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## Weight gain for gestational-age charts in dichorionic twins: Tool for establishing optimal weight gain in twin pregnancies

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When I was born at 32 weeks gestation at 3 lbs. 10 oz. and my sister at 3 lbs. 11 oz., my parents had no idea they were having twins. My mom didn't have an ultrasound, which was much less common then; but were there other clues that were missed (i.e., was my mom's weight gain abnormally high for her gestational age?). Even now, we only have provisional standards for pregnancy weight gain for multiple gestations, and these are based on a single study of mothers and do not include women with underweight prepregnancy body-mass index (BMI).<sup>1</sup>

There is an urgent need to establish evidenced-based recommendations for pregnancy weight gain in twin gestations for clinical research and practice. Women carrying twins experience higher rates of adverse pregnancy, obstetrical and birth outcomes linked to low and excessive pregnancy weight gain in singletons, and the risks are even higher among those conceived with assisted reproductive techniques.<sup>2, 3</sup> But whether these outcomes are linked to pregnancy weight gain remains unclear. With the widespread adoption of fertility therapies and delayed childbearing, the occurrence of multiple births has increased substantially over the past few decades.<sup>4</sup> Rates of twinning continue to remain high in the United States and globally.<sup>4, 5</sup> In the United States, more than one out of every 30 births is now a twin, and in 2014, the rate peaked at 33.9 twins per 1000 live births.<sup>4</sup>

Despite these high rates of twinning and an increase in research on prepregnancy body size and pregnancy weight gain, few studies have focused on pregnancy weight gain in twins and higher-order multiples. Therefore, the evidence base for recommendations remains small. One reason for this may be the methodological challenges facing researchers. Studying pregnancy weight gain among twins and higher-order multiples poses more challenges than for singleton pregnancies. To establish sound recommendations, an ideal reference cohort would include participants with good baseline health, minimal pregnancy complications, gestational ages at delivery close to term and birth weights above the threshold for low birthweight. However, with multiples and with multiples conceived via assisted reproduction methods, preterm birth is the norm and many babies are born small, even at term.<sup>3</sup> Most studies of twin pregnancy weight gain and pregnancy/birth outcomes have been conducted in dichorionic twin gestations, have evaluated total weight gain rather than the pattern across pregnancy, and have had insufficient numbers to draw meaningful conclusions about women with prepregnancy underweight or severe obesity. Moreover, disentangling the effects of

pregnancy weight gain from the duration of pregnancy on perinatal outcomes is challenging and sometimes prone to reverse causation, as adverse outcomes and gestational age are highly correlated and, understandably, women who deliver early have less time to gain weight.<sup>2</sup>

To overcome this barrier, Hutcheon and colleagues in this issue of *PPE* have developed gestational age-specific charts for twin pregnancy weight gain that have the potential to guide the establishment of clinical recommendations for pregnancy weight gain in twin gestations.<sup>6</sup> The charts are based on 1,109 women with uncomplicated dichorionic pregnancies who delivered at or beyond 35 weeks gestation from 1998 to 2013 in Pittsburgh. Pregnancies that were reduced from higher-order multiples and those without ultrasound-confirmed gestational age were excluded. Prepregnancy weight was self-reported, and longitudinal prenatal weight data were abstracted from the medical charts with electronic data entry. Gestational age was calculated using last menstrual period, and updated with ultrasound-estimated gestational age, as appropriate. The study included predominately Non-Hispanic White (80%), and a small proportion of women were Non-Hispanic Black (15%), Hispanic (1%) and other race (4%). About half of the cohort was normal weight prior to pregnancy, while the remaining women were almost evenly split between overweight and obese; unfortunately, the number of underweight women (n=37) were too few for the creation of a chart for this group. As expected, average total weight gain decreased with increasing prepregnancy BMI values. Interestingly, the maternal weight gain patterns were similar to those of singleton gestations until about 17-19 weeks, at which point they became noticeably higher than singletons, with a gradual flattening of the slope after 28 weeks gestation.

The authors used rigorous methods to model weight gain across gestation,<sup>6</sup> specifically, hierarchical linear regression models with restricted cubic splines allowed for non-linear curves and, importantly, random effects accounted for the correlation between repeated weight measurements over time. With the strong association between assisted reproductive techniques and twinning, it is not surprising that nearly a third of the study participants conceived with infertility treatment. Unfortunately, we have no idea whether or how the exogenous hormones these women were prescribed might have affected their pregnancy weight gain trajectory; hence, these women may need separate charts and recommendations. The authors present separate curves for each prepregnancy BMI category (normal, overweight, obese), and although these groupings are useful for pragmatic and policy reasons, the variability in adiposity across a BMI category range is wide (e.g., the percentage body fat in a woman whose BMI=19 is much lower than a women whose BMI=24). The implications of weight gain across this range of adiposity on different outcomes may be important to examine, especially among women beginning pregnancy with lower prepregnancy BMI values who may need to gain more weight for optimal pregnancy outcomes. While the predominately White study population may not be fully generalisable, recent evidence supports the generalisability of existing gestational age-specific z-score charts, developed in singletons at the same hospital in Pittsburgh with a similar racial-ethnic distribution, to diverse US populations.<sup>7</sup> Moreover, the proportion of twin infants born small for gestational age was not discussed, which may impact the generalisability of these charts.

There are many other interrelated factors that may be associated with the pattern and timing of weight gain, which need to be considered in future research. These factors include zygosity, sex of the twins, chorionicity, fetal growth and perhaps even the composition of weight gain—each adding additional layers of complexity and potentially influencing the course and outcome of twin pregnancies.<sup>1, 8</sup> The composition of maternal weight gain (fat, fat-free mass, and supporting tissues) in twin pregnancies likely differs from singleton pregnancies, and may be important for neonatal size and developmental programming.<sup>9, 10</sup> However, even among singleton gestations, robust measures of body composition changes across pregnancy have only been conducted in a handful of studies,<sup>9, 10</sup> and these do not disentangle the fetal from maternal components. In particular, the expansion of body water compartments—which is a component of the lean mass and a physiologic adaptation of all pregnancies—is often believed to occur earlier and remain generally higher among multiple gestations compared to singletons, with implications for the pattern of weight gain. Clearly, the additional fetus and supporting tissues (e.g., placenta) are components of the additional weight gain typical in twin gestations, but whether the remaining weight gain is predominantly fat or lean mass, and whether the composition of weight gain is important for neonatal and child outcomes remains unknown.

Thanks to Hutcheon et al., gestational age-specific charts are now available for evaluation of pregnancy weight gain in dichorionic twins. Future studies should expand upon this important work to evaluate curves for high and low prepregnancy BMI values and for monozygotic twins; explore whether curves differ by fetal sex, use of assisted reproductive technologies or race/ethnicity and if need be, develop customized charts for specific groups. Additional areas include examining patterns and composition of maternal weight gain in twin pregnancies, and assessing associations between twin pregnancy weight gain and both perinatal and long-term outcomes among mothers and children. If these studies come to fruition, we may eventually have sound evidence-based recommendations for pregnancy weight gain in twin gestations to guide prenatal care.

## Biography

Elizabeth Widen is Research Scientist and future Assistant Professor in the Department of Nutritional Sciences at the University of Texas at Austin. Widen is an interdisciplinary nutritional and reproductive epidemiologist with a research program that examines the links between preconception, prenatal, and postnatal nutrition with short- and long-term health outcomes of mothers and their children, including obesity/body composition, micronutrient status and child cognitive development. Widen was awarded a Pathway to Independence Award (K99/R00 HD086304) from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and an Early Career Award from the Thrasher Research Fund.

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