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Running Head: Trajectories of Depression Symptoms

Long-Term Trajectories of Depression Symptoms in Mothers of Children with Cancer

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Abstract

Objective: To identify trajectories of depression symptoms in mothers of children with cancer from diagnosis/relapse through five years and examine maternal factors at diagnosis/relapse predicting membership in these trajectories. **Method:** Mothers ($n = 327$; $M_{\text{age}} = 37.6$ years, $SD = 7.7$ years; 85% white) reported depression symptoms near the time of their child's diagnosis/relapse and then again at one-, three-, and five-years post-diagnosis/relapse. Mothers also reported perceived stress, coping (primary control, secondary control, and disengagement coping), and spirituality near the time of diagnosis. Latent class growth analysis was used to identify latent trajectories of depression symptoms, and a 3-step multinomial logistic regression tested covariate predictors of membership in the trajectories. **Results:** Three trajectories were identified: "Low Depression Symptoms" (63.3%), "Moderate Depression Symptoms" (31.5%), and "High Depression Symptoms" (5.2%). Mothers who used more primary and secondary control coping were more likely to be in the low depression symptom trajectory as compared to the moderate ($OR = 1.64, p = .024$ and $OR = 1.38, p = .013$, respectively) or high trajectories ($OR = 1.99, p = .008$ and $OR = 1.81, p = .001$, respectively). **Conclusions:** Although mothers of children with cancer generally displayed improved mental health further from diagnosis, mothers with more depression symptoms after diagnosis/relapse displayed substantial stability in depression symptoms over the five years. Mothers of children with cancer may benefit from early screening of mental health and coping strategies, as well as interventions to bolster effective coping for those with elevated depression symptoms.

Keywords: coping, mothers' depressive symptoms, Latent class growth analysis, pediatric cancer, trajectories

Long-Term Trajectories of Depression Symptoms in Mothers of Children with Cancer

With improved survival rates for pediatric cancer (DeSantis et al., 2014), it is increasingly important to understand the long-term effects of pediatric cancer on families. A child's diagnosis of cancer affects the entire family, particularly parents. Parental distress after diagnosis has critical implications for parents' physical health, family/marital adjustment, and child adjustment (Kearney, Salley, & Muriel, 2015). However, relatively little is known about which parents are at risk for long-term adjustment problems and what protective factors may mitigate their distress. By better understanding trajectories of parent adjustment and factors that predict risk for long-term distress, interventions may be introduced earlier to foster resilience.

Although many parents of children with cancer are resilient (Kearney et al., 2015; Phipps et al., 2015), a subset experience marked distress or mental health problems (e.g., anxiety, depression), even years after diagnosis (Compas et al., 2015; Creswell, Wisk, Litzelman, Allchin, & Witt, 2014; Kazak et al., 2015; Norberg & Boman, 2008; Wijnberg-Williams, Kamps, Klip, & Hoekstra-Weebers, 2006). Parents of children with cancer also report more emotional distress than healthy comparison parents (Creswell et al., 2014; Maurice-Stam, Oort, Last, & Grootenhuis, 2008; Norberg & Boman, 2008; Pai et al., 2007; Wijnberg-Williams et al., 2006). Specifically, parents of children with cancer may be more likely to experience prolonged clinically elevated depression symptoms than either anxiety or posttraumatic stress symptoms (Katz et al., 2018). In contrast with parents of healthy children, parents of children with cancer display more depression symptoms at multiple time points from diagnosis through five years post-diagnosis (Katz et al., 2018; Norberg & Boman, 2008; Vrijmoet-Wiersma et al., 2008; Wijnberg-Williams et al., 2006). Furthermore, mothers tend to report more adjustment difficulties than do fathers across the illness trajectory (Clarke, McCarthy, Downie, Ashley, &

Anderson, 2009; Pai et al., 2007; Vrijmoet-Wiersma et al., 2008), perhaps because mothers are often the primary caregiver and typically accompany the child to cancer-related procedures (Kazak et al., 1996). Given elevated risk for depression symptoms in mothers, it is particularly important to elucidate trajectories of mothers' depression symptoms after their children's diagnosis of cancer.

Bonanno and Diminich (2013) suggest that adults' long-term adjustment patterns to stressful life events are most appropriately differentiated by comparing latent trajectories of functioning in the years after the stressor. Three trajectories have consistently emerged across studies and types of potentially traumatic events (e.g., natural disaster, breast cancer): (1) minimal-impact resilience, characterized by a mild and transient stress response at the time of the stressor followed by stable, low levels of distress; (2) chronically high distress; and (3) recovery, characterized by moderate to high distress that decreases to low levels (Bonanno & Diminich, 2013). In cases of pediatric cancer, longitudinal studies of mothers' adjustment have generally measured mean levels of distress, documenting elevated depression symptoms after diagnosis that decrease over subsequent months (Katz et al., 2018; Kazak et al., 2015; Kearney et al., 2015). However, variance in trajectories of caregiver depression symptoms suggests the presence of distinct latent trajectories of depression symptoms (Katz et al., 2018). Indeed, distinct latent trajectories of parent distress have emerged in the 6 months after diagnosis (Dolgin et al., 2007; Steele, Dreyer, & Phipps, 2004), including high, moderate, decreasing, and low distress trajectories. However, it is unknown whether these trajectories remain stable beyond 6 months. Approximately one-fourth of parents report clinically elevated distress even five years after their child's diagnosis (Kazak et al., 2015; Wijnberg-Williams et al., 2006), suggesting the possibility of a chronically distressed or delayed distress trajectory. Therefore, it is critical to elucidate long-

term trajectories of adjustment (e.g., chronically high depression symptoms, resilience) and to identify risk and resilience factors that predict membership in these trajectories.

Studies examining protective factors in parents of children with cancer have generally focused on external (e.g., high socioeconomic status, social support; Bemis et al., 2015) or trait-based factors (e.g., personality; Kearney et al., 2015). However, internal processes, such as perception of stress, coping, and spirituality, have received less attention and may shed light on modifiable protective factors that can be enhanced in interventions to promote resilience. The diagnosis and treatment of pediatric cancer results in marked stress for parents, including stresses of daily/role functioning (e.g., job-related changes), cancer communication (e.g., talking to children about cancer), and cancer caregiving (e.g., child's treatment-related effects; Rodriguez et al., 2012). In contrast to measuring external stress exposure or context-specific types of stress (e.g., cancer-related stressors, caregiver stress), perceived stress reflects individuals' subjective stress reactions. In other words, high perceived stress indicates that an individual subjectively experiences their current life circumstances as stressful. In the broader depression literature, more perceived stress has been linked with a trajectory of chronically high depression symptoms, with those in a consistently low depression trajectory reporting less perceived stress compared to those with fluctuating depression (increasing or decreasing; Repetto, Caldwell, & Zimmerman, 2004). Thus, elevated perceived stress following diagnosis might be expected to relate to patterns of chronically elevated depression symptoms or recovery. Although perceived stress is broadly related to adjustment in mothers of children with cancer (Bemis et al., 2015; Hae-Ra, 2003), it has not been examined as a predictor of mothers' adjustment over time; thus, it is unknown whether perceived stress following diagnosis might relate to patterns of minimal-impact resilience, recovery, or more chronic distress.

Adaptive coping may serve as a resource for parents of children with cancer (Compas et al., 2015; Compas, Jaser, Dunn, & Rodriguez, 2012; Maurice-Stam et al., 2008). A control-based model of coping has been used to understand parental coping with pediatric chronic illness and posits three voluntary coping factors: primary control, secondary control, and disengagement, (Compas et al., 2015; Connor-Smith, Compas, Wadsworth, Thomsen, & Saltzman, 2000). Primary control coping includes active, voluntary efforts to alter the situation or a person's emotional state (e.g., problem-solving, emotional regulation, emotional expression). Secondary control coping refers to efforts to adapt to or fit into present conditions (e.g., positive thinking, cognitive restructuring, acceptance). Disengagement coping refers to voluntarily retreating from addressing or acknowledging stressors (e.g., avoidance, denial,). Coping responses corresponding to primary or secondary control coping are associated with fewer depression symptoms for mothers and fathers near diagnosis (Compas et al., 2015; Maurice-Stam et al., 2008; Turner-Sack, Menna, Setchell, Maan, & Cataudella, 2016). In contrast, disengagement coping at diagnosis is linked with elevated maternal distress or depression symptoms (Greening & Stoppelbein, 2007; Lindahl Norberg, Pöder, & von Essen, 2011). Mothers with a tendency to cope with cancer-related stressors by disengaging might thus be expected to exhibit a pattern of chronic depression symptoms. Longitudinal research to determine the role of coping across the cancer continuum has been recommended (Vrijmoet-Wiersma et al., 2008); however, cancer-specific coping has yet to be examined as a predictor of long-term maternal depression.

Lastly, spirituality is hypothesized to serve a protective function against the uncertainty of illness and treatment (Cadell, 2012; Landis, 1996; Weaver & Flannelly, 2004). Separate from religion (Hill et al., 2000), spirituality refers to existential questioning and a search for spiritual meaning (Hatch, Burg, Naberhaus, & Hellmich, 1998; Hill et al., 2000). Although spirituality has

not been previously linked with depression in mothers of children with cancer, it has been associated with depression more generally (Koenig, 2009). Moreover, spirituality is associated with more active coping, meaning-making, and posttraumatic growth in caregivers of chronically ill children (Cadell, 2012; Landis, 1996; Schneider & Mannell, 2006; Weaver & Flannelly, 2004), which may in turn reduce the risk for depression. Thus, spirituality may promote resilience for mothers of children newly diagnosed with cancer, suggesting that mothers who are more spiritual may exhibit patterns of distress more consistent with minimal-impact resilience.

This study empirically identified subgroups of mothers with qualitatively different trajectories of depression symptoms over the five years after their child's initial diagnosis/relapse using a large sample and longitudinal prospective design. Based on contemporary theory (Bonanno & Diminich, 2013) and prior pediatric cancer studies using smaller samples and shorter time frames (Steele et al., 2004), it was predicted that 3 to 6 trajectories would emerge, including patterns of chronically high, chronically low, and decreasing depression symptoms. As a second aim, mothers' trajectory membership was examined in relation to their perceived stress, coping (primary control, secondary control, and disengagement coping), and spirituality near the time of diagnosis. To the extent that trajectories were characterized by chronic and/or elevated depression symptoms, it was hypothesized that trajectory membership would be predicted by more perceived stress, less primary and secondary control coping, less spirituality, and more disengagement coping. In contrast, it was predicted that less perceived stress, more primary and secondary control coping, more spirituality, and less disengagement coping would predict trajectory membership characterized by chronically low or transient, decreasing symptoms.

Method

Procedure

Mothers were recruited as participants in a larger, longitudinal study examining family adjustment to childhood cancer (Compas et al., 2015). However, the present analyses were secondary and not a priori aims of the larger study. Following institutional review board approval at Nationwide Children's Hospital and Vanderbilt University, eligible families were identified from cancer registries. Families were eligible if their child was: (a) aged 5–17 years, (b) recently diagnosed with new or relapsed cancer, (c) English-speaking, and (d) without a pre-existing developmental delay. Eligible families were approached for recruitment by trained research assistants in outpatient oncology clinics and inpatient rooms at both children's hospitals. All parents were invited to participate; however, only one parent was required to participate for a family to be enrolled, with the current analyses only examining the maternal caregivers. Parents provided written informed consent. Mothers completed questionnaires in the hospital or at home after diagnosis/relapse ($M = 2.5$ months, $SD = 2.0$ months) and at one year ($M = 14.0$ months post diagnosis/relapse, $SD = 3.1$ months), three years ($M = 41.0$ months post diagnosis/relapse, $SD = 3.8$ months), and five years ($M = 63.3$ months post diagnosis/relapse, $SD = 5.2$ months) after enrollment. Families were compensated for their time.

Participants

Three-hundred and twenty-seven mothers reported on symptoms of depression at one or more study time point(s). Mothers of enrolled families were eligible to participate at all time points (even if they did not participate in baseline data collection) unless their child died. However, mothers' pre-death data were included in the analyses if their child had died during the course of the study to prevent exclusion of the families of children with poor prognoses. At enrollment, 336 of 380 eligible families consented to participate, and 321 mothers completed questionnaires. At approximately one-year post-diagnosis, 10% ($n = 34$) of children had died,

and one child became ineligible because of a diagnosis of developmental disability. Of the remaining 301 eligible families, most mothers had complete data at one-year post-diagnosis ($n = 217$, 72%). At the three-year follow-up, an additional 21 children had died, another child was ineligible because of a diagnosis of developmental disability, and 47 families were not approached because they were already past three years post-diagnosis at the time that three- and five-year follow-ups were IRB approved. Of the 232 remaining families who were approached, 46% ($n = 107$) of mothers participated. At the five-year follow-up, four additional children had died. Of the 275 families approached, 39% ($n = 108$) of mothers participated.

Attrition was not significantly related to primary variables of interest in this study: depression, spirituality, coping (all p -values ns). Mothers who did not participate at one-year post diagnosis reported more perceived stress following diagnosis ($t = 2.00$, $p = .047$), had children with higher treatment intensity ($t = 2.31$ [204], $p = .022$), and were more likely to have a child who had relapsed ($\chi^2 [1] = 7.04$, $p = .008$). However, only treatment intensity significantly differentiated attrition when controlling for families lost to follow-up due to child death ($n = 34$, 10%; $t = 2.41$ [200], $p = .017$; other p -values ns). At three- and five-year follow-ups, attrition was more likely for mothers of older children ($t = 1.98$ [230.42], $p = .049$ and $t = 2.41$ [322], $p = .016$, respectively) and mothers of children who had relapsed ($\chi^2 [1] = 17.60$, $p < .001$ and $\chi^2 [1] = 8.91$, $p = .003$, respectively). After controlling for child death, attrition was higher at three-year follow-up for children who had relapsed ($\chi^2 [1] = 3.91$, $p = .048$) and at five-year follow-up for older children ($t = 2.10$ [259], $p = .037$). No other demographic (age, marital status, years of education, family income, SES, child gender) or clinical variables (CNS directed treatment [yes/no], diagnosis, length of treatment) significantly differentiated attrition (all p -values ns).

Measures

Demographic and Clinical Variables. Mothers reported their age, marital status, race, education, family income, number of children, SES, and child gender. Children's medical diagnosis, date of diagnosis, date of final treatment, and treatment information were collected through medical chart review. Length of treatment was calculated by subtracting date of diagnosis from date of final treatment. The Intensity of Treatment Rating Scale 2.0 (ITR-2) provided an overall rating of treatment intensity using diagnosis, stage/risk level, and treatment modality (Werba et al., 2007). Chart reviews were completed at 5-years post-enrollment for participants who had re-consented during a three- or five-year follow-up, yielding incomplete length of treatment data due to missing date of final treatment for dropouts or deceased patients.

Depression Symptoms. Mothers completed the BDI-II (Beck, Steer, & Brown, 1996), which contains 21 items ranging from 0 to 3. The total score corresponds to increasing severity of depression symptoms, with clinical ranges of minimal (0–13), mild (14–19), moderate (20–28), and severe (29–63; Beck et al., 1996). This is a well-established and standardized measure that demonstrates good construct validity and internal consistency (Steer, Ball, Ranieri, & Beck, 1997). Internal consistency in the current study was excellent ($\alpha = .93$).

Perceived Stress. The Perceived Stress Scale is a 10-item questionnaire using a Likert scale ranging from 0 (*never*) to 4 (*very often*) that measures the extent to which one appraises events during the past month as stressful (Cohen, Kamarck, & Mermelstein, 1983; Cohen & Williamson, 1988). This measure has strong psychometric properties (Cohen et al., 1983; Cohen & Williamson, 1988) and demonstrated good internal consistency in the present study ($\alpha = .85$).

Coping. The Responses to Stress Questionnaire-Pediatric Cancer version (RSQ-PC) is a 57-item, validated measure of maternal coping responses to pediatric cancer (Compas et al., 2012; Connor-Smith et al., 2000). Mothers rated how they coped with cancer-specific stressors

on a Likert scale ranging from 1 (*not at all*) to 4 (*a lot*). The current study examined voluntary coping factors of the RSQ-PC (i.e., primary control coping, secondary control coping, and disengagement). Ratio scores representing total individual factor scores divided by the total score for the entire measure were used as recommended (Compas et al., 2015; Connor-Smith et al., 2000). Internal consistency for these factors was acceptable in this sample ($\alpha = .74-.75$).

Spiritual Involvement and Beliefs. The Spiritual Involvement and Beliefs Scale (SIBS; Hatch et al., 1998) is a 24-item questionnaire assessing engagement in spiritual actions and beliefs without religion-specific language. Mothers rated items on a Likert scale from 1 (*strongly agree*) to 5 (*strongly disagree*). The SIBS consists of four subscales with strong psychometric properties, including strong internal consistency and construct validity (Hatch et al., 1998). However, given the high subscale intercorrelations in the current study ($r = .5-.89$) and low internal consistency for the Humility/Application subscale ($\alpha = .45$), all items were summed for an overall spirituality score with excellent internal consistency ($\alpha = .91$).

Statistical Analyses

Descriptive statistics and Pearson correlations were calculated in SPSS (version 25), with subsequent analyses conducted in MPlus (version 7.3). The average pattern of change in maternal depression symptoms was first characterized using latent growth curve modeling (LGCM). Single-group LGCMs were analyzed for intercept-only, linear, and quadratic models and empirically compared. Strong model fit is indicated by a nonsignificant χ^2 test statistic, comparative fit index (CFI) $> .95$, root mean square error of approximation (RMSEA) $< .05$, and standardized root mean square residual (SRMR) $< .08$ (Hu & Bentler, 1999).

Homogeneous trajectories were empirically identified using latent class growth analysis with maximum likelihood estimation. Unconditional models with an increasing number of class

solutions were compared according to interpretability, theory, parsimony, and model fit criteria (i.e., Bayesian information criteria [BIC; Schwarz, 1978], entropy, average class assignment probabilities, and likelihood ratio tests). Lower BIC suggests better fit, with BIC differences of 0–2, 2–6, 6–10, and >10 considered weak, positive, strong, and very strong evidence for one model over another, respectively (Kass & Raftery, 1995; Raftery, 1995). Entropy and average class assignment probabilities (ranging from 0–1) reflect classification accuracy and certainty of class assignment, respectively, with larger values reflecting higher accuracy and certainty of assignment and >.80 considered strong evidence (Rost, 2006). Lastly, the Lo-Mendell-Rubin test (LMR; Lo, Mendell, & Rubin, 2001) and the bootstrap likelihood ratio difference test (BLRT; McLachlan & Peel, 2000) compare each model with the model containing one fewer class (e.g., 4-class solution versus the 3-class solution). Models were estimated using all available data and missing data were estimated using maximum likelihood, which is suitable for small sample sizes and yields similar to less biased estimates compared to multiple imputation (Shin, 2017).

The 3-step approach was used (Asparouhov & Muthén, 2014; Vermunt, 2010) to examine how perceived stress, coping, and spirituality at diagnosis related to mothers' membership in the identified latent trajectories. This approach conducts a multinomial logistic regression predicting latent class membership while maintaining the probabilistic nature of the latent class variable and accounting for the variance of all predictors. Therefore, rather than assigning participants to their most likely class, participants retained partial membership in classes according to their probability of class membership. Given that maternal age, education, income, race, relapse, and child death are associated with maternal depression in this population (Bemis et al., 2015; Wijnberg-Williams et al., 2006), these variables were included as covariates (i.e., 1 = relapse before/during study, 0 = never relapsed; 1 = child deceased, 0 = child living) in the model with

significant predictors. Treatment intensity was also included as a covariate given that it significantly differentiated attrition at one-year follow-up. Missing data for these analyses were estimated using multiple imputation given that MPlus version 7.3 does not permit estimation of missing data using maximum likelihood for the 3-step approach.

Results

Preliminary Analyses

Demographic information for patients and mothers is presented in Table 1. Means, standard deviations, and correlations are presented in Table 2. On average, mothers' BDI-II scores were in the mild range (Beck et al., 1996) at diagnosis ($M = 15.00$, $SD = 10.59$) and in the minimal range one- to five-years after study enrollment ($M = 8.61$ - 12.27 , $SD = 8.74$ - 10.95). At diagnosis/relapse, 11% ($n = 35$) of mothers reported BDI-II scores in the severe range, and 18% ($n = 57$) reported scores in the moderate range. At one-year follow-up, 7% ($n = 16$) reported scores in the severe range, and 16% ($n = 35$) reported scores in the moderate range. At three-years post diagnosis/relapse, 5% ($n = 5$) reported scores in the severe range, and 10% ($n = 11$) reported scores in the moderate range. At five-years post diagnosis/relapse, 6% ($n = 6$) reported scores in the severe range, and 3% ($n = 3$) reported scores in the moderate range.

Depression symptoms were negatively correlated with primary and secondary control coping and positively correlated with disengagement coping and perceived stress (Table 2). Spirituality was significantly correlated with depression symptoms at diagnosis/relapse and one-year, but not at three- or five-years. Coping variables were associated with perceived stress and spirituality in expected directions, and coping factors were highly intercorrelated. Tolerance (all $>.47$) and the variance inflation factor (VIF; all < 2.12) suggest no multicollinearity despite significant correlations between coping, spirituality, and perceived stress.

Longitudinal Analyses

Fit indices supported a quadratic model of change over time ($\chi^2 [1, N = 327] = 0.06; p = .80; CFI = 1.00; RMSEA < .01, 95\% CI [<.01, .09]; SRMR = 0.01$) in contrast to linear growth ($\chi^2 [5, N = 327] = 12.83; p = .02; CFI = .96; RMSEA = .07, 95\% CI [.02, .12]; SRMR = .10$) or an intercept-only model ($\chi^2 [8, N = 327] = 92.74; p < .001; CFI = .59; RMSEA = .18, 95\% CI [15, .21]; SRMR = 0.28$). Overall, a significant decreasing slope was evident in mean maternal depression scores ($B = -2.71, SE = 0.55, p < .001$). Although a four-class solution was supported by the lowest BIC (Table 3) and a significant change in LMR between the three- and four-class solutions (without a significant change in LMR between four- and five-classes), the BIC difference between the three- (5397.19) versus four-class models (5394.55) did not reflect strong evidence against a 3-class model (Kass & Raftery, 1995; Raftery, 1995). The three- and four-class models also both exhibited relatively high entropy and average class assignment probabilities, reflecting similar accuracy and certainty in categorizing mothers into classes. Visual inspection of the four-class model revealed one class of only two people. In contrast, the patterns observed in the three-class model were clinically meaningful and consistent with theory and prior research; therefore, the three-class model was retained as the final model.

The largest class was labeled “Low Depression Symptoms” ($n = 207, 63.3\%$; Figure 1) and characterized by few to no depression symptoms across the five year study period. Mothers in the low depression symptoms trajectory began with an average BDI-II score of 9.09 ($SE = 0.56, p < .001$; intercept) consistent with the minimal depression range; however, the average growth pattern of $-2.66 (SE = 0.48, p < .001; slope)$ demonstrated significant decreases in depression symptoms, primarily from diagnosis to one-year. The second largest class was labeled “Moderate Depression Symptoms” ($n = 103, 31.5\%$) and characterized by consistently moderate

levels of depression symptoms. These mothers initially reported an average BDI-II score of 22.16 ($SE = 1.27, p < .001$; intercept), consistent with moderate depression symptoms. Although the moderate depression symptoms trajectory appeared to be decreasing over time (Figure 1), the slope of this trajectory was not significant ($B = -0.86, SE = 1.35, p = .52$), perhaps due to considerable slope variance. The smallest class was labeled “High Depression Symptoms” ($n = 17, 5.2\%$) and was characterized by the highest levels of depression symptoms at all time points. Mothers in this trajectory reported an average BDI-II score at diagnosis/relapse of 40.00 ($SE = 3.53, p < .001$; intercept), consistent with severe depression symptoms. Despite significantly decreasing depression symptoms over time ($B = -6.24, SE = 3.15, p = .048$), their BDI-II scores were still within the severe depression range (32.13) five years after diagnosis.

Predictors of Trajectory Membership

Primary and secondary control coping were predictive of mothers’ trajectory membership. More primary and secondary control coping predicted that mothers were more likely to be assigned to the low depression trajectory as compared to either the high depression ($OR = 1.99, p = .008$ and $OR = 1.81, p = .001$, respectively) or moderate depression trajectories ($OR = 1.64, p = .024$ and $OR = 1.38, p = .013$, respectively). More secondary control coping also predicted that mothers were more likely to be assigned to the moderate depression trajectory ($OR = 1.31, p = .035$) as compared to the high depression trajectory; however, primary control coping did not differentiate membership in the moderate versus high trajectories. Perceived stress, spirituality, and disengagement coping did not significantly predict trajectory membership ($p = .10-.71$). Table 4 depicts odds ratios comparing predictors across classes. Significant comparisons between the low versus high and moderate trajectories remained significant after controlling for maternal age, education, income, race, child relapse, child death, and treatment

intensity for both primary ($OR = 2.13, p = .014$ and $OR = 1.59, p = .007$, respectively) and secondary control coping ($OR = 2.10, p = .018$ and $OR = 1.42, p = .003$, respectively); however, secondary control coping no longer significantly differentiated moderate versus high trajectories ($OR = 1.48, p = .179$). No covariates significantly predicted membership ($p = .089-.981$).

Discussion

Using a longitudinal prospective design and a large sample, this study empirically identified three trajectories of depression symptoms in mothers during the five years following their child's cancer diagnosis/relapse. On average, mothers' depression symptoms decreased over time, and most displayed a trajectory of few to no depression symptoms (63.3%), supporting the resilience of this population (Kearney et al., 2015; Phipps et al., 2015). However, a small but notable group of mothers (5.2%) displayed marked depression symptoms across the five years following their child's diagnosis/relapse, with a third group reporting moderate, stable depression symptoms (31.5%). These findings suggest a link between mothers' coping at diagnosis and long-term patterns of adjustment.

Consistent with prior findings (Katz et al., 2018), mothers displayed significant decreases in depression symptoms over time, particularly in the first year after diagnosis, suggesting that mothers of children with cancer may experience a natural decline in distress as the initial acute cancer-related stressors remit. Despite decreases in average depression symptoms, the trajectories remained relatively stable across children's course of illness, with average within-trajectory scores generally remaining within the same BDI-II severity ranges (e.g., severe, moderate, minimal). For example, mothers in the high depression trajectory continued to display scores within the severe range of the BDI-II despite marked decreases from diagnosis to five-

years. These findings highlight the importance of early intervention for mothers experiencing distress or mental health problems at diagnosis.

The presence of consistently high and low depression symptom trajectories is consistent with trajectories identified in smaller samples followed over a shorter period of time (Steele et al., 2004), as well as adjustment patterns observed following other potentially traumatic events (Bonanno & Diminich, 2013). Furthermore, the proportion of mothers in the high and low trajectories (i.e., 5.2% and 63.3%) is consistent with other stressors (5-30% and 35-65%, respectively; Bonanno & Diminich, 2013). The pattern of decreasing depression symptoms from diagnosis to one year in the low depression trajectory was consistent with the mild, transient distress of minimal-impact resilience (Bonanno & Diminich, 2013), as were findings that a pattern of low-impact resilience was most prevalent. Although not described in the broader literature (Bonanno & Diminich, 2013), the trajectory of moderate depression symptoms is in line with a pattern of stable, moderate distress described in pediatric oncology studies (Dolgin et al., 2007; Steele et al., 2004). Considerable variability was observed in this trajectory; therefore, with a larger sample, this subgroup may diverge into separate groups more consistent with established patterns. However, the emergence of this unexpected trajectory may also be attributed to unique features of pediatric cancer. Unlike other acute stressors (e.g., natural disasters) with a clearly identifiable offset, the stressors parents experience with pediatric cancer may be ongoing, including a transition from initial stressors at diagnosis to treatment-related and then survivorship stressors (e.g., late effects). These long-term trajectories suggest that the low, moderate, and high distress patterns observed during the first 6 months after diagnosis (Dolgin et al., 2007; Steele et al., 2004) may persist past treatment.

Surprisingly, a trajectory characterized by steeply decreasing depression symptoms did not emerge. Although this is inconsistent with prior literature (Bonanno & Diminich, 2013; Dolgin et al., 2007; Steele et al., 2004), it is noteworthy that significant decreases occurred in both the high and low trajectories, suggesting that symptoms generally improve over time. These findings expand upon previous reports suggesting that mothers' resilience in the context of pediatric cancer may be most consistent with a pattern of minimal-impact resilience rather than recovery (Bonanno & Diminich, 2013). The absence of a recovery trajectory may also be accounted for by the resilience of mothers in this sample, with relatively few depression symptoms in most mothers, potentially creating a floor effect. It is also possible that any recovery is most apparent within the first year (Steele et al., 2004), with more frequent assessments perhaps revealing more nuanced changes in mothers' adjustment.

Similar to Steele et al. (2004), trajectories were differentiated only by maternal coping. The use of primary and secondary control coping was linked with a pattern of resilience, consistent with cross-sectional studies (Compas et al., 2015; Maurice-Stam et al., 2008; Turner-Sack et al., 2016). Primary and secondary control coping remained statistically significant even after controlling for maternal age, education, income, race, relapse, child death, and treatment intensity. Mothers who cope effectively after diagnosis may experience less distress, setting them on a course of resilience. In contrast, perhaps mothers who apply appropriate coping strategies at diagnosis continue to cope effectively throughout the course of illness and thus display more stable, low levels of distress. Further studies are needed to examine longitudinal coping patterns to understand how changes in coping relate to patterns of adjustment. Interestingly, coping did not differentiate high and moderate groups when controlling for covariates, suggesting that the key distinction may be between patterns of resilience versus elevated depression.

Surprisingly, perceived stress, disengagement coping, and spirituality did not significantly predict mothers' trajectory assignment despite significant bivariate correlations with maternal depression at multiple time points. Mothers' perceived stress at diagnosis may have less bearing on long-term functioning than more proximal measures of stress during treatment and survivorship. Perceived stress may also be more transient and may decrease over time, with coping likely being stable and thus more characteristic of long-term patterns of psychosocial functioning. The lack of findings for disengagement coping may be attributed to the variance accounted for by primary and secondary control coping in the models. The role of spirituality may evolve over the illness trajectory (e.g. diagnosis versus after treatment; Schneider & Mannell, 2006), and thus changes in spirituality may be more predictive of changes in mothers' distress. This is further supported by nonsignificant associations between spirituality at diagnosis and depression at three- and five-years. Future studies should examine how these factors vary across the illness trajectory and relate differently to mothers' adjustment at various timepoints.

These findings may not generalize to the larger population. Importantly, a sizable number of mothers were lost to follow-up in this study; specifically, mothers of older children and children who had relapsed or experienced higher intensity cancer treatment were more likely to be lost to follow-up. Thus, findings may not translate to families of older children and may underrepresent distress at later time points for mothers of children with more disease severity. However, given findings of higher distress for mothers of children who relapsed or died, inclusion of relapsed and deceased children is also a strength of the current study. Generalizability may have been further reduced by the somewhat limited racial/ethnic diversity of participants. These findings can also only be generalized to mothers. Further studies should

include non-maternal caregivers. Because of the single-reporter design, method variance may have inflated the association between depression symptoms and coping.

Mothers' mental health before diagnosis was not assessed; therefore, chronic depression symptoms may have confounded long-term cancer-related distress with trajectories possibly reflecting pre-existing differences in mothers' mental health. Although the low and high trajectories significantly decreased in depression symptoms over time, the relative stability within trajectories supports the possibility of pre-existing symptom differences. One possibility is that differences in mothers' approach to coping pre-diagnosis yielded differences in pre-diagnosis depression symptoms that continued following diagnosis. This possibility continues to support the importance of mothers' active coping for their mental health. However, trajectory percentages for the present study were also consistent with patterns observed across other potentially traumatic events (Bonanno & Diminich, 2013), further validating these findings. Regardless of whether mothers' distress began prior to their child's cancer diagnosis, the number of mothers with long-term elevated depression symptoms suggests that a subset of families may benefit from psychosocial intervention beyond the current standard of care.

This study also has strengths that bolster potential implications of the results. This study includes one of the largest longitudinal samples of mothers of children with cancer, improving on the relatively small sample numbers reported in prior studies of parental long-term adjustment. Families were all recruited close to diagnosis/relapse; therefore, their trajectories can be compared and meaningfully reflect adjustment from diagnosis into survivorship. This study also used well-validated, established measures and a longitudinal analytic approach described as the gold standard for examining patterns of adjustment in adults (Bonanno & Diminich, 2013).

Findings support early screening of mothers' adjustment (e.g., depression symptoms) and coping (i.e., primary/secondary control coping). Such screening is consistent with psychosocial standards of care for parents and psychosocial assessment, which state that caregivers should experience "early and ongoing assessment" of their emotional adjustment and psychosocial needs (Kazak et al., 2015; Kearney et al., 2015). Use of brief, validated screeners of maternal distress may assist clinicians in identifying mothers at risk. Although no brief screening tools are available to assess coping, assessment may be performed through clinical interviews. These findings primarily support screening at diagnosis; however, providers should integrate family psychosocial screeners into follow-up care during treatment and survivorship (Kearney et al., 2015). Although several interventions have been developed for parents of children newly diagnosed with cancer (Surviving Cancer Competently Intervention Program and Bright IDEAS; Kazak et al., 1999; Sahler et al., 2013), evidence-based interventions for explicitly fostering coping in this population are limited (Kearney et al., 2015). These findings and prior coping research (Compas et al., 2015; Maurice-Stam et al., 2008) suggest that coping interventions promoting the use of primary and secondary control coping may effectively reduce mothers' risk for long-term distress. Moreover, the timing of coping interventions may be essential, with intervention near diagnosis critical for preventing long-term patterns of maternal distress.

These findings also have several implications for further research on interventions for parents of children with cancer. Despite an overall pattern of resilience, a subset of mothers displayed marked distress that remained relatively stable over 5 years and would benefit from early psychosocial intervention. Consistent with cross-sectional studies (Compas et al., 2015), these longitudinal findings suggest that a targeted intervention promoting primary and secondary

control coping may help a subgroup of mothers at risk for long-term distress. Thus, developing such interventions is a critical next step in fostering caregiver mental health.

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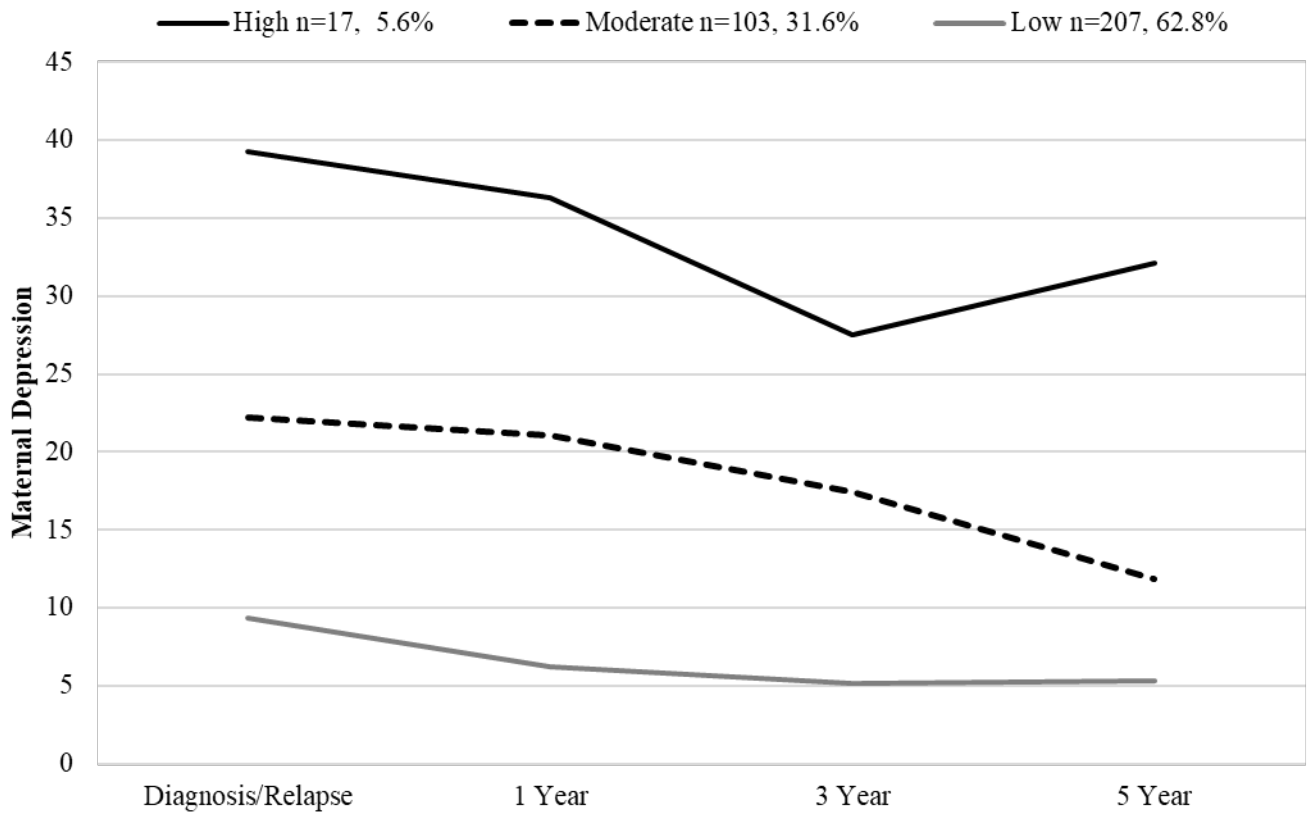


Figure 1. Estimated mean depression symptoms (BDI-II) for each trajectory.

Table 1

Patient and Mother Demographic and Clinical Characteristics

	Percent/Mean (SD)
Child Age (years)	
Mean (SD)	10.6 (3.9)
Child Gender	
Male	51.7%
Parent Age (years)	
Mean (SD)	37.6 (7.7)
Parent Ethnicity	
Hispanic (yes)	5.7%
Parent Race	
White	85.9%
African-American	9.7%
American Indian/Native Alaskan	0.5%
Asian	0.5%
Other	3.4%
Marital Status	
Married/Cohabiting	74.8%
Single	11.2%
Divorced/Separated/Widowed	14.0%
Parental Education	
Mean Years (SD)	13.96 (2.32)*
Number of children	
Mean (SD)	2.5 (1.13)
Family Income	
< \$25,000	29.3%
25,001–\$50,000	28.8%
\$50,001–\$75,000	15.1%
\$75,001–\$100,000	12.2%
> \$100,001	14.6%
Diagnostic Category	
Leukemia	35.8%
Lymphoma	25.0%
Solid Tumor	30.6%
Brain Tumor	8.6%
CNS Directed Treatment Received	52.6%
Enrolled following Relapsed Cancer	11.0%
Relapsed during Study	3.9%
Deceased	17.6%

Note. All percentages taken from available data. *Most completed high school and some college/technical school

Table 2

Means, Standard Deviations, and Correlations between all Study Variables

	<i>N</i>	<i>M</i> (<i>SD</i>)	1	2	3	4	5	6	7	8
1. Depression T1	318	15.00 (10.59)								
2. Depression T2	217	12.27 (10.95)	.68***							
3. Depression T3	107	9.58 (8.74)	.53***	.59***						
4. Depression T4	108	8.61 (9.07)	.52***	.51***	.71***					
5. Primary Control Coping T1	316	.20 (.04)	-.51***	-.44***	-.25*	-.39***				
6. Secondary Control Coping T1	320	.26 (.05)	-.64***	-.50***	-.37***	-.44***	.35***			
7. Disengagement Coping T1	321	.13 (.03)	.39***	.38***	.37***	.44***	-.59***	-.56***		
8. Perceived Stress T1	320	21.12 (7.04)	.64***	.42***	.40***	.43***	-.40***	-.64***	.37***	
9. Spirituality T1	319	96.09 (14.83)	-.21***	-.21**	-.07	-.18	.34***	.18**	-.29***	-.10

Note. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 3

Comparison of Model Fit for Latent Class Growth Analysis

Classes per model	Bayesian	Entropy	Average class	Lo-Mendell-Rubin Test (<i>p</i>)	Bootstrap Likelihood
	Information Criteria		assignment probabilities		Ratio Test <i>p</i> -values (comparisons)
2	5452.04	.77	.88–.95	206.64 (.002)	< .001 (1 vs. 2 classes)
3	5397.19	.81	.86–.95	74.78 (.049)	< .001 (2 vs. 3 classes)
4	5394.55	.81	.87–1.00	24.74 (.02)	< .001 (3 vs. 4 classes)
5	5397.05	.67	.73–.97	19.81 (.84)	< .001 (4 vs. 5 classes)

Note. Bold indicates the selected model.

Table 4

Odds Ratios Comparing Predictors across Classes

Predictors	Low vs. Moderate		Low vs. High		Moderate vs. High	
	<i>OR</i>	<i>p</i>	<i>OR</i>	<i>p</i>	<i>OR</i>	<i>p</i>
Primary Control Coping	1.64	.024	1.99	.008	1.21	.250
Secondary Control Coping	1.38	.013	1.81	.001	1.31	.035
Disengagement Coping	1.14	.488	1.14	.595	1.00	.997
Spirituality	1.04	.138	1.05	.140	1.01	.609
Perceived Stress	0.91	.101	0.88	.186	0.97	.706

Note. The second class listed in each column is used as the reference class.