2.º CICLO

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Assessing the COVID-19 pandemic effects on child development

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effects on child development

Avaliação dos efeitos da pandemia de COVID-19

no desenvolvimento infantil

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Resumo

Introdução: A pandemia de COVID-19 emergiu como um desafio a nível global, com implicações para a saúde pública e para a sociedade em geral. As estratégias de contenção implementadas, incluindo confinamentos, produziram mudanças no estilo de vida das populações, levantando questões sobre o seu impacto no crescimento e desenvolvimento infantojuvenil.

Objetivos: Analisar o impacto da pandemia de COVID-19 nos padrões de crescimento de uma coorte de crianças e jovens da região Norte de Portugal.

Materiais e Métodos: Foi realizado um estudo observacional retrospetivo, com dados dos registos de saúde eletrónicos de duas unidades de saúde, no âmbito dos Cuidados de Saúde Primários. O estudo centrou-se nos parâmetros ao nascimento e nos dados de crescimento de crianças nascidas entre 2002 e 2023. A análise de dados foi realizada com recurso aos softwares R e IBM SPSS Statistics. A investigação envolveu uma comparação de z-scores com populações de referência validadas a nível internacional, assim como uma comparação com a população índice do próprio estudo, referente ao período pré-pandémico. Para mitigar fatores confundidores, os dados foram ajustados através de modelos ANCOVA.

Resultados: Foram incluídos dados de 4298 crianças, sendo 2183 (50,8%) rapazes e 2115 (49,2%) raparigas. A idade gestacional média foi de 38,6 (DP 1,7) semanas, o comprimento médio ao nascimento foi de 48,8 (DP 2,4) cm, o peso médio ao nascimento foi de 3,167 (DP 0,502) kg e o perímetro cefálico médio ao nascimento foi de 34,1 (DP 1,6) cm. A análise multivariada revelou diferenças significativas no perímetro cefálico ao nascimento nos rapazes, entre o grupo de controlo e o grupo do pico da pandemia, que incluiu nascidos em 2021 (p=0,002). Quanto ao desenvolvimento infantil, foi realizada a análise de 202 452 medições antropométricas e de pressão arterial, revelando algumas alterações entre os grupos de controlo e da pandemia. Para as idades de 0 a 1 ano, os z-scores de IMC foram menores durante a pandemia, com uma diferença de 0,088 ($p<0,001$). Para as idades de 5 a 9 anos, os z-scores de IMC foram maiores durante a primeira fase de confinamento e respetiva reabertura, com uma diferença de 0,181 ($p=0,005$) em comparação com os valores pré-pandemia, e menores do que o grupo controlo durante a terceira fase de confinamento e respetiva reabertura, com uma diferença de 0,079 ($p=0,047$). Quanto às crianças com idades entre 10 e 16 anos, os z-scores de IMC foram significativamente maiores durante a pandemia, com uma diferença de 0,172 ($p<0,001$), mas sem significância estatística durante a terceira fase de confinamento e respetiva reabertura. Os z-scores de pressão arterial sistólica foram mais elevados entre crianças com idades entre 5 e 9 anos durante a pandemia, com uma diferença de 0,127 ($p<0,001$), mas sem significância estatística durante o primeiro ano de restrições. O aumento nesses z-scores foi detetado mais cedo e de forma mais expressiva em crianças com mais de 10 anos, com uma diferença de 0,185 ($p=0,002$) em comparação com os dados pré-pandemia. Os z-scores de pressão arterial diastólica foram mais elevados durante a pandemia em todas as idades, em comparação com o grupo pré-pandemia: 0,159 para idades de 2 a 4 anos ($p=0,027$), 0,214 para idades entre os 5 e os 9 anos ($p<0,001$) e 0,331 para idades acima de 10 anos.

Conclusões: A pandemia de COVID-19 teve impacto nas medidas ao nascimento e no desenvolvimento infantojuvenil. A resiliência, a adaptabilidade e a prestação adequada de cuidados de saúde infantil apontam para um caminho de recuperação na era pós-pandemia, em vez de um efeito de dano permanente.

Palavras-Chave

Parâmetros ao nascimento; Idade gestacional; Padrões de crescimento; Desenvolvimento infantil; Desenvolvimento juvenil; COVID-19; Gráficos de crescimento; Análise multivariada.

Abstract

Introduction: The COVID-19 outbreak emerged as a global challenge with far-reaching implications for public health and society at large. The implemented mitigation strategies, including lockdowns, have prompted changes in lifestyles, raising questions about their impact on children's growth and development.

Objectives: To analyse the impact of the COVID-19 pandemic on the growth patterns of a child and youth cohort from the North region of Portugal.

Materials and Methods: An observational retrospective study was carried, with data retrieved from the electronic health records of two Primary Care units. The analysis focused on birth parameters and child growth data for children born between 2002 and 2023. Data analysis was performed using R software and IBM SPSS Statistics. The study involved a comparison with internationally validated reference standards using z-scores and a comparison with the study's own index population from the pre-pandemic period. To account for confounding factors, data were adjusted through ANCOVA models.

Results: Data from 4,298 children, 2,183 (50.8%) boys and 2,115 (49.2%) girls were included for analysis. Mean gestational age was 38.6 (SD 1.7) weeks, mean birth length was 48.8 (SD 2.4) cm, mean birth weight was 3.167 (SD 0.502) kg, and mean birth head circumference was 34.1 (SD 1.6) cm. The multivariate assessment revealed significant differences in birth head circumference among boys between the control group and the peak pandemic group, comprising infants born in 2021 (p=0.002). As for child growth development, the analysis of 202,452 measurements was carried out, unveiling some changes between the control and the pandemic groups. For ages 0 to 1 years old, BMI z-scores were lower during the pandemic by 0.088 (p<0.001). For ages 5 to 9 years old, BMI z-scores were higher during the first lockdown and reopening phases by 0.181 (p=0.005) when compared to the pre-pandemic values, and lower than the pre-pandemic group during the third lockdown and reopening periods by 0.079 (p=0.047). As for children aged 10 to 16 years old, BMI z-scores were significantly higher during the pandemic by 0.172 (p<0.001), but with no statistical significance during the third lockdown and reopening stages. Systolic blood pressure (BP) z-scores were higher among children aged 5 to 9 years old during the pandemic, by 0.127 (p<0.001), but with no statistical significance within the first year of restrictions. The rise in systolic BP z-scores was detected sooner and more expressively in children aged over 10 years, by 0.185 (p=0.002) compared to the pre-pandemic data. Diastolic BP z-scores were higher during the pandemic among all ages, when compared to the pre-pandemic group: by 0.159 for ages 2 to 4 years old (p=0.027), by 0.214 for ages 5 to 9 years old (p<0.001) and by 0.331 for ages over 10 years old.

Conclusions: The COVID-19 pandemic prompted changes in birth parameters and child growth development. Child and youth's resilience, adaptability, and adequate healthcare provision point towards a path of recovery in the post-pandemic era rather than a permanent damage effect.

Keywords

Birth parameters; Gestational age; Growth patterns; Child development; Adolescent development; COVID-19; Growth Charts; Multivariate analysis.

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List of Abbreviations

2-way ANCOVA	2-way Analysis of Covariance
BMI	Body Mass Index
BP	Blood pressure
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus Disease 2019
DBP	Diastolic Blood Pressure
EMM	Estimated Marginal Means
NHLBI	National Heart, Lung, and Blood Institute
SNS	National Health Service - "*Serviço Nacional de Saúde*"
SBP	Systolic Blood Pressure
SD	Standard deviation
SITAR	Super Imposition by Translation and Rotation
PNSIJ	National Child and Youth Health Surveillance Programme - "*Programa Nacional de Saúde Infantil e Juvenil*"
WHO	World Health Organization

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Introduction

Background

The coronavirus disease 2019 (COVID-19) outbreak, caused by the novel coronavirus SARS-CoV-2, has emerged as a global challenge with far-reaching implications for public health, the global economy and society. The outbreak was designated a public health emergency of international concern by the World Health Organization (WHO) on 30th January 2020.[1] Due to its rapid spread worldwide, it was declared a pandemic by 11th March 2020, resulting in unique global circumstances aimed at restraining disease transmission.[2]

The implemented strategies, which involved the definition of lockdown periods in many countries, prompted changes in the lifestyles of the affected populations.[3] The impact of these restrictions on dietary habits, physical activity and mental health has been a topic of interest and analysis within the scientific community.[4-7] Specifically, the consequences of the COVID-19 pandemic on key health parameters, such as anthropometric measurements and blood pressure values, have been documented in several studies.[8,9] While variations in methodology exist among works, particularly concerning data collection methods such as online questionnaires and self-reported participant values, systematic reviews and meta-analyses published in this domain consistently indicate a noteworthy trend: confinement periods have broadly contributed to a rise in weight and body mass index (BMI) among adults.[8,10]

In light of this findings, pregnant women may have been similarly impacted, with changes in their weight throughout gestation potentially affecting the birth parameters of newborns. On the other hand, evidence published prior to the pandemic indicates that exposure to high levels of stress could potentially have adverse effects on intrauterine development, a higher risk of prematurity and translate in low birth weight.[11] Some studies conducted during the COVID-19 pandemic suggested a potential increase in preterm births during this period, while others reported no significant changes in gestational age.[12] There were also conflicting reports of both an increase and a decrease in birth weight, with the direction of this change appearing to vary across different geographic regions.[13,14] Moreover, data on birth head circumference during the pandemic is still very limited. Considering the contradictory and occasionally scarce information available, it remains crucial to pursue further research on the effects of the COVID-19 pandemic on gestational age and birth anthropometric parameters.

The repercussions of the COVID-19 pandemic may be even more relevant on paediatric growth, if one considers the already established evidence that greater than expected weight gain at any time in childhood is associated with increased BMI in adolescence and adulthood.[15–17] The disruption of daily routines among children and adolescents has been accompanied by an increase in sedentary behaviour and stress.[18,19] This shift is primarily attributed to restricted physical space at home, limitations on organized physical activities like sports, and the greater amount of screen time associated with remote learning and reduced social interaction.[20] Furthermore, changes in dietary habits, either due to food availability or as a response to stress, may have led to uneven weight changes.[21,22] Consequently, it is plausible that the growth and development of children and adolescents affected by the COVID-19 pandemic may have been notably influenced, which was already documented by several works in this domain.[21,23,24]

In a study in Greece, body weight increased in 35% of children and adolescents during the first COVID-19 lockdown.[21] In Austria, BMI z-scores in children aged 7 to 10 years old significantly increased within six months of the pandemic onset, particularly among boys.[23] A large American retrospective cohort study presented a significant change in adjusted-for-age BMI among middle childhood individuals within a period of nine months following the onset of the pandemic.[24]

It is important to note, however, that due to the recent nature of this situation there is a lack of published studies that comprehensively assess whether the pandemic's impact on the anthropometric measurements of children and adolescents persisted beyond the period of restrictive measures. Many of the studies conducted thus far relied on self-reported measurements and have primarily focused on comparing pre-pandemic data with measurements taken during and immediately after lockdown periods, without considering the longer-term effects. Additionally, these works do not provide insight into the ongoing trajectory of growth charts for the individuals under investigation. Since anthropometric parameters play a crucial role in assessing the nutritional status of children, these aspects hold significant relevance and implications within the field of Clinical Nutrition.

National Child and Youth Health Surveillance Programme

The Portuguese National Health Service (SNS) is a public, universal, tendentially free of charge health system that provides healthcare coverage to all residents. Portugal's National Child and Youth Health Surveillance Programme (PNSIJ) is a governmental initiative dedicated to monitoring and promoting the health of children and youth across the country.[25] This program aims to ensure the physical, mental, and social well-being of children while assessing their development over time. It relies on interdisciplinary collaboration among healthcare professionals, including physicians, nurses, dentists, psychologists, and social workers.

Growth curves serve as a fundamental tool for tracking the nutritional status and growth of children and adolescents. Achieving harmonious development within normal parameters is crucial for a healthy adult life, and as a result, it holds significant implications for the overall health of populations. Accordingly, PNSIJ relies on WHO child growth standards and on the American National Heart, Lung, and Blood Institute (NHLBI) blood pressure charts.[26-28]

To achieve PNSIJ goals, medical appointments to the family physician are scheduled at key developmental milestones that correspond to significant events encompassing several domains, such as physical, psychomotor, cognitive, emotional, social, nutritional, and educational stages (Figure 1). These visits are coordinated with the national vaccination schedule to ensure comprehensive protection against preventable diseases. If an appointment is scheduled for any other reason, whether shortly before or after the designated key age, the recommended examination for that age should be conducted opportunistically.

Primary Care setting medical appointments according to PNSIJ
(Portuguese National Child and Youth Health Surveillance Programme)

< 1 year	1 to 4 years	5 to 9 years	≥ 10 years
1st week of life	12 months old 💉	5 years old 💉	10 years old 💉
1 month old	15 months old	6 to 7 years old	12 to 13 years old
2 months old 💉	18 months old 💉	8 years old	15 to 18 years old
4 months old 💉	2 years old		
6 months old 💉	3 years old		
9 months old	4 years old		

💉 Vaccine administration within the national vaccination schedule

Figure 1. Primary Care setting medical appointments according to PNSIJ.

Portuguese Pandemic Timeline

The COVID-19 pandemic officially began in Portugal on 2nd March 2020, with the report of the first confirmed case of infection (Figure 2).[29] Schools were closed by March 16th, and a state of emergency was declared between March 19th and May 2nd, resulting in a mandatory 45-day home confinement period (1st lockdown). High schools reopened on May 18th, but other education levels continued with remote learning until the end of the school year in late June. The government gradually eased restrictions during the summer.[29]

A second COVID-19 wave emerged in October 2020. By the end of the month, mask-wearing in public spaces became mandatory. Starting in November, partial confinement measures were implemented, including weekend stay-at-home orders and evening curfews.[29] In line with other European countries, vaccination began on December 27th.

In early 2021, due to a sharp surge in infection cases that propelled Portugal to the status of the country with the highest number of new cases per million inhabitants at that point, a 59-day period of mandatory home confinement was imposed from January 15th to March 14th (2nd lockdown).[29,30] This wave saw the highest number of hospitalizations and deaths. Kindergartens and elementary schools (for 6 to 10-year-old children) reopened on March 15th. Middle schools (10 to 15-year-old children) remained closed until April 5th. High schools resumed activities on April 19th. Many restrictions persisted through the summer of 2021 to control the Delta variant spread, despite there were no additional lockdowns.[30]

As of October 9th, 85% of the population had completed their primary vaccination. However, the rapid spread of the Omicron variant in the community began the following month, leading to the sequential reintroduction of restrictions.[30] On December 1st, 2021, the Portuguese government reinstated a state of calamity, predominantly revolved around the use of masks, the mandatory presentation of the digital certificate of vaccination, and the widespread testing of the population.[30] Although a complete lockdown was not established, on December 21st, mandatory teleworking was implemented, and bars and clubs were closed.

After the holiday season, there was a notable raise in the number of positive COVID-19 cases. The peak in new daily cases was achieved on 27th January 2022, with 65,706 positive tests, however, discussions among healthcare professionals focused on the reduced disease severity of these cases.[30] Restrictions began to be gradually lifted starting on February 7th.

On April 22nd, 2022, the mandatory use of masks in most enclosed spaces was lifted, except for public transport and healthcare facilities.[31] The state of alert concluded on September 30th, and with it, most of the COVID-19 related regulations were lifted, including mandatory isolation for infected individuals and population-wide testing. The sole remaining regulation was the requirement to wear masks in healthcare facilities, which was lifted on April 6th, 2023.[31]

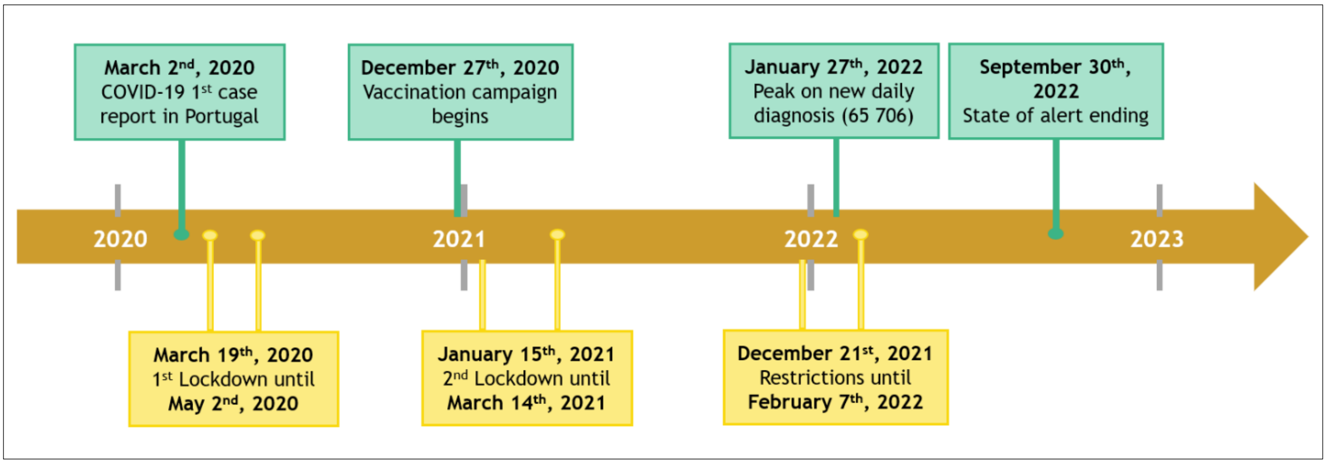


Figure 2. Portuguese pandemic timeline.

Objectives

Main goal

To analyse the impact of the COVID-19 pandemic on the growth patterns of a child and youth cohort from the North region of Portugal.

Specific goals

- To examine the evolution of several parameters at birth, including gestational age, birth length, birth weight and birth head circumference.
- To track the progression of several anthropometric parameters and blood pressure measurements in a child and adolescent cohort: length/height, weight, BMI, head circumference, systolic blood pressure and diastolic blood pressure.
- To develop the pre-pandemic growth charts of the child-adolescent cohort under investigation.
- To compute the z-score variation of several anthropometric parameters and blood pressure measurements using internationally validated standards as reference.
- To analyse the differences between distinct pandemic timespan divisions regarding the z-scores of anthropometric parameters and blood pressure measurements.

Material and Methods

Study Design

An observational retrospective study was conducted in a Primary Care setting during the first semester of 2023. The study protocol was approved by the North Regional Administration Health Ethics Committee (reference CE/2022/120) and designed in accordance with the principles of the World Medical Association's Declaration of Helsinki and the European General Data Protection Regulation.

The study is composed of two sections:

- Section A focuses on assessing birth parameters, including gestational age, newborn anthropometric measurements at birth, and maternal COVID-19 infection during pregnancy.
- Section B deals with child growth development data, encompassing several anthropometric parameters and blood pressure measurements.

The results are initially presented for the entire study sample and subsequently divided into different timespan categories, considering the COVID-19 pandemic timeline. The obtained data are compared to the following reference populations:

- Index population, comprising children's measurements obtained from the study sample before the onset of the pandemic when they were aged 0 to 18 years at the time of assessment.
- Fenton growth charts for preterm infants.[32]
- WHO child growth standards.[26,27]
- American NHLBI blood pressure report and Centers for Disease Control and Prevention (CDC) blood pressure charts.[33,34]

Study Population and Study Sample

The study population includes children born from 1st January 2002 to 30th June 2023 that are registered users at two Primary Care units within the Portuguese SNS. The facilities of Santa Justa Family Healthcare Unit and Valongo Family Healthcare Unit are located in Valongo, a city in the North region of Portugal included in a large metropolitan area in Porto district.

For Section A, all individuals with available data for at least one of the birth parameters under investigation were included in the study sample, regardless of their birth date. For Section B, individuals who had at least one visit to the study's sites with recorded anthropometric measurements were included in the study sample. Individuals who did not meet these criteria or had transferred their clinical records to another healthcare facility at the time of data collection were excluded.

Definitions

Preterm birth is defined by WHO as babies born alive before 37 weeks of pregnancy are completed.[35] Preterm birth is further categorized into different groups based on gestational age:

- Extremely preterm: born before 28 weeks of gestation.
- Very preterm: born between 28 and 32 weeks of gestation.
- Moderate to late preterm: born between 32 and 37 weeks of gestation.

In line with the Portuguese pandemic timeline (Figure 2), four divisions for data analysis and group comparisons were established and are presented on Figure 3.

<table>
<tr><th colspan="2">Pandemic Timeline</th><th>Division IV</th><th>Division III</th><th>Division II</th><th>Division I</th></tr>
<tr><td>Pre-pandemic</td><td>Until March 1st, 2020</td><td>Control Group</td><td>Control Group</td><td>Control Group</td><td>Control Group</td></tr>
<tr><td rowspan="5">COVID-19 Pandemic</td><td>2nd March 2020 to 17th May 2020</td><td>Group A
1st Lockdown</td><td rowspan="2">Group 1
1st Lockdown + 1st Reopening</td><td rowspan="5">Group α
Pandemic with restrictions</td><td rowspan="6">Pandemic Group</td></tr>
<tr><td></td><td>Group B
1st Reopening</td></tr>
<tr><td>15th January 2021 to 14th March 2021</td><td>Group C
2nd Lockdown</td><td rowspan="2">Group 2
2nd Lockdown + 2nd Reopening</td></tr>
<tr><td></td><td>Group D
2nd Reopening</td></tr>
<tr><td>21st December 2021 to 6th February 2022</td><td>Group E
3rd Lockdown</td><td rowspan="2">Group 3
3rd Lockdown + 3rd Reopening</td></tr>
<tr><td>Restrictions lifted</td><td>From February 7th, 2022</td><td>Group F
3rd Reopening</td><td>Group β
Pandemic after restriction lifting</td></tr>
</table>

Figure 3. Pandemic timeline divisions for statistical analysis.

The control group consisted of individuals from the pre-pandemic dataset, encompassing those born or measured before March 2nd, 2020. Division I, comprising two groups, was devised as a broad distinction between the periods preceding and succeeding the Portuguese pandemic onset (March 2nd, 2020).

Division II facilitated a comparison between the pre-pandemic group and data from two distinct pandemic stages: a period with restrictions (group α, covering the peak pandemic timespan) and a period following the lifting of restrictions (group β). Division III subdivides the pandemic group into three subgroups, each encompassing a lockdown phase followed by the respective period of restriction lifting (groups 1, 2, and 3). Lastly, Division IV is the most finely segmented, dividing the pandemic group into six subcategories, including three lockdowns (groups A, C and E) and three reopening phases (groups B, D and F).

The 1st lockdown (group A) was defined as the period between the detection of the first COVID-19 infection case in Portugal until 17th May 2020, coinciding with the lifting of restrictions and the reopening of high schools the following day. The 2nd lockdown (group C) ranged from 15th January 2021 to 14th March 2021, in line with the establishment of a 59-day mandatory home confinement. The 3rd lockdown (group E) was not linked with a real government-imposed lockdown but was labelled as such for the sake of easy and consistent group naming. It comprised the period between 21st December 2021 (mandatory teleworking and clubs closing) and 6th February 2022, at which point restrictions began to be gradually lifted.

In Section B, youths were divided into four age categories:

- 0 to 1 years old (inclusive).
- 2 to 4 years old (inclusive).
- 5 to 9 years old (inclusive).
- over 10 years old.

Although some of these groups encompass a wide age range, this division was essential to ensure group homogenization regarding the number of participants.

Data Collection

At the study sites, electronic registries from surveillance appointments are available from September 2006 onward. Children's appointments are scheduled according to PNSIJ's recommendations (Figure 1) and opportunistic measurements may be conducted by doctors and nurses beyond the recommended age ranges.

The list of registered users at the healthcare units was retrieved in January 2023 and updated in July 2023. After applying the inclusion criteria, data were manually collected from the electronic health records of the eligible participants by individually consulting each file. Information was registered in a Microsoft Excel secured spreadsheet (Microsoft Office 2016). Data were pseudo-anonymized by assigning a participant identification code, the key to which was exclusively accessible to the principal researcher of the study.

The initial study protocol specified that data would be sourced from the electronic health records of children born between 1st January 2004 to 31st December 2021. However, it was deemed necessary to extend the data collection timeframe:

- For children born from January 2002 to December 2003, half of the available health records were randomly selected for data retrieval. This addition was required to complete the development of the index population's growth charts, particularly for individuals aged 16 to 18 years old. Birth parameters were included, when available.
- For individuals born from January 2022 to June 2023, data were collected by the end of July 2023 to broaden the post-pandemic dataset, including birth parameters and anthropometric measurements.

Birth date, sex and twinship information were collected from all included clinical files. For Section A, gestational age (in weeks), birth length (in centimetres), birth weight (in kilograms) and birth head circumference (in centimetres) were retrieved. Additionally, data concerning maternal COVID-19 infection during pregnancy, including gestational age (in weeks) at the time of diagnosis, were collected for children born after 2nd March 2020. For Section B, length/height (in centimetres) and weight (in kilograms) measurements were retrieved for all ages, head circumference (in centimetres) measurements were collected up to 5 years old and systolic and diastolic blood pressure (in millimetres of mercury) were collected from 3 years old onward.

Over the years, measurement equipment was regularly calibrated at the study's healthcare facilities, yet not standardized for all assessments. Each healthcare unit maintained its own set of materials, which might have been updated or replaced over time. Nevertheless, it can be generally stated that:

- Height/length recumbent boards or stadiometers (either portable or wall-mounted) were used for length/height measurements.
- Digital or analogue scales were used for weight measurements.
- Flexible measuring tapes were used for head circumference.
- Digital or analogue sphygmomanometers were used for blood pressure.

It is noteworthy that birth anthropometric measurements were typically measured at hospitals or maternity facilities outside of this study's sites. The information was later transcribed to the study sites' electronic health records by doctors and nurses.

Data Treatment

Data management was performed using R software version 4.3.1 and R Studio software version 2023.06.0. These tools were primarily used for the conversion of the data spreadsheet into a suitable database. The process was extensive and involved creating programming code from the ground up to address the specific requirements for statistical analysis.

Firstly, since the data retrieved from health records that had been maintained by healthcare providers over the years, the database underwent screening to detect potential errors. To accomplish this, a programming code was designed to generate warnings that were subsequently reviewed and manually corrected.

After this process, some variables were computed from the revised data:

- BMI (kg/m^2) was calculated from length/height and weight measurements.
- Age at time of measurement (in years) was determined from birth date and date of appointment, and subsequently transformed.
- Transformed logarithmic birth parameters were created.
- Newborn anthropometric birth parameters' z-scores were calculated from Fenton growth charts.[32]
- Anthropometric measurements' logarithms (base 10) were determined, with the BMI ones being transformed.
- Anthropometric measurements' z-scores were calculated from WHO child growth standards (until 18 years, inclusive) and from the index population (after logarithmic transformation, until 16 years old, inclusive).[26,27]
- Blood pressure's z-scores were calculated from NHLBI/CDC data (until 19 years) and from the index population (from 3 to 16 years old, inclusive).[33,34]

As unveiled above, some adjustments were deemed necessary to improve the computed variables, thus creating transformed variables.

Acknowledging the impact of gestational age and twinship in child anthropometric measurements, and the positive skewness on age distribution, transformed age at time of measurement was computed according to the following formula:

$$\begin{aligned} Transformed\ age = \ & 1 + \log_{10}\ (0.1 + age - [0.005]_{if\ twins} \\ & + \{0.002 \times (gestational\ age - 38) \times (1 - age)\}_{if\ age < 0.2}) \end{aligned}$$

The term in square brackets was considered only if the child had a twin, while the term in curly brackets was added only if the age at time of measurements was below 0.2 (approximately 10 weeks). Coefficient values for the transformed age variable were selected to align the anthropometric measurements of preterm children and/or children with twins more closely to those of the index population. This adjustment was made due to the observed similarity in growth patterns, although with a time delay that was positively linked with prematurity and twinship. To ensure the result was positive, a requirement of the "Gamlss" package, a value of 1 was added to the final expression. Table 1 shows examples of the transformed age values, used in the horizontal axis of growth charts.

Table 1. Transformed age at time of measurement examples.

Age at time of measurement	Gestational age	Twinship	Transformed age
1 week	38 weeks	No	0.076 years
2 weeks	28 weeks	No	0.076 years
2 weeks	31 weeks	Yes	0.079 years
2 months	38 weeks	No	0.426 years
1 year	38 weeks	No	1.041 years
3 years	38 weeks	No	1.491 years
10 years	38 weeks	No	2.004 years
18 years	38 weeks	No	2.258 years

In Section A, since birth parameters had negative skewness, the scale was reversed before computing a logarithmic transformation to those variables. Afterwards, a linear transformation was applied to obtain values that were close to the original ones. Hence, transformed birth anthropometric parameters were computed according to the following formula:

$$Transformed\ birth\ parameter = C + (D - C) \times \frac{\log_{10}\left(\frac{M-x}{M-C}\right)}{\log_{10}\left(\frac{M-D}{M-C}\right)}$$

In this formula, x are birth anthropometric measurements (birth length, birth weight and birth head circumference) and C, D and M are parameters. M is chosen so that all measurements remain below such value. C and D are values that will be fixed points of the transformation: if measurement equals C, the transformed measurement is also equal to C; if measurement equals D, the transformed measurement is also equal to D. In general, C parameter is close to a central tendency value (*e.g.*, the median) and D parameter is close to a value related with the dispersion (*e.g.*, percentiles 25 or 75). The values chosen for these parameters depend on the birth anthropometric variable and are presented in Table 2.

Table 2. Values used for the transformed measurement variable parameters.

Birth Parameter	C	D	M
Birth length	49	47.5	59
Birth weight	3.19	2.89	9
Birth head circumference	34	33	48

In Section B, concerning child growth data, length/height, weight, BMI and head circumference presented positive skewness. Therefore, a logarithmic (base 10) transformation was applied to normalize data by reducing the observed positive skewness. As for BMI, however, the formula was adjusted, since the logarithm alone was insufficient to achieve a large enough decrease in skewness:

$$Transformed\ BMI\ logarithm = \log_{10}(BMI - 6)$$

Table 3 presents the correspondence between logarithmic anthropometric measurements, including BMI transformed logarithm, and the respective absolute values. These values were used on the vertical axis of the growth charts.

Table 3. Logarithmic correspondence with anthropometric measurements.

Length/height logarithm	Length/height
1.6	39.8 cm
1.7	50.1 cm
1.8	63.1 cm
1.9	79.4 cm
2.0	100.0 cm
2.1	125.9 cm
2.2	158.5 cm
2.3	199.5 cm

Weight logarithm	Weight
0.5	3.16 kg
1.0	10.0 kg
1.5	31.6 kg
2.0	100.0 kg

Head circumference logarithm	Head circumference
1.50	31.6 cm
1.55	35.5 cm
1.60	39.8 cm
1.65	44.7 cm
1.70	50.1 cm
1.75	56.2 cm

BMI transformed logarithm	BMI
0.6	10.0 kg/m^2
0.8	12.3 kg/m^2
1.0	16.0 kg/m^2
1.2	21.9 kg/m^2
1.4	31.1 kg/m^2
1.6	45.8 kg/m^2

Finally, still relying on R software, growth charts were created for the index population, including accordingly designed centile curves, and violin plots were generated to illustrate weight variation across time.

For the described data treatment process, the following R packages were used:

- “Tidyverse”, a set of packages for generic tasks and calculations.
- “Dplyr”, to work with data frame, allowing for database management.
- “Haven”, to import and export Microsoft Excel and IBM SPSS Statistics formats into and from the R software.
- “Psych”, for basic descriptive statistics.
- “Tibble”, for checking and formatting dates.
- “Lubridate”, to work with date-times and timespans.
- “Gamlss”, fitting the Generalized Additive Models for Location Scale and Shape, required to calculate centile curves.[36]
- “Sitar”, for fitting and plotting SITAR (Super Imposition by Translation and Rotation) growth curve models and to compute length/height, weight, BMI and head circumference z-scores using WHO child growth standards.[26-28,37]
- “Childsds”, for calculation of length/height, weight, BMI and head circumference z-scores and centiles using WHO child growth standards.[26-28]
- “Pedbp”, for estimating paediatric systolic and diastolic blood pressure percentiles by sex, age, and height according to NHLBI and CDC data.[33,34]

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics software version 28.0.0.0. Variables were assessed for normal distribution through an analysis of skewness and kurtosis.

In descriptive analyses, absolute frequencies, percentages, mean, standard deviation and range were used. Descriptive statistics were presented for the total sample and divided by sex or according to age categories.

Differences between groups were analysed with the Mann-Whitney U test (two independent groups) or the Kruskal-Wallis test (three or more independent groups) for non-parametric variables. Post Hoc analysis included Bonferroni corrections.

General Linear Models were used for analysing relationships between one or more independent variables and one dependent variable, through 2-way ANCOVA. These models allowed control for confounding variables (including age, sex, gestational age and twinship), in order to assess interactions between factors, and to evaluate the effects of multiple predictors on a response variable. Post Hoc analysis included Bonferroni and Sidak corrections, used to determine which specific pairs of variables had significant differences.

For statistical analysis purposes, the significance level was set at 0.05.

Results

Out of 4,818 health records within the defined birth dates span, the data of 4,298 children born between 3rd January 2002 and 23rd June 2023 were included for analysis. In this study's sample, there are 2,183 boys (50.8%) and 2,115 girls (49.2%). A set of 124 twins (2.9%) was identified, 67 of them being boys (54.0%).

Section A *- Birth parameters assessment*

A.1. Date of Birth

Concerning date of birth, 3,799 children (88.4%) were born before the pandemic onset, while 499 (11.6%) were born after 2nd March 2020. Table 4 presents the distribution of births each year.

Table 4. Sample characterization by year of birth.

Year of birth	Total Sample	Boys	Girls
2002[a)]	173 (4.0%)	86	87
2003[a)]	129 (3.0%)	58	71
2004	249 (5.8%)	138	111
2005	239 (5.6%)	122	117
2006	275 (6.4%)	133	142
2007	282 (6.6%)	141	141
2008	253 (5.9%)	142	111
2009	227 (5.3%)	120	107
2010	230 (5.4%)	115	115
2011	224 (5.2%)	98	126
2012	215 (5.0%)	108	107

Year of birth	Total Sample	Boys	Girls
2013	166 (3.9%)	78	88
2014	193 (4.5%)	98	95
2015	213 (5.0%)	105	108
2016	195 (4.5%)	98	97
2017	195 (4.5%)	101	94
2018	167 (3.9%)	88	79
2019	151 (3.5%)	79	72
2020	158 (3.7%)	85	73
2021	147 (3.4%)	80	67
2022	143 (3.3%)	73	70
2023[b)]	74 (1.7%)	37	37
All	4298	2183	2115

a) Only a sample of the available data was collected. b) Data available until June 30th, 2023.

After excluding years with incomplete data, the average number of births is 206.4 annually. From 2004 to 2012, the annual number of births was above the expected value. Starting from 2013, except for the year 2015, the annual birth rate has consistently remained below the average number of births, exhibiting a declining trend after the onset of the COVID-19 pandemic.

Table 5. Sample characterization by season of birth.

Year	Season	Number of Births
2004	Winter [a]	39
	Spring	52
	Summer	70
	Autumn	59
2005	Winter	63
	Spring	55
	Summer	65
	Autumn	66
2006	Winter	56
	Spring	55
	Summer	71
	Autumn	86
2007	Winter	76
	Spring	59
	Summer	74
	Autumn	80
2008	Winter	52
	Spring	60
	Summer	65
	Autumn	73
2009	Winter	61
	Spring	51
	Summer	60
	Autumn	63
2010	Winter	45
	Spring	59
	Summer	57
	Autumn	61
2011	Winter	58
	Spring	56
	Summer	65
	Autumn	47
2012	Winter	53
	Spring	55
	Summer	56
	Autumn	56
2013	Winter	46
	Spring	38
	Summer	38
	Autumn	43
2014	Winter	48
	Spring	56
	Summer	39
	Autumn	53
2015	Winter	43
	Spring	53
	Summer	58
	Autumn	55
2016	Winter	45
	Spring	55
	Summer	45
	Autumn	50
2017	Winter	48
	Spring	42
	Summer	58
	Autumn	53
2018	Winter	31
	Spring	43
	Summer	40
	Autumn	50
2019	Winter	45
	Spring	35
	Summer	31
	Autumn	44
2020	Winter	33
	Spring	39
	Summer	42
	Autumn	45
2021	Winter	32
	Spring	41
	Summer	37
	Autumn	33
2022	Winter	36
	Spring	40
	Summer	34
	Autumn	35
	Winter [a]	11
Total of Births		3922

a) Incomplete season.

Seasonality effect between 2004 and 2022 is presented on Table 5. The maximum number of births was registered in the autumn of 2006 and the minimum in the winter of 2018 and the summer of 2019. The average number of births is 50.9 per season, remaining below this threshold since the winter of 2018.

A.2. Gestational Age

Table 6 provides an overview of the sample characterization regarding gestational age. Out of the 4,298 healthcare records consulted, 551 were excluded from this subsection's analysis due to missing data. Descriptives are presented for the total sample, divided by sex and analysing twins. Sample characterization by gestational age categories is also displayed, with 91.8% (n=3,443) of pregnancies matching term deliveries.

Table 6. Sample characterization by gestational age and gestational age categories.

Gestational Age		Total Sample	Boys	Girls	Twins
Gestational age (weeks)	n	3,747	1,904	1,843	120
	Mean (SD)	38.6 (1.7)	38.6 (1.6)	38.6 (1.7)	35.4 (2.2)
	Range	[24;42]	[31;42]	[24;42]	[28;38]
Gestational age categories (weeks)					
Term born ≥ 37 weeks	n	3,443	1,743	1,700	42
	Mean (SD)	39.0 (1.1)	39.0 (1.1)	39.0 (1.1)	37.5 (0.5)
Moderate to Late Preterm born 32 to 36 weeks	n	274	145	129	70
	Mean (SD)	35.1 (1.2)	35.0 (1.2)	35.1 (1.3)	34.8 (1.4)
Very Preterm born 28 to 31 weeks	n	27	16	11	8
	Mean (SD)	29.7 (1.2)	30.0 (1.2)	29.4 (1.2)	30.0 (1.3)
Extremely Preterm born ≤ 27 weeks	n	3	-	3	-
	Mean (SD)	25.3 (1.2)	-	25.3 (1.2)	-

The following set of tables presents the comparison between the control group and the pandemic group for gestational age, displayed by the four different divisions of the COVID-19 pandemic timeline (Figure 3).

In Table 7, outcomes are classified based on the periods preceding and following the pandemic onset (division I), and *p* values are provided to compare independent samples using the Mann-Whitney U test. As for this division, no statistically significant differences were found between the control and the pandemic groups. This finding remained consistent when applying multivariate analysis (p=0.886), after adjusting for sex, twinship and division I timespan categories.

Table 7. Gestational age comparative analysis of the control and the pandemic groups by division I.

Gestational Age		Control Group	Pandemic Group	*p* value
Boys	n	1,645	259	0.578
	Mean (SD)	38.6 (1.7)	38.6 (1.7)	
Girls	n	1,618	225	0.937
	Mean (SD)	38.6 (1.8)	38.7 (1.5)	
Total	n	3,263	484	0.713
	Mean (SD)	38.6 (1.7)	38.6 (1.6)	

Looking more closely to the pandemic group, Table 8 presents data displayed according to division II timespans. In this scenario, using Kruskal-Wallis test, significant differences emerged among groups regarding mean gestational age of the entire sample (p=0.009), though no such differences were clear when analysing by sex. Post-hoc tests with Bonferroni correction revealed, through pairwise comparisons, that these differences are of significance between group α and group β (p=0.007).

Table 8. Gestational age comparative analysis of the control and the pandemic groups by division II.

Gestational Age		Control Group	Pandemic Group		*p* value
			Group α Pandemic with restrictions	Group β Pandemic without restrictions	
Boys	n	1645	161	98	0.085
	Mean (SD)	38.6 (1.7)	38.4 (1.8)	38.9 (1.4)	
Girls	n	1618	129	96	0.101
	Mean (SD)	38.6 (1.8)	38.5 (1.6)	39.0 (1.2)	
Total	n	3263 [a,b]	290 [a]	194 [b]	0.009 *
	Mean (SD)	38.6 (1.7)	38.4 (1.7)	38.9 (1.3)	

Post-hoc tests: equal superscript letters indicate absence of significant differences between groups.
* Statistically significant, $p \leq 0.05$.

Multivariate analysis of birth parameters regarding division II timespans is displayed on Table 9. After adjusting for sex, twinship and division II timespan categories, differences on gestational age remained of significance between the three groups ($p=0.042$, partial $\eta^2=0.002$), when comparing with the index population. There was a significant positive difference in mean gestational age between the control group and group β. A closer look through pairwise comparisons with Sidak correction confirmed differences to be of significance between group α and group β ($p=0.036$). When splitting data by sex, differences on gestational age between the three groups were not significant ($p=0.192$ for girls, $p=0.220$ for boys).

Table 9. Gestational age multivariate analysis by division II groups.

Pandemic Timeline Groups	B	Std. Error	*p* value	Partial η^2
Control Group	0	-	-	-
Group α Pandemic with restrictions	-0.141	0.100	0.158	0.001
Group β Pandemic without restrictions	0.239	0.120	0.047 *	0.001

Values adjusted for sex, twinship and division II timespan groups. * Statistically significant, $p \leq 0.05$.

Table 10 provides the comparative analysis between the control group and three pandemic groups, considering division III. In this setting, using Kruskal-Wallis test, no significative differences were found between groups regarding gestational age. Consistent results were found when applying multivariate analysis (*p*=0.174), after adjusting for sex, twinship and division III timespan categories.

Table 10. Gestational age comparative analysis of the control and the pandemic groups by division III.

Gestational Age		Control Group	Pandemic Group			*p* value
			Group 1 1st Lockdown (A) + 1st Reopening (B)	Group 2 2nd Lockdown (C) + 2nd Reopening (D)	Group 3 3rd Lockdown (E) + 3rd Reopening (F)	
Boys	n	1,645	80	69	110	0.416
	Mean (SD)	38.6 (1.7)	38.6 (1.6)	37.9 (1.7)	38.7 (1.7)	
Girls	n	1,618	57	63	105	0.146
	Mean (SD)	38.6 (1.8)	38.5 (1.5)	38.5 (1.7)	39.0 (1.2)	
Total	n	3,263	137	132	215	0.073
	Mean (SD)	38.6 (1.7)	38.5 (1.6)	38.4 (1.7)	38.8 (1.5)	

When comparing the control group with the pandemic group, categorized into six subgroups (division IV), no significative differences were observed when using either Kruskal-Wallis test (Table 11) or the multivariate analysis (*p*=0.114), after adjusting for sex, twinship and division IV timespan categories.

Table 11. Gestational age comparative analysis of the control and the pandemic groups by division IV.

Gestational Age		Control Group	Pandemic Group						*p* value
			Group A 1st Lockdown	Group B 1st Reopening	Group C 2nd Lockdown	Group D 2nd Reopening	Group E 3rd Lockdown	Group F 3rd Reopening	
Boys	n	1,645	15	65	13	56	12	98	0.109
	Mean (SD)	38.6 (1.7)	38.5 (0.6)	38.6 (1.8)	38.9 (1.3)	38.2 (1.8)	37.2 (3.0)	38.9 (1.4)	
Girls	n	1,618	12	45	6	57	9	96	0.275
	Mean (SD)	38.6 (1.8)	37.7 (2.1)	38.7 (1.2)	38.3 (1.5)	38.5 (1.8)	39.0 (1.2)	39.0 (1.2)	
Total	n	3,263	27	110	19	113	21	194	0.051
	Mean (SD)	38.6 (1.7)	38.2 (1.5)	38.6 (1.6)	38.7 (1.4)	38.3 (1.8)	38.0 (2.5)	39.0 (1.3)	

A.3. Anthropometric Birth Parameters

Table 12 provides an overview of the sample characterization regarding neonatal anthropometric measurements. Out of the 4,298 healthcare records consulted, 434 to 626 were excluded from this section's sample due to missing data, depending on the birth parameter under consideration. Data are presented for the total sample, divided by sex and analysing twins.

Table 12. Sample characterization by birth anthropometric parameters.

Birth Parameters		Total Sample	Boys	Girls	Twins
Birth length (cm)	n	3,785	1,916	1,869	108
	Mean (SD)	48.8 (2.4)	48.9 (2.2)	48.8 (2.5)	44.4 (3.4)
	Range	[29.0;55.5]	[41;55.5]	[29.0;55.5]	[34.3;51.0]
Birth weight (kg)	n	3,864	1956	1,908	116
	Mean (SD)	3.167 (0.502)	3.152 (0.470)	3.169 (0.508)	2.25 (0.441)
	Range	[0.520;5.312]	[1.770;4.640}	[0.520;5.312]	[0.995;3.285]
Birth head circumference (cm)	n	3,672	1,851	1,821	106
	Mean (SD)	34.1 (1.6)	34.3 (1.5)	34.1 (1.6)	32.3 (2.0)
	Range	[24.7;39.5]	[28.0;39.0]	[24.7;39.5]	[26.6;36.0]

The following set of tables presents the comparison between the control group and the pandemic group for birth anthropometric measurements, displayed by the four different divisions of the COVID-19 pandemic timeline (Figure 3).

In Table 13, outcomes are classified based on the periods preceding and following the pandemic onset (division I), and *p* values are provided to compare independent samples using the Mann-Whitney U test. Mean birth head circumference was significantly different between the control group and the pandemic group (p=0.017). This distinction was particularly noticeable among boys, whose mean birth head circumference was significantly lower in the control group, compared to the pandemic group (p=0.002).

Table 13. Comparative analysis of birth parameters between the control and the pandemic groups by division I.

Birth Anthropometric Parameters			Control Group	Pandemic Group	p value
Birth length (cm)	**Boys**	n	1,662	254	0.477
		Mean (SD)	49.1 (2.5)	49.2 (2.1)	
	Girls	n	1,647	222	0.701
		Mean (SD)	48.4 (2.5)	48.5 (2.1)	
	Total	n	3,309	476	0.972
		Mean (SD)	48.8 (2.5)	48.9 (2.2)	
Birth weight (kg)	**Boys**	n	1,703	253	0.400
		Mean (SD)	3.227 (0.508)	3.208 (0.486)	
	Girls	n	1,685	223	0.314
		Mean (SD)	3.111 (0.501)	3.088 (0.422)	
	Total	n	3,388	476	0.227
		Mean (SD)	3.169 (0.508)	3.152 (0.46)	
Birth head circumference (cm)	**Boys**	n	1,600	317	0.002 *
		Mean (SD)	34.3 (1.6)	34.6 (1.5)	
	Girls	n	1,605	216	0.879
		Mean (SD)	33.8 (1.5)	33.9 (1.4)	
	Total	n	3,205	467	0.017 *
		Mean (SD)	34.1 (1.6)	34.3 (1.5)	

* Statistically significant, $p \leq 0.05$.

In addition, a multivariate assessment with transformed birth anthropometric parameters was performed using division I cut-off points. Results are presented on Table 14. After adjusting for sex, twinship, gestational age and division I timespan categories, transformed birth head circumference remained significantly divergent in the control group when compared to the pandemic group (p=0.006, partial η^2=0.002). When splitting by gender, it was found that this disparity was due to the boys' sample ($p<0.001$, partial $\eta^2=0.008$), but not present among girls ($p=0.998$). There were no significative differences in transformed birth length ($p=0.712$) or transformed birth weight ($p=0.149$).

When using Fenton growth charts as the reference population, birth head circumference z-scores were significantly divergent in the control group when compared to the pandemic group ($p=0.008$, partial $\eta^2=0.002$). In this setting, there were no significative differences in birth length ($p=0.559$) or birth weight ($p=0.225$) z-scores between the two groups.

Table 14. Birth parameters' multivariate analysis by division I groups.

Pandemic Timeline Groups	Study sample				Fenton growth charts z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
Transformed birth length					**Birth length**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.036	0.097	0.712	0.000	0.023	0.04	0.559	0.000
Transformed birth weight					**Birth weight**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.029	0.02	0.149	0.001	-0.053	0.043	0.225	0.000
Transformed birth head circumference					**Birth head circumference**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.195	0.071	0.006 *	0.002	0.125	0.047	0.008 *	0.002

Values adjusted for sex, twinship, gestational age and division I timespan groups.
* Statistically significant, $p \leq 0.05$.

Looking more closely to the pandemic group, Table 15 presents data displayed according to division II timespans. In this scenario, differences were found when analysing mean birth head circumference between the three groups using Kruskal-Wallis test ($p=0.044$), particularly in boys ($p=0.006$). Post-hoc tests with

Bonferroni correction did not confirm these differences among groups for the total sample. Notwithstanding, as for boys, pairwise comparisons revealed significative differences between the control group and group α (p=0.043).

Table 15. Comparative analysis of birth parameters between the control and the pandemic groups by division II.

Birth Parameter			Control Group	Pandemic Group		p value
				Group α Pandemic with restrictions	Group β Pandemic without restrictions	
Birth length (cm)	Boys	n	1,662	159	95	0.760
		Mean (SD)	49.1 (2.5)	49.2 (2.1)	49.2 (2.2)	
	Girls	n	1,647	129	93	0.259
		Mean (SD)	48.4 (2.5)	48.3 (2.2)	48.8 (2.1)	
	Total	n	3,309	288	188	0.546
		Mean (SD)	48.8 (2.5)	48.8 (2.2)	49.0 (2.1)	
Birth weight (kg)	Boys	n	1,703	158	95	0.702
		Mean (SD)	3.227 (0.508)	3.202 (0.48)	3.227 (0.508)	
	Girls	n	1,685	130	93	0.361
		Mean (SD)	3.111 (0.501)	3.057 (0.446)	3.131 (0.385)	
	Total	n	3,388	288	188	0.419
		Mean (SD)	3.169 (0.508)	3.137 (0.47)	3.174 (0.446)	
Birth head circumference (cm)	Boys	n	1,600	158	93	0.006 *
		Mean (SD)	34.3 (1.6) [a]	34.6 (1.4) [b]	34.7 (1.5) [a,b]	
	Girls	n	1,605	127	89	0.499
		Mean (SD)	33.8 (1.5)	33.8 (1.4)	34.0 (1.4)	
	Total	n	3,205	285	182	0.044 *
		Mean (SD)	34.1 (1.6) [a]	34.2 (1.5) [a]	34.4 (1.5) [a]	

Post-hoc tests: equal superscript letters indicate absence of significant differences between groups.
* Statistically significant, $p \leq 0.05$.

A multivariate assessment with transformed anthropometric measurements was performed using division II cut-off points (Table 16). After adjusting for sex, twinship, gestational age and division II timespan categories, transformed birth head circumference was significantly divergent between groups (p=0.022, partial η^2=0.002). When splitting the analysis by sex, it was found that such disparity was due to the boys' sample (p=0.001, partial η^2=0.008), but not the girls' (p=0.905). There was a positive difference in transformed birth head circumference between the control group and the pandemic groups, with significance regarding group α (p=0.034). Post-hoc pairwise comparisons confirmed significant differences between the control group and group α for boys (p=0.005), but not for the total sample (p=0.088). There were no significative differences among groups in transformed birth length (p=0.824) or transformed birth weight (p=0.202).

Table 16. Birth parameters' multivariate analysis by division II groups.

Pandemic Timeline Groups	Study sample				Fenton growth charts z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
Transformed birth length					**Birth length**			
Control Group	0	-	-	-	0	-	-	-
Group α Pandemic with restrictions	0.073	0.122	0.55	0.000	0.046	0.05	0.359	0.000
Group β Pandemic without restrictions	-0.02	0.148	0.891	0.000	-0.011	0.06	0.854	0.000
Transformed birth weight					**Birth weight**			
Control Group	0	-	-	-	0	-	-	-
Group α Pandemic with restrictions	-0.013	0.025	0.612	0.000	-0.016	0.055	0.769	0.000
Group β Pandemic without restrictions	-0.054	0.031	0.081	0.001	-0.108	0.066	0.102	0.001
Transformed birth head circumference					**Birth head circumference**			
Control Group	0	-	-	-	0	-	-	-
Group α Pandemic with restrictions	0.192	0.088	0.030 *	0.001	0.124	0.059	0.034 *	0.001
Group β Pandemic without restrictions	0.201	0.109	0.065	0.001	0.125	0.072	0.082	0.001

Values adjusted for sex, twinship, gestational age and division II timespan groups.
* Statistically significant, $p \leq 0.05$.

When using Fenton growth charts as the reference, birth head circumference z-scores were significantly divergent between groups (*p*=0.030, partial η^2=0.002), particularly between the control group when compared to group α. In this setting, there were also no significative differences in birth length (*p*=0.636) or weight (*p*=0.259) z-scores between groups.

Table 17 provides the comparative analysis between the control group and three pandemic groups, considering division III.

Table 17. Comparative analysis of birth parameters between the control and the pandemic groups by division III.

Birth Parameter		Control Group	Pandemic Group			*p* value
			Group 1 1st Lockdown (A) + 1st Reopening (B)	Group 2 2nd Lockdown (C) + 2nd Reopening (D)	Group 3 3rd Lockdown (E) + 3rd Reopening (F)	
Birth length (cm)						
Boys	n	1,662	80	69	105	0.228
	Mean (SD)	49.1 (2.5)	49.6 (2.0)	48.8 (2.2)	49.2 (2.1)	
Girls	n	1,647	57	63	102	0.136
	Mean (SD)	48.4 (2.5)	48.0 (2.2)	48.5 (2.3)	48.8 (2.0)	
Total	n	3,309	137	132	207	0.694
	Mean (SD)	48.8 (2.5)	48.9 (2.2)	48.7 (2.2)	49.0 (2.1)	
Birth weight (kg)						
Boys	n	1,703	79	69	105	0.871
	Mean (SD)	3.227 (0.508)	3.21 (0.463)	3.199 (0.499)	3.212 (0.498)	
Girls	n	1,685	58	63	102	0.176
	Mean (SD)	3.111 (0.501)	2.981 (0.473)	3.138 (0.425)	3.119 (0.382)	
Total	n	3,388	137	132	207	0.448
	Mean (SD)	3.169 (0.508)	3.112 (0.479)	3.17 (0.464)	3.166 (0.446)	
Birth head circumference (cm)						
Boys	n	1,600	79	69	103	0.005 *
	Mean (SD)	34.3 (1.6) [a]	34.4 (1.4) [a,b]	34.8 (1.4) [b]	34.7 (1.5) [a,b]	
Girls	n	1,605	58	62	98	0.335
	Mean (SD)	33.8 (1.5)	33.5 (1.5)	34.0 (1.3)	34.0 (1.4)	
Total	n	3,205	135	131	201	0.021 *
	Mean (SD)	34.1 (1.6) [a]	34.0 (1.5) [a]	34.4 (1.4) [a]	34.3 (1.5) [a]	

Post-hoc tests: equal superscript letters indicate absence of significant differences between groups.
* Statistically significant, $p \leq 0.05$.

When using the Kruskal-Wallis test, birth head circumference was the only parameter revealing statistically significant mean differences between groups (p=0.021), specifically when assessing boys (p=0.005). Post-hoc pairwise comparisons did not confirm significative differences between groups when analysing the total sample. Notwithstanding, when considering the boys' sample, significative differences between the control group and group 2 (p=0.036) were exposed using post-hoc tests.

A multivariate assessment using transformed neonatal anthropometric parameters was performed considering division III cut-off points, as presented on Table 18. After adjusting for sex, gestational age, twinship and division III timespan categories, there were significant differences in transformed birth head circumference between groups (p=0.002, partial η^2=0.004), but not in transformed birth length (p=0.703) or transformed birth weight (p=0.112). These significant differences in transformed birth head circumference between groups were found to be due to the boys' sample (p<0.001, partial η^2=0.011), but were not seen among girls (p=0.824). There was a significative positive difference in transformed birth head circumference between the control group and group 2.

Pairwise comparisons for timeline division III confirmed the following statistically significant differences concerning transformed birth head circumference:

- for the total sample, between the control group and group 2 (p=0.003).
- for the total sample, between group 1 and group 2 (p=0.045).
- for the boys' sample, between the control group and group 2 (p=0.001).

Tests of between-subjects-effect also revealed statistically significant differences between the control group and group 3, regarding transformed birth weight. Notwithstanding, these differences were not confirmed by post-hoc analysis.

Table 18. Birth parameters' multivariate analysis by division III groups.

Pandemic Timeline Groups	Study sample				Fenton growth charts z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
Logarithmic birth length					**Birth length**			
Control Group	0	-	-	-	0	-	-	-
Group 1 1st Lockdown + 1st Reopening	0.195	0.172	0.257	0.000	0.092	0.070	0.191	0.000
Group 2 2nd Lockdown + 2nd Reopening	-0.009	0.176	0.957	0.000	0.011	0.072	0.875	0.000
Group 3 3rd Lockdown + 3rd Reopening	-0.041	0.142	0.773	0.000	-0.015	0.058	0.796	0.000
Logarithmic birth weight					**Birth weight**			
Control Group	0	-	-	-	0	-	-	-
Group 1 1st Lockdown + 1st Reopening	-0.039	0.036	0.279	0.000	-0.072	0.077	0.352	0.000
Group 2 2nd Lockdown + 2nd Reopening	0.03	0.037	0.417	0.000	0.077	0.079	0.330	0.000
Group 3 3rd Lockdown + 3rd Reopening	-0.06	0.030	0.042 *	0.001	-0.122	0.063	0.055	0.001
Logarithmic birth head circumference					**Birth head circumference**			
Control Group	0	-	-	-	0	-	-	-
Group 1 1st Lockdown + 1st Reopening	-0.026	0.125	0.837	0.000	-0.018	0.083	0.825	0.000
Group 2 2nd Lockdown + 2nd Reopening	0.441	0.128	<0.001 *	0.003	0.291	0.085	<0.001 *	0.003
Group 3 3rd Lockdown + 3rd Reopening	0.185	0.104	0.075	0.001	0.112	0.069	0.101	0.001

Values adjusted for sex, twinship, gestational age and division III timespan groups.
* Statistically significant, $p \leq 0.05$.

For division III, when using Fenton growth charts as the reference population, there were significant differences in birth head circumference z-scores between groups (p=0.003, partial η^2=0.004), but not in birth length (p=0.608) or birth weight (p=0.133) z-scores. These significant differences in birth head circumference were found to be due to the boys' sample (p<0.001, partial η^2=0.010), but were not identified among girls (p=0.393). Alike what was described when using the index population as reference, a significant positive difference in birth head circumference was observed between the control group and group 2. Pairwise comparisons confirmed the following statistically significant differences concerning birth head circumference z-scores:

- for the total sample, between the control group and group 2 (p=0.003).
- for the total sample, between group 1 and group 2 (p=0.045).
- for the boys' sample, between the control group and group 2 (p=0.002).

Finally, when comparing the control group with the pandemic group, categorized into six divisions (Table 19), noticeable differences were observed between groups for mean birth head circumference in both the total sample (p=0.014) and the boys' sample (p=0.015). These differences, however, were not validated by post-hoc tests with Bonferroni correction.

No significant differences between groups arose in birth length (p=0.881) or weight (p=0.632) for the total sample. However, among girls, significant differences among groups were identified through Kruskal-Wallis tests for mean birth length (p=0.045) and mean birth weight (p=0.047). These differences were confirmed through post-hoc analysis with Bonferroni correction solely for birth weight. In this setting, subsequently performed pairwise comparisons exposed differences between the control group and group A (*p*=0.038), as well as between the latter and group D (*p*=0.036).

Table 19. Comparative analysis of birth parameters between the control and the pandemic groups by division IV.

Birth Parameter		Control Group	Pandemic Group						*p* value
			Group A 1st Lockdown	Group B 1st Reopening	Group C 2nd Lockdown	Group D 2nd Reopening	Group E 3rd Lockdown	Group F 3rd Reopening	
Birth length (cm)									
Boys	n	1,662	15	65	13	56	10	95	0.148
	Mean (SD)	49.1 (2.5)	50.4 (1.4)	49.4 (2.1)	49.0 (1.8)	48.8 (2.3)	48.7 (1.8)	49.2 (2.2)	
Girls	n	1,647	12	45	6	57	9	93	0.045 *
	Mean (SD)	48.4 (2.5) [a]	46.7 (2.3) [a]	48.4 (2.0) [a]	47.2 (2.0) [a]	48.6 (2.3) [a]	48.9 (1.3) [a]	48.8 (2.1) [a]	
Total	n	3,309	27	110	19	113	19	188	0.881
	Mean (SD)	48.8 (2.5)	48.8 (2.6)	49.0 (2.1)	48.4 (2.0)	48.7 (2.3)	48.8 (1.5)	49.0 (2.1)	
Birth weight (kg)									
Boys	n	1,703	15	64	13	56	10	95	0.486
	Mean (SD)	3.227 (0.508)	3.38 (0.361)	3.17 (0.477)	3.43 (0.390)	3.145 (0.509)	3.167 (0.531)	3.217 (0.497)	
Girls	n	1,685	12	46	6	57	9	93	0.047 *
	Mean (SD)	3.111 (0.501) [a]	2.657 (0.445) [b]	3.065 (0.447) [a,b]	3.031 (0.329) [a,b]	3.15 (0.434) [a]	2.98 (0.334) [a,b]	3.131 (0.385) [a,b]	
Total	n	3,388	27	110	19	113	19	188	0.632
	Mean (SD)	3.169 (0.508)	3.059 (0.536)	3.126 (0.465)	3.304 (0.410)	3.147 (0.471)	3.078 (0.447)	3.174 (0.446)	
Birth head circumference (cm)									
Boys	n	1,600	14	65	13	56	10	93	0.015 *
	Mean (SD)	34.3 (1.6) [a]	34.5 (1.5) [a]	34.3 (1.4) [a]	35.4 (1.3) [a]	34.7 (1.4) [a]	34.8 (1.4) [a]	34.7 (1.5) [a]	
Girls	n	1,605	12	44	5	57	9	89	0.112
	Mean (SD)	33.8 (1.5)	32.4 (1.8)	33.8 (1.4)	33.9 (1.1)	34.0 (1.3)	33.4 (1.1)	34.0 (1.4)	
Total	n	3,205	26	109	18	113	19	182	0.014 *
	Mean (SD)	34.1 (1.6) [a]	33.5 (1.9) [a]	34.1 (1.4) [a]	35.0 (1.4) [a]	34.3 (1.4) [a]	34.1 (1.4) [a]	34.4 (1.5) [a]	

Post-hoc tests: equal superscript letters indicate absence of significant differences between groups.
* Statistically significant, *p*≤0.05.

Table 20. Birth parameters' multivariate analysis by division IV groups.

Pandemic Timeline Groups	Study sample				Fenton growth charts z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
Transformed birth length					**Birth length**			
Control Group	0	-	-	-	0	-	-	-
Group A 1st Lockdown	0.418	0.380	0.272	0.000	0.171	0.155	0.27	0.000
Group B 1st Reopening	0.140	0.192	0.465	0.000	0.072	0.078	0.355	0.000
Group C 2nd Lockdown	-0.696	0.453	0.125	0.001	-0.265	0.184	0.151	0.001
Group D 2nd Reopening	0.108	0.190	0.569	0.000	0.059	0.077	0.449	0.000
Group E 3rd Lockdown	-0.242	0.453	0.592	0.000	-0.052	0.184	0.779	0.000
Group F 3rd Reopening	-0.021	0.148	0.889	0.000	-0.011	0.06	0.852	0.000
Transformed birth weight					**Birth weight**			
Control Group	0	-	-	-	0	-	-	-
Group A 1st Lockdown	-0.022	0.079	0.782	0.000	-0.048	0.17	0.777	0.000
Group B 1st Reopening	-0.043	0.040	0.281	0.000	-0.078	0.086	0.366	0.000
Group C 2nd Lockdown	0.083	0.095	0.377	0.000	0.179	0.203	0.377	0.000
Group D 2nd Reopening	0.021	0.040	0.603	0.000	0.059	0.085	0.487	0.000
Group E 3rd Lockdown	-0.119	0.095	0.207	0.000	-0.253	0.203	0.213	0.000
Group F 3rd Reopening	-0.054	0.031	0.081	0.001	-0.108	0.066	0.102	0.001
Transformed birth head circumference					**Birth head circumference**			
Control Group	0	-	-	-	0	-	-	-
Group A 1st Lockdown	-0.314	0.280	0.262	0.000	-0.251	0.185	0.175	0.001
Group B 1st Reopening	0.044	0.139	0.754	0.000	0.038	0.092	0.681	0.000
Group C 2nd Lockdown	0.798	0.336	0.017 *	0.002	0.508	0.222	0.022 *	0.001
Group D 2nd Reopening	0.383	0.137	0.005 *	0.002	0.256	0.091	0.005 *	0.002
Group E 3rd Lockdown	0.029	0.327	0.929	0.000	-0.008	0.216	0.969	0.000
Group F 3rd Reopening	0.201	0.109	0.064	0.001	0.125	0.072	0.082	0.001

Values adjusted for sex, twinship, gestational age and division IV timespan groups.
* Statistically significant, $p \leq 0.05$.

Analysing division IV cut-off points, a multivariate analysis with transformed neonatal anthropometric measurements was performed, the results being presented on Table 20. After adjusting for sex, twinship, gestational age and division IV timespan categories, there were significant differences in transformed birth head circumference between groups (*p*=0.007, η^2=0.005), but not in transformed birth length (*p*=0.574) or transformed birth weight (*p*=0.333).

The significant differences in transformed birth head circumference between groups were related to the boys' sample (*p*=0.002, partial η^2=0.012), and were not found among girls (*p*=0.192). There was a significative positive difference in transformed birth head circumference between the control group and groups C and D, as presented on Table 20. However, these differences were not confirmed by post-hoc analysis with Sidak correction.

For division IV, when using Fenton growth charts as the reference population, there were significant differences in birth head circumference z-scores between groups (*p*=0.007, partial η^2=0.005), but not in birth length (*p*=0.563) or birth weight (*p*=0.381) z-scores. These significant differences in birth head circumference z-scores between groups were found to be due to the boys' sample (*p*=0.003, partial η^2=0.011), but were not identified among girls (*p*=0.139). A significant positive difference in birth head circumference was observed between the control group and groups C and D. However, these differences were not confirmed by post-hoc analysis.

A.4. Maternal COVID-19 Infection

Considering individuals born after 2nd March 2020, 83 cases of maternal COVID-19 infection during pregnancy were identified. Data on maternal COVID-19 infection was missing in 7 of the 499 analysed health records. Regarding gestational age categories, 3 individuals fell into the "moderate to late term" category, born at 36 weeks, with the remaining being “term” newborns (ranging from 37 to 41 weeks).

Table 21. Comparative analysis of the control and the pandemic groups by maternal COVID-19 infection during pregnancy.

Birth Parameter			Control Group	Pandemic Group		*p* value
				Without maternal COVID-19 infection	With maternal COVID-19 infection	
Gestational age (weeks)	**Boys**	n	1,645	219	37	0.755
		Mean (SD)	38.6 (1.7)	38.6 (1.8)	38.6 (1.2)	
	Girls	n	1,618	176	46	0.547
		Mean (SD)	38.6 (1.8)	38.6 (1.6)	38.9 (1.1)	
	Total	n	3,263	395	83	0.817
		Mean (SD)	38.6 (1.7)	38.6 (1.7)	38.8 (1.2)	
Birth length (cm)	**Boys**	n	1,662	213	37	0.663
		Mean (SD)	49.1 (2.5)	49.2 (2.1)	49.3 (2.2)	
	Girls	n	1,647	175	44	0.973
		Mean (SD)	48.4 (2.5)	48.5 (2.2)	48.6 (2.1)	
	Total	n	3,309	388	81	0.979
		Mean (SD)	48.8 (2.5)	48.9 (2.2)	48.9 (2.1)	
Birth weight (cm)	**Boys**	n	1,703	212	37	0.668
		Mean (SD)	3.227 (0.508)	3.202 (0.499)	3.234 (0.422)	
	Girls	n	1,685	176	44	0.561
		Mean (SD)	3.111 (0.501)	3.089 (0.442)	3.076 (0.35)	
	Total	n	3,388	388	81	0.442
		Mean (SD)	3.169 (0.508)	3.151 (0.4767)	3.148 (0.390)	
Birth head circumference (cm)	**Boys**	n	1,600	210	37	0.008 *
		Mean (SD)	34.3 (1.6) [a]	34.6 (1.5) [b]	34.7 (1.4) [a,b]	
	Girls	n	1,605	171	43	0.835
		Mean (SD)	33.8 (1.5)	33.8 (1.5)	33.9 (1.2)	
	Total	n	3,205	381	80	0.083
		Mean (SD)	34.1 (1.6) [a]	34.3 (1.5) [b]	34.3 (1.4) [a,b]	

Post-hoc tests: equal superscript letters indicate absence of significant differences between groups.
* Statistically significant, $p \leq 0.05$.

Table 21 displays the gestational age and neonatal anthropometric characteristics of the subgroup of newborns exposed to maternal COVID-19 infection, while providing the results of a comparison between this subgroup, the subgroup without maternal infection and the control group, using Kruskal-Wallis test. Significant differences were observed between groups for birth head circumference when analysing the boys' sample (p=0.008) with Kruskal-Wallis test, but not the girls' or the total sample. These differences were found to be of significance between the control group and the pandemic subgroup without maternal infection (p=0.004).

Table 22 presents a multivariate analysis of gestational age and transformed birth anthropometric parameters regarding the diagnosis of maternal COVID-19 infection during pregnancy. This analysis unveils significant differences between groups for transformed birth head circumference, both for the total sample (p=0.031, partial η^2=0.002) and for the boy's sample (p=0.001, partial η^2=0.008), but not for the girl's sample (p=0.972). In both scenarios, there was a significant positive difference between the control group and the pandemic subgroup without maternal COVID-19 infection. This significance was confirmed through pairwise comparisons (p=0.044 for the total sample, p=0.004 for the boys' sample).

When using Fenton growth charts as the reference population, there were significant differences in birth head circumference z-scores between groups (p=0.041, partial η^2=0.002), but not in birth length (p=0.877) or birth weight (p=0.439) z-scores. A significant positive difference in birth head circumference was observed between the control group and the pandemic subgroup without maternal COVID-19 infection during pregnancy, both for the total sample and for the boys' sample. Post-hoc pairwise comparisons with Sidak correction proved these differences to be of significance only for the boy's sample (p=0.003).

Table 22. Gestational age and birth parameters' multivariate analysis by maternal COVID-19 infection.

Pandemic Timeline Groups	Study sample				Fenton growth charts z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
Gestational age $^{\Delta}$								
Control Group	0	-	-	-				
Pandemic Group Without maternal COVID-19 infection	-0.017	0.087	0.846	0.000				
Pandemic Group With maternal COVID-19 infection	0.150	0.181	0.408	0.000				
Transformed birth length #					**Birth length**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group Without maternal COVID-19 infection	0.018	0.106	0.864	0.000	0.02	0.043	0.643	0.000
Pandemic Group With maternal COVID-19 infection	0.084	0.222	0.705	0.000	0.022	0.090	0.808	0.000
Transformed birth weight #					**Birth weight**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group Without maternal COVID-19 infection	-0.025	0.022	0.255	0.000	-0.048	0.048	0.311	0.000
Pandemic Group With maternal COVID-19 infection	-0.050	0.046	0.279	0.000	-0.083	0.099	0.402	0.000
Transformed birth head circumference #					**Birth head circumference**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group Without maternal COVID-19 infection	0.189	0.077	0.015 *	0.002	0.122	0.051	0.018 *	0.002
Pandemic Group With maternal COVID-19 infection	0.182	0.161	0.258	0.000	0.108	0.107	0.311	0.000

$^{\Delta}$ Values adjusted for sex, twinship and maternal COVID-19 infection during pregnancy. # Values adjusted for sex, twinship, gestational age and maternal COVID-19 infection. * Statistically significant, $p \leq 0.05$.

It was subsequently assessed whether the timing of maternal COVID-19 infection had any influence on gestational age and neonatal anthropometric measurements. Table 23 displays the distribution of maternal infection cases across pregnancy trimesters.

Table 23. Comparative analysis of the control and the pandemic groups by maternal COVID-19 infection during pregnancy, split in pregnancy trimesters.

Birth Parameter			Control Group	Pandemic Group				*p* value
				Without maternal COVID-19	With maternal COVID-19 infection			
					1st Trimester	2nd Trimester	3rd Trimester	
Gestational age (weeks)	**Boys**	n	1,645	219	13	12	12	0.840
		Mean (SD)	38.6 (1.7)	38.6 (1.8)	38.5 (1.2)	38.9 (1.2)	38.4 (1.4)	
	Girls	n	1,618	176	12	19	15	0.570
		Mean (SD)	38.6 (1.8)	38.6 (1.6)	38.8 (1.1)	39.2 (1.3)	38,7 (1.0)	
	Total	n	3,263	395	25	31	27	0.525
		Mean (SD)	38.6 (1.7)	38.6 (1.7)	38.6 (1.1)	39.1 (1.2)	38.6 (1.2)	
Birth length (cm)	**Boys**	n	1,662	213	13	12	12	0.855
		Mean (SD)	49.1 (2.5)	49.2 (2.1)	49.4 (3.1)	49.3 (0.8)	49.4 (2.1)	
	Girls	n	1,647	175	12	17	15	0.355
		Mean (SD)	48.4 (2.5)	48.5 (2.2)	48.6 (1.6)	49.2 (2.6)	47.9 (1.5)	
	Total	n	3,309	388	25	29	27	0.801
		Mean (SD)	48.8 (2.5)	48.9 (2.2)	49.0 (2.5)	49.2 (2.0)	48.5 (1.9)	
Birth weight (cm)	**Boys**	n	1,703	212	13	12	12	0.639
		Mean (SD)	3.227 (0.508)	3.202 (0.499)	3.109 (0.434)	3.348 (0.402)	3.255 (0.428)	
	Girls	n	1,685	176	12	17	15	0.680
		Mean (SD)	3.111 (0.501)	3.089 (0.442)	3.061 (0.281)	3.135 (0.424)	3.021 (0.317)	
	Total	n	3,388	388	25	29	27	0.451
		Mean (SD)	3.169 (0.508)	3.151 (0.4767)	3.086 (0.362)	3.223 (0.421)	3.125 (0.382)	
Birth head circumfe-rence (cm)	**Boys**	n	1,600	210	13	12	12	0.005 *
		Mean (SD)	34.3 (1.6) [a]	34.6 (1.5) [b]	34.1 (1.3) [a,b]	35.3 (1.1) [a,b]	34.8 (1.7) [a,b]	
	Girls	n	1,605	171	12	16	15	0.642
		Mean (SD)	33.8 (1.5)	33.8 (1.5)	34.0 (1.4)	34.3 (1.3)	33.6 (0.8)	
	Total	n	3,205	381	25	28	27	0.056
		Mean (SD)	34.1 (1.6)	34.3 (1.5)	34.0 (1.4)	34.7 (1.3)	34.1 (1.4)	

Post-hoc tests: equal superscript letters indicate absence of significant differences between groups.
* Statistically significant, $p \leq 0.05$.

Using Kruskal-Wallis test for comparisons, differences in mean birth head circumference among boys (p=0.005) were confirmed to be significant only in the subgroup without maternal COVID-19 infection when compared to the control group (p=0.037). No significative differences between groups on gestational age or transformed birth anthropometric parameters were found when using a multivariate model to analyse the total sample (p=0.064).

Notwithstanding, when analysing the boy's sample with a multivariate model (Table 24), significant differences were noticed between groups (p=0.001, partial η^2=0.010) for transformed birth head circumference. These included positive significant differences between the control group and the subgroup without maternal COVID-19 infection, which was confirmed through pairwise comparisons (p=0.012), and between the control group and the subgroup with 2nd trimester maternal COVID-19 infection, which was not confirmed by post-hoc tests.

Using Fenton growth charts for boys as reference, significant differences were also observed among groups (p=0.001, partial η^2=0.010) for birth head circumference z-scores. These included overlapping positive significant differences between the control group and the subgroups without maternal infection and with 2nd trimester maternal infection, only the first being confirmed by post-hoc tests (p=0.010).

Table 24. Boys' birth head circumference multivariate analysis by maternal COVID-19 infection during pregnancy, split in pregnancy trimesters.

Pandemic Timeline Groups	Study sample				Fenton growth charts z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
Boys' transformed birth head circumference					**Boys' birth head circumference**			
Control Group	0	-	-	-	0	-	-	-
Pandemic Group With 1st Trim infection	-0.205	0.406	0.614	0.000	-0.144	0.262	0.582	0.000
Pandemic Group With 2nd Trim infection	0.992	0.424	0.019 *	0.003	0.636	0.273	0.020 *	0.003
Pandemic Group With 3rd Trim infection	0.638	0.422	0.131	0.001	0.371	0.272	0.173	0.001
Pandemic Group Without infection	0.350	0.107	0.001 *	0.006	0.229	0.069	<0.001*	0.006

Values adjusted for sex, twinship, gestational age and maternal COVID-19 infection during pregnancy.
* Statistically significant, $p \leq 0.05$.

Section B *- Child growth assessment*

B.1. Number of measurements

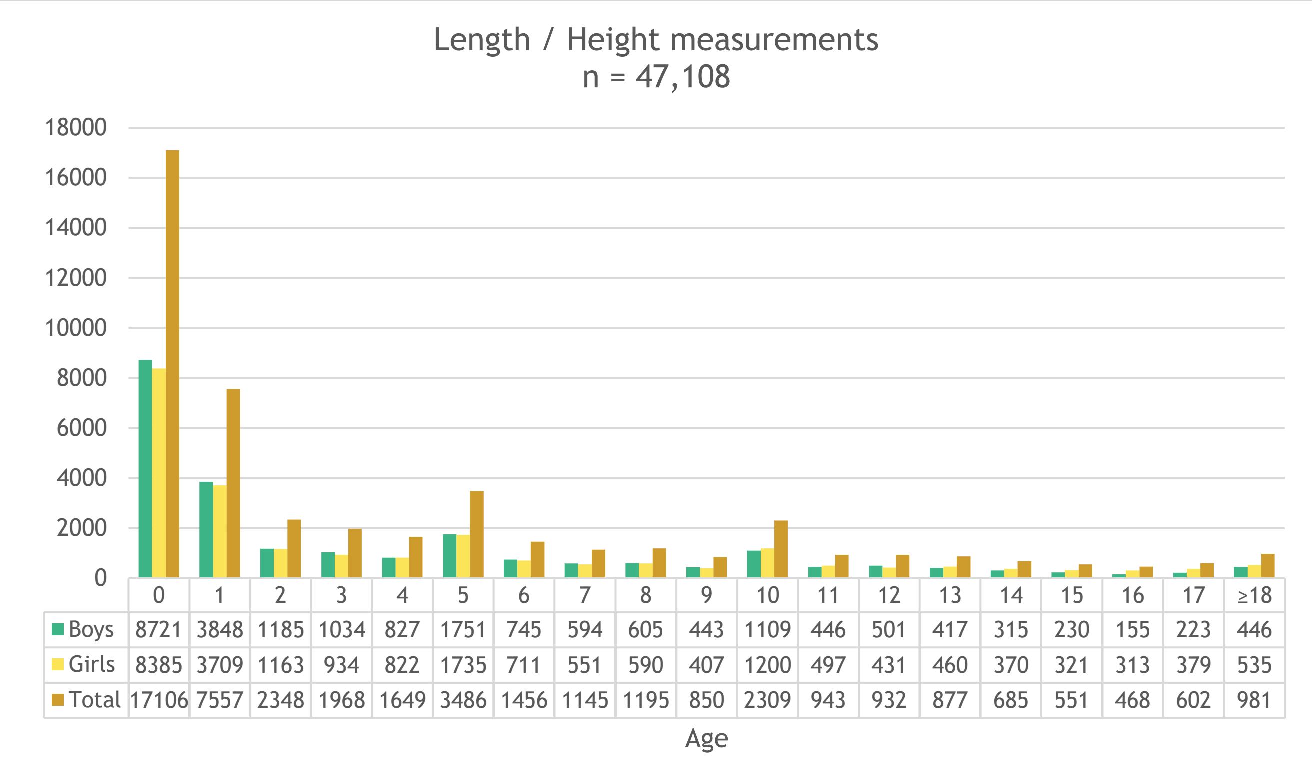
Out of the 4298 individuals included in the study sample, 4282 had at least one visit to the study sites' facilities with recorded anthropometric measurements. Hence, data from a total 202,452 measurements were manually retrieved from health records, covering the period from 27th September 2006 to 27th July 2023. Each subject had a mean of 12.5 appointments (SD=6.3), ranging from 1 to 53 different dates of healthcare facilities' visits with measurement records. General sample characterization by sex is presented on Table 25.

Table 25. Sample characterization by anthropometric measurements and blood pressure.

Parameter Measurements		Total Sample	Boys	Girls
Length/ Height (cm)	n	47,108	23,595	23,513
	Mean (SD)	94.1 (35.5)	93.7 (35.0)	94.4 (36.1)
	Range	[39.0;199.0]	[41.0;199.0]	[39.0;185.0]
Weight (kg)	n	51,442	25,659	25,783
	Mean (SD)	18.11 (18.36)	17.65 (16.78)	18.56 (17.91)
	Range	[1.87;145.0]	[1.93;145.0]	[1.87;121.0]
BMI (kg/m^2)	n	46,057	23,160	22,897
	Mean (SD)	17.2 (3.1)	17.2 (2.8)	17.3 (3.2)
	Range	[8.84;47.8]	[8.90;45.3]	[8.84;47.8]
Head circumference (cm)	n	26,636	13,524	13,112
	Mean (SD)	43.2 (3.9)	43.7 (5.0)	42.7 (4.8)
	Range	[30.8;55.0]	[31.0;55.0]	[30.8;55.0]
SBP (mmHg)	n	15,607	7,513	8,094
	Mean (SD)	96.0 (13.4)	95.7 (13.3)	96.4 (13.4)
	Range	[50.0;160.0]	[50.0;160.0]	[50.0;148.0]
DBP (mmHg)	n	15,602	7,512	8,090
	Mean (SD)	56.3 (10.7)	55.4 (10.2)	57.2 (11.0)
	Range	[30.0;97.0]	[30.0;97.0]	[30.0;96.0]
	Total n	202,452 measurements	100,963 measurements	101,489 measurements

B.2. Length/Height

A total 47,108 measurements of length/height were retrieved from health records. The distribution of these measurements across age is presented in Figure 4.



	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	≥18
Boys	8721	3848	1185	1034	827	1751	745	594	605	443	1109	446	501	417	315	230	155	223	446
Girls	8385	3709	1163	934	822	1735	711	551	590	407	1200	497	431	460	370	321	313	379	535
Total	17106	7557	2348	1968	1649	3486	1456	1145	1195	850	2309	943	932	877	685	551	468	602	981

Figure 4. Distribution of length/height measurements by age.

In accordance with the PNSIJ recommended appointments (Figure 1), the highest number of measurements was observed during the first and second years of life. There is a peak in measurements at both the 5-year and the 10-year age milestones, in line with the vaccination schedule. The lowest number of height measurements was recorded at 16 years.

Descriptive statistics on length/height measurements for the study sample are presented on Table 26, divided by age groups (from 0 to 18 years old).

Table 26. Length/height sample characterization by age groups.

Length/Height (cm)		0 to 1 years	2 to 4 years	5 to 9 years	10 to 18 years
Boys	n	12,569	3,046	4,138	3,396
	Mean (SD)	66.7 (11.5)	97.5 (8.1)	121.7 (10.5)	155.4 (14.0)
	Range	[41.0;98.0]	[78.0;123.0]	[100.0;160.0]	[120.0;199.0]
Girls	n	12,094	2,919	3,994	3,971
	Mean (SD)	65.2 (11.1)	96.2 (8.3)	120.6 (10.5)	153.8 (10.2)
	Range	[39.0;96.0]	[74.5;124.0]	[99.0;156.0]	[120.0;185.0]
Total	n	24,663	5,965	8,132	7,367
	Mean (SD)	66.0 (11.3)	96.9 (8.2)	121.2 (10.5)	154.5 (12.1)
	Range	[39.0;98.0]	[74.5;124.0]	[99.0;160.0]	[120.0;199.0]

Data from measurements made before the pandemic onset were used to create length/height-for-age growth charts for the index population (Figure 5). These are presented by sex, in a logarithmic scale, and include percentile curves. Information on transformed age and length/height logarithm can be found on Tables 1 and 3, respectively.

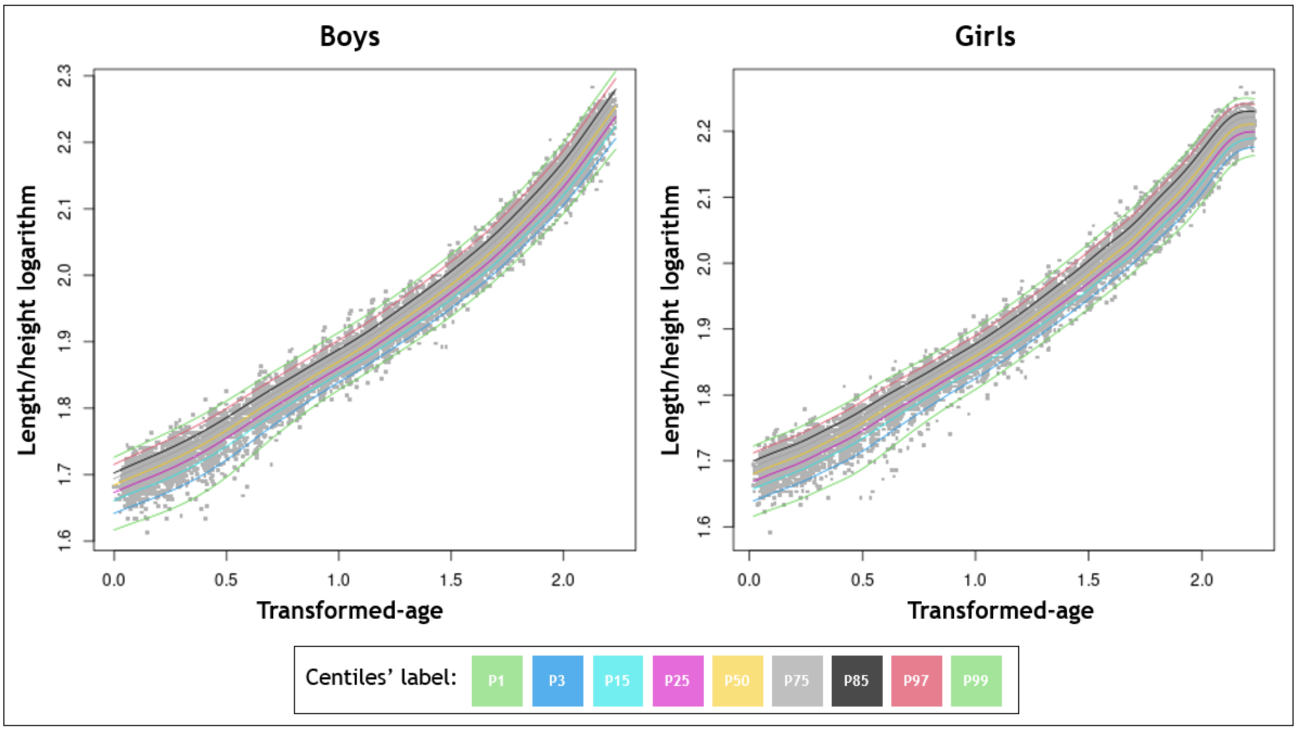


Figure 5. Length/height-for-age growth charts for the index population.

As can be observed, the length/height-for-age growth curve for girls stabilizes at an earlier age compared to the boys', which presents a steeper slope. A few outliers can be observed for lower lengths/heights, related with preterm children.

Using the index population as reference, the z-scores of logarithmic length/height measurements were obtained and used in a multivariate analysis across different time divisions. In parallel, using WHO child growth standards as reference, the z-scores of length/height measurements for that setting were calculated. Models were adjusted for sex, twinship, gestational age, transformed age and timeline.

Starting with timeline division I, statistically significant differences in logarithmic length/height z-scores were observed for all ages (p=0.005, partial η^2<0.001), but not among specific age ranges. Differences are explored on Table 27.

Table 27. Length/height z-scores' differences across division I groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.024	0.016	0.127	0.000	0.034	0.018	0.05 *	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.003	0.036	0.929	0.000	0.000	0.036	0.998	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.048	0.030	0.105	0.000	0.039	0.029	0.175	0.000
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.052	0.027	0.059	0.001	0.051	0.026	0.051	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.032	0.012	0.005 *	0.000	-0.037	0.012	0.003 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division I timespan groups.
* Statistically significant, $p \leq 0.05$.

Significantly positive coefficients in logarithmic length/height z-scores were observed in the pandemic group when compared to the control group while considering all ages (p=0.005), but not for specific age ranges.

When adopting WHO child growth standards as reference, statistically significant general differences were observed among groups for all ages (p=0.003, partial η^2<0.001), as well as among 0 to 1 years old (p=0.050, partial η^2<0.001). In this scenario, when considering all ages, a significant negative difference was spotted in length/height z-scores for the pandemic group, compared to the control group. As for ages 0 to 1 years old, it was spotted a positive significant difference.

When applying timeline division II while considering the index population as reference, statistically significant differences were observed among groups for all ages (p=0.015, partial η^2<0.001), as well as among specific age ranges, including 0 to 1 years old (p=0.036, partial η^2<0.001) and 2 to 4 years old (p=0.027, partial η^2=0.001). Differences between groups are depicted in Table 28.

There was a significative positive difference in logarithmic length/height z-scores in group α when compared to the control group, both for all ages and for ages 0 to 1 years old. As for group β, there was a significant negative difference of logarithmic height z-scores when compared to the control group in ages 2 to 4 years old. On the contrary, for the age group over 10 years old, there was a significant positive difference in group β when compared to the control group.

Post-hoc analysis confirmed the following statistically significant differences:

- in age group 0 to 1 years, between the control group and group α (p=0.038)
- in age group 2 to 4 years old, between group α and group β (p=0.022).

Table 28. Length/height z-scores' differences across division II groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.051	0.020	0.013 *	0.000	0.064	0.022	0.004 *	0.000
Group β	-0.010	0.023	0.669	0.000	-0.004	0.025	0.861	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.076	0.046	0.102	0.000	0.082	0.047	0.081	0.001
Group β	-0.101	0.051	0.048 *	0.001	-0.101	0.052	0.051	0.001
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.022	0.039	0.572	0.000	0.010	0.038	0.791	0.000
Group β	0.075	0.040	0.061	0.000	0.071	0.040	0.075	0.000
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.032	0.033	0.334	0.000	0.034	0.032	0.286	0.000
Group β	0.073	0.034	0.035 *	0.001	0.070	0.032	0.030 *	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Group α	0.040	0.015	0.008 *	0.000	-0.017	0.016	0.288	0.000
Group β	0.024	0.016	0.140	0.000	-0.061	0.017	<0.001 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division II timespan groups.
Group α: Pandemic with restrictions. Group β: Pandemic without restrictions.
* Statistically significant, $p \leq 0.05$.

When adopting WHO child growth standards as reference for division II analysis, general results were overlapping, with significative differences identified for all ages (p=0.001, partial η^2<0.001), for ages 0 to 1 years old (p=0.015, partial η^2<0.001), and for ages 2 to 4 years old (p=0.023, partial η^2=0.001). In this setting, there was a positive significant difference in group α when compared to the control group, when analysing ages 0 to 1 years old. Considering all ages, there was a significant negative difference in in group β in comparison to the control group. The difference between group β and the control group displayed a significant positive trend in age range over 10 years old. Post-hoc analysis confirmed the following statistically significant differences:

- for all ages, between the control group and group β (p<0.001).
- in age group 0 to 1 years, between the control group and group α (p=0.012).
- in age group 2 to 4 years old, between group α and group β (p=0.018).

Considering timeline division III, with the index population as reference, statistically significant differences in logarithmic length/height z-scores were generally observed between groups, both for all ages (p<0.001, partial η^2<0.001) and for specific age ranges, including 0 to 1 years old (p=0.002, partial η^2=0.001), 2 to 4 years old (p=0.029, partial η^2=0.002), and over 10 years old (p=0.029, partial η^2=0.002). Distinctions between groups are detailed in Table 29.

There was a significant positive difference in logarithmic length/height in group 2 when compared to the control group, both for all ages and for ages 0 to 1 years old. As for group 3, there was a significant negative difference in logarithmic length/height when compared to the control group in ages 2 to 4 years old, yet displaying a positive difference in ages over 10 years old.

Post-hoc analysis for timeline division III confirmed the following statistically significant differences among groups:

- for ages 0 to 1 years, between the control group and group 2 (p=0.001).
- for ages 0 to 1 years, between group 1 and group 2 (p=0.025).
- for ages 0 to 1 years, between group 2 and group 3 (p=0.007).
- for age range 2 to 4 years old, between group 2 and group 3 (p=0.06).

Table 29. Length/height z-scores' differences across division III groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.007	0.030	0.800	0.000	0.003	0.033	0.928	0.000
Group 2	0.107	0.029	<0.001 *	0.001	0.124	0.032	<0.001 *	0.001
Group 3	-0.005	0.022	0.811	0.000	0.001	0.024	0.976	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.101	0.076	0.184	0.000	0.105	0.077	0.172	0.000
Group 2	0.090	0.060	0.136	0.000	0.097	0.061	0.112	0.000
Group 3	-0.103	0.049	0.036 *	0.001	-0.102	0.049	0.039 *	0.001
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.004	0.063	0.946	0.000	-0.014	0.062	0.824	0.000
Group 2	0.031	0.050	0.537	0.000	0.022	0.050	0.664	0.000
Group 3	0.073	0.039	0.061	0.000	0.069	0.038	0.074	0.000
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.053	0.053	0.309	0.000	-0.041	0.049	0.406	0.000
Group 2	0.070	0.041	0.086	0.001	0.069	0.038	0.073	0.001
Group 3	0.075	0.033	0.024 *	0.001	0.071	0.031	0.023*	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.009	0.023	0.681	0.000	-0.039	0.024	0.105	0.000
Group 2	0.077	0.020	<0.001 *	0.000	0.008	0.021	0.712	0.000
Group 3	0.025	0.015	0.108	0.000	-0.061	0.016	<0.001 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
Group 1: 1st Lockdown + Reopening. Group 2: 2nd Lockdown + Reopening. Group 3: 3rd Lockdown + Reopening.
* Statistically significant, *p*≤0.05.

When adopting WHO child growth standards as reference, results were similar to the previously described, with the identification of significative differences for all ages (p<0.001, partial η^2<0.001), for ages 0 to 1 years old (p=0.001, partial η^2=0.001), for ages 2 to 4 years old (p=0.026, partial η^2=0.002), and for ages over 10 years old (p=0.034, partial η^2=0.001). Length/height z-scores exhibited a significant negative difference in group 3 in comparison to the control group. For age groups 0 to 1 years old, 2 to 4 years old and over 10 years old, trends were similar to those described for the index population. Post-hoc analysis confirmed many statistically significant differences:

- for all ages, between the control group and group 3 (p<0.001).
- for all ages, between group 2 and group 3 (p=0.035).
- for ages 0 to 1 years, between the control group and group 2 (p<0.001).
- for ages 0 to 1 years old, between group 1 and group 2 (p=0.035).
- for ages 0 to 1 years old, between group 2 and group 3 (p=0.008)
- for ages 2 to 4 years old, between group 2 and group 3 (p=0.05).

When analysing timeline division IV, considering the index population as reference, statistically significant general differences were observed among groups for all ages (p=0.005, partial η^2<0.001), for ages 0 to 1 years old (p<0.001, partial η^2=0.001) and for ages 2 to 4 years old (p=0.031, partial η^2=0.002). These discrepancies in logarithmic length/height z-scores are explored in Table 30.

There was a significant positive difference in group D, when compared to the control group, both for all ages and for 0 to 1 years old. On the contrary, for ages 2 to 4 years old, there was a significant negative z-score difference in group F when compared to the control group. Post-hoc analysis, however, only confirmed statistically significant differences in age group 0 to 1 years old, between the control group and group D (p<0.001), and between group D and group F (p=0.001).

When adopting WHO child growth standards as reference, results were similar, with significative differences in length/height z-scores being identified between groups for all ages (p<0.001, partial η^2=0.001), for ages 0 to 1 years old (p<0.001, partial η^2=0.001), and for ages 2 to 4 years old (p=0.027, partial η^2=0.002).

Table 30. Length/height z-scores' differences across division IV groups.

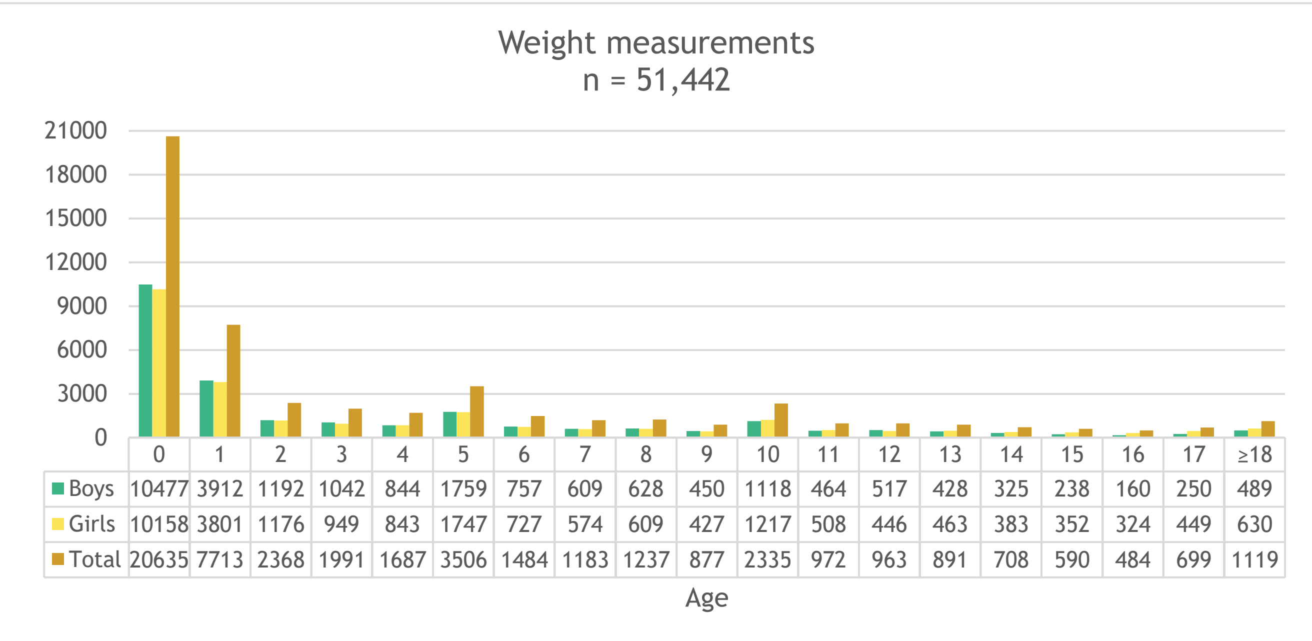
Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.060	0.060	0.320	0.000	-0.055	0.066	0.408	0.000
Group B - 1st R	0.008	0.034	0.804	0.000	0.02	0.037	0.581	0.000
Group C - 2nd L	-0.051	0.067	0.443	0.000	-0.06	0.074	0.418	0.000
Group D - 2nd R	0.141	0.031	<0.001 *	0.001	0.163	0.035	<0.001 *	0.001
Group E - 3rd L	0.039	0.069	0.569	0.000	0.051	0.076	0.501	0.000
Group F - 3rd R	-0.010	0.023	0.669	0.000	-0.004	0.025	0.861	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.409	0.248	0.100	0.000	-0.418	0.25	0.094	0.000
Group B - 1st R	0.153	0.080	0.056	0.001	0.158	0.081	0.050 *	0.001
Group C - 2nd L	0.032	0.145	0.824	0.000	0.048	0.146	0.745	0.000
Group D - 2nd R	0.101	0.066	0.123	0.000	0.106	0.066	0.108	0.000
Group E - 3rd L	-0.116	0.150	0.441	0.000	-0.109	0.151	0.469	0.000
Group F - 3rd R	-0.101	0.051	0.048 *	0.001	-0.101	0.052	0.051	0.001
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.174	0.155	0.262	0.000	-0.189	0.152	0.215	0.000
Group B - 1st R	0.037	0.068	0.581	0.000	0.019	0.067	0.776	0.000
Group C - 2nd L	0.124	0.134	0.354	0.000	0.108	0.132	0.414	0.000
Group D - 2nd R	0.017	0.054	0.753	0.000	0.008	0.053	0.875	0.000
Group E - 3rd L	0.04	0.142	0.776	0.000	0.042	0.14	0.766	0.000
Group F - 3rd R	0.075	0.040	0.061	0.000	0.071	0.04	0.075	0.000
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.038	0.158	0.811	0.000	-0.044	0.155	0.778	0.000
Group B - 1st R	-0.055	0.055	0.316	0.000	-0.041	0.051	0.428	0.000
Group C - 2nd L	0.061	0.103	0.557	0.000	0.090	0.095	0.348	0.000
Group D - 2nd R	0.072	0.043	0.098	0.000	0.066	0.040	0.105	0.000
Group E - 3rd L	0.092	0.092	0.318	0.000	0.068	0.082	0.407	0.000
Group F - 3rd R	0.074	0.034	0.032 *	0.001	0.071	0.032	0.027 *	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.095	0.053	0.072	0.000	-0.096	0.056	0.086	0.000
Group B - 1st R	0.009	0.025	0.707	0.000	-0.027	0.026	0.312	0.000
Group C - 2nd L	0.012	0.049	0.808	0.000	-0.029	0.052	0.573	0.000
Group D - 2nd R	0.089	0.022	<0.001 *	0.000	0.014	0.023	0.523	0.000
Group E - 3rd L	0.034	0.049	0.479	0.000	-0.066	0.050	0.190	0.000
Group F - 3rd R	0.024	0.016	0.135	0.000	-0.060	0.017	<0.001 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division IV timespan groups.
* Statistically significant, $p \leq 0.05$. L - Lockdown. R - Reopening.

There was a significant negative difference in group F in comparison to the control group, when analysing all ages, which was confirmed by post-hoc pairwise comparisons (p=0.007). As for age range 0 to 1 years old, there was a positive z-score difference in group D in comparison to the control group. In this age range, post-hoc analysis unveiled significant differences between the control group and group D (p<0.001), and between group D and group F (p=0.001). There was also a significant positive z-score difference in group B when compared to the control group for ages 2 to 4 years old. Post-hoc analysis, however, did not confirm these differences in length/height z-scores.

B.3. Weight

A total 51,442 weight measurements were collected from health records. The distribution of these measurements across age is presented in Figure 6.



Age	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	≥18
Boys	10477	3912	1192	1042	844	1759	757	609	628	450	1118	464	517	428	325	238	160	250	489
Girls	10158	3801	1176	949	843	1747	727	574	609	427	1217	508	446	463	383	352	324	449	630
Total	20635	7713	2368	1991	1687	3506	1484	1183	1237	877	2335	972	963	891	708	590	484	699	1119

Figure 6. Distribution of weight measurements by age.

In accordance with the PNSIJ recommended appointments (Figure 1), the highest number of measurements was observed during the first and second years of life. There is a peak in measurements at both the 5-year and the 10-year age milestones. The lowest number of weight measurements was recorded at 16 years.

Descriptive statistics on weight measurements for the whole study sample are presented on Table 31, divided by age groups (between 0 and 18 years old).

Table 31. Weight sample characterization by age groups.

Weight (kg)		0 to 1 years	2 to 4 years	5 to 9 years	10 to 18 years
Boys	n	14,389	3,078	4,203	3,500
	Mean (SD)	7.31 (3.09)	15.88 (3.16)	26.04 (7.54)	50.61 (15.56)
	Range	[1.93;19.05]	[8.95;32.0]	[13.8;69.0]	[22.5;145.0]
Girls	n	13,959	2,968	4,084	4,142
	Mean (SD)	6.83 (2.89)	15.48 (3.38)	25.96 (7.74)	50.78 (13.89)
	Range	[1.87;18.5]	[8.49;35.5]	[13.2;77.0]	[22.0;115.0]
Total	n	28,348	6,046	8,287	7,642
	Mean (SD)	7.07 (3.0)	15.68 (3.27)	26.0 (7.64)	50.7 (14.68)
	Range	[1.87;19.05]	[8.49;35.5]	[13.2;77.0]	[22.0;145.0]

Data from measurements made before the pandemic onset were used to create weight-for-age growth charts for the index population (Figure 7). These are presented by sex, in a logarithmic scale, and include percentile curves. Information on transformed age and weight logarithm can be found on Table 1 and Table 3, respectively. As presented on Figure 7, the weight-for-age growth curve for girls stabilizes at an earlier age compared to boys. Boys seem to display heavier weight than girls, in average. A few outliers can be observed for lower weights, which are related with preterm children.

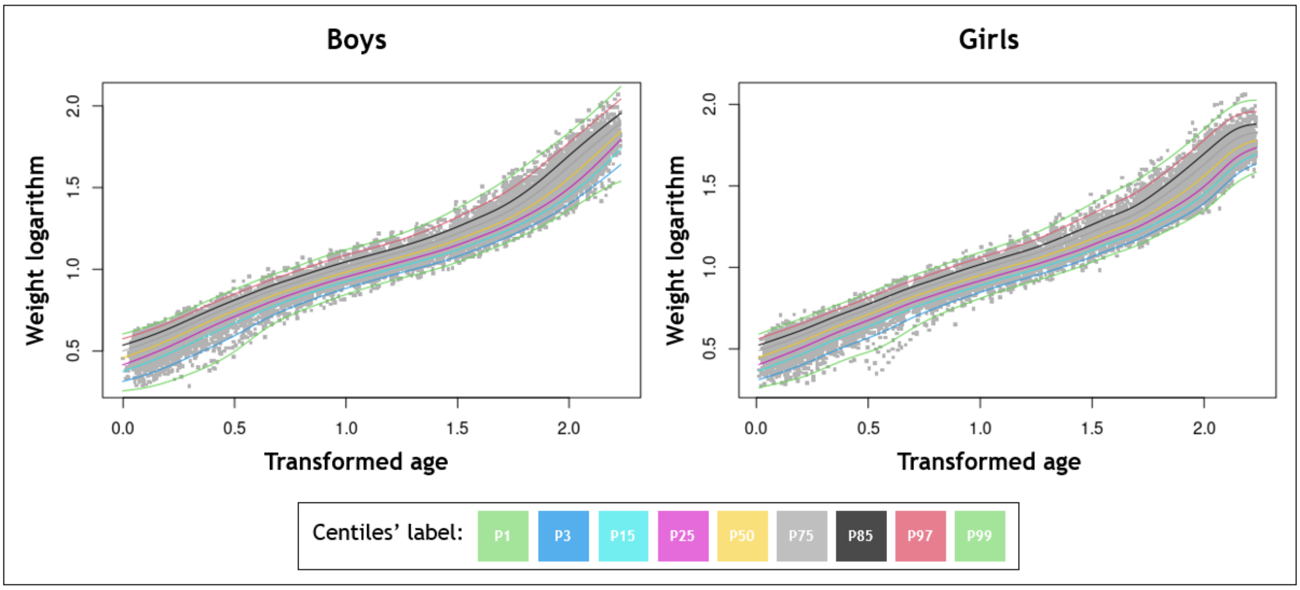


Figure 7. Weight-for-age growth charts for the index population.

Using the index population as reference, the z-scores of logarithmic weight measurements were obtained and used in a multivariate analysis across different time divisions. In parallel, using WHO child growth standards as reference, the z-scores of length/height measurements for that setting were calculated and used for a multivariate model analysis. Models were adjusted for sex, twinship, gestational age, transformed age and pandemic timeline.

Regarding timeline division I, with the index population as reference, statistically significant differences in logarithmic weight z-scores were observed among groups for ages 0 to 1 years old (p<0.001, partial η^2<0.001) and for ages over 10 years old (p<0.001, partial η^2=0.001), but not when analysing for all ages (p=0.981). Differences between groups are explored in Table 32. When adopting WHO child growth standards as the reference population, statistically significant differences were observed in weight z-scores solely among ages 0 to 1 years old (p=0.05, partial η^2<0.001). In both scenarios, these differences displayed a negative trend in comparison to the control group.

Table 32. Weight z-scores' differences across division I groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.055	0.015	<0.001*	0.000	-0.042	0.015	0.005 *	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.014	0.036	0.683	0.000	-0.019	0.038	0.616	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.027	0.029	0.359	0.000	0.028	0.034	0.407	0.000
Over 10 years old								
Control Group	0	-	-	-				
Pandemic Group	0.052	0.027	0.059	0.001				
All ages								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.000	0.011	0.981	0.000	-0.022	0.013	0.095	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division I timespan groups.
* Statistically significant, $p \leq 0.05$.

Considering the index population as reference, stratified according to timeline division II, statistically significant differences were observed in logarithmic weight z-scores among groups for all ages (p=0.008, partial η^2<0.001), as well as among specific age ranges, including 0 to 1 years old (p<0.001, partial η^2=0.001) and over 10 years old (p<0.001, partial η^2=0.003). Differences between groups are explored in Table 33. In this setting, there was a significative negative difference in logarithmic weight z-scores in group β when compared to the control group, both when considering all ages and for ages 0 to 1 years old. As for age range over 10 years old, there was a significative positive difference of logarithmic weight z-scores in both groups when compared to the control group.

Post-hoc analysis through pairwise comparisons for timeline division II confirmed the following significant differences:

- for all ages, between group α and group β (*p*=0.006).
- for ages 0 to 1 years old, between the control group and group β (*p*<0.001), and between group α and group β (*p*=0.040).
- for ages over 10 years old, between the control group and group α (*p*<0.001), and between the control group and group β (*p*=0.038).

Table 33. Weight z-scores' differences across division II groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	-0.025	0.019	0.192	0.000	-0.009	0.019	0.643	0.000
Group β	-0.092	0.021	<0.001 *	0.001	-0.085	0.022	<0.001 *	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.038	0.046	0.409	0.000	0.039	0.049	0.431	0.000
Group β	-0.078	0.050	0.122	0.000	-0.088	0.053	0.099	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.074	0.039	0.058	0.000	0.080	0.045	0.076	0.000
Group β	-0.021	0.039	0.586	0.000	-0.025	0.046	0.583	0.000
Over 10 years old								
Control Group	0	-	-	-				
Group α	0.143	0.033	<0.001 *	0.003				
Group β	0.084	0.034	0.013 *	0.001				
All ages								
Control Group	0	-	-	-	0	-	-	-
Group α	0.028	0.014	0.051	0.000	0.015	0.017	0.396	0.000
Group β	-0.033	0.015	0.031 *	0.000	-0.066	0.019	<0.001 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division II timespan groups.
Group α: Pandemic with restrictions. Group β: Pandemic without restrictions.
* Statistically significant, *p*≤0.05.

When adopting WHO child growth standards as reference, significative differences were generally identified for weigh z-scores regarding all ages (p<0.001, partial η^2<0.001) and ranging from 0 to 1 years old (p<0.001, partial η^2=0.001). There was a significative negative difference in weight z-scores in group β when compared to the control group, for both all ages and for ages 0 to 1 years old. Post-hoc analysis for timeline division II confirmed the following statistically significant differences between groups:

- for all ages, between the control group and group β (p=0.001), and between group α and group β (p=0.002)
- for ages 0 to 1 years old, between the control group and group β (p<0.001), and between group α and group β (p=0.018).

Narrowing the timeline to division III (Table 34) and considering the index population as reference, statistically significant differences in logarithmic weight z-scores were noticed between groups for all ages (p=0.011, partial η^2<0.001) and for specific age ranges, including 0 to 1 years old (p<0.001, partial η^2=0.001) and over 10 years old (p<0.001, partial η^2=0.004). There was a significant negative difference in group 3 when compared to the control group, both for all ages and for ages 0 to 1 years. As for group 1, there was a significant positive difference in logarithmic weight z-scores when compared to the control group in age range 5 to 9 years old. Regarding ages over 10 years old, all three pandemic groups presented a statistically significative positive difference in comparison to the control group.

Post-hoc analysis confirmed the following statistically significant differences:

- for all ages, between group 1 and group 3 (p=0.041), and between group 2 and group 3 (p=0.036).

- for ages 0 to 1 years old, between the control group and group 3 ($p<0.001$).
- for ages over 10 years old, between the control group and group 1 ($p=0.004$), and between the control group and group 2 ($p=0.003$).

Table 34. Weight z-scores' differences across division III groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.029	0.028	0.293	0.000	-0.012	0.028	0.662	0.000
Group 2	-0.010	0.027	0.722	0.000	0.004	0.027	0.873	0.000
Group 3	-0.092	0.020	<0.001 *	0.001	-0.083	0.021	<0.001 *	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.037	0.076	0.632	0.000	0.033	0.081	0.682	0.000
Group 2	0.037	0.060	0.544	0.000	0.041	0.064	0.516	0.000
Group 3	-0.065	0.048	0.178	0.000	-0.075	0.051	0.140	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.151	0.063	0.017 *	0.001	0.157	0.073	0.032 *	0.001
Group 2	0.030	0.050	0.557	0.000	0.031	0.058	0.588	0.000
Group 3	-0.016	0.038	0.672	0.000	-0.017	0.044	0.700	0.000
Over 10 years old								
Control Group	0	-	-	-				
Group 1	0.174	0.051	<0.001 *	0.002				
Group 2	0.138	0.040	<0.001 *	0.002				
Group 3	0.081	0.033	0.013 *	0.001				
All ages								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.036	0.022	0.101	0.000	0.028	0.026	0.277	0.000
Group 2	0.030	0.019	0.113	0.000	0.009	0.023	0.707	0.000
Group 3	-0.032	0.015	0.027 *	0.000	-0.062	0.018	<0.001 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
Group 1: 1st Lockdown + Reopening. Group 2: 2nd Lockdown + Reopening. Group 3: 3rd Lockdown + Reopening.
* Statistically significant, $p \leq 0.05$.

When adopting WHO child growth standards as reference, significative differences were identified for weight z-scores regarding all ages (p=0.003, partial η^2<0.001) and ranging from 0 to 1 years old (p<0.001, partial η^2=0.001), in general. Difference trends between groups were similar to the ones described for the index population regarding all ages and age group 0 to 1 years old. As for ages 5 to 9 years old, there was a significant positive difference in weight z-scores between the control group and group 1. Post-hoc analysis confirmed the following statistically significant differences between groups:

- for all ages, between the control group and group 3 (p=0.003), and between group 1 and group 3 (p=0.018).
- for ages 0 to 1 years old, between the control group and group 3 (p<0.001), and between group 2 and group 3 (p=0.046).

Considering the index population as reference, regarding timeline division IV, statistically significant differences in logarithmic weight z-scores were observed among groups for all ages (p=0.013, partial η^2<0.001), for ages 0 to 1 years old (p=0.001, partial η^2=0.001), for ages 5 to 9 years old (p=0.03, partial η^2=0.002) and for ages over 10 years old (p<0.001, partial η^2=0.004). Differences between groups are explored in Table 35.

Logarithmic weight z-scores featured a significant negative difference when comparing group F with the control group, both for all ages and for 0 to 1 years old. In addition, there was a significant positive z-score difference in group B when compared to the control group, both for all ages and for 5 to 9 years old. As for over 10 years old, there was a positive difference during timespans B, D and F, in comparison to the control group.

Table 35. Weight z-scores' differences across division IV groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.046	0.057	0.420	0.000	-0.038	0.058	0.517	0.000
Group B - 1st R	-0.024	0.032	0.439	0.000	-0.005	0.032	0.879	0.000
Group C - 2nd L	0.034	0.064	0.598	0.000	0.013	0.065	0.843	0.000
Group D - 2nd R	-0.018	0.029	0.531	0.000	0.003	0.030	0.930	0.000
Group E - 3rd L	-0.091	0.063	0.150	0.000	-0.069	0.065	0.286	0.000
Group F - 3rd R	-0.092	0.021	<0.001 *	0.001	-0.085	0.022	<0.001 *	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.013	0.247	0.958	0.000	-0.051	0.262	0.845	0.000
Group B - 1st R	0.042	0.080	0.603	0.000	0.042	0.085	0.622	0.000
Group C - 2nd L	0.102	0.145	0.483	0.000	0.128	0.153	0.405	0.000
Group D - 2nd R	0.024	0.066	0.718	0.000	0.024	0.069	0.725	0.000
Group E - 3rd L	0.055	0.146	0.706	0.000	0.042	0.155	0.788	0.000
Group F - 3rd R	-0.078	0.050	0.123	0.000	-0.088	0.053	0.100	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.232	0.158	0.141	0.000	-0.265	0.182	0.145	0.000
Group B - 1st R	0.221	0.069	0.001 *	0.001	0.234	0.079	0.003 *	0.001
Group C - 2nd L	0.104	0.132	0.429	0.000	0.107	0.152	0.482	0.000
Group D - 2nd R	0.018	0.054	0.743	0.000	0.019	0.062	0.754	0.000
Group E - 3rd L	0.058	0.141	0.682	0.000	0.096	0.163	0.557	0.000
Group F - 3rd R	-0.021	0.039	0.587	0.000	-0.025	0.046	0.584	0.000
Over 10 years old								
Control Group	0	-	-	-				
Group A - 1st L	0.035	0.152	0.817	0.000				
Group B - 1st R	0.190	0.054	<0.001 *	0.002				
Group C - 2nd L	0.005	0.101	0.959	0.000				
Group D - 2nd R	0.158	0.042	<0.001 *	0.002				
Group E - 3rd L	0.063	0.091	0.492	0.000				
Group F - 3rd R	0.084	0.034	0.013 *	0.001				
All ages								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.064	0.050	0.202	0.000	-0.057	0.056	0.308	0.000
Group B - 1st R	0.058	0.024	0.016 *	0.000	0.050	0.029	0.084	0.000
Group C - 2nd L	0.042	0.047	0.369	0.000	0.047	0.057	0.410	0.000
Group D - 2nd R	0.028	0.021	0.172	0.000	0.001	0.026	0.955	0.000
Group E - 3rd L	-0.025	0.046	0.584	0.000	-0.019	0.057	0.744	0.000
Group F - 3rd R	-0.033	0.015	0.031 *	0.000	-0.066	0.019	<0.001 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
* Statistically significant, $p \leq 0.05$. L - Lockdown. R - Reopening.

Post-hoc analysis confirmed the following statistically significant differences:

- for all ages, between group B and group F (p=0.02).
- for ages 0 to 1 years old, between the control group and group F (p<0.001).
- for ages 5 to 9 years old, between the control group and group B (p=0.027), and between group B and group F (p=0.034).
- for ages over 10 years old, between the control group and group B (p=0.009), and between the control group and group D (p=0.004).

When using WHO child growth standards as reference, significant weight z-score differences emerged for all ages (p=0.006, partial η^2<0.001), and among ages 0 to 1 years (p=0.011, partial η^2=0.001). Group B exhibited higher weight z-scores when compared to the control group for ages 5 to 9 years, while group F exhibited lower weight z-scores when compared to the control group for all ages and for ages 0 to 1 years. Post-hoc analysis confirmed these differences: for all ages, between the control group and group F (p=0.008), and group B versus group F (p=0.011); for 0 to 1 years, between the control group and group F (p=0.002).

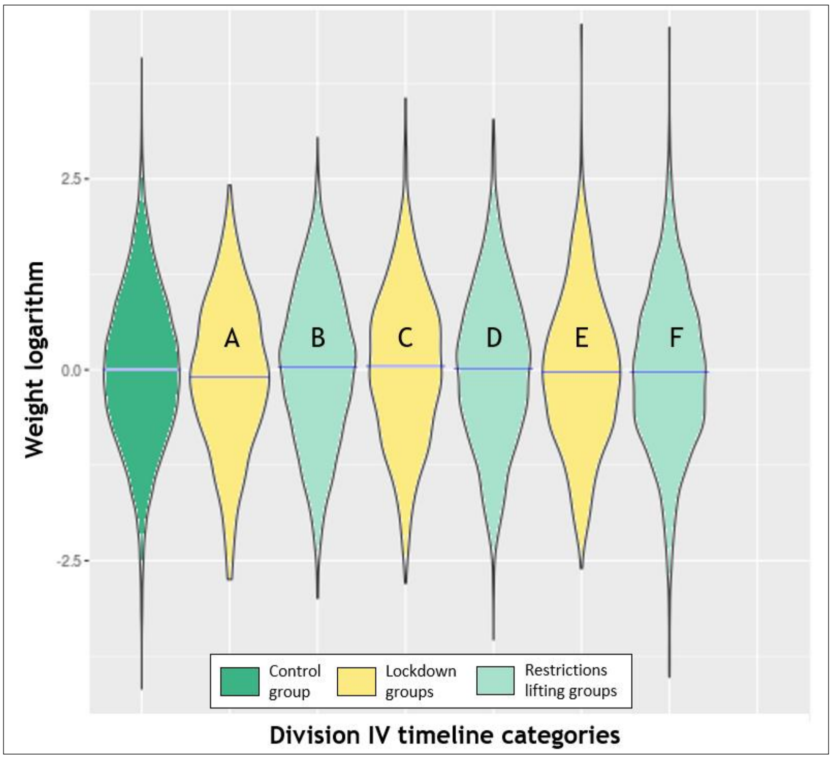


Figure 8. Logarithmic weight distribution across the COVID-19 pandemic.

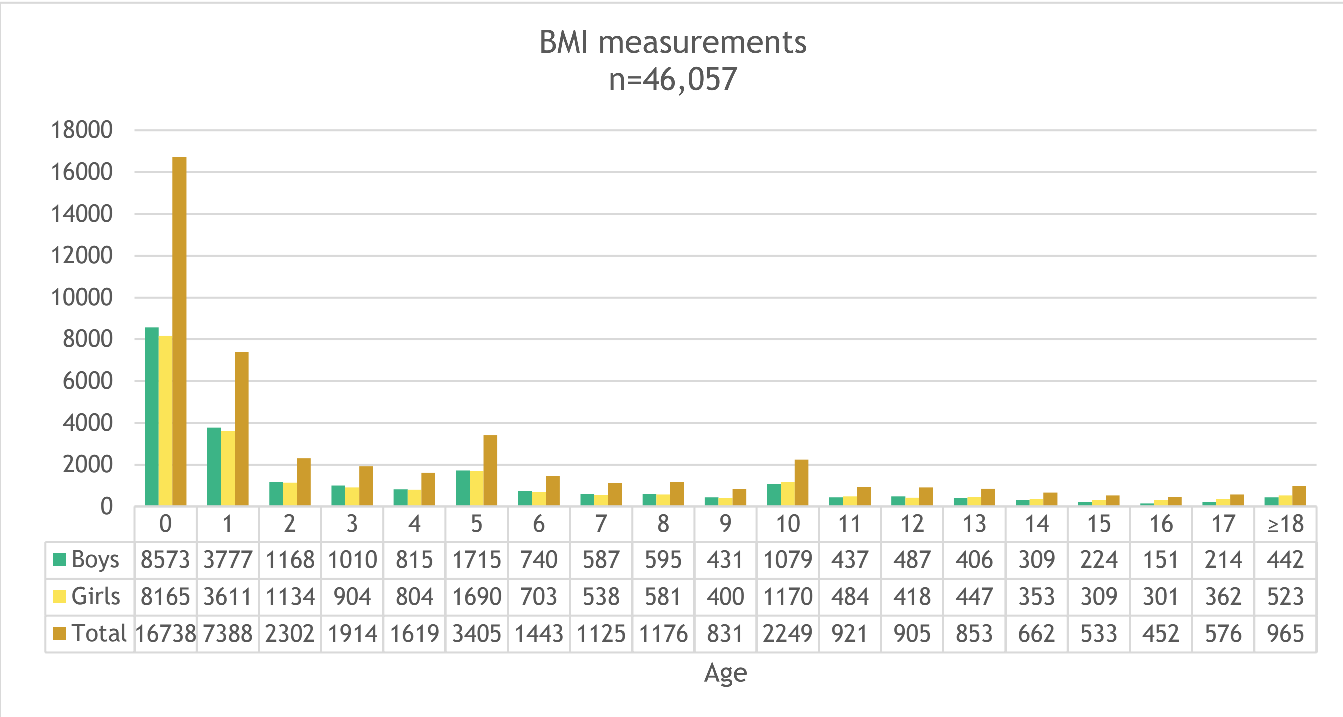
The distribution of weight logarithms across division IV categories is presented in Figure 8, using a violin plot. More detailed comparisons can be found on Table 36. Notably, the control group exhibits significant differences from pandemic groups B through F, with these displaying a significant positive difference when compared to the control group. Group A exhibits significant differences from pandemic groups B, D, E, and F, all showing a positive trend of weight gain in comparison to group A. Group B, corresponding to the 1st restriction lifting phase, is significantly different from the other two reopening groups (D and F).

Table 36. Comparison of logarithmic weight parameters across division IV timespans.

Pandemic Timeline Groups	Mean	Std. Error of the Mean	*p* value for pairwise comparisons	
Control Group	1.052	0.001	**Group A** - 1st Lockdown	0.957
			Group B - 1st Reopening	<0.001 *
			Group C - 2nd Lockdown	<0.001 *
			Group D - 2nd Reopening	<0.001 *
			Group E - 3rd Lockdown	<0.001 *
			Group F - 3rd Reopening	<0.001 *
Group A	1.059	0.004	**Group B** - 1st Reopening	0.008 *
			Group C - 2nd Lockdown	0.086
			Group D - 2nd Reopening	<0.001 *
			Group E - 3rd Lockdown	<0.001 *
			Group F - 3rd Reopening	<0.001 *
Group B	1.075	0.002	**Group C** - 2nd Lockdown	1.000
			Group D - 2nd Reopening	<0.001 *
			Group E - 3rd Lockdown	0.112
			Group F - 3rd Reopening	0.008 *
Group C	1.075	0.004	**Group D** - 2nd Reopening	0.205
			Group E - 3rd Lockdown	0.457
			Group F - 3rd Reopening	0.593
Group D	1.086	0.002	**Group E** - 3rd Lockdown	1.000
			Group F - 3rd Reopening	0.994
Group E	1.087	0.004	**Group F** - 3rd Reopening	1.000
Group F	1.083	0.002		

B.4. Body Mass Index

A total of 46,057 BMI measurements were collected for analysis. This number is inferior to the total number of length/height and weight measurements, since they may not have always coincided in date of measurement. The distribution of BMI measurements across age is presented in Figure 9.



Age	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	≥18
Boys	8573	3777	1168	1010	815	1715	740	587	595	431	1079	437	487	406	309	224	151	214	442
Girls	8165	3611	1134	904	804	1690	703	538	581	400	1170	484	418	447	353	309	301	362	523
Total	16738	7388	2302	1914	1619	3405	1443	1125	1176	831	2249	921	905	853	662	533	452	576	965

Figure 9. Distribution of BMI measurements by age.

In accordance with the PNSIJ recommended appointments (Figure 1), the highest number of measurements was observed during the first and second years of life. There is a peak in measurements at both the 5-year and the 10-year age milestones. Since the lowest number of height and weight measurements was recorded at 16 years, this is also the age range with less BMI measurements.

Descriptive statistics on BMI measurements for the entire study sample are presented on Table 37, divided by age groups (from 0 to 18 years old).

Table 37. BMI sample characterization by age groups.

BMI (kg/m^2)		0 to 1 years	2 to 4 years	5 to 9 years	10 to 18 years
Boys	n	12,350	2,993	4,068	3,307
	Mean (SD)	16.4 (2.1)	16.6 (1.6)	17.2 (2.6)	20.4 (3.9)
	Range	[8.9;25.8]	[12.4;26.0]	[12.0;29.7]	[12.5;45.3]
Girls	n	11,776	2,842	3,912	3,844
	Mean (SD)	16.1 (2.0)	16.5 (1.8)	17.4 (2.9)	21.0 (4.2)
	Range	[8.8;25.3]	[12.0;27.8]	[12.1;33.8]	[12.1;47.8]
Total	n	24,126	5,835	7,980	7,151
	Mean (SD)	16.3 (2.0)	16.5 (1.7)	17.3 (2.7)	20.7 (4.1)
	Range	[8.8;25.8]	[12.0;27.8]	[12.0;33.8]	[12.1;47.8]

Data from measurements made before the pandemic onset were used to create BMI-for-age growth charts for the index population (Figure 7), presented by sex and including percentile curves. Information on transformed age and transformed BMI logarithms can be found on Table 1 and Table 3, respectively. The BMI-for-age growth curve is similar for both sexes.

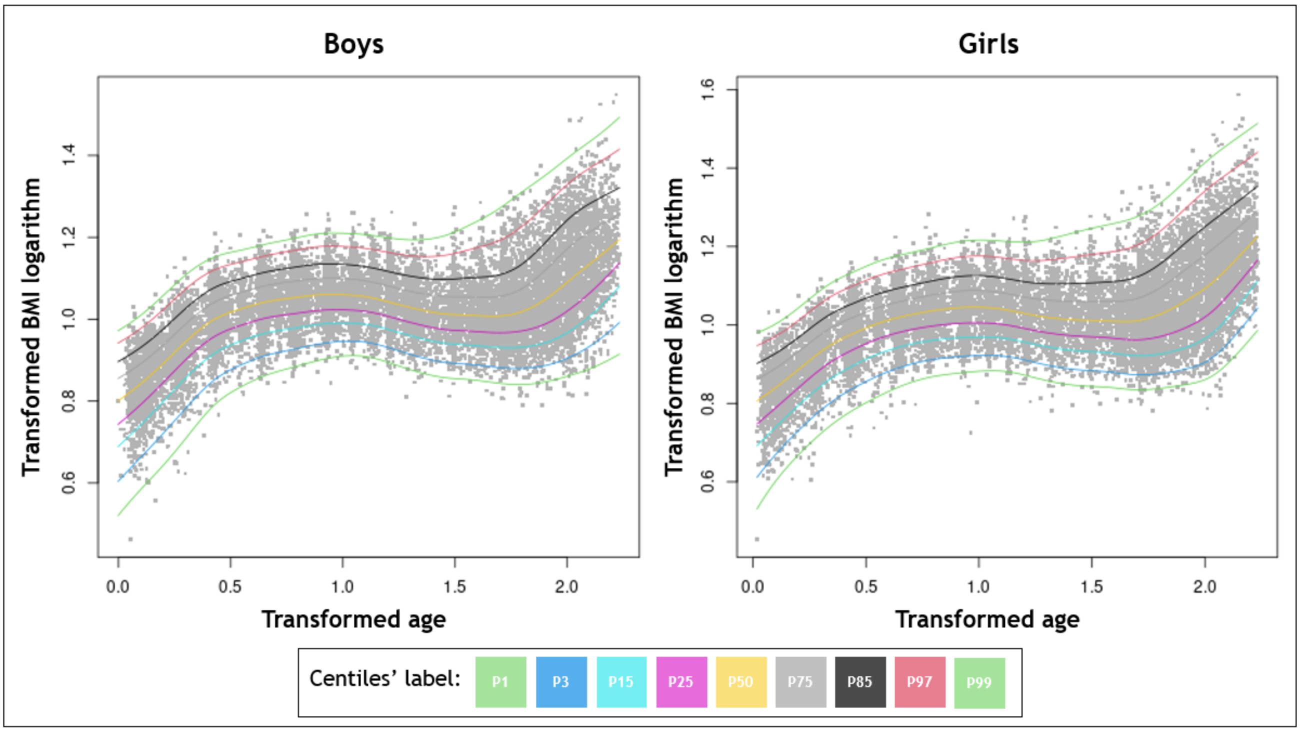


Figure 10. BMI-for-age growth charts for the index population.

Using the index population as reference, the z-scores of transformed BMI logarithm measurements were obtained and used in multivariate analysis across time divisions. In parallel, using WHO child growth standards as reference, the z-scores of BMI measurements for that setting were calculated and used for another multivariate analysis. Models were adjusted for sex, twinship, gestational age, transformed age and pandemic timeline.

Regarding timeline division I (Table 38), statistically significant differences in transformed BMI logarithm z-scores were observed among groups in general, for ages 0 to 1 years old (p<0.001, partial η^2=0.001), displaying a negative trend, and for ages over 10 years old (p<0.001, partial η^2=0.003), with a positive trend. No differences were found when analysing for all ages (p=0.138).

Table 38. BMI z-scores' differences across division I groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	p value	Partial η^2	B	Std. Error	p value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.088	0.017	<0.001*	0.001	-0.087	0.017	<0.001 *	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.009	0.037	0.802	0.000	-0.016	0.042	0.696	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.001	0.030	0.975	0.000	0.002	0.036	0.961	0.000
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.122	0.028	<0.001*	0.003	0.134	0.032	<0.001 *	0.003
All ages								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	-0.018	0.012	0.138	0.000	-0.117	0.013	<0.001 *	0.002

Values adjusted for sex, twinship, gestational age, transformed age and division I timespan groups.
* Statistically significant, $p\leq0.05$.

When adopting WHO child growth standards as reference, statistically significant differences in BMI z-scores were observed between groups for all ages (p<0.001, partial η^2=0.002), for ages 0 to 1 years old (p<0.001, partial η^2=0.001) and for ages over 10 years old (p<0.001, partial η^2=0.005). Alike the index population analysis, the statistically significant differences in this setting were related to a negative difference in the pandemic group, when compared to the control group.

Considering the index population as reference, when applying timeline division II (Table 39), statistically significant differences were observed in transformed BMI logarithm z-scores among groups for all ages (p<0.001, partial η^2<0.001) and for specific age ranges, including 0 to 1 years (p<0.001, partial η^2=0.001), 5 to 9 years (p=0.005, partial η^2=0.001) and over 10 years (p<0.001, partial η^2=0.005).

In this scenario, there was a significant negative difference in transformed BMI logarithm z-scores in group α when compared to the control group for ages 0 to 1 years old. As for ages 5 to 9 years old and over 10 years old, the significant differences exhibited a positive trend. When comparing group β to the control group, significant negative differences were observed for all ages, for ages 0 to 1 years old and for ages 5 to 9 years old. Post-hoc analysis for timeline division II confirmed the following significant differences:

- for ages 0 to 1 years old and for ages over 10 years old, between the control group and group α (p=0.006 and p<0.001, respectively)
- for all ages and for ages 0 to 1 years old, between the control group and group β (p=0.002 and p<0.001, respectively).
- for all ages, for ages 5 to 9 years old and for over 10 years old, between group α and group β (p=0.002, p=0.003 and p=0.003, respectively).

Table 39. BMI z-scores' differences across division II groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	-0.066	0.021	0.002 *	0.000	-0.066	0.022	0.003 *	0.000
Group β	-0.116	0.024	<0.001*	0.001	-0.116	0.024	<0.001*	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	-0.008	0.047	0.859	0.000	-0.009	0.054	0.864	0.000
Group β	-0.010	0.052	0.845	0.000	-0.025	0.059	0.674	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.084	0.040	0.035 *	0.001	0.105	0.048	0.027 *	0.001
Group β	-0.091	0.041	0.026 *	0.001	-0.108	0.049	0.027 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.172	0.034	<0.001*	0.005	0.196	0.039	<0.001*	0.004
Group β	0.067	0.035	0.054	0.001	0.067	0.040	0.092	0.000
All ages								
Control Group	0	-	-	-	0	-	-	-
Group α	0.015	0.015	0.322	0.000	-0.063	0.017	<0.001*	0.000
Group β	-0.057	0.017	<0.001*	0.000	-0.180	0.018	<0.001*	0.002

Values adjusted for sex, twinship, gestational age, transformed age and division II timespan groups.
Group α: Pandemic with restrictions. Group β: Pandemic without restrictions.
* Statistically significant, $p \leq 0.05$.

When adopting WHO child growth standards as reference, overlapping significative differences in BMI z-scores were identified for all ages ($p<0.001$, partial $\eta^2=0.003$) and for specific age ranges, including 0 to 1 years old ($p<0.001$, partial $\eta^2=0.001$), 5 to 9 years old ($p=0.004$, partial $\eta^2=0.002$) and over 10 years old ($p<0.001$, partial $\eta^2=0.004$). The significant differences found between the control group and the pandemic groups had a negative trend, with the exception of age range 5 to 9 years old and over 10 years old, for which group α exhibited a positive difference when compared to the control group. Post-hoc analysis for timeline division II confirmed the following significant differences in BMI z-scores:

- for all ages, between all groups, with a significance of $p<0.001$ between the control group and each of the pandemic groups, as well as between group α and group β.
- for ages 0 to 1 years old, between all groups, with $p=0.008$ between the control group and group α, $p<0.001$ between the control group and group β, and $p=0.050$ between group α and group β.
- for ages 5 to 9 years old, between group α and group β ($p=0.003$).
- for ages over 10 years old, between the control group and group α ($p<0.001$), and between group α and group β ($p=0.012$).

Narrowing the timeline to division III, distinctions between groups are presented in Table 40. When considering the index population as the reference, statistically significant differences in transformed BMI logarithm z-scores were noticed between groups, both for all ages ($p=0.001$, partial $\eta^2<0.001$) and for specific age ranges, including 0 to 1 years old ($p<0.001$, partial $\eta^2=0.001$), 5 to 9 years old ($p=0.005$, partial $\eta^2=0.002$) and over 10 years old ($p<0.001$, partial $\eta^2=0.005$).

In this setting, group 1 displayed a significant positive difference in transformed BMI logarithm z-scores compared to the control group across all ages, and in age ranges 5 to 9 years old and over 10 years old. Conversely, group 2 exhibited a significant negative transformed BMI logarithm z-scores' difference in the age range of 0 to 1 years old when compared to the control group. However, in the age range of over 10 years old, the difference between the control group and group 2 displayed a significant positive trend. Group 3 presented a significant negative transformed BMI logarithm z-score difference compared to the control group across all ages, as well as in age ranges 0 to 1 years old and 5 to 9 years old.

Table 40. BMI z-scores' differences across division III groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.036	0.031	0.242	0.000	-0.035	0.032	0.270	0.000
Group 2	-0.091	0.030	0.003 *	0.000	-0.093	0.031	0.002 *	0.000
Group 3	-0.114	0.023	<0.001*	0.001	-0.112	0.023	<0.001*	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.037	0.078	0.634	0.000	-0.044	0.089	0.622	0.000
Group 2	-0.036	0.062	0.563	0.000	-0.034	0.070	0.630	0.000
Group 3	0.018	0.050	0.714	0.000	0.005	0.057	0.925	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.181	0.064	0.005 *	0.001	0.215	0.077	0.005 *	0.001
Group 2	0.023	0.051	0.653	0.000	0.036	0.061	0.559	0.000
Group 3	-0.079	0.040	0.047 *	0.001	-0.093	0.047	0.050 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.244	0.054	<0.001*	0.004	0.263	0.061	<0.001 *	0.003
Group 2	0.157	0.042	<0.001*	0.003	0.186	0.047	<0.001 *	0.003
Group 3	0.062	0.034	0.068	0.001	0.063	0.039	0.104	0.000
All ages								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.047	0.024	0.046 *	0.000	0.001	0.026	0.956	0.000
Group 2	-0.005	0.020	0.789	0.000	-0.100	0.022	<0.001*	0.000
Group 3	-0.052	0.016	0.001 *	0.000	-0.176	0.017	<0.001*	0.002

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
Group 1: 1st Lockdown + Reopening. Group 2: 2nd Lockdown + Reopening. Group 3: 3rd Lockdown + Reopening.
* Statistically significant, $p \leq 0.05$.

Post-hoc analysis for timeline division III confirmed the following statistically significant differences among groups:

- for all ages, between the control group and group 3 (p=0.006), and between group 1 and group 3 (p=0.002).
- for ages 0 to 1 years old, between the control group and group 2 (p=0.016) and between the control group and group 3 (p<0.001).
- for ages 5 to 9 years old, between the control group and group 1 (p=0.028) and between group 1 and group 3 (p=0.002).
- for ages over 10 years old, between the control group and group 1 (p<0.001), between the control group and group 2 (p<0.001), and between group 1 and group 3 (p=0.010).

When adopting WHO child growth standards as reference, significative differences were identified between BMI z-scores' groups for all ages (p<0.001, partial η^2=0.003) and specific ages ranges, including 0 to 1 years old (p<0.001, partial η^2=0.001) and 5 to 9 years old (p=0.005, partial η^2=0.002). Group 1 presented a significant positive difference in BMI z-scores when compared to the control group in age ranges 5 to 9 years old and over 10 years old. Group 2 and group 3 BMI z-scores' differences when compared to the control group were similar to the ones described when considering the index population as reference.

Post-hoc analysis confirmed the following statistically significant differences between groups when using WHO child growth standard as reference:

- for all ages, between the control group and groups 2 (p<0.001) and 3 (p<0.001); between group 1 and group 2 (p=0.012), between group 1 and group 3 (p<0.001), and between group 2 and group 3 (p=0.026).

- for ages 0 to 1 years old, between the control group and group 2 (p=0.014) and between the control group and group 3 (p<0.001).
- for ages 5 to 9 years old, between the control group and group 1 (p=0.031) and between group 1 and group 3 (p=0.003).
- for ages over 10 years old, between the control group and group 1 (p<0.001), between the control group and group 2 (p<0.001), and between group 1 and group 3 (p=0.012).

Considering the index population as reference, analysing data by timeline division IV, statistically significant differences were observed in transformed BMI logarithm among groups for all ages (p=0.001, partial η^2=0.001), for ages 0 to 1 years old (p<0.001, partial η^2=0.002), for ages 5 to 9 years old (p=0.001, partial η^2=0.003) and for ages over 10 years old (p<0.001, partial η^2=0.006). These differences are explored in Table 41.

Transformed BMI logarithm z-scores featured a significant positive difference when comparing group B with the control group, for all ages, and for age groups 5 to 9 years old and over 10 years old. In addition, there was a significant positive z-score difference in group D when compared to the control group, for over 18 years old. On the other hand, there was a significant negative difference between the control group and group D for ages 0 to 1 years old. When comparing group F with the control group, the difference also exhibited a negative trend for all ages, and for age groups 0 to 1 years old and 5 to 9 years old.

Post-hoc analysis confirmed the following statistically significant differences:

- for all ages, between the control group and group F (p=0.012), and between group B and group F (p=0.001).

- for ages 0 to 1 years old, between the control group and group D (p=0.002), and between the control group and group F (p<0.001).
- for ages 5 to 9 years old, between the control group and group B (p=0.006), and between group B and group F (p<0.001).
- for ages over 10 years old, between the control group and group B (p<0.001), between the control group and group D (p=0.001), and between group B and group D (p=0.03).

When adopting WHO child growth standards as reference, significative differences in BMI z-scores arose for all ages group (p<0.001, partial η^2=0.003) and for specific age ranges, including 0 to 1 years old (p<0.001, partial η^2=0.002), 5 to 9 years old (p=0.001, partial η^2=0.003), and over 10 years old (p<0.001, partial η^2=0.005).

BMI z-scores featured a significant positive difference when comparing group B with the control group, for age groups 5 to 9 years old and over 10 years old. In addition, there was a significant positive z-score difference in group D when compared to the control group, for ages over 10 years old, but not for all ages or ages 0 to 1 years old, in which the significant difference displayed a negative trend in comparison to the control group. In addition, there was a significant negative difference when comparing group F with the control group, for all ages, and for age groups 0 to 1 years old and 5 to 9 years old.

Post-hoc analysis of BMI z-scores with WHO child growth standards as the reference population confirmed the following significant differences:

- for all ages, between the control group and groups D (p<0.001) and F (p<*0.001*); between group B and group D (p=0.007), between group B and group F (p<0.001) and between group C and group F (p=0.031).

Table 41. BMI z-scores' differences across division IV groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.035	0.063	0.576	0.000	-0.043	0.064	0.504	0.000
Group B - 1st R	-0.037	0.035	0.298	0.000	-0.032	0.036	0.366	0.000
Group C - 2nd L	0.085	0.070	0.227	0.000	0.067	0.071	0.350	0.000
Group D - 2nd R	-0.128	0.033	<0.001*	0.001	-0.128	0.034	<0.001*	0.001
Group E - 3rd L	-0.089	0.072	0.217	0.000	-0.074	0.074	0.316	0.000
Group F - 3rd R	-0.116	0.024	<0.001*	0.001	-0.116	0.024	<0.001*	0.001
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.309	0.250	0.217	0.000	0.306	0.285	0.283	0.000
Group B - 1st R	-0.073	0.082	0.373	0.000	-0.080	0.093	0.391	0.000
Group C - 2nd L	0.113	0.146	0.440	0.000	0.145	0.167	0.384	0.000
Group D - 2nd R	-0.066	0.067	0.328	0.000	-0.070	0.076	0.360	0.000
Group E - 3rd L	0.276	0.151	0.069	0.001	0.281	0.172	0.104	0.000
Group F - 3rd R	-0.010	0.052	0.845	0.000	-0.025	0.059	0.674	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.212	0.160	0.184	0.000	-0.252	0.191	0.188	0.000
Group B - 1st R	0.253	0.069	<0.001*	0.002	0.300	0.083	<0.001*	0.002
Group C - 2nd L	0.080	0.135	0.556	0.000	0.088	0.162	0.587	0.000
Group D - 2nd R	0.014	0.055	0.795	0.000	0.028	0.065	0.672	0.000
Group E - 3rd L	0.090	0.144	0.532	0.000	0.119	0.173	0.493	0.000
Group F - 3rd R	-0.091	0.041	0.026 *	0.001	-0.108	0.049	0.027 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.091	0.161	0.572	0.000	0.117	0.191	0.541	0.000
Group B - 1st R	0.260	0.056	<0.001*	0.004	0.278	0.063	<0.001*	0.003
Group C - 2nd L	0.021	0.104	0.843	0.000	0.089	0.116	0.442	0.000
Group D - 2nd R	0.178	0.044	<0.001*	0.003	0.201	0.050	<0.001*	0.003
Group E - 3rd L	0.017	0.094	0.857	0.000	0.042	0.101	0.681	0.000
Group F - 3rd R	0.067	0.035	0.057	0.001	0.066	0.040	0.099	0.000
All ages								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.025	0.054	0.643	0.000	-0.043	0.060	0.475	0.000
Group B - 1st R	0.063	0.026	0.015 *	0.000	0.011	0.028	0.699	0.000
Group C - 2nd L	0.066	0.050	0.187	0.000	0.000	0.055	0.998	0.000
Group D - 2nd R	-0.019	0.022	0.401	0.000	-0.118	0.024	<0.001*	0.001
Group E - 3rd L	-0.004	0.050	0.942	0.000	-0.128	0.054	0.017 *	0.000
Group F - 3rd R	-0.057	0.017	<0.001*	0.000	-0.180	0.018	<0.001*	0.002

Values adjusted for sex, twinship, gestational age, transformed age and division IV timespan groups.
* Statistically significant, $p \leq 0.05$. L - Lockdown. R - Reopening.

- for ages 0 to 1 years old, between the control group and group D (p=0.003), and between the control group and group F (p<0.001).
- for ages 5 to 9 years old, between the control group and group B (p=0.006) and between group B and group F (p<0.001).
- for ages over 10 years old, between the control group and group B (p<0.001), between the control group and group D (p=0.001) and between group B and group F (p=0.036).

B.5. Head Circumference

A total 26,088 head circumference measurements were retrieved from health records. Of these, only measurements between 0 and 4 years old were considered for analysis. The distribution of head circumference measurements across age is presented in Figure 11.

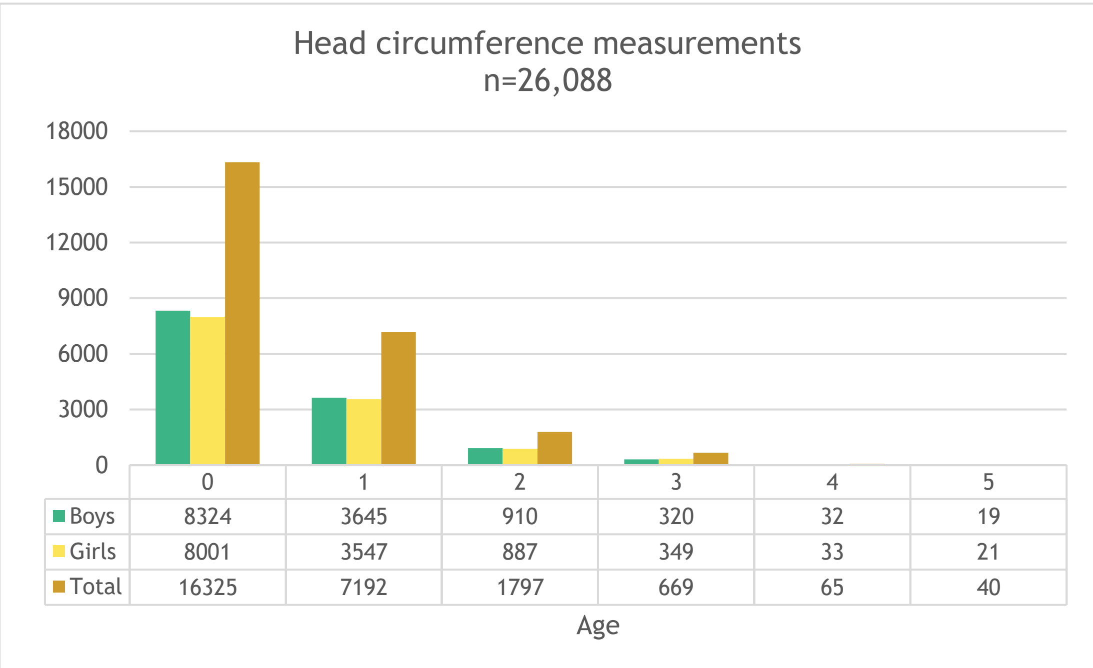


Figure 11. Distribution of head circumference measurements by age.

In accordance with the PNSIJ recommendations, head circumference was primarily evaluated from birth through 2 years old, with a greater frequency of measurements occurring during the first year of life due to the schedule of recommended appointments (Figure 1).

Descriptive statistics on head circumference measurements for the study sample are presented on Table 42, divided by age groups (from 0 to 4 years old).

Table 42. Head circumference sample characterization by age groups.

Head Circumference (cm)		0 to 1 years	2 to 4 years
Boys	n	11,969	1,262
	Mean (SD)	43.0 (4.7)	50.0 (1.4)
	Range	[31.0;55.0]	[43.7;55.0]
Girls	n	11,548	1,269
	Mean (SD)	41.9 (4.5)	49.0 (1.6)
	Range	[30.8;53.0]	[45.0;55.0]
Total	n	23,517	2,531
	Mean (SD)	42.5 (4.6)	49.5 (1.6)
	Range	[30.8;55.0]	[43.7;55.0]

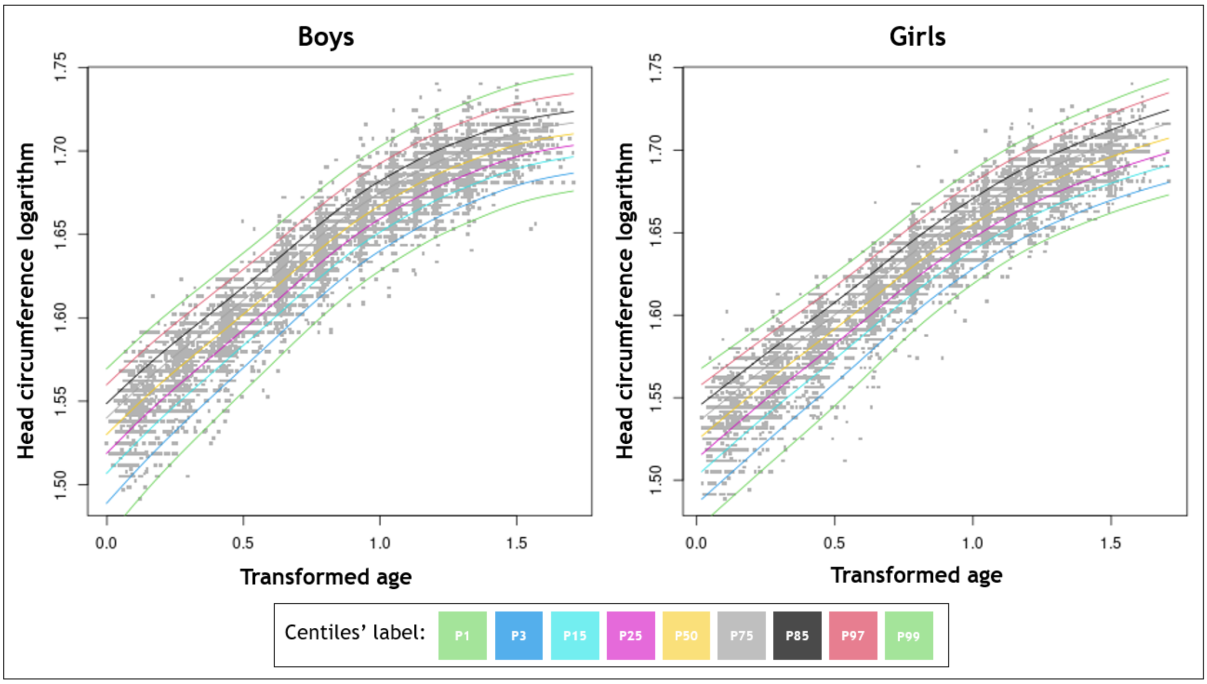


Figure 12. Head circumference-for-age growth charts for the index population.

Data from measurements made before the pandemic onset were used to create head circumference-for-age growth charts for the index population (Figure 12). These are presented by sex, in a logarithmic scale, and include percentile curves. Information on transformed age and head circumference logarithm can be found on Table 1 and Table 3, respectively. The boys' sample appears to exhibit a greater initial data dispersion, thus confirming the wider range and standard deviation values identified in Table 42.

Using the index population as reference, the z-scores of logarithmic head circumference measurements were obtained and used in a multivariate analysis across different time divisions. In parallel, using WHO child growth standards as reference, head circumference measurements' z-scores for that setting were calculated and used for a multivariate analysis. Models were adjusted for sex, twinship, gestational age, transformed age and pandemic timeline.

Table 43. Head circumference z-scores' differences across division I groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.014	0.017	0.407	0.000	0.020	0.017	0.241	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.132	0.066	0.044 *	0.002	0.132	0.065	0.044 *	0.002
All ages								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.023	0.016	0.156	0.000	0.040	0.017	0.017 *	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division I timespan groups.
* Statistically significant, $p \leq 0.05$.

Regarding timeline division I, statistically significant differences between groups in logarithmic head circumference z-scores were observed only for ages 2 to 4 years old (p=0.044, partial η^2=0.002). When adopting WHO child growth standards as reference, statistically significant differences were observed in head circumference z-scores for all ages (p=0.017, partial η^2<0.001), and for ages 2 to 4 years old (p=0.044, partial η^2=0.002). Head circumference z-scores' differences between the control group and the pandemic group are presented in Table 43, the ones with statistical significance displaying a positive trend.

Considering the index population as reference, when applying timeline division II, no statistically significant differences were observed in logarithmic head circumference z-scores between groups. Differences are presented on Table 44.

Table 44. Head circumference z-scores' differences across division II groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.021	0.021	0.318	0.000	0.031	0.022	0.166	0.000
Group β	0.004	0.024	0.861	0.000	0.007	0.025	0.780	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.143	0.083	0.086	0.001	0.147	0.083	0.076	0.001
Group β	0.117	0.098	0.231	0.001	0.110	0.097	0.257	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Group α	0.031	0.021	0.139	0.000	0.051	0.021	0.018 *	0.000
Group β	0.013	0.023	0.575	0.000	0.026	0.024	0.273	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division II timespan groups.
Group α: Pandemic with restrictions. Group β: Pandemic without restrictions.
* Statistically significant, p≤0.05.

When adopting WHO child growth standards as reference, statistically significant differences in head circumference z-scores were observed between groups for all ages (p=0.042, partial η^2<0.001), but not among specific age groups. There was a significant positive difference between the control group and group α, when. These differences, however, were not confirmed through post-hoc tests.

Narrowing the timeline to division III (Table 45), no statistically significant differences were generally observed in logarithmic head circumference z-scores between groups when considering the index population as reference. Notwithstanding, group 2 displayed a significant positive difference in logarithmic head circumference compared to the control group across all ages, and in age ranges 0 to 1 years old. Post-hoc analysis did not confirm these differences.

Table 45. Head circumference z-scores' differences across division III groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.016	0.031	0.615	0.000	-0.006	0.032	0.864	0.000
Group 2	0.073	0.030	0.014 *	0.000	0.081	0.031	0.009 *	0.000
Group 3	-0.004	0.023	0.846	0.000	-0.001	0.024	0.978	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.079	0.122	0.515	0.000	0.084	0.121	0.489	0.000
Group 2	0.109	0.117	0.350	0.000	0.110	0.116	0.344	0.000
Group 3	0.177	0.094	0.059	0.001	0.173	0.093	0.063	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Group 1	-0.007	0.030	0.806	0.000	0.013	0.031	0.683	0.000
Group 2	0.076	0.029	0.008 *	0.000	0.095	0.030	0.002 *	0.000
Group 3	0.008	0.022	0.707	0.000	0.023	0.023	0.319	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
Group 1: 1st Lockdown + Reopening. Group 2: 2nd Lockdown + Reopening. Group 3: 3rd Lockdown + Reopening.
* Statistically significant, p≤0.05.

When using WHO child growth standards, significant differences in head circumference z-scores' groups were observed for all ages (p=0.014, partial η^2<0.001), but not among specific age ranges. Group 2 displayed a positive difference compared to the control group, for all ages and for ages 0 to 1 years old. Post-hoc analysis confirmed significant differences only for all ages, between the control group and Group 2 (p=0.009).

When analysing data by division IV timespans, no statistically significant differences were observed in logarithmic head circumference z-scores between groups. In this setting, explored in Table 46, a statistically significant positive difference was found between the control group and group D, when considering all ages. There was also a significant positive difference between the control group and group E, among those with 2 to 4 years old. Post-hoc analysis through pairwise comparisons, however, did not confirm these significances.

When considering WHO child growth standards as reference, significative differences in head circumference z-scores were generally found between groups for ages 2 to 4 years old (p=0.046, partial η^2=0.005), but not for all ages (p=0.081). When analysing Table 46, there is a significant positive difference between the control group and group D, for all ages and for age range 0 to 1 years old. There is also a significant positive difference between the control group and group E, when narrowing the logarithmic head circumference z-scores' analysis to age range 2 to 4 years old. Post-hoc analysis, however, did not confirm the identified statistical significances.

Table 46. Head circumference z-scores' differences across division IV groups.

Pandemic Timeline Groups	Index population z-scores				WHO child growth standards z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
0 to 1 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.022	0.065	0.731	0.000	-0.015	0.068	0.822	0.000
Group B - 1st R	-0.014	0.035	0.694	0.000	-0.003	0.037	0.938	0.000
Group C - 2nd L	0.128	0.070	0.067	0.000	0.130	0.073	0.074	0.000
Group D - 2nd R	0.061	0.032	0.060	0.000	0.071	0.034	0.037 *	0.000
Group E - 3rd L	-0.089	0.072	0.215	0.000	-0.075	0.075	0.314	0.000
Group F - 3rd R	0.004	0.024	0.861	0.000	0.007	0.025	0.780	0.000
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.182	0.348	0.602	0.000	-0.180	0.345	0.602	0.000
Group B - 1st R	0.113	0.129	0.381	0.000	0.118	0.128	0.358	0.000
Group C - 2nd L	-0.284	0.285	0.318	0.000	-0.284	0.283	0.315	0.000
Group D - 2nd R	0.185	0.127	0.145	0.001	0.186	0.126	0.141	0.001
Group E - 3rd L	0.827	0.311	0.008 *	0.003	0.855	0.309	0.006 *	0.003
Group F - 3rd R	0.117	0.098	0.232	0.001	0.110	0.097	0.258	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.028	0.064	0.665	0.000	-0.010	0.067	0.885	0.000
Group B - 1st R	-0.002	0.034	0.955	0.000	0.019	0.035	0.591	0.000
Group C - 2nd L	0.111	0.068	0.102	0.000	0.125	0.071	0.077	0.000
Group D - 2nd R	0.069	0.032	0.029 *	0.000	0.088	0.033	0.007 *	0.000
Group E - 3rd L	-0.038	0.070	0.589	0.000	-0.011	0.073	0.884	0.000
Group F - 3rd R	0.013	0.023	0.574	0.000	0.026	0.024	0.273	0.000

Values adjusted for sex, twinship, gestational age, transformed age and division IV timespan groups.
* Statistically significant, $p \leq 0.05$. L - Lockdown. R - Reopening.

B.6. Systolic Blood Pressure

A total 15,605 SBP measurements were collected for analysis. The distribution of SBP measurements across age is presented in Figure 12. In accordance with the PNSIJ recommendations, SBP was primarily evaluated from 3 years old onward, with a peak in measurements at both the 5-year (maximum) and the 10-year age milestones, in line with the vaccination schedule.

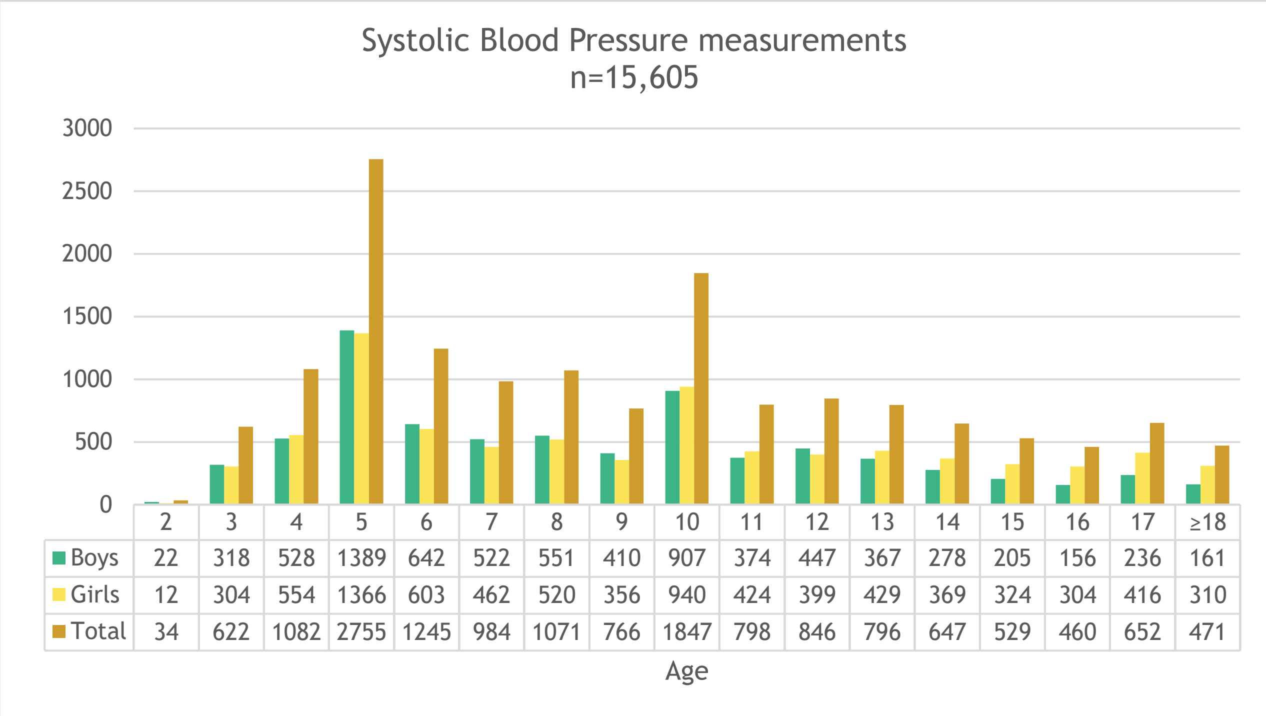


Figure 13. Distribution of systolic blood pressure measurements by age.

Descriptive statistics on SBP measurements for the study sample are presented on Table 47, divided by age groups (from 2 to 18 years old).

Table 47. SBP sample characterization by age groups.

SBP (mmHg)		2 to 4 years	5 to 9 years	10 to 18 years
Boys	n	846	3,514	2,970
	Mean (SD)	84.8 (8.6)	91.1 (8.6)	103.8 (13.0)
	Range	[59.0;120.0]	[50.0;136.0]	[70.0;160.0]
Girls	n	858	3,307	3,605
	Mean (SD)	84.1 (8.8)	90.2 (9.2)	104.1 (12.0)
	Range	[50.0;117.0]	[53.0;140.0]	[65.0;148.0]
Total	n	1,704	6,821	6,575
	Mean (SD)	84.5 (8.7)	90.6 (9.4)	104.0 (12.4)
	Range	[50.0;120.0]	[50.0;140.0]	[65.0;160.0]

Data from measurements made before the pandemic onset were used to create SBP-for-age growth charts for the index population (Figure 14). These are presented by sex and include percentile curves.

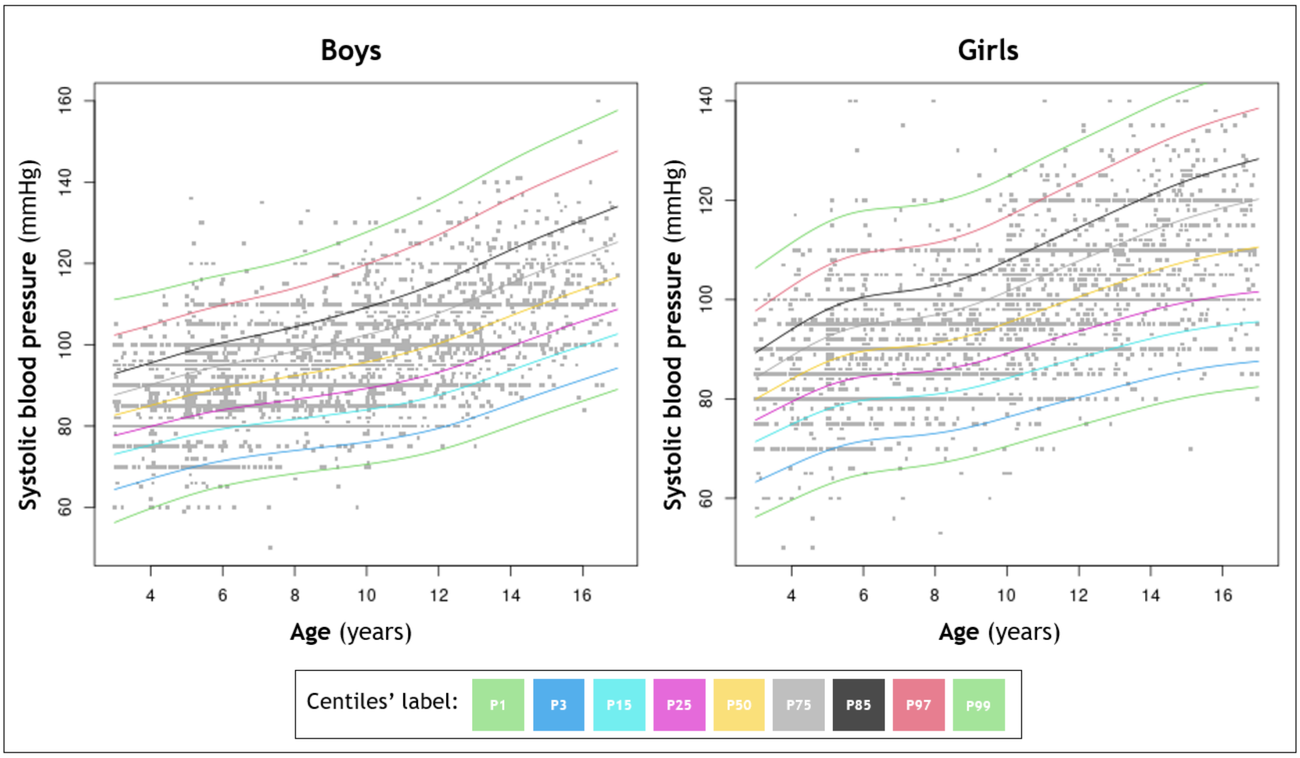


Figure 14. SBP-for-age growth charts for the index population.

Using the index population as reference, the z-scores of SBP measurements were obtained and used in a multivariate analysis across different time divisions. In parallel, using NHLBI and CDC data as reference, SBP measurements' z-scores for that setting were calculated and used for a multivariate analysis. Models were adjusted for sex, twinship, gestational age, transformed age and timeline.

Regarding timeline division I, statistically significant differences were observed in SBP z-scores among groups in general, for all ages (p<0.001, partial η^2=0.002), for ages 5 to 9 years (p<0.001, partial η^2=0.002), and for over 10 years old (p<0.001, partial η^2=0.003). When adopting NHLBI and CDC data as reference, statistically significant differences in SBP z-scores were observed between groups for all ages (p<0.001, partial η^2=0.002), for ages 5 to 9 years (p=0.002, partial η^2=0.002) and for over 10 years old (p=0.008, partial η^2=0.001). Differences between groups are explored in Table 48, the ones with significance displaying a negative trend.

Table 48. SBP z-scores' differences across division I groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.010	0.071	0.887	0.000	0.000	0.055	0.996	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.127	0.033	<0.001*	0.002	0.080	0.029	0.002 *	0.002
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.108	0.028	<0.001*	0.003	0.078	0.030	0.008 *	0.001
All ages								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.096	0.020	<0.001*	0.002	0.093	0.019	<0.001*	0.002

Values adjusted for sex, twinship, gestational age, transformed age and division I timespan groups.
* Statistically significant, $p \leq 0.05$.

Considering the index population as reference, when applying timeline division II (Table 49), statistically significant differences were observed in SBP z-scores among groups for all ages (p<0.001, partial η^2=0.002), as well as for specific age ranges, including 5 to 9 years old (p<0.001, partial η^2=0.003) and over 10 years old (p<0.001, partial η^2=0.004). When exploring differences between groups, there was a significant positive difference in SBP z-scores between the control group and each of the pandemic subgroups, both for all ages and for age range 5 to 9 years old. In age range over 10 years old, this positive difference was only significant between the control group and group α.

Table 49. SBP z-scores' differences across division II groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.075	0.096	0.435	0.000	0.054	0.074	0.465	0.000
Group β	-0.099	0.098	0.312	0.001	-0.057	0.076	0.451	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.097	0.045	0.032 *	0.001	0.064	0.039	0.102	0.000
Group β	0.156	0.044	<0.001*	0.002	0.112	0.038	0.003 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.159	0.036	<0.001*	0.004	0.135	0.037	<0.001*	0.003
Group β	0.061	0.035	0.083	0.001	0.026	0.036	0.471	0.000
All ages								
Control Group	0	-	-	-	0	-	-	-
Group α	0.123	0.027	<0.001*	0.002	0.124	0.024	<0.001*	0.002
Group β	0.070	0.026	0.008 *	0.001	0.064	0.024	0.006 *	0.001

Values adjusted for sex, twinship, gestational age, transformed age and division II timespan groups.
Group α: Pandemic with restrictions. Group β: Pandemic without restrictions.
* Statistically significant, $p \leq 0.05$.

Post hoc analysis confirmed the following significant differences:

- for all ages and for ages over 10 years old, between the control group and group α ($p<0.001$ for both).
- for all ages and for ages 5 to 9 years old, between the control group and group β ($p=0.023$ and $p=0.001$, respectively).

When considering NHLBI and CDC data as reference, significative differences in SBP z-scores were generally identified for all ages (p<0.001, partial η^2=0.002) and for specific age ranges, including 5 to 9 years old (p=0.005, partial η^2=0.002), and over 10 years old (p<0.001, partial η^2=0.003). The significant differences found between the control group and the pandemic subgroups had a positive trend.

Post-hoc analysis through pairwise comparisons for timeline division II confirmed the following significant differences:

- for all ages and for ages over 10 years old, between the control group and group α (p<0.001 and p=0.023, respectively).
- for all ages and for ages 5 to 9 years old, and between the control group and group β (p=0.019 and p=0.009, respectively).

Narrowing the timeline to division III, distinctions between groups are presented in Table 50. When considering the index population as the reference, statistically significant differences in SBP z-scores were noticed between groups for all age categories: all ages (p<0.001, partial η^2=0.002), 2 to 4 years (p=0.039, partial η^2=0.005), 5 to 9 years old (p=0.001, partial η^2=0.003) and over 10 years old (p<0.001, partial η^2=0.004). All significant differences identified for the pandemic subgroups exhibited a positive trend when compared to the control group.

In this setting, post-hoc analysis through pairwise comparisons confirmed the following statistically significant differences in SBP z-scores among groups:

- for all ages, between the control group and group 1 (p<0.001), and between the control group and group 2 (p=0.004).
- for ages 2 to 4 years old, between group 1 and group 3 (p=0.025).

- for ages 5 to 9 years old, between the control group and group 3 (p=0.004).
- for ages over 10 years old, between the control group and group 1 (p=0.011), and between the control group and group 2 (p=0.001).

Table 50. SBP z-scores' differences across division III groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	p value	Partial η^2	B	Std. Error	p value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.444	0.186	0.017 *	0.003	0.211	0.142	0.139	0.001
Group 2	0.027	0.117	0.816	0.000	0.060	0.090	0.503	0.000
Group 3	-0.139	0.093	0.134	0.001	-0.088	0.073	0.223	0.001
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.149	0.074	0.045	0.001	0.090	0.064	0.161	0.000
Group 2	0.081	0.058	0.162	0.000	0.064	0.050	0.203	0.000
Group 3	0.145	0.043	<0.001*	0.002	0.101	0.037	0.006 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.185	0.059	0.002 *	0.002	0.146	0.060	0.015 *	0.001
Group 2	0.162	0.044	<0.001*	0.003	0.144	0.044	0.001*	0.002
Group 3	0.062	0.034	0.068	0.001	0.029	0.035	0.402	0.000
All ages								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.187	0.045	<0.001*	0.001	0.140	0.041	<0.001*	0.001
Group 2	0.113	0.033	<0.001*	0.001	0.132	0.030	<0.001*	0.002
Group 3	0.062	0.025	0.014 *	0.000	0.061	0.023	0.007 *	0.001

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
Group 1: 1st Lockdown + Reopening. Group 2: 2nd Lockdown + Reopening. Group 3: 3rd Lockdown + Reopening.
* Statistically significant, $p\leq0.05$.

When considering NHLBI and CDC data as reference, statistically significant differences in SBP z-scores were noticed between groups for all ages (p<0.001, partial η^2=0.002), and for specific age ranges, namely 5 to 9 years old (p=0.018, partial η^2=0.002) and over 10 years old (p=0.002, partial η^2=0.003). All significant differences identified in Table 50 for the pandemic subgroups exhibited a positive trend when compared to the control group. Post-hoc analysis with Sidak correction confirmed the following statistically significant differences in SBP z-scores:

- between the control group and group 1, for all ages (p=0.004).
- between the control group and group 2, both for all ages (p<0.001), and for ages over 10 years old (p=0.007).
- between the control group and group 3, both for all ages (p=0.042), and for ages 5 to 9 years old (p=0.035).

Considering the index population as reference, when analysing data by timeline division IV, statistically significant differences were observed in SBP z-scores between groups for all age categories: all ages (p<0.001, partial η^2=0.002), 5 to 9 years old (p=0.005, partial η^2=0.003) and over 10 years old (p=0.001, partial η^2=0.004). All significant differences identified in Table 51 for the pandemic subgroups exhibited a positive trend when compared to the control group.

Post-hoc analysis for division IV, when using the index population as reference, confirmed the following statistically significant differences:

- for all ages, between the control group and group B (p<0.001), and between the control group and group D (p=0.008).
- for ages 5 to 9 years old, between the control group and group F (p=0.008).
- for ages over 10 years old, between the control group and group B (p=0.037), and between the control group and group D (p=0.005).

Table 51. SBP z-scores' differences across division IV groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.807	1.022	0.430	0.000	0.306	0.796	0.701	0.000
Group B - 1st R	0.432	0.189	0.022 *	0.003	0.208	0.145	0.151	0.001
Group C - 2nd L	-0.181	0.285	0.525	0.000	-0.031	0.222	0.888	0.000
Group D - 2nd R	0.068	0.127	0.594	0.000	0.078	0.098	0.426	0.000
Group E - 3rd L	-0.513	0.285	0.072	0.002	-0.373	0.222	0.093	0.002
Group F - 3rd R	-0.098	0.097	0.314	0.001	-0.057	0.076	0.454	0.000
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.010	0.190	0.956	0.000	-0.001	0.162	0.996	0.000
Group B - 1st R	0.173	0.080	0.031 *	0.001	0.106	0.069	0.127	0.000
Group C - 2nd L	-0.044	0.147	0.767	0.000	-0.062	0.127	0.623	0.000
Group D - 2nd R	0.102	0.062	0.101	0.000	0.085	0.054	0.113	0.000
Group E - 3rd L	-0.015	0.155	0.922	0.000	-0.053	0.134	0.696	0.000
Group F - 3rd R	0.156	0.044	<0.001*	0.002	0.112	0.038	0.003 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.101	0.179	0.573	0.000	0.058	0.192	0.762	0.000
Group B - 1st R	0.195	0.062	0.002 *	0.002	0.154	0.063	0.014	0.001
Group C - 2nd L	0.104	0.105	0.321	0.000	0.101	0.105	0.336	0.000
Group D - 2nd R	0.172	0.047	<0.001*	0.003	0.152	0.047	0.001 *	0.002
Group E - 3rd L	0.075	0.092	0.416	0.000	0.063	0.089	0.479	0.000
Group F - 3rd R	0.060	0.035	0.084	0.001	0.026	0.036	0.472	0.000
All ages								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.075	0.130	0.564	0.000	0.029	0.122	0.813	0.000
Group B - 1st R	0.202	0.048	<0.001*	0.001	0.153	0.043	<0.001*	0.001
Group C - 2nd L	0.030	0.082	0.720	0.000	0.051	0.074	0.492	0.000
Group D - 2nd R	0.127	0.036	<0.001*	0.001	0.146	0.032	<0.001*	0.002
Group E - 3rd L	-0.014	0.077	0.856	0.000	0.033	0.067	0.622	0.000
Group F - 3rd R	0.069	0.026	0.008 *	0.001	0.064	0.007	0.007 *	0.001

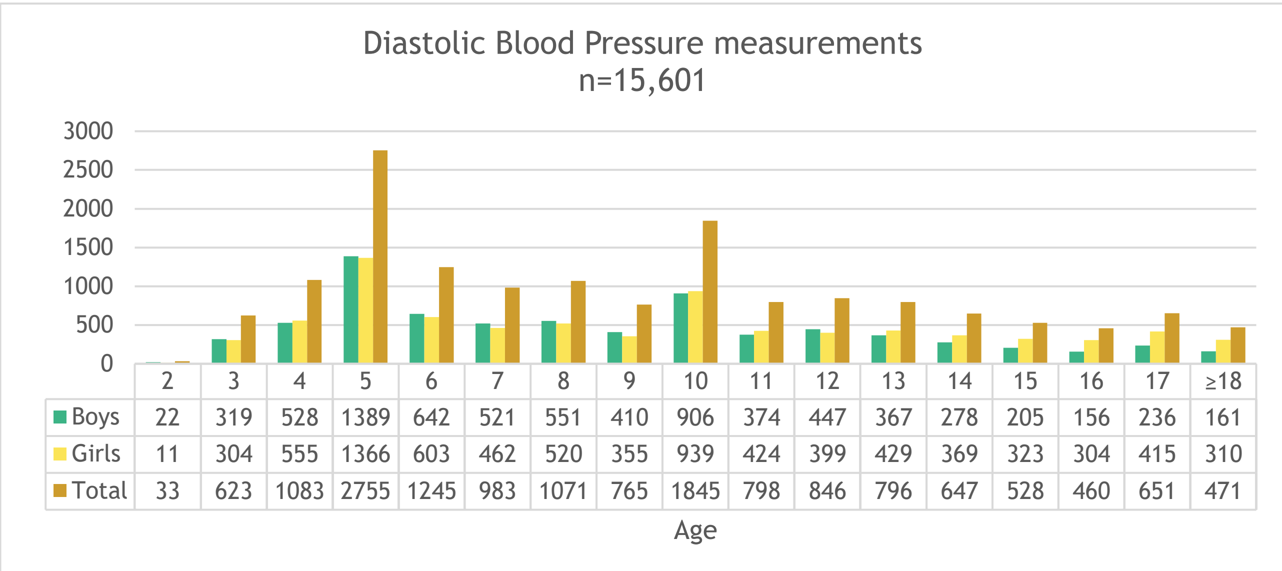
Values adjusted for sex, twinship, gestational age, transformed age and division IV timespan groups.
* Statistically significant, $p \leq 0.05$. L - Lockdown. R - Reopening.

When using NHLBI and CDC data as the reference population, statistically significant differences in SBP z-scores were observed between groups for all ages ($p<0.001$, partial $\eta^2=0.003$), for age range 5 to 9 years ($p=0.043$, partial $\eta^2=0.002$) and for over 10 years ($p=0.019$). The significant differences identified in Table 51 for the pandemic subgroups exhibited a positive trend when compared to the control group. Post-hoc analysis confirmed the following significant differences:

- for all ages, between the control group and group B ($p=0.008$), and between the control group ad group D ($p<0.001$).
- for ages over 10 years, between the control group and group D ($p=0.028$).

B.7. Diastolic Blood Pressure

A total 15,601 DBP measurements were collected from health records. Their distribution across age is presented in Figure 16. In accordance with the PNSIJ recommendations, DBP was primarily evaluated from 3 years old onward, with a peak in measurements at the 5-year and the 10-year age milestones.



	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	≥18
Boys	22	319	528	1389	642	521	551	410	906	374	447	367	278	205	156	236	161
Girls	11	304	555	1366	603	462	520	355	939	424	399	429	369	323	304	415	310
Total	33	623	1083	2755	1245	983	1071	765	1845	798	846	796	647	528	460	651	471

Figure 15. Distribution of diastolic blood pressure measurements by age.

Descriptive statistics on DBP measurements for the study sample are presented on Table 52, divided by age groups (from 2 to 18 years old).

Table 52. DBP sample characterization by age groups.

DBP (mmHg)		2 to 4 years	5 to 9 years	10 to 18 years
Boys	n	847	3,513	2,969
	Mean (SD)	47.4 (7.5)	53.0 (8.7)	60.5 (9.7)
	Range	[30.0;80.0]	[30.0;95.0]	[34.0;96.0]
Girls	n	859	3,306	3,602
	Mean (SD)	47.4 (8.2)	52.7 (8.6)	62.8 (9.9)
	Range	[30.0;90.0]	[30.0;95.0]	[30.0;96.0]
Total	n	1,706	6,819	6,571
	Mean (SD)	47.4 (7.9)	52.8 (8.6)	61.8 (9.8)
	Range	[30.0;90.0]	[30.0;95.0]	[30.0;96.0]

Data from measurements made before the pandemic onset were used to create DBP-for-age growth charts for the index population (Figure 17). These are presented by sex and include percentile curves.

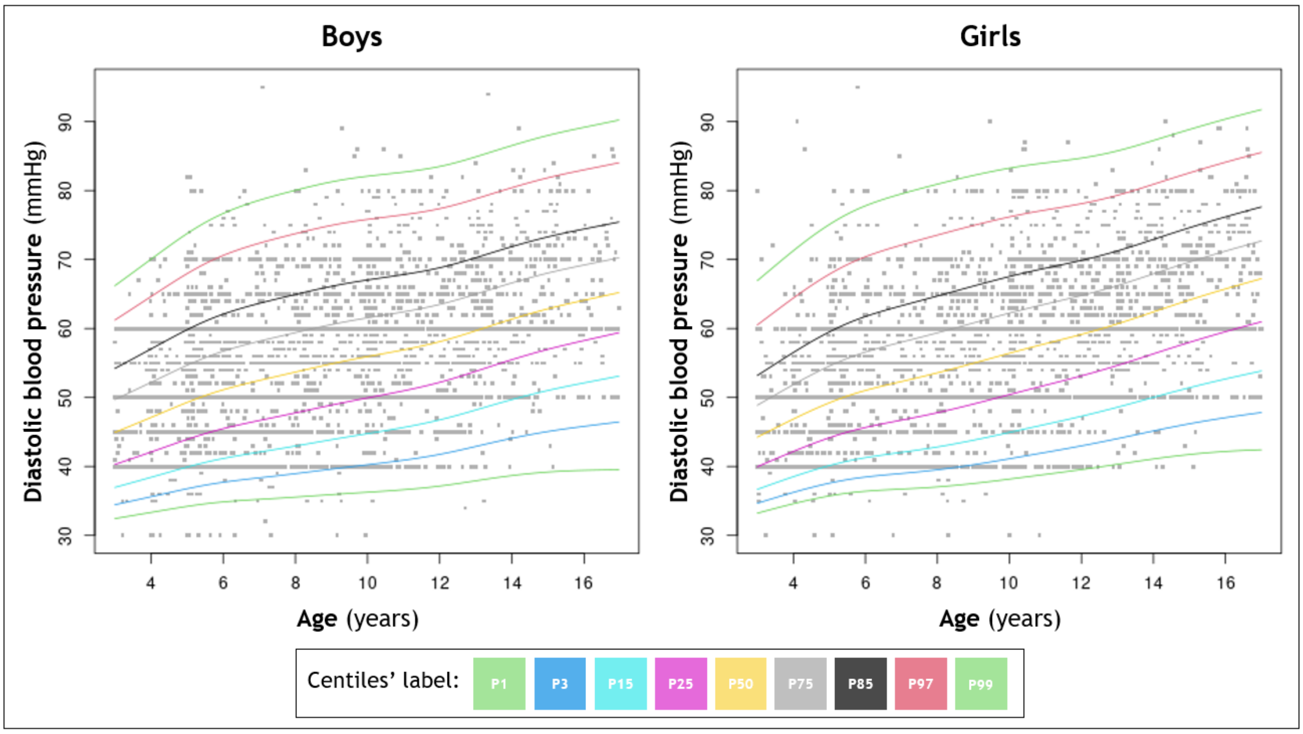


Figure 16. DBP-for-age growth charts for the index population

Using the index population as reference, the z-scores of DBP measurements were obtained and used in a multivariate analysis across different time divisions. In parallel, using NHLBI and CDC data as reference, the z-scores of DBP measurements for that setting were calculated. Models were adjusted for sex, twinship, gestational age, transformed age and timeline.

Regarding timeline division I, statistically significant differences in DBP z-scores were observed among groups for all ages (p<0.001, partial η^2=0.013), for ages 2 to 4 years old (p=0.027, partial η^2=0.003), for ages 5 to 9 years old (p<0.001, partial η^2=0.006), and for ages over 10 years old (p<0.001, partial η^2=0.024). DBP z-scores' differences between groups are explored in Table 53, the ones with statistical significance displaying a positive trend.

Table 53. DBP z-scores' differences across division I groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.159	0.072	0.027 *	0.003	0.143	0.047	0.002 *	0.006
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.214	0.034	<0.001*	0.006	0.154	0.060	0.001 *	0.001
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.331	0.030	<0.001*	0.024	0.270	0.023	<0.001*	0.026
All ages								
Control Group	0	-	-	-	0	-	-	-
Pandemic Group	0.272	0.021	<0.001*	0.013	0.257	0.016	<0.001*	0.021

Values adjusted for sex, twinship, gestational age, transformed age and division I timespan groups.
* Statistically significant, $p \leq 0.05$.

When adopting NHLBI and CDC data as reference, statistically significant differences in DBP z-scores were observed between groups for all age categories: all ages (p<0.001, partial η^2=0.021), 2 to 4 years (p=0.002, partial η^2=0.026), 5 to 9 years old (p<0.001, partial η^2=0.006) and over 10 years old (p<0.001, partial η^2=0.026). DBP z-scores' differences between the control and the pandemic groups display a positive trend.

Considering the index population as reference, when applying timeline division II (Table 54), statistically significant differences were observed in DBP z-scores among groups for all ages (p<0.001, partial η^2=0.013), as well as for specific age ranges, including 5 to 9 years old (p<0.001, partial η^2=0.007) and over 10 years old (p<0.001, partial η^2=0.024).

When exploring differences between groups, there were significant positive differences in DBP z-scores between the control group and the two pandemic subgroups, regarding all ages and specific age ranges, including 5 to 9 years old and over 10 years old. Among these three age categories, post hoc analysis with pairwise comparisons confirmed significant differences between the control group and group α (p<0.001), and between the control group and group β (p<0.001).

When considering NHLBI and CDC data as reference, overlapping significative differences in DBP z-scores were generally identified between groups in every age category: all ages (p<0.001, partial η^2=0.021), 2 to 4 years (p=0.006, partial η^2=0.006), 5 to 9 years old (p<0.001, partial η^2=0.007) and over 10 years old (p<0.001, partial η^2=0.026). The significant differences found between the control group and the pandemic subgroups exhibited a positive trend.

Table 54. DBP z-scores' differences across division II groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.094	0.097	0.331	0.001	0.101	0.063	0.108	0.002
Group β	0.228	0.099	0.022 *	0.003	0.188	0.065	0.004 *	0.005
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.162	0.047	<0.001*	0.002	0.113	0.034	<0.001*	0.002
Group β	0.262	0.045	<0.001*	0.005	0.193	0.033	<0.001*	0.006
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group α	0.321	0.038	<0.001*	0.014	0.271	0.029	<0.001*	0.017
Group β	0.342	0.037	<0.001*	0.017	0.270	0.028	<0.001*	0.018
All ages								
Control Group	0	-	-	-	0	-	-	-
Group α	0.245	0.028	<0.001*	0.006	0.238	0.020	<0.001*	0.011
Group β	0.298	0.027	<0.001*	0.009	0.275	0.020	<0.001*	0.015

Values adjusted for sex, twinship, gestational age, transformed age and division II timespan groups.
* Statistically significant, $p \leq 0.05$.

In this setting, post-hoc analysis through pairwise comparisons with Sidak correction confirmed the following significant differences:

- for all ages and for ages over 10 years old, between the control group and both the pandemic subgroups ($p<0.001$).
- for ages 2 to 4 years old, between the control group and group β ($p=0.011$).
- for age ranges 5 to 9 years old, between the control group and group α ($p=0.003$), and between the control group and group β ($p<0.001$).

Narrowing the timeline to division III, distinctions between groups regarding DBP z-scores are presented in Table 55. When considering the index population as the reference statistically significant differences in DBP z-scores were noticed among groups in general, for all ages (p<0.001, partial η^2=0.013), for ages 5 to 9 years old (p<0.001, partial η^2=0.007), and for ages over 10 years old (p<0.001, partial η^2=0.024). All significant differences identified in Table 55 for the pandemic subgroups exhibited a positive trend when compared to the control group.

In this setting, post-hoc analysis confirmed the following statistically significant differences in DBP among groups:

- for all ages and age range over 10 years old, between the control group and all the pandemic subgroups, with a significance of p<0.001.
- for ages 5 to 9 years old, between the control group and group 1 (p=0.018), and between the control group and group 3 (p<0.001).

In division III setting, when considering NHLBI and CDC data as reference, statistically significant differences in DBP z-scores were noticed between groups in every age category: all ages (p<0.001, partial η^2=0.021), 2 to 4 years (p=0.019, partial η^2=0.006), 5 to 9 years old (p<0.001, partial η^2=0.007) and over 10 years old (p<0.001, partial η^2=0.026). All significant differences identified in Table 55 between the control group and the pandemic subgroups presented positive trends.

Post-hoc analysis through pairwise comparisons with Sidak correction confirmed the following statistically significant differences in DBP among groups:

- for all ages and for over 10 years old, between the control group and all the pandemic subgroups, with a significance of p<0.001.
- for 2 to 4 years old, between the control group and group 3 (p=0.025).
- for 5 to 9 years old, between the control group and group 1 (p=0.038), and between the control group and group 3 (p<0.001).

Table 55. DBP z-scores' differences across division III groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.250	0.189	0.186	0.001	0.093	0.121	0.441	0.000
Group 2	0.048	0.118	0.685	0.000	0.108	0.077	0.160	0.001
Group 3	0.206	0.094	0.029 *	0.003	0.177	0.062	0.004 *	0.005
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.227	0.077	0.003 *	0.001	0.154	0.056	0.006 *	0.001
Group 2	0.137	0.060	0.022 *	0.001	0.096	0.044	0.029 *	0.001
Group 3	0.250	0.044	<0.001*	0.005	0.183	0.032	<0.001*	0.005
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.253	0.063	<0.001*	0.003	0.224	0.047	<0.001*	0.004
Group	0.347	0.046	<0.001*	0.011	0.286	0.035	<0.001*	0.013
Group 3	0.344	0.036	<0.001*	0.018	0.275	0.027	<0.001*	0.019
All ages								
Control Group	0	-	-	-	0	-	-	-
Group 1	0.245	0.047	<0.001*	0.002	0.207	0.034	<0.001*	0.003
Group 2	0.246	0.034	<0.001*	0.004	0.246	0.025	<0.001*	0.007
Group 3	0.293	0.026	<0.001*	0.010	0.276	0.019	<0.001*	0.016

Values adjusted for sex, twinship, gestational age, transformed age and division III timespan groups.
Group 1: 1st Lockdown + Reopening. Group 2: 2nd Lockdown + Reopening. Group 3: 3rd Lockdown + Reopening.
* Statistically significant, $p \le 0.05$.

Considering the index population as reference, when analysing DBP data by timeline division IV, statistically significant differences were observed between groups for all ages ($p<0.001$, partial $\eta^2=0.015$), ages 2 to 4 years old ($p=0.034$, partial $\eta^2=0.008$), ages 5 to 9 years old ($p<0.001$, partial $\eta^2=0.009$) and over 10 years old ($p<0.001$, partial $\eta^2=0.026$). Differences between the control group and the pandemic subgroups are explored in Table 56.

All significant differences for the pandemic subgroups exhibited a positive trend when compared to the control group, except for group C in age ranges 2 to 4 years and 5 to 9 years old, which displayed a negative difference.

Post-hoc analysis through pairwise comparisons confirmed the following statistically significant differences:

- for all ages, between the control group and the restrictions' lifting subgroups, group B (p<0.001), group D (p<0.001) and group F (p<*0.001*); between groups B and C (p=0.002); between groups C and D (p<0.001); between groups C and E (p=0.025); and between groups C and F (p<0.001).
- for ages 5 to 9 years, between the control group and the restrictions' lifting subgroups, group B (p=0.021) group D (p=0.014) and group F (p<0.001); between groups B and C (p=0.008), groups C and D (p=0.015), and groups C and F (p=0.003).
- for ages over 10 years old, between the control group and four pandemic subgroups, namely group B (p=0.008), group D (p<0.001), group E (p=0.005) and group F (p<0.001).

When using NHLBI and CDC data as the reference population, statistically significant differences were observed between groups for all age categories: all ages (p<0.001, partial η^2=0.011), 2 to 4 years old (p=0.008), 5 to 9 years old (p<0.001, partial η^2=0.09) and over 10 years old (p<0.001, partial η^2=0.028). In this setting, all significant differences identified in Table 55 for the pandemic subgroups exhibited a positive trend when compared to the control group, except for group C in age range 5 to 9 years old, which displayed a negative difference.

Table 56. DBP z-scores' differences across division IV groups.

Pandemic Timeline Groups	Index population z-scores				NHLBI and CDC data z-scores			
	B	Std. Error	*p* value	Partial η^2	B	Std. Error	*p* value	Partial η^2
2 to 4 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.257	10.038	0.804	0.000	-0.353	0.676	0.601	0.000
Group B - 1st R	0.267	0.192	0.164	0.001	0.108	0.123	0.381	0.000
Group C - 2nd L	-0.628	0.289	0.030 *	0.003	-0.338	0.188	0.072	0.002
Group D - 2nd R	0.177	0.128	0.168	0.001	0.192	0.083	0.021 *	0.003
Group E - 3rd L	0.009	0.289	0.976	0.000	0.072	0.188	0.700	0.000
Group F - 3rd R	0.228	0.099	0.021 *	0.003	0.188	0.065	0.004 *	0.005
5 to 9 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	-0.032	0.196	0.869	0.000	-0.026	0.143	0.856	0.000
Group B - 1st R	0.272	0.083	0.001 *	0.002	0.185	0.061	0.002 *	0.002
Group C - 2nd L	-0.335	0.151	0.027 *	0.001	-0.241	0.112	0.031 *	0.001
Group D - 2nd R	0.218	0.064	<0.001*	0.002	0.155	0.047	0.001 *	0.002
Group E - 3rd L	0.066	0.162	0.683	0.000	0.054	0.118	0.644	0.000
Group F - 3rd R	0.263	0.045	<0.001*	0.005	0.193	0.033	<0.001*	0.006
Over 10 years old								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.437	0.192	0.023 *	0.001	0.399	0.151	0.008	0.001
Group B - 1st R	0.234	0.066	<0.001*	0.003	0.207	0.049	<0.001*	0.003
Group C - 2nd L	0.053	0.111	0.635	0.000	0.069	0.083	0.405	0.000
Group D - 2nd R	0.397	0.049	<0.001*	0.013	0.323	0.037	<0.001*	0.015
Group E - 3rd L	0.358	0.097	<0.001*	0.003	0.309	0.070	<0.001*	0.004
Group F - 3rd R	0.343	0.037	<0.001*	0.017	0.271	0.028	<0.001*	0.018
All ages								
Control Group	0	-	-	-	0	-	-	-
Group A - 1st L	0.199	0.136	0.143	0.000	0.158	0.102	0.123	0.000
Group B - 1st R	0.251	0.049	<0.001*	0.002	0.213	0.036	<0.001*	0.003
Group C - 2nd L	-0.133	0.085	0.120	0.000	-0.042	0.062	0.504	0.000
Group D - 2nd R	0.311	0.037	<0.001*	0.005	0.296	0.027	<0.001*	0.009
Group E - 3rd L	0.242	0.080	0.002 *	0.001	0.279	0.056	<0.001*	0.002
Group F - 3rd R	0.298	0.027	<0.001*	0.009	0.276	0.020	<0.001*	0.015

Values adjusted for sex0. twinship0. gestational age0. transformed age and division IV timespan groups.
* Statistically significant0. $p \leq 0.05$. L - Lockdown. R - Reopening.

Post-hoc analysis of DBP z-scores through pairwise comparisons with Sidak correction confirmed the following significant differences:

- for all ages, between the control group and four pandemic subgroups, namely group B ($p<0.001$), group D ($p<0.001$), group E ($p<0.001$) and group F ($p<0.001$); and between group C and four other pandemic subgroups, specifically group B ($p=0.007$), group D ($p<0.001$); group E ($p=0.002$) and group F ($p<0.001$).
- for ages 5 to 9 years, between the control group and the restrictions' lifting subgroups, namely group B ($p=0.049$), group D ($p=0.023$) and group F ($p<0.001$); between groups B and C ($p=0.015$); between groups C and D ($p=0.021$); and between groups C and F ($p=0.004$).
- for ages over 10 years old, between the control group and four pandemic subgroups, namely group B ($p<0.001$), group D ($p<0.001$), group E ($p<0.001$) and group F ($p<0.001$).

Discussion

Birth parameters assessment

Most children in the study sample were born before the pandemic onset, while 11.6% were born after 2nd March 2020. The observed demographic changes in this study align with those observed in the country and beyond its borders. From 2004 to 2007, the annual number of births exhibited an upward trend, which then reversed from 2008 to 2012, aligned with the European financial crisis.[38] Despite this, the annual number of births remained above this sample's average during those years. This pattern contrasts with the period starting in 2013 (except for the year 2015), during which the annual birth rate fell below the average level of 206.4 births per year. This is overlapping with an average decline in births of 2.9% annually that was observed in Europe between 2015 and 2019.[39]

Following the onset of the COVID-19 pandemic, there was a reduction in the annual number of births within the study sample. This decline in birth rates is consistent with a pattern observed in previous pandemics.[39] In Europe, the COVID-19 pandemic was associated with a notable decrease of 4.1% in births by January 2021, approximately nine months after the pandemic's outbreak, particularly affecting countries with a declining birth rate prior to the pandemic.[39] In Portugal, this decrease amounted to 17.8% when compared to the average number of births in January 2018 and 2019.[39] In the specific context of this study, there were 32 births in Winter 2021, compared to an average of 38 births in Winter 2018 and 2019, indicating a 15.8% decrease.

The COVID-19 pandemic did not significantly impact pregnancy duration when comparing this study's control group with various pandemic timeline divisions. Statistically significant differences were only found when splitting timeline according to division II, between peak pandemic (group α) and post-restriction (group β) periods, in which there was an increase in mean gestational age. There was also no impact of maternal COVID-19 infection during pregnancy on gestational age, regardless of the timing of disease diagnosis.

In France, gestational age outcomes were also not modified by the COVID-19 pandemic.[40] However, some studies have documented a reduction in preterm birth rates, as presented in a meta-analysis.[12] In South Korea, for example, birth during the COVID-19 pandemic was associated with lower odds of preterm delivery.[41] In Austria, there was a decrease in the rate of very low gestational age during the lockdown phase compared to the pre-lockdown, but the rate of low gestational age births presented a slight increase during the lockdown period.[14] In China, however, the COVID-19 lockdown restrictions were linked to a slightly elevated risk of preterm birth.[42] Regarding maternal COVID-19 infection, two multicentric studies concluded that having this diagnosis during pregnancy was associated with a higher proportion of preterm deliveries.[43,44]

Of the three birth anthropometric parameters under analysis in this study, only head circumference was affected by the COVID-19 pandemic, particularly in boys. There was a significant increase in mean birth head circumference for children born during the 2nd lockdown and the corresponding restriction lifting phase (group 2 for division III, groups C and D for division IV) in comparison to the control group. This period, spanning from January 15th to December 20th, 2021, encompasses pregnancies conceived within the first year of the pandemic.

Lockdowns and quarantine measures may have influenced the dietary habits of pregnant women, with a potential impact on newborn anthropometrics. A Canadian cross-sectional study revealed that more than half of pregnant individuals altered their dietary patterns during the pandemic.[45] Some shifted toward healthier choices (increasing fruits and vegetables intake), while others moved toward less healthy options (including frozen goods, canned products, and pastries). Interestingly, there was a curvilinear relationship between these dietary changes and mental health symptoms.[45] In Italy, the impact of the COVID-19 pandemic on maternal diet during pregnancy may have been adverse, as there were reports of reduced adherence to the Mediterranean diet in that context.[46]

Research on the precise impact of the COVID-19 pandemic on newborn head circumference is quite limited. In Austria, birth head circumference was only slightly higher during the lockdown months.[14] A notable observation was made that newborns from pregnancies involving gestational diabetes in 2020 had larger birth head circumferences than those of 2018.[47] Within this study, data regarding maternal conditions other than COVID-19 infection was not considered.

When examining the effect of maternal COVID-19 infection during pregnancy, the observed statistically significant differences in birth head circumference were primarily due to discrepancies between the control group and the subgroup without maternal infection. Hence, there was no effect of maternal COVID-19 infection on birth parameters in this cohort.

Research on the impact of maternal COVID-19 infection on newborn head circumference is relatively scarce, since the majority of works concern other birth parameters, including birth weight and birth BMI.[13,14] One study suggests that a maternal diagnosis of COVID-19 is associated with a higher likelihood of reduced head circumference at birth.[44] Two works analysing data by severity of maternal disease reached the conclusion that there was a statistically significant decrease in newborn head circumference in cases of exposure to severe maternal COVID-19 infection when compared to mild disease.[48,49]

Child growth assessment

The COVID-19 pandemic's effects on child anthropometrics have been studied by research groups globally, with variations in study approaches and sample sizes.

As for this study, in children aged 0 to 1 years old, the 2nd reopening phase exhibited significant higher standardized length/heigh z-scores in comparison to the pre-pandemic control group, by 0.107 (p<0,001). Subsequently, in this age group, length/height z-scores were lower at the ending of restrictive governmental rules, yet with no statistical significance when compared to the control group. For ages 2 to 4 years old, standardized height z-scores were significantly lower in the post-pandemic period by 0.101 (p=0.048), when compared to the control group, and with a significance of p=0.018 in comparison to the pandemic peak. These findings were validated through the z-scores' comparison with WHO child growth standards.

Regarding weight measurements, different trends could be identified, depending on the age range under analysis. For children between 0 and 1 years old, weight z-scores were lower during the pandemic by 0.055 (p<0.001), with a particular significant difference during the third lockdown and reopening phases, by 0.092

(p<0.001). Regarding children between 5 and 9 years old, weight z-scores were higher during the first lockdown and reopening phases by 0.151 (p=0.017) when compared to the pre-pandemic values. This may reflect the initial impact of the 1st lockdown. Weight z-scores were then lower during the unwind of the pandemic, without statistically significant differences when compared to the control group. As for ages over 10 years old, the onset of the pandemic was associated with a significant increase in weight z-scores, by 0.143 (p<0.001), which persisted even after the lifting of restrictions, by 0.084 (p=0.013) when compared to the control group. These differences suggest that the initial stages of the pandemic might have encountered distinct influences compared to the subsequent months.

Differences in weight are better understood when considered in the context of BMI. For ages 0 to 1 years old, BMI z-scores were lower during the pandemic by 0.088 (p<0.001) and persisted below the control group by 0.116 (p<0.001), even after the lifting of restrictions. For ages 5 to 9 years old, BMI z-scores were higher during the first lockdown and reopening phases by 0.181 (p=0.005) when compared to the pre-pandemic values. Subsequently, BMI z-scores were lower than the pre-pandemic group during the third set of lockdown and reopening periods by 0.079 (p=0.047). As for children aged 10 to 16 years old, BMI z-scores were significantly higher during the pandemic by 0.122 (p<0.001), specifically by 0.172 (p<0.001) during peak pandemic. However, no statistical significative differences compared to the control group were found when comparing the pre-pandemic group with the third lockdown and respective reopening stages. This suggests a potential trend of BMI recovery over time.

A group of Austrian researchers conducted a set of studies under this topic, focusing on a cohort of children aged 7 to 10 years. When examining the impact of the 2020 confinement, they reported a significant increase in BMI z-scores, approximately by 0.16, resulting in a 3.8% increase in the proportion of children classified as having excess weight or obesity.[23] Their follow-up publication extended the longitudinal study until March 2021, confirming the ongoing trend of increased excess weight and obesity, particularly among boys.[50] Interestingly, they also observed an increase in the standard deviation scores of girls' height, which may contribute to the differences observed between sexes.[50]

In a large retrospective American cohort study, the most significant difference in age-adjusted BMI compared to the median was found in the 5 to 11-year-old group, with an increase of 1.57 kg/m^2 between 2019 and the period spanning from June 2020 to January 2021.[24] In a Czech study, the most pronounced BMI raise was registered at around 12 years of age in both sexes.[51] In a large study in Massachusetts, obesity prevalence increased in 2020 to a greater extent than expected based on the increase in pre–COVID-19 years, particularly among boys aged 6 to 11 years, with a 2.8% increase.[52] A German study dividing a 153,508 children sample by age categories (1 to 6, 6 to 12 and over 12 years old) found a substantial weight gain across all weight and age groups.[53] Other than this study, evidence is limited on infants aged 0 to 1 years old.

Throughout the pandemic, changes in dietary patterns and decreased physical activity have potentially engendered noteworthy consequences for the children's BMI.[18,21] The imposition of restrictions and changes in daily routines limited opportunities for outdoor activities and facilitated a more sedentary lifestyle, while dietary habits may have shifted towards increased consumption of energy-dense foods.[54] In Portugal, children aged 6 to 8 years old increased their consumption of sweet and savoury snacks during the pandemic.[55] Nearly half of the child population displayed an increase in sedentary behaviours. The Portuguese results align with findings from 12 other European countries that have shared their data, with consistency observed across most analysed dimensions.[55] These observations underscore the significance of addressing lifestyle modifications and promoting balanced nutritional choices for children, even during challenging public health circumstances.

When examining head circumference, although statistical significance was observed for newborns, differences for growth development measurements were relatively subtle. These became more noticeable when broadly dividing the sample into pre-pandemic and pandemic periods, particularly with regards to an increase in head circumference observed in children aged 2 to 4 years old. No statistical significance was observed when further subdividing the sample. No published evidence is available so far regarding the pandemic's impact on head circumference among toddlers.

In this study, systolic blood pressure z-scores were higher among children aged 5 to 9 years old during the pandemic, by 0.127 ($p<0.001$), but with no statistical significance within the first year of restrictions. The rise in systolic blood pressure z-scores was detected sooner and more expressively in children aged over 10 years, by 0.185 ($p=0.002$) compared to the pre-pandemic data. Diastolic blood pressure z-scores were higher during the pandemic among all ages, when compared to the pre-pandemic group: by 0.159 for ages 2 to 4 years old ($p=0.027$), by 0.214 for ages 5 to 9 years old ($p<0.001$) and by 0.331 for ages over 10 years old. Unlike other parameters, diastolic blood pressure appears to have been more significantly and enduringly affected over time in this study.

The pandemic has brought about increased stress and anxiety levels in children.[19,20] The fear of contracting the virus, social isolation, and the uncertainty surrounding the future may have taken a toll on their mental well-being.[19] Chronic stress can trigger the body's "fight or flight" response, leading to elevated blood pressure over time.[56] Moreover, dietary habits may also have been affected by the pandemic.[21] With more time spent at home, there has been a tendency towards increased consumption of processed and unhealthy foods and a decrease in physical activity.[18,21] High-sodium and high-sugar diets can contribute to hypertension in children, further exacerbating the issue. In a study with a Chinese cohort, the proportion of school-aged boys and girls with pre-elevated blood pressure and elevated blood pressure increased by 46.6% during the COVID-19 quarantine.[57]

Strengths and Limitations

This study enabled a comprehensive evaluation of the impact of the COVID-19 pandemic on the birth parameters and child growth development of a Portuguese local cohort, incorporating data from before, during, and after the core pandemic period. Its design, which includes the establishment of an index population from data gathered between 2002 and 2020, enhances the validity and robustness of the results. Throughout the assessment of multiple birth, growth and blood pressure parameters, the results were consistently compared to validated reference populations, including Fenton growth charts, WHO child growth charts, and NHLBI/CDC blood pressure data.[26,27,32-34] The overlapping results between this study's index population and the reference charts further underscores the reliability of the findings.

The present study is not without its limitations. It adopts a retrospective design, relying on data collected over a span of 17 years from various healthcare professionals. This approach introduces potential biases, including issues related to data accuracy, completeness, and possible variations in record-keeping practices over time. Moreover, this study did not include data on dietary habits or physical activity. These factors could enhance the overall robustness of the investigation, considering their relevance to child and youth nutritional status.

Furthermore, a significant limitation arises from the lack of standardization in anthropometric measurements. These measurements depended on the equipment that was available on the healthcare office where they were taken (there are several possible consulting rooms in each of the study sites) and on the individual healthcare professional responsible for recording them. This lack of uniformity in data collection could lead to inconsistencies and hinder the precise interpretation of results. Despite that, the fact that data stemmed from measurements taken over an extended period of time and was collected for observational purposes rather than research lends a certain authenticity to the dataset, as the measurements were not influenced by the intention of conducting a study, reducing the likelihood of bias. Moreover, the dataset is impressively robust, comprising over 11,000 birth parameters' measurements and 200,000 growth measurements across various age groups. In particular, the sample born after the pandemic onset included 499 health records, with 83 of them being exposed to maternal infection during pregnancy. While not a large sample, it is more substantial than many of the previously published works in this domain.

This study's measurements are not reliant on self-reported values but rather represent objective measurements obtained by healthcare professionals, increasing their reliability and accuracy. To enhance the handling of this study's extensive dataset, presenting results using logarithms may have offered several advantages, particularly when dealing with growth data, which often exhibits a skewed distribution with a wide range of values.[58] Logarithmic transformations help normalizing the data by compressing the scale, thereby facilitating the visualization and interpretation of trends. Additionally, this approach can mitigate data variability and make trends and patterns more evident.[58] For instance, sudden changes that might be less noticeable on a linear scale can become more apparent on a logarithmic scale.

The application of a multivariate analysis model represents a significant advantage of this study, allowing for the consideration of potential confounding factors that may have arisen due to the non-standardized measurements and other variables, including sex, twinship, gestational age, age at time of measurement and pandemic timeline divisions. By statistically accounting for these confounders, the investigation enhances its ability to discern genuine relationships between the measured parameters and the outcomes of interest.

Additionally, the fact that the children in this study reside in the same municipality is a significant strength. While it may not entirely eliminate confounding variables, it does mitigate their impact by reducing the influence of regional or environmental factors. This homogeneity within the study population enhances the internal validity of the findings and allows for more confident inferences about the relationships being investigated.

Future challenges

While this study has shed light on the immediate impact of the COVID-19 pandemic on childhood development, several future challenges remain. The documented increases in weight, BMI, and blood pressure during the lockdown phases, along with the recovery of weight and BMI in the 0 to 1-year-old group after the easing of restrictions, underscore the complex interplay between pandemic-related disruptions and child health. Notably, a more modest reduction in weight observed in the 10 to 18-year-old age group, which is closer to adulthood, suggests that the long-term effects of this event may require further investigation and attention. While statistically significant results were observed, it's important to note that the actual impact of these differences was relatively modest. As only three years and a half have passed since the pandemic's onset, a comprehensive understanding of its lasting consequences on childhood development is still in the making. These findings have far-reaching implications for future health policies, particularly in the face of the persistent concern of childhood obesity. Collaborative efforts from governments, communities, and schools are also essential in promoting healthy eating habits, encouraging physical activity, and preventing chronic diseases. Continued research and a longer-term perspective are imperative as the evolving landscape of child health in a post-pandemic era is navigated.

Conclusions

This study provides valuable insights into the impact of the COVID-19 pandemic on child growth development, through an analysis of the z-score variations of several anthropometric parameters and blood pressure data across time. Results were compared to internationally validated reference standards, as well as with the study's sample own index population, comprising over 17 years of information.

The analysis of 499 children born after the pandemic onset, unveiled a small yet significant increase in mean birth head circumference for children born in 2021 in comparison to the control group, particularly in boys. Maternal COVID-19 infection during pregnancy did not influence gestational age or newborn birth parameters.

As for child growth development, distinct trends of pandemic impact on BMI were identified, despite the small effect sizes: there was a global decrease in BMI for ages 0 to 1 years old, an increase followed by a soon BMI recovery in ages 5 to 9 years old, and a sustained rise in children 10 years to 16 years old followed by a less pronounced BMI decrease during the reopening phase. There was no substantial effect of the COVID-19 pandemic on head circumference. Conversely, there was a consistent increase in blood pressure among children over 5 years old, which was detected earlier in children over 10 years.

These findings emphasize the need for long-term research and targeted interventions to promote the well-being of children and adolescents. Blood pressure may require ongoing monitoring over time. All in all, amid the difficult challenges posed by the COVID-19 pandemic, children's adaptability, and adequate healthcare provision suggest a path of recovery rather than of irreversible harm.

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