

Habilitationsschrift

SARS-CoV-2 in children and adolescents

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List of original articles used in the Habilitation

Article I

A Ulytè, T Radtke, I A Abela, S R Haile, C Berger, M Schanz, M Schwarzmüller, A Trkola, Jan Fehr, M A Puhon, and S Kriemler. Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school-children: prospective cohort study of 55 schools in the canton of Zurich, Switzerland. *BMJ*, 372:n616, 2021. doi:10.1136/bmj.n616

Article II

S R Haile, A Raineri, S Rueegg, T Radtke, A Ulytè, M A Puhon, and S Kriemler. Heterogeneous evolution of SARS-CoV-2 seroprevalence in school-age children: Results from the school-based cohort study Ciao Corona in November-December 2021 in the canton of Zurich. *Swiss Med Wkly*, 153(1):40035, January 2023. doi:10.57187/smw.2023.40035

Article III

G P Peralta, A-L Camerini, S R Haile, C R Kahlert, E Lorthe, L Marciano, A Nussbaumer, T Radtke, A Ulytè, M A Puhon, and S Kriemler. Lifestyle behaviours of children and adolescents during the first two waves of the COVID-19 pandemic in Switzerland and their relation to well-being: a population-based study. *Int J Public Health*, 67, September 2022. doi:10.3389/ijph.2022.1604978

Article IV

S R Haile, S Gunz, G P Peralta, A Ulytè, A Raineri, S Rueegg, V Yasenok, T Radtke, M A Puhon, and S Kriemler. Health-related quality of life and adherence to lifestyle recommendations in schoolchildren during the COVID-19 pandemic: results from the longitudinal cohort study Ciao Corona. *Int J Public Health*, 68(1606033), 2023. doi:10.3389/ijph.2023.1606033

Article V

S R Haile, G P Peralta, A Raineri, S Rueegg, A Ulytè, M A Puhon, T Radtke, and S Kriemler. Determinants of health-related quality of life in healthy children and adolescents during the COVID-19 pandemic: results from a prospective longitudinal cohort study. *Eur J Pediatr*, 2024. doi:10.1007/s00431-024-05459-w

Summary

The COVID-19 global pandemic, caused by the SARS-CoV-2 virus, was declared in early 2020. The disease, and restrictive measures introduced to slow its spread, caused significant societal disruption. The role of children and adolescents in the transmission of SARS-CoV-2, and how they were impacted by restrictive measures, was unclear. We conducted Ciao Corona, a longitudinal school-based cohort study to assess how children and adolescents were affected by the COVID-19 pandemic. With repeated serological antibody testing, seroprevalence of SARS-CoV-2 among schoolchildren in the Swiss canton of Zurich was estimated at 5 time-points from 2020 to 2022. Baseline questionnaires and periodic follow-up questionnaires were used to collect a variety of other outcomes, including symptoms, changes in lifestyle (physical activity, screen time and sleep), family situation, and well-being (health-related quality of life). Ciao Corona provided a high-quality evidence base to inform decisions related to mitigation measures in children and adolescents in Switzerland, including vaccination strategy. We observed that SARS-CoV-2 seroprevalence in children and adolescents was similar to that of adults with low evidence of outbreaks within schools or classes, and most children had few symptoms (**Article I** (1) and **Article II** (2)). Physical activity decreased and screen time increased during the pandemic period, and children and adolescents who continued to meet World Health Organization recommendations for both reported better health-related quality of life than those who did not meet either recommendation (**Article III** (3) and **Article IV** (4)). Stress, anxiousness and sadness were also identified as key determinants of health-related quality of life (**Article V** (5)). Further research opportunities include identification of which children and adolescents are least likely to meet lifestyle recommendations, and most likely to experience sadness, anxiousness or stress, which would enable targeted interventions aimed at improving health-related quality of life in schoolchildren. While the COVID-19 global health emergency has ended, the results of Ciao Corona can be used to inform preparedness strategy in children and adolescents for the next pandemic.

Introduction

Throughout human history, highly infectious diseases have been observed to spread quickly across wide geographic areas, leading them to be referred to as “pandemic”. Some well-known pandemics include the black death, cholera, the 1918 flu, SARS and the swine flu (6). While there is no single accepted definition of the word pandemic, it generally involves a novel highly contagious disease with high attack rates, minimal population immunity, and often high disease severity spread across a large geographic area with the potential to move between places (7). Alongside acute measures to treat infected persons, strategies to mitigate the severity and spread of pandemics are of great public health interest. These strategies include a range of non-pharmaceutical approaches, as well as antiviral therapies and vaccination (8). Such non-pharmaceutical strategies include isolation of cases, quarantine of potentially infected persons, restrictions of travel, and school and workplace closures.

In December 2019, the first Coronavirus disease 2019 (COVID-19) case was identified, caused by the SARS-CoV-2 virus. Within a few short weeks, a global pandemic had been declared, with the first case noted in Switzerland in February 2020. The disease and restrictive measures to stop its spread caused significant social and economic disruption. At the time, it was not known how the virus was transmitted, how severe it was, or who was susceptible (9). Research was necessary to understand the disease itself, how it spread, how to contain it and how to treat it.

Much early research on the spread and impact of COVID-19 focused on the adult population. These findings were, however, not always transferable to children and adolescents, who are often considered more vulnerable than the adult population (10). Children and adolescents often spend more time in crowded settings, e.g. schools and daycare centers, further increasing their risk of contracting the disease. Mitigation measures should therefore consider the unique situation of children and adolescents.

Due to lack of knowledge about infection and susceptibility, many countries, including Switzerland, implemented very restrictive lockdowns in early 2020. Generally, these included measures such as mask mandates, travel restrictions, and closing of public facilities, as had been outlined in response to previous pandemics (8). From the perspective of children and adolescents, relevant measures included school closings (or conversely, the decision to keep

schools open), restrictions in sporting and other leisure activities, and vaccination strategies. Good quality research was necessary to inform decisions about further implementation of measures to contain the spread of the SARS-CoV-2 virus (11). The first year of the COVID-19 pandemic saw a large number of new studies trying to understand the new pandemic, including heterogeneous populations of interest and study designs (12). Population-based studies, rather than those focusing on e.g. children with symptoms or those admitted to hospitals, were necessary to estimate seroprevalence in an unbiased manner and to explore other outcomes in the general population.

After an initial emphasis on studying disease transmission, research quickly also turned to the myriad other effects of the SARS-CoV-2 pandemic. In a matter of days, normal patterns of life were completely overtaken by restrictive measures. Even as highly restrictive lockdowns gave way to milder restrictions, patterns of work, school, leisure and other activities remained changed for months to come. The extent to which such disruption affected children and adolescents was unclear, including for example its effect on key lifestyle factors like physical activity (PA), screen time (ST) and sleep, or on quality of life indicators such as well-being and health-related quality of life (HRQOL) (13). There is only sparse data from previous pandemics on the effect of a pandemic on mental health (10). Mental health is affected not only because of the disease itself, but also because of mitigation strategies like school closures. General aspects of well-being such as health-related quality of life have also been shown to be impacted during pandemics (14).

To explore the impact of the COVID-19 pandemic on children and adolescents in Switzerland, we therefore developed Ciao Corona (15), a school-based longitudinal cohort study of children and adolescents in the canton of Zurich, one of the many studies in the Switzerland-wide research network Corona Immunitas. Overall, 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), participated. Using serological testing, SARS-CoV-2 seroprevalence was assessed in June 2020, November 2020, March 2021, December 2021 and June 2022. Schools and classes participating in June 2020 were also invited to participate in later testing periods. By July 2022, 4250 children and adolescents had been tested, ranging from 1875 to 2500 participants or 43 to 55 schools per testing round. Children (or their parents) were also asked to fill out a baseline

questionnaire at the time of their first antibody test which was shortly after the lockdown, and then they completed follow-up questionnaires on a periodic basis (July 2020, January 2021, March 2021, September 2021, and July 2022). These questionnaires further examined a large range of other factors, including symptoms, lifestyle behaviors (PA, screen time, and sleep), HRQOL, parents' working situation. Many children in Ciao Corona participated at multiple timepoints. The sampling strategy ensured that children in all districts of the canton of Zurich were tested, in both urban and rural areas, and across all school levels. The Bayesian analysis strategy adjusted seroprevalence estimates for the age and sex structure of the entire canton of Zurich, corrected for possible school-level clustering, and corrected also for sensitivity and specificity of the diagnostic test. Seroprevalence results from the initial round of serological testing in June/July 2020 were published in (16), and final results from July 2022 in (17).

In this Habilitation, five publications related to Ciao Corona are summarized, which address important research questions regarding the role of children and adolescents in the COVID-19 pandemic. **Article I** examined the SARS-CoV-2 seroprevalence in children and adolescents in November 2020, as well as clustering of infections within schools and classes, and reported symptoms (1). **Article II** updated the seroprevalence estimates in December 2021, and examined the role of the vaccination in 12-15-year-olds (2). **Article III** examined changes in lifestyle (PA, ST and sleep) and their relationship with well-being and life satisfaction in Ciao Corona and 3 other cohorts of children across Switzerland (3). **Article IV** assessed whether adherence to lifestyle recommendations was associated with HRQOL across two years of the pandemic (4). Finally, **Article V** aimed to identify other determinants of HRQOL from a broad set of biological, social and psychological candidate variables (5).

Summary of the original articles

In our analysis of Ciao Corona serological testing from November 2020 (**Article I**) (1), we reported that seroprevalence had increased to 4.5% among school-age children, with no significant differences between children of different ages. Newly seropositive children reported more symptoms than negative children, but the most common symptoms (headache, runny nose, cough, sore throat, fatigue) were not specific to COVID-19. Though 7 / 275 classes had multiple seropositive children, this was within the range of classes that could have occurred by chance if all infections were independent. There was therefore no strong evidence for clus-

tering of infections in our sample. Symptoms were generally mild, not specific to COVID-19 and did not differ significantly between seropositive and seronegative participants.

By December 2021, the COVID-19 vaccination was approved in Switzerland for adolescents aged 12-15, but not yet available to those aged 5-11. Seroprevalence had increased to 31% among unvaccinated children and 46% overall (**Article II**) (2). Secondary school children had on average higher seroprevalence than those in primary school, and this difference was only partly explained by the new vaccination strategy. Variability between geographic districts, between schools, and between classes increased substantially in the first two years of the pandemic, mirroring an increasingly complex pattern of SARS-CoV-2 transmission, even in a small geographic region. Observed seroprevalence in our sample was similar to other studies of COVID-19 seroprevalence in children, and to other studies in adults.

As the pandemic progressed, it became clear that few children or adolescents suffered longterm physical effects from COVID-19. Nevertheless, other consequences, for example impacted lifestyle, mental health or quality of life, remained possible. Combining Ciao Corona data from Zurich with three other COVID-19 cohorts of children in St. Gallen, Graubünden and Ticino (**Article III**), we examined adherence to World Health Organization (WHO) recommendations on PA (≥ 1 hr/day), ST (≤ 2 hr/day) and sleep (9-11 hr/night for those 6-13 years old and 8-10 hr/night for those 14-16 years old) between June 2020 and April 2021 (3), as well as the association between such lifestyle factors and overall well-being. Fewer children met WHO recommendations for PA and ST during the first wave of the COVID-19 pandemic, with a slight recovery during the second wave. Children and adolescents meeting all three of the WHO recommendations for PA, ST and sleep were significantly more likely to report excellent health and higher life satisfaction than those not meeting any of the recommendations. We therefore demonstrated a substantial impact of the COVID-19 pandemic on key lifestyle behaviors, and a positive association between lifestyle and well-being.

If the pandemic impacted PA and ST in children and adolescents, a logical next question is whether these changes affected HRQOL in this population? Using the Ciao Corona data (**Article IV**), we investigated changes in adherence to WHO recommendations on PA and ST during the first two years of the pandemic (4). Using inverse probability weighting with propensity scores, we were further able to examine whether adherence to these recommenda-

tions was associated with HRQOL. We found that while adherence to PA recommendations dropped early in the pandemic and then recovered, adherence to ST recommendations remained lower than pre-pandemic. Further, children and adolescents meeting both recommendations had significantly higher HRQOL than those not meeting either recommendation.

Naturally, HRQOL is affected not only by lifestyle, but also by other factors, especially during a pandemic with various restrictive mitigation strategies. In **Article V**, we therefore aimed to identify determinants of HRQOL using a broad range of biological, psychological and social factors in a large longitudinal population-based sample from the Ciao Corona study (5). Using a data driven approach, sadness, anxiousness and stress were identified as the most important determinants of HRQOL, more so than other factors such as PA or chronic health conditions. Public health strategies to improve mental health may therefore be effective in improving HRQOL in this age group.

Discussion

In the early months of the COVID-19 pandemic, our team developed the Ciao Corona study, a prospective longitudinal school-based cohort study to examine seroprevalence and transmission of SARS-CoV-2 in children and adolescents in Switzerland, as well as assess the impact of the pandemic on other aspects, including lifestyle and well-being. This Habilitation has described 5 selected papers reporting on results from Ciao Corona, taken from a larger collection of publications about the study. In this section, the greater context of Ciao Corona results are discussed.

SARS-CoV-2 seroprevalence estimates from serological antibody testing were described from June 2020 (16), November 2020 (**Article I**: 1), March 2021 (18), December 2021 (**Article II**: 2), and June 2022 (17). **Article I** described how overall SARS-CoV-2 seroprevalence in our sample increased to 7.8% by November 2020, with minimal differences between age groups. Infections did not appear to cluster within classes, school levels or schools. Symptoms reported were mostly general (e.g. headache, runny nose, sore throat, and fatigue), and were observed in similar rates in seronegative and seropositive participants. **Article II** later discussed the increase in seroprevalence by December 2021 to 46%, with much heterogeneity between classes, schools, and geographic districts. Much, but not all, of the difference in seroprevalence be-

tween primary and secondary school participants could be explained by the introduction of the vaccine for 12-15-year-olds in June 2021. The observed SARS-CoV-2 seroprevalence in children and adolescents in Switzerland was similar to that of adults, as seen also in systematic reviews (19). As many SARS-CoV-2 infections in children and adolescents were not reported, often due to lack of PCR testing, the use of serological antibody testing is essential to capture unbiased estimates of SARS-CoV-2 seroprevalence in this age group (20). Infections in children and adolescents often presented with mild symptoms or were even asymptomatic (21). School infection rates appeared similar to those of the general population, providing further evidence that transmission in school settings did not substantially contribute to community transmission (19,22). Older children and adolescents generally had high transmission rates than younger children (21), even accounting for vaccination status.

Alongside much research related directly to transmission of the SARS-CoV-2 virus, we and other researchers have explored the effect of the virus and strategies to mitigate it have had on other aspects of life. **Article III** described changes in PA, ST and sleep in a cross-sectional analysis of 4 cohorts of children and adolescents across Switzerland, and the relationship between lifestyle and well-being (3). Few children and adolescents met recommendations for PA and ST during the pandemic than before, with only a slight recovery during the second wave of infections. Those meeting all three recommendations were more likely to report excellent health (odds ratio: 1.95, 95% confidence interval 1.00 - 2.76). **Article IV** went on to examine whether adherence to international recommendations on key lifestyle behaviors as associated with HRQOL in a longitudinal analysis of Ciao Corona data (4). Adherence to PA recommendations dropped in 2020 but returned to pre-pandemic levels by 2022. Similarly, fewer children met ST recommendations in 2020 and 2021 than pre-pandemic. HRQOL was 9.7 points higher on a scale from 0 to 100 (95% CI 3.0 - 16.3) among those who met both PA and ST recommendations compared to those who did not meet either recommendation. Similar changes in lifestyle have been reported during the early phases of the COVID-19 pandemic (23,24). The onset of the pandemic was also associated with increased mental health problems, such as anxiety and depression, and decreased HRQOL (25,13,26). **Article V** identified sadness, anxiousness and stress as the most important determinants of HRQOL, even other factors such as PA, ST, chronic health conditions or nationality (5). Mental health has been observed to be associated with chronic health conditions, PA, family relationships and social support (25). The need for high quality research on mental health and HRQOL to

address future crises has also been emphasized (25,13,26). Few studies have taken a global view on HRQOL in children and adolescents 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.

Results from Ciao Corona enabled evidence-based decision making with regards to mitigation strategies for school-age children in Switzerland, including school closures and vaccination strategy. Along with providing updates in SARS-CoV-2 seroprevalence in schoolchildren over time, the Ciao Corona study's school-based approach enabled the examination of potential clustering of infections, which would indicate outbreaks in classes or schools. The Swiss National COVID-19 Science Task Force used Ciao Corona to inform their policy brief on measures in schools (27), noting that as schools had experienced few outbreaks, there was little need to implement additional measures. With this evidence, schools in Switzerland were able to stay open much longer than in many other countries (28). As the pandemic situation progressed, mitigation measures were adapted and vaccines protecting against COVID-19 were developed. The Federal Commission for Vaccination Questions ("Eidgenössische Kommission für Impffragen" (EKIF)) considered whether to recommend vaccination in children and adolescents. For these age groups, Ciao Corona provided important evidence that COVID-19 was primarily asymptomatic to mild with few longterm effects. Therefore, the EKIF recommended the COVID-19 vaccine to 12-15-year-olds (in June 2021 (29)) who wished to be vaccinated, and later to 5-11-year-olds (in December 2021 (31,30)) whose parents requested it. A general recommendation was not made, as Ciao Corona and similar studies (19) had observed few children and adolescents with severe disease or long-lasting symptoms. Evidence from this and other studies was important to guide policy decisions on vaccination strategy (19,32), safe schooling (27,33), and other mitigation measures.

A closer look at the literature reveals a heterogeneous mix of studies, both in terms of study design and risk of bias (34). In contrast, Ciao Corona is a randomly selected school-based longitudinal cohort study, where the school-based sampling approach closely matched that of the general population of schoolchildren in the canton of Zurich. Ciao Corona was also one of the few large studies to focus on the spread of SARS-CoV-2 in schools (16). To minimize selection bias in enrolled children, serological testing was performed in schools, and study information provided in multiple formats and languages. The longitudinal structure, with

repeated serological testing in schools mixed with periodic online questionnaires, provided much needed data on a variety of topics related to SARS-CoV-2 infection, transmission in children and adolescents as well as other changes during the pandemic period (e.g. (19,35)).

Some limitations must be recognized. As with any diagnostic test, misclassification in Ciao Corona was possible, both false negative and false positive. Some children may have lost antibodies and therefore appeared seronegative despite having been infected with the virus (36). Antibody testing does not identify recent infections as antibodies take some time to develop. Ciao Corona used two different antibody tests, each with high sensitivity and high specificity (ABCORA 2.0 from University of Zurich's Institute for Medical Virology with sensitivity 94.3% and specificity 99.0% (37), and SenASTrIS from Lausanne University Hospital's (CHUV) Service of Immunology and Allergy and EPFL's Laboratory of Virology and Genetics with sensitivity 94.0% and specificity 99.2% (38)). The estimation of seroprevalence in Ciao Corona adjusted explicitly for sensitivity and specificity of the diagnostic test using a Bayesian methodology (39), in line with other seroprevalence studies in Corona Immunitas (40). The Bayesian approach we employed also assumed a range of plausible sensitivity and specificity values for the diagnostic test, making the results more robust than if point estimates had been assumed (36). The serological antibody testing used in the Ciao Corona study to assess seroprevalence is inherently retrospective. It cannot be used to assess the temporal sequence of infections, e.g. to identify patterns of transmission within a specific class. As we did not only test confirmed cases, Ciao Corona is unlikely to suffer from differential misclassification bias.

Sources of selection bias also need to be considered. Ciao Corona's school-based sampling scheme was described previously (15), and implemented by myself prior to study begin. Schools with fewer than 40 total children across any of the school levels (lower levels: grades 1-3; middle level: grades 4-6; upper level: grades 7-9) were excluded, as were schools for children with special needs (15). A random sample of primary schools was selected by geographic district, proportional to the population. For those selected primary schools, the corresponding secondary school was selected. The list of schools obtained from the canton of Zurich's Department of Education did not include "Gymnasium" schools, secondary schools leading to university education, which correspond to approximately 18% of the secondary school population. The school sampling procedure did not take into account that the canton of Zurich has relatively more primary schools than secondary schools (in that students in

multiple primary schools may attend the same secondary school, depending on school district). Classes within schools were chosen randomly, rather than testing all classes within each school, so that the sampling distribution should be similar to that of the overall population. Use of post-stratification weights in the analysis of seroprevalence corrects for a mismatch in the age and sex distribution of the sample and population (40). While the school-based sampling approach may not have been strictly population-based, it did not recruit participants that are more likely than average to be positive (as in e.g. hospital-based studies), or less likely (e.g. only asymptomatic participants). We did not have information on how many eligible children could not attend testing due to an acute SARS-CoV-2 infection.

Bias may also occur due to nonrandom willingness to participate. We do not know if some subjects participated to determine if a previous bout of symptoms could have been COVID-19 or did not participate to avoid a positive test result (36). The participation rate of 50% in Ciao Corona was nonetheless high despite the use of venous blood sampling (see Supplementary Material in 18). The majority of Ciao Corona participants had highly educated parents, at least one of whom was Swiss, but it is unlikely that SARS-CoV-2 infections differed among children without Swiss nationality, as all came from the same community and attended the same school.

In the analysis of lifestyle and HRQOL, other limitations played a role. Recent pre-pandemic data on HRQOL in children and adolescents was not available for comparison and was not possible to collect once the pandemic had begun. The four cohorts of schoolchildren described in the cross-sectional analysis of lifestyle (3) used somewhat different questionnaires which were at times challenging to combine. With more time to prepare the respective studies, uniform questionnaires could have been used in these Corona Immunitas centers. We did not consider other measures of social situation, for example parents' mental health, family cohesion, or social isolation, and did not include many positive predictors of HRQOL. Switzerland had a relatively short lockdown period and shorter school closings than other countries, and therefore the association between HRQOL and lifestyle or mental health may have weaker than in other countries (28). As the majority of Ciao Corona participants had highly educated Swiss parents, our results may only partially hold for children from more vulnerable, socially disadvantaged families. Finally, while our analysis implied that a focus on mental health and lifestyle could improve overall HRQOL, the identified determinants of HRQOL are not

guaranteed to translate beyond the pandemic setting.

The results of Ciao Corona as described here suggest several possibilities for further research. As the COVID-19 pandemic has become endemic, studies of seroprevalence are no longer of great interest. Pandemic-related changes to lifestyle and well-being nonetheless continue to be important and are key to mental health preparedness in case of disasters and other crises (41). We observed that adherence to international recommendations on PA, ST and sleep were impacted during the pandemic, and not all returned to pre-pandemic levels. However, it remains unclear which children and adolescents were likely not to meet these recommendations, and which were able to meet all recommendations, even despite pandemic restrictions. Identification of determinants of low PA, high ST and insufficient sleep could serve to indicate potential public health interventions in this age group. We observed that not meeting any of the WHO recommendations implied a significant reduction in HRQOL compared to those who met all recommendations, implying that public health interventions targeting lifestyle could potentially be used to improve HRQOL. Components of mental health (sadness, anxiety and stress) were identified as key determinants of HRQOL in children and adolescents during the COVID-19 pandemic, even more so than lifestyle behaviors. Further examination of who is at risk of poor mental health would enable tailoring of mental health interventions which could in turn improve both mental health and HRQOL (26). One likely scenario is that there is a complex bidirectional interplay between mental health and lifestyle behaviors such as PA (42), ST (43) and sleep (44). Even if, as we have observed, mental health is a main determinant of HRQOL, public health interventions may be more easily implementable if they target PA, ST or sleep directly and mental health only indirectly. Validation studies are also needed to determine whether these results hold outside of the pandemic setting.

In May 2023, the WHO declared the end of the global health emergency that was the COVID-19 pandemic. Life in Switzerland and around the world is mostly back to normal, at least in terms of infectious disease outbreaks and measures to restrict them. Nevertheless, preparedness for the next Public Health emergency is key to act quickly to mitigate it, and to maintain the physical and mental health of the population. Children and adolescents are a subset of the general population, with particular needs. Patterns of social contact in this age group, due to close contact with their peers in schools, are not necessarily comparable to the general adult population. And stressors, pandemic or otherwise, impact the development of children

and adolescents that could influence their lives as they grow into adulthood (45). Multidisciplinary research specific to children and adolescents is needed to ensure that they receive the physical, mental and social support they need in the next pandemic and beyond.

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Appendix: Original articles of the Habilitation

Article I: Ulytè et al 2021, BMJ

A Ulytè, T Radtke, I A Abela, S R Haile, C Berger, M Schanz, M Schwarzmüller, A Trkola, Jan Fehr, M A Puhán, and S Kriemler. Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school-children: prospective cohort study of 55 schools in the canton of Zurich, Switzerland. *BMJ*, 372:n616, 2021. doi:10.1136/bmj.n616

Article II: Haile et al 2023, Swiss Med Wkly

S R Haile, A Raineri, S Rueegg, T Radtke, A Ulytè, M A Puhán, and S Kriemler. Heterogeneous evolution of SARS-CoV-2 seroprevalence in school-age children: Results from the school-based cohort study Ciao Corona in November-December 2021 in the canton of Zurich. *Swiss Med Wkly*, 153(1):40035, January 2023. doi:10.57187/smw.2023.40035

Article III: Peralta et al 2022, Int J Public Health

G P Peralta, A-L Camerini, S R Haile, C R Kahlert, E Lorthe, L Marciano, A Nussbaumer, T Radtke, A Ulytè, M A Puhán, and S Kriemler. Lifestyle behaviours of children and adolescents during the first two waves of the COVID-19 pandemic in Switzerland and their relation to well-being: a population-based study. *Int J Public Health*, 67, September 2022. doi:10.3389/ijph.2022.1604978

Article IV: Haile et al 2023, Int J Public Health

S R Haile, S Gunz, G P Peralta, A Ulytè, A Raineri, S Rueegg, V Yasenok, T Radtke, M A Puhán, and S Kriemler. Health-related quality of life and adherence to lifestyle recommendations in schoolchildren during the COVID-19 pandemic: results from the longitudinal cohort study Ciao Corona. *Int J Public Health*, 68(1606033), 2023. doi:10.3389/ijph.2023.1606033

Article V: Haile et al 2024, Eur J Pediatr

S R Haile, G P Peralta, A Raineri, S Rueegg, A Ulytè, M A Puhán, T Radtke, and S Kriemler. Determinants of health-related quality of life in healthy children and adolescents during the COVID-19 pandemic: results from a prospective longitudinal cohort study. *Eur J Pediatr*, 2024. doi:10.1007/s00431-024-05459-w