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Work package 3- Task 3.2 – Deliverable:

D3.5 Report on patterns of core and integrated socio-economic, migration, urban environment and lifestyle related stressors across Europe. (Mo54)

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D3.5 Report on patterns of core and integrated socio-economic, migration, urban environment and lifestyle related stressors across Europe

1 INTRODUCTION

WP3 of LifeCycle focusses on the integration of integrated, harmonized measures of early-life stressors in the cohorts that make part of the EU Child Cohort Network. Such measures will allow better comparison between cohorts, populations, and countries participating in the network, and facilitate aetiological studies relating early life stressors with health. Therefore, WP3 (task 3.1) generated new early-life stressor data related to socio-economic, migration, urban environment, and lifestyle factors in a large set of cohorts. These variables have been detailed in previous deliverables (3.1-3.4) and are summarized in Table 1. Distributions of these variables across the European cohorts have already been reported in Deliverables 3.1-3.4.

Task 3.2 aims to describe and compare patterns of early-life stressors across Europe, with a particular focus on describing how various early-life stressors co-exist across Europe and on describing the social and urban inequalities in stressor patterns. Participating partner cohorts in each analysis are those for which the key variables were available. Three specific analyses make part of this task:

1) Urban stressors and health-related behaviour patterns in 6 European Birth Cohorts

2) Socioeconomic position (SEP) influence on the early-life individual exposome

3) Lifestyle patterns of preschool children

Table 1: Summary of new hamonised early-life stressor data generated in WP3 of LifeCycle (task 3.1).

	SEP	Ethnicity	Urban	Lifestyle - Behaviour	Lifestyle - Diet	Upload to the infrastructure (July 2021)
Periods covered:	na	na	pregnancy preschool 1r school	preschool	pregnancy preschool 1r school	
Cohort:						
ALSPAC	X	-	X	X	X	Complete
BiB	X	X	X	X	X	Complete
CHOP	X	X	-	-	X	Complete
DNBC	X	-	X	-	X	Complete
EDEN	X	X	X	X	X	Complete
ELFE	X	X	-	X	X	Complete
GECKO	X	X	-	-	-	Complete
Gen R	X	X	X	-	X	Complete
INMA	X	X	X	X	X	Complete
MOBA	X	-	X	X	X	Complete
NFBC66	-	-	-	-	-	Complete
NFBC86	X	-	-	-	-	Complete
NINFEA	X	X	X	-	X	Complete
RAINE	-	X	-	-	-	Complete
RHEA	X	X	X	X	X	Complete
SWS	X	-	-	X	X	Complete
Non-partner cohorts (EU Child Cohort Netowrk):						
ABCD			X			Complete
GASPII			X			Complete
KANC			X			Complete
Piccolipiù	X	X	X	X	X	Complete

2 Urban stressors and health-related behaviour patterns in 6 European cohorts

Sílvia Fernández-Barrés, Serena Fossati, Sandra Márquez, José Urquiza, and Martine Vrijheid (ISGlobal), and members of the LifeCycle cohorts.

Aim

As part of task 3.2 in LifeCycle we evaluated the association of the urban environment stressors with health-related behaviours in childhood. For this analyses, we used existing data from 6 European cohorts, 5 of which are also partner cohorts in LifeCycle (BiB, EDEN, INMA, MoBa, RHEA). The database was created as part of a previous European FP7 project (HELIX). The early life stressor variables available in this dataset are very similar to the ones that were being generated for all the LifeCycle cohorts, which made this an important first database to start evaluating the interrelationships between early-life stressors, before the total LifeCycle database was available. A publication of the results is in preparation and is expected to be submitted in September 2021.

Introduction

Unhealthy behaviours are one of the main causes of non-communicable diseases, including cardiovascular diseases and obesity, especially insufficient physical activity, sedentary time and inadequate sleep. The current Word Health Organization (WHO) recommendation is to achieve at least 60 minutes a day of moderate-to-vigorous physical activity, but less than 45% of children, and 20% of the adolescents worldwide meet this recommendation, indicating a physical activity decrease with age. Children and adolescents are becoming more sedentary and it is estimated that 22% to 60% European children spend more than 2 hours per day of screen time (a proxy of sedentary time) at week days, and 52% to 91% at weekends depending of the country.

Several interventions targeting these behaviours at individual level have been conducted but with limited success. As indicated by ecological models, lifestyle is influenced by individual factors but also by environmental factors. Thus, there is an increasing interest in studying the role of the urban environment in the increase of unhealthy behaviours among children and adolescents, and in evaluating whether a change in the urban design may be beneficial for promoting a healthier lifestyle

Given the potential for the urban environment to influence health-related behaviours, and the lack of studies in children and of studies assessing multiple urban environment exposures, our aim was to evaluate the association between several objectively measured urban environment indicators from different domains (built environment, traffic and natural spaces), and several health behaviours (physical activity, active transport, sedentary behaviours and sleep duration) and their patterns, in childhood from six European cohorts.

Methods

We estimated exposure to the urban environment, including measures of built environment, natural spaces and road traffic for 1,581 children age 6-11 years from six European Birth Cohorts, using data collected as part of the Human Early Life Exposome (HELIX) project. We collected questionnaire information on moderate-to-vigorous physical activity, physical activity outside school hours, active transport, sedentary behaviours and sleep duration and used principal component analysis to create patterns of behaviours.

Urban environment exposures were estimated for home and school adresses during childhood, including: **Population density** (number of inhabitants/km^2); **Building density** (m^2 built/km^2) within a buffer of 300m; **Connectivity density** (number of intersections / km^2) within a buffer of 300m; **Access to public transport** in terms of lines (meters of bus public transport mode lines inside each 300m buffer); **Access to public transport** in terms of stops (number of bus public transport mode stops inside each 300m buffer); **Facility density** (number of facilities present divided by the area of the 300m buffer); **Facility richness** (number of different facility types present divided by the maximum potential number of facility types (at a 300m buffer); **Mixed land use** (Land use Shannon's Evenness Index); **Walkability index** (as mean of deciles of facility richness index, land use Shannon's Evenness Index, population density, connectivity density); **Total traffic load** of major roads in 100m buffer; **Total traffic load** of all roads in 100m buffer; **Traffic density** on nearest road; **Inverse distance** to nearest road; **Average of Normalized Difference Vegetation Index** (NDVI) values within a buffer of 100m; **Green and blues space** within 300m; **Green distance**: Straight line distance to nearest green space > 5,000m^2.

We analysed associations between the urban environment exposures and health behaviours (individual and patterns) through an exposome-wide association study (ExWAS) approach for single exposures, and we built final multi-exposure models using the Deletion-Substitution-Addition (DSA) algorithm.

Results

Physical activity

Seven environmental exposures were nominally associated with moderate-to-vigorous physical activity in the ExWAS analysis (p<0.05), and the association between higher NDVI at 100-m buffer at home passed the multiple testing corrected p-value threshold of 0.003 (β 8.72 (95%CI 3.22, 14.21). This association was attenuated in the final multi-exposure model (β 7.00 (95%CI -0.38, 14.38) (Table 1). In this multi-exposure model, building density within a 300m from home (β 6.39 (95%CI 1.80, 10.98) and presence of green spaces close to the school (β -5.06 (95%CI -10.11, 0.00) were associated with moderate-to-vigorous physical activity.

For physical activity outside the school hours, seven urban exposures showed nominal associations in the ExWAS, but none passed correction for multiple testing (p value 0.003). In the multi-exposure model, population density near the home address was associated with a decrease in the time performing physical activity outside the school hours (β -3.80 (95%CI -6.97, -0.64) and building density with an increase (β 6.59 (95%CI 2.33, 10.86); Table 1).

Active transport

In the ExWAS analysis, nine exposures were associated with active transport from home to school, and three of the exposures passed the multiple correction threshold: greater facility richness and density were associated with increased active transport, and land use with a decrease of active transport. In the multi-exposure model, distance to the nearest green space, greater land use diversity within home area, and street connectivity around the school were associated with decreased active transport (Table 1). Facility density around the home was associated with increased active transport.

Sleep duration

The only variable that was associated with sleep duration was home proximity to a major road, which was associated with a decrease of 0.08 (95%CI -0.15,-0.01) hours of sleep per day, both in the ExWAS and in multi-exposure models (Table 1).

Table 1. Analysis of the association between home and school exposures, and single lifestyle behaviours in childhood (N=1,581). Only results associated with at least with one exposure with a p-value in the DSA model below 5% are shown.

	Moderate-to-vigorous physical activity (min/day)	Physical activity outside the school hours (min/day)	Active transport (min/day)	Sleep duration (hours/day)	Sedentary time (min/day)
Exposure (IQR or category)[a]	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)
Home					
NDVI-100m (0.31)	7.00 (-0.38, 14.38)	5.70 (-1.43, 12.83)	ns	ns	**-22.71 (-39.90, -5.51)**
Green distance (213.25 m)	ns	ns	**-0.94 (-1.67, -0.22)**	ns	ns
Major roads-100m (*vs.* no major road)	ns	ns	0.69 (-0.26, 1.64)	**-0.08 (-0.15, -0.01)**	ns
Population density (7,550.89 people/km^2)	-1.37 (-4.40, 1.65)	**-3.80 (-6.97, -0.64)**	ns	ns	5.53 (-1.60, 12.67)
Building density-300m (174,887.9 m^2 built/km^2)	**6.39 (1.80, 10.98)**	**6.59 (2.33, 10.86)**	ns	ns	**-10.55 (-20.27, -0.82)**
Facility density 300m (38.90 facilities/km^2)	ns	ns	**1.25 (0.41, 2.09)**	ns	5.96 (-4.78, 16.70)
Land use (0.19)	2.44 (-0.83, 5.70)	ns	**-1.35 (-2.05, -0.65)**	ns	ns

	Moderate-to-vigorous physical activity (min/day)	Physical activity outside the school hours (min/day)	Active transport (min/day)	Sleep duration (hours/day)	Sedentary time (min/day)
Exposure (IQR or category)[a]	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)
School					
Green spaces Yes (*vs.* No)	-5.06 (-10.11, 0.00)	ns	ns	-	-
Connectivity (117.47 number of intersections/km^2)	-3.01 (-6.80, 0.78)	-2.94 (-6.23, 0.35)	**-1.16 (-1.94, -0.37)**	-	-

[a] Reference category as indicated inside brackets for the categorical variables. For continuous variables, estimates are calculated per IQR increase in exposure, as indicated inside brackets; IQRs calculated on the first imputed dataset after back transforming the variables. Models adjusted for cohort, child age, child sex, maternal education, family affluence score and area level SES. Beta estimates for all exposure variables selected in 10% or more of

Sedentary behaviours

Some urban indicators were related to sedentary behaviours. Higher vegetation (NDVI within a 100 m from home) was associated with a decrease of -20.40 (95%CI -32.98, -7.82) overall sedentary time in the ExWAS analysis. This decrease was observed also in the sedentary sub-activities (television viewing and time playing computer games (data not shown)). In multi-exposure models, higher vegetation was associated with overall sedentary time (Table 1). Population density was associated with greater time spent in sedentary activities in the ExWAS, but this association was attenuated in the multiple exposure model. Building density was associated with a decrease of sedentary time in the multi-exposure models (β -10.55 (95%CI -20.27, -0.82).

Behavioural patterns

To study the behaviours in combination, we performed PCA and the loadings are shown in Figure 1. PC1 (explaining 26.2% of variance) described higher moderate-to-vigorous physical activity and physical activity outside the school hours. PC2 (explaining 19.7 % of variance) described more screen time and less sleep, and PC3 (Explaining 15.3 % of variance) described more time of active transport. Results for the behavioural patterns generally reflected those for the individual behaviours (Figure 1).

Discussion and conclusions

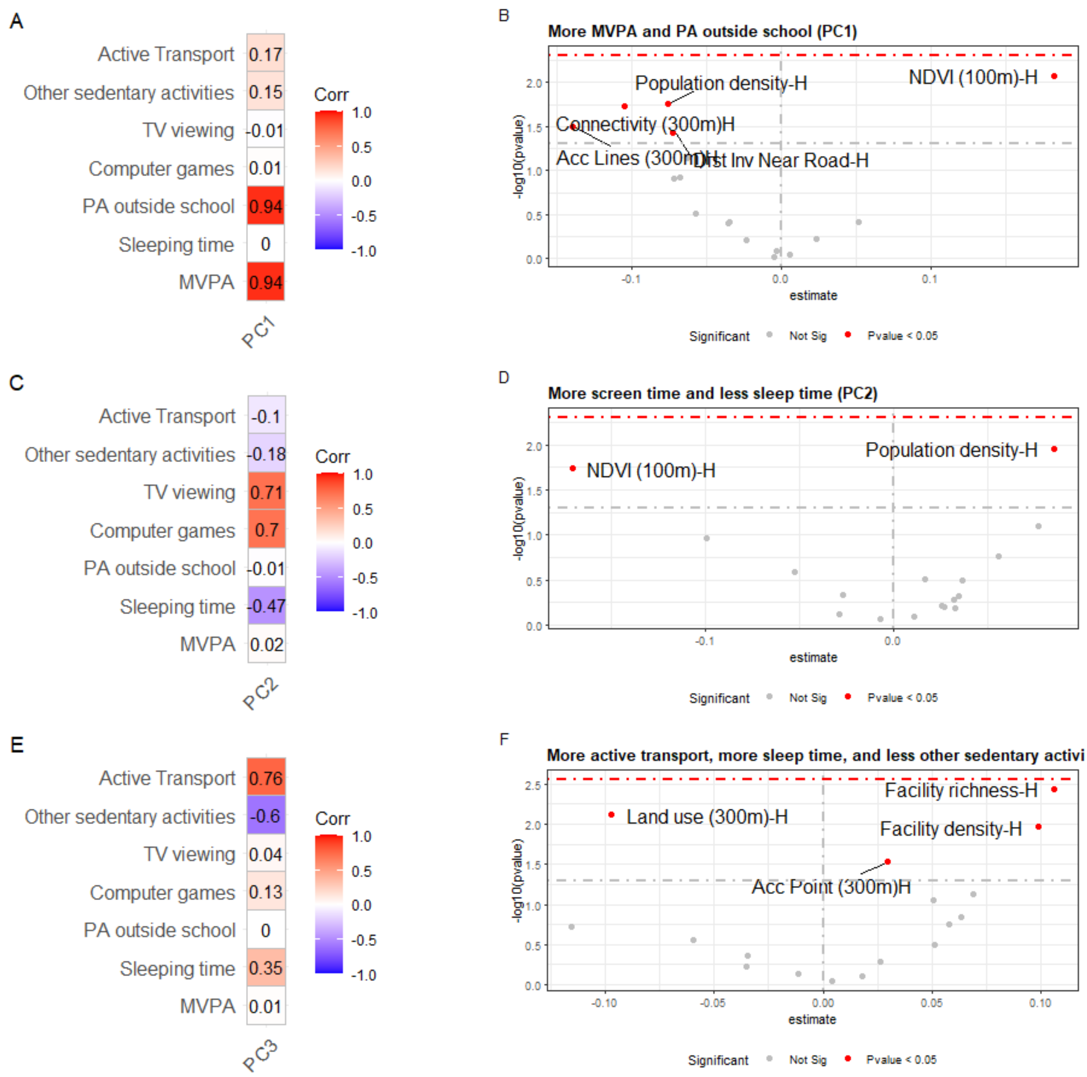
This multicohort study identified several urban environment characteristics that may beneficially influence health-related behaviours in children. Our findings suggest that areas of the cities with more vegetation, more building and facility density, less population density and without major roads may be more supportive for more physical activity, less sedentary behaviours, more sleep and more active transport.

A high proportion of the children included in this study (63.6%) does not meet the current WHO guidelines for moderate-to-vigorous physical activity and 58.6% spend more than two hours per day watching TV or playing computer and video games. Moreover, active transport is considerably low, being the daily average time spent from home to school of 6.9 minutes. Our results reinforce the need for policymakers to reconsider the cities designs in order to improve children lifestyle behaviours. Our study found the relationship between built environment and lifestyle behaviours to be similar across the cohorts in six countries, what may indicate that investment in new urban designs may be applied across Europe to benefit children health. Our study also indicates that these designs need to be comprehensive and take into account several urban indicators. One of the strategies should be improving vegetation in the streets and green spaces, if they are more attractive and well maintained may improve the perception of safety of parents and children. One of the most common strategies is to promote public transportation use, even though we do not observe an association of transport accessibility with lifestyle in childhood, this initiative may be positive to reduce traffic load and the subsequent air pollution and noise.

Future research is needed, including other urban indicators that may be relevant for children and adolescent lifestyles (such as: pedestrian zones and sport facilities (e.g. tennis table and volley courts)), the combination of perceived and objective measures of the urban environment (such as crime and attractiveness), the use of objectively measures of lifestyle behaviours, including countries from Eastern Europe and other areas less studied, and implement longitudinal studies and intervention studies to assess the change in the urban environment and its impact on health behaviours.

In conclusion, this comprehensive and systematic study suggests that more vegetation, more building and facility density, less population density and without major roads may be more supportive for health behaviours in childhood. These results reinforce the need of interventions on the urban design that include multiple aspects of the urban environment and are addressed to all age groups, including children.

Figure 1. Association between the urban environment exposures and behavioural patterns in childhood in single-exposure ExWAS model. (A,C,E): Heatmap showing outcome loadings of first three components. (B,D,F): Volcano plots showing significance (*p*-value) against beta coefficient. Black dashed horizontal line at *p*-values of 0.05; red solid horizontal line at TEF of 0.005.



3 Socioeconomic position (SEP) influence on the early-life individual exposome in LifeCycle cohorts

Costanza Pizzi, Lorenzo Richiardi, Chiara Moccia, Giovenale Moirano, Antonio D'Errico, Milena Maule (UNITO), Serena Fossati and Martine Vrijheid (ISGlobal), and members of the LifeCycle cohorts.

Aim

As part of task 3.2 in LifeCycle we evaluated the association of child SEP at birth with the personal exposome during infancy, accounting for geographical variability among cities and countries. For this analysis, we use existing data from 8 European partner cohorts in LifeCycle (ALSPAC, BiB, DNBC, EDEN, GENR, INMA, MoBa, NINFEA). The SEP is measured using the EHII (Equivalized Household Income Indicator) developed within LifeCycle task 3.1.1. The exposures considered for this analysis include the urban environment exposures created within LifeCycle task 3.1.3, the lifestyle exposures created within LifeCycle task 3.1.4, breastfeeding, passive smoking and exposure to pets. A pilot study has been conducted on the Turin centre of the Italian NINFEA study. We are currently carrying out the analyses on the other cohorts. A publication of the results is expected to be submitted in mid 2022.

Introduction

Early exposure to unhealthy lifestyles and environmental risk factors is known to affect health throughout the life-course. There is also evidence that the exposure patterns are influenced by SEP.

Methods

All analyses are city/cohort-specific and will be conducted using the DataShield platform. Exposures variables with a skewed distribution are transformed to achieve normality or dichotomized using the median as cut-off when no transformation will work. In order to enhance comparability across the different cities/countries, continuous exposures are also standardized within each cohort, subtracting the cohort-specific mean and dividing by the cohort-specific standard deviation.

Within each exposome domain, variables with a correlation greater than 0.9 with another variable measuring the same /similar exposure are excluded from the analysis. Similarly, for the spatial variables measured at increasing range of distances, only one variable is considered. For exposures assessed repeatedly over time, one measure for each period analysed is used.

The EHII is available as a continuous variable (log-euro); in each cohort the categorical variable (low/medium/high income) will be constructed using as cut-offs either the tertiles or the first and third quartiles of the log equivalized total disposable household income distribution of the country-specific 2011 EUSILC (European Union statistics on Income and Living Conditions) database used to derive the indicator. When analysing the association between the EHI and the exposome a two-levels variable dichotomised as low/medium SEP vs high SEP is used, as well as the continuous variable, checking the linearity assumption.

Statistical analyses are performed according to the following steps:

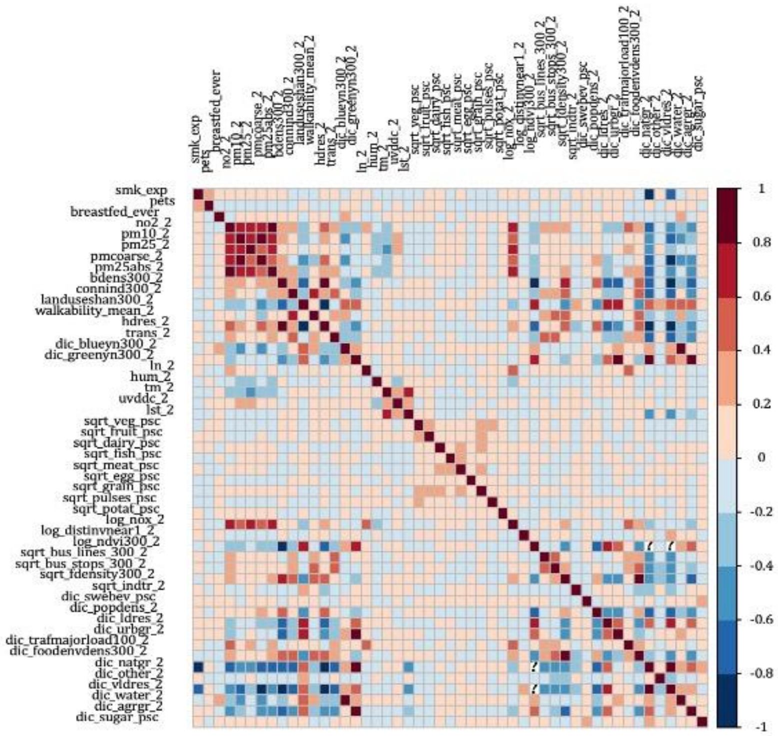
- Exploratory analysis on the exposome by computing the correlation between all pairs of exposures and comparison of the derived correlation matrices across the different cohorts/cities. In particular, within each cohort, Pearson correlations between all pairs of continuous exposures, tetrachoric correlations between pairs of binary variables and polyserial correlations between pairs of continuous and binary exposures are used. For the continuous variables, correlations are calculated using both the non-standardized and the standardized variables. Cohort-specific correlation matrices are displayed and compared using heat maps.

-Standard regression models to evaluate the cohort-specific effect of the SEP driver on each exposure included in the exposome accounting for multiple comparisons and potential confounders (Drivers-Exposome Wide Association Study - DExWAS, that is with the exposome variables as the dependent variables). Linear regression models are used for continuous variables and logistic regression models for binary exposures variables. Three sets of exposome data will be analysed: i) normally distributed continuous variables (transformed to achieve normality if necessary) plus dichotomized variables for the variables for which normality cannot be achieved; ii) standardized continuous variables plus dichotomized variables for the variables for which normality cannot be achieved, iii) all variables dichotomized. Cohort/cities-specific analysis to take into account the fact that the role of SEP likely varies among cities and countries are conducted with maternal age, parity and ethnicity (e.g. maternal country of birth) treated as potential confounders. Exposome-wide associations with the EHII by city/countries are presented both as beta coefficients (with 95% confidence intervals) and as volcano plots. The latter shows the strength of association (p-value) on they-axis and the effect size on the x-axis.

Results

Results from the pilot study conducted on the Turin participants of the Italian NINFEA birth cohort (n~2500) are included in this report. The heat map in Figure 1 shows the correlation matrix calculated on these data, with dark red squares indicating highly positively correlated variables (e.g. the air pollution exposures on the top left corner) and dark blue squares indicating pair of variables that are highly negatively correlated (e.g. percentage of forest land use and passive smoking in the bottom left corner).

Figure 1. Correlation matrix of the 0-2 years individual exposome variables – the Turin-NINFEA data.



Figures 2 and 3 show the results of the DExWAS analyses for the continuous and binary exposure variables respectively, derived from the model adjusted for the potential confounders. The low/medium EHII vs high EHII (baseline) effect estimates are reported. The graphs show that low EHII is associated with lower consumption of fruit and vegetables, lower levels of NO2, building and facilities densities, traffic, walkability and connectivity index, higher land-use diversity index, and higher exposure to pets.

Figure 2. Volcano plot showing the results of the DExWAS analysis for the continuous exposome variables. Low/medium EHII vs high EHII effects are standardized and derived from linear regression model adjusted for potential confounders.

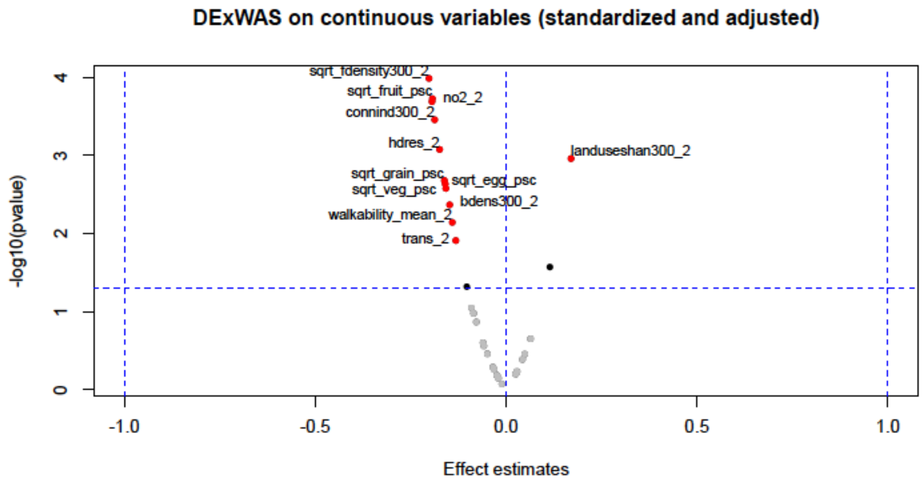
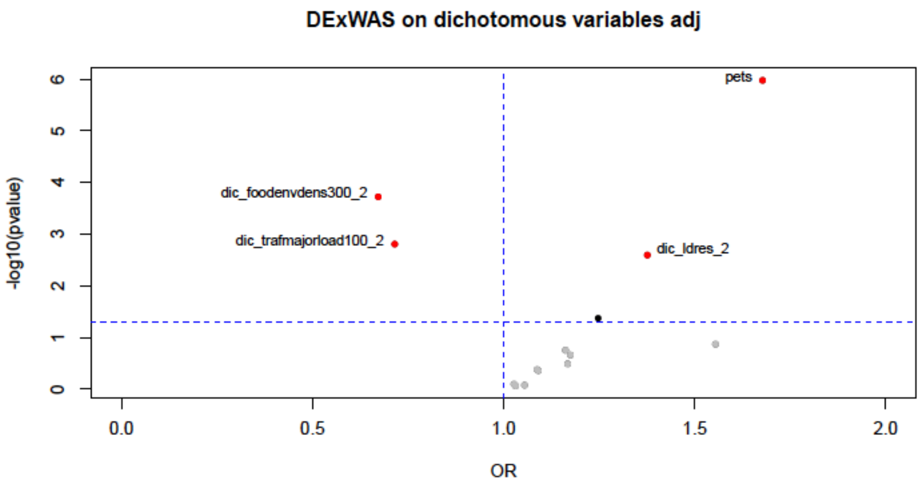


Figure 3. Volcano plot showing the results of the DExWAS analysis for the binary exposome variables. Low/medium EHII vs high EHII effects are derived from logistic regression models adjusted for potential confounders.



Conclusions

In the Italian city of Turin children from low SEP families are exposed to higher levels of environmental risk factors and unhealthy lifestyles during infancy.

Next steps

These SEP-early life exposome analyses will be replicated in the LifeCycle ALSPAC, BiB, DNBC, EDEN, GENR, INMA and MoBa birth cohorts in the next months.

If available on DataShield analyses based on principal component analysis (PCA) methods, used to reduce the exposome dimension, will be conducted. In particular, as the exposome data include both continuous and categorical variables instead of a standard PCA analysis, factor analysis of mixed data (FAMD) will be considered.

4 Lifestyle patterns in preschool children in LifeCycle cohorts.

Sandrine Lioret, Lucinda Calas, Patricia Dargent, Marie Aline Charles (INSERM), and members of the LifeCycle cohorts.

Background and objectives

Children's energy balance-related behaviours, *i.e.* diet, screen sedentary behaviour, physical activity and sleep, combine into the so-called "lifestyle patterns" and may have a synergic effect on health. However, the link of such lifestyle patterns with obesity related outcomes is not always consistent across studies, and has been sparsely investigated in preschool children.

The first objective is this proposal was to identify and compare such lifestyle patterns across nine cohorts involved in the LIFECYCLE project (i.e. Eden, Elfe, Bib, SWS, INMA, ALSPAC, MoBa, RHEA, Piccolipiù). Then we aimed at investigating the associations between demographic and socioeconomic factors and such lifestyle patterns; and to assess the cross-sectional relations of the latter with child BMI, accounting for demographic and socioeconomic factors.

Methods

Lifestyle pattern derivation.

We ran a principal component analysis (PCA) including the following harmonised energy balance-related behaviours: vegetables, fruits, fish, savouries, processed meat, sweets and sweet beverages intake (servings per day); TV time (hours per day); other screen time (usual hours per day); time spent playing outside (seasonal z-scores); and time spent sleeping per day (hours per day). The resulting harmonised variables are PCA scores for each lifestyle pattern. These were calculated at the individual level by summing the observed standardized values for each harmonised variable weighted according to the PCA loadings.

Two components were retained in each cohort, based on eigenvalues >1.1, the scree plot and their interpretability:

- Pattern A: only one pattern was consistent across all cohorts: it was characterised by intake of non-core foods and beverages (savouries, sweets, sweet beverages and processed meat) and high screen time; it was also generally characterized by low intake of core foods (vegetables, fruits and fish). This lifestyle pattern was labelled "**Sweet drinks, discretionary foods and TV"**.
- Pattern B: the other PCA component, commonly characterised by relatively high consumption of fruit and vegetable, was however less consistent across cohorts regarding the other energy balance-related behaviours.

Associations of lifestyle pattern A with demographic and socioeconomic factors; and BMI.

1st analysis: In each cohort, we are currently analysing the associations between demographic (maternal age at the childbirth and parity), socio-economic factors (maternal education level and the EUSILC income indicator from subtask 3.1.1, in quintiles), chid sex and lifestyle pattern A scores (outcome), using multivariable regression analysis. The current intermediate results are presented in Table 1.

2nd analysis: We will next analyse cross-sectional associations between lifestyle pattern A (main exposure) and BMI zscores (ouctome), accounting for the above-mentioned demographic and socio-economic factors, and using multivariable regression analysis.

Intermediate results (work in progress) and conclusions

We have so far found consistent results across the analysed cohorts (Table 1), which confirm findings described in the literature, such as maternal education level and age being negatively associated with the adherence to the "Sweet drinks, discretionary foods and TV" lifestyle pattern. This is also coherent with the negative association observed with the EULSIC indicator, although there is more variability between cohorts with this indicator. The higher scores observed in boys, as compared to girls, are also consistent with other studies.

Overall, the various associations are consistent across these six European cohorts, which adds robustness to these findings; we are hoping to see the same consistency in the three cohorts left to analyse.

Next steps

We are still in the DAA process for the three cohorts left and should be getting access in the upcoming months. We will shortly start the second analysis. All these analyses are planned to be finished by November 2021.

5 Conclusions and further work

The wide range of data on early-life stressors available in the EU Child Cohort Network provides a unique opportunity to describe how early-life stressors co-exist across Europe and which key predictors determine an individual's stressor experience. The work in Task 3.2, WP3, of LifeCycle focused on using the stressor data newly generated in the project to uncover the underlying dependencies and inequalities and to define stressor patterns.

This information will inform policymakers and potential interventions. For example, the work presented in this report shows that characteristics of the urban environment (more vegetation, more building and facility density, less population density and less major roads) may lead to more beneficial health behaviours during childhood. These results reinforce the need for urban design interventions that include multiple aspects of the urban environment and are addressed to all age groups, including children. Moreover, the ongoing work in the LifeCycle cohorts presented in this report will provide systematic information regarding socio-economic and geographic inequalities in the early-life stressors, including environmental risk factors and unhealthy lifestyles during infancy. Final conclusions from this work are expected by the end of the project.

Importantly, the data contained within the infrastructure provide the opportunity to answer many policy-related questions on early-life stressors in the future, now that harmonized variables are available. This report provides an example of how these variables can be used to unravel such questions.