Weight Trajectories from Birth and Bone Mineralization at 7 Years of Age

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Objective To assess whether different trajectories of weight gain since birth influence bone mineral content (BMC) and areal bone mineral density (aBMD) at 7 years of age.

Study design We studied a subsample of 1889 children from the Generation XXI birth cohort who underwent whole-body dual-energy radiograph absorptiometry. Weight trajectories identified through normal mixture modeling for model-based clustering and labeled "normal weight gain," "weight gain during infancy," "weight gain during childhood," and "persistent weight gain" were used. Differences in subtotal BMC, aBMD, and size-corrected BMC (scBMC) at age 7 years according to weight trajectories were estimated through analysis of covariance.

Results Compared with the "normal weight gain" trajectory, children in the remaining trajectories had significantly greater BMC, aBMD, and scBMC at age 7 years, with the strongest associations for "persistent weight gain" (girls [BMC: 674.0 vs 559.8 g, aBMD: 0.677 vs 0.588 g/cm^2, scBMC: 640.7 vs 577.4 g], boys [BMC: 689.4 vs 580.8 g, aBMD: 0.682 vs 0.611 g/cm^2, scBMC: 633.0 vs 595.6 g]). After adjustment for current weight, and alternatively for fat and lean mass, children with a "weight gain during childhood" trajectory had greater BMC and aBMD than those with a "normal weight gain" trajectory, although significant differences were restricted to girls (BMC: 601.4 vs 589.2 g, aBMD: 0.618 vs 0.609 g/cm^2).

Conclusion Overall, children following a trajectory of persistent weight gain since birth had clearly increased bone mass at 7 years, but weight gain seemed slightly more beneficial when it occurred later rather than on a normal trajectory during the first 7 years of life. *(J Pediatr 2017;■■:■■-■■).*

The theoretical approach currently used to model peak adult bone mass and subsequent fracture risk builds on the premise that there is important tracking of this characteristic throughout the life course, modulated by gene–environment interactions.[1] Empirically, there is also growing evidence of early life influences on bone accrual.[2,3]

The anthropometric phenotype comprises a set of partially modifiable influences on bone strength from as early as intrauterine life.[3-5] Strong cross-sectional relations between body size and bone mass and density have been established clearly in children, reflecting, to a large extent, the adaptation of skeletal modeling to loading.[6-9] More recently, sensitive periods for the effect of height and weight on children's bone mass and geometry have been found,[10-12] suggesting that qualitative differences in the timing of growth may have relevant quantitative impact on bone accrual. However, it is not clear whether differences in the overall shape of growth since birth, particularly weight trajectories, also have differential impact on bone mineral mass and density. Indeed, increased overall exposure to weight during growth, in dose and/or duration, may positively influence bone health as a consequence of greater and/or longer exposure to loading, especially from the lean component.[13] Among the statistical approaches to examine the role of growth trajectories in later health and disease, group-based modeling methods seek to identify distinctive subgroups of individuals that follow similar growth patterns.[14,15]

aBMD	Areal bone mineral density
BMC	Bone mineral content
BMI	Body mass index
DXA	Dual-energy radiograph absorptiometry
scBMC	Size-corrected bone mineral content

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Generation XXI was funded by European Regional Development Fund (FEDER) through the Operational Programme Competitiveness and Internationalization and national funding from the Foundation for Science and Technology (FCT) – Portuguese Ministry of Science, Technology and Higher Education (POCI-01-0145-FEDER-016838 and POCI-01-0145-FEDER-016837), under the projects "BioAdversity: Como a adversidade social na infância condiciona a saúde: A biologia da adversidade social" (Ref. FCT PTDC/DTP-EPI/1687/2014) and "PathMOB.: Risco cardiometabólico na infância: desde o início da vida ao fim da infância" (Ref. FCT PTDC/DTP-EPI/3306/2014); by the Unidade de Investigação em Epidemiologia - Instituto de Saúde Pública da Universidade do Porto (EPIUnit) (POCI-01-0145-FEDER-006862; Ref. UID/DTP/04750/2013); and by Administração Regional de Saúde Norte (Regional Department of Ministry of Health) and Fundação Calouste Gulbenkian; PhD Grant SFRH/BD/92370/2013 (T.M.) and the Postdoc grant SFRH/BPD/88729/2012 (R.L.), co-funded by the FCT and the Human Potential Operating Programme of the European Social Fund (POPH/FSE Program); and the FCT Investigator contract IF/01060/2015 (A.C.S.). This study is also a result of the project DOCnet (NORTE-01-0145-FEDER-000003), supported by Norte Portugal Regional Operational Programme (NORTE 2020), under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF). The authors declare no conflicts of interest.

Portions of this study were presented as an oral presentation during the European Congress of Epidemiology in Munich, Germany, August 28-September 2, 2016, and at the XXXIV Reunión Científica de la SEE, XI Congresso da Associação Portuguesa de Epidemiologia in Seville, Spain, September 14-16, 2016 and published in abstract form.

0022-3476/$ - see front matter.
https://doi.org10.1016/j.jpeds.2017.08.033

So far, few studies have explored the relationship between growth and bone and research has focused on age-delimited periods, rather than capturing the overall shape of weight gain.[10-12,16-19]

The aim of this study was to estimate the influence of distinct weight trajectories since birth on bone mineral content (BMC) and areal bone mineral density (aBMD) at 7 years of age. Specifically, we aimed to assess whether those trajectories have explanatory power for bone mass at age 7 years in addition to concurrent anthropometrics.

Material and Methods

This work was embedded in the Generation XXI study, a prospective population-based birth cohort established in Porto, Portugal.[20,21] To summarize, recruitment took place between April 2005 and August 2006 at all level III public units providing obstetric and neonatal care that covered the metropolitan area of Porto. Of the invited mothers, 8495 agreed to participate (91.4%), and a total of 8647 infants (gestational age ≥24 weeks) were enrolled. At 4 years of age (April 2009 to July 2011), 7459 children were reevaluated (86.3% of the initial cohort). Again, at 7 years of age (April 2012 to April 2014), 6889 children were reassessed (79.7% of the initial cohort).

The Generation XXI study protocol conforms to the ethical principles outlined in the 1964 Declaration of Helsinki and was approved by the Ethics Committee of Hospital de São João and the University of Porto Medical School and by the Portuguese Data Protection Authority. Written informed consent from parents (or legal substitute) and oral assent from children were obtained at each evaluation.

In the follow-up evaluation at 7 years of age, children assessed between December 1, 2012, and August 31, 2013, were invited to undergo a whole-body dual-energy radiograph absorptiometry (DXA) scan. From the 5225 children with a weight trajectory assignment, DXA scanning was performed successfully in 1889 children (48.3% girls), who comprised our final sample for analysis (**Figure 1**). Following standard manufacturer protocols, total body BMC (g), bone area (cm^2), and aBMD (g/cm^2) were obtained while children were barefoot in light clothing and without metal accessories with a Hologic Discovery QDR 4500W device (Hologic Inc, Bedford, Massachusetts), software version 13.3.0.1. To ensure that the lines between adjacent subregions of the body were placed correctly, scans were examined twice, directly after the scanning procedure and at a later time point by a second, well-trained research assistant. We performed daily quality assurance tests using a spine phantom. As recommended by the International Society for Clinical Densitometry for research in pediatric populations, total body less head (subtotal) measures were used.[22] Size-corrected bone mineral content (scBMC) was derived separately for girls and boys by linear regression of BMC on bone area and addition of the residuals of the regression to the mean sample BMC.[23]

Birth weights were abstracted from clinical records. At ages 4 and 7 years, anthropometric measurements were

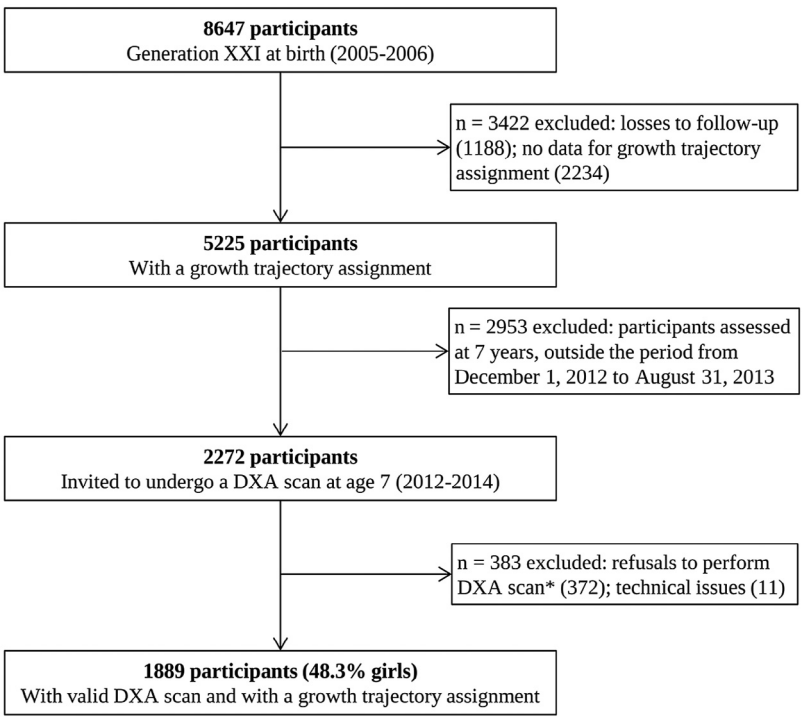

Figure 1. Flowchart of the participants included for analysis from the Generation XXI cohort, Porto, Portugal. *Participants who refused to participate in the DXA evaluation (n = 171) + participants who scheduled 3 different appointments but did not show up for evaluation or did not respond to our invitation after at least 5 attempts (n = 201).

FLA 5.5.0 DTD ■ YMPD9396_proof ■ October 12, 2017