

RESEARCH ARTICLE

Cohort Profile: Multimorbidity in Children and Youth Across the Life-course (MY LIFE) Study

Mark A Ferro PhD¹; Ellen L Lipman MD, MSc²; Ryan J Van Lieshout MD, PhD²; Brian Timmons PhD³; Lilly Shanahan PhD^{4,5}; Jan Willem Gorter MD PhD³; Kathy Georgiades PhD²; Michael Boyle PhD²

Abstract

Objective: This manuscript serves to provide an overview of the methods of the Multimorbidity in Children and Youth across the Life-course (MY LIFE) study, profile sample characteristics of the cohort, and provide baseline estimates of multimorbidity to foster collaboration with clinical and research colleagues across Canada. **Method:** MY LIFE is comprised of 263 children (2-16 years) with a physical illness recruited from McMaster Children's Hospital, their primary caregiving parent, and their closest-aged sibling. Participants are followed with data collection at recruitment, 6, 12, and 24 months which includes structured interviews, self-reported measures, and biological samples and occur in a private research office or at participants' homes. Post-COVID-19, data collection transitioned to mail and telephone surveys. **Results:** At recruitment, children were 9.4 (4.2) years of age and 52.7% were male. The mean duration of their physical illness was 4.5 (4.1) years; 25% represent incident cases (duration <1 year). Most (69.7%) had healthy body weight and intelligence in the average range (73.5%). Overall, 38.2% of children screened positive for ≥ 1 mental illness according to parent report (24.8% screened positive based on child self-report). Compared to 2016 Census data, the MY LIFE cohort overrepresents families of higher socioeconomic status. **Conclusions:** Multimorbidity is common among children and these baseline data will serve to measure relative changes in the mental health of children with physical illness over time. MY LIFE will provide new information for understanding multimorbidity among children, though underrepresentation of lower socioeconomic families may have implications for the generalizability of findings.

Key Words: *adolescent; child; chronic disease; longitudinal study; mental illness; physical illness*

Résumé

Objectif: Le présent manuscrit sert à présenter un aperçu des méthodes de l'étude sur la multimorbidité chez les enfants et les jeunes tout au long de la vie (MA VIE), à esquisser des caractéristiques d'échantillon de la cohorte et à fournir des estimations de base de la multimorbidité pour faciliter la collaboration avec les collègues cliniques et chercheurs du Canada. **Méthode:** MA VIE comprend 263 enfants (de 2 à 16 ans) souffrant d'une maladie physique recrutés à

¹School of Public Health and Health Systems, University of Waterloo, Waterloo, Ontario

²Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario

³Department of Pediatrics, McMaster University, Hamilton, Ontario

⁴Department of Psychology, University of Zurich, Zurich, Switzerland

⁵Jacobs Center for Productive Youth Development, University of Zurich, Zurich, Switzerland

Corresponding E-mail: mark.ferro@uwaterloo.ca

Submitted: June 12, 2020; Accepted: November 12, 2020

l'hôpital pour enfants de McMaster, leur principal parent aidant, et leurs frères et sœurs les plus rapprochés en âge. Les participants sont suivis par une collecte de données lors du recrutement, à 6, 12, et 24 mois, ce qui comporte des entrevues structurées, des mesures auto-déclarées, et des échantillons biologiques qui sont prélevés dans un bureau privé de la recherche ou au domicile de participants. La collecte de données post-COVID-19 a effectué une transition par la poste et les sondages par téléphone. **Résultats:** Lors du recrutement, les enfants avaient 9,4 (4,2) ans et 52,7 % étaient de sexe masculin. La durée moyenne de leur maladie physique était de 4,5 (4,1) ans; 25 % représentaient des cas incidents (durée < 1 an). La plupart (69,7 %) avait un poids corporel sain et une intelligence dans la moyenne (73,5 %). En général, 38,2 % des enfants avaient un dépistage positif pour ≥ 1 maladie mentale selon le rapport des parents (24,8 % avaient un dépistage positif selon l'auto-déclaration des enfants). Comparativement aux données du recensement de 2016, la cohorte MA VIE surreprésente les familles de statut socio-économique plus élevé. **Conclusions:** La multimorbidité est commune chez les enfants et ces données de départ serviront à mesurer les changements relatifs de la santé mentale des enfants souffrant de maladie physique avec le temps. MA VIE fournira de nouvelles informations pour comprendre la multimorbidité chez les enfants, quoique la sous-représentation des familles au faible statut socio-économique puisse avoir des implications pour la généralisabilité des résultats.

Mots clés: adolescent; enfant, maladie chronique; étude longitudinale; maladie mentale, maladie physique

Background and Rationale for the Cohort

The co-occurrence of physical and mental illness—multimorbidity—is common in children, with prevalence estimates of 20%-30% in epidemiological and $\geq 50\%$ in clinical samples (Butler et al., 2018; Ferro, 2016; Tegethoff, Belardi, Stalujanis, & Meinschmidt, 2015). The Multimorbidity in Children and Youth across the Life-course (MY LIFE) study was established to address the needs of this understudied population and the health professionals who provide their care (Ferro, Lipman, Van Lieshout, Gorter, et al., 2019). MY LIFE was guided by our integration of the Stress Process Model (Pearlin, 1989, 1999; Pearlin, Lieberman, Menaghan, & Mullan, 1981; Pearlin, Schieman, Fazio, & Meersman, 2005) and the Behavioral Model of Health Services Use (Andersen, 1995, 2008; Andersen & Newman, 1973), which conceptualized the predisposing, enabling, and need influences on health (i.e., multimorbidity) and behaviours (i.e., mental health service use). Through the relations among predisposing, enabling, and need factors, we can elucidate potential causal mechanisms leading to the onset of multimorbidity and identify potential targets for intervention. Within this conceptual framework, MY LIFE was designed with a multi-level (individual, family, community), multi-method (structured interviews, questionnaires, linkage to administrative records, biological assessments), and multi-informant (child, parent) approach to data collection. The selection of measures was informed by our pilot study and consideration of administration time, participant burden, relevance across developmental periods, and psychometric properties, particularly in the subpopulation

of families who have a child with a physical or mental illness (Butler et al., 2018). A summary of the health-related constructs and associated questionnaires (e.g., intelligence testing) used in MY LIFE is shown in Table 1.

MY LIFE is designed to provide solutions to five main knowledge gaps in child multimorbidity research. First, with rare exceptions, clinical studies have been small, cross-sectional in design, and have focused on a single physical illness (Jones et al., 2017; Reaume & Ferro, 2019). MY LIFE recruited a sample of children with a variety of physical illnesses and their families and are being followed prospectively. This will increase the generalizability of findings, provide novel information on the natural course of multimorbidity, and inform opportunities for preventive interventions. For instance, primary interventions aiming to prevent the onset of mental comorbidity in children with physical illness by adopting routine mental health screening soon after diagnosis; secondary interventions to reduce symptoms in children with subclinical symptoms by focusing on positive mental health; and, tertiary interventions to improve function in children with multimorbidity with comprehensive mental health services.

Second, previous studies have typically assessed symptoms of psychopathology, but were unable to generate diagnoses of mental illness (Pinquart & Shen, 2011a, 2011b, 2011c). MY LIFE implemented a multi-method (e.g., measures of physiological and psychological stress for both children and parents; accelerometers to measure habitual physical activity), multi-informant (e.g., child and parent reports on questionnaires; linkage with administrative data) approach to assess mental illness in children at both the symptom and

Table 1. Summary of questionnaires and scales included in MY LIFE			
Construct	Measure or description	Informant	Internal consistency (α)
Child psychopathology	Mini International Neuropsychiatric Interview for Children and Adolescents ^a (Sheehan et al., 2010)	Child Parent	N/A
	Ontario Child Health Study Emotional Behavioural Scales (Boyle, Duncan, et al., 2019; Duncan et al., 2019)	Child Parent	0.66-0.87 0.82-0.92
	Strengths and Difficulties Questionnaire (Goodman, 2001)	Parent	0.63-0.81
Child psychosocial health	KIDSCREEN-27 (Oltean & Ferro, 2019; Qadeer & Ferro, 2018; Ravens-Sieberer et al., 2007; Tompke & Ferro, 2019)	Child Parent	0.74-0.87 0.76-0.88
	Self-Description Questionnaire (Ferro & Boyle, 2013; Marsh, 1992)	Child	0.83
	Self Perception Profile for Children (Ferro & Tang, 2017; Harter, 2012)	Child	0.82-0.89
Child physical health	World Health Organization Disability Assessment Schedule 2.0 (Kimber, Rehm, & Ferro, 2015; Tompke et al., 2020; Üstün, Kostanjsek, Chatterji, & Rehm, 2010)	Child Parent	0.84 0.87
	Kaufmann Brief Intelligence Test, second edition ^a (Bain & Jaspers, 2010)	Child	N/A
Parent psychopathology	Center for Epidemiological Studies Depression Scale (Radloff, 1977)	Parent	0.92
	Generalized Anxiety Disorder 7 (Spitzer, Kroenke, Williams, & Lowe, 2006)	Parent	0.87
Parent quality of life	Short Form-36 (Ware, Snow, Kosinski, & Gandek, 1993)	Parent	0.82-0.93
Family environment	McMaster Family Assessment Device (Byles, Byrne, Boyle, & Offord, 1988)	Parent	0.86
	Parental Stress Scale (J. O. Berry & Jones, 1995; Zelman & Ferro, 2018)	Parent	0.85
	Sibling Inventory of Differential Experience (Daniels & Plomin, 1985)	Child	0.73
School environment and peers	Items from 2014 Ontario Child Health Study assessing school climate, bullying, extracurricular activities (Boyle, Georgiades, et al., 2019)	Child	N/A
Mental health services	Items from 2014 Ontario Child Health Study assessing access and use of services (Boyle, Georgiades, et al., 2019)	Parent	N/A
Sociodemographics	Items from Statistics Canada	Parent	N/A
Only children ≥ 10 years of age complete self-reported measures. All measures were completed at each measurement occasion, with the exception of the Kaufmann Brief Intelligence Test, second edition, which was administered once, at baseline, or at the first follow-up after the child turned four years of age.			
^a Research staff-led structured interview.			

diagnostic level. This approach will inform allocation of mental health resources.

Third, little is known about mechanisms implicated in the development of multimorbidity, and particularly how the interplay of biological and psychosocial processes interact in the onset of child multimorbidity (Buske-Kirschbaum et al., 2013; Ferro, 2015; Ferro & Boyle, 2015; Ferro & Gonzalez, 2020; Kornelsen, Buchan, Gonzalez, & Ferro, 2019). MY LIFE measures multiple markers of inflammation, stress, physical activity, gross motor functioning, and contextual factors at multiple levels (e.g., family environment, sibling health, differential parenting, neighbourhood characteristics). Accordingly, a more comprehensive understanding of the development of multimorbidity will be ascertained and targets for intervention identified.

Fourth, despite the large increase in the use of mental health services among children in the past decade (Gandhi et al., 2016), it is unclear whether multimorbidity impacts use patterns of such services (Ferro, Lipman, Van Lieshout, Boyle, et al., 2019). Through data linkage with health records, MY LIFE will generate knowledge of services use that can be disseminated to support children and families as they navigate the mental health system, as well as inform strategies to integrate physical and mental health services.

Fifth, the extent to which findings from clinical studies on child multimorbidity can be applied to the general population is unknown. MY LIFE has implemented many of same measures of mental, psychosocial, and family health used in the recently completed 2014 Ontario Child Health Study, a province-wide study of the mental health of Canadian youth, conducted by Statistics Canada. Thus, investigations can be undertaken to determine whether findings related to burden, risk factors, and outcomes of child multimorbidity are sample-dependent and thus, may inform the development of public health policies to reduce the incidence of child multimorbidity.

MY LIFE will build on previous research to document the natural course of mental illness (symptoms and diagnoses) in children diagnosed with a physical illness; identify predictors of multimorbidity; test whether these predictors are moderated by biological or psychosocial factors; explore potential mediating effects of inflammatory or stress response markers in the development of multimorbidity; examine the extent to which multimorbidity influences the use of mental health services; and, determine if findings are

sample-dependent in comparison to the 2014 Ontario Child Health Study.

This manuscript serves to provide an overview of the methods of the Multimorbidity in Children and Youth across the Life-course (MY LIFE) study, profile sample characteristics of the cohort, and provide baseline estimates of multimorbidity to foster collaboration with clinical and research colleagues across Canada. In profiling the cohort, we will make descriptive comparisons to 2016 Census data to determine the extent to which the cohort is representative of the population. Highlighting the prevalence of multimorbidity among children is important to establish the baseline from which the mental health of children with physical illness and their families may change over time. It is our aim that presenting these data in this descriptive format will facilitate collaboration with researchers and health professionals across Canada, and globally, to forward the agenda in child multimorbidity research.

Participants in the Cohort

The MY LIFE cohort is comprised of a sample of 263 children aged 2-16 years at the time of recruitment who have been diagnosed by a health professional with one chronic physical illness (e.g., asthma, diabetes, epilepsy, juvenile arthritis), as well as their primary caregiving parent or guardian (herein parent). Operationally, these are physical illnesses that are expected to be present for ≥ 12 months (i.e., chronic) and result in ≥ 1 of the following: 1—functional limitations; 2—dependencies to compensate for functional limitations (e.g., medication, use of assistive devices); or, 3—need for additional health services. Children were recruited from McMaster Children's Hospital, an academic paediatric tertiary care centre, with a large catchment area covering much of southwestern and central Ontario—the most sociodemographically diverse regions of Canada's most populated province. Because evidence suggests that the risk for mental illness across different physical illnesses is negligible (suggesting some common underlying risk for multimorbidity) (Butler et al., 2018; Ferro, 2016), children were recruited from the outpatient clinics in the paediatric subspecialties of dermatology, endocrinology, gastroenterology, hematology, neurology, respirology, and rheumatology. Informed by our pilot study (Butler et al., 2018), the age range for inclusion in the MY LIFE cohort is intentionally broad to increase coverage and generalizability for those physical illnesses that are diagnosed early in life, as well as to ensure that during the follow-up of the cohort,

all participants continue to receive care in the paediatric health system (i.e., they have not yet transitioned to adult health services). Because health outcomes and service use among children with multiple chronic physical illnesses are already well-known, these individuals were excluded from the MY LIFE cohort (Berry et al., 2014; Cohen et al., 2012; Cohen & Patel, 2014). Likewise, children and parents without adequate English language skills were excluded, as the measures selected for use in MY LIFE have not all been validated in other languages.

A unique feature of the MY LIFE cohort is the inclusion of sibling data. In cases where participating children have a sibling within three years of age, parents report on the psychopathology and quality of life of siblings, and children with physical illness report on perceived differences between their and their sibling's relationship with their parents. The three-year age-gap criterion was chosen to ensure similarity of developmental periods for the two siblings (Pediatrics, 2020). Nearly two thirds (65.9%) of the MY LIFE cohort have eligible siblings whose data are being collected.

Results from our simulation studies suggested that a sample size of 250 children would provide adequate statistical power ($1-\beta \geq 0.80$) at $\alpha=0.05$ to accurately and reliably address our overall objectives for the MY LIFE cohort once all data are collected: estimate trajectories of psychopathology, model risk factors for multimorbidity, and test for mediating and moderating effects in the onset of multimorbidity.

Procedures and Follow-up

The MY LIFE cohort is being followed for 24 months with data collection at recruitment (baseline) and at 6, 12, and 24 months. *A priori* considerations for this follow up schedule were based on the timing of typical clinical follow ups for their physical illness, and allowing sufficient time between assessments to identify detectable changes in mental and psychosocial outcomes, as well as in biomarkers of inflammation and the stress response. Our previous experience suggested that a 24-month follow up would be adequate for detecting and modelling such changes in the MY LIFE cohort.

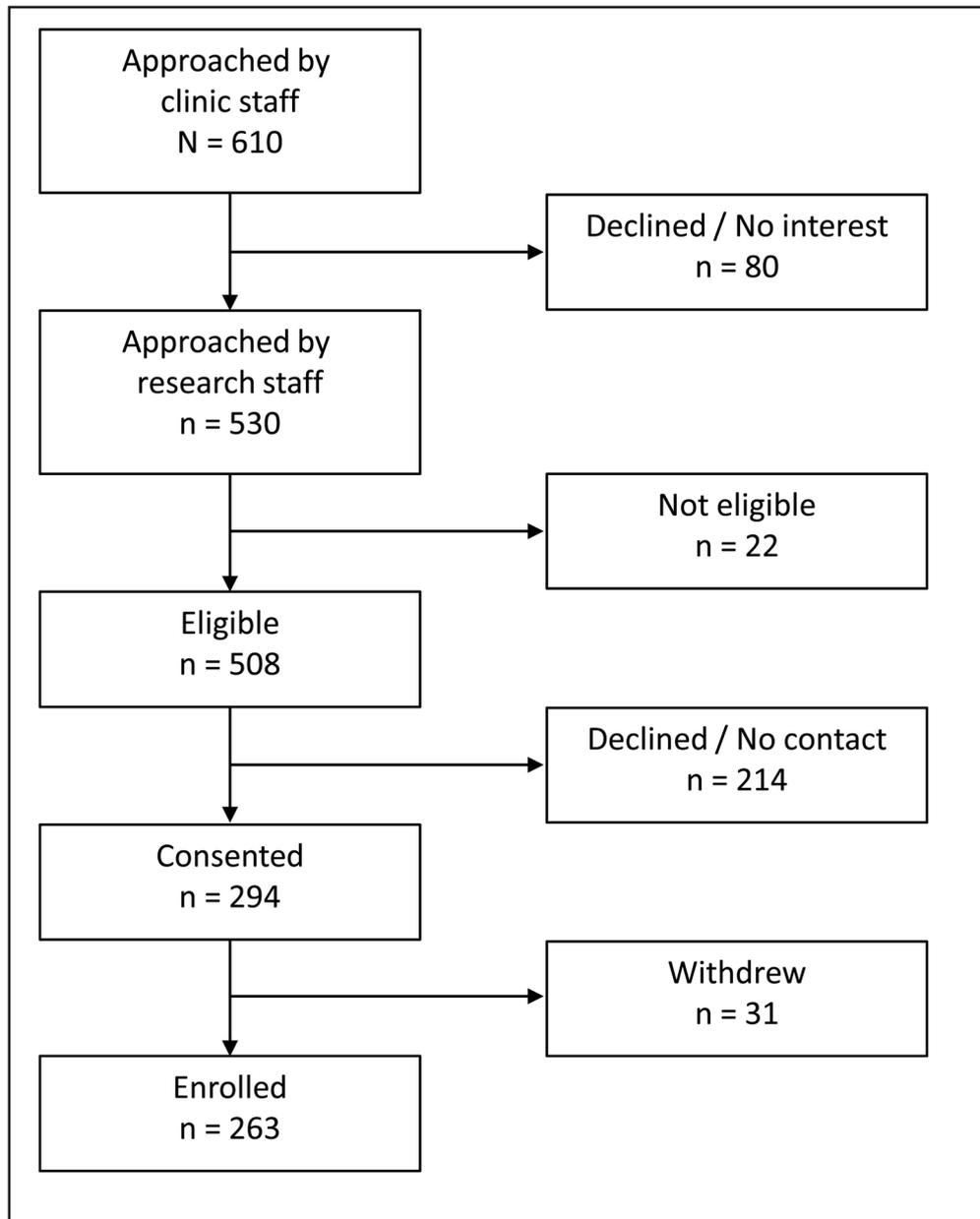
Recruitment into the MY LIFE cohort followed these steps: research staff worked with health professionals within the clinics to identify eligible children and families, whereby clinic nurses, either before or after the medical appointment, invited families to speak with research staff about enrolling

into MY LIFE. Research staff verified eligibility, described the study and what participation entailed, and obtained permission from interested families for the study manager to contact them a few days later to schedule the baseline data collection interview. Data collection includes structured interviews, self-reported measures, and biological samples and occur in a private research office within the hospital. Computer-assisted data collection is used to minimize data entry and coding errors, as well as minimize missing data. In rare situations prior to the COVID-19 pandemic (e.g., to accommodate travel, work schedules, or child care), research staff would conduct data collection interviews at families' homes or send out mail survey packages. In maintaining the MY LIFE cohort during the COVID-19 pandemic, all data collection was switched to mail surveys and telephone interviews in March 2020 to minimize risk exposure for participants and research staff, as well as support the social/physical distancing initiative. Prior to participation, informed written consent was obtained from all parents and children 16 years of age, whereas informed written assent was obtained from children 7-15 years of age. Oral assent was obtained from younger children in the MY LIFE cohort.

As shown in Figure 1, 610 children and their families were approached about MY LIFE in their respective clinics, of which 508 were eligible to enroll. In total, 57.9% of eligible families provided consent to participate and 51.8% enrolled and completed the baseline data collection (representing 89.4% of families who consented). By the end of the first follow-up (six months post-recruitment), 2.3% of children had withdrawn from MY LIFE. There were no differences in the sex or age distribution of children who did versus did not participate in MY LIFE [53% vs. 52% male; Mean (SD) 9.4 (4.2) vs. 9.4 (4.3) years]. These findings were robust when stratifying on *when* families declined participation (e.g., declined to speak to research staff in clinic, declined participation after eligibility screening).

Measurement

The primary outcome in MY LIFE is child mental illness which is assessed using a structured interview and self-reported measure. First, the Mini International Neuropsychiatric Interview for Children and Adolescents is a diagnostic interview that measures mental illness in the past six months according to the Diagnostic and Statistical Manual of Mental Disorders v5 and International Statistical Classification of Diseases and Health Related Problems v10

Figure 1. MY LIFE participant recruitment chart

(Boyle et al., 2017; Duncan et al., 2018; Sheehan et al., 2010). The modules that assess major depressive episode, generalised, separation, and social anxiety, specific phobia, attention-deficit hyperactivity, oppositional defiant, and conduct disorders are used in MY LIFE, as these represent the most common mental illnesses affecting children (Georgiades et al., 2019). Second, the Ontario Child Health Study Emotional Behavioural Scales is a self-reported checklist measuring child psychopathology in the past six months (Boyle, Duncan, et al., 2019; Duncan et al., 2019). In addition to summing total, internalizing, and externalizing

symptomatology scores, subscale scores for major depressive episode, generalised and separation anxiety, social phobia, attention-deficit hyperactivity, oppositional defiant, and conduct disorder are computed.

Biological assessments within the MY LIFE cohort focus on indicators of inflammation, stress, gross motor functioning, and physical activity. Blood specimens—whole blood and dried blood spots—are collected from children at each assessment to assay levels of proinflammatory cytokines that may mediate the development of multimorbidity.

These cytokines include tumour necrosis factor α , interleukin 1 β , interleukin 6, and C-reactive protein. Whole blood is collected from children ≥ 10 years of age at the hospital laboratory by a phlebotomist and then processed and stored by research staff. Of the 120 age-eligible children, 41.7% provided a baseline whole blood sample. All children are eligible to provide dried blood spots. Collected by research staff, 35.7% of children provided baseline dried blood spots. Both types of blood specimens will be assayed using high sensitivity ELISA and samples are stored at -80°C to permit analysis of additional cytokines as the field moves forward. Blood specimens are not collected during study visits that occur in participants' homes or when mail surveys are used.

Hair samples are also collected at each assessment from children (88.6%) and parents (89.0%) to measure hair cortisol concentration as an indicator of chronic physiological stress and potential mediator of multimorbidity onset. Extracting cortisol from hair is a non-invasive procedure (hair is cut close to, not pulled from the scalp) making it agreeable to children and parents. Samples can be stored at room temperature prior to processing, which permits sampling at home and submission to our research office in postal envelopes. Factors thought to influence hair cortisol concentrations (e.g., hair washes per week, chemical processes, smoke exposure) are collected on a standard form reported by parents. On account of the COVID-19 pandemic, blood and hair specimens remain in storage and have yet to be assayed.

The Peabody Developmental Motor Scale, second edition is being administered at each data collection to children aged 2-5 years in order to conduct sub-studies comparing the gross motor functioning of this subgroup within the MY LIFE cohort to population norms (Folio & Fewell, 2000). Relatedly, children in the MY LIFE cohort are provided with an accelerometer at each assessment, which is to be worn for seven consecutive days to measure the duration, intensity, and frequency of movement (i.e., habitual physical activity). Thresholds for levels of physical activity have been validated and will be used to examine the extent to which physical activity moderates the association between physical and mental illness in children (Takken et al., 2010). Finally, height (standing and sitting) and weight are measured using a standardized protocol to calculate body mass index percentiles for the MY LIFE cohort of children.

As part of the baseline assessment, parents were asked to provide their child's health insurance number and consent

to linking their MY LIFE study data to their records in existing health care administrative databases. These linkage activities will permit more comprehensive examinations of the patterns of mental health service use for children in the MY LIFE cohort with multimorbidity and whether these patterns differ compared to children with mental, but not physical illnesses, in the population. In total, 89.4% of the MY LIFE cohort provided their health insurance number.

Sample Characteristics

Sociodemographic and health-related characteristics of the MY LIFE cohort are shown in Table 2. Children were, on average, Mean (SD): 9.4 (4.2) years of age and 52.7% were male. The majority of children were born in Canada (93.9%). The most common diagnoses were rheumatological (27.8%), respiratory (20.5%), and endocrine (14.4%). The mean duration of their physical illness was 4.5 (4.1) years at baseline, with 25% of the cohort representing incident cases (i.e., duration < 1 year). Over two thirds (69.7%) had a healthy body weight and 73.5% had intelligence in the average range.

The majority of parents were biological mothers (87.8%). The mean age of parents was 40.4 (6.5) years and 15.3% were immigrants to Canada. Families generally represented high socioeconomic status—87.0% were partnered (married or common law), 76.0% had obtained postsecondary education, and 59.9% reported annual household incomes of $\geq \$90,000$ (median income for > 1 -person households; Statistics Canada, 2016). Data from the 2016 Canadian Census data were used to describe the characteristics of families within the catchment area of our recruitment site (Canada, 2016). Census data showed that while the proportion of families with > 1 child was similar to MY LIFE (61.6% vs. 65.9%), the distribution of parent age was different; 38.5% of the general population were aged 30-49 years versus 90.0% within MY LIFE. This was expected given the age criteria for participation in MY LIFE. Other notable differences with the general population included the proportion of immigrants (24.7%), partnered parents (54.9%), and postsecondary education (52.4%). It is important contextualize these differences; Census data represents the general population and not our target population of families who have a child with a physical illness.

With regards to our primary outcome, 24.8% of the MY LIFE cohort screened positive for ≥ 1 mental illness (using the Mini International Neuropsychiatric Interview) according to child self-reports. This proportion was higher for

Table 2. Selected sociodemographic and health-related characteristics of MY LIFE participants				
Characteristic	Response option	n	% ^a	Missing
Child (n=263)				
Sex	Male	138	52.7	1 (0.4%)
Age (years)	2-4	51	19.4	0 (0.0%)
	5-7	55	20.9	
	8-10	61	23.2	
	11-13	45	17.1	
	14-16 ^b	51	19.4	
Country of birth	Born in Canada	246	93.9	1 (0.4%)
Diagnosis	Dermatological	23	8.7	0 (0.0%)
	Endocrine	38	14.4	
	Gastroenterological	34	12.9	
	Hematological	29	11	
	Neurological	12	4.6	
	Respiratory	54	20.5	
	Rheumatological	73	27.8	
Years since diagnosis	<1.0	63	25	11 (4.2%)
	1.0 to <2.5	37	14.7	
	2.5 to <5.0	54	21.4	
	5.0 to <7.5	46	18.3	
	≥7.5	52	20.6	
Body mass index ^c	Underweight (<5th percentile)	11	4.5	19 (7.2%)
	Healthy weight (5th to <85th percentile)	170	69.7	
	Overweight (85th to <95th percentile)	32	13.1	
	Obese (≥95th percentile)	31	12.7	
Composite IQ	Lower extreme (≤69)	3	1.3	29 (11.0%) ^d
	Below average (70-84)	9	3.8	
	Average (85-115)	172	73.5	
	Above average (116-130)	47	20.1	
	Upper extreme (≥131)	3	1.3	
Parent (n=263)				
Sex	Female	235	89.7	1 (0.4%)
Age (years)	20-29	11	4.2	2 (0.8%)
	30-39	115	44.1	
	40-49	120	46	
	50-59	13	5	
	60-69	2	0.8	
Relation to child	Biological parent	257	98.1	1 (0.4%)
Country of birth	Born in Canada	222	84.7	1 (0.4%)
Marital status	Married	202	77.1	1 (0.4%)
	Common law	26	9.9	
	Widowed	2	0.8	
	Separated	12	4.6	
	Divorced	10	3.8	
	Never married	10	3.8	

continued

Table 2. Continued				
Characteristic	Response option	n	% ^a	Missing
Education	Never married	10	3.8	1 (0.4%)
	Some secondary	7	2.7	
	Secondary graduate	46	17.6	
	Vocational/Technical graduate	10	3.8	
	Post-secondary graduate	150	57.3	
	Graduate/Professional school graduate	49	18.7	
Household income	≤\$29 999	23	8.8	3 (1.1%)
	\$30 000-\$59 999	29	11.2	
	\$60 000-\$89 999	52	20	
	\$90 000-\$119 999	35	13.5	
	\$120 000-\$149 999	46	17.7	
	≥\$150 000	85	32.7	
Sibling (n=169)				
Sex	Male	79	46.7	89 (33.8%) ^e
Age (years)	0-4	33	19.4	89 (33.8%) ^e
	5-7	32	18.8	
	8-10	38	22.4	
	11-13	32	18.8	
	14-18	35	20.6	
	^a Refers to valid percent, which excludes participants with missing data in the denominator. ^b Includes one child who was 16 years at the time of recruitment into MY LIFE, but turned 17 years at the time of the baseline data collection. ^c Percentiles based on the Centers for Disease Control in the United States. ^d Includes 18 children not yet old enough (<4 years) to complete the Kaufmann Brief Intelligence Test, second edition. These children will complete the test at the first follow-up at which they are age eligible. ^e Represents valid missingness; that is, the participating child did not have an eligible sibling.			

Table 3. Prevalence of multimorbidity		
	Parent report (n=263)	Child report (n=117)
Mental illness	n (%)	n (%)
Any	101 (38.4)	29 (24.8)
Internalizing		
Major depressive episode	21 (8.0)	13 (11.1)
Generalized anxiety disorder	28 (10.7)	10 (8.5)
Separation anxiety disorder	22 (8.4)	9 (7.7)
Social phobia	23 (8.8)	3 (2.6)
Specific phobia	25 (9.8)	9 (7.7)
Externalizing		
Attention-deficit hyperactivity disorder	41 (15.6)	11 (9.4)
Oppositional defiant/conduct disorder	17 (6.5)	3 (2.6)
Mental illness was measured using the Mini International Neuropsychiatric Interview for Children and Adolescents. Children ≥10 years of age were eligible to provide self-reported responses to the Mini International Neuropsychiatric Interview for Children and Adolescents. Data are n (%).		

Children and Adolescents, 38.2%, according to parent report. As shown in Table 3, comorbidity of mental illnesses was common in this sample of children.

Strengths and Weaknesses

There are four main strengths of MY LIFE that distinguishes it from other cohorts. First, it has a sample size that is adequately powered to assess changes in mental health over time, model potential mediating and moderating effects, and compare outcomes across different physical illnesses. Should findings replicate previous preliminary findings that differences in risk for mental illness across different physical illnesses is negligible (Butler et al., 2018; Ferro, 2016), aggregated analyses will allow the identification of common determinants, mechanism, and outcomes of child multimorbidity. These critical findings can then inform strategies to reduce the incidence of multimorbidity in children. Second, the rigorous assessment of multimorbidity and relevant covariates, including the integration of multi-level biological and psychosocial measures, will result in the most comprehensive understanding of child multimorbidity to date. Further, this information will help elucidate the mechanisms leading to the onset and persistence of multimorbidity and inform targets for intervention. Third, the large proportion of incident cases (i.e., children who were recruited into MY LIFE within the first year of their physical illness diagnosis) will allow for the identification of periods of elevated vulnerability for multimorbidity and inform windows of opportunity for the appropriate level of intervention. Comparisons with sibling controls will contribute novel information about the natural course of psychopathology for children newly diagnosed with a physical illness. Fourth, extensive data linkage opportunities will generate critical information to help families navigate the health care system, optimize the provision of mental health services, and inform integrated physical and mental health care models.

Limitations surrounding the MY LIFE cohort should also be highlighted. Most notably, recruitment from a single site and including only individuals with adequate English language skills (many measures have only been validated in English) may limit the generalizability of the MY LIFE cohort and subsequent inferences from this cohort to inform interventions aimed at reducing child multimorbidity. Similarly, selection bias may be present given the relatively affluent socioeconomic characteristics reported by parents. While initial evidence suggests that attrition within MY LIFE is very low, missing blood specimen data were higher.

Analyses that examine factors associated with such missingness are needed to assess the extent to which inferences using blood specimen data are biased. Further, the 24-month follow-up may be of inadequate length to determine the natural course of many mental illnesses in the youngest participants. Likewise, if evidence suggests that risk for mental illness is different across physical illness classifications, stratified analyses that are illness-specific may be underpowered. At the start of MY LIFE, a number of child mental health services were funded by the Ministry of Children, Community and Social Services (MCCSS), which are not included in the administrative datasets in which we will link MY LIFE data. Our previous experience has shown that linkage with MCCSS is not possible and thus, parents are asked directly to report on the MCCSS-funded mental health services their children utilize. The shift to mail surveys in response to the COVID-19 pandemic may result in substantial loss of biological data in future follow ups as blood specimens are not collected with this approach. It may also skew the natural course of multimorbidity given the expectation that this crisis will increase symptoms of psychopathology and increase risk for mental illness.

Data Availability

Research ethical approval for MY LIFE does not permit the public sharing of study data. However, requests to access data from the MY LIFE cohort should be made in writing by contacting the corresponding author by email to initiate discussions regarding potential research projects.

Acknowledgements

We acknowledge the children, parents, health professionals, and clinic staff without whose participation MY LIFE would not be possible. We thank Jessica Zelman, Robyn Wojcicki, and Charlene Attard for coordinating the study. Health professionals who facilitated recruitment were Drs. Michelle Batthish, Tania Cellucci, Liane Heale, Karen McAssey, Linda Pedder, Anthony Chan, Mihir Bhatt, Elyanne Ratcliffe, Mary Sherlock, Robert Issenman, Mary Zachos, Herbert Brill, Nikhil Pai, Susan Wasserman, Herminio Lima, Brandon Meaney, and Gabriel Ronen. MY LIFE was funded by the Canadian Institutes of Health Research (PJT-148602). Drs. Ferro, Van Lieshout, and Timmons are funded by the Canada Research Chairs Program. Dr. Ferro is the recipient of the Early Researcher Award from the Ministry of Research, Innovation and Science. Dr. Van Lieshout holds the Albert Einstein/Irving Zucker Chair in Neuroscience, Dr. Gorter holds the Scotiabank Chair in

Child Health Research, and Dr. Georgiades holds the Dan Offord Chair in Child Studies.

Conflicts of Interest

The authors have no financial relationships to disclose.

References

- American Academy of Pediatrics (2020). Ages & stages. Retrieved from <https://www.healthychildren.org/English/ages-stages/Pages/default.aspx>
- Andersen, R. (1995). Revisiting the behavioral model and access to medical care: Does it matter? *Journal of Health and Social Behavior*, 36(1), 1-10.
- Andersen, R. (2008). National health surveys and the behavioral model of health services use. *Medical Care*, 46(7), 647-653. doi:10.1097/MLR.0b013e31817a835d
- Andersen, R., & Newman, J. F. (1973). Societal and individual determinants of medical care utilization in the United States. *The Milbank Memorial Fund Quarterly: Health and Society*, 51(1), 95-124.
- Bain, S. K., & Jaspers, K. E. (2010). Kaufman Brief Intelligence Test, 2nd edition. *Journal of Psychoeducational Assessment*, 28(2), 167-174. doi:10.1177/0734282909348217
- Berry, J. G., Hall, M., Neff, J., Goodman, D., Cohen, E., Agrawal, R.,... Feudtner, C. (2014). Children with medical complexity and Medicaid: Spending and cost savings. *Health Affairs (Millwood)*, 33(12), 2199-2206. doi:10.1377/hlthaff.2014.0828
- Berry, J. O., & Jones, W. H. (1995). The Parental Stress Scale: Initial psychometric evidence. *Journal of Social and Personal Relationships*, 12(3), 463-472.
- Boyle, M. H., Duncan, L., Georgiades, K., Bennett, K., Gonzalez, A., Van Lieshout, R. J.,...Janus, M. (2017). Classifying child and adolescent psychiatric disorder by problem checklists and standardized interviews. *International Journal of Methods in Psychiatric Research*, 26(4), e1544. doi:10.1002/mpr.1544
- Boyle, M. H., Duncan, L., Georgiades, K., Wang, L., Comeau, J., Ferro, M. A.,...Kata, A. (2019). The 2014 Ontario Child Health Study Emotional Behavioural Scales (OCHS-EBS) Part II: Psychometric Adequacy for Categorical Measurement of Selected DSM-5 Disorders. *Canadian Journal of Psychiatry*, 64(6), 434-442. doi:10.1177/0706743718808251
- Boyle, M. H., Georgiades, K., Duncan, L., Comeau, J., Wang, L., & 2014 Ontario Child Health Study Team (2019). The 2014 Ontario Child Health Study-Methodology. *Canadian Journal of Psychiatry*, 64(4), 237-245. doi:10.1177/0706743719833675
- Buske-Kirschbaunn, A., Schmitt, J., Plessow, F., Romanos, M., Weidinger, S., & Roessner, V. (2013). Psychoendocrine and psychoneuroimmunological mechanisms in the comorbidity of atopic eczema and attention deficit/hyperactivity disorder. *Psychoneuroendocrinology*, 38(1), 12-23. doi:10.1016/j.psyneuen.2012.09.017
- Butler, A., Van Lieshout, R. J., Lipman, E. L., MacMillan, H. L., Gonzalez, A., Gorter, J. W.,...Ferro, M. A. (2018). Mental disorder in children with physical conditions: A pilot study. *BMJ Open*, 8(1), e019011. doi:10.1136/bmjopen-2017-019011
- Byles, J., Byrne, C., Boyle, M. H., & Offord, D. R. (1988). Ontario Child Health Study: Reliability and validity of the general functioning subscale of the McMaster Family Assessment Device. *Family Process*, 27(1), 97-104.
- Cohen, E., Berry, J. G., Camacho, X., Anderson, G., Wodchis, W., & Guttman, A. (2012). Patterns and Costs of Health Care Use of Children With Medical Complexity. *Pediatrics*, 130(6), e1463-e1470.
- Cohen, E., & Patel, H. (2014). Responding to the rising number of children living with complex chronic conditions. *CMAJ*, 186(16), 1199-1200. doi:10.1503/cmaj.141036
- Daniels, D., & Plomin, R. (1985). Differential experience of siblings in the same family. *Developmental Psychology*, 21(5), 747-760.
- Duncan, L., Boyle, M., Ferro, M. A., Georgiades, K., Van Lieshout, R. J., Bennett, K.,...Szatmari, P. (2018). Psychometric evaluation of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). *Psychological Assessment*, 30(7), 916-928. doi:10.1037/pas0000541
- Duncan, L., Georgiades, K., Wang, L., Comeau, J., Ferro, M. A., Van Lieshout, R. J.,...Boyle, M. H. (2019). The 2014 Ontario Child Health Study Emotional Behavioural Scales (OCHS-EBS) Part I: A Checklist for Dimensional Measurement of Selected DSM-5 Disorders. *Canadian Journal of Psychiatry*, 64(6), 423-433. doi:10.1177/0706743718808250
- Ferro, M. A. (2015). Mediated moderation of the relation between maternal and adolescent depressive symptoms: Role of adolescent physical health. *Social Psychiatry and Psychiatric Epidemiology*, 50(11), 1743-1751. doi:10.1007/s00127-015-1103-5
- Ferro, M. A. (2016). Major depressive disorder, suicidal behaviour, bipolar disorder, and generalised anxiety disorder among emerging adults with and without chronic health conditions. *Epidemiology and Psychiatric Science*, 25(5), 462-474. doi:10.1017/S2045796015000700
- Ferro, M. A., & Boyle, M. H. (2013). Longitudinal invariance of measurement and structure of global self-concept: A population-based study examining trajectories among adolescents with and without chronic illness. *Journal of Pediatric Psychology*, 38(4), 425-437. doi:10.1093/jpepsy/jss112
- Ferro, M. A., & Boyle, M. H. (2015). The impact of chronic physical illness, maternal depressive symptoms, family functioning, and self-esteem on symptoms of anxiety and depression in children. *Journal of Abnormal Child Psychology*, 43(1), 177-187. doi:10.1007/s10802-014-9893-6
- Ferro, M. A., & Gonzalez, A. (2020). Hair cortisol concentration mediates the association between parent and child psychopathology. *Psychoneuroendocrinology*, 114, 104613. doi:10.1016/j.psyneuen.2020.104613
- Ferro, M. A., Lipman, E. L., Van Lieshout, R. J., Boyle, M. H., Gorter, J. W., MacMillan, H. L.,...Georgiades, K. (2019). Mental-physical multimorbidity in youth: Associations with individual, family, and health service use outcomes. *Child Psychiatry and Human Development*, 50(3), 400-410.
- Ferro, M. A., Lipman, E. L., Van Lieshout, R. J., Gorter, J. W., Shanahan, L., Boyle, M.,...Timmons, B. (2019). Multimorbidity in children and youth across the life-course (MY LIFE): Protocol of a Canadian prospective study. *BMJ Open*, 9(11), e034544. doi:10.1136/bmjopen-2019-034544
- Ferro, M. A., & Tang, J. (2017). Psychometric properties of the Self-Perception Profile for Children in children with chronic physical conditions. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, 26(2), 119-124.
- Folio, M. R., & Fewell, R. R. (2000). *Peabody developmental motor scales: Examiner's manual*. Austin: Pro-ed.
- Gandhi, S., Chiu, M., Lam, K., Cairney, J. C., Guttman, A., & Kurdyak, P. (2016). Mental Health Service Use Among Children and Youth in Ontario: Population-Based Trends Over Time. *Canadian Journal of Psychiatry*, 61(2), 119-124. doi:10.1177/0706743715621254
- Georgiades, K., Duncan, L., Wang, L., Comeau, J., Boyle, M. H., & Ontario Child Health Study, T. (2019). Six-Month Prevalence of Mental Disorders and Service Contacts among Children and Youth in Ontario: Evidence from the 2014 Ontario Child Health Study. *Canadian Journal of Psychiatry*, 64(4), 246-255. doi:10.1177/0706743719830024
- Goodman, R. (2001). Psychometric Properties of the Strengths and Difficulties Questionnaire. *Journal of the American Academy*

- of *Child and Adolescent Psychiatry*, 40(11), 1337-1345. doi:10.1097/00004583-200111000-00015
- Harter, S. (2012). *Self-Perception Profile for Children: Manual and Questionnaires*. Denver: University of Denver.
- Jones, L. C., Mrug, S., Elliott, M. N., Toomey, S. L., Tortolero, S., & Schuster, M. A. (2017). Chronic physical health conditions and emotional problems from early adolescence through midadolescence. *Academic Pediatrics*, 17(6), 649-655. doi:10.1016/j.acap.2017.02.002
- Kimber, M., Rehm, J., & Ferro, M. A. (2015). Measurement invariance of the WHODAS 2.0 in a population-based sample of youth. *PLoS One*, 10(11), e0142385.
- Kornelsen, E., Buchan, M. C., Gonzalez, A., & Ferro, M. A. (2019). Hair cortisol concentration and mental disorder in children with chronic physical illness. *Chronic Stress*, 3. doi:10.1177/2470547019875116
- Marsh, H. W. (1992). *Self-Description Questionnaire (SDQ) I: a theoretical and empirical basis for the measurement of multiple dimensions of preadolescent self-concept. An interim test manual and research monograph*. University of Western Sydney, Macarthur.
- Oltean, I. I., & Ferro, M. A. (2019). Agreement of child and parent-proxy reported health-related quality of life in children with mental disorder. *Quality of Life Research*, 28(3), 703-712. doi:10.1007/s11136-018-2026-x
- Pearlin, L. I. (1989). The sociological study of stress. *Journal of Health and Social Behavior*, 30(3), 241-256.
- Pearlin, L. I. (1999). The Stress Process Model revisited. In C. S. Aneshensel & J. C. Phelan (Eds.), *Handbook of the sociology of mental health*. New York: Kluwer Academic/Phenum Publishers.
- Pearlin, L. I., Lieberman, M. A., Menaghan, E. G., & Mullan, J. T. (1981). The stress process. *Journal of Health and Social Behavior*, 22(4), 337-356.
- Pearlin, L. I., Schieman, S., Fazio, E. M., & Meersman, S. C. (2005). Stress, health, and the life course: Some conceptual perspectives. *Journal of Health and Social Behavior*, 46(2), 205-219. doi:10.1177/002214650504600206
- Pinquart, M., & Shen, Y. (2011a). Anxiety in children and adolescents with chronic physical illnesses: A meta-analysis. *Acta Paediatrica*, 100(8), 1069-1076. doi:10.1111/j.1651-2227.2011.02223.x
- Pinquart, M., & Shen, Y. (2011b). Behavior problems in children and adolescents with chronic physical illness: A meta-analysis. *Journal of Pediatric Psychology*, 36(9), 1003-1016. doi:jsr042 [pii] 10.1093/jpepsy/jsr042
- Pinquart, M., & Shen, Y. (2011c). Depressive symptoms in children and adolescents with chronic physical illness: An updated meta-analysis. *Journal of Pediatric Psychology*, 36(4), 375-384. doi:jsq104 [pii] 10.1093/jpepsy/jsq104
- Qadeer, R. A., & Ferro, M. A. (2018). Child-parent agreement on health-related quality of life in children with newly diagnosed chronic health conditions: A longitudinal study. *International Journal of Adolescent Youth*, 23(1), 99-108. doi:10.1080/02673843.2017.1297242
- Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1(3), 385-401.
- Ravens-Sieberer, U., Auquier, P., Erhart, M., Gosch, A., Rajmil, L., Bruil, J.,...European, K. G. (2007). The KIDSCREEN-27 quality of life measure for children and adolescents: Psychometric results from a cross-cultural survey in 13 European countries. *Quality of Life Research*, 16(8), 1347-1356. doi:10.1007/s11136-007-9240-2
- Reaume, S. V., & Ferro, M. A. (2019). Chronicity of mental comorbidity in children with new-onset physical illness. *Child: Care, Health and Development*, 45(4), 559-567. doi:10.1111/cch.12667
- Sheehan, D. V., Sheehan, K. H., Shytle, R. D., Janavs, J., Bannon, Y., Rogers, J. E.,...Wilkinson, B. (2010). Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). *Journal of Clinical Psychiatry*, 71(3), 313-326. doi:10.4088/JCP.09m05305whi
- Spitzer, R. L., Kroenke, K., Williams, J. B., & Lowe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine*, 166(10), 1092-1097. doi:10.1001/archinte.166.10.1092
- Statistics Canada (2016). Census Program. Retrieved from <http://www12.statcan.gc.ca/census-recensement/index-eng.cfm>
- Takken, T., Stephens, S., Balemans, A., Tremblay, M. S., Esliger, D. W., Schneiderman, J.,...Feldman, B. M. (2010). Validation of the Actiheart activity monitor for measurement of activity energy expenditure in children and adolescents with chronic disease. *European Journal of Clinical Nutrition*, 64(12), 1494-1500. doi:10.1038/ejcn.2010.196
- Tegethoff, M., Belardi, A., Stalujanis, E., & Meinschmidt, G. (2015). Association between mental disorders and physical diseases in adolescents from a nationally representative cohort. *Psychosomatic Medicine*, 77(3), 319-332. doi:10.1097/PSY.0000000000000151
- Tompke, B. K., & Ferro, M. A. (2019). Measurement invariance and informant discrepancies of the KIDSCREEN-27 in children with mental disorder. *Applied Research on Quality of Life*, 10.1007/s11482-019-09801-5.
- Tompke, B. K., Tang, J., Oltean, I., Buchan, M. C., Reaume, S. V., & Ferro, M. A. (2020). Measurement invariance of the WHODAS 2.0 across youth with and without physical or mental conditions. *Assessment*, 27(7), 1490-1501. doi:10.1177/1073191118816435
- Üstün, T. B., Kostanjsek, N., Chatterji, S., & Rehm, J. (2010). *Measuring health and disability: manual for WHO Disability Assessment Schedule: WHODAS 2.0*. Geneva: World Health Organization.
- Ware, J. E., Snow, K. K., Kosinski, M., & Gandek, B. (1993). *SF-36 Health Survey manual and interpretation guide*. Boston: New England Medical Center, The Health Institute.
- Zelman, J. J., & Ferro, M. A. (2018). Psychometric properties of the Parental Stress Scale in families of children with chronic physical conditions. *Family Relations*, 67(April 2018), 240-252.