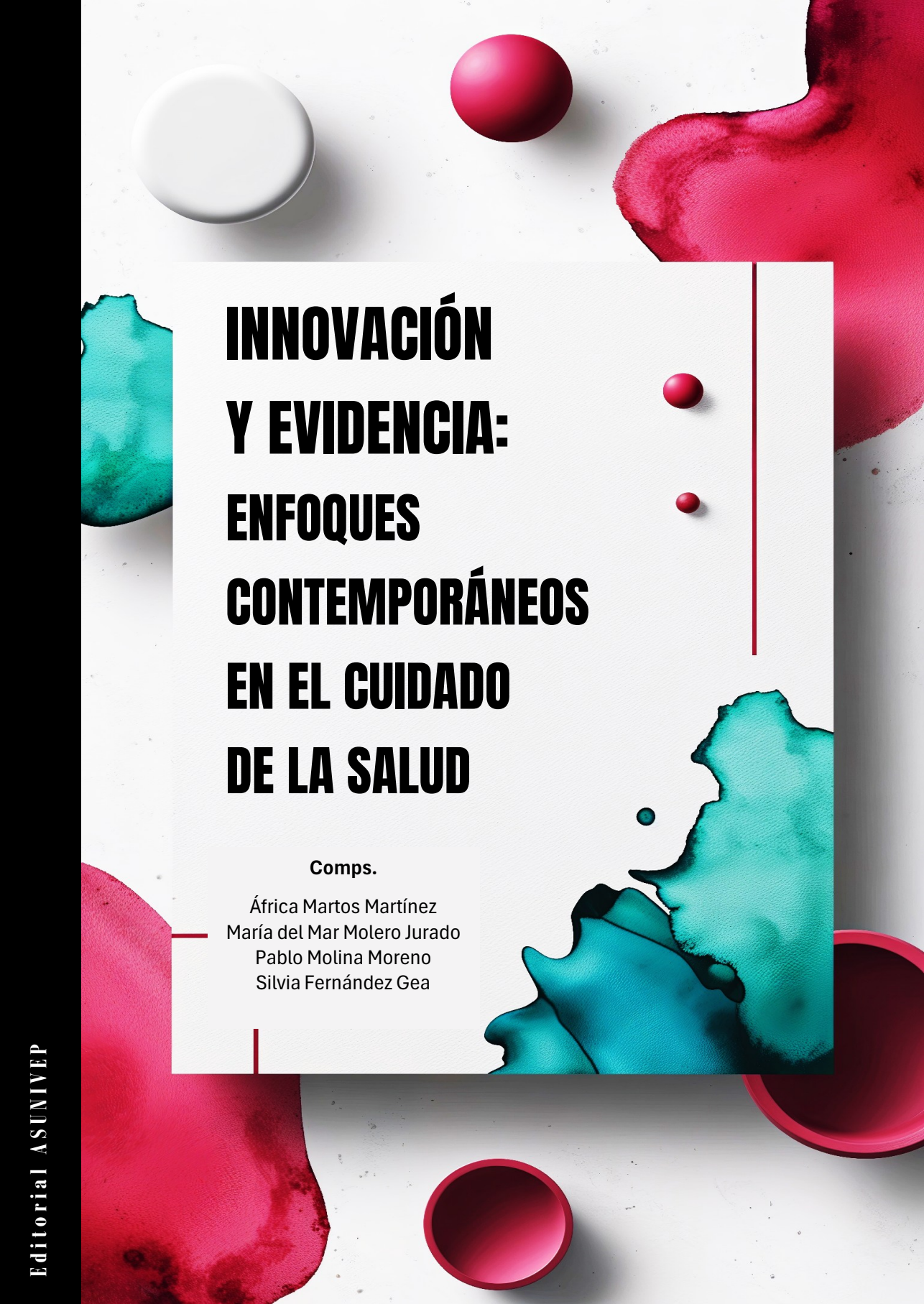




# **INNOVACIÓN Y EVIDENCIA: ENFOQUES CONTEMPORÁNEOS EN EL CUIDADO DE LA SALUD**

**Comps.**

África Martos Martínez  
María del Mar Molero Jurado  
Pablo Molina Moreno  
Silvia Fernández Gea



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## CAPÍTULO 23

### **Early Detection of Cardiometabolic Risk in Adolescents Through a Multidimensional Assessment of Adiposity, Metabolism, and Inflammation: A Prospective Project Proposal**

Carlos Manuel Pérez Pérez\* & Francisco José Vera Serrano\*\*

*\*Universidad de Cádiz; \*\*Servicio Andaluz de Salud*

#### **Introduction**

##### *Project description*

##### *Current state of knowledge*

Obesity during childhood and adolescence represents one of the major contemporary public health challenges. Its relevance extends beyond increased body weight, as excess adiposity from an early age is associated with metabolic, endocrine, and inflammatory alterations that may contribute to the subsequent development of chronic diseases (Blüher, 2019).

Furthermore, obesity during youth has been associated with a greater likelihood of persistent excess weight and the development of complications in adulthood (Dietz, 1998), reinforcing the importance of the early identification and assessment of associated cardiometabolic risk factors during childhood and adolescence (Valerio et al., 2024).

Adolescence represents a particularly relevant period for studying the early development of cardiometabolic risk. During this stage, substantial hormonal, metabolic, and body composition changes occur and may interact with the degree of adiposity and lifestyle habits. Identifying alterations during this period therefore provides an opportunity to advance prevention and early detection strategies before unfavorable cardiometabolic profiles become established.

The assessment of excess weight in pediatric populations has traditionally relied on anthropometric indicators such as body mass index (BMI), interpreted using age- and sex-specific cut-off points (Cole et al., 2000). Although BMI is a useful tool for classifying weight status, no single anthropometric indicator can fully characterize body composition and individual cardiometabolic risk. Recent evidence indicates that different measures of general and central adiposity may provide complementary information on cardiometabolic risk factors during childhood and adolescence (Joisten et al., 2024; Kim et al., 2024; Xie et al., 2024).

Central adiposity is of particular interest from a cardiometabolic perspective. Recent trends in abdominal obesity among Spanish pediatric populations and its association with risk factors reinforce the need to consider body fat distribution when assessing children and adolescents (Schröder et al., 2024). Likewise, waist circumference-based indicators may provide information complementary to BMI regarding the presence of cardiometabolic abnormalities (Kim et al., 2024; Xie et al., 2024).

This approach becomes particularly relevant when adipose tissue is considered a metabolically active endocrine organ capable of producing bioactive substances involved in energy regulation, metabolism, and inflammatory processes (Galic et al., 2010; Kershaw & Flier, 2004). The expansion and dysfunction of adipose tissue may promote a state of chronic low-grade inflammation through interactions among adipocytes, immune cells, and various inflammatory mediators, thereby contributing to the development of obesity-related metabolic alterations (Kawai et al., 2021).

Chronic low-grade inflammation associated with excess adiposity is particularly relevant during childhood and adolescence because of its potential involvement in the early development of metabolic alterations and its possible implications for future health. Although the available evidence in pediatric

populations remains more limited than in adults, the study of these mechanisms represents a growing area of interest for improving our understanding of the early onset of metabolic complications (Polak-Szczybyło, 2023).

Among the molecules associated with adipose tissue, leptin is of particular interest. This adipokine is closely related to fat mass and the regulation of energy balance. In obesity, elevated leptin concentrations may occur alongside alterations in leptin signaling and a reduced biological response to its effects, a phenomenon associated with leptin resistance (Zhang & Scarpace, 2006). In addition, adipokines are involved in metabolic and inflammatory mechanisms that are relevant to understanding the complications associated with pediatric obesity (Martos-Moreno et al., 2013). More recent evidence continues to support the relevance of leptin as a biomarker associated with adiposity and metabolic alterations during the early stages of life (Al Zein et al., 2024).

Alongside leptin, pentraxin-3 (PTX3) is a biomarker of interest because of its involvement in innate immunity and various inflammatory and cardiovascular processes (Norata et al., 2010). However, its behavior across different metabolic contexts is complex, and its interpretation is not necessarily equivalent to that of other inflammatory markers (Miyazaki et al., 2014). The available evidence on PTX3 in pediatric and adolescent populations remains comparatively limited, supporting the need for further investigation into its potential relationship with adiposity and other cardiometabolic indicators.

From a preventive perspective, it is particularly important to consider the heterogeneity that may exist among adolescents with apparently similar anthropometric characteristics. The relationships among BMI, body fat, and cardiometabolic risk factors are not necessarily equivalent across individuals, and different anthropometric indicators may differ in their ability to identify specific metabolic abnormalities (Joisten et al., 2024; Kim et al., 2024; Xie et al., 2024). Therefore, the aim of the present project is not to replace BMI with a single alternative measure, but rather to integrate the complementary information provided by different dimensions of adiposity.

In this regard, the estimation of adiposity using skinfold measurements represents a feasible approach in pediatric research when standardized procedures and equations specifically developed for children and adolescents are used (Slaughter et al., 1988). Combining these measurements with BMI, indicators of central adiposity, biochemical parameters, and biomarkers may provide a broader approach to the assessment of cardiometabolic risk.

#### *Detailed project description of the project*

In this context, the present project proposes the joint assessment of anthropometric and body composition indicators, parameters of glucose and lipid metabolism, dietary habits, and biomarkers related to metabolic regulation and inflammation in an adolescent population. Particular attention will be given to leptin and PTX3 and their relationships with different dimensions of adiposity and the metabolic profiles identified.

The main contribution of the project therefore lies in moving beyond an approach based on indicators considered in isolation toward a multidimensional characterization of early cardiometabolic risk. The integration of anthropometric, metabolic, and inflammatory variables may contribute to a better characterization of the heterogeneity observed during adolescence and generate useful knowledge for future early detection strategies.

#### *Project objectives*

The overall objective of the project is to comprehensively analyze the relationship between body adiposity, metabolic profile, and selected biomarkers related to metabolic regulation and inflammation, with the aim of characterizing profiles potentially associated with early cardiometabolic risk in adolescents.

The specific objectives are:

1. To analyze the association between anthropometric and body composition indicators and the assessed parameters of glucose and lipid metabolism.
2. To examine the relationship between leptin concentrations and indicators of general and central adiposity.
3. To analyze the association between PTX3 concentrations and the anthropometric and metabolic characteristics of the participants.
4. To compare the metabolic and inflammatory profiles of adolescents with different adiposity characteristics and weight status.
5. To explore the relationship between dietary habits and the anthropometric, metabolic, and inflammatory indicators assessed.
6. To explore, through the integrated analysis of the variables studied, the existence of combinations of indicators potentially associated with distinct cardiometabolic risk profiles.

#### *Rationale and feasibility*

The early identification of cardiometabolic abnormalities represents an important opportunity for prevention, particularly during a stage of life when metabolic changes associated with excess adiposity may begin to emerge. The integration of anthropometric, metabolic, and inflammatory indicators will make it possible to investigate the heterogeneity among adolescents with different adiposity characteristics and to explore whether the combined assessment of leptin and PTX3 provides information complementary to conventionally used parameters.

The scientific relevance of the project also lies in the integrated assessment of variables representing different dimensions potentially associated with cardiometabolic risk. This approach will enable the joint analysis of general and central adiposity, metabolic profile, selected biomarkers, and dietary habits, thereby providing a broader characterization of the study population and generating new hypotheses for future research.

The project is methodologically feasible because it combines standardized anthropometric procedures, structured instruments for the assessment of dietary habits, and available analytical techniques for the determination of biochemical parameters and biomarkers. Access to the adolescent population through collaborating educational institutions will facilitate recruitment and the systematic implementation of the planned assessments. Furthermore, the availability of the necessary human, technical, and laboratory resources will enable the different phases of the project to be carried out once the corresponding ethical and administrative approvals have been obtained.

### **Methodology**

#### *Description of the study design, materials, and planned activities*

An observational, analytical, and prospective study is proposed to characterize different profiles potentially associated with early cardiometabolic risk. The study population will consist of adolescents aged 12 to 18 years enrolled in the participating educational institutions. The sample size will be determined through a statistical calculation conducted before recruitment begins, taking into account the study objectives, the main variables of interest, and an estimated proportion of potential losses or incomplete records.

Participation will be voluntary and will require informed consent from parents or legal guardians and, when appropriate, assent from the adolescent. Recruitment will begin only after the necessary ethical and administrative approvals have been obtained.

Participants with previously diagnosed inflammatory, endocrine, or metabolic diseases that could substantially affect the biomarkers under investigation will be excluded, as will those receiving treatments

with a relevant influence on the variables analyzed. Recent acute infectious processes and inability to complete the required study procedures will also be considered exclusion criteria.

The planned activities will include anthropometric and body composition assessment, metabolic characterization, biomarker determination, and assessment of dietary habits.

Anthropometric measurements will be performed by previously trained personnel using standardized procedures. Weight and height will be measured to calculate BMI and classify weight status according to age- and sex-specific criteria (Cole et al., 2000).

The assessment will be complemented by waist circumference as an indicator of central adiposity and skinfold measurements to estimate body adiposity using equations developed for pediatric populations (Slaughter et al., 1988). The instruments used will be calibrated, and measurements will be performed under standardized conditions to reduce procedure-related variability.

Biochemical characterization will include parameters related to glucose and lipid metabolism, including fasting glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

Leptin and PTX3 concentrations will also be determined. Biological samples will be collected under standardized conditions by qualified healthcare professionals and subsequently processed and stored according to established procedures to ensure appropriate traceability and stability. Biomarkers will be determined using validated immunoenzymatic techniques and the corresponding quality-control procedures.

Dietary habits will be assessed using a structured instrument appropriate for the adolescent population. The frequency of consumption of different food groups will be analyzed and, when permitted by the characteristics of the instrument and the quality of the information obtained, energy intake and macronutrient distribution will be estimated.

#### *Methodological rationale and alignment with the objectives*

The proposed methodology is directly aligned with the objectives of the project. Anthropometric and body composition indicators will enable the characterization of different dimensions of adiposity; biochemical parameters will provide information on the metabolic profile; and the determination of leptin and PTX3 will allow their relationships with adiposity and the metabolic abnormalities under investigation to be explored.

The assessment of dietary habits will incorporate a behavioral dimension potentially associated with these variables. Thus, combining anthropometric, metabolic, inflammatory, and dietary information will enable cardiometabolic risk to be addressed from a multidimensional perspective and allow the exploration of distinct profiles among participants.

#### *Suitability of materials and procedures for the planned activities*

The materials and procedures will be selected according to the specific characteristics of each activity.

Calibrated equipment will be used for anthropometric measurements, and standardized procedures will be applied to minimize measurement variability.

Biological samples will be collected using appropriate medical supplies by qualified professionals. Sample processing, storage, and analysis will be performed using the necessary laboratory resources to ensure traceability, stability, and reliable analytical determination.

Dietary habits will be assessed using a structured instrument adapted to the study population, and the information obtained will be entered into a coded database for subsequent analysis.

#### *Available resources and their suitability for the project*

The development of the project will require coordination among the research team, healthcare professionals, and collaborating educational institutions.

The participating institutions will facilitate access to the study population and provide appropriate facilities for assessments that can be conducted within the school setting.

Technical resources will include calibrated anthropometric equipment, materials for biological sample collection and processing, and laboratory resources for the planned analyses.

Information and communication technology (ICT) tools will also be used for data management, database creation and maintenance, and statistical analysis. Data will be recorded using identification codes and managed through procedures designed to preserve confidentiality and data quality.

The combined availability of human, technical, institutional, and laboratory resources will enable the different phases of the project to be carried out once the corresponding approvals have been obtained.

#### *Indicators and evaluation methods*

The main anthropometric indicators will include BMI, waist circumference, and estimates of body adiposity. Metabolic indicators will include fasting glucose and lipid profile components, while leptin and PTX3 will constitute the specific biomarkers assessed in the project.

Variables related to dietary habits and potential confounding factors, particularly age and sex, will also be included.

The statistical analysis will initially include a description of the sample characteristics and the distribution of the variables under study. Subsequently, comparisons will be performed among participants with different adiposity characteristics, and associations among anthropometric indicators, metabolic parameters, and biomarkers will be analyzed. When methodologically appropriate, multivariable models will be used to explore independent associations and control for potential confounding factors.

Project implementation indicators will include the extent to which the target sample size is achieved, the proportion of participants who complete the planned assessments, the availability of valid biological samples for the planned determinations, and the percentage of complete records. As expected performance levels, the project will aim to achieve the calculated sample size and a high proportion of complete assessments, valid biological samples, and complete records. These indicators will be monitored throughout the project to identify potential deviations from the expected targets and, when necessary, implement measures to optimize recruitment, data collection, and the quality and completeness of the information obtained.

#### *Project organization and planning*

The project will have an estimated duration of 12 months and will be organized into five consecutive phases. The timing of the different activities will be adapted to the progress of recruitment and the operational conditions of the participating institutions. Responsibilities will be assigned according to the expertise of the different team members. The research team will be responsible for the overall coordination of the project, qualified healthcare professionals will carry out activities related to biological sample collection, and research and technical staff will perform the corresponding assessment, sample processing, data management, and analysis tasks. The work plan will be continuously monitored to assess progress, identify potential deviations, and address any issues that may arise during project implementation.

- Phase 1. Preparation and coordination. Obtaining the necessary ethical and administrative approvals, coordinating with collaborating institutions, preparing materials, and standardizing the assessment procedures.

- Phase 2. Recruitment. Providing information to educational institutions, families, and potential participants; obtaining the corresponding informed consent and assent; and applying the eligibility criteria.

- Phase 3. Assessment and sample collection. Conducting anthropometric and body composition measurements, assessing dietary habits, and collecting biological samples.
- Phase 4. Sample processing and data analysis. Processing biological samples, determining biochemical parameters and biomarkers, cleaning the database, and conducting the statistical analyses.
- Phase 5. Integration and dissemination of results. Integrating and interpreting the findings, drawing conclusions, and preparing research outputs for scientific dissemination.

Ongoing coordination among the professionals involved will enable continuous monitoring of the work plan, assessment of progress across the different phases, and implementation of any necessary measures in response to potential issues. This process will facilitate compliance with the established procedures and contribute to ensuring the quality of the information obtained.

## **Results**

### *Expected results*

#### *Aspects to be evaluated*

Once data collection and analysis have been completed, the participants' anthropometric and body composition characteristics, metabolic parameters, leptin and PTX3 concentrations, and dietary habits will be evaluated in an integrated manner.

Associations between indicators of general and central adiposity and parameters of glucose and lipid metabolism will be analyzed. Likewise, the relationships between leptin and PTX3 concentrations and the participants' anthropometric and metabolic characteristics will be assessed.

The metabolic and inflammatory profiles of adolescents with different adiposity characteristics and weight status will also be compared, and potential associations between dietary habits and the assessed indicators will be explored. Finally, the information obtained will be analyzed jointly to explore the existence of combinations of indicators potentially associated with distinct cardiometabolic profiles.

From an implementation perspective, the extent to which the target sample size is achieved, the proportion of participants with complete assessments, the availability of valid biological samples, and the completeness of the records obtained will also be evaluated. These indicators will enable an assessment of the feasibility of the proposed methodology and the quality of the information generated.

### *Expected findings*

A multidimensional characterization of the participants is expected to be obtained through the integration of anthropometric and body composition indicators, metabolic parameters, biomarkers, and dietary habits.

Regarding leptin, it is hypothesized that adolescents with greater general and central adiposity will exhibit higher circulating concentrations. This expectation is consistent with evidence linking leptin to adiposity in pediatric populations and supporting its potential relevance as a complementary biomarker (Al Zein et al., 2024; Bravo et al., 2024).

Differences in selected parameters of glucose and lipid metabolism are also expected to be identified among participants with different adiposity characteristics. Nevertheless, individual variability within similar anthropometric categories is also anticipated, given the complex relationships among BMI, body adiposity, and cardiometabolic risk factors and the complementary information that different anthropometric indicators may provide (Joisten et al., 2024; Kim et al., 2024; Xie et al., 2024).

For this reason, no single anthropometric measure is hypothesized a priori to have superior ability to characterize all components of cardiometabolic risk. Instead, the combined analysis of BMI, waist circumference, estimates of body adiposity, and metabolic parameters is expected to identify differences that may not be fully captured when any of these indicators is considered in isolation.

Regarding PTX3, its relationship with adiposity characteristics and metabolic profile will be explored without prespecifying a single direction for the expected associations. Given the biological complexity of

this biomarker and the more limited evidence available in adolescent populations, the findings will be interpreted exploratorily and in conjunction with the remaining variables (Miyazaki et al., 2014; Norata et al., 2010).

The relationship between dietary habits and the anthropometric, metabolic, and inflammatory indicators assessed will also be explored. Patterns of association between specific dietary characteristics and less favorable profiles may be identified; however, given the observational design and the inherent limitations of self-reported dietary information, the findings will not allow causal relationships to be established.

Finally, the integrated analysis of the variables under study will enable the exploration of combinations of indicators associated with distinct cardiometabolic profiles. This approach is intended to investigate the heterogeneity among participants and determine whether the joint consideration of different dimensions provides additional information for their characterization. The purpose of the project is not to develop or validate a diagnostic or predictive tool, but rather to generate knowledge and new hypotheses that may provide a basis for future longitudinal research.

### Conclusions

The present project proposes a multidimensional approach to the study of early cardiometabolic risk during adolescence by integrating indicators of general and central adiposity, metabolic parameters, dietary habits, and biomarkers related to metabolic regulation and inflammation.

Its main contribution lies in moving beyond a characterization based exclusively on weight status and examining the potential heterogeneity among adolescents with similar anthropometric characteristics. The integration, within a single assessment strategy, of different dimensions of adiposity, metabolic profile, and leptin and PTX3 concentrations represents one of the distinctive features of the proposed project. This approach will make it possible to explore whether specific metabolic and inflammatory profiles exhibit characteristics that are not fully captured when conventional anthropometric indicators are considered in isolation.

Future findings should be interpreted in light of the inherent limitations of the observational design, which will allow associations to be identified but will not permit causal relationships to be established. The biological variability of the biomarkers, potential age- and sex-related differences, and the limitations inherent in self-reported dietary information should also be considered. Furthermore, the absence of longitudinal follow-up will limit the ability to determine the temporal evolution of the identified profiles.

Despite these limitations, the project may expand current knowledge of the relationships among adiposity, metabolism, and inflammation during a stage of life that is particularly relevant for prevention. The findings may generate new hypotheses and provide a basis for future longitudinal studies aimed at examining the evolution of the identified profiles and determining which combinations of indicators are most useful for the early characterization of cardiometabolic risk.

Ultimately, the implementation of the project will make it possible to assess the feasibility of a multidimensional approach to the study of cardiometabolic risk in adolescents. Although the proposed project is not intended to develop a diagnostic or predictive tool, its findings may help guide future research aimed at improving early detection and prevention strategies during adolescence.

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