

Why key determinants of childhood obesity?

The development of childhood obesity involves a complex interplay of genetic susceptibility, environmental, and lifestyle factors (key determinants). The effects of current obesity prevention programmes (mainly school based) have been limited, with best results achieved in younger children. Scientific research must further the evidence base on the determinants of childhood obesity. This factsheet summarises key STOP research related to the **exposome approach** for the identification of risk factors for childhood obesity (see keywords).



Keywords

- **Adiposity:** referring to body fat
- **Cholesterol:** is a fat-like, waxy substance that helps your body make cell membranes, many hormones, and vitamin D. Too much low density lipoprotein (LDL) cholesterol in the bloodstream is linked to cardiovascular disease
- **Exposome:** refers to the totality of exposures from a variety of external and internal sources including chemical agents, biological agents, or radiation, from conception onward, over a complete lifetime. It encompasses also "psychosocial components" including the impact of social relations and socio-economic position on health (Vineis et al. What is new in the exposome? 2020 Environ Int (143))
- **Epigenetics:** the study of how your behaviours and environment can cause changes that affect the way your genes work
- **Insulin:** is a hormone created by the pancreas that controls the amount of glucose in your bloodstream at any given moment. It also helps store glucose in your liver, fat, and muscles. It also regulates the body's metabolism of carbohydrates, fats, and proteins
- **Metabolomics:** is the systematic study of small-molecule metabolites in a biological system
- **The gut microbiome:** is located in the digestive system and is made up of trillions of bacteria, fungi and other microorganisms
- **Metabolites:** a substance made or used when the body breaks down food, drugs or chemicals, or its own tissue (for example, fat or muscle tissue).
- **Urinary metabolomic profiles:** urine specimens have high concentrations of food-derived metabolites and can provide an objective measure of dietary intake

STOP project findings: Mini-summary

STOP published over 20 papers related to childhood determinants. A selection of STOP publications are referenced (1-10). Additional publications in this area can be accessed from the [special supplement in the scientific journal Obesity Reviews](#) and from www.stopchildobesity.eu.

External Exposome

- **Built environment and childhood obesity:** Findings indicate effect of some characteristics of the built environment on childhood obesity, mainly related to traffic-related air pollution and characteristics supporting walking. (1) An additional study found that a higher density of vegetation, more building density, less population density, and no major roads, are associated with improved health behaviours in childhood. (2)

Internal Exposome

- **Overall, findings from literature reviews on metabolomics** (3) and **epigenetics** (4) were not robust enough to make a consistent contribution to inform childhood obesity policy.
- **Cord blood metabolic signatures predictive of childhood overweight and obesity:** There was a relationship identified between higher levels of cholestenone (a cholesterol derivative) and rapid growth. Lower level of the branched chain amino acid (BCAA) valine were predictive of overweight in childhood. Cholestenone and (BCAAs) suggest a role of the gut microbiome in child growth trajectories. (5)
- **Multiomic analysis (based on multiple measurements of changes in different compartments of molecules) and birthweight:** Data suggested that cholesterol and related metabolic pathways are related to birthweight. The identified biological signals may create a molecular basis for the onset of health outcomes associated with birthweight variation. (6)
- **Direct and indirect effects of prenatal exposures:** Information on seven prenatal exposures (maternal education, pre-pregnancy BMI, weight gain and tobacco smoke during pregnancy, age at delivery, parity, and child gestational age) was collected and cord blood levels of 31 metabolites, associated with rapid postnatal growth and/or childhood overweight in a previous study, were measured. Although findings showed evidence of the effect of in utero metabolism in the predisposition to rapid postnatal growth and rapid postnatal growth linked to predisposition to childhood overweight, evidence on the role of epigenetics was still limited. (7)



Ultra-processed food (UPF)

According to the **NOVA food classification** - UPF's are 'formulations of ingredients, mostly of exclusive industrial use, typically created by series of industrial techniques and processes'.

They typically contain high levels of fats, refined sugars and salt.

Examples of common UPF's include carbonated soft drinks, mass produced bread and buns and processed foods.

It should be acknowledged that the NOVA classification system is imperfect, but does provide a guide to classifying food types.

Monteiro, C.A., Cannon, G., Lawrence, M., Costa Louzada, M.L. and Pereira Machado, P. 2019. Ultra-processed foods, diet quality, and health using the NOVA classification system. Rome, FAO.



Implications of findings for policy design

- **Creating opportunities** for physical activity, including urban planning (safe areas reserved for children, green spaces, biking lanes) are better for children's health and better for planetary health. Development of green areas have an impact on climate change policies (less cars, more carbon dioxide absorption by plants, less use of energy).
- **UPF has been implicated as connected with childhood obesity.** UPF may also be associated with increased land use and GHG emissions compared to less processed foods. Mutually enforcing policies that disincentive UPF within the food system and the food environment, with particular emphasis on the school food environment are needed.

STOP project findings: Mini-summary (cont.)

In recent decades children have shifted to consuming ultra-processed foods (UPF). The following research investigates the effects of this consumption.

Diet in children and molecular pathways

- **Diet quality and insulin secretion in children in the Helix consortium (six population based cohorts in France, Greece, Lithuania, Norway, Spain, and the UK):** Urinary metabolomic profiles can reflect diet quality in childhood. Findings identified a common panel of 4 urinary metabolites that was predictive of the Mediterranean diet adherence and UPF consumption. Greater adherence to the Mediterranean diet was associated with lower C-peptide levels. C-peptide concentrations are associated with diabetes risk. (8)
- **The ALSPAC cohort:** Women living in Avon, in United Kingdom, with an expected delivery date between 1 April 1991 and 31 December 1992 were recruited. Subsequently, participants were followed up with questionnaires and clinical measurements at regular time intervals, providing lifestyle, behavioural and biological data. Findings from a study utilising the ALSPAC cohort to investigate associations between UPF consumption and adiposity trajectories from childhood to early adulthood, provide important and novel evidence that higher UPF consumption is associated with greater increases in adiposity from childhood to early adulthood. (9)
- Another study with the **ALSPAC cohort** tested the association between UPF consumption (using food diaries) and metabolic profiles for children. It was found that at the age of 7, UPF was associated with metabolic traits linked to child obesity risk. Greater UPF intake relative to total energy consumed was related to lower levels of BCAA's (associated with underlying control of food intake and obesity risk). (10)

Socio-economic position

- **Metabolic profiles of socio-economic position (SEP):** Metabolic profiles associated with SEP among almost 30 000 adults participating in 10 prospective cohorts, in both Finland and the UK, were investigated. Findings showed that social and economic factors have a significant impact on human physiology. The metabolites found to be associated with SEP are known to predict cardiovascular disease and cognitive decline in later life. (11)



Childhood obesity needs to be tackled at a global level with individual, population and planetary facets influencing policy interventions

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Future research priorities

The findings from the STOP project have provided new evidence and insights regarding the key determinants of childhood obesity.

Examples of future research opportunities include:

- metabolomics and epigenetics
- the role of UPF in childhood obesity risk



STOP Publications (see www.stopchildobesity.eu for an up-to-date list)

The following papers are referenced within this factsheet. Additional publications in this area can be accessed from the Special supplement in the scientific journal *Obesity Reviews* and from www.stopchildobesity.eu.

- (1) Malacarne D, Handakas E, Robinson O, et al. The built environment as determinant of childhood obesity: A systematic literature review. *Obes Rev.* 2021. <https://doi.org/10.1111/obr.13385>.
- (2) Fernández-Barrés S, Robinson O, Fossati S, et al. Urban environment and health behaviours in children from six European countries. *Enviro Int.* 2022 (165) <https://doi.org/10.1016/j.envint.2022.107319>.
- (3) Handakas E, Lau C H, Alfano R, et al. A systematic review of metabolomic studies of childhood obesity: State of the evidence for metabolic determinants and consequences. *Obes Rev.* 21. <https://doi.org/10.1111/obr.13384>.
- (4) Alfano R, Robinson O, Handakas E, et al. Perspectives and challenges of epigenetic determinants of childhood obesity: A systematic review. *Obes Rev.* 2021. <https://doi.org/10.1111/obr.13389>.
- (5) Handakas E, Keski-Rahkonen P, Chatzi L, et al. Cord blood metabolic signatures predictive of childhood overweight and rapid growth. *Int J Obes* 2021. 45, pages2252–2260. <https://www.nature.com/articles/s41366-021-00888-1>.
- (6) Alfano R, Chadeau-Hyam M, Ghantous A, et al. A multi-omic analysis of birthweight in new-born cord blood reveals new underlying mechanisms related to cholesterol metabolism. 2020. *Metabolism.* (10) <https://doi.org/10.1016/j.metabol.2020.154292>.
- (7) Alfano R, Plushquin M, Robinson O, et al. Cord blood metabolites and rapid postnatal growth as multiple mediators in the prenatal propensity to childhood overweight 2022. 46, pages1384–1393 <https://www.nature.com/articles/s41366-022-01108-0>.
- (8) Stratakis N, Siskos P A, Papadopoulou E. Urinary metabolic biomarkers of diet quality in European children are associated with metabolic health. *eLife.* 2022. <https://doi.org/10.7554/eLife.71332>.
- (9) Chang K, Khandpur N, Neri D, Touvier M, Huybredts I, Millet C, Vamos E. Ultra-processed food consumption and adiposity trajectories from 2 childhood: a prospective analysis of the ALSPAC birth cohort. *Obes Review* 2021; 23 (1) [doi:10.1001/jamapediatrics.2021.1573](https://doi.org/10.1001/jamapediatrics.2021.1573).
- (10) Handakas E, Chang K, Khadphur N. Metabolic profiles of ultra-processed food consumption in British children and their role in childhood obesity risk. 2022. *Clinical Nutrition.* <https://doi.org/10.1016/j.clnu.2022.09.002>.
- (11) Robinson O, Carter AR, Ala-Korpela M, et al. Metabolic profiles of child socio-economic position- a multi-cohort analysis. *International journal of Epidemiology.* 2021. 50 (3) <https://doi.org/10.1093/ije/dyaa188>.



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For more information, visit www.stopchildobesity.eu.

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