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Fetal growth and ethnic variation

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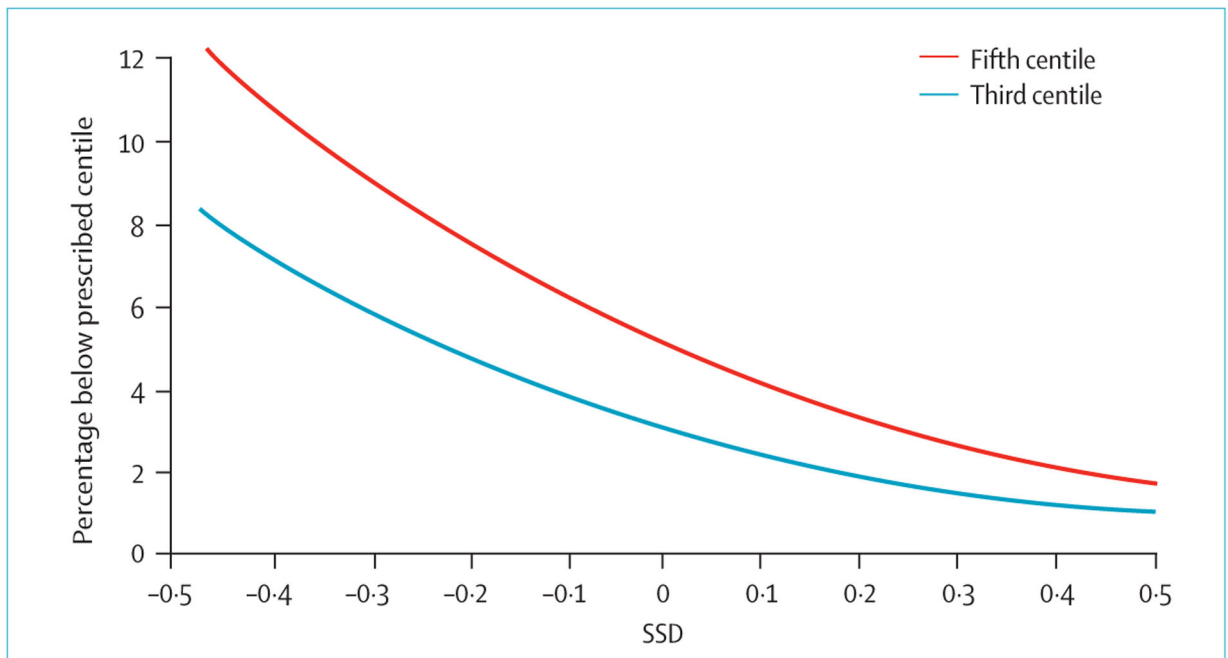
We read with interest the Article by Villar and colleagues¹, which suggests no differences in fetal growth exist as shown by crown-rump length or head circumference from eight geographically diverse study sites. A key determinant of their decision to pool across sites was whether the standardised site difference (SSD; defined as the difference between the site and overall mean standardised by the overall SD) at different gestational ages was less than 0.5. We believe that this criterion could be too liberal, resulting in potentially inappropriate pooling of sites. To show this potential, we calculated the probability of a newborn baby's measurements being below the lower limit of the standard for a particular site when the standard was constructed using data pooled across different sites for different values of SSD from -0.5 to 0.5 as recommended. Probabilities were computed as a function of SSD when constructing both the third and fifth centiles (figure). When the SSD is zero, the site-specific and pooled centiles are the same. However, when the SSD is -0.50, the probability of being less than the 5th centile is 12.6%, with a probability of 1.6% for an SSD of 0.50. This discrepancy could have important clinical implications. If a pooled standard is used when the SSD is 0.50, 3.4% of fetuses (targeted centile-pooled centile = 5.0%-1.6%) would be misclassified as not extreme. Likewise, when the SSD is 0.50, 7.6% (targeted centile-pooled centile = 12.6%-5.0%) of fetuses would be misclassified as extreme. Thus, even with a small SSD, the estimated centiles could be seriously biased when pooling sites. Our calculation, along with figures 2 and 3 in Villar and colleagues' paper,¹ suggests that we have to be very careful when interpreting the pooled standard in this situation. Further, Villar and colleagues'¹ proposed sensitivity analysis that computes the standard leaving out only a single site lacks the ability to detect meaningful differences between these potentially different sites.

References

1. Villar J, Papageorgiou AT, Pang R, et al. , for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st).The likeness of fetal growth and newborn size across non-isolated populations in the INTERGROWTH-21st Project: the Fetal Growth Longitudinal Study and Newborn Cross-Sectional Study.*Lancet Diabetes Endocrinol* 2014; published online July 7. 10.1016/S2213-8587(14)70121-4.

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**Figure:**

Percentage less than the prescribed fifth and third centile as a function of SSD when using a pooled standard

Percentage less than the fifth and third centiles when pooling as a function of SSD.

These probabilities are computed from $f = \Phi(-SSD - 1.6449)$ for the fifth centile and $f = \Phi(-SSD - 1.8808)$ for the third centile, where Φ denotes the cumulative normal distribution. SSD=standardised site difference.