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Prevention of Depression in At-Risk Adolescents: Identification of Course and Predictors of Intervention Response

A dissertation submitted in partial satisfaction of the requirements for the degree of

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in

Clinical Psychology

by

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The Dissertation of Karen T. G. Schwartz is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

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ABSTRACT OF THE DISSERTATION

Prevention of Depression in At-Risk Adolescents: Identification of Course and Predictors of Intervention Response

by

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Doctor of Philosophy in Clinical Psychology

University of California San Diego, 2020
San Diego State University, 2020

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Depression is a prevalent and disabling disorder. Parental depression predicts onset and treatment resistance in offspring, and adolescent onset has been associated with severe and chronic course. Thus, much work has been done to prevent depression, particularly in adolescent offspring of depressed parents. Few prevention trials have evaluated disorder course. Understanding long-term patterns and predictors of prevention

response in at-risk adolescents may inform new intervention development. As such, the current study aimed to empirically derive longitudinal patterns of response to prevention and test predictors of response. Adolescents (N = 316) at personal and familial risk for depression were enrolled in a multi-site randomized controlled trial testing a nine-month group-based cognitive-behavioral prevention program (CBP). The Depression Symptom Rating Scale (DSR) was used to establish patterns of prevention response across 6 years of study participation. Candidate predictors included intervention assignment, current parental depression at baseline, adolescent risk (i.e., a history of depressive episode, subsyndromal depressive symptoms, both), adolescent functioning, anxiety symptoms, and hopelessness. Repeated Measures Latent Class Analysis (RMLCA) was used to identify patterns of response across follow-up. Predictors of class membership were then analyzed using Multinomial Logistic Regression. All analyses employed an intent-to-treat design, used an alpha level of .05, and were run using M*plus*8. RMLCA model fit indices (i.e., AIC = 3211.24, BIC = 3476.76, BLMRT: $p < .001$; entropy = 87%) supported a four-class solution: well/late onset (n = 213; 68.5%), recurrent/brief episodes (n = 38; 12.2%), recurrent/persistent episodes (n = 19; 6.1%), early discontinuation (i.e., n = 41; 13.2%). Multinomial logistic regression revealed that increased odds of categorization in the well/late onset class vs. the recurrent/persistent class were related to being randomized to CBP and having better functioning and less hopelessness at baseline. Interestingly, adolescents at highest risk for depression were also more likely categorized in the well/late onset class compared to the recurrent/persistent class. The four distinct trajectories of prevention response identified have implications for booster session timing

and prevention program content. Results also support the feasibility of using RMLCA and multinomial logistic regression in future work, progressing the understanding long-term depression prevention effects in at-risk adolescents.

INTRODUCTION

Depression is a highly prevalent and debilitating disorder, impacting up to 20% of teens in the United States. Prevalence rates increase across adolescence, with 1 out of 5 older teens experiencing a depressive episode (Avenevoli, Knight, Kessler, & Merikangas, 2008). Depression can be chronic, recurrent, and disruptive of developmental transitions (Kessler, 2012; Kessler & Bromet, 2013). Studies have shown that adolescent depression predicts grave social and academic dysfunction, including increased social withdrawal, risky behaviors, substance use, suicidality, and academic dropout (e.g., Kessler, 2012). Additionally, impairment has been shown to compound over time, leaving a trail of dysfunction across domains into adulthood (e.g., Lewinsohn, Clarke, Seeley, & Rohde, 1994). Thus, adolescence is a key developmental period during which depression prevention efforts may be most effective in derailing this substantial public health concern.

In addition to clear impacts on mental health and functioning, depression is costly. Monetary costs directly associated with depression management and treatment have culminated in a total economic burden of $210.5 billion (Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015). Early-onset depression has been related to increased depression severity, prolonged course, decreased family and financial stability, disrupted social support, and increased rates of teen pregnancy. Finally, depression has been identified as a significant predictor of persistent and debilitating physical health problems and early death (Kessler, 2012). These cascading and compounding disturbances of societal functioning place increased demands on government relief programs, which translates to

an additional $102 million in indirect costs (Greenberg et al., 2015). Remarkably, a majority of adolescents meeting depression criteria do not receive indicated specialty mental health services or experience insufficiency in care, failing to upset the negative course of disease and increasing economic burden (e.g., Merikangas et al., 2011). Furthermore, evidence-based treatments for youth with depression have yielded the lowest effect sizes of major psychological disorders (Weisz et al., 2017). However, depression prevention efforts have been shown to be cost effective (Lynch et al., 2005), further supporting the importance of prevention research.

Much work has been done to prevent depression onset in youth, supporting the use of cognitive-behavioral programs over other prevention modalities; however, reviews have evidenced substantial variability in effect sizes of prevention programs (Brunwasser & Garber, 2016; Stice, Shaw, Bohon, Marti, & Rohde, 2009). Trials have looked towards identifying moderators of outcome to understand the heterogeneity in findings, and level of risk has been a central, consistent moderator of response. Prevention studies have employed three broad theoretical frameworks capturing levels of adolescent depression risk: (1) universal prevention (i.e., administering the intervention to all youth within a given catchment area), (2) selective prevention (i.e., administering the intervention to subgroups of youth endorsing familial and/or environmental risk factors of disorder), and (3) indicated prevention (i.e., administering the intervention to youth reporting personal risk factors of disorder; Horowitz & Garber, 2006). Both selective and indicated methods have been identified as superior preventative designs compared to universal efforts, as defined by increased magnitude of effect sizes (Hendricks Brown et al., 2018; Horowitz

& Garber, 2006; Stice et al., 2009). This could be due to increased opportunity for symptom movement, as participants in selective and indicated trials were more likely to endorse baseline symptoms compared to those enrolled in universal trials (Horowitz & Garber, 2006). However, increased efficacy may also reflect greater relevance of skills to participants due to personal symptoms and/or family structure, promoting greater attention and opportunities for mastery. Either way, superiority of selective studies supports the potency of family as a risk factor.

Depression runs in families, and parental depression has been shown to be a robust predictor of depression onset in youth as well as treatment failure (Beardslee, Versage, & Gladstone, 1998; Garber et al., 2009; Korhonen, Luoma, Salmelin, & Tamminen, 2014). Genetic factors play a role in intergenerational transmission of depression, with genetics accounting for $\geq$ 50% of transmission variance. Additionally, genetic load seems to interact with environmental risk factors, such that individuals at genetic risk for depression seem to be more sensitive than those without genetic risk to aversive environmental experiences (Birmaher et al., 1996). This is particularly concerning, as parental depression has also been shown to impact the rearing environment.

Substantial research on the environmental mechanisms through which parental depression impacts offspring has been published. First, depression seems to interfere with parents' abilities to model important skills such as emotion regulation and healthy coping (e.g., Goodman & Gotlib, 1999). Second, parental depression may challenge offspring notions of self-efficacy, as youth may feel excessive guilt, particularly for unsuccessful in

attempts to improve parental dysphoria (Zahn-Waxler, Kochanska, Krupnick, & McKnew, 1990). Similarly, parents with depression have been shown to vacillate between warm and hostile parenting styles as a function of mood, promoting perceived behavioral ineffectiveness in youth that can lead to the adoption of maladaptive secondary coping strategies (Elgar et al., 2007). Finally, parental depression has been associated with increased levels of stress within the home (e.g., marital conflict, parent-youth conflict, general uncertainty), which has been consistently identified as a depression risk factor (e.g., Cummings, Keller, & Davies, 2005; Goodman & Gotlib, 1999). Developmental changes associated with adolescence (e.g., increased emotional reactivity combined with insufficient cognitive control, heightened sensitivity to social contexts, drive for independence from parental influence; Arnett, 1999; Rudolph, 2014) can increase the negative impact of these familial risk factors, further promoting the heightened prevalence of depression in these markedly at-risk youth.

In sum, adolescence has been shown to be a key developmental period during which intervention efforts are highly indicated and yet under delivered; further, familial depression conveys substantial additional risk of depression development and poor outcomes. The Prevention of Depression study (POD; Garber et al., 2009) is the largest multi-site prevention trial published to date with the longest reported follow-up period (6 years). POD built on these findings by enrolling a selective *and* indicated sample of adolescents in a randomized controlled trial comparing a cognitive-behavioral prevention program to usual care. The trial was successful, as intervention effects in favor of the active arm were maintained across the full assessment period; additional questions

regarding depression development and maintenance have not yet been explored by POD or the literature at broad, and answers may guide the development and implementation of the next generation of intervention programs. Key questions include: (a) considering that depression is often categorized as chronic, what are the long-term, unfolding patterns of disorder in high-risk individuals? (b) Can intervention shift high-risk individuals onto a better long-term course? (c) Do risk variables, such as parental psychopathology and individual experiences with depression symptoms, matter within the context of defining course and/or have implications for intervention delivery timing (e.g., implementation of booster sessions), and (d) Are there other modifiable individual predictors that influence depression course?

This dissertation aimed to contribute answers to these questions using the archival POD dataset. To frame aims and provide rationale for specific predictors of prevention response, theoretical frameworks of depression development, findings speaking to longitudinal course both within and outside of an intervention context, patterns of symptom trajectories, and predictors of long-term findings were reviewed.

CHAPTER 1. LITERATURE REVIEW

Definition and course of depression

Depressive disorders are defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM; American Psychiatric Association, 2013) as prolonged and impairing periods characterized by negative affect and/or loss of interest or pleasure in typically-enjoyed activities, accompanied by a combination of other cognitive and neurovegetative traits. Diagnoses under this umbrella can be distinguished from one another by the number of symptoms present and their duration. For instance, Major Depressive Disorder (MDD) can be diagnosed if one reports a period of $\geq$ 2 weeks during which $\geq$ 5 symptoms are experienced for most of the day, nearly every day, accompanied by functional impairment. MDD is typically evident in episodes that remit and reoccur across the lifespan. In contrast, a diagnosis of Persistent Depressive Disorder (PDD; formerly Dysthymia) requires fewer symptoms (depressed mood plus $\geq$ 2 supporting symptoms) for a substantial period of time ($\geq$ 1 year in youth), with no more than 2 months of welltime within the interval discussed. Across these two major diagnoses, depression is characterized as a chronic disease with a waxing and waning course.

To standardize research on the course of depressive illness, Frank and colleagues (1991) proposed rationally-developed operationalized descriptors, in efforts to segregate psychopathology from normative changes in mood state: *episode* (i.e., a period during which one endorses concurrent, clinically significant symptoms, numerous enough to meet diagnostic criteria on a validated measure; duration of $\geq$ 2 weeks, per the DSM-5), *remission* (i.e., an asymptomatic [$\leq$ 2 mild symptoms, per the DSM-5] period that is not

necessarily catalyzed by an intervention; duration of ≥ 2 months, per the DSM-5), *recurrence* (i.e., onset of an independent episode after recovery criteria have been met). As described below, definitions of terms have varied in their operationalizations across the literature.

Evidence informing the longitudinal course of depression

The review of current literature speaking to depression course was separated into three categories: studies of natural course of untreated depression, prevention programs for non-diagnosed youth, and treatment programs for diagnosed youth. To match the current focus on depression trajectories and their predictors, the literature review on prevention and treatment literatures was confined to trials with published findings at follow-up.

Natural course. Studies informing natural course assessed individuals longitudinally to evaluate changes in depression symptoms, independent of intervention-based manipulation. Methods included national surveys and cohort studies. Findings speak to rates of disease in large, representative samples and outline expectations of natural course. The latter provided guidelines for practical significance of intervention response.

Prevalence and length of episode. Current depression has been identified in approximately 9% to 14% of adolescents enrolled in naturalistic longitudinal trials (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993; Rushton, Forcier, & Schectman, 2002), among the highest prevalence rates of all major DSM disorders assessed (Lewinsohn et al., 1993). Depressive episode duration in these studies ranged

considerably, with an average length of approximately 6 to 8 months (Kovacs, Feinberg, Crouse-Novak, Paulauskas, & Finkelstein, 1984a; Lewinsohn et al., 1993). Chronic and prolonged episodes were also common with 44% of youth enrolled with moderate-severe levels of depression symptom severity maintaining that status 1 year later (Rushton et al., 2002).

Remission. Less data were available in community samples informing rates of depression remission following episode. Recovery data from two cohorts of treatment-seeking children ages 8 to 13 years old at high risk due to low socioeconomic status and trauma histories, indicated that recovery prior to 3 months post-depression onset was unlikely. Rates of remission peaked by months 15 to 18, with 92% of children meeting remission criteria (Kovacs et al., 1984a).

Recurrence. In children, those who had recovered evidenced a 26% chance of recurrence of a depressive episode within the first year at risk, and 40% chance of recurrence within 2 years. Highest window of risk immediately followed the required welltime to meet recurrence criteria (i.e., 2-4 months post initial episode offset; Kovacs et al., 1984a). In adolescents, a depression relapse rate of 18.4% was reflected by the full sample (Lewinsohn et al., 1993; Lewinsohn, Clarke et al., 1994). Time to relapse occurred 6 months post-recovery in 5% of the sample, by 1 year in 12% of the sample, and by 4 years in 33% of the sample (Lewinsohn, Clarke et al., 1994), and 45% of those with adolescent MDD experienced recurrence between 19-24 years of age (Lewinsohn, Rohde, Klein, & Seeley, 1999). In a sample comprised solely of adolescent women, 70% experienced depression recurrence (Daley, Hammen, & Rao, 2000).

Trajectories of depression. To date, patterns of depression symptoms over time have been difficult to elucidate, as most longitudinal studies have not reported on variations between individuals, opting instead to evaluate rates of onset or mean rates of change overall or by treatment group. However, four naturalistic, longitudinal trials (Hammen, Brennan, & Keenan-Miller, 2008; Lewinsohn, Clarke et al., 1994; Lewinsohn, Roberts et al., 1994; Rushton et al., 2002) evaluated within-person changes over the course of time.

Rushton et al. (2002) and Lewinsohn, Clarke, and colleagues (1994) reported on within-person symptom maintenance, findings from which have been reported above. In contrast the remaining two publications that reported on within-person depression symptom changes over the course of time utilized patterns of symptom change in their samples to group participants rationally into one of four groups. First, Lewinsohn, Roberts et al. (1994) grouped participants based on depression symptoms at two time points. Youth were categorized as never depressed (66.3%), formerly depressed (12.7%; i.e., evidence of depressive episode prior to Time 1), future cases (6.5%; i.e., onset of a depressive episode between Time 1 and Time 2), and currently depressed at Time 1 (2.6%). Similarly, Hammen and colleagues (2008) defined four courses of depression based on observations of change in youth with familial history of depression. Their four groups were defined as follows: onset-recurrent (i.e., depression onset prior to 15 years old with evidence of episode recurrence between ages 15-20), early-onset (i.e., depression onset prior to 15 years old with no evidence of episode recurrence between ages 15-20), later-onset (i.e., depression onset after age 15), never depressed (i.e., no

evidence of depression onset by age 20). In their sample, the largest number of participants did not evidence depression onset (57.5%). The second largest group was the later-onset group, encompassing 16.1% of the sample. The onset-recurrent and early-onset-desist groups were similar in size (6.1% vs. 6.0% respectively).

Taken together, findings from unselected, naturalistic studies were remarkable for depression symptom stability and high rates of recurrence among those evidencing previous or baseline symptoms of depression, while individuals with later-onset or absence of depression seem to maintain wellness at higher rates. Remarkably, few of the larger natural survey studies reported data at multiple time points and were therefore not included in this summary, which highlights the need for additional information on longitudinal within-person changes in depression symptoms. Investigations of longitudinal symptom trajectories laid the groundwork for fine-tuning our understanding of personal course and how intervention might be incorporated to meet the needs of individuals.

Prevention programs. Much work has been done to prevent depression onset in youth. As stated above, depression, particularly with pediatric onset, has long-lasting debilitating effects across domains, is difficult to treat, and is associated with substantial economic burden. As such, researchers have taken the logical approach to direct efforts towards avoiding such hardship through prevention. Prevention programs have been tested in multiple settings, including in schools, primary care settings, and research laboratories. Programs have varied in their use of groups, inclusion of parents, and symptom requirements for eligibility. As stated above, sampling youth at personal or

familial risk of depression development have yielded the highest effect sizes, rather than providing intervention to universal and unselected samples (e.g., Horowitz & Garber, 2006). In support of this dissertation's aims and chosen dataset, cognitive-behavioral programs identified as most efficacious in preventing depression development that assessed maintenance of findings across follow-up were examined.

Penn Resiliency Program. The Penn Resiliency Program (PRP; Gillham, Reivich, & Jaycox, 2008) is one of the most widely evaluated depression prevention programs for youth between the ages of 10 and 14. However, evidence of program efficacy has varied considerably across studies, with some trials supporting superior effects of PRP compared to control conditions, while others found no significant differences by group. Taken together, the mean effect size of PRP at post is small (0.11-0.21; Brunwasser & Garber, 2016; Brunwasser, Gillham, & Kim, 2009).

Across follow-up, evidence of maintained PRP effects has also been mixed. Some explorations identified group differences in depression symptom severity at 6-months (Gillham, Reivich, Jaycox, & Seligman, 1995; Wijnhoven, Creemers, Vermulst, Scholte, & Engels, 2014) and 2-year post-intervention (Cardemil, Reivich, Beevers, Seligman, & James, 2007; Gillham et al., 1995), while others did not (Gillham et al., 2007).

One trial provided sufficient data to illustrate the shape of change in depression symptoms by group. Findings depicted linear increases in depression symptoms, within the control group, beginning immediately (post-intervention) and continuing through 2-year follow-up; however, those in the PRP group showed continued maintenance of reduced symptoms through the 12-month assessment, after which depression scores

increased. Authors inferred that the receipt of PRP may have provided youth with tools necessary to cope effectively with stressors associated with increased academic and social demands during the pubertal window, while those in the control group maintained vulnerability illustrated by depressive symptoms in response to these stressors. The patterns of depression symptom change within PRP highlighted the importance of considering time in studies of prevention outcome and suggested that the implementation of booster sessions may be valuable 1 year post-intervention to maintain gains, long-term (Gillham et al., 1995).

Coping with Stress. The Coping with Stress (CWS) intervention is a cognitive-behavioral group intervention for adolescents who were not currently experiencing a depressive episode, adapted from Clarke and Lewinsohn's (1986) Coping with Depression treatment program. Unlike, PRP, CWS was intended to be implemented with older adolescents (i.e., high school students). CWS was also particularly notable as it served as the basis of the manual used in POD.

Overall, CWS has evidenced consistent prevention effects compared to usual care (UC; Clarke et al., 1995, Clarke et al., 2001; Stice, Rohde, Seeley, & Gau, 2008). Specifically, CWS was superior to UC in preventing depression at post and 1 year later in terms of prevalence of depression onset and magnitude of scores on dimensional measures of depression symptom severity (Clarke et al., 1995, Clarke et al., 2001; Stice et al., 2008). Significant group differences in rates of depression onset persisted but diminished 18 and 24 months post-intervention (Clarke et al., 2001; Stice, Rohde, Gau, & Wade, 2010). Of those who did experience depression onset, members of the CWS group

met onset criteria significantly later than those receiving UC, promoting a delay effect as a result of intervention (Clarke et al., 2001). It is notable that adolescents recruited for enrollment in Clarke and colleagues' (2001) study were all offspring of depressed adults.

In contrast, Dobson, Hopkins, Fata, Scherrer, and Allan (2010) published null findings in their comparison of CWS to an attention-control condition. Participants across groups evidenced declines in dimensional measures of depression symptoms through the 6-month follow-up assessment, possibly suggesting evidence of natural remission and the potential importance of nonspecific supportive factors common to instances of clinical contact. However, the small initial sample size (N = 46) and high attrition (39.1% lost-to-follow-up) may have also driven findings.

Taken together, the evidence base for CWS supported its use to prevent depression in teens, as it has consistently separated from comparison conditions in studies exhibiting methodological rigor. Additionally, findings inform course as CWS groups exhibited a delay in depression onset compared to those receiving assessment contact only. This suggested that prevention efforts may be effective in helping youth avoid depression during a developmental stage known to be ripe with risk factors and associated with impairment that may be more impactful long-term (e.g., negative influences during the development of self-concept, missing key social milestones, falling behind academically).

POD. As stated previously, the current study utilized archival data on 316 adolescents enrolled in a four-site, randomized, pre-test/post-test effectiveness trial comparing a cognitive behavioral depression prevention program (CBP), based on CWS,

to usual care (UC; Garber et al., 2009). The implementation of CWS in POD varied in terms of the number of implementation sites included in the trial, length of the acute intervention period (shorter), continuation period (longer, to try to address the need for longer follow-up care), and the addition of a module on problem solving to promote self-efficacy in adolescents (Weersing et al., 2016).

Primary outcomes supported decreased rates of depression onset after completion of CBP compared to UC; however, 21.4% of adolescents within the CBP group and 32.7% in UC developed depression by the post-intervention assessment (Garber et al., 2009). Effects were substantially modified as a function of parental depression at baseline, such that differential efficacy by intervention assignment was no longer apparent in the subset of adolescents whose caregivers met for current depression at baseline. The adolescent indicator of individual depression risk did not significantly impact rates of onset at Month 9 by intervention assignment (Garber et al., 2009).

Primary findings were maintained approximately two years post-continuation (i.e., the month 33 assessment), such that the impact of intervention on rates of depression onset was still detectable. By the month 33 assessment, 36.8% of adolescents within the CBP group and 47.7% who received UC experienced at least one depressive episode; parental depression at baseline continued to moderate effects, such that differences in outcome by intervention assignment were no longer significant if the parent was in episode at baseline (Beardslee et al., 2013). During the follow-up period, intervention groups did not significantly differ in terms of service use, indicating that

findings were best attributed to trial intervention efforts rather than external continuation services (Beardslee et al., 2013).

At the final assessment, approximately six years (75 months) post-intervention, adolescents who received CBP had a significantly lower hazard ratio compared to those in the UC group, illustrated by differences in rates of onset by group ($61.9\%_{CBP}$ vs. $70.5\%_{UC}$; Brent et al., 2015). Analyses highlighted that the core differences in effects occurred within the first 9 months of study participation and were then maintained across the follow-up period. Notably, the impact of parental depression at baseline on the pattern of findings at the final assessment remained, such that the lack of parental depression at baseline was associated with increased prevention effects of CBP compared to UC, as well as increased depression-free days (DFD), while the presence of parental depression at baseline eliminated group-based discrepancies in rates of onset and DFD as participants entered young adulthood (Brent et al., 2015).

Summary. Across prevention programs, cognitive-behavioral interventions in adolescents exhibited predominantly positive effects in prolonging welltime compared to control conditions. Findings reflect the importance of intervention timing, as they highlighted the increased benefits of engaging adolescents in prevention programs in comparison to enrolling younger children who may have been less able to digest abstract content associated with prevention-focused skill building. Furthermore, the success of POD supported the utility of monthly booster sessions to inform timing of implementation to further decrease rates of depression onset and recurrence.

Treatment programs. Treatment programs refer to randomized controlled trials that compared a cognitive behavioral paradigm to a control condition, and published results over follow-up; enrolled youth had diagnosed depression and/or depression symptoms indicative of clinically significant elevations. Although not a target of the current study, understanding depression trajectories of youth starting from a position of disorder was particularly relevant to the current study as 80.1% of the POD sample had a history of depression prior to intervention and 13.9% experienced a depressive episode during the acute phase of intervention. Furthermore, response to an intervention program similar to those used in treatment trials was a central aim of POD. Trials of cognitive behavioral therapy (CBT) were drawn from the most-recent evidence base update of psychosocial treatments for pediatric depression, focusing again on findings over follow-up (Weersing, Jeffreys, Do, Schwartz, & Bolano, 2017).

The Coping with Depression Course (CWD) is a cognitive-behavioral group treatment for adolescents and involves the dissemination of the following skills: behavioral activation, relaxation, cognitive restructuring, and improving social effectiveness (e.g., communication, negotiation, conflict resolution; Clarke & Lewinsohn, 1986). CWD is the treatment version of the CWS manual utilized in POD. Explorations of the CWD manual were remarkable for the evaluation of parental involvement in treatment and the value of content on familial conflict and coping, to understand the impact of promoting parent buy-in and support of youth follow-through (Clarke, Rohde, Lewinsohn, Hops, & Seeley, 1999; Lewinsohn et al., 1990).

Acute findings supported the active conditions over the waitlist control group in terms of diagnostic improvements (i.e., no longer meeting criteria for a depression diagnosis) and dimensional depression symptom scores (Clarke et al., 1999; Lewinsohn, Clarke, Hops, & Andrews, 1990).

Follow-up comparisons at 1 month and 6 months posttreatment evaluating increased efficacy of parental involvement in adolescent treatment did not suggest statistical advantage of parental involvement in treatment; however, it was notable that groups in which parents were involved consistently scored lower on outcome measures of interest than those with adolescents alone (Lewinsohn et al., 1990). Use of booster sessions in efforts to maintain effects was successful, as adolescents receiving booster sessions evidenced increased rates of depression recovery (i.e., $\geq$ 8 weeks of minimal or absent symptoms; 100% recovery) compared to the assessment-only conditions (50% recovery) at the 12-month assessment. Recurrence rates did not significantly differ from those observed in assessment-only conditions at the same time point. Similarly, significance on rates of remission and recurrence was lost by group across measures of outcome by 24 months, although the receipt of boosters promoted faster time to remission achievement compared to those in assessment-only conditions (Clarke et al., 1999). These positive findings reflected the patterns reported in the CWS prevention literature, particularly the initial support of active over comparison conditions and the positive impact of booster sessions on outcomes. Prevention trials have evidenced longer-term maintenance of CWS superiority, supporting the increased utility of prevention efforts compared to treating symptoms after diagnostic onset.

In sum, CWD findings replicated across two trials such that CWD superiority was initially evident but not maintained over follow-up. Clarke and colleagues' (1999) test of the impact of booster sessions on long-term outcomes did not support the implementation of additional care, overall. Despite parental involvement not statistically separating from lack-of-involvement conditions, visual inspection of measures suggested potential benefits of the inclusion of parents in treatment across measures and time points (Clarke et al., 1999; Lewinsohn et al., 1990). Thus, findings promoted family factors for consideration when thinking about long-term depression recovery in teens.

The Treatment for Adolescent Depression Study (TADS; TADS, 2004) expanded on the CWD literature base by testing a compilation manual consisting of CWD and Brent et al. (1997) manual content to medication alone, combined medication and CBT treatment, and pill placebo in a sample of adolescents with moderate depression symptom severity. Measures of treatment response, sustained response (i.e., the maintenance of treatment responder status for $\geq$ 2 consecutive assessments; Rohde et al., 2008), and dimensional depression symptom severity consistently promoted combination treatment as the most efficacious arm through 18 weeks post-randomization. Surprisingly, CBT treatment, alone, was steadily outperformed by both active arms and did not differ significantly from the effects of pill placebo (Rohde et al., 2008; TADS, 2004; TADS 2007).

Rates of treatment response converged at the week 24 assessment (6 months post-randomization) and beyond (TADS, 2009). Although combination treatment seemed to yield the greatest benefits in this sample (TADS, 2007), CBT response rates, when

delivered alone, neared those of combined care by week 36 and also had the lowest rates of relapse of the four arms (Rohde et al., 2008). These findings supported the use of CBT to promote long-term changes in adolescent depression trajectories. Findings also highlighted the utility of longitudinal assessment and evaluating course.

A second landmark study (i.e., Treatment of Resistant Depression in Adolescents; TORDIA; Brent et al., 2008) tested the efficacy of individual CBT using the same manual employed by TADS implemented by independent investigators in a much more severe sample of depressed adolescents (Brent et al., 2008). Findings evaluated after the delivery of acute treatment (12 weeks) comparing combined medication and CBT treatment to medication alone suggested that the inclusion of CBT promoted superior effects as evidenced by higher rates of treatment response compared to the exclusion of CBT (Brent et al., 2008).

Remission and recurrence were evaluated after all elements of treatment had been delivered (i.e., acute phase and booster sessions). Treatment groups did not significantly differ on either measure of depression status 24, 48, or 72 weeks post-randomization (Emslie et al., 2010; Vitiello et al., 2011). Authors attempted to inform depression trajectory and found that CDRS-R scores decreased through the week 72 assessment; however, differences in terms of rate of decline did not significantly differ by group. Adolescents who achieved remission status compared to those who did not evidenced divergence in CDRS-R score decline at week 6 that was still detectable by week 72 (Vitiello et al., 2011). Similar to TADS, these findings corroborated the utility of combined treatment in adolescents with severe depression; however, without a CBT

alone group, it was difficult to conclude whether combination treatment would have outperformed CBT alone. Additionally, findings suggested that prolonged symptom improvement was initiated and detectable very early in participation (6 weeks), which may inform timing of treatment delivery and hypotheses of trajectory to be observed in the current study.

Predictors of depression course

Predictors are defined as baseline variables that may impact the directionality and magnitude of outcome, across a sample (Kraemer, Wilson, Fairburn, & Agras, 2002). Individual differences in risk of depression development have been used to inform trajectories of onset, maintenance of symptoms across time, future development of intervention content, and timing of implementation. Predictors of outcome from the reviewed trials were synthesized by outcome status tested: wellness, onset, remission, recurrence. Findings reported below covered a broader range of predictors than those tested in the current study; however, the breath provided context for the targeted aims.

Wellness. The following demographic variables predicted substantial symptom improvement in treatment studies and prolonged wellness in prevention trials: younger age at enrollment (Clarke et al., 2001; Curry et al., 2006), higher parental education levels, and living in a home that included both biological parents (Clarke et al., 2001). Race, ethnicity, family income, and adolescent verbal intelligence did not significantly predict symptom improvement or wellbeing in the reviewed trials (Curry et al., 2006; Lewinsohn et al., 1990). Evidence of gender predicting wellness was mixed, as one prevention trial identified that male gender predicted better outcomes (Clarke et al., 2001)

while another rendered gender as non-significant (Lewinsohn et al., 1990). It is notable that these demographic factors were only evaluated as predictors within prevention and treatment contexts.

Participant characteristics were also evident predictors of wellbeing. In terms of depression features, younger age of depression onset (Clarke et al., 1992), shorter duration of first episode (Curry et al., 2006; Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000), single as opposed to multiple episodes evident in the participant's history, and fewer symptoms endorsed during the participant's worst endorsed episode all predicted heightened wellbeing (Lewinsohn et al., 2000). Additionally, minimal melancholic features, lower endorsement of hopelessness or suicidal ideation (Curry et al., 2006) and absence of history of suicide attempts (Curry et al., 2006, Lewinsohn et al., 2000) were shown to predict wellness. Comorbidity was explored using general as well as specific criteria. Per Curry and colleagues (2006), minimal comorbid conditions predicted acute symptom improvements within the TADS sample. More specifically, absence of comorbid substance use disorders and lower scores on dimensional measures of borderline and antisocial personality traits were also associated with wellness in a naturalistic longitudinal study (Lewinsohn et al., 2000). Surprisingly, increased number of past psychiatric diagnoses was shown in one trial to predict symptom improvement across treatment groups (Clarke et al., 1992). Finally, wellness was significantly associated with improved functioning (Curry et al., 2006), low emotional reliance on others, and low endorsement of academic difficulties (Clarke et al., 2001; Lewinsohn et al., 2000).

Family features such as the number of first-degree relatives with depression, the number of first-degree relatives with recurrent depression, family conflict, and daily hassles predicted wellness in the direction that lower levels of variables predicted better outcomes (Lewinsohn et al., 2000). Parental depression was not significantly associated with symptom improvement (Curry et al., 2006).

Lastly, treatment-related variables were explored by treatment trials to understand the impact of referral source, expectations, and parental involvement on positive outcomes. Findings suggest that parental involvement in treatment (Clarke et al., 1992) and adolescent expectations of good outcomes (Curry et al., 2006) significantly predicted symptom improvement post-treatment. Referral source and parental expectations were not significantly associated with symptom decline (Curry et al., 2006).

Onset. Predictors of depression onset were tested within the context of naturalistic longitudinal designs. Gender significantly predicted rates of depression onset over time, such that female participants met onset criteria at higher rates than males (Lewinsohn et al., 1999; Lewinsohn, Clarke et al., 1994). In contrast, a majority of the demographic variables tested (i.e., age at study enrollment, race, ethnicity, presence of biological parents within the home, parental occupation) were nonsignificant predictors of depression onset in youth (Lewinsohn et al., 1999; Lewinsohn, Clarke et al., 1994). Findings regarding parental educational attainment were mixed, such that one trial reported that lower parental education predicted depression onset (Lewinsohn, Clarke et al., 1994), while Lewinsohn and colleagues (1999) reported that the relationship between parental education and depression onset was nonsignificant.

In terms of individual characteristics, increased stress levels (Daley et al., 2000), history of suicide attempts (Lewinsohn, Clarke et al., 1994), and comorbid conditions predicted depression onset (Daley et al., 2000; Lewinsohn, Clarke et al., 1994). Age of depression onset, episode duration, depression severity, suicidal ideation, and general impairment as a function of psychopathology did not significantly predict onset of a depressive episode (Lewinsohn, Clarke et al., 1994). Additionally, previous receipt of intervention did not significantly impact rates of depression onset in youth (Lewinsohn, Clarke et al., 1994).

Family factors, such as parental psychopathology (Daley et al., 2000) and family violence predicted depression onset in adolescents. Specifically, parental depression was associated with onset in offspring at an earlier age than observed in those without depressed parents (Weissman et al., 2006).

Remission. Rates of remission (also referred to in the literature as recovery) were explored by naturalistic longitudinal studies, as well as landmarking treatment trials. No demographic variables (i.e., age, gender, race, ethnicity, family income) achieved significance when using remission as the outcome variable of interest (Clarke et al., 1999; Curry et al., 2011; Kovacs et al., 1984a; Vitiello et al., 2011).

Age of initial depression onset predicted shorter time to recovery (Kovacs et al., 1984a), while decreased depression symptom severity during the initial episode (Clarke et al., 1992; Curry et al., 2011; Emslie et al., 2010; Vitiello et al., 2011) and absence of residual symptoms of depression post-treatment (Curry et al., 2011) significantly predicted increased rates of remission. Similarly, lower scores on dimensional measures

of anxiety symptom severity (Clarke et al., 1992; Emslie et al., 2010) and higher functioning (Clarke et al., 1992; Curry et al., 2011) also predicted rates of remission. Duration of initial depressive episodes, suicidality, endorsement of melancholic features, presence of comorbid conditions (i.e., any, dysthymia, anxiety, behavioral disorders), and history of abuse did not significantly impact rates of remission across trials (Curry et al., 2011; Kovacs et al., 1984a; Vitiello et al., 2011). Hopelessness and endorsement of cognitive distortions were mixed in terms of their reported impact on remission rates, such that less hopelessness was significantly predictive of remission across TORDIA follow-up assessments (Emslie et al., 2010; Vitiello et al., 2011); however, TADS long-term follow-up did not evidence significant differentiation between remission and lack of remission as a function of baseline hopelessness (Curry et al., 2011). Clarke and colleagues (1992) identified increased endorsement of rational thoughts as a significant predictor of episode remission, but Curry and colleagues (2011) did not.

Parental depression at baseline mitigated treatment effects (CWD vs. UC) in a selective sample of depressed offspring of depressed adults (Clarke et al., 2002). Although not tested explicitly as a predictor, as it was a risk factor across enrolled youth, CWD superiority was not evident across measures of depression outcome, across time points. Rushton et al. (2002) found that family cohesion (i.e., family having fun together, participant-father closeness) was associated with remission, as did an endorsement of a family member completing suicide. Vitiello and colleagues (2011) replicated their finding that decreased family conflict was predictive of remission. In contrast, TADS did

not find a significant relationship between family conflict and remission rates (Curry et al., 2011).

Finally, lack of previous psychosocial treatment was associated with shorter times to recovery (Kovacs et al., 1984a); yet, previous evidence of treatment response (Curry et al., 2011; Emslie et al., 2010) and continued use of antidepressant medication (Vitiello et al., 2011) also reportedly promoted remission. Referral source and treatment expectancy did not significantly impact remission rates when tested (Curry et al., 2011).

Recurrence. The largest number of variables was examined within the context of identifying salient risk factors of depression recurrence in enrolled youth. Participant age and indicators of socioeconomic status, such as family income, parental education level, and parental occupation, were nonsignificant predictors of recurrence (Curry et al., 2011; Lewinsohn, Clarke et al., 1994). Findings regarding gender as a predictor of depression recurrence were mixed, such that female gender significantly predicted recurrence in most trials (Curry et al., 2011; Lewinsohn et al., 1993; Lewinsohn et al., 2000; Lewinsohn, Clarke et al., 1994), but not all (Kovacs et al., 1984b). Similarly, minority status is TORDIA was associated with depression relapse rates by the week 72 assessment (Vitiello et al., 2011), but not in TADS ($p > .05$; Curry et al., 2011).

Regarding youth features of depression, previous episodes of depression (Daley et al., 2000; Lewinsohn et al., 1999), increased depression severity during episodes (Curry et al., 2011; Emslie et al., 2010; Lewinsohn, Clarke et al., 1994), increased number of episodes within one's history (Lewinsohn et al, 2000), and residual symptoms of depression (de Zwart, Jeronimus, & de Jonge, 2018) promoted increased rate of and

decreased time to recurrence. Age of onset of initial depressive episodes did not influence recurrence rates (Kovacs et al., 1984b). Suicidal ideation during the initial depressive episode and history of suicide attempts predicted shorter time to recurrence (Lewinsohn, Clarke et al., 1994), and the former also predicted higher recurrence rates (Curry et al., 2011). Presence of comorbid conditions, including dysthymia (Kovacs et al., 1984b), non-mood disorders (Daley et al., 2000), borderline and antisocial personality traits (Lewinsohn et al., 2000), and episodic, but not chronic, stress (Daley et al., 2000), were positively associated with recurrence rates. Curry et al. (2011) also identified comorbid anxiety as a significant predictor of increased recurrence rates; however, this finding was contradicted by Kovacs and colleagues (1984b; nonsignificant finding). General indicators of comorbidity (e.g., any condition, count) did not significantly predict recurrence (Curry et al., 2011; Lewinsohn, Clarke et al., 1994). In terms of measures of functioning predicting recurrence, findings were mixed based on the operationalization of the construct. Poorer functioning (Emslie et al., 2010) and increased emotional reliance (Lewinsohn et al., 2000) significantly predicted recurrence in youth; however, this finding did not generalize to the TADS sample (Curry et al., 2011), nor to a measure of impairment collected by Lewinsohn, Clarke and colleagues (1994).

Familial saturation of depression (e.g., proportion of family members with MDD; Lewinsohn, Clarke et al., 1994) and witnessing family violence (Daley et al., 2000) predicted increased risk of recurrence. However, neither parental psychopathology nor family conflict reached statistical significance as predictors of depression recurrence (Curry et al., 2011; Daley et al., 2000). None of the treatment-related variables (i.e.,

history of psychosocial intervention, previous intervention response, referral source, treatment expectancy) tested in relation to recurrence rates reached statistical significance, either (Curry et al., 2011; Lewinsohn, Clarke et al., 1994).

Predictors of depression trajectories. Explorations of demographic factors revealed that female gender significantly impacted trajectory, such that higher proportion of women were present in a group characterized by recurrent course, followed by early-onset, later-onset, and least present in a group that never met criteria for depression (Hammen et al., 2008; Lewinsohn, Roberts et al., 1994). Similarly, female gender was associated with the maintenance of moderate/severe depression symptom endorsement over the course of a 1-year period (Rushton et al., 2002) but failed to meet significance in a second evaluation of predictors of maintained symptom duration (Lewinsohn, Clarke et al., 1994). Younger age at study enrollment also predicted membership in a never-depressed group compared to other classes (Lewinsohn, Roberts et al., 1994). Finally, Lewinsohn, Roberts and colleagues (1994) identified that living with both biological parents predicted an absence of depression compared to those categorized as having a history of depression, but findings were not maintained when evaluated in groups characterized by other trajectories (Lewinsohn, Roberts et al., 1994; Rushton et al., 2002). Race, ethnicity, other indicators of household makeup (e.g., number of individuals in the home, birth order), and socioeconomic status did not significantly categorize participants into predetermined, rationally derived groups (Lewinsohn, Clarke et al., 1994; Lewinsohn, Roberts et al., 1994; Rushton et al., 2002).

Depression symptom severity and earlier age of onset predicted trajectory, such that both predicted depression symptom maintenance (Lewinsohn, Clarke et al., 1994). Depression symptom severity also distinguished adolescents with current depression from those with historical episodes and those who would go on to meet criteria for an episode, and never-depressed youth (Lewinsohn, Roberts et al., 1994). Suicidal ideation, worse general health, and somatic complaints also predicted prolonged symptom maintenance (Lewinsohn, Clarke et al., 1994; Rushton et al., 2002). Poor functioning significantly distinguished currently depressed youth from those who would develop depression prior to the next time point, from those with historical or absent depression (Lewinsohn, Roberts et al., 1994). Additionally, increased social dysfunction was associated with early-onset episodes compared to later-onset or absence of depression (Hammen et al., 2008). Lastly, suspension from school predicted symptom maintenance over time (Rushton et al., 2002). Self-esteem (Rushton et al., 2002), history of suicide attempts, general comorbidity (Lewinsohn, Clarke et al., 1994), substance use, and alternate definitions of functioning did not reach statistical significance in terms of differentiating trajectories of depression course (Rushton et al., 2002).

Maternal depression significantly predicted depression trajectories, such that onset-recurrence and early-onset groups had larger proportions of adolescents with depressed mothers compared to those in the later-onset or never depressed groups (Hammen et al., 2008). Parental age (Lewinsohn, Roberts et al., 1994) and family support (Rushton et al., 2002) did not predict trajectory groupings, significantly. Finally, the receipt of counseling (Lewinsohn, Clarke et al., 1994; Rushton et al., 2002) as well as

difficulties obtaining medical care (Rushton et al., 2002) were both positively associated with depression symptom duration.

Findings from POD. The POD study is the largest longitudinal prevention trial published to date, and was the source of the dataset for this investigation. As stated above, intervention assignment consistently predicted prevention outcome, supporting CBP superiority over UC. However, parental depression served as a substantial moderator through month 33, such that active parental depression at baseline diminished the effects of CBP. Additional candidate predictors and moderators of depression onset by month 9 were explored, including demographic characteristics, parental and adolescent clinical characteristics at baseline, and contextual factors (e.g., family conflict, life events). Findings revealed that increased depression symptoms (self-report), hopelessness, aggression, dysfunction, parent-adolescent conflict, parental psychological control, stressful life events, and decreased parental acceptance were all associated with elevated chances of depression onset by month 9, with hopelessness and dysfunction being the most robust predictors in the final model (Weersing et al., 2016). In addition to parental depression at baseline, parental history of hypomania, higher adolescent depressive and anxious symptoms (self-report), dysfunction, and hopelessness also moderated intervention effects by month 9. Utilizing significant moderators to create clusters of elevated risk of onset within the CBP condition, high functioning youth with a caregiver classified as currently depressed at baseline and high endorsement of hopelessness were at greatest risk for developing depression by month 9 (57% onset), closely followed by lower functioning adolescents receiving CBP (56% onset). In

contrast, higher functioning youth with neither current parental depression nor anxiety symptoms were predicted to fare the best in CBP (0% onset; Weersing et al., 2016).

Risk clusters initially defined at month 9 were reviewed at month 33. Relatively low-risk youth, characterized at baseline by higher functioning, no current parental depression at baseline, and decreased self-reported anxiety symptoms, again evidenced superior effects of CBP compared to UC (i.e., longest time to depression onset by month 33, increased number of DFD since baseline; Garber et al., 2018).

In sum, psychopathology and poor functioning were associated with negative outcomes, such as depression onset and recurrence. Limitations in summarizing the literature on predictors included incongruence in variables assessed and differences in definitions of targeted constructs.

Summary

In sum, across naturalistic, prevention, and treatment studies, findings illustrated chronicity and high rates of recurrence of depression in adolescents. However, temporal patterns of change between studies paired with within-person explorations and analyses of predictors supported substantial variability in depression trajectories, as well as profiles of risk. Findings overwhelmingly suggested that individuals vary in their intervention needs to increase welltime. While these investigations laid the groundwork for improved understanding of longitudinal patterns of symptom course, limitations included use of rational groupings, unbalanced sample sizes, attrition, and focus on symptoms at static time points by group, rather than evaluating the full spectrum of

possible trajectories within individuals. This dissertation planned to expand upon this literature utilizing POD data to inform long-term depression trajectories.

THE CURRENT STUDY

The objective of the current study was to identify 1) classes of longitudinal depression trajectories and 2) predictors of those trajectories that could be targeted by future prevention programs. The POD sample lent itself well to these objectives by including adolescents at individual *and* familial risk for depression development, utilizing a rich measurement schedule that allowed for an empirical approach to establish prevention response trajectories (including onset, recurrence, maintenance, and recovery), incorporating intervention, and covering a follow-up period that spanned the adolescent/emerging adult transition. To my knowledge, this type of empirical exploration has not previously been done. Furthermore, this study expanded substantially on the POD literature. Published findings from POD reported on rates of depression onset and wellness through 75 months post-randomization, which was a considerably longer time period than other prevention trials (Brunwasser & Garber, 2016; Horowitz & Garber, 2006). However, outcome measures focused on incidence (i.e., % onset) and absolute figures of DFD that limited the understanding of variability of effects and changes in depression course that may be clinically informative. Thus, the current study contributed information novel to this dataset as well as to the prevention of depression evidence base as a whole.

Findings may have implications for intervention design and implementation. Characterizing multiple paths of response may inform depression theory by illustrating

long-term post-intervention ebb and flow of symptoms. The longitudinal illustration of response may highlight when individuals could maximally benefit from booster sessions. Additionally, predictors could inform new intervention targets and support allocation of mental health resources to those who are most at-risk. Fine-tuning who receives intervention, when delivery may be most useful, and identifying elements that seem to promote wellness to the greatest extent may yield more effective and long-lasting prevention of depression. If prevalence rates of depression can be further reduced, with it will decrease the profound, negative public health impact of the disease. Additionally, findings can inform efficient use of resources, which increases chances that services may be available to those who need them at the time of highest need. To this end, two aims are outlined to achieve study goals.

Chapter 1, in part, is currently being prepared for submission for publication of the material. Schwartz, Karen T. G.; Garber, Judy; Weersing, V. Robin. The dissertation author was the primary investigator and author of this material.

CHAPTER 2. AIMS

Aim 1: To empirically **derive classes of prevention response**, utilizing longitudinal depression symptom severity data from a large intervention sample of adolescents at individual and familial risk for depression development.

Hypothesis 1. It was hypothesized that participants would be classified into four trajectories differentiated by time to depression onset and number of episodes experienced across participation: prolonged wellness, early to episode, late to episode, and recurrent course.

Aim 2: To evaluate **predictors of the prevention response trajectories** defined by Aim 1. Predictors of interest encompassed variables central to study design and original aims, including intervention assignment (UC, CBP), indicators of individual depression risk, and current parental depression at baseline. Additionally, predictors that evidenced impact previously within the POD dataset (i.e., adolescent functioning, anxiety, hopelessness) were explored. Lastly, current parental depression was implicated in previously published study findings as a strong moderator that diminished CBP superiority on time to depression onset. As such, moderation of intervention effects by baseline parental depression status on class membership was evaluated in an exploratory analysis.

Hypothesis 2. It was hypothesized that intervention assignment would significantly predict pattern of prevention response, such that those assigned to CBP would be classified as having trajectories of relative wellness, while those who received UC would be more likely to evidence trajectories characterized by increased depression,

replicating CBP superiority identified in previously published findings from the same dataset. In contrast, parental depression at baseline and adolescent depression history were expected to promote more severe and chronic classifications of prevention response.

Chapter 2, in part, is currently being prepared for submission for publication of the material. Schwartz, Karen T. G.; Garber, Judy; Weersing, V. Robin. The dissertation author was the primary investigator and author of this material.

CHAPTER 3. METHOD

The POD dataset, an archival dataset from a multi-site randomized controlled trial (RCT) testing the efficacy of a nine-month group-based cognitive behavioral prevention program (CBP) compared to usual care (UC), was utilized to meet these goals. Adolescents (N = 316) retrospectively reported weekly ratings of depression symptoms during five assessment timepoints that were used to inform trajectory. In addition to the weekly symptom ratings, adolescents and caregivers provided questionnaire data that informed predictor variables. Written informed consent was obtained from parents or caregivers, and informed assent was obtained from adolescent participants.

Subjects

The utilized archival dataset included 316 13-17 year olds (M = 14.79 years, SD = 1.35; 58.5% female; 24.3% racial and/or ethnic minority; see Table 1) at personal and familial risk for depression development, who were out of episode at the time of enrollment. Adolescents were enrolled with at least one consenting caregiver who had a personal history of depression during the adolescent's lifetime. All participants spoke sufficient English to understand study proceedings, complete assessments written in English, and engage in an intervention solely presented in English (Garber et al., 2009).

Inclusion Criteria. As stated above, recruitment efforts aimed to identify adolescents at personal and familial risk for depression, who were not currently in episode at the time of enrollment. Personal risk criteria included (1.a) meeting criteria for a prior major depressive episode (MDE) that had been in complete remission for $\geq$ 2 months (n = 175; 55.4%), (1.b) the endorsement of elevated depression symptoms at

baseline (Center for Epidemiologic Studies Depression Scale [CES-D] ≥ 20; Radloff, 1991) without simultaneously meeting criteria for a current depressive episode (*n* = 63; 19.9%), or (1.c) both (*n* = 78; 24.7%). Familial risk was operationalized as follows: (2) having ≥ 1 consenting caregiver who (2.a) met criteria for a MDE within the past 3 years, (2.b) endorsed ≥ 3 cumulative years in MD/Dysthymic episode within the youth's lifetime, or (2.c) both (Garber et al., 2009). Families were ineligible for enrollment if (1) adolescents or consenting caregivers met diagnostic criteria for Bipolar I or Schizophrenia, (2) adolescents had a current diagnosis of mood disorder (DSM-IV), (3) adolescents endorsed taking a therapeutic dose of an anti-depressant medication, or (4) adolescents reported previous receipt of > 8 sessions of cognitive behavioral therapy for depression (Garber et al., 2009).

Procedures

Recruitment. Recruitment occurred between 8/2003-2/2006 across four sites: Vanderbilt University (*n* = 80; Nashville, TN); University of Pittsburgh (*n* = 80; Pittsburgh, PA); Kaiser Permanente Center for Health Research (*n* = 78; Portland, OR); Judge Baker Children's Center/Children's Hospital (*n* = 78; Boston, MA). Recruitment strategies included announcements and letters via health maintenance organization computerized database, e-mail listserves, physicians in the community, and local schools. Advertisements were also disseminated by newspapers, radio, and television (Garber et al., 2009).

Randomization. Eligible families were randomized to receive CBP or UC using the Begg and Iglewicz (1980) modification of the Efron (1971) biased coin toss.

Randomization was blocked on age, sex, race/ethnicity, and personal risk status (i.e., history of depressive episode, elevated CES-D score) to ensure that these features were evenly distributed across groups. Siblings meeting eligibility criteria were invited to participate and were yoke-randomized to promote intervention consistency within family units. The final sample included 33 sets of siblings, including 1 set of triplets (n = 67; see analytical plan for management of sibling data). Randomization was successfully balanced across all blocked variables (Garber et al., 2009; see Table 1).

CBP. The Cognitive-Behavioral Prevention Program (CBP) utilized a modified version of a previously tested cognitive behavioral intervention manual developed by the OR site listed above (Clarke et al., 1995; Clarke et al., 2001). The current version included 8 group-based sessions that occurred once per week for 90 minutes (acute; mean number of sessions attended: 6.5; Garber et al., 2009), followed by 90-minute booster sessions that occurred monthly for 6 months (continuation; mean number of sessions attended: 3.5; Garber et al., 2009). Sessions were led by masters-level clinicians, trained and supervised by an experienced clinician. Targeted skills during the acute phase included cognitive restructuring and problem solving. Targeted skills during the continuation phase included a review of cognitive restructuring and problem solving, with additional focus on behavioral activation, relaxation, and assertiveness training. Caregivers were involved in sessions 1 and 8, where they were received general information were briefed on skills taught during group sessions. Therapist compliance to the intervention manual ranged from 88.1%-95.8%.

UC. Recipients of Usual Care (UC) were able to engage in any non-study service, which was cataloged post hoc by study personnel (Garber et al., 2009). This control condition served as a benchmark to identify if CBP effects surpassed typically available service alternatives.

Assessment. Families completed an assessment battery prior to randomization to determine eligibility and provide a baseline measurement of symptoms and functioning. Families were reassessed five times over the course of 6 years at intervals of increasing magnitude over time (month 2, month 9, month 21, month 33, young adult follow-up). Of note, the original grant award funded study activities from baseline through the month 33 follow-up assessment; a second grant was awarded to capture the impact of intervention on the transition to early adulthood, around the adolescent's 21st birthday (at approximately month 75 of participation; Brent et al., 2015). Each assessment consisted of parent- and self-report questionnaires, as well as semi-structured interviews querying the presence of psychopathology in caregivers and adolescents since the last time point. The first follow-up assessment took place in the midst of the active intervention phase, and the second assessment occurred following the conclusion of the intervention phase of the study (approximately 9 months post-randomization).

Retention. Overall retention was excellent, with 98.4% (N = 311) of the original sample providing any post-baseline DSR data. Of the original 316 participants, 88.0% (n = 278) provided a dataset through the young adult assessment. On average, participants completed 4.48 (SD = 1.04; range: 0-5) assessments, including 300 (94.9%) reporting at month 2, 290 (91.8%) reporting at month 9, 251 (79.4%) reporting at month 21, 296

(93.7%) reporting at month 33, and 278 (88.0%) reporting at the young adult follow-up (see Table 2). The high retention across timepoints decreased plausibility that substantial bias would threaten the validity of findings (Schulz & Grimes, 2002).

In terms of early discontinuation from study participation as a whole (n = 38, 12.0%), few participants (n = 5; 1.6%) refused to return to any follow-up assessment. The month 2 assessment served as the final timepoint for three participants (0.9%), eight participants (2.5%) discontinued after the post-intervention assessment (month 9), three (0.9%) did not return after the month 21 follow-up, and 19 youth (6%) terminated their involvement after the month 33 assessment.

Measures

Sample characteristics. Sociodemographic characteristics such as participant age, gender, minority status (i.e., identification as an ethnic and/or racial minority) and socioeconomic status were collected at baseline via paper/pencil questionnaire. Socioeconomic status (SES) was measured by the Hollingshead Index (Hollingshead, 1975), such that higher scores indicated higher SES. Sibling status was noted dichotomously (N/Y) to capture violations of independence in observations, given shared genetic and environmental factors. Sibling status was included as a covariate in all analyses evaluating predictors of classification of prevention response.

Eligibility criteria (i.e., familial risk for depression development, absence of active depressive episode in youth) were assessed using semi-structured clinical interviews administered by trained and reliable assessors. Caregivers completed the Structured Clinical Interview for DSM-IV axis I disorders (SCID-I; First, Spitzer,

Gibbon, & Williams, 1997), which probed history of depression and was used to establish family risk. The absence of current depression in adolescents was evaluated using the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiological Version (K-SADS-PL; Kaufman et al., 1997; interrater agreement $\geq$ 85.9%; Garber et al., 2009).

Prevention response trajectory. Depression symptom severity across follow-up was assessed using the Longitudinal Interval Follow-up Evaluation (LIFE; Keller et al., 1987), a semi-structured interview that yields weekly depression symptom scores, ranging from 1-6 (Depression Symptom Ratings; DSR). Lower DSR scores reflected fewer symptoms with less associated impairment, while higher scores were more indicative of clinically significant symptoms. A DSR score of 4 was equivalent to DSM-IV's symptom criteria for Depression, Not Otherwise Specified. A depressive episode was defined as a DSR $\geq$ 4 for $\geq$ 2 consecutive weeks. Onset referred to the first occurrence of an episode between baseline and participation completion. Episodes were determined to be independent from one another, if a participant endorsed > 8 consecutive weeks of welltime (i.e., DSR < 4) between the initial episode offset and new episode onset.

Adolescents and consenting caregivers were interviewed independently at each timepoint to obtain retrospective reports of the adolescent's symptoms and functioning since the last visit. This methodology allowed assessors to "fill in" scores continuously for any missed assessment interviews. Considering the high retention by timepoint, the

flexibility of the protocol did not seem to mask threats to assessment reliability or validity by imposing extensive cognitive burden on participants.

Interviews began with a creation of a mood-focused timeline to aid in recall by eliciting indicators of context (see Figure 1 for an illustrative sample of a timeline form). Adolescents and consenting caregivers were each provided with a blank timeline that included a -1 and -2 on the y-axis to reflect subthreshold and threshold depression symptoms, respectively. The x-axis or indicator of time also served as what one might consider a typical or neutral mood. Respondents then marked the timeline to indicate "dips" in their mood, including dates and a brief discussion of the events, triggers, and/or circumstances surrounding those dates. Assessors utilized the timeline to guide their query of depression symptoms, starting with the most severe dip, per the respondent's report, and systematically assessing each indicated dip in order of most to least severe. The assessment concluded with queries of depression symptoms during indicated welltime, to ensure a thorough capture of symptoms across the period between the last and current assessments. Trained and reliable independent evaluators (97.5% interrater agreement; Garber et al., 2009) unaware of the adolescent's intervention assignment considered both reports in addition to clinical judgment when assigning weekly DSR scores after the assessment's conclusion.

To manage the substantial number of weeks that youth participated in the study, weekly DSR data were summarized into 9-month, 6-month, and 3-month coding sets using the following three steps. 1) Weekly DSR scores were dichotomized (0 = no, 1 = yes) to reflect if a weekly score was part of a depressive episode, following the criteria

for episodes detailed above. 2) Weeks of participation were then sectioned into broader time intervals (i.e., 9-month, 6-month, 3-month). Calendar-based variations in number of weeks per month and impact of date of enrollment were standardized by beginning timelines at Week 0 (baseline) and equating 4 consecutive DSR ratings (i.e., a 4-week period) to one month. 3) Finally, each interval received a single DSR summary score reflecting the presence or absence of *any* depressive episode during that interval. If no episodes were evident (i.e., all DSR < 4 or DSR $\underline{\geq}$ 4 for < 2 consecutive weeks), the interval received a summary score of 0. If at least one episode was present (i.e., DSR $\underline{\geq}$ 4 for $\underline{\geq}$ 2 consecutive weeks), the interval received a summary score of 1.

Some episodes spanned the imposed interval boundaries. For instance, an 8-week episode that onset at week 32 and offset at week 39 spanned the first and second 9-month time intervals. In such cases, the following decision rules were applied. An episode was coded within the interval during which a majority of the episode (> 50%) occurred, to avoid double-counting time in episode. In cases where an episode spanned time boundaries equally without encompassing a majority of either timeframe (such as the example above), the episode was counted as present in the earlier timeframe. However, if the episode was sufficiently long that it encompassed > 50% of multiple intervals, it was counted as present in both summary scores. In the event that a DSR score was missing for $\underline{\geq}$ 2 consecutive weeks of a timeframe and there was no additional evidence of an episode within that same timeframe, the entire timeframe was coded as missing due to the possibility of an episode occurring during the missing weeks.

Predictors of prevention response. Intervention assignment was determined using the randomization procedure detailed above (Begg and Iglewicz, 1980; Efron, 1971). The presence of a major depressive episode in consenting caregivers at baseline (*n* = 157; 49.7%) was determined by the SCID-I (First, Spitzer, Gibbon, & Williams, 1997). The individual risk indicator in adolescents was informed by two measures. First, history of depressive episodes was assessed using the K-SADS-PL (Kaufman et al., 1997; interrater agreement $\geq$ 85.9%). Second, adolescents completed the CES-D, a 20-item self-report of depression symptoms within the past week; adolescents were identified as currently subsyndromal if they endorsed a CES-D score of 20 or higher (range: 0-60) at baseline without meeting concurrent criteria for a depressive episode, per the K-SADS-PL (Garber et al., 2009). This three-level variable was re-coded to allow for bivariate comparisons in prediction analyses.

Additional candidate predictors were drawn from Weersing and colleagues' (2016) evaluation of predictors and moderators of acute POD outcomes. First, the Children's Global Adjustment Scale (CGAS; Shaffer et al., 1983) was used to capture adolescent functional impairment at baseline. Independent evaluators considered both parent and adolescent reports on adolescent symptoms and functioning obtained during the LIFE interview. The single-item summary of adolescent functional impairment at baseline reflected a balance of symptom levels and associated impairment. The measure ranged from 0-100, with higher scores indicating better functioning across domains (ICC = 0.60; Weersing et al., 2016). The Screen for Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997), an adolescent-reported measure of anxiety symptoms

within the past 2 weeks, was utilized to capture current, dimensional symptoms of anxiety. Total scores reflected a sum of the 41 items, each scored 0, 1, or 2 points, with higher scores indicating greater severity of anxiety symptoms ($\alpha = .91$). Finally, pessimism about the future was measured by the Beck Hopelessness Scale (BHS; Beck, Weissman, Lester, & Trexler, 1974), a 20-item true/false measure with higher scores indicating increased hopelessness, per adolescent report ($\alpha = .85$).

Chapter 3, in part, is currently being prepared for submission for publication of the material. Schwartz, Karen T. G.; Garber, Judy; Weersing, V. Robin. The dissertation author was the primary investigator and author of this material.

CHAPTER 4. DATA ANALYTIC PLAN

Data cleaning and preparation

All statistical analyses involved in the current study were designed to utilize an intent-to-treat design and an alpha of .05. Examinations of descriptive data, including measures of central tendency (for continuous variables), prevalence rates (for categorical variables), skew (cutoff: > |2|) and kurtosis (cutoff: > |10|) were planned for all variables to understand if measures of interest had sufficient variability and met appropriate distributional assumptions to power the planned analyses. A thorough examination of the impact of not returning for the young adult assessment on classification was also planned. First, demographic (e.g., age, gender, race, ethnicity) and clinical (e.g., intervention assignment, baseline DSR score, depression history, parental depression status at baseline) characteristics of adolescents who had DSR data through the young adult assessment were compared to those who did not, using independent sample t-tests for continuous characteristics and chi-square statistical procedures for categorical characteristics. Then, an evaluation of the number of weeks assessed was planned to identify any outlier timepoints informed by < 20% of the sample, as truncation of such timepoints would be considered. Last, the impact of not returning for the young adult assessment on classification was examined. Data preparation and preliminary descriptive analyses to define the sample and explore missing data were performed in IBM SPSS Statistics (25); analyses defined by each aim were run in M*plus*8.

Classification of Prevention Response (Aim 1)

Repeated Measures Latent Class Analysis (RMLCA) was selected to determine independent trajectories of depression prevention response, based on summarized Depression Severity Rating (DSR) scores. RMLCA is a person-centered statistical method used to examine categorical variables in multivariate, longitudinal datasets. This method groups participants into classes based similar patterns of depressive episodes (0/1) by time interval across study participation, using conditional response probabilities (CRP; Collins & Lanza, 2010; Flaherty & Kiff, 2012). The exploration of class solutions began with the analysis of a 1-Class solution and increase by one class to allow for model comparisons (i.e., 1-Class, 2-Class, 3-Class…*k*-Class). Repeated model comparisons (N_{class} vs N_{class}-1) identified the most parsimonious model that maximized the associations among the observed variables. A final solution would be settled upon when fit indices (see below) suggested that the inclusion of an additional class no longer explained sufficient additional systematic variance. A solution with fewer classes was preferred to uphold parsimony.

Overall model fit was evaluated by multiple indices. The Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) are descriptive fit indices, such that smaller values when comparing solutions categorized by different numbers of classes (i.e., N_{class} vs N_{class}-1) indicate better model fit (Flaherty & Kiff, 2012). The Bootstrapped Lo-Mendell-Rubin Test (BLMRT) is a statistical test that uses a repeated sampling procedure to compare the class solution in question to the fit of a solution with one fewer class. Significant findings ($p < .05$) supported the inclusion of more classes, while $p > .05$ suggested better fit with fewer classes to promote parsimony. In the event that indicators

were directionally inconsistent, a majority rule would be applied to determine model fit. Practical utility of findings would be informed by classification accuracy (i.e., entropy > 80%; Flaherty & Kiff, 2012) and rational interpretability of resulting classes.

Classification procedure. Procedures were executed in the following order to identify and clarify the most specific model of best fit. First, timeframe was examined to understand whether 9-month, 6-month, or 3-month intervals yielded the best fitting solutions. The selection of 9-month intervals to start was meaningful as it reflected the full period of intervention delivery, including acute weekly sessions and monthly continuation sessions. This step incorporated summarized timepoints as indicators of the RMLCA. Then, the impact of missing data and variability in study participation time was evaluated. The variability of weeks between the baseline and young adult assessments was to be examined by truncating time points that were informed by few participants from the upper tail of the distribution. Second, the inclusion of the early discontinuation indicator representing participants who did not return for the young adult assessment was evaluated. Classifications resulting from the most sensitive combination of model elements promoting best fit was then to be interpreted and applied to Aim 2 prediction models as the nominal dependent variable.

Predictors of Classification (Aim 2)

Multinomial logistic regression that accounted for uncertainty in the classes established by Aim 1 was to be used to evaluate predictors of class membership (i.e., prevention response). Prior to running the statistical models, assumptions will be examined. Given the presence of siblings in the current sample, it was determined *a*

priori that a dichotomous sibling variable (i.e., membership to a sibling set: no = 0, yes = 1) would be included in the proposed models as an auxiliary variable, to account for variance introduced by violations of independence. Multicollinarity, or the inclusion of redundant predictors in the same model, would be determined by tolerance ($T < 0.10$) and the variance inflation factor ($VIF > 10$). The Box-Tidwell Test (Box & Tidwell, 1962) would be performed to test the relation between continuous predictor variables the logit transformation of the dependent variable. Lastly, standardized residuals ($> |2|$), centered leverage values (> 0.013), and Cook's Distance scores (> 1) were to be considered to identify influential data points that had substantial leverage or served as outliers. Again, majority rule would be used to determine points of concern. If identified, sensitivity analyses (i.e., analyzing models with and without the points of concern included) would be run to illustrate the impact of individual datapoints on the pattern of findings.

If assumptions were met, multinomial logistic regressions would examine predictors of prevention response, using the RMLCA output as a single, nominal dependent variable in M*plus*8 (Asparouhov & Muthén, 2014). An alpha level of .05 was used to determine statistical significance and corresponding effect sizes (Odds Ratio [OR]) qualified practical significance (i.e., increased effect size is associated with increased OR distance from 1; Chen, Cohen, & Chen, 2010). The six candidate predictors were to be evaluated in a step-wise fashion. First, univariate models were planned to identify the impact of isolated predictors on classification of depression trajectory. If significant at the .05 level, predictors would then be included in a second, multivariate model to determine robustness of predictive power. Differential impact of certain

characteristics may be more useful in determining profiles of risk. Therefore, univariate predictors achieving significance may be informative, even if significance is not maintained at the multivariate level.

Moderation. Given previous findings within the POD dataset, a multinomial logistic regression model was planned to identify the impact of current parental depression on the relationship between intervention assignment and class membership as an exploratory analysis.

Power

The technical literature on power analysis for RMLCA is substantially underdeveloped. Similarly, there is limited evidence of acceptable and plausible methodology for power analysis for multinomial logistic regression. Given our sample size of 316 participants, having up to 10 independent variables within a given model, providing a 30:1 ratio, was estimated to likely protect results from bias (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996). This conservative ratio allowed for the detection of groups and group differences, if present, supporting reasonable inferences based on findings.

Chapter 4, in part, is currently being prepared for submission for publication of the material. Schwartz, Karen T. G.; Garber, Judy; Weersing, V. Robin. The dissertation author was the primary investigator and author of this material.

CHAPTER 5. RESULTS

Baseline sample characteristics are displayed overall and by group in Table 1. Intervention group differences were explored at baseline using independent sample t-tests for continuous variables and chi-square statistical procedures to examine group differences in categorical variables. As reported in Table 1, there were no significant differences based on group assignment, further supporting successful randomization procedures. All variables of interest were deemed acceptable for analysis in the current study.

Classification of Prevention Response (Aim 1)

Repeated Measures Latent Class Analysis (RMLCA) was used to determine independent trajectories of depression prevention response by evaluating within-subject endorsement of depressive episodes across study participation.

Assessment of timeframe. Summarization of Depression Severity Rating (DSR) scores yielded 12 timepoints in the 9-month coding set, 18 timepoints in the 6-month coding set, and 36 timepoints in the 3-month coding set. RMLCA commands that included timepoints as indicators with no additional auxiliary variables identified the coding set of best comparative fit to the data. The 9-month and 6-month models yielded viable results. Findings from both models were consistent in their promotion of a solution of best fit. However, the 6-month coding offered increased specificity, due to the increased number of timepoints. It also included a larger sample ($N_{6\text{-Month}}$ = 308 vs. $N_{9\text{-Month}}$ = 307) and increased entropy (73.9% vs. 67.2%). Taken together, the model comparison promoted the 6-month coding over the 9-month set. The statistics associated

with the 3-month coding were unstable due to the large number of parameters estimated. While entropy was higher, the improvement was deemed artificial due to many parameters being constrained at their extremes. Lastly, the upper tail of 3-month timepoints was informed by very few participants (six timepoints informed by < 20% of the sample), to a greater degree than the other coding schemas. As such, 3-month coding was eliminated from further consideration.

Missing data. Table 2 illustrates DSR descriptive statistics. The current dataset reflected minimal missing data overall. The potential influence of DSR missingness was accounted for in the exploration of aims by the use of M*plus*8, which automatically adjusted for missing data using the Full Information Maximum Likelihood approach (FIML). However, while the distribution of weeks assessed was normal (i.e., it did not evidence skew or kurtosis), visual inspection of the distribution revealed a gap separating participants who did not completed the young adult assessment (n = 38) from those who did (n = 278). No comparison on any demographic or clinical variable reached statistical significance in the current sample, when evaluating differences between those who did and did not complete the young adult assessment (see Table 3). Despite these null findings, sensitivity analyses evaluating time outliers and early discontinuation of study participation on trajectory formation were conducted using the 6-month coding set.

Time outliers. Variability in the number of weeks assessed was observed among participants who completed the young adult follow-up. As such, the number of participants informing each timepoint in the upper tail of the distribution of weeks assessed was examined (see Table 2). The last three timepoints of the 6-month coding set

were considered for truncation as they were informed by < 20% of the sample (Timepoint 16: n = 36; Timepoint 17: n = 13; Timepoint 18: n = 2); truncation of timepoints informed by few participants could increase precision of estimates. Iterative RMLCA models systematically omitted one timepoint at a time. The fit indices from the three models were compared and yielded consistency in their promotion of a solution of best fit as evidenced by comparable index values. As such, the investigation of early discontinuation of assessment activities was done in all three models.

Early discontinuation. A dichotomous early discontinuation variable (i.e., missing the young adult follow-up) was computed and included as an indicator in the three models that varied by number of truncated timepoints. Fit indices and statistical tests of model fit promoted the inclusion of the early discontinuation variable and the truncation of the final two timepoints as the preferred model, as evidenced by the comparatively higher entropy and consistent indices of best fit. Thus, the employed analytical model differed from the proposed model depicted in Figure 2, as the model of choice included an indicator capturing early discontinuation, in addition to the DSR scores summarized into 6-month time intervals. Despite the truncation of final timepoints, all remaining data from the full sample were included in analyses.

Class creation and evaluation of model fit. RMLCAs testing 3 and 4 classes were fit to the data, evaluating 17 binary indicators. The 6-month coding yielded 16 binary indicators that reflected truncation of the final two timepoints. The last indicator included in the RMLCA was the early discontinuation variable, specifying lack of

participation in the young adult assessment (No = 0, Yes = 1; n_{Yes} = 33). No auxiliary variables were included at the class formation stage.

The model fit indices for each RMLCA solution are available in Table 4. Overall model fit indices (i.e., AIC, BIC) differed in their indication of favored class solution. The AIC index indicated that the 4-class solution fit better than the 3-class solution, as evidenced by the smaller AIC index. The 4-class BIC index was larger than those reflecting solutions with smaller class numbers; however, the differences in index magnitude was small and was contrasted by a statistically significant Bootstrapped Lo-Mandell-Rubin Test ($p < .001$) and improvements in entropy. Considering the majority rule in place, indices taken together suggested a 4-class solution fit better than a 3-class solution; therefore, the Conditional Response Probabilities (CRP) were evaluated to further explore model fit.

Per the CRPs (see Table 5) reflecting the probability of endorsing a "Yes" response per indicator (i.e., any depressive episode within the timepoint, early discontinuation from study participation) and the descriptive statistics calculated by class (see Table 6), the 4-class solution was defined predominantly by number of episodes endorsed, time to onset, and the overall proportion of time spent in episode across participation, as well as early discontinuation from study participation. As such, class 1 was defined as the well/late onset class; class 2 was defined as the recurrent/brief episode class; class 3 was defined as the recurrent/persistent class; and, class 4 was defined as the early discontinuation class (CRP of early discontinuation indicator = .71). A 4-class solution fit the data better than a 3-class solution, for it provided an additional coherent

category defined by early discontinuation from assessment activities that allowed for further distinction of the boundaries between the other three clinically informative classes. Latent class probabilities for each of the four classes were 68.5% (n = 213) in class 1, 12.2% (n = 38) in class 2, 6.1% (n = 19) in class 3, and 13.2% (n = 41) in class 4.

Validation of class interpretations. To probe this face-valid interpretation of classes, secondary analyses were run to identify if depression characteristics (i.e., weeks assessed, number of episodes, week of first episode onset, proportion of participation spent in episode) statistically separated classes. Multinomial logistic regression was used, accounting for sibling status as a covariate. Number of weeks spent in episode was excluded as it evidenced redundancy with proportion of time spent in episode (r = .98, p < .001); the latter was used to validate the classes, as it accounted for individual variability in weeks assessed and provided context for the potential impact of episode length on individual experiences. Overall, the pattern of results mapped on to the rational class interpretations at the .05 level, supporting the validity of class interpretation (see Table 7).

Predictors of Classification (Aim 2)

All assumptions were met, supporting the use of multinomial logistic regression without methodological accommodation by altering any predictors or the sample. As stated above, a dichotomous sibling variable was incorporated into each regression model to account for variance introduced by shared genes and environment. This addition of a covariate differed from the proposed analytical model in Figure 2. There was no evidence of multicollinearity between predictor variables (Tolerance $\geq$ 0.708; Variance Inflation

Factors $\leq$ 1.473). The Box-Tidwell Test (Box & Tidwell, 1962) yielded consistently non-significant findings (all *p*s > .05). Lastly, explorations of influential data points did not suggest points of concern that surpassed index thresholds. Thus, multinomial logistic regressions were completed per the data analytic plan.

Table 6 displays descriptive statistics for predictor variables by class. No hypotheses were made *a priori* regarding the selection of a reference group within the nominal dependent variable. As such, bivariate class comparisons were conducted for each multinomial logistic regression model. Table 8 displays findings by class comparison to illustrate the clinical profiles significantly predicting likelihood of classification at the univariate level, with additional notation for predictors that maintained significance in a multivariate framework.

Intervention as a predictor. As data were drawn from a clinical trial of which intervention assignment was a central aim, I will first review the findings that implicated intervention assignment as a predictor of classification of prevention response. Of all the bivariate comparisons, intervention assignment served as a central predictor of classification in the recurrent/persistent class. As expected, participants randomized to receive CBP were less likely to be classified in the recurrent persistent class compared to the well/late onset class (*OR* = 0.38, *S.E.* = 0.47, *p* = .039). Intervention assignment also distinguished participants in the recurrent/persistent class from those in the early discontinuation class, such that participants randomized to receive CBP rather than UC were less likely to be categorized in the recurrent/persistent class compared to the early

discontinuation class (*OR* = 5.42, *S.E.* = 0.68, *p* = .013). Intervention assignment did not predict odds of classification in the recurrent/brief class at the .05 level.

Additional predictors of classification. The remainder of univariate findings supported predictors distinguishing participants categorized in the well/late onset class from other categorizations of depression course. First, increased likelihood of being categorized in the well/late onset class rather than in the early discontinuation class was associated with decreased endorsement of anxiety symptoms (*OR* = 1.06, *S.E.* = 0.02, *p* = .010) and hopelessness (*OR* = 1.13, *S.E.* = 0.05, *p* = .017) at baseline, although neither maintained significance when included in a multivariate framework. Second, increased odds of participant categorization in the well/late onset class vs. the recurrent/persistent class was related to increased functioning (*OR* = 0.92, *S.E.* = 0.03, *p* = .005) and decreased hopelessness (*OR* = 1.14, *S.E.* = 0.05, *p* = .005) at baseline. Interestingly, individuals at highest risk at study entry (i.e., endorsed both a history of depression and elevated depressive symptoms at baseline, compared to a history of depression alone) were more likely to be categorized in the well/late onset class rather than the recurrent/persistent class (*OR* = 0.30, *S.E.* = 0.49, *p* = .014). Multivariate analyses supported baseline functioning as a robust difference in classification between these two groups (*p* = .038; see Table 8). Third, participants categorized in the well/late onset class also endorsed less severe anxiety symptoms (*OR* = 1.05, *S.E.* = 0.02, *p* = .019) compared to those placed in the recurrent/brief episodes class. All other models evaluating the impact of individual predictors on prevention response classification did not achieve statistical significance.

Secondary analyses. Additional analyses aiming to understand the impact of sociodemographic characteristics (i.e., age, gender, minority status, SES) on classification were explored. Findings distinguished the recurrent/brief class from other classes. Specifically, participants were more likely to be classified in the recurrent/brief class compared to the well/late onset class if they were younger at enrollment (*OR* = 0.74, S.E. = 0.14, *p* = .035). In a multivariate framework, only anxiety symptoms maintained significance as a predictor separating the recurrent/brief and well/late onset classes (see Table 8).

Sociodemographic characteristics also informed likelihood of being classified in the recurrent/brief vs. the recurrent/persistent class. Identifying as non-Hispanic White rather than an ethnic and/or racial minority substantially increased the likelihood of classification in the recurrent/brief class (*OR* = 10.49, S.E. = 1.06, *p* = .026). Additionally, increased SES impacted classification in the same direction (*OR* = 1.06, S.E. = 0.03, *p* = .038). However, neither maintained significance when both were included in a multivariate model (*p*s > .05).

Moderation. Current parental depression did not significantly moderate the relationship between intervention assignment and trajectory classification at the .05 level in this sample. Additionally, intervention assignment did not significantly moderate exploratory findings implicating parental depression as a predictor of onset rather than maintained wellness within the well/late onset class (*p* = .449).

Chapter 5, in part, is currently being prepared for submission for publication of the material. Schwartz, Karen T. G.; Garber, Judy; Weersing, V. Robin. The dissertation author was the primary investigator and author of this material.

CHAPTER 6. DISCUSSION

The current study aimed to empirically derive longitudinal trajectories of depression in a high-risk sample of adolescents enrolled in a randomized trial evaluating the impact of a cognitive behavioral prevention program. This is the first investigation to empirically derive trajectory groupings that characterize both frequency and timing of depressive episodes. The current study further examined predictors of these groupings, to understand clinical indicators of depression trajectories. Univariate prediction analyses were run first to facilitate hypothesis generation. The potentially low power for multivariate models promoted caution when interpreting robustness of effects. Taken together, univariate findings were discussed in detail as candidate variables for future work.

Overall, the initial hypotheses of the study were supported. Four classes of prevention response emerged, distinguished by the number of episodes endorsed, time to onset, and the overall proportion of time spent in episode across follow-up, as well as early discontinuation from study participation. Intervention significantly predicted membership in the least severe class, and other clinical indicators logically related to prevention response class membership. The statistical methods employed show promise for identifying clinically useful and theoretically interesting subgroups of youth. The following paragraphs delve into the characteristics of classes, followed by a discussion of predictors, clinical implications, limitations, and directions for future research.

The well/late onset class. The largest class defined represented participants who maintained wellness or exhibited late onset compared to other classes. In the current

study, maintained wellness equated to the absence of a depressive episode across follow-up. Those who did convert to depression during the follow-up period within this class did so on average 126.82 weeks post-baseline. This finding is in line with the primary POD outcomes (Garber et al., 2009) and CWS (Clarke et al., 2001) reports of prevention efforts promoting a delay effect in youth.

Considering the average age of group members at enrollment was 15 years, this 2.5-year delay implied that onset occurred between 17 and 18 years old. Lewinsohn et al. (1999) cited the window between 19-24 years as a high-risk window for relapse in previously depressed youth. As 80.1% of the POD sample had a history of depressive episode at study entry, it is not surprising that timing of episode co-occurred with this developmental period. At this age, teens face increased stress associated with changes in societal and social demands, increasing risk for mental health problems particularly in those who have histories of psychopathology (Arnett, 1999; Burt & Paysnick, 2012; Daley et al., 2000).

However, it is notable and encouraging that a majority of those who did experience onset reported incidence of a single episode, rather than recurrent course. The well/late onset group reported on the most weeks of study participation compared to other groups identified, with the lowest proportion of time spent in episode – 6% of study participation was spent in episode, which equates to 4.8 months. This time may not have been consecutive across participants and may not have achieved remission by study completion. Still, naturalistic studies of adolescent depression report that untreated episodes resolve after 6 to 8 months (Kovacs et al., 1984a; Lewinsohn et al., 1993),

making the experiences of youth in this class relatively mild and transient. As such, this group may be particularly resilient and resourceful compared to adolescents categorized to other trajectories.

The recurrent/brief class. The second-largest group to emerge from the latent class analysis reflected recurrent course with brief episodes. Of the 38 youth categorized to this group, zero maintained wellness and 37 reported more than two independent depressive episodes across participation (range: 1-7 episodes). Of note, youth in this group experienced the earliest onset of all the classes, a mere 8.5 months post-enrollment, which corresponded with the monthly continuation of the intervention phase. Despite the comparable number of episodes to the recurrent/persistent class, youth in the recurrent/brief class reported being in episode during 20% of their study participation, with episode length being rather stereotyped on average, lasting for approximately one month each. This suggests that the recurrent/brief group may be susceptible to episode but resilient.

It is possible that the brevity may have allowed youth in this class to maintain involvement in developmentally appropriate activities. Behavioral activation has been shown to promote positive mood, maintain support systems including extra-familial supports and increase opportunities to obtain evidence countering unhelpful thoughts (Martin & Oliver, 2019). Furthermore, experiencing the ebb and flow of symptoms may have promoted understanding that depression is transient, decreasing hopelessness during episodes that may have allowed for faster recovery.

The recurrent/persistent class. In contrast to the recurrent/brief class, the recurrent/persistent class included adolescents with the most severe course. Despite maintaining wellness for over 1 year on average, participants endorsed being in episode approximately half of their study participation (range: 1-6 episodes). Examination of individual episode length revealed that episodes on average lasted approximately 1 year each, which is twice as long as the reported naturalistic course of untreated depressive episodes (Kovacs et al., 1984a; Lewinsohn et al., 1993). It is possible that this course reflected dysthymia or persistent depressive disorder; however, considering that youth had to evidence consistent symptoms that equated to a DSR $\geq$ 4, it is likely that adolescents in this class evidenced prolonged MDD.

Persistent depression may have gross implications on how depression during adolescence may impact functioning in early adulthood. It is possible that persistent time in episode may impede on activity engagement, learning effective social and life skills, and future planning. However, persistent depression could also relate to habituation to mood-state, suggesting that youth with more persistent depression may be less functionally jarred by being in episode, compared to those less used to negative mood states (i.e., participants in the recurrent/brief class). Promotion of adaptive functioning despite depressed mood could be best reinforced by engagement in CBP and/or supportive parenting, which speaks to the inclusion of intervention assignment and parental depression as candidate predictors.

The early discontinuation class. The final class identified was interpreted as a methodological artifact representing participants who discontinued study participation

prior to the final timepoint. A 3-class RMLCA solution converged without the inclusion of the early discontinuation indicator; however, use of the indicator promoting this fourth class clarified fit indices substantially, which sharpened the boundaries between the remaining classes. Table 3 supported that sample characteristics did not relate to missing data; however, this category is clearly coherent, suggesting there may be other unmeasured factors driving class membership (e.g., life events, stress, match-to-intervention, non-specific factors associated with research proceedings). Understanding this class has implications for intervention engagement and implementation of skills. Yet, it is difficult to make inferences regarding early discontinuation class membership due to the absence of information that could confirm motives for early discontinuation, such as intolerance of study-related burden or clinical decline.

Predictors of Prevention Response

The current study evaluated candidate predictors of prevention response identified previously within the POD sample as impactful on outcome. Weersing and colleagues (2016) reported lowest onset was evident in youth randomized to CBP, who reported higher functioning, absence of current parental depression, and lower anxiety symptoms. In contrast, low functioning or high functioning with current parental depression and hopelessness promoted the highest rates of onset (Garber et al., 2018; Weersing et al., 2016). As expected, findings predicting prevention response trajectory mapped onto the POD risk clusters, such that lower incidents of psychopathology was related to high functioning and lower levels of anxiety and hopelessness, while the inverse was implicated in the more severe trajectories.

Maintained wellness. The well/late onset class highlights the success of prevention efforts and is a natural class of interest when evaluating predictors of maintained wellness. Thus, it was not surprising that a majority of the predictor models yielded findings that involved membership in the well/late onset class. Findings supported that those who entered the study with higher functioning and less severe symptoms of anxiety and hopelessness were most likely to be categorized as maintaining wellness.

Interestingly, adolescents in this class also reported to baseline with highest indicated risk for depression (i.e., history of episode plus subsyndromal symptom elevations at baseline). This contradicts with naturalistic investigations of depression trajectory that found lack of personal experience with depression to be a promoter of wellness (Hammen et al., 2008; Lewinsohn, Clarke et al., 1994; Lewinsohn, Roberts et al., 1994; Rushton et al., 2002). While a majority of the sample (80.1%) met criteria for a depressive episode prior to enrollment, current symptom elevations on top of a history of episode seems clinically meaningful when determining long-term response to prevention efforts. It is possible that this clinical profile reflects adolescents most ready for change. The personal experience with depression and potential recognition of warning signs of onset (i.e., heightened symptoms), both in the adolescent and perhaps caregivers, may have increased urgency and interest in engaging in prevention efforts. This rationale is contrary to the initial thought within the prevention literature that observing parental depression would be reason enough to increase adolescents' interest in and commitment to participating. Previous findings published by the POD investigative team highlighted

the prolonged impact of current parental depression at baseline as a moderator of outcomes, diminishing the positive effects of CBP compared to UC, through the young adult assessment (Brent et al., 2015). However, the prolonged effect originated as intervention group differences by the month 9 assessment that maintained parallel paths across follow-up (Brent et al., 2015), and the mechanism underlying this interference is unknown (Weersing et al., 2016). Thus, the practical magnitude of deviation in findings is difficult to assert. It is possible that the longitudinal capture of disease in the current study reflects decreased salience of parental influence in adolescence and similarly illustrates favor of personal investment in independence and commitment to long-term success.

Of further benefit, the increased functioning, hope, and decreased or absent anxiety symptoms may have allowed for meaningful engagement and successful skill uptake. Of note, findings also indicated that those likely to be categorized in the well class were randomized to receive CBP over UC, compared to those categorized by the most severe clinical course (i.e., recurrent/persistent depression), suggesting successful match to intervention in those likely to respond.

Recurrent course. Two recurrent classes emerged capturing participants who met criteria for $\geq$ 2 independent episodes across study participation; however the groups were distinguished by severity of recurrent course, such that those in the persistent class experienced elongated episodes translating to their being depressed on average for half of the time they participated in the trial. In contrast, the brief class evidenced fewer weeks to initial onset and increased numbers of independent episodes that were each shorter in

duration, summing to participants in this class being depressed on average for 20% of their participation. Adolescents more likely to be classified in either category evidenced increased psychopathology at baseline compared to those classified in the well/late onset class, which is consistent with the previous literature (Curry et al., 2011; Emslie et al., 2010)

There were no significant differences in intervention assignment between brief and persistent classes; however, participants randomized to CBP were less likely to be classified in the recurrent/persistent class compared to the early discontinuation class and more likely to be classified in the well/late onset vs. the recurrent/persistent class. Furthermore, it is notable that minority status and SES distinguished severity of recurrent course, such that those who identified as an ethnic and/or racial minority and those endorsing lower SES were more likely to be classified in the recurrent/persistent class rather than the recurrent brief class. As neither variable maintained significance in the multivariate model, it is possible that the difference in severity of recurrence may be driven by an unmeasured characteristic, such as service use. Inclusion of service use was outside of the scope of the current study due to the time-varying nature of service use variables. However, previous work in the POD sample found that identifying as non-Hispanic White increased the odds and intensity of cumulative outpatient service between the baseline and month 33 assessments (Do et al., 2015). This finding maps onto the broader service use literature that corroborates a disparity in service use as a function of racial and/or ethnic identity (e.g., Merikangas et al., 2011).

Of interest, gender did not significantly impact trajectory classification in the current sample. Gender has been implicated as a robust predictor of depression onset in adolescents, with girls converting to depression twice as often as boys (Lewinsohn et al., 1999; Lewinsohn, Clarke et al., 1994). Again, it is important to note that 80.1% of the current sample experienced a depressive episode prior to enrollment, suggesting that previously established predictors of depression onset may be less relevant to the current findings than predictors of remission and recurrence, and the evidence of gender impacting depression course has been mixed (e.g., Clarke et al., 2001 vs. Curry et al., 2011 vs. Kovacs et al., 1984b). Taken together, our null finding may not be unusual within the context of the literature at broad.

Statistical Proof-of-Concept

The current study aimed to answer empirical questions central to the prevention of depression in youth and understand long-term impact of prevention efforts into adulthood. Benefits of this methodology included the ability to obtain data-driven trajectories, rather than specifying trajectories *a priori* (e.g., growth mixture modeling). While many studies have evaluated the efficacy of depression prevention programs, few have included such a long interval of follow-up data and most have described trajectories of outcome through rational groupings of participants. Thus, there was limited empirical evidence informing the specification of trajectories, in advance. Second, RMLCA allowed for the identification of multiple trajectories capturing different patterns of outcome, rather than forcing a single course illustrating averaged data across participants (e.g., multilevel modeling). RCT findings consistently report at least two outcomes

following intervention: those who met study-defined criteria for clinical improvement (e.g., offset of diagnosis, substantial decrease in symptom endorsement), and those who did not. Therefore, it was clear that fitting the data to a single trajectory would not accurately capture the dynamic possibilities for post-intervention course, nor would it be clinically informative.

As such, the current study provided a statistical proof-of-concept that the RMLCA protocol (Asparouhov & Muthén, 2014) could accommodate 17 indicators and produce viable and rational results. This may open doors to other longitudinal trials aiming to make inferences of increased specificity, particularly in studies with relatively brief follow-up periods. The current study aimed to summarize patterns of depressive episodes across a 6-year follow-up period, resorting to the use of 6-month time intervals. The 24 weeks represented by each 6-month timepoint matched the average episode length reported in POD (M = 21.91 weeks, SD = 35.49); thus, the coding schema held promise that it could support inferences regarding dynamic differences in episode timing (e.g., recurrence corresponding with the college transition); however, episode length varied substantially (range: 2 to 302 weeks), and the classes obtained suggested increased likelihood that individuals experienced more prominent patterns defined by episode length rather than timing. Other protocols using dynamic data measurement methods such as the DSR could potentially evaluate more sensitive changes in depression trajectory by using the same amount of indicators in the RMLCA that each represent smaller periods of time.

Of course, the current aims were completed using iterative processes due to minimal literature investigating comparable research questions. The employed methodology was unique in that some indices required decisions that were not informed by *p*-values or established cutoffs. For example, it is possible that the use of alternative decision rules could implicate data points of concern that might require sensitivity analyses. To combat potential bias, the first author took a conservative approach to data cleaning and preparation, consulted with a statistical expert and thoroughly reviewed the available literature to ensure accuracy of method execution. Lastly, interpretability of findings was utilized to support plausibility of inferences detailed above, further increasing confidence in this report.

Implications for Intervention

Intervention assignment did not consistently implicate classification across class comparisons. However, when significant, the odds of classification as a function of intervention assignment were some of the largest observed and targeted classification in the recurrent/persistent group. Participants randomized to UC compared to CBP were two times more likely to be classified as having a recurrent/persistent trajectory than a well/late onset trajectory and five times more likely to be classified in the recurrent/persistent group than the early discontinuation group. Both findings support the decreased efficacy of usual care, which in turn promotes CBP as a tool to prolong wellness and decrease severity of depression course. Findings did not implicate intervention in comparing recurrent/persistent to recurrent/brief classes. However, the racial/ethnic disparities and previous findings regarding service use in the POD sample

imply that those in the recurrent/persistent class were unlikely to receive sufficient and/or high-quality care.

It has been reported that the efficacy (Warren, Nelson, Mondragon, Baldwin, & Burlingame, 2010) and content of usual care practices in pediatric mental health vary, with the content consisting of tools that span the evidence-based and non-evidence based domains (Benjamin Wolk et al., 2016). Despite statements made by the World Health Organization (2004) and National Institute of Mental Health (Reiss & Price, 1996) promoting prevention efforts, implementation in community mental health has proved difficult due to limited resources and prioritization of more acute cases. Additionally, once in services, inconsistencies in the level of expertise and licensure of mental health providers has been shown to further promote observed differences in approaches and orientations (Benjamin Wolk et al., 2016). However, the well/late onset profile supports an ideal clinical window for prevention intervention that yields long-lasting effects in adolescents and minimizes both time and money costs associated with more persistent depression management. Thus, findings call on health advocates, such as pediatricians and school counselors, to better inform families of the benefits of depression prevention, particularly promoting structured, cognitive-behavioral programs.

Furthermore, the mean timing of episode onset in the well/late onset class reflects a key developmental transition time, suggesting that engagement in booster sessions towards the end of high school and/or beginning of college may be key in promoting effective navigation of the adolescent/emerging adult transition and prolonging wellness. Unfortunately, there is a substantial gap in mental health services for transitional-aged

youth, such that services are sparse and often a lower priority in established mental health systems (Paul, Street, Wheeler, & Singh, 2015). Yet, active efforts to improve accessibility and acceptability of university counseling centers, particularly for students identifying as ethnic and/or racial minorities, are apparent (Banks, 2019). Joining efforts to understand and further promote mental health services for transitional-aged youth may be an important area of future research.

Limitations

The statistical methods utilized were exploratory and limitations to inferences based on current findings are important to consider. First, the POD dataset is classified as a prevention sample, as adolescents did not exhibit active disorder at the time of enrollment. However, a majority of the sample (80.1%) met criteria for a depressive episode prior to enrollment. Previous work has implicated previous episode occurrence (Daley et al., 2000; Lewinsohn et al., 1999), frequency (Lewinsohn et al., 1990), and severity (Curry et al., 2011; Emslie et al., 2010; Lewinsohn, Clarke et al., 1994) as negative predictors of depression course. In the current sample, history of depression was summarized dichotomously, making it impossible to evaluate the impact of prior episode characteristics on long-term response to prevention.

POD is the largest published prevention trial to date, with a sample size of 316 at enrollment and maintenance of 88.0% of participants across the 6-year follow-up period. Additionally, the available literature on power supported a sample size of this magnitude as appropriate for the planned analyses. However, considering the exploratory nature of the completed analyses and the number of parameters estimated by the aims, replication

in a larger sample could potentially corroborate the plausibility of inferences. Additionally, the imbalance of group sizes in the RMLCA's 4-class solution may have limited the stability of the multinomial logistic regressions. The classes were empirically derived and their interpretations made consistent, logical clinical sense. Furthermore, multinomial logistic regression assumptions do not dictate necessity of group equality in size, and the findings yielded by the regressions were also logical in direction; still, it is possible that a larger sample yielding more consistently sized groupings would result in different patterns of findings. As such, replication is warranted.

Future directions

The current study made promising contributions to the prevention literature by using advanced statistical methods to inform long-term trajectories of intervention response and highlighting clinical characteristics that seemed to promote particular trajectories. Future studies can further inform the trajectories identified by incorporating time varying predictors in the analysis. Intervention is an invaluable resource that has been shown to decrease the impact of genetic and environmental risk on depression development in youth; however, it is naïve to assume that one episode of preventative care could be solely responsible for wellness across the lifespan. Many factors could assist in maintaining prevention effects across time, such service use, maintenance of a support system, adaptive habit formation (e.g., exercise, sleep) and avoidance of maladaptive coping (e.g., substance use). In contrast, the experience of unexpected stressors, such as negative life events, could have the opposite effect. Furthermore, previous work observed how residual symptoms increased risk of relapse (Curry et al.,

2011; de Zwart et al., 2018). Although not examined in the current study, coding and analyzing DSR scores between episodes may reveal addition differentiations between courses. The current study served as a basis of support that evaluating such vibrant trajectories is possible. Future work can build on this by incorporating time-varying maintenance factors to further illustrate ways to prolong wellness.

Understanding trajectories of prevention response and their predictors is important for prevention recruitment among at-risk youth as well as informing how to maintain wellness. The natural next step of interest is to utilize the trajectories to understand how depression course during adolescence impacts functioning in early adulthood. As discussed above, the experience of brief versus persistent course may have differentially interfered with the development of life and social skills. Without additional intervention, it is expected that deficits would similarly impede functioning into adulthood (Hammen et al., 2008; Lewinsohn, Clarke et al., 1994; Lewinsohn, Roberts et al., 1994; Rushton et al., 2002). Furthermore, transitional-aged youth are at high risk for developing maladaptive habits (e.g., substance use; Burt & Paysnick, 2012) due to added responsibilities associated with independence, potentially increasing stress which increases risk for depression relapse (Daley et al., 2000). As such, understanding domains of functioning in adulthood and how patterns of prevention response inform them can be applied in conjunction with the current findings to the development of the next generation of depression prevention programs.

Chapter 6, in part, is currently being prepared for submission for publication of the material. Schwartz, Karen T. G.; Garber, Judy; Weersing, V. Robin. The dissertation author was the primary investigator and author of this material.

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FIGURES

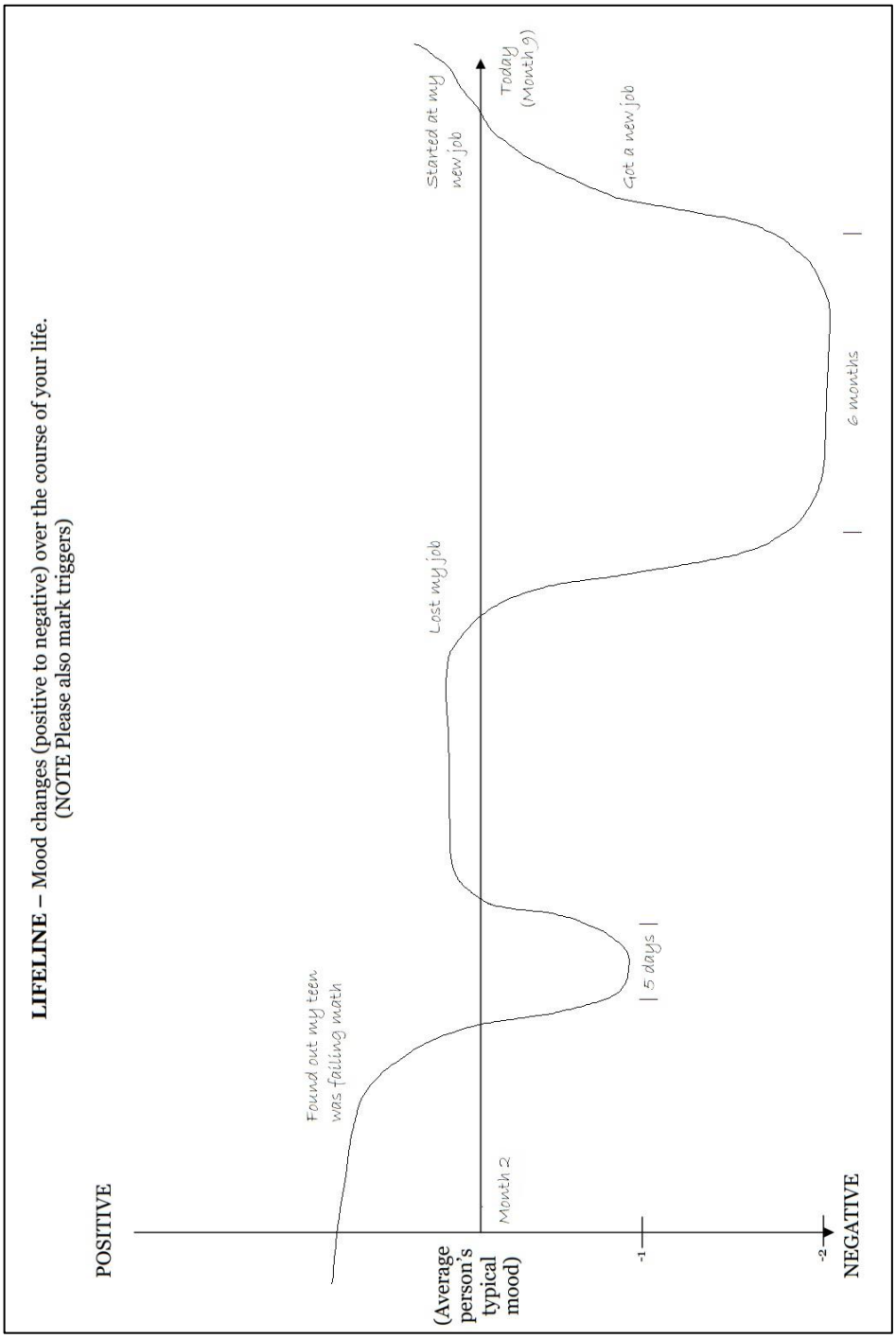

Figure 1. Example timeline used to aid in recall during follow-up assessments. *Note:* information reflected is fabricated and for illustration purposes only.

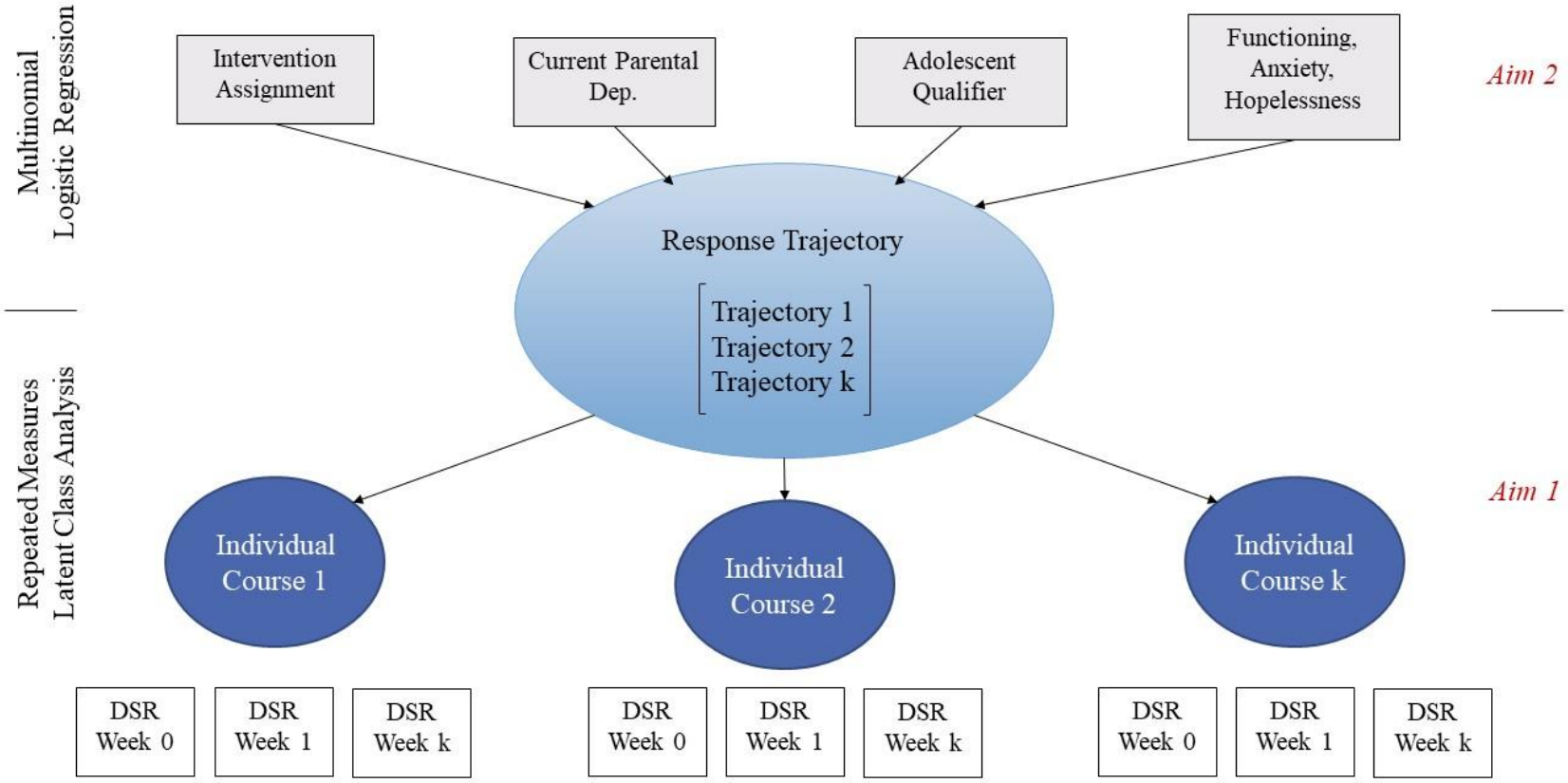

Figure 2. Proposed analytical model. *Note:* DSR = Depression Severity Rating Scale; *k* reflects the last number in a series.

TABLES

Table 1. Sample characteristics at baseline. *Note.* Continuous variables are reported as *M* (*SD*), and group differences were tested using independent samples t-tests; categorical variabels are reported as *N* (%), and group differences were tested using chi-square statistical procedures. UC = Usual Care; CBP = Cognitive-Behavioral Prevention Program; CES-D = Center for Epidemiologic Studies Depression Scale; CGAS = Children's Global Adjustment Scale; SCARED = Screen for Anxiety Related Emotional Disorders; BHS = Beck Hopelessness Scale.

	Full Sample	UC	CBP	*p*
N	316	157 (49.7%)	159 (50.3%)	
Age	14.79 (1.35)	14.83 (1.25)	14.76 (1.46)	.660
Gender (% female)	185 (58.5%)	92 (58.6%)	93 (58.5%)	.984
Minority status (% racial and/or ethnic minority)	76 (24.3%)	40 (25.8%)	36 (22.8%)	.533
Sibling (% yes)	67 (21.2%)	28 (17.8%)	39 (24.5%)	.146
Current parental depression (% yes)	157 (49.7%)	76 (48.4%)	81 (50.9%)	.652
Adolescent study qualifier				.653
Depression history (% yes)	175 (55.4%)	87 (55.4%)	88 (55.3%)	
CES-D $\geq$ 20	63 (19.9%)	34 (21.7%)	29 (18.2%)	
Both	78 (24.7%)	36 (22.9%)	42 (26.4%)	
Functioning (CGAS)	76.26 (8.74)	76.09 (9.28)	76.42 (8.20)	.736
Anxiety (SCARED)	22.57 (12.18)	22.40 (12.01)	22.73 (12.39)	.812
Hopelessness (BHS)	4.64 (4.03)	4.81 (4.01)	4.47 (3.97)	.466

Table 2. DSR characteristics across study participation. *Note*. DSR = Depression Severity Rating Scale.

	N (%)/*M* (*SD*)
Any DSR data	311 (98.4%)
Early discontinuation	33 (10.6%)
Month 2	3 (1.0%)
Month 9 (i.e., post-intervention)	8 (2.6%)
Month 21	3 (1.0%)
Month 33 (i.e., 3 years post-intervention)	19 (6.1%)
Full dataset	
Young adult follow-up (i.e., 21st birthday)	278 (89.4%)
Timepoints completed across participants	
Month 2	300 (94.9%)
Month 9	290 (91.8%)
Month 21	251 (79.4%)
Month 33	296 (93.7%)
Young adult follow-up	278 (88.0%)
Timepoints completed within participant	
0	5 (1.6%)
1	6 (1.9%)
2	10 (3.2%)
3	16 (5.1%)
4	54 (17.1%)
5	225 (71.2%)
Weeks assessed	
Range	6-438
Mean	304.09 (80.10)
Median	316
Mode	305
Skew	-1.69 (0.14)
Kurtosis	3.36 (0.28)
Percentiles	
25%	285
50%	316
75%	354

Table 3. Examiniation of DSR missingness. *Note.* Continuous variables are reported as *M* (*SD*), and group differences were tested using independent samples t-tests; categorical variabels are reported as *N* (%), and group differences were tested using chi-square statistical procedures. CBP = Cognitive-Behavioral Prevention Program; CES-D = Center for Epidemiologic Studies Depression Scale; CGAS = Children's Global Adjustment Scale; SCARED = Screen for Anxiety Related Emotional Disorders; BHS = Beck Hopelessness Scale.

	Full Sample	Completion of the Young Adult Follow-Up	Early Dis-continuation	*p*
N	316	278	38	
Age	14.79 (1.35)	14.85 (1.37)	14.42 (1.18)	.070
Gender (% female)	185 (58.5%)	165 (59.4%)	20 (52.6%)	.430
Minority status (% racial and/or ethnic minority)	76 (24.3%)	69 (24.9%)	7 (19.4%)	.472
Sibling (% yes)	67 (21.2%)	59 (21.2%)	8 (21.1%)	.981
Intervention assignment (% CBP)	159 (50.3%)	139 (50.0%)	20 (52.6%)	.761
Current parental depression (% yes)	157 (49.7%)	133 (47.8%)	24 (63.2%)	.077
Adolescent study qualifier				.180
Depression history (% yes)	175 (55.4%)	158 (56.8%)	17 (44.7%)	
CES-D $\geq$ 20	63 (19.9%)	56 (20.1%)	7 (18.4%)	
Both	78 (24.7%)	64 (23.0%)	14 (36.8%)	
Functioning (CGAS)	76.26 (8.74)	76.55 (8.40)	74.11 (10.80)	.187
Anxiety (SCARED)	22.57 (12.18)	22.15 (11.80)	25.58 (14.53)	.104
Hopelessness (BHS)	4.64 (4.03)	4.53 (3.96)	5.50 (4.50)	.175

Table 4. RMLCA overall model fit by class solution. *Note.* N = 311; estimator used is MLR; * indicates that spurious classes that included less than 5% (n = 15) of the sample were present in the solution. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; BLMRT = Bootstrapped Lo-Mendell-Rubin Test.

Solution	AIC	BIC	BLMRT (p-value)	Entropy
1-Class	3512.014	3575.590	N/A	N/A
2-Class	3256.560	3387.452	< .001	.812
3-Class	3222.202	3420.411	< .001	.731
4-Class	3211.235	3476.760	< .001	.872
5-Class*	3216.003	3548.845	.500	.872

Table 5. RMLCA conditional response probabilities for a 4-Class solution

Indicator	Start	Class			
		1	2	3	4
		(*n* = 213)	(*n* = 38)	(*n* = 19)	(*n* = 41)
Timepoint 1	Week 0	.152	.432	.325	.051
Timepoint 2	Week 24	.052	.303	.200	.238
Timepoint 3	Week 48	.032	.513	.142	.000
Timepoint 4	Week 72	.044	.385	.218	.259
Timepoint 5	Week 96	.047	.508	.349	.000
Timepoint 6	Week 120	.086	.234	.359	.285
Timepoint 7	Week 144	.089	.166	.706	.344
Timepoint 8	Week 168	.075	.295	.824	.000
Timepoint 9	Week 192	.082	.220	.810	.000
Timepoint 10	Week 216	.069	.254	.857	.282
Timepoint 11	Week 240	.062	.129	1.000	.750
Timepoint 12	Week 264	.072	.159	.741	1.000
Timepoint 13	Week 288	.099	.302	.813	.700
Timepoint 14	Week 312	.080	.147	.730	1.000
Timepoint 15	Week 336	.087	.408	.252	1.000
Timepoint 16	Week 360	.076	1.000	.589	1.000
Early Discontinuation	---	.000	.102	.000	.705

Table 6. Sample characteristics by RMLCA 4-Class solution. *Note.* Continuous variables are reported as *M* (*SD*); categorical variabels are reported as *N* (%); significance testing utlized multinomial logistic regression, including Sibling as a covaraite; see Table 7 and Table 8 for elaboration on findings. SES = socioeconomic status; CBP = Cognitive-Behavioral Prevention Program; CES-D = Center for Epidemiologic Studies Depression Scale. * $p < .05$.

	Class			
	1: Well/late onset	2: Recurrent/ brief	3: Recurrent/ persistent	4: Early Disc.
N	213	38	19	41
Weeks assessed	326.86 (41.79)*	320.89 (60.66)*	321.89 (35.48)*	162.00 (112.38)*
SOCIODEMOGRAPHICS				
Age	14.90 (1.40)*	14.42 (1.08)*	14.95 (1.55)	14.54 (1.23)
Gender (% Female)	118 (55.5%)	24 (63.2%)	15 (78.9%)	24 (58.5)
Minority status (% racial and/or ethnic minority)	56 (26.4%)	3 (7.9%)*	8 (42.1%)*	9 (22.5%)
SES	46.32 (11.81)	48.25 (12.35)*	40.66 (13.38)*	44.30 (11.65)
Sibling (% yes)[a]	48 (22.5%)	5 (13.2%)	6 (31.6%)	6 (14.6%)
CANDIDATE PREDICTORS				
Intervention assignment (% CBP)	110 (51.6%)*	11 (28.9%)	13 (68.4%)*	21 (51.2%)*
Current parental depression (% yes)	104 (48.8%)	18 (47.4%)	9 (47.4%)	22 (53.7%)
Adolescent study qualifier				
Depression history (% yes)	129 (60.6%)	16 (42.1%)	8 (42.1%)	20 (48.8%)
CES-D $\geq$ 20	43 (20.2%)	6 (15.8%)	6 (31.6%)	8 (19.5%)
Both	41 (19.2%)*	16 (42.1%)	5 (26.3%)*	13 (31.7%)
Functioning	77.31 (8.31)*	72.29 (8.65)	73.47 (8.52)*	76.22 (9.07)
Anxiety	20.76 (11.05)*	26.79 (13.33)*	26.84 (11.05)	25.12 (15.18)*
Hopelessness	4.04 (3.58)*	6.03 (4.78)	5.89 (3.76)*	5.56 (4.66)*
DEPRESSION PREVALENCE				
Maintained wellness	84 (39.4%)	0 (0.0%)	0 (0.0%)	21 (51.2%)
Single episode	72 (33.8%)	1 (2.6%)	4 (21.1%)	10 (24.4%)
Recurrent episodes	57 (26.8%)	37 (97.4%)	15 (78.9%)	10 (24.4%)

Table 6. Sample characteristics by RMLCA 4-Class solution, continued. *Note*. Continuous variables are reported as *M* (*SD*); categorical variabels are reported as *N* (%); significance testing utlized multinomial logistic regression, including Sibling as a covaraite; see Table 7 and Table 8 for elaboration on findings. SES = socioeconomic status; CBP = Cognitive-Behavioral Prevention Program; CES-D = Center for Epidemiologic Studies Depression Scale. * $p < .05$.

	Class			
	1: Well/late onset	2: Recurrent/ brief	3: Recurrent/ persistent	4: Early Disc.
EPISODE DESCRIPTIVES				
No. of episodes	0.94 (0.95)*	3.50 (1.33)*	2.58 (1.35)*	1.02 (1.39)*
Week of first-episode onset	126.82 (106.02)*	33.95 (31.32)*	71.95 (67.55)*	84.35 (82.20)*
No. of weeks in episode	19.34 (18.21)	64.34 (38.68)	165.95 (68.29)	60.95 (57.04)
Prop. of participation spent in episode	.06 (.05)*	.20 (.12)*	.51 (.19)*	.21 (.15)*

Table 7. Validation of interpretation of RMLCA classes. *Note.* The second class listed served as the reference group; the large odds ratios observed when proportion of participation spent in episode served as the predictor were confirmed using SPSS. [a] maintained significance in a multivariate framework. OR = odds ratio; S.E. = standard error; ref. = reference group.

Contrast	Estimate	OR	S.E.	*p*
RECURRENT/BRIEF VS. WELL/LATE ONSET				
No. of episodes	2.89	17.99	0.57	< .001
Week of first episode onset[a]	-0.02	0.98	0.00	< .001
Prop. of participation spent in episode	23.19	1.18×10^{10}	4.23	< .001
RECURRENT/PERSISTENT VS. WELL/LATE ONSET				
No. of episodes[a]	2.22	9.21	0.46	< .001
Week of first episode onset[a]	-0.01	0.99	0.00	.001
Prop. of participation spent in episode[a]	37.52	1.97×10^{16}	5.58	< .001
EARLY DISC. VS. WELL/LATE ONSET				
No. of weeks assessed[a]	-0.04	0.96	0.01	< .001
Prop. of participation spent in episode[a]	24.01	2.68×10^{10}	5.44	< .001
RECURRENT/BRIEF VS. RECURRENT/PERSISTENT				
Week of first episode onset	-0.01	0.99	0.00	.006
Prop. of participation spent in episode[a]	-14.33	5.98×10^{-7}	3.34	< .001
RECURRENT/BRIEF VS. EARLY DISC.				
No. of weeks assessed	0.03	1.03	0.01	.004
No. of episodes	3.55	34.81	0.82	< .001
Week of first episode onset[a]	-0.02	0.98	0.00	< .001
RECURRENT/PERSISTENT VS. EARLY DISC.				
No. of weeks assessed	0.04	1.04	0.01	< .001
No. of episodes	2.89	17.99	0.72	< .001
Prop. of participation spent in episode[a]	13.52	7.44×10^{5}	3.94	.001

Table 8. Significant findings from univariate multinomial logistic regression analyses. *Note.* The sibling variable was included in all models as an auxiliary variable. [a] indicates that predictor maintained significance in a multivariate framework; the second class listed served as the reference group. OR = odds ratio; S.E. = standard error; ref. = reference group; CBP = Cognitive-Behavioral Prevention Program; NHW = non-Hispanic White; SES = socioeconomic status.

Contrast	Estimate	OR	S.E.	*p*
RECURRENT/BRIEF VS. WELL/LATE ONSET				
Age	-0.30	0.74	0.14	.035
Anxiety[a]	0.05	1.05	0.02	.019
RECURRENT/PERSISTENT VS. WELL/LATE ONSET				
Intervention assignment (CBP as ref.)	-0.98	0.38	0.47	.039
Adolescent study qualifier (depression history vs. both as ref.)	-1.21	0.30	0.49	.014
Functioning[a]	-0.08	0.92	0.03	.005
Hopelessness	0.13	1.14	0.05	.005
EARLY DISC. VS. WELL/LATE ONSET				
Anxiety	0.06	1.06	0.02	.010
Hopelessness	0.12	1.13	0.05	.017
RECURRENT/BRIEF VS. RECURRENT/PERSISTENT				
Minority status (NHW as ref.)	2.35	10.49	1.06	.026
SES	0.06	1.06	0.03	.038
EARLY DISC. VS. RECURRENT/PERSISTENT				
Intervention assignment (CBP as ref.)	1.69	5.42	0.68	.013