Published in final edited form as:

Ann Nutr Metab. 2014 ; 65(2-3): 110–113. doi:10.1159/000365893.

Importance of characterizing growth trajectories

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Abstract

In the era of the obesity epidemic in children, characterizing childhood growth trajectories (weight, height or BMI/ weight-for-length) is becoming essential for surveillance. Clinicians routinely use growth curves to identify abnormal growth trajectories. Clinical epidemiologists use growth trajectories for different purposes. They are interested in the determinants of growth but also in the consequences of certain patterns of growth on later health and diseases. Characterizing growth trajectories is also necessary if one wants to predict future growth based on past growth and might be useful in the future to compare the anticipated impact of various interventions.

Keywords

growth trajectories; surveillance; etiology; prediction; categorization

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“All models are wrong, but some are useful”

--H. Box

Human growth and development are characterized and defined by the way in which we change in size, shape and maturity with age. [1] An early example of the study of growth was the Comte de Montbeliard's measurement of his son every 6 months for 18 years in the 18th century. [2] Since then many others have characterized growth of children, but questions remain unanswered. What causes the patterns of growth? How different are they for different people? Can we put these people into categories? Why are patterns different for different people in different categories? Can we identify inflection points to discover their drivers? How well can we construct growth references for surveillance and prevention? To answer these questions, simplifying assumptions are required, which is why many investigators have developed statistical models to describe growth. Many such models exist; the papers in this supplement describe several of them, including their applications,

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Conflict of interest

The authors declare that they have no conflict of interest.

advantages and disadvantages. Here, we provide an overview of the purposes of modeling growth trajectories.

Surveillance

Clinicians routinely use growth curves—for body length, weight, and sometimes weight/length ratios (e.g, body mass index— kg/m^2) to identify abnormal growth trajectories. In the prenatal period, clinicians use such curves to detect inadequate fetal weight gain, which failure can have severe consequences including fetal or neonatal death. [3] Controversy exists over whether or not fetal weight gain curves should be customized. [4] As reviewed by Gaillard et al. in this issue, customised fetal weight growth charts take into account the individual variation in fetal growth potential based on non-pathological maternal and fetal characteristics. [5] These customised weight charts may improve the distinction between growth restricted fetuses and constitutionally small fetuses. However, it is unclear whether incorporation of physiological characteristics into customised growth charts really improves this distinction. [5]

After birth, length/height and weight surveillance is a cornerstone of well-child visits, a visible record for both clinicians and parents. Crossing percentile lines downward is a traditional signal of failure to thrive. In the era of obesity, upward crossing gets more attention. Although weight-for-length varies substantially in the first few months of life, crossing several percentile lines can be worrying even in the first 6 months of life. In one study, we looked at how upward crossing of 2 percentile lines predicted later obesity. [6] Such upward crossing in the first 6 months was actually more predictive of later obesity than similar crossing in any of the other three 6-month intervals in the first two years of life. [6] If pediatricians are interested in surveillance in their daily practice, one area of interest to clinical epidemiologists is what causes observed patterns of growth, or more specifically, what underlies the variation between children in linear and adiposity growth.

Etiology of growth

In addition to genetics, several prenatal factors, such as gestational diabetes, and postnatal factors, such as early feeding, may have an impact on later growth. In the fetus, exposition to hyperglycemia is an important driver of adiposity. We have known for a long time that higher maternal glucose level or its extreme version, clinical gestational diabetes, is associated with higher weight and adiposity at birth. [7] Glucose passes the placenta easily whereas insulin does not. Excess glucose is presented to the fetal pancreas which produces insulin, an anabolic hormone.[8] But the extent to which gestational diabetes causes obesity and metabolic dysfunction in a growing child is still under debate. Gestational diabetes seems associated with slower weight for length gain in infancy. [9, 10] The increased adiposity in offspring of mothers with gestational diabetes seems to reappear only later in childhood. In Project Viva gestational diabetes was associated with increased skin folds and blood pressure at 3 year, but not with BMI. [11] In the EPOCH study, Crume et al. used mixed linear effects models (with polynomials and splines) to assess differences in BMI and BMI growth velocity from birth through 13 years of age.[12] They observed that the overall BMI growth trajectory was slightly lower for children exposed to gestational diabetes in

utero from birth through 2 years of age, but this difference was not significant. In contrast they observed higher BMI growth velocity among exposed youth between 10 and 13 years. [12]

Another major postnatal determinant of length and weight is infant feeding. In a recent study of 4680 children from the UK, Johnson et al. examined associations between breastfeeding duration and weight growth trajectories using a method developed by T. Cole, the SuperImposition by Translation And Rotation (SITAR), a shape invariant model. One important strength of SITAR is that it summarises individual growth relative to the average trajectory in three key parameters: size, tempo and velocity. In this study, the authors showed that infants breastfed for longer had slower weight growth velocities in the first months of life and later age at peak weight growth velocity. [13] In a different study in US children, Wen et al. used another kind of key parameters: milestones derived from BMI growth trajectories.[14] Using mixed effect models with fractional polynomial functions, they calculated age and BMI at infancy peak and adiposity rebound, as well as BMI growth velocity and area under curve between 1 week, infancy peak, adiposity rebound, and 18 years. In this study in US children, higher birth weight z-score predicted earlier adiposity rebound and higher BMI at infancy peak and adiposity rebound. [14]

These studies provide examples of various methods of characterizing individuals' change of weight or BMI with age and how they can be used to address etiological questions, either when studying determinants of growth or, as we will discuss now, when studying the long term consequences of early growth.

Prediction

By prediction, we mean the extent to which early growth patterns are associated with later health outcomes, for etiology or potentially for risk stratification. One highly-researched topic is the extent to which “catch-up growth” predicts later adiposity and dysmetabolism. The term “catch-up growth” is befuddling. Traditionally it refers to linear growth in the first 6 months of life. Catch-down occurs to the same extent as catch-up in well-nourished populations. Body length z-score may be quite variable at birth, but by 6 months of age, it tends to canalize toward values halfway between the extremes, presumably mostly due to genetic factors.[15] However, many authors now use the term “catch-up” to refer to rapid infant weight gain among babies who were born small; the time period can vary from a few months to a few years. This use has several disadvantages: it conflates weight with length. Weight is an amalgam of linear growth and adiposity. Its positive valence, i.e., catching up sounds like a good thing, even though rapid weight gain is associated with adverse consequences. [16] It also tends to ignore that babies born at higher weights also have long-term adverse health consequences. [17] With regard to weight and weight-for-length measures, it is preferable to avoid the term “catch-up” and instead 1.) specify which growth parameter is under study; and 2.) use less value-laden terms such as rapid weight gain. One way to look at weight or length/height patterns is to subtract weight or length/height at an earlier age from a later age. In this issue, Van Dommelen et al explored the impact of gain in weight and length in the first year on cognition, health-related quality of life and problem behavior in young adults born small for gestational age [18] In this Dutch study, the

exposure variable was weight or length SDS at 1 year of age adjusted for weight or length SDS at birth. They showed that a higher weight growth in the first year was associated with better cognition and fewer disabilities, but not with problem behavior. [18] Another way to look at weight-for-length patterns is to divide it into different age intervals of biological interest. An example of this approach is the work carried out by Belfort et al who looked in a cohort from the 1980s, at weight gain, linear growth and weight for length gain and divided this into term to 4 months and 4–12 months. They showed different relationships depending on the kinds of growth and the different intervals. For higher blood pressure, for example, the strongest associations were for greater linear growth from term to 4 months and higher weight-for-length gain during 4–12 months.[19] Another important issue in preterm and small-for-gestational-age babies (SGA) is trade-offs for different outcomes, especially obesity and cardio-metabolic risk on the one hand and neurodevelopment on the other. [20] In reviewing several studies, among term, preterm, and SGA babies, we showed that more rapid gain in weight-for-length predicts obesity and cardio metabolic risk.[21] However, linear growth and probably gain in weight-for-length were directly associated with neurodevelopment among preterm babies, but to date associations appear null among full-term adequate-for-gestational-age or SGA babies. These findings encourage clinicians not to overfeed term SGA babies.

Infancy is not the only period of growth that predicts later outcomes. Sun and Himes in this issue provide a good example of a study that relates height growth in adolescence and the risk of metabolic syndrome later in life. Using data from the Fels study, they showed that early attainment of the peak height velocity engenders greater risks for chronic disease. [22] In contrast to etiological studies, risk stratification in clinical practice requires very high predictive values. In this issue, Van Buuren et al present a new technique to improve prediction of future growth of an individual child.[23] The key idea is to find children in existing databases who are similar to this child. The growth patterns of the matched children suggest how the current child might evolve in future. [23] Using this method, Van Buuren suggests that it might be possible to materialize the effects of an intervention on a child's growth curve before the intervention starts by finding and comparing matches from the group that got the intervention in the past and from the group that did not. Prediction of future growth based on past growth makes sense because growth is largely driven by genetics. Yet, growth is also sensitive to a range of non-genetic factors, in particular environmental factors, and these might be difficult to predict. Thus, grouping children into categories should always be done with caution.

Categorization versus characterization of individual growth

Some growth trajectory modeling approaches provide individual growth trajectories, such as those proposed in Botton et al. or in Tilling et al., while others are based on classification of children into different groups [24, 25], such as the Group-based Modeling method proposed by Nagin [26]. In this issue, Van Rossem et al studied 3550 children participating in a birth cohort with repeated measures until age 11 years.[27] They used group-based modeling and showed that children in the category of persistent overweight were more likely to have overweight parents than those in the overweight reduction pattern, while birth weight and breastfeeding did not differ between the two groups of children.[27] In this issue, Twisk asks

whether it is necessary to classify subjects into different trajectories to answer research questions. [28] Even if classification is useful for description, he questions how useful it can be for analytic purposes. Among the issues related to the classification of growth trajectories are that choosing the number (and name) of categories can be subjective, and that categorizing data results in a loss of information.

In conclusion, in the era of the obesity epidemic in children, characterizing childhood trajectories of weight, length/height or BMI is becoming more important for surveillance, etiology, and clinical practice. Studying growth trajectories may very well allow more accurate identification and quantification of modifiable risk factors, as well as prediction of health outcomes. Characterization of these trajectories may also help to identify critical windows during which intervention may be especially useful.

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