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## Mental Disorder in Children with Physical Conditions: A Pilot Study

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|---------------------------------|--|
| Journal:                        | <i>BMJ Open</i>  |
| Manuscript ID                   | bmjopen-2017-019011  |
| Article Type:                   | Research   |
| Date Submitted by the Author:   | 04-Aug-2017  |
| Complete List of Authors:       | Butler, Alexandra; University of Waterloo<br>Van Lieshout, Ryan ; McMaster University<br>Lipman, Ellen; McMaster University<br>MacMillan, Harriet; McMaster University<br>Gonzalez, Andrea; McMaster University<br>Gorter, Jan Willem; McMaster University<br>Georgiades, Kathy; McMaster University<br>Speechley, Kathy ; Western University,<br>Boyle , Michael ; McMaster University<br>Ferro, Mark; University of Waterloo, School of Public Health and Health Systems |
| <b>Primary Subject Heading</b>: | Mental health  |
| Secondary Subject Heading:      | Paediatrics  |
| Keywords:                       | multimorbidity, mental disorder, chronic disease, pilot study  |
|                                 |  |

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## Mental Disorder in Children with Physical Conditions: A Pilot Study

Butler A<sup>1</sup>, Van Lieshout RJ<sup>2</sup>, Lipman EL<sup>2</sup>, MacMillan HL<sup>2</sup>, Gonzalez A<sup>2</sup>, Gorter JW<sup>3</sup>, Georgiades K<sup>2</sup>,  
Speechley KN<sup>4,5</sup>, Boyle MH<sup>2</sup>, Ferro MA<sup>1,\*</sup>

[1] School of Public Health & Health Systems, University of Waterloo

[2] Department of Psychiatry & Behavioural Neurosciences, McMaster University

[3] Department of Pediatrics, McMaster University

[4] Department of Paediatrics, Western University

[5] Department of Epidemiology & Biostatistics, Western University

[\*] Corresponding author

### Contact information for corresponding author

Mark A. Ferro, University of Waterloo, School of Public Health and Health Systems, 200 University  
Avenue West, Waterloo, Ontario, Canada, N2L 3G1, Phone: 519.888.4567, Fax: 519.746.6776, Email:  
[mark.ferro@uwaterloo.ca](mailto:mark.ferro@uwaterloo.ca))

### Authors' contributions

MAF led the study. MAF, MHB, KNS, KG, JWG, AG, HLM, ELL, and RJV conceptualized and designed the study and were responsible for acquiring funding. MHB, KNS, KG, and AG provided methodological insights. JWG, HLM, ELL, and RJV provided clinical insights. KNS and HLM helped facilitate clinic participation. AB and MAF analyzed and interpreted data and drafted the manuscript. All authors critically reviewed and revised and then approved the final manuscript as submitted.

## Funding

This work was supported by the Canadian Institutes of Health Research (MOP-133645). At the time of the study, MAF was supported by a Research Early Career Award from Hamilton Health Sciences. MAF currently holds the Canada Research Chair in Youth Mental Health; MHB holds the Canada Research Chair in the Social Determinants of Child Health; KG holds the Dan Offord Chair in Child Studies (McMaster); JWG holds the Scotiabank Chair in Child Health Research (McMaster); AG is supported by a Canadian Institutes for Health Research New Investigator Award; HLM holds the Chedoke Chair in Child Psychiatry (McMaster); and, RJV holds the Albert Einstein/Irving Zucker Chair in Neuroscience.

## Competing interests

The authors declare that they have no competing interests.

## Data sharing statement

Data will not be shared in order to protect the confidentiality of participants. This was a multisite study and we do not have approval to make the data publically available.

## Acknowledgements

The authors gratefully acknowledge the children, parents, and health professionals and their staff without whose participation, this study would not have been possible. We especially thank Jane Terhaerd for assisting with ethical approval. Health professional contributors to this study were: Janice Falcone, Karen McAssey, Marilyn Rothney, Susan Wasserman (McMaster Children's Hospital) and Roberta Berard, Craig Campbell, Margo Devries-Rizzo, Michelle Diebold, Patti Guertjens, Simon Levin, Narayan Prasad (Children's Hospital London Health Sciences).

**Abstract**

**Objectives:** Methodologically, to assess the feasibility of participant recruitment and retention, as well as missing data in studying mental disorder among children newly-diagnosed with chronic physical conditions (i.e., multimorbidity). Substantively, to examine the prevalence of multimorbidity, identify sociodemographic correlates, and model the influence of multimorbidity on changes in child quality of life and parental psychosocial outcomes over a six-month follow-up.

**Design:** Pilot study.

**Setting:** Two children's tertiary hospitals.

**Participants:** Children aged 6-16 years diagnosed in the past six months with one of asthma, diabetes, epilepsy, food allergy, or juvenile arthritis and their parents.

**Outcome measures:** Response, participation, and retention rates. Child mental disorder using the Mini International Neuropsychiatric Interview at baseline and six months. Child quality of life, parental symptoms of stress, anxiety, and depression, and family functioning. All outcomes were parent reported.

**Results:** Response, participation, and retention rates were 90%, 83%, and 88%, respectively. Of the 50 children enrolled in the study, the prevalence of multimorbidity 58% at baseline and 42% at six months. No sociodemographic characteristics were associated with multimorbidity. Multimorbidity at baseline was associated with declines over six months in the following domains of quality of life: physical well-

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3 being,  $\beta=-4.82$  (-8.47, -1.17), psychological well-being,  $\beta=-4.10$  (-7.62, -0.58), and school environment,  
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5  $\beta=-4.17$  (-8.18, -0.16). There was no association with parental psychosocial outcomes over time.  
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10 **Conclusions:** Preliminary evidence suggests that mental disorder in children with a physical condition is  
11 very common and has a negative impact on quality of life over time. Based on the strong response rate  
12 and minimal attrition, our approach to study child multimorbidity appears feasible and suggests that  
13 and minimal attrition, our approach to study child multimorbidity appears feasible and suggests that  
14 multimorbidity is an important concern for families. Methodological and substantive findings from this  
15 pilot study have been used to implement a larger, more definitive study of child multimorbidity out of  
16 which should come important clinical implications.  
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For peer review only

### Strengths and limitations of this study

- This pilot study includes children newly-diagnosed with chronic physical conditions.
- This is the first study to examine child physical-mental multimorbidity across a number of different conditions.
- This study was likely underpowered to detect differences between children with and without multimorbidity and the small sample size limits generalizability.
- All outcomes were parent-reported.

## Introduction

The global prevalence of children with a chronic physical condition—a health problem that requires ongoing management over a period of years or decades—is common, affecting approximately 25% of children, and increasing.<sup>1</sup> Many of these children will be adversely affected by their disorders or their treatment, subsequently developing additional conditions, including mental disorders.<sup>2</sup> Compared to their peers with a physical or mental disorder only, children with multimorbidity (physical-mental comorbidity) experience greater symptom severity and impairment in both physical and mental health domains.<sup>3</sup> Understandably, the onset of multimorbidity remains an important concern for children, parents, health professionals, and payers.<sup>4</sup>

Mental disorders are common in children<sup>5</sup> and disproportionately affect children and young people with chronic physical conditions (herein physical conditions).<sup>6,7</sup> Estimates from clinical samples suggest that nearly half of children with physical conditions meet criteria for a mental disorder diagnosis.<sup>8</sup> In general population samples, this estimate is lower, with approximately 20-30% of children being affected.<sup>3</sup>

Evidence of the association between physical and mental health is robust,<sup>9-11</sup> but with few exceptions,<sup>7,12</sup> the literature base consists mostly of cross-sectional studies. This limits our understanding of mental health at the time children are diagnosed with a physical condition and how their mental health may change over time. One study found more parent-reported symptoms of problem behavior in children 6-7 years newly diagnosed with a chronic illness compared to healthy controls.<sup>7</sup> This effect was stable through to 10-11 years of age, highlighting the chronicity of multimorbidity in childhood. In a prospective study of children with diabetes, hazard ratios for mental disorder were highest within six-months of the diabetes diagnosis (3.0 [2.7-3.4]) compared to those with a duration of diabetes of five years or more (1.9 [1.7-2.1]), regardless of age at diagnosis,<sup>12</sup> suggesting that the peri-diagnostic period



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3 may be a time of particular mental health risk. While these studies have advanced the field,  
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5 opportunities exist to overcome the limitations in these studies associated with the ascertainment of  
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7 physical conditions based on parent-report,<sup>13</sup> assessment of symptoms of problem behaviors rather  
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9 than mental disorder,<sup>14,15</sup> and inherent weaknesses of using register-based data related to data quality  
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11 and variable availability.<sup>16</sup>  
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16 Existing research also suggests that physical conditions and mental disorders are independently  
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18 associated with poorer psychosocial outcomes including quality of life<sup>17,18</sup> and self-esteem,<sup>19,20</sup> as well as  
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20 academic performance.<sup>21,22</sup> These adverse effects can also extend to parents and families who  
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22 experience elevated stress and psychological distress, worse family functioning, and financial  
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24 hardship.<sup>23-26</sup> Effects on child and parent psychosocial outcomes appear similar when physical and  
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26 mental disorders are examined separately; however, there is little research examining whether  
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28 multimorbidity exerts a compounding effect. Cross-sectional evidence suggests that children with  
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30 multimorbidity experience worse quality of life compared to children with a physical or mental disorder  
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32 alone.<sup>27,28</sup> One prospective study showed that adults who experienced multimorbidity during  
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34 adolescence had lower quality of life compared to those who had a physical or mental disorder only.<sup>29</sup>  
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36 These researchers found that among those with multimorbidity, physical conditions affected physical  
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38 quality of life only; while their mental disorder negatively affected multiple domains of life quality,  
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40 including physical, emotional, and social well-being. The extent to which multimorbidity influences other  
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42 aspects of parental health and well-being, including parenting stress, psychopathology, and family  
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44 relationships, is unknown.  
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52 Despite the progress made in understanding child multimorbidity and its effects on psychosocial  
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54 outcomes, important knowledge gaps remain. First, the burden and correlates of multimorbidity,  
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3 particularly in clinical samples of children who represent the largest consumers of health services,<sup>30</sup> is  
4 not well known. This information is needed to inform resource allocation and the provision of services  
5 within the health system. Second, the timing of multimorbidity onset, how it changes, and its influence  
6 on psychosocial outcomes over time are not well-understood, limiting our ability to identify  
7 opportunities for intervention to prevent the development of mental disorder in children with physical  
8 conditions. This includes a lack of understanding how mental disorders may change or appear in relation  
9 to the onset of the physical condition. For example, are anxiety disorders more common at the time of  
10 diagnosis given the uncertainty surrounding prognosis? Third, effects of child multimorbidity on parental  
11 health and well-being have not been explored in much detail. Understanding these effects is key to  
12 designing, implementing, and evaluating family-centered approaches to care within the pediatric setting  
13 to promote the best possible health outcomes for children, parents, and families.<sup>31</sup>

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30 We conducted a pilot study to assess the feasibility of recruiting of eligible participants, estimating  
31 respondent burden related to data collection, and the extent of missing data and attrition.

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33 Substantively, the aims of the pilot study were to: 1—examine the initial prevalence of multimorbidity in  
34 a clinical sample of children newly-diagnosed with a physical condition, as well as rates six months later;  
35 2—identify correlates of multimorbidity in children and parents; and, 3—explore the influence of  
36 multimorbidity on changes in child quality of life and parental psychosocial outcomes over six-months of  
37 follow-up. We hypothesized that at the time of diagnosis 50% of children would screen positive for  
38 mental disorder (anxiety disorders being most common). Based on limited evidence,<sup>12</sup> we hypothesized  
39 that six months later, there would be a decrease in the proportion of multimorbidity (depressive  
40 disorder being most common). Finally, we hypothesized that socioeconomic disadvantage would be  
41 associated with multimorbidity; children with multimorbidity would have worse quality of life over time;  
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3 their parents, more symptoms of parenting stress, anxiety, and depression; and, their families, worse  
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5 functioning compared to children with physical conditions only.  
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## 10 **Methods**

### 11 **Sample**

12 Data come from the Researching Adolescent and Child Health Study (REACH), a multisite, prospective,  
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14 pilot study aimed at examining mental disorder(s) in children with physical conditions. Families were  
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16 recruited from two pediatric academic hospitals in Ontario, Canada to assess mental and psychosocial  
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18 outcomes in children with newly-diagnosed with physical conditions. Health professionals at the  
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20 hospitals were involved at the initial point of contact and provided eligible families with an overview of  
21  
22 the study and details regarding participation. The eligibility criteria for the study were children who: 1—  
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24 were aged 6-16 years old; 2—had received a diagnosis of asthma, diabetes, epilepsy, food allergy or  
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26 juvenile idiopathic arthritis within the six months prior to recruitment; and, 3—had a parent who could  
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28 read English. We aimed to recruit 60 children and families (12 per condition) over a 12-month period.  
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### 37 **Data Collection**

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39 After the medical encounter, eligible families were invited by clinic nurses to speak with research staff  
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41 about the study. Research staff briefly introduced the study and provided families an information letter.  
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43 Families interested in participating in the study consented for clinic nurses to send their contact  
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45 information to study investigators who then followed-up with families by telephone to confirm  
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47 eligibility, obtain oral consent from parents and children, and arrange for a convenient time to conduct a  
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49 telephone interview to assess child mental health. Parents also completed two mailed surveys to assess  
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51 psychosocial outcomes and demographic characteristics; one at baseline and one six months later, when  
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53 a second telephone interview to assess mental health was conducted. Parents of all participating  
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3 children provided proxy reports and children who were  $\geq 11$  years of age self-reported on the telephone  
4 interview and to the mail survey. Parents and children also consented to have health professionals  
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6 provide clinical information at the same measurement occasions. The study protocol received ethical  
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8 approval from the relevant research ethics boards.  
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## 11 12 13 14 **Measures**

### 15 16 *Mental disorder*

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18 Child mental disorder(s) were assessed using the Mini International Neuropsychiatric Interview for  
19 Children and Adolescents (MINI-KID).<sup>32</sup> The MINI-KID is a structured diagnostic interview used to assess  
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21 DSM-IV disorders in children aged 6-17 years and has been validated against the Schedule for Affective  
22  
23 Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version.<sup>32</sup> It is composed of  
24  
25 diagnostic modules that contain screening questions and skip patterns for each disorder. Phone  
26  
27 interviews were administered separately: the MINI-KID(c), to children  $\geq 11$  years; and the MINI-KID(p)  
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29 (proxy version) to all parents at both measurement occasions. The MINI-KID was administered by a  
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31 single interviewer who underwent training that included monitored practice. The presence of eight  
32  
33 current disorders was assessed: major depressive episode, separation anxiety disorder, social phobia,  
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35 specific phobia, generalized anxiety disorder, attention deficit/hyperactivity disorder, oppositional  
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37 defiant disorder, and conduct disorder. The MINI-KID has demonstrated strong test-retest reliability  
38  
39 compared to other instruments.<sup>14</sup> Mental disorder was classified according to parent reports on the  
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41 MINI-KID.  
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### 50 51 *Quality of life*

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53 Child quality of life between the two visits was measured using the KIDSCREEN-27,<sup>33</sup> a 27-item child and  
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55 parent-reported generic measure that assesses five domains: physical well-being (five items; examines  
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3 physical activity and energy), psychological well-being (seven items; examines emotional balance and  
4 life satisfaction), autonomy and parent relations (seven items; examines family dynamics and age-  
5 appropriate freedoms), social support and peers (four items; examines nature of peer relationships) and  
6 school environment (four items; examines perception of cognition, learning, and feelings about school).  
7 Responses are scored using a five-point Likert scale and domain scores are transformed into T-values  
8 with a mean of 50 and a standard deviation of 10 (higher scores indicate better quality of life). The  
9 KIDSCREEN-27 has been found to be valid and reliable in children with and without physical  
10 conditions<sup>33,34</sup> and demonstrated adequate agreement between children and parents.<sup>35</sup> Internal  
11 consistency reliabilities for each domain from this study were good for both child ( $\alpha=0.75-0.89$ ) and  
12 parent reports ( $\alpha=0.83-0.92$ ). Because only children  $\geq 11$  years self-reported the KIDSCREEN-27 ( $n=28$ ,  
13 56%), only parent-reported KIDSCREEN-27 scores were used in these analyses.  
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### 30 *Parental stress*

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32 The Parental Stress Scale (PSS) measures parental stress across the domains of rewards, stressors, loss  
33 of control, and satisfaction.<sup>36</sup> The 18 items are rated on a five-point Likert scale (eight items are reverse-  
34 coded) with higher scores (range: 18-90) indicating more parental stress. The psychometric properties of  
35 the PSS are robust: test-retest reliability ( $r=0.81$ ) and convergent validity with the Parenting Stress Index  
36 ( $r=0.75$ ) and Perceived Stress Scale ( $r=0.41$ ).<sup>36</sup> Internal consistency for the PSS in this study was  $\alpha=0.84$ .  
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### 46 *Parental anxiety*

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48 The State Trait Anxiety Inventory (STAI) is a widely used tool for measuring anxiety. Of the 40 questions  
49 in the STAI survey, REACH considered "trait anxiety" items only which aim to measure how parents  
50 generally feel, as well as their propensity for perceived anxiety.<sup>37</sup> Survey responses were scored from 1-4  
51 (seven items are reverse-coded). Scores were summed together (range: 20-80) with higher scores  
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3 indicating higher levels of anxiety. The STAI has robust psychometric properties, with trait-specific test-  
4 retest reliabilities of  $r=0.73-0.86$  and has been shown to be valid with other questionnaires used to  
5 assess anxiety ( $r=0.73-0.85$ ).<sup>37,38</sup> In this study, internal consistency for the STAI was  $\alpha=0.89$ .  
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### 10 11 12 *Parental depression*

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14 Parental symptoms of depression were measured with the Center for Epidemiological Studies  
15 Depression Scale (CES-D), a 20-item scale designed to assess depressive symptomatology in the general  
16 adult population over the past week.<sup>39</sup> The CES-D includes items that survey the domains of positive and  
17 negative affect, somatic activity, and interpersonal relations. A four-point Likert scale is used to rate the  
18 frequency of symptoms experienced. Higher scores (range: 0-60) indicate greater frequency of  
19 depressive symptoms and individuals with total scores  $\geq 16$  are typically identified as having clinically  
20 significant levels of depression.<sup>39</sup> Extensive research has shown the CES-D to be valid and reliable.<sup>38,40</sup> In  
21 this study, internal consistency for the CES-D was  $\alpha=0.93$ .  
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### 34 *Family functioning*

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36 The 12-item General Functioning subscale of the McMaster Family Assessment Device provided a valid  
37 and reliable measure of the health/pathology of the family (i.e., family functioning).<sup>41,42</sup> The scale is  
38 derived by summing items from six domains: problem solving, communication, roles, affective  
39 responsiveness, affective involvement, and behavioral control. Items are rated on a four-point Likert  
40 scale with higher scores (range: 0-36) indicating poorer overall family functioning. Internal consistency  
41 for the FAD in this study was  $\alpha=0.92$ .  
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### 52 *Physical Condition Disease severity*

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3 Disease severity in children was assessed and measured by a health professional using a 10 cm visual  
4 analog scale (VAS). The VAS represents a continuum of disease severity.<sup>43</sup> Health professionals marked  
5 the VAS at the point at which best reflected the disease severity of the child, according to their clinical  
6 judgment. The distance from the zero point of the VAS (left side) to the mark was measured and  
7 recorded as the disease severity of the child. The VAS and its scoring method has been used in a variety  
8 of populations and settings to assess well-being and pain and has the advantage of being easily  
9 comparable across study samples.<sup>44,45</sup>

### 20 21 *Demographic characteristics*

22 Sociodemographic data were collected on child and parent age, sex and immigrant status, parent  
23 marital status and educational attainment, as well as annual household income.

### 29 30 **Analysis**

31 Comparisons between children with and without multimorbidity were made using Mann-Whitney  
32 (continuous variables) and Fisher's Exact tests (categorical variables). Changes in the prevalence of  
33 multimorbidity from baseline to six months was using the McNemar test. Analysis of variance with post  
34 hoc Scheffé tests were conducted to compare KIDSCREEN-27 scores with available population norms.<sup>33</sup>  
35 Generalized linear modeling was used to examine the association between multimorbidity and  
36 children's quality of life and parent psychosocial outcomes at six-months. Outcomes were regressed on  
37 presence of multimorbidity, controlling for baseline scores for each respective outcome, as well as child  
38 age, sex, and physical condition. These covariates were included in the models to present unbiased  
39 estimates of effect. All analyses were conducted using SPSS 21 (IBM Corporation). Due to the pilot  
40 nature of this study, statistical tests were two-tailed using a significance level of  $\alpha=0.10$ . There were no  
41 missing item-level data.

## Results

### *Sample characteristics*

Over 12 months, 62 families were approached to participate in REACH. Of these, 56 (90% response) agreed to participate. Four families were not interested in participating and two families had a child that did not meet the eligibility criteria. Fifty families (83% participation) completed the baseline assessment (telephone and mail) and forty-four (88% retention) completed the six-month follow-up (telephone and mail). Repeated attempts to contact the six families who completed the telephone interview, but did not return the complete mail survey were unsuccessful, thus the reasons for withdrawal from the study are unknown. There were no baseline differences between families lost to follow-up and those who completed the study.

Baseline characteristics are shown in Table 1. The mean age of children was 11.3 (SD 3.3) years and 52% were male. There was no difference in the number of children across physical condition subgroup, though asthma was the most common (28%) and epilepsy and food allergy, the least common (16%). Parents had a mean of age of 44.0 (5.7) years and 90% were female. Most parents were married (78%), had completed post-secondary education (78%), and had annual household incomes of  $\geq$ \$90,000 Canadian dollars (58%).

### *Prevalence of multimorbidity*

The prevalence of multimorbidity declined from 58% at baseline to 42% at six-months ( $p=0.09$ ; Table 2). At baseline, 11 (22%) children had multiple mental disorders. This decreased to nine (18%) at six months. Anxiety disorder (at least one of separation anxiety, phobias, or generalized anxiety) was the most common disorder at baseline (36%) and six months (26%). Differences across physical conditions



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3 were found for the prevalence of attention-deficit hyperactivity disorder ( $\chi^2=6.44$ ;  $p=.06$ ) and  
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5 oppositional defiant disorder ( $\chi^2=7.53$ ;  $p=0.07$ ) at baseline and for attention-deficit hyperactivity  
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7 disorder ( $\chi^2=7.98$ ;  $p=.09$ ) at six months. In each case, the proportion of mental disorder was elevated in  
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9 children with food allergy.  
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### 11 12 13 14 *Correlates of multimorbidity*

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16 Results showed no differences in child and parent characteristics between children with and without  
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18 multimorbidity with two exceptions (Table 1): children with multimorbidity had lower KIDSCREEN-27  
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20 psychological well-being (43.6 vs. 49.4;  $p=0.08$ ) and parents reported higher STAI scores (44.2 vs. 38.2;  
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22  $p=0.05$ ).  
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### 26 27 28 *Multimorbidity and psychosocial outcomes*

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30 Comparisons of KIDSCREEN-27 scores between our sample and population norms are shown in Figure 1.  
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32 Overall differences were found for the physical well-being, psychological well-being, and peer support  
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34 domains. Post hoc tests showed that compared to population norms, children with multimorbidity had  
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36 significantly poorer psychological well-being ( $t=4.21$ ;  $p<0.01$ ) and children without multimorbidity had  
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38 lower peer support ( $t=2.66$ ;  $p<0.01$ ). Results of the unadjusted and adjusted generalized linear models  
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40 of the association of multimorbidity with quality of life over time are shown in Table 3. Adjusting for  
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42 child age, sex, type of physical condition, and baseline KIDSCREEN-27 score, multimorbidity was  
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44 associated with lower scores in the following domains at six months: physical well-being ( $\beta=-4.82$ ;  
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46  $p=0.03$ ), psychological well-being ( $\beta=-4.10$ ;  $p=0.06$ ), and school environment ( $\beta=-4.17$ ;  $p=0.09$ ). With the  
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48 exception of autonomy and parent relations, the strength of the association increased after covariate  
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50 adjustment.  
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3 The same modeling strategy was used to examine the associations with parental stress, anxiety,  
4 depression, and family functioning. In both unadjusted and adjusted models, multimorbidity was not  
5 associated with any psychosocial outcomes in parents over time (Table 4). Similarly, the strength of  
6 association (though not statistically significant) increased after covariate adjustment.  
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## 14 **Discussion**

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16 In this pilot study, over half of children screened positive for mental disorder(s) soon after being  
17 diagnosed with a physical condition and this proportion appeared to decrease six months later. Anxiety  
18 disorders were found to be the most common disorders affecting children at diagnosis and six-months  
19 later. There were no sociodemographic differences between children with and without multimorbidity.  
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21 While multimorbidity did have a negative effect on child quality of life over time, our hypothesis that it  
22 would also influence parental outcomes was unsupported.  
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32 Methodologically, this pilot study has implications for the study of child multimorbidity within the  
33 clinical setting. Regarding participant recruitment, we limited the amount of contact between research  
34 staff and families during the initial contact in the clinic. This served two purposes: one, it minimized  
35 burden on the physicians and nurses whose primary focus is clinical care, as well as clinical staff  
36 managing large patient volumes. Two, it reduced the amount of information passed to families at a time  
37 when they may have felt overwhelmed with the clinical information provided by the physician about  
38 their child's diagnosis. We provided an information letter and then followed up by telephone a few days  
39 later when families were away from the clinic and had a chance to review this letter and determine if  
40 they wanted to participate. Our approach of engaging families personally in clinic, followed by  
41 telephone contact, and data collection via mail survey was found to be acceptable to families. Our  
42 strong response and retention rates contrast evidence showing reduced response rates in research  
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3 studies.<sup>46</sup> The majority of families in our study also noted that mail survey was the preferred method for  
4 data collection compared to online surveys and home interviews (data not shown). Overall, our  
5 methodology resulted in good coverage, with over 80% of consecutively approached eligible families  
6 participating in the study. Participation requirements had minimal burden on families as shown by the  
7 strong retention rate and lack of missing data. This suggests that the mental health of children with  
8 physical conditions is an important concern for families and that they are willing to contribute their time  
9 to such research studies. Our recruitment experience suggested that a number of children were  
10 ineligible for the study because their illness duration was greater than six months (i.e., diagnosed before  
11 six years of age). To ensure a more efficient recruitment that encompasses an even larger coverage of  
12 our target population, the larger study will include children as young as two years of age and we are  
13 expanding the number of physical conditions (e.g., bowel diseases, chronic headache, lupus).  
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30 Our estimate of the proportion of children with multimorbidity was similar to previous reports<sup>8</sup> and  
31 supports the chronicity of multimorbidity during the early stages of being diagnosed with a physical  
32 condition.<sup>7</sup> As shown in previous work in children with diabetes<sup>12</sup> the peri-diagnostic period represents a  
33 critical developmental period for mental health. Elevated rates of anxiety disorder may be attributable  
34 to the uncertainty that children may experience regarding the prognosis of their physical condition,  
35 including unpredictability of exacerbations, fear of death, loss of control, stigma associated with their  
36 condition, or adverse effects of medical treatment.<sup>10</sup> From this perspective, anxiety arises from  
37 negatively-biased thought patterns that exaggerate adverse effects of the physical condition and can  
38 undermine confidence in adapting to threatening situations.<sup>47</sup> Anxiety in these children may be an  
39 inherited trait or learned behavior—parents of children with multimorbidity in our sample reported  
40 more symptoms of anxiety compared to parents of children without multimorbidity. There is also  
41 emerging evidence of shared biological pathways that underlie multimorbidity. In adults, symptoms of  
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3 anxiety are associated with systemic inflammation,<sup>48</sup> which is elevated in individuals with physical  
4 conditions. Whether markers of inflammation, such as pro-inflammatory cytokines mediate the  
5 relationship between physical and mental disorder is unknown.  
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12 These findings also contribute to the converging evidence that risk for mental disorder is relatively  
13 consistent among children with various physical conditions.<sup>49</sup> One exception was that attention-deficit  
14 hyperactivity disorder was more common among children with food allergy. This increased risk is  
15 supported by some previous studies.<sup>50,51</sup> As in this work, attention-deficit hyperactivity disorder in our  
16 sample of children with food allergy was mainly of the inattentive subtype. Inattentiveness may co-  
17 occur with core symptoms of generalized anxiety disorder, manifesting because of hypervigilance in  
18 avoiding food allergens. From a biological perspective, there is evidence of shared immunological<sup>52</sup> and  
19 inflammatory<sup>53</sup> responses for allergic conditions and attention-deficit hyperactivity disorder which may  
20 explain this association. Given the small number of children with food allergy in our sample, these  
21 interpretations are by no means definitive, but instead are offered as hypotheses to be tested rigorously  
22 in larger samples.  
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39 In general, the sample consisted of high socioeconomic two-parent families, which may have  
40 contributed to the lack of sociodemographic differences between children with and without  
41 multimorbidity. Placing the finding in the context of previous work is difficult given the absence of  
42 studies examining sociodemographic correlates of multimorbidity. Previous population-based studies  
43 conducted in Canada also showed no socioeconomic differences between children with and without  
44 physical conditions.<sup>23,54-56</sup> In our larger study, we will work towards a recruitment strategy that will  
45 include wider variation in the socioeconomic status to families to increase the representativeness of the  
46 sample. Contrary to expectation, no effect of multimorbidity on parental outcomes was found.  
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3 Nevertheless, information related to parental psychopathology and family environment may be  
4 important control variables used to isolate the effects of multimorbidity on child outcomes. Such family  
5 processes may also be implicated in complex pathways linking physical and mental health in children. As  
6 a result, these variables will be included in the larger study.  
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14 Multimorbidity appears to have a negative effect on children's quality of life, above and beyond the  
15 effect of having a physical condition alone.<sup>17</sup> This effect is pervasive, affecting multiple domains of  
16 quality of life during the first six months after a diagnosis. Of interest is the finding that the magnitude  
17 of effect seen for physical well-being, psychological well-being, and school environment was  
18 approximately half a standard deviation. This metric has been validated as the minimal clinically  
19 important difference for measures of quality of life<sup>57</sup> and provides evidence to support the perception  
20 that changes in child quality of life due to multimorbidity are clinically relevant. Given the early onset of  
21 multimorbidity, health professionals in the pediatric setting should consider engaging children and  
22 families in discussions about mental health soon after the diagnosis of a physical condition is made and  
23 discussion surrounding the physical condition completed. Within a holistic family-centered approach,  
24 health professionals are encouraged to apply brief screening tools to identify at-risk children and  
25 provide referrals to supportive services on a case-by-case basis. This is a critical window of opportunity  
26 given that mental disorder is strong predictor of youth suicide<sup>58</sup> and that risk for suicide is highest soon  
27 after an adolescent is diagnosed with a physical condition.<sup>59</sup> Because of the chronicity and pervasiveness  
28 of multimorbidity and its influence on child and parent psychosocial functioning, continuing monitoring  
29 during routine clinical assessments may also be warranted.  
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52 There are two noteworthy limitations. First, the study was likely underpowered to detect differences  
53 between children with and without multimorbidity and the small sample size may limit the  
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3 generalizability of findings. However, our sample size was consistent with considerations for  
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5 implementing pilot studies<sup>60</sup> and our coverage of eligible families was good. Second, measurement of  
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7 child mental health and child and parent outcomes were parent-reported. While we have found  
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9 adequate agreement between parents and a small subset of children who provided self-reported quality  
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11 of life,<sup>35</sup> significant associations may be the result of shared-method variance.  
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## 16 **Conclusion**

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18 These preliminary findings indicate that mental disorder in children newly-diagnosed with a physical  
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20 condition is common and negatively affects their quality of life over time. If these results are replicated  
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22 in a subsequent larger study, health professionals should be aware of the burden of multimorbidity and  
23  
24 prepare themselves to discuss mental health with children and their parents. Findings from this pilot  
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26 study have been used to implement a large-scale study that will examine child multimorbidity in greater  
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28 depth and provide more definitive clinical implications.  
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For peer review only

**Table 1. Baseline sample characteristics**

|                                | Full sample | Multimorbid | Not multimorbid | P-value |
|--------------------------------|-------------|-------------|-----------------|---------|
| N                              | 50          | 29          | 21              |         |
| <b>Child</b>                   |             |             |                 |         |
| Age, years                     | 11.3 (3.3)  | 11.6 (3.2)  | 11.0 (3.4)      | 0.62    |
| Male, n (%)                    | 26 (52)     | 15 (52)     | 11 (52)         | 0.96    |
| Diagnoses, n (%)               |             |             |                 | 0.98    |
| Asthma                         | 14 (28)     | 9 (31)      | 5 (24)          |         |
| Diabetes                       | 9 (18)      | 4 (14)      | 5 (24)          |         |
| Epilepsy                       | 8 (16)      | 4 (14)      | 4 (19)          |         |
| Food allergy                   | 8 (16)      | 5 (17)      | 3 (14)          |         |
| Juvenile arthritis             | 11 (22)     | 7 (24)      | 4 (19)          |         |
| Disease severity, VAS          | 1.3 (1.2)   | 1.5 (1.3)   | 0.9 (0.9)       | 0.16    |
| Quality of life, KIDSCREEN-27  |             |             |                 |         |
| Physical well-being            | 48.0 (12.0) | 47.4 (11.0) | 48.8 (13.4)     | 0.77    |
| Psychological well-being       | 46.1 (9.8)  | 43.6 (8.1)  | 49.4 (11.2)     | 0.08    |
| Autonomy/Parent relations      | 48.9 (9.6)  | 47.5 (7.0)  | 50.8 (12.1)     | 0.72    |
| Peer support                   | 46.1 (11.4) | 46.7 (12.1) | 45.4 (10.5)     | 0.35    |
| School environment             | 50.1 (10.8) | 47.7 (8.8)  | 53.3 (12.4)     | 0.12    |
| <b>Parent</b>                  |             |             |                 |         |
| Age, years                     | 44.0 (5.7)  | 43.0 (4.8)  | 45.2 (6.3)      | 0.43    |
| Female, n (%)                  | 45 (90)     | 26 (90)     | 19 (91)         | 0.92    |
| Married, n (%)                 | 39 (78)     | 22 (76)     | 17 (81)         | 0.67    |
| Post-secondary graduate, n (%) | 39 (78)     | 22 (76)     | 17 (81)         | 0.67    |
| Income ≥\$90,000, n (%)        | 29 (58)     | 17 (59)     | 12 (57)         | 0.87    |
| Parental stress, PSS           | 35.9 (7.9)  | 37.1 (7.3)  | 34.4 (8.5)      | 0.32    |
| Parental anxiety, STAI         | 41.6 (9.8)  | 44.2 (9.1)  | 38.2 (10.0)     | 0.05    |
| Parental depression CES-D      | 12.7 (9.9)  | 13.0 (9.6)  | 12.2 (10.5)     | 0.58    |
| Family functioning, FAD        | 25.5 (6.3)  | 24.7 (6.2)  | 26.5 (6.6)      | 0.20    |

Results are reported as mean (standard deviation) unless otherwise noted.

**Table 2. Prevalence of multimorbidity**

|                                 | Full sample | Asthma | Diabetes | Epilepsy | Food allergy | Juvenile arthritis | P-value |
|---------------------------------|-------------|--------|----------|----------|--------------|--------------------|---------|
| <b>Baseline</b>                 |             |        |          |          |              |                    |         |
| Any disorder                    | 29 (58)     | 9 (64) | 4 (44)   | 4 (50)   | 5 (63)       | 7 (64)             | 0.88    |
| Major depressive episode        | 12 (24)     | 4 (29) | 2 (22)   | 1 (13)   | 1 (13)       | 4 (36)             | 0.74    |
| Separation anxiety              | 2 (4)       | 0      | 0        | 1 (13)   | 0            | 1 (9)              | 0.43    |
| Phobia*                         | 15 (30)     | 6 (46) | 1 (11)   | 1 (13)   | 3 (38)       | 4 (36)             | 0.35    |
| Generalized anxiety             | 6 (12)      | 0      | 0        | 2 (25)   | 2 (25)       | 2 (18)             | 0.11    |
| Attention-deficit hyperactivity | 5 (10)      | 1 (7)  | 0        | 1 (13)   | 3 (38)       | 0                  | 0.06    |
| Oppositional defiant            | 9 (18)      | 2 (14) | 1 (11)   | 2 (25)   | 4 (50)       | 0                  | 0.07    |
| Conduct                         | 3 (6)       | 1 (7)  | 0        | 1 (13)   | 1 (13)       | 0                  | 0.65    |
| <b>Six months</b>               |             |        |          |          |              |                    |         |
| Any disorder                    | 21 (42)     | 9 (64) | 1 (11)   | 4 (50)   | 2 (25)       | 5 (56)             | 0.10    |
| Major depressive episode        | 2 (4)       | 0      | 0        | 0        | 0            | 2 (22)             | 0.11    |
| Separation anxiety              | 3 (6)       | 2 (14) | 0        | 1 (13)   | 0            | 0                  | 0.56    |
| Phobia*                         | 10 (20)     | 5 (36) | 1 (11)   | 1 (13)   | 0            | 3 (33)             | 0.25    |
| Generalized anxiety             | 4 (8)       | 1 (7)  | 0        | 1 (13)   | 0            | 2 (22)             | 0.55    |
| Attention-deficit hyperactivity | 3 (6)       | 0      | 0        | 0        | 2 (25)       | 1 (11)             | 0.09    |
| Oppositional defiant            | 6 (12)      | 2 (14) | 0        | 2 (25)   | 2 (25)       | 0                  | 0.31    |
| Conduct                         | 4 (8)       | 1 (7)  | 0        | 2 (25)   | 1 (13)       | 0                  | 0.33    |

Results are the number (%) of children with multimorbidity. Fisher's Exact tests examined multimorbidity across the five physical conditions.

\*Includes generalized, non-generalized, and specific phobias.



**Table 3. Longitudinal effects of multimorbidity on child quality of life**

| KIDSCREEN-27              | Unadjusted   |         | Adjusted     |         |
|---------------------------|--------------|---------|--------------|---------|
|                           | B (SE)       | P-value | B (SE)       | P-value |
| Physical well-being       | -3.76 (2.23) | 0.09    | -4.82 (2.22) | 0.03    |
| Psychological well-being  | -2.06 (2.44) | 0.40    | -4.10 (2.14) | 0.06    |
| Autonomy/Parent relations | 0.77 (2.53)  | 0.76    | -0.67 (2.40) | 0.78    |
| Peer support              | -0.59 (2.83) | 0.84    | -1.23 (2.66) | 0.64    |
| School environment        | -3.56 (2.88) | 0.22    | -4.17 (2.44) | 0.09    |

Models adjusted for child age and sex, physical condition, and baseline quality of life.

**Table 4. Longitudinal effects of multimorbidity on parental outcomes**

|                           | Unadjusted  |         | Adjusted     |         |
|---------------------------|-------------|---------|--------------|---------|
|                           | B (SE)      | P-value | B (SE)       | P-value |
| Parental stress, PSS      | 0.28 (1.60) | 0.86    | -1.50 (1.51) | 0.32    |
| Parental anxiety, STAI    | 0.14 (2.05) | 0.95    | -0.24 (2.15) | 0.91    |
| Parental depression CES-D | 0.30 (1.12) | 0.80    | 0.62 (1.13)  | 0.58    |
| Family functioning, FAD   | 1.21 (1.32) | 0.36    | 1.47 (1.28)  | 0.25    |

Models adjusted for child age and sex, physical condition, and baseline psychosocial outcome.

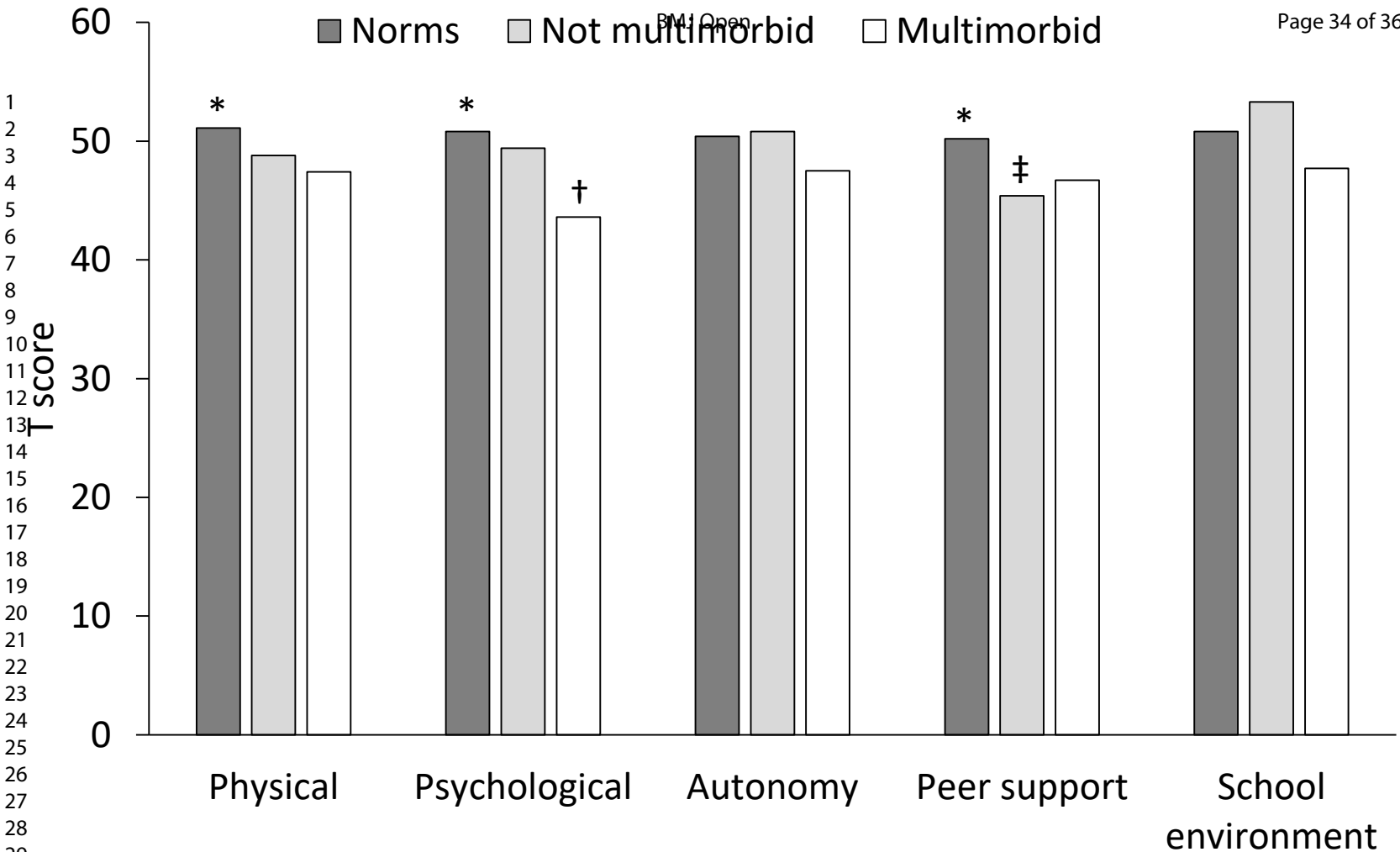
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3 **Figure 1. Comparison of KIDSCREEN-27 scores with population norms**  
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5 \*p<0.10 for overall F-test across the three groups.  
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7 †Multimorbid group significantly lower than normative and not multimorbid groups.  
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9 ‡Not multimorbid group significantly lower than normative group.  
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**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies**

| Section/Topic             | Item # | Recommendation   | Reported on page # |
|---------------------------|--------|--|--------------------|
| Title and abstract        | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract   | 1                  |
|                           |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found  | 3                  |
| <b>Introduction</b>       |        |  |                    |
| Background/rationale      | 2      | Explain the scientific background and rationale for the investigation being reported   | 6-8                |
| Objectives                | 3      | State specific objectives, including any prespecified hypotheses   | 8                  |
| <b>Methods</b>            |        |  |                    |
| Study design              | 4      | Present key elements of study design early in the paper  | 9-10               |
| Setting                   | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  | 9                  |
| Participants              | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up   | 9                  |
|                           |        | (b) For matched studies, give matching criteria and number of exposed and unexposed  | N/A                |
| Variables                 | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   | 10-13              |
| Data sources/ measurement | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 10-13              |
| Bias                      | 9      | Describe any efforts to address potential sources of bias  | 13                 |
| Study size                | 10     | Explain how the study size was arrived at  | 9                  |
| Quantitative variables    | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why   | 13                 |
| Statistical methods       | 12     | (a) Describe all statistical methods, including those used to control for confounding  | 13                 |
|                           |        | (b) Describe any methods used to examine subgroups and interactions  | 13                 |
|                           |        | (c) Explain how missing data were addressed  | 13                 |
|                           |        | (d) If applicable, explain how loss to follow-up was addressed   | 13                 |
|                           |        | (e) Describe any sensitivity analyses  | N/A                |
| <b>Results</b>            |        |  |                    |

|                          |     |  |        |
|--------------------------|-----|--|--------|
| Participants             | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed            | 14     |
|                          |     | (b) Give reasons for non-participation at each stage   | 14     |
|                          |     | (c) Consider use of a flow diagram   | N/A    |
| Descriptive data         | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders   | 14     |
|                          |     | (b) Indicate number of participants with missing data for each variable of interest  | 14     |
|                          |     | (c) Summarise follow-up time (eg, average and total amount)  | 14     |
| Outcome data             | 15* | Report numbers of outcome events or summary measures over time   | 14     |
| Main results             | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 31-32  |
|                          |     | (b) Report category boundaries when continuous variables were categorized  | N/A    |
|                          |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period   | N/A    |
| Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   | 15-16  |
| <b>Discussion</b>        |     |  |        |
| Key results              | 18  | Summarise key results with reference to study objectives   | 16     |
| <b>Limitations</b>       |     |  |        |
| Interpretation           | 20  | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                   | 16-19  |
| Generalisability         | 21  | Discuss the generalisability (external validity) of the study results  | 18, 19 |
| <b>Other information</b> |     |  |        |
| Funding                  | 22  | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based  | 2      |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Mental Disorder in Children with Physical Conditions: A Pilot Study

|                                 |  |
|---------------------------------|--|
| Journal:                        | <i>BMJ Open</i>  |
| Manuscript ID                   | bmjopen-2017-019011.R1   |
| Article Type:                   | Research   |
| Date Submitted by the Author:   | 10-Oct-2017  |
| Complete List of Authors:       | Butler, Alexandra; University of Waterloo<br>Van Lieshout, Ryan ; McMaster University<br>Lipman, Ellen; McMaster University<br>MacMillan, Harriet; McMaster University<br>Gonzalez, Andrea; McMaster University<br>Gorter, Jan Willem; McMaster University<br>Georgiades, Kathy; McMaster University<br>Speechley, Kathy ; Western University,<br>Boyle , Michael ; McMaster University<br>Ferro, Mark; University of Waterloo, School of Public Health and Health Systems |
| <b>Primary Subject Heading</b>: | Mental health  |
| Secondary Subject Heading:      | Paediatrics  |
| Keywords:                       | multimorbidity, mental disorder, chronic disease, pilot study  |
|                                 |  |

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Manuscripts

## Mental Disorder in Children with Physical Conditions: A Pilot Study

Butler A<sup>1</sup>, Van Lieshout RJ<sup>2</sup>, Lipman EL<sup>2</sup>, MacMillan HL<sup>2</sup>, Gonzalez A<sup>2</sup>, Gorter JW<sup>3</sup>, Georgiades K<sup>2</sup>,  
Speechley KN<sup>4,5</sup>, Boyle MH<sup>2</sup>, Ferro MA<sup>1,\*</sup>

[1] School of Public Health & Health Systems, University of Waterloo

[2] Department of Psychiatry & Behavioural Neurosciences, McMaster University

[3] Department of Pediatrics, McMaster University

[4] Department of Paediatrics, Western University

[5] Department of Epidemiology & Biostatistics, Western University

[\*] Corresponding author

### Contact information for corresponding author

Mark A. Ferro, University of Waterloo, School of Public Health and Health Systems, 200 University  
Avenue West, Waterloo, Ontario, Canada, N2L 3G1, Phone: 519.888.4567, Fax: 519.746.6776, Email:  
[mark.ferro@uwaterloo.ca](mailto:mark.ferro@uwaterloo.ca)

### Authors' contributions

MAF led the study. MAF, MHB, KNS, KG, JWG, AG, HLM, ELL, and RJV conceptualized and designed the study and were responsible for acquiring funding. MHB, KNS, KG, and AG provided methodological insights. JWG, HLM, ELL, and RJV provided clinical insights. KNS and HLM helped facilitate clinic participation. AB and MAF analyzed and interpreted data and drafted the manuscript. All authors critically reviewed and revised and then approved the final manuscript as submitted.



## Funding

This work was supported by the Canadian Institutes of Health Research (MOP-133645). At the time of the study, MAF was supported by a Research Early Career Award from Hamilton Health Sciences. MAF currently holds the Canada Research Chair in Youth Mental Health; MHB holds the Canada Research Chair in the Social Determinants of Child Health; KG holds the Dan Offord Chair in Child Studies; JWG holds the Scotiabank Chair in Child Health Research; AG is supported by a Canadian Institutes for Health Research New Investigator Award; HLM holds the Chedoke Health Chair in Child Psychiatry; and, RJV holds the Albert Einstein/Irving Zucker Chair in Neuroscience.

## Competing interests

The authors declare that they have no competing interests.

## Data sharing statement

Data will not be shared in order to protect the confidentiality of participants. This was a multisite study and we do not have approval to make the data publically available.

## Acknowledgements

The authors gratefully acknowledge the children, parents, and health professionals and their staff without whose participation, this study would not have been possible. We especially thank Jessica Zelman for coordinating the study and Jane Terhaerd for assisting with ethical approval. Health professional contributors to this study were: Janice Falcone, Karen McAssey, Marilyn Rothney, Susan Wasserman (McMaster Children's Hospital) and Roberta Berard, Craig Campbell, Margo Devries-Rizzo, Michelle Diebold, Patti Guertjens, Simon Levin, Narayan Prasad (Children's Hospital London Health Sciences).

**Abstract**

**Objectives:** Methodologically, to assess the feasibility of participant recruitment and retention, as well as missing data in studying mental disorder among children newly-diagnosed with chronic physical conditions (i.e., multimorbidity). Substantively, to examine the prevalence of multimorbidity, identify sociodemographic correlates, and model the influence of multimorbidity on changes in child quality of life and parental psychosocial outcomes over a six-month follow-up.

**Design:** Prospective pilot study.

**Setting:** Two children's tertiary-care hospitals.

**Participants:** Children aged 6-16 years diagnosed in the past six months with one of asthma, diabetes, epilepsy, food allergy, or juvenile arthritis and their parents.

**Outcome measures:** Response, participation, and retention rates. Child mental disorder using the Mini International Neuropsychiatric Interview at baseline and six months. Child quality of life, parental symptoms of stress, anxiety, and depression, and family functioning. All outcomes were parent reported.

**Results:** Response, participation, and retention rates were 90%, 83%, and 88%, respectively. Of the 50 children enrolled in the study, the prevalence of multimorbidity was 58% at baseline and 42% at six months. No sociodemographic characteristics were associated with multimorbidity. Multimorbidity at baseline was associated with declines over six months in the following quality of life domains: physical well-being,  $\beta=-4.82$  (-8.47, -1.17), psychological well-being,  $\beta=-4.10$  (-7.62, -0.58), and school

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3 environment,  $\beta=-4.17$  (-8.18, -0.16). There was no association with parental psychosocial outcomes over  
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5 time.  
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10 **Conclusions:** Preliminary evidence suggests that mental disorder in children with a physical condition is  
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12 very common and has a negative impact on quality of life over time. Based on the strong response rate  
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14 and minimal attrition, our approach to study child multimorbidity appears feasible and suggests that  
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16 multimorbidity is an important concern for families. Methodological and substantive findings from this  
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18 pilot study have been used to implement a larger, more definitive study of child multimorbidity, which  
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20 should lead to important clinical implications.  
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### Strengths and limitations of this study

- This pilot study includes children newly-diagnosed with chronic physical conditions.
- This is the first study to examine mental disorder in children newly-diagnosed with a number of different conditions.
- This study was likely underpowered to detect differences within and between children with and without multimorbidity and the small sample size limits generalizability.
- All outcomes were parent-reported.

## Introduction

The global prevalence of children with a chronic physical condition—a health problem that requires ongoing management over a period of years or decades—is common, affecting approximately 25% of children, and increasing.<sup>1</sup> These children may be adversely affected by their disorders or their treatment, subsequently developing additional conditions, including mental disorders.<sup>2</sup> Compared to their peers with a physical or mental disorder only, children with multimorbidity (physical-mental comorbidity) experience greater symptom severity and impairment in both physical and mental health domains.<sup>3</sup> Understandably, the onset of multimorbidity remains an important concern for children, parents, health professionals, and payers.<sup>4</sup>

Mental disorders of any type are common in children and adolescents<sup>5</sup> and disproportionately affect young people with chronic physical conditions (herein physical conditions).<sup>6,7</sup> Estimates from clinical samples suggest that nearly half of children with physical conditions meet criteria for a mental disorder diagnosis.<sup>8</sup> In general population samples, this estimate is lower, with approximately 20-30% of children being affected.<sup>3</sup>

Evidence of the association between physical and mental health is robust,<sup>9-11</sup> but with few exceptions,<sup>7,12,13</sup> the literature base consists mostly of cross-sectional studies. This limits our understanding of mental health at the time children are diagnosed with a physical condition and how their mental health may change over time. One study found more parent-reported symptoms of problem behavior in children 6-7 years newly diagnosed with a chronic illness compared to healthy controls.<sup>7</sup> This effect was stable through to 10-11 years of age, highlighting the chronicity of multimorbidity in childhood. In a prospective study of children with diabetes, hazard ratios for mental disorder were highest within six-months of the diabetes diagnosis (3.0 [2.7-3.4]) compared to those with

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3 a duration of diabetes of five years or more (1.9 [1.7-2.1]), regardless of age at diagnosis,<sup>12</sup> suggesting  
4 that the peri-diagnostic period may be a time of particular mental health risk. Another prospective study  
5 showed changes over time in associations of mental health with physical conditions being associated  
6 with depressive symptoms during childhood, and with anxiety symptoms during early adolescence.<sup>13</sup>  
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8 While these studies have advanced the field, opportunities exist to overcome the limitations in these  
9 studies associated with the ascertainment of physical conditions based on parent-report,<sup>14</sup> assessment  
10 of symptoms of problem behaviors rather than mental disorder,<sup>13,15,16</sup> and inherent weaknesses of using  
11 register-based data related to data quality and variable availability.<sup>17</sup>  
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14 Existing research also suggests that physical conditions and mental disorders are independently  
15 associated with poorer psychosocial outcomes including quality of life<sup>18,19</sup> and self-esteem,<sup>20,21</sup> as well as  
16 academic performance.<sup>22,23</sup> These adverse effects can also extend to parents and families who  
17 experience elevated stress and psychological distress, worse family functioning, and financial  
18 hardship.<sup>24-28</sup> Effects on child and parent psychosocial outcomes appear similar when physical and  
19 mental disorders are examined separately; however, there is little research examining whether  
20 multimorbidity exerts a compounding effect. Cross-sectional evidence suggests that children with  
21 multimorbidity experience worse quality of life compared to children with a physical or mental disorder  
22 alone.<sup>29,30</sup> One prospective study showed that adults who experienced multimorbidity during  
23 adolescence had lower quality of life compared to those who had a physical or mental disorder only.<sup>31</sup>  
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25 These researchers found that among those with multimorbidity, physical conditions affected physical  
26 quality of life only; while their mental disorder negatively affected multiple domains of life quality,  
27 including physical, emotional, and social well-being. The extent to which multimorbidity influences other  
28 aspects of parental health and well-being, including parenting stress, psychopathology, and family  
29 relationships, is not well known.  
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5 Despite the progress made in understanding child multimorbidity and its effects on psychosocial  
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7 outcomes, important knowledge gaps remain. First, the burden and correlates of multimorbidity,  
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9 particularly in clinical samples of children who represent the largest consumers of health services,<sup>32</sup> is  
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11 not well known. While other studies have examined prevalence of multimorbidity, those studies were  
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13 based on population, not clinical samples of prevalent cases and did not measure DSM-aligned  
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15 diagnoses;<sup>3,13</sup> are out-dated;<sup>8</sup> or, focus on a single physical condition.<sup>12</sup> This information is needed to  
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17 inform resource allocation and the provision of services within the health system. Second, the timing of  
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19 multimorbidity onset, how it changes, and its influence on psychosocial outcomes over time are not  
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21 well-understood, limiting our ability to identify opportunities for intervention to prevent the  
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23 development of mental disorder in children with physical conditions. This includes a lack of  
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25 understanding how mental disorders may change or appear in relation to the onset of the physical  
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27 condition. For example, are anxiety disorders more common at the time of diagnosis given the  
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29 uncertainty surrounding prognosis? Third, effects of child multimorbidity on parental health and well-  
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31 being have not been explored in much detail. Understanding these effects is key to designing,  
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33 implementing, and evaluating family-centered approaches to care within the pediatric setting to  
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35 promote the best possible health outcomes for children, parents, and families.<sup>33</sup>  
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43 Anticipating substantial hardship and stress associated with receiving a diagnosis of a physical condition  
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45 in childhood within families, as well as the uncertainty surrounding prognosis, we conducted a pilot  
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47 study to assess the feasibility of recruiting of eligible participants, estimating respondent burden related  
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49 to data collection, and the extent of missing data and attrition. Substantively, the aims of the pilot study  
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51 were to: 1—examine the initial prevalence of multimorbidity in a clinical sample of children newly-  
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53 diagnosed with a physical condition, as well as rates six months later; 2—identify correlates of  
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3 multimorbidity in children and parents; and, 3—explore the influence of multimorbidity on changes in  
4 child quality of life and parental psychosocial outcomes over six-months of follow-up. Based on previous  
5 clinical studies,<sup>8</sup> we hypothesized that at the time of diagnosis, 50% of children would screen positive for  
6 mental disorder. Based on limited evidence,<sup>12</sup> we hypothesized that six months later, there would be a  
7 decrease in the proportion of multimorbidity. Finally, we hypothesized that children with multimorbidity  
8 would have worse quality of life over time; their parents, more symptoms of parenting stress, anxiety,  
9 and depression; and, their families, worse functioning compared to children with physical conditions  
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## 23 **Methods**

### 24 **Sample**

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26 Data come from a multisite, prospective, pilot study aimed at examining mental disorder(s) in children  
27 with physical conditions. Families were recruited from four outpatient clinics from two pediatric  
28 academic hospitals (specialized tertiary care centres; two clinics per hospital) in Ontario, Canada to  
29 assess mental and psychosocial outcomes in children with newly-diagnosed with physical conditions.  
30 Health professionals at the hospitals were involved at the initial point of contact and provided eligible  
31 families with an overview of the study and details regarding participation. The eligibility criteria for the  
32 study were children who: 1—were aged 6-16 years old (six is the youngest age at which our measure of  
33 mental disorder is validated; the ceiling age of 16 years ensured that during the follow-up, participants  
34 did not transfer out of the pediatric health system); 2—had received a diagnosis of asthma, diabetes,  
35 epilepsy, food allergy or juvenile idiopathic arthritis (which represent the most common physical  
36 conditions among children)<sup>34</sup> within the six months prior to recruitment; and, 3—had a parent who  
37 could read English (not all measures have been validated in other languages). Children were excluded if  
38 they had a degenerative neurological disorder because child and parental outcomes are well-established  
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3 in this population. Child IQ was not tested and children were not excluded if their parents indicated  
4 intellectual disability, maximizing the coverage and representativeness of our sample. Following sample  
5 size guidelines suggested for the conduct of pilot studies,<sup>35</sup> we aimed to recruit 60 children and families  
6 (12 per condition) over a 12-month period.  
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## 14 **Data Collection**

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16 After the medical encounter, eligible families were invited by clinic nurses to speak with research staff  
17 about the study. Research staff briefly introduced the study and provided families an information letter.  
18 Families interested in participating in the study consented for clinic nurses to send their contact  
19 information to study investigators who then followed-up with families by telephone to confirm  
20 eligibility, obtain oral consent from parents and children, and arrange for a convenient time to conduct a  
21 telephone interview to assess child mental health. Parents also completed two mailed surveys to assess  
22 psychosocial outcomes and demographic characteristics; one at baseline and one six months later, when  
23 a second telephone interview to assess mental health was conducted. Parents of all participating  
24 children provided proxy reports and children who were  $\geq 11$  years of age self-reported on the telephone  
25 interview and to the mail survey. Parents and children also consented to have health professionals  
26 provide clinical information at the same measurement occasions. The study protocol received ethical  
27 approval from the Hamilton Integrated Research Ethics Board (14-130) and Research Ethics Board  
28 (105505).  
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## 48 **Measures**

### 49 *Mental disorder*

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51 Child mental disorder(s) were assessed using the Mini International Neuropsychiatric Interview for  
52 Children and Adolescents (MINI-KID).<sup>36</sup> The MINI-KID is a structured diagnostic interview used to assess  
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3 DSM-IV disorders in children aged 6-17 years and has been validated against the Schedule for Affective  
4 Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version.<sup>36</sup> It is composed of  
5 diagnostic modules that contain screening questions and skip patterns for each disorder. Phone  
6 interviews were administered separately: the MINI-KID(c), to children  $\geq 11$  years; and the MINI-KID(p)  
7 (proxy version) to all parents at both measurement occasions. The MINI-KID was administered by a  
8 single interviewer who underwent training that included monitored practice. The presence of the most  
9 common mental disorders was assessed: major depressive episode, separation anxiety disorder, social  
10 phobia, specific phobia, generalized anxiety disorder, attention deficit/hyperactivity disorder,  
11 oppositional defiant disorder, and conduct disorder.<sup>37</sup> The MINI-KID has demonstrated strong test-retest  
12 reliability compared to other instruments.<sup>15</sup> Mental disorder was classified according to parent reports  
13 on the MINI-KID.  
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### 30 *Quality of life*

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32 Child quality of life between the two visits was measured using the KIDSCREEN-27,<sup>38</sup> a 27-item child and  
33 parent-reported generic measure that assesses five domains: physical well-being (five items; examines  
34 physical activity and energy), psychological well-being (seven items; examines emotional balance and  
35 life satisfaction), autonomy and parent relations (seven items; examines family dynamics and age-  
36 appropriate freedoms), social support and peers (four items; examines nature of peer relationships) and  
37 school environment (four items; examines perception of cognition, learning, and feelings about school).  
38 Responses are scored using a five-point Likert scale and domain scores are transformed into T-values  
39 with a mean of 50 and a standard deviation of 10 (higher scores indicate better quality of life). The  
40 KIDSCREEN-27 has been found to be valid and reliable in children with and without physical  
41 conditions<sup>38,39</sup> and demonstrated adequate agreement<sup>38,39</sup> between children and parents.<sup>40</sup> Internal  
42 consistency reliabilities for each domain from this study were good for both child ( $\alpha=0.75-0.89$ ) and  
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3 parent reports ( $\alpha=0.83-0.92$ ). Because only children  $\geq 11$  years self-reported the KIDSCREEN-27 ( $n=28$ ,  
4 56%), only parent-reported KIDSCREEN-27 scores were used in these analyses.  
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### 10 *Parental stress*

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12 The Parental Stress Scale (PSS) measures parental stress across the domains of rewards, stressors, loss  
13 of control, and satisfaction.<sup>41</sup> The 18 items are rated on a five-point Likert scale (eight items are reverse-  
14 coded) with higher scores (range: 18-90) indicating more parental stress. The psychometric properties of  
15 the PSS are robust: test-retest reliability ( $r=0.81$ ) and convergent validity with the Parenting Stress Index  
16 ( $r=0.75$ ) and Perceived Stress Scale ( $r=0.41$ ).<sup>41</sup> Internal consistency for the PSS in this study was  $\alpha=0.84$ .  
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### 26 *Parental anxiety*

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28 The State Trait Anxiety Inventory (STAI) is a widely used tool for measuring anxiety. Of the 40 questions  
29 in the STAI survey, REACH considered “trait anxiety” items only which aim to measure how parents  
30 generally feel, as well as their propensity for perceived anxiety.<sup>42</sup> Survey responses were scored from 1-4  
31 (seven items are reverse-coded). Scores were summed together (range: 20-80) with higher scores  
32 indicating higher levels of anxiety. The STAI has robust psychometric properties, with trait-specific test-  
33 retest reliabilities of  $r=0.73-0.86$  and has been shown to be valid with other questionnaires used to  
34 assess anxiety ( $r=0.73-0.85$ ).<sup>42,43</sup> In this study, internal consistency for the STAI was  $\alpha=0.89$ .  
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### 46 *Parental depression*

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48 Parental symptoms of depression were measured with the Center for Epidemiological Studies  
49 Depression Scale (CES-D), a 20-item scale designed to assess depressive symptomatology in the general  
50 adult population over the past week.<sup>44</sup> The CES-D includes items that survey the domains of positive and  
51 negative affect, somatic activity, and interpersonal relations. A four-point Likert scale is used to rate the  
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3 frequency of symptoms experienced. Higher scores (range: 0-60) indicate greater frequency of  
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5 depressive symptoms and individuals with total scores  $\geq 16$  are typically identified as having clinically  
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7 significant levels of depression.<sup>44</sup> Extensive research has shown the CES-D to be valid and reliable.<sup>43,45</sup> In  
8  
9 this study, internal consistency for the CES-D was  $\alpha=0.93$ .

#### 14 *Family functioning*

16 The 12-item General Functioning subscale of the McMaster Family Assessment Device provided a valid  
17  
18 and reliable measure of the health/pathology of the family (i.e., family functioning).<sup>46,47</sup> The scale is  
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20 derived by summing items from six domains: problem solving, communication, roles, affective  
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22 responsiveness, affective involvement, and behavioral control. Items are rated on a four-point Likert  
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24 scale with higher scores (range: 0-36) indicating poorer overall family functioning. Internal consistency  
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26 for the FAD in this study was  $\alpha=0.92$ .

#### 32 *Physical Condition Disease severity*

34 Disease severity in children was assessed and measured by a health professional using a 10 cm visual  
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36 analog scale (VAS). The VAS represents a continuum of disease severity.<sup>48</sup> Health professionals marked  
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38 the VAS at the point at which best reflected the disease severity of the child, according to their clinical  
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40 judgment. The distance from the zero point of the VAS (left side) to the mark was measured and  
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42 recorded as the disease severity of the child. The VAS and its scoring method has been used in a variety  
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44 of populations and settings to assess well-being and pain and has the advantage of being easily  
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46 comparable across study samples.<sup>49,50</sup>

### *Demographic characteristics*

Sociodemographic data were collected on child and parent age, sex and immigrant status, parent marital status and educational attainment, as well as annual household income.

### **Analysis**

Comparisons between children with and without multimorbidity were made using Mann-Whitney (continuous variables) and Fisher's Exact tests (categorical variables). Changes in the prevalence of multimorbidity from baseline to six months was using the McNemar test. Analysis of variance with post hoc Scheffé tests were conducted to compare KIDSCREEN-27 scores with available population norms.<sup>38</sup> Generalized linear modeling was used to examine the association between multimorbidity and children's quality of life and parent psychosocial outcomes at six months. Outcomes were regressed on presence of multimorbidity, controlling for baseline scores for each respective outcome, as well as child age, sex, and physical condition. These covariates were included in the models to present unbiased estimates of effect. All analyses were conducted using SPSS 21 (IBM Corporation). Due to the pilot nature of this study, statistical tests were two-tailed using a significance level of  $\alpha=0.10$ . As there were no missing item-level data, complete case analysis was used.

### **Results**

#### *Sample characteristics*

Over 12 months, 62 families were approached to participate in REACH. Of these, 56 (90% response) agreed to participate. Four families were not interested in participating and two families had a child that did not meet the eligibility criteria. Fifty families (83% participation) completed the baseline assessment (telephone and mail) and forty-four (88% retention) completed the six-month follow-up (telephone and mail). Repeated attempts to contact the six families who completed the telephone interview, but did not

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3 return the complete mail survey, were unsuccessful, thus the reasons for withdrawal from the study are  
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5 unknown. There were no baseline differences between families lost to follow-up and those who  
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7 completed the study.  
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12 Baseline characteristics are shown in Table 1. The mean age of children was 11.3 (SD 3.3) years and 52%  
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14 were male. There was no difference in the number of children across physical condition subgroup,  
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16 though asthma was the most common (28%) and epilepsy and food allergy, the least common (16%).  
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18 Parents had a mean of age of 44.0 (5.7) years and 90% were female. Most parents were Caucasian  
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20 (94%), married (78%), had completed post-secondary education (78%), and had annual household  
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22 incomes of  $\geq$ \$90,000 Canadian dollars (58%).  
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### 28 *Prevalence of multimorbidity*

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30 The prevalence of multimorbidity declined from 58% at baseline to 42% at six-months ( $p=0.09$ ; Table 2).  
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32 At baseline, 11 (22%) children had multiple mental disorders. This decreased to nine (18%) at six  
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34 months. Anxiety disorder (at least one of separation anxiety, phobias, or generalized anxiety) was the  
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36 most common disorder at baseline (36%) and six months (26%). Differences across physical conditions  
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38 were found for the prevalence of attention-deficit hyperactivity disorder ( $\chi^2=6.44$ ;  $p=.06$ ) and  
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40 oppositional defiant disorder ( $\chi^2=7.53$ ;  $p=0.07$ ) at baseline and for attention-deficit hyperactivity  
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42 disorder ( $\chi^2=7.98$ ;  $p=.09$ ) at six months. In each case, the proportion of mental disorder was elevated in  
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44 children with food allergy.  
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### 50 *Correlates of multimorbidity*

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52 Results showed no differences in child and parent characteristics between children with and without  
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54 multimorbidity with two exceptions (Table 1): children with multimorbidity had lower KIDSCREEN-27  
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3 psychological well-being (43.6 vs. 49.4;  $p=0.08$ ) and parents reported higher STAI scores (44.2 vs. 38.2;  
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5  $p=0.05$ ).

### 6 7 8 9 10 *Multimorbidity and psychosocial outcomes*

11 Comparisons of KIDSCREEN-27 scores between our sample and population norms are shown in Figure 1.  
12  
13 Overall differences were found for the physical well-being, psychological well-being, and peer support  
14 domains. Post hoc tests showed that compared to population norms, children with multimorbidity had  
15 significantly poorer psychological well-being ( $t=4.21$ ;  $p<0.01$ ) and children without multimorbidity had  
16 lower peer support ( $t=2.66$ ;  $p<0.01$ ). Results of the unadjusted and adjusted generalized linear models  
17 of the association of multimorbidity with quality of life over time are shown in Table 3. Adjusting for  
18 child age, sex, type of physical condition, and baseline KIDSCREEN-27 score, multimorbidity was  
19 associated with lower scores in the following domains at six months: physical well-being ( $\beta=-4.82$ ;  
20  $p=0.03$ ), psychological well-being ( $\beta=-4.10$ ;  $p=0.06$ ), and school environment ( $\beta=-4.17$ ;  $p=0.09$ ). With the  
21 exception of autonomy and parent relations, the strength of the association increased after covariate  
22 adjustment.  
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39 The same modeling strategy was used to examine the associations with parental stress, anxiety,  
40 depression, and family functioning. In both unadjusted and adjusted models, multimorbidity was not  
41 associated with any psychosocial outcomes in parents over time (Table 4). Similarly, the strength of  
42 association (though not statistically significant) increased after covariate adjustment.  
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### 50 **Discussion**

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52 In this pilot study, over half of children screened positive for mental disorder(s) soon after being  
53 diagnosed with a physical condition and this proportion appeared to decrease six months later. Anxiety  
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3 disorders were found to be the most common disorders affecting children at diagnosis and six months  
4 later. There were no sociodemographic differences between children with and without multimorbidity.  
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6 While multimorbidity did have a negative effect on child quality of life over time, our hypothesis that it  
7  
8 would also influence parental outcomes was unsupported.  
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13 Methodologically, this pilot study has implications for the study of child multimorbidity within the  
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15 clinical setting. Regarding participant recruitment, we limited the amount of contact between research  
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17 staff and families during the initial contact in the clinic. This served two purposes: one, it minimized  
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19 burden on the physicians and nurses whose primary focus is clinical care, as well as clinical staff  
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21 managing large patient volumes. Two, it reduced the amount of information passed to families at a time  
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23 when they may have felt overwhelmed with the clinical information provided by the physician about  
24  
25 their child's diagnosis. We provided an information letter and then followed up by telephone a few days  
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27 later when families were away from the clinic and had a chance to review this letter and determine if  
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29 they wanted to participate. Our approach of engaging families personally in clinic, followed by  
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31 telephone contact, and data collection via mail survey was found to be acceptable to families. Our  
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33 strong response and retention rates contrast evidence showing reduced response rates in research  
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35 studies.<sup>51</sup> The majority of families in our study also noted that mail survey was the preferred method for  
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37 data collection compared to online surveys and home interviews (data not shown). Overall, our  
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39 methodology resulted in good coverage, with over 80% of consecutively approached eligible families  
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41 participating in the study. This suggests that the mental health of children with physical conditions is an  
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43 important concern for families and that they are willing to contribute their time to such research  
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45 studies. Our recruitment experience suggested that a number of children were ineligible for the study  
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47 because their illness duration was greater than six months. To ensure a more efficient recruitment that  
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49 encompasses an even larger coverage of our target population, the larger study will include children as  
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3 young as two years of age and we are expanding the number of physical conditions (e.g., bowel  
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5 diseases, chronic headache, lupus).  
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10 Our estimate of the proportion of children with multimorbidity was similar to previous reports<sup>8</sup> and  
11 supports the chronicity of multimorbidity during the early stages of being diagnosed with a physical  
12 condition.<sup>7</sup> As shown in previous work in children with diabetes<sup>12</sup> the peri-diagnostic period represents a  
13 critical developmental period for mental health. While this study did not measure mental disorder prior  
14 to the diagnosis of a physical condition, elevated rates of anxiety disorder at the time of diagnosis may  
15 be attributable to the uncertainty that children may experience (either before or after diagnosis)  
16 regarding the prognosis of their physical condition, including unpredictability of exacerbations, fear of  
17 death, loss of control, stigma associated with their condition, or adverse effects of medical treatment.<sup>10</sup>  
18 From this perspective, anxiety arises from negatively-biased thought patterns that exaggerate adverse  
19 effects of the physical condition and can undermine confidence in adapting to threatening situations.<sup>52</sup>  
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21 Anxiety in these children may be an inherited trait or learned behavior—parents of children with  
22 multimorbidity in our sample reported more symptoms of anxiety compared to parents of children  
23 without multimorbidity. There is also emerging evidence of shared biological pathways that underlie  
24 multimorbidity. In adults, symptoms of anxiety are associated with systemic inflammation,<sup>53</sup> which is  
25 elevated in individuals with physical conditions. Whether markers of inflammation, such as pro-  
26 inflammatory cytokines mediate the relationship between physical and mental disorder is unknown.  
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48 These findings also contribute to the converging evidence that risk for mental disorder is relatively  
49 consistent among children with various physical conditions.<sup>54</sup> One exception was that attention-deficit  
50 hyperactivity disorder was more common among children with food allergy. This increased risk is  
51 supported by some previous studies.<sup>55,56</sup> As in this work, attention-deficit hyperactivity disorder in our  
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3 sample of children with food allergy was mainly of the inattentive subtype. Inattentiveness may co-  
4 occur with core symptoms of generalized anxiety disorder, manifesting because of hypervigilance in  
5 avoiding food allergens. From a biological perspective, there is evidence of shared immunological<sup>57</sup> and  
6 inflammatory<sup>58</sup> responses for allergic conditions and attention-deficit hyperactivity disorder which may  
7 explain this association. Given the small number of children with food allergy in our sample, these  
8 interpretations are by no means definitive, but instead are offered as hypotheses to be tested rigorously  
9 in larger samples.  
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21 In general, the sample consisted of high socioeconomic two-parent families, which may have  
22 contributed to the lack of sociodemographic differences between children with and without  
23 multimorbidity and limits the generalizability of the findings. Placing the finding in the context of  
24 previous work is difficult given the absence of studies examining sociodemographic correlates of  
25 multimorbidity. Previous population-based studies conducted in Canada also showed no socioeconomic  
26 differences between children with and without physical conditions.<sup>24,59-61</sup> In our future larger study, we  
27 will work towards a recruitment strategy that will include wider variation in the socioeconomic status to  
28 families to increase the representativeness of the sample. Contrary to expectation, no effect of  
29 multimorbidity on parental outcomes was found. Nevertheless, information related to parental  
30 psychopathology and family environment may be important control variables used to isolate the effects  
31 of multimorbidity on child outcomes. Such family processes may also be implicated in complex pathways  
32 linking physical and mental health in children. As a result, these variables will be included in the larger  
33 study.  
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52 Multimorbidity appears to have a negative effect on children's quality of life, above and beyond the  
53 effect of having a physical condition alone.<sup>18</sup> This effect is pervasive, affecting multiple domains of  
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3 quality of life during the first six months after a diagnosis. Of interest is the finding that the magnitude  
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5 of effect seen for physical well-being, psychological well-being, and school environment was  
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7 approximately half a standard deviation. This metric has been validated as the minimal clinically  
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9 important difference for measures of quality of life<sup>62</sup> and provides evidence to support the perception  
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11 that changes in child quality of life due to multimorbidity are clinically relevant. Given the early onset of  
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13 multimorbidity, health professionals in the pediatric setting should consider engaging children and  
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15 families in discussions about mental health soon after the diagnosis of a physical condition is made and  
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17 discussion surrounding the physical condition completed. Within a holistic family-centered approach,  
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19 health professionals are encouraged to apply brief screening tools to identify at-risk children and  
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21 provide referrals to supportive services on a case-by-case basis. This is a critical window of opportunity  
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23 given that mental disorder is strong predictor of youth suicide<sup>63</sup> and that risk for suicide is highest soon  
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25 after an adolescent is diagnosed with a physical condition.<sup>64</sup> Because of the chronicity and pervasiveness  
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27 of multimorbidity and its influence on child and parent psychosocial functioning, continuing monitoring  
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29 during routine clinical assessments may also be warranted.  
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37 There are two noteworthy limitations. First, the study was likely underpowered to detect differences  
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39 between children with and without multimorbidity and the small sample size may limit the  
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41 generalizability of findings. However, our sample size was consistent with considerations for  
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43 implementing pilot studies<sup>35</sup> and our coverage of eligible families was good. Second, measurement of  
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45 child mental health and child and parent outcomes were parent-reported. While we have found  
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47 adequate agreement between parents and a small subset of children who provided self-reported quality  
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49 of life,<sup>40</sup> significant associations may be the result of shared-method variance.  
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## 54 **Conclusion**

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3 These preliminary findings indicate that mental disorder in children newly-diagnosed with a physical  
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5 condition is common and negatively affects their quality of life over time. If these results are replicated  
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7 in a subsequent larger study, health professionals should be aware of the burden of multimorbidity and  
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9 prepare themselves to discuss mental health with children and their parents. Findings from this pilot  
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11 study have been used to implement a large-scale study that will examine child multimorbidity in greater  
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13 depth and provide more definitive clinical implications.  
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For peer review only

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**Table 1. Baseline sample characteristics**

|                                | Full<br>sample | Multimorbid | Not<br>multimorbid | P-value |
|--------------------------------|----------------|-------------|--------------------|---------|
| N                              | 50             | 29          | 21                 |         |
| <b>Child</b>                   |                |             |                    |         |
| Age, years                     | 11.3 (3.3)     | 11.6 (3.2)  | 11.0 (3.4)         | 0.62    |
| Male, n (%)                    | 26 (52)        | 15 (52)     | 11 (52)            | 0.96    |
| Diagnoses, n (%)               |                |             |                    | 0.98    |
| Asthma                         | 14 (28)        | 9 (31)      | 5 (24)             |         |
| Diabetes                       | 9 (18)         | 4 (14)      | 5 (24)             |         |
| Epilepsy                       | 8 (16)         | 4 (14)      | 4 (19)             |         |
| Food allergy                   | 8 (16)         | 5 (17)      | 3 (14)             |         |
| Juvenile arthritis             | 11 (22)        | 7 (24)      | 4 (19)             |         |
| Disease severity, VAS          | 1.3 (1.2)      | 1.5 (1.3)   | 0.9 (0.9)          | 0.16    |
| Quality of life, KIDSCREEN-27  |                |             |                    |         |
| Physical well-being            | 48.0 (12.0)    | 47.4 (11.0) | 48.8 (13.4)        | 0.77    |
| Psychological well-being       | 46.1 (9.8)     | 43.6 (8.1)  | 49.4 (11.2)        | 0.08    |
| Autonomy/Parent relations      | 48.9 (9.6)     | 47.5 (7.0)  | 50.8 (12.1)        | 0.72    |
| Peer support                   | 46.1 (11.4)    | 46.7 (12.1) | 45.4 (10.5)        | 0.35    |
| School environment             | 50.1 (10.8)    | 47.7 (8.8)  | 53.3 (12.4)        | 0.12    |
| <b>Parent</b>                  |                |             |                    |         |
| Age, years                     | 44.0 (5.7)     | 43.0 (4.8)  | 45.2 (6.3)         | 0.43    |
| Female, n (%)                  | 45 (90)        | 26 (90)     | 19 (91)            | 0.92    |
| Immigrant, n (%)               | 10 (20)        | 8 (28)      | 2 (10)             | 0.16    |
| Married, n (%)                 | 39 (78)        | 22 (76)     | 17 (81)            | 0.67    |
| Post-secondary graduate, n (%) | 39 (78)        | 22 (76)     | 17 (81)            | 0.67    |
| Income ≥\$90,000, n (%)        | 29 (58)        | 17 (59)     | 12 (57)            | 0.87    |
| Parental stress, PSS           | 35.9 (7.9)     | 37.1 (7.3)  | 34.4 (8.5)         | 0.32    |
| Parental anxiety, STAI         | 41.6 (9.8)     | 44.2 (9.1)  | 38.2 (10.0)        | 0.05    |
| Parental depression CES-D      | 12.7 (9.9)     | 13.0 (9.6)  | 12.2 (10.5)        | 0.58    |
| Family functioning, FAD        | 25.5 (6.3)     | 24.7 (6.2)  | 26.5 (6.6)         | 0.20    |

Results are reported as mean (standard deviation) unless otherwise noted.

**Table 2. Prevalence of multimorbidity**

|                                 | Full sample | Asthma | Diabetes | Epilepsy | Food allergy | Juvenile arthritis | P-value |
|---------------------------------|-------------|--------|----------|----------|--------------|--------------------|---------|
| <b>Baseline</b>                 |             |        |          |          |              |                    |         |
| Any disorder                    | 29 (58)     | 9 (64) | 4 (44)   | 4 (50)   | 5 (63)       | 7 (64)             | 0.88    |
| Major depressive episode        | 12 (24)     | 4 (29) | 2 (22)   | 1 (13)   | 1 (13)       | 4 (36)             | 0.74    |
| Separation anxiety              | 2 (4)       | 0      | 0        | 1 (13)   | 0            | 1 (9)              | 0.43    |
| Phobia*                         | 15 (30)     | 6 (46) | 1 (11)   | 1 (13)   | 3 (38)       | 4 (36)             | 0.35    |
| Generalized anxiety             | 6 (12)      | 0      | 0        | 2 (25)   | 2 (25)       | 2 (18)             | 0.11    |
| Attention-deficit hyperactivity | 5 (10)      | 1 (7)  | 0        | 1 (13)   | 3 (38)       | 0                  | 0.06    |
| Oppositional defiant            | 9 (18)      | 2 (14) | 1 (11)   | 2 (25)   | 4 (50)       | 0                  | 0.07    |
| Conduct                         | 3 (6)       | 1 (7)  | 0        | 1 (13)   | 1 (13)       | 0                  | 0.65    |
| <b>Six months</b>               |             |        |          |          |              |                    |         |
| Any disorder                    | 21 (42)     | 9 (64) | 1 (11)   | 4 (50)   | 2 (25)       | 5 (56)             | 0.10    |
| Major depressive episode        | 2 (4)       | 0      | 0        | 0        | 0            | 2 (22)             | 0.11    |
| Separation anxiety              | 3 (6)       | 2 (14) | 0        | 1 (13)   | 0            | 0                  | 0.56    |
| Phobia*                         | 10 (20)     | 5 (36) | 1 (11)   | 1 (13)   | 0            | 3 (33)             | 0.25    |
| Generalized anxiety             | 4 (8)       | 1 (7)  | 0        | 1 (13)   | 0            | 2 (22)             | 0.55    |
| Attention-deficit hyperactivity | 3 (6)       | 0      | 0        | 0        | 2 (25)       | 1 (11)             | 0.09    |
| Oppositional defiant            | 6 (12)      | 2 (14) | 0        | 2 (25)   | 2 (25)       | 0                  | 0.31    |
| Conduct                         | 4 (8)       | 1 (7)  | 0        | 2 (25)   | 1 (13)       | 0                  | 0.33    |

Results are the number (%) of children with multimorbidity. Fisher's Exact tests examined multimorbidity across the five physical conditions.

\*Includes generalized, non-generalized, and specific phobias.

**Table 3. Longitudinal effects of multimorbidity on child quality of life**

| KIDSCREEN-27              | Unadjusted   |         | Adjusted     |         |
|---------------------------|--------------|---------|--------------|---------|
|                           | B (SE)       | P-value | B (SE)       | P-value |
| Physical well-being       | -3.76 (2.23) | 0.09    | -4.82 (2.22) | 0.03    |
| Psychological well-being  | -2.06 (2.44) | 0.40    | -4.10 (2.14) | 0.06    |
| Autonomy/Parent relations | 0.77 (2.53)  | 0.76    | -0.67 (2.40) | 0.78    |
| Peer support              | -0.59 (2.83) | 0.84    | -1.23 (2.66) | 0.64    |
| School environment        | -3.56 (2.88) | 0.22    | -4.17 (2.44) | 0.09    |

Models adjusted for child age and sex, physical condition, and baseline quality of life.

**Table 4. Longitudinal effects of multimorbidity on parental outcomes**

|                           | Unadjusted  |         | Adjusted     |         |
|---------------------------|-------------|---------|--------------|---------|
|                           | B (SE)      | P-value | B (SE)       | P-value |
| Parental stress, PSS      | 0.28 (1.60) | 0.86    | -1.50 (1.51) | 0.32    |
| Parental anxiety, STAI    | 0.14 (2.05) | 0.95    | -0.24 (2.15) | 0.91    |
| Parental depression CES-D | 0.30 (1.12) | 0.80    | 0.62 (1.13)  | 0.58    |
| Family functioning, FAD   | 1.21 (1.32) | 0.36    | 1.47 (1.28)  | 0.25    |

Models adjusted for child age and sex, physical condition, and baseline psychosocial outcome.



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2  
3 **Figure 1. Comparison of KIDSCREEN-27 scores with population norms**  
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5 \*p<0.10 for overall F-test across the three groups.  
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7 †Multimorbid group significantly lower than normative and not multimorbid groups.  
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9 ‡Not multimorbid group significantly lower than normative group.  
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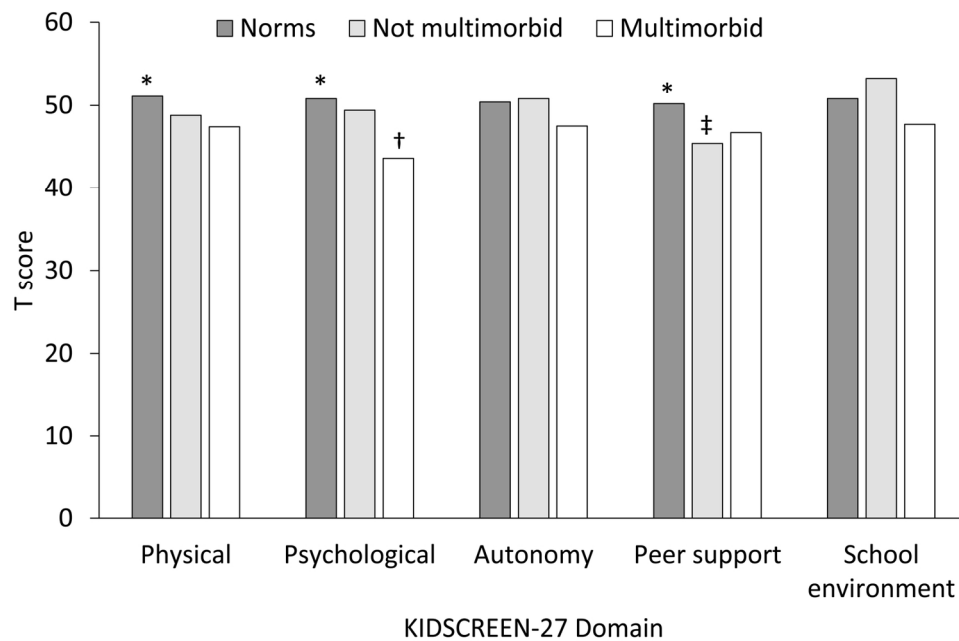


Figure 1. Comparison of KIDSCREEN-27 scores with population norms  
 \* $p < 0.10$  for overall F-test across the three groups.  
 †Multimorbid group significantly lower than normative and not multimorbid groups.  
 ‡Not multimorbid group significantly lower than normative group.

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**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies***

| Section/Topic                | Item # | Recommendation   | Reported on page # |
|------------------------------|--------|--|--------------------|
| Title and abstract           | 1      | (a) Indicate the study's design with a commonly used term in the title or the abstract   | 1                  |
|                              |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found  | 3                  |
| <b>Introduction</b>          |        |  |                    |
| Background/rationale         | 2      | Explain the scientific background and rationale for the investigation being reported   | 6-8                |
| Objectives                   | 3      | State specific objectives, including any prespecified hypotheses   | 8                  |
| <b>Methods</b>               |        |  |                    |
| Study design                 | 4      | Present key elements of study design early in the paper  | 9-10               |
| Setting                      | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  | 9                  |
| Participants                 | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up   | 9                  |
|                              |        | (b) For matched studies, give matching criteria and number of exposed and unexposed  | N/A                |
| Variables                    | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   | 10-13              |
| Data sources/<br>measurement | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 10-13              |
| Bias                         | 9      | Describe any efforts to address potential sources of bias  | 13                 |
| Study size                   | 10     | Explain how the study size was arrived at  | 9                  |
| Quantitative variables       | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why   | 13                 |
| Statistical methods          | 12     | (a) Describe all statistical methods, including those used to control for confounding  | 13                 |
|                              |        | (b) Describe any methods used to examine subgroups and interactions  | 13                 |
|                              |        | (c) Explain how missing data were addressed  | 13                 |
|                              |        | (d) If applicable, explain how loss to follow-up was addressed   | 13                 |
|                              |        | (e) Describe any sensitivity analyses  | N/A                |
| <b>Results</b>               |        |  |                    |

|                          |     |  |        |
|--------------------------|-----|--|--------|
| Participants             | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed            | 14     |
|                          |     | (b) Give reasons for non-participation at each stage   | 14     |
|                          |     | (c) Consider use of a flow diagram   | N/A    |
| Descriptive data         | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders   | 14     |
|                          |     | (b) Indicate number of participants with missing data for each variable of interest  | 14     |
|                          |     | (c) Summarise follow-up time (eg, average and total amount)  | 14     |
| Outcome data             | 15* | Report numbers of outcome events or summary measures over time   | 14     |
| Main results             | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 31-32  |
|                          |     | (b) Report category boundaries when continuous variables were categorized  | N/A    |
|                          |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period   | N/A    |
| Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   | 15-16  |
| <b>Discussion</b>        |     |  |        |
| Key results              | 18  | Summarise key results with reference to study objectives   | 16     |
| <b>Limitations</b>       |     |  |        |
| Interpretation           | 20  | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                   | 16-19  |
| Generalisability         | 21  | Discuss the generalisability (external validity) of the study results  | 18, 19 |
| <b>Other information</b> |     |  |        |
| Funding                  | 22  | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based  | 2      |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Mental Disorder in Children with Physical Conditions: A Pilot Study

|                                 |  |
|---------------------------------|--|
| Journal:                        | <i>BMJ Open</i>  |
| Manuscript ID                   | bmjopen-2017-019011.R2   |
| Article Type:                   | Research   |
| Date Submitted by the Author:   | 22-Nov-2017  |
| Complete List of Authors:       | Butler, Alexandra; University of Waterloo<br>Van Lieshout, Ryan ; McMaster University<br>Lipman, Ellen; McMaster University<br>MacMillan, Harriet; McMaster University<br>Gonzalez, Andrea; McMaster University<br>Gorter, Jan Willem; McMaster University<br>Georgiades, Kathy; McMaster University<br>Speechley, Kathy ; Western University,<br>Boyle , Michael ; McMaster University<br>Ferro, Mark; University of Waterloo, School of Public Health and Health Systems |
| <b>Primary Subject Heading</b>: | Mental health  |
| Secondary Subject Heading:      | Paediatrics  |
| Keywords:                       | multimorbidity, mental disorder, chronic disease, pilot study  |
|                                 |  |

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## Mental Disorder in Children with Physical Conditions: A Pilot Study

Butler A<sup>1</sup>, Van Lieshout RJ<sup>2</sup>, Lipman EL<sup>2</sup>, MacMillan HL<sup>2</sup>, Gonzalez A<sup>2</sup>, Gorter JW<sup>3</sup>, Georgiades K<sup>2</sup>,  
Speechley KN<sup>4,5</sup>, Boyle MH<sup>2</sup>, Ferro MA<sup>1,\*</sup>

[1] School of Public Health & Health Systems, University of Waterloo

[2] Department of Psychiatry & Behavioural Neurosciences, McMaster University

[3] Department of Pediatrics, McMaster University

[4] Department of Paediatrics, Western University

[5] Department of Epidemiology & Biostatistics, Western University

[\*] Corresponding author

### Contact information for corresponding author

Mark A. Ferro, University of Waterloo, School of Public Health and Health Systems, 200 University  
Avenue West, Waterloo, Ontario, Canada, N2L 3G1, Phone: 519.888.4567, Fax: 519.746.6776, Email:  
[mark.ferro@uwaterloo.ca](mailto:mark.ferro@uwaterloo.ca)

### Authors' contributions

MAF led the study. MAF, MHB, KNS, KG, JWG, AG, HLM, ELL, and RJV conceptualized and designed the study and were responsible for acquiring funding. MHB, KNS, KG, and AG provided methodological insights. JWG, HLM, ELL, and RJV provided clinical insights. KNS and HLM helped facilitate clinic participation. AB and MAF analyzed and interpreted data and drafted the manuscript. All authors critically reviewed, revised, and then approved the final manuscript as submitted.

## Funding

This work was supported by the Canadian Institutes of Health Research (MOP-133645). At the time of the study, MAF was supported by a Research Early Career Award from Hamilton Health Sciences. MAF currently holds the Canada Research Chair in Youth Mental Health; MHB holds the Canada Research Chair in the Social Determinants of Child Health; KG holds the Dan Offord Chair in Child Studies; JWG holds the Scotiabank Chair in Child Health Research; AG is supported by a Canadian Institutes for Health Research New Investigator Award; HLM holds the Chedoke Health Chair in Child Psychiatry; and, RJV holds the Canada Research Chair in the Perinatal Programming of Mental Disorders and Albert Einstein/Irving Zucker Chair in Neuroscience.

## Competing interests

The authors declare that they have no competing interests.

## Data sharing statement

Data will not be shared in order to protect the confidentiality of participants. This was a multisite study and we do not have approval to make the data publically available.

## Acknowledgements

The authors gratefully acknowledge the children, parents, and health professionals and their staff without whose participation this study would not have been possible. We especially thank Jessica Zelman for coordinating the study and Jane Terhaerd for assisting with ethical approval. Health professional contributors to this study were: Janice Falcone, Karen McAssey, Marilyn Rothney, Susan Wasserman (McMaster Children's Hospital) and Roberta Berard, Craig Campbell, Margo Devries-Rizzo,

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Michelle Diebold, Patti Guertjens, Simon Levin, Narayan Prasad (Children’s Hospital London Health Sciences).

For peer review only



## Abstract

**Objectives:** Methodologically, to assess the feasibility of participant recruitment and retention, as well as missing data in studying mental disorder among children newly-diagnosed with chronic physical conditions (i.e., multimorbidity). Substantively, to examine the prevalence of multimorbidity, identify sociodemographic correlates, and model the influence of multimorbidity on changes in child quality of life and parental psychosocial outcomes over a six-month follow-up.

**Design:** Prospective pilot study.

**Setting:** Two children's tertiary-care hospitals.

**Participants:** Children aged 6-16 years diagnosed in the past six months with one of asthma, diabetes, epilepsy, food allergy, or juvenile arthritis and their parents.

**Outcome measures:** Response, participation, and retention rates. Child mental disorder using the Mini International Neuropsychiatric Interview at baseline and six months. Child quality of life, parental symptoms of stress, anxiety, and depression, and family functioning. All outcomes were parent reported.

**Results:** Response, participation, and retention rates were 90%, 83%, and 88%, respectively. Of the 50 children enrolled in the study, the prevalence of multimorbidity was 58% at baseline and 42% at six months. No sociodemographic characteristics were associated with multimorbidity. Multimorbidity at baseline was associated with declines over six months in the following quality of life domains: physical well-being,  $\beta=-4.82$  (-8.47, -1.17), psychological well-being,  $\beta=-4.10$  (-7.62, -0.58), and school

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3 environment,  $\beta=-4.17$  (-8.18, -0.16). There was no association with parental psychosocial outcomes over  
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5 time.  
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10 **Conclusions:** Preliminary evidence suggests that mental disorder in children with a physical condition is  
11  
12 very common and has a negative impact on quality of life over time. Based on the strong response rate  
13  
14 and minimal attrition, our approach to study child multimorbidity appears feasible and suggests that  
15  
16 multimorbidity is an important concern for families. Methodological and substantive findings from this  
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18 pilot study have been used to implement a larger, more definitive study of child multimorbidity, which  
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20 should lead to important clinical implications.  
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For peer review only

### Strengths and limitations of this study

- This pilot study includes children newly-diagnosed with chronic physical conditions.
- This is the first study to examine mental disorder in children newly-diagnosed with a number of different conditions.
- This study was likely underpowered to detect differences within and between children with and without multimorbidity and the small sample size limits generalizability.
- All outcomes were parent-reported.

## Introduction

The global prevalence of children with a chronic physical condition—a health problem that requires ongoing management over a period of years or decades—is common, affecting approximately 25% of children, and increasing.<sup>1</sup> These children may be adversely affected by their disorders or their treatment, subsequently developing additional conditions, including mental disorders.<sup>2</sup> Compared to their peers with a physical or mental disorder only, children with multimorbidity (physical-mental comorbidity) experience greater symptom severity and impairment in both physical and mental health domains.<sup>3</sup> Understandably, the onset of multimorbidity remains an important concern for children, parents, health professionals, and payers.<sup>4</sup>

Mental disorders of any type are common in children and adolescents<sup>5</sup> and disproportionately affect young people with chronic physical conditions (herein physical conditions).<sup>6,7</sup> Estimates from clinical samples suggest that nearly half of children with physical conditions meet criteria for a mental disorder diagnosis.<sup>8</sup> In general population samples, this estimate is lower, with approximately 20-30% of children being affected.<sup>3</sup>

Evidence of the association between physical and mental health is robust,<sup>9-11</sup> but with few exceptions,<sup>7,12,13</sup> the literature base consists mostly of cross-sectional studies. This limits our understanding of mental health at the time children are diagnosed with a physical condition and how their mental health may change over time. One study found more parent-reported symptoms of problem behavior in children 6-7 years newly diagnosed with a chronic illness compared to healthy controls.<sup>7</sup> This effect was stable through to 10-11 years of age, highlighting the chronicity of multimorbidity in childhood. In a prospective study of children with diabetes, hazard ratios for mental disorder were highest within six-months of the diabetes diagnosis (3.0 [2.7-3.4]) compared to those with

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3 a duration of diabetes of five years or more (1.9 [1.7-2.1]), regardless of age at diagnosis,<sup>12</sup> suggesting  
4 that the peri-diagnostic period may be a time of particular mental health risk. Another prospective study  
5 showed changes over time in associations of mental health with physical conditions being associated  
6 with depressive symptoms during childhood, and with anxiety symptoms during early adolescence.<sup>13</sup>  
7  
8 While these studies have advanced the field, opportunities exist to overcome the limitations in these  
9 studies associated with the ascertainment of physical conditions based on parent-report,<sup>14</sup> assessment  
10 of symptoms of problem behaviors rather than mental disorder,<sup>13,15,16</sup> and inherent weaknesses of using  
11 register-based data related to data quality and variable availability.<sup>17</sup>  
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14 Existing research also suggests that physical conditions and mental disorders are independently  
15 associated with poorer psychosocial outcomes including quality of life<sup>18,19</sup> and self-esteem,<sup>20,21</sup> as well as  
16 academic performance.<sup>22,23</sup> These adverse effects can also extend to parents and families who  
17 experience elevated stress and psychological distress, worse family functioning, and financial  
18 hardship.<sup>24-28</sup> Effects on child and parent psychosocial outcomes appear similar when physical and  
19 mental disorders are examined separately; however, there is little research examining whether  
20 multimorbidity exerts a compounding effect. Cross-sectional evidence suggests that children with  
21 multimorbidity experience worse quality of life compared to children with a physical or mental disorder  
22 alone.<sup>29,30</sup> One prospective study showed that adults who experienced multimorbidity during  
23 adolescence had lower quality of life compared to those who had a physical or mental disorder only.<sup>31</sup>  
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25 These researchers found that among those with multimorbidity, physical conditions affected physical  
26 quality of life only; while their mental disorder negatively affected multiple domains of life quality,  
27 including physical, emotional, and social well-being. The extent to which multimorbidity influences other  
28 aspects of parental health and well-being, including parenting stress, psychopathology, and family  
29 relationships, is not well known.  
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5 Despite the progress made in understanding child multimorbidity and its effects on psychosocial  
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7 outcomes, important knowledge gaps remain. First, the burden and correlates of multimorbidity,  
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9 particularly in clinical samples of children who represent the largest consumers of health services,<sup>32</sup> is  
10  
11 not well known. While other studies have examined prevalence of multimorbidity, those studies were  
12  
13 based on population, not clinical samples of prevalent cases and did not measure DSM-aligned  
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15 diagnoses;<sup>3,13</sup> are out-dated;<sup>8</sup> or, focus on a single physical condition.<sup>12</sup> This information is needed to  
16  
17 inform resource allocation and the provision of services within the health system. Second, the timing of  
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19 multimorbidity onset, how it changes, and its influence on psychosocial outcomes over time are not  
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21 well-understood, limiting our ability to identify opportunities for intervention to prevent the  
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23 development of mental disorder in children with physical conditions. This includes a lack of  
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25 understanding how mental disorders may change or appear in relation to the onset of the physical  
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27 condition. For example, are anxiety disorders more common at the time of diagnosis given the  
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29 uncertainty surrounding prognosis? Third, effects of child multimorbidity on parental health and well-  
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31 being have not been explored in much detail. Understanding these effects is key to designing,  
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33 implementing, and evaluating family-centered approaches to care within the pediatric setting to  
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35 promote the best possible health outcomes for children, parents, and families.<sup>33</sup>  
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43 Anticipating substantial hardship, stress, and psychological distress associated with receiving a diagnosis  
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45 of a physical condition in childhood within families, as well as prognostic uncertainty,<sup>12,34-38</sup> we  
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47 conducted a pilot study to assess the feasibility of recruiting of eligible participants, estimating  
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49 respondent burden related to data collection, and the extent of missing data and attrition.  
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51 Substantively, the aims of the pilot study were to: 1—examine the initial prevalence of multimorbidity in  
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53 a clinical sample of children newly-diagnosed with a physical condition, as well as rates six months later;  
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3 2—identify correlates of multimorbidity in children and parents; and, 3—explore the influence of  
4 multimorbidity on changes in child quality of life and parental psychosocial outcomes over six-months of  
5 follow-up. Based on previous clinical studies,<sup>8</sup> we hypothesized that at the time of diagnosis, 50% of  
6 children would screen positive for mental disorder. Based on limited evidence,<sup>12</sup> we hypothesized that  
7 six months later, there would be a decrease in the proportion of multimorbidity. Finally, we  
8 hypothesized that children with multimorbidity would have worse quality of life over time; their parents,  
9 more symptoms of parenting stress, anxiety, and depression; and, their families, worse functioning  
10 compared to children with physical conditions only.  
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## 23 **Methods**

### 24 **Sample**

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26 Data come from a multisite, prospective, pilot study aimed at examining mental disorder(s) in children  
27 with physical conditions. Families were recruited from four outpatient clinics from two pediatric  
28 academic hospitals (specialized tertiary care centres; two clinics per hospital) in Ontario, Canada to  
29 assess mental and psychosocial outcomes in children with newly-diagnosed with physical conditions.  
30 Health professionals at the hospitals were involved at the initial point of contact and provided eligible  
31 families with an overview of the study and details regarding participation. The eligibility criteria for the  
32 study were children who: 1—were aged 6-16 years old (six is the youngest age at which our measure of  
33 mental disorder is validated; the ceiling age of 16 years ensured that during the follow-up, participants  
34 did not transfer out of the pediatric health system); 2—had received a diagnosis of asthma, diabetes,  
35 epilepsy, food allergy or juvenile idiopathic arthritis (which represent the most common physical  
36 conditions among children)<sup>39</sup> within the six months prior to recruitment; and, 3—had a parent who  
37 could read English (not all measures have been validated in other languages). Children were excluded if  
38 they had a degenerative neurological disorder because child and parental outcomes are well-established  
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3 in this population. Child IQ was not tested and children were not excluded if their parents indicated  
4 intellectual disability, maximizing the coverage and representativeness of our sample. Following sample  
5 size guidelines suggested for the conduct of pilot studies,<sup>40</sup> we aimed to recruit 60 children and families  
6 (12 per condition) over a 12-month period.  
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## 14 **Data Collection**

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16 After the medical encounter, eligible families were invited by clinic nurses to speak with research staff  
17 about the study. Research staff briefly introduced the study and provided families an information letter.  
18 Families interested in participating in the study consented for clinic nurses to send their contact  
19 information to study investigators who then followed-up with families by telephone to confirm  
20 eligibility, obtain oral consent from parents and children, and arrange for a convenient time to conduct a  
21 telephone interview to assess child mental health. Parents also completed two mailed surveys to assess  
22 psychosocial outcomes and demographic characteristics; one at baseline and one six months later, when  
23 a second telephone interview to assess mental health was conducted. Parents of all participating  
24 children provided proxy reports and children who were  $\geq 11$  years of age (n=33) self-reported on the  
25 telephone interview and to the mail survey. Parents and children also consented to have health  
26 professionals provide clinical information at the same measurement occasions. The study protocol  
27 received ethical approval from the Hamilton Integrated Research Ethics Board (14-130) and Research  
28 Ethics Board (105505).  
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## 48 **Measures**

### 49 *Mental disorder*

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51 Child mental disorder(s) were assessed using the Mini International Neuropsychiatric Interview for  
52 Children and Adolescents (MINI-KID).<sup>41</sup> The MINI-KID is a structured diagnostic interview used to assess  
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3 DSM-IV disorders in children aged 6-17 years and has been validated against the Schedule for Affective  
4 Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version.<sup>41</sup> It is composed of  
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6 diagnostic modules that contain screening questions and skip patterns for each disorder. Phone  
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8 interviews were administered separately: the MINI-KID(c), to children  $\geq 11$  years; and the MINI-KID(p)  
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10 (proxy version) to all parents at both measurement occasions. The MINI-KID was administered by a  
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12 single interviewer who underwent training that included monitored practice. The presence of the most  
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14 common mental disorders was assessed: major depressive episode, separation anxiety disorder, social  
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16 phobia, specific phobia, generalized anxiety disorder, attention deficit/hyperactivity disorder,  
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18 oppositional defiant disorder, and conduct disorder.<sup>42</sup> The MINI-KID has demonstrated strong test-retest  
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20 reliability compared to other instruments.<sup>15</sup> Mental disorder was classified according to parent reports  
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22 on the MINI-KID.  
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### 30 *Quality of life*

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32 Child quality of life between the two visits was measured using the KIDSCREEN-27,<sup>43</sup> a 27-item child and  
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34 parent-reported generic measure that assesses five domains: physical well-being (five items; examines  
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36 physical activity and energy), psychological well-being (seven items; examines emotional balance and  
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38 life satisfaction), autonomy and parent relations (seven items; examines family dynamics and age-  
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40 appropriate freedoms), social support and peers (four items; examines nature of peer relationships) and  
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42 school environment (four items; examines perception of cognition, learning, and feelings about school).  
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44 Responses are scored using a five-point Likert scale and domain scores are transformed into T-values  
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46 with a mean of 50 and a standard deviation of 10 (higher scores indicate better quality of life). The  
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48 KIDSCREEN-27 has been found to be valid and reliable in children with and without physical  
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50 conditions<sup>43,44</sup> and demonstrated adequate agreement between children and parents.<sup>45</sup> Internal  
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3 consistency reliabilities for each domain from this study were good for both child ( $\alpha=0.75-0.89$ ) and  
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5 parent reports ( $\alpha=0.83-0.92$ ).  
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#### 10 *Parental stress*

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12 The Parental Stress Scale (PSS) measures parental stress across the domains of rewards, stressors, loss  
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14 of control, and satisfaction.<sup>46</sup> The 18 items are rated on a five-point Likert scale (eight items are reverse-  
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16 coded) with higher scores (range: 18-90) indicating more parental stress. The psychometric properties of  
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18 the PSS are robust: test-retest reliability ( $r=0.81$ ) and convergent validity with the Parenting Stress Index  
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20 ( $r=0.75$ ) and Perceived Stress Scale ( $r=0.41$ ).<sup>46</sup> Internal consistency for the PSS in this study was  $\alpha=0.84$ .  
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#### 26 *Parental anxiety*

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28 The State Trait Anxiety Inventory (STAI) is a widely used tool for measuring anxiety. Of the 40 questions  
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30 in the STAI survey, REACH considered “trait anxiety” items only which aim to measure how parents  
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32 generally feel, as well as their propensity for perceived anxiety.<sup>47</sup> Survey responses were scored from 1-4  
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34 (seven items are reverse-coded). Scores were summed together (range: 20-80) with higher scores  
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36 indicating higher levels of anxiety. The STAI has robust psychometric properties, with trait-specific test-  
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38 retest reliabilities of  $r=0.73-0.86$  and has been shown to be valid with other questionnaires used to  
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40 assess anxiety ( $r=0.73-0.85$ ).<sup>47,48</sup> In this study, internal consistency for the STAI was  $\alpha=0.89$ .  
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#### 46 *Parental depression*

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48 Parental symptoms of depression were measured with the Center for Epidemiological Studies  
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50 Depression Scale (CES-D), a 20-item scale designed to assess depressive symptomatology in the general  
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52 adult population over the past week.<sup>49</sup> The CES-D includes items that survey the domains of positive and  
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54 negative affect, somatic activity, and interpersonal relations. A four-point Likert scale is used to rate the  
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3 frequency of symptoms experienced. Higher scores (range: 0-60) indicate greater frequency of  
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5 depressive symptoms and individuals with total scores  $\geq 16$  are typically identified as having clinically  
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7 significant levels of depression.<sup>49</sup> Extensive research has shown the CES-D to be valid and reliable.<sup>48,50</sup> In  
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9 this study, internal consistency for the CES-D was  $\alpha=0.93$ .  
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#### 14 *Family functioning*

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16 The 12-item General Functioning subscale of the McMaster Family Assessment Device provided a valid  
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18 and reliable measure of the health/pathology of the family (i.e., family functioning).<sup>51,52</sup> The scale is  
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20 derived by summing items from six domains: problem solving, communication, roles, affective  
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22 responsiveness, affective involvement, and behavioral control. Items are rated on a four-point Likert  
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24 scale with higher scores (range: 0-36) indicating poorer overall family functioning. Internal consistency  
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26 for the FAD in this study was  $\alpha=0.92$ .  
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#### 32 *Physical Condition Disease severity*

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34 Disease severity in children was assessed and measured by a health professional using a 10 cm visual  
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36 analog scale (VAS). The VAS represents a continuum of disease severity.<sup>53</sup> Health professionals marked  
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38 the VAS at the point at which best reflected the disease severity of the child, according to their clinical  
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40 judgment. The distance from the zero point of the VAS (left side) to the mark was measured and  
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42 recorded as the disease severity of the child. The VAS and its scoring method has been used in a variety  
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44 of populations and settings to assess well-being and pain and has the advantage of being easily  
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46 comparable across study samples.<sup>54,55</sup>  
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### *Demographic characteristics*

Sociodemographic data were collected on child and parent age, sex and immigrant status, parent marital status and educational attainment, as well as annual household income.

### **Analysis**

Comparisons between children with and without multimorbidity were made using Mann-Whitney (continuous variables) and Fisher's Exact tests (categorical variables). Changes in the prevalence of multimorbidity from baseline to six months was using the McNemar test. Analysis of variance with post hoc Scheffé tests were conducted to compare KIDSCREEN-27 scores with available population norms.<sup>43</sup> Generalized linear modeling was used to examine the association between multimorbidity and children's quality of life and parent psychosocial outcomes at six months. Outcomes were regressed on presence of multimorbidity, controlling for baseline scores for each respective outcome, as well as child age, sex, and physical condition. These covariates were included in the models to present unbiased estimates of effect. All analyses were conducted using SPSS 21 (IBM Corporation). Due to the pilot nature of this study, statistical tests were two-tailed using a significance level of  $\alpha=0.10$ . As there were no missing item-level data, complete case analysis was used.

### **Results**

#### *Sample characteristics*

Over 12 months, 62 families were approached to participate in REACH. Of these, 56 (90% response) agreed to participate. Four families were not interested in participating and two families had a child that did not meet the eligibility criteria. Fifty families (83% participation) completed the baseline assessment (telephone and mail) and forty-four (88% retention) completed the six-month follow-up (telephone and mail). Repeated attempts to contact the six families who completed the telephone interview, but did not

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3 return the complete mail survey, were unsuccessful, thus the reasons for withdrawal from the study are  
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5 unknown. There were no baseline differences between families lost to follow-up and those who  
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7 completed the study.  
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12 Baseline characteristics are shown in Table 1. The mean age of children was 11.3 (SD 3.3) years and 52%  
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14 were male. There was no difference in the number of children across physical condition subgroup,  
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16 though asthma was the most common (28%) and epilepsy and food allergy, the least common (16%).  
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18 Parents had a mean of age of 44.0 (5.7) years and 90% were female. Most parents were Caucasian  
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20 (94%), married (78%), had completed post-secondary education (78%), and had annual household  
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22 incomes of  $\geq$ \$90,000 Canadian dollars (58%).  
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### 28 *Prevalence of multimorbidity*

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30 The prevalence of parent-reported multimorbidity declined from 58% at baseline to 42% at six months  
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32 ( $p=0.09$ ; Table 2). At baseline, 11 (22%) children had multiple mental disorders. This decreased to nine  
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34 (18%) at six months. Anxiety disorder (at least one of separation anxiety, phobias, or generalized  
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36 anxiety) was the most common disorder at baseline (36%) and six months (26%). Differences across  
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38 physical conditions were found for the prevalence of attention-deficit hyperactivity disorder ( $\chi^2=6.44$ ;  
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40  $p=.06$ ) and oppositional defiant disorder ( $\chi^2=7.53$ ;  $p=0.07$ ) at baseline and for attention-deficit  
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42 hyperactivity disorder ( $\chi^2=7.98$ ;  $p=0.09$ ) at six months. In each case, the proportion of mental disorder  
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44 was elevated in children with food allergy.  
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50 The prevalence of child-reported multimorbidity was substantially lower than that reported by  
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52 parents—18% at baseline and 15% at six months. Given the low number of child age-eligible to provide  
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3 self-reports, differences in mental disorder across physical conditions were not examined. Parent-child  
4 agreement on the MINI-KID for any mental disorder was  $\kappa=0.15$ .  
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### 8 9 10 *Correlates of multimorbidity*

11 Results showed no differences in child and parent characteristics between children with and without  
12 parent-reported multimorbidity with two exceptions (Table 1): children with multimorbidity had lower  
13 KIDSCREEN-27 psychological well-being (43.6 vs. 49.4;  $p=0.08$ ) and parents reported higher STAI scores  
14 (44.2 vs. 38.2;  $p=0.05$ ). Among children who provide self-reports, those with multimorbidity reported  
15 lower KIDSCREEN-27 scores in the following domains: psychological well-being (38.1 vs. 49.1;  $p<0.01$ ),  
16 peer support (41.6 vs. 50.7;  $p<0.01$ ), and school environment (41.8 vs. 51.5;  $p=0.01$ ).  
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### 26 27 28 *Multimorbidity and psychosocial outcomes*

29 Comparisons of parent-reported KIDSCREEN-27 scores between our sample and population norms are  
30 shown in Figure 1. Overall differences were found for the physical well-being, psychological well-being,  
31 and peer support domains. Post hoc tests showed that compared to population norms, children with  
32 multimorbidity had significantly poorer psychological well-being ( $t=4.21$ ;  $p<0.01$ ) and children without  
33 multimorbidity had lower peer support ( $t=2.66$ ;  $p<0.01$ ). Results of the unadjusted and adjusted  
34 generalized linear models of the association of parent-reported multimorbidity with quality of life over  
35 time are shown in Table 3. Adjusting for child age, sex, type of physical condition, and baseline  
36 KIDSCREEN-27 score, multimorbidity was associated with lower scores in the following domains at six  
37 months: physical well-being ( $B=-4.82$ ;  $p=0.03$ ), psychological well-being ( $B=-4.10$ ;  $p=0.06$ ), and school  
38 environment ( $B=-4.17$ ;  $p=0.09$ ). With the exception of autonomy and parent relations, the strength of  
39 the association increased after covariate adjustment. Though similar estimates of association were  
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3 found for child reports (multimorbidity and KIDSCREEN-27), only the association between  
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5 multimorbidity and psychological well-being was statistically significant ( $B=-10.66$ ;  $p=0.03$ ).  
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10 The same modeling strategy was used to examine the associations with parental stress, anxiety,  
11  
12 depression, and family functioning. In both unadjusted and adjusted models, multimorbidity was not  
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14 associated with any psychosocial outcomes in parents over time (Table 4). Similarly, the strength of  
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16 association (though not statistically significant) increased after covariate adjustment.  
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## 21 Discussion

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23 In this pilot study, over half of children screened positive, based on parent-report, for mental disorder(s)  
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25 soon after being diagnosed with a physical condition and this proportion appeared to decrease six  
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27 months later. This contrasted self-reported mental disorder, in which approximately one in five children  
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29 screened positive and which remained relatively stable over time. Anxiety disorders were found to be  
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31 the most common disorders affecting children at diagnosis and six months later. There were no  
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33 sociodemographic differences between children with and without multimorbidity. While multimorbidity  
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35 did have a negative effect on child quality of life over time, our hypothesis that it would also influence  
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37 parental outcomes was unsupported.  
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43 Methodologically, this pilot work has implications for the study of child multimorbidity within the clinical  
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45 setting. Regarding participant recruitment, we limited the amount of contact between research staff  
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47 and families during the initial contact in the clinic. This served two purposes: one, it minimized burden  
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49 on the physicians and nurses whose primary focus is clinical care, as well as clinical staff managing large  
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51 patient volumes. Two, it reduced the amount of information passed to families at a time when they may  
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53 have felt overwhelmed with the clinical information provided by the physician about their child's  
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3 diagnosis. We provided an information letter and then followed up by telephone a few days later when  
4 families were away from the clinic and had a chance to review this letter and determine if they wanted  
5 to participate. Our approach of engaging families personally in clinic, followed by telephone contact, and  
6 data collection via mail survey was found to be acceptable to families. Our strong response and  
7 retention rates contrast evidence showing reduced response rates in research studies.<sup>56</sup> The majority of  
8 families in our study also noted that mail survey was the preferred method for data collection compared  
9 to online surveys and home interviews (data not shown). Overall, our methodology resulted in good  
10 coverage, with over 80% of consecutively approached eligible families participating in the study. This  
11 suggests that the mental health of children with physical conditions is an important concern for families  
12 and that they are willing to contribute their time to such research studies. Our recruitment experience  
13 suggested that a number of children were ineligible for the study because their illness duration was  
14 greater than six months. To ensure a more efficient recruitment that encompasses an even larger  
15 coverage of our target population, the larger study will include children as young as two years of age  
16 and we are expanding the number of physical conditions (e.g., bowel diseases, chronic headache, lupus).

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37 Our study reaffirms the need to consider the perspective of multiple informants when assessing the  
38 presence of child mental disorder.<sup>57,58</sup> Parent-child agreement was nearly identical to previous  
39 research,<sup>58</sup> suggesting that the presence of a physical condition in children does not appear to influence  
40 the level of agreement between child and parent reports of mental disorder. The extent to which the  
41 excess proportion of multimorbidity identified by parents is clinically relevant requires additional study  
42 that include assessments by mental health professionals to verify clinical diagnoses of mental disorder.

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52 Our estimate of the proportion of children with multimorbidity was similar to previous reports<sup>8</sup> and  
53 supports the chronicity of multimorbidity during the early stages of being diagnosed with a physical  
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3 condition.<sup>7</sup> As shown in previous work in children with diabetes<sup>12</sup> the peri-diagnostic period represents a  
4 critical developmental period for mental health. While this study did not measure mental disorder prior  
5 to the diagnosis of a physical condition, elevated rates of anxiety disorder at the time of diagnosis may  
6 be attributable to the uncertainty that children may experience (either before or after diagnosis)  
7 regarding the prognosis of their physical condition, including unpredictability of exacerbations, fear of  
8 death, loss of control, stigma associated with their condition, or adverse effects of medical treatment.<sup>10</sup>  
9 From this perspective, anxiety arises from negatively-biased thought patterns that exaggerate adverse  
10 effects of the physical condition and can undermine confidence in adapting to threatening situations.<sup>59</sup>  
11 Anxiety in these children may be an inherited trait or learned behavior—parents of children with  
12 multimorbidity in our sample reported more symptoms of anxiety compared to parents of children  
13 without multimorbidity. There is also emerging evidence of shared biological pathways that underlie  
14 multimorbidity. In adults, symptoms of anxiety are associated with systemic inflammation,<sup>60</sup> which is  
15 elevated in individuals with physical conditions. Whether markers of inflammation, such as pro-  
16 inflammatory cytokines mediate the relationship between physical and mental disorder is unknown.  
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18 These findings also contribute to the converging evidence that risk for mental disorder is relatively  
19 consistent among children with various physical conditions.<sup>61</sup> One exception was that attention-deficit  
20 hyperactivity disorder was more common among children with food allergy. This increased risk is  
21 supported by some previous studies.<sup>37,62</sup> As in this work, attention-deficit hyperactivity disorder in our  
22 sample of children with food allergy was mainly of the inattentive subtype. Inattentiveness may co-  
23 occur with core symptoms of generalized anxiety disorder, manifesting because of hypervigilance in  
24 avoiding food allergens. From a biological perspective, there is evidence of shared immunological<sup>63</sup> and  
25 inflammatory<sup>64</sup> responses for allergic conditions and attention-deficit hyperactivity disorder which may  
26 explain this association. Given the small number of children with food allergy in our sample, these  
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3 interpretations are by no means definitive, but instead are offered as hypotheses to be tested rigorously  
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5 in larger samples.  
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10 In general, the sample consisted of high socioeconomic two-parent families, which may have  
11 contributed to the lack of sociodemographic differences between children with and without  
12 multimorbidity and limits the generalizability of the findings. Placing the finding in the context of  
13 previous work is difficult given the absence of studies examining sociodemographic correlates of  
14 multimorbidity. Previous population-based studies conducted in Canada also showed no socioeconomic  
15 differences between children with and without physical conditions.<sup>24,65-67</sup> In our future larger study, we  
16 will work towards a recruitment strategy that will include wider variation in the socioeconomic status to  
17 families to increase the representativeness of the sample. Contrary to expectation, no effect of  
18 multimorbidity on parental outcomes was found. Nevertheless, information related to parental  
19 psychopathology and family environment may be important control variables used to isolate the effects  
20 of multimorbidity on child outcomes. Such family processes may also be implicated in complex pathways  
21 linking physical and mental health in children. As a result, these variables will be included in the larger  
22 study.  
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41 Multimorbidity appears to have a negative effect on children's quality of life, above and beyond the  
42 effect of having a physical condition alone.<sup>18</sup> This effect is pervasive, affecting multiple domains of  
43 quality of life during the first six months after a diagnosis. Of interest is the finding that the magnitude  
44 of effect seen for physical well-being, psychological well-being, and school environment was  
45 approximately half a standard deviation. This metric has been validated as the minimal clinically  
46 important difference for measures of quality of life<sup>68</sup> and provides evidence to support the perception  
47 that changes in child quality of life due to multimorbidity are clinically relevant. Given the early onset of  
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3 multimorbidity, health professionals in the pediatric setting should consider engaging children and  
4 families in discussions about mental health soon after the diagnosis of a physical condition is made and  
5 discussion surrounding the physical condition completed. Within a holistic family-centered approach,  
6 health professionals are encouraged to apply brief screening tools to identify at-risk children and  
7 provide referrals to supportive services on a case-by-case basis. This is a critical window of opportunity  
8 given that mental disorder is strong predictor of youth suicide<sup>69</sup> and that risk for suicide is highest soon  
9 after an adolescent is diagnosed with a physical condition.<sup>34</sup> Because of the chronicity and pervasiveness  
10 of multimorbidity and its influence on child and parent psychosocial functioning, continuing monitoring  
11 during routine clinical assessments may also be warranted.  
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26 There is one noteworthy limitation: the study was likely underpowered to detect differences between  
27 children with and without multimorbidity and the small sample size may limit the generalizability of  
28 findings. However, our sample size was consistent with considerations for implementing pilot studies<sup>40</sup>  
29 and our coverage of eligible families was good.  
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### 37 **Conclusion**

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39 These preliminary findings indicate that mental disorder in children newly-diagnosed with a physical  
40 condition is common and negatively affects their quality of life over time. If these results are replicated  
41 in a subsequent larger study, health professionals should be aware of the burden of multimorbidity and  
42 prepare themselves to discuss mental health with children and their parents. Findings from this pilot  
43 study have been used to implement a large-scale study that will examine child multimorbidity in greater  
44 depth and provide more definitive clinical implications.  
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**Table 1. Baseline sample characteristics**

|                                | Full<br>sample | Multimorbid | Not<br>multimorbid | P-value |
|--------------------------------|----------------|-------------|--------------------|---------|
| N                              | 50             | 29          | 21                 |         |
| <b>Child</b>                   |                |             |                    |         |
| Age, years                     | 11.3 (3.3)     | 11.6 (3.2)  | 11.0 (3.4)         | 0.62    |
| Male, n (%)                    | 26 (52)        | 15 (52)     | 11 (52)            | 0.96    |
| Diagnoses, n (%)               |                |             |                    | 0.98    |
| Asthma                         | 14 (28)        | 9 (31)      | 5 (24)             |         |
| Diabetes                       | 9 (18)         | 4 (14)      | 5 (24)             |         |
| Epilepsy                       | 8 (16)         | 4 (14)      | 4 (19)             |         |
| Food allergy                   | 8 (16)         | 5 (17)      | 3 (14)             |         |
| Juvenile arthritis             | 11 (22)        | 7 (24)      | 4 (19)             |         |
| Disease severity, VAS          | 1.3 (1.2)      | 1.5 (1.3)   | 0.9 (0.9)          | 0.16    |
| Quality of life, KIDSCREEN-27  |                |             |                    |         |
| Physical well-being            | 48.0 (12.0)    | 47.4 (11.0) | 48.8 (13.4)        | 0.77    |
| Psychological well-being       | 46.1 (9.8)     | 43.6 (8.1)  | 49.4 (11.2)        | 0.08    |
| Autonomy/Parent relations      | 48.9 (9.6)     | 47.5 (7.0)  | 50.8 (12.1)        | 0.72    |
| Peer support                   | 46.1 (11.4)    | 46.7 (12.1) | 45.4 (10.5)        | 0.35    |
| School environment             | 50.1 (10.8)    | 47.7 (8.8)  | 53.3 (12.4)        | 0.12    |
| <b>Parent</b>                  |                |             |                    |         |
| Age, years                     | 44.0 (5.7)     | 43.0 (4.8)  | 45.2 (6.3)         | 0.43    |
| Female, n (%)                  | 45 (90)        | 26 (90)     | 19 (91)            | 0.92    |
| Immigrant, n (%)               | 10 (20)        | 8 (28)      | 2 (10)             | 0.16    |
| Married, n (%)                 | 39 (78)        | 22 (76)     | 17 (81)            | 0.67    |
| Post-secondary graduate, n (%) | 39 (78)        | 22 (76)     | 17 (81)            | 0.67    |
| Income ≥\$90,000, n (%)        | 29 (58)        | 17 (59)     | 12 (57)            | 0.87    |
| Parental stress, PSS           | 35.9 (7.9)     | 37.1 (7.3)  | 34.4 (8.5)         | 0.32    |
| Parental anxiety, STAI         | 41.6 (9.8)     | 44.2 (9.1)  | 38.2 (10.0)        | 0.05    |
| Parental depression CES-D      | 12.7 (9.9)     | 13.0 (9.6)  | 12.2 (10.5)        | 0.58    |
| Family functioning, FAD        | 25.5 (6.3)     | 24.7 (6.2)  | 26.5 (6.6)         | 0.20    |

Results are reported as mean (standard deviation) unless otherwise noted.

**Table 2. Prevalence of multimorbidity**

|                                 | Full sample | Asthma | Diabetes | Epilepsy | Food allergy | Juvenile arthritis | P-value |
|---------------------------------|-------------|--------|----------|----------|--------------|--------------------|---------|
| <b>Baseline</b>                 |             |        |          |          |              |                    |         |
| Any disorder                    | 29 (58)     | 9 (64) | 4 (44)   | 4 (50)   | 5 (63)       | 7 (64)             | 0.88    |
| Major depressive episode        | 12 (24)     | 4 (29) | 2 (22)   | 1 (13)   | 1 (13)       | 4 (36)             | 0.74    |
| Separation anxiety              | 2 (4)       | 0      | 0        | 1 (13)   | 0            | 1 (9)              | 0.43    |
| Phobia*                         | 15 (30)     | 6 (46) | 1 (11)   | 1 (13)   | 3 (38)       | 4 (36)             | 0.35    |
| Generalized anxiety             | 6 (12)      | 0      | 0        | 2 (25)   | 2 (25)       | 2 (18)             | 0.11    |
| Attention-deficit hyperactivity | 5 (10)      | 1 (7)  | 0        | 1 (13)   | 3 (38)       | 0                  | 0.06    |
| Oppositional defiant            | 9 (18)      | 2 (14) | 1 (11)   | 2 (25)   | 4 (50)       | 0                  | 0.07    |
| Conduct                         | 3 (6)       | 1 (7)  | 0        | 1 (13)   | 1 (13)       | 0                  | 0.65    |
| <b>Six months</b>               |             |        |          |          |              |                    |         |
| Any disorder                    | 21 (42)     | 9 (64) | 1 (11)   | 4 (50)   | 2 (25)       | 5 (56)             | 0.10    |
| Major depressive episode        | 2 (4)       | 0      | 0        | 0        | 0            | 2 (22)             | 0.11    |
| Separation anxiety              | 3 (6)       | 2 (14) | 0        | 1 (13)   | 0            | 0                  | 0.56    |
| Phobia*                         | 10 (20)     | 5 (36) | 1 (11)   | 1 (13)   | 0            | 3 (33)             | 0.25    |
| Generalized anxiety             | 4 (8)       | 1 (7)  | 0        | 1 (13)   | 0            | 2 (22)             | 0.55    |
| Attention-deficit hyperactivity | 3 (6)       | 0      | 0        | 0        | 2 (25)       | 1 (11)             | 0.09    |
| Oppositional defiant            | 6 (12)      | 2 (14) | 0        | 2 (25)   | 2 (25)       | 0                  | 0.31    |
| Conduct                         | 4 (8)       | 1 (7)  | 0        | 2 (25)   | 1 (13)       | 0                  | 0.33    |

Results are the number (%) of children with multimorbidity. Fisher's Exact tests examined multimorbidity across the five physical conditions.

\*Includes generalized, non-generalized, and specific phobias.

**Table 3. Longitudinal effects of multimorbidity on child quality of life**

|                           | Unadjusted   |         | Adjusted      |         |
|---------------------------|--------------|---------|---------------|---------|
|                           | B (SE)       | P-value | B (SE)        | P-value |
| <b>Parent Report</b>      |              |         |               |         |
| Physical well-being       | -3.76 (2.23) | 0.09    | -4.82 (2.22)  | 0.03    |
| Psychological well-being  | -2.06 (2.44) | 0.40    | -4.10 (2.14)  | 0.06    |
| Autonomy/Parent relations | 0.77 (2.53)  | 0.76    | -0.67 (2.40)  | 0.78    |
| Peer support              | -0.59 (2.83) | 0.84    | -1.23 (2.66)  | 0.64    |
| School environment        | -3.56 (2.88) | 0.22    | -4.17 (2.44)  | 0.09    |
| <b>Child Report</b>       |              |         |               |         |
| Physical well-being       | -7.76 (4.23) | 0.07    | -5.43 (4.36)  | 0.21    |
| Psychological well-being  | -8.58 (5.52) | 0.12    | -10.66 (4.78) | 0.03    |
| Autonomy/Parent relations | 1.20 (4.07)  | 0.77    | -0.26 (4.16)  | 0.95    |
| Peer support              | -3.19 (5.75) | 0.58    | -1.48 (5.52)  | 0.79    |
| School environment        | 0.09 (5.12)  | 0.99    | -2.02 (4.72)  | 0.67    |

Parent models include parent-reported MINI-KID and KIDSCREEN-27, whereas child models included child-reported MINI-KID and KIDSCREEN-27. Models adjusted for child age and sex, physical condition, and baseline quality of life.

**Table 4. Longitudinal effects of multimorbidity on parental outcomes**

|                           | Unadjusted  |         | Adjusted     |         |
|---------------------------|-------------|---------|--------------|---------|
|                           | B (SE)      | P-value | B (SE)       | P-value |
| Parental stress, PSS      | 0.28 (1.60) | 0.86    | -1.50 (1.51) | 0.32    |
| Parental anxiety, STAI    | 0.14 (2.05) | 0.95    | -0.24 (2.15) | 0.91    |
| Parental depression CES-D | 0.30 (1.12) | 0.80    | 0.62 (1.13)  | 0.58    |
| Family functioning, FAD   | 1.21 (1.32) | 0.36    | 1.47 (1.28)  | 0.25    |

Models adjusted for child age and sex, physical condition, and baseline psychosocial outcome.



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3 **Figure 1. Comparison of KIDSCREEN-27 scores with population norms**  
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5 \*p<0.10 for overall F-test across the three groups.  
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7 †Multimorbid group significantly lower than normative and not multimorbid groups.  
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9 ‡Not multimorbid group significantly lower than normative group.  
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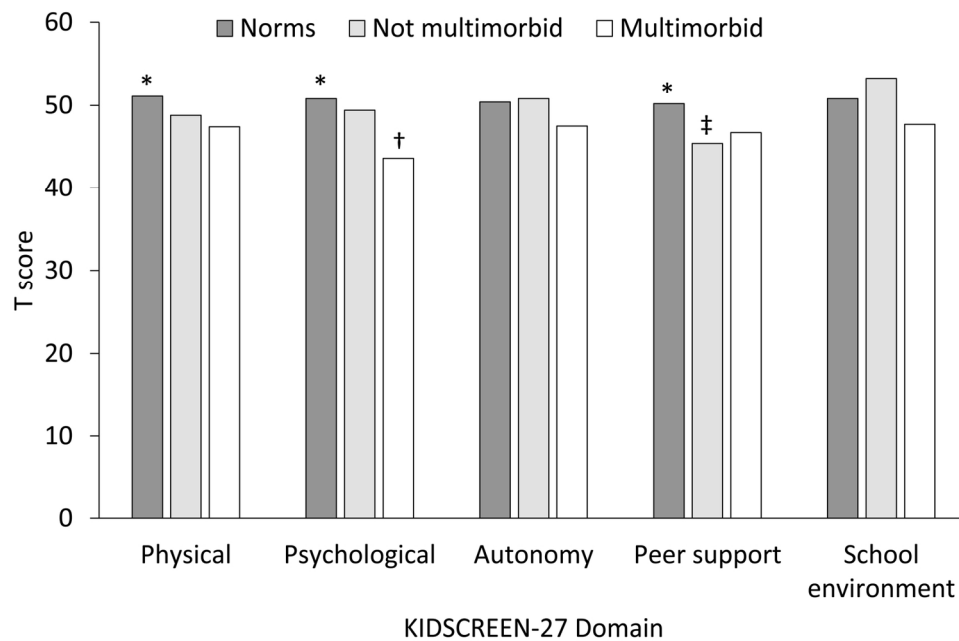


Figure 1. Comparison of KIDSCREEN-27 scores with population norms  
 \* $p < 0.10$  for overall F-test across the three groups.  
 †Multimorbid group significantly lower than normative and not multimorbid groups.  
 ‡Not multimorbid group significantly lower than normative group.

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**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies***

| Section/Topic                | Item # | Recommendation   | Reported on page # |
|------------------------------|--------|--|--------------------|
| Title and abstract           | 1      | (a) Indicate the study's design with a commonly used term in the title or the abstract   | 1                  |
|                              |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found  | 3                  |
| <b>Introduction</b>          |        |  |                    |
| Background/rationale         | 2      | Explain the scientific background and rationale for the investigation being reported   | 6-8                |
| Objectives                   | 3      | State specific objectives, including any prespecified hypotheses   | 8                  |
| <b>Methods</b>               |        |  |                    |
| Study design                 | 4      | Present key elements of study design early in the paper  | 9-10               |
| Setting                      | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  | 9                  |
| Participants                 | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up   | 9                  |
|                              |        | (b) For matched studies, give matching criteria and number of exposed and unexposed  | N/A                |
| Variables                    | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   | 10-13              |
| Data sources/<br>measurement | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 10-13              |
| Bias                         | 9      | Describe any efforts to address potential sources of bias  | 13                 |
| Study size                   | 10     | Explain how the study size was arrived at  | 9                  |
| Quantitative variables       | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why   | 13                 |
| Statistical methods          | 12     | (a) Describe all statistical methods, including those used to control for confounding  | 13                 |
|                              |        | (b) Describe any methods used to examine subgroups and interactions  | 13                 |
|                              |        | (c) Explain how missing data were addressed  | 13                 |
|                              |        | (d) If applicable, explain how loss to follow-up was addressed   | 13                 |
|                              |        | (e) Describe any sensitivity analyses  | N/A                |
| <b>Results</b>               |        |  |                    |

|                          |     |  |        |
|--------------------------|-----|--|--------|
| Participants             | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed            | 14     |
|                          |     | (b) Give reasons for non-participation at each stage   | 14     |
|                          |     | (c) Consider use of a flow diagram   | N/A    |
| Descriptive data         | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders   | 14     |
|                          |     | (b) Indicate number of participants with missing data for each variable of interest  | 14     |
|                          |     | (c) Summarise follow-up time (eg, average and total amount)  | 14     |
| Outcome data             | 15* | Report numbers of outcome events or summary measures over time   | 14     |
| Main results             | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 31-32  |
|                          |     | (b) Report category boundaries when continuous variables were categorized  | N/A    |
|                          |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period   | N/A    |
| Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   | 15-16  |
| <b>Discussion</b>        |     |  |        |
| Key results              | 18  | Summarise key results with reference to study objectives   | 16     |
| <b>Limitations</b>       |     |  |        |
| Interpretation           | 20  | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                   | 16-19  |
| Generalisability         | 21  | Discuss the generalisability (external validity) of the study results  | 18, 19 |
| <b>Other information</b> |     |  |        |
| Funding                  | 22  | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based  | 2      |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).