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Childhood adiposity trajectories: discerning order amongst the chaos

Izzuddin M Aris[1] *and Emily Oken*[1,2]

[1]Division of Chronic Disease Research Across the Lifecourse, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA;; and [2]Department of Nutrition, Harvard TH Chan School of Public Health, Boston, MA, USA

Childhood obesity tracks into later life (1), suggesting that BMI (a growth metric commonly used to define obesity) in early childhood may affect cardiometabolic risks such as metabolic syndrome and type 2 diabetes. Many epidemiological studies examining associations between childhood BMI and later cardiometabolic outcomes have focused on single-point exposures of BMI (2, 3), which does not adequately reflect the complex and dynamic BMI changes that vary over time during the child's development. Groups of children may also follow distinct BMI developmental patterns, which may confer different risks for cardiometabolic disease later in life. Identifying heterogeneous growth patterns during early childhood, rather than simply assessing size at a single point in time, could prove more useful in predicting health outcomes in later childhood and even adulthood.

In this issue of the Journal, Wibaek and colleagues (4) report on their study of 453 healthy Ethiopian children with repeated measures of BMI assessed in the first 5 y of life. Using latent trajectory modeling techniques, the authors identified 4 distinct patterns of BMI development, which they label "stable low BMI," "normal BMI," "rapid catch-up to high BMI," and "slow catch-up to high BMI." Compared to children with the "normal BMI" pattern, those with the "rapid catch-up to high BMI" pattern exhibited greater accretion of fat mass during infancy and increased cardiometabolic risk (i.e., higher triglycerides, C-peptide, insulin, and HOMA-IR) at 5 y, whereas those with the "stable low BMI" pattern exhibited generally lower cardiometabolic risk, with the exception of higher triglyceride concentrations.

It is noteworthy that these findings from a predominantly low-income population in a developing country are consistent with those from higher-income populations (5–7), despite differences in stunting and obesity prevalence, health care systems, and socioeconomic circumstances. This similarity suggests that any bias attributable to uncontrolled (residual) confounding is an unlikely explanation for the observed associations. Moreover, these results add substantively to the growing body of literature that has been utilizing "group-based approaches" to address population heterogeneity of growth or adiposity trajectories (8, 9). Throughout the years, investigators have acknowledged the existence of heterogeneous growth patterns within a population (5, 10), signifying the need for more research on identifying distinct developmental patterns that are predictive of future disease risk, especially in diverse study populations.

The clinical utility of these "group-based approaches," however, has been the subject of long-standing debate. Clinicians often identify "abnormal" childhood growth patterns as crossing of major percentile lines on a standard growth chart. This method is simple and straightforward to implement. Latent trajectory modeling techniques, however, are typically implemented in research settings only and are relatively computer-intensive (11). The choices of the correct model and number of distinct patterns are also not always straightforward because they depend on the investigator's judgment (11). The assignment of children to a distinct developmental pattern is also based on their highest estimated group-membership probability to the identified pattern; thus, these latent patterns should not be considered as the actual developmental patterns but, rather, as approximations of more complex ones (12). Furthermore, these latent trajectory methods do not characterize individual trajectory milestones, such as the exact age of the infant BMI peak or childhood BMI rebound of each child, which are typically estimated from visual inspection of individual BMI-for-age curves (13) or using other statistical methods such as mixed-effect models (14). Recent studies have shown that the timing of these milestones, especially an early age at BMI rebound, are strong risk factors for an adverse cardiometabolic profile in later life (14). Children with "at-risk" developmental patterns also cannot be identified until after these patterns have occurred. Hence, any prevention or intervention strategies may be implemented only during school age rather than at earlier periods.

It is also worth mentioning that such BMI patterns are not "exposures" in the true causal sense. The observed growth patterns are likely the result of exposure to other factors related to growth and body composition (e.g., diet and physical activity), and these exposures are most likely the "causes" of health status later in life. This distinction is crucial when attempting

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Address correspondence to IMA (e-mail: Izzuddin_Aris@harvardpilgrim.org).

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to extrapolate such findings to plan prevention or intervention strategies that aim to mitigate the onset of future obesity and cardiometabolic disease. Furthermore, these exposures are themselves entangled with several other genetic, epigenetic, behavioral, and environmental factors throughout the life course in a time-invariant and/or time-dependent manner, thus requiring more advanced approaches to make the appropriate causal inferences (15).

Nevertheless, as Wibaek et al. (4) note, these findings may be helpful for health professionals caring for children to gain a better understanding of the pathways leading to cardiometabolic risk. Ultimately, more work is needed to unravel the complex etiology of growth patterns observed in life-course research and its relationships with early life exposures and later health outcomes. Future studies would likely need a combination of different methodological approaches to better address these issues.

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