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Early-life multimorbidity and health-related quality of life in adolescence: insights from the Norwegian Mother, Father and Child Cohort Study (MoBa)

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Abstract

Background

Health-related quality of life (HRQoL) is a multidimensional measure of well-being in relation to one's health and comprises physical, mental, and social dimensions. Multimorbidity – the co-occurrence of two or more health conditions – is linked to poor HRQoL among older adults. However, multimorbidity is prevalent across the lifespan – including in childhood, adolescence and early adulthood, where it is characterised by relatively higher rates of neurodevelopmental and psychiatric conditions. In this study, we investigate early-life multimorbidity of somatic, psychiatric, and neurodevelopmental conditions and links to HRQoL in adolescence.

Methods

Diagnostic codes from linked secondary care registry data were used to ascertain health conditions diagnosed during childhood and adolescence among participants in the Norwegian Mother, Father, and Child Cohort Study (MoBa, N = 113,964). HRQoL was operationalised via self-report measures of pain frequency, mental wellbeing and school enjoyment at age 14 (N ~ 22,800). We explored differences in HRQoL by multimorbidity status among the most commonly diagnosed conditions in the sample and among commonly observed comorbidity patterns. Next, in preregistered confirmatory analyses, we tested the relationship between both quantitative (the number of distinct diagnoses an individual had received) and qualitative (having vs. not having > 1 diagnoses) indices of multimorbidity and HRQoL in adolescence.

Results

Health-related quality of life in adolescence was typically lower across all domains for those with multimorbidity (10.7% of the sample) than for individuals with one or none conditions. Descriptives analyses showed that among the most common patterns of multimorbidity, this was typically the result of an additive combination of the individual effect estimates of each condition. Associations between a quantitative index of multimorbidity and HRQoL were strongest for mental wellbeing, with each additional health condition predicting a 0.39 (95% CI: -0.41 – -0.37) standard deviation decrease in quality of life scores, and a significantly lower magnitude for both increased pain frequency (|β|=0.16 [0.14 – 0.18]) and decreased school enjoyment (|β|=0.17 [-0.19– – 0.14]). Additional qualitative effects of having vs. not having multimorbidity were not found.

Conclusions

The number of somatic, psychiatric, and neurodevelopmental conditions experienced in early life is linked to reduced HRQoL in adolescence. The relationship appears to be mostly additive and is strongest for the mental dimension of HRQoL. Negative correlates of multimorbidity in early-life justify focus on this patient group for tailored intervention programmes.

Background

Multimorbidity, defined as the co-occurrence of two or more chronic health conditions, presents a challenge both in clinical practice and research. Overlapping conditions can lead to delayed or missed diagnoses (1), under-treatment (2), complications in treatment (3), and can make etiological investigations more challenging (4). Patients with multimorbidity are often underrepresented in clinical trials (5), which contributes to a lack of knowledge about the applicability of treatment interventions in this group.

While multimorbidity has most often been considered as a feature of later life, co-occurring conditions are also prevalent in early-life (defined here as childhood, adolescence and early adulthood up to 25 years old) (6, 7). One distinguishing feature of early-life multimorbidity is that, more often than not (8), it involves psychiatric conditions – such as anxiety disorders (9), conduct disorder (10), depression (11), bipolar disorder (12), eating disorders (13) – and/or neurodevelopmental conditions like autism and attention-deficit hyperactivity disorder (ADHD) (14–16). In terms of somatic conditions contributing to multimorbidity in early-life, the most common are asthma (17) epilepsy (18), migraine (19), allergies (20, 21), type 1 diabetes (22), as well as juvenile arthritis and skin conditions (23).

In the general population, the prevalence of multimorbidity has been estimated at 25%, which accounts for nearly two thirds of those with a chronic condition (24). Multimorbidity earlier in life is generally considered to be less common, but its prevalence has not been precisely estimated, with differences in definitions resulting in a wide range of estimates between 2–46% (8, 19–22). Given the predominant involvement of psychiatric and neurodevelopmental conditions in early-life multimorbidity, and the evidence that such conditions may have been increasing in prevalence in recent years (29), it is plausible that multimorbidity among young people is also increasingly common.

Among populations where it has been most extensively studied, multimorbidity is often noted for its broad impacts on health-related quality of life (HRQoL) (30–32). HRQoL is defined by three domains of wellbeing and functioning: physical wellbeing (e.g., pain, sleep quality), social functioning (e.g., relationships and societal participation), and mental wellbeing (e.g., emotional distress and mood). (33) Among child and adolescent populations, HRQoL has been shown to be poorer among those with co-occurring mental and physical health symptoms than among those with either physical or mental health problems alone or neither type of condition (34). Currently, relatively less is known about the specific relationship between clinical multimorbidity of early-life and HRQoL in adolescence.

The overall aim of the current study was to investigate the relationship between multimorbidity in early-life and adolescent HRQoL. Specifically, we set out to explore and estimate associations between early-

life multimorbidity and three adolescent HRQOL domains (physical pain, mental wellbeing, and school enjoyment).

Methods

Analytic methods for this study were pre-registered prior to commencement of the analyses (35). Deviations from the pre-registered analysis plan are listed, with a description of their potential impact on the interpretation of results (if applicable) in Supplementary Table 1.

Sample

The Norwegian Mother, Father and Child Cohort Study (MoBa) is a population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health (36). Participants were recruited from all over Norway from 1999–2008. The women consented to participation in 41% of the pregnancies. The cohort includes approximately 114,500 children, 95,200 mothers and 75,200 fathers. MoBa is regulated by the Norwegian Health Registry Act. The current study was approved by The Regional Committees for Medical and Health Research Ethics (2016/1702). Pregnant women were asked to provide information about their health and lifestyle. After giving birth, the recruited women were asked to fill out questionnaires about their children, health, and environmental exposures at 0.5, 1.5, 3, 5, 8, and 14 years of age. Fathers were also asked to participate by filling out a questionnaire at enrolment and again in 2015. Blood samples were obtained from both parents during pregnancy and from mothers and children (umbilical cord) at birth (37). Observational analyses were performed on the entire MoBa sample with valid consent as of October 2025 (N = 113,964).

Measures

Exposures

Multimorbidity

Health conditions were selected and extracted from linked secondary care health registry data (Norwegian Patient Registry; NPR) where they are reported using ICD-10 diagnostic codes. The list of 33 conditions included in this study, and the relative ICD-10 codes used to identify them, is available in Supplementary Table 2. The conditions were chosen as part of a broader project investigating multimorbidity in early-life, based on the following criteria: a) somatic conditions relevant to our target population of interest (children and adolescents); b) from a list of the 40 most common chronic morbidities (5); c) that are feasibly identifiable based on administrative health data. Despite not being chronic in nature, severe respiratory infections requiring hospitalisation (with multiple registrations in the patient registry; see below) were included to index susceptibility to infections during early-life.

Individuals were registered as having a diagnosis if they received the diagnostic code at least twice during the follow-up period of the MoBa study (2008–2023). This criterion was used to improve the specificity of case ascertainment and reduce potential misclassification. The participant age range at the end of follow-up was 15–23 years.

Quantitative and qualitative indices of multimorbidity

We prepared two specific multimorbidity exposure variables for our preregistered confirmatory hypothesis testing analyses. The first was a count variable of the number of different diagnoses each individual received, representing a *quantitative index* of multimorbidity. The highest counts were collapsed into a single level (6+) to avoid identifying small groups (< 20 individuals). The second exposure variable was a binary variable indicating whether or not individuals had received 2 or more diagnoses. In the analytic models, this variable therefore represents a *qualitative index* of the impact of multimorbidity *over and above* the quantitative exposure.

Outcomes

The physical, mental, and social domains of HRQoL in adolescence were indexed, respectively, by self-reported measures of pain frequency, mental wellbeing, and school enjoyment, collected from MoBa participants when they were 14 years old. These outcomes were selected as the most thematically appropriate, continuously coded variables in the relevant questionnaire.

Pain frequency was measured using a single item that asked participants to respond on a five-point scale (ranging from “Never” to “All the time”) to the question: “During the past 4 weeks, how often have you had physical pain?”. This variable was treated as continuous.

Mental wellbeing was assessed using the 10-item Hopkins Symptoms Checklist (SCL-10 (38)). SCL-10 is based on a SCL-8 with two additional items (one for the anxiety and one for the depression subscales) added specifically for MoBa to increase reliability. Answers to the checklist are a four-point response scale and asks participants about symptoms related to anxiety and depression within the preceding two weeks. The scale showed acceptable internal consistency in the sample, with an ordinal Cronbach’s alpha of 0.92. A total score was calculated by multiplying the mean of all available items by the total number of items in the scale. If more than 50% of items were missing, the total score was set to missing. The SCL total score was reversed, so that higher scores corresponded to higher mental wellbeing.

School enjoyment was measured using a single item that asked participants the extent, on a four-point response scale (*completely disagree* to *completely agree*), to which they agreed with the statement *“I like being at school*”. The variable was treated as continuous.

More information about these variables coding in the MoBa questionnaire can be found in Supplementary table 3.

Covariates

We included child sex and birth year as covariates in all analyses. These variables were obtained through linkage with the Medical Birth Registry of Norway.

Handling of missing data

Within our analytic sub-sample of MoBa, data on outcome variables were primarily missing due to participant attrition by the time of the 14-year questionnaire. Given the well-documented non-randomness of attrition from cohort studies (in MoBa (39) and elsewhere (40–42), we assumed that complete case analysis would be biased due to not being missing completely at random (MCAR). For this reason, and to improve the precision of our estimates, we performed multiple imputation under the missing at random (MAR) assumption. Imputation of missing outcomes was carried out in the *mice* R package(43), and included all variables used in the main analyses, along with auxiliary variables identified as likely to be predictive of missingness in this dataset: household income, parental education, psychometric instruments result at 8 years old for the child and mother, and for the father at the designated timepoint, and for the mother at the 14 years timepoint, questionnaire results on experiencing bullying and parental cohabitation were also included. The list of potential missingness predictors was tailored to the different HRQoL traits (Supplementary table 5) and tested for each trait individually (Supplementary table 6) and we imputed 30 datasets.

To evaluate the potential impact of missing data assumptions, we conducted sensitivity analyses using complete-case data (Supplementary table 7).

Statistical analyses

In exploratory analyses, we first calculated mean levels of pain frequency, mental wellbeing, and school enjoyment by diagnosis, for all included conditions present at N ≧ 100 in the sample. Next, we grouped the most commonly co-occurring conditions (restricting again to N ≧ 100 for each comorbidity pairing), and compared mean scores on each HRQoL domain. In pre-registered confirmatory analyses, scores in each HRQoL domain were then regressed on the quantitative multimorbidity exposure (i.e., number of diagnoses) in linear models. To account for the possibility of non-linearity in this relationship, we added the qualitative multimorbidity exposure (having vs. not having multiple health conditions) to the regression models. Effects were evaluated with pre-registered one-tailed tests (assuming a negative relationship between multimorbidity and HRQoL).

All analyses were carried out on all N = 112,934 MoBa participants across all 30 imputed datasets, with results pooled according to Rubin's rules (44). Analyses were conducted in R (45), version 4.5.1, with data preparation using *phenotools* (46), multiple imputation using *mice* (43), wrangling using *tidyverse* (47), and *sandwich* (48) to calculate robust standard errors.

Multiple Testing

To account for multiple testing in confirmatory analyses, we applied the Benjamini–Hochberg false discovery rate (FDR) correction procedure. Families of tests within which the FDR corrections were applied corresponded to hypothesis tests specified in the preregistration (35) to preserve a type 1 error rate of 5%.

Availability of data and code

Data from the Norwegian Mother, Father and Child Cohort Study is managed by the Norwegian Institute of Public Health. Access requires approval from the Regional Committees for Medical and Health Research Ethics (REK), compliance with GDPR, and data owner approval. Participant consent does not allow individual-level data storage in repositories or journals. Researchers seeking access for replication must apply via www.helsedata.no.

Analytic code for the project is publicly available at https://github.com/psychgen/hrqol-multimorbidity.

Results

Descriptive statistics

Descriptive statistics for the sample prior to imputation are presented in Table 1. From our overall 112,934 sample, 55083 (48.8%) were females, 34,908 (30.6%) had at least one condition recorded by the end of the follow-up period, and 12,230 (10.7%) had multiple diagnoses. The most common sources of multimorbidity were co-occurrences of anxiety and depression N = 2129 (1.8%), ADHD and anxiety N = 1807 (1.5%), and asthma and repeated severe respiratory infections N = 1278 (1.1%). The mean ages at first diagnosis for individuals with one condition and with multiple conditions were 10.1 and 9.5 years respectively, and 51.3% / 55.3% of each group were females. As expected, individuals with missing data at age 14 differed systematically in terms of demographic characteristics and the prevalence of multimorbidity (see Supplementary Table 4). Subsequent analyses were therefore performed on multiply imputed data.

Table 1
Descriptive statistics for pain frequency, mental wellbeing, and school enjoyment, stratified by (top section) specific diagnoses and (bottom section) number of diagnoses

			Pain frequency		Mental wellbeing (SCL-10)		School enjoyment	
	N	% females	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Diagnosis								
Anxiety	9612	68.1	1788	0.37 (1.13)	1646	-1.00 (1.37)	1638	-0.47 (1.15)
Asthma	9554	43.1	1987	0.12 (1.04)	1880	-0.03 (0.99)	1877	-0.01 (1.01)
ADHD	7619	42.0	1115	0.19 (1.08)	1015	-0.53 (1.30)	1010	-0.33 (1.12)
Severe respiratory infections	4468	48.8	774	0.12 (1.07)	743	-0.01 (1.00)	744	0.05 (0.97)
Depression	4151	69.9	892	0.42 (1.12)	793	-1.23 (1.41)	787	-0.63 (1.15)
Autism	2480	36.0	426	0.08 (1.08)	394	-0.61 (1.39)	394	-0.44 (1.16)
Learning disorders	2289	43.0	274	0.15 (1.10)	260	-0.43 (1.26)	256	-0.41 (1.18)
Migraine	1785	63.3	389	0.58 (1.18)	365	-0.34 (1.20)	362	-0.13 (1.00)
Eating disorders	1748	90.7	442	0.22 (1.08)	407	-0.90 (1.27)	403	-0.27 (1.09)
Epilepsy	1421	46.8	248	0.07 (1.08)	233	-0.10 (1.07)	232	-0.01 (1.05)
ODD/CD	1017	30.4	121	0.01 (1.10)	108	-0.39 (1.44)	107	-0.18 (1.14)
Kidney disease	985	60.7	193	0.09 (1.04)	175	0.08 (0.88)	175	0.01 (1.00)
Type 1 diabetes	825	45.5	185	-0.00 (1.03)	178	-0.04 (1.01)	177	0.06 (1.00)
IBS	731	55.5	151	0.46 (1.15)	133	-0.45 (1.22)	133	-0.21 (1.12)
Chronic pain	713	63.5	143	0.96 (1.21)	131	-0.37 (1.35)	128	-0.13 (1.08)

			Pain frequency		Mental wellbeing (SCL-10)		School enjoyment	
	N	% females	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Diagnosis								
IBD	546	44.7	131	0.26 (1.02)	121	-0.08 (1.12)	122	-0.00 (0.90)
Psoriasis	440	54.1	90	0.17 (1.05)	80	-0.11 (1.08)	79	0.01 (0.96)
Hypothyroidism	421	67.2	84	0.04 (1.05)	73	-0.28 (1.21)	73	-0.08 (1.21)
Alcohol use disorder	289	54.3	31	0.01 (1.09)	29	-0.73 (1.21)	29	-0.46 (1.02)
Hypertension	187	43.9	34	0.04 (1.12)	27	-0.09 (0.95)	26	0.01 (1.08)
COPD	155	50.3	29	-0.08 (0.95)	29	0.03 (0.98)	29	0.16 (1.00)
Dyspepsia	153	60.8	33	0.61 (1.24)	28	-0.27 (0.98)	28	0.01 (0.99)
Arthritis	143	53.1	32	-0.07 (0.97)	30	0.18 (0.75)	30	-0.11 (1.02)
Cancer	108	38.0	21	-0.03 (1.05)	19	0.02 (1.05)	19	-0.27 (1.16)
Constipation	103	16.5	17	0.24 (1.13)	15	0.42 (0.44)	15	-0.18 (1.27)
Number of diagnoses								
0	78161	47.7	18056	-0.07 (0.96)	16847	0.13 (0.87)	16820	0.06 (0.96)
1	22590	49.1	4629	0.12 (1.04)	4319	-0.19 (1.11)	4310	-0.09 (1.04)
2	8292	53.6	1484	0.28 (1.13)	1370	-0.57 (1.32)	1368	-0.28 (1.12)
3	2791	57.1	464	0.32 (1.13)	428	-0.85 (1.38)	422	-0.50 (1.15)
4	812	61.7	120	0.79 (1.18)	108	-1.42 (1.45)	106	-0.50 (1.20)
5	223	66.4	32	0.57 (1.35)	27	-1.29 (1.60)	27	-0.28 (1.14)

			Pain frequency		Mental wellbeing (SCL-10)		School enjoyment	
	N	% females	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Diagnosis								
6+*	65	76.9	-	0.22 (-)	-	-1.24 (-)	-	-1.16 (-)

ADHD, attention-deficit/hyperactivity disorder; ODD/CD, oppositional defiant disorder/conduct disorder; IBS, irritable bowel syndrome; IBD, inflammatory bowel disease; COPD, chronic obstructive pulmonary disease. *Values in this row are suppressed due to small cell counts.

Exploratory analyses: HRQoL by conditions and patterns of multimorbidity

Figure 1 shows estimated mean levels of pain frequency, school enjoyment, and mental wellbeing among adolescents with the most commonly diagnosed neurodevelopmental, psychiatric, and somatic conditions, stratified by multimorbidity status. Across all outcome domains – and most markedly for mental wellbeing – individuals with multimorbidity had, on average, poorer HRQoL in adolescence. The strongest effect was observed among individuals with a recorded depression diagnosis plus at least one other condition, whose mental wellbeing was nearly two standard deviations below the sample average (-1.88; 95% CIs: -1.94–1.82). Average levels of pain frequency and school enjoyment were generally less extreme in the context of all diagnoses, regardless of multimorbidity status. For school enjoyment, it was notable that, in the *absence* of multimorbidity, only those with depression, anxiety, and ADHD showed reductions relative to the overall sample mean.

The results of our exploratory analyses looking at specific sources of multimorbidity and their relationship to adolescent HRQoL are presented in Fig. 2. Red dots indicate standardised average scores for pain frequency, school enjoyment, and mental wellbeing among those with both conditions in a given pairing, while the grey dots indicate the same for those with only one or the other of the conditions in the pairing. Overall, the results follow one of two patterns. Often differences appear approximately equivalent to an additive combination of what is observed for each condition alone. This is the case for those with co-occurring anxiety and depression, whose absolute scores on pain frequency (0.54 [0.44–0.63]), school enjoyment (-0.74 [-0.86–0.63) and mental wellbeing (-1.87 [-1.98–1.76]) are greater than those with either condition individually. In other cases – for example, in the co-occurrence between anxiety and asthma or between ADHD and depression – differences appear more attributable to the relationship with one condition in the pairing (e.g., anxiety rather than asthma, depression rather than ADHD).

When comparing average scores on each adolescent HRQoL domain among those with different numbers of recorded diagnoses (Fig. 3), we saw evidence of linear trends for all domains, and possible non-linearity with an inflection point at 2 conditions for mental wellbeing. These effects were tested in pre-registered confirmatory analyses.

Confirmatory analyses: relationships between HRQoL and multimorbidity

We ran linear regressions predicting scores on the three adolescent HRQoL domains as a function of, first, quantitative (i.e., number of diagnosed conditions), and then both quantitative and qualitative (> 1 condition or not) multimorbidity exposures. In the model including only the quantitative measure of multimorbidity, each additional condition was associated with significant decreases in mental wellbeing (β = − 0.41 [95% CI: − 0.42, − 0.40], one-tailed $p_{FDR} < 0.001$), increases in pain frequency (β = 0.16 [0.14, 0.18], one-tailed $p_{FDR} < 0.001$) and decreases school enjoyment (β = − 0.18, [−0.20, − 0.16], one-tailed $p_{FDR} < 0.001$). When adding in the qualitative measure of multimorbidity to the model, we initially observed a small additional worsening of mental wellbeing over and above the linear trend but this did not survive correction for multiple testing; nor were there any significant effects for pain frequency or school enjoyment. Parameter estimates from the model including both predictors are presented in Table 2.

Table 2
Results from linear regression models of HRQoL related outcomes (pain frequency, school enjoyment, and mental wellbeing) on multimorbidity

Predictor	**Outcome**	**95% CI**	***p* FDR**
Number of conditions	Pain frequency	0.161 (0.137–0.184)	< .001
Number of conditions	School enjoyment	-0.167 (-0.194 - -0.141)	< .001
Number of conditions	Mental wellbeing	-0.391 (-0.41 - -0.373)	< .001
Multimorbidity (0/1)	Pain frequency	0 (-0.054–0.054)	0.495
Multimorbidity (0/1)	School enjoyment	-0.034 (-0.121–0.053)	0.322
Multimorbidity (0/1)	Mental wellbeing	-0.052 (-0.103 - -0.001)	0.068

CI: confidence intervals; pFDR: false discovery rate-corrected p-value

Discussion

The current study presents an investigation into adolescent health-related quality of life (HRQoL) in the context of early-life multimorbidity. We found multimorbidity to reduced HRQoL in adolescence. Of the most commonly diagnosed conditions, most appeared to be linked to only minor reductions in HRQoL

when present on their own, with more substantial differences appearing only when multiple conditions were present. In confirmatory analyses, we confirmed a linear relationship between the number of co-occurring conditions and pain frequency, school enjoyment, and mental wellbeing in adolescence.

Results from our confirmatory analyses clearly illustrated that a greater number of lifetime conditions across childhood, adolescence and early adulthood was associated with more frequent pain, poorer mental wellbeing, and lower enjoyment of school at age 14. These findings align with previous work showing poorer HRQoL among adolescents with co-occurring somatic, psychiatric, and neurodevelopmental conditions (49–52). We found little evidence that the association between condition count and HRQoL outcomes deviated substantially from linearity. This is consistent with prior evidence in older adults suggesting that the burden of multimorbidity follow a linear increase by number of condition added (53). Combinations of conditions may interact synergistically to worsen health-related quality of life deviating from a linear pattern, as previously reported (54), but It is likely that where such synergistic effects exist, they are more specific than general: for example, one condition may hinder the effective management of another, (e.g., ADHD affecting adherence to treatment and management of diabetes (55, 56)(57, 58)) or the presence of a second condition may intensify the perceived or functional burden of the first (e.g., depression increasing perception of pain (59)).

While the results of our confirmatory analyses present a relatively straightforward picture of the relationship between multimorbidity and adolescent HRQoL, our exploratory analyses revealed several noteworthy patterns that contextualise this relationship. Those with multimorbidity –around 10% of the sample – were indeed substantially more likely to have reduced HRQoL in adolescence than those with only one condition registered. However, strikingly, those with only single diagnoses in the neurodevelopmental or somatic condition categories, had hardly any increased pain frequency, decreased school enjoyment, or decreased mental wellbeing at age 14 compared to those in the sample with no registered diagnoses at all. Instead, adolescent HRQoL for individuals with neurodevelopmental or somatic diagnoses was *only* substantially reduced when they also had co-occurring conditions. For example, among the nearly 2000 migraine sufferers in our sample, those with migraine alone showed somewhat more frequent pain in adolescence compared to their peers, but no reduction in school enjoyment or mental wellbeing. In contrast, those with migraine *and* at least one other condition had more than twice as much pain, reduced enjoyment of school, and mental wellbeing nearly one standard deviation below the sample average. Accordingly, the third clear pattern from our exploratory analyses was that co-occurring mental disorders largely explained adolescent HRQoL reductions among those with neurodevelopmental and somatic conditions. Of the 17 condition pairings that occurred in more than 100 individuals, 10 included either anxiety or depression. ADHD may be a notable exception, where co-occurring anxiety appears associated with substantially poorer wellbeing than anxiety alone, potentially indicating a more specific interaction between ADHD and anxiety. This pattern is consistent with previous findings by Sciberras et al., who reported substantially poorer quality of life and functioning among children with ADHD and co-occurring anxiety disorders compared to those with ADHD alone (60). Among these pairings, stratified analyses clearly indicate that anxiety and depression play a key role in reduced adolescent HRQoL linked to psychiatric, somatic, and neurodevelopmental multimorbidity in

early-life. This interpretation is likely strongest for pain frequency and school enjoyment, whereas associations with mental wellbeing should be considered in light of the partial conceptual overlap between anxiety/depression diagnoses and the mental wellbeing measure itself.

Previous work has established that psychiatric conditions are prominent in early-life multimorbidity and are associated with poorer HRQoL (61, 62). Our findings extend this literature by demonstrating that, within a multimorbidity framework encompassing somatic, psychiatric, and neurodevelopmental conditions, the cumulative burden of diagnosed conditions throughout early-life is associated with poorer HRQoL across multiple domains in adolescence.

Accordingly, we feel it is reasonable to speculate on potential clinical implications of our results. If co-occurring anxiety and depression among individuals with other psychiatric, and both neurodevelopmental and somatic conditions are major drivers of the reduced HRQoL seen among these patient groups during adolescence, these represent plausible targets for interventions to increase HRQoL. However, the present analyses did not investigate the causal pathways underlying these associations. Consequently, it remains unclear whether co-occurring anxiety and depression directly contribute to reduced HRQoL, whether they partly reflect the impact of underlying neurodevelopmental or somatic conditions, or whether both mechanisms are involved. Future work should therefore investigate not only whether treatment of anxiety and depression improves HRQoL in multimorbid populations, but also whether interventions tailored to specific neurodevelopmental or somatic conditions, or to particular multimorbidity profiles, may be required. This may be especially important in neurodevelopmental populations such as autistic individuals, where co-occurring anxiety and depression are common and where questions remain regarding the effectiveness and accessibility of existing interventions for these conditions (63, 64).

Limitations

Although the current study was strengthened by pre-registration, the use of a large and generally representative sample, and registry linkage to ascertain diagnoses from secondary healthcare services, it is subject to several limitations. First, the HRQoL measures we used were self-reported and – particularly in the case of the measures of pain frequency and school enjoyment – represented relatively coarse measures of the domains of interest. Second, a clear caveat to our finding that anxiety and depression drive multimorbidity-HRQoL links in adolescence, is that our measure of mental wellbeing is based on items assessing symptoms of anxiety and depression. This risks a certain circularity – those with diagnosed anxiety and depression are clearly more likely to have elevated symptoms of these conditions in when assessed using questionnaires. However, several factors mitigate this limitation. Firstly, the mental wellbeing is an important HRQoL domain, and when assessed by other means it shows a strong negative correlation with symptoms of anxiety and depression. Secondly, this means of assessment has face validity – it is reasonable to assume that most people would assess better mood and less worry with a better overall quality of life. Thirdly, whilst our results demonstrating the primacy of anxiety and depression in driving multimorbidity-HRQoL associations are strongest in the mental

wellbeing domain, the patterns are directly replicated in school enjoyment and mirrored in pain frequency. An additional limitation concerns our use of lifetime co-prevalence of diagnoses (i.e., ever within the available follow-up period) as an indicator of multimorbidity, which is quite a liberal definition that potential includes conditions experienced some years apart, without temporal overlap. This was a pragmatic decision to allow us to characterise the links between multimorbidity and adolescent HRQoL in the broadest possible terms, but future refinement is warranted to assess the importance of different diagnoses occurring close together in time for adolescent outcomes.

Conclusions

Multimorbidity during early-life shows links with adolescent health-related quality of life, with individuals receiving more distinct diagnoses experiencing more frequent pain, poorer mental wellbeing, and less enjoyment of school than their peers. Multimorbidity among younger patients is characterised by an important role for neurodevelopmental and psychiatric conditions. Our findings underscore the importance of these conditions – particularly anxiety and depression – both individually and in co-occurrence, for driving associations between diagnoses and health-related quality of life in adolescence. The consistently poorer HRQoL observed among adolescents with multiple co-occurring conditions suggests that this group may represent an important target for intervention efforts. In particular, our findings highlight co-occurring anxiety and depression as potentially important contributors to reduced HRQoL and therefore plausible targets for strategies aimed at improving wellbeing among adolescents with multimorbidity.

Declarations

Competing Interests

OAA has received a speaker´s honorarium from Lundbeck and Janssen and is a consultant to cortechs.ai. All the other authors report no conflicts of interest.

Author Contribution

Conceptualization: D.B. and L.J.H.; Data analysis: D.B.; Figures: D.B.; Code checking: J.H.P.; Writing—original draft: L.J.H.; Writing—review and editing: D.B., L.H., J.H.P., M.M.B., E.C.C., C.D., A.S., O.A., H.A., A.H., and L.J.H. All authors reviewed and approved the final manuscript.

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Data Availability

Data from the Norwegian Mother, Father and Child Cohort Study is managed by the Norwegian Institute ofPublic Health. Access requires approval from the Regional Committees for Medical and Health Research Ethics(REC), compliance with GDPR, and data owner approval. Participant consent does not allow individual-leveldata storage in repositories or journals. Researchers seeking access for replication must apply viawww.helsedata.no. Disclaimer: Data from the Norwegian Patient Registry has been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Patient Registry is intended nor should be inferred.

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Figures

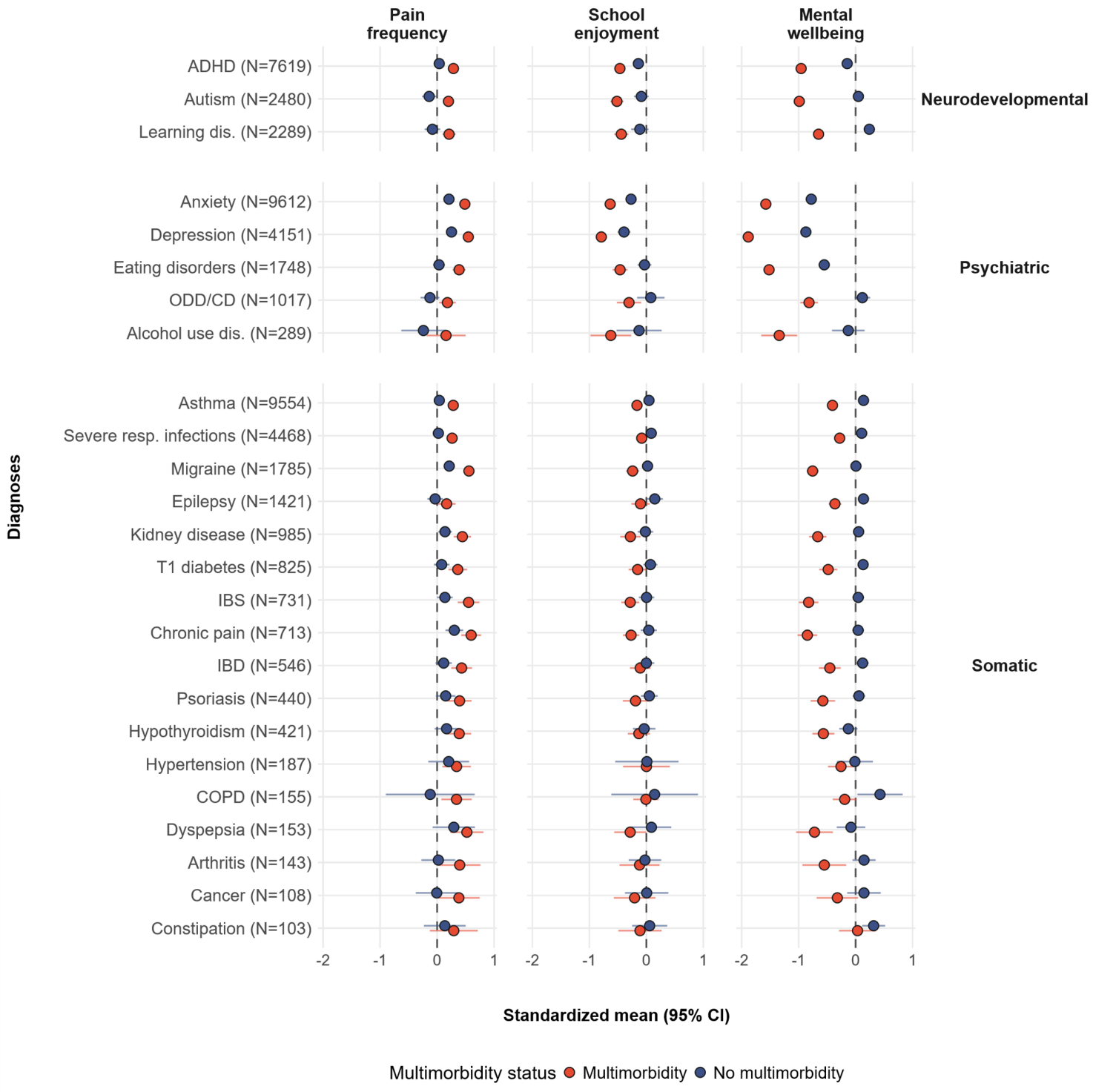


Figure 1

Average scores for pain frequency, school enjoyment, and mental wellbeing in adolescence across conditions with N>100, and by multimorbidity status. (ADHD, attention-deficit/hyperactivity disorder; ODD/CD, oppositional defiant disorder/conduct disorder; IBS, irritable bowel syndrome; IBD, inflammatory bowel disease; COPD, chronic obstructive pulmonary disease).

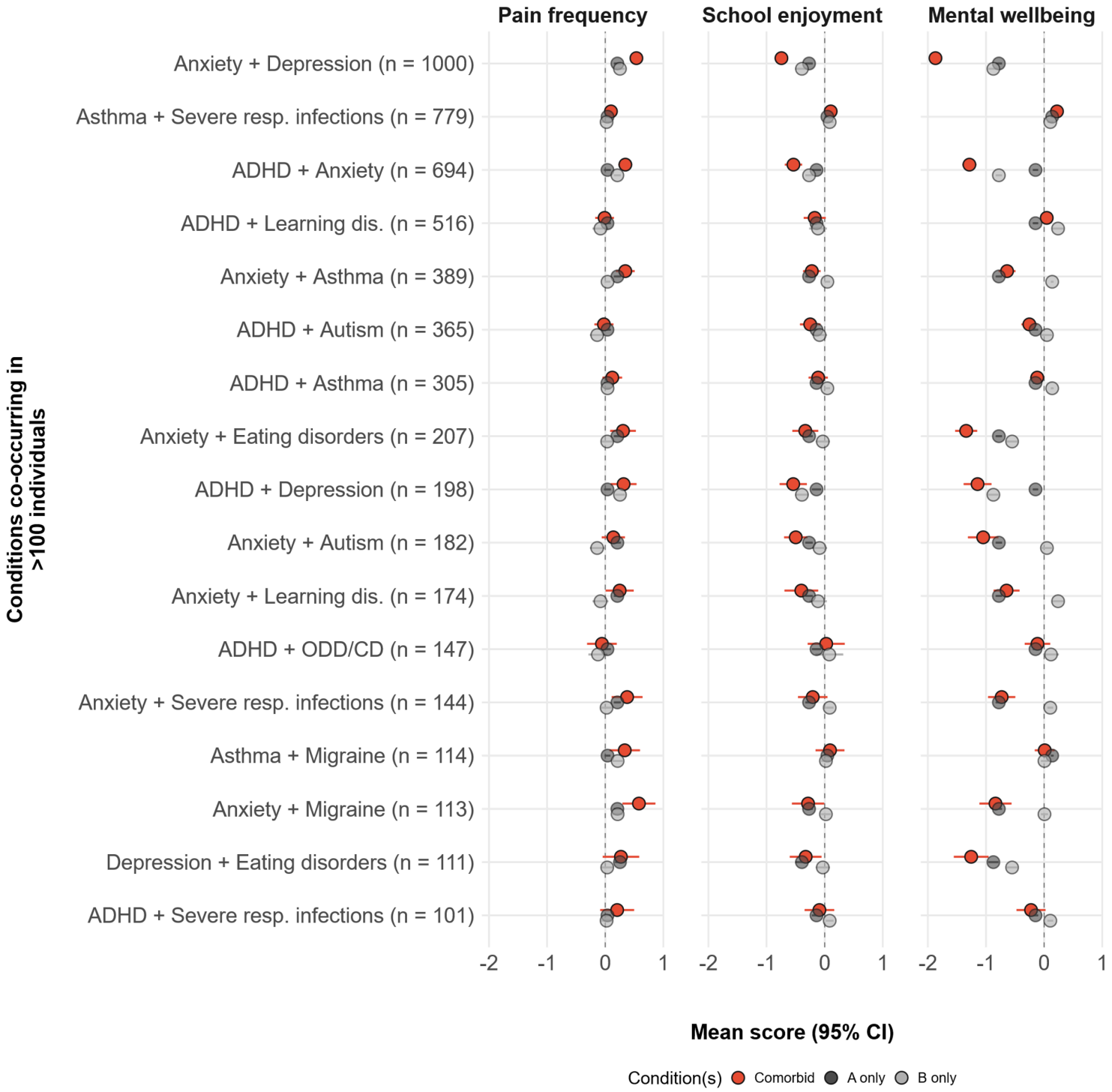


Figure 2

Average scores for pain frequency, school enjoyment, and mental wellbeing in adolescence across condition pairings with N>100 (grey reference points show equivalent scores from individuals with either condition A, the first listed, or B from a given pairing only; ADHD, attention-deficit/hyperactivity disorder; ODD/CD, oppositional defiant disorder/conduct disorder; IBS, irritable bowel syndrome; IBD, inflammatory bowel disease; COPD, chronic obstructive pulmonary disease).

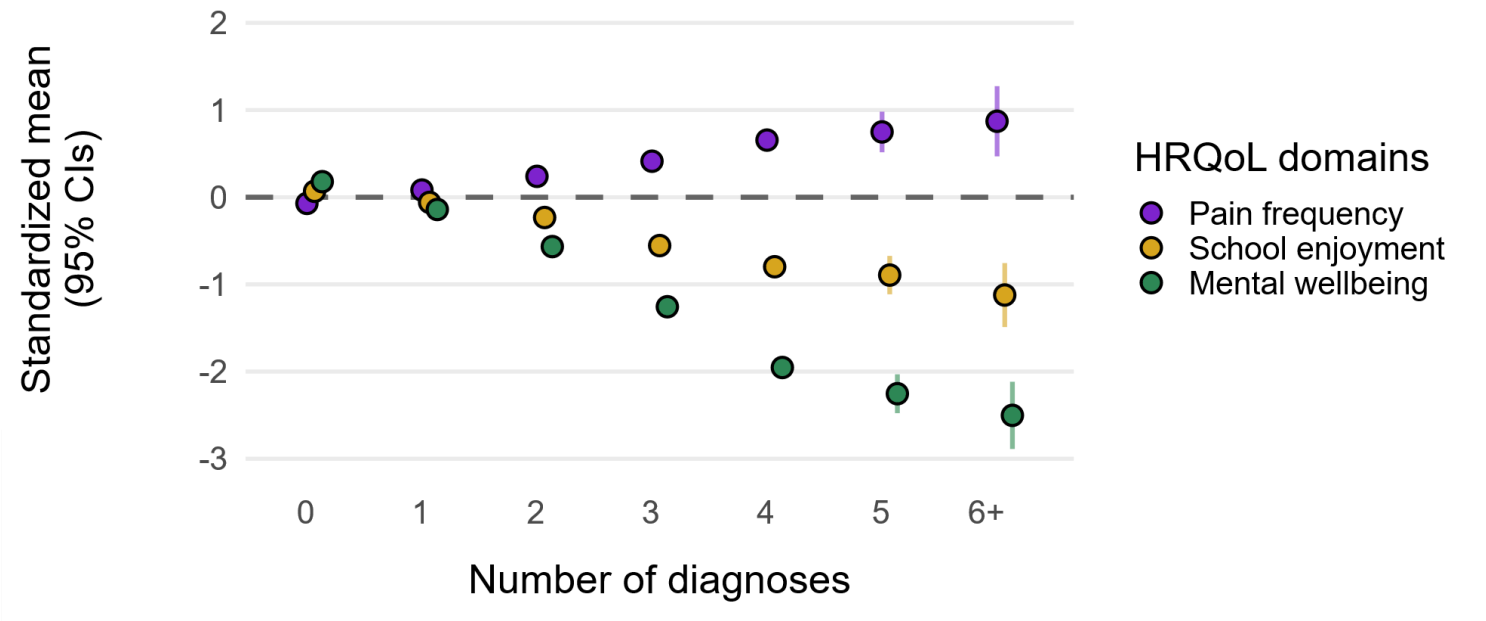


Figure 3

Average scores for pain frequency, school enjoyment, and mental wellbeing in adolescence across by number of recorded diagnoses

Supplementary Files

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