and interesting approach of identifying children at risk of adult overweight or obesity. In summary, the i3C cutoff points take us one step closer to the challenging question of how to define childhood overweight and obesity on the basis of the prediction of adverse adult health effects.

Lise G Bjerregaard
Centre for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, 2000 Frederiksberg, Copenhagen, Denmark
lise.geisler.bjerregaard@regionh.dk

I declare no competing interests.

1 Kartiosuo N, Ramakrishnan R, Lemeshow S, et al. Predicting overweight and obesity in young adulthood from childhood body-mass index: comparison of cutoffs derived from longitudinal and cross-sectional data. *Lancet Child Adolesc Health* 2019; published online Aug 23. http://dx.doi.org/10.1016/S2352-4642(19)30204-4.

2 Aarestrup J, Bjerregaard LG, Gamborg M, et al. Tracking of body mass index from 7 to 69 years of age. *Int J Obesity* 2016; **40:** 1376–83.

3 Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obes Rev* 2008; **9:** 474–88.

4 Freedman DS, Lawman HG, Galuska DA, Goodman AB, Berenson GS. Tracking and variability in childhood levels of BMI: the Bogalusa Heart Study. *Obesity* 2018; **26:** 1197–202.

5 Bjerregaard LG, Jensen BW, Angquist L, Osler M, Sørensen TIA, Baker JL. Change in overweight from childhood to early adulthood and risk of type 2 diabetes. *N Engl J Med* 2018; **378:** 1302–12.

6 Bjerregaard LG, Adelborg K, Baker JL. Change in body mass index from childhood onwards and risk of adult cardiovascular disease. *Trends Cardiovasc Med* 2019; published online Feb 5. DOI:10.1016/j.tcm.2019.01.011.

7 Zimmermann E, Bjerregaard LG, Gamborg M, Vaag AA, Sørensen TIA, Baker JL. Childhood body mass index and development of type 2 diabetes throughout adult life-A large-scale danish cohort study. *Obesity* 2017; **25:** 965–71.

8 Gjærde LK, Gamborg M, Ängquist L, Truelsen TC, Sørensen TIA, Baker JL. association of childhood body mass index and change in body mass index with first adult ischemic stroke. *JAMA Neurol* 2017; **74:** 1312–18.

Language delays in children with prenatal exposure to HIV and antiretroviral therapy

Flickr/Valerie Hinojosa

Published **Online** September 9, 2019 http://dx.doi.org/10.1016/S2352-4642(19)30291-3

See **Articles** page 803

Catherine Wedderburn and colleagues' birth cohort study[1] makes an important contribution to the current understanding of the neurodevelopment—and particularly the language development—of the expanding population of children with prenatal exposure to HIV and antiretroviral therapy (ART). The aim of the study was to compare the neurodevelopmental outcomes of HIV-exposed uninfected children with an HIV-unexposed uninfected group at 6 months and 24 months of age. Using a large cohort from two low-resourced settings in the Western Cape province of South Africa, Wedderburn and colleagues' study is the first to show clear delays in receptive and expressive language at 24 months, measured on the Bayley Scales of Infant and Toddler Development, third edition (BSID-III), in the absence of any other neurodevelopmental delay. The group of HIV-exposed uninfected children, controlled for male sex bias, showed increased odds of clinically significant delays in receptive language (odds ratio 1·96 [95% CI 1·09 to 3·52]) and expressive language (2·14 [1·11 to 4·15]) at 2 years of age compared with HIV-unexposed children. Among several subgroup analyses done, only maternal immunosuppression was significantly associated with increased prevalence of receptive and expressive language delays, with maternal CD4 cell counts of 500 cells per mL or less associated with increased likelihood of such delays. These findings advance our understanding of the language development of HIV-exposed uninfected children in several ways.

The significance of delayed language acquisition in HIV-exposed uninfected children, the time at which the delay was detected, and the distinct pattern of language impairment reported in the study deserve further discussion. The study identifies a new population at risk of language impairment. Several studies have now alluded to an early and continued risk of language delay in the HIV-exposed uninfected population, especially those in low-resource settings. For example, decreased vocalisation was detected in late infancy in a smaller study from a similar sample in South Africa,[2] while decreased language skills were found in prenatally HIV-exposed uninfected young people (aged 9–16 years) living in stressful New York neighbourhoods, which were characterised by violence, poverty, and unemployment.[3] Early delayed language learning poses a risk for continued language impairment, which is not outgrown and which considerably affects a child's communication with family and peers, their emotional wellbeing, social acceptance, school readiness, reading and writing, and overall academic success.[4]

Because language acquisition is a complex and protracted process, beginning very early in life, it is possible that differences in language between the study groups might have already emerged before 24 months of age. Auditory processing of the maternal voice, language, and music starts when the neurosensory part of the auditory system becomes active from 25 weeks' gestation.[5] The foetal beginnings of language development and the potential for interfering factors are, therefore, relevant to the population of children prenatally exposed to HIV and ART.

Wedderburn and colleagues[1] further found an unusual pattern of language delay in the HIV-exposed uninfected group. A higher proportion of HIV-exposed uninfected children showed receptive language delay (23 [14%] of 165) than expressive language delay (18 [11%] of 158), indicating that children in the study sample were not late talkers, whose language delay is mostly evident in expressive language, with reduced vocabulary size and grammatical development.[6] Cassidy and colleagues[7] found a similar pattern of lower receptive language scores among 24-month-old children who were exposed to efavirenz-based ART in utero, particularly those with longer exposure, from conception onwards. More research is required to investigate the characteristics of language impairment in HIV-exposed uninfected children who also received antiretroviral therapy. Wedderburn and colleagues[1] did not report whether children in any of the groups had temporary or permanent hearing loss, or any other form of neurodevelopmental disability. Concerns regarding the overestimation of development by the BSID-III[8] highlight the need for careful selection of language assessment tools for research. Assessments of children's hearing should be included in future studies.

The second notable finding in the study was the association between the severity of maternal HIV and language delay. Because language is acquired within the context of early responsive interactions and conversations between a caregiver and a child, consistent maternal linguistic input is key to developing language.[9] Independent of family income and education, the amount of adult–child conversational turns that a young child experiences is related to the strength of white matter connections between Wernicke's and Broca's areas.[10] The implication is that early communication interventions might be effective when mothers' health care is improved and when they are trained to increase naturally occurring interactive conversations with their HIV-exposed uninfected infants and young children. Since the increased susceptibility of the HIV-exposed uninfected infant population to language delay has become clearer, informing caregivers of the risk, without alarming them, is a professional responsibility. Increased child-care support to mothers with HIV is important as they are already burdened by their own disease. Another area in need of support is breastfeeding, as highlighted by the low prevalence in this study's sample.[1]

Wedderburn and colleagues' study[1] thus provides evidence of two factors contributing to language delays observed in the HIV-exposed uninfected group: prenatal HIV and ART exposure, and the severity of maternal HIV infection. Further longitudinal behavioural and neuroimaging data of the same study cohort are anticipated.

Alta Kritzinger
Department of Speech-Language Pathology and Audiology, University of Pretoria, Private bag X20, Hatfield 0028, Pretoria, South Africa
alta.kritzinger@up.ac.za

I declare no competing interests.

1 Wedderburn CJ, Yeung S, Rehman AM, et al. Neurodevelopment of HIV-exposed uninfected children in South Africa: outcomes from an observational birth cohort study. *Lancet Child Adolesc Health* 2019; published online Sept 9. http://dx.doi.org/10.1016/S2352-4642(19)30250-0.
2 Springer PE, Slogrove AL, Laughton B, et al. Neurodevelopmental outcome of HIV-exposed but uninfected infants in the Mother and Infants Health Study, Cape Town, South Africa. *Trop Med Int Health* 2018; **23:** 69–78.
3 Kang E, Leu CS, Snyder J, Robbins RN, Bucek A, Mellins CA. Caregiver perceptions of environment moderate relationship between neighborhood characteristics and language skills among youth living with perinatal HIV and uninfected youth exposed to HIV in New York City. *AIDS Care* 2018; **31:** 61–68.
4 Owens RE. Language disorders. Boston: Pearson, 2014.
5 Graven SN, Browne JV. Auditory development in the fetus and infant. *Newborn Infant Nurs Rev* 2008; **8:** 187–92.
6 Rescorla LA, Dale PS. Late talkers. Baltimore: Paul H Brooks, 2013.
7 Cassidy AR, Williams PL, Leidner J, et al. In utero efavirenz exposure and neurodevelopmental outcomes in HIV-exposed uninfected children in Botswana. *Pediatr Infect Dis J* 2019; **38:** 828–34.
8 Anderson PJ, Burnett A. Assessing developmental delay in early childhood—concerns with the Bayley-III scales. *Clin Neuropsychol* 2017; **31:** 371–81.
9 Owens RE. Language development. Boston: Pearson, 2016.
10 Romeo RR, Segaran J, et al. Language exposure relates to structural neural connectivity in childhood. *J Neurosci* 2018; **38:** 7870–77.