Research Paper

Exposome changes in primary school children following the wide population non-pharmacological interventions implemented due to COVID-19 in Cyprus: A national survey

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A B S T R A C T

Background: Non-pharmacological interventions (NPI), including lockdowns, have been used to address the COVID-19 pandemic. We describe changes in the environment and lifestyle of school children in Cyprus before the lockdown and during school re-opening, and assess compliance to NPI, using the exposome concept.

Methods: During June 2020, parents completed an online questionnaire about their children's lifestyle/behaviours for two periods; school re-opening (May 21-June 26) following the population-wide lockdown, and the school period before lockdown (before March).

Findings: Responses were received for 1509 children from over 180 primary schools. More than 72% of children complied with most NPI measures; however, only 48% decreased the number of vulnerable contacts at home. Sugary food consumption was higher in the post-lockdown period with 37% and 26% of the children eating sugary items daily and 4–6 times/week, compared to 33% and 19%, respectively, for the pre-lockdown period ($p<0.001$). Children's physical activity decreased compared to pre-lockdown ($p<0.001$), while screen time increased in the post-lockdown period, with 25% of children spending 4-7 hours/day in front of screens vs. 10% in the pre-lockdown period ($p<0.001$). About half of the children washed their hands with soap 4–7 times/day post-lockdown vs. 30% in the pre-lockdown period ($p<0.001$).

Interpretation: This national survey showed a high degree of compliance to NPI measures among school children. Furthermore, the exposome profile of children may be affected in the months following NPI measures due to alterations in diet, physical activity, sedentary behaviour, and hand hygiene habits.

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1. Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared as a global pandemic by the World Health Organization on March 11, 2020 [1, 2]. As of December 6, 2020, over 65.87 million cases and 1.5 million deaths had been reported globally since the start of the pandemic [3] and 12,181 cases of COVID-19 and 59 associated deaths had been reported in Cyprus [4]. The first two COVID-19 cases in Cyprus were reported on March 10, 2020, and non-pharmacological interventions (NPI) were subsequently implemented to restrict the

spread of the virus [4]. School closures were among the first measures (March 13), followed by closures of dining and recreation areas (March 16) [5]. Stay-at-home orders, also widely referred to as lockdown, went in effect on March 24 [5]. As the daily reported cases started decreasing, the gradual easing of measures was introduced in early May 2020. Schools re-opened on May 21, following a strict protocol that included among others, a rotation of students with a maximum of 12 allowed in class and a defined break area for each class, and with the Cyprus Ministry of Health conducting a random screening for SARS-CoV-2 infection among students and school personnel [6, 7]. During the same period, recommendations were also made for the implementation of personal measures including limitations in the number of contacts (physical distancing) and reinforcement of personal hygiene habits.

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Research in context

Evidence before this study

We searched PubMed for studies published until September 30, 2020 using the terms: COVID-19, children and lifestyle. Only six peer-reviewed, English-language studies on the effect of COVID-19 measures on children's lifestyle were retrieved. The impact of non-pharmacological intervention (NPI) measures on children's health during the pandemic period has been sporadically studied by focusing on a few risk factors at a time, without using the methodological framework of the exposome, which is defined as the comprehensive characterization of all environmental exposures during one's lifetime.

Added value of this study

A survey was used to target all primary schools in Cyprus to comprehensively study the impact of the initial population-wide NPI measures (lockdown) (March 13 - May 4) on the children's exposome during the school re-opening period (May 21 – June 26). To the best of our knowledge, this is the first study looking at the post-confinement (lockdown) exposome profile changes of children during school re-opening, after the initial population-wide NPI measures as part of the COVID-19 response. The comprehensive and agnostic description of the children's exposome profile may help to comprehensively account for both known and possibly unknown effects of NPI measures on children's health, and for delineating the children's degree of compliance to infection prevention and control protocols at school and at home.

Implications of all the available evidence

This dataset documented changes in the lifestyle and behaviours of primary school children following the lockdown period when schools re-opened. Changes in food frequency consumption, physical activity, screen time, digital communication and hand hygiene habits were observed. Findings could inform COVID-19 risk-based public health response strategies targeted for school settings. Future response strategies to epidemics should consider elements of promoting a healthy lifestyle for children at school and at home. Public health policy could ultimately benefit from the inclusion of the human exposome methodological framework and its tools towards the improved identification of susceptible sub-population groups and to facilitate the deployment of site-tailored public health measures.

The implemented NPI measures required changes in routine behaviours of primary school children, including changes in attending classes face to face or not, commuting to school, conducting extracurricular activities and meeting with friends. These routine behaviours, as well as the context in which they take place, the associated environmental exposures, and personal and contextual parameters, define the exposome profile of children (i.e. the totality of environmental exposures during one's lifetime) [8, 9]. Given that routine activities are associated with a suite of exposures, compliance to the NPI measures is expected to have led to changes in the exposome profile of primary school children. The comprehensive assessment of the totality of changes in lifestyle and behaviours could be conducted by implementing the methodological framework of the human exposome and through the description of changes in exposome profiles between different time frames.

So far, there have been limited data about the magnitude and extent of possible changes in children's lifestyle and behaviour profile due to the implemented NPI measures for the COVID-19 pandemic. Studies on changes of children's lifestyle in Spain, Italy, Canada, U.S., and China during periods in which strict COVID-19 measures (e.g. lockdowns) were implemented showed that parameters, such as physical activity, screen time, diet, as well as sleep time were affected [10–15]. Specifically, it was shown that physical activity levels decreased and screen time/sedentary behaviour increased in all studied children's populations during the measures [10–15], whereas sleep time increased for the studied children in Canada and Italy [10, 11], and changes in diet were observed for Spanish and Italian children [11, 12, 14]. Conversely, in a study among the Italian population aged ≥ 12 years, a slight increase in physical activity was reported [16].

In parallel, the role of children in the COVID-19 disease spread as well as the severity of COVID-19 in younger populations is still under investigation. A meta-analysis conducted early on the COVID-19 pandemic provided preliminary evidence that children younger than 10 to 14 years have lower susceptibility to SARS-CoV-2 infection when compared to adults [17], and a systematic review concluded that children do not present with a different transmission potential of SARS-CoV-2 infection compared to adults [18]. Moreover, it seems that a lower percentage of children develop severe COVID-19-related symptoms compared to adults, with cardiovascular disease being the most frequent comorbidity in severe cases [19]. As new data become available, they add to the knowledge on the role of children in SARS-CoV-2 transmission and to the ongoing scientific discourse, that will likely inform the implementation of NPI and compliance to them.

We implemented a national survey to study changes in the children's exposome upon primary schools re-opening (after the population-wide lockdown) and compared it against the children's exposome during the pre-lockdown period in Cyprus. The objectives of this study were: (i) to describe the children's environment, individual behaviour and lifestyle at school and at home (exposome profiles) before and after the lockdown in Cyprus, and (ii) to assess the children's compliance to the COVID-19 NPI protocols and recommendations, with special focus on personal hygiene and physical distancing at both school and home settings, by adopting the methodological context of the human exposome.

2. Methods

2.1. Study design and population

The Exposome@School | COVID-19 national survey was conducted online. Information about the survey and links to the questionnaire were forwarded to parents of primary school children via school administrations, during the re-opening of schools following the lockdown in the Republic of Cyprus (June 2020). Public schools and private schools teaching in Greek language (330 and 6, respectively) located in all government-controlled areas of the Republic of Cyprus were contacted, and 253 of them agreed to distribute the survey to their children's parents. Eligible participants were children attending a primary school. Per the study protocol, participants living in Cyprus less than one year were not eligible. However, this exclusion was amended, and in the main study all participants were included.

2.2. Data collection and ethics

Data was collected from June 1 until July 17, 2020 using REDCap hosted on a server at the Cyprus University of Technology [20]. The survey questionnaire was available in Greek, and parents were asked to respond on behalf of the children. The study was approved by the Cyprus National Bioethics Committee (ΕΕΒΚ/ΕΠ/2020.01.113) and the Ministry of Education, Culture, Youth and Sport (21.11.06.10). Parents were informed that the data collection was anonymous and
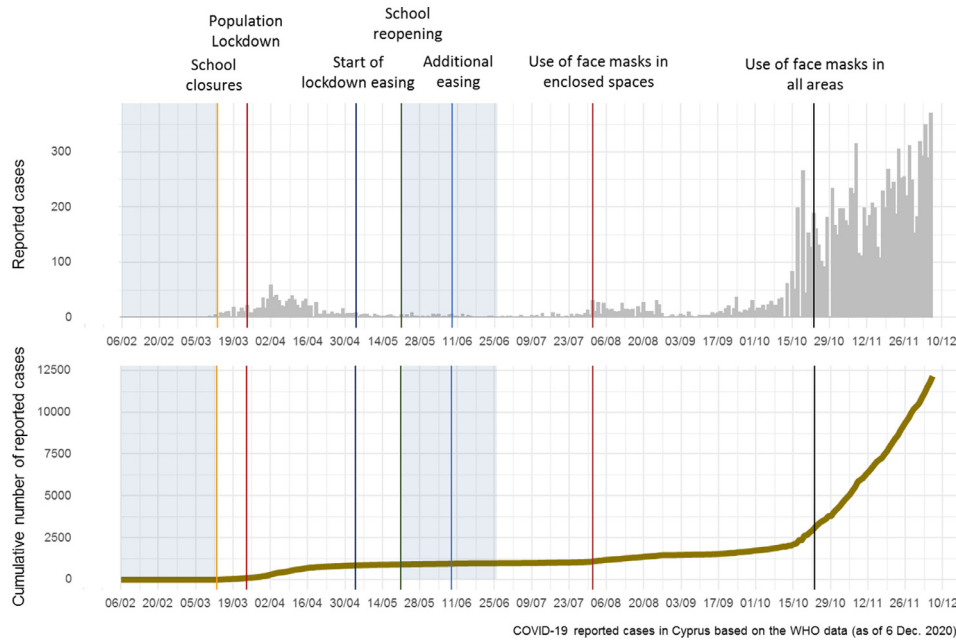
Fig. 1. Epidemiological curves for COVID-19 reported cases (top) and cumulative number of cases (bottom) in Cyprus based on WHO data (1). NPI measures are denoted with vertical lines. The blue shaded areas indicate the two study periods for which the primary school children's lifestyle is described in our study.

that, if they wished to, they could withdraw from the study at any time while completing the questionnaire.

The study included questions about the children's lifestyle and behaviours for two periods (Fig. 1): (a) pre-lockdown, i.e. before March 2020 and (b) post-lockdown when schools reopened (May 21-June 26, 2020). The whole set of NPI measures implemented in Cyprus during the period until September 2020 can be found in Fig. S1. In this analysis, we included components from all three exposome domains, i.e. the general external domain (socio-economic status), the specific external domain (lifestyle and COVID-19 related parameters) and the internal domain (background characteristics, intrinsic properties, medical history) (Table 1). The BMI-for-age was calculated based on the measurements reported by parents for child's weight and height, standardized for age and sex, using the WHO 2007 growth reference standard for children [21].

More specifically, the online survey consisted of questions related to demographic and general characteristics of children (e.g., age, sex, health status, height, weight, city, returned or not to school) and their parents (educational level) as well as questions about the children's lifestyle/behaviour (physical activity, diet, digital communication, screen time, personal hygiene, number of contacts and hours spent at home) and parents' habits (smoking and household cleaning activities) for the two study periods (pre- and post-lockdown). Questions from four validated questionnaires and one diary were used: i) Diary of contacts [22]: a contact was defined as either a two-way conversation with three or more words in the physical presence of another

person or physical skin-to-skin contact (e.g. handshake, hug and kiss) [22], ii) European Health Interview Survey for 2014 based on the Cyprus Statistical Services [23], iii) European Urban Health Indicators survey [24, 25], iv) Questionnaire on hand hygiene and cleaning of home areas [26], and v) Questionnaire on physical activity for children PAQ-C [27−29], where we used 3 out of 9 items included in the original questionnaire, so a spare time activity score could be calculated by taking the mean of all activities (e.g. basketball, cycling, ballet). The questionnaire and details about methodology can be found in the Supplementary Material S2.

2.3. Statistical analysis

2.3.1. Description of the children's exposome profile

Frequencies and percentages were used for the description of categorical variables and means (standard deviations) or medians (interquartile ranges) for the continuous variables, depending on the distribution of the variable. In all categorical variables the "I don't know/I don't want to answer" responses were re-coded to "missing". The pre- and post-lockdown differences in lifestyle/habits parameters were compared using the non-parametric Wilcoxon rank sum paired test and/or chi-square test for continuous and/or categorical variables, respectively. For continuous variables with pre- and post-lockdown values, the percent change was calculated as $[(post - pre)/pre]*100$ for use in the analysis.

Table 1.

Exposome domains and their specific components/variables included in the Exposome@School|COVID-19 survey. The number of variables is based on the main questions of the questionnaire and not on sub-questions.

Exposome domain	Study group of components	Variables	# variables
General external	Socio-economic status	Parents' educational level	2
Specific external	Lifestyle (children)	Exercise, diet, screen time, digital communication	34
	Lifestyle (children) − related with NPI measures	Personal hygiene, number of contacts, time spent at home weekdays and weekend	22
	Lifestyle (parents)	Parents' smoking and household cleaning activities frequency	10
Internal external	Anthropometrics	Weight, height	2
	Medical history	Chronic disease, vaccination	4
	Background characteristics	Age, sex, place of birth, years living in Cyprus, district/city of residence, municipality, postal code, school	8

2.3.2. Exposome-wide association study

We performed an exposome-wide association study (ExWAS) to agnostically assess associations of demographic, lifestyle and behavioural parameters with the degree of compliance to COVID-19 recommended measures (Tables S1-S4). In a correlation analysis, all variables were used as continuous with categorical variables being assigned a score (Table S5). Spearman correlation coefficients were calculated and results were visualized with a circo-plot.

Four indicators of compliance to COVID-19 protocols were used as binary outcomes (1 and 0) in separate logistic regression models, adjusted for age, sex, parents' educational level and number of days since school re-opening: (i) increase in the hours staying at home during weekdays, (ii) decrease in the number of vulnerable contacts at home during weekdays, (iii) decrease in the number of contacts at school, and (iv) increase of hand washing frequency using antiseptic or soap. People belonging in the vulnerable group were those over 60 years, pregnant, or having a chronic disease. These indicators were categorized as 0 or 1 based on the responses for the pre- and post-lockdown period for the number of hours staying at home (1 if post > pre), the number of contacts at school (1 if post < pre), the number of vulnerable contacts at home during weekdays (1 if post < pre) and the hand washing frequency using antiseptic or soap (1 if post > pre and 1 if post: > 7 times/day & pre: > 7 times/day). For the compliance indicator of decreased number of contacts at school, we used only the data from children who returned to school following the re-opening of schools ($n = 1331$).

Categorical variables were grouped so that they would have a maximum of 4 levels (2−4 levels) in order to decrease the number of tests in the regression models. The p-values of all model parameters that were used for inference (i.e., excluding the intercept, age, sex, days since school re-opening and parents' educational level coefficients) were summarized and adjusted for Benjamini−Hochberg false discovery rate (FDR) [30]. Only parameters with FDR-adjusted p-value ≤ 0.05 were considered statistically significant.

2.3.3. Sensitivity analysis

We conducted a sensitivity analysis by excluding seven children that either reported living in Cyprus less than 1 year ($n = 2$) or they had no response about the years living in Cyprus ($n = 5$), as per the original study protocol.

All analyses were conducted in R 4.0.2 with RStudio 1.3.1093 [31, 32]. The input data, scripts, and output are available in the Supplementary Material S3.

2.4. Role of the funding source

The funders of this study had no role in the study design, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data and final responsibility for the decision to submit for publication.

3. Results

3.1. Study population characteristics

A total of 1509 primary school children from more than 180 schools all over Cyprus were included in the study analysis (Fig. 2). There were 2807 entries which were not complete, and they were not included in the analysis (visits of the questionnaire link but not submitted questionnaire). Participating children had a mean age of 9.6 years (SD: 1.7), a balanced sex ratio (52% males and 48% females), and the majority of them were born in Cyprus (96%) (Table 2). The reported parents' educational level was relatively high with about half of them holding at least one university degree (57% of mothers and 44% of fathers). Most parents completed the survey for one child
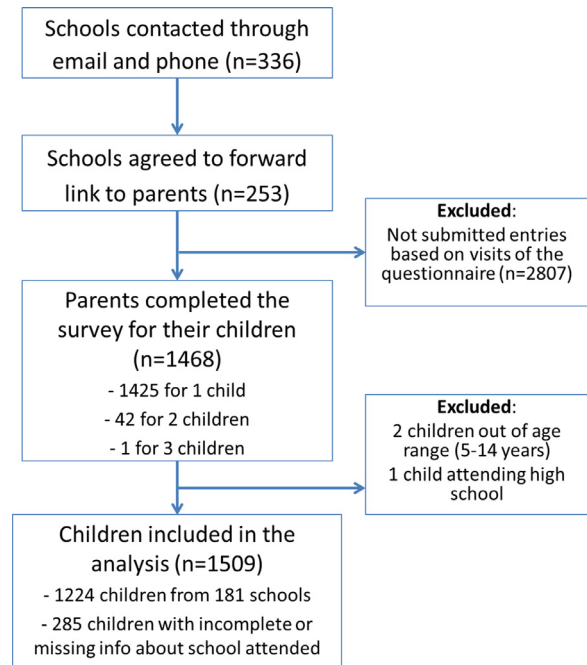

Fig. 2. Flow chart including number of schools contacted for the survey, those that agreed to forward questionnaire to parents, number of parents who completed the survey and number of children included in the analysis.

(97%), 42 parents for two children (2.9%) and 1 for three children (0.1%).

Most children's health status was reported as healthy (92%) while for 8%, a chronic disease was reported by their parents; the most frequently reported diseases were allergies (34%) and asthma (33%) (Table S6). Most children were vaccinated according to the recommended vaccination schedule and received all recommended vaccine doses (93% and 92%, respectively). About half of the children had a normal BMI for their age (57%), while 23% were overweight and 15% were obese. We observed higher obesity levels for boys compared to girls (18% and 10%, respectively, Table S7).

A small portion of children did not go to school following the re-opening of schools on May 21 (12%). Out of the 1331 children who returned to school, 211 (16%) were tested for SARS-CoV-2 with a diagnostic test (PCR) in random sampling taking place in school premises; this testing campaign was initiated by the Cyprus Ministry of Health [7] and only one child was tested positive (0.5%).

3.2. Children's exposome profile in the pre- and post-lockdown periods

3.2.1. Diet

Some of the children's dietary habits seem to have changed between the pre- and post-lockdown periods (fish, sugar, salty/savoury foods, breakfast, ready-made food and supplements), whereas for others no change was observed (fruits, vegetables, legumes and meat). In effect, about half of the children consumed fruits daily (54% for both pre- and post-lockdown periods), whereas a third of them consumed vegetables daily (34% and 31%, pre- and post-lockdown, respectively) (Fig. S2). The weekly meat consumption frequency was relatively high, with half of the children eating meat 2−3 times per week and about one third of them, eating meat 4−6 times per week in both study periods (Fig. S3). Regarding legumes consumption, half of the children consumed legumes 2−3 times per week and one third of them, once a week (Fig. S3).

There were statistically significant differences in the frequency of fish consumption before and post-lockdown ($p<0.001$), however the ratio of children consuming fish once per week before was similar to

Table 2.
Demographics and general characteristics of participating children.

	Overall (n = 1509)
Sex (%)	
Female	709 (47.6)
Male	780 (52.4)
Age in years (mean (SD))	9.6 (1.7)
Age groups (%)	
5−6 year old	4 (0.3)
7−8 year old	476 (31.5)
9−10 year old	481 (31.9)
11−12 year old	531 (35.2)
13−14 year old	17 (1.1)
BMI for age* (%)	
Thinness	77 (5.5)
Normal	789 (56.8)
Overweight	320 (23.1)
Obese	202 (14.6)
Place of birth (%)	
Cyprus	1448 (96.0)
EU country	49 (3.2)
Non-EU country	12 (0.8)
Years living in Cyprus (mean (SD))	9.1 (2.1)
District/City (%)	
Nicosia	613 (40.6)
Limassol	375 (24.9)
Larnaca	274 (18.2)
Paphos	97 (6.4)
Famagusta	150 (9.9)
Self-reported chronic disease (%)	
No	1367 (91.5)
Yes	127 (8.5)
Vaccination with at least one of the recommended vaccines (%)	
Yes	1460 (98.9)
No	16 (1.1)
Vaccine doses (if more than one dose is required) (%)	
Yes	1304 (92.3)
No, vaccine not available	15 (1.1)
No, we thought that more than one dose wasn't needed	13 (0.9)
No, we neglected but they will be provided	73 (5.2)
No, only one dose was needed	8 (0.6)
Vaccination, according to recommended schedule (%)	
Yes	1302 (93.2)
No	95 (6.8)
Returned to school following school re-opening (%)	
Yes	1330 (88.1)
No	179 (11.9)
Tested for SARS-CoV-2 in school (%)	
No	1119 (84.1)
Yes	211 (15.9)
Result of test for SARS-CoV-2 in school (%)	
Negative	135 (99.3)
Positive	1 (0.7)
Mother's educational level (%)	
Has not completed primary school	70 (4.6)
Primary School	68 (4.5)
Middle School (3 years)	21 (1.4)
High School/Vocational High School (diploma)	207 (13.7)
Higher (after high school) non-tertiary Education	83 (5.5)
Higher Tertiary Education (non-University)	195 (12.9)
University (bachelor's degree)	445 (29.5)
University-postgraduate (only Master's degree)	385 (25.6)
PhD	32 (2.1)
Father's educational level (%)	
Has not completed primary school	13 (0.9)
Primary School	35 (2.3)
Middle School (3 years)	78 (5.2)
High School/Vocational High School (diploma)	480 (31.9)
Higher (after high school) non-tertiary Education	89 (5.9)
Higher Tertiary Education (non-University)	146 (9.7)
University (bachelor's degree)	320 (21.3)
University-postgraduate (only Master's degree)	300 (19.9)
PhD	44 (2.9)
Primary school children in family (mean (sd))	1.4 (0.6)
Siblings participating in the survey (%)	87 (5.8)

* Based on WHO 2007 cut-off points for BMI-for-age (21). BMI standard deviation scores taking in account age and sex were calculated and then based on the specific cut-offs, the BMI-for-age categories were created (≤−2: Thinness; −2 ⟨ Normal ≤1; 1< Overweight ≤ 2; ⟩ 2: Obese).

the ratio of children consuming fish once per week post-lockdown (45.8% and 46.3%, respectively) and there was a slight decrease in the percentage of children consuming fish 2−3 times per week (15% and 13%, respectively). Moreover, the consumption frequency of salty/savoury foods decreased with 33% of children eating them 2−3 times per week in the post-lockdown period compared to 37%, in the pre-lockdown period (Fig. S4, $p<0.001$). The consumption of food items that contained sugar was high in both periods, but even higher in the post-lockdown period with 37% and 26% of the children eating sugary items every day and 4−6 times per week, respectively, in the post-lockdown period, compared to 33% and 19% for the pre-lockdown period ($p<0.001$) (Fig. S4). Similarly, the proportion of children eating breakfast daily increased in the post-lockdown period (80% compared to 76%, $p = 0.002$) (Fig. S5). On the other hand, following the re-opening of schools, children ate ready-made food less frequently with 20% of children never consuming ready-made food in the post-lockdown period, compared to 6% in the pre-lockdown period ($p<0.001$) (Fig. S6). Furthermore, there were statistically significant differences in the use or not of supplements pre- and post-lockdown ($p<0.001$), however the percentage of people not using supplements was similar for the two periods (80 and 82%, respectively) (Fig. S7).

3.2.2. Physical activity

Following the re-opening of schools, children's physical activity decreased both in school and in their free time compared to the period before lockdown ($p<0.001$). The spare time activity score, which is based on the weekly frequency of activities children engage with during their free-time, was significantly reduced in the post-lockdown period (median [Q1, Q3]: 1.38 [1.25, 1.62]) vs. 1.5 [1.38, 1.75] in the pre-lockdown period, suggesting that the children's physical activity was reduced following the lockdown ($p<0.001$, Fig. S8). About half of the children engaged with activities that involved little physical effort during their free time (51%) and were sitting down during school break (46%) in the post-lockdown period compared to 29% and 9%, respectively for the pre-lockdown period ($p<0.001$, Figs. S9 and S10).

3.2.3. Digital communication and screen time

Daily communication of children with friends and family using telephone or internet increased in the post-lockdown period (46% and 45%, respectively compared to 32% and 34% for the pre-lockdown period, $p<0.001$) (Fig. S11). Screen time in the form of watching TV or using a computer, mobile phone, tablet, and game console also increased in the post-lockdown period ($p<0.001$), with screen time being 1−3 h/day for 62% of children, and 4−7 h/day for 25% of children (Fig. S12).

3.2.4. Personal hygiene habits

Children increased the frequency of hand hygiene with antiseptic products and hand washing with soap in the post-lockdown period, with about half of the children washing their hands with soap 4−7 times/day (51% vs. 30% in the pre-lockdown period) and using hand antiseptic 1−3 times/day (44% vs. 19% in the pre-lockdown period, $p<0.001$) (Fig. S13).

3.2.5. Number of contacts and number of hours staying at home

Children decreased the number of physical contacts during school re-opening after the population-wide lockdown ($p<0.001$) (Fig. 3). Specifically, the median number of contacts during weekdays was about halved in school, home and elsewhere (10, 4 and 4, respectively, compared to 24, 6 and 10, in the pre-lockdown period) ($p<0.001$, Fig. S14). Similar decreases in contacts were observed during weekends (Fig. S15). Children of all ages (5−14 years) decreased
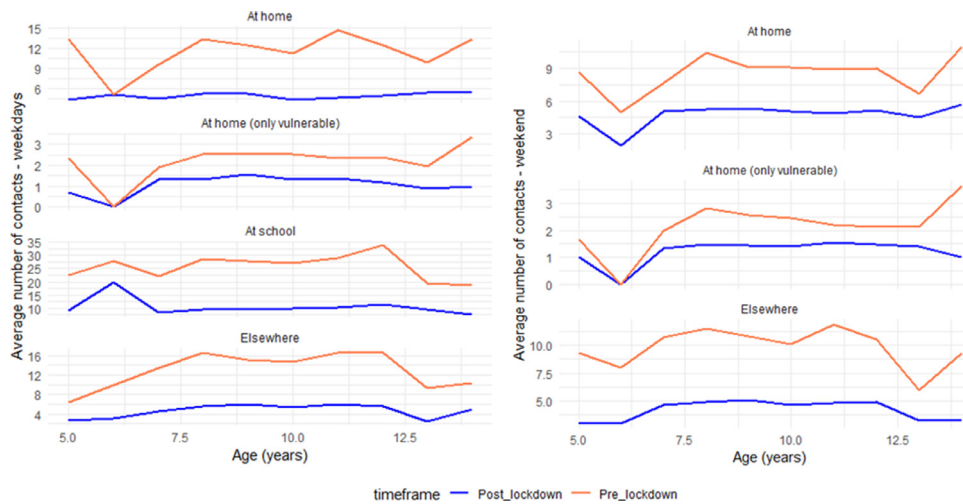
Fig. 3. Average number of contacts at home (separately for vulnerable contacts), at school and elsewhere by age for the 2 periods: (a) following the re-opening of schools (post-lockdown) and (b) before the lockdown (pre-lockdown) during weekdays and weekends.

their average number of contacts in all settings during both weekends and weekdays, with children of younger age (6 years old) having a low number of vulnerable and total contacts at home in both pre- and post-lockdown periods (Fig. 3).

Statistically significant ($p<0.001$) decreases were also observed in the number of vulnerable group contacts at home, for both weekends and weekdays (median [Q1, Q3]: 2[1, 3] in the pre-lockdown period and 1[0, 2] in the post-lockdown period) (Figs. S14 and S15). It is important to note that, before the lockdown, the percentage of children who were coming in contact at their home with at least one person belonging to the vulnerable groups (i.e., those > 60 years old, pregnant, or presence of chronic diseases) was higher compared to the period following the lockdown, for both weekends and weekdays (Table S8).

The median change (%) in the number of contacts during weekdays was negative for contacts at home, school and elsewhere, but it was zero for vulnerable contacts at home (-30 [-67, 0], -60 [-76, -47], -60 [-81, -30] and 0 [-60, 0], respectively) (Fig. S16). Similar changes were observed for contacts during weekends (Fig. S17).

Similarly to the decrease in contacts, children stayed more hours at home following the re-opening of schools ($p<0.001$), both in weekends and weekdays (median [Q1, Q3]: 20 [12, 24] and 15 [10, 20], respectively, compared with 15 [10, 19] and 12 [7, 15] in the pre-lockdown period) (Fig. S18). The median change (%) in the hours staying at home was positive for both weekdays and weekends (31 [0, 67] and 20 [0, 60], respectively) (Fig. S19).

3.2.6. Parents' smoking habits and household cleaning activities frequency

Parents' smoking habits did not change between the two study periods with most parents not smoking in the house (about 70%) and about 26% of them smoking in the house daily (median [Q1, Q3]: 10 [5, 15] cigarettes per day) in both periods ($p>0.05$, Fig. S20). As parents reported, the frequency of all household cleaning activities with the use of disinfectants or antiseptic products increased in the post-lockdown period, with the majority of parents cleaning the kitchen 7 times/week (72% compared to 51% in the pre-lockdown period); about half of them reported cleaning the bathroom 7 times/week (43% compared to 29%) and about one third of them mopping and cleaning other surfaces 7 times/week (33% and 32%, compared to 21% and 22%, accordingly) ($p<0.001$, Fig. S21).

3.3. Exposome-wide associations

3.3.1. Correlations among exposome variables

A circo plot for all exposome variables adjusted for age, sex, mother's and father's educational level did not show any unexpected patterns of correlation among the variables (Fig. 4). Notable positive correlations ($r \geq 0.7$) were observed for dietary variables [fish, vegetables, sugar, fruits, meat, savoury/salty foods (snacks) and legumes] among the pre- and post-lockdown study periods (Table S9).

3.3.2. Assessment of children's compliance to COVID-19 recommendations and hygiene protocols

Based on three out of four compliance indicators, the children's compliance to COVID-19 measures following the lockdown was relatively high (73–85%), with the exception of the indicator of reduced number of contacts belonging in the vulnerable groups at home
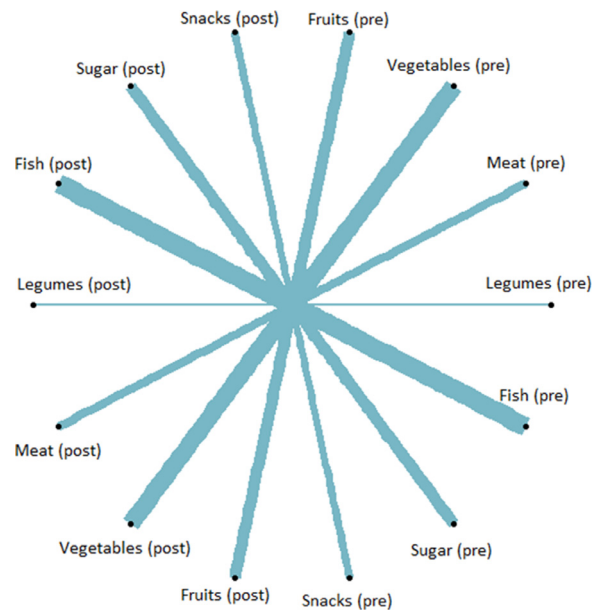

Fig. 4. Circo plot for exposome variables adjusted for age, sex, mother's and father's educational level. Only correlations with |r| ≥ 0.7 are shown. Only positive correlations were observed for |r| ≥ 0.7. "Post" refers to the post-lockdown period and "pre" to the pre-lockdown period. The width of the line indicates the level of correlation (larger width indicates higher r).

Table 3.
Summary tables for compliance indicators.

Outcome	OverallN (%)	MalesN (%)	FemalesN (%)
Increase in hours staying at home − weekdays ($n = 1509$)	1096 (72.9)	562 (72.4)	515 (72.9)
Decrease in number of vulnerable contacts at home - weekdays ($n = 1190$)	573 (48.2)	308 (48.4)	257 (48.2)
Decrease in number of contacts at school ($n = 1330$)	1100 (85.1)	569 (85.1)	516 (84.9)
Increase in hand washing using soap or antiseptic ($n = 1509$)	1099 (74.4)	549 (71.5)	532 (77.2)

during weekdays, for which only about half of the children (48%) decreased the number of vulnerable contacts at home (Table 3). No significant differences were observed for the compliance indicators between boys and girls ($p > 0.05$).

3.3.3. ExWAS associations with indicators of compliance to COVID-19 protocols

In the ExWAS models of compliance to COVID-19 measures for which the outcome was the increase in hours staying at home during weekdays, four parameters had an FDR-corrected p-value < 0.05. In effect, consuming meat 4−7 times/week, and not returning to school in the post-lockdown period were positively associated with increased time spent at home. Living in Paphos (smaller town compared to the capital of Nicosia), and use of hand antiseptic ≥ 4 times/day in the pre-lockdown period were negatively associated with this compliance indicator (Fig. 5).

The percent change in the total number of contacts at home during weekdays and of vulnerable contacts at home during weekends were negatively associated with the indicator of reduced number of vulnerable contacts at home during weekdays (FDR-adjusted p-value < 0.05).

The only variable positively associated with the compliance indicator of reduced number of contacts at school was never communicating with friends using phone or internet in the pre-lockdown

period, whereas < 4 times/week sugar consumption before and after the lockdown, use of hand antiseptic ≥ 4 times/day in the pre-lockdown period, change (%) in the number of contacts outside of home and school and change (%) in the number of hours staying at home on weekends were negatively associated with this compliance indicator (FDR-adjusted p-value < 0.05). No variable was found to be associated with the compliance indicator of increase of hand hygiene frequency. All significant parameters with FDR-adjusted p-value ≤ 0.05 can be found in Table S10.

In the sensitivity analysis, in which seven children living in Cyprus for less than a year or with missing information were excluded, the trends observed were the same as those of the main analysis. The number of missing data per variable can be found in Table S11.

4. Discussion

The pandemic and its impact on lifestyle and behaviours can be better understood using comprehensive frameworks such as the one of the human exposome, which has been previously used in the assessment of chronic health outcomes due to environmental exposures [33]. In this national survey, we employed the exposome concept and its tools to evaluate the impact of the population-wide lockdown and other restrictive measures on lifestyle and behaviours of children. A representative sample was obtained from the majority of schools located in all government-controlled areas of the Republic of Cyprus (Table S12). The study also described children's compliance to post-lockdown NPI measures and health protocols during school re-opening period (May-June 2020).

The impact of the COVID-19 pandemic and its associated NPI measures (lockdown, school closures) on children's exposome profile was evident by the changes in relevant exposome parameters, such as physical activity, diet, digital communication, screen time, personal hygiene habits, number of contacts and hours staying at home as well as their parents' frequency of household cleaning activities. Specifically, the changes observed in the children's exposome (behaviours and living environment) within 1−2 months after the lockdown compared to the period before the introduction of NPI measures in
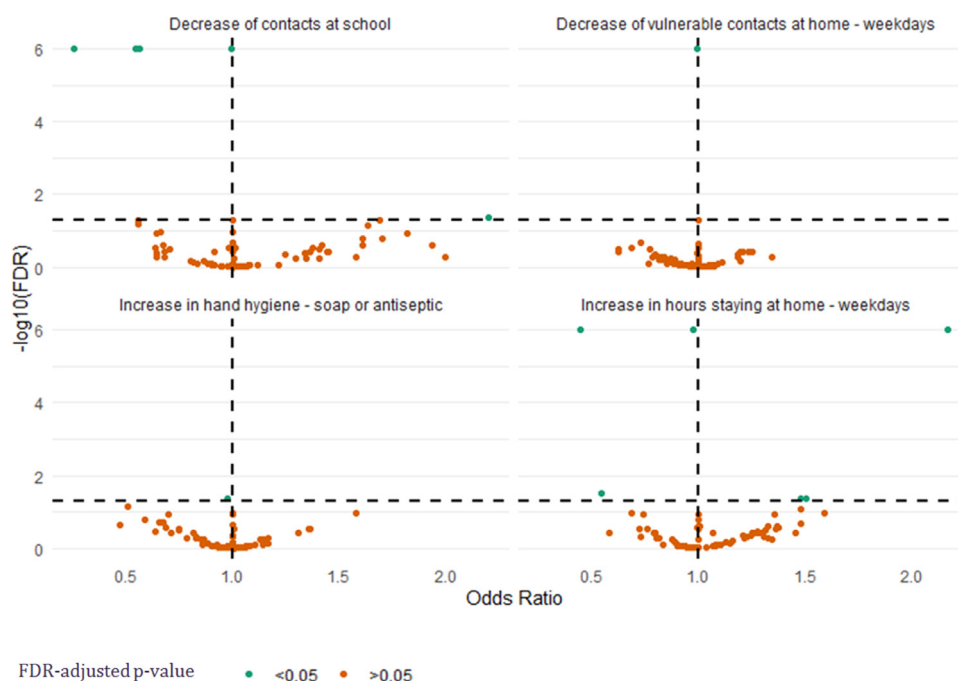

Fig. 5. Odds ratios vs. -$\log_{10}$ (FDR-adjusted p-value) for ExWAS models of compliance indicators. Compliance indicators from top left to bottom right: Decrease in the number of contacts at school, decrease in the number of vulnerable contacts at home during weekdays, increase in hand hygiene using soap or antiseptic and increase in hours staying at home during weekdays.

March were the following: reduced physical activity, increased consumption of sugary food items, decreased consumption of ready-made food, increased screen time, increased frequency of digital communication with friends and family, decreased number of contacts at home, school and elsewhere, increased time spent at home, increased frequency of hand washing and antiseptic use and higher frequency of passive exposure to cleaning products through the increased frequency of household cleaning activities [34]. Several of these changes in exposome parameters were observed in factors/parameters already linked with population health trends such as increasing obesity [35], and include inadequate daily consumption of sugary items and sedentary lifestyle including lower physical activity and higher screen time.

The degree of children's compliance to NPI measures (assessed with either increasing time spent at home, or decreasing number of contacts at school, or decreasing number of vulnerable contacts at home, or increasing frequency of personal hygiene) was associated with certain lifestyle habits. These habits/behaviours were: higher consumption of sugar and meat, or using less frequently hand antiseptic and never communicating with friends in the pre-lockdown period. Such habits and lifestyle changes might be presumably driven by recommendations to stay at home and reduce contacts at school, and limit face-to-face extracurricular activities. On the other hand, living in the smaller district/city of Paphos (with population of about 36,000) was negatively associated with increased time spent at home when compared with living in the district/city of Nicosia (capital city of Cyprus). This association could be attributed to the fact that living in smaller in population size urban settings may provide easier access to green/blue spaces, such as parks and the beach, and it may be also linked with perceptions of higher sense of safety and trust being outdoors, when compared with people living in larger cities [36]. Reducing contact with vulnerable individuals at home was the metric that children followed the least among all compliance indicators. This may be important to consider in future public health response measures for better protecting vulnerable population groups during pandemics.

Previous studies showed that the COVID−19 confinement may have affected specific parameters in children's lifestyle e.g. decreased physical activity and increased sedentary behaviour [10−15], increased sleep time [11, 13], and diet changes [11, 12, 14]. These studies were mainly focused on the period during COVID-19 strict restrictions (lockdown and school closures), whereas our study describes the children's lifestyle in the period following the gradual relaxation of measures and re-opening of schools in Cyprus, using the exposome approach. Our results are aligned with those of previous studies for the parameters of physical activity and screen time [10−15], indicating that possibly these changes in children's lifestyle may have occurred during the COVID-19 lockdown period and persisted afterwards. However, our data cannot provide information about the lifestyle/behaviour changes during the lockdown period for primary school children in Cyprus.

It is necessary to examine whether these exposome changes persist in the longer-term and to assess the impact of children's sedentary behaviour and sugary food consumption on their later in life odds of developing chronic diseases. The fact that the majority of children conformed to a sedentary lifestyle in combination with the higher consumption of sugar following the re-opening of schools needs to be reassessed in future prospective studies and should inform future policy making of promoting healthy lifestyle for children when measures such as stay-at-home orders are in place. The use of exposome tools will be important to identify susceptible sub-population groups and to facilitate the deployment of site-tailored public health measures [37], promoting a healthier lifestyle during periods in which physical distancing is necessary.

Strengths of this study are its relatively large sample size (at a minimum, children from 54% of the contacted schools were included), being representative of the Cyprus children's population. This is also the first study demonstrating the application of the exposome's concept during the COVID-19 pandemic, where comprehensive understanding of primary school children's behaviours took place. Limitations of this study include the possible recall bias of the participating parents, the cross-sectional design, the fact that parents completed the questionnaire on behalf of their children and that the survey was limited to parents who had access to the internet and who were comfortable completing an online survey using their device (e.g. mobile phone, computer). Recall bias might have differentially affected the responses about the period before the lockdown compared to the responses about the period after the lockdown that referred to the current habits/activities of the children. The interpretation of the results should be done cautiously taking into account both the strengths and the limitations.

Overall, the methodology on the description of the profile of children following and before the lockdown can be used for future exposome studies in primary school children. Detailed and agnostic description of the children's exposome helps in weighing in known and possibly unknown effects of NPI measures, and thereby better informing decision making for pandemic response. Future studies could further benefit from broadening the number and type of exposome variables considered and by including biospecimen in their study design so that children's internal exposome may be better captured (biomarkers of effect, omics platforms).

The NPI measures implemented were deemed necessary to reduce the SARS-CoV-2 transmission. However, as our results show, they modified the exposome profile of primary school children. If the modifications, e.g. sedentary lifestyle have a longer-term effect, they can potentially alter chronic disease risk. Modifiable risk factors for chronic diseases such as diabetes, obesity and cardiovascular diseases are unhealthy diet and physical inactivity [38], and as seen in our results, diet and physical activity are parameters which were affected between the two studied periods. Hence, it is important that the impacts of any NPI measure are considered in their totality prior to its implementation and strategies are developed to minimize health risks when population-wide measures are in effect. The study's findings could inform health policy guidelines towards decreasing the impacts of future epidemics and the impact of NPI measures. The COVID-19 pandemic brought up challenges for all sectors (health, social, and economic) and revealed the urgent need for an integrated assessment of the impacts and response plans to major public health events, as well as for sustainable development that benefit both the environment and public health [39]. Monitoring the degree of compliance of children to NPI measures and health protocols could ultimately help towards improving interventions that, within the context of a public health emergency, do not compromise multiple determinants of health. Additionally, this study could inform the monitoring of determinants of compliance to emergency public health measures, such as those implemented during the pandemic for children, towards further improvement of the degree of compliance at school and home settings.

Author contributions

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Declaration of Competing Interests

All authors declare no competing interests.

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Data sharing statement

The datasets utilised in this study can be found in the Supplementary Material. Sensitive data like municipality, school name and postal code were removed prior sharing the current datasets for data protection purposes.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2021.100721.

References

[1] WHO. Q&A on coronaviruses (COVID-19) https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-coronaviruses (Accessed 10 May 2020).

[2] WHO. Coronavirus disease 2019 (COVID-19) situation report − 51 https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf (Accessed 10 May 2020).

[3] WHO. WHO coronavirus disease (COVID-19) dashboard https://covid19.who.int/ (Accessed 7 December 2020).

[4] World Health Organization. https://covid19.who.int/region/euro/country/cy (Accessed 10 February 2020).

[5] Press Information Office. Coronavirus covid-19 - Cyprus https://www.pio.gov.cy/coronavirus/ (Accessed 9 May 2020).

[6] Ministry of Education, Culture, Sports and Youth. Ενημερωνόμαστε για τον Κορωνοϊό (Covid-19) http://www.moec.gov.cy/covid_19.html (Accessed 8 December 2020).

[7] Press Information Office. Διενέργεια 20.000 δωρεάν διαγνωστικών εξετάσεων στα σχολεία https://www.pio.gov.cy/%CE%B1%CE%BD%CE%B1%CE%BA%CE%BF%CE%B9%CE%BD%CF%89%CE%B8%CE%AD%CE%BD%CF%84%CE%B1-%CE%AC%CF%81%CE%B8%CF%81%CE%BF.html?id=14430#flat (Accessed 15 November 2020).

[8] Miller GW, Jones DP. The nature of nurture: refining the definition of the exposome. Toxicol Sci 2014;137(1):1–2. doi: 10.1093/toxsci/kft251.

[9] Wild CP. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol Biomark Prev 2005;14(8):1847–50. doi: 10.1158/1055-9965.EPI-05-0456.

[10] Dunton GF, Do B, Wang SD. Early effects of the COVID-19 pandemic on physical activity and sedentary behavior in children living in the U.S. BMC Public Health 2020;20(1):1351. doi: 10.1186/s12889-020-09429-3.

[11] López-Bueno R, López-Sánchez GF, Casajús JA, Calatayud J, Gil-Salmerón A, Grabovac I, Tully MA, Smith L. Health-related behaviors among school-aged children and adolescents during the Spanish Covid-19 confinement. Front Pediatr 2020;8:573. doi: 10.3389/fped.2020.00573.

[12] Medrano M, Cadenas-Sanchez C, Oses M, Arenaza L, Amasene M, Labayen I. Changes in lifestyle behaviours during the COVID-19 confinement in Spanish children: a longitudinal analysis from the MUGI project. Pediatr Obes 2020. doi: 10.1111/ijpo.12731.

[13] Moore SA, Faulkner G, Rhodes RE, Brussoni M, Chulak-Bozzer T, Ferguson LJ, Mitra R, O'Reilly N, Spence JC, Vanderloo LM, Tremblay MS. Impact of the COVID-19 virus outbreak on movement and play behaviours of canadian children and youth: a national survey. Int J Behav Nutr Phys Act 2020;17(1):85. doi: 10.1186/s12966-020-00987-8.

[14] Pietrobelli A, Pecoraro L, Ferruzzi A, Heo M, Faith M, Zoller T, Antoniazzi F, Piacentini G, Fearnbach SN, Heymsfield SB. Effects of COVID-19 lockdown on lifestyle behaviors in children with obesity living in Verona, Italy: a longitudinal study. Obesity 2020;28(8):1382–5. doi: 10.1002/oby.22861.

[15] Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. Prog Cardiovasc Dis 2020;63(4):531–2. doi: 10.1016/j.pcad.2020.04.013.

[16] Di Renzo L, Gualtieri P, Pivari F, Soldati L, Attinà A, Cinelli G, Leggeri C, Caparello G, Barrea L, Scerbo F, Esposito E, De Lorenzo A. Eating habits and lifestyle changes during COVID-19 lockdown: an Italian survey. J Transl Med 2020;18(1):229. doi: 10.1186/s12967-020-02399-5.

[17] Viner RM, Mytton OT, Bonell C, Melendez-Torres GJ, Ward J, Hudson L, Waddington C, Thomas J, Russell S, van der Klis F, Koirala A, Ladhani S, Panovska-Griffiths J, Davies NG, Booy R, Eggo RM. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. JAMA Pediatr 2020. doi: 10.1001/jamapediatrics.2020.4573.

[18] Rajmil L. Role of children in the transmission of the COVID-19 pandemic: a rapid scoping review. bmjpo 2020;4(1):e000722. doi: 10.1136/bmjpo-2020-000722.

[19] De Luca CD, Esposito E, Cristiani L, Mancino E, Nenna R, Cortis E, Midulla F. Covid-19 in children: a brief overview after three months experience. Paediatr Respir Rev 2020;35:9–14. doi: 10.1016/j.prrv.2020.05.006.

[20] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42(2):377–81. doi: 10.1016/j.jbi.2008.08.010.

[21] de Onis M. Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ 2007;85(09):660–7. doi: 10.2471/BLT.07.043497.

[22] Mossong J, Hens N, Jit M, Beutels P, Auranen K, Mikolajczyk R, Massari M, Salmaso S, Tomba GS, Wallinga J, Heijne J, Sadkowska-Todys M, Rosinska M, Edmunds WJ. Social contacts and mixing patterns relevant to the spread of infectious diseases. PLoS Med 2008;5(3):e74. doi: 10.1371/journal.pmed.0050074.

[23] Republic of Cyprus, Ministry of Finance. European health interview Survey. Statistical Service; 2014.

[24] European urban health indications system part 2. EURO-URHIS; 2012.

[25] Pope D, Puzzolo E, Birt C, Guha J, Higgerson J, Patterson L, van Ameijden E, Steels S, Owusu MW, Bruce N, Verma A. Collecting standardised urban health indicator data at an individual level for adults living in urban areas: methodology from EURO-URHIS 2. Eur J Public Health 2016:ckv220. doi: 10.1093/eurpub/ckv220.

[26] Ioannou S, Ioannou S, Andrianou XD, Charisiadis P, Christophi CA, Yiasoumi G, Makris KC. Occupational exposures to disinfectants and pre-diabetes status among active nurses in Cyprus. Scand J Work Environ Health 2019;45(5):505–13. doi: 10.5271/sjweh.3804.

[27] Chortiatinou S, Risvas G, Zampelas A. Eat healthy - live like scout», a nutrition behaviour change program in scouts, aged 12-15 years. Clin Nutr ESPEN 2016;13:e58. doi: 10.1016/j.clnesp.2016.03.016.

[28] Kowalski KC, Crocker PRE, Donen RM. The physical activity questionnaire for older children (PAQ-C) and adolescents (PAQ-A) manual. Canada: college of kinesiology, University of Saskatchewan, 1−38. College of Kinesiology, University of Saskatchewan: Canada; 2004. p. 1−38.

[29] Kowalski KC, Crocker PRE, Faulkner RA. Validation of the physical activity questionnaire for older children. Pediatr Exerc Sci 1997;9(2):174–86. doi: 10.1123/pes.9.2.174.

[30] Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc 1995;57(1):289–300.

[31] R Core Team. The R Project for Statistical Computing. The R Foundation. http://www.r-project.org.

[32] RStudio Team. RStudio: integrated development environment for R. http://www.rstudio.com/.

[33] Haddad N, Andrianou XD, Makris KC. A scoping review on the characteristics of human exposome studies. Curr Pollut Rep 2019;5(4):378–93. doi: 10.1007/s40726-019-00130-7.

[34] Andra SS, Charisiadis P, Karakitsios S, Sarigiannis DA, Makris KC. Passive exposures of children to volatile trihalomethanes during domestic cleaning activities of their parents. Environ Res 2015;136:187–95. doi: 10.1016/j.envres.2014.10.018.

[35] WHO. Childhood obesity surveillance initiative - highlights 2015-17. Factsheet; 2018.

[36] European Commission, Directorate-General for Regional and Urban Policy. Report on the quality of life in European cities, 2020. Luxembourg: Publications Office of the European Union; 2020.

[37] Andrianou XD, Pronk A, Galea KS, Stierum R, Loh M, Riccardo F, Pezzotti P, Makris KC. Exposome-based public health interventions for infectious diseases in urban settings. Environ Int 2021;146:106246. doi: 10.1016/j.envint.2020.106246.

[38] Chronic diseases are the major cause of death and disability worldwide. World Health Organization; 2005.

[39] Barouki R, Kogevinas M, Audouze K, Belesova K, Bergman A, Birnbaum L, Boekhold S, Denys S, Desseille C, Drakvik E, Frumkin H, Garric J, Destoumieux-Garzon D, Haines A, Huss A, Jensen G, Karakitsios S, Klanova J, Koskela I-M, Laden F, Marano F, Franziska Matthies-Wiesler E, Morris G, Nowacki J, Paloniemi R, Pearce N, Peters A, Rekola A, Sarigiannis D, Šebková K, Slama R, Staatsen B, Tonne C, Vermeulen R, Vineis P. The COVID-19 pandemic and global environmental change: emerging research needs. Environ Int 2021;146:106272. doi: 10.1016/j.envint.2020.106272.