



ObMetrics

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This manual corresponds to version 1.0 of the ObMetrics.

List of Abbreviations

1. Body Mass Index (**BMI**).
2. Blood Pressure (**BP**).
3. Centers for Disease Control and Prevention (**CDC**).
4. Copenhagen School Child Intervention Study (**CoSCIS**).
5. Diastolic Blood Pressure (**DBP**).
6. European Youth Heart Study (**EYHS**).
7. Systolic Blood Pressure (**SBP**).
8. High-Density Lipoprotein Cholesterol (**HDL-C**).
9. Homeostatic Model Assessment for Insulin Resistance (**HOMA-IR**).
10. Identification and Prevention of Dietary and Lifestyle-Induced Health Effects In Children and Infants (**IDEFICS**).
11. International Diabetes Federation (**IDF**).
12. International Obesity Task Force (**IOTF**).
13. KInder Sports Studie (**KISS**).
14. Metabolic Syndrome (**MetS**).
15. National Cholesterol Education Program Adult Treatment Panel III (**NCEP-ATP III**).
16. National Health And Nutrition Examination Survey (**NHANES**).

17. National High Blood Pressure Education Program (**NHBPEP**).
18. Physical Activity among Norwegian Children Study (**PANCS**).
19. Triacylglycerols (**TAG**).
20. Waist Circumference (**WC**).
21. World Health Organization (**WHO**).

1. Introduction

The assessment of Metabolic Syndrome (MetS) in at-risk pediatric patients requires the measurement of the following components:

- 1) **Systolic and Diastolic Blood Pressure** (SBP and DBP, respectively).
- 2) **Excess adiposity**, such as Body Mass Index (BMI) or Waist Circumference (WC).
- 3) **Lipid profile** including Triacylglycerols (TAG) and High-Density Lipoprotein Cholesterol (HDL-C).
- 4) **Glucose homeostasis**, evaluated via direct glucose measurement and insulin resistance assessments using the Homeostasis Model Assessment (HOMA-IR) index.

While the MetS assessment in adults is straightforward due to well-established definitions, evaluating MetS in pediatric populations presents unique challenges. Clinicians and researchers must navigate two primary issues: 1) selecting an appropriate definition that aligns with the patient's age group, and 2) ensuring that the reference data's ethnic background is suitable for the population studied. In some cases, clinicians create tailored definitions of MetS to better serve the needs of specific populations.

To address these complexities, **ObMetrics** was designed as a flexible Shiny app that enables users to calculate MetS outputs based on published or customizable definitions. The choice of MetS definition can significantly impact prevalence rates, particularly in pediatric populations. In the absence of a universal consensus on MetS definitions for children, ObMetrics provides researchers and clinicians with a valuable tool for comparing outputs across multiple definitions, aiding in the clinical monitoring of pediatric patients with obesity. ObMetrics provides results in both classification and z-score formats, supporting diverse clinical and research needs:

- **Metabolic Syndrome Classification:** ObMetrics offers a binary (yes/no) calculation of MetS and its components, allowing users to choose among several definitions. Please consult Tables 1 and 2 for further details.
- **Continuous Metabolic Syndrome Score:** ObMetrics also calculates z-scores for MetS and its components, with options to select among various reference tables. Refer to Tables 3, 4, and 5 for details on the scoring process.

We anticipate that this application will be particularly useful to researchers across epidemiology, pediatrics, and public health fields and will serve as a practical tool for clinicians in the ongoing monitoring of pediatric patients.

Table 1: Proposed definitions for the classification of MetS across different studies, including age ranges, study populations, and specific cutoff points for each MetS component.

<u>Definition</u>	<u>Study population</u>	<u>Age range</u>	<u>Components of MetS</u>					
			<u>Excess adiposity</u>	<u>Blood pressure</u>	<u>Triacylglycerols</u>	<u>HDL-C</u>	<u>Glucose</u>	<u>Insulin resistance</u>
Cook et al 2003 (NCEP ATP III) ¹	White, Black, and Mexican-American 12-19 years old (N = 2420, NHANES III, 1988-1994)	2-18 years old	WC \geq 90th percentile (age, sex and ethnic-specific, NHANES III) ¹⁰	SBP or DBP \geq 90th percentile (age, sex and height percentile specific, NHBPEP) ^{11,12}	TAG \geq 110 mg/dL (NCEP) ^{13,14}	HDL-C \leq 40 mg/dL (NCEP) ^{13,14}	Glucose \geq 110 mg/dL (ADA) ¹	Insulin resistance is not considered
de Ferranti et al 2004 ²	White, Black, and Mexican American 12-19 years old (N = 1960, NHANES III, 1988-1994)	2-18 years old	WC \geq 75th percentile (age, sex and ethnic specific, NHANES III) ¹⁰	SBP \geq 90th percentile (age, sex and height percentile specific NHBPEP) ^{11,12}	TAG \geq 100 mg/dL (NCEP) ^{13,14}	HDL-C \leq 50 and \leq 45 mg/dL for age <15 and \geq 15 respectively ^{1,3,14}	Glucose \geq 110 mg/dL ²	Insulin resistance is not considered
Ford et al 2005 ³	White, Black, and Mexican American 12-17 years old (N = 1370, NHANES, 1999-2000)	2-18 years old	WC \geq 90th percentile (age, sex and ethnic specific, NHANES III) ¹⁰	SBP or DBP \geq 90th percentile (age, sex and height percentile specific, NHBPEP) ^{11,12}	TAG \geq 110 mg/dL (NCEP) ^{13,14}	HDL-C \leq 40 mg/dL (NCEP) ^{13,14}	Glucose \geq 100 mg/dL ¹⁵	Insulin resistance is not considered
Viner et al 2005 ⁴	White, Black, South Asian, and other or mixed ethnicity 2-18 years old (N = 103, everyone with obesity)	2-18 years old	BMI \geq 95th percentile (Cole et al 2000) ¹⁶	SBP \geq 95th percentile (age, sex and height percentile specific, NHBPEP) ^{11,12}	TAG \geq 150 mg/dL ⁴	HDL-C \leq 35 mg/dL ^{13,14}	Glucose \geq 110 mg/dL or Insulin \geq 15 μ UI/ml, \geq 30 μ UI/ml and \geq 20 μ UI/ml for pre-, mid- and postpubertal children, respectively ¹⁷	See the footnote for more details ¹ .

¹ Viner et al 2005. Pre, mid- and postpubertal children are defined as Tanner I, Tanner II-IV and Tanner V, respectively.

<u>Definition</u>	<u>Study population</u>	<u>Age range</u>	<u>Excess adiposity</u>	<u>Blood pressure</u>	<u>Triacylglycerols</u>	<u>HDL-C</u>	<u>Glucose</u>	<u>Insulin resistance</u>
Zimmet et al 2007 (IDF) ^{5,6}	It was a report. See the footnote for more details ² .	10-18 years old <u>* ObMetrics uses an extended version that can be used from 2 to 18 years of age⁹</u>	WC ≥ 90th percentile or adult cut-points if lower (age ≤ 16, sex and ethnic-specific, NHANES III) and adult cut-points (age > 16, sex and ethnic-specific) ¹⁰	SBP or DBP ≥ 130 or 85 mmHg ^{5,6,11,12}	TAG ≥ 150 mg/dL ^{5,6}	HDL-C ≤ 40 mg/dL (age ≥ 16, NCEP) and HDL-C ≤ 40 mg/dL in males and 50 mg/dL in females (age ≥ 17, NCEP) ^{5,6,13,14}	Glucose ≥ 100 mg/dL (ADA) ¹⁵	Insulin resistance is not considered
Olza et al 2011 ^{7,8}	White European (Spanish) 5-10.9 years old (N=930)	4-18 years old	BMI ≥ 95th percentile (Cole et al 2000) ¹⁶ <u>2-18 years old</u>	SBP or DBP ≥ 90th percentile (age, sex and height percentile specific, NHBPEP) ^{11,12} <u>2-18 years old</u>	TAG ≥ 90th percentile (age and sex specific, NCEP) ^{13,14} <u>0-19 years old</u>	HDL-C ≤ 10th percentile (age and sex specific) ¹⁸ <u>4-19 years old</u>	Glucose ≥ 100 mg/dL ^{7,8}	HOMA-IR ≥ 2.5 and ≥ 5.38 for prepubertal (Tanner I) and pubertal children (Tanner II-IV) ^{7,8}
Ahrens et al 2014 (IDEFICS study, monitoring/action level) ⁹	European 2-10.9 years old (N=18745, IDEFICS)	3-10 years old	WC ≥ 90th/95th percentile (age and sex specific, IDEFICS) ⁹	SBP/DBP ≥ 90th/95th percentile (age and sex specific, IDEFICS) ⁹	TAG ≥ 90th/95th percentile / HDL-C ≤ 10th/05th percentile (age and sex specific, IDEFICS) ⁹	Glucose/HOMA-IR ≥ 90th/95th percentile or (age and sex specific, IDEFICS) ⁹		

² Zimmet et al 2007 (IDF). Cut-points of WC in adults are 94 and 80 cm in males and females, in the case of Mexican-American males is 90 cm. The presence of obesity is considered a sine qua non-condition for MetS.

Table 2. Available tables of reference values for customizing MetS definitions in ObMetrics.

<u>Tailor your definition</u>	<u>Excess adiposity</u>	<u>Blood pressure</u>	<u>Triacylglycerols</u>	<u>HDL-C</u>	<u>Glucose</u>	<u>Insulin resistance</u>
<u>Customizable option</u> (the user can choose between all the reference tables)	<p>1) WC ≥ 90th percentile (Cook and Ford definitions)^{1,3}</p> <p>2) WC ≥ 75th percentile (de Ferranti definition)²</p> <p>3) WC ≥ 90th percentile or adult cutoff point if lower (Zimmet definition)^{5,6}</p> <p>4) WC ≥ 90th percentile (Ahrens definition, monitoring level)⁹</p> <p>5) WC ≥ 95th percentile (Ahrens definition, action level)⁹</p> <p>6) WC ≥ 90th percentile (CDC)¹⁹</p> <p>7) WC ≥ 90th percentile (McCarthy et al 2001)²⁰</p> <p>8) WC ≥ 90th percentile (Ferrandez et al 2005)²¹</p> <p>1) BMI ≥ 95th percentile (Viner and Olza definitions)^{4,7,8}</p> <p>2) BMI ≥ 95th percentile (WHO)²²</p> <p>3) BMI ≥ 90th percentile (CDC)¹⁹</p> <p>4) BMI ≥ 95th percentile (Sobradillo et al 2004)²³</p>	<p>1) SBP or DBP ≥ 90th percentile (Cook, Ford and Olza definitions)^{1,3,7,8,11,12}</p> <p>2) SBP (or DBP) ≥ 90/95th percentile (de Ferranti and Viner definitions)^{2,4,11,12}</p> <p>3) SBP or DBP ≥ 130 or 85 cutoff points (Zimmet definition)^{5,6}</p> <p>4) SBP or DBP ≥ 90th percentile (Ahrens definition, monitoring level)⁹</p> <p>5) SBP or DBP ≥ 95th percentile (Ahrens definition, action level)⁹</p>	<p>1) TAG ≥ 110 cutoff point (Cook and Ford definitions)^{1,3}</p> <p>2) TAG ≥ 100 cutoff point (de Ferranti definition)²</p> <p>3) TAG ≥ 150 cutoff point (Viner and Zimmet definitions)^{4,5,6}</p> <p>4) TAG ≥ 90th percentile (Olza definition)^{7,8}</p> <p>5) TAG ≥ 90th percentile (Ahrens definition, monitoring level)⁹</p>	<p>1) HDL-C ≤ 40 cutoff point (Cook and Ford definitions)^{1,3}</p> <p>2) HDL-C ≤ cutoff point (de Ferranti definition)²</p> <p>3) HDL-C ≤ 35 cutoff point (Viner definition)⁴</p> <p>4) HDL-C ≤ cutoff point (Zimmet definition)^{5,6}</p> <p>5) HDL-C ≤ 10th percentile (Olza definition)^{7,8}</p> <p>6) HDL-C ≤ 10th percentile (Ahrens definition, monitoring level)⁹</p>	<p>1) Glucose ≥ 110 cutoff point (Cook, de Ferranti and Viner definitions)^{1,2,4}</p> <p>2) Glucose ≥ 100 cutoff point (Ford, Zimmet and Olza definitions)^{3,5,6,7,8}</p> <p>3) Glucose ≥ 90th percentile (Ahrens definition, monitoring level)⁹</p> <p>4) Glucose ≥ 90th percentile (Ahrens definition, action level)⁹</p>	<p>1) HOMA-IR ≥ cutoff points according to Tanner index (Olza definition)^{7,8}</p> <p>2) HOMA-IR ≥ 90th percentile (Ahrens definition, monitoring level)⁹</p> <p>3) HOMA-IR ≥ 90th percentile (Ahrens definition, action level)⁹</p> <p>4) HOMA-IR ≥ cutoff points based on Tanner index (Anguita et al 2020)^{24*}</p> <p>* HOMA-IR cutoff point for the prepubertal stage (Tanner I) is ≥ 2.5 to be considered insulin resistance. For the pubertal stage (Tanner II-IV), the cutoff points are 3.38 and 3.905 for males and females, respectively²⁴</p>

Table 3. Proposed continuous MetS definitions with details on study populations and age ranges.

<u>Definitions</u>	<u>Study population</u>	<u>Age range</u>
Ahrens et al 2014 ⁹	European (N=18745, IDEFICS study)	3-10 years old
Stravnsbo et al 2018 ²⁵	European (Denmark, Estonia, Portugal, Switzerland) and United States (N = 22479, EYHS, CoSCIS, PANCS, KISS and NHANES studies)	6-18 years old

Table 4. Standardized method for calculating continuous MetS scores, showing the step-by-step process for determining z-scores for each component⁹. BP z-score is the mean between SBP and DBP z-score. Lipid z-score is the mean of TAG z-score and HDL-C z-score.

<u>Continuos MetS z-scores</u>						
<u>Steps</u>	<u>Excess adiposity</u>	<u>Blood pressure</u>	<u>Triacylglycerols</u>	<u>HDL-C</u>	<u>Glucose</u>	<u>Insulin resistance</u>
Step 1	WC z-score	SBP and DBP z-score	TAG z-score	HDL-C z-score (-)	Glucose z-score	HOMA-IR z-score
Step 2	WC z-score	BP z-score (mean of both)	Lipid z-score (mean of both)		HOMA-IR z-score	
Final step	MetS z-score = (WC z-score + BP z-score + Lipid z-score + HOMA-IR z-score)/4					

Please note that before calculating the Lipid z-score, the HDL-C z-score is multiplied by -1. Find below further information regarding the calculation of the MetS z-score on the source codes: https://github.com/bips-hb/IDEFICS-Score_Calculator/.

Table 5. Customizable options for defining continuous MetS scores, allowing users to choose reference values for each component to match the study's requirements.

<u>Define your score</u>	<u>Excess adiposity</u>	<u>Blood pressure</u>	<u>Triacylglycerols</u>	<u>HDL-C</u>	<u>Glucose</u>	<u>Insulin resistance</u>
Customizable option (the user can choose between all the available options)	1) WC z-score (Ahrens et al 2014) ⁹ 2) WC z-score (Stravnsbo et al 2018) ²⁵ 3) WC z-score (Sharma et al 2015, NHANES) ²⁶ 4) WC z-score (Ferrández et al 2005) ²¹ 1) BMI z-score (Stravnsbo et al 2018) ²⁵ 2) BMI z-score (WHO) ²⁷ 3) BMI z-score (Cole et al 2012) ²⁸ 4) BMI z-score (Sobradillo et al 2004) ²³	1) SBP z-score and DBP z-score (Ahrens et al 2014) ⁹ 2) SBP z-score and DBP z-score (Stravnsbo et al 2018) ²⁵ 2) SBP z-score and DBP z-score (NHBPEP et al 2004) ¹²	1) TAG z-score (Ahrens et al 2014) ⁹ 2) TAG z-score (Stravnsbo et al 2018) ²⁵	1) HDL-C z-score (Ahrens et al 2014) ⁹ 2) HDL-C z-score (Stravnsbo et al 2018) ²⁵	1) Glucose z-score (Ahrens et al 2014) ⁹ 2) Glucose z-score (Stravnsbo et al 2018) ²⁵	1) HOMA-IR z-score (Ahrens et al 2014) ⁹ 2) HOMA-IR z-score (Stravnsbo et al 2018) ²⁵

2. Prerequisites

- **Access:** ObMetrics is accessible through any standard web browser, including Google Chrome, Mozilla Firefox, Safari, and others. Users can access the application at <https://coblabugr.shinyapps.io/obmetrics/>.
- **Required Data:** ObMetrics requires data input in an Excel file structured according to the provided template. You can download the Excel template directly from the application interface by clicking the "**Download Excel Template**" button. The required variables include:
 - **ID:** Unique identifier for each participant.
 - **decimal_age:** Age in years, expressed as a decimal.
 - **sex:** Coded as 0 for males and 1 for females.
 - **height_m:** Height in meters.
 - **weight_kg:** Weight in kilograms.
 - **wc_cm:** WC in centimeters.
 - **dbp_mmHg:** DBP in millimeters of mercury.
 - **sbp_mmHg:** SBP in millimeters of mercury.
 - **tag_mg_dl:** TAG in milligrams per deciliter (mg/dL).
 - **hdlc_mg_dl:** HDL-C in milligrams per deciliter (mg/dL).
 - **glucose_mg_dl:** Glucose in milligrams per deciliter (mg/dL).
 - **insulin_microU_ml:** Insulin in microinternational units per milliliter (μ U/mL).
 - **tanner_index:** Tanner stage, coded as 1 for prepubertal, 2-3-4-5 for pubertal stages.

Make sure to use a period (.) as the decimal separator and leave columns blank if data is unavailable. For additional guidance on data preparation, you can also download a sample dataset by clicking the "**Download demo data**" button in the application.

3. Interface Description

Sidebar Overview: The sidebar in ObMetrics is designed to guide users through a logical workflow, with each numbered section representing a step in the data analysis process. The sections are as follows:

- 1) **Upload Your Data:** In this section, users can upload their data in Excel format by clicking on the "Browse" button. Users are encouraged to download and use the provided Excel template, which includes all required input variables. Additionally, a toggle switch allows users to load demo data, enabling them to explore the application's features without uploading their own dataset.
- 2) **Select a Definition:** This section allows users to choose from various MetS definitions to apply in their analysis. Options are provided to select reference values and thresholds for each component of MetS, such as WC, BP, TAG, HDL-C, and glucose. Users can also specify whether to include insulin resistance (HOMA-IR) as an additional component in their MetS analysis. Each selection is designed to provide flexibility and adaptability to different clinical and research needs.
- 3) **Visualize Results:** Here, users can view the results of their analysis. ObMetrics displays an interactive table with calculated outputs for each component of MetS, including binary classification and z-score metrics. Additionally, graphical tools allow users to visualize the data with one-dimensional and two-dimensional plots, which can be customized by selecting specific variables. These visualization options provide an intuitive way to examine individual results and trends within the dataset.
- 4) **Download Results:** In this final section, users can download their analyzed data in Excel format. The application generates a modified version of the original uploaded file, now enriched with calculated MetS classifications and z-scores, facilitating further data analysis or record-keeping.
- 5) **About:** The About section is designed to provide users with resources and support, enhancing their overall experience with ObMetrics and encouraging engagement with the development team. It includes the following subsections:
 - **User Guide:** This subsection displays a comprehensive user guide within the application interface. The user guide contains detailed instructions on each aspect of the application, including how to prepare data, select MetS definitions, interpret results, and troubleshoot common issues. The guide is displayed in a PDF format for

ease of navigation, and users are encouraged to review it thoroughly before using ObMetrics.

- **Quick Tutorial:** This subsection provides a brief video tutorial that walks users through the main functionalities of ObMetrics. The tutorial serves as a quick-start guide, covering the essential steps for uploading data, selecting definitions, viewing results, and downloading outputs. It is ideal for users who prefer a visual overview to get acquainted with the application's features.
- **Contact Us:** This subsection offers contact information for the developers and researchers responsible for ObMetrics. Users can reach out to the team with questions, suggestions, or issues encountered while using the application. Profiles and contact icons (e.g., email, LinkedIn, and institutional links) for each team member are provided to facilitate communication.
- **Feedback:** The Feedback subsection invites users to complete a usability survey to share their experience and satisfaction with ObMetrics. The survey is based on the Post-Study System Usability Questionnaire (PSSUQ) and collects responses on aspects such as ease of use, system usefulness, information quality, and interface quality. User feedback is valuable for improving future versions of the application and ensuring it meets the needs of the research and clinical communities.

Input Section: In the "Upload Your Data" section, users input data by uploading a structured Excel file that follows the template provided by the app. Each variable required for MetS calculation must be correctly formatted, as specified in the template. The option to load demo data is available for users who want to explore the functionality without preparing a dataset.

Output Section: ObMetrics generates two primary types of outputs: MetS Classification (binary "yes" or "no") and Continuous Metabolic Syndrome Score (z-scores). The results are displayed in the "Visualize Results" section, which provides both tabular and graphical representations of the calculated values for each MetS component. Users are encouraged to consult the guide's reference tables to interpret these results correctly. The download option in the "Download Results" section allows users to obtain a complete Excel file with all calculated outputs, supporting easy integration into subsequent research workflows.

4. Step-by-Step Workflow

Upon accessing the provided link to the ObMetrics web application, users are greeted with a structured interface featuring a sidebar menu on the left (highlighted in orange) and a main content area in the center (highlighted in red). The **Overview** section in the sidebar provides a brief introduction and background information about the purpose and scope of the application.

The sidebar menu organizes the app's functions into distinct sections, allowing users to navigate through various features. By selecting different sections in the sidebar, users can interact with the main content area (central menu), which dynamically updates to display relevant tools and information for each chosen section.

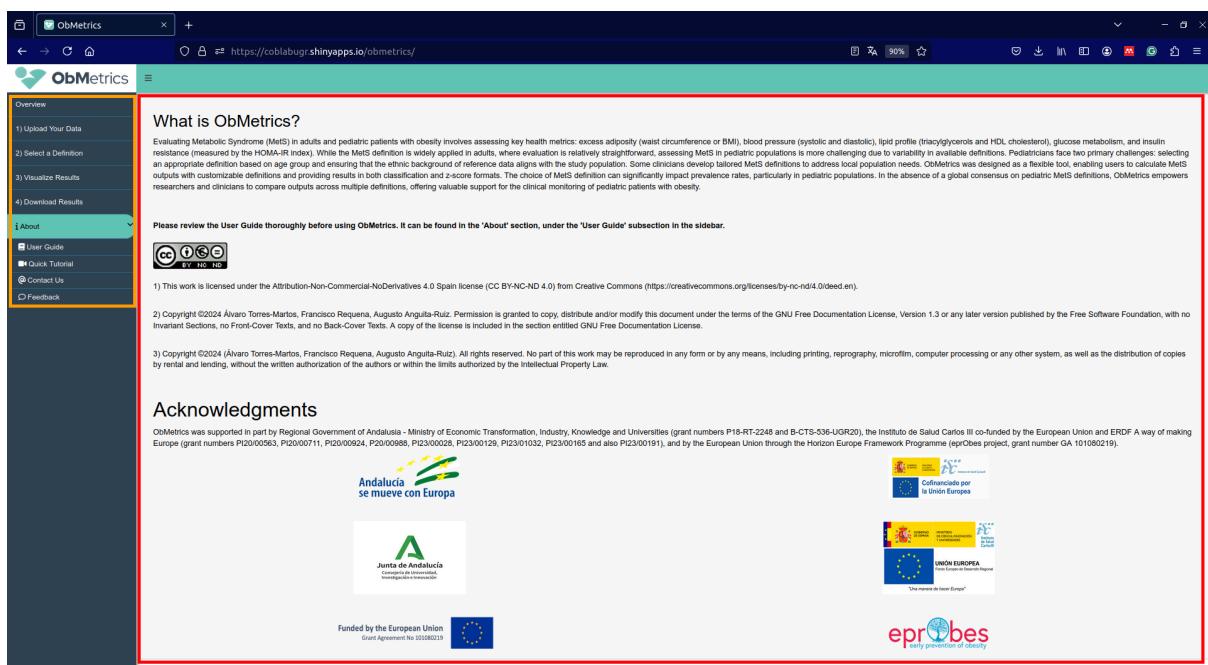


Figure 1. Main interface of the ObMetrics web application, with the sidebar menu highlighted in orange and the central content area highlighted in red.

To begin using the app, click on **Section 1: Upload Your Data** in the sidebar, highlighted in orange. This initiates the workflow, guiding the user through each step necessary to analyze MetS and its components in pediatric populations.

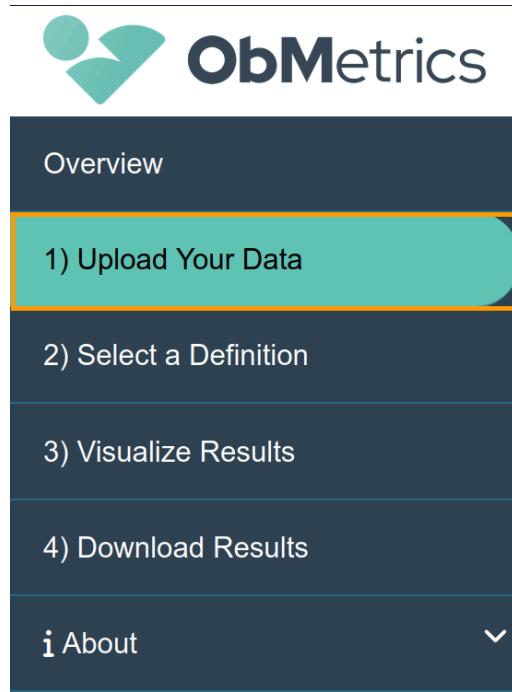


Figure 2. Sidebar menu of the ObMetrics application, highlighting Section 1: Upload Your Data in orange to guide users on where to start the data entry process.

4.1. Data Upload and Template Options

In Section 1: Upload Your Data, users can prepare and upload their data for analysis, with multiple options to facilitate data input and preparation. This section provides several essential functionalities:

1. **Uploading Data** (highlighted in orange): Users can upload their data file by clicking the Browse button. It is recommended to use the provided template to ensure that all necessary variables are included and correctly formatted. To test the functionalities of the Shiny app, users can activate the demo dataset by toggling the switch located to the right of the phrase: “If you wish to use demo data to explore ObMetrics functionality, toggle the demo data option on the right.”
2. **Downloading the Excel Template** (highlighted in red): To help users structure their data correctly, an Excel template is available for download. This template includes predefined columns and formats that match the input requirements of the application. Users should ensure that data is entered as specified and use a period (.) as the decimal separator. If any data fields are unavailable, they can leave the relevant cells blank.

3. Downloading the Demo Dataset (highlighted in yellow): For users who wish to explore the app's functionality before uploading their own data, a demo dataset is available for download. This sample file provides an example of a completed template, offering guidance on how to organize and format data.

4. Input Variables Table (highlighted in green): This table lists all required input variables, specifying the variable names, expected units, and data types (e.g., id as unique numbers, decimal_age as years, sex coded as 0 for males and 1 for females). Users should consult this table to ensure all variables are prepared correctly according to the required specifications. Not all variables are mandatory for every calculation, as required fields depend on the selected MetS definitions.

We strongly recommend first downloading the **demo dataset** (highlighted in yellow) and consulting the **Input Variables Table** (highlighted in green) to understand how each variable should be coded. This step will help users familiarize themselves with the data structure and coding requirements.

Once you are familiar with the data coding, download the **Excel template** (highlighted in red) and carefully fill it out, following the same coding and units specified in the **Input Variables Table** (highlighted in green).

The screenshot shows the ObMetrics application interface. On the left is a dark sidebar with navigation links: Overview, 1) Upload Your Data (highlighted in yellow), 2) Select a Definition, 3) Visualize Results, 4) Download Results, and About. The main content area has three main sections:

- Upload your data:** A form with a 'Browse...' button and a placeholder 'No file selected'. A note says: "Please download the Excel template (available in the right panel) and enter your data as instructed. Once completed, upload the Excel file using the 'Browse' button." A yellow box highlights this section.
- Download Excel template:** A button labeled 'Download Excel template'. A red box highlights this section.
- Input variables:** A table titled 'Name.variable.input' with columns 'Name', 'variable', 'input', 'Unit', and 'Description'. The table lists various variables with their units and descriptions. A green box highlights this section.

At the bottom of the page is a note: "Table 1: Required input variables for calculating outputs. Note that not all variables are necessary for every calculation; required fields depend on the chosen MetS criteria. Refer to the User Guide for more details."

Figure 3. Overview of Section 1 in the ObMetrics application, showing options for uploading data, downloading a structured template, downloading a demo dataset, and reviewing required input variables.

The screenshot shows a LibreOffice Calc spreadsheet titled "2024-11-05_Obmetrics_example_dataset.xlsx - LibreOffice Calc". The sheet is named "Sheet1". The data consists of 21 rows of information across 14 columns. The columns are labeled: id, decimal_age, sex, height_m, weight_kg, wc_cm, dbp_mmHg, sbp_mmHg, tag_mg_dl, hdlc_mg_dl, glucose_mg_dl, insulin_microU_ml, and tanner_index. The data entries are numerical values representing age, sex, height, weight, waist circumference, blood pressure, triglycerides, HDL cholesterol, glucose levels, insulin concentration, and Tanner index.

Figure 4. Example of the ObMetrics demo dataset, displaying required variables and their respective formats, including decimal age, sex (coded as 0 for males and 1 for females), anthropometric measurements, BP values, lipid profile markers, glucose levels, insulin concentration, and Tanner index. This dataset provides a reference for users to correctly format and organize their own data for analysis.

The screenshot shows a LibreOffice Calc spreadsheet titled "2024-11-05_Obmetrics_input_template.xlsx - LibreOffice Calc". The sheet is named "Sheet1". The data consists of 21 rows of information across 14 columns. The columns are labeled: id, decimal_age, sex, height_m, weight_kg, wc_cm, dbp_mmHg, sbp_mmHg, tag_mg_dl, hdlc_mg_dl, glucose_mg_dl, insulin_microU_ml, and tanner_index. All cells in the data range are currently empty, indicating a template for data entry.

Figure 5. Excel template provided by ObMetrics for data entry, showing the required variables and column headers. This template ensures that all necessary data is formatted correctly for analysis.

Please note that not all variables are required to calculate MetS; you can refer to the various tables for specific requirements. In general, age, sex, and height are usually necessary, while the Tanner index is only needed in certain cases, such as in the definitions by Viner *et al.*

(2005) and Olza *et al.* (2011). If a variable is not required for your analysis, such as insulin or Tanner index, and you do not wish to include it in the template, **leave the corresponding column blank but do not delete it**. Additionally, ensure that all columns are formatted as numeric to avoid errors, and always use a period (.) as the decimal separator to prevent potential issues.

Once the data is filled in, click the **Browse button** (highlighted in red). A notification will appear (highlighted in orange), indicating that you can now proceed to **Section 2: Select a Definition** (highlighted in yellow) to continue with the analysis setup.

The figure consists of three vertically stacked screenshots of the ObMetrics application interface, showing the progression of the data upload process.

- Screenshot 1 (Top): Initial Data Upload Screen**
 - The sidebar on the left shows steps: 1) Upload Your Data (highlighted in green), 2) Select a Definition, 3) Visualize Results, 4) Download Results, and About.
 - The main panel has a heading "Upload your data". It contains instructions: "Please download the Excel template (available in the right panel) and enter your data as instructed. Once completed, upload the Excel file using the 'Browse' button." Below this is a "Browse" button highlighted with a red box.
 - To the right, there's a "Download Excel template" section with a "Download Excel template" button.
 - At the bottom, a note says: "If you wish to use demo data to explore ObMetrics functionality, toggle the demo data option on the right." A toggle switch is shown.
 - A small note at the bottom: "After uploading the data, proceed to Section 2) Select a Definition. Choose your desired output, and don't forget to click 'Run Analysis' once you've made your selection."
- Screenshot 2 (Middle): Confirmation Message**
 - The same interface as Screenshot 1, but with a confirmation message box in the center: "Your data has been uploaded successfully." This message is highlighted with an orange box.
 - The "Upload" button is now labeled "Upload complete".
 - The "Dismiss" button is visible in the message box.
 - The sidebar step "2) Select a Definition" is highlighted in yellow.
- Screenshot 3 (Bottom): Step 2 Selection**
 - The sidebar step "2) Select a Definition" is highlighted in yellow.
 - The main panel shows the "Upload your data" section with the "Upload complete" message.
 - The "Download Excel template" section is visible on the right.
 - The note at the bottom remains the same: "After uploading the data, proceed to Section 2) Select a Definition. Choose your desired output, and don't forget to click 'Run Analysis' once you've made your selection."

Figure 6. Data upload process in the ObMetrics application. The first panel shows the initial step where users can upload their data file by clicking the "Browse" button (highlighted in red). After selecting the file, a confirmation message appears (highlighted in orange), indicating successful data upload and prompting users to proceed to Section 2: Select a Definition (highlighted in yellow).

Once the Select a Definition button is clicked, the central menu updates to display the interface shown in Figure 7.

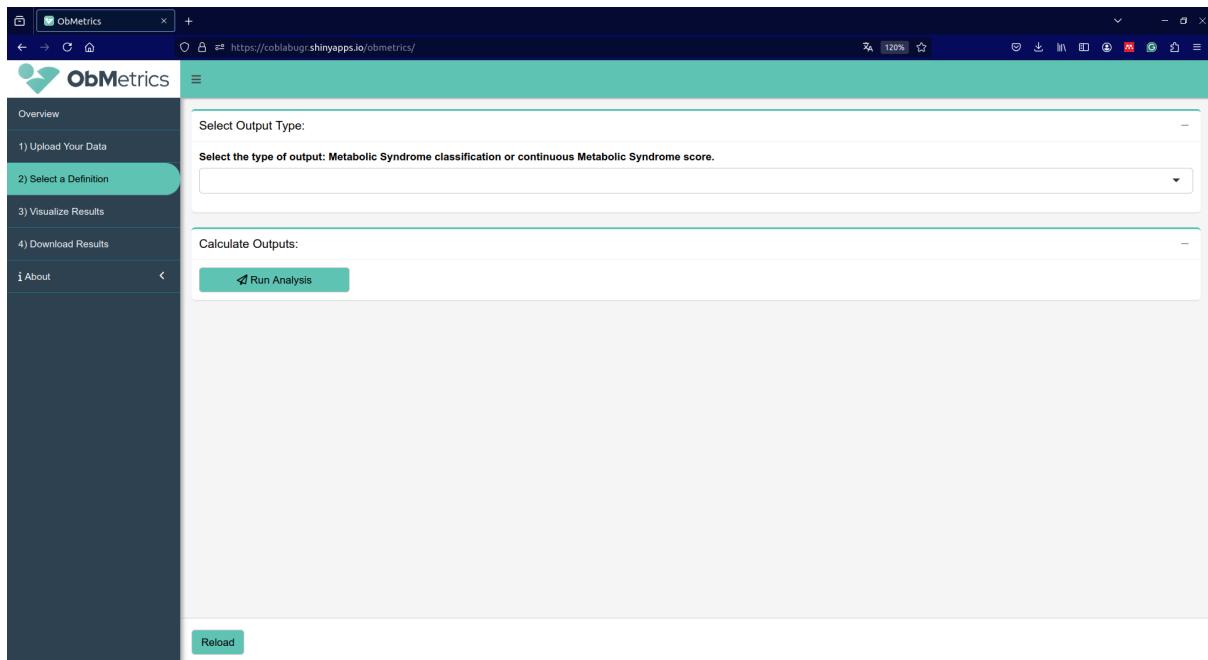


Figure 7. Interface of Section 2: Select a Definition in the ObMetrics application. Users can choose between a Metabolic Syndrome Classification or a Continuous Metabolic Syndrome Score by selecting the appropriate option in the dropdown menu.

4.2. Selecting MetS Outcome Type and Definition

The user should click on the Select the type of output: **Metabolic Syndrome Classification** or **Continuous Metabolic Syndrome Score** button within the Select Output Type panel. Different fields and settings will appear depending on whether the user selects the classification or z-score option, each offering unique analysis choices.

To streamline this User Guide and ensure clarity, we will divide this section into two distinct subsections. First, we will explore the classification options, which allow for a binary (yes/no) assessment of MetS and its individual components according to selected definitions. Second, we will detail the z-score options, which enable a continuous evaluation of MetS and each component through standardized scores. In both classification and z-score analyses, users are provided with a comprehensive assessment of MetS as a whole and a detailed evaluation of each individual component. This approach will offer a clear, structured overview of the available options, guiding users through the setup and selection process in an organized manner.

4.2.1. Metabolic Syndrome Classification: Definitions and Customization Options

When users select the **Metabolic Syndrome Classification** option (highlighted in red), they are provided with a comprehensive list of all available definitions, as outlined in **Table 1**. Based on the selected definition (highlighted in orange), an additional option appears, allowing users to choose specific reference populations. This feature enables the selection of reference values from the NHANES III study across different ethnic populations, specifically Multi-ethnic, European-American, African-American, and Mexican-American, to assess obesity based on WC (highlighted in yellow). This customization ensures that users can align their analysis with the most appropriate population standards for accurate classification.

The figure consists of three vertically stacked screenshots of the ObMetrics web application interface. Each screenshot shows a navigation sidebar on the left with links: Overview, 1) Upload Your Data, 2) Select a Definition (which is highlighted in teal), 3) Visualize Results, 4) Download Results, and About. The main content area has a teal header bar with the title 'Select Output Type:'. Below it, a dropdown menu says 'Select the type of output: Metabolic Syndrome classification or continuous Metabolic Syndrome score.' A red box highlights the 'Metabolic Syndrome Classification' option in the dropdown. In the second screenshot, a yellow box highlights the 'Cook (NCEP ATP III) Definition (United States (Multi-ethnic), Cook et al. 2003) [1]' option under 'Metabolic Syndrome (MetS) Classification Options'. In the third screenshot, a yellow box highlights the 'NHANES III Study (United States (Multi-ethnic), used in Cook, de Ferranti, Ford, and Zimmet Definitions) [10]' option under '2.1) Select Reference Values for Obesity Based on Waist Circumference:'. At the bottom of each screenshot is a teal button labeled 'Run Analysis'.

ObMetrics

Overview

- 1) Upload Your Data
- 2) Select a Definition**
- 3) Visualize Results
- 4) Download Results

i About

Select Output Type:

Select the type of output: Metabolic Syndrome classification or continuous Metabolic Syndrome score.

Metabolic Syndrome Classification

Metabolic Syndrome (MetS) Classification Options:

- Ford Definition (United States (Multi-ethnic), Ford et al. 2005) [3]

2.1) Select Reference Values for Obesity Based on Waist Circumference:

- NHANES III Study (United States (Multi-ethnic), used in Cook, de Ferranti, Ford, and Zimmet Definitions) [10]

Calculate Outputs:



ObMetrics

Overview

- 1) Upload Your Data
- 2) Select a Definition**
- 3) Visualize Results
- 4) Download Results

i About

Select Output Type:

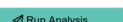
Select the type of output: Metabolic Syndrome classification or continuous Metabolic Syndrome score.

Metabolic Syndrome Classification

Metabolic Syndrome (MetS) Classification Options:

- Viner Definition (United Kingdom (Multi-ethnic), Viner et al. 2005) [4]

Calculate Outputs:



ObMetrics

Overview

- 1) Upload Your Data
- 2) Select a Definition**
- 3) Visualize Results
- 4) Download Results

i About

Select Output Type:

Select the type of output: Metabolic Syndrome classification or continuous Metabolic Syndrome score.

Metabolic Syndrome Classification

Metabolic Syndrome (MetS) Classification Options:

- Zimmet (IDF) Definition (Multi-ethnic, Zimmet et al. 2007) [5-6]

2.1) Select Reference Values for Obesity Based on Waist Circumference:

- NHANES III Study (United States (Multi-ethnic), used in Cook, de Ferranti, Ford, and Zimmet Definitions) [10]

Calculate Outputs:



ObMetrics

Overview

- 1) Upload Your Data
- 2) Select a Definition**
- 3) Visualize Results
- 4) Download Results

i About

Select Output Type:

Select the type of output: Metabolic Syndrome classification or continuous Metabolic Syndrome score.

Metabolic Syndrome Classification

Metabolic Syndrome (MetS) Classification Options:

- Olza Definition (Spain (European Ethnic), Olza et al. 2011) [7-8]

Calculate Outputs:



ObMetrics

Overview

- 1) Upload Your Data
- 2) Select a Definition**
- 3) Visualize Results
- 4) Download Results

i About

Select Output Type:

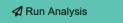
Select the type of output: Metabolic Syndrome classification or continuous Metabolic Syndrome score.

Metabolic Syndrome Classification

Metabolic Syndrome (MetS) Classification Options:

- Ahrens (Monitoring Level, IDEFICS) Definition (Europe (Multi-ethnic), Ahrens et al. 2014) [9]

Calculate Outputs:



The figure consists of two vertically stacked screenshots of the ObMetrics software. Both screenshots show the same user interface for selecting a Metabolic Syndrome classification. In the top screenshot, a red box highlights the 'Metabolic Syndrome Classification' option in a dropdown menu under 'Select Output Type'. Below this, an orange box highlights the 'Ahrens (Action Level, IDEFICS) Definition (Europe (Multi-ethnic), Ahrens et al. 2014) [9]' option in a dropdown menu under 'Metabolic Syndrome (MetS) Classification Options'. At the bottom, a green button labeled 'Run Analysis' is visible. In the bottom screenshot, a yellow box highlights a list of reference values for WC based on the NHANES III study, including options for Multi-ethnic, European-American, African-American, and Mexican-American populations.

Figure 8. Workflow for selecting a Metabolic Syndrome Classification in ObMetrics. After choosing the Metabolic Syndrome Classification option (highlighted in red), users can select from various predefined definitions (highlighted in orange), each offering specific parameters for MetS classification. Depending on the chosen definition, users are then prompted to select reference values for WC based on the NHANES III study, with options for Multi-ethnic, European-American, African-American, and Mexican-American populations (highlighted in yellow). This flexible setup allows for tailored analyses that match the population context of the study.

If the user selects the **Customizable Definition** option (highlighted in red), they can choose from various reference values or cutoff points available in Table 2. First, the user can select either **Waist Circumference** or **Body Mass Index** as the measure to evaluate the obesity component depending on the choice, different options will appear (highlighted in orange). Additionally, there are distinct reference values or cutoff points for other components (Blood Pressure, Triacylglycerols, HDL-C, and Glucose) (highlighted in yellow). Finally, the user can decide whether to include **HOMA-IR** as a measure for assessing insulin resistance. Only if the user selects "Yes" will an additional option appear, allowing them to choose among different reference values or cutoff points (highlighted in green). Based on findings from the case study used to evaluate ObMetrics, we strongly recommend including insulin resistance as an additional component of MetS.

Figure 9: Interface view when the Customizable Definition option is selected, showing options for obesity measurement, reference values for MetS components, and the inclusion of HOMA-IR for insulin resistance.

4.2.2. Continuos Metabolic Syndrome Scores: Definitions and Customization Options

When the user selects the **Continuous Metabolic Syndrome Score** option (highlighted in red), they can choose from predefined MetS scoring definitions based on published studies. The selected definitions include reference standards from multi-ethnic population studies that provide consistent methodology. Each definition reflects different population studies, such as the **IDEFICS Study** or combined data from various international cohorts like **CosCIS, EYHS, KISS, PANCS, and NHANES** (also highlighted in orange), as shown in

Table 3. These standardized definitions allow for a robust and reliable calculation of MetS scores across diverse demographic groups.

To gain a comprehensive understanding of how the global MetS score is calculated, users are encouraged to refer to **Table 4**, which outlines the standardized methodology for aggregating individual component scores into an overall MetS score. This continuous score offers a nuanced evaluation of metabolic risk by integrating each component's z-score, allowing for a more detailed assessment across different population subgroups.

Figure 10: Interface options for selecting predefined continuous MetS score definitions, illustrating choices from the IDEFICS study (top) and multi-cohort studies (bottom).

If the user selects the **Customizable Definition** option (highlighted in red), they can choose from various reference values as outlined in **Table 5**. Initially, the user can select between **Waist Circumference** and **Body Mass Index** as the measure for assessing the obesity component. Based on this selection, different options appear (highlighted in orange). Additionally, the user can choose from various reference values for the other components of MetS, allowing for a tailored approach to each parameter.

The figure consists of two vertically stacked screenshots of the ObMetrics web application. Both screenshots show the 'Customizable Definition' section highlighted with a red border.

Screenshot 1 (Top): This screenshot shows the 'Continuous Metabolic Syndrome (MetS) Score Options' section. A red box highlights the 'Customizable Definition' button. Below it, a yellow box highlights the 'Select Anthropometric Measure for Obesity' section, which includes options for 'Waist circumference (WC)' and 'Body mass index (BMI)'. Further down, a yellow box highlights the 'Select Reference Values for Blood Pressure Score' section, which includes options for 'NHBPEP 2004 (United States (Multi-ethnic)) [12]' and 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]'. Another yellow box highlights the 'Select Reference Values for Triacylglycerols Score' section, which includes options for 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]' and 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]'. A third yellow box highlights the 'Select Reference Values for HDL-C Score' section, which includes options for 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]' and 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]'. A fourth yellow box highlights the 'Select Reference Values for Glucose Score' section, which includes options for 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]' and 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]'. A fifth yellow box highlights the 'Select Reference Values for HOMA-IR Score' section, which includes options for 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]' and 'CosCIS, EYHS, KISS, PANCs, and NHANES Studies (Worldwide (Multi-ethnic), Stavnsbo et al. 2018) [25]'. At the bottom, a green 'Run Analysis' button is visible.

Screenshot 2 (Bottom): This screenshot is similar to the first one but shows a different anthropometric measure selected: 'Body mass index (BMI)'. The 'Customizable Definition' button is highlighted in red. The 'Select Anthropometric Measure for Obesity' section is highlighted in orange, showing 'Body mass index (BMI)'. The other sections (Reference Values for Blood Pressure, Triacylglycerols, HDL-C, Glucose, and HOMA-IR) are highlighted in yellow, showing the same reference values as in Screenshot 1. The 'Run Analysis' button is also present at the bottom.

Figure 11: Interface for the Customizable Definition option (highlighted in red) for Continuous Metabolic Syndrome Score in ObMetrics. Users can select between Waist Circumference and Body Mass Index as the anthropometric measure for obesity assessment (highlighted in orange), with each option providing specific reference values based on the selected definitions. Additionally, users can customize reference values for other MetS components—Blood Pressure, Triacylglycerols, HDL-C, Glucose, and HOMA-IR (highlighted in yellow). This customization allows users to adapt the MetS scoring system according to population-specific and study-specific definitions, as outlined in Table 5.

Once the user has selected the desired definition, they can proceed by clicking the **Run Analysis** button (highlighted in red) to initiate the calculation. Please note that before selecting and confirming a definition, it is essential to consider details such as the age range, ethnicity of the study population used to derive the reference values, cutoff points, original publications, and relevant clinical guidelines.

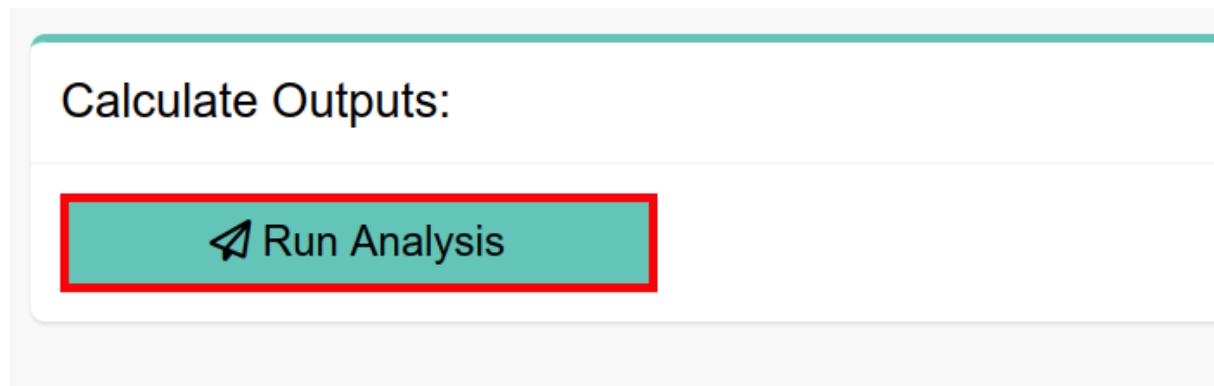


Figure 12: "Run Analysis" button highlighted in red, allowing users to initiate calculations after selecting their preferred definition for MetS analysis.

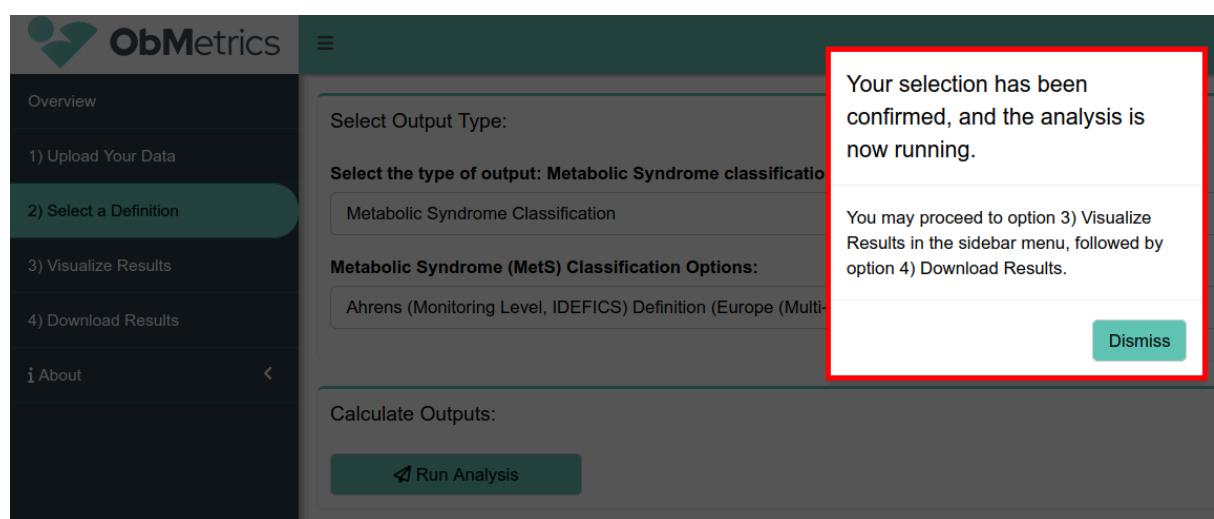


Figure 13: Confirmation notification displayed after initiating the analysis, highlighted in red, indicating that the user may proceed to the 3) Visualize Results and 4) Download Results sections.

Once the **Run Analysis** button is clicked, a notification (highlighted in red) will appear, confirming that the analysis has started. The message informs the user that they can now proceed to the next sections to view and download the results by selecting **3) Visualize Results** and **4) Download Results** from the sidebar menu.

When the user clicks on section **3) Visualize Results** in the sidebar menu, the central menu updates to display an interactive results table. An alert box appears (highlighted in red) with a message reminding the user to verify that all data entries fall within the appropriate age range, as discrepancies could lead to missing values. The message also notes that the estimation process may take a few seconds to complete. Click **Dismiss** on the alert box to fully access and view the results.

Figure 14: Interface for Visualize Results section in ObMetrics, showing the alert message reminding users to verify data consistency before visualizing the output results.

4.5. Interactive Results Visualization

In the **3) Visualize Results** section in the sidebar, the central menu is organized into three distinct panels for interactive data exploration. At the top, the **Interactive Table of Results** (highlighted in red) provides an interactive table displaying both input and output variables, allowing users to examine each component of the dataset. Below, two additional panels offer graphical representations of the data: the **Interactive One-Dimensional Plot** (highlighted in orange), which allows users to visualize individual variables, and the **Interactive Two-Dimensional Plot** (highlighted in yellow), which supports comparison between two variables, facilitating a deeper exploration of relationships within the dataset.

Figure 14. 3) Visualize Results section, featuring the Interactive Table of Results (top, highlighted in red) and two graphical panels below: Interactive One-Dimensional Plot (highlighted in orange) and

Interactive Two-Dimensional Plot (highlighted in yellow). These components provide a comprehensive view of the dataset's input and output variables.

Note that depending on the definition selected in Section 2) **Select a Definition**, the **Insulin Resistance (IR)** component may or may not appear in the results table (highlighted in red). This inclusion or exclusion of IR directly influences the output for **Altered_components**, which tallies the number of altered MetS components for each individual. This difference in definition parameters demonstrates the customization options available in ObMetrics to tailor the MetS evaluation definitions.

The screenshot displays two versions of the 'Interactive Table of Results' from the ObMetrics platform. Both tables include columns for various metabolic and anthropometric variables: BMI, QUICKI, HOMA_IR, Height_zscore, DBP, SBP, Blood_pressure, Excess_adiposity, Triglycerols, HDL_C, Glucose, Insulin_resistance, Altered_components, and Metabolic_Syndrome.

The upper table is associated with the Ahrens definition, as indicated by the highlighted 'Insulin_resistance' column. This column shows values such as 0.3, 0.32, 0.33, 0.31, 0.29, 0.31, 0.29, 0.27, 0.32, 0.39, and 0.32. The 'Altered_components' column for this table shows counts of 4, 3, 3, 4, 0, 4, 3, 0, 4, 0, and 0 respectively, contributing to a total of 22 altered components across the 12 rows.

The lower table is associated with the Zimmet definition, where the 'Insulin_resistance' column is not highlighted. Instead, it lists 'tanner_index' values (1, 2, 4, 2, 1, 4, 2, 1, 4, 1, 3, 3). The 'Altered_components' column for this table shows counts of 0, 2, 1, 1, 2, 2, 2, 1, 2, 3, 0, and 0 respectively, contributing to a total of 18 altered components across the 12 rows.

Figure 15: Interactive Table of Results in the "3) Visualize Results" section. The upper table applies the Ahrens definition, displaying the Insulin Resistance component (highlighted in red), which contributes to the Altered_components count. In contrast, the lower table uses the Zimmet definition, where IR is excluded, affecting the total altered components reported for each case.

In the **Interactive Table of Results**, users can explore the input and output variables with various color palettes representing variable ranges and the status of each component as normal or altered (green and red, respectively). Users can interact with the table for enhanced data interpretation by sorting, filtering, and highlighting specific records. For instance, variables can be sorted in ascending or descending order by clicking the icon next

to the variable name (highlighted in red) and toggling the order with a second click (highlighted in orange). Additionally, users can filter results based on variable values by selecting the icon below each variable name (highlighted in yellow). Individual rows can also be highlighted by clicking on the desired entry (highlighted in blue). Finally, users have the option to minimize the table by clicking the icon in the upper corner of the panel (highlighted in green), and can maximize it again by clicking the icon once more.

The figure consists of three vertically stacked screenshots of an "Interactive Table of Results". Each screenshot shows a table with 15 columns and approximately 15 rows of data. The columns are labeled: id, decimal_age, sex, height_m, weight_kg, wc_cm, dbp_mmHg, sbp_mmHg, tag_mg_dl, hdlc_mg_dl, glucose_mg_dl, insulin_microU_ml, tanner_index, BMI, QUICKI, and HOMA.

- Screenshot 1:** The "decimal_age" column header is highlighted with a red box, and the "sex" column header is highlighted with an orange box. The entire table has a light gray background.
- Screenshot 2:** The "decimal_age" column header is highlighted with an orange box. The table has a light gray background.
- Screenshot 3:** The "id" column header is highlighted with a yellow box. The "decimal_age" column header is highlighted with a yellow box. The "sex" column header is highlighted with a yellow box. The "height_m" column header is highlighted with a yellow box. The "weight_kg" column header is highlighted with a yellow box. The "wc_cm" column header is highlighted with a yellow box. The "dbp_mmHg" column header is highlighted with a yellow box. The "sbp_mmHg" column header is highlighted with a yellow box. The "tag_mg_dl" column header is highlighted with a yellow box. The "hdlc_mg_dl" column header is highlighted with a yellow box. The "glucose_mg_dl" column header is highlighted with a yellow box. The "insulin_microU_ml" column header is highlighted with a yellow box. The "tanner_index" column header is highlighted with a yellow box. The "BMI" column header is highlighted with a yellow box. The "QUICKI" column header is highlighted with a yellow box. The "HOMA" column header is highlighted with a yellow box. The "id" column contains several blue-highlighted rows (e.g., row 20, row 4, row 8, row 15, row 7, row 18, row 10, row 3, row 5, row 11).

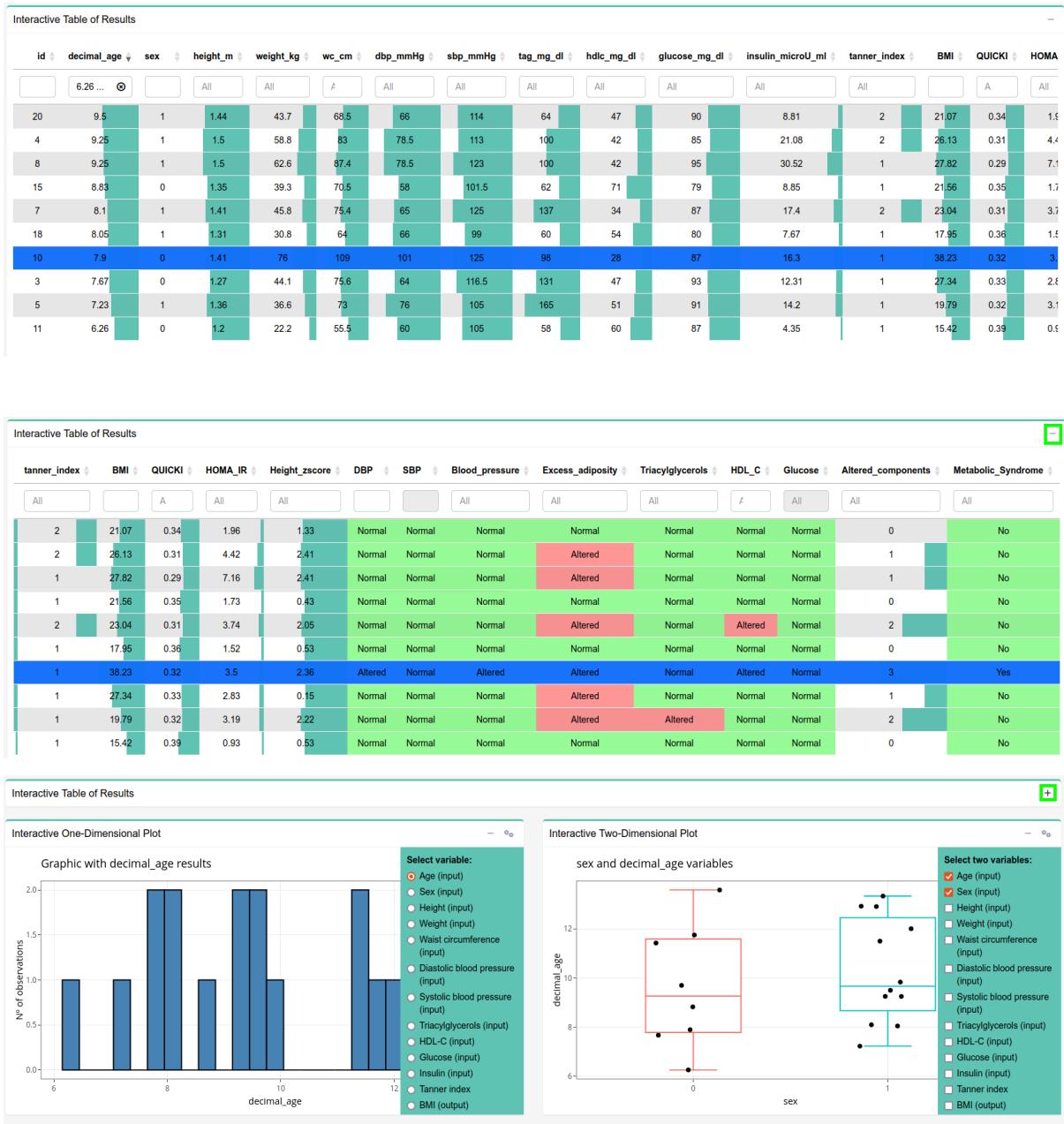
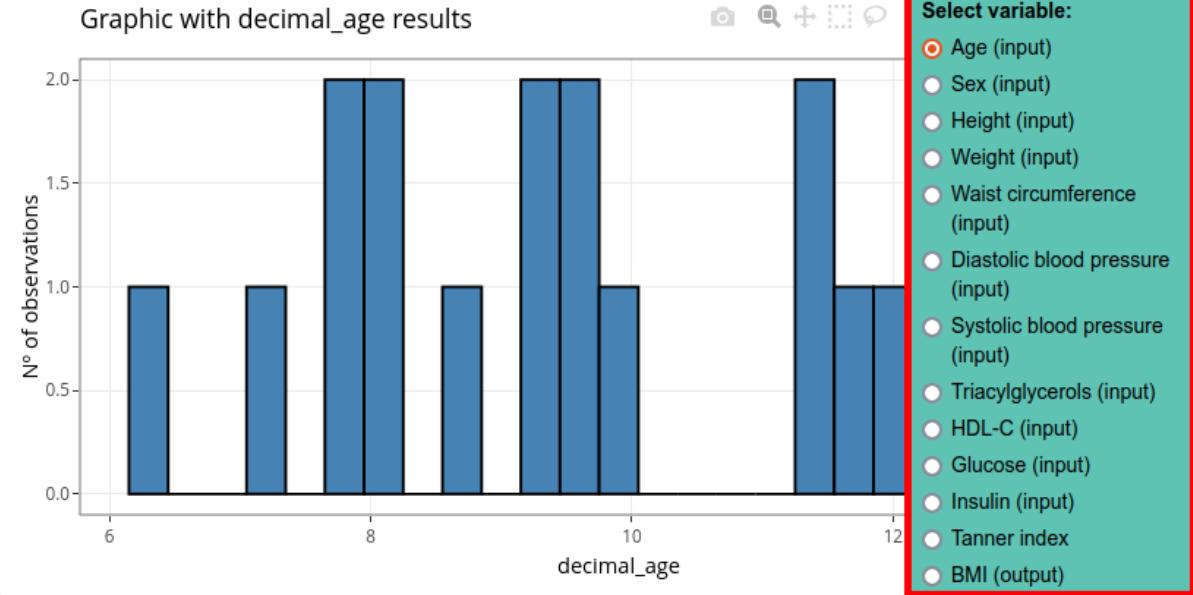


Figure 16: Overview of the Interactive Table of Results, showcasing sorting, filtering, highlighting, and minimization functionalities.

The user can select the variable(s) they wish to visualize from the side panel (highlighted in red). For the one-dimensional plot, a single variable can be selected, while for the two-dimensional plot, two variables are required. Once the desired variables are selected, the user can click the gear icon to hide the side panel, allowing for an expanded view and interaction with the plot (highlighted in orange).

Interactive One-Dimensional Plot



Interactive One-Dimensional Plot

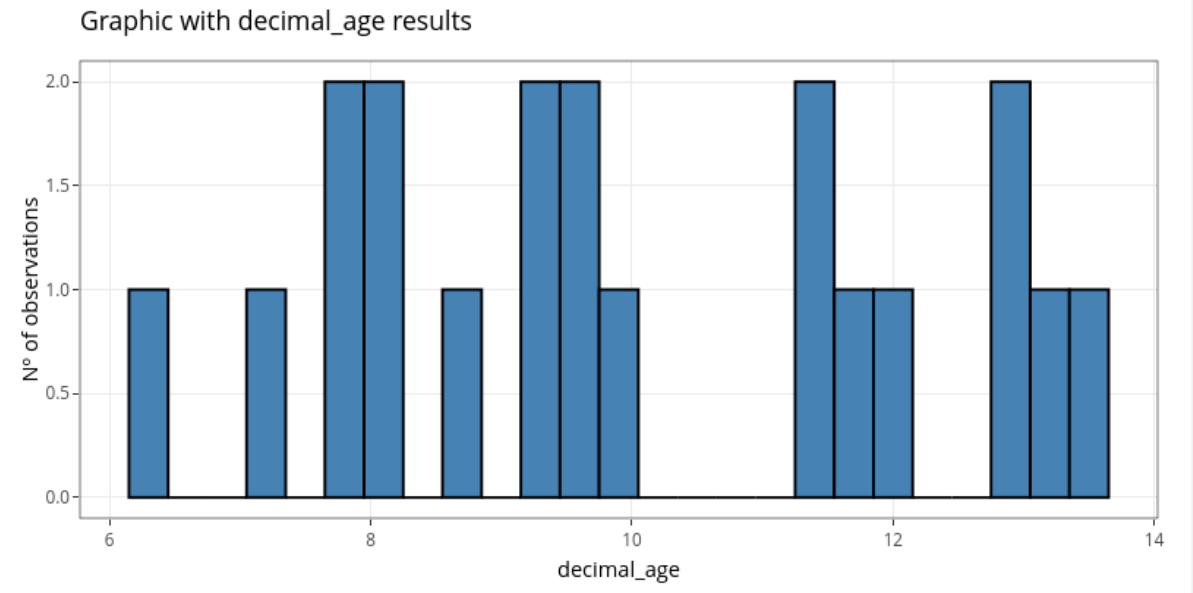


Figure 17: Interactive One-Dimensional Plot with options for selecting and visualizing variables, with controls for hiding the selection panel.

Both plot panels in the ObMetrics interface are interactive, leveraging Plotly's functionality. When hovering over the plots, users can view specific data points, percentages, or basic descriptive statistics, enhancing the interpretability of the visualized variables (highlighted in red). Each Plotly icon serves a purpose: [the download icon allows saving the plot as a PNG](#), zoom and pan icons enable users to focus on specific plot areas, box and lasso selection tools assist in selecting subsets of data points, and zoom in/out buttons adjust the

view. Additionally, autoscale and reset axis functions return the plot to its default view, while the "show closest data on hover" and "compare data on hover" options control data display interactions for hover events (highlighted in orange).

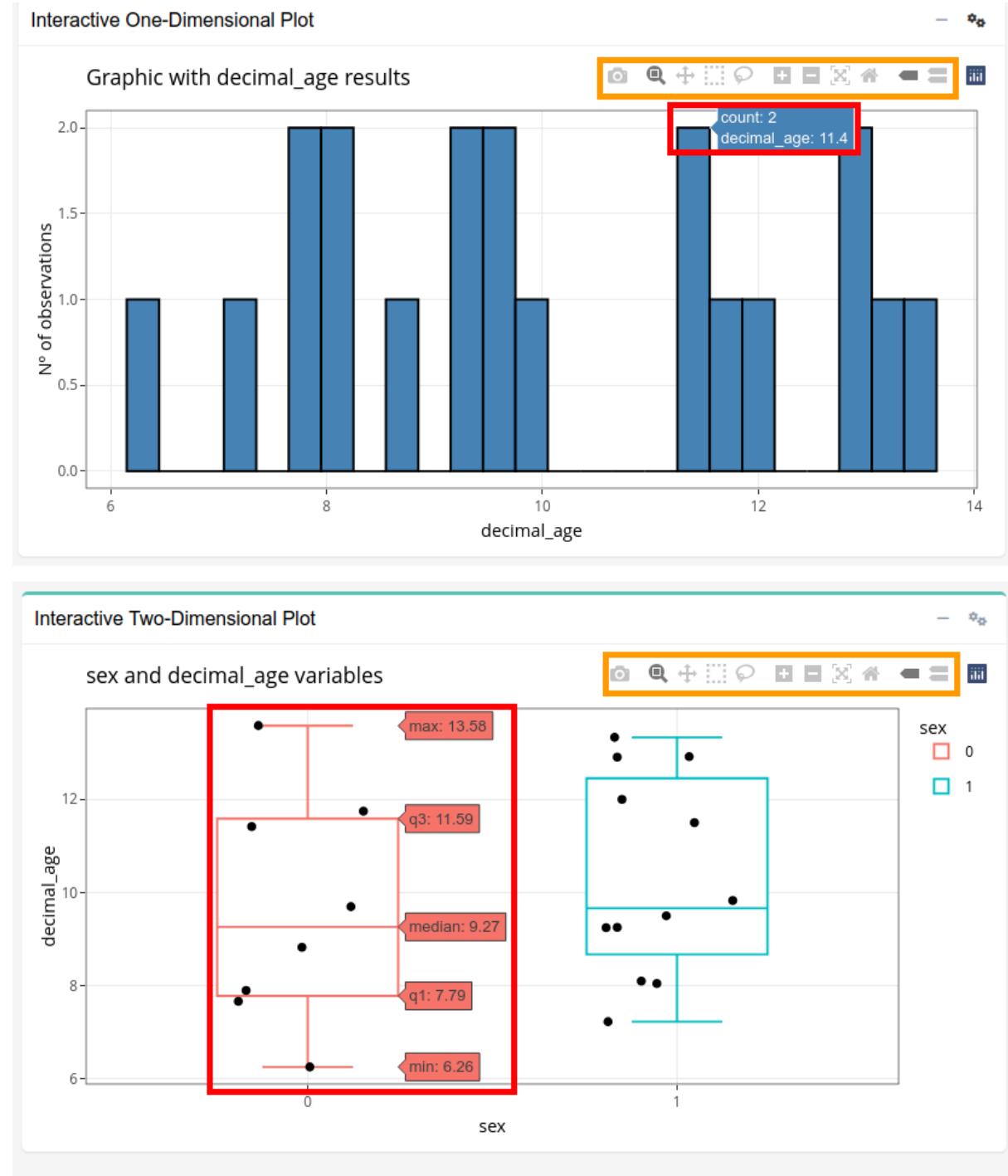
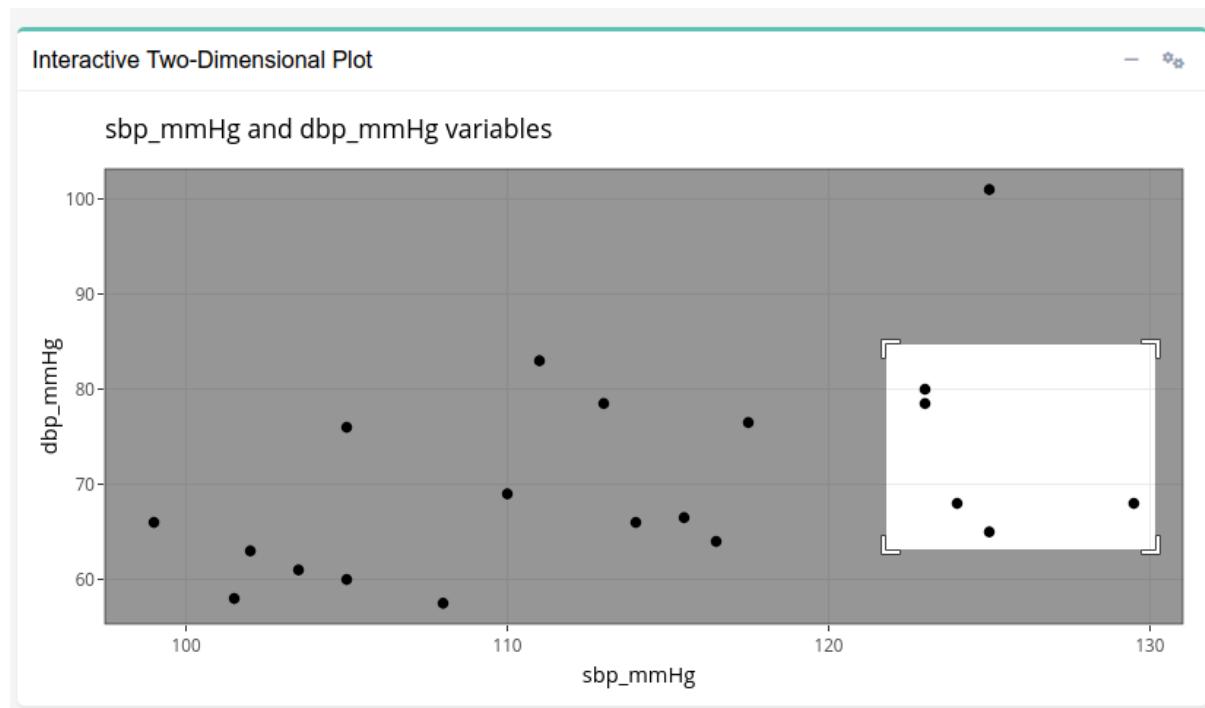
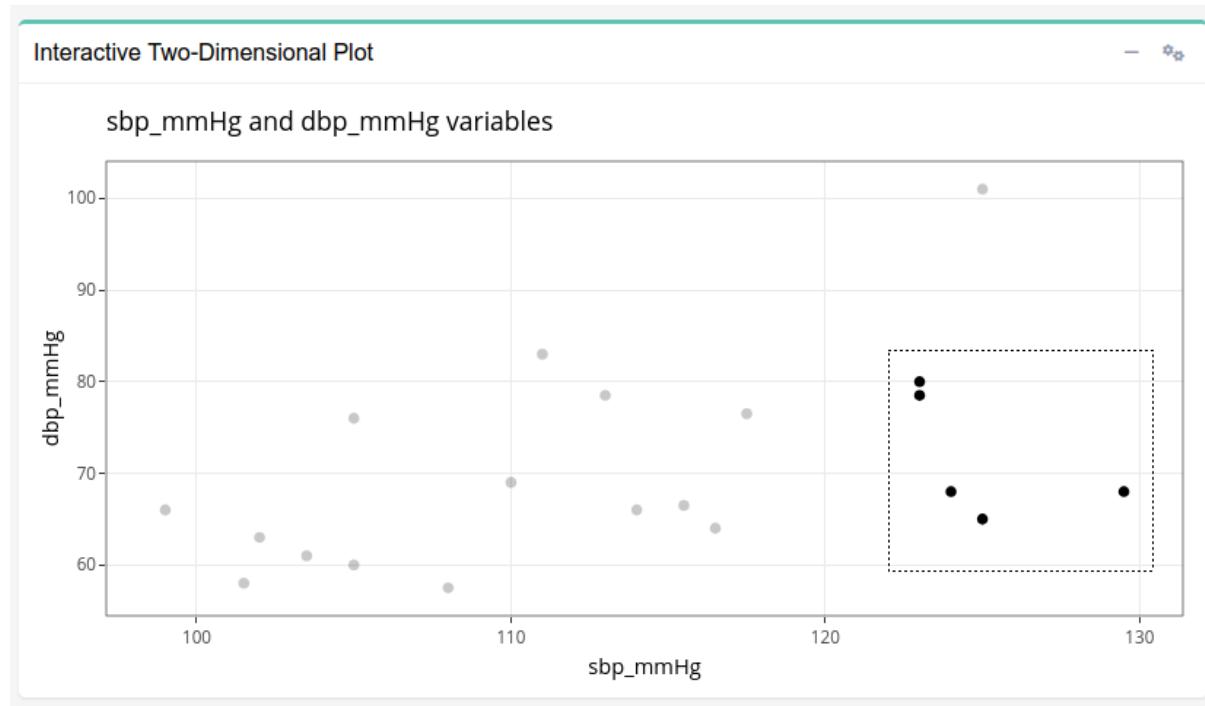


Figure 18. Interactive One-Dimensional and Two-Dimensional Plot panels with Plotly functionality for in-depth data visualization and analysis.

Some examples of these functionalities include using the box select tool to highlight specific patients of interest or zooming in to examine particular data points in greater detail, as

illustrated in Figure 19. These tools allow for a more focused and nuanced analysis of the data, aiding in the identification of patterns or individual outliers within the dataset.



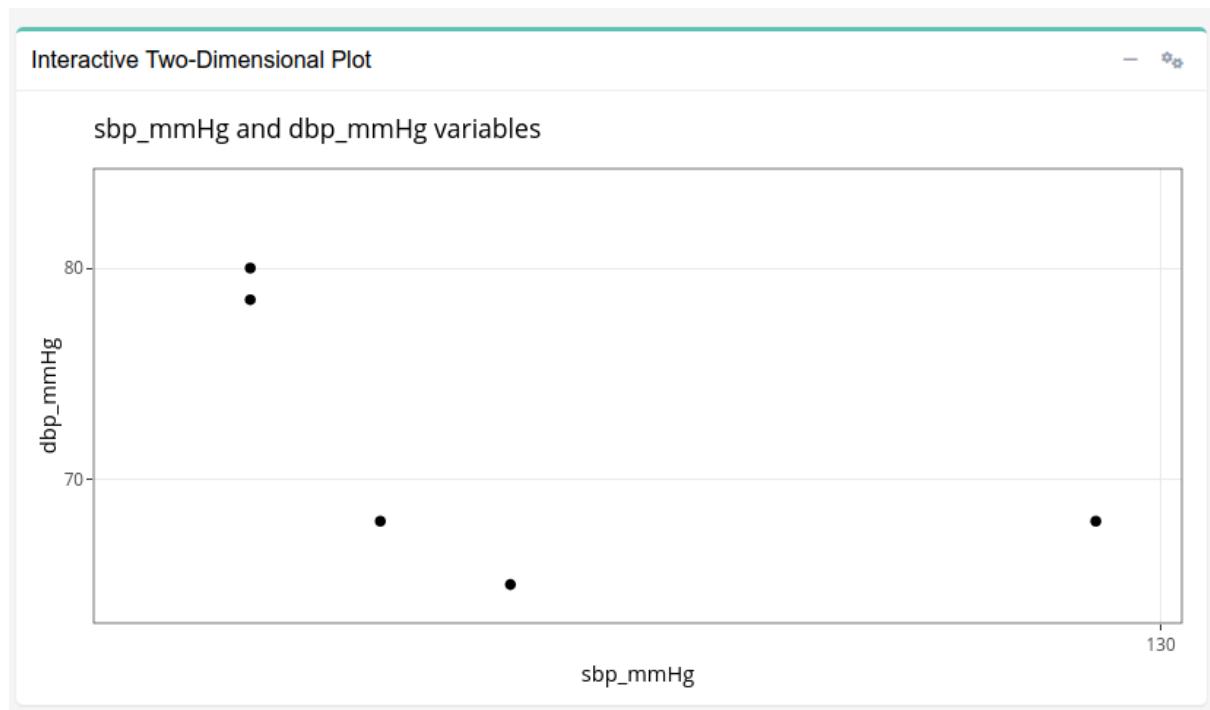
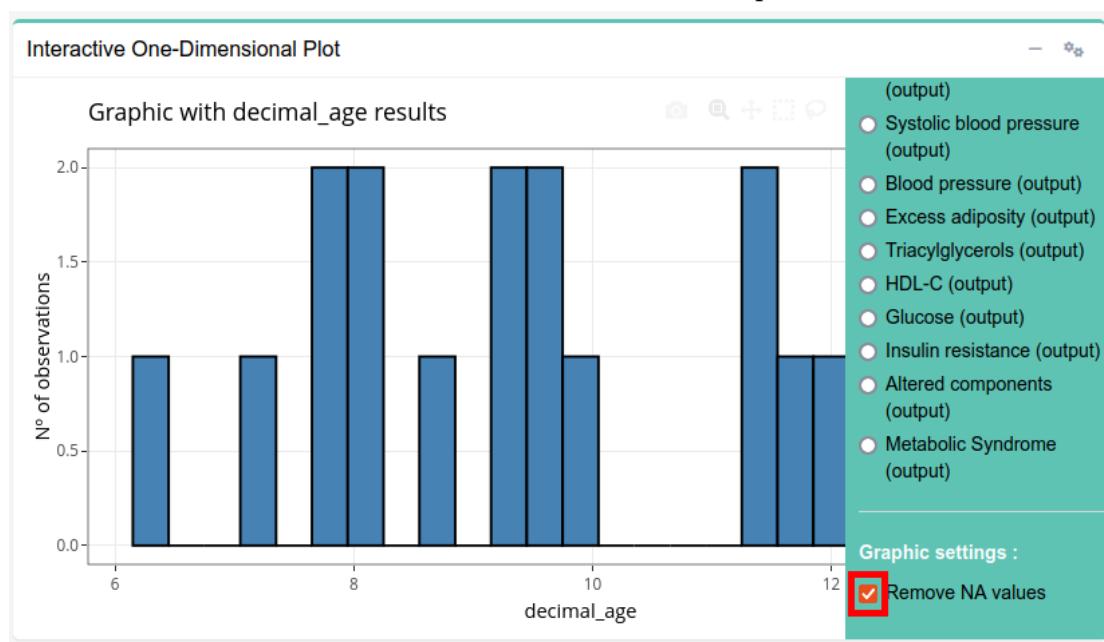


Figure 19. Demonstration of Plotly's interactive tools, such as box select (first screenshot) and zoom (second and third screenshot), for highlighting and examining selected patient data points in the ObMetrics interface.

In the interactive plot settings, users have the option to enhance their data visualization experience by selecting specific settings. For one-dimensional plots, users can choose to exclude missing values by enabling the "**Remove NA values**" option (highlighted in red). In the two-dimensional plots, the "**Change order axis**" feature (highlighted in orange) allows users to swap the axes, providing greater flexibility in data interpretation. These settings contribute to a more tailored and efficient visualization experience.



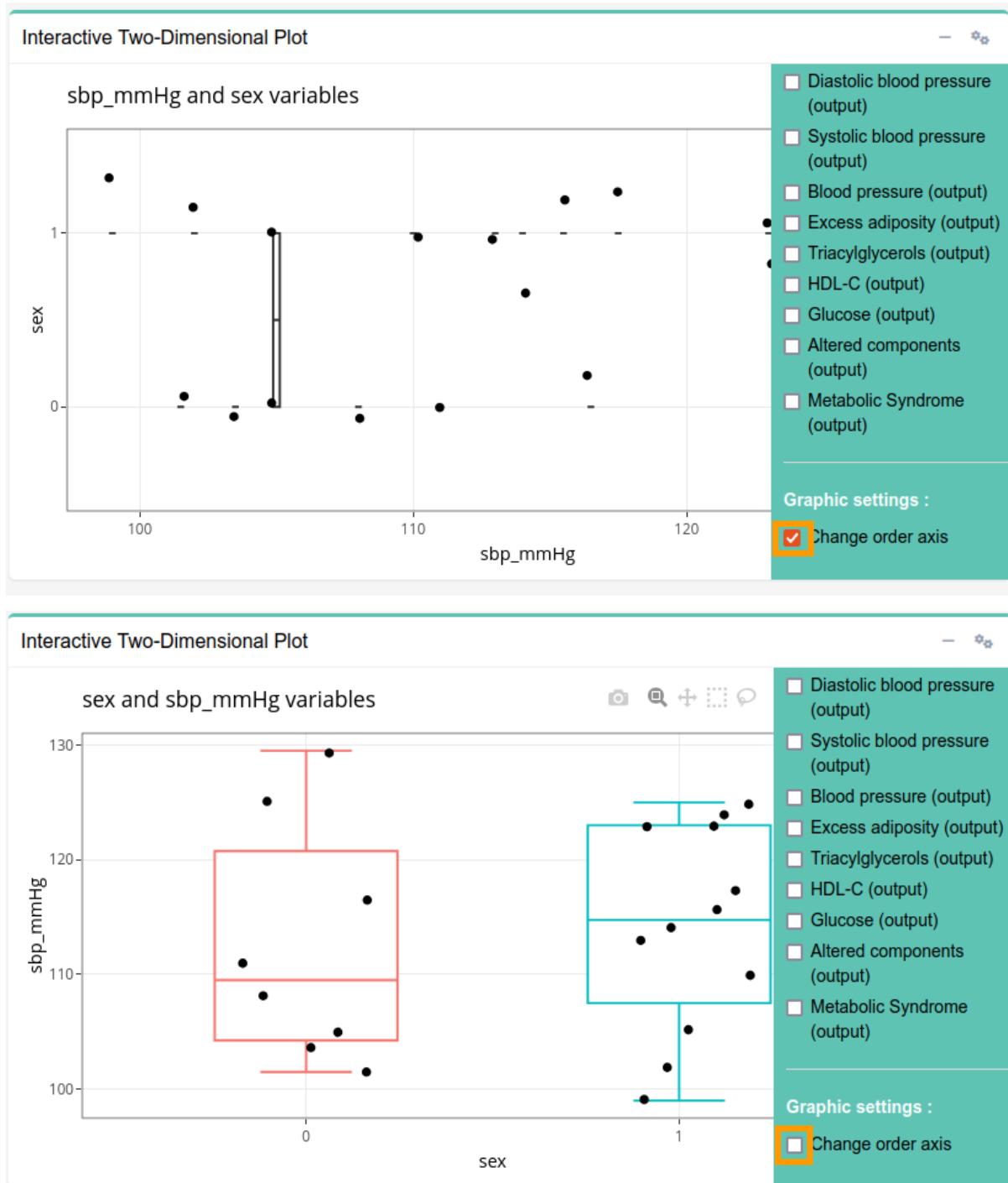


Figure 20: Illustration of user customization options in ObMetrics' interactive plots, showing the ability to remove missing values in one-dimensional plots and switch axis order in two-dimensional plots for optimal data exploration.

The user can minimize and maximize the plot panels using the same icon as in the Interactive Results Table. Finally, once the user has finished working in section **3) Visualize Results**, they can proceed to subsection **4) Download Results**. Upon clicking this option, the central menu layout will change accordingly.

4.5. Download Results

In section 4) **Download Results**, the user is presented with a single panel labeled "Download Results" in the central menu, featuring a button with the same name (highlighted in red). By clicking this button, the user can download the original data template uploaded to ObMetrics, now filled with all calculated outputs based on the previously selected definition. To provide a clear record of the chosen options, a log is displayed within this panel (highlighted in orange). Upon downloading, the output file includes two sheets: the first sheet contains the calculated results (highlighted in yellow), and the second sheet (highlighted in green) shows the same log as displayed on the panel, ensuring traceability of the definitions and thresholds applied.

The screenshot shows the ObMetrics software interface. On the left, there's a sidebar with navigation links: Overview, 1) Upload Your Data, 2) Select a Definition, 3) Visualize Results, 4) Download Results (which is highlighted in teal), and i About. The main area is titled "Download Results" and contains a large red button labeled "Download Results". Below the button is a log window with a yellow border, titled "ObMetrics_logs". The log content is as follows:

```

Definition Ahrens et al. 2014 (Monitoring Level, IDEFICS)
Excess_adiposity IDEFICS (Europe (Multi-ethnic)): WC >= 90th percentile by age and sex
Blood_pressure IDEFICS (Europe (Multi-ethnic)): BP >= 90th percentile of any pressures by age and sex
Triacylglycerols IDEFICS (Europe (Multi-ethnic)): TAG >= 90th percentile by age and sex
HDL_C IDEFICS (Europe (Multi-ethnic)): HDL-C <= 10th percentile by age and sex
Glucose IDEFICS (Europe (Multi-ethnic)): Glucose >= 90th percentile by age and sex
Insulin_resistance IDEFICS (Europe (Multi-ethnic)): HOMA-IR >= 90th percentile by age and sex
Version ObMetrics 1.0 ( 2024-11-06 )

```

Below this is a LibreOffice Calc spreadsheet window titled "2024-11-06_Obmetrics_output.xlsx - LibreOffice Calc". The spreadsheet has several tabs at the bottom: Archivo, Editar, Ver, Insertar, Formato, Estilos, Hoja, Datos, Herramientas, Ventana, Ayuda. The visible sheet is the "Output" tab, which contains a table of data. The table has columns: Q, O, P, R, S, T, U, V, W, X, Y, Z, AA. The rows contain various numerical and categorical values, such as "QUICKI", "HOMA_IR", "Height_zscore", "DBP", "SBP", "Blood_pressure", "Excess_adiposity", "Triacylglycerols", "HDL_C", "Glucose", "Insulin_resistance", "Altered_components", and "Metabolic_Syndrome". A yellow box highlights the entire table area. At the bottom of the calc window, there are buttons for Buscar (Search), Log, and PageStyle.

2024-11-06_Obmetrics_output.xlsx - LibreOffice Calc

	ObMetrics_logs
Definition	Ahrens et al. 2014 (Monitoring Level, IDEFICS)
Excess_adiposity	IDEFICS (Europe (Multi-ethnic)): WC >= 90th percentile by age and sex
Blood_pressure	IDEFICS (Europe (Multi-ethnic)): BP >= 90th percentile of any pressures by age and sex
Triacylglycerols	IDEFICS (Europe (Multi-ethnic)): TAG >= 90th percentile by age and sex
HDL-C	IDEFICS (Europe (Multi-ethnic)): HDL-C <= 10th percentile by age and sex
Glucose	IDEFICS (Europe (Multi-ethnic)): Glucose >= 90th percentile by age and sex
Insulin_resistance	IDEFICS (Europe (Multi-ethnic)): HOMA-IR >= 90th percentile by age and sex
Version	ObMetrics 1.0 (2024-11-06)

Figure 21: The "Download Results" panel in ObMetrics, showing the download button and the log of selected options. The downloaded file includes the filled output on the first sheet and the applied definitions log on the second sheet, as shown in the additional screenshots.

It is advisable to retain not only the first sheet with the output results but also the second sheet of the downloaded Excel file, which contains detailed information on the selected definition, cutoff points, reference values used, as well as the date and version of ObMetrics. This additional sheet serves as essential documentation, providing context and ensuring the reproducibility of the results for future reference.

5. Support and Documentation

In the "About" section, users can find comprehensive information to facilitate the use of ObMetrics. By selecting "User Guide" in the sidebar, the main panel displays this same user guide, where users can access details about the app, reference values, prerequisites, interface description, step-by-step instructions, additional information, best practices, FAQs, and references. If users select "Quick Tutorial," the central menu changes to show a short video tutorial that provides an intuitive walkthrough of the Shiny app's main functions.

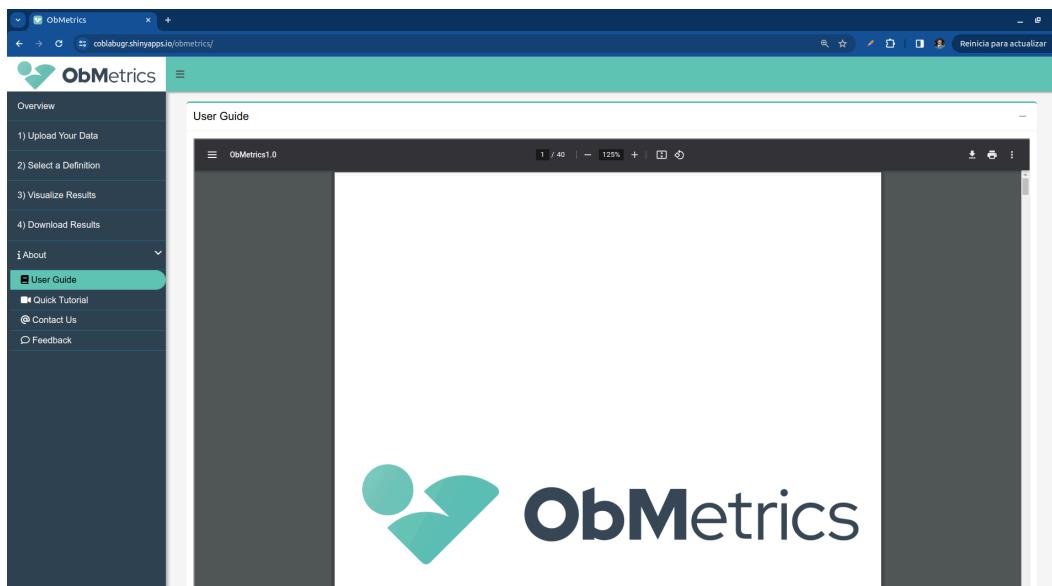


Figure 22: The "User Guide" panel within the "About" section, displaying the user guide directly in the application for easy reference.

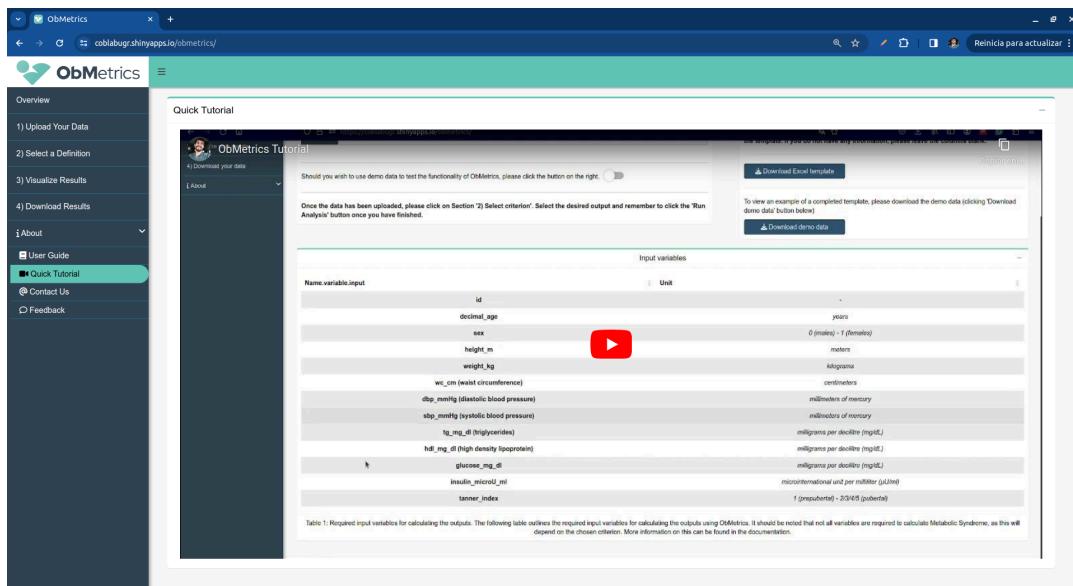


Figure 23: The "Quick Tutorial" section, featuring a video tutorial that provides a brief overview of ObMetrics' primary functionalities.

For users who have questions, suggestions, or feedback, the "Contact Us" section in the sidebar presents information about the primary developers of ObMetrics. Each developer's panel includes icons linking to their email, ORCID, LinkedIn, and GitHub profiles. Lastly, by clicking "Feedback" in the sidebar, users are redirected to a [Google Form](#) for usability testing. All users are encouraged to complete this survey to help the development team assess user satisfaction and improve ObMetrics.

The screenshot shows the 'Contact Us' section of the ObMetrics application. On the left, a sidebar lists navigation options: Overview, 1) Upload Your Data, 2) Select a Definition, 3) Visualize Results, 4) Download Results, i About, User Guide, Quick Tutorial, Contact Us (which is highlighted in green), and Feedback. The main area displays four developer profiles in cards:

- Álvaro Torres-Martos**: Postdoctoral Researcher at University of Granada. Description: Álvaro Torres-Martos is a postdoctoral bioinformatician and biostatistician at the University of Granada's Institute of Nutrition and Food Technology (INYTA) and a member of the Bionut research group. His PhD work centers on using multi-omics and explainable AI to advance molecular insights into childhood obesity. He is also interested in applying omics and exposome data to public health, which led to an international research stay at the University of Oxford's Nuffield Department of Primary Care Health Sciences. Buttons: Email, GitHub, LinkedIn, GitHub.
- Augusto Anguita-Ruiz**: Postdoctoral Researcher at ISGlobal. Description: Augusto Anguita-Ruiz is a biological data scientist specialised in the analysis of complex epidemiological datasets such as those composed of clinical, omics, biochemical, and environmental data. At ISGlobal he is an investigator of the EU-H2020 ATHLETE exposome project. His main technical skills include a strong statistical, programming and data visualisation background, with special emphasis on the use of machine learning models. He has also experience in personalised medicine with the development of e-health apps for clinicians and health professionals and a predictive genetic algorithm. Buttons: Email, GitHub, LinkedIn, GitHub.
- Francisco Requena**: Postdoctoral Researcher at Weill Cornell Medicine. Description: Francisco-Requena did his PhD at the Clinical Bioinformatics lab in the Imagine Institute (Paris). His current work focuses on the development of computational methods, including machine-learning, for the clinical interpretation of variants in rare disease patients. Buttons: Email, GitHub, LinkedIn, GitHub.
- Jesús Alcalá-Fdez**: Full Professor at University of Granada and DaSCI. Description: He is a full professor at the Department of Computer Science and Artificial Intelligence of the University of Granada, where he is a member of the research group 'Soft Computing and Intelligent Information Systems' (SCIS), TIC-186, the Andalusian Interuniversity Institute in Data Science and Computational Intelligence (DaSCI), and the research centre in Information and Communication Technologies (CITIC-UGR). His research activity is supported by a high number of publications in the best journals in the research areas in which he works and by the number of citations they have obtained. He currently has an H-index of 26 and more than 5357 citations according to the Web of Science and an H-index of 30 and more than 8877 citations according to Google Scholar, which shows that these publications have produced a certain impact on the research community. In 2020 he has been included in the list of researchers 'World Scientist, World's Top 2% Scientists' published in the prestigious journal Plos Biology, which lists the world's elite in the world of scientific research. Buttons: Email, GitHub, LinkedIn, GitHub.

Figure 24: The "Contact Us" panel, where users can access the contact details and professional profiles of the primary ObMetrics developers.

The screenshot shows the 'Feedback' section of the ObMetrics application. The sidebar is identical to Figure 24. The main area displays a Google Form titled 'Usability testing on ObMetrics'. The form includes:

- A header message: 'Please fill out the form! We want to know your opinion!' followed by the ObMetrics logo.
- An input field for 'Correo *': 'alvarotorresmartos@gmail.com' with a 'Cambiar de cuenta' link.
- A note: '* Indica que la pregunta es obligatoria'.
- An input field for 'Correo *': 'Tu dirección de correo electrónico'.
- A text box for 'PSSUQ (Post-Study System Usability Questionnaire)':
 - PSSUQ Questionnaire: Questions 1 to 16: Overall; Questions 1 to 6: System Usefulness (SYSUSE); Questions 7 to 12: Information Quality (INFOQUAL); Questions 13 to 16: Interface Quality (INTERQUAL)
- A rating scale: '1. Overall, I am satisfied with how easy it is to use this system. *' with a range from 'Strongly Disagree' to 'Strongly Agree'.

Figure 25: The "Feedback" section, with a Google Form for users to provide usability feedback, supporting continuous improvement of ObMetrics.

6. More information.

For users seeking deeper insights into the technical aspects and foundational research behind ObMetrics, we invite you to explore our GitHub repository, accessible at <https://github.com/AlvaroTorresMartos/ObMetrics>. This repository provides the scripts used to generate tables and figures derived from the case study employed in validating ObMetrics' utility.

In addition to the source code, users will find comprehensive documentation detailing the application's structure and the analytical pipeline followed to produce the outputs. The repository further outlines the license under which ObMetrics is shared, fostering transparency and promoting collaborative contributions from the research community. Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND 4.0), ObMetrics welcomes usage in academic and research settings, with attribution to the authors while maintaining the integrity of the original tool.

We encourage you to explore this resource to gain a complete understanding of the methodologies implemented within ObMetrics and to potentially expand or customize the application for your own research needs.

7. Best Practices for Using ObMetrics

Pediatric MetS is intricately linked to the future risk of type II diabetes and cardiovascular diseases in adulthood. Despite its importance, there is currently no universally accepted definition of pediatric MetS, and ongoing debate persists regarding whether each component should carry equal weight. Furthermore, there is ambiguity about the inclusion of HOMA-IR as an additional component of MetS versus its use solely in conjunction with glucose levels to assess glucose homeostasis. As noted in the introduction of this guide, defining MetS in pediatric populations remains complex, and various expert opinions highlight different approaches to diagnosis, each with unique advantages and limitations.

Currently, two predominant approaches exist among pediatric experts for defining MetS in children. The first approach supports using MetS definitions and reference tables as presented in the original publications, given that these definitions often have high diagnostic accuracy for the ethnically specific population studied. However, a limitation of this approach is that these definitions may not be as accurate when applied to populations with differing ethnic backgrounds, potentially leading to diagnostic discrepancies. This has led to a second approach, wherein pediatricians modify internationally accepted definitions by incorporating national or region-specific reference tables. This strategy aims to enhance diagnostic accuracy for populations with different ethnic profiles than those studied in the original definition. However, modifying a MetS definition to fit a different population may alter its diagnostic power, an adjustment that requires careful consideration by a team of expert pediatric researchers who can evaluate the trade-offs between diagnostic accuracy and potential biases.

For researchers and clinicians using ObMetrics, pediatric experts involved in this study recommend several critical factors to optimize MetS assessment. First and foremost, it is advisable to select a MetS definition derived from a reference population that closely resembles the study population in terms of ethnicity and geography. In addition, including insulin resistance as an additional metabolic component is strongly recommended to provide a comprehensive evaluation of metabolic risk factors in children. Instead of relying on fixed cutoff points, using percentiles based on sex, age, and Tanner stage can offer a more nuanced and accurate diagnostic value. Given the variability in growth and pubertal development, age-based percentiles should ideally be supplemented with Tanner-based percentiles, and for BP, height percentiles should also be considered to ensure diagnostic precision across a wide age range.

Another essential consideration is the ethnic applicability of the selected MetS definition. When using reference values and definitions derived from a specific ethnic population, it is crucial to assess whether these thresholds are appropriate for different ethnic backgrounds.

Applying definitions with ethnic-specific reference values to populations outside that ethnic context may lead to misclassification and inaccurate diagnoses. Conversely, editing an existing MetS definition may diminish its original diagnostic power, as the adjusted definitions may no longer reflect the population for which it was validated.

An alternative to categorical MetS classification is the use of a continuous MetS z-score, both globally and for individual components. The MetS z-score provides a quantitative assessment of MetS severity, which may be especially valuable for tracking changes in metabolic health over time or comparing metabolic risk across populations. Using z-scores can also offer a more refined picture of metabolic risk progression than binary classification, which may be more appropriate for certain research or clinical contexts. The choice between categorical classification and z-score assessment should align with the clinical or research objectives at hand, recognizing that MetS definitions may vary in their suitability for diagnostic, monitoring, or investigative purposes.

In conclusion, selecting and applying a MetS definition in pediatric populations requires a careful, context-sensitive approach. Considerations should include age range applicability, pubertal development stage (assessed through Tanner staging), ethnicity, and the type of MetS assessment (categorical vs. continuous). Additionally, MetS may serve different clinical objectives—diagnosis, monitoring, and research—and not all definitions are equally suited to these varied purposes. By thoughtfully selecting MetS definitions and adjusting parameters in ObMetrics, users can optimize the accuracy and relevance of MetS assessments, ultimately contributing to better pediatric health outcomes.

8. Frequently Asked Questions (FAQ)

1. What types of data are required to use ObMetrics?

- ObMetrics requires an Excel file structured according to the provided template. Key variables include anthropometric data, BP, lipid profiles, glucose, and optionally insulin levels and Tanner stage. Ensure all data entries follow the format specified in the template for accurate analysis.

2. How do I choose the right MetS definition for my study population?

- Selecting a MetS definition depends on factors like the age, sex, and ethnicity of your study population. ObMetrics provides multiple definitions and customization options, allowing you to align with populations similar to your cohort. For instance, if your population is ethnically diverse, you may opt for definitions validated in multi-ethnic studies.

3. Can I use ObMetrics for longitudinal studies?

- Yes, ObMetrics can be used for both cross-sectional and longitudinal studies. For longitudinal studies, using the continuous MetS z-score option may provide a more nuanced view of changes over time in metabolic health.

4. What is the difference between Metabolic Syndrome Classification and Continuous MetS Score in ObMetrics?

- The Metabolic Syndrome Classification provides a binary outcome for each component, indicating if an individual meets MetS definitions (Yes/No). The Continuous MetS Score option, on the other hand, calculates z-scores for each component and an overall MetS score, which may be more suitable for identifying trends over time or making comparisons across different groups.

5. How do I interpret the Interactive Results Table?

- The Interactive Results Table displays both input and output data for each individual. Green indicates normal levels, while red indicates altered levels. You can sort, filter, and highlight rows to better examine specific data points, helping you identify patterns or outliers in your dataset.

6. How can I include or exclude Insulin Resistance (IR) as a MetS component?

- In the "Select a Definition" section, you can choose whether to include IR by selecting the HOMA-IR option. Including IR can provide additional insights into metabolic health for all populations.

7. What are the best practices for using ObMetrics with different age groups?

- For pediatric populations, it's essential to select definitions that consider growth and development stages. Using percentiles based on age and sex, where available, will enhance diagnostic accuracy. For BP, incorporating height percentiles is also recommended for a more precise assessment.

8. How do I handle missing data in ObMetrics?

- If your dataset contains missing values, ObMetrics allows you to choose the "Remove NA values" option in the plot settings. This feature excludes missing data from the visualization, providing a cleaner analysis. However, it's best to complete data as much as possible before analysis for comprehensive results.

9. Why do the results differ when I use national versus international reference values?

- MetS definitions may vary in diagnostic power depending on the population for which they were developed. Definitions based on international definitions might not be as accurate for some ethnic groups. Adjusting reference values based on national data may improve diagnostic precision, but this requires validation to ensure consistent results.

10. Can ObMetrics output be used for clinical diagnosis?

- ObMetrics is intended primarily for research and epidemiological studies rather than direct clinical diagnosis. It provides diagnostic definitions for MetS as per various definitions, but clinical judgment and local guidelines should guide any diagnostic or treatment decisions.

11. How can I download and document my analysis results?

- In the "Download Results" section, you can download the analyzed dataset in Excel format. The output includes two sheets: the first contains calculated results, while the second logs the definitions, cutoff points, and reference values used, along with the version of ObMetrics and the date of analysis. Retaining both sheets is recommended for traceability and documentation.

12. How is the feedback provided in the "Feedback" section used?

- Feedback gathered through the Google Form in the "Feedback" section is used to evaluate user satisfaction and identify areas for improvement. All input is reviewed by the development team to enhance the app's usability, accuracy, and relevance for future versions.

13. Where can I find additional technical resources or code for custom analysis?

- Detailed technical resources, including R scripts for generating case study results and figures, are available in our GitHub repository at <https://github.com/AlvaroTorresMartos/ObMetrics>. This repository also includes license details and additional documentation to support advanced users interested in further customization.

14. Is ObMetrics suitable for all types of pediatric research?

- ObMetrics can be used for various research purposes, such as diagnostic studies, monitoring metabolic risk over time, or exploring epidemiological patterns. However, each MetS definition may vary in suitability based on study objectives. For instance, continuous MetS scores might be more appropriate for monitoring trends, while binary classification may suit prevalence studies.

15. Can I contribute to the development of ObMetrics?

- ObMetrics is open to collaborative input. If you have suggestions or wish to contribute to its development, please contact us via the "Contact Us" section, where you can find links to the development team's contact information and GitHub profiles.

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