

Parental Depressive Symptoms and Physical-Mental Multimorbidity in Children

by

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AUTHOR'S DECLARATION

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

STATEMENT OF CONTRIBUTIONS

This thesis is the work of Gurkiran Dhuga with the collaboration of her supervisor, Dr. Mark Ferro with contributions from Dr. Jennifer Yessis and Dr. Scott Leatherdale.

ABSTRACT

Background: Children with a chronic physical illness represent a substantial proportion of the child population. These children are at an elevated risk for mental illness (i.e., physical-mental multimorbidity). Additionally, their parents may experience elevated levels of depressive symptoms. Parental depression is a robust risk factor for mental illness in children; an association that is stronger when a child has a chronic physical illness. Unfortunately, current research assessing parental depressive symptoms and child physical-mental multimorbidity is primarily cross-sectional, focuses on specific chronic physical illnesses, and excludes children under 10 years of age, limiting the generalizability of study findings.

Objectives: The objectives of this work were to: (1) delineate trajectories of depressive symptoms among parents of children with a chronic physical illness over 24 months; (2) identify baseline factors predictive of trajectory group membership; and (3) examine the association between trajectory group membership and child physical-mental multimorbidity.

Methods: Data came from a longitudinal study of 246 children and their parents recruited from outpatient clinics at McMaster Children's Hospital. Latent class growth modelling identified trajectories of parental depressive symptoms. Multinomial logistic regression determined baseline predictors of trajectory group membership, and logistic regression examined the association between trajectory group membership and child physical-mental multimorbidity.

Results: Three trajectory groups were identified based on level of symptomatology: low (52%), subclinical (32%), and clinical (16%). Predictors of parental depressive symptom trajectories were more parental anxiety symptoms (OR = 1.55, 95% CI = 1.31-1.83 [subclinical]; OR = 1.81, 95% CI = 1.48-2.21 [clinical]), poorer parental physical health (OR = 0.94, 95% CI = 0.90-0.99; OR = 0.88, 95% CI = 0.82-0.95), living in areas with more residential instability (OR = 1.93,

95% CI = 1.17-3.20; OR = 3.15, 95% CI = 1.54-6.46), and more parenting stress (OR = 1.11, 95% CI = 1.02-1.19 [clinical]). Parental depressive symptom trajectory group membership was not associated with child physical-mental multimorbidity.

Conclusion: Findings suggest that most parents do not present with elevated levels of depressive symptoms. Predictors of parental depressive symptom trajectories and child physical-mental multimorbidity may help identify individuals with an increased susceptibility for poorer mental health outcomes. These findings highlight the need to integrate physical and mental health services as well as parental mental health services within pediatric settings. Future research should explore additional predictors of parental depressive symptom trajectories and child physical-mental multimorbidity.

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LIST OF ABBREVIATIONS

BIC	Bayesian Information Criteria
CES-D	Center for Epidemiologic Studies Depression Scale
CPI	Chronic Physical Illness
CwCPI	Children with a Chronic Physical Illness
FAD	McMaster Family Assessment Device
GAD	Generalized Anxiety Disorder
LCGM	Latent Class Growth Model
LMR-LRT	Lo-Mendell-Rubin Ad-hoc Adjusted Likelihood Ratio Test
MINI-KID	Mini International Neuropsychiatric Interview for Children and Adolescents
MY LIFE	Multimorbidity in Children and Youth Across the Life-course
ON-MARG	Ontario Marginalization Index
PHQ	Patient Health Questionnaire
PSS	Parental Stress Scale
SF	Short Form
WHODAS	World Health Organization Disability Assessment Schedule

BACKGROUND

1.1. Chronic Physical Illness in Children

A substantial proportion of children are impacted by a chronic physical illness (CPI), such as diabetes mellitus, asthma, or epilepsy (1–3). Definitions used to classify CPIs vary across the literature, making it difficult to estimate prevalence among children (2–4). Current research suggests that approximately 25% of children have a CPI, but some studies report prevalence > 50% (1,3,4). Notably, prevalence has been increasing over time and, as a result of medical advancements, more children with a CPI (CwCPI) are living into adulthood (1,5). This has important implications because in Ontario the estimated healthcare cost of CPIs is \$10.5B each year (6). Based on data from the United States, CwCPI can have annual medical expenditures of \$9,000 more than healthy children (7,8). Furthermore, CwCPI may have poorer health-related quality of life, worse school experiences, and more difficulty reaching psychosocial milestones (9–11).

1.2. Mental Illness in Children

Children are not only affected by CPIs, but also mental illnesses (12). Estimates suggest that at least one in five children have a mental illness; anxiety and disruptive disorders are the most common among children, with 6.5% of children having any anxiety disorder and 5.7% having any disruptive disorder (12–14). Some of the most prevalent mental illnesses amongst children are attention deficit hyperactivity disorder, oppositional defiant disorder, generalized anxiety disorder, and major depressive episode (13). Concerningly, several mental illnesses onset during childhood, including attention deficit hyperactivity disorder, oppositional defiant disorder, phobias, and separation anxiety disorder (15). Unfortunately, mental illness can impact

children throughout the life course; diagnosis with a mental illness early in life increases the risk of persistent mental illness in adulthood (12). Children with a mental illness may also have poorer health-related quality of life, poorer academic performance, and lower educational attainment (16–18).

1.3. Physical-Mental Multimorbidity in Children

One group that has an elevated risk of developing a mental illness is CwCPI (19). Research suggests they have a 43% higher risk of developing a mental illness (i.e., physical-mental multimorbidity) in comparison to children without a CPI (19). Although estimates are wide-ranging, within population-based samples up to 35% of children have physical-mental multimorbidity (3,20). In clinical samples the prevalence is greater, with estimates $\geq 50\%$ (21,22). Children with physical-mental multimorbidity often have poorer health-related quality of life and are typically high-cost users within the Ontario healthcare system (23,24).

1.4. Depression in Parents of Children with a Chronic Physical Illness

The impact of a CPI extends beyond the child and can also affect parents (25–27). Findings suggest that parents of CwCPI have poorer physical health, increased levels of anxiety symptoms, and elevated levels of depressive symptoms in comparison to parents of healthy children (26–30). Research indicates that parents of CwCPI have over twice the odds of reporting elevated depressive symptoms (25). They are also more likely to have depressive symptoms that reach the cut-off for clinical depression (28). Few studies assess how parental depressive symptoms change over time; longitudinal studies on maternal depressive symptom trajectories often observe four trajectory groups (27,31–33). A substantial proportion of mothers

present with low levels of depressive symptoms over time that are not of subclinical or clinical significance (31–33). However, current findings indicate that up to 20% of mothers of children with epilepsy may have depressive symptoms indicative of clinical depression for durations as long as ten years (31,33). Importantly, these trajectories may be impacted by the time from diagnosis of the child CPI; parents of children with shorter illness durations present with more depressive symptoms (27).

A weakness of current research on parental depressive symptoms, especially within longitudinal studies, is the exclusion of fathers (27,31–33). It is well established that primary caregivers are often mothers and women typically spend more time caring for children than men (25,34). Moreover, research findings indicate that mothers may experience more negative outcomes from having a CwCPI in comparison to fathers (35–37). However, studies that include fathers generally assess depressive symptoms amongst parents rather than primary caregivers, limiting the generalizability of the findings to male primary caregivers (35–38). The findings from an exploratory study suggest that the impact of having a CwCPI on parental depressive symptoms may be the same across male and female primary caregivers (38). Specifically, differences in depressive symptoms may be associated with being the primary caregiver rather than biological sex (38). Therefore, research should examine depressive symptoms among both male and female primary caregivers.

A multitude of factors may be involved in the association between having a CwCPI and increased parental depressive symptoms. For instance, parents of CwCPI may experience a number of chronic stressors, such as balancing work with medical visits, ensuring proper medical care, and affording medical care. This elevation in chronic stressors may be associated with more depressive symptoms (39). Parents may also face uncertainty regarding child CPI

which can be associated with distress (40). This could include uncertainty about the prognosis, medical care, or treatment options (40,41). Other potential mechanisms include feelings of grief or hopelessness which can be associated with depressive symptoms (42,43). Grief could include feelings of loss regarding their healthy child or old life (43). Feelings of hopelessness could be due to thoughts that the child condition is unchangeable or that the condition will prevent children from having a normal life (42). In general, there are no clearly established mechanisms that may lead to parental depression in parents of CwCPI.

Identifying factors that may be associated with poorer depressive symptom trajectories could allow for prevention efforts to identify parents at risk of poor outcomes. The comorbidity of anxiety and depression is well-established (44–46). Therefore, parents with anxiety may be at an increased risk for more depressive symptoms. Parents of CwCPI also have more parenting stress, and in certain circumstances, parenting stress is associated with more psychological distress (47). Furthermore, poorer family functioning is a risk factor for less favourable depressive symptom trajectories (31,33). On the other hand, physically healthy mothers have more favourable depressive symptom trajectories (32,48). Another important factor to consider is socioeconomic disadvantage; being unmarried, younger, and having lower socioeconomic status is associated with less favourable trajectories (31–33). Research has also observed shorter illness durations to be associated with more parental depressive symptoms; thus, parents of children with more recently diagnosed CPIs may be more negatively impacted (27). There are also neighbourhood-level variables associated with depression and depressive symptoms, such as residential instability and deprivation (49–53).

1.5. Parental Depression and Physical-Mental Multimorbidity in Children

Not only may several factors be associated with parental depressive symptom trajectories, but these trajectory groups may be associated with physical-mental multimorbidity in children (32,37,54). The association between parental depression and child mental illness is well-established within the literature (55–58). Children of parents with depression are more likely to have both internalizing and externalizing disorders (55,57,58). They have at least double the risk of anxiety disorders, major depressive disorder, and attention deficit hyperactivity disorder (58). Importantly, the association between parental depression or depressive symptoms and child mental illness is greater when a child has a CPI (32,59). Amongst mothers with less favourable depressive symptom trajectories, CwCPI have more depressive symptoms in comparison to healthy children (32). Unfortunately, the literature examining the association between parental depressive symptoms and child mental illness in CwCPI is limited; studies have primarily focused on symptoms of child anxiety or depression (29,32,37,54). Furthermore, there is limited information on whether child sex may moderate the association between parental depressive symptoms and child mental illness. Some studies observe moderation by child sex for certain mental illnesses, whereas others do not (48,55,60–63).

1.6. Theoretical Orientation

Pearlin's Stress Process Model aligns with the objectives of this study (64–66). The model outlines three key domains of social stress: sources of stress, mediators or moderators, and outcomes (64,65). The first domain is the sources of stress which can include life events and chronic strains (65). Life events are considered to be discrete occurrences whereas chronic strains are considered to be ongoing (65). Chronic strains can include interpersonal conflicts and

economic problems (65,66). It is suggested that life events and chronic strains interact; for instance, a life event such as having a child diagnosed with a CPI may result in chronic strains including depressive symptoms (65,66). Stressors can also be classified as either primary or secondary (66). The classification is based on whether stressors occur first (primary) or second (secondary) (66). For instance, in the example above, having a child diagnosed with a CPI could be a primary stressor and parental depressive symptoms could be a secondary stressor. The second domain in the model consists of mediators or moderators between the stressors and the outcome; these can include self-esteem, social support, and biological sex (64,65). Finally, the outcomes, or manifestations of stress, can include mental illnesses such as depression or anxiety (65,66). The most recent iterations of this model consider these three domains within the context of socioeconomic variables; it also includes neighbourhood ambient stressors that can be associated with the stressors and outcome (64). For this study, the stressor was parental depressive symptoms, and the outcome was physical-mental multimorbidity in children (Appendix A). Child sex was assessed as a potential moderator in this association.

STUDY RATIONALE AND RESEARCH OBJECTIVES

The overall goal of this study was to better understand depressive symptoms in parents of CwCPI. Previous studies examining parental depressive symptoms and physical-mental multimorbidity in children have several limitations. Fathers are often excluded, limiting the ability to identify potential differences in outcomes between male and female primary caregivers (27,29,32,33,67). Children less than 10 years of age have been excluded, ignoring early life experiences (29,32,67). Studies have primarily been cross-sectional, resulting in an inability to model the course of symptoms over time (27,28). Previous findings using population-based samples may not extrapolate to high-risk clinical samples of children (29,32,67). Participant recruitment has had a narrow focus of CPIs, with most studies focusing on one or a few CPIs, limiting the generalizability of the findings (28,31,33,68,69). Finally, most studies assess symptoms of child mental illness rather than mental illness diagnosis, which may impact the magnitude of the findings (29,32,70–73).

The specific aims of this study were to:

1. Delineate trajectories of depressive symptoms among parents of children with a chronic physical illness over 24 months.
 - a. Explore if there were differences in depressive symptom trajectories between mothers and fathers.

It was hypothesized that there would be four depressive symptom trajectory groups - low, subclinical, decreasing, and clinical (31–33). Additionally, it was hypothesized that depressive symptom trajectories would not differ between mothers and fathers (38).

2. Identify baseline factors predictive of trajectory group membership.

It was hypothesized that baseline predictors of poorer depressive symptom trajectories would be poorer parental physical health (32,48), elevated parental anxiety symptoms (44,45), increased parenting stress (47), less time from diagnosis (27), poorer family functioning (31,33), younger parental age, and socioeconomic disadvantage (31–33).

3. Examine the association between trajectory group membership and the presence of physical-mental multimorbidity in children.

a. Explore the moderating effect of child sex on the association between trajectory group membership and physical-mental multimorbidity in children.

It was hypothesized that less favourable trajectories would more adversely impact the mental health of CwCPI (32,58). Given insufficient research regarding child sex as a moderator, a hypothesis was not formed (48,55,60,61).

METHODS

3.1. Study Design and Sample

The data for this study came from the Multimorbidity in Children and Youth Across the Life-course (MY LIFE) study. This was a longitudinal study that focused on understanding the mental health of CwCPI (74,75). Recruitment of primary caregivers (hereafter referred to as parents) and children occurred through outpatient clinics at McMaster Children's Hospital, in Hamilton, Ontario (74,75).

To be included in the study, children must have been between the ages of 2 to 16 years and diagnosed with a CPI by a physician. Physician-diagnosed CPIs were defined as those that would last 12 months or longer and result in one or more of the following: (a) functional limitations, (b) dependencies due to their limitations, and/or (c) additional healthcare (74,75). Families were recruited from the following outpatient clinics: dermatology, endocrinology, gastroenterology, haemophilia, immunology, neurology, respirology, and rheumatology. Exclusion criteria were diagnosis with multiple CPIs at recruitment and parents or children with inadequate English proficiency. Data was collected at baseline, 6, 12, and 24 months; surveys and structured interviews were completed at these time points by parents and children aged 10 years or older (74,75). Due to the COVID-19 restrictions, as of March 2020, all data collection was completed through mail surveys and telephone interviews (75).

3.2. Procedure

Ethics approval for the MY LIFE study was obtained from the University of Waterloo Human Research Ethics Board and the Hamilton Integrated Research Ethics Board. Eligible families were identified by research assistants alongside healthcare professionals within

outpatient clinics (74,75). The study was then introduced to eligible families by a clinic nurse. Families interested in participating in the study had the opportunity to speak with a research assistant before or after their medical appointment. The research assistant confirmed that the family was eligible for the study, provided an explanation of the study, and received written permission to contact the family in a few days (74,75). For more details regarding the study procedure, see the MY LIFE protocol and cohort profile (74,75).

In total, 610 families were approached by clinic staff, 530 (87%) were approached by research staff, and 508 (83%) were eligible. Of these families, 294 (58%) consented to participate and baseline data was collected for 263 (52%) (75). Some parents had multiple children enrolled in the MY LIFE study; to avoid duplicate parent-reports, one child per parent was randomly selected to be included in the present study. This resulted in 17 (6.5%) children being removed and a final sample of 246 parent-child dyads.

3.3. Measures

3.3.1. Center for Epidemiologic Studies Depression Scale

The Center for Epidemiologic Studies Depression Scale (CES-D) measured parental depressive symptoms. This 20-item self-report assesses depressed affect, positive affect, somatic activity, and interpersonal relations (76). For each item, the frequency of symptom occurrence within the past week is assessed. Items are scored on a four-point Likert scale with scores ranging from 0 (rarely or none of the time [less than once a week]) to 3 (most or all of the time [five to seven days a week]). Total scores range from 0 to 60 and higher scores indicate more depressive symptoms (76). A score of 16 or higher is indicative of clinically-relevant depressive symptoms and scores ranging from 8 to 15 are associated with subclinical depression (76,77). If

up to four items were missing, mean imputation was used whereby the available items were averaged (76,78). This scale has shown evidence of validity across populations; internal consistency reliability was shown to be acceptable in the present sample ($\alpha = 0.92-0.93$) (79,80).

3.3.2. Generalized Anxiety Disorder-7

The Generalized Anxiety Disorder (GAD)-7 measured symptoms of anxiety among parents. This self-report assesses symptoms of anxiety experienced during the previous two weeks (81). The measure contains seven items that are scored on a four-point Likert scale with scores ranging from 0 (not at all) to 3 (nearly every day). Total scores range from 0 to 21 and higher scores denote more symptoms of anxiety. Scores of 5-9, 10-14, and 15-21 are indicative of mild, moderate, and severe anxiety, respectively (81). Mean imputation by averaging the available items was used if up to four items were missing. Across populations, the GAD-7 has demonstrated strong psychometric properties (81,82). In this sample, adequate internal consistency reliability was observed ($\alpha = 0.88$).

3.3.3. Parental Stress Scale

The Parental Stress Scale (PSS) assessed parenting stress. The scale contains 18 items categorized into four subscales: parental rewards, parental stressors, lack of control, and parental satisfaction (83). Each item is scored on a five-point Likert scale with scores ranging from 1 (strongly disagree) to 5 (strongly agree). To obtain a final score, eight items on the scale that indicate less parenting stress are reverse coded. Total scores range from 18 to 90 and higher scores signify more parenting stress (83). If up to three items were missing, mean imputation was used whereby the available items were averaged. Acceptable internal consistency reliability of

the PSS was observed in this sample ($\alpha = 0.86$); evidence of construct validity has been observed in Canadian populations (80,84).

3.3.4. Short Form-36

The Short Form (SF)-36 assessed the health-related quality of life of parents. The SF-36 is composed of eight domains which are physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health (85). Items on the scale have varying response options including multiple Likert scales and binary options of yes or no. Domain scores, ranging from 0 to 100, can be obtained where higher scores indicate better health-related quality of life (85). If up to half of the scale items were missing, mean imputation was used whereby the available scale items were averaged. To assess parental physical health, the physical component score was used (85). The physical component score is calculated by converting all domain scores into z-scores and then factor score coefficients are applied to the z-scores. Next, the weighted scores are summed and standardized through a linear T-score transformation with a mean of 50 and a standard deviation of 10 (85,86). Higher physical component scores indicate better physical health (85). The SF-36 has shown evidence of strong psychometric properties across populations and was shown to have adequate internal consistency reliability in the current sample ($\alpha = 0.91$) (85,87,88).

3.3.5. McMaster Family Assessment Device

The General Functioning subscale of the McMaster Family Assessment Device (FAD) assessed family functioning (89). This subscale contains 12 items that examine problem-solving,

communication, roles, affective responses, affective involvement, and behaviour control. Each item is scored on a four-point Likert scale with scores ranging from 0 (strongly agree) to 3 (strongly disagree) (89). To obtain an overall score, six positive items are reverse coded. The summed scores range from 0 to 36 and higher scores signify better family functioning (89). Mean imputation by averaging the available items was used if up to 40% of the items were missing (90). The General Functioning subscale has shown adequate internal consistency reliability in this sample ($\alpha = 0.86$) and demonstrated acceptable validity in Canadian populations (91,92).

3.3.6. Mini International Neuropsychiatric Interview for Children and Adolescents

The Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) assessed the presence of mental illness (i.e., physical-mental multimorbidity) in children. This structured interview assesses the presence of mental illness within the past six months based on the Diagnostic and Statistical Manual of Mental Disorders 5 and the International Classification of Diseases 10 (93). For the MY LIFE study, the presence of the most common mental illnesses was assessed. These were major depressive episode, separation anxiety disorder, social anxiety disorder, specific phobia, generalized anxiety disorder, attention deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder (74). For each disorder, there is an associated diagnostic module which contains two to four screening questions. If children screen positive to these initial questions, then the rest of the module is completed. All responses for the MINI-KID are binary with options of yes or no (93). For the MY LIFE study, both parent- and child-reports were available; however, for this study, only the

parent-reports were used to ensure that all children were included in the analysis (74). The MINI-KID has shown evidence of validity and reliability across populations (93–95).

3.3.7. World Health Organization Disability Assessment Schedule 2.0

The World Health Organization Disability Assessment Schedule (WHODAS) 2.0 assessed the level of disability among children. This 12-item questionnaire assesses six domains of functioning within the past 30 days (96). The domains are cognition, mobility, self-care, getting along, life activities, and participation. Each domain has two associated questions which are scored on a five-point Likert scale with scores ranging from 1 (none) to 5 (extreme or cannot do) (96). Simple scoring was used whereby the scores for all items were totalled and higher scores denoted more disability. If one item was missing, mean imputation by averaging the available items was used (96). Two adjustments were made to the questionnaire; item 2 was modified to "...household responsibilities/chores" and item 12 was modified to "... work/school." The inclusion of "chores" and "school" made the questions more relevant to the study population. Although both parent- and child-reports were available, to ensure all children were included in the analysis, only the parent-reports were used (74). Across populations, the WHODAS 2.0 has demonstrated strong psychometric properties (97–99). In this sample, adequate internal consistency reliability ($\alpha = 0.87$) and validity was observed (100–102).

3.3.8. Ontario Marginalization Index

The Ontario Marginalization Index (ON-MARG) measured neighbourhood-level marginalization. The index consists of four factors: residential instability, material deprivation, dependency, and ethnic concentration (103). Residential instability is the area-level

concentration of people facing family or housing instability. Material deprivation refers to the lack of access and attainment of basic material needs among individuals and communities. Dependency is the area-level concentration of those without income from employment (103). Ethnic concentration is the concentration of people who identify as a visible minority and/or are recent immigrants. Each factor is reported as a factor score with a mean of zero and a standard deviation of one, higher scores indicate more marginalization (103). To obtain the factor scores, participant postal codes were linked to dissemination areas using the 2017 Statistics Canada's Postal Code^{OM} Conversion File Plus (104).

3.3.9. Additional Variables

Sociodemographic variables assessed were marital status (partnered or single), education (less than post-secondary education or at least post-secondary education), and household income before taxes. Yearly household income was categorized as being above or below the median household income for >1-person households (\$90,000) (105). For both parents and children, data was collected on sex (male or female), age, ethnicity (Caucasian or other), and country of birth (Canada or other). Additionally, the time from diagnosis of the CPI was determined (74).

3.4. Statistical Analysis

3.4.1. Objective 1: Parental Depressive Symptom Trajectories

Latent class growth modelling identified parental depressive symptom trajectories over 24 months. This approach uses finite mixture modelling to identify trajectory groups that may not otherwise be observed (106,107). Unlike growth curve modelling, latent class growth modelling does not assume that there is an average population trajectory (106). Additionally, in

comparison to growth mixture modelling, it does not make assumptions regarding the distribution of trajectories or include random effects (107). As a result, the parents in each trajectory group are assumed to be homogenous (108).

Censored normal latent class growth models (LCGMs), with study time in months as the time variable, were run in MPlus (106,109). Based on previous literature, a model with four trajectory groups was used as the starting point; models with fewer trajectory groups were then examined (31–33). Non-significant higher-order terms were sequentially removed from the model until only linear terms remained or all the highest-order terms in the model were significant (31,33,110). To identify the best fitting model, four fit indices were used: the Bayesian Information Criteria (BIC), the Lo-Mendell-Rubin ad-hoc adjusted likelihood ratio test (LMR-LRT), average posterior probability, and class sizes based on maximum probability assignment. Better model fit was indicated by lower BIC values, a significant LMR-LRT p -value, higher average posterior probabilities, and class sizes $> 5\%$ (106,111,112). In general, differences in BIC values of ≥ 10 indicate very strong evidence in support of a model and average posterior probabilities should be > 0.70 (106,113).

To investigate the potential impact of parental sex on depressive symptom trajectories a sensitivity analysis was conducted, whereby LCGMs with and without fathers were compared for substantive differences. The parameter estimates and 95% confidence intervals for the final parental (mothers and fathers) and maternal LCGMs were plotted to identify potential differences. Mean scores across trajectory groups in the final model were assessed using Welch's analysis of variance and post-hoc Tukey-Kramer.

Time from diagnosis was included as a covariate in the final model. Non-significant higher-order terms were removed from the model until only linear terms remained or all the

highest-order terms in the model were significant (31,33,110). The parameter estimates and 95% confidence intervals of the adjusted and unadjusted LCGMs were plotted to identify differences.

3.4.2. Objective 2: Baseline Predictors of Trajectory Group Membership

Comparisons of baseline variables identified predictors of parental depressive symptom trajectory group membership. The baseline variables assessed were parental anxiety symptoms, parenting stress, parental physical health, time from diagnosis, child disability, family functioning, parental sex, parental age, child sex, child age, and household income. To investigate neighbourhood-level effects, residential instability, material deprivation, dependency, and ethnic concentration were also included. Due to the limited socioeconomic heterogeneity within the sample (see Table 1), additional sociodemographic variables were not assessed.

Analysis of variance compared continuous variables; Welch's analysis of variance was used for variables that violated the assumption of homogenous variance. χ^2 tests were used to compare categorical variables; Fisher's exact test was used for variables with small cell counts (114). Non-parametric variables were compared using the Kruskal-Wallis test (103). To control for multiple comparisons, the Benjamini-Hochberg procedure, with a false discovery rate of 0.05, identified variables for which pairwise comparisons were conducted (31,115). Pairwise comparisons were conducted using post-hoc Tukey, χ^2 tests, or the Dwass-Steel-Critchlow-Fligner method, as appropriate. Any variables that were significant at $p < 0.05$ in the bivariate comparisons were included in a multinomial logistic regression model.

3.4.3. Objective 3: Trajectory Group Membership and Child Physical-Mental Multimorbidity

Logistic regression assessed the association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity at 24 months. Significant variables ($p < 0.05$) from the bivariate comparisons in objective 2 were included in the model. However, family functioning was excluded due to its mediating effect in the association between maternal depressive symptoms and child mental illness (29,67). Additional variables included based on prior literature were child age and material deprivation (52,116–118). Child sex was included to assess for moderation; an interaction term between parental depressive symptom trajectory group membership and child sex was included.

An unadjusted model with only parental depressive symptom trajectory group membership was assessed. Then, blocks of independent variables were sequentially added (see Appendix C) (119). Sociodemographic variables were added first – parental age, child age, child sex, and household income. Neighbourhood-level marginalization variables were then added – residential instability and material deprivation. The following model added child disability. Finally, parental health variables were added – anxiety symptoms, parenting stress, and physical health.

3.4.4. Statistical Software

Mplus version 8.8 (109) was used for the LCGMs and RStudio (120) was used for plotting the trajectories; all other analyses used SAS Studio software version 9.4 (SAS Institute, Cary, NC). Unless otherwise stated, results were considered statistically significant if $p < 0.05$.

3.5. Sample Size

Although there are no clear guidelines for sample size in latent class growth modelling, prior work has delineated four trajectory groups with a sample size of 110 (121). Research on maternal depressive symptom trajectories used samples of 339 and 356 to identify four trajectory groups (31,33). Although the current sample was not as large, multiple start values enhanced the robustness of the results (122).

Previous research using multinomial logistic regression to identify predictors of depressive symptom trajectory groups include seven or ten predictors and have class sizes < 30 (31,33). The multinomial logistic regression model in this study included eight predictors and had class sizes > 30 . The logistic regression model in this study included ten predictors and had class sizes > 80 . Furthermore, a simulation study demonstrated that a sample size of $n = 250$ with four assessments was adequately powered ($1-\beta = 0.80$) at $\alpha = 0.05$ to detect measures of association that were medium in magnitude and moderating effects (74). Although the sample size in this study was slightly smaller than 250, the difference was negligible.

Given the longitudinal nature of this study, missing data was expected. For this study, item-level missingness was handled using imputation methods recommended for each measure; analyses for all objectives used the imputed dataset. Furthermore, for the LCGMs, missingness was handled using full-information maximum likelihood (48).

RESULTS

4.1. Sample Characteristics

Fourteen (5.7%) parent-child dyads withdrew from the study. The baseline characteristics of the parents and children are outlined in Table 1. Most parents were female (90.2%, $n = 222$), born in Canada (84.6%, $n = 208$), and Caucasian (86.2%, $n = 212$). Parents had a mean age of 40.55 years ($SD = 6.61$), 77.2% ($n = 190$) had at least a post-secondary education, 58.9% ($n = 145$) had a household income \geq \$90,000, and 85.8% ($n = 211$) were partnered. They had low levels of anxiety symptoms (mean = 4.53, $SD = 4.33$), minimal parenting stress (mean = 36.03, $SD = 8.90$), and physical health similar to population norms (mean = 47.22, $SD = 10.55$).

Children had a mean age of 9.43 years ($SD = 4.24$) and 48.4% ($n = 119$) were female. They had low levels of disability (mean = 19.40, $SD = 6.82$) and a mean time from diagnosis of 4.20 years ($SD = 3.93$). The most common CPI diagnoses were rheumatological (28.1%, $n = 69$), respiratory (19.9%, $n = 49$), and endocrine (15.0%, $n = 37$). At baseline, 37.8% ($n = 93$) of children had physical-mental multimorbidity.

4.2. Objective 1

4.2.1. Prevalence of Depressive Symptoms

Mean parental CES-D scores were 10.60 ($SD = 9.66$) at baseline, 10.63 ($SD = 10.14$) at 6 months, 11.39 ($SD = 10.28$) at 12 months, and 11.97 ($SD = 9.95$) at 24 months. Mean maternal CES-D scores were 11.11 ($SD = 9.87$) at baseline and 12.58 ($SD = 10.07$) at 24 months. Mean paternal CES-D scores were 5.92 ($SD = 5.82$) at baseline and 6.19 ($SD = 6.46$) at 24 months. At baseline, 26.8% ($n = 66$) of parents had clinically-relevant depressive symptoms and at 6 months this changed to 25.2% ($n = 62$). At 12 months, 25.6% ($n = 63$) of parents had clinically-relevant

depressive symptoms and by 24 months 27.2% ($n = 67$) of parents did. At baseline, 28.8% ($n = 64$) of mothers had clinically-relevant depressive symptoms and 8.3% ($n = 2$) of fathers. At 24 months, 29.3% ($n = 65$) of mothers had clinically-relevant depressive symptoms and 8.3% ($n = 2$) of fathers.

4.2.2. Parental Depressive Symptom Trajectories

The fit indices for the LCGMs including both mothers and fathers are presented in Table 2. Based on the model fit indices, a 3-class model was selected. This model had a BIC score of 6303.24, a significant LMR-LRT p -value ($p = 0.0274$), average posterior probabilities > 0.85 , and no class sizes $< 5\%$. In comparison, the 4-class model had a non-significant LMR-LRT p -value ($p = 0.6028$), one class consisting of 4.5% of the sample, and no replication of the maximum log-likelihood. The 2-class model had a BIC score of 6392.37, indicating very strong evidence in support of the 3-class model.

The parameter estimates of the final parental LCGM are shown in Table 3. The best fitting 3-class model consisted of two classes with linear terms and one class with a cubic term. Figure 1 depicts the observed and predicted trajectories of the three classes. The model identified a low, subclinical, and clinical class. The majority ($n = 129, 52.4\%$) of parents were in the low class. This class had low levels of depressive symptoms that remained stable over time; mean CES-D scores were 4.34 ($SD = 4.28$) at baseline and 5.24 ($SD = 3.96$) at 24 months. The subclinical class consisted of 32.1% ($n = 79$) of the sample. This class fell above the CES-D subclinical cut-off for the entire 24 months. At baseline, the mean CES-D score was 13.84 ($SD = 6.36$). At 24 months, the mean CES-D score was above the clinical cut-off (mean = 16.84, $SD = 7.38$). The clinical class ($n = 38, 15.5\%$) had scores that remained above the CES-D clinical cut-

off throughout the 24 months. The mean CES-D score at baseline was 25.51 (SD = 9.40), at 6 months the mean CES-D score peaked to 29.00 (SD = 7.52), and at 24 months the mean CES-D score was 26.90 (SD = 7.99). The mean scores across the three classes are outlined in Table 4. There was a significant difference ($p < 0.0001$) in mean CES-D scores across classes at all four timepoints and all post-hoc pairwise group comparisons were significant at $p < 0.01$. Individual trajectories and the predicted trajectory for each class can be found in S2.

4.2.3. Maternal Depressive Symptom Trajectories

The fit indices for the models only including mothers are presented in Table 5. Based on the model fit indices, a 3-class model was selected. This model had a BIC score of 5747.53, a significant LMR-LRT p -value ($p = 0.0210$), average posterior probabilities > 0.85 , and no class sizes $< 5\%$. A 4-class model was explored; however, after some simplification, the parameters of one class were fixed to avoid singularity of the information matrix. Thus, this model was not further explored. The 2-class model had a BIC score of 5830.29, indicating very strong evidence in support of the 3-class model. The residual variances for the 2-class model were fixed to avoid singularity of the information matrix.

The parameter estimates of the final maternal LCGM are shown in Table 6. The best fitting 3-class model consisted of two classes with linear terms and one class with a cubic term. Figure 2 depicts the observed and predicted trajectories of the three classes. The model identified a low, subclinical, and clinical class. The low class had low levels of depressive symptoms that remained relatively stable; the majority ($n = 117, 52.7\%$) of mothers were in the low class. The subclinical class consisted of 30.6% ($n = 68$) of the sample. This class fell above the CES-D

subclinical cut-off for the entire 24 months. The clinical class ($n = 37$, 16.7%) remained above the CES-D clinical cut-off throughout the 24 months.

The parameter estimates and 95% confidence intervals for the parental and maternal LCGMs are plotted in Figure 3. There was substantial overlap in the parameter estimates and confidence intervals between the two models, suggesting no difference between the models. Therefore, objectives two and three used the parental LCGM.

4.2.4. Adjusted LCGM

The LCGM with time from diagnosis as a covariate identified three classes, all with linear terms. The first model that was explored included all quadratic terms because all models including one or more cubic terms had fixed parameters. The parameter estimates and model fit indices of the final adjusted LCGM are shown in S3 and S4, respectively. Figure 4 presents the parameter estimates and 95% confidence intervals for the unadjusted and adjusted LCGMs. There was substantial overlap between the two models. The unadjusted LCGM was used for further analyses due to the similarity between the two models and the simplicity of the unadjusted model.

4.3. Objective 2

Bivariate comparisons of baseline predictors across trajectory groups are shown in Table 7. Baseline predictors of parental depressive symptom trajectory group membership were parental anxiety symptoms ($p < 0.0001$), parenting stress ($p < 0.0001$), parental physical health ($p < 0.0001$), child disability ($p < 0.0001$), family functioning ($p < 0.0001$), household income ($p = 0.0021$), and residential instability ($p = 0.0126$). In comparison to the low class, the subclinical

and clinical classes had more anxiety symptoms, more parenting stress, poorer physical health, children with higher levels of disability, worse family functioning, and lower household income. In comparison to the low class, the clinical class lived in areas with more residential instability. The clinical class also had more anxiety symptoms, poorer physical health, and children with higher levels of disability in comparison to the subclinical class.

The results of the multinomial logistic regression model identifying baseline predictors of parental depressive symptom trajectory group membership are presented in Table 8. Due to missingness on the predictors, five parent-child dyads were removed from the model. Baseline predictors were parental anxiety symptoms, parenting stress, parental physical health, and residential instability. Compared to the low class, the subclinical had more anxiety symptoms (OR = 1.55, 95% CI = 1.31-1.83), worse physical health (OR = 0.94, 95% CI = 0.90-0.99), and lived in areas with more residential instability (OR = 1.93, 95% CI = 1.17-3.20). The clinical class had more anxiety symptoms (OR = 1.81, 95% CI = 1.48-2.21), more parenting stress (OR = 1.11, 95% CI = 1.02-1.19), poorer physical health (OR = 0.88, 95% CI = 0.82-0.95), and lived in areas with more residential instability (OR = 3.15, 95% CI = 1.54-6.46) compared to the low class.

4.4. Objective 3

At 24 months, 82 children (33.3%) had physical-mental multimorbidity. Child sex was not a moderator in the association between child physical-mental multimorbidity and parental depressive symptom trajectory group membership ($\beta = 0.14$, $p = 0.5754$ for the subclinical class; $\beta = 0.53$, $p = 0.1069$ for the clinical class). Table 9 presents the logistic regression model investigating the association between parental depressive symptom trajectory group membership

and child physical-mental multimorbidity. Nineteen parent-child dyads were removed from the model due to missingness on either the predictors or outcome variable. Child age violated the assumption of linearity in the logit ($p = 0.0002$); however, the removal of this variable from the model did not change the significance of the findings or the odds ratio for the significant variable in the final model. In the unadjusted model (model 1), parental depressive symptom trajectory group membership was significantly associated with child physical-mental multimorbidity. The odds ratio was larger in the clinical class (OR = 3.75, 95% CI = 1.73-8.12) than in the subclinical class (OR = 2.33, 95% CI = 1.25-4.33). However, this association was not significant once parental health variables were added (model 5). In the fully adjusted model, only child disability (OR = 1.07, 95% CI = 1.02-1.13) was associated with child physical-mental multimorbidity.

DISCUSSION

5.1. Objective 1

Three parental depressive symptom trajectory groups were identified: low, subclinical, and clinical. Most parents were in the low class; however, almost half of parents presented with subclinical or clinically-relevant levels of depressive symptoms. Depressive symptom trajectories did not differ between mothers and fathers, nor did they change substantially following the inclusion of time from diagnosis as a covariate in the LCGM.

The three delineated trajectories align with the hypothesis and are consistent with previous studies (31–33,123). Over one-quarter of parents had clinically-relevant depressive symptoms at each timepoint. This is similar to prior estimates among parents of CwCPI (23% to 38%) and higher than estimates in control groups (19%) (28,31,33). In alignment with previous research, the low class was the largest, consisting of just over half of the sample (31,32,123,124). This indicates that most parents of CwCPI do not experience elevated levels of depressive symptoms, which may be beneficial for child mental health (32,55–58). The subclinical class may be the most burdensome because this group of parents may not qualify for mental health services (125–127). Subclinical levels of depressive symptoms are also associated with at least double the odds of incident major depression (128,129). The clinical class may have implications for child physical-mental multimorbidity given the well-established association between parental depression and child mental illness (55–58).

Contrary to what was hypothesized, a decreasing class was not observed. The sample size may have been too small to elucidate this trajectory group. Furthermore, three of the previous studies identifying a decreasing trajectory group span more than two years (32,33,124). Thus, the duration of the current study may not have been long enough to delineate this trajectory group.

As hypothesized, there was no difference in depressive symptom trajectories between mothers and fathers. This provides further support that depressive symptoms among parents of CwCPI are associated with being the primary caregiver rather than biological sex (38). Although the sample of fathers in the study was small, it may be representative of the general population. Canadian data suggests that mothers represent 83-90% of persons most knowledgeable about a child (25,32).

Contrary to what was anticipated, time from diagnosis did not impact parental depressive symptom trajectories. This opposes findings that illness duration is a study-level moderator of parental depressive symptoms, whereby shorter illness durations are associated with more depressive symptoms (27). Because the mean time from diagnosis in this study was 4.2 years, most parents may have adapted to child CPI. Some research suggests parents may adapt within the first 2.5 years after diagnosis (43,130). Additionally, due to the range of CPIs in the sample, the disease courses may have differed across children which could have attenuated the association.

5.2. Objective 2

Parental anxiety symptoms, parenting stress, parental physical health, child disability, family functioning, household income, and residential instability were associated with parental depressive symptom trajectory group membership in the bivariate comparisons. In the multinomial logistic regression model, anxiety symptoms, parenting stress, physical health, and residential instability were associated with parental depressive symptom trajectory group membership. A dose-response effect was observed whereby the less favourable trajectory groups had poorer baseline characteristics.

As hypothesized, anxiety symptoms, parenting stress, physical health, poorer family functioning, and household income were predictors of parental depressive symptom trajectory group membership. This is consistent with research examining factors associated with depression and depressive symptoms (31–33,35,44,45,47,131). However, in the multinomial logistic regression model, parenting stress was only a significant predictor in the clinical class, and both income and family functioning were not significant predictors. This may suggest that these associations are attenuated by other parental health factors. For instance, studies identifying family functioning as a predictor do not control for maternal anxiety symptoms or physical health (31,33). Additionally, in some studies household income is not a significant predictor of maternal depressive symptom trajectories (31,33).

Although not hypothesized, child disability was a predictor of parental depressive symptom trajectory group membership in the bivariate comparisons; this association was attenuated in the multinomial logistic regression model. This suggests that child disability may not have a significant effect on parental depressive symptom trajectories when considering other parental health variables. Prior work indicates that the complexity of the child condition is associated with caregiver depressive symptoms, and there is some support that parents of children with more life-limiting conditions present with more depressive symptoms (27,132). In support of the attenuated effect, prior work has not found an association between child illness severity and parental depressive symptoms when controlling for other variables (35). Additionally, other studies did not find an association between epilepsy severity and maternal depressive symptom trajectories (31,33).

Residential instability was also associated with parental depressive symptom trajectory group membership and was the strongest predictor in the multinomial logistic regression model.

This finding is supported by research in the general population demonstrating associations between social fragmentation and depression or mental health scores, as well as between neighbourhood cohesion and depressive symptoms (49,50,133). This highlights the importance of considering neighbourhood-level factors when assessing parental depressive symptoms.

Both parental age and time from diagnosis were hypothesized to be predictors of parental depressive symptom trajectory group membership, but this was not observed. Importantly, research supporting an effect of maternal age does not control for factors such as maternal anxiety symptoms and physical health, or observe an effect of maternal age for all trajectory groups (31,33). Because the mean time from diagnosis in this study was 4.2 years most parents may have adapted to child CPI, explaining why time from diagnosis was not a predictor (43,130).

Overall, the predictors of parental depressive symptom trajectory group membership were primarily factors proximal to the parent, rather than child or CPI characteristics. This suggests that child CPI may not have the largest impact on parental depressive symptom trajectories. Given the dose-response effect, these predictors could identify parents who are more likely to experience poor mental health outcomes (see Screening). Furthermore, this may identify additional factors involved in the theoretical model (see Application to the Theoretical Model).

5.3. Objective 3

Child sex was not a moderator in the association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity. Parental depressive symptom trajectory group membership was not associated with child physical-mental multimorbidity; the only significant predictor was child disability.

The baseline prevalence of child physical-mental multimorbidity was 38%, and at 24 months it was 33%. This finding suggests that most CwCPI do not experience physical-mental multimorbidity. This aligns with research that estimates physical-mental multimorbidity prevalence to be 35%; however, estimates can range from approximately 20% to over 50% based on the sample (3,20–22,134). Importantly, the prevalence of child mental illness in the general population is approximately 20%, suggesting that CwCPI have a higher prevalence of mental illness (12,13).

The finding that child sex did not moderate the association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity adds to the limited literature on this topic. This suggests children of either sex are similarly impacted by parental depressive symptom trajectories. Previous findings are mixed, with some studies observing moderation for specific mental illnesses and others not (48,55,60–63). A moderating effect of child sex may not have been observed because this study did not stratify by type of mental illness (i.e., internalizing or externalizing disorder). The most consistent finding in previous research is between maternal depression or depressive symptoms and child internalizing symptoms, whereby the association is stronger among female children (48,55).

Contrary to what was hypothesized, there was no association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity. This is inconsistent with literature identifying an association between parental depression and child mental illness (55–58). However, this finding aligns with a few studies that have not observed an association between parental depressive symptoms and child physical-mental multimorbidity (21,116). This suggests there may be an unmeasured variable attenuating the association between parental depressive symptom trajectory group membership and child physical-mental

multimorbidity. The variables that attenuated the association - parental anxiety symptoms, parental physical health, and parenting stress - could be components of health-related quality of life (85). Prior research supports an association between depression or depressive symptoms and quality of life in the general population and among parents of CwCPI (135–139). Additionally, research supports an association between depressive symptom severity and health-related quality of life amongst those with major depressive disorder (140,141). Thus, parental health-related quality of life may moderate the association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity, whereby the association is stronger among parents with poorer health-related quality of life.

The sole predictor of child physical-mental multimorbidity was child disability. This finding is supported by literature demonstrating an association between disability and mental illness (142–145). This suggests that parental variables and other distal variables may not significantly impact the mental health of CwCPI. Therefore, interventions could focus on factors more proximal to the child. Importantly, the impact of child disability on child physical-mental multimorbidity may be substantial. In the present study, a 3.5 unit increase on the WHODAS 2.0 represented a clinically meaningful difference and increased the odds of physical-mental multimorbidity by approximately 25% (146). This finding suggests that level of disability may be an additional factor to include in the theoretical model.

5.4. Application to the Theoretical Model

The study did not provide support for the proposed theoretical model. Furthermore, additional variables potentially involved in the theoretical model were not assessed (see Future Directions). However, this study did identify potential avenues to expand the model, including

the addition of stressors. For instance, parental anxiety symptoms, parenting stress, and parental physical health may be primary stressors of parental depressive symptoms. Child disability may be a stressor of child physical-mental multimorbidity. Furthermore, residential instability could be a neighbourhood ambient stressor of parental depressive symptoms. Although the study did not find a moderating effect of child sex, or an association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity, the potential moderating effect of parental health-related quality of life could be explored. Overall, the findings provide information on potential adaptations to the proposed theoretical model.

5.5. Strengths and Limitations

This study had several strengths. To our knowledge, it was the first study to examine depressive symptom trajectories among parents of children with a broad array of CPIs in a clinical population, expanding the generalizability of the findings. Additionally, findings expanded the limited literature on paternal depressive symptoms. It provided information on neighbourhood-level variables to explore. This study also explored a wide range of mental illness diagnoses across a broad age range of children.

There are important caveats to this study. Despite the sufficient sample size, a larger sample may have delineated additional trajectory groups and allowed for more robust comparisons of trajectories between mothers and fathers. Furthermore, the socioeconomic advantage of the sample may have underestimated the effects of sociodemographic variables. The minimal socioeconomic heterogeneity in the sample limited the ability to assess variables such as marital status and education. Therefore, these findings may have more limited applicability to the general population and those who are socioeconomically disadvantaged.

The reliance on parent-reports for child characteristics could have implications for the identified associations. Research suggests there is poor agreement between parent- and youth-reports on the WHODAS 2.0 whereby parents report lower levels of child disability (98,100). Therefore, parent-child disagreement would bias towards the null, suggesting the impact of child disability may be larger than observed. Parent-child disagreement is also observed on the MINI-KID, with parents reporting more mental illnesses compared to children (94,147). This may suggest that the prevalence of child physical-mental multimorbidity is lower than estimated in this study. However, among CwCPI there is some indication that parent-child agreement increases as the time from diagnosis increases (148).

The study did not stratify based on CPI, limiting the ability to identify differences across CPIs. However, findings indicate that a noncategorical approach may be appropriate (149,150). This approach is useful to assess the psychosocial impacts a CPI may have on children, which may not be dependent on the type of CPI (149). Additionally, in the MY LIFE sample, CPI classification is not associated with physical-mental multimorbidity (119).

The findings in the study may partly be associated with the impact of the COVID-19 pandemic as part of data collection occurred during this time. Some research indicates an increased prevalence of major depressive disorder associated with COVID-19 (151,152). In a subsample of the MY LIFE study, both parents and children present with increased distress compared to pre-COVID (153). Therefore, parental depressive symptoms and child physical-mental multimorbidity could partly be due to the impact of the COVID-19 pandemic, rather than child CPI. However, mean parental depressive symptoms and child physical-mental multimorbidity prevalence were similar throughout the study.

5.6. Implications

5.6.1. Integration of Parental Mental Health Services in Pediatrics

Given the substantial proportion of parents presenting with elevated levels of depressive symptoms, it is important to monitor and provide care to these parents. Subclinical or clinically-relevant levels of depressive symptoms can be detrimental to parents, but it can also negatively impact the mental health of children (32,55–58,128,129). Therefore, it is critical to assess parental mental health within a family-centered care model. Family-centered care can involve including the family in the decision-making process and providing support for family members (154,155).

Parents of CwCPI may spend a substantial amount of time in a pediatric hospital, making this a well-suited environment to address parental mental health. Quittner et al. highlight the need to annually screen at least one parent for anxiety and depression (156). Given the lack of association between parental health variables and child physical-mental multimorbidity identified in the present study, a single test for parental mental health could be administered. This could be the Patient Health Questionnaire (PHQ)-9 or the mental component score of the SF-12 (156–158). Importantly, mental health service options need to be available prior to screening parents. This could include educational materials, plans to address suicidal ideation, and a list of mental health services (156,159).

Furthermore, Salley et al. suggest three approaches to integrate parental mental health in pediatric settings. The first approach involves addressing parental mental health needs as part of child medical care. However, this approach may result in a conflict of interest and a lack of privacy because parental information is documented with child information (159). The second approach involves referring the parent to a mental health professional external to the hospital.

Although this addresses some of the issues of the first approach, there are other potential barriers, such as the limited availability of community providers and the provider not having a strong understanding of child CPI (159). The third approach involves parents receiving care in the pediatric setting. In this case, the parent is treated separately from the child but at the same location. This can help address the legal and ethical issues of the first approach and the logistic issues of the second approach (159). Mental health services for parents could be provided by psychologists that use a family-centered approach. Alternatively, providers trained in adult mental health could work within the pediatric setting (159).

Pediatric facilities have begun to integrate parental mental health services. For instance, a pediatric oncology facility has a three-tiered approach to treat parents. The three tiers include social worker support accessible to all parents, specialized counselling such as supportive counselling with a social worker, and tele-health referrals, respectively (160). This approach provides mental health services that best align with parent needs and allows parents to receive some services in the pediatric facility. Furthermore, a pediatric medical center in the United States offers weekly psychologist visits to parents who qualify for the service. The visits with the psychologist can be scheduled in advance, but this is not required, allowing for more flexibility based on the caregiving demands of the parent (161). The center also has an adult psychiatrist who works two-half days a week. On average, parents in this program complete 7.5 sessions (161). This suggests a similar approach could be effective. In a Canadian context, The Hospital for Sick Children has a five-year plan that involves creating avenues for parents to receive mental health services; however, there are no details regarding the integration of services within the hospital (162). Although there has been some uptake of integrating parental mental health

within pediatric settings, there is a need for evaluation of these approaches and other approaches to determine the feasibility and effectiveness for both parental and child mental health.

5.6.2. Integration of Physical and Mental Health Services in Pediatrics

There is a need to further integrate physical and mental health services in pediatric settings (163,164). CwCPI highlight the need for mental health providers to understand both the mental and physical aspects of conditions (163). Researchers also indicate the need to screen CwCPI for mental illnesses (156). For instance, using the Strengths and Difficulties Questionnaire (165,166). Importantly, integrated care from the outset of child CPI diagnosis could allow for early detection of a mental illness or elevated symptoms (164).

In a primary care setting, the Queens Family Health Team in Nova Scotia provides patients with referrals to see a counsellor within the practice (167). A similar approach could be expanded in pediatric settings, where children receive services from an on-site mental health professional. Another example is the Foundry Centres in British Columbia which offer integrated services using a stepped care model to young people. In this model, the needs of young people are assessed and used to determine the services needed. Young people can receive active engagement such as peer support, low intensity supports such as family education, moderate intensity supports such as individual therapy, or high intensity supports such as psychiatric services (167,168). A similar stepped approach could be implemented in pediatric settings. Furthermore, The Hospital for Sick Children is developing an approach which involves integrating mental, behavioural, and physical healthcare (162). Despite these steps towards integrated physical and mental health services, future research on the effectiveness and feasibility of these approaches and other approaches in pediatric settings is needed.

5.6.3. Screening

By assessing predictors of parental depressive symptom trajectory group membership, healthcare professionals may be able to identify the trajectory that a parent will follow. Furthermore, predictors of parental depressive symptom trajectories and child physical-mental multimorbidity may help identify parents and children at risk of poor mental health outcomes. Parents and children who present with these predictors may require additional follow-up and support and be good candidates for preventative interventions. Most measures in this study could be utilized in a clinical setting given their brevity (i.e., CES-D, WHODAS 2.0). Other potential brief measures include the PHQ-9, and the SF-12, which looks at both physical and mental health (157,158).

5.6.4. Interventions

A variety of interventions exist for parents of CwCPI (169,170). Problem-solving therapy has a small benefit on parental mental health (170,171). However, there is a lack of information and support for other interventions addressing mental health among parents of CwCPI (170). Interventions with limited research include family therapy, motivational interviewing, and multisystemic therapy (170). Mindfulness-based interventions are effective for stress among parents of CwCPI and depression in an adult psychiatric population (169,172). Additionally, acceptance and commitment therapy has similar benefits to traditional cognitive behavioural therapy for depression in the general population (173). Given the limited information on effective interventions for parents of CwCPI, there is a need for further studies.

Additional factors that could be targeted in interventions are predictors of parental depressive symptom trajectory group membership, such as parental anxiety symptoms and

physical health. However, factors such as residential instability are less modifiable, indicating more systematic issues need to be addressed. Identifying neighbourhoods with greater residential instability could help identify parents in greater need of intervention. Additionally, given the association between social cohesion and mental health, area-based initiatives, community engagement programs, and urban regeneration programs could be explored (174–178). Furthermore, level of disability could be a target for mental illness interventions among CwCPI.

5.7. Future Directions

There are a variety of avenues for future research. One such avenue is the inclusion of male primary caregivers. The literature on paternal depressive symptoms in this population is limited, even more so for longitudinal studies, and often consists of small sample sizes which limits the robustness of the results (27,28,38). Through the over-recruitment of male primary caregivers, stratified analyses by parental sex could be conducted. This could more robustly assess whether depressive symptom trajectories among parents of CwCPI differ based on caregiver status or biological sex. Additionally, the recruitment of a more socioeconomically diverse sample would allow for the assessment of a variety of sociodemographic factors, enhancing the external validity of the findings.

The inclusion of a control group, such as children seeking care in the emergency department or those attending the fracture clinic could expand the knowledge in this research area. By including a control group, potential mediators and moderators in the association between child CPI and parental depressive symptom trajectories could be assessed. This could include factors such as grief, chronic stressors, uncertainty, and hopelessness (39–43). A control group would also help adjust for external variables, such as a pandemic.

Furthermore, the potential bidirectionality of these associations should be assessed (143,179,180). This could involve assessing children with recently diagnosed CPIs. By focusing on children recently diagnosed with a CPI, the temporality of parental depressive symptoms and child mental illness with respect to child CPI could be established. Addressing these factors would also provide a better understanding of the theoretical model.

Additional variables potentially involved in the association between parental depressive symptom trajectories and child physical-mental multimorbidity should be investigated. For instance, family functioning may be a mediator in the association between parental depressive symptom trajectories and child physical-mental multimorbidity. However, studies assessing this mediator focus on children over the age of 10 years and maternal depressive symptoms, limiting the generalizability of the findings (29,67). Prior mental health status and biological factors such as cortisol may also be associated with parental depressive symptom trajectories and child physical-mental multimorbidity (123,181). Additionally, the mental health of other caregivers of the child may be associated with child physical-mental multimorbidity (57,58). Future research should also extend beyond parental depressive symptoms. For instance, assessing parental health-related quality of life and anxiety symptoms.

CONCLUSION

The findings from this study demonstrate that most parents of CwCPI do not present with elevated depressive symptoms. However, there is a large group of parents that present with subclinical or clinically-relevant levels of depressive symptoms. A variety of factors may be predictors of parental depressive symptom trajectory group membership. Most of these predictors are proximal to the parent, suggesting a limited impact of child characteristics on parental depressive symptom trajectories. Comparatively, parental depressive symptoms trajectories may not be associated with child physical-mental multimorbidity, but child disability is. The predictors of parental depressive symptom trajectories and child physical-mental multimorbidity may help identify parents and children at risk of poorer mental health outcomes. In pediatric settings, there is a need to integrate parental mental health services as well as physical and mental health services. Future work should explore additional variables that may be involved in the association between parental depressive symptoms trajectories and child physical-mental multimorbidity.

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FIGURES AND TABLES

Table 1: Baseline characteristics of the MY LIFE sample

Characteristic	Mean (SD)	Imputed (n [%])	Missing (n [%])
Parental age, years	40.55 (6.61)	0 (0%)	0 (0%)
Child age, years	9.43 (4.24)	0 (0%)	0 (0%)
Parental depressive symptoms, CES-D	10.60 (9.66)	1 (0.41)	1 (0.41)
Parental anxiety symptoms, GAD-7	4.53 (4.33)	0 (0%)	1 (0.41)
Parenting stress, PSS	36.03 (8.90)	1 (0.41)	1 (0.41)
Parental physical health, SF-36	47.22 (10.55)	1 (0.41)	1 (0.41)
Time from child diagnosis, years	4.20 (3.93)	0 (0%)	0 (0%)
Child disability, WHODAS 2.0	19.40 (6.82)	0 (0%)	1 (0.41)
Family functioning, FAD	27.90 (5.40)	0 (0%)	1 (0.41)
Marginalization, ON-MARG		0 (0%)	2 (0.81)
Residential instability	-0.40 (0.78)		
Material deprivation	-0.34 (0.91)		
Dependency	-0.22 (0.96)		
Ethnic concentration	-0.19 (0.67)		

Characteristic	N (%)	Missing (n [%])
Female parent	222 (90.24)	0 (0%)
Female child	119 (48.37)	0 (0%)
Caucasian parent	212 (86.18)	0 (0%)
Canadian born parent	208 (84.55)	0 (0%)
Married/common-law parent	211 (85.77)	0 (0%)
Post-secondary education or higher	190 (77.24)	0 (0%)
Household income, ≥ \$90,000	145 (58.94)	2 (0.81)
Child diagnosis classification		0 (0%)
Dermatological	22 (8.94)	
Endocrine	37 (15.04)	
Gastroenterological	31 (12.60)	
Hematological	26 (10.57)	
Neurological	12 (4.88)	
Respiratory	49 (19.92)	
Rheumatological	69 (28.05)	
Child multimorbidity, MINI-KID	93 (37.80)	1 (0.41)

Missing refers to the number of participants with missing scores, excluding those who had scores imputed.

Table 2: Model fit indices for the LCGM of parental depressive symptoms

Number of Classes	BIC	LMR-LRT (<i>p</i> -value)	Average Posterior Probability	Maximum Probability Assignment (%)
1	6770.56	-	Class 1: 1.00	100.00
2	6392.37	<0.0001	Class 1: 0.98 Class 2: 0.93 Mean: 0.96	66.67 33.33
3	6303.24	0.0274	Class 1: 0.95 Class 2: 0.88 Class 3: 0.93 Mean: 0.92	52.44 32.11 15.45
4	6278.59	0.6028	Class 1: 0.95 Class 2: 0.97 Class 3: 0.88 Class 4: 0.90 Mean: 0.93	49.59 4.47 31.30 14.63

Table 3: Parameter estimates for the LCGM of parental depressive symptoms

Group	Parameter	Estimate (SE)	<i>p</i> -value
Low	Intercept	3.606 (0.571)	<0.001
	Linear	0.064 (0.022)	0.004
Subclinical	Intercept	12.991 (1.095)	<0.001
	Linear	0.155 (0.059)	0.009
Clinical	Intercept	25.319 (1.951)	<0.001
	Linear	1.695 (0.617)	0.006
	Quadratic	-0.210 (0.082)	0.011
	Cubic	0.006 (0.002)	0.015

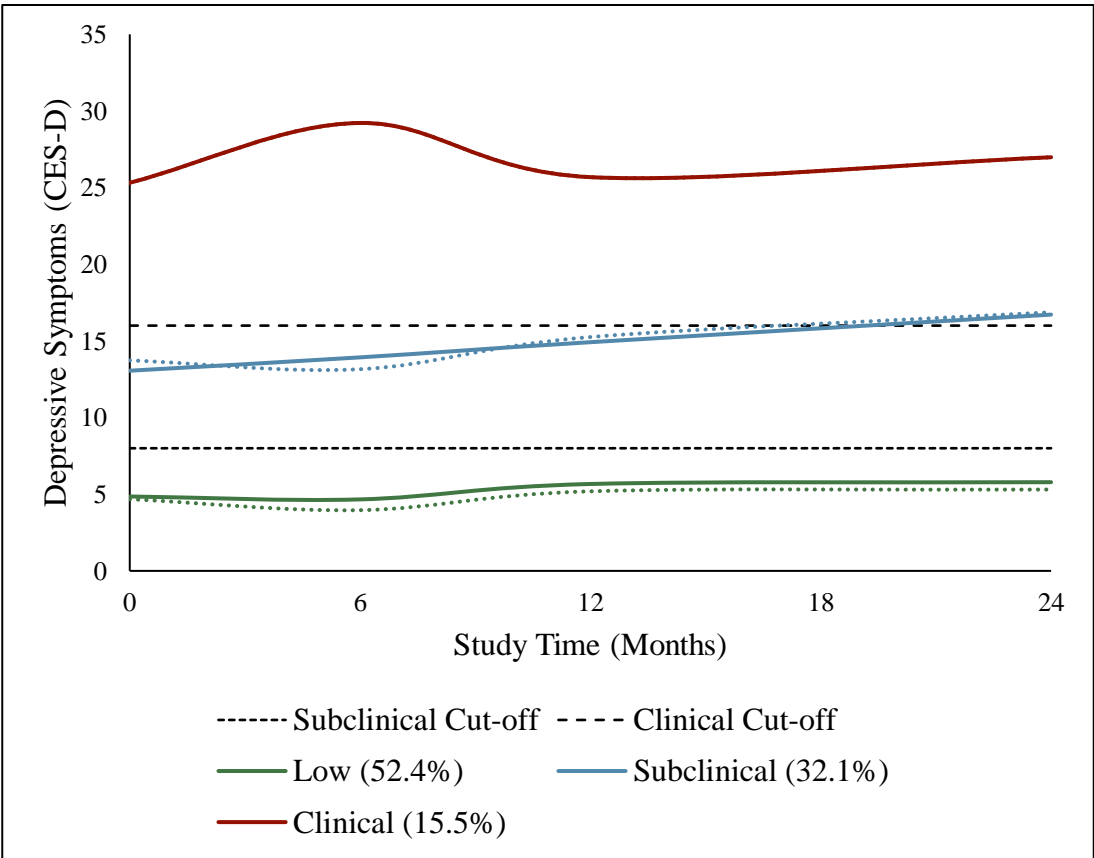


Figure 1: Parental depressive symptom trajectories. The solid lines represent the predicted trajectories, and the coloured dashed lines represent the observed trajectories.

Table 4: Parental depressive symptoms over time, stratified by trajectory group

Timepoint	Trajectory Group			F	<i>p</i> -value
	Low	Subclinical	Clinical		
Baseline	4.34 (4.28)	13.84 (6.36)	25.51 (9.40)	140.76	<0.0001
6 months	3.81 (3.17)	13.05 (5.48)	29.00 (7.52)	261.14	<0.0001
12 months	5.06 (4.58)	15.18 (9.33)	25.53 (8.36)	124.73	<0.0001
24 months	5.24 (3.96)	16.84 (7.38)	26.90 (7.99)	165.74	<0.0001

CES-D scores are reported as mean (standard deviation).

Table 5: Model fit indices for the LCGM of maternal depressive symptoms

Number of Classes	BIC	LMR-LRT (<i>p</i> -value)	Average Posterior Probability	Maximum Probability Assignment (%)
1	6154.29	-	Class 1: 1.00	100.00
2	5830.29	<0.0001	Class 1: 0.96 Class 2: 0.96 Mean: 0.96	27.48 72.52
3	5747.53	0.0210	Class 1: 0.93 Class 2: 0.88 Class 3: 0.93 Mean: 0.91	52.70 30.63 16.67

Table 6: Parameter estimates for the LCGM of maternal depressive symptoms

Group	Parameter	Estimate (SE)	<i>p</i> -value
Low	Intercept	3.961 (0.703)	<0.001
	Linear	0.065 (0.025)	0.008
Subclinical	Intercept	12.991 (1.271)	<0.001
	Linear	0.179 (0.065)	0.006
Clinical	Intercept	25.390 (2.094)	<0.001
	Linear	1.799 (0.625)	0.004
	Quadratic	-0.223 (0.085)	0.008
	Cubic	0.006 (0.003)	0.012

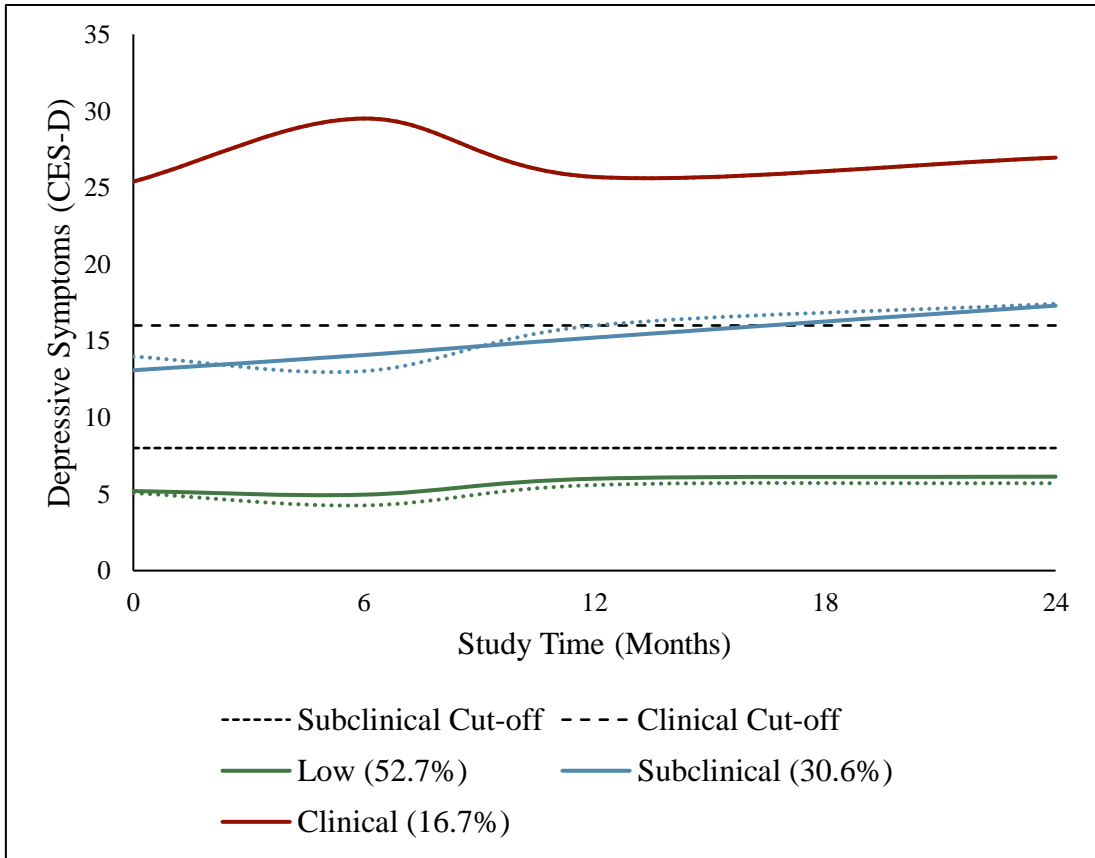


Figure 2: Maternal depressive symptom trajectories. The solid lines represent the predicted trajectories, and the coloured dashed lines represent the observed trajectories.

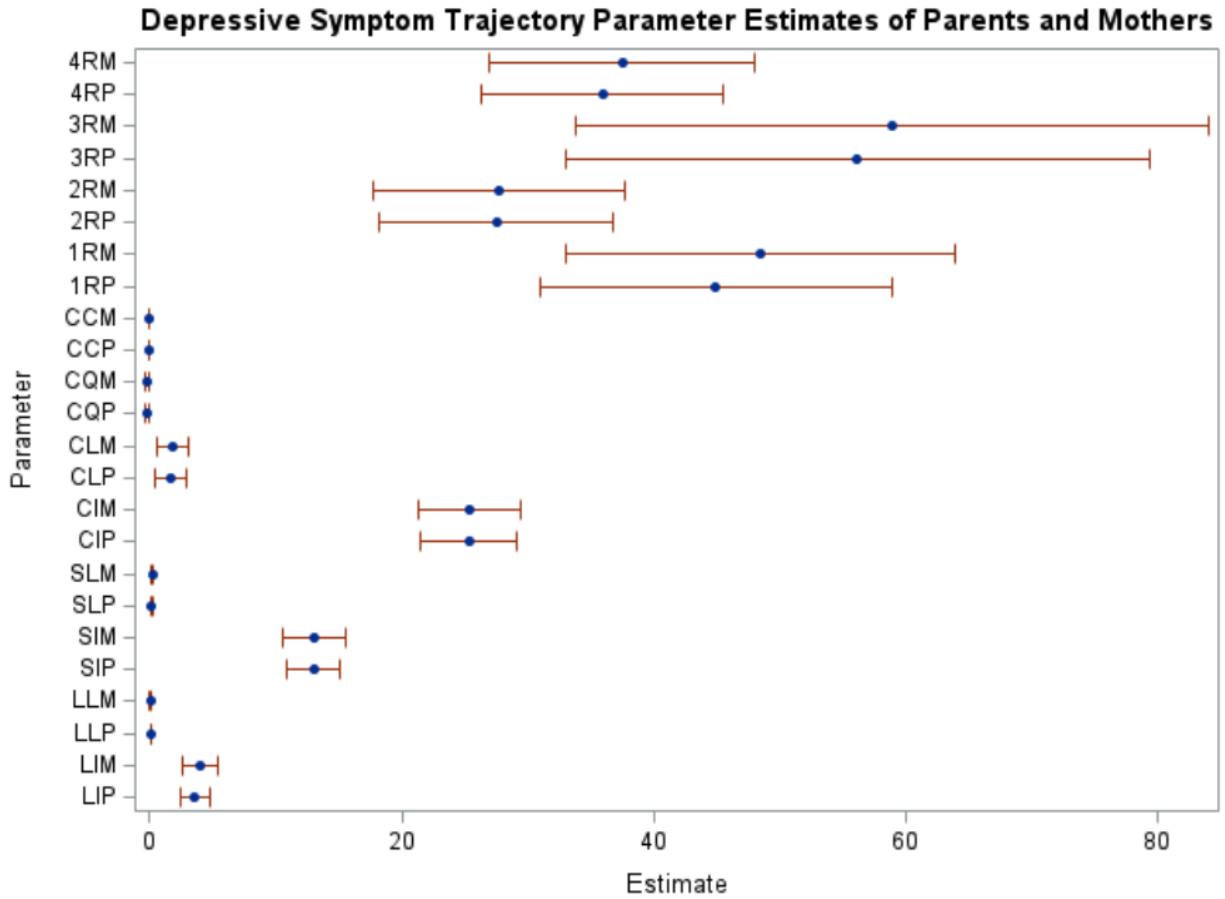


Figure 3: Comparison of model estimates between the parental LCGM and the maternal LCGM. The blue dots represent the estimated values, and the red bands represent the 95% confidence intervals. The parameters are named as follows: the first letter indicates the class (L=low, S=subclinical, C=clinical) whereas the number indicates the study timepoint (1, 2, 3, or 4), the second letter indicates the estimate (I=intercept, L=linear, Q=quadratic, C=cubic, R=residual variance), and the third letter indicates the model (M=mothers only, P=all parents).

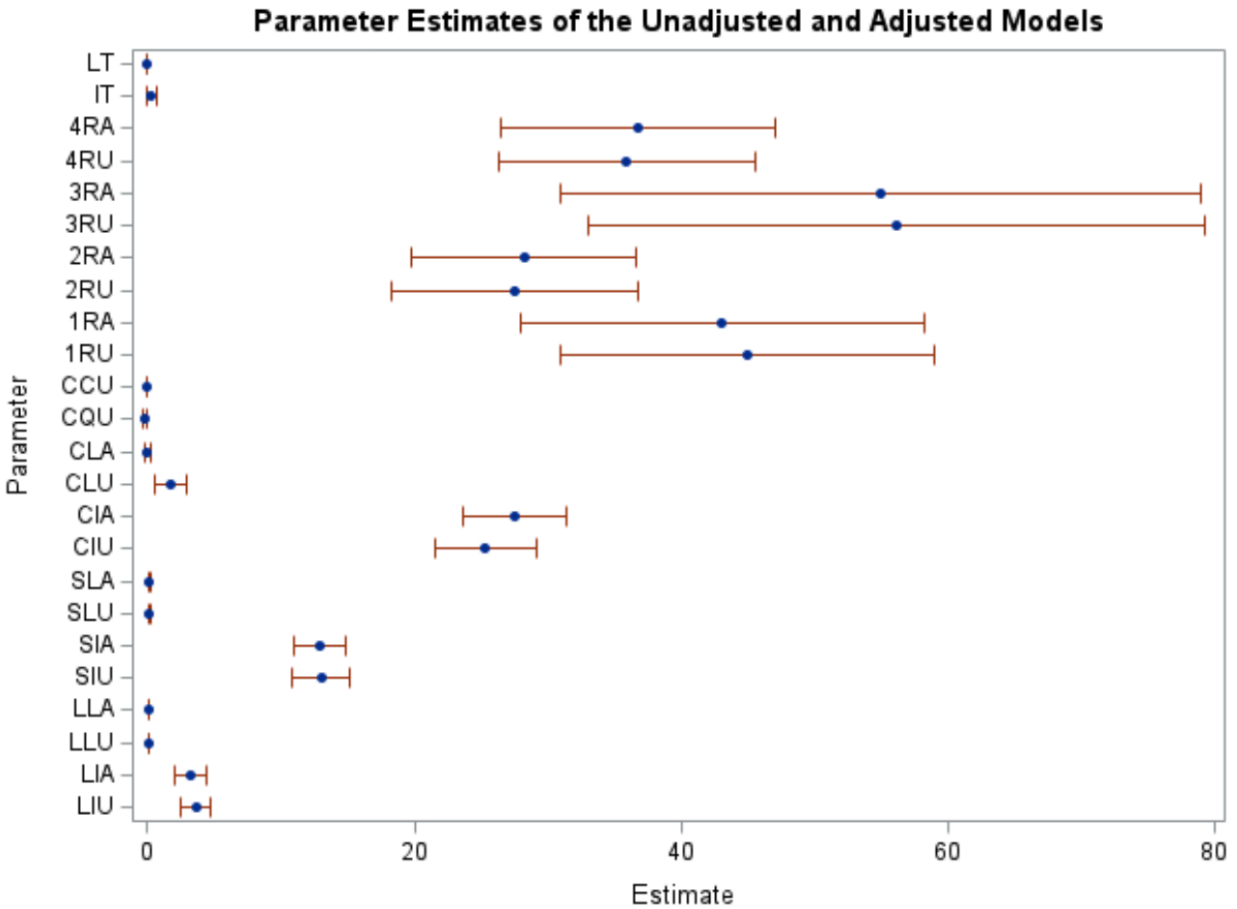


Figure 4: Comparison of model estimates between the unadjusted LCGM and the LCGM with mean-centered time from diagnosis as a covariate. The blue dots represent the estimated values, and the red bands represent the 95% confidence intervals. The parameters are named as follows: the first letter indicates the class (L=low, S=subclinical, C=clinical) whereas the number indicates the study timepoint (1, 2, 3, or 4), the second letter indicates the estimate (I=intercept, L=linear, Q=quadratic, C=cubic, R=residual variance), and the third letter indicates the model (U=unadjusted, A=adjusted). IT and LT represent the intercept and linear factors being regressed on time from diagnosis, respectively.

Table 7: Baseline characteristics of parents, stratified by trajectory group

Baseline characteristic	Trajectory Group			F/ χ^2	p-value	Contrasts ^a
	Low (n = 129)	Subclinical (n = 79)	Clinical (n = 38)			
Parent						
Female, % ^b	111 (86.05)	74 (93.67)	37 (97.37)	-	0.0675	
Age, years	41.34 (6.38)	40.45 (7.00)	38.11 (6.09)	3.59	0.0292	
Anxiety symptoms, GAD-7 ^c	2.02 (2.18)	6.10 (3.83)	9.97 (4.44)	83.81	<0.0001*	C > S > L
Parenting stress, PSS ^c	32.44 (7.13)	38.86 (7.93)	42.49 (10.63)	26.54	<0.0001*	C, S > L
Physical health, SF-36 ^c	52.27 (6.88)	44.07 (9.92)	36.36 (11.74)	45.08	<0.0001*	L > S > C
Child						
Female, %	55 (42.64)	40 (50.63)	24 (63.16)	5.19	0.0747	
Age, years	9.48 (4.34)	9.46 (4.29)	9.19 (3.87)	0.07	0.9325	
Time from diagnosis, years	4.34 (4.08)	4.46 (3.92)	3.16 (3.29)	1.58	0.2074	
Disability, WHODAS 2.0	17.47 (5.51)	20.37 (7.12)	24.05 (7.71)	16.42	<0.0001*	C > S > L
Family						
Functioning, FAD	29.77 (4.68)	26.01 (5.25)	25.43 (5.80)	18.77	<0.0001*	L > S, C
Household income \geq \$90,000, %	89 (68.99)	40 (50.63)	16 (42.11)	12.29	0.0021*	L > S, C
Marginalization, ON-MARG						
Residential instability ^d	-0.52 (0.70)	-0.30 (0.91)	-0.19 (0.73)	8.74	0.0126*	C > L
Deprivation ^d	-0.44 (0.78)	-0.23 (1.03)	-0.22 (1.04)	1.45	0.4841	
Dependency ^d	-0.37 (0.74)	-0.06 (1.20)	-0.06 (0.99)	4.51	0.1048	
Ethnic concentration ^d	-0.17 (0.73)	-0.19 (0.59)	-0.29 (0.63)	1.16	0.5611	

Reported as mean (standard deviation), unless stated otherwise.

L, S and C denote the low, subclinical and clinical classes, respectively.

^a Denotes significant pairwise contrasts at $p < 0.05$.

^b Indicates that Fisher's exact test was used.

^c Indicates that Welch's ANOVA was used.

^d Indicates that a Kruskal-Wallis test was used.

*Significant based on the Benjamini-Hochberg procedure.

Table 8: Multinomial logistic regression investigating baseline predictors of parental depressive symptom trajectory group membership

Baseline Characteristic	Trajectory Group	
	Subclinical	Clinical
<i>Parent</i>		
Age	1.03 (0.97, 1.10)	0.98 (0.89, 1.07)
Anxiety symptoms, GAD-7	1.55 (1.31, 1.83)***	1.81 (1.48, 2.21)***
Parenting stress, PSS	1.06 (1.00, 1.12)	1.11 (1.02, 1.19)*
Physical health, SF-36	0.94 (0.90, 0.99)*	0.88 (0.82, 0.95)***
<i>Child</i>		
Disability, WHODAS 2.0	0.97 (0.90, 1.04)	0.97 (0.88, 1.06)
<i>Family</i>		
Functioning, FAD	0.94 (0.87, 1.02)	0.95 (0.85, 1.05)
Household income < \$90,000	1.36 (0.61, 3.04)	0.67 (0.20, 2.31)
Residential Instability, ON-MARG	1.93 (1.17, 3.20)*	3.15 (1.54, 6.46)**

Reported as odds ratio (95% confidence interval). The low trajectory group was set as the reference group.

Bolded items indicate significant associations. *p<0.05, **p<0.01, ***p<0.001

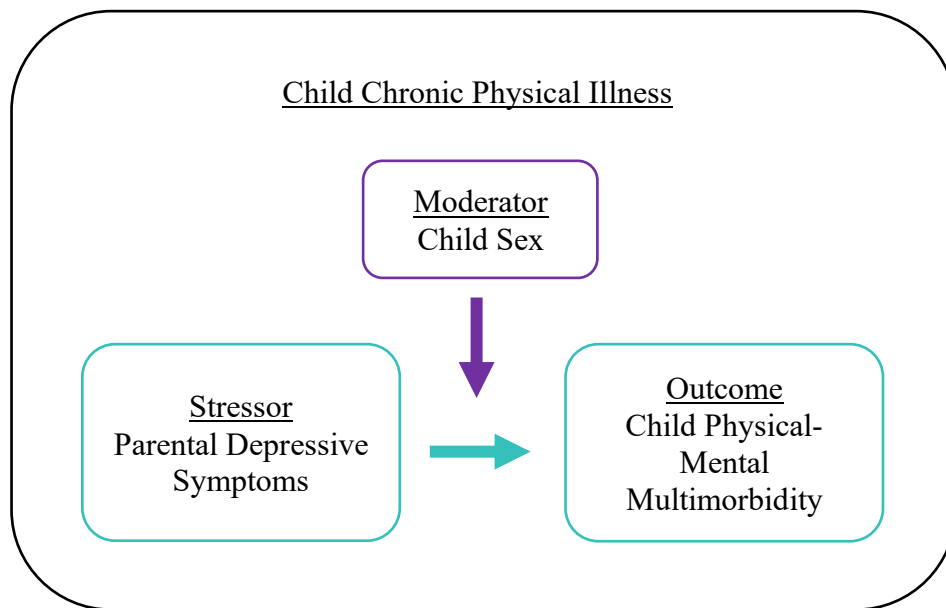
Table 9: Logistic regression investigating the association between parental depressive symptom trajectory group membership and child physical-mental multimorbidity

Characteristic	Model 1	Model 2	Model 3	Model 4	Model 5
<i>Trajectory group</i>					
Subclinical class	2.33 (1.25, 4.33)**	2.27 (1.19, 4.33)*	2.41 (1.25, 4.64)**	2.04 (1.03, 4.01)*	1.55 (0.70, 3.41)
Clinical class	3.75 (1.73, 8.12)***	3.29 (1.44, 7.48)**	3.65 (1.58, 8.46)**	2.73 (1.11, 6.71)*	1.68 (0.53, 5.32)
<i>Sociodemographic</i>					
Parent age		0.94 (0.89, 1.00)*	0.94 (0.88, 1.00)*	0.95 (0.89, 1.01)	0.95 (0.89, 1.02)
Child age		1.09 (1.00, 1.19)	1.10 (1.00, 1.20)	1.09 (0.99, 1.20)	1.10 (1.00, 1.21)
Male child		1.31 (0.73, 2.33)	1.27 (0.71, 2.29)	1.45 (0.79, 2.68)	1.53 (0.82, 2.83)
Household income < \$90,000		1.22 (0.67, 2.20)	1.28 (0.69, 2.37)	1.18 (0.62, 2.24)	1.13 (0.58, 2.20)
<i>Marginalization</i>					
Residential instability, ON-MARG			0.72 (0.46, 1.13)	0.74 (0.47, 1.17)	0.77 (0.48, 1.23)
Material deprivation, ON-MARG			1.14 (0.79, 1.65)	1.09 (0.75, 1.59)	1.10 (0.75, 1.62)
<i>Child health</i>					
Disability, WHODAS 2.0				1.08 (1.03, 1.13)**	1.07 (1.02, 1.13)**
<i>Parental health</i>					
Anxiety symptoms, GAD-7					1.06 (0.96, 1.17)
Parenting stress, PSS					1.01 (0.97, 1.05)
Physical health, SF-36					1.00 (0.96, 1.04)
<i>Model fit</i>					
c-statistic	0.64	0.67	0.69	0.73	0.74

Reported as odds ratio (95% confidence interval).

Bolded items indicate significant associations. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

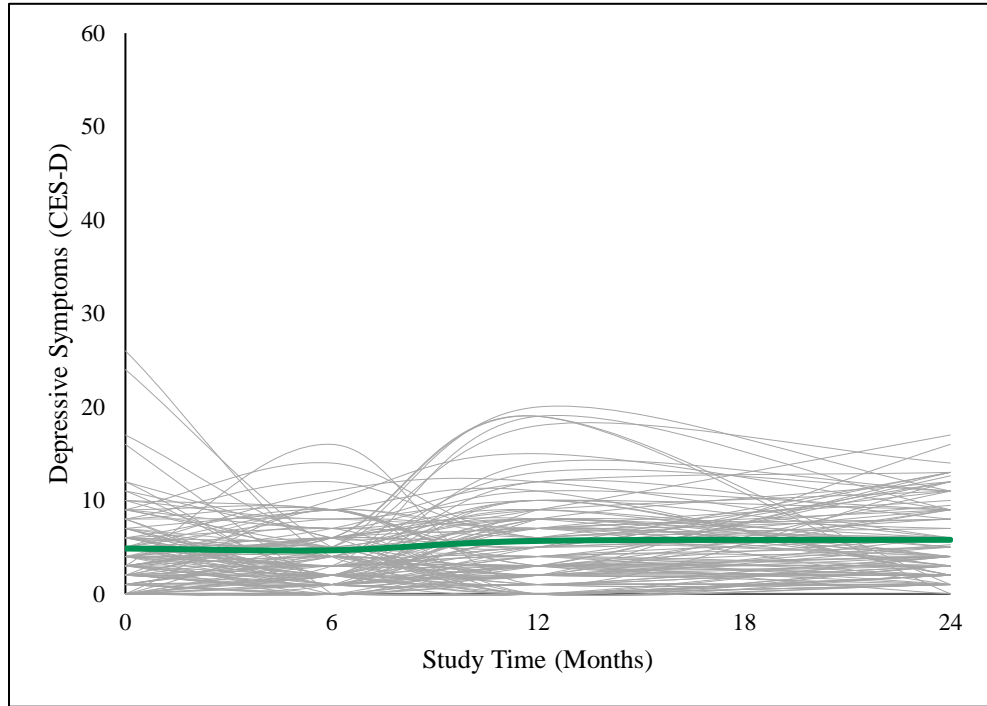
APPENDIX A – THEORETICAL MODEL



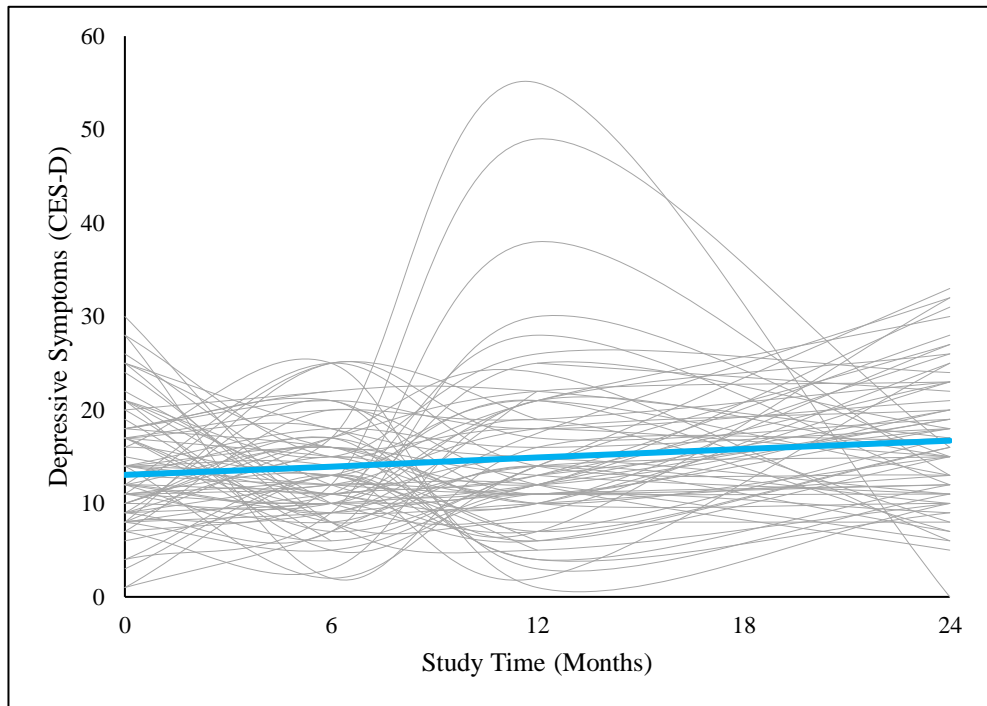
S1: Theoretical model

APPENDIX B – INDIVIDUAL DEPRESSIVE SYMPTOM TRAJECTORIES

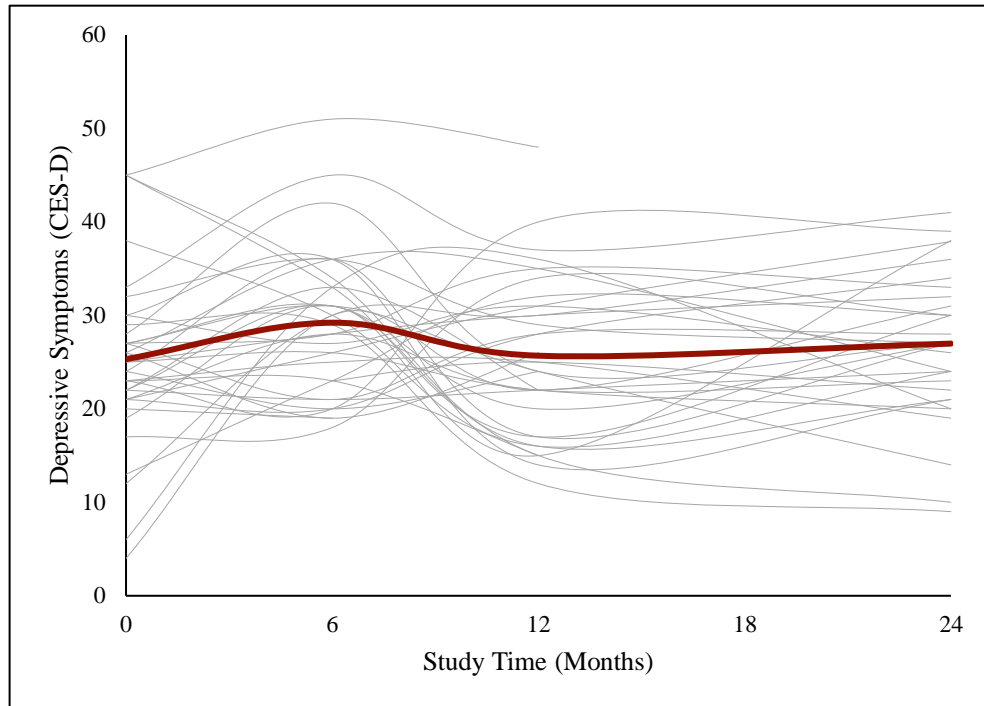
A



B



C



S2: Observed and predicted parental depressive symptom trajectories. The grey lines depict the observed trajectories of individuals belonging to the specified class. The coloured lines depict the predicted trajectory for the class. A) The graph represents the trajectories for the low class. B) The graph represents the trajectories for the subclinical class. C) The graph represents the trajectories for the clinical class.

APPENDIX C – ADJUSTED LCGM

S3: Parental depressive symptom trajectories with mean-centered time from diagnosis as a covariate

Class	Parameter	Estimate (SE)	<i>p</i> -value
1	Intercept	3.234 (0.633)	<0.001
	Linear	0.069 (0.023)	0.002
2	Intercept	12.861 (0.996)	<0.001
	Linear	0.141 (0.058)	0.015
3	Intercept	27.536 (1.949)	<0.001
	Linear	-0.002 (0.118)	0.984
	Intercept on Time	0.271 (0.187)	0.148
	Linear on Time	-0.004 (0.006)	0.549

S4: Model fit indices for the adjusted LCGM of parental depressive symptoms

Number of Classes	BIC	LMR-LRT (<i>p</i> -value)	Average Posterior Probability	Maximum Probability Assignment (%)
3	6302.90	0.0399	Class 1: 0.95 Class 2: 0.89 Class 3: 0.92 Mean: 0.92	50.41 34.15 15.45

APPENDIX D – STATISTICAL MODELS

Objective 2

$$\eta_i^{(j)} = \beta_0^{(j)} + \beta_1^{(j)} PAGE_i + \beta_2^{(j)} GAD_i + \beta_3^{(j)} PSS_i + \beta_4^{(j)} SF_i + \beta_5^{(j)} WHODAS_i + \beta_6^{(j)} FAD_i + \beta_7^{(j)} INC_i + \beta_8^{(j)} INST_i$$

where

j is the trajectory group membership category, reference is the low class,

$\eta_i^{(j)}$ = is the log-odds of $Y_i = j$ for subject i , which is unobserved and random,

$PAGE_i$ is the observed (fixed) predictor variable parental age for subject i ,

GAD_i is the observed (fixed) predictor variable parental anxiety symptoms for subject i ,

PSS_i is the observed (fixed) predictor variable parenting stress for subject i ,

SF_i is the observed (fixed) predictor variable parental physical health for subject i ,

$WHODAS_i$ is the observed (fixed) predictor variable child disability for subject i ,

FAD_i is the observed (fixed) predictor variable family functioning for subject i ,

INC_i is the observed (fixed) predictor variable household income (reference is $\geq \$90,000$) for subject i ,

$INST_i$ is the observed (fixed) predictor variable residential instability for subject i ,

$\beta_0^{(j)}$ is the fixed and unknown intercept,

$\beta_1^{(j)}, \beta_2^{(j)}, \dots, \beta_8^{(j)}$ are the fixed and unknown regression coefficients for each of the predictors listed above,

for any $i \neq k$, $(PAGE_i, GAD_i, PSS_i, SF_i, WHODAS_i, FAD_i, INC_i, INST_i, \eta_i^{(j)}) \perp$

$(PAGE_k, GAD_k, PSS_k, SF_k, WHODAS_k, FAD_k, INC_k, INST_k, \eta_k^{(j)})$.

Objective 3

Moderation analysis

$$\eta_i = \beta_0 + \beta_1 SUB_i + \beta_2 CLIN_i + \beta_3 PAGE_i + \beta_4 CAGE_i + \beta_5 CSEX_i + \beta_6 INC_i + \beta_7 INST_i + \beta_8 DEPR_i + \beta_9 WHODAS_i + \beta_{10} GAD_i + \beta_{11} PSS_i + \beta_{12} SF_i + \beta_{13} SUB_i * CSEX_i + \beta_{14} CLIN_i * CSEX_i$$

where

η_i is the log-odds of having physical-mental multimorbidity for subject i , which is unobserved and random,

SUB_i is the observed (fixed) predictor variable the subclinical class (reference is the low class) for subject i ,

$CLIN_i$ is the observed (fixed) predictor variable the clinical class (reference is the low class) for subject i ,

$CAGE_i$ is the observed (fixed) predictor variable child age for subject i ,

$CSEX_i$ is the observed (fixed) predictor variable child sex (reference is female) for subject i ,

$DEPR_i$ is the observed (fixed) predictor variable material deprivation for subject i ,

β_0 is the fixed and unknown intercept,

$\beta_1, \beta_2, \dots, \beta_{14}$ are the fixed and unknown regression coefficients for the variables $SUB_i, CLIN_i,$

$PAGE_i, CAGE_i, CSEX_i, INC_i, INST_i, DEPR_i, WHODAS_i, GAD_i, PSS_i, SF_i$, the interaction

between SUB_i and $CSEX_i$, and the interaction between $CLIN_i$ and $CSEX_i$ respectively,

for any $i \neq k$,

$(SUB_i, CLIN_i, PAGE_i, CAGE_i, CSEX_i, INC_i, INST_i, DEPR_i, WHODAS_i, GAD_i, PSS_i, SF_i,$

$SUB_i * CSEX_i, CLIN_i * CSEX_i, \eta_i) \perp$

$(SUB_k, CLIN_k, PAGE_k, CAGE_k, CSEX_k, INC_k, INST_k, DEPR_k, WHODAS_k, GAD_k, PSS_k, SF_k, SUB_k * CSEX_k, CLIN_k * CSEX_k, \eta_k)$.

Analysis without moderation

Block 1: Adds parental depressive symptom trajectory group membership

$$\eta_i = \beta_0 + \beta_1 SUB_i + \beta_2 CLIN_i$$

Block 2: Adds sociodemographic variables

$$\eta_i = \beta_0 + \beta_1 SUB_i + \beta_2 CLIN_i + \beta_3 PAGE_i + \beta_4 CAGE_i + \beta_5 CSEX_i + \beta_6 INC_i$$

Block 3: Adds marginalization indices

$$\eta_i = \beta_0 + \beta_1 SUB_i + \beta_2 CLIN_i + \beta_3 PAGE_i + \beta_4 CAGE_i + \beta_5 CSEX_i + \beta_6 INC_i + \beta_7 INST_i + \beta_8 DEPR_i$$

Block 4: Adds child disability

$$\eta_i = \beta_0 + \beta_1 SUB_i + \beta_2 CLIN_i + \beta_3 PAGE_i + \beta_4 CAGE_i + \beta_5 CSEX_i + \beta_6 INC_i + \beta_7 INST_i + \beta_8 DEPR_i + \beta_9 WHODAS_i$$

Block 5: Adds parental health variables

$$\eta_i = \beta_0 + \beta_1 SUB_i + \beta_2 CLIN_i + \beta_3 PAGE_i + \beta_4 CAGE_i + \beta_5 CSEX_i + \beta_6 INC_i + \beta_7 INST_i + \beta_8 DEPR_i + \beta_9 WHODAS_i + \beta_{10} GAD_i + \beta_{11} PSS_i + \beta_{12} SF_i$$