Variables Associated with Performance on a Cognitive Screening Measure and Cognitive Remediation Training Outcome in the Acute Phase of Major Depressive Disorder

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Abstract

Major Depressive Disorder (MDD) is associated with cognitive deficits, particularly in the domains of attention, memory, and executive functioning (EF). Previous research has demonstrated that residual cognitive deficits secondary to depressive disorders are associated with risk of relapse. Established treatments for depression, such as cognitive behavioural therapy (CBT) and psychotropic medications, have been shown to improve cognition in MDD. More recently, cognitive remediation therapy has been associated with improvement of cognitive deficits in depression. This project consisted of two studies which sought to investigate the relationship between several clinical variables and (a) cognitive functioning, and (b) changes in cognitive functioning following cognitive remediation training in the acute phase of major depressive disorder. Study 1 used a retrospective study method and made use of a secondary database from a tertiary-care outpatient clinic. The purpose was to investigate the relationship between two variables (number of past depressive episodes and past hospitalization due to depression) and attention, memory, and executive functioning scores on a cognitive screening battery, in 125 individuals with acute depression, while controlling for psychiatric medication use. These two variables were unrelated to cognitive performance, after controlling for use of psychotropic medications. Study 2 was an exploratory pre-post community-based pilot study with 12 individuals with acute depression that examined the association of three clinical variables (number of comorbidities, severity of depression, and perceived cognitive deficit) with changes in memory, attention, and reasoning performance following an 8-weeks of CRT with six sessions per week. Participants completed 44.67 sessions (93.06%) with a range of 29 to 48 and showed improvement in memory scores. In univariate, but not multivariate models, comorbidity

and depression severity were positively associated with reasoning and memory score increases. Findings are discussed within the context of the strengths and limitations of the studies.

Keywords: depression, cognitive functioning, cognitive remediation training

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Major Depressive Disorder (MDD) is a common and debilitating mental health disorder characterized by sadness, loss of interest, and other affective, cognitive, and somatic symptoms (American Psychological Association, 2013). Recent studies indicate that the lifetime prevalence of major depressive disorder (MDD) in Canada is between 11.2% (Knoll & MacLennan, 2017) and 19% (Government of Canada, 2021). The prevalence of MDD has been found to be higher in women than in men (APA, 2013; Knoll et al., 2017; Shields et al., 2021). Further, the prevalence of MDD in Canada more than doubled (from 7% to 16%) during the COVID-19 pandemic (Shields et al., 2021).

The Burden of Depression

Over fifteen years ago, MDD was projected to become the second leading cause of disability worldwide by 2020 (Murray & Lopez, 1996). However, even before the COVID-19 pandemic was declared by WHO in 2020, this estimate was surpassed, as MDD was found to be the second leading cause of disability and poor health worldwide in 2019 (Ferrari et al., 2022).

The annual cost of depression in the USA has been estimated to be approximately $236 billion, which represents an increase of 35% since 2010 (Greenberg et al., 2021). The majority (61%) of this estimate is attributable to workplace costs (e.g., absenteeism and presenteeism), whereas 35% is attributable to direct costs (e.g., medical, pharmaceutical, inpatient, outpatient, and emergency-room services), and 4% to suicide-related mortality costs.

Few studies have investigated the cost of depression in Canada. Chiu and colleagues (2017) found the annual per-capita direct health-care costs in Ontario were 20% higher for a group of patients with depression compared to a nondepressed control group ($3,210 vs. $2,629).

Another study (Tanner et al., 2020) found that in Manitoba, depression added a total average health-care cost of almost $10,000 per person per year. The authors extrapolated their results to estimate the cost of depression to the entire Canadian health-care system. They estimated that the cost of MDD is approximately $12 billion annually in Canadian health system spending. However, in reality, it is likely that the current costs are higher due to the increase in depression during the COVID-19 pandemic (Shields et al., 2021).

Furthermore, treatment-resistant depression, which is defined as the failure to respond to at least two antidepressants used at an adequate dose and duration (Fava, 2003), occurs in approximately 50% to 70% of patients. It is estimated to result in an additional 30% increase in costs associated with health care utilization and direct medical expenditures when compared to depression that is not considered treatment-resistant (Amos et al., 2018; McCrone et al., 2017; Olchanski et al., 2013).

Functional Deficits in Depression

Depression adversely affects human functioning (Hammer-Helmich et al., 2018; McKnight & Kashdan, 2009). Those with depression report substantial functional deficits, which refers to the limitations that one may experience due to a physical or mental illness (Üstün & Kennedy, 2009). Thus, individuals with depression are less likely to be able to carry out certain activities in their daily lives, such as the ability to form and maintain healthy interpersonal relationships (e.g., De Aquino et al., 2017; Weinstock et al., 2006) and to work productively (e.g., Melnyk et al., 2018). Research suggests that depression is related to poorer functioning across many domains; however, the domains of individual, occupational and social-interpersonal functioning in depression have received the most research attention (McKnight & Kashdan, 2009; Üstün & Kennedy, 2009).

Individual Functioning. Individuals with depression often have difficulty in their individual functioning in addition to their depressive symptoms. For example, those with depression tend to have poorer self-efficacy, which refers to an individual's confidence in their own ability to execute their behaviours towards a desired goal (Bandura, 1994). Relative to nondepressed controls, individuals with depression have been found to have significantly poorer adaptive functioning (daily living skills) and interpersonal functioning (skills required to initiate and maintain social relationships), as well as significantly lower self-efficacy for adaptive and interpersonal behaviours (Milanovic, 2016).

Feelings of hopelessness, defined as the negative expectations regarding oneself and a negative emotional state characterized by the lack of finding a solution for one's problems (Beck et al., 1974) are common in those with depression (APA, 2013, Beck et al., 1993). This is of particular concern, as hopelessness has been associated with increased risk of suicide (Ribeiro et al., 2018).

Individuals with depression also exhibit more unhealthy behaviours compared to healthy controls. For example, people with depression who smoke cigarettes are more likely to increase their smoking behaviour over time compared to their nondepressed counterparts. A 5-year follow-up study (Breslau et al., 1998) looked at cigarette smoking patterns in smokers with a history of depression at baseline (depressed group) compared to smokers who had no history of depression at baseline (control group). The authors found that 23% of the depressed group progressed to daily smoking after 5 years, compared to only 9.3% of the control group. They also found that at 5-year follow-up, the rate of smoking cessation in the depressed group was lower than the rate of smoking cessation in control group. Individuals with depression also tend

to drink more alcohol than nondepressed controls (Graham & Massak, 2007). Those with MDD also have higher rates of substance use than healthy controls (Calarco & Lobo, 2021).

Individuals with depression also struggle to maintain healthy physical lifestyles. A meta-analysis (Roshanaei-Moghaddam et al., 2009) found that of 11 studies looking at the effects of depression on physical activity, eight studies found that depression at baseline was associated with significant risk of development of a sedentary lifestyle or decreased level of physical activity.

Occupational Functioning. The impact of depression on job performance has been estimated to be greater than that of other chronic and debilitating conditions such as arthritis, hypertension, back problems, and diabetes (Hays, 1995; Kessler et al., 2001). Those with depression are at high risk for early termination of education, which can in turn reduce future employment opportunities (Berndt, 2000; Kessler & Bromet, 2013). Depression is associated with increased absenteeism, as workers with depression are more likely to take time off work and to utilize mental health days compared to workers without depression (Gilmour & Patten, 2007; Lerner et al., 2010). Those with depression are also less productive at work, as they make more errors on the job (Melnyk et al., 2018) than nondepressed workers. Conversely, remission of depression is associated with significantly improved occupational functioning, particularly self-rated productivity (Daremo et al., 2015). Workers with depression have also been found to report more work conflict (arguments or other difficulties with coworkers), which in turn can lead to even greater loss of productivity in the work domain (Smith et al., 2002).

Research has found that depression affects worker productivity by reducing cognitive processing, attention, memory, concentration, and energy levels (McKnight & Kashdan, 2009). This is further supported by studies that have found specific symptoms of depression to be

associated with work deficit. For example, sleep-onset insomnia (Fried & Nesse, 2014) and cognitive problems, specifically concentration and memory problems (McIntyre et al., 2013), have been found to be more strongly related to poorer work functioning than other symptoms of depression. Thus, symptoms of depression, particularly sleep and cognitive problems, make it more difficult for workers to do their jobs effectively, leading to decreased productivity and in some cases absenteeism.

Social-Interpersonal Functioning. In addition to the work domain, depression is also associated with poorer social-interpersonal functioning. Research has found that depression is associated with a number of interpersonal problems, such as poor family functioning (Weinstock et al., 2006), marital dissatisfaction and discord (Coyne et al., 2002; Fink & Shapiro, 2013; Goldfarb & Trudel, 2019; Kessler & Bromet, 2013), and poor parent-child relationships and friendships (Kessler & Bromet, 2013; Mickelson, 2001; Nasser & Overholser, 2005; Windle, 1994).

A number of theories attempt to explain why those with depression have social-interpersonal problems. According to the interpersonal theory of depression (Coyne, 1976; Hames et al., 2013), individuals with depression want reassurance from others and engage in maladaptive interpersonal behaviours (e.g., excessive reassurance-seeking). These maladaptive interpersonal behaviours cause other people to negatively think about, avoid, and/or reject those with depression. The symptoms of those with depression then start to worsen as a result of other people's rejection and avoidance of them. Another theory, the self-verification theory (Hames et al., 2013; Swann & Greenwald, 1983), posits that people desire interpersonal feedback that confirms their self-concept because it enhances their ability to predict and control their own environment. Consistent with this theory, individuals with depression have been found to

engage in negative feedback-seeking whereby they actively solicit criticism from others. Receiving this negative feedback, however, leads to an increase in negative affect, thereby perpetuating depressive symptoms. According to the social reinforcement theory of depression (Lewinsohn, 1974), certain environmental changes and/or avoidant behaviours inhibit individuals from experiencing positive environmental reward and reinforcement, which in turn can lead to the development and persistence of depression. For example, certain life events, such as losing one's job, can induce depression because this reduces the positive reinforcement that the job offered (i.e., being around others). Other research suggests that those with depression may have social deficits, such as impaired social communication (e.g., impaired emotion recognition, lack of eye contact) and impaired social perception (e.g., reduced empathy), which may lead to problems in social-interpersonal functioning (Kupferberg et al., 2016).

In sum, research to date supports the notion that depression adversely affects human functioning (Hammer-Helmich et al., 2018; McKnight & Kashdan, 2009). At the individual level, depression is associated with functional deficit, such that those with depression may be less able to carry out certain functions in their daily lives (Üstün & Kennedy, 2009). Those with depression also tend to engage in unhealthier behaviour compared to controls (Calarco & Lobo, 2021; Graham & Massak, 2007; Roshanaei-Moghaddam et al., 2009). At the societal level, depression is associated with increased use of medical resources, productivity losses due to short-term and long-term disability, and reductions in health-related quality of life (Olchanski et al., 2013). Depression is associated with poorer occupational functioning, as represented by decreased work productivity (Melnyk et al., 2018; Smith et al., 2002) and absenteeism (Lerner et al., 2010). In addition, those with depression are at high risk for early termination of education, which can in turn reduce future occupational prospects (Berndt, 2000; Kessler & Bromet, 2013).

Depression is also associated with poor social-interpersonal functioning, including poor family functioning (Weinstock et al., 2006), marital dissatisfaction and discord (Coyne et al., 2002; Fink & Shapiro, 2013; Goldfarb & Trudel, 2019; Kessler & Bromet, 2013), and poor parent-child relationships and friendships (Kessler & Bromet, 2013; Mickelson, 2001; Nasser & Overholser, 2005; Windle, 1994). Given the significant burdens associated with depression, the literature suggests that depression is an important area in which to dedicate future research efforts.

Cognitive Deficits in Depression

Cognition refers to a broad set of abilities that allows an individual to perceive, process, manipulate, and respond to information and includes a number of mental functions including awareness, perception, attention, memory, processing speed, and higher order cognitive functions (i.e., executive functioning), such as planning, problem solving, and reasoning (McIntyre et al., 2015; Medalia et al., 2017). Problems with cognition are common in depression and are listed in the DSM-5 criteria for MDD as a "diminished ability to think or concentrate, or indecisiveness, nearly every day" (APA, 2013, pg. 161).

A distinction has been made between different types of cognition in depression. "Hot" cognition in depression involves cognitive function that is emotion-laden. Depression involves a cognitive bias towards emotional, specifically negative, information. For example, individuals with depression have been found to respond faster to negative stimuli than to positive stimuli (Mitterschiffthaler, et al, 2007). This negativity bias has been well-established by past research (for a review, see Miskowiak & Carvalho, 2014). Cognitive distortions in depression typically present as negative beliefs. They are considered "hot" cognitions because they are emotion-laden.

"Cold" cognition, on the other hand, involves cognitive function that does not involve emotion, such as reading a list of nonsense syllables (Ahern et al., 2019, Gonda et al., 2015; Roiser & Sahakian, 2013). Research suggests that up to 90% of individuals with depression experience deficits in different domains of "cold" cognition such as attention, memory, and executive functioning (Chakrabarty et al., 2016; Douglas et al., 2018; Hasselbalch et al., 2012; McIntyre et al., 2015; Murrough et al., 2011; Nuño et al., 2021). Cognitive deficits are deficits in non-emotionally laden tasks.

MDD is associated with neuroanatomical and neurochemical changes. The primary brain regions that have found to be compromised in MDD include the amygdala, the prefrontal cortex, and the hippocampus (Bergmann et al., 2025). Cold cognitive deficits in MDD have been associated with lower prefrontal cortex activation (Nord et al., 2020), while hot cognitive deficits in MDD have been associated with lower activation in the limbic system, particularly the amygdala (Schulze et al., 2020). Additionally, MDD symptoms have been associated with changes in neurotransmitters, particularly with decreases in dopamine, norepinephrine, and serotonin (Nut, 2008).

A number of studies (Conradi et al., 2010; Fava et al., 2007; Hasselbalch et al., 2012; Nierenberg et al., 2010; Potter et al., 2004; Rock et al., 2014; Semkovska et al., 2019) have supported the finding that cognitive deficits continue to linger after treatment even when other symptoms of depression (i.e., affective and somatic) remit. For example, Conradi et al. (2011) found that cognitive symptoms, specifically, concentration difficulties and indecisiveness, were the most prevalent symptoms in those with depression and were present during 85% to 94% of the duration of a depressive episode as well as during 39% to 44% of the duration of periods of remission. A meta-analysis conducted by Rock and colleagues (2014) looked at cognitive

functioning, assessed with a performance-based neuropsychological test battery, in patients with depression during acute (i.e., depressed) and remitted (i.e., euthymic) states. They found that the magnitude of cognitive deficits during acute and remitted states were not comparable and that those in remitted states had better memory scores than those in the acute state. Similarly, other studies have found that although cognitive deficits often present residually during the remitted phase of MDD, they have been found to be less severe during these remitted periods than during acute phases of the disorder (Hammar et al., 2022; Ji et al., 2020; Kriesche et al., 2022). Not surprisingly, even during periods of remission, residual cognitive deficits continue to interfere with daily functioning (Jaeger et al., 2006; Lam et al., 2012).

Not only do residual cognitive symptoms affect one's daily functioning, but residual depressive symptomatology has also been associated with risk of relapse (Paykel, 2008). The effect or "toxicity" of repeated depressive episodes (Gorwood et al., 2008) on cognition has been proposed to explain the persistence of cognitive deficits seen in depression. According to this view, each depressive episode leads to an accumulation of vulnerability, such that each depressive episode leads to further decline in functioning over time (Kaser et al., 2016). Furthermore, research supports the notion that "episodes beget episodes," such that the more depressive episodes one experiences, the more likely they will experience a subsequent episode (Post, 1992). Research suggests that 60% of individuals who have had one depressive episode will have a second, 70% of individuals who have had two depressive episodes will have a third, and 90% of individuals with three episodes will have a fourth episode (Bockting et al., 2015; Solomon et al., 2000).

In sum, cognitive deficits are a core symptom of depression. They are very common and are often resistant to treatment and linger even when other symptoms of the disorder remit

(Conradi et al., 2011). These residual cognitive deficits in turn can increase the risk of relapse of depression (Paykel, 2008).

Cognitive Deficits and Functional Deficit

According to Kielhofner (2009), cognition involves "a process of identifying, selecting, interpreting, storing, and using information to make sense of and interact with the physical and social world, to conduct one's everyday activities, and to plan and enact the course of one's occupational life" (p. 85). Thus, success in everyday life relies, in part, on one's level of cognitive functioning. Conversely, cognitive dysfunction can impair one's ability to function in daily life (i.e., functional deficit). For example, if one has significant difficulty in remembering information, they will likely have difficulty in maintaining a home, in keeping a job, and in establishing and keeping meaningful interpersonal relationships.

Not surprisingly, research shows that cognitive symptoms, such as attention and memory problems, are associated with functional deficit in patients with MDD (Hammer-Helmich et al., 2018). Fried and Nesse (2014) investigated the degree to which symptoms of depression differed in their associations with deficit in five domains (work, home management, social activities, private activities, and close relationships). They found that concentration problems had the second highest association with all deficit domains, second only to sad mood. The results of this study suggest that cognitive deficits, specifically concentration difficulties, in depression are among the most disabling symptoms of the disorder. Cognitive deficits seen in depression can affect occupational and social-interpersonal functioning. Hammer-Helmich and colleagues (2018) found that perceived cognitive symptoms were more strongly associated with presenteeism (i.e., working when sick) than with absenteeism, suggesting that those who perceive their cognitive symptoms to be worse are more likely to remain working when they

have depression rather than taking time off work. The authors suggest that these individuals may either be reluctant to disclose their diagnosis to their employers and/or they may not be able to miss work or take extended leaves due to economic reasons. Presenteeism can, in turn, have negative consequences for the individual and for others. For example, Melnyk et al. (2018) found that nurses with depression were more likely to make medical errors on the job than those who did not have depression.

In terms of social-interpersonal functioning, those with depression may have a reduced ability to concentrate on the topic of conversation (Schwartz-Mette & Rose, 2016), which in turn can negatively affect interpersonal relationships. Furthermore, individuals with depression may not have sufficient cognitive resources to process incoming social signals (Mor & Winquist, 2002) and thus may misinterpret the behaviours of others. Cognitive symptoms can also have a direct negative effect on one's mental health. For example, other research suggests that cognitive deficits in depression can increase the risk for psychological decompensation (i.e., deterioration of mental health) by compromising an individual's ability to follow and implement psychiatric or psychological treatment plans (Medalia et al., 2017). That is, an individual's mental health may deteriorate because he or she is unable to follow a treatment plan effectively due to cognitive deficits.

Research suggests that improvement in cognitive deficits over time may play an important role in functional recovery (i.e., improvement in life functioning) for patients with depression. Jaeger et al. (2006) found that in a sample of patients hospitalized for MDD, cognitive improvement over time was associated with a higher likelihood of functional recovery and those who showed no improvement or worse cognitive functioning were more likely to be significantly or totally disabled, which was defined as "virtually total care provided in

institutional or specialized environments with no independent functioning" (p. 42). Thus, when looking at the different symptoms of depression and how they impact one's functioning, research suggests that cognitive symptoms may be among the most disabling symptoms of depression (e.g., Fried & Nesse, 2014).

Age and Cognitive Functioning

Age is a factor that can markedly influence performance on cognitive tasks. Studies have documented the finding that cognitive performance generally declines with age (Harada et al., 2013). Research suggests that older individuals (older than 65 years of age) with depression tend to have worse cognitive deficits than their younger counterparts (Albert et al., 2018). For example, Fossati and colleagues (2002) found a significant effect of age on verbal memory performance in young and older adult patients with depression, with older adult patients performing more poorly than younger patients on a verbal memory task. Furthermore, MDD has been associated with different age-related neurobiological changes. More specifically, older individuals with depression have been found to have greater atrophy in their hippocampus, whereas younger individuals with depression have been found to have greater atrophy in the prefrontal cortex (Bergmann et al., 2025).

Thus, a distinction can be made between the extent of cognitive functioning in late-life depression and the extent of cognitive functioning in individuals who are younger than 65 years of age. The differences in cognitive deficits between older and younger depressed samples suggest that the research on cognitive deficits associated with depression in older samples may be less applicable to younger samples, and vice-versa.

Assessing Cognitive Deficits in Depression

Cognitive deficits in depression have been assessed using subjective self-reports and objective psychometric neuropsychological tests. Self-report measures are questionnaires that are completed either by the individual or a collateral informant. They are considered to be subjective measures because they measure the individual's subjective experience of cognitive functioning as reported by the self or another party. Self-report measures are often used in primary care settings (Svendsen et al., 2012), particularly as screening instruments, because they are relatively inexpensive and easy to administer. Examples of often-used self-report measures of depression symptoms include the Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001) and the Beck Depression Inventory-II (BDI, Beck et al., 1996). These measures contain some items assessing cognitive difficulties associated with depression. To measure the full scope of perceived cognitive deficits, the Perceived Deficits Questionnaire (PDQ; Sullivan et al., 1999) has been used.

In addition to self-report measures, objective psychometric neuropsychological tests are also used to assess cognitive deficits in depression. Neuropsychological assessment can be defined as "a performance-based method to assess cognitive functioning and is performed with a battery approach, which involves a variety of cognitive ability areas" (Harvey, 2012, p. 91). These tests are considered objective because they make use of normative comparison stratified by various demographic variables, such as age, sex, and education, based on standardized samples. Examples of neuropsychological tests include Coding subtest from the Weschler Adult intelligence Scale (WAIS; Wechsler, 2008) and Ray Auditory Verbal Learning test (RAVLT; Rey, 1958).

There are several specific uses of neuropsychological assessment, including collection of diagnostic information, differential diagnostic information, assessment of treatment response,

and prediction of functional potential and functional recovery. Some examples of well-validated measure of cognition include the Digit Symbol Substitution test (DSST) or the Coding subtest from the Weschler Adult Intelligence Scale (WAIS). Neuropsychological testing has important practical implications in depression treatment settings. Results from these types of tests can inform treatment planning which might be tailored in accordance with patients' identified cognitive strengths and weaknesses with the hope of improving treatment response and outcome.

Self-Reported Cognitive Deficits in Depression

The most common self-reported cognitive deficits in depression are attention/concentration and memory (Gaynes et al., 2007). In a study of 164 outpatients with depression (Lam et al., 2012), 96% noted difficulty concentrating and 93% reported problems with memory. Furthermore, 52% of these patients perceived these cognitive symptoms as interfering substantially with their occupational functioning. The presence of memory and attentional complaints also differentiates individuals with depression from nondepressed, healthy controls. Naismith and colleagues (2007) found that patients with acute depression rated themselves as experiencing higher levels of cognitive dysfunction in the domains of speed, concentration, and short-term memory than nondepressed controls.

Performance-based Cognitive Deficits in Depression.

There is ample research on cognitive functioning in depression using neuropsychological tests. Many studies have used full neuropsychological batteries, whereas others have used only a few subtests from these batteries to tap into the various cognitive domains. Neuropsychological deficits in individuals with depression have been documented in a number of domains such as general intelligence, motor functioning, processing speed, visuospatial processing, attention, verbal and nonverbal memory, and executive functioning to name a few (Harrison et al., 2016;

Jaeger et al., 2006; Roiser & Sahakian, 2013); however, not all studies have consistently found deficits in each of these domains (Jaeger et al., 2006). Most studies that have investigated cognitive deficits in depression have been small, cross-sectional studies that have used different patient populations (e.g., combining bipolar and unipolar depression) and widely varying neurocognitive batteries (Russo et al., 2015). As a result, not all studies have assessed the same cognitive domains. Furthermore, the sensitivity of the assessment tools used to assess cognitive deficits in depression have also varied (Russo et al., 2015). Despite this, attention, memory, and executive functioning are the domains in which cognitive deficits in depression are most commonly found (Harrison et al., 2016; Hasselbalch et al., 2012; Jaeger et al., 2006; Mohn &; Murrough et al., 2011; Papakostas, 2014; Rock et al., 2014; Roiser & Sahakian, 2013; Rund, 2016; Stordal et al., 2004; Zakzanis et al., 1998) with many studies showing moderate effect sizes between individuals with depression compared to nondepressed controls in these neurocognitive domains.

Given that the depression-related cognitive deficits seen in late life (i.e., after the age of 65) differ from those seen in younger adults, the literature reviewed below only includes studies that investigate cognitive deficits associated with depression with a younger adult population between the ages of 18 and 65.

Attention. Attentional deficits are considered to be a core symptom of depression (APA, 2013). Attention refers to "several different capacities or processes that are related aspects of how the organism becomes receptive to stimuli and how it may begin processing incoming or attended-to excitation" (Lezak et al., 2004, p. 34). Attention can involve both automatic (involuntary) and controlled (voluntary) processes. Automatic attentional processes occur without conscious awareness and thus require no or very few cognitive resources, whereas

controlled attentional processes tend to be more effortful as they require conscious awareness and more cognitive resources (Schneider & Shiffrin, 1977). Hasher and Zacks (1979) have postulated that effortful, but not automatic, attentional processes are compromised in depression. Research has generally supported this hypothesis, with studies showing that individuals with depression tend to perform worse than healthy controls on more effortful attentional tasks but not automatic tasks (e.g., Thomas et al., 1998). Furthermore, research has also shown that an important characteristic of attention is its limited capacity (e.g., Lavie, 2005); this aspect of attention implies that individuals can selectively attend to only a small portion of the stimuli with which they are presented, whereas the vast majority of concurrent stimuli remains in the background. Lezak et al. (2004) have identified several domains of attention, including: (1) immediate span of attention; (2) selective or focused attention; (3) sustained attention; (4) divided attention; and (5) alternating attention. In particular, depression has been found to be associated with deficits in selective attention, sustained attention, and divided attention. In the cognitive literature, cognitive deficit in depression has been classified as cognitive performance scoring 1 or 1.5 standard deviations lower than the mean scores of healthy controls (Liu et al., 2023).

Selective, also called focused, attention refers to an individual's ability to attend to certain stimuli to the exclusion of others (Lezak et al., 2004). A recent study by Keller et al. (2019) compared selective attention deficits in a sample of over 1,000 participants with MDD and a sample of 336 age- and sex-matched healthy controls using a non-emotional Stroop color-word task. They found that those with MDD had longer reaction times than controls, indicating that the MDD group had more difficulty in selective attention. Similarly, other studies have found selective attention deficits in "cold" (or emotion-independent) cognition in depression

(Holmes & Pizzagalli, 2008; Rock et al., 2014; Semkovska et al., 2019). Several other studies have also found that "hot" (or emotionally-laden) cognitive deficits are also present in depression. These studies have found that individuals with depression show a negative cognitive bias in that they are more likely to attend to negative stimuli rather than positive or neutral stimuli (e.g., Joorman & Gotlib, 2007; Joormann, et al., 2015; Kaser et al., 2016; Koster et al., 2005; Mathews et al., 1996; Surguladze et al., 2005).

Sustained attention, also called vigilance, refers to an individual's ability to focus on certain stimuli for an extended period of time and is often measured using tasks in which individuals must attend and respond to specific stimuli consistently during a repetitive or continuous task (Lezak et al., 2004). Several studies have demonstrated that compared to nondepressed controls, individuals with depression make more errors of omission and commission and display longer reaction times on sustained attention tasks (Agarwal et al., 2002; Farrin et al., 2003; Keller et al., 2019; Kemp et al., 2009; Lim et al., 2013; Porter et al, 2003; Tenke et al., 2008; van der Meere & Borger, 2007).

Divided attention involves the ability to engage and respond to several tasks at the same time (Lezak et al., 2004). Divided attention tasks typically require participants to simultaneously pay attention to two or more different stimuli and respond only to target stimuli. Several authors have found that participants with depression are slower than nondepressed controls to react to target stimuli when required to divide their attention (e.g., Keller et al., 2019; Lautenbacher et al., 2002; Majer et al. 2004; Thomas et al., 1998). This is consistent with Hasher and Zacks' hypothesis (1979) that more effortful attentional processes (i.e., dividing one's attention) are compromised in depression.

Taken together, these results suggest that depression is associated with significant deficits in selective, sustained, and divided attention compared to nondepressed controls. Specifically, individuals with depression often show attentional biases that influence the type of information that they attend to, are less able to sustain their attention, and are less able to divide their attention as needed.

Memory. Depression is also commonly associated with a number of memory deficits. Research has established that memory is a complex concept involving several distinct processes (Squire & Zola, 1996). One important distinction is between explicit and implicit memory. Explicit memory, also referred to as declarative memory, involves knowledge that is consciously available, whereas implicit, or procedural, memory involves knowledge that is not consciously available but is often expressed in performance, such as riding a bike (Lezak et al., 2004). Depression is associated with an implicit memory bias towards negative stimuli compared to positive stimuli (Gaddy & Ingram, 2014; Phillips et al., 2010). Depression is also associated with declarative memory deficits (Deuschle et al., 2004; Zakzanis et al., 1998).

Another important distinction within the memory domain is that between verbal and visual memory (Moscovitch, 1992). Several studies have shown that depression is associated with impaired verbal memory (e.g., Burt et al., 1995; Chen et al., 2018; Fossati et al., 2002; Gregory et al., 2020; Hermens et al., 2010). Specifically, compared to healthy controls, individuals with depression recall fewer words on tests of immediate recall and show deficits on tests of story learning and recall (Hammar et al., 2011; Kizilbash, 2002)

Visual memory has also been found to be impaired in individuals with depression (Chen et al., 2018; Hammar et al., 2011; Hammar & Schmid, 2013). Several studies have found that individuals with depression performed significantly worse on the delayed recall and recognition

trials of visual memory tests than controls (Behnken et al., 2010; Hammar et al., 2011; Hammar & Schmid, 2013). Furthermore, research suggests that those with depression are more likely to show deficits in recall, rather than recognition, as the former is considered to be more cognitively demanding (Brand et al., 1992; Kizilbash, 2002). Thus, depression is associated with deficit in a number of different types of memory including declarative, verbal, and visual memory.

Executive functioning (EF). Depression is also associated with significant deficits in executive functioning (EF). EF includes self-regulated, higher-level cognitive processes that control and regulate lower, more automatic processes towards goal-directed behavior (Snyder, 2013). More specifically, EF involves the ability to flexibly adjust behaviours/actions, engage in strategic planning, and complete goal-oriented tasks (DeBattista, 2005; Millan et al., 2012). There are many different aspects of EF, some of which include set-shifting, inhibition, and working memory; empirical studies have found evidence of EF deficits due to depression with respect to all of these areas of EF (Ahern & Semkovska, 2017; Rogers et al., 2004).

Set-shifting refers to the ability to adapt behaviour and thoughts to new, changing, or unexpected circumstances and/or situations (Pender et al., 2014). Set-shifting is also sometimes referred to as cognitive flexibility which can be defined as the ability to adapt behaviours in response to changes in the environment (Dajani & Uddin, 2015). Merriam and colleagues (1999) have shown that individuals with depression perform more poorly on the Wisconsin Card Sorting Test (WCST), a widely used neuropsychological index of prefrontal cortical function, than controls. Other set-shifting tasks have also been found to differentiate between individuals with depression and controls (Christensen et al., 1997; Gabrys et al., 2018; Gregory et al., 2020; Liu et al., 2021; Snyder, 2013; Trivedi & Greer, 2014; Veiel, 1997).

Response inhibition refers to the ability to suppress or avoid an automatic response in order to make a less automatic but task-relevant response (Miyake et al., 2000; Snyder, 2013). Several studies have found that individuals with depression display significant inhibition deficits compared to controls (Schmid et al., 2011; Snyder, 2013; Veiel, 1997; Zakzanis et al., 1998). Research has found that individuals with depression show enhanced attention for depressive stimuli relative to neutral stimuli (e.g., Leung et al., 2009). It has been suggested that this attentional bias in depression is in fact due to the lack of inhibition of mood-congruent material (i.e., negative material) (Joorman & Gotlib, 2007). However, inhibition deficits in individuals with depression have also been shown for non-emotional stimuli, such as non-emotional Go/No-Go tasks that involve responding to target images, while simultaneously withholding response to distractor images, using non-emotional stimuli, such as using letters of the alphabet. (Burdette et al., 2021; Gregory et al., 2020; Keller et al., 2019).

A final aspect of EF, working memory, is defined as the ability to temporarily maintain and manipulate information in short-term memory (Baddeley et al., 1996). Several studies have found that depression is associated with working memory deficits (Gärtner et al., 2018; Joorman & Gotlib, 2007; Nikolin et al., 2021; Pelosi et al., 2000; Rose & Ebmeier, 2006; Sweeney et al., 1998).

In sum, research has looked at specific cognitive deficits associated with depression in the domains of attention, memory, processing speed, and EF. Using a variety of neuropsychological tests in each of these domains, the literature supports the notion that compared to nondepressed controls, those with depression show deficits in selective, sustained, and divided attention, verbal and visual memory, and several domains of EF, notably, verbal fluency, set-shifting, working memory, and inhibition.

Variables Associated with Cognitive Deficits in Depression

Understanding variables that are related to cognitive functioning in individuals with depression may provide insight into the processes by which depression can cause cognitive deficits and how they can be treated. Several investigations have looked at clinical variables that may contribute to cognitive dysfunction in depression.

Number of Past Depressive Episodes

One variable that has been studied in relation to cognitive functioning in depression is number of past depressive episodes. A recent review (Kriesche et al., 2022) looking at cognitive deficits in the acute and remitted phases of depression found a positive correlation between the number of episodes of depression and cognitive deficits. One study (MacQueen et al., 2002) found that the higher number of depressive episodes predicted poorer performance on a computerized memory task in a sample of individuals with depression. However, the authors did not distinguish between participants with past or current depression. Another study (Paelecke-Habermann et al., 2005) compared EF performance in two depression groups: a "mild group" which consisted of individuals with one or two previous depressive episodes and a "severe group" which consisted of individuals with three or more previous depressive episodes. They found that the severe group showed greater deficits in the EF domains of planning and monitoring compared to the mild group. Basso and Bornstein (1999) compared memory functioning in individuals with recurrent depression, individuals with first-episode depression, and healthy nondepressed controls. They found that the recurrent group demonstrated greater deficits on measures of episodic verbal memory recall than the single-episode group and healthy controls and that the nature of these group differences reflected a deficit in acquisition rather than in retrieval or retention for the recurrent group. Importantly, the two groups with

depression were not found to differ in overall severity of depression, suggesting that the memory deficits seen in the recurrent group were not due to greater emotional distress, but instead due to recurrent depressive episodes. In contrast to these results, a study by Miskowiak et al. (2016) found that in a sample of bipolar and unipolar patients, number of previous depressive episodes did not predict cognitive change over an 8-week period.

A recent meta-analysis (Semkovska et al., 2019) reviewed over 250 studies on depression and cognitive functioning and found that the number of previous depressive episodes negatively affected cognitive functioning in individuals with a past history of depression who were currently euthymic. That is, they reported that the higher the number of previous episodes, the more severe the cognitive deficits relative to healthy controls. However, this review focused on the remitted (i.e., euthymic) phase of depression; thus, their results are not generalizable to what happens to individuals during the acute (i.e., currently depressed) phase of depression. Also, many of the studies reviewed in this meta-analysis did not control for past head injuries, an issue that the authors do not discuss. Another limitation of this meta-analysis is that the authors were unable to assess the influence of age on the relationship between the number of past depressive episodes and cognitive functioning. A study by Gregory and colleagues (2020) found that older age (>65) was associated with poorer cognitive functioning across a number of neurocognitive domains. Individuals who are older are more likely to have had depression for a longer duration than individuals with depression who are younger. Since the more depressive episodes one experiences, the more likely he or she will experience a subsequent episode (Post, 1992), older individuals would likely have experienced more episodes of depression than their younger counterparts (Gorwood et al., 2008), creating a potential confound. Most research has not

controlled for this current age effect when looking at the relationship between the number of past depressive episodes and cognitive functioning to ensure that age does not confound the findings.

Past Hospitalization Due to Depression

Several studies have found that hospitalization due to depression is associated with poorer cognitive functioning in one or more cognitive domains. More specifically, greater number of past hospitalizations due to depression have been associated with greater deficits on measures of EF (Harvey et al., 2004) and verbal memory (Elgamal et al., 2010). Of note, the study by Elgamal et al. (2010) used participants with an age range of 15 to 75. Part of this is due to normal age-related cognitive decline (Salthouse, 2009). Thus, the results of this study may not be relevant to individuals between the ages of 18-65 with depression.

A study by Preiss et al. (2009), found that patients with MDD who had more previous hospitalizations performed significantly worse on measures of attention and EF than controls. However, the authors used a different diagnostic system for the identification of depression (i.e., ICD-10) as the study was conducted in Europe, rather than North America's diagnostic system (i.e., DSM-5). Furthermore, the authors only included individuals with remitted depression but excluded those with acute depression. Cognitive deficits present during the remitted phase of MDD have been found to be less severe than cognitive deficits present during acute phases of the disorder (Hammar et al., 2022; Ji et al., 2020; Kriesche et al., 2022).

Number of hospitalizations due to depression has been linked to severity of depression. A systematic review by Prina et al. (2015) found an association between depressive symptoms and subsequent admission to a general hospital, longer length of stay, and higher re-admission risk. Suicidal behaviours are the most concerning symptoms of depression and often result in hospitalization. Suicide risk has been associated with cognitive deficit. Using a measure of

risky decision-making, Zheng and colleagues (2022) compared hospitalized individuals with MDD who had attempted suicide and compared them to hospitalized nondepressed controls. They found that the MDD group was more likely to make risky decisions than controls, which would signify problems with EF. Other research suggests that risk of rehospitalization after a suicide attempt is high, especially for the first month after release from the hospital (Cepeda et al., 2020). Thus, the more hospitalizations for depression that a person experiences, the more severe their symptoms were.

The current age of participants was not taken into account in most of these studies. For example, Elgamal et al. (2010) included participants up to age 75. Older and late-life depression (above age 65) is associated with a distinct profile of cognitive deficits that differs from that of younger individuals with depression (Fossati et al., 2002). In particular, older individuals with depression tend to have worse verbal memory and other age-related cognitive decline compared to adults who are age 18 to 65 (Albert et al., 2018; Salthouse, 2009).

As noted, age is a factor that can significantly influence performance on some cognitive tasks. Studies have documented the finding that cognitive performance generally declines with age (Harada et al., 2013). Research suggests that that older individuals (older than 65 years of age) with depression tend to have worse cognitive deficits than their younger counterparts (Albert et al., 2018). For example, Fossati and colleagues (2002) found a significant effect of age on verbal memory performance in young and older adult patients with depression, with older adult patients performing more poorly than younger patients on a verbal memory task. Thus, a distinction can be made between the extent of cognitive functioning in late-life depression and the extent of cognitive functioning in individuals who are younger than 65 years of age. The differences in cognitive deficits between older and younger depressed samples suggests that the

research on cognitive deficits associated with depression in older samples may not be applicable to younger samples, and vice-versa.

Individuals who are older are more likely to have had depression for a longer duration than individuals with depression who are younger (Gregory et al., 2020). Furthermore, those who have had depression longer are more likely to have experienced a greater burden of illness (or more hospitalizations) due to depression.

Limitations to Previous Research

In sum, investigations have led to inconsistent results, with some studies finding an association between certain clinical variables and cognitive deficits (e.g., Paelecke-Habermann et al., 2005) whereas others have not (Miskowiak et al., 2016). These inconsistencies are likely due to methodological differences between studies, which have utilized different methods of assessment of both clinical factors and cognitive functioning (McClintock et al., 2010; McDermott & Ebmeier, 2009). Furthermore, other studies (e.g., Preiss et al., 2009) have not distinguished between remitted and acute phases of MDD. Previous research has found that, as expected, cognitive deficits are less severe during remitted periods than during acute phases of the disorder (Hammar et al., 2022; Ji et al., 2020). As well, a review by Krieske and colleagues (2022) found that there may be differences in the types of cognitive deficits exhibited by those with acute depression and those remitted depression. Individuals with acute depression showed deficits in processing speed, learning, and memory. Although they did find less pronounced cognitive deficits in those with remitted depression, some deficits were still present, particularly in the domains of attention, learning and memory, and working memory. Another limitation to previous research is that self-reports of individuals' functioning are often not corroborated with more objective information, such as information that is documented by a psychiatrist that could

be obtained from individuals' clinical chart. A limitation to self-report measures is that they can suffer from limited reliability and validity (Dang et al., 2020). For example, patients may over-report or under-report their symptoms for a variety of reasons (e.g., social desirability, inconsistency of responses due to negligence). Thus, it is important to distinguish acute and remitted depression in research, as they are associated with different cognitive deficits and to corroborate self-reported information.

More research is needed to fully understand the clinical variables that are associated with cognitive deficits in depression. Future work needs to address these limitations in previous research by using large homogeneous samples consisting of outpatient adults with unipolar depression, by distinguishing between acute and remitted states of depression, by excluding individuals without acute MDD, by controlling for the possible confounding effects of age, and by corroborating self-report with information obtained through chart review. Understanding the clinical variables that are associated with cognitive performance of patients with depression may provide insight into the processes by which depression leads to cognitive dysfunction. This might help to inform the development of more effective treatments for cognitive deficits in depression.

Treatment of Cognitive Deficits in Depression

There are several established treatments for MDD, including cognitive behavioural therapy (which is discussed below) as well as psychotropic medication. According to the Anxiety and Depression Association of America (ADAA; 2020), pharmacotherapy, including antidepressants, selective serotonin reuptake inhibitors (SSRIs), and selective norepinephrine reuptake inhibitors (SNRIs), is considered a first-line treatment for depression.

Cognitive Behavioural Therapy

Cognitive behavioural therapy (CBT) is a short-term, evidence-based treatment for depression and is arguably the most recognizable and widely used forms of psychotherapy (Hofmann et al., 2012). CBT is based on the cognitive model of depression put forth by Beck, Rush, Shaw and Emery in 1979. CBT is based on the premise that psychopathology is caused by dysfunctional and repetitive negative thinking patterns, that in turn cause emotional and behavioural difficulties. CBT teaches individuals to modify their dysfunctional cognitions and maladaptive behaviours, and to alter the manner in which they interpret and act on negative emotions. Treatment is delivered through a psychoeducational approach, in which clients are provided a rationale for CBT through a consideration of the relationship between cognition, emotions, and behaviour (Beck, 1995; Hamilton & Dobson, 2002). Treatment is focused on solving current problems, is structured and directive, and is brief and time-limited, usually lasting 12 to 16 sessions (Beck, 1995).

CBT is recommended as a first-line treatment for depression (ADAA, 2020; American Psychological Association, 2019). Several meta-analyses have compared the efficacy of pharmacotherapy and various psychotherapies, including CBT, for depression. The results of these have indicated that antidepressants and psychotherapies are approximately equivalent in terms of their efficacy. However, psychotherapies may provide some additional prophylactic (i.e., protective) effect in terms of recurrence of depression (Cuijpers et al., 2013; De Maat et al., 2006; Imel et al., 2008). One benefit of psychotherapy is that it does not pose the risk of negative side effects that can accompany pharmacotherapy (Martin-Vazquez, 2016; Sansone & Sansone, 2012). Thus, for some individuals, psychotherapy may be a more attractive option.

Research on CBT shows it to be more effective than waitlist or no treatment conditions (Butler et al., 2006; Cuijpers et al., 2013; Hofmann et al., 2012). However, studies comparing the effectiveness of CBT to other psychological treatments have found mixed results (Hofmann et al., 2012). A few meta-analyses have found CBT to be as effective compared to other treatments such as supportive-expressive therapies, peer support interventions, interpersonal, and psychodynamic therapies (Beltman et al., 2010; Pfeiffer et al., 2011). Recently, Cuijpers and colleagues (2023) conducted a meta-analysis that included 87 studies comparing the effects of CBT to other psychotherapies. They found that CBT had a small, but significant, effect over other psychotherapies. Other research has found favourable results for CBT. For example, CBT has been found to be superior to relaxation techniques and psychodynamic therapy (Jorm et al., 2008; Tolin, 2010). Other research suggests that CBT can also have beneficial effects on occupational and psychosocial functioning (Matsunaga et al., 2010).

Despite research that supports CBT as one of the most effective treatments for depression, many individuals do not improve with standard CBT. For example, Thimm and Antonsen (2014) looked at the effectiveness of group CBT for depression in a sample of outpatients. Their results showed that 56% of individuals did not show a significant improvement in depression from CBT. Other research shows that CBT does not specifically improve the cognitive deficits seen in depression. A study conducted by Porter and colleagues (2015) examined the effect of CBT and schema therapy on cognitive functioning in a sample of outpatients with depression and a sample of nondepressed controls. They found that after 16 weeks of psychotherapy, the group with depression showed a significant decrease in affective symptoms but no improvement on cognitive measures. Thus, although CBT and schema therapy can alleviate affective symptoms of depression, it appears that these therapies do not improve the

cognitive deficits seen in depression. The authors concluded that their results "suggest a need to modify psychological treatments to include components targeting cognitive functioning" (p. 393). This is further supported by research showing that cognitive deficits often persist even when affective symptoms of depression remit (e.g., Conradi et al., 2010; Fava et al., 2007; Hasselbalch et al., 2012; Nierenberg et al., 2010; Potter et al., 2004; Rock et al., 2014; Semkovska et al., 2019). Since residual cognitive symptoms can increase the risk of relapse (Paykel, 2008), this research has led to important questions about how standard treatments for depression can be improved.

Cognitive Remediation Therapy

Cognitive remediation therapy (CRT) is a form of behavioural training for people who are experiencing cognitive deficits and involves a collection of techniques that is designed to help people develop and strengthen underlying cognitive skills in domains such as attention, memory, and EF (Galletly & Rigby, 2013; Medalia et al., 2016; Thérond et al., 2021). CRT involves structured training in particular cognitive domains using either paper-and-pencil tests or computer programs. More recent studies have utilized computerized CRT, delivered in clinics or in clients' homes, as these methods have the advantage of being standardized and more efficient (Galletly & Rigby, 2013). A training session often includes a mixture of visual, auditory, and cross-modality tasks or 'games' in different cognitive domains. For example, a task for focused attention may require respondents to click on certain types of stimuli (e.g., apples) while simultaneously ignoring distracting stimuli (e.g., other types of fruit). An example of a recognition memory task may require respondents to identify stimuli (e.g., animals) that they were previously presented with. These tasks are presented repeatedly to the respondent in subsequent training sessions at increasing levels of difficulty. Often, CRT programs will provide

feedback on respondents' performance. This can offer behavioural reinforcement, motivating respondents to continue CRT training to further improve their cognitive skills (Corbo & Abreu, 2028).

CRT is based in part on the principle of neuroplasticity (Rabipour & Raz, 2012). Neuroplasticity refers to the notion that a change in neural structure and function can occur in response to experience or environmental simulation (Shaw et al., 1994). Research shows that repeated practice of a certain skill can result in lasting changes in neural structures. Maguire and colleagues (2006) found that taxi drivers have larger gray matter volumes in brain areas associated with spatial memory. Similarly, professional typists have greater development of neural regions related to the programming of motor tasks (Cannonieri et al., 2007). In further support of neuroplasticity, some research suggests that CRT can generalize beyond task-specific skills and apply to untrained overarching abilities (Jaeggi et al., 2010). In this study, the authors looked at whether training individuals on the n-back test would improve their fluid intelligence. The authors defined fluid intelligence as involving "the ability to adapt thinking to new cognitive problems" (p. 1). They compared two groups of participants (n = 104), who were trained on either the single n-back test or the dual n-back test for a total of eight weeks. The n-back test is a neuropsychological test that measures working memory. The authors compared these two student groups with a control group who had no training on the n-back test. Results showed that the two cognitive training groups saw improved working memory compared to the non-trained control group. Furthermore, there was also an improvement to the training groups' fluid intelligence, which refers to the ability to solve problems in novel situations (Jaeggi et al., 2010). This effect may be due to the fact that working memory and fluid intelligence share overlapping neural networks in the prefrontal cortex; thus, improvement in one ability can lead to improvement in

the other (Klingberg, 2010). Thorsen et al. (2014) conducted a review of neurobiological changes associated with CRT in individuals with schizophrenia focusing on studies using brain imaging techniques before and after CRT. They found that CRT affects the activity and structure of multiple brain regions, including prefrontal, parietal, and limbic areas. They also found that changes in prefrontal brain areas were the most reported finding across studies, which is consistent with the finding that schizophrenia is associated with dysfunction in this region. The results of this review support the notion that CRT is associated with both cognitive as well as neurobiological improvement, thus supporting the role of neuroplasticity in CRT.

There are several commercially available types of computerized online training. Some of the more popular programs are from the companies Cogmed, Lumosity, and Cognifit. Users are able to sign up for an online account, can purchase products (e.g., assessments and training programs) based on their needs (e.g., memory problems, cognitive problems associated with depression), and can monitor their progress.

A debate exists in the literature as to whether CRT programs are truly effective, with some researchers arguing that CRT has limited empirical evidence of efficacy (Melby-Lervåg & Hulme, 2013; Nguyen et al., 2021), whereas other researchers have argued that empirical evidence of its efficacy does exist (Harvey et al., 2018; Jaeggi et al, 2008; Redick et al., 2013). Unfortunately, it seems that such a debate is warranted, as there are many inconsistencies in the CRT literature. The difficulty in determining if CRT is truly effective or not is likely due to methodological differences between past studies, which have utilized different CRT programs, different methods of assessment, and different populations. This had made comparisons across studies difficult. Furthermore, replication of research findings is uncommon in the CRT literature.

The Role of CRT in Mental Health. CRT was originally developed to treat cognitive deficits seen in schizophrenia and there is substantial empirical support for the use of CRT in schizophrenia treatment (for a recent review, see Fitapelli & Lindenmayer, 2022). CRT has more recently been found to be effective in the improvement of several mental health disorders, including eating disorders, schizoaffective disorder, mild cognitive deficit, psychiatric symptoms, and the daily functioning of patients with early-stage dementia (Fan et al., 2017). It has also recently been adapted to treat such deficits in mood and anxiety disorders with promising results (Gold et al., 2016). For example, in a study by Preiss et al. (2013), participants with unipolar or bipolar depression completed online training, which involved three 20-minute training sessions per week for eight weeks, in the domains of attention, memory, and EF, using Cognifit, a validated online cognitive training program. Compared to the control group who received standard care, the group that received the CRT training showed reduced depressive symptomatology and fewer self-reports of cognitive failures. Yet another study found that 15 sessions of CRT significantly improved attention and memory capacities in a sample of inpatients with depression (Priyamvada, 2015). Other studies have found that CRT improves processing speed and EF in individuals with depression (Elgamal, 2007).

A recent meta-analysis (Thérond et al., 2021) analyzed results from eight studies to estimate the efficacy of CRT on cognitive functioning in depression. They found that CRT improved global cognition, verbal memory, attention/processing speed, working memory, and executive functioning in individuals with depression. No significant improvements were found for visuospatial memory or verbal fluency. In addition, no significant moderating effect of participant age was found. Another meta-analysis (Legemaat et al., 2021) with 24 studies reported that cognitive remediation with patients with depression showed improvement in

cognitive functioning, especially in the area of attention, memory, processing speed, working memory and verbal learning, but not in EF. There was no effect found for age.

Thus, in MDD, CRT has been found to improve cognitive functioning in the domains of attention, memory, and processing speed; the findings in EF seems uncertain. Overall, it appears that CRT may be a promising option to help improve cognitive functioning among individuals with depression; however, more research is needed.

In sum, research has demonstrated that CRT is effective in improving cognitive deficits for individuals with schizophrenia (Fitapelli & Lindenmayer, 2022) with promising results for MDD (Legemaat et al., 2021; Thérond et al., 2021). Unfortunately, limited research is available on the effectiveness of CRT for use with other mental health disorders (Kim et al., 2018). More research is needed, particularly replication research, to fully understand the effectiveness of CRT for mental health-related cognitive symptoms.

An important factor in the cognitive remediation literature is the distinction between near and far transfer effects (Barnett & Sala, 2002). Near transfer refers to the generalization of acquired skills across similar domains. Conversely, far transfer refers to the generalization of acquired skills across dissimilar domains. For example, if an individual completes training in focused attention, it will be easier to transfer this acquired skill to tasks that involve focused attention (near transfer) than to tasks that do not involve focused attention (far transfer).

Lineras et al. (2019) looked at the transfer effects of working memory in two working memory training programs using working memory tasks (near transfer) and fluid intelligence tasks (far transfer). They found that the working memory training was associated with gains in the working memory tasks. They also found that the working memory training was not associated with gains in fluid intelligence tasks. Thus, they found evidence of near transfer but

not far transfer effects. Barnett and Ceci (2002) suggest that near transfer is more likely to occur when training and testing tasks are identical. Consistent with this, Sala and colleagues (2019) noted that improvements seen in cognitive-training programs rarely generalize beyond the trained task (i.e., near transfer).

Variables Associated with CRT Outcome. Although several studies have analyzed moderators of CRT improvement in schizophrenia (for a review, see Seccomandi et al., 2020), unfortunately, current research on the variables associated with CRT efficacy for depression is very limited. One study (Listunova et al., 2020) looked at predictors of CRT treatment change in individuals with partially remitted depression. Researchers split their sample into two groups: one group of participants whose cognitive functioning improved from baseline to post-treatment ("improvers") and another group of participants whose cognitive functioning did not improve from baseline to post-treatment ("non-improvers") and compared these groups on several sociodemographic, psychopathological, psychosocial and training factors. They found that the two groups differed significantly in the domain of attention, with the "non-improvers" having a significantly longer duration of illness than the "improvers." No other differences were found between the groups. A limitation to this study is that the authors only included individuals with partially remitted depression. Thus, their results are not generalizable to those with acute depression or those in full remission. A recent meta-analysis by Thérond and colleagues (2021) looked at three moderators of CRT outcome: session format (individual vs. group), treatment duration, and age. They did not find any significant effects for the moderators. Finally, Goldberg et al. (2023) found that IQ moderated CRT outcome, such that those with lower IQ showed greater improvements in working memory. They also found that session format moderated the results, with CRT delivered in an individual format (vs. group format) was

associated with greater gains in EF. Age, education, gender, or baseline depression were not found to moderate the effect of CRT.

Severity of Depression. Severity of depression has been investigated as a predictor of CRT treatment response. A recent meta-analysis (Legemaat et al., 2021), which included 21 studies, found that CRT had a small effect on post-treatment depressive symptomatology. More specifically, they found that CRT improved depressive symptomatology in those with severe baseline symptoms but not in those with moderate baseline symptoms. This suggests that severity of depression at baseline may predict outcome in CRT, such that those with more severe depression at the start of therapy may see more improvement in their symptoms at the end of therapy than those with less severe depression. The authors argue that this finding "is not surprising, since more depressive symptoms mean more room for improvement" (p. 11).

Duration of illness has been found to predict CRT response. Individuals who have had depression for a shorter period of time have been found to show more improvement in their cognitive symptoms after CRT than those who have had depression for a longer period of time (Myklebost et al., 2022). This highlights the importance of early intervention. Duration of illness is associated with severity of depression (Galimberti et al., 2020). The longer an individual has depression, if it is not properly treated, the more likely their depressive symptomology will be classified as severe. This is especially true of cognitive symptoms in depression (Gorwood et al., 2008).

Comorbidity. There have been no studies to date that have investigated the association between comorbidity and CRT outcome in depression. However, research has found that severity of depression is linked to comorbidity such that individuals with severe depression are likely to have more comorbidities than individuals with mild or moderate depression. In support

of this, Steffan et al. (2020) found that the prevalence of comorbid disorders increased with depression severity, amounting to an almost 50% higher prevalence for most comorbid disorders in severe compared to mild depression cases. Thus, it is possible that comorbidity would be associated with CRT change. The greater the number of comorbid disorders an individual with depression has, the more severe their depression is likely to be. This, in turn, could affect their response to CRT.

Perceived Cognitive Deficits. Myklebost and colleagues (2022) looked at predictors of a CRT treatment program in a sample of individuals with partially remitted depression. They found that higher levels of perceived treatment credibility and expectancy measured using the Credibility and Expectancy Scale (CEQ; Borkovec & Nau, 1972), predicted a positive CRT response. However, perceived treatment credibility and expectancy is different than perceived cognitive deficits. There are no studies that look and the relationship between perceived cognitive deficits and CRT. In addition, the authors caution the interpretation of this finding, as their sample was self-referred to the CRT intervention and the role of treatment credibility may be different in a routine care setting. Furthermore, they found that pre-treatment levels of self-reported self-efficacy were not significantly associated with treatment response. Perceived cognitive deficits are cognitive deficits that a person believes he or she has, whether or not these deficits actually are detected when tested objectively. In line with this, several studies have failed to find a concordance between individuals with depression's self-reports of their cognitive functioning and their performance-based cognitive functioning (e.g., Svendsen et al., 2012). It seems that those with depression are not accurately able to predict their own cognitive abilities. However, previous studies have only compared perceived (self-reported) deficits and assessment measures of cognitive functioning and not with CRT outcome. The link between perceived

cognitive functioning and cognitive treatment outcome has not been investigated. It is possible that how one believes they are functioning cognitively may influence their progress in therapy.

Overall, research on the variables related to treatment response in CRT for depression is scarce. Of the few studies available on this topic, most focus on outcome variables such a reduction of depression symptomatology.

General summary

Individuals with depression often experience cognitive deficits in addition to their affective symptoms. These cognitive deficits have been found to negatively impact on individuals' occupational and social functioning, and quality of life.

Several clinical variables have been postulated to influence the likelihood that one will experience cognitive deficits as part of their depression presentation, such as number of past depressive episodes and past hospitalization due to depression (Elgamal et al., 2010; Semkovska et al., 2019). However, studies that have examined such variables of cognitive deficits in depression have led to inconsistent results. These inconsistencies are likely due to methodological differences between studies, which have utilized different methods of assessment of both clinical factors and cognitive functioning. More research is needed to fully understand the clinical variables that are associated with cognitive deficits in depression.

Study 1 sought to address limitations in previous research in four ways. First, participants were selected from a clinical database of adult outpatients with unipolar depression who did not meet criteria for other mood-related disorders (i.e., bipolar disorder or schizoaffective disorder). Second, only individuals with acute (i.e., current) depression were included and those with remitted depression were excluded. Third, self-report information was corroborated with information obtained through chart review. Fourth, use of psychotropic medication was

considered as covariates to offset its potentially confounding influence on the results. Understanding clinical variables that are associated with the cognitive performance of patients with depression may provide insight into the processes by which depression leads to cognitive dysfunction. This in turn can inform the development of more effective treatments for depression.

Depression is most often treated with pharmacotherapy or cognitive behavioural therapy (CBT). However, research suggests that a significant proportion of patients do not improve from such treatment (Hofmann et al., 2012). Specifically, CBT does not appear to affect the cognitive functioning of individuals with depression (Porter et al., 2015). Cognitive remediation programs have shown promising results in treating cognitive deficits associated with depression (Gold et al., 2016). Given this, studies investigating the variables related to CRT outcome allow clinicians a way of identifying who may or may not benefit from particular treatments. Study 2 was a community-based study that examined the relationship between several predictors and change in CRT in three cognitive domains (attention, memory, and reasoning). This information is useful in the appropriate allocation of resources so as to help as many individuals with mental health needs as effectively as possible.

Study 1

Study 1 used a retrospective study method and made use of a secondary database from the START Clinic for Mood and Anxiety Disorders, which is a tertiary-care outpatient clinic located in Toronto, Ontario. The purpose of Study 1 was to investigate the relationship between two variables, past depressive episodes and past hospitalization due to depression, and scores on a screening measure of cognitive functioning in individuals with acute depression, while controlling for the effects of age and use of psychotropic medication. The cognitive functioning

domains that were assessed included attention, memory, and executive functioning (EF). These domains were the domains chosen for this study because they are the domains in which cognitive deficits in depression are most commonly found (Harrison et al., 2016; Hasselbalch et al., 2012; Jaeger et al., 2006; Mohn &; Murrough, et al. 2011; Papakostas, 2014; Rock et al., 2014; Roiser & Sahakian, 2013; Rund, 2016; Stordal et al., 2004; Zakzanis et al., 1998).

Data Source

The anonymized data for this study came from a clinical research database that was maintained by START Clinic. The database contained intake information of patients who had consented for their anonymous data to be used for research purposes.

As part of the intake process at the clinic, all new patients at the clinic complete a brief neuropsychological screener, a semi-structured diagnostic clinical interview, as well as medical and sociodemographic questionnaires (Appendices A and B, respectively) on their first visit for clinical purposes. During their first appointment, new patients are also asked if they would like to include their personal data in the clinic's research database. Those who are interested are provided a consent form to sign (see Appendix C). Data from these intake measures were collected by a team of trained and supervised research associates at the clinic. The development of the database at the START Clinic has received ethics approval from the Optimum Review Board (see Appendix D).

Trained research associates from the clinic (not including the principal investigator) reviewed the clinic's database, which consisted of outpatients seen at the clinic from 2015 to 2020, and identified individuals who met the inclusion criteria for Study 1 (see below). No further data was added to the clinic base after 2020 because intakes were suspended due to the

COVID-19 pandemic that was declared in March 2020, and the government-mandated public lockdowns that went on for an extended period of time to contain the virus.

Study 1 Hypotheses

Hypothesis one stated that a higher number of lifetime depressive episodes would be associated with poorer performance on cognitive tasks that are related to attention, memory, and EF. Hypothesis two stated that past hospitalization for depression would be associated with poorer performance on cognitive tasks that assess attention, memory, and EF.

Study 1 Method

Study Population

A total of 169 individuals from the intake database at the START clinic were identified for the study based on their having completed the entire intake procedure. Inclusionary criteria included 1) between the ages of 18 and 65; 2) currently experiencing a major depressive episode, as determined by a semi-structured diagnostic clinical interview, i.e., the Mini International Neuropsychiatric Interview (M.I.N.I.); and 3) attended the START Clinic between 2015 to 2020.

Of the 169 identified individuals, 24 with a DSM-5 diagnosis of bipolar I or bipolar II were excluded, and another nine were excluded because they had MDD but were not currently experiencing a major depressive episode (MDE) at the time of testing. Although cognitive deficits often present residually during the remitted phase of MDD, they have been found to be less severe during remitted periods than during acute or "active" phases of the disorder (Hammar et al., 2022; Ji et al., 2020; Kriesche et al., 2022). Finally, 11 individuals were excluded for missing data. After these exclusions, a total of 125 individuals (68 women, 57 men) were included in the study. All of them met DSM-5 criteria for MDD and were also experiencing a current MDE at the time of testing.

The mean age of the study sample (N = 125) was 38.52 years (SD = 13.03, range = 18 to 64). Participants reported experiencing an average of 4.57 past depressive episodes, including the depressive episode that they were currently experiencing.

Almost half of individuals (n = 51; 40.80%) were on psychotropic medication and 16 participants (12.80%) were taking non-psychotropic medication at the time of testing. A total of 23 (18.40%) participants reported experiencing a concussion or head injury that did not produce symptoms following the injury. The large majority of participants (n = 119, 95.20%) reported receiving mental health services in the past, whereas 121 (96.80%) participants reported being diagnosed with another psychiatric disorder. Finally, 13 (10.40%) participants experienced past hospitalization due to depression, whereas 112 (89.60%) did not.

Over half of the participants (n = 73; 58.34%) reported themselves as single, whereas 31 (24.80%) identified themselves as married. The majority of participants (n = 78; 62.40%) chose not to identify their ethnicity; of those who did, 37 (29.60%) identified as Caucasian. In terms of education, 50 participants (40.00%) reported that their highest level of education was a Bachelor's degree, whereas 27 (21.60%) reported that their highest level of education was a high school diploma. Finally, 58 participants (46.40%) reported working full-time and 26 participants (20.80%) reported themselves as retired. For a complete summary of the demographic and clinical characteristics of the sample, see Table 1 below.

Diagnostic information for participants was obtained from the semi-structured diagnostic clinical interview used during intake. All participants in the study met the criteria for a current major depressive episode and the criteria for major depressive disorder at the time of testing.

Table 1

Demographic and Clinical Characteristics in the Study 1 Total Sample

Demographic Characteristics	*n*	%
Age (years)	38.52 (*SD* = 13.03)	
Sex		
Female	68	54.40
Male	57	45.60
Past head injury	23	18.40
Previous diagnoses of MDD	122	97.60
Previous diagnosis of mental health disorder other than MDD	121	96.80
Past mental health services	119	95.20
Past hospitalization due to depression	13	10.40
Current medications	101	80.80
Psychotropic	51	40.80
Non-psychotropic	16	12.80
Marital status		
Single	73	58.40
Married	31	24.80
Cohabitating	12	9.60
Separated	2	1.60
Divorced	5	4.00
Widowed	0	0.00
Did not report	2	1.60
Highest educational degree earned		
Less than high school	4	3.20
High school or GED	27	21.60
College degree	10	8.00
Bachelor degree	50	40.00
Master's degree	15	12.00

PhD degree	4	3.20
Professional degree	8	6.40
Did not report	7	5.60
Work status		
Working full-time	58	46.40
Working part-time	16	12.80
Unemployed/laid off	20	16.00
Keeping house/raising children full-time	2	1.60
Retired	26	20.80
Student	0	0.00
Ethnicity	0	0.00
Caucasian	37	29.60
Asian	5	4.00
Hispanic	1	.80
African American	2	1.60
Indigenous	0	0.00
Other	2	1.60
Did not report	78	62.40

Note. $N = 125$

The majority of participants ($n = 100$; 80.00%) reported experiencing multiple lifetime episodes of depression and thus met criteria for recurrent MDD, whereas 25 (20.00%) participants reported having had a single depressive episode which was the current episode.

Many of the individuals also met criteria for one or more anxiety disorders ($n = 112$; 89.60%), the most common of which was generalized anxiety disorder ($n = 97$; 77.60%), followed by social anxiety disorder ($n = 76$; 60.80%) and current panic disorder ($n = 18$; 14.40%). Agoraphobia was also observed in 44 (35.20%) participants and over a quarter met DSM-5 diagnostic criteria for OCD ($n = 35$; 28.00%) and PTSD ($n = 33$; 26.40%), respectively. See

Table 2 below for the complete diagnostic findings from the structured clinical interview using the Mini International Neuropsychiatric Interview (MINI).

Measures

The assessment tools that were used in the clinic intake procedure and that are relevant to the current study are described below.

Neuropsychological Assessment Battery Screening Module (S-NAB). The Neuropsychological Assessment Battery Screening Module (S-NAB; Stern & White, 2003) was used in Study 1 to screen participants for the presence of cognitive deficits. The full version of the NAB is a comprehensive battery of tests comprised of the following domain-specific modules: screening, attention, language, memory, visuospatial, and executive functioning. The first module, the Screening Module (S-NAB), is an abbreviated version of the full NAB. The S-NAB consists of 14 brief individual tests, which yield five index scores reflecting the five cognitive domains assessed by the full version of the NAB. The domains (and individual tests) of the S-NAB that were of interest are listed below.

1. Attention (Orientation, Digits Forward, Digits Backward, Numbers & Letters Efficiency-Part A and Part B)
2. Memory (Shape Learning Immediate Recall, Shape Learning Delayed Recognition, Story Learning Immediate Recall, and Story Learning Delayed Recognition)
3. Executive Functioning (Mazes and Word Generation)

The Screening Module takes less than one hour to administer and is an option for rapid assessment of cognition. The Screening Module yields standardized scores similar to IQ scores (M = 100, SD = 15) for the five indexes. The demographically corrected norms for the S-NAB are based on age, education level, and sex. There are two parallel forms (Form 1 and Form 2) for

Table 2

Frequency of Psychiatric Diagnoses as Assessed with the Mini International Neuropsychiatric Interview (MINI) in the Study 1 Total Sample

Psychiatric diagnoses	*n*	%
Mood disorders	125	100.00
Major depressive episode (current)	125	100.00
Major depressive episode (past)	100	80.00
Major depressive disorder	125	100.00
Bipolar I	0	0.00
Bipolar II	0	0.00
Psychotic disorder	4	3.20
Anxiety disorders	112	89.60
Panic disorder	18	14.40
Agoraphobia	44	35.20
Social anxiety disorder	76	60.80
Generalized anxiety disorder	97	77.60
Obsessive compulsive disorder	35	28.00
Post-traumatic stress disorder	33	26.40
Substance-related disorders	28	22.40
Substance use disorder	15	12.00
Alcohol use disorder	18	14.40
Eating disorders	7	5.60
Anorexia	2	1.60
Bulimia	5	4.00
Attention Deficit Hyperactivity Disorder	63	50.40

Note. N = 125.

each of the domain modules. Form 1 was used in the present study. The standardized scores were used as the primary measure of cognitive functioning in Study 1. Higher scores indicate better cognitive functioning. Cognitive deficit is determined by an S-NAB composite score below 85, which corresponds to one standard deviation (*SD* = 15) below the mean score of 100. Previous studies examining traumatic brain injury and substance using samples with the S-NAB have also used this cut-off (Copersino et al. 2009; Lange et al., 2010). The S-NAB has been found to discriminate between cognitively impaired and unimpaired substance-abusing patients (Grohman & Fals-Stewart, 2004). Zgaljardic and Temple (2010) also found that the S-NAB demonstrated good reliability and validity in a sample of patients with moderate-to-severe brain injury. They also found acceptable internal consistency (α = .600) for the S-NAB total score. However, internal consistency was lower for the individual domain scores: The internal consistency for each domain in the study by Zgaljardic and Temple (2010) study was found to be α = .390 (S-NAB Attention), α = .420 (S-NAB Memory), and α = -.370 (S-NAB EF). The authors also found convergent validity between the S-NAB and the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), a measure that has been validated in depression (Srisurpanon et al., 2017).

Consistent with previous research which shows attention, memory, and executive functioning to be the cognitive deficits most commonly found in depression with the use of performance-based tests, (Harrison et al., 2016; Hasselbalch et al., 2012; Jaeger et al., 2006; Mohn & Rund, 2016; Murrough, et al. 2011, Papakostas, 2014; Rock et al., 2014; Roiser &. Sahakian, 2013; Stordal et al., 2004; Zakzanis et al., 1998), only the scores of these cognitive domains from the S-NAB were analyzed for the purpose of Study 1.

Reliable Digit Span (RDS). Due to the nature of depression, individuals with depression may put forth suboptimal effort during cognitive testing. For example, poor effort has been invoked to explain the observation that patients with depression underperform on cognitively demanding tasks, despite matching control participants on less demanding tasks (Cohen et al., 2001). Given this, participants were administered a performance validity test to assess whether suboptimal effort was contributing to their cognitive test performance. The RDS performance validity test is within the Neuropsychological Assessment Battery Screening Module (S-NAB; Stern & White, 2003). The S-NAB consists of the Digits Forward and the Digits Backward subtests. On both subtests, participants hear a sequence of numerical digits and are tasked to recall the sequence correctly, either in normal order (Digits Forward) or in reverse order (Digits Backward), with increasingly longer sequences being tested in each trial. An RDS score is calculated by taking the longest span of Digit Forward on which both trials are passed plus the longest span on Digit Backwards on which both trials are passed. An RDS score of 6 or less has been demonstrated to be the optimal cut-off score to indicate invalid performance, with specificity of 86% and a sensitivity of 21% (Mueller et al., 2015). The RDS was used to check for suboptimal effort during cognitive testing on the S-NAB.

Mini International Neuropsychiatric Interview (M.I.N.I.) 7.0.2. The MINI (Sheehan et al., 1998) is a short, semi–structured diagnostic interview intended to explore the most common disorders based upon the Diagnostic and Statistical Manual for Mental Disorders (DSM). It consists of standardized, structured, closed-end questions throughout its diagnostic procedure. Psychiatric diagnosis is made according to the number of affirmative replies to the specific questions. The original MINI (Sheehan et al., 1998) has similar reliability and validity properties to both the Structured Clinical Interview for Diagnostic and Statistical Manual (SCID)

for DSM-III-R and the Composite International Diagnostic Interview for the International Classification of Diseases, tenth edition, but has a much shorter administration time (Lecrubier et al., 1997; Sheehan et al., 1998). The MINI 7.0.2. is an updated version of the original MINI and assesses 17 disorders based upon the Diagnostic and Statistical Manual for Mental Disorders, fifth edition (DSM-5; APA, 2013). The 17 disorders that it assesses include: major depressive disorder, bipolar I and bipolar II, generalized anxiety disorder, panic disorder, agoraphobia, social anxiety disorder, obsessive-compulsive disorder, posttraumatic stress disorder, alcohol use disorder, substance use disorder, any psychotic disorder, anorexia nervosa and bulimia nervosa. The MINI has demonstrated excellent inter-rater and test-retest reliabilities (Pettersson et al, 2018). For the purpose of the current study, the MINI for Attention-Deficit/Hyperactivity Disorder Studies, which is an extended version of the MINI 7.0.2., was used to describe the sample and establish diagnoses in both Study 1 and 2.

Medical questionnaire (Appendix A). The medical questionnaire is a self-report measure that consists of nine questions to assess the participant's medical history that is of interest to this study. Questions 5 and 7 assess, respectively, the number of lifetime depression episodes and past hospitalization for depression, both of which are the variables of interest in the current study. The total number of lifetime episodes of depression included both past (where applicable) as well as the current depression episode. Past hospitalization for depression was assessed with a Yes/No response. Diagnostic information obtained from the medical questionnaire was corroborated with information from the clinical chart review.

Clinical chart. Diagnostic information from the medical questionnaire was corroborated with information obtained from the clinical chart review. The medical questionnaire is a self-reported questionnaire and represents individuals' perception about their own medical history.

Since self-report measures suffer from limited reliability and validity (Dang et al., 2020), the diagnostic information obtained from their medical questionnaire was corroborated with information obtained from their clinical chart at the START Clinic. Individuals' charts contain diagnostic information from psychiatrist and clinical director of the START Clinic. There were no inconsistencies between these two types of information.

Sociodemographic questionnaire (Appendix B). The sociodemographic questionnaire is a self-report measure that assesses participants' sociodemographic information that are pertinent to this study (e.g., sex, age, marital status, ethnicity, education, and employment status).

Study 1 Results

Pre-analysis Issues

Missing Data. The data were entered into the Statistical Package for the Social Sciences (SPSS) and were screened for missing items. For participants with a small number (less than 5%) of missing scale or subscale items, each missing item was replaced with the mean value for that item (Tabachnick & Fidell, 2007). There were no participants with more than 5% missing values.

Univariate and Multivariate Outliers. The data were also screened for univariate and multivariate outliers. Within group univariate outliers are cases within each group with extreme values on one variable that can distort results (Tabachnick & Fidell, 2007). To screen for univariate outliers, scores on all scale items were standardized into *z*-scores in SPSS. Once transformed, any cases with a z-score that exceeded ±3.29 were identified as univariate outliers (Tabachnick & Fidell, 2007). Using this method, no univariate outliers were identified.

Multivariate outliers are cases with unusual combinations of scores on two or more variables that can distort results (Tabachnick & Fidell, 2007). Multivariate outliers were

assessed using Mahalanobis' distance and Cook's *D*. The Mahalanobis distance measures the distance between a case and its distribution. Cook's *D* measures the combined influence of a case being an outlier on *y* and on a set of predictors (Stevens, 2009). Influential outliers were defined as those with a Mahalanobis distance with χ^2 value that was significant at $p < .001$ and a Cook's *D* that exceeded the value of one (Stevens, 2009). Using this method, no multivariate outliers were identified.

Correlations. A pooled-sample bivariate correlation analysis was conducted with all variables to check for redundancy and to examine the relationships. Redundancy and possibly multicollinearity is suspected if two or more variables are highly correlated with one another, i.e., at $r = .90$ or greater (Tabachnick & Fidell, 2007). In the present analysis, a number of variables were significantly correlated. The S-NAB domains (Attention, Memory and EF) were correlated with each other and ranged from $r = .18$, $p < .04$ (Memory with EF) to $r = .36$, $p < .00$ (Memory with Attention). Use of psychotropic medication was significantly associated with Attention ($r = .204$, $p < .05$). See Table 3 below for the full correlation matrix.

Multicollinearity. Multicollinearity was assessed with two metrics. First, multicollinearity is very likely in the case of redundancy when two or more predictor variables are highly correlated with one another ($r = .90$ or greater), which can lead to unstable matrix inversion (Tabachnick & Fidell, 2007), and to biased and unstable standard errors and unstable *p*-values (Vatcheva et al., 2016). Table 3 shows no correlations that exceeded .90. Second, multicollinearity was also assessed by looking at the variance inflation factor (VIF) which indicates the degree to which the variance in the regression coefficients is inflated. The guidelines by Daoud (2017) were used to interpret the VIF where values higher than 5 would suggest the presence of multicollinearity. All the VIF estimates (Lifetime depressive episodes =

Table 3

Bivariate Correlations Among Variables in the Study 1 Total Sample

Measure	1	2	3	4	5	6	7
1. S-NAB-Attention	–						
2. S-NAB-Memory	.36**	–					
3. S-NAB-EF	.27**	.18*	–				
4. Depressive episodes	.05	-.05	.07	–			
5. Past hospitalization	.00	.00	-.07	-.03	–		
6. Age	.08	.04	.13	-.03	.07	–	
7. PsychMeds	.20*	.07	-.12	.02	-.12	.05	–

Note. N = 125*;* S-NAB-Attention = Neuropsychological Assessment Battery Screening module attention subscale; S-NAB-Memory = Neuropsychological Assessment Battery Screening module memory subscale; S-NAB-EF = Neuropsychological Assessment Battery Screening; module executive functioning subscale; Depressive episodes = number of depressive episodes (including current episode); Past hospitalization = past hospitalization due to depression (yes/no); PsychMeds = whether participants were taking psychotropic medication time of testing.

*$p < .05$. **$p < .01$.

1.00, Past hospitalization due to depression = 1.00) were well below the cut-off value of 5. Thus, multicollinearity was not considered to be likely.

S-NAB Performance Validity. All participants had an S-NAB RDS score that was equal to or greater than the cut-off score (i.e., 6). Thus, all participants were deemed to be putting forth optimal effort on the S-NAB.

Clinical Chart. Diagnostic information from the medical questionnaire was corroborated with information obtained from the clinical chart review. There were no inconsistencies between what participants reported and the information in their clinical file.

Primary Analyses

Cognitive deficit is determined by an S-NAB domain score below 85. All mean scores for the three S-NAB domains were above this cut-off: S-NAB Attention $M = 94.46$ ($SD = 15.96$, range = 55.00-136.00), S-NAB Memory $M = 97.60$ ($SD = 14.68$, range = 63.00 – 138.00), and S-NAB EF $M = 96.81$ ($SD = 16.68$, range = 15.00 – 134.00). The range of S-NAB scores showed that some individuals were below the *T*-score of 85 which suggested cognitive deficit. Further examination revealed that 33 (26.40%) participants were below the cut-off on S-NAB Attention, 27 (21.60%) on S-NAB Memory, and 23 (18.40%) on S-NAB EF. See Table 4 below for means and standard deviations for all variables for Study 1.

A repeated measures ANOVA was performed to compare the scores on the three S-NAB domains (Attention, Memory, and EF). There was no statistically significant differences between the domain scores, $F(2, 123) = 2.17$, $p = .12$, Wilk's $\lambda = .97$, partial $\eta^2 = .034$.

Evaluation of Covariates. Age and psychotropic medication use were considered for use as covariates to address their potential confounding effects on the results. To assess their suitability, both of these variables were examined to determine whether they met the following criteria: (a) covariates must be correlated with the criterion variable; (b) covariates must be uncorrelated with the predictors; and (c) the regression slopes between the covariate and criterion variable must be parallel for each level of the predictor, i.e., the interaction term between the covariate and the predictor when predicting the criterion variable must be nonsignificant (Loftin & Madison, 1991, p. 134). Meeting all three assumptions are required for the variable to be used as a covariate.

Regression Analyses with Number of Lifetime Depression Episodes and Past Hospitalization for Depression as Predictors. Separate regression analyses were conducted on

Table 4

Mean (Standard Deviation) of Scores for Variables in Study 1 Total Sample

Variable	*M* (*SD*)
S-NAB-A	94.45 (15.96)
S-NAB-M	97.60 (14.68)
S-NAB-EF	96.81 (16.68)
Number of depressive episodes	4.58 (3.49)
Past hospitalization (yes/no)	13/125

Note. $N = 125$; S-NAB-A = Neuropsychological Assessment Battery Screening module attention subscale; S-NAB-M = Neuropsychological Assessment Battery Screening module memory subscale; S-NAB-EF = Neuropsychological Assessment Battery Screening module executive functioning subscale; Number of depressive episodes = number of depressive episodes (including current episode).

each of the three criterion S-NAB domains (Attention, Memory, and EF) with the number of lifetime depressive episodes and past hospitalization for depression as predictors. Age was not correlated with any of the criterion variables (Attention, Memory, and EF) and was excluded from further consideration for its use as a covariate.

Use of psychotropic medication was significantly correlated with the S-NAB attention domain ($r = .204$, $p = .022$), but was not correlated with either S-NAB memory or S-NAB EF. Thus, it was not included as a covariate in analysis involving S-NAB memory or S-NAB EF Psychotropic medication was investigated further for its potential role as a covariate in analysis involving Attention. A regression analysis with S-NAB Attention as the criterion variable on Number of Lifetime Depression Episodes, Past Hospitalization for Depression, Psychotropic Medication Use, and their interaction terms showed that there were no significant findings for the interaction terms. The assumption of parallelism or homogeneity of regression slopes was

met (Bump, 1992), indicating that Psychotropic Medication Use could be used as a covariate in the regression analyses involving Attention. Parallelism states that the slopes of the regression lines between the covariate and dependent variable are the same across all levels of the independent variable.

Three sets of regressions were run with S-NAB Attention, S-NAB Memory, and S-NAB EF as the criterion variable, respectively. The two predictors were Number of Lifetime Depression Episodes and Past Hospitalization for Depression. Psychotropic Medication Use was used as a covariate in the regression involving S-NAB Attention, and was entered into the regression model in Step 1, followed by the predictors in Step 2. A Bonferroni split approach was used where significance was interpreted at $p < .017$ so as to keep the overall Type 1 error rate at .05. A summary of the regression results is displayed in Table 5.

S-NAB Attention as Criterion. The results showed that the number of lifetime depressive episodes and past hospitalization for depression did not significantly predict S-NAB Attention scores, $F(3, 121) = 1.84$, $p = .14$, $R^2 = .04$ after controlling for use of psychotropic medication.

S-NAB Memory as Criterion. The results showed that number of lifetime depressive episodes and past hospitalization for depression did not significantly predict S-NAB Memory scores, $F(2, 122) = 0.69$, $p = .50$, $R^2 = .01$.

S-NAB EF as Criterion. The results showed that number of lifetime depressive episodes and past hospitalization due to depression did not significantly predict S-NAB Executive Functioning scores, $F(2, 122) = 1.49$, $p = .21$, $R^2 = .05$.

Supplementary Analyses. Previous research suggests that each depressive episode that one experiences leads to an accumulation of vulnerability, such that each depressive episode leads to further decline in functioning over time (Post, 1992). Thus, supplementary multivariate

Table 5

Regression of S-NAB Domains on Number of Depressive Episodes and Past Hospitalization

Variable	*B*	*SE*	*t*	*p*	95% CI	*sr*
			S-NAB-A			
Step 1						
PsychMeds	0.20	2.86	2.31	.022	[0.96, 12.29]	.20
Step 2						
Dep. Episode	0.04	0.41	0.42	.63	[-0.62, 0.98]	.04
Past hosp.	0.02	4.66	0.25	.80	[-8.05, 10.41]	.02
			S-NAB-M			
Dep. Episode	-0.60	0.38	-0.66	.51	[-1.00, 0.50]	-.06
Past hosp.	0.00	4.33	0.02	.99	[-8.95, 8.65]	.00
			S-NAB-EF			
Dep. Episode	0.08	0.43	0.88	.38	[-0.47, 1.23]	.08
Past hosp.	-0.07	4.90	-0.76	.45	[-13.41, 5.99]	-.07

Note. $N = 125$; PsychMeds = whether participants were taking psychotropic medication time of testing; Dep. Episode = number of lifetime depressive episodes (including current episode); Past hosp. = past hospitalization due to depression (yes/no); S-NAB-A = S-NAB attention domain; S-NAB-M = S-NAB memory domain; S-NAB-EF = S-NAB executive functioning domain.

*$p < .017$

analyses were conducted to compare the cognitive scores (Attention, Memory, EF) of those with a single episode of depression and those with multiple episodes of depression.

In order to ascertain whether Psychotropic Medication Use could be used as a covariate, an initial MANOVA was conducted with number of past depressive episodes (single vs, multiple), psychotropic medication use, and their interaction term as independent variables. The dependent variables were the three S-NAB domains (attention, memory, and EF). It was found

that the interaction term was not significant, meeting the test of parallelism. Thus, Psychotropic Medication Use was used as a covariate in the multivariate analyses below.

A multivariate analysis of covariance (MANCOVA) with Group (single vs. multiple episodes) as the independent variable and Psychotropic Medication Use as the covariate was carried out (see means and SDs in Table 6). The three S-NAB domains (Attention, Memory, and EF) were the dependent variables. No significant multivariate effect was found, $F(3, 120) = 1.45$, $p = .23$, Pillai's Trace = .04, partial $\eta^2 = .05$, suggesting that overall cognition did not differ between those who had one versus multiple episodes of depression.

Univariate ANOVAs were conducted on each of the S-NAB domains of Memory and EF, with Group (single vs. multiple episodes) as the independent variable. A separate ANCOVA was employed for S-NAB Attention with Psychotropic Medication Use as the covariate. A Bonferroni split approach was used where significance was interpreted at $p < .017$ so as to keep the overall Type 1 error rate at .05. As can be seen in Table 6, no significant effects were found for S-NAB Attention, $F(1, 122) = 4.287$, $p = .04$, partial $\eta^2 = .03$; for S-NAB Memory, $F(1, 123) = 0.27$, $p = .61$; or for S-NAB EF, $F(1, 123) = 0.19$, $p = .67$.

Overall, it was observed that there were no differences between those who experienced a single episode of depression and those who experienced multiple episodes of depression on the S-NAB.

Study 1 Summary and Discussion

The objective of Study 1 was to investigate the association between two clinical variables, which included number of lifetime depressive episodes and past hospitalization for

Table 6

Supplementary Analyses of Variance Comparing Participants with a Single Depressive Episode to Those with Multiple Depressive Episodes on Cognitive Scores in Study 1 Total Sample

S-NAB domain	Single episode (n =25)		Multiple episodes (n = 100)		df_1	df_2	F	p	Partial n^2
	M	*SD*	*M*	*SD*					
Attention	87.74	15.68	96.14	15.66	1	122	4.29	.04	.03
Memory	96.24	15.67	97.94	14.49	1	123	0.27	.61	.00
EF	95.52	20.31	97.13	15.74	1	123	0.19	.67	.00

Note. N = 125; Dep. Episode = number of lifetime depressive episodes (including current episode); Past hosp. = past hospitalization due to depression (yes/no); S-NAB = Neuropsychological Assessment Battery-Screening Module; Attention = S-NAB attention domain; Memory = S-NAB memory domain; EF = S-NAB executive functioning domain; Single episode = participants who have experienced only one past and/or current depressive episode; Multiple episodes = participants who have experienced more than one past and/or current depressive episode.

*$p < .017$

depression, and scores on a screening measure of cognitive functioning in individuals with acute depression. The cognitive functioning domains that were assessed included attention, memory, and executive functioning.

Hypothesis one stated that greater number of lifetime depressive episodes would be associated with poorer performance on cognitive tasks that are associated with attention, memory, and executive functioning (EF). This hypothesis was not supported. Contrary to the hypothesis, the number of lifetime depressive episodes of depression was not related to performance on cognitive tasks.

Hypothesis two stated that past hospitalization due to depression would also be associated with poorer performance on cognitive tasks that are associated with attention, memory, and EF. This hypothesis was not supported. Contrary to the hypothesis, past hospitalization due to depression was not related to performance on cognitive tasks.

The absence of significant results for hypothesis one suggests that the number of episodes of depression that one experiences is not related to cognitive functioning. These results are not consistent with previous research. A recent systematic review by Kriesche and colleagues (2022) looking at cognitive deficits in the acute and remitted phases of depression found a positive correlation between the number of episodes of depression one had experienced and cognitive deficits. This inconsistency may be partly due to the fact that the current study is a single study whereas a systematic review examines the results of several studies, including those with no significant findings, to arrive at an overall conclusion. However, many of the studies that they included in their review did not control for psychiatric medication use. This study is novel in that it controlled for psychiatric medication use.

The lack of significant results from hypothesis two suggests that past hospitalization due to depression is not associated with cognitive functioning. These results are inconsistent with previous research suggesting that greater number of past hospitalizations due to depression have been associated with greater deficits on measures of EF (Harvey et al., 2004; Preiss et al., 2009), verbal memory (Elgamal et al., 2010), and attention (Preiss et al., 2009). While it is possible that there is no relationship between past hospitalization due to depression and cognitive functioning, it is also possible that the lack of significant findings may be due to limitations of the study (see below).

Supplementary analyses. Supplementary analyses were also conducted to determine if participants with multiple episodes of depression performed worse on cognitive measures than those who had only experienced a single episode of depression. A multivariate analysis of covariance on the three cognitive domains revealed no significant multivariate effect. Follow-up univariate analyses also showed no differences between these two groups for the attention, memory or EF domains.

These findings are inconsistent with a recent meta-analysis by Varghese and colleagues (2022) who found evidence that individuals with recurrent depressive episodes performed significantly worse than those with a single depressive episode on measures of memory. This contrast is made even more stark by the finding in the current study that when individual facets of cognitive functioning were looked at, individuals with recurrent depressive episodes scored better on attention than those with a single depressive episode.

One possible explanation for the current findings relates to participants being newly diagnosed. Those who are experiencing their first episode of depression may be more likely to be newly diagnosed than those who have experienced multiple episodes. Being newly diagnosed with a mental health disorder can be difficult to accept and cope with due to the experience of perceived stigma (Patten et al., 2016). The stress caused by being newly diagnosed may have lowered the cognitive performance in those with a single-episode of depression. However, this cannot be confirmed as no information was available on the timing of diagnosis for these individuals. Another possibility is that individuals who have had multiple episodes of depression might have learned to cope through experience, and therefore, might present as not as severely compromised as one would expect. This is an area for future research.

Strengths and Limitations

The results must be viewed in the context of the strengths and limitations of the present study. This study addresses limitations in previous research by using a clinical database of adult outpatients with unipolar depression and who did not meet criteria for other mood-related disorders (i.e., bipolar disorder or schizoaffective disorder), by only including individuals with acute (i.e., current) depression, excluding those with remitted depression, and by corroborating self-report with information obtained through chart review.

One strength of this study is that it focused only on acute depression and not remitted depression. Much of the literature does not distinguish between acute (i.e., individuals who were depressed at the time of testing) and remitted depression (i.e., individuals who were not depressed at the time of testing) that can confound the findings. Several studies have shown that although cognitive deficits are often present residually during the remitted phase of MDD, they have been found to be less severe during these remitted periods than during acute phases of the disorder (Hammar et al., 2022; Ji et al., 2020; Rock et al., 2014). Thus, by combining those with acute and remitted depression in a research study and not distinguishing between the two groups, it would be impossible to determine the extent to which the cognitive dysfunction is due to acute or remitted MDD.

Another strength of this study was that information self-reported by participants regarding their diagnostic information was corroborated with information in their clinical file. Diagnostic information in their clinical files was documented by psychiatrist Dr. Martin Katzman. This allowed for accuracy verification, as what participants reported was compared to what their clinical file said. Of note, there were no inconsistencies between what participants reported and the information in their clinical file. Previous studies often do not compare participant's self-report with more objective information that is in their clinical file.

As well, the findings were not influenced by confounding effects of age and psychotropic medication use as both were investigated as plausible covariates and, where relevant, their impact on the results were controlled statistically.

A potential limitation of the study could be that the S-NAB might not be sensitive enough to detect cognitive deficits in depression. In particular, studies have found that processing speed is impaired in those with depression compared to healthy controls (e.g., Jaeger et al., 2006; Mohn & Rund, 2016). The S-NAB does not include a separate processing speed subtest. This should be examined in future studies.

No other studies on depression have used the S-NAB. The S-NAB was chosen for this study based on its brevity, its ease of administration, and its potential to be used in primary care settings. Many studies on cognitive functioning in depression use extensive batteries of neuropsychological tests and although the assessment through neuropsychological tests is preferable for a more exhaustive analysis of patients' cognitive deficits (Galimberti et al., 2020), this approach is not feasible in other settings. For example, in primary care settings, brief screening tools that can indicate if individuals would benefit from a full neuropsychological assessment are more useful. However, even though the S-NAB has not been used in depression studies, it has been utilized in other clinical studies that look at substance use (Grohman & Fals-Stewart, 2004) traumatic brain injury (Zgaljardic & Temple, 2010). Both of these conditions are comorbid with depression (APA, 2013).

Another limitation of this study is that the data for this project were collected from the clinic's existing database that was developed by five different trained research assistants. These assistants would carry out the intake with new clients when they come to the clinic for their first appointment and enter the information into the database. Even though the research assistants

were trained on the standardized use of the clinical tools, the subjective nature of clinical interviews could have led to assessor variability which is common (Fung et al., 2022) and may have affected results.

Furthermore, the absence of significant findings might be linked to the relative healthy cognitive functioning of the sample. The average S-NAB scores were above the threshold for cognitive deficit, indicating that the cognitive difficulties experienced by the sample, for the most part, were not severe enough to be considered as cognitive deficits. However, there was a fairly large minority who were below this cut-off and did show deficits: 15.20% on attention, 10.40% on memory, and 15.20% on executive functioning.

More research is needed to fully understand the clinical factors that predict cognitive deficits in depression. Future work needs to address the limitations of previous research by using a large homogeneous sample consisting of outpatient adults with unipolar depression, by distinguishing between acute and remitted states of depression, by excluding individuals without MDD, by corroborating self-report with information obtained through chart review, and by comparing patients with depression who endorse cognitive difficulties and those who do not. Ideally, the sample reporting cognitive difficulties should meet the criteria for cognitive deficits. Nevertheless, the present study suggests that individuals with acute depression who have past hospitalizations and recurrent episodes may not have lower attention, memory, or executive functioning than acutely depressed individuals without this history.

Study 2

The purpose of Study 2 was to investigate variables associated with changes in attention, memory, and reasoning (which represents the domain of executive functioning) among individuals with depression following cognitive remediation training (CRT). The variables that

were considered were severity of depression, comorbidity of other mental health disorders, and perceived cognitive deficit prior to the CRT. This study was carried out under the aegis of the START Clinic after receiving ethics approval from the Optimum Review Board (see Appendix G), and under the clinical supervision of Dr. Martin Katzman, a psychiatrist and the Director of the START Clinic.

Study 2 Hypotheses

Three hypotheses were generated for this study. It was expected that greater number of comorbidities, greater severity of depression, and greater perceived cognitive deficit reported by participants prior to CRT would be associated with greater improvements in attention (hypothesis one), greater improvements in memory (hypothesis two), and greater improvements in reasoning (hypothesis three) following CRT.

Study 2 Method

Participants

Fourteen individuals who had completed the clinic intake process (i.e., were administered the MINI, the S-NAB, and the self-report questionnaires as identified in the *Measures* section below) were invited to participate in Study 2 for the following reasons: (a) they were on the waitlist and had not yet begun any treatment at the clinic; (b) they were not receiving any other forms of psychological therapy; (c) they had not received formal cognitive therapy (CBT) in the past; (d) the MINI indicated that they were experiencing current MDE; and (e) the MINI showed that they did not meet the criteria for ADHD. ADHD has been found to be associated with additional cognitive impairment above that seen in depression alone (Larochette, Harrison, Rosenblum, & Bowie, 2011). One individual dropped out of the study and another did not have sufficient data, leaving 12 participants for the data analysis.

As can be seen in Table 7 which provides a complete summary of the demographic characteristics of the final sample (N = 12; 8 women and 4 men), the mean age of the participants was 44.08 years (SD = 16.16). At the time of testing, three participants (25.00%) were on non-psychotropic medication and one was using psychotropic medication (8.33%). Three participants (25.00%) had a history of receiving mental health services, one was previously diagnosed with a mental health disorder other than major depression (8.33%), and three (25.00%) were previously hospitalized for major depression.

The majority of participants (n = 8; 66.67%) chose not to disclose their marital status; the rest identified as single (n = 2; 16.67%), married (n = 1; 8.33%), or divorced (n = 1; 8.33%). Similarly, the majority of participants (n = 8; 66.67%) chose not to disclose their highest educational level, whereas the rest who did (n = 4; 33.33%) noted that they had a university bachelor degree or less. Finally, two-thirds of the sample (n = 8; 66.67%) chose not to disclose their ethnicity, whereas the remaining (n = 4; 33.33%) self-identified as Caucasian.

Table 8 presents the diagnostic findings from the structured clinical interview using the MINI. As can be seen, all the participants met the diagnostic criteria for current major depressive disorder, and three had experienced previous major depressive episodes, which meant that they met the criteria for recurrent major depressive disorder. The MINI also revealed that several individuals met the criteria for anxiety disorders, of which generalized anxiety disorder was the most frequent (n = 10; 83.33%), followed by social anxiety disorder (n = 5; 41.67%), panic disorder, and agoraphobia (n =1; 8.33% for each). Three (25.00%) participants also met the criteria for PTSD and one person (8.33%) was diagnosed with substance use disorder.

Table 7

Demographic Characteristics in the Study 2 Total Sample

Demographic Characteristics	*n*	%
Age (years)	44.08 (*SD* = 16.161)	
Sex		
Female	8	66.67
Male	4	33.33
Previous diagnoses of MDD	3	25.00
Previous diagnosis of mental health disorder other than MDD	1	8.33
Past mental health services	3	25.00
Past hospitalization due to depression	3	25.00
Current medications	4	25.00
Psychotropic	1	8.33
Non-psychotropic	3	25.00
Marital status		
Single	2	16.67
Married	1	8.33
Cohabitating	0	0.00
Separated	0	0.00
Divorced	1	8.33
Widowed	0	0.00
Did not report	8	66.67
Highest educational degree earned		
Less than high school	1	8.33
High school or GED	1	8.33
College degree	1	8.33
Bachelor degree	1	8.33
Master's degree	0	0.00
PhD degree	0	0.00

Professional degree	0	0.00
Did not report	8	66.67
Work status		
Working full-time	1	8.33
Working part-time	1	8.33
Unemployed/laid off	1	8.33
Keeping house/raising children full-time	1	8.33
Retired	0	0.00
Student	0	0.00
Did not report	8	66.67
Ethnicity		
Caucasian	4	33.30
Asian	0	0.00
Hispanic	0	0.00
African American	0	0.00
Indigenous	0	0.00
Other	0	0.00
Did not report	8	66.67

Note. $N = 12$.

Table 8

Study 2: Frequency of Psychiatric Diagnoses as Assessed by the *Mini International Neuropsychiatric Interview (MINI)* in the Study 2 Total Sample

Psychiatric diagnoses	*n*	%
Mood disorders	0	
Major depressive episode (current)	12	100.00
Major depressive episode (past)	3	25.00
Major depressive disorder	12	100.00
Bipolar I	0	0.00
Bipolar II	0	0.00
Psychotic disorder	0	0.00
Anxiety disorders		
Panic disorder	1	8.33
Agoraphobia	1	8.33
Social anxiety disorder	5	41.67
Generalized anxiety disorder	10	83.33
Obsessive compulsive disorder	0	0.00
Post-traumatic stress disorder	3	25.00
Substance-related disorders	1	8.33
Substance use disorder	1	8.33
Alcohol use disorder	0	0.00
Eating disorders		
Anorexia	0	0.00
Bulimia	0	0.00
Attention Deficit Hyperactivity Disorder	0	0.00

Note. $N = 12$.

Measures

Mini International Neuropsychiatric Interview (M.I.N.I.) 7.0.2. A detailed description of the MINI is provided in Study 1. The MINI was used in Study 2 to assess for the presence of psychiatric disorders and to establish whether or not there was comorbidity, and the number of disorders involved. It was also used to establish current MDE and to rule out ADHD.

Patient Health Questionnaire (PHQ-9). The PHQ-9 (Kroenke et al., 2001) is a brief self-report instrument designed to assess depression. Although the PHQ-9 can be used to establish provisional MDD diagnoses, it was used in Study 2 to assess the severity of depressive symptoms. The PHQ-9 was originally developed to assess DSM-IV criteria for depression; however, the symptoms that its nine items assess remain unchanged in the DSM-5 update. Thus, the PHQ-9 can be used to assess DSM-5 criteria for MDD. Respondents indicate how much they have been bothered by the nine symptoms over the past two weeks by responding to a scale that ranges from 0 ("*not at all*") to 3 ("*nearly every day*"). Responses to items are summed to yield a single PHQ-9 total score, where a higher score reflects greater severity of depression. The severity levels of the PHQ-9 are: 0-4 (none/minimal), 5-9 (mild), 10-14 (moderate), 15-19 (moderately severe), and 20-27 (severe). Test sensitivity for the PHQ-9 ranges from 68% to 95% and test specificity ranges from 84% to 95% for MDD. The positive predictive value of the PHQ-9 ranges from 31% to 51% depending on the cut-off value and is similar to those of other instruments. Internal consistency estimates of the PHQ-9 range from .83 to .92 (Cameron et al., 2008). In the current study, its internal consistency was $\alpha = .85$. Severity scores from the PHQ-9 were not used for this study. Severity was treated as a continuous instead of categorical variable in the analysis.

Perceived Deficits Questionnaire (PDQ). The Perceived Deficits Questionnaire (PDQ; Sullivan et al., 1999) is a 20-item self-report scale that was used to measure subjective cognitive functioning. It assesses self-perceived cognitive deficits in several domains of cognitive functioning that have been found to be compromised in multiple sclerosis (MS): prospective memory, retrospective memory, attention/concentration, and planning/organization. Individuals indicate how often they have experienced such difficulties during the previous four weeks. Each of the 20 items is scored on a 5-point Likert scale (0 = *never*, 1 = *rarely*, 2 = *sometimes*, 3 = *often*, 4 = *almost always*). The total score for the PDQ is calculated by taking the sum of the raw scores across the 20 items. Total scores can range from 0 to 80, with higher scores indicating greater self-reported cognitive deficit. The PDQ also generates scores for each of the four subscales. Subscale scores range from 0 to 20 and are generated by calculating the sum of the raw scores of specific sets of items as follows: attention/concentration (items 1, 5, 9, 13, 17), retrospective memory (items 2, 6, 10, 14, 18), prospective memory (items 3, 7, 11, 15, 19), and planning/organization (items 4, 8, 12, 16, 20). The total PDQ score was used in the present study as a measure of perceived cognitive deficit. Its internal consistency was found to be $\alpha = .906$.

Lam et al. (2018) analyzed the psychometric properties of the PDQ in a sample with MDD and found that it displayed high internal consistency, with Cronbach's alpha ranging from .81 and .96. Their results also showed that the PDQ has good convergent and discriminant validity. The authors concluded that the PDQ is a reliable and valid measure of cognitive dysfunction in patients with MDD. The PDQ has also been found to differentiate between levels of depression; PDQ scores for individuals with severe depression have been found to be significantly higher than PDQ scores for nondepressed controls on all four subscales (Lawrence et al., 2013).

Medical questionnaire (Appendix A). The medical questionnaire was used to obtain the participant's self-reported medical history. A fuller description of this measure is provided in Study 1.

Sociodemographic questionnaire (Appendix B). This questionnaire was used to collect background information on the participants. A fuller description of this measure is provided in Study 1.

Intervention

Cognitive Remediation Training (CRT). CogniFit is a personalized, computer-based, online cognitive training program that has been validated in several different populations including dyslexia (Kraus & Breznitz, 2009), multiple sclerosis (Shatil et al., 2010), older adults at risk for falls (Verghese et al., 2010), normally aging older adults (Peretz et al., 2011), as well as depression (Preiss et al, 2013). In their review of commercial brain training programs, Shah and colleagues (2017) ranked commonly used computerized training programs based on their research evidence. Programs were ranked as Level 1 if they had at least two well-designed RCTs, one of which had to be of high quality and a second had to be of at least moderate quality. Programs were ranked as Level II if they had at least one well-designed RCT of high quality. Finally, programs were ranked as Level III if they had one or more moderate/poorly designed RCTs. Shah and colleagues rated Cognifit as possessing the highest level of research evidence (i.e., Level I). The version that was used for the present study has been found to improve cognitive functioning in a sample with depression (Preiss et al., 2013). This program offers training on multiple cognitive domains and trains 23 cognitive skills that fall under five general cognitive domains, as follows: attention, memory, coordination, perception, and reasoning. Each training session includes a mixture of visual, auditory, and cross-modality tasks. Personalization

of learning is accomplished by using a baseline neurocognitive evaluation, the results of which determine the individual content and level of subsequent training for each participant. During training, personalization is maintained by an adaptive feature that continually measures the participant's performance, adapts the difficulty level of the training tasks, and provides detailed graphic and verbal performance feedback during and after each training task. Since the training program is designed based on the results on the neurocognitive evaluation of the individual and because the program continually adapts to each person's strengths and weaknesses, it is unlikely that two participants would receive an identical training program in regards to choice of training tasks, amount, and intensity of training on each cognitive domain. An individual's Cognifit scores are compared to a normative group based on age and sex. The norms used in the personalized training program are based on the nearly five million users. However, given that people use Cognifit every day, new data is added and information about updated norms is unavailable. Scores can range from 0 to 800, with higher scores signifying better cognitive functioning and are interpreted as follows: below average (0-200), low average (200-400), high average (400-600), and above average (600-800). Given that previous research shows attention, memory, and executive functioning (the latter of which is akin to reasoning) to be the domains in which performance-based cognitive deficits in depression are most commonly found (Harrison et al., 2016; Hasselbalch et al., 2012; Jaeger et al., 2006; Mohn & Rund, 2016; Murrough, et al. 2011, Papakostas, 2014; Rock et al., 2014; Roiser & Sahakian, 2013; Stordal et al., 2004; Zakzanis et al., 1998), only the scores of these domains were analyzed for the purpose of Study 2. A subscription account was held by the START Clinic and the use of the Cognifit program was made freely accessible to the participants in Study 2 for the purpose of CRT.

Procedure

The study took place from September 2019 to January 2020. Individuals from the clinic's wait list were called to see if they were interested in participating in Study 2. Fourteen individuals who met the Study 2 inclusion criteria (see *Participants* section above) were contacted by phone for their interest in participating in Study 2. Study 2 was designed and presented as an investigation to look at the effectiveness of a cognitive remediation training (CRT) in improving cognitive behavioural therapy (CBT) outcomes for individuals depression but without ADHD (see Appendix F for the original consent form for study 2 that was approved by Optimum Ethics Review Board). All of the individuals who were contacted expressed interest and were scheduled for individual in-person meetings with the investigator.

During this in-person meeting, the original purpose and design of Study 2 was described to each participant where they would be randomly assigned to one of two treatment conditions. One group would complete the CRT program followed by a 12-week in-person CBT program, and the other group would complete just the 12-week in-person CBT program without the CRT. The performance of the two groups on cognitive tests would be compared to determine whether CRT had any effect in terms of boosting cognitive functioning after CBT. The second group would have the option of taking the CRT at a later time if they wished. Details of the original study procedure for both groups as described in the Consent Form (Appendix F) were provided to the participant, and the risks and benefits of participation were discussed. The investigator answered any questions the participant might have before they signed the Consent Form.

All 14 participants had home internet access which meant that they were able to undertake the CRT in the form of an eight-week Cognifit training program in their own homes. They were thus assigned to the CRT plus CBT condition. These participants were given detailed instructions on how to access the Cognifit online training program. The investigator helped each

participant create a Cognifit online account and showed them how to complete the training sessions.

Unfortunately, by the time the participants had completed their CRT and were ready to begin the CBT portion of the original study, the COVID-19 pandemic was declared, resulting in a nation-wide pandemic lockdown that lasted more than two years from 2020 to 2022. Consequently, it was not possible to fulfill the CBT portion of the study as the clinic could provide only remote services. Participants were told that the CBT portion of the study could not be fulfilled and were instead offered immediate virtual individual therapy by Dr. Martin Katzman.

The research design of Study 2 was thus modified to reflect only the CRT portion, and the objectives of Study 2 were revised to examine how three variables (number of comorbidities, severity of depression, and perceived cognitive deficit) were associated with change in cognitive functioning following CRT training. The findings of this revised Study 2 are reported in this dissertation.

The Cognifit program lasted eight weeks. In each week, the participants engaged in six 10-minute Cognifit training sessions. These six weekly training sessions could be completed all at once or on separate days over the week. This method was used in a similar study by Preiss and colleagues (2013), who found that those with depression improved significantly more in the domains of attention and EF than nondepressed controls. Individual's Pre-CRT scores were the scores they received from the first session of the 8-week program (baseline). Post-CRT scores were the scores they received from the final session of the 8-week program.

In order to maximize treatment adherence, at the beginning of each week (Monday), all participants were sent an e-mail informing them which Cognifit sessions they were to complete

for that week. This was possible because the number of training sessions completed by each participant could be tracked using the Cognifit account that was held by the START Clinic. At the end of each week (Friday), participants were sent another e-mail reminding them to complete their six Cognifit sessions for the week if they had not already done so. Participant cognitive scores were recorded by Cognifit after each training session and could be accessed by the principal investigator. Participants were told to contact the investigator in case a problem arose or if they had questions during their training sessions. Following the completion of the training sessions by all participants, anonymized data was released by START Clinic for subsequent analyses. All the data collected are maintained in the START Clinic and are considered to be property of the clinic.

Study 2 Results

Pre-analysis Issues

Comorbidity. Comorbidity was determined by counting the number of mental health disorders for which the participant met the criteria for in addition to MDD. For example, if the participant met the criteria for generalized anxiety in addition to MDD, their comorbidity score was listed as "1". Thus, the comorbidity score reflected the number of comorbid disorders that the participant had, excluding MDD. All diagnoses were assessed using the MINI that was administered as part of the clinic intake process. See Table 9 below for the pre, post and change CRT scores for each of the 12 participants.

Table 9

Study 2: Scores For the PHQ-9, PDQ, Number of Comorbidities and Pre-post CRT and Change Scores For Each of the 12 Participants in Study 2

Part.	Co.	PHQ-9	PDQ	Pre-CRT-A	Post-CRT-A	ΔCRT-A	Pre-CRT-M	Post-CRT-M	ΔCRT-M	Pre-CRT-R	Post-CRT-R	ΔCRT-R
1	2	17	34	622.500	631.000	8.500	438.570	430.440	-8.125	635.670	698.070	62.400
2	2	5	37	679.750	733.250	53.500	425.340	405.68	-19.750	619.000	596.800	-22.200
3	3	26	51	425.000	498.000	73.000	343.860	467.990	124.125	327.000	446.200	119.200
4	3	7	17	601.500	645.500	44.000	514.860	566.240	51.375	454.000	502.400	48.400
5	0	15	54	719.750	634.250	-85.500	328.430	332.810	4.375	619.330	615.130	-4.200
6	1	8	25	632.850	553.350	-79.500	413.290	426.170	12.875	564.670	546.270	-18.400
7	2	4	21	706.500	686.000	-20.500	554.000	533.620	-20.375	715.670	651.260	-64.400
8	4	19	31	515.500	526.000	10.500	389.140	473.640	84.500	405.330	528.530	123.200
9	1	18	48	638.250	683.750	45.500	414.710	411.960	-1.750	530.670	549.670	19.000
10	2	15	31	569.750	558.250	-11.500	430.860	495.610	64.750	535.000	480.600	-54.400
11	4	23	55	548.750	563.750	15.000	174.860	249.860	102.000	680.000	746.200	66.200
12	2	9	25	579.000	629.000	50.000	450.860	491.360	40.500	405.333	440.730	35.400

Note. N = 12; Part. = participant; Co. = Number of comorbidities in addition to MDD; PHQ-9 = Patient Health Questionnaire (depression severity measure); PDQ = Perceived Deficits Questionnaire; Pre CRT-A = score on CRT attention domain before initiating CRT; Post CRT-A = score on CRT attention domain after completing CRT; Pre CRT-M = score on CRT memory domain before initiating CRT; Post CRT-M = score on CRT memory domain after completing CRT; Pre CRT-R = score on CRT reasoning domain before initiating CRT; Post CRT-R = score on CRT reasoning domain after completing CRT; ΔCRT-A = post-pre change score in CRT attention domain; ΔCRT-M = post-pre change score in CRT memory domain; ΔCRT-R = post-pre change score in CRT reasoning domain; CRT scores range from 0 to 800, with higher scores signifying better cognitive functioning.

Missing Data. The data was entered into the Statistical Package for the Social Sciences (SPSS) and was screened for missing items. There were no missing data.

Univariate and Multivariate Outliers. The data were also screened for univariate and multivariate outliers using the method outlined in Study 1. Using this method, no univariate or multivariate outliers were identified.

Simple Correlations and Multicollinearity. Bivariate correlational analyses (see Table 10) were carried out with the variables in the study: Comorbidity, severity of depression (PHQ-9), perceived cognitive deficit (PDQ), and the change in cognitive scores following cognitive remediation training in memory (ΔCRT-M), attention (ΔCRT-A), and reasoning (ΔCRT-R) as measured with the Cognifit program.

There was a significant and strong positive correlation between PDQ and PHQ-9 (r = .740, $p < .01$), which suggests against using both as predictors because of the high proportion of shared variance between them which could lead to a redundancy problem. Notably, PDQ did not have any significant correlation with any of the change scores, i.e., ΔCRT-A, ΔCRT-M, and ΔCRT-R (see Table 10). In contrast, PHQ-9 was significantly correlated with ΔCRT-M (r = .688, $p < .05$), and with ΔCRT-R (r = .687, $p < .05$), indicating that PHQ-9 would be a better choice than the PDQ as a predictor of the pre-post CRT changes in memory and reasoning

There were also significant and strong negative relationships between the pre-scores in attention, pre-CRT-A, with Comorbidity (r = -.695, p = .012), the PHQ-9 (r = -.690, p = .013), post-scores in attention or post-CRT-A (r = .796, $p < .01$), ΔCRT-R (r = -.749, p = .005), and ΔCRT-M (r = -.911, $p < .001$); and between post-CRT-A with the PHQ-9 (r = -.656, p = .021), and ΔCRT-M (r = -.827, $p < 001$). This suggests that participants who had poorer attention prior to undertaking CRT were likely to have more comorbidities, greater severity of depression,

Table 10

Study 2: Bivariate Correlations Among Variables in Study 2

	1	2	3	4	5	6	7	8	9	10	11	12
1. Comorbidity	–											
2. PHQ-9	.353	–										
3. PDQ	-.072	.740**	–									
4. ΔCRT-R	.623*	.687*	.295	–								
5. ΔCRT-M	.705*	.688*	.272	.662*	–							
6. ΔCRT-A	.533	.208	.034	.472	.330	–						
7. Pre-CRT-A	-.695*	-.690*	-.174	-.749**	-.911**	-.519	–					
8. Post-CRT-A	-.431	-.656*	-.179	-.538	-.827**	.104	.796**	–				
9. Pre-CRT-M	-.247	-.726**	-.825**	-.416	-.535	.060	.362	.464	–			
10. Post-CRT-M	.085	-.451	-.803**	-.103	-0.61	.251	-.100	.062	.875**	–		
11. Pre-CRT-R	-.292	-.311	.089	-.606*	-.599*	-.489	.730**	.504	-.061	-.441	–	
12. Post-CRT-R	.030	.046	.298	-.125	-.328	-.312	.438	.289	-.339	-.616*	-.864**	–

Note. N = 12; Comorbidity = number of comorbid mental health diagnoses identified using the M.I.N.I; PHQ-9 = Patient Health Questionnaire total score (depression severity measure); PDQ = Perceived Deficits Questionnaire total score; ΔCRT-A = post-pre change score in CRT attention domain; ΔCRT-M = post-pre change score in CRT memory domain; ΔCRT-R = = post-pre change score in CRT reasoning domain; Pre CRT-A = score on CRT attention domain before initiating CRT; Post CRT-A = score on CRT attention domain after completing CRT; Pre CRT-M = score on CRT memory domain before initiating CRT; Post CRT-M = score on CRT memory domain after completing CRT; Pre CRT-R = score on CRT reasoning domain before initiating CRT; Post CRT-R = score on CRT reasoning domain after completing CRT; CRT scores range from 0 to 800, with higher scores signifying better cognitive functioning.

*$p < .05$. **$p < .01$.

higher post-scores in attention, and more improvement in memory and reasoning domains of CRT.

In addition, there were also significant and strong positive relationships among ΔCRT-M and Comorbidity ($r = .705$, $p = .010$), PHQ-9 ($r = .688$, $p = .013$), and ΔCRT-R ($r = .662$, $p < .05$). There were also significant and strong positive relationships among ΔCRT-R and Comorbidity ($r = .623$, $p = .031$) and PHQ-9 ($r = .687$, $p = .014$). This suggests that number of comorbidities and severity of depression are related to pre-post change in CRT for memory and reasoning.

There were also significant and strong negative relationships among the pre-scores in memory with the PHQ-9, ($r = -.726$, $p = .007$) and the PDQ ($r = -.825$, $p < .001$); and between the post-scores in memory and the PDQ ($r = -.803$, $p = .002$), pre-scores in memory (.875, $p < .001$), and post reasoning scores ($r = -.616$, $p = .033$). These correlations suggest that those with poorer memory prior to starting CRT were more likely to have greater severity of depression and greater perceived cognitive deficits and also that those with higher perceived deficits did more poorly on the CRT memory domain. Further, those who had better memory prior to starting CRT did better in the memory domain at the end of CRT.

Those who had higher pre-CRT-R also had higher pre-CRT-A ($r = .730$, $p < .01$) and greater change in their memory scores ΔCRT-M ($r = .599$, $p < .05$). Finally, those who had higher reasoning scores at the end of CRT also had lower memory scores after CRT ($r = -.616$, $p = .033$).

Multicollinearity was assessed with two metrics. First, multicollinearity is very likely when two or more predictor variables are highly correlated with one another ($r = .90$ or greater), which can lead to unstable matrix inversion (Tabachnick & Fidell, 2007); in the case of

regression analysis, multicollinearity can lead to biased and unstable standard errors and unstable *p*-values (Vatcheva et al., 2016). Table 10 shows that highest correlation coefficient among the three predictors (Comorbidity, PHQ-9, and PDQ) was between PHQ-9 and PDQ at .740. Second, multicollinearity was also assessed by looking at the variance inflation factor (VIF) which indicates the degree to which the variance in the regression coefficients is inflated. The guidelines by Daoud (2017) were used to interpret the VIF where values higher than 5 would suggest the presence of multicollinearity. All the VIF estimates (Comorbidity = 1.588, PHQ-9 = 3.488, PDQ = 3.068) were below the cut-off value of 5. Thus, multicollinearity was not considered to be likely.

Primary Analyses

CRT Sessions. The average number of CRT sessions completed by the participants was 44.67 sessions (93.062%) out of a total of 48 sessions. The majority of participants (n = 9/12, 75.00%) completed all 48 sessions.

On average, participants completed 75% of the CRT sessions. Overall, there was no significant relationship between the number of CRT sessions completed and the pre/post change scores in the three CRT domains of attention (r = -.109, p = .737), memory (r = -.482, p = .112), and reasoning (r = -.010, p =.975). Table 9 displays the means and standard deviations for all variables for Study 2. Comorbidity, PHQ-9 (measure of depression severity), and PDQ (measure of perceived cognitive deficit), all served as variables of interest in the regression analyses.

Before the regression analyses were carried out, an examination of the change scores in the sample (n = 12) was completed. As seen in Table 9, eight individuals (66.667%) saw improvement in their pre-post change scores (range of change scores = 8.500 to 73.000 increase) in the attention domain, whereas four individuals (33.333%) showed a deterioration (range of

change scores = 11.500 to 85.500 decrease). Similarly, for the memory domain, eight individuals (66.667%) saw improvement in their pre-post change scores (range of change scores = 4.375 to 124.125 increase) in the memory domain, whereas four individuals (33.333%) showed a deterioration (range of change scores = 1.750 to 20.375 decrease). For the reasoning domain, seven individuals (58.333%) saw improvement in their pre-post change scores (range of change scores = 19.000 to 123.2000 increase) in this domain, whereas five individuals (41.667%) saw a deterioration (range of change scores = 4.200 to 64.400 decrease). To determine the overall effect of the CRT on the cognitive domains, further analysis using paired sample *t*-tests were carried out (see next section).

Effect of cognitive remediation training over time. Paired sample *t*-tests were conducted to test whether there was a significant difference between post-CRT scores and pre-CRT scores for each of the CRT domains. For the domain of attention, no significant difference between the post-scores (M = 611.842, SD = 71.758) and the pre-scores (M = 603.258, SD = 83.510) was found, $t(11) = 0.585$, $p = .285$, $d = .169$. For the domain of memory, a significant difference between the post-scores (M = 440.448, SD = 86.463) and the pre-scores (M = 406.573, SD = 96.076) was found, $t(11) = 2.515$; $p = .014$; $d = .726$, with memory performance improving with the training. For the domain of reasoning, no significant difference between the post-scores (M = 566.822, SD = 97.225) and the pre-scores (M = 540.963, SD = 121.316) was found, $t(11) = -1.457$; $p = .087$; $d = .421$.

Regression Analyses with Comorbidity and PHQ-9 as Predictors. Separate multiple regression analyses on each of the post-CRT scores with PHQ-9 and Comorbidity as predictors were conducted. Their corresponding pre-CRT scores were used as covariates. The PDQ was excluded as a predictor due to the lack of significant association with any of the change scores

(see Table 10) as previously mentioned, and the need to restrict predictors due to the low sample size (n = 12).

Since there were three sets of regression (one for each of CRT domains of attention, memory, and reasoning), a Bonferroni split approach was used where significance was interpreted at $p < .017$ so as to keep the overall Type 1 error rate at .05.

Post-CRT-A as Criterion. It was found that the addition of Comorbidity and PHQ-9 did not significantly add to the prediction of post-CRT-A scores when controlling for pre-CRT-A scores at step 1, F^{change} (2, 8) = 0.502, p = .623, $R^2change$ = .041.

Post-CRT-M as Criterion. It was found that the addition of Comorbidity and PHQ-9 did not significantly add to the prediction of post-CRT-M scores when controlling for pre-CRT-M scores at step 1, F^{change} (2, 8) = 5.273, p = .035, $R^2change$ = .134.

Post-CRT-R as Criterion. The addition of Comorbidity and PHQ-9 did not significantly add to the prediction of post-CRT-R scores when controlling for pre-CRT-R scores at step 1, F^{change} = (2, 8) 6.145, p = .024, $R^2change$ = .153.

Study 2 Discussion

The objective of Study 2 was to investigate clinical variables associated with changes in attention, memory, and reasoning among individuals with acute depression following cognitive remediation training. The variables that were examined included comorbidity of other mental health disorders, severity of depression (PHQ-9), and perceived cognitive deficits (PDQ). All of these variables are typically available prior to treatment and their ability to predict outcome was investigated. The first hypothesis stated that a greater number of comorbidities, greater severity of depression, and greater perceived cognitive deficits would be associated with greater

improvements in attention. This hypothesis was not supported. There were no significant associations between any of the variables and change in attention.

While the small sample size likely played a major role, the lack of significant findings for attention may be due to the types of attention measured by the Cognifit program. Cognifit measures attention in the following areas: focused attention, divided attention, inhibition, and updating. Inhibition and updating are commonly considered core executive functions (e.g., Daucourt et al., 2018; Rodríguez-Nieto et al., 2022) rather than attentional processes. Furthermore, updating has been found to have neural overlap with working memory (Rodríguez-Nieto et al., 2022). In addition, there are several areas of attention that are not assessed by Cognifit. For example, the Cognifit program does not assess sustained attention, which has been found to be compromised in those with depression compared to their nondepressed counterparts (Agarwal et al., 2002; Farrin et al., 2003; Keller et al., 2019; Kemp et al., 2009; Lim et al., 2013; Porter et al, 2003; Tenke et al., 2008; van der Meere & Borger, 2007). Thus, the lack of findings for the CRT attention domain may be at least partly due to the Cognifit program, which may have excluded important aspects of attention that are compromised in depression (e.g., sustained attention), as well as included other cognitive skills that are not relevant based on past research to the attention domain (e.g., updating). It is difficult to compare these findings to the extant literature because there have been no studies to date that have investigated variables associated with CRT outcome for the domain of attention. Thus, as the first study in the area, this study suggests that there may be no association with attention, but that there is also a need to train and assess all types of attention (e.g., sustained attention) in future studies and to examine the predictive value of comorbidity and severity of depression for treatment outcome.

Hypothesis two stated that a greater number of comorbidities, greater severity of

depression, and greater perceived cognitive deficit would be associated with greater improvements in memory. Hypothesis three stated that greater number of comorbidities, greater severity of depression, and greater perceived cognitive deficit would be associated with greater improvements in reasoning. Although the multivariate results did not support either hypothesis, the bivariate correlation analysis showed that both comorbidity and greater severity of depression were positively associated with changes in memory and reasoning.

The small size of the sample made it more difficult to obtain significant findings in the multivariate context. Even so, the findings do suggest that number of comorbidities and severity of depression are worthy factors to examine in future research given their positive correlations with change in memory and reasoning scores. To put it in another way, individuals who had more comorbidities or who reported more severe depression symptoms prior to starting the cognitive remediation training ended up showing greater improvements in their memory and reasoning scores at the end of the training. Further, even despite the sample size limitation and nonsignificant regression models, comorbidity and depression severity prior to CRT together explained 13.40% and 15.30 % of the variance in memory and reasoning final scores, respectively, when initial scores were statistically controlled.

The current study also found that participants overall showed an improvement in memory following CRT, but did not show improvements in attention or reasoning. This is inconsistent with a recent meta-analysis by Mokhtari et al. (2015), which reported that CRT improved executive functioning, but not memory in MDD. This inconsistency may be partly due to the fact that this study is a single study whereas a meta-analysis combines the results of several studies, including those with no significant findings, to arrive at an overall effect.

An examination of the simple correlations between predictors and cognition scores

indicated that those who had poorer CRT attention scores as well as poorer CRT reasoning scores at baseline reported greater improvements in their CRT memory and CRT reasoning scores following their cognitive remediation training or CRT. This suggests that better outcomes in memory and reasoning are obtained following the training for individuals who are worse in their attention and reasoning at baseline, as assessed with performance-based tasks. Other studies have also found CRT to improve verbal and working memory, and executive functioning, which includes reasoning. Consistent with this, a recent meta-analysis by Thérond et al. (2021), who found that CRT improved verbal memory, attention, working memory, and executive functioning in individuals with depression.

In contrast, participants' subjective scores on the Perceived Deficits Questionnaire, which is a self-report measure, were not associated with pre-post changes in their CRT scores in the attention, memory, or reasoning domains. This suggests that one's subjective assessment of one's own cognitive deficits has no association with cognitive changes as measured with performance tasks following cognitive remediation training. This lack of an association between self-reports of cognitive functioning and objective performance-based measures in depression has been found in previous research (Svendsen et al., 2012).

Severity of depression has previously been found to be positively associated with number of psychiatric comorbidities (Steffan et al., 2020). Interestingly, this was not borne out in the current study which showed that the positive correlation of severity of depression with comorbidity was not significant. This is likely due to the sample size being too small to detect the association, as well as a problem with restricted sampling. More specifically, the participants' scores on severity of depression (PHQ-9) were concentrated towards the lower end of the range of possible scores (the mean was 13.830 out of a possible 27), which shows that the

participants were mildly or moderately depressed (Kroenke et al., 2001a). The results might have turned out differently had a fuller range of depression severity scores been sampled.

Another factor to consider is the extent to which the training and outcome tasks are similar to (near transfer), or different (far transfer) from each other (Barnett & Sala, 2002). In Study 2, outcome tasks were embedded in the CRT training. The cognitive training tasks (attention, memory, and reasoning) were the same as the outcome tasks. Thus, results reflect near-transfer effects. It is unclear if there were far-transfer effects because the study did not assess whether the gains learned in CRT generalized to other areas of the participants' lives. It is possible that although participants saw benefit from CRT in their outcome measures, these improvements may have only been relevant to the training task and might not generalize to other areas of cognition or unrelated areas of their lives. Consistent with this, Sala and colleagues (2019) note that improvement seen in cognitive-training programs rarely generalizes beyond the trained task and similar tasks. Future studies should include both near- and far-transfer measures.

Strengths and Limitations

One strength of the study is the use of a clinical population. Results of Study 2 are applicable to individuals with acute MDD who are in out-patient treatment settings. A second strength is that it was established that participants were experiencing a current MDE at the time of the study. Many previous studies do not differentiate between those with acute or remitted phases of depression (e.g., Preiss et al., 2009). Research has found that cognitive deficits during acute and remitted states significantly differ (Rock et al., 2014). However, whether participants remained in the acute phase for the duration of the training could not be determined. This is an area for future research.

A major limitation in this study is its small sample size of 12 participants. According to the G*Power program (Faul et al., 2009), it was estimated that a sample of size of 91 would have been required to be adequately powered. The low sample size meant that the study was underpowered, making it harder to detect significant findings. Another major limitation is the lack of a control group. Without a control group, it is not possible to determine whether the changes in the CRT scores were the result of the CRT training, or due to other factors, such as regression to the mean over time (Yu & Chen, 2015).

Additionally, participants completed, on the average, 75% of the cognitive remediation training sessions. The participants might not have received the full benefits of the CRT as a result. This could have influenced the findings, and to a greater extent given the small sample size.

Both limitations of the study were the direct result of the COVID-19 pandemic which made it impossible to continue with the recruitment of more participants and data collection. The COVID lockdown in Canada lasted for over two years; movements in public were restricted, and the clinic where the data were collected was closed to in-person appointments. Virtual appointments for recruitment and data collection purposes were not considered given the high level of anxiety, stress, and uncertainty experienced by all in the population. The psychological climate had changed over the course of the pandemic (Penninx et al., 2022) which could have introduced a confound in the study if new data were collected and combined.

Study 2 should be regarded as an exploratory effectiveness study or pilot study, and not as an efficacy study. Effectiveness studies are conducted in “real world” settings under more pragmatic conditions compared to efficacy studies that are carried out under highly controlled conditions (Singal et al., 2014). The findings from effectiveness studies are not generalized to

other settings because they are influenced by external factors (patient-, provider-, system-, or environment-related) that are not, or cannot be, controlled. However, their findings can offer insight into directions for future research.

In spite of the limitations in this study, the findings suggest that cognitive remediation training might be helpful for memory difficulties but not necessarily for attention or reasoning, and that those with more severe depression symptoms or who have more comorbidities might benefit more from the training. However, the study needs to be repeated with a larger sample size, a control group, and participants with a wider range of depression severity scores. Future research could also look into the generalization of any benefits gained from cognitive remediation training to real life functioning.

General Discussion

Two studies were carried out with the overall aims of providing information that might potentially guide the identification of depressed patients who have a higher probability of cognitive difficulties (study 1), and the identification of clinical characteristics that might predict response to cognitive remediation training (study 2).

The results of the two studies cannot be compared as the participants differed in one important aspect. Although both studies looked at individuals experiencing a current MDE, half of the participants in Study 1 also had a diagnosis of ADHD, whereas none of the participants in Study 2 did. Similar variables were not considered for use across both studies for this reason. Additionally, in Study 1, out of a total sample of 125, 63 people had ADHD and 25 of those with ADHD were taking psychotropic medication. Thus, it is unlikely that ADHD significant results were found for the S-NAB attention domain because psychiatric medication use was use as a covariate. Thus, the influence of medication use was removed.

The first study investigated the number of lifetime depressive episodes and past hospitalization for depression as predictors of cognitive functioning in attention, memory, and executive functioning among depressed outpatients after controlling for psychotropic medication use. Neither variable was found to be a significant predictor. Additional analyses did not reveal significant differences in cognitive functioning between individuals who had experienced a single depressive episode versus those who had multiple episodes. The results from this study contradict previous research, and this could be related to the use of the S-NAB.

The S-NAB is a screening tool that is quick and easy to use. This makes it an attractive option compared to full neuropsychological test batteries that are time-consuming and expensive to use. However, the findings from study 1 cast doubt on the utility of the S-NAB to detect cognitive difficulties in depressed patients. The tool shows good psychometric properties when used with other clinical populations, such as those with substance abuse (Grohman & Fals-Stewart, 2004) and brain injury (Zgaljardic & Temple, 2010). It also shows convergent validity with the MoCA, a test of cognitive dysfunction, that has been validated in depression (Srisurpanon et al., 2017). Even so, study 1 suggests that the S-NAB might not be a sufficiently sensitive test of individual differences in cognitive difficulties in acutely depressed patients.

Study 2 examined number of comorbidities, severity of depression, and perceived cognitive deficit as predictors of responses to an eight-week cognitive remediation training among depressed outpatients. Findings revealed that participants showed an improvement in their memory, but not in their attention or reasoning abilities, following the training.

The PDQ was removed as a predictor in regression models as it was not correlated with the outcome measures. Number of comorbidities and severity of depression, when considered together in the regression, were not found to be significant predictors of change in memory and

reasoning in cognitive functioning after the training. However, bivariate correlations indicate that greater number of comorbidities and greater severity of depression were both linked to greater improvements in memory and reasoning after the training.

It is acknowledged that study 2 suffered from the absence of a control group, which made it difficult to interpret whether the improvement in memory was a training effect. The study was disrupted by the COVID pandemic and that made it impossible to continue with more participant recruitment and data collection. However, the investigation should be regarded as exploratory in nature and as an effectiveness study that was conducted in an outpatient clinic under real world conditions that pose more challenges than what investigators would face in an experimental setting with rigorous controls in place.

It is noted that the samples in the studies had high rates of comorbidities, particularly anxiety. High rates of comorbidity, particularly anxiety disorders, are common in depression (Ittasakul et al., 2014). Previous research has shown the anxiety can significantly impact cognitive functioning (Majeed et al., 2023; Yang et al., 2015). As anxiety was not assessed in the current study, its role in cognitive changes following cognitive remediation training could not be investigated. This is an area for future research.

There are few treatments that specifically target the “cold” cognitive deficits in depression, despite the fact that cognitive deficits in depression are associated with significant burden in different areas of life. The results of this project suggest that more research is needed on the effects of CRT as a possible treatment for the “cold” cognitive deficits seen in depression.

Although not tested here, improved cognition in depression may lead to better treatment outcomes overall. For example, a possible reason why some individuals may not improve with standard CBT treatment (Thimm & Antonsen, 2014) is that cognitive dysfunction associated

with depression can make it difficult for individuals to learn the cognitive and behavioural strategies taught in session and implement them in their daily lives. If an individual is unable to sustain his or her attention during a CBT session, it is unlikely that this person will be able to learn and remember the skills that are taught in session and as a result will be unable to implement these skills in daily life. Given this, it may be possible that adding CRT as an adjunctive treatment to standard CBT for depression may improve standard CBT treatment outcomes by training and strengthening cognitive abilities that will enable individuals to learn and implement the cognitive and behavioural strategies that are taught in CBT. Future research should investigate the use of CRT in combination with other depression treatment, such as psychotropic medication and/or psychotherapy (CBT).

One general issue in the literature is the great variability in the methods and instruments used to assess and treat cognition in depression, making it difficult to compare results across studies. What one instrument defines as a cognitive domain may differ significantly from another instrument. For example, the S-NAB (Stern & White, 2003), used in Study 1, defines memory as shape (visual) and story (auditory) immediate recall and delayed recognition, whereas the Cognifit program used in this study defines memory as: auditory short-term memory, contextual memory, non-verbal memory, visual short-term memory, working memory, short-term memory, naming, and recognition. Although many of the Cognifit memory tests are traditionally considered memory tests, working memory can sometimes be classified as an EF test such as the Digits Backward test (Faria et al., 2015); naming can be classified as an EF test, for example, the FAS test of Verbal Fluency (Gustavson et al., 2019); or naming can be a language test, for example the Neuropsychological Assessment Battery (NAB; Stern & White, 2003). The lack of consistency in terms of which tests reflect which domains makes it difficult to

assess and treat cognitive deficits effectively and explains why a trained neuropsychologist is needed to interpret findings.

In conclusion, neither the number of lifetime depressive episodes nor past hospitalization for depression were associated with performance on a cognitive screening task that measured attention, memory, and executive functioning, after accounting for the effects of age and the use of psychotropic medications (Study 1). Further, participants with acute depression in an 8-week cognitive remediation training program showed that number of comorbidities and severity of depression were positively associated with the change in memory and reasoning scores when the bivariate correlations were looked at (Study 2). The findings in both studies have to be interpreted with their aforementioned limitations in mind. Importantly, it has to be kept in mind that Study 2 had a small sample size which would have made it difficult to detect significant changes in cognitive functioning following the cognitive remediation training. As well, it was not possible to attribute the improvement in memory scores to the training because of the absence of a control group.

Directions for Future Research

Taken together, it seems that cognitive functioning and CRT is an interesting area of investigation for future researchers of depression. Future research should replicate the current studies with larger samples and control group. Since there was no control group to compare the results to, it is not possible to determine if the changes in the CRT scores where a result of the CRT training. Changes could have been due to other factors, such as time or regression to the mean.

Future research should also separate individuals with a single-episode of depression from those with multiple episodes. Although not found in this project, previous research has shown

that individuals with a single episode of depression differ from those with multiple episodes in their cognitive functioning (Varghese et al., 2022). Furthermore, distinguishing between individuals in the acute and remitted phases of depression is an important consideration for future researchers. Finally, the cognitive domains examined in both studies included attention, memory, and executive functioning. There might be value in looking at other cognitive domains as well, such as motor function, involving psychomotor speed, and social cognition, which includes affective and emotional functioning (APA, 2013). As these domains were not specifically examined in the present study, a suggestion is that future research should investigate variables associated with cognitive functioning in these areas.

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Appendix A: Medical Questionnaire

Medical Questionnaire

Please answer the following questions:

1. **Have you ever had a concussion or head injury resulting in loss of consciousness, or which produced any symptoms following the injury?** YES _____ NO _____

2. **Have you ever received mental health services in the past (e.g., have you participated in group therapy). If so, when and where?**

_____

_____

_____

3. **Have you ever been diagnosed with depression? If so, when and by whom?**

_____

_____

_____

4. **Have you ever been diagnosed with another psychiatric disorder (e.g., ADHD, bipolar disorder, anxiety disorders)? If so, when and by whom?**

_____

_____

_____

5. **How many depressive episodes have you had in your lifetime? (Note: a depressive episode is a period of two weeks or longer in which a person experiences certain symptoms of depression: feelings of sadness and hopelessness, fatigue, weight gain or weight loss, changes in sleeping habits, loss of interest in activities, or thoughts of suicide.**

_____

_____

_____

6. **Have you ever been hospitalized? If so, when, for how long, and for what reason?**

_____

_____

_____

7. **Have you ever been hospitalized due to depression? If so, when, for how long, and for what reason?**

_____

_____

_____

8. **Please list all prescription medications that you are currently taking (include the dosage per day and the reason for taking).**

_____

_____

_____

9. **Please list all prescription medications that you have taken in the past (include the dosage per day and the reason for taking).**

_____

_____

_____

Appendix B: Sociodemographic Questionnaire

Sociodemographic Questionnaire

Please answer the following questions:

1. **Sex:**

   ___ Female

   ___ Male

   ___ Other

2. **Date of birth:** (dd/mm/yy): _____
3. **Age:** _____
4. **Marital Status:**

   ___ Single

   ___ Married

   ___Cohabitating

   ___ Separated

   ___ Divorced

   ___ Widowed

5. **Ethnic background:**

   ___ White

   ___ Asian

   ___Hispanic

   ___ African American

   ___ Indigenous (please specify: _____)

   ___ Other (please specify: _____)

6. **What is the highest degree you have earned?**

___ High school diploma or equivalency (GED)

___ Associate degree (junior college)

___ Bachelor's degree

___ Master's degree

___ Doctorate

___ Professional degree (MD, JD, etc)

___ None of the above (less than high school)

7. **Which of the following best describes your current main daily activities and/or responsibilities:**

___ Working full-time (40+ hours per week)

___ Working part-time (less than 40 hours per week)

___ Unemployed/laid off

___ Keeping house/raising children full-time

___ Retired

___ Student

8. **If you are working or you have worked in the past, what kind of work do (did) you do?**

_____

_____

Appendix C: Clinic Consent Form to include Data into Research Database

START Clinic for Mood
and Anxiety Disorders
32 Park Road
Toronto, Ontario
M4W 2N4

Dear Patients of the START Clinic,

Just before your first visit to the START Clinic, you are asked to complete a series of questionnaires which allow us the opportunity to assess you and your mental health. The information gathered for the packages is used individually to aid in your assessment. In addition, it may be added together with the information from other people to examine generally what people are like when they arrive in the clinic.

This information is very important for us and other therapists of patients with anxiety disorder in order to study and develop new treatment options that we can in turn offer our patients.

Please be aware that all of the information you provide us with is kept with strict confidentiality, and also be aware that your name will not be used in any publications.

If you have any further questions regarding the questionnaires used or the research we are conducting please do not hesitate to ask.

Thank you,

Martin A. Katzman BSc, MD, FRCPC
Clinic Director

I _____ understand and am confortable with the above.
Patient Name (PLEASE PRINT)

_____ _____
Signature Date

Phone: (416) 598-9344 Fax: (416) 598-8198

Appendix D: Ethics Approval from Optimum Review Board for Original Database

OPTIMUM
CLINICAL RESEARCH INC

March 27, 2007

Dr. Martin A. Katzman
START Clinic for Mood and Anxiety Disorders
790 Bay Street Suite 900
Toronto, Ontario
M5G 1N8
Fax: 416-598-8198

FAXED MAR 2 8 2007

TITLE: **START CLINIC DATABASE PACKAGE**
OUR FILE NO. **575**

Dear Dr. Katzman:

At the meeting held on March 22, 2007, the Board reviewed the proposed Clinic Database information. The Board provided approval of the data analysis.

The Board recommended that a statement be added to the Confidentiality Agreement to cover this possible use of data in future analyses. In addition, if data from current or past files will be included, these patients should be notified of this possible anonymous use of pooled data, either by a documented telephone call, or by mail. Thank you.

Sincerely,

Bill Wilson
Chair - Ethics Review Board

BW/pgh

*** THIS NOTIFICATION WILL BE SENT BY FAX ONLY ***

Optimum Ethics Review Board is constituted and functions according to Division 5 of the Food and Drug Regulations, ICH Harmonized Tripartite Guideline (GCP Consolidated Guideline) and FDA Information Sheets: Guidance for IRBs and Clinical Investigators.

231 King Street East, Oshawa, Ontario L1H 1C5 Tel: (905) 723-4694 Fax: (905) 723-7590

OPTIMUM
CLINICAL RESEARCH INC

April 29, 2015

Attn: Melissa Furtado
c/o Dr. Martin Katzman, M.D., FRCPC
S.T.A.R.T Clinic
32 Park Road
TORONTO ONTARIO
M4W 2N4

RE DATABASE PACKAGE ADDENDUM
PROTOCOL NO : WS2382578

Dear Dr. Katzman:

At the meeting held on April 29, 2015, the Board reviewed your letter emailed on April 14, 2015, notifying of the addendum to the above database. The Board provided approval for the implementation of the addendum.
Thank you.

Sincerely,

Bill Wilson
Chair - Ethics Review Board

BW/pgh

Optimum Ethics Review Board is constituted and functions according to Division 5 of the Food and Drug Regulations, ICH/GCP Guidelines, FDA 21 CFR Parts 50 & 56, DHHS Section 45 CFR 46, the Declaration of Helsinki, FDA Information Sheets: Guidance for IRBs and Clinical Investigators and the Tri-Council Policy Statement for Ethical Conduct of Research Involving Humans.

604 Taunton Rd. W., Oshawa, Ontario L1H 7K4 Tel: (905) 723-4694 Fax: (905) 723-7590

Appendix E Clinic Consent Form for Study 2 Approved by Optimum Ethics Review Board

INFORMED CONSENT - B

Title of Study: The effectiveness of CRT as an adjunct to CBT for depression

Study Investigators: Rebecca Tzalazidis, M.A.
Ph.D. Student
Lakehead University
Thunder Bay, ON
rtzalazi@lakeheadu.ca

Dr. Josephine Tan, Ph.D., C. Psych
Associate Professor
Lakehead University
Thunder Bay, ON
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Dr. Martin A. Katzman, M.D., F.R.C.P. (C)
Adjunct Faculty
Lakehead University
Thunder Bay, ON
mkatzman@startclinic.ca

Description and Purpose

The purpose of the study is to investigate whether cognitive remediation therapy (CRT) can improve outcomes in standard cognitive behavioural therapy (CBT) for depression.

Description of Procedures

During this study, you will be randomly assigned to one of two groups, the CRT+CBT group or the CBT-only group. Both groups will complete an online cognitive assessment and will complete several questionnaires before the start of treatment. The CRT+CBT group will then complete an online cognitive training in their homes that will last approximately 20 minutes three times per week for a total duration of 8 weeks. During this time, the other group will be waitlisted. After this, both groups will again complete the online cognitive assessment and will complete several questionnaires. Both groups will then complete a 12-week cognitive behavioural therapy (CBT) program for depression, which will last approximately 1.5 hours per week. At the end of the CBT program, both groups will be asked to complete the online cognitive assessment and several questionnaires for a final time. Individuals in the CBT-only group will have an opportunity to complete the CRT program once the study is complete.

The CRT program will take place in your home, while the three cognitive assessments and CBT sessions will take place at the START Clinic for Mood and Anxiety Disorders, located at 32 Park Rd, Toronto, ON M4W 2N4.

Costs/Compensation

The treatment provided as part of this study will be offered at no cost to you.

Patient initials: _____

Benefits

The benefit of participation in this study is an opportunity to contribute to scientific research in clinical psychology which will provide insight into improving psychological treatments for depression. The study may also benefit you by providing strategies to help you cope with your depression. It is also possible that you may not experience any direct benefit as a result of your participation in this study, beyond the exposure to information regarding the management of your depression.

Risks

During the study you may feel mild fatigue or discomfort when completing some of the tasks. If needed, you may take breaks during the study. You may also experience psychological distress, such as depressive symptoms, anxiety symptoms, frustration, sleep disturbances, irritability, and increased fatigue as a result of discussing issues related to your depression and from answering questions about these issues on the questionnaires. Your participation in this study will not affect the treatment you are receiving from your physician at the START Clinic.

Exclusion from the Study

You will not be eligible for participation in this study if you are under 17 years of age or over 65 years of age, if you have previously experienced or are currently experiencing a manic, hypomanic, or psychotic episode, or if you have attention-deficit/hyperactivity disorder (ADHD).

Confidentiality

All information collected about you during this study will be kept confidential and your identity will not be revealed when the results of this study are reported in presentations and publications. Your confidentiality will be protected.

It is important for you to know that all information discussed with the researchers will be held in the strictest of confidence. However, there are some exceptions and limits to confidentiality that you should be aware of:

1. If there are reasonable grounds to suspect that a child under the age of 18 is or may be in need of protection, we are bound to report these matters to the Children's Aid Society.
2. When an allegation of sexual abuse by a health practitioner is disclosed, we are required to report to the abusing practitioner's regulatory college.
3. If subpoenaed by a court order, it is required that personal health information is released.
4. When there is a serious threat of harm to you or another identified individual, may break confidentiality (i.e., call the police).
5. If you experience a serious medical or mental health crisis that requires hospital intervention we will be required to break confidentiality by having you brought to the hospital for care.

Patient initials: _____

Data Storage
All electronic data (through Cognifit) will only be shared with the investigator (Rebecca Tzalazidis) through the investigator's research account. Your online data will be deleted by the investigator once the study is complete.

Data at the START Clinic will go into a file that is stored under locked conditions. Participants' data are de-identified. These files are stored at the Clinic for a minimum of five year. Only Dr. Martin Katzman and the investigator (Rebecca Tzalazidis) will have access to the data, and the research coordinators employed at the Clinic will have access to the data during this time. All data will then be shipped to and stored in an offsite storage facility for a period of 25 years. After this, the files will be confidentially shredded and there will be no paper record of participations' data.

Anonymized data in electronic form will also be securely stored in Dr. Josephine Tan's research lab located at Lakehead University in Thunder Bay, Ontario for a minimum of five years.

Voluntary Participation:
Your participation in this study is entirely voluntary and will have no bearing on the services that you are currently receiving or will be receiving from the START Clinic. You can choose to not participate, or to withdraw from the study at any time, and this will not have any foreseen undesirable consequences. If you withdraw from the study, all information collected to that point will be retained within the study records.

Additional Information
By participating in this study, and providing that you meet other eligibility criteria, you may have the opportunity of participating in a second study at a later date, which will compare the effectiveness of psychological treatments for depression.

This study has been reviewed by the Lakehead University Research Ethics Board. If you have any questions related to the ethics of the research and would like to speak to someone outside of the research team please contact Sue Wright from the Research Ethics Board at 807-343-8283 or research@lakeheadu.ca. This study has also been reviewed through the START Clinic by the Optimum Research Ethics Board. You can contact the Optimum Ethics Review Board Coordinator, Paula Hutchings, at optimumerb@yahoo.com.

Contacts:
If you have any further questions about the study, you may contact Rebecca Tzalazidis at rtzalazi@lakeheadu.ca, Dr. Martin Katzman at mkatzman@startclinic.ca, or Dr. Josephine Tan at jtan@lakeheadu.ca.

Conflicts of Interest
There are no foreseen conflicts of interest with respect to this study.

Patient initials: _____

OPTIMUM ETHICS REVIEW BOARD

Version: April 15, 2019

Summary of Findings

If you wish to receive a summary of the results obtained from this study, please provide either your e-mail address or mailing address below. If you do not wish to receive a summary of the results obtained from this study, please leave the space below blank. A brief report of the findings will be available to those interested once the study is complete.

E-mail address: _____

or

Mailing address: _____

_____

Consent

Study Title: The effectiveness of CRT as an adjunct to CBT for depression

I confirm that I have been given sufficient time to consider the above information and to seek advice if I choose to do so. In addition, I confirm that to the best of my knowledge and belief, all technical language used by the research team members has been explained and that I received satisfactory answers to all questions which I asked. I have read all and understand this consent form and I voluntarily agree to participate in this research study. I have received a copy of this consent form.

_____ _____

Participant's Printed Name Signature & Date

_____ _____

Researcher's Printed Name Signature & Date

Patient initials: _____