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## Predictors of health-related quality of life for children with neurodevelopmental conditions

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Neurodevelopmental conditions can be associated with decreased health-related quality of life; however, the predictors of these outcomes remain largely unknown. We characterized the predictors of health-related quality of life (HRQoL) in a sample of neurodiverse children and youth. We used a cross-sectional subsample from the Province of Ontario Neurodevelopmental Disorders Network (POND) consisting of those children and young people in the POND dataset with complete study data (total  $n = 615$ ; 31% female; age: 11.28 years  $\pm$  2.84 years). Using a structural equation model, we investigated the effects of demographics (age, sex, socioeconomic status), core features (Social Communication Questionnaire, Toronto Obsessive Compulsive Scale, Strengths and Weaknesses of attention deficit/hyperactivity disorder (ADHD)-symptoms and Normal Behavior), co-occurring symptoms (Child Behaviour Checklist), and adaptive functioning (Adaptive Behaviour Assessment System) on HRQoL (KINDL). A total of 615 participants had complete data for this study (autism = 135, ADHD = 273, subthreshold ADHD = 7, obsessive-compulsive disorder (OCD) = 38, sub-threshold OCD = 1, neurotypical = 161). Of these participants, 190 (31%) identified as female, and 425 (69%) identified as male. The mean age was 11.28 years  $\pm$  2.84 years. Health-related quality of life was negatively associated with co-occurring symptoms ( $B = -0.6$ ,  $SE = 0.20$ ,  $CI (-0.95, -0.19)$ ,  $p = 0.004$ ) and age ( $B = -0.1$ ,  $SE = 0.04$ ,  $CI (-0.19, -0.01)$ ,  $p = 0.037$ ). Fewer co-occurring symptoms were associated with higher socioeconomic status ( $B = -0.5$ ,  $SE = -0.05$ ,  $CI (-0.58, -0.37)$ ,  $p < 0.001$ ). This study used a cross-sectional design. Given that one's experiences, needs, supports, and environment and thus HrQoL may change significantly over the lifespan and a longitudinal analysis of predictors is needed to capture these changes. Future studies with more diverse participant groups are needed. These results demonstrate the importance of behavioural and sociodemographic characteristics on health-related quality of life across neurodevelopmental conditions.

**Keywords** Quality of life, Neurodevelopmental disorders, Structural equation modelling

### Abbreviations

ABAS	Adaptive Behaviour Assessment System
ADHD	Attention-deficit/hyperactivity disorder
ADOS	Autism Diagnostic Observation Schedule
ASD	Autism spectrum disorder

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CBCL	Child Behaviour Checklist
CFI	Comparative fit index
GAC	General Adaptive Composite
HrQoL	Health-related quality of life
OCD	Obsessive–compulsive disorder
PICS	Parent Interview for Child Symptoms
POND	Province of Ontario Neurodevelopmental Disorders Network
QoL	Quality of life
SEM	Structural equation modelling
SES	Socioeconomic status
RMSEA	Root mean square error of approximation
SCQ	Social Communication Questionnaire
SRMR	Standardized root mean squared residual
SWAN	Strengths and Weaknesses of ADHD-Symptoms and Normal Behavior
TD	Typical development
TLI	Tucker Lewis index
TOCS	Toronto Obsessive Compulsive Scale
WLSMV	Weighted least square estimator

Autism spectrum disorder (ASD; autism), attention deficit/hyperactivity disorder (ADHD), and obsessive–compulsive disorder (OCD) are diagnostic labels referring to groups of neurodevelopmental conditions that manifest early in life and can be associated with differences in personal, social, occupational, and academic abilities<sup>1,2</sup>. These conditions are highly heterogeneous and have been associated with significant overlap in etiology, biology, and phenotype<sup>3</sup>. For example, a recent meta-analysis estimated the prevalence of ADHD and OCD in autism as 28% and 9%, respectively<sup>4</sup>. Furthermore, several neuroimaging studies have reported shared patterns of brain structure<sup>3,5</sup> and function<sup>6,7</sup> among these conditions. Constellation of the core and co-occurring autism, ADHD, and OCD features, combined with environmental and societal factors can significantly impact an individual's function and overall quality of life (QoL)<sup>8–10</sup>.

QoL is a subjective construct defined as one's satisfaction with life in relation to culture, value systems, goals, expectations, standards, and concerns<sup>11</sup>. Diagnoses of autism, ADHD, and OCD have been associated with decreases in health-related quality of life<sup>12</sup> (Health-related QoL; HrQoL) for children with these conditions<sup>13</sup>. The significant heterogeneity within neurodevelopmental conditions, including variability in the strength and presentation of core and co-occurring symptoms<sup>3</sup>, translates to large variability in HrQoL outcomes<sup>14</sup>. Some of the factors that may contribute to this variability include individual differences in profiles of strengths and needs, and social, demographic, economic, and environmental factors; however, the contribution of these factors to HrQoL remains relatively unknown for children with neurodevelopmental conditions. Our recent systematic review revealed significant gaps in our understanding of predictors of HrQoL in neurodevelopmental conditions<sup>15</sup>. At the same time, the review found that many predictors of HrQoL transcend diagnosis boundaries (e.g., adaptive functioning, mental health), motivating a transdiagnostic approach.

In samples of children with diagnoses of autism, ADHD, and OCD, in particular, a handful of studies suggest that the extent of core-domain symptoms (social communication and repetitive behaviours in autism<sup>9</sup>; hyperactivity in ADHD<sup>8</sup>; obsessions and compulsions in OCD<sup>16</sup>) as well as adaptive functioning<sup>9</sup> may decrease HrQoL. In addition to these domains, autism, ADHD, and OCD are also associated with increased risk of mental health symptoms including internalizing (inwardly focused behaviours including anxiety and depression) and externalizing behaviours (outwardly focused behaviours including impulsivity, rule breaking, and aggression)<sup>13,17,18</sup>, associated with decreased psychological well-being<sup>19,20</sup> and can negatively impact HrQoL<sup>9,16,21</sup>. However, studies examining the effect of these challenges on HrQoL in autism, ADHD, and OCD are limited, have small sample sizes, and only consider a subset of variables in isolation<sup>10,15,22,23</sup>.

Demographic variables and other social determinants of health can also impact HrQoL. Sex and gender may influence HrQoL through inequitable access to health services, social demands, and higher rates of mental health challenges in females<sup>24</sup>. Age is suggested to influence HrQoL through changes in age-related developmental<sup>25</sup> and social experiences<sup>26</sup>. In samples of children with autism, ADHD, and OCD, studies examining the effects of age and sex and gender on HrQoL have reported mixed findings when comparing diagnosis groups<sup>26–28</sup>.

In addition to age and sex and gender, other social factors, such as race/ethnicity and socioeconomic status, can impact HrQoL directly through access to resources to improve well-being<sup>29</sup> and experiences of oppression and discrimination<sup>30</sup>. These factors can also indirectly impact HrQoL through their influence on symptoms (e.g., access to supports). However, the effects of these determinants on overall HrQoL has limited investigation in children with autism<sup>31</sup> or ADHD<sup>22</sup> and no investigation in children with OCD.

Another critical limitation of the existing literature is the focus on diagnostic categories in isolation. Autism, ADHD, and OCD co-occur at high rates with significant overlap in symptoms<sup>32–35</sup>. There is emerging evidence to question the validity of these diagnostic labels as a result of the heterogeneity and suggestions for transdiagnostic approaches across autism, ADHD, and OCD based on clinical and neuroanatomical attributes<sup>3</sup>. From a dimensional perspective<sup>36</sup>, many symptom domains are also shared among these diagnoses. To this end, the goal of this study was to study the correlates of HrQoL for children with autism, ADHD, and OCD with a diagnosis-agnostic lens.

Based on the previous literature, we hypothesize that symptoms, co-occurring symptoms, and demographic variables are associated with HrQoL in neurodiverse groups.

## Methods

### Participants

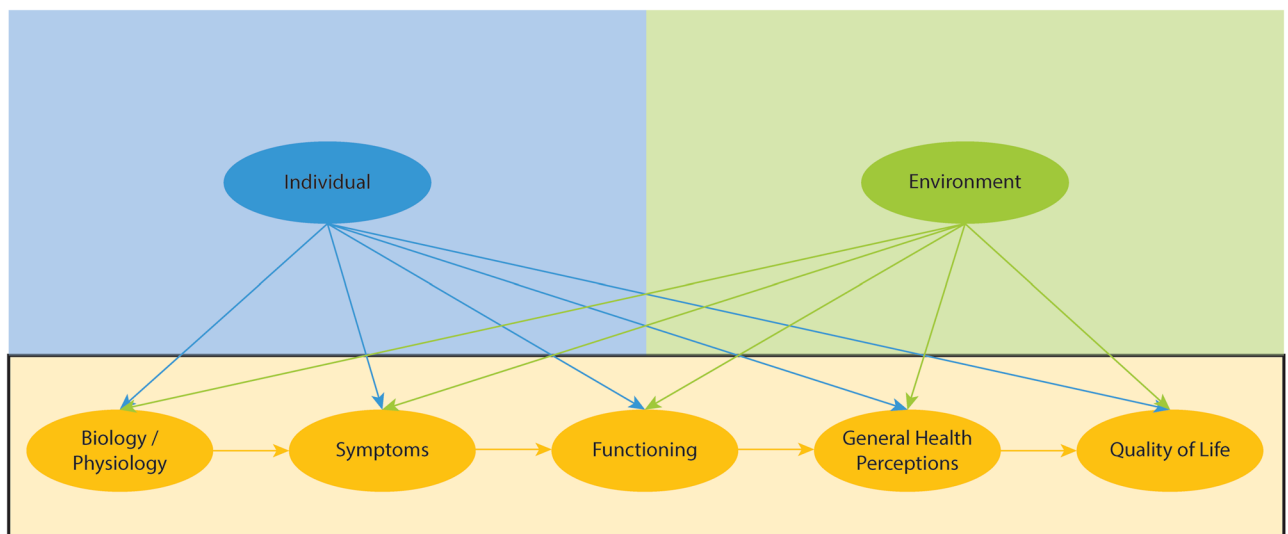
This study conducted a secondary analysis of a subset of the data from the Province of Ontario Neurodevelopmental Disorders (POND) Network, consisting of children and youth with complete study data (Additional File 5). The data were exported on July 23, 2021, and contained a total of 1472 participants aged 7 to 17 years old (autism = 541, ADHD = 445, sub-threshold ADHD = 154, OCD = 119, sub-threshold OCD = 6, typically developing, TD = 207). This age range was chosen based on the availability of the HrQoL measure. Sub-threshold participants were included in part of the transdiagnostic approach of our analysis, as symptoms which do not meet clinical thresholds for a diagnosis may still influence quality of life. Sub-threshold participants were seen at the Hospital for Sick Children and received their designation through clinical judgement. Diagnoses were supported by gold-standard assessment: The Autism Diagnostic Observation Schedule (ADOS)<sup>37</sup> and the Autism Diagnostic Interview - Revised (ADI-R) for autism<sup>38</sup>, Parent Interview for Child Symptoms (PICS) for ADHD<sup>39</sup>, and the Children's Yale-Brown Obsessive Compulsive Scale for OCD<sup>40</sup>. The TD participants part of POND did not have a neurodevelopmental, psychiatric, or neurological condition, were not born prematurely and had no first-degree family history of a neurodevelopmental condition. Informed consent was provided by participants who were determined to have capacity to consent. Otherwise, consent was obtained from guardians and assent was provided by the participants. Research ethics approval was provided at each participating POND institution (Holland Bloorview Kids Rehabilitation Hospital, Hospital for Sick Children, McMaster University, McMaster Children's Hospital, St Joseph's Hospital, Western University, Children's Hospital at London Health Sciences Centre, Queen's University). All methods were performed in accordance with the relevant guidelines and regulations.

### Theoretical framework

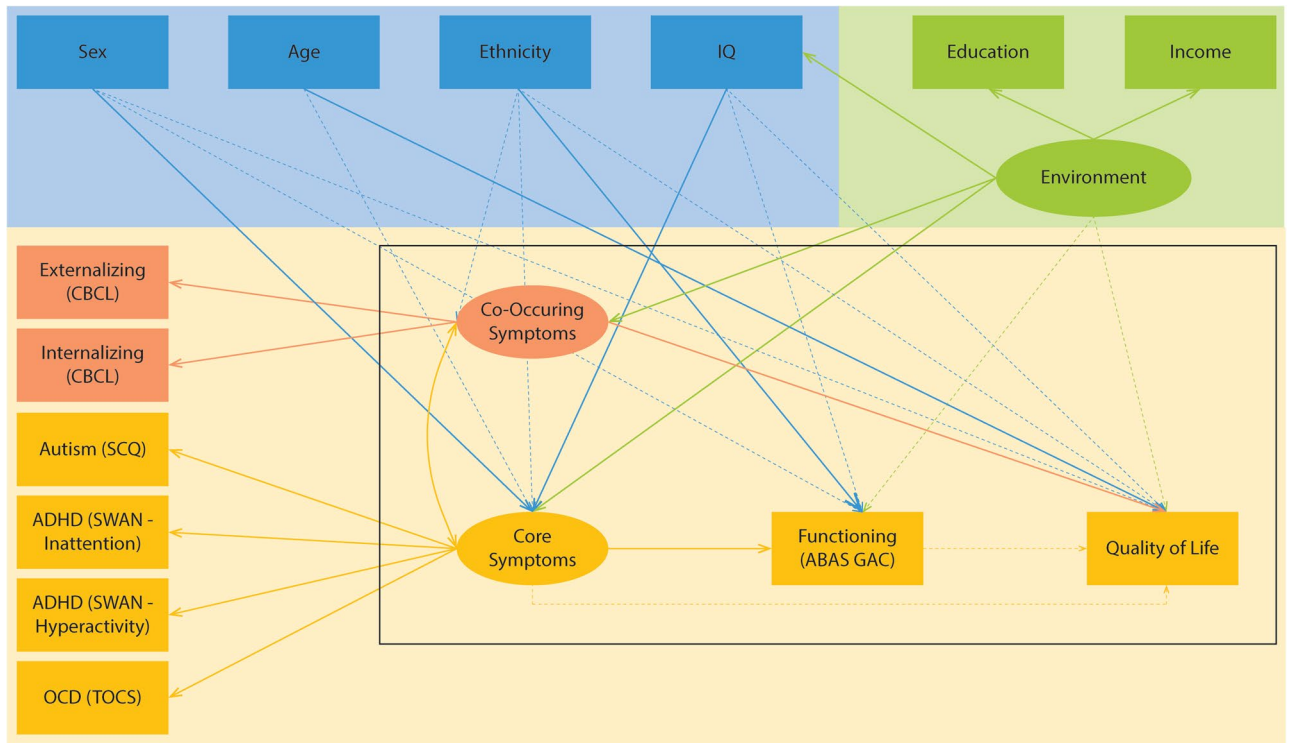
Various conceptual models have been developed to theorize determinants of HrQoL. In this study, we built upon the revised version of the 1995 Wilson and Cleary Model made by Ferrans et al. in 2005<sup>41</sup> (Fig. 1), to model the interrelationships among dimensions impacting HRQoL. According to a systematic review of 100 articles evaluating HrQoL, the revised version of the 1995 Wilson and Cleary Model was one of the most frequently and most comprehensive used models in HrQoL research<sup>42</sup>. The Wilson and Cleary model of HRQoL predictors includes seven domains. These include biological/physiological factors (variables that quantify the function of cells, organs, or body systems), symptoms (quantifies perception of a person's physical, emotional, or cognitive state, measured on a global or condition/domain-specific measure, functioning (the ability to perform tasks across multiple domains), general health perceptions (subjective rating integrating previous health concepts), overall quality of life (subjective rating of wellbeing), and characteristics of the individual (demographic, development, psychological, and biological influences of health outcomes) and environment (social and physical influencers of health outcomes).

### Measures

We operationalized the Revised Wilson and Cleary model for use in our analyses as shown in Fig. 2. HrQoL was quantified using the KINDL<sup>43</sup>. The KINDL is a self- or parent-reported measure of HrQoL in clinical or non-clinical pediatric populations<sup>43</sup>. Our study used the self-reported KINDL, which included the Kid-KINDL (ages 7 to 13) and the Kiddo-KINDL (ages 14 to 17)<sup>43</sup>. The Kid- and Kiddo-KINDL contain 6 domains of physical well-being, emotional well-being, self-esteem, family, friends, and everyday functioning<sup>43</sup>. Each question is scored on a 5-point Likert scale (never, seldom, sometimes, often, all the time), with high scores indicating worse HrQoL. In a sample of clinical and non-clinical populations, the KINDL has demonstrated a high degree



**Figure 1.** Revised Wilson and Cleary Model adapted from Ferrans et al.



**Figure 2.** Adaptation of the Revised Wilson and Cleary Model.

of internal consistency (Cronbach’s = 0.84) and a moderate convergent validity ( $r = 0.40\text{--}0.72$ ) to similar instruments (e.g. Child Health Questionnaire and the SF-36).

For symptoms, core-domain features of autism, ADHD, and OCD as well as co-occurring domains of internalizing and externalizing symptoms were used. Autism traits were quantified using the Social Communication Questionnaire Lifetime Version (SCQ)<sup>44</sup>. ADHD symptoms were measured using the Strengths and Weaknesses of ADHD-symptoms and Normal Behavior (SWAN) rating scale<sup>45</sup> for ADHD traits. OCD symptoms were characterized using the Toronto Obsessive Compulsive Scale (TOCS)<sup>46</sup>. Internalizing and externalizing symptoms were quantified using the subscales of the Child Behaviour Checklist (CBCL)<sup>47</sup>.

Functional abilities were assessed by the Adaptive Behaviour Assessment System (ABAS) parent-report questionnaire for ages 5 to 21<sup>48</sup>. The General Adaptive Composite (GAC) score, a standardized measure of conceptual, social, and practical scores, was used.

Individual factors included age, IQ, sex, and ethnicity. Full scale IQ was quantified using the Weschler Abbreviated Scale of Intelligence (first or second edition)<sup>49</sup>, the Weschler Intelligence Scale for Children (Fourth or Fifth Edition)<sup>50</sup>, the Stanford-Binet Intelligence Scale<sup>51</sup>, or the Weschler Preschool and Primary Scale of Intelligence (Fourth Edition)<sup>52</sup>. Ethnicity was modeled as a binary variable, white (European descent) versus non-white (Latin, Black, East Asian, Southeast Asia, Indigenous, Middle Eastern, and South Asian) due to our sample size and composition.

Environmental characteristics consisted of socioeconomic status (SES), which integrated information on the caregiver’s educational status and the household income. We hypothesized SES would be associated with all primary domains in the model, co-occurring symptoms, and IQ. Due to the well-established link between the influence of SES on mental health<sup>53</sup> and on IQ<sup>54</sup>, a regression path between SES and these individual indicators was included. The domains of general health perceptions and biology/physiology were not attainable from the POND database, and thus were excluded from the model. Table 1 summarizes each variable in its appropriate domain, based on the revised Wilson and Cleary Model.

Individual	Environment	Symptoms	Functioning	HRQoL
Sex Age Ethnicity Full Scale IQ	Household Income Primary Caregiver Education	SCQ SWAN TOCS CBCL Internalizing CBCL Externalizing	ABAS General Composite Score	Kiddo/Kid KINDL

**Table 1.** Study variables categorized in domains of revised Wilson and Cleary model.

## Statistical analysis

To explore pairwise associations between variables, Pearson correlations were used. Alpha was set at 0.05, and P-values were corrected using the Holm-Bonferroni correction<sup>55</sup>.

To understand the correlates of HrQoL, we employed Structural equation modelling (SEM)<sup>56</sup>. SEM is a multivariate analysis technique that provides a flexible framework for analyzing complex associations among multiple measured and latent variables. Latent variables are unobserved variables whose values are inferred mathematically from the model. SEM can be used to test the validity of theoretical models using empirical data<sup>57</sup>. In this study, we used the revised Wilson and Cleary model to construct the SEM model (Fig. 2). In this model, environment and symptoms were constructed as latent variables. Participant-reported education and income were considered as indicators of environment as noted by direct paths among these variables. The symptom domain of the Wilson and Cleary model was conceptualized as core symptoms relevant to autism (SCQ), ADHD (SWAN), and OCD (TOCS) as well as co-occurring mental health symptoms (CBCL internalizing and externalizing symptoms). Five variables were included as individual factors, namely sex, age, ethnicity, and IQ. Finally, the functioning domain of the Wilson and Cleary model was quantified by the adaptive functioning measure in POND (ABAS II). In total, 14 measured variables and three latent variables were included in the model. The paths in the SEM model were informed by the Wilson and Cleary model as well as prior literature, including a recent systematic review<sup>15</sup>. In particular, core and co-occurring symptoms were linked to model the potential association among these domains<sup>58,59</sup>. Individual factors were connected to symptoms to model sex- and age-related differences in symptoms<sup>60–63</sup> as well as diagnosis effects on prevalence of co-occurring intellectual disability. Individual factors were also connected to the functioning domain to reflect associations based on theoretical considerations in the Ferrans model<sup>41</sup> as well as literature findings characterizing these associations<sup>64–66</sup>. Finally, the environment variable was connected to symptoms, functioning, and quality of life to reflect the impact of social determinants of health on these domains.

SEM analysis was completed using the lavaan package in R studio 4.1.2<sup>67</sup>. The measures (CBCL internalizing, CBCL externalizing, KINDL total score, the ABAS general adaptive composite, and IQ) were normalized prior to application of the SEM. Standardized coefficients were used to determine the relative contribution of each measure to the model. Acceptable model fit was determined based on the following: normed Chi-square value ( $< 5$  for good model fit<sup>68</sup>); Comparative Fit Index (CFI) and Tucker Lewis-Index (TLI) ( $\geq 0.95$  indicating excellent model fit,  $> 0.9$  indicating acceptable model fit<sup>69,70</sup>); Root Mean Square Error of Approximation (RMSEA) and Standard Root Mean Residual (SRMR) ( $\leq 0.08$  indicating good model fit, with values  $< 0.05$  indicating excellent model fit<sup>71</sup>). The model was fitted with the diagonally weighted least square estimator (WLSMV) estimator<sup>72</sup> due to the categorical data in the model. Based on commonly used estimates of 5–10 samples per parameter or 10 samples per variable, a sample size of 615 provides sufficient power for our analysis<sup>73</sup>.

## Ethics approval and consent to participate

The POND study was approved by each participating institution's research ethics boards; written informed consent or assent was obtained from the primary caregiver or participant where appropriate.

## Results

### Participant demographics

A total of 615 children and youth had complete data (from the 1472 original participants, Additional File 1) and were included in the SEM models (Table 2). The Kid-KINDL was completed by 460 participants and the Kiddo-KINDL was completed by 155 participants (Additional File 2). Two participants reported a non-binary gender or not specified and were removed from the analyses given the small sample size.

### Pairwise correlations

Figures 3 and 4 depicts pairwise Pearson correlations among the model variables. Across the entire participant pool, medium correlations were found between HrQoL and internalizing ( $r = -0.35$ ,  $p < 0.001$ ) and externalizing symptoms ( $r = -0.28$ ,  $p < 0.001$ ), while small correlations were found with adaptive functioning ( $r = 0.17$ ,  $p < 0.001$ ), autism traits ( $r = -0.12$ ,  $p < 0.001$ ), hyperactivity ( $r = -0.12$ ,  $p < 0.001$ ), inattention ( $r = -0.17$ ,  $p < 0.001$ ), obsessive-compulsive symptoms ( $r = -0.16$ ,  $p < 0.001$ ), parental education ( $r = 0.11$ ,  $p < 0.001$ ), income ( $r = 0.10$ ,  $p < 0.001$ ), and age ( $r = -0.09$ ,  $p = 0.001$ ).

### Structural equation modelling

When the entire participant pool was used, the structural equation model fit was good to excellent (SRMR = 0.06, normed Chi-square = 4.428 TLI = 0.932, CFI = 0.956, and RMSEA = 0.075). The model explained 17.9% of variance in HrQoL in our sample.

The results are shown in Fig. 5. In this model, HrQoL was negatively associated with co-occurring symptoms ( $B = -0.6$ ,  $SE = 0.20$ ,  $CI (-0.95, -0.19)$ ,  $p = 0.004$ ) and age ( $B = -0.1$ ,  $SE = 0.04$ ,  $CI (-0.19, -0.01)$ ,  $p = 0.037$ ). The direct effects of functioning, environment, sex, ethnicity, or IQ on HrQoL were not statistically significant. Co-occurring symptoms were negatively associated with SES ( $B = -0.5$ ,  $SE = -0.05$ ,  $CI (-0.58, -0.37)$ ,  $p < 0.001$ ), and correlated with core symptoms ( $B = 0.9$ ,  $SE = 0.04$ ,  $CI (0.79, 0.94)$ ,  $p < 0.001$ ). This correlation with core symptoms was expected, given the overlap between externalizing behaviours and ADHD symptoms, and internalizing behaviours and OCD symptoms (e.g., anxiety).

Greater adaptive functioning was significantly associated with decreased core symptoms ( $B = -0.9$ ,  $SE = 0.155$ ,  $CI (-1.20, -0.60)$ ,  $p < 0.001$ ) and white ethnicity ( $B = 0.1$ ,  $SE = 0.03$ ,  $CI (0.002, 0.13)$ ,  $p = 0.043$ ). Decreased core symptoms were associated with female sex ( $B = 0.3$ ,  $SE = 0.04$ ,  $CI (0.18, 0.34)$ ,  $p < 0.001$ ), higher IQ ( $B = -0.3$ ,

	ADHD N = 135	Autism N = 273	OCD N = 38	SubADHD N = 7	SubOCD N = 1	TD N = 161	Total N = 615	Adjusted P-Value (group) <sup>1</sup>
Sex								< 0.001
Female (n (%))	41 (30%)	61 (22%)	17 (45%)	2 (29%)	1 (100%)	68 (42%)	190 (31%)	
Male (n (%))	94 (69%)	212 (78%)	21 (55%)	5 (71%)	0	93 (58%)	425 (69%)	
Age in years (mean ± standard deviation)	10.38 ± 2.54	11.63 ± 2.88	12.87 ± 2.72	9.86 ± 3.48	13.00	11.12 ± 2.78	11.28 ± 2.84	< 0.001
Income								< 0.001
High (>\$150,000) (n (%))	28 (20%)	59 (22%)	12 (32%)	3 (43%)	1 (100%)	65 (40%)	168 (27%)	
Middle (\$50,000–\$150,000)	62 (46%)	134 (49%)	18 (47%)	3 (43%)	0 (0%)	74 (46%)	291 (47%)	
Low (\$0–\$49,999)	45 (33%)	80 (29%)	8 (21%)	1 (14%)	0 (0%)	22 (14%)	156 (26%)	
Education								< 0.001
Graduate/professional (n (%))	19 (14%)	48 (18%)	9 (24%)	4 (57%)	1 (100%)	55 (34%)	136 (22%)	
Associate (n (%))	40 (30%)	84 (31%)	7 (18%)	1 (14%)	0 (0%)	29 (18%)	161 (26%)	
Undergraduate (n (%))	39 (29%)	71 (26%)	9 (24%)	1 (14%)	0 (0%)	57 (35%)	177 (29%)	
High school (n (%))	31 (23%)	65 (24%)	11 (29%)	1 (14%)	0 (0%)	19 (12%)	127 (21%)	
Did not complete high school (n (%))	6 (< 1%)	5 (< 1%)	2 (5%)	0 (0%)	0 (0%)	1 (< 1%)	14 (< 1%)	
Ethnicity								0.037
Non-White (n (%))	9 (7%)	46 (17%)	4 (11%)	2 (29%)	0	19 (12%)	80 (13%)	
White (n (%))	126 (93%)	227 (83%)	34 (89%)	5 (71%)	1 (100%)	142 (88%)	535 (87%)	
KINDL questionnaire								
Kid KINDL (n (%))	118 (87%)	191 (70%)	21 (55%)	6 (86%)	1 (100%)	123 (76%)	460 (75%)	< 0.001
Kiddo KINDL (n (%))	17 (13%)	82 (30%)	17 (45%)	1 (14%)	0 (0%)	38 (24%)	155 (25%)	< 0.001
KINDL score <sup>a</sup>	64.04 ± 13.16	63.75 ± 12.26	64.14 ± 12.82	68.01 ± 9.04	87.50	72.16 ± 11.15	66.13 ± 12.71	< 0.001
SWAN inattention <sup>b</sup>	5.49 ± 2.86	4.42 ± 2.93	2.15 ± 2.80	3.00 ± 2.58	0.00	0.16 ± 0.47	4.08 ± 3.27	< 0.001
SWAN Hyperactivity <sup>c</sup>	4.13 ± 3.13	3.36 ± 3.04	0.88 ± 1.61	2.43 ± 1.62	0.00	0.08 ± 0.46	3.03 ± 3.09	< 0.001
SWAN Inattentive or Hyperactivity ≥ 6 <sup>b,c</sup> (n(%))	83 (62%)	127 (47%)	5 (15%)	1 (14%)	0 (0%)	0 (0%)		< 0.001
TOCS <sup>d</sup>	− 26.74 ± 27.55	− 11.92 ± 24.11	18.62 ± 18.72	− 25.86 ± 27.37	12.00	− 40.85 ± 23.77	− 19.13 ± 28.52	< 0.001
SCQ <sup>e</sup>	7.67 ± 6.33	19.27 ± 7.33	5.37 ± 4.11	4.29 ± 5.47	4.00	2.32 ± 2.25	11.23 ± 9.50	< 0.001
SCQ ≥ 11 <sup>e</sup>	35 (26%)	234 (87%)	5 (13%)	1 (14%)	0 (0%)	2 (1%)	227 (37%)	< 0.001
IQ <sup>f</sup>	97.50 ± 14.65	92.28 ± 24.13	113.16 ± 11.87	103.29 ± 8.64	118.00	109.71 ± 12.13	99.45 ± 20.39	< 0.001
ABAS GAC <sup>g</sup>	78.90 ± 16.95	65.47 ± 15.77	93.13 ± 17.30	87.57 ± 16.72	120.00	103.98 ± 12.80	80.55 ± 22.25	< 0.001
CBCL internalizing T-Score <sup>h</sup>	61.79 ± 11.01	63.79 ± 9.90	64.34 ± 8.95	51.29 ± 8.52	67.00	46.95 ± 9.10	58.84 ± 12.23	< 0.001
CBCL Externalizing T-Score <sup>i</sup>	59.96 ± 12.04	57.96 ± 10.55	52.71 ± 10.57	52.14 ± 11.57	52.00	43.10 ± 8.47	54.11 ± 12.40	< 0.001

**Table 2.** Participant characteristics. <sup>a</sup>KIDNL Range (0–100). <sup>b</sup>SWAN Inattention Range (− 18 to 18) ≥ 6 Clinical Cut-off. <sup>c</sup>SWAN Hyperactivity Range (− 18 to 18), ≥ 6 Clinical Cut-off. <sup>d</sup>TOCS Range (− 23 to 23). <sup>e</sup>SCQ Range (0–39), ≥ 11 Clinical Cut-off. <sup>f</sup>IQ Range (0–144+). <sup>g</sup>ABAS GAC Range (40–120). <sup>h</sup>CBCL Internalizing T-Score Range (0–100) ≥ 64 Clinical Cut-off. <sup>i</sup>CBCL Externalizing T-Score (0–100) ≥ 64 Clinical Cut-off. <sup>1</sup>(1) continuous normal distributed, p-value derived from ANOVA, (2) continuous non-normal, p-value derived from Kurskall-Wallis test, (3) categorical, p-value derived from Fisher Exact test.

SE = 0.04, CI (− 0.42, − 0.27),  $p < 0.001$ ), and greater SES ( $B = -0.3$ , SE = 0.05, CI (− 0.40, − 0.18.9)  $p < 0.001$ ). IQ was positively associated with SES ( $B = 0.3$ , SE = 0.05, CI (0.19, 0.38)  $p < 0.001$ ).

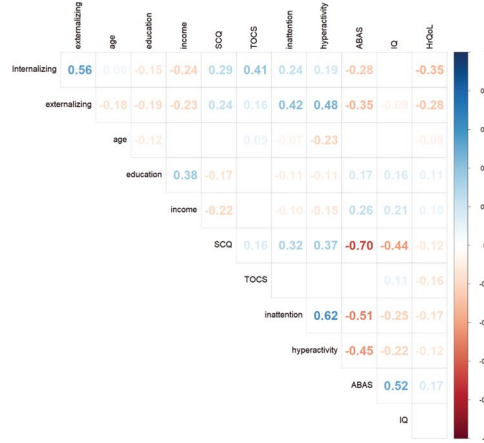
To further investigate the effect of sex, the model was run separately for male/female. For the sex analysis, the model accounted for 57% and 14% of variance in HrQoL for the female and male groups, respectively, but the overall conclusions remained unchanged (Additional File 4).

## Discussion

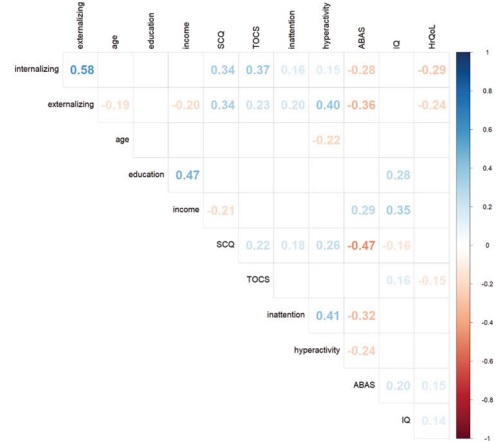
The purpose of this study was to characterize the correlates of HrQoL in a pediatric neurodiverse population. We constructed a model based on the Revised Wilson and Cleary framework. To our knowledge, this study is the first HrQoL study using a transdiagnostic approach across neurodevelopmental conditions.

Our model explained less than 20% of the variance in HrQoL for the overall sample. This variation is in line with other studies that measured HrQoL in clinical pediatric populations<sup>74</sup>. Given that most of the variability in HrQoL is not accounted for by the variables included in our model, future studies are needed to understand what other factors may contribute to QoL. These factors may include the general health perceptions and biology/

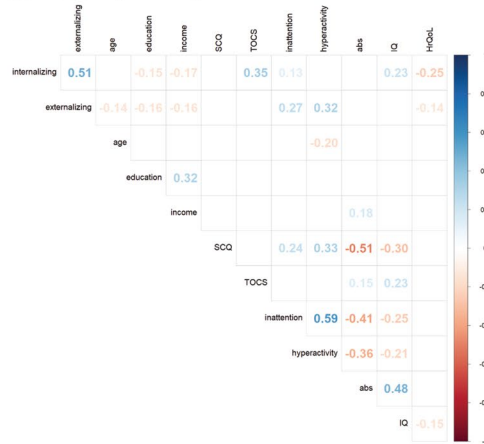
(A) All participants (n = 615)



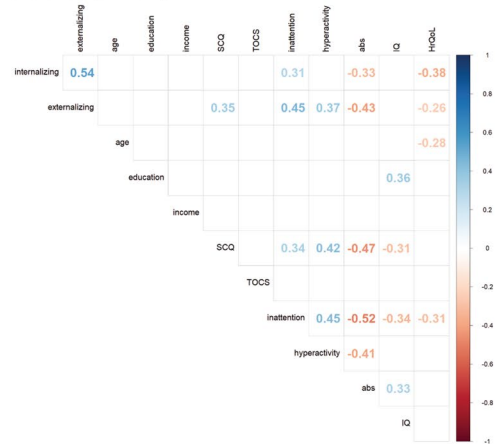
(B) ADHD (n = 135)



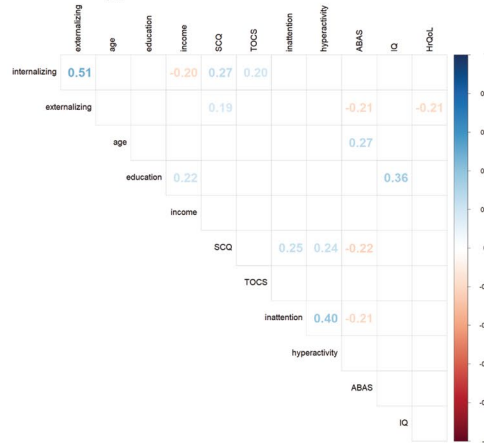
(C) Autism (n = 273)



(D) OCD (n = 38)



(E) Neurotypical (n = 161)

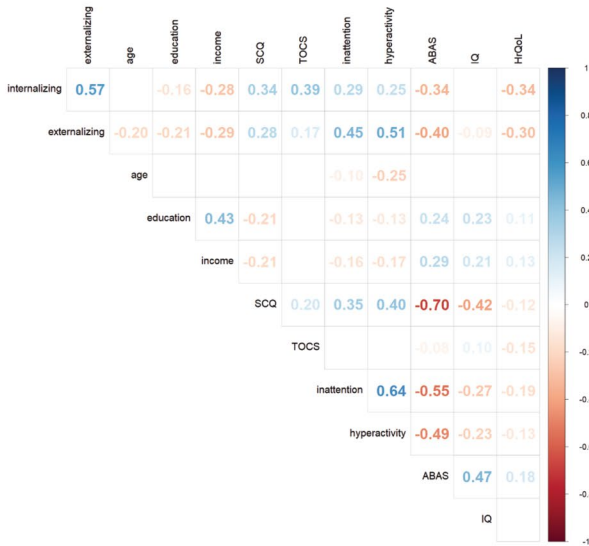


**Figure 3.** Correlation Matrix for (A) Total (B) ADHD, (C) autism, (D) OCD (E) TD.

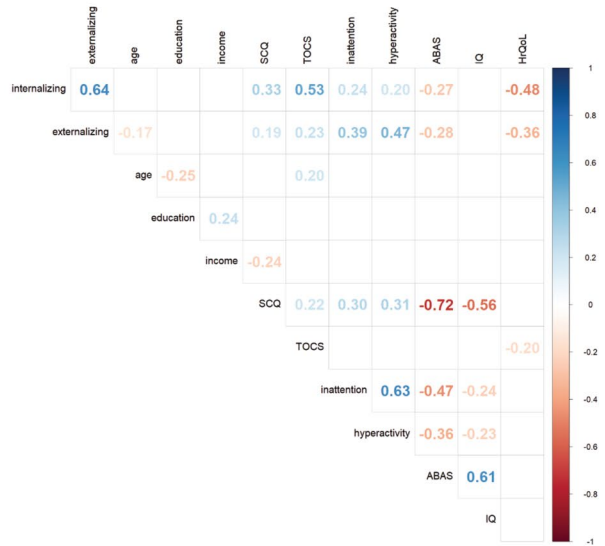
physiology of the Wilson and Cleary’s model of HrQoL as well as a measure to quantify the gap between one’s experience and expectation of life<sup>75</sup>.

Contrary to our hypothesis, only co-occurring conditions and age were directly associated with HrQoL. The association between HrQoL and externalizing/internalizing symptoms remained consistent when stratifying the sample by sex. Internalizing and externalizing behaviours have been previously associated with QoL<sup>21</sup> and one’s subjective well-being<sup>76</sup>. These results are consistent with the findings of a recent systematic review which highlighted the negative impact of mental health symptoms on HrQoL in neurodevelopmental conditions<sup>15</sup>, as

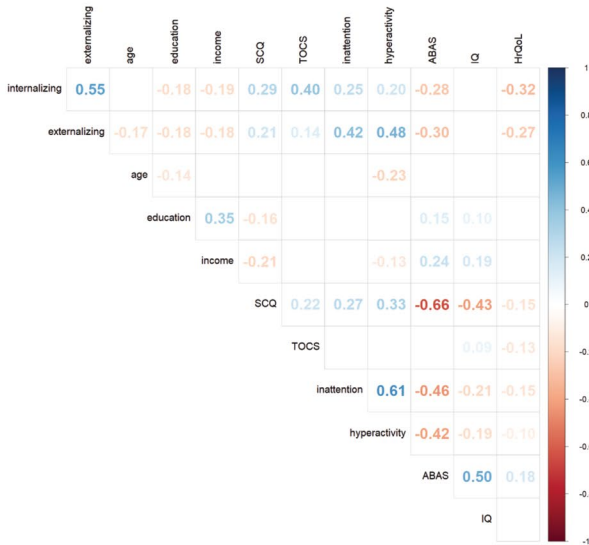
(A) White (n = 535)



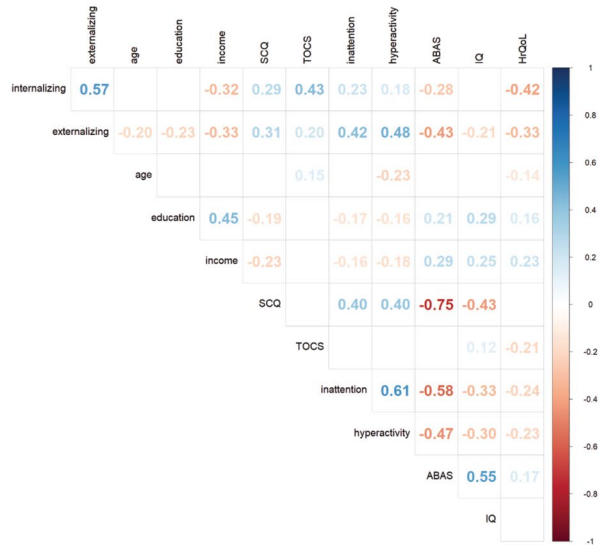
(B) Non-white (n = 80)



(C) Males (n = 425)



(D) Females (n = 190)



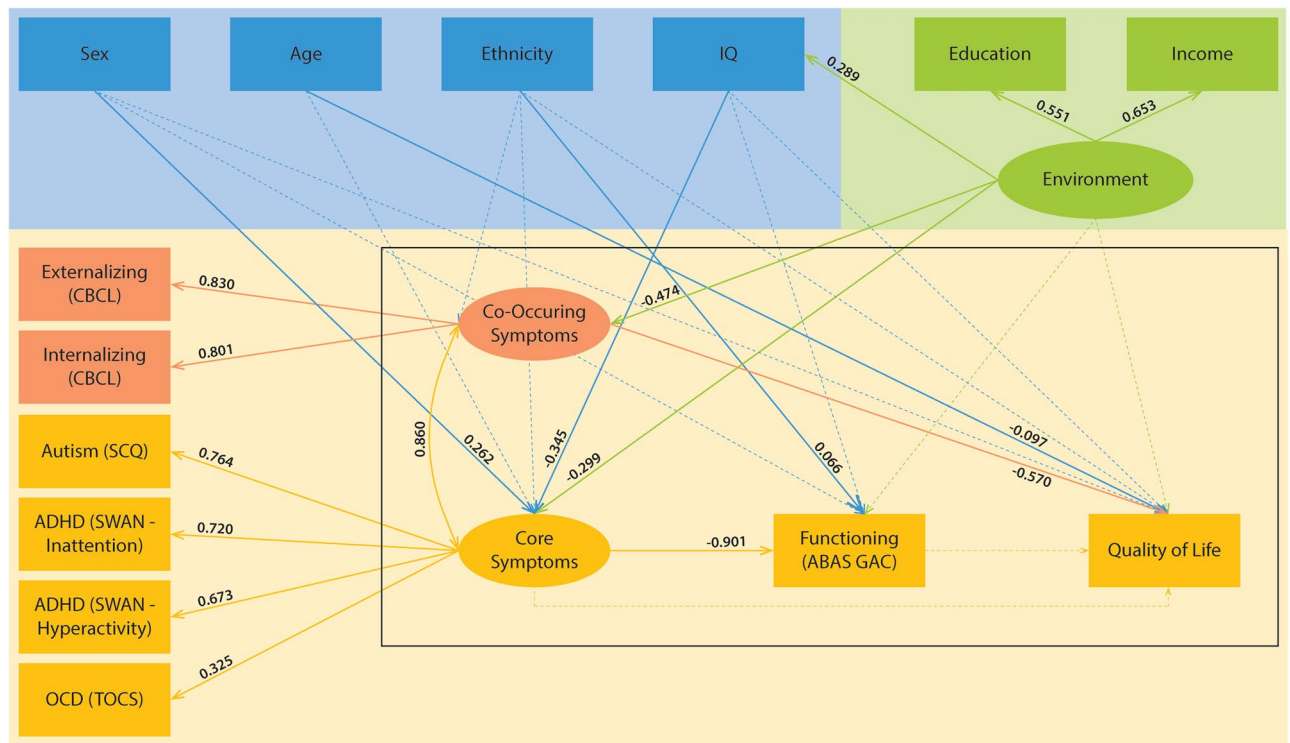
**Figure 4.** Correlation matrices by race/ethnicity: (A) white (B) non-white and sex: (C) male (D) female.

well as the results of a study examining perspectives of autistic adults on quality of life<sup>77</sup>. Mental health symptoms, including externalizing and internalizing behaviours, are also transdiagnostic domains which are impacted across neurodivergent groups<sup>78–81</sup>. In this context, our results highlight the strength of a transdiagnostic approach to understanding the predictors of QoL. Future studies comparing neurodiverse groups with matched participants of internalizing/externalizing behaviours and no neurodevelopmental condition can further clarify the interactions among neurodevelopmental differences, mental health conditions, and HrQoL.

Unlike previous studies<sup>9,82,83</sup>, we did not find a direct association between HrQoL, functioning, and core symptoms, but our results suggest that these domains may indirectly impact QoL through affecting internalizing and externalizing behaviours. This is consistent with previous findings that anxiety is a moderator of the association between autism features and quality of life<sup>84</sup>. It is also important to note that these findings should be interpreted in the context that our measures of symptoms and adaptive functioning reflect the perception of caregiver informants whereas our QoL measure reflects the participants' subjective experiences.

Our model also examined the association of sociodemographic factors with HrQoL. The results suggest a direct and negative association between age and HrQoL. This is consistent with the existing literature on the association of age and QoL in neurodivergent children<sup>9,14,16</sup>. This association may reflect the age-related differences in societal expectations, stressors, perceptions of disability, and support<sup>85</sup>. These findings should be interpreted with caution given the cross sectional nature of our data. It is also interesting to note that when stratifying the participant pool by diagnosis and sex, the pairwise correlation between HrQoL and age was only significant for





**Figure 5.** SEM Model for HrQoL. Solid lines represent significant pathways, dotted lines represent insignificant pathways.

female participants and those with a diagnosis of OCD. Future studies are needed to understand the differential contribution of age across demographic and diagnostic subgroups.

Our structural equation model did not reveal a significant direct association between HrQoL and sex; however, our model suggests that sex may influence HrQoL indirectly through modulation of symptoms. This finding should be interpreted in the context that neurodevelopmental condition-related symptoms may present differently in girls and that our measures may be limited in capturing these differences.

We also found that higher socioeconomic status was indirectly associated with increased HrQoL, through internalizing and externalizing behaviour. The connection between these co-occurring symptoms and SES is well established in previous literature<sup>33</sup> as lower SES may reflect the greater likelihood of negative life events; for example, parental employment stress or housing challenges<sup>86</sup>. Additionally, children from higher SES households may have greater access to mental health services. Since children with disabilities typically have increased healthcare and educational costs<sup>87</sup>, the socioeconomic barrier to accessing mental health services is exacerbated.

Our results did not show a significant direct or indirect association between HrQoL and race/ethnicity, although this variable is a well-established correlate of health and HrQoL<sup>30</sup>. Our findings should be interpreted with caution given the large imbalance in sample sizes for the white and racialized groups and the dichotomization of the race/ethnicity variable into white and non-white categories as this approach does not capture the diversity of experience in the racialized group. Given the many systemic barriers experienced by racialized families, it is critical future studies include diverse participant samples so that the diversity of experiences can be characterized.

### Limitations

A limitation of our study is the cross-sectional nature. One's experiences, needs, supports, and environment and thus HrQoL may change significantly over the lifespan and a longitudinal analysis of predictors is needed to capture these changes. In particular, future longitudinal studies on predictors of HrQoL are highly needed.

Another limitation of this study is the construct of HrQoL used as the outcome as this measure is based on neurotypical notions of life quality. An example of this is the social wellbeing subscale which includes having and spending time with friends, a construct that may not be predictive of HrQoL for some autistic individuals. Instead, other people's knowledge and acceptance of autism, support and services, and sensory differences may be more relevant to the QoL construct in autism<sup>77</sup>. The development of a subjective HrQoL measure that can be applied across neurodiverse populations is critically needed.

Thirdly, the ability to capture distinguishable co-occurring symptoms in the neurodiverse groups was limited by the instruments used. As some externalizing and internalizing behaviours can overlap with ADHD and OCD respectively, this may have hampered the ability of our model to capture distinct relationships between HrQoL and co-occurring symptoms. Further, future studies comparing predictors of HrQoL in neurodivergent populations with those in individuals with psychiatric conditions can further clarify the role of mental health symptoms.

Additionally, our analysis focused on sex and did not include gender and our participant pool did not include gender-diverse participants. Our coding of ethnicity may not reflect the heterogeneity of ethnicities white versus non-white groups. Finally, other than our diagnostic tools, the variables used in the study were based on parent-report questionnaires. Future studies with clinician-administered measures are likely to add greater understanding.

The study has several strengths. First, this study used a self-report measure of HrQoL. This is important as parental reports may be subject to biases due to the negative perceptions of symptoms<sup>28</sup>. Second, we used a transdiagnostic and dimensional approach to identifying correlates for HrQoL in children with autism, ADHD, OCD, and typical development. Through combining the data from participants across these groups and using core symptom domains rather than the primary diagnosis in the SEM model, we investigated the impact of different symptom domains on HrQoL, rather than the effect of diagnostic criteria. Third, the methodology of this study provided a unique and comprehensive way to understand predictors of HrQoL. The use of an SEM model enabled us to base our analysis on a theoretical model for HrQoL and create latent constructs for unobservable variables. Altogether, this created a thorough model accounting for the interrelationships between numerous variables. The variables used in our study were not restricted to functioning or symptoms, but also included a range of demographic and environmental variables to create a profile of participants in our study outside of their diagnosis.

## Conclusion

Our results suggest internalizing and externalizing symptoms are key contributors to HrQoL in children with neurodevelopmental conditions, highlighting the need for consideration of transdiagnostic symptom domains in assessment and provision of interventions and supports.

## Data availability

Participants were drawn from the Province of Ontario Neurodevelopmental Disorders (POND) network (exported July 2021). Data from the POND network is available via a controlled data release through Ontario Brain Institute's Brain-CODE: <https://www.braincode.ca/>.

Received: 15 February 2023; Accepted: 11 March 2024

Published online: 16 March 2024

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## Acknowledgements

This research was conducted with the support of the Canadian Institute for Health Research and the Province of Ontario Neurodevelopmental Network, as part of the Ontario Brain Institute. The opinions, results, and conclusions are those of these authors and no endorsement by the Ontario Brain Institute is intended or should be inferred.

## Author contributions

M.M. conceptualized and designed the study, analysed study data, drafted the original manuscript, interpreted the results, and revised the manuscript. R.C. generated manuscript figures, and critically reviewed and revised the manuscript. M.P., E.A., and B.A. contributed to the concept and design of the study, acquisition of study data, interpretation of results, and the critical review and revision of the manuscript. J.C., E.K., M.A., J.B., A.I., R.S., S.G., R.N., and J.J. contributed to the acquisition of data and the critical review and revision of the manuscript. A.K. substantially contributed to the drafting of the manuscript, concept and design of the study, analytic plan, interpretation of results, and critical review and revision of the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

## Funding

This work was supported by the Canadian Institute of Health Research (CIHR).

## Competing interests

This work was supported by research funds from Samsung Canada, Autism Speaks Canada, and Mitacs. All co-authors meet the requirements for authorship and have reviewed and approved this manuscript. Dr Kushki is the inventor of a software called the "Anxiety Meter". She is involved in commercialising the Anxiety Meter (patents US 9,844,332 B2 and US 16/276,208 (pending)) and will financially benefit from its sales. Dr Kushki served on the board of advisors for Shaftesbury, a media company developing virtual reality products for autistic children, from February 2020 to February 2021, and was compensated financially for this role. Dr Kushki has received donations of hardware for her research program from Samsung Canada. Dr Anagnostou reports grants from Roche, grants from Anavex, personal fees from Roche, personal fees from Quadrant, personal fees from Impel, personal fees from Ono, personal fees from Wiley, book royalties from Springer, book royalties from APPI, and non-financial support from AMO Pharma outside the submitted work. In addition, Dr Anagnostou holds a patent on the software called the "Anxiety Meter"; the Anxiety Meter is being commercialised and she will financially benefit from its sales. The other authors report no potential conflicts of interest.

## Additional information

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1038/s41598-024-56821-9>.

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