before in the general population (dbSNP, Exome Variant Server); however, a mutation involving a different nucleotide change at the same position has been reported in a Marfan syndrome patient, suggesting that this position is important for correct RNA processing.[6] The genetic analysis also identified 2 mutations of unknown pathogenicity, in *TGFBR1* (c.409G>A; p.Val137Ile) and in *LMNA* (c.1158-6C>T, NM_170707.3).

A familial study confirmed that the mother meets the diagnostic criteria for Marfan syndrome (aortic dissection and family history) with a systemic score of 3 (scoliosis, myopia > 3 diopters, and *pectus excavatum*). She has 3 sisters with no disease phenotype, and both elderly parents died several years ago, apparently from noncardiovascular causes, although no data are available.

The familial cosegregation analysis began with the mother and was directed at *FBN1* and at *TGFBR1*, included because of its association with familial aortic syndromes. The study showed that the mother does not carry the *TGFBR1* mutation but is mosaic for the *FBN1* mutation (Figure). The presence of this somatic mosaicism indicates that the mutation arose *de novo* during the mother's embryonic development, and the analysis was therefore not continued in her sisters. Following recommended procedures for confirmation of suspected mosaicism, we extended the genetic analysis to another tissue (bucal mucosa) and confirmed the results with a second independent primer pair. These tests yielded a similar percentage of cells containing the mutant allele, indicating that the mutation event occurred in the early stages of embryogenesis.

The literature on mosaicism in Marfan syndrome reveals that parent carriers have less severe phenotypes than probands or express no manifest phenotype, independently of sex.[2–5] However, in the family studied here, the mother has a prominent vascular phenotype, despite carrying the mutation in mosaicism. This discrepancy could in principle reflect differences in the type of genetic alteration; however, this hypothesis is not supported by the published data, which show that a weaker phenotype in the mosaic parent is found with all types of mutation, whether causing amino acid substitution or protein truncation.[2–5] We therefore recommend close clinical follow-up of patients with a mosaic mutation, even if it is present in a low percentage of cells.

The intrafamiliar variation encountered here might be explained by a protective effect of the *TGFBR1* variant found in the son. Another possible explanation is the age difference, since aortic dilatation in Marfan syndrome is progressive and therefore likely to worsen with age. Moreover, pregnancy is an additional risk factor for aortic dilatation in patients with underlying aortic disease.[1]

In summary, we present an example of somatic mosaicism in *FBN1* that illustrates the importance of considering this possibility in genetic counseling programs. This would permit a more focused strategy than would be possible otherwise. This case also shows that somatic mosaicism is not always associated with a less severe progression of Marfan syndrome.

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The Longitudinal Childhood Obesity Study (ELOIN): Design, Participation and Characteristics of the Baseline Sample

Estudio Longitudinal de Obesidad Infantil (ELOIN): diseño, participación y características de la muestra

To the Editor,

Controlling childhood obesity is a global health priority.[1] Obesity is associated with comorbidity in childhood and, if it persists, leads to a higher risk for diseases in adulthood.[2] According to the Spanish National Health Survey, the prevalence of obesity in the 2- to 17-year-old population age group increased from 8.4% in 1993 to 10.5% in 2011.[3] The factors most widely studied by researchers to explain the high incidence of childhood obesity are energy balance, food intake, physical activity, and sedentary behavior.[4]

The Longitudinal Childhood Obesity Study (ELOIN) is a prospective, population cohort study that started in 2012 and aims to describe variations in overweight and obesity, determine the association of overweight and obesity with sociodemographic and lifestyle factors, and estimate their impact on health. This dynamic cohort and the baseline sample are composed of children aged 4 years. Follow-up measurements are being recorded at ages 6, 9, 12, and 14 years. The target population is children born between 15 January 2008 and 30 November 2009, living in the Madrid Autonomous Community, and under the care of one of the 31 pediatricians in the Madrid Sentinel Primary Care Physician Network. The study design has already been described in the literature.[5] We collected data for the baseline sample in 2 consecutive steps: at a physical examination performed by the

Table 1
Study Variables, Data Collection Methods, and Follow-up Timeline

Methods	Measurements	Variables
Physical examination: anthropometry	Weight status	Mean values for weight, height, waist circumference, and systolic and diastolic blood pressure. Body mass index. Child's weight and height, reported by accompanying adult. Diagnosed comorbidities: allergies, asthma, hypertension, etc.
Computer-assisted telephone interview questionnaire on eating and lifestyle	Eating habits, quality of life, diet assessment, physical exercise, sleep, use of TV/gaming/computer screens, and neighborhood facilities	*Child:* breast milk and introduction of solids (4 y). Energy intake: food types, macronutrients and micronutrients based on food composition tables. Eating habits: diet changes, school meals, daily meal patterns, frequency of fast food intake. Physical activity (h/wk), sleep (h/d), use of computer, TV and game console (h/d). Health-related quality of life score (from age 6 y). *Parents:* reported weight and height. Physical activity and sedentary behavior. Neighborhood sports and exercise facilities.
	Social factors	Socioeconomic status, family size/structure, and parents' educational level and purchasing power.
Blood sample at ages 9 and 14 y	Blood-based biomarkers	*All samples:* lipids (total cholesterol, HDL-C, LDL-C, triglycerides), glucose, insulin, glycated hemoglobin (HbA_{1c}), C-reactive protein, calcium, phosphate, alkaline phosphatase, ferritin, and transferrin. Vitamins A, B12, E, folic acid, D, and individual carotinoids. *Subsample for genetic markers:* selected gene testing of expression in lymphocytes.
Medical records: primary care electronic medical record (APMADRID) and specialist records (MBDS)	Past medical history and medications	Anthropometric values, health problems and diagnosed comorbidities, eating habits and sleep. Laboratory tests: blood lipids, glucose, minerals, vitamins. Prescription medication and vaccinations. Use of health care services (These variables will be collected from records from birth onwards.)

Follow-up timeline				
2012-2013	2014-2015	2017-2018	2020-2021	2023-2024
T_0	T_1	T_2	T_3	T_4
Age 4 y	Age 6 y	Age 9 y	Age 12 y	Age 14 y
Data collection - Physical examination - Questionnaire - Medical records	- Physical examination - Questionnaire - Medical records	- Physical examination - Questionnaire - Medical records - Blood samples	- Physical examination - Questionnaire - Medical records	- Physical examination - Questionnaire - Medical records - Blood samples

HDL-C, high-density lipoprotein cholesterol; HT, hypertension; LDL-C, low-density lipoprotein cholesterol; MBDS, Minimum Basic Data Set; TV, television.

pediatrician at the health center, followed by a structured computer-assisted telephone interview with the person in charge of the child's nutrition.

We sent a letter to the children's families to explain the study aims and obtained the families' written informed consent. The study protocol was approved by the Ethics Committee of Hospital Ramón y Cajal, Madrid.

Table 1 shows the study variables and procedures. At the physical examination, 2 standard measurements were taken of the child's weight, height, waist circumference, and blood pressure. Digital scales were used for weight, a telescopic measuring rod for height, a nonstretchable measuring tape to measure the waist circumference above the iliac crests, and a validated aneroid sphygmomanometer was used to record blood pressure. Obesity was defined in accordance with the criteria of the World Health Organization, the International Obesity Task Force, and the Spanish anthropometric tables designed by *Fundación Orbegozo*.

The questionnaire included the following modules: sociodemographic variables, dietary patterns and lifestyles, semiquantitative food frequency based on the Martin-Moreno et al questionnaire,[6] and quality of life (KINDSCREEN-10).

Laboratory tests were performed following standard procedures and quality controls. The following data were collected from the child's medical records from birth: growth and development (weight and height), health problems (cardiometabolic and musculoskeletal disorders, upper respiratory tract obstruction, anxiety, depression and behavior disorders), laboratory tests, medication, vitamin supplements, and vaccinations. Data were taken from the child's single primary care electronic medical record (APMADRID program) and hospitalization records (Minimum Data Set). A unique identity code was applied to each child to ensure medical record traceability throughout the Madrid Autonomous Community.

In 2011, we conducted a pilot study and trained staff to standardize measurements. To encourage participation, we organized activities with families and pediatricians. The project was published in the Madrid Autonomous Community Health Website.

For the statistical analysis, qualitative variables are expressed as relative frequencies and quantitative variables as mean and standard deviation. The association between determinants was assessed with multilevel logistic regression models using anthropometric status (body mass index at baseline and changes during follow-up) as a dependent variable. In view of the complex sampling design, we applied a 95% confidence interval in all analyses.

In total, 2627 of the 4571 children screened at aged 4 years participated in the questionnaire and examination, representing a response rate of 57.5%. Participants (Table 2) had a mean body mass index of 15.9 and a systolic and diastolic blood pressure of 88.5 and 51.6 mmHg, respectively. Mean daily intake for carbohydrates, proteins and fats was 226.9 g, 87.5 g and 82.4 g, respectively. Mean fruit and vegetable portions per day were 1.9 and 1.7, respectively. Weekly physical activity was 2.7 hours and daily use of television, game console and computer was 2.7 hours.

Table 2
Anthropometric, Nutritional and Lifestyle Characteristics, and Blood Pressure in the Baseline Sample

	Total (N = 2627)	Boys (N = 1334)	Girls (N = 1293)
Age, mo	48.6 ± 1.6	48.6 ± 1.6	48.6 ± 1.5
Weight, kg	17.0 ± 2.5	17.2 ± 2.4	16.9 ± 2.5
Height, cm	103.4 ± 4.4	103.9 ± 4.4	103.0 ± 2.3
BMI, kg/m^2	15.9 ± 1.6	15.9 ± 1.5	15.9 ± 1.7
Waist circumference, cm	52.0 ± 4.1	51.8 ± 3.9	52.3 ± 4.3
Systolic blood pressure, mmHg	88.5 ± 8.9	88.8 ± 8.9	88.1 ± 9.0
Diastolic blood pressure, mmHg	51.6 ± 8.8	51.5 ± 8.7	51.7 ± 8.8
Frequency of daily breakfast, %	97.5	98.2	96.8
Breast milk only, mo	3.3 ± 2.4	3.2 ± 2.5	3.4 ± 2.4
Carbohydrate intake, g/d	226.9 ± 66.6	231 ± 68.9	222.2 ± 63.8
Protein intake, g/d	87.5 ± 24.6	88.0 ± 24.9	86.9 ± 24.3
Fat intake, g/d	82.4 ± 20.1	83.2 ± 20.3	81.4 ± 19.7
Fruit intake, portions/d	1.9 ± 1.1	1.8 ± 1.1	1.9 ± 1.1
Vegetable intake, portions/d	1.7 ± 2.9	1.6 ± 0.9	1.7 ± 4.0
Sleep, h/d	10.5 ± 1.1	10.5 ± 1.1	10.5 ± 1.1
Physical activity, h/wk	2.7 ± 1.7	2.7 ± 1.7	2.7 ± 1.6
Use of TV, game console or computer, h/d	2.7 ± 1.6	2.8 ± 1.7	2.7 ± 1.7

BMI, body mass index; TV, television.
Unless otherwise indicated, the data are expressed as mean ± standard deviation.

The ELOIN study lays the foundations to prospectively follow upa representative sample of children. Its main strength lies in its longitudinal, population cohort design that includes children with a broad socioeconomic status, geographical residence, and origin. The data from the ELOIN study cohort through to adult age will help improve our clinical-epidemiological knowledge of the factors associated with the onset and persistence of childhood obesity and its short- and long-term impact on health.

The characteristics of the baseline sample are quite similar to the characteristics of the general population. However, the percentage of mothers with primary school education or below is slightly lower in the ELOIN study than in Madrid in general. The main challenge in follow-up will be to maintain high participation levels, and to achieve this we have designed engagement strategies to be implemented by the pediatricians and a telephone call and alert system for the families.

We believe that the ELOIN study is a viable project with a design that makes efficient use of health resources. The study results will provide an excellent opportunity to strengthen prevention strategies and control childhood obesity in our region.

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