: A moderated-mediation model. *Journal of Studies on Alcohol and Drugs, 75*(1), 83–92. https://doi.org/10.15288/jsad.2014.75.83

Christ, C., Schouten, M. J., Blankers, M., van Schaik, D. J., Beekman, A. T., Wisman, M. A., Stikkelbroek, Y. A., & Dekker, J. J. (2020). Internet and computer-based cognitive behavioral therapy for anxiety and depression in adolescents and young adults: Systematic review and meta-analysis. *Journal of Medical Internet Research, 22*(9), e17831. https://doi.org/10.2196/17831

Cochran, G., Field, C., DiClemente, C., & Caetano, R. (2016). Latent classes among recipients of a brief alcohol intervention: A replication analysis. *Behavioral Medicine, 42*(1), 29–38. https://doi.org/10.1080/08964289.2014.951305

Colder, C. R., Lee, Y. H., Frndak, S., Read, J. P., & Wieczorek, W. F. (2019). Internalizing symptoms and cannabis and alcohol use: Between- and within-person risk pathways with coping motives. *Journal of Consulting and Clinical Psychology, 87*(7), 629–644. https://doi.org/10.1037/ccp0000413

Constantino, M. J., Boswell, J. F., Coyne, A. E., Swales, T. P., & Kraus, D. R. (2021). Effect of matching therapists to patients vs assignment as usual on adult psychotherapy outcomes: A randomized clinical trial. *JAMA Psychiatry, 78*(9), 960–969. https://doi.org/10.1001/jamapsychiatry.2021.1221

Conway, K. P., Compton, W., Stinson, F. S., & Grant, B. F. (2006). Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *The Journal of Clinical Psychiatry, 67*(2), 247–257. https://doi.org/10.4088/jcp.v67n0211

Cook, S., Heather, N., & McCambridge, J. (2015). Posttreatment motivation and alcohol treatment outcome 9 months later: Findings from structural equation modeling. *Journal of Consulting and Clinical Psychology, 83*(1), 232–237.https://doi.org/10.1037/a0037981

Cooper, M. L. (1994). Motivations for alcohol use among adolescents: Development and validation of a four-factor model. *Psychological Assessment, 6*(2), 117-128. https://doi.org/10.1037/1040-3590.6.2.117

Corace, K., Arès, I., Overington, L., & Kim, H. S. (2021). Substance use and mental health disorders: Psychologists' role in bridging the gap. *Canadian Psychology*. Advance online publication. https://doi.org/10.1037/cap0000299

Cunningham, J. A., Hodgins, D. C., Keough, M. T., Hendershot, C. S., Schell, C., & Godinho, A. (2020). Online interventions for problem gamblers with and without co-occurring unhealthy alcohol use: Randomized controlled trial. *Internet Interventions, 19*, 100307. https://doi.org/10.1016/j.invent.2020.100307

Davidson, K. M., & Ritson, E. B. (1993). The relationship between alcohol dependence and depression. *Alcohol and Alcoholism, 28*(2), 147–155.

Davis, L. M., Uezato, A., Newell, J., & Frazier, E. (2008). Major depression and comorbid substance use disorders. *Current Opinion in Psychiatry, 21*(1), 14-18. https://doi.org/10.1097/YCO.0b013e3282f32408

Deady, M., Mills, K. L., Teesson, M., & Kay-Lambkin, F. (2016). An online intervention for co-occurring depression and problematic alcohol use in young people: Primary outcomes from a randomized controlled trial. *Journal of Medical Internet Research, 18*(3), e71. https://doi.org/10.2196/jmir.5178

Deeken, F., Banaschewski, T., Kluge, U., & Rapp, M. A. (2020). Risk and protective factors for alcohol use disorders across the lifespan. *Current Addiction Reports, 7*(3), 245–251. https://doi.org/10.1007/s40429-020-00313-z

Del Boca, F., McRee, B., Vendetti, J., & Damon, D. (2017). The SBIRT program matrix: A conceptual framework for program implementation and evaluation: SBIRT program matrix. *Addiction, 112*(Suppl. 2), 12–22. https://doi.org/10.1111/add.13656

DeVido, J. J., & Weiss, R. D. (2012). Treatment of the depressed alcoholic patient. *Current Psychiatry Reports, 14*(6), 610–618. https://doi.org/10.1007/s11920-012-0314-7

Domínguez-Salas, S., Díaz-Batanero, C., Lozano-Rojas, O. M., & Verdejo-García, A. (2016). Impact of general cognition and executive function deficits on addiction treatment outcomes: Systematic review and discussion of neurocognitive pathways. *Neuroscience and Biobehavioral Reviews, 71*, 772–801.https://doi.org/10.1016/j.neubiorev.2016.09.030

Drake, R. E., Mueser, K. T., & Brunette, M. F. (2007). Management of persons with co-occurring severe mental illness and substance use disorder: Program implications. *World Psychiatry, 6*(3), 131-136.

Drake, R. E., O'Neal, E. L., & Wallach, M. A. (2008). A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders. *Journal of Substance Abuse Treatment, 34*(1), 123–138. https://doi.org/10.1016/j.jsat.2007.01.011

Dube, P., Kroenke, K., Bair, M. J., Theobald, D., & Williams, L. S. (2010). The P4 Screener. *The Primary Care Companion to The Journal of Clinical Psychiatry*, e1–e8. https://doi.org/10.4088/pcc.10m00978blu

Ebert, D. D., Mortier, P., Kaehlke, F., Bruffaerts, R., Baumeister, H., Auerbach, R. P., Alonso, J., Vilagut, G., Martínez, K. I., Lochner, C., Cuijpers, P., Kuechler, A. M., Green, J., Hasking, P., Lapsley, C., Sampson, N. A., Kessler, R. C., & WHO World Mental Health-International College Student Initiative collaborators (2019). Barriers of mental health treatment utilization among first-year college students: First cross-national results from the WHO World Mental Health International College Student Initiative. *International Journal of Methods in Psychiatric Research, 28*(2), e1782. https://doi.org/10.1002/mpr.1782

Eisenberg, D., & Chung, H. (2012). Adequacy of depression treatment among college students in the United States. *General Hospital Psychiatry, 34*(3), 213–220. https://doi.org/10.1016/j.genhosppsych.2012.01.002

Etzelmueller, A., Vis, C., Karyotaki, E., Baumeister, H., Titov, N., Berking, M., Cuijpers, P., Riper, H., & Ebert, D. D. (2020). Effects of internet-based cognitive behavioral therapy in routine care for adults in treatment for depression and anxiety: Systematic review and meta-analysis. *Journal of Medical Internet Research, 22*(8), e18100. https://doi.org/10.2196/18100

Eysenbach, G. (2011). CONSORT-EHEALTH: Improving and standardizing evaluation reports of web-based and mobile health interventions. *Journal of Medical Internet Research, 13*(4), e126. https://doi.org/10.2196/jmir.1923

Faulkner, G., Ramanathan, S., Kwan, M., & the CCWS Expert Panel Group (2019). Developing a coordinated Canadian post-secondary surveillance system: A Delphi survey to identify

measurement priorities for the Canadian Campus Wellbeing Survey (CCWS). *BMC Public Health, 19*(935). https://doi.org/10.1186/s12889-019-7255-6

Fergusson, D. M., Boden, J. M., & Horwood, L. J. (2009). Tests of causal links between alcohol abuse or dependence and major depression. *Archives of General Psychiatry, 66*(3), 260–266. https://doi.org/10.1001/archgenpsychiatry.2008.543

Flückiger, C., Del Re, A. C., Wampold, B. E., & Horvath, A. O. (2018). The alliance in adult psychotherapy: A meta-analytic synthesis. *Psychotherapy, 55*(4), 316–340. https://doi.org/10.1037/pst0000172

Frohlich, J. R., Rapinda, K. K., Schaub, M. P., Wenger, A., Baumgartner, C., Johnson, E. A., O'Connor, R. M., Vincent, N., Blankers, M., Ebert, D. D., Hadjistavropoulos, H., Mackenzie, C. S., & Keough, M. T. (2018). Efficacy of an online self-help treatment for comorbid alcohol misuse and emotional problems in young adults: Protocol for a randomized controlled trial. *JMIR Research Protocols, 7*(11), e11298. https://doi.org/10.2196/11298

Frohlich, J. R., Rapinda, K. K., Schaub, M. P., Wenger, A., Baumgartner, C., Johnson, E. A., O'Connor, R. M., Vincent, N., Blankers, M., Ebert, D. D., Hadjistavropoulos, H. D., Mackenize, C. S., Wardell, J. D., Augsburger, M., Goldberg, J. O., & Keough, M. T. (2021). Efficacy of a minimally guided internet treatment for alcohol misuse and emotional problems in young adults: Results of a randomized controlled trial. *Addictive Behaviors Reports, 14,* 100390. https://doi.org/10.1016/j.abrep.2021.100390

Garrido, S., Millington, C., Cheers, D., Boydell, K., Schubert, E., Meade, T., & Nguyen, Q. V. (2019). What works and what doesn't work? A systematic review of digital mental health interventions for depression and anxiety in young people. *Frontiers in Psychiatry, 10*, 1–19. https://doi.org/10.3389/fpsyt.2019.00759

Gill, S., Contreras, O., Muñoz, R. F., & Leykin, Y. (2014). Participant retention in an automated online monthly depression rescreening program: Patterns and predictors. *Internet Interventions, 1*(1), 20–25. https://doi.org/10.1016/j.invent.2014.02.003

González, P., Nuñez, A., Merz, E., Brintz, C., Weitzman, O., Navas, E. L., Camacho, A., Buelna, C., Penedo, F. J., Wassertheil-Smoller, S., Perreira, K., Isasi, C. R., Choca, J., Talavera, G. A., & Gallo, L. C. (2017). Measurement properties of the Center for Epidemiologic

Studies Depression Scale (CES-D 10): Findings from HCHS/SOL. *Psychological Assessment, 29*(4), 372–381. https://doi.org/10.1037/pas0000330

Government of Canada. (2015). *The chief public health officer's report on the state of public health in Canada, 2015: Alcohol consumption in Canada.* Ottawa, ON: Public Health Agency of Canada. Retrieved from http://healthycanadians.gc.ca/publications/department-ministere/state-public-health-alcohol-2015-etat-sante-publique-alcool/alt/state-phac-alcohol-2015-etat-aspc-alcool-eng.pdf

Government of Canada. (2020). *Alcohol use among Canadians.* Retrieved from https://health-infobase.canada.ca/alcohol/ctads/

Grant, B., Goldstein, R., Saha, T., Chou, S., Jung, J., Zhang, H., . . . Hasin, D. (2015). Epidemiology of DSM-5 alcohol use disorder: Results from the national epidemiologic survey on alcohol and related conditions III. *JAMA Psychiatry, 72*(8), 757-66. https://doi.org/10.1001/jamapsychiatry.2015.0584

Grant, V. V., Stewart, S. H., & Mohr, C. D. (2009). Coping-anxiety and coping-depression motives predict different daily mood-drinking relationships. *Psychology of Addictive Behaviors, 23*(2), 226-237. https://doi.org/10.1037/a0015006

Gratzer, D., & Khalid-Khan, F. (2016). Internet-delivered cognitive behavioural therapy in the treatment of psychiatric illness. *Canadian Medical Association Journal, 188*(4), 263–272. https://doi.org/10.1503/cmaj.150007

Greenfield, S. F., Pettinati, H. M., O'Malley, S., Randall, P. K., & Randall, C. L. (2010). Gender differences in alcohol treatment: An analysis of outcome from the COMBINE study. *Alcoholism: Clinical and Experimental Research, 34*(10), 1803-1812. https://doi.org/10.1111/j.1530-0277.2010.01267.x

Groenwold, R. H. H., Moons, K. G. M., & Vandenbroucke, J. P. (2014). Randomized trials with missing outcome data: How to analyze and what to report. *Canadian Medical Association Journal*, *186*(15), 1153–1157. https://doi.org/10.1503/cmaj.131353

Grothues, J. M., Bischof, G., Reinhardt, S., Meyer, C., John, U., & Rumpf, H. J. (2008). Effectiveness of brief alcohol interventions for general practice patients with problematic drinking behavior and comorbid anxiety or depressive disorders. *Drug and Alcohol Dependence, 94*, 214–220. https://doi.org/10.1016/j.drugalcdep.2007.11.015

Gustavson, K., Knudsen, A. K., Nesvåg, R., Knudsen, G. P., Vollset, S. E., & Reichborn-Kjennerud, T. (2018). Prevalence and stability of mental disorders among young adults: Findings from a longitudinal study. *BMC Psychiatry, 18*(1), 65. https://doi.org/10.1186/s12888-018-1647-5

Hadjistavropoulos, H. D., Mehta, S., Wilhelms, A., Keough, M. T., & Sundström, C. (2020). A systematic review of internet-delivered cognitive behavior therapy for alcohol misuse: Study characteristics, program content and outcomes. *Cognitive Behaviour Therapy, 49*(4), 327–346. https://doi.org/10.1080/16506073.2019.1663258

Hadjistavropoulos, H. D., Chadwick, C., Beck, C. D., Edmonds, M., Sundström, C., Edwards, W., Ouellette, D., Waldrop, J., Adlam, K., Bourgeault, L., & Nugent, M. (2021). Improving internet-delivered cognitive behaviour therapy for alcohol misuse: Patient perspectives following program completion. *Internet Interventions, 26*, 100474. https://doi.org/10.1016/j.invent.2021.100474

Hasin, D. S., Stinson, F. S., Ogburn, E., Grant, B. F. (2007). Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry, 64*(7), 830–842. https://doi.org/10.1001/archpsyc.64.7.830

Haug, S., & Schaub, M. P. (2016). Treatment outcome, treatment retention, and their predictors among clients of five outpatient alcohol treatment centres in Switzerland. *BMC Public Health, 16*(1), 581–581. https://doi.org/10.1186/s12889-016-3294-4

Hawke, L. D., Sheikhan, N. Y., MacCon, K., & Henderson, J. (2021). Going virtual: Youth attitudes toward and experiences of virtual mental health and substance use services during the COVID-19 pandemic. *BMC Health Services Research, 21*(1), 340. https://doi.org/10.1186/s12913-021-06321-7

Henson, P., Wisniewski, H., Hollis, C., Keshavan, M., & Torous, J. (2019). Digital mental health apps and the therapeutic alliance: Initial review. *BJPsych Open, 5*(1), E15. doi:10.1192/bjo.2018.86

Hofmann, S. G., Asnaani, A., Vonk, I. J. J., Sawyer, A. T., & Fang, A. (2012). The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cognitive Therapy and Research, 36*(5), 427–440. https://doi.org/10.1007/s10608-012-9476-1

Hobbs, J. D., Kushner, M. G., Lee, S. S., Reardon, S. M., & Maurer, E. W. (2011). Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for alcohol dependence. *The American Journal on Addictions, 20*(4), 319–329. https://doi.org/10.1111/j.1521-0391.2011.00140.x

Humeniuk, R., Ali, R., Babor, T., Farrell, M., Formigoni, M., Jittiwutikarn, J., de Lacerda, R., Ling, W., Marsden, J., Monteiro, M., Nhiwatiwa, S., Pal, H., Poznyak, V., & Simon, S. (2008). Validation of the alcohol, smoking and substance involvement screening test (ASSIST). *Addiction, 103*(6), 1039–1047. https://doi.org/10.1111/j.1360-0443.2007.02114.x

Hunt, S. A., Baker, A. L., Michie, P. T., & Kavanagh, D. J. (2009). Neurocognitive profiles of people with comorbid depression and alcohol use: Implications for psychological interventions. *Addictive Behaviors, 34*(10), 878–886. https://doi.org/10.1016/j.addbeh.2009.03.036

Hussong, A. M., Jones, D. J., Stein, G. L., Baucom, D. H., & Boeding, S. (2011). An internalizing pathway to alcohol use and disorder. *Psychology of Addictive Behaviors, 25*(3), 390–404. https://doi.org/10.1037/a0024519

Iarussi, M. M. (2019). *Integrating motivational interviewing and cognitive behavior therapy in clinical practice* (1st ed.). Routledge.

Ibrahim, A. K., Kelly, S. J., Adams, C. E., & Glazebrook, C. (2013). A systematic review of studies of depression prevalence in university students. *Journal of Psychiatric Research, 47*(3), 391-400. https://doi.org/10.1016/j.jpsychires.2012.11.015

Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Miech, R. A. (2015). *Monitoring the future national survey results on Drug Use, 1975-2014: Volume II, college students and adults ages 19-55*. Ann Arbor, MI: Institute for Social Research, The University of Michigan.

Jung, H., von Sternberg, K., & Davis, K. (2017). The impact of mental health literacy, stigma, and social support on attitudes toward mental health help-seeking. *International Journal of Mental Health Promotion, 19*(5), 252-267. https://doi.org/10.1080/14623730.2017.1345687

Jung, T., & Wickrama, K. A. S. (2007). An introduction to latent class growth analysis and growth mixture modeling. *Social and Personality Psychology Compass 2*(1), 302–317. https://doi.org/10.1111/j.1751-9004.2007.00054.x

Kaal, E., Schaub, M.P., Wenger, A., Ülesoo, T., Blankers, M., Haug, S., Ebert, D.D., Riper, H., Keough, M., Noormets, H., Kilp, K. (2020). Testing the efficacy of a minimal-guidance online self-help intervention for alcohol misuse in Estonia: Study protocol of a randomized controlled trial. *BMC Public Health, 20*(1), 790. https://doi.org/10.1186/s12889-020-08791-6

Kalodner, C. R., Delucia, J. L., & Ursprung, A. W. (1989). An examination of the tension reduction hypothesis: the relationship between anxiety and alcohol in college students. *Addictive Behaviors, 14*(6), 649–654. https://doi.org/10.1016/0306-4603(89)90007-5

Karyotaki, E., Riper, H., Twisk, J., Hoogendoorn, A., Kleiboer, A., Mira, A., Mackinnon, A., Meyer, B., Botella, C., Littlewood, E., Andersson, G., Christensen, H., Klein, J. P., Schröder, J., Bretón-López, J., Scheider, J., Griffiths, K., Farrer, L., Huibers, M. J. H., … Cuijpers, P. (2017). Efficacy of self-guided internet-based cognitive behavioral therapy in the treatment of depressive symptoms. *JAMA Psychiatry, 74*(4), 351. https://doi.org/10.1001/jamapsychiatry.2017.0044

Karyotaki, E., Efthimiou, O., Miguel, C., Bermpohl, F., Furukawa, T., Cuijpers, P., & the Individual Patient Data Meta-Analyses for Depression (IPDMA-DE) Collaboration. (2021). Internet-Based cognitive behavioral therapy for depression: A systematic review and individual patient data network meta-analysis. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2020.4364

Kelly, T. M., Daley, D. C., & Douaihy, A. B. (2012). Treatment of substance abusing patients with comorbid psychiatric disorders. *Addictive Behaviors, 37*(1), 11–24. https://doi.org/10.1016/j.addbeh.2011.09.010

Keough, M. T., & O'Connor, R. M. (2016). Interactive effects of the BIS and the BAS on trajectories of alcohol misuse after university graduation. *Substance Abuse: Research and Treatment, 9*(Suppl 1), 33–40. https://doi.org/10.4137/SART.S31434

Kessler, R. C., Sampson, N. A., Berglund, P., Gruber, M. J., Al-Hamzawi, A., Andrade, L., Bunting, B., Demyttenaere, K., Florescu, S., de Girolamo, G., Gureje, O., He, Y., Hu, C., Huang, Y., Karam, E., Kovess-Masfety, V., Lee, S., Levinson, D., Medina Mora, M. E.,

Moskalewicz, J., … Wilcox, M. A. (2015). Anxious and non-anxious major depressive disorder in the World Health Organization World Mental Health Surveys. *Epidemiology and Psychiatric Sciences, 24*(3), 210–226. https://doi.org/10.1017/S2045796015000189

Khantzian, E. J. (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harvard Review of Psychiatry, 4*(5), 231–244. https://doi.org/10.3109/10673229709030550

Kirouac, M., Stein, E. R., Pearson, M. R., & Witkiewitz, K. (2017). Viability of the World Health Organization quality of life measure to assess changes in quality of life following treatment for alcohol use disorder. *Quality of Life Research, 26*(11), 2987–2997. https://doi.org/10.1007/s11136-017-1631-4

Kraemer H. C. (2016). Messages for clinicians: Moderators and mediators of treatment outcome in randomized clinical trials. *The American Journal of Psychiatry*, *173*(7), 672–679. https://doi.org/10.1176/appi.ajp.2016.15101333

Kuntsche, E., & Kuntsche, S. (2009). Development and validation of the Drinking Motive Questionnaire Revised Short Form (DMQ-R SF). *Journal of Clinical Child and Adolescent Psychology, 38*(6), 899-908. https://doi.org/10.1080/15374410903258967

Kushner, M. G., Sher, K. J., & Erickson, D. J. (1999). Prospective analysis of the relation between DSM-III anxiety disorders and alcohol use disorders. *The American Journal of Psychiatry, 156*(5), 723–732. https://doi.org/10.1176/ajp.156.5.723

Kuteesa, M. O., Cook, S., Weiss, H. A., Kamali, A., Weinmann, W., Seeley, J., Ssentongo, J. N., Kiwanuka, T., Namyalo, F., Nsubuga, D., & Webb, E. L. (2019). Comparing Alcohol Use Disorders Identification Test (AUDIT) with Timeline Follow Back (TLFB), DSM-5 and Phosphatidylethanol (Peth) for the assessment of alcohol misuse among young people in Ugandan fishing communities. *Addictive Behaviors Reports, 10*, 100233. https://doi.org/10.1016/j.abrep.2019.100233

Kwan, M. Y., Faulkner, G. E., Arbour-Nicitopoulos, K. P., & Cairney, J. (2013). Prevalence of health-risk behaviours among Canadian post-secondary students: Aescriptive results from the National College Health Assessment. *BMC Public Health, 13*, 548. https://doi.org/10.1186/1471-2458-13-548

Lai, H. M. X., Cleary, M., Sitharthan, T., & Hunt, G. E. (2015). Prevalence of comorbid substance use, anxiety and mood disorders in epidemiological surveys, 1990–2014: A

systematic review and meta-analysis. *Drug and Alcohol Dependence, 154*, 1–13. https://doi.org/10.1016/j.drugalcdep.2015.05.031

Lanza, S. T., & Rhoades, B. L. (2013). Latent class analysis: an alternative perspective on subgroup analysis in prevention and treatment. *Prevention Science, 14*(2), 157–168. https://doi.org/10.1007/s11121-011-0201-1

Littlefield, A. K., King, K. M., Acuff, S. F., Foster, K. T., Murphy, J. G., & Witkiewitz, K. (2021). Limitations of cross-lagged panel models in addiction research and alternative models: An empirical example using project MATCH. *Psychology of Addictive Behaviors.* https://doi.org/10.1037/adb0000750

Livingston, J. D., Milne, T., Fang, M. L., & Amari, E. (2011). The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. *Addiction*, *107*(1), 39–50. https://doi.org/10.1111/j.1360-0443.2011.03601.x

Lo, Y. (2001). Testing the number of components in a normal mixture. *Biometrika, 88*, 767–778. https://doi.org/10.1093/biomet/88.3.767

Lubman, D. I., Allen, N. B., Rogers, N., Cementon, E., & Bonomo, Y. (2007). The impact of co-occurring mood and anxiety disorders among substance-abusing youth. *Journal of Affective Disorders, 103*, 105–112. https://doi.org/10.1016/j.jad.2007.01.011

Lungu, A., & Sun, M. (2016). Time for a change: College students' preference for technology-mediated versus face-to-face help for emotional distress. *Telemedicine Journal and E-Health, 22*(12), 991–1000. https://doi.org/10.1089/tmj.2015.0214

Luo, C., Sanger, N., Singhal, N., Pattrick, K., Shams, I., Shahid, H., Hoang, P., Schmidt, J., Lee, J., Haber, S., Puckering, M., Buchanan, N., Lee, P., Ng, K., Sun, S., Kheyson, S., Chung, D. C., Sanger, S., Thabane, L., & Samaan, Z. (2020). A comparison of electronically-delivered and face to face cognitive behavioural therapies in depressive disorders: A systematic review and meta-analysis. *EClinicalMedicine, 24*, 100442. https://doi.org/10.1016/j.eclinm.2020.100442

Mangrum, L. F., Spence, R. T., & Lopez, M. (2006). Integrated versus parallel treatment of co-occurring psychiatric and substance use disorders. *Journal of Substance Abuse Treatment, 30*(1), 79–84. https://doi.org/10.1016/j.jsat.2005.10.004

Marmorstein, N. R. (2009). Longitudinal associations between alcohol problems and depressive symptoms: early adolescence through early adulthood. A*lcoholism: Clinical and Experimental research, 33*(1), 49–59. https://doi.org/10.1111/j.1530-0277.2008.00810.x

Marel, C., Mills, K. L., Kingston, R., Gournay, K., Deady, M., Kay-Lambkin, F., Baker, A., Teesson, M. (2016). *Guidelines on the management of co-occurring alcohol and other drug and mental health conditions in alcohol and other drug treatment settings.* Sydney, Australia: NHMRC Centre of Research Excellence in Mental Health and Substance Use. Retrieved from: https://extranet.who.int/ncdccs/Data/AUS_B9_Comorbidity-Guidelines-2016.pdf

Martínez-González, J. M., Caracuel, A., Vilar-López, R., Becoña, E., & Verdejo-García, A. (2020). Evaluation of motivation for the treatment of drug addicts with personality disorders. *The Spanish Journal of Psychology, 23*(e15), 1–9. https://doi.org/10.1017/SJP.2020.13

Matud, M. P., Díaz, A., Bethencourt, J. M., & Ibáñez, I. (2020). Stress and psychological distress in emerging adulthood: A gender analysis. *Journal of Clinical Medicine, 9*(9), 2859. https://doi.org/10.3390/jcm9092859

McKee, S. A. (2017). Concurrent substance use disorders and mental illness: Bridging the gap between research and treatment. *Canadian Psychology, 58*(1), 50–57. https://doi.org/10.1037/cap0000093

McNeish, D., & Wolf, M. G. (2020). Thinking twice about sum scores. *Behavior Research Methods, 52*(6), 2287–2305. https://doi.org/10.3758/s13428-020-01398-0

Merrill, J. E., Wardell, J. D., & Read, J. P. (2014). Drinking motives in the prospective prediction of unique alcohol-related consequences in college students. *Journal of Studies on Alcohol and Drugs, 75*(1), 93–102. https://doi.org/10.15288/jsad.2014.75.93

Miller, W. R., & Rollnick, S. (2002). *Motivational interviewing: Preparing people for change (2nd Edition)*. New York, NY: Guilford Press.

Miller, W. R., & Rollnick, S. (2013). *Motivational Interviewing: Helping people change, 3rd Edition (Applications of Motivational Interviewing)*. The Guilford Press.

Mohr, D. C., Cuijpers, P., & Lehman, K. (2011). Supportive accountability: A model for providing human support to enhance adherence to ehealth interventions. *Journal of Medical Internet Research*, *13*(1), e30. https://doi.org/10.2196/jmir.1602

Morley, K., Baillie, A., Leung, S., Sannibale, C., Teesson, M., & Haber, P. (2016). Is specialized integrated treatment for comorbid anxiety, depression and alcohol dependence better than treatment as usual in a public hospital setting? *Alcohol and Alcoholism, 51*(4), 402-409. https://doi.org/10.1093/alcalc/agv131

Mueser, K. T., Noordsy, D. L., Drake, R. E., & Fox, L. (2003). *Integrated treatment for dual disorders: A guide to effective practice* (1st ed.). The Guilford Press.

Müller, M., Ajdacic-Gross, V., Vetrella, A. B., Preisig, M., Castelao, E., Lasserre, A., … Vandeleur, C. (2020). Subtypes of alcohol use disorder in the general population: A latent class analysis. *Psychiatry Research*, *285*, 112712–112712. https://doi.org/10.1016/j.psychres.2019.112712

Mushquash, A. R., Stewart, S. H., Sherry, S. B., Sherry, D. L., Mushquash, C. J., & MacKinnon, A. L. (2013). Depressive symptoms are a vulnerability factor for heavy episodic drinking: A short-term, four-wave longitudinal study of undergraduate women. *Addictive Behaviors, 38*(5), 2180–2186. https://doi.org/10.1016/j.addbeh.2012.11.008

Muthén, L. K., & Muthén, B. O. (2012). *Mplus user's guide: Version 7*. Los Angeles, CA: Muthén and Muthén.

Naps, M. S., Maass, D., Kranzler, H. R., Smith, R. V., Ingram, E., & Oslin, D. W. (2018). Predictors of Treatment Referral after AUDIT-C Screening for Heavy Drinking. *Addictive Disorders & Their Treatment, 17*(3), 124–133. https://doi.org/10.1097/ADT.0000000000000134

National Institute on Drug Abuse. (2009). *NIDA-Modified ASSIST-Prescreen V1.0*. World Health Organization. Retrieved from http://www.drugabuse.gov/nidamed/screening/nmassist.pdf

Ning, K., Gondek, D., Patalay, P., & Ploubidis, G. B. (2020). The association between early life mental health and alcohol use behaviours in adulthood: A systematic review. *PloS One, 15*(2), e0228667–e0228667. https://doi.org/10.1371/journal.pone.0228667

Oliveira, S., Carvalho, H., & Esteves, F. (2016). Toward an understanding of the quality of life construct: Validity and reliability of the WHOQOL-Bref in a psychiatric sample. *Psychiatry Research*, *244*, 37–44. https://doi.org/10.1016/j.psychres.2016.07.007

Orui, K., Frohlich, J. R., Stewart, S. H., Sherry, S. B., & Keough, M. T. (2020). Examining subgroups of depression and alcohol misuse in emerging adults during university: A

replication and extension study. *International Journal of Mental Health and Addiction*, *19,* 2323–2341. https://doi.org/10.1007/s11469-020-00325-w

Oswalt, S. B., Lederer, A. M., Chestnut-Steich, K., Day, C., Halbritter, A., & Ortiz, D. (2020). Trends in college students' mental health diagnoses and utilization of services, 2009-2015. *Journal of American College Health, 68*(1), 41–51. https://doi.org/10.1080/07448481.2018.1515748

Otasowie, J. (2021). Co-occurring mental disorder and substance use disorder in young people: Aetiology, assessment and treatment. *BJPsych Advances, 27*(4), 272-281. https://doi.org/10.1192/bja.2020.64

Patrick, M. E., Terry-McElrath, Y. M., Kloska, D. D., & Schulenberg, J. E. (2016). High-intensity drinking among young adults in the united states: Prevalence, frequency, and developmental change. *Alcoholism, Clinical and Experimental Research, 40*(9), 1905–1912. https://doi.org/10.1111/acer.13164

Pedersen, E. R., Grow, J., Duncan, S., Neighbors, C., & Larimer, M. E. (2012). Concurrent validity of an online version of the Timeline Followback assessment. *Psychology of Addictive Behaviors*, *26*(3), 672–677. https://doi.org/10.1037/a0027945

Pedrelli, P., Shapero, B., Archibald, A., & Dale, C. (2016). Alcohol use and depression during adolescence and young adulthood: A summary and interpretation of mixed findings. *Current Addiction Reports, 3*(1), 91–97. https://doi.org/10.1007/s40429-016-0084-0

Polak, K., Haug, N., Drachenberg, A., & Svikis, H. (2015). Gender considerations in addiction: Implications for treatment. *Current Treatment Options in Psychiatry, 2*(3), 326-338. https://doi.org/10.1007/s40501-015-0054-5

Preacher, K. J., Zyphur, M. J., & Zhang, Z. (2010). A general multilevel SEM framework for assessing multilevel mediation. *Psychological Methods*, *15*(3), 209–233. https://doi.org/10.1037/a0020141

Priester, M. A., Browne, T., Iachini, A., Clone, S., Dehart, D., & Seay, K. D. (2016). Treatment access barriers and disparities among individuals with co-occurring mental health and substance use disorders: An integrative literature review. *Journal of Substance Abuse Treatment, 61*, 47-59. https://doi.org/10.1016/j.jsat.2015.09.006

Prior, K., Mills, K., Ross, J., & Teesson, M. (2017). Substance use disorders comorbid with mood and anxiety disorders in the Australian general population. *Drug and Alcohol Review, 36*(3), 317–324. https://doi.org/10.1111/dar.12419

Radloff, L. S. (1977). The CES-D Scale. *Applied Psychological Measurement*, *1*(3), 385–401. https://doi.org/10.1177/014662167700100306

Raftery, A. (1995). Bayesian model selection in social research. *Sociological Methodology*, 25, 111-163. https://doi.org/10.2307/271063

Ramsey, S. E., Engler, P. A., & Stein, M. D. (2005). Alcohol use among depressed patients: The need for assessment and intervention. *Professional Psychology, Research and Practice, 36*(2), 203–207. https://doi.org/10.1037/0735-7028.36.2.203

Reins, J. A., Buntrock, C., Zimmermann, J., Grund, S., Harrer, M., Lehr, D., Baumeister, H., Weisel, K., Domhardt, M., Imamura, K., Kawakami, N., Spek, V., Nobis, S., Snoek, F., Cuijpers, P., Klein, J. P., Moritz, S., & Ebert, D. D. (2021). Efficacy and moderators of internet-based interventions in adults with subthreshold depression: An individual participant data meta-analysis of randomized controlled trials. *Psychotherapy and Psychosomatics*, *90*(2), 94–106. https://doi.org/10.1159/000507819

Riper, H., Andersson, G., Hunter, S. B., Wit, J., Berking, M., & Cuijpers, P. (2014). Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: a meta-analysis. *Addiction*, *109*(3), 394–406. https://doi.org/10.1111/add.12441

Riper, H., Hoogendoorn, A., Cuijpers, P., Karyotaki, E., Boumparis, N., Mira, A., Andersson, G., Berman, A. H., Bertholet, N., Bischof, G., Blankers, M., Boon, B., Boß, L., Brendryen, H., Cunningham, J., Ebert, D., Hansen, A., Hester, R., Khadjesari, Z., Kramer, J., … Smit, J. H. (2018). Effectiveness and treatment moderators of internet interventions for adult problem drinking: An individual patient data meta-analysis of 19 randomised controlled trials. *PLoS medicine, 15*(12), e1002714. https://doi.org/10.1371/journal.pmed.1002714

Robinson, J., Sareen, J., Cox, B. J., & Bolton, J. (2009). Self-medication of anxiety disorders with alcohol and drugs: Results from a nationally representative. *Journal of Anxiety Disorders*, *23*(1), 38-45. https://doi.org/10.1016/j.janxdis.2008.03.013

Rollnick, S., Heather, N., Gold, R., & Hall, W. (1992). Development of a short 'readiness to change' questionnaire for use in brief, opportunistic interventions among excessive drinkers. *British Journal of Addiction, 87*(5), 743–754. https://doi.org/10.1111/j.1360-0443.1992.tb02720.x

Salaheddin, K., & Mason, B. (2016). Identifying barriers to mental health help-seeking among young adults in the UK: a cross-sectional survey. *The British Journal of General Practice, 66*(651), e686–e692. https://doi.org/10.3399/bjgp16X687313

Saunders, J. B., Aasland, O. G., Barbor, T. F., de la Fuente, J. R., & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction, 88*(6), 791-804. https://doi.org/10.1111/j.1360-0443.1993.tb02093.x

Schaub, M. P., Blankers, M., Lehr, D., Boss, L., Riper, H., Dekker, J., Goudriaan, A. E., Maier, L. J., Haug, S., Amann, M., Dey, M., Wenger, A., & Ebert, D. D. (2016). Efficacy of an internet-based self-help intervention to reduce co-occurring alcohol misuse and depression symptoms in adults: study protocol of a three-arm randomised controlled trial. *BMJ Open, 6*(5), e011457. https://doi.org/10.1136/bmjopen-2016-011457

Schaub, M. P., Tiburcio, M., Martinez, N., Ambekar, A., Balhara, Y., Wenger, A., Monezi Andrade, A. L., Padruchny, D., Osipchik, S., Gehring, E., Poznyak, V., Rekve, D., Souza-Formigoni, M., & WHO e-Health Project on Alcohol and Health Investigators Group. (2018). Alcohol e-Help: Study protocol for a web-based self-help program to reduce alcohol use in adults with drinking patterns considered harmful, hazardous or suggestive of dependence in middle-income countries. *Addiction*, *113*(2), 346–352. https://doi.org/10.1111/add.14034

Schouten, M. J. E., Christ, C., Dekker, J. J. M., Riper, H., Goudriaan, A. E., & Blankers, M. (2021). Digital interventions for people with co-occurring depression and problematic alcohol use: A systematic review and meta-analysis. *Alcohol and Alcoholism*, 1–13. https://doi.org/10.1093/alcalc/agaa147

Schry, A. R., & White, S. W. (2013). Understanding the relationship between social anxiety and alcohol use in college students: A meta-analysis. *Addictive Behaviours, 38*, 2690-2706. https://doi.org/10.1016/j.addbeh.2013.06.014

Schwartz, G. (1978). Estimating the dimension of a model. *Annals of Statistics, 6*, 461–464. https://doi.org/10.1214/aos/1176344136

Schuckit M. A. (2006). Comorbidity between substance use disorders and psychiatric conditions. *Addiction, 101*(Suppl 1), 76–88. https://doi.org/10.1111/j.1360-0443.2006.01592.x

Schuler, M. S., Puttaiah, S., Mojtabai, R., & Crum, R. M. (2015). Perceived barriers to treatment for alcohol problems: A latent class analysis. *Psychiatric Services, 66*(11), 1221–1228. https://doi.org/10.1176/appi.ps.201400160

Scott, C. K. (2004). A replicable model for achieving over 90% follow-up rates in longitudinal studies of substance abusers. *Drug and Alcohol Dependence*, *74*(1), 21–36. https://doi.org/10.1016/j.drugalcdep.2003.11.007

Settipani, C. A., Hawke, L. D., Cleverley, K., Chaim, G., Cheung, A., Mehra, K., Rice, M., Szatmari, P., & Henderson, J. (2019). Key attributes of integrated community-based youth service hubs for mental health: a scoping review. *International Journal of Mental Health Systems, 13*, 52. https://doi.org/10.1186/s13033-019-0306-7

Sher, K. J., & Grekin, E. R. (2007). Alcohol and affect regulation. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 560–580). Guilford Press.

Smetanin, P., Stiff, D., Briante, C., Adair, C. E., Ahmad, S. & Khan, M. (2011). The life and economic impact of major mental illnesses in Canada: 2011 to 2041. *Mental Health Commission of Canada.* Retrieved from https://www.mentalhealthcommission.ca/wp-content/uploads/drupal/MHCC_Report_Base_Case_FINAL_ENG_0_0.pdf

Smith, J. P., & Book, S. W. (2010). Comorbidity of generalized anxiety disorder and alcohol use disorders among individuals seeking outpatient substance abuse treatment. *Addictive Behaviors, 35*(1), 42–45. https://doi.org/10.1016/j.addbeh.2009.07.002

Sobell, L. C., & Sobell, M. B. (1992). Timeline Follow-back: A technique for assessing self-reported ethanol consumption. In J. Allen & R. Z. Litten (Eds.), *Measuring Alcohol Consumption: Psychosocial and Biological Methods* (pp. 41-72). Humana Press.

Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder. *Archives of Internal Medicine, 166*(10), 1092. https://doi.org/10.1001/archinte.166.10.1092

Stacy, A. W., & Wiers, R. W. (2010). Implicit cognition and addiction: A tool for explaining paradoxical behavior. *Annual Review of Clinical Psychology, 6*, 551–575. https://doi.org/10.1146/annurev.clinpsy.121208.131444

Stanton, A. M., Batchelder, A. W., Kirakosian, N., Scholl, J., King, D., Grasso, C., Potter, J., Mayer, K. H., & O'Cleirigh, C. (2021). Differences in mental health symptom severity and care engagement among transgender and gender diverse individuals: Findings from a large community health center. *PloS One*, *16*(1), e0245872. https://doi.org/10.1371/journal.pone.0245872

Stapinski, L. A., Sannibale, C., Subotic, M., Rapee, R. M., Teesson, M., Haber, P. S., & Baillie, A. J. (2021). Randomised controlled trial of integrated cognitive behavioural treatment and motivational enhancement for comorbid social anxiety and alcohol use disorders. *The Australian and New Zealand Journal of Psychiatry, 55*(2), 207–220. https://doi.org/10.1177/0004867420952539

Stewart, S. H., Grant, V. V., Mackie, C. J., & Conrod, P. J. (2016). Comorbidity of anxiety and depression with substance use disorders. In K. J. Sher (Ed.), *The Oxford handbook of substance use and substance use disorders* (p. 149–186). Oxford University Press.

Stewart, S. J., Samoluk, S. B., & MacDonald, A. B. (1999). Anxiety sensitivity and substance use and abuse. In S. Taylor (Ed.). *Anxiety sensitivity* (pp. 287–319). Mahwah, NJ: Lawrence Erlbaum.

Stewart, S. H., Sherry, S. B., Comeau, M. N., Mushquash, C. J., Collins, P., & Van Wilgenburg, H. (2011). Hopelessness and excessive drinking among aboriginal adolescents: The mediating roles of depressive symptoms and drinking to cope. *Depression Research and Treatment, 2011*, 1–11. https://doi.org/10.1155/2011/970169

Stoltenberg, S. F., Mudd, S. A., Blow, F. C., & Hill, E. M. (1998). Evaluating measures of family history of alcoholism: Density versus dichotomy. *Addiction, 93*(10), 1511–1520. https://doi.org/10.1046/j.1360-0443.1998.931015117.x

Substance Abuse and Mental Health Services Administration. (2009). Integrated treatment for co-occurring disorders: Building your program. Retrieved from https://store.samhsa.gov/sites/default/files/d7/priv/ebp-kit-building-your-program-10112019.pdf

Substance Abuse and Mental Health Services Administration. (2020). *Substance use disorder treatment for people with co-occurring disorders*. Retrieved from https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP20-02-01-004_Final_508.pdf

Sundström, C., Hadjistavropoulos, H., Wilhelms, A., Keough, M., & Schaub, M. (2020). Optimizing internet-delivered cognitive behaviour therapy for alcohol misuse: a study protocol for a randomized factorial trial examining the effects of a pre-treatment assessment interview and health educator guidance. *BMC Psychiatry, 20*(1), 126. https://doi.org/10.1186/s12888-020-02506-2

Tait, R. J., Paz Castro, R., Kirkman, J., Moore, J. C., & Schaub, M. P. (2019). A digital intervention addressing alcohol use problems (the "Daybreak" program): Quasi-experimental randomized controlled trial. *Journal of Medical Internet Research, 21*(9), e14967. https://doi.org/10.2196/14967

Valentine, S. E., & Shipherd, J. C. (2018). A systematic review of social stress and mental health among transgender and gender non-conforming people in the United States. *Clinical Psychology Review, 66*, 24–38. https://doi.org/10.1016/j.cpr.2018.03.003

Vasilaki, E. I., Hosier, S. G., & Cox, M. W. (2006). The efficacy of motivational interviewing as a brief intervention for excessive drinking: A meta-analytic review. *Alcohol and Alcoholism, 41*(3), 328-335. https://doi.org/10.1093/alcalc/agl016

Verhoog, S., Dopmeijer, J., de Jonge, J., van der Heijde, C., Vonk, P., Bovens, R., de Boer, M., Hoekstra, T., Kunst, A., Wiers, R., & Kuipers, M. (2020). The use of the alcohol use disorders identification test – Consumption as an indicator of hazardous alcohol use among university students. *European Addiction Research*, *26*(1), 1–9. https://doi.org/10.1159/000503342

Vîslă, A., Constantino, M. J., & Flückiger, C. (2021). Predictors of change in patient treatment outcome expectation during cognitive-behavioral psychotherapy for generalized anxiety disorder. *Psychotherapy, 58*(2), 219–229. https://doi.org/10.1037/pst0000371

Wardell, J. D., Kempe, T., Rapinda, K. K., Single, A., Bilevicius, E., Frohlich, J. R., Hendershot, C. S., & Keough, M. T. (2020). Drinking to cope during covid-19 pandemic: The role of external and internal factors in coping motive pathways to alcohol use, solitary drinking,

and alcohol problems. *Alcoholism, clinical and experimental research*, *44*(10), 2073–
2083. https://doi.org/10.1111/acer.14425

Wendlandt, N. M., & Rochlen, A. B. (2008). Addressing the college-to-work transition:
Implications for university career counselors. *Journal of Career Development, 35*(2),
151–165. http://dx.doi.org/10.1177/0894845308325646

Werlen, L., Puhan, M. A., Landolt, M. A., & Mohler-Kuo, M. (2020). Mind the treatment gap:
The prevalence of common mental disorder symptoms, risky substance use and service
utilization among young Swiss adults. *BMC Public Health, 20*(1), 1470.
https://doi.org/10.1186/s12889-020-09577-6

Westra, H., Constantino, M., & Antony, M. (2016). Integrating motivational interviewing with
cognitive-behavioral therapy for severe generalized anxiety disorder: An allegiance-
controlled randomized clinical trial. *Journal of Consulting and Clinical Psychology,
84*(9), 768–782. https://doi.org/10.1037/ccp0000098

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E… & Vos,
T. (2013). Global burden of disease attributable to mental and substance use disorders:
Findings from the Global Burden of Disease Study 2010. *Lancet, 382*, 1575–1586.
https://doi.org/10.1016/S0140-6736(13)61611-6

WHOQOL GROUP. (1998). Development of the World Health Organization WHOQOL-BREF
Quality of Life Assessment. *Psychological Medicine, 28*(3), 551–558.
https://doi.org/10.1017/s0033291798006667

Witkiewitz, K., Pearson, M. R., Hallgren, K. A., Maisto, S. A., Roos, C. R., Kirouac, M., …
Heather, N. (2017). Who achieves low risk drinking during alcohol treatment? An
analysis of patients in three alcohol clinical trials. *Addiction*, *112*(12), 2112–2121.
https://doi.org/10.1111/add.13870

Wolitzky-Taylor, K., Bobova, L., Zinbarg, R. E., Mineka, S., & Craske, M. G. (2012).
Longitudinal investigation of the impact of anxiety and mood disorders in adolescence on
subsequent substance use disorder onset and vice versa. *Addictive behaviors, 37*(8), 982–
985. https://doi.org/10.1016/j.addbeh.2012.03.026

Wood, D., Crapnell, T., Lau, L., Bennett, A., Lotstein, D., Ferris, M., & Kuo, A. (2017).
Emerging adulthood as a critical stage in the life course. In N. Halfon et al. (eds.),

Handbook of Life Course Health Development, (pp. 123–143). https://doi.org/10.1007/978-3-319-47143-3_7

World Health Organization. (2014). *Global status report on alcohol and health 2014*. World Health Organization.

Wüsthoff, L. E., Waal, H., & Gråwe, R. W. (2014). The effectiveness of integrated treatment in patients with substance use disorders co-occurring with anxiety and/or depression: A group randomized trial. *BMC Psychiatry, 14*(67). https://doi.org/10.1186/1471-244X-14-67

Yang, C. C. (2006). Evaluating latent class analysis models in qualitative phenotype identification. *Computational Statistics and Data Analysis, 50*(4), 1090–1104. https://doi.org/10.1016/j.csda.2004.11.004

Yates B. T. (2020). Research on improving outcomes and reducing costs of psychological interventions: Toward delivering the best to the most for the least. *Annual Review of Clinical Psychology, 16*, 125–150. https://doi.org/10.1146/annurev-clinpsy-071519-110415

Yule, A. M., & Kelly, J. F. (2019). Integrating Treatment for co-occurring mental health conditions. *Alcohol Research: Current Reviews, 40*(1), e1-13. https://doi.org/10.35946/arcr.v40.1.07