

## **Determinants of health-related quality of life in healthy children and adolescents during the COVID-19 pandemic: results from the longitudinal cohort study Ciao Corona**

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## Abstract

**Purpose:** Understanding health-related quality of life (HRQOL) in children and adolescents, during a pandemic and afterwards, aids in understanding how circumstances in their lives impact their well-being. We aimed to identify determinants of HRQOL from a set of biological, psychological and social factors.

**Methods:** Data was taken from a longitudinal sample (n = 1843) of children and adolescents enrolled in the prospective school-based cohort study Ciao Corona in Switzerland. The primary outcome was HRQOL, assessed using the KINDL total score and its subscales (each from 0, worst, to 100, best). Potential determinants, including biological (physical activity, screen time, sleep, chronic conditions, etc), psychological (sadness, anxiousness, stress) and social (nationality, parents' education, etc) factors, were assessed in 2020 and 2021, and HRQOL in 2022. Determinants were identified in a data-driven manner using recursive partitioning to define homogeneous subgroups, stratified by school level.

**Results:** Median KINDL total score in the empirically identified subgroups ranged from 68 to 83 in primary school children and from 69 to 82 in adolescents in secondary school. The psychological factors sadness, anxiousness and stress in 2021 were identified as the most important determinants of HRQOL in both primary and secondary school children. Other factors, such as physical activity, screen time, chronic conditions or nationality, were determinants only in individual subscales.

**Conclusion:** Recent mental health, more than biological, physical or social factors, played a key role in determining HRQOL in children and adolescents during pandemic times. Public health strategies to improve mental health may therefore be effective in improving HRQOL in this age group.

**Keywords:** youth, mental health, well-being, COVID-19, pandemic

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### List of abbreviations

- BMI: body mass index
- HBSC: Health-Behaviour in School-Aged Children survey
- HRQOL: health-related quality of life
- IQR: interquartile range
- PA: physical activity
- ST: screen time

## Introduction

Children and adolescents are formed by the environment they live in and their social engagement with those around them. The assessment of health-related quality of life (HRQOL) allows us to better understand how circumstances in their lives impact their well-being, especially during disasters like the coronavirus disease 2019 (COVID-19) pandemic. Many children and adolescents remain resilient over time or may recover rapidly. However, others may suffer from multiple stressors (e.g. illness, disruption of the family system, isolation, social separation from peers and home confinement) thereby impacting their short and long-term mental health and well-being [1]. Understanding HRQOL and building knowledge about physical, emotional and social challenges that children and adolescents may have experienced during the pandemic will allow to raise Public Health awareness and build the foundation for action now and in future difficult periods that may evolve.

Various studies have shown that HRQOL in children and adolescents has worsened during the COVID-19 pandemic [2–4], though there is some evidence that it has at least partially recovered to prepandemic levels [5]. HRQOL is a complex construct, defined as a subjective perception

that an individual has about the impact their health has on their life, involving not only biological factors (e.g. body mass index (BMI), or chronic health conditions) [6], but also psychological (e.g. stress, anxiety or depression) and social factors (e.g. family support, social integration, or family atmosphere) [7,8]. In line with this bio-psycho-social construct [7], several studies have demonstrated positive associations between physical activity and HRQOL [9–11], and negative associations between BMI and HRQOL [12,13]. Other studies have explored associations with screen time [14–16], sleep [17], self-esteem and emotions [18], parents' education and family wealth [19], and nationality [20]. While determinants of HRQOL in children with a range of chronic diseases have been previously studied, generally prior to the pandemic, fewer have sought to identify possible determinants of HRQOL in healthy children, often with small sizes [11,14,20]. Surprisingly few studies took a global view on HRQOL in youth by trying to understand the influence of the broader bio-psycho-social construct on their well-being and teasing out which factors alone or in combination are most influential.

Using data from the Ciao Corona study, a prospective school-based cohort study of children and adolescents during the COVID-19 pandemic (2020 - 2022), we aimed to identify determinants of HRQOL at the end of the pandemic, June 2022, in a cohort of children and adolescents from randomly selected schools, using conditional inference trees to identify patterns of determinants that indicate clusters of children and adolescents with similar HRQOL.

## Methods

### Study

The data for this analysis come from the school-based longitudinal cohort study Ciao Corona [21], in which 55 randomly selected schools (primary school grades 1-6 and secondary school grades 7-9, ages 6-17 years) in the canton of Zurich, the largest canton in Switzerland of

approximately 1.5 million inhabitants (18% of the total Swiss population), took part. Subjects (or their parents) were also asked to fill out a baseline questionnaire at the time of their first antibody test, and to complete follow-up questionnaires on a periodic basis (July 2020, January 2021, March 2021, September 2021, and July 2022). The analysis set of this study included children and adolescents who had KINDL total scores in June 2022 and at least one questionnaire filled out earlier during the pandemic.

The study was approved by the ethical committee of the canton of Zurich (2020-01336), and the study design has been published elsewhere [21] (ClinicalTrials.gov identifier: NCT04448717). All participants provided written informed consent before being enrolled in the study. Results relating to lifestyle behaviors [22] and HRQOL [23] have been reported previously.

## **Outcomes**

The primary outcome was HRQOL in June 2022, assessed using the KINDL questionnaire, filled out either by primary school students and parents together, or by students in secondary school on their own. KINDL is a reliable and valid measure of HRQOL in children and adolescents [24,25], on a scale from 0 (worst) to 100 (best). It has 6 subscales, each from 0 to 100: physical, emotional, self-esteem, family, friends, and school. Several slightly different versions of KINDL are available, of which the parent version for children 7-17 years old was used [26]. Age group was determined by the highest grade level achieved during the study period. Children who were in 6th grade or lower were in the primary school group (having never gone to secondary school), while those who were in at least 7th grade by 2022 were in the secondary school group, even if they were still in primary school in 2020.

Possible determinants of HRQOL were pulled from questionnaires and categorized into three categories: biological, psychological and social determinants, as has previously been described as a model for HRQOL [6,7,27,28] (Figure 1). Biological variables included sex (male, female,

other), body mass index (BMI), physical activity (PA), screen time (ST), sleep duration, presence of chronic diseases, symptoms possibly compatible with post-COVID-19 condition (PCC, also known as Long Covid) and self-rated health. BMI was calculated according to weight and height, and compared with the standard Swiss population [29] to derive z-scores. BMI was then categorized as overweight if its z-score was 1 or higher. PA, ST and sleep were recorded in hours per week, which were then compared with World Health Organization recommendations [30] ( $\geq 1$  h/day of PA,  $\leq 2$  h/day of ST, and 9-11 h/night of sleep for 6-13 year olds or 8-10 h/night for 14-16 year olds). Chronic conditions included asthma, celiac disease, neurodermatitis, type I diabetes, inflammatory bowel disease, hypertension, attention deficit hyperactivity disorder (ADHD), epilepsy, joint disorders, and depression / anxiety. Possible post-COVID-19 condition [31,32] was identified if participants reported any number of symptoms lasting 3 months or longer that might be related to a COVID-19 infection in seropositive participants. For self-rated health [33], children were asked how they would describe their health status (excellent, good, moderately good, bad).

Psychological variables included sadness, anxiousness and stress that were taken from Health-Behaviour in School-Aged Children (HBSC) questionnaires [34]. For sadness, children were asked how often they felt sad or depressed in the last 6 months (daily, multiple times per week, once per week, once per month, seldom or never). For anxiousness, they were asked how often in the last six months they felt scared or anxious (same responses as for depression). For stress, parents were asked how they would assess the level of stress in the child's life on a scale from 1 (no stress) to 6 (extreme stress).

Social variables collected were parents' nationality (at least 1 Swiss parent vs other), parents' highest education level (at least one with college prep high school or university vs usual high school or professional school or lower), presence of household financial difficulties (yes/no), and

change of parents' working situation (reduction in or loss of work, vs no change), or change or loss of employment due to parents' health [35].

Data were collected in a series of online questionnaires: June 2020, September 2020, October 2020, January 2021, March 2021, September 2021, November 2021, December 2021 and June 2022. For data analysis, timepoints were grouped by year: 2019 (retrospective questions in the June 2020 questionnaire relating to the pre-pandemic period), 2020, 2021 and 2022. HRQOL was taken from the June 2022 questionnaire while possible determinants were taken from 2019-2021. If multiple questionnaires existed for a subject in the same year with the same question, the mean or most frequent response was taken.

## **Statistical Methods**

We used conditional inference trees [36,37] estimated by binary recursive partitioning to identify possible determinants of HRQOL in children and adolescents. This procedure was repeated for the KINDL total score as well as for each of its subscales, and stratified by age group (primary vs secondary school). As a sensitivity analysis, multiple imputation using chained equations was used to impute missing covariates [38] ( $m = 100$ ), and then recursive partitioning was used to identify significant predictors of HRQOL in each of the imputed datasets. We then counted how often each variable was included in the model selection procedure, with more important variables appearing more often than variables which are not determinants. All analysis was performed in R (R version 4.2.1 (2022-06-23)) using the packages partykit [36,39] and mice [40]. For further details, see supplementary material.

## Results

There were 1843 children and adolescents who had KINDL total scores in June 2022 and at least one questionnaire filled out since June 2020 (Table 1). Approximately 8% of children were overweight, and 76% had highly educated parents. KINDL total scores remained stable in the period 2020 - 2022 (median primary school in 2020 82.3 [IQR 77.1 - 86.5], in 2022 80.2 [74.0 - 85.4], and in secondary school 2020 79.2 [72.9 - 85.1] and 2020 74.0 [67.7 - 81.2]), but were somewhat lower in secondary school children than in those remaining in primary school (Supplementary Figure S1). Covariates considered to be potential determinants of HRQOL are displayed graphically in Figure 1 and listed in Table 1 by age group and timepoint (2019, 2020, or 2021).

KINDL total score in primary school children ranged from 38 to 100 with an interquartile range (IQR) of 11.5 points. Most of the variation in KINDL total score in 2022 in primary school children was explained by stress, sadness, and anxiousness in 2021 (Figure 2). Median KINDL total score in the identified subgroups ranged from 66 [IQR 57 to 73] (in those with frequent sadness, frequent anxiousness and moderate to high stress) to 81 [76 to 85] (in those reporting no stress), a difference which corresponded to 1.3 times the overall IQR. The same variables were generally chosen for the subscales, along with self-rated health and parents' education level (Figure 3, see boxes denoted "P" or "P, S"). Notably, variables from 2021 were more often chosen than their 2020 counterparts.

Similarly, most of the variation in KINDL total score in secondary school children, ranging from 33 to 99 with IQR = 13.5, was explained by stress, anxiety and self-rated health (Figure 4). Median KINDL total score in the identified subgroups ranged from 68 [IQR 62 to 73] (among those with moderate to high stress and frequent anxiety) to 81 [73 to 88] (among those with no stress and excellent self-rated health), a difference of 1 IQR. Anxiousness was a predictor of



KINDL total score in primary school children, but not secondary school, though it was identified as a determinant for some of the subscales. Additionally, sex, PA, sleep, ST, chronic diseases and nationality were identified as predictors of various subscales (Figure 3, see boxes denoted “S” or “P, S”). These additional variables were determinants of single subscales. However, most of these additional factors were not identified as determinants for overall HRQOL in secondary school children.

As there is some uncertainty in recursive partitioning where models may not always choose the same factors in the presence of missing data, we repeated the model for total KINDL score 100 times each for primary and secondary school children (Figure 5, Supplementary Material Tables S4 and S5). For primary school children, the models most often included stress, anxiousness and sadness, and included self-rated health about 25% of the time. For secondary school children, the models generally included stress, sadness, self-rated health and anxiousness, with PA included in 40% of the models.

## Discussion

Psychological factors from 2021 such as stress, sadness, anxiousness and self-rated health were most predictive of HRQOL in 2022, in both primary and secondary school children from a longitudinal cohort of schoolchildren during the COVID-19 pandemic from 2020-2022. Mid-2022 represented the end of the pandemic after most restrictions had been lifted. Determinants from 2021 rather than 2022, explained a difference in KINDL total score of 13-15 points out of 100 in clusters of children and adolescents with or without these factors. Our study suggests that social and biological factors did not play a role in determining HRQOL, especially in primary school children. Only for adolescents in secondary school factors such as PA, sleep, ST, chronic health conditions, and nationality were identified as determinant of individual KINDL subscales. These

results show that a major part of HRQOL in children and adolescents during the COVID-19 pandemic was explained by mental health determinants from periods when restrictions were still in place (in 2021).

The existence of sadness, anxiousness and stress as components of mental health led to a reduction in HRQOL of 13-15 points on a 0-100 scale in our children and adolescents which is likely relevant from a clinical and public health perspective. This difference corresponds to or is even higher than the impact of chronic health conditions such as asthma, headache, or hemophilia [41–44]. Considering that Switzerland had experienced one of the mildest restrictions during the COVID-19 pandemic, and that our study population was predominantly of high socio-economic state, the impact of the pandemic on mental health in children and adolescents and consequently on their HRQOL is expected to be much larger in a more disadvantaged population and countries with more severe confinements [45].

A number of publications have examined the relationship between HRQOL and a small number of mostly single factors in children, primarily before the COVID-19 pandemic. For instance, it has been observed that parental education and family wealth [19], as well as cardiorespiratory fitness are correlated with HRQOL [14], along with PA [9–11], BMI [12], obesity [13] and ST [15]. Fewer studies have examined a broad range of potential factors and their association with HRQOL. These have identified psychological factors (self-esteem and emotions [18]), lifestyle factors (PA, sleep, ST, diet [17]), and sociodemographic factors (family education, poverty and race [46]; or unemployed parents, single parents, and non-western background [20]) as well as biological factors (disease burden, overweight, and chronic conditions [20,46]).

Studies examining determinants of HRQOL since the onset of the pandemic have often focused on only a few potentially determining factors. Associations have been reported with body composition, PA and nutrition [47], Mediterranean diet [48], ST [4,49], and household education [50]. International comparisons of HRQOL in children during the pandemic are however

complicated by the wide range and severity of restrictions, especially school closures.

Switzerland, for example, had a much shorter period of complete school closures than many other countries [45], though the assessment period for HRQOL was generally later in the pandemic, after re-opening of schools. However, our analysis remains one of few studies that examined a broad range of possible determinants for HRQOL in a pandemic setting.

If sadness, anxiousness and stress are key determinants of HRQOL, the key public health implication is that reducing these three factors could improve HRQOL in children and adolescents. Improving mental health in children and adolescents likely requires individual, social and community strategies in order to be effective [51]. School-based interventions [52] are particularly attractive as they also reach those who might not seek out such changes individually. These programs could also include self-help strategies, including daily activities to reduce stress and development of social support systems, especially in adolescents [51,53], interactions with nature and green space [54–56] or strategies to improve lifestyle as integral part of the school setting [15,57]. Although our analysis identified stress, anxiousness and sadness as key determinants of HRQOL, it may be that they are only the nearest predictors in the pathway determining HRQOL. Changes to other factors, like PA, sleeping patterns or social support, may nevertheless improve mental health, thereby increasing HRQOL. It remains however unclear whether our findings relate only to HRQOL in pandemic settings, or whether they can be generalized also to other settings.

This analysis has a number of strengths. It comprised a large sample ( $n = 1843$ ), compared to similar studies on HRQOL, and was based on a sample from randomly selected schools for a whole canton that is quite representative for health behaviors of overall Switzerland [58].

Prospective data was collected across 2 years during a pandemic. This was the period where significant changes in life conditions throughout different levels of society (government, schools, families, peers) took place potentially affecting HRQOL. We considered around 30 biological,

social, and psychological factors, in line with a well-established conceptual model of HRQOL [6].

The stratification by age group allowed us to account for differing behavior patterns and perceptions in primary school children versus adolescents in secondary school [59].

There are also several limitations. We did not measure HRQOL prior to the pandemic. While data collection for Ciao Corona did seek to examine changes in lifestyle and mental health during the COVID-19 pandemic, it did not *a priori* intend to explore determinants of HRQOL. Therefore, we have no information on some potentially interesting factors, for example mental status and/or substance abuse or lifestyle of parents. Depression and anxiety were not based on clinical criteria, but on single questions taken from the Health Behaviour in School-aged Children survey [60]. Study participants were more likely to have Swiss nationality and more highly educated parents than the general population [61]. Had we been able to include also a more vulnerable, socially disadvantaged population, the study may have revealed an even stronger impact of mental health and other factors on HRQOL [19]. Additionally, data collection in our study leaned towards factors with possible negative impact, even though HRQOL is influenced by both positive and negative factors [62,63]. Future studies may improve data collection by including a better balance between positive and negative factors.

In conclusion, in one of the few studies to look at a broad range of possible determinants of HRQOL in predominantly healthy children and adolescents, we observed the psychological factors such as stress, sadness and anxiousness in 2021 (when many pandemic related restrictions were still in place) were the main determinants of HRQOL in June 2022 (after the end of public COVID-19 restrictions). Social and biological factors were generally not selected by our data-driven approach as determinants of overall HRQOL, but may have been determinants of individual subscales. Most recent variables determined HRQOL better than the same variables assessed at an earlier timepoint. A range of individual, family, community or

school-based strategies are likely needed to improve mental health and consequently HRQOL in children and adolescents during such difficult pandemic-related times and beyond.

## Statements and Declarations

- **Competing Interests:** All authors have completed the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.
- **Ethics approval and Informed Consent:** The study was approved by the Ethics Committee of the Canton of Zurich, Switzerland (2020-01336). All participants provided written informed consent before being enrolled in the study.
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- **Data, Material and/or Code availability:** The data used for this analysis can be obtained by request from the corresponding author.
- **Authors' contributions:** SK and MAP initiated the project and preliminary design. SK, TR, SRH developed the design and methodology. SK, TR, AU, AR, SR, GPP, recruited study participants, collected, and managed the data. SRH performed statistical analysis and wrote the first draft of the manuscript. All authors contributed to the design of the study and interpretation of its results and revised and approved the manuscript for intellectual content. SK and SRH had access to and verified all underlying data. The corresponding

author SK attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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## Tables and Figures

*Table 1: Covariates considered as potential determinants of health-related quality of life (HRQOL) in study participants, by age group and timepoint.*

	Primary school			Secondary school		
	2019 <sup>1</sup>	2020 <sup>1</sup>	2021 <sup>1</sup>	2019 <sup>1</sup>	2020 <sup>1</sup>	2021 <sup>1</sup>
<b>Biological:</b>						
Sex						
Male		441 / 891 (49%)			466 / 952 (49%)	
Chronic health condition		109 / 891 (12%)			149 / 952 (16%)	
Self-rated health	na	1.51±0.55 [434]	1.56±0.49 [708]	na	1.54±0.54 [556]	1.66±0.49 [759]
Symptoms compatible with Long Covid	na	na	9 / 891 (1.0%)	na	na	21 / 952 (2.2%)
BMI category						
Normal weight	na	349 / 389 (90%)	332 / 361 (92%)	na	460 / 520 (88%)	427 / 461 (93%)
Overweight/ Obese	na	40 / 389 (10%)	29 / 361 (8.0%)	na	60 / 520 (12%)	34 / 461 (7.4%)
PA met (%) <sup>2</sup>	82%±38% [390]	63%±48% [388]	76%±37% [661]	80%±40% [517]	54%±50% [510]	67%±41% [723]
ST met (%) <sup>3</sup>	98%±13% [389]	85%±36% [393]	96%±17% [657]	87%±34% [518]	51%±50% [517]	63%±44% [721]
Sleep met (%) <sup>4</sup>	93%±26% [393]	90%±30% [394]	93%±23% [658]	68%±47% [517]	80%±40% [516]	62%±43% [722]
<b>Psychological:</b>						
Sadness	na	4.10±0.98 [386]	4.30±0.80 [659]	na	4.26±0.91 [518]	4.09±0.89 [722]
Anxiousness	na	4.48±0.90 [383]	4.48±0.77 [658]	na	4.55±0.83 [519]	4.38±0.80 [723]
Stress	na	2.12±0.97 [363]	2.17±0.96 [652]	na	2.86±1.17 [480]	2.82±1.07 [716]
<b>Social:</b>						
Swiss nationality <sup>5</sup>		739 / 869 (85%)			805 / 918 (88%)	
High parental education		698 / 861 (81%)			647 / 903 (72%)	
Household financial difficulties	na	na	15 / 891 (1.7%)	na	na	20 / 952 (2.1%)

Change in parents' working situation for health reasons	0 / 891 (0%)	na	5 / 891 (0.6%)	0 / 951 (0%)	na	2 / 952 (0.2%)
Change in working situation parent(s)	0 / 891 (0%)	161 / 891 (18%)	18 / 891 (2.0%)	0 / 951 (0%)	177 / 952 (19%)	16 / 952 (1.7%)

na = not assessed

<sup>1</sup>n / N (%); Mean±SD [N]

<sup>2</sup>Percent of WHO physical activity (PA) recommendations met

<sup>3</sup>Percent of WHO screen time (ST) recommendations met

<sup>4</sup>Percent of WHO sleep recommendations met

<sup>5</sup>At least one parent with Swiss nationality

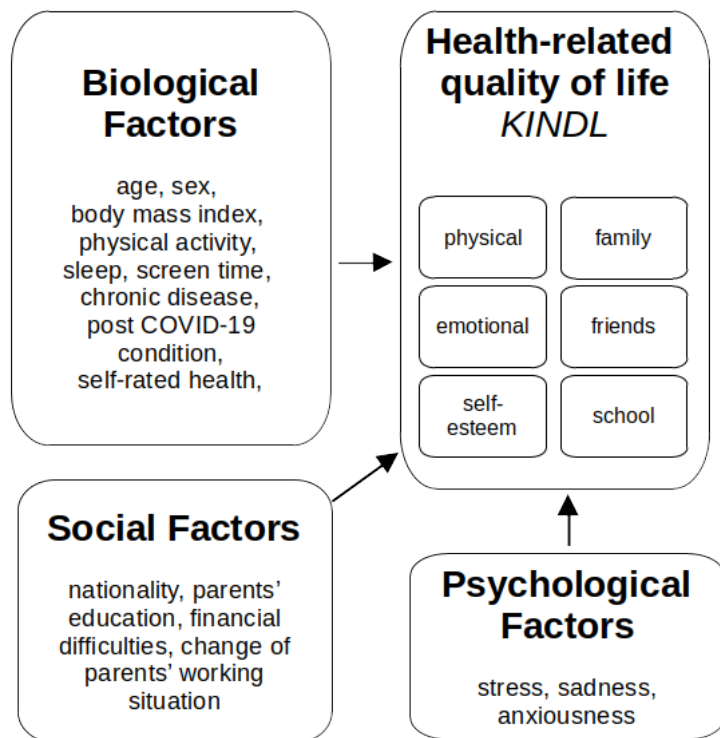
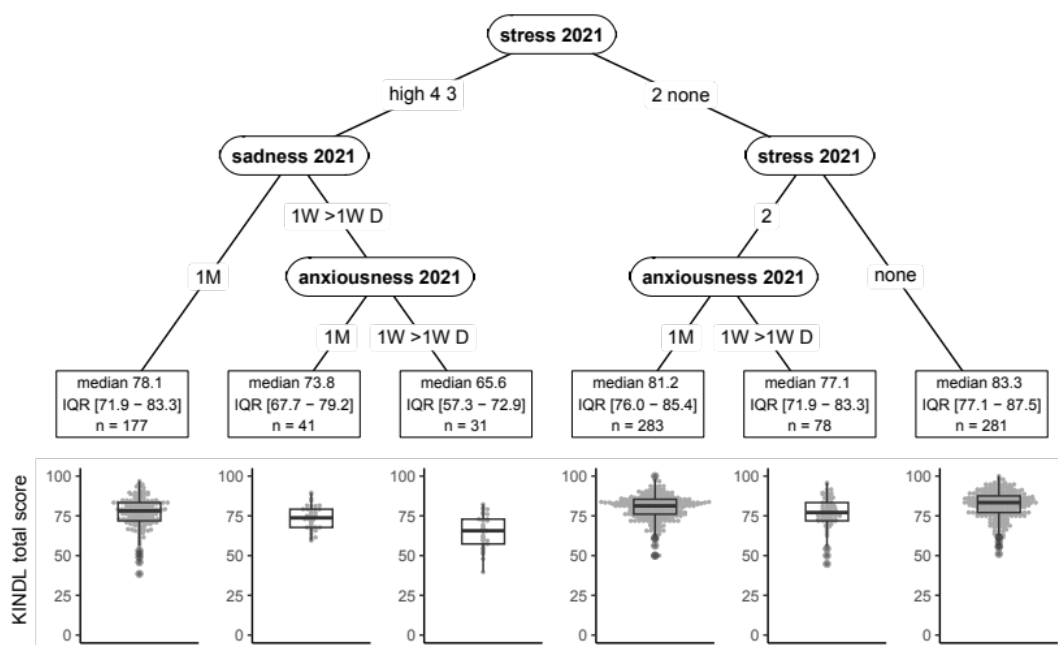


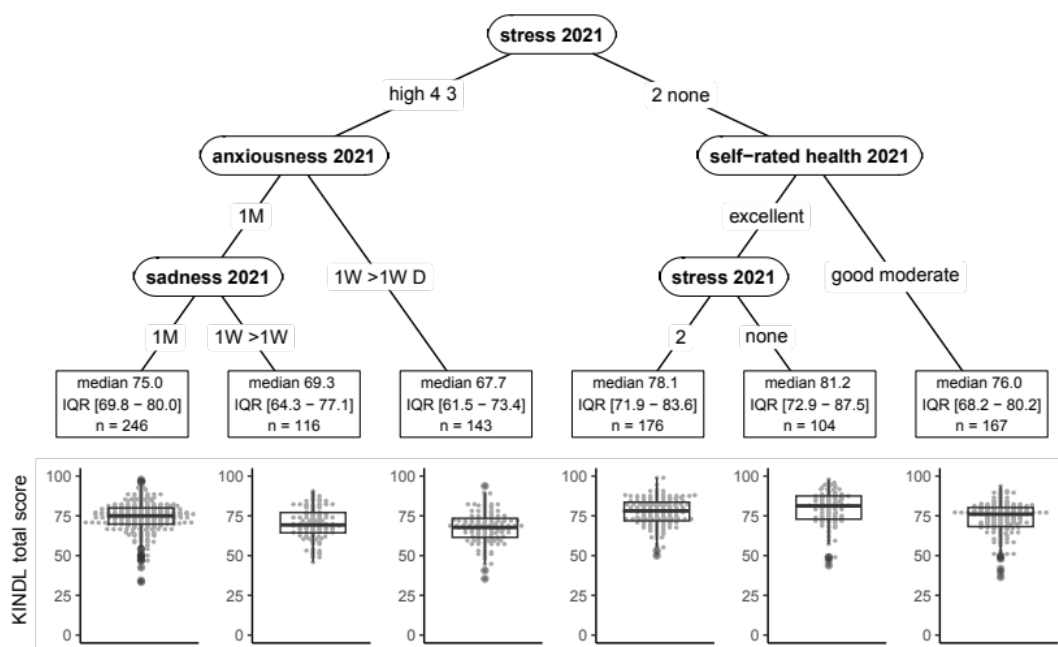
Figure 1: Potential determinants of health-related quality of life (HRQOL), grouped into biological, social and psychological factors.



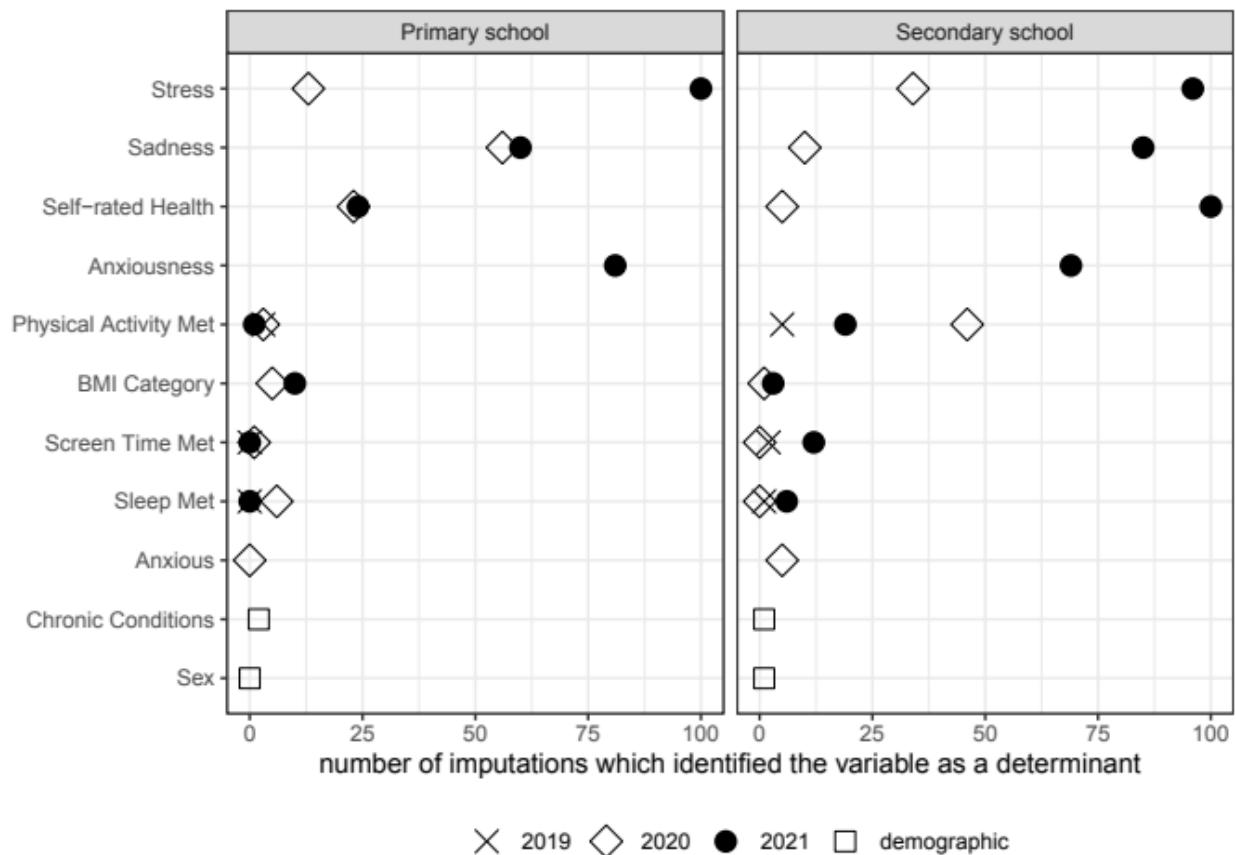
*Figure 2: Recursive partitioning tree for health-related quality of life (HRQOL, KINDL total score) in 2022 in primary school children. Identified determinants are stress, sadness and anxiousness in 2021. Sadness and anxiousness could have occurred once per month (1M), once per week (1W), more than once per week (>1W) or daily (D). Stress was considered on a 5-point scale from 1 (no stress) to 4 (high stress). Other variables included in the model could not be used to create more homogeneous groups with respect to KINDL total score. For each subgroup, median KINDL total score, interquartile range (IQR), mean  $\pm$  standard deviation and sample size (n) are given.*

	Total score	Physical	Emotional	Self-esteem	Family	Friends	School
Stress 2021	P, S	P, S	P	P, S	P, S	P	P, S
Anxiousness 2021	P, S		S	P, S		P, S	S
Sadness 2021	P, S	P	P, S			S	P
Self-rated Health 2021	S	S	S	P, S			P
Chronic Health Conditions		P	S			P, S	
Physical Activity Met 2021				S		S	
Sex		S					
Sleep Met 2021					S		
Self-rated Health 2020						S	
Stress 2020							S
Screen Time Met 2021							S

*Figure 3: Overview of all variables identified as determinants of health-related quality of life assessed by the KINDL total score and its subscales: physical, emotional, self-esteem, family, friends, and school. 'P' indicate variables identified for primary school only, 'S' for secondary school only and 'P, S' for both primary and secondary school. Variables not shown were not identified for any of the subscales.*



*Figure 4: Recursive partitioning tree for health-related quality of life (HRQOL, KINDL total score) in 2022 in secondary school children. Identified determinants are stress, sadness, anxiousness, and self-rated health in 2021. Sadness and anxiousness could have occurred once per month (1M), once per week (1W), more than once per week (>1W) or daily (D). Stress was considered on a 5-point scale from 1 (no stress) to 4 (high stress). Self-rated health was rated as excellent, good, moderately good or bad. Other variables included in the model could not be used to create more homogeneous groups with respect to KINDL total score. For each subgroup, median KINDL total score, interquartile range (IQR), mean  $\pm$  standard deviation and sample size (n) are given.*



*Figure 5: Variables identified as determinants of KINDL total scores by recursive partitioning after multiple imputation (with 100 imputations). More frequently identified variables are of greater importance than those identified in few imputations. For example, stress in 2021 was identified in all 100 imputed datasets for primary school children, indicating it to be an important determinant. On the contrary, chronic conditions were identified in only a few imputations, implying that they are not main determinants of HRQOL in children.*