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Classifying gestational weight gain trajectories using the SITAR growth model

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Abstract

Background—Gestational weight gain is often characterized by the total amount of weight gained during pregnancy, however, the pattern of gain may be an important determinant of health outcomes. The SITAR (Super Imposition by Translation And Rotation) model has been used to describe childhood growth trajectories and has appeal because of the biological interpretability of its parameters. The objective of this study was to determine the feasibility of applying this model to gestational weight gain trajectories.

Methods—The study cohort included 3470 normal-weight, overweight, and obese women delivering at Magee-Womens Hospital in Pittsburgh, Pennsylvania, 1998 to 2010. We applied the SITAR model, a non-linear mixed effects model, to serial prenatal weight gain measurements in each pre-pregnancy body mass index (BMI) category. We fit models of varying complexity, and chose the best-fitting model to describe the pattern of weight gain (by its absolute amount, timing, and acceleration) for each BMI group.

Results—The most complex SITAR models failed to converge, but reduced models could successfully be fit by specifying fewer random effects and simplifying the modeling of gestational age. Best-fitting models for each BMI group explained between 95 and 97% of the variation in weight gain trajectories. Peak rates of weight gain were reached between the 20th and 22nd weeks, and were higher for normal and overweight women (0.59 kg/week and 0.57 kg/week, respectively) than obese women (0.46 kg/week).

Conclusions—Following some modifications, the SITAR model can be used to characterize pregnancy weight gain patterns.

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Keywords

gestational weight gain; growth modeling; and pregnancy

INTRODUCTION

Maternal weight gain during pregnancy is a predictor of perinatal and maternal health outcomes.¹ However, our understanding of the relationship between gestational weight gain and maternal and child health is based almost entirely on studies of the total amount of weight gained in pregnancy.² Women can follow different trajectories to achieve the same total weight gain, so it is possible that the pattern of gain is important. For example, several studies have found that weight gain during the first trimester is a better predictor of some infant (neonatal body fat),³ child (overweight/obesity and cardiometabolic risk),^{4,5} and maternal outcomes (gestational diabetes, weight retention)^{6,7} compared to weight gain later in pregnancy. Modeling weight gain trajectories is ideally-suited to extending this research, as it overcomes downfalls of alternative methods that conduct multiple tests comparing weight gain to internal or external standards.

While evaluating differences in trajectories is intuitively appealing, it is challenging in practice.⁸ Simple approaches, such as piecewise linear regression,⁹ require choosing arbitrary gestational age cut-points and assume the rate of weight gain is linear within each cut-point defined interval, and estimate biologically implausible abrupt changes at these cut-points. More complex approaches, such as latent class models,¹⁰ can better describe growth trajectories, but the biological interpretation of the parameters is unclear. An approach for summarizing growth trajectories that captures the complexity of weight gain patterns while allowing for biologically meaningful interpretation is needed.

The SITAR model (Super-Imposition by Translation And Rotation) has been used to describe child growth trajectories.^{11–15} Its parameters summarize trajectories in terms of the absolute amount, timing, and acceleration of growth. Using the model, a population-average weight gain curve is estimated, and each woman's variation from the curve is expressed using woman-specific random effects estimates for absolute amount, timing, and acceleration. These three woman-specific estimates can be used as exposure variables to explore associations with adverse outcomes. For example, literature on the effects of first trimester weight gain could be extended by examining how timing of onset of weight gain affects adverse maternal, infant, or childhood health outcomes and be used to estimate the effect of earlier weight gain on the risk of adverse events. Such literature could lead to important effects on policy and clinical care, if earlier weight gain appeared problematic and signaled a need for weight gain interventions earlier in pregnancy than what is currently recommended. Given the potential of this new approach for characterizing weight gain trajectories, the objective of this study was to determine the feasibility of applying the SITAR model to gestational weight gain trajectories.

METHODS

Data sources and study cohort

Our study cohort was drawn from women delivering singleton, non-anomalous infants at Magee-Womens Hospital in Pittsburgh, Pennsylvania, from 1998 to 2010 as part of an ongoing study of pregnancy weight gain. We grouped women according to pre-pregnancy body mass index (BMI, pre-pregnancy weight self reported at the initial visit (kg)/self-reported height (m)²) categories and randomly sampled 1676 normal weight (18.5–24.9 kg/m²), 1241 overweight (25–29.9 kg/m²), and 1200 obese (≥ 30 kg/m²) women whose serial antenatal weight measurements were abstracted from medical records. The University of Pittsburgh's Institutional Review Board approved this project.

Measurement

Weight gain (kg) was calculated as the difference between measured weight at the time of a prenatal visit or delivery admission and self-reported pre-pregnancy weight. Women were excluded if their gestational weight gain measurement was implausible (defined as a gain ≥ 36.4 kg or < −18.2 kg). Gestational age was estimated using last menstrual period confirmed or revised with early ultrasound.¹⁶

Statistical Analyses

Gestational weight gain trajectories were modeled using SITAR growth curve analysis.¹¹ A non-linear mixed effects model was fit to the serial prenatal weight gain measurements using the equation:

$$y_{it} = a_i + h\left(\frac{t - b_i}{\exp(-c_i)}\right) + \eta_{it}$$

where y_{it} is the gestational weight gain measurement for woman i at gestational age t and η_{it} represent the error terms, assumed to be normally distributed. $h(t)$ is a non-linear function of gestational age, which allows the relationship between weight gain and gestational age to be represented using the best-fitting curve. The remaining parameters are comprised of both a fixed and a random effect, where the random effects allows each woman's curve to deviate from the population-average curve in three ways (Figure 1). For example, $a_i = a_0 + a_{1i}$, where a_0 represents the model-estimated average weight gain at conception and a_{1i} represents each woman's deviation from this value, represented as a vertical shift to the population-average curve (i.e., the absolute amount of weight gain). Theoretically, a_i should equal 0 for all women (since weight gain should begin at 0 kgs), but allowing it to vary partially captures the measurement error induced by self-reported pre-pregnancy weight while also allowing for the best fit of the model to the observed data. Thus, a_i reflects a combination of measurement error in self-reported pre-pregnancy weight and model misspecification. Secondly, the population-average curve can be shifted horizontally by the value of b_{1i} (timing of weight gain). Finally, the slope of the curve (i.e., the acceleration of weight gain) is modified for each individual by the value of c_{1i} .

To fit the model, we used the `sitar` package (version 1.0.3) in the R language and environment (version 3.1.3).^{17,18} Separate models were built for each pre-pregnancy BMI category because the association between gestational weight gain and adverse pregnancy outcome differs by pre-pregnancy BMI.^{19,20} Using the `sitar` package, we identified outliers in weight gain using the `velout` function and visualizes these trajectories using the `codeplot` function. We removed measurements where the rate of change from contiguous measures was more than 5 standard deviations away in absolute value from the median estimated using the data (i.e., Code 4 outliers as categorized by the `velout` function). The relationship between maternal weight gain and gestational age was modeled using a regression B-spline with five knots to allow a smooth, non-linear pattern of weight gain across gestation.

We began with simple models that estimated the random effects for each of absolute amount, timing, and acceleration alone. We successively increased the complexity of the model by estimating two, then all three of the random effects. For each of these models, we also included the corresponding fixed effect(s), and always included a fixed effect for absolute timing, as the model required.

For models that did not converge or resulted in error messages, we tried the following commonly-applied simplifications/transformations:^{11,14,21} a) decreasing the number of spline knots from 5 to 3, b) centering gestational age at the average, c) log-transforming the weight gain measurements (after adding the absolute value of the lowest weight gain (a weight loss) plus one to the weight gain measurements to avoid negative values, which cannot be log-transformed), d) applying a more restrictive outlier definition by decreasing the threshold of detection, and e) removing fixed effects for timing (i.e., $b_0=0$) and acceleration (i.e., $c_0=0$) in the model containing all three random effects.

We reported the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and the percent of variance explained by each model (compared to a reduced model containing no SITAR parameters). Adjusted AIC and BIC were calculated if the outcome was log-transformed.²² Better-fitting models will have lower AIC and BIC values and explain a higher percentage of the variance. For each pre-pregnancy BMI category, we chose which model fit the data best based on the lowest AIC value. For the best models, we estimated peak acceleration and its corresponding gestational age. We compared population-average curves across BMI categories to explore the extent that the data supports different trajectories of gain.

To determine the impact of mis-reported pre-pregnancy weight on the results, we performed a sensitivity analysis in the subgroup of women who had prenatal weight gain measurements before the 13th week of gestation. For these women, we calculated weight gain by substituting their first measured prenatal weight for their self-reported pre-pregnancy weight.

We conducted an additional sensitivity analysis to illustrate the effect of having fewer measurements on the fit of the model for normal weight women. To do so, we kept the first and last measurements for each woman, and then sampled from the middle visits. We sampled the middle 50% and 60% of visits for each woman and refit the best-fitting model

in the normal weight women. Across all the models, we compared the population-averaged trajectories and the estimates for the three SITAR random effects.

RESULTS

We included 3470 women with a total of 35274 weight gain measurements. We excluded 19 inconsistent measures (multiple visits per woman at a given gestational age but with discordant weight measures) and nine measures that were determined to be erroneous/outliers, for a total of 35246 analyzed measurements. On average, women were weighed 10.2 times during their pregnancies (Table S1). Total pregnancy weight gain was approximately 15.0 kg among normal weight and overweight women and 12.5 kg among obese women.

Table 1 shows the application of the SITAR model to serial weight gain measurements. Under the original model specification, convergence was only achieved in models that included a single random effect for absolute amount or timing. The acceleration-only model converged among normal weight and overweight women. Models specifying multiple random effects failed to converge without modification in all BMI groups. Of the models that achieved convergence without simplification/transformation, the model containing only a random effect for timing fit best in terms of AIC and BIC, and explained between 87.3% and 88.8% of the variance across the BMI categories.

Table 1 also overviews the modeling simplifications or transformations that were attempted to fit models that did not initially converge. The acceleration-only model could be fit after reducing the knots of the gestational age spline from five to three. This simplification also led to convergence in the model containing random effects for both amount and timing, and the model containing random effects for amount and acceleration.

Models containing random effects for both timing and acceleration could be successfully fit after reducing the number of knots and log-transforming gestational weight gain for the normal and overweight women, but could not be fit under any of the attempted transformations for the obese women. These models fit the data better than the models containing only one random effect. Of the models containing two random effects, the model with random effects for amount and acceleration fit best and explained between 94.4% and 95.9% of the variation across BMI categories.

The model containing random effects for all three parameters could only be fit when the fixed effect for acceleration was constrained to zero in the normal weight women, and when the fixed effect for timing was constrained to zero in the overweight women. For obese women, the model converged under either constraint. The model with acceleration constrained to zero fit better than all preceding models for the normal weight and obese women (95.9% and 96.9% of variance explained, respectively), while the model with timing constrained to zero was the best-fitting model for the overweight women (96.8% variance explained).

Figure 2(a) illustrates the crude weight gain trajectories for women with normal pre-pregnancy BMI. Figures 2(b)–(d) illustrate the extent that adjustment for each random effect

explains variability in trajectories. If variation were completely accounted for by a model, all individual trajectories would be shifted to align perfectly on the population average. Thus, models leading to a (vertically) narrower distribution of adjusted trajectories better explain variation. In the model with only a fixed and a random effect for the absolute amount of weight gain, each woman's smoothed fitted trajectory looks exactly like the population-averaged curve, except shifted vertically (up or down) according to the value of her individual random effect; Figure 2(b) reflects the extent to which differences in trajectories are explained by differences in absolute amount of weight gain. Likewise, Figures 2(c) and 2(d) show the effects of adjusting for timing (a horizontal shift, Figure 2(c)) or acceleration ('stretching' the shape of the slope, Figure 2(d)).

Figures 2(e)–(g) illustrate the effect of adjusting for two random effects simultaneously, and Figure 2(h) illustrates the effect of adjusting for all three random effects. As more random effects were added, the adjusted trajectories became closer to the population average, implying increasingly better model fit. Results for overweight and obese women shown in the Supplementary File: Figure S1 and Figure S2, respectively.

Figure S3 and S4 illustrate crude weight gain measurements for a sample of women alongside their fitted trajectories from the best-fitting model and the population-average trajectory for normal and obese women, respectively. For these women, the estimated trajectories fit the data very well. The normal weight women exhibit less variation in their curves, with the fitted trajectories often overlapping the population-average trajectory. Obese women exhibited more variation in their weight gain trajectories, however, the SITAR model was able to flexibly model the individual variation well.

Figure 3(a)–(c) illustrate the population-average weight gain trajectories and acceleration curves for the best-fitting models within each BMI classification. Normal and obese women were estimated to lose weight in the first few weeks of gestation. All groups of women were estimated to have positive "weight gains" at conception, which is biologically infeasible, and may reflect measurement error in self-reported pre-pregnancy BMI. Furthermore, there are fewer prenatal visits during the earliest gestational ages, implying that the precision of the trajectories is lowest at these gestational ages. In the second and third trimesters, the curves appeared similar across BMI categories. Normal and overweight women had higher peak velocities (0.59 kg/week and 0.57 kg/week, respectively) of weight gain than obese women (0.46 kg/week), with all groups of women estimated to reach their peak velocities of gain between the 20th and 22nd week of gestation.

To explore how sensitive these curves were to the chosen model, we also examined these curves for the models that included fixed and random effects for the absolute amount and acceleration parameters (Figure S5). The shapes were somewhat different from the best-fitting models, and the estimated peak velocities were reached later in gestation. The estimated trajectory was most different for the obese women, in terms of shape and timing of peak velocity (occurring during the 20th week in the best-fitting model and during the 32nd week in the second best-fitting model). While a difference of twelve weeks in the age at peak velocity is striking, in both models it is apparent that acceleration becomes near constant sometime after the 20th week of gestation. Thus, choosing an exact age

corresponding to the peak velocity is somewhat arbitrary since any ages after constancy is reached correspond to the maximum (or near maximum) rate.

Sensitivity analyses

2719 women had their first prenatal visit prior to the 13th week of gestation. When we redefined gestational weight gain using the first measured weight rather than self-reported pre-pregnancy weight, the model did not converge for the overweight women, and the results for the normal and obese women are presented in Figure S6. Using the measured first-trimester weight leads to a downward shift to the fitted trajectories, implying that women had under-estimated their pre-pregnancy weights on average. These curves look very similar to those estimates using self-reported pre-pregnancy weight, although the estimated age at peak velocity is two weeks later using the modified outcome for obese women.

Our second sensitivity analysis examined how having fewer measurements affects the fit of the best-fitting model and parameter estimation of the SITAR random effects. The population-averaged trajectories were very similar after ten weeks gestation comparing the best-fitting model in normal weight women to the same model fit on a sample of the dataset (Figure S7). Before this time, the fit of the model differs, likely because there were fewer visits during earlier gestational ages and so removing some of these has a larger effect on the fit during the first trimester. Removing measurements did not have a large effect on the estimate of the random effects for absolute amount or acceleration, while the timing random effect was estimated less consistently across the models (Figure S8).

COMMENTS

We investigated the practical utility of the SITAR model to describe patterns of pregnancy weight gain among women of varying pre-pregnancy BMI. While the full model using original SITAR specifications could not be fit, modified versions of the model converged and explained between 95% and 97% of the variation in the data. These models can be used in future studies to evaluate the association of weight gain timing and acceleration with health outcomes.

Growth mixture models and latent class models could have been used to study gestational weight gain trajectories. The strength of growth mixture models is the ability to identify distinct classes of trajectories.⁸ The SITAR model only allows variation from the average spline according to three parameters, implying that women with very different shapes may have poorer fits. The latent class model estimates different accelerations across gestational age and these latent variables can be used in studies of health outcomes. However, as these models require mutual adjustment for all latent variables, the interpretation of these conditional coefficients is unclear. These alternative approaches also require similar timing of measurements across individuals, which is rare in most observational studies of weight gain.⁸

This is the first study we are aware of to apply the SITAR model to the study of pregnancy weight gain. Our cohort of 3470 women of varying pre-pregnancy weights with roughly 10 weight gain measures per woman represents a unique and relatively large dataset. For

researchers designing a study that may benefit from such an analysis, it is more important to have more measurements per woman than more women each having fewer measurements. While we did not formally study an acceptable lower bound, other researchers have applied the SITAR model to a population of eighty participants each with seven measurements, illustrating that the model can be successfully applied to smaller populations.²¹

In this context, interpretation of results is limited to the degree that weight gain is a relatively crude marker of maternal nutrition and body composition and contains measurement error due to its reliance on self-reported pre-pregnancy weight. Another important limitation is that advanced statistical knowledge is required to implement the SITAR model. Such non-linear models are often difficult to fit and may require a combination of variable transformations and/or simplifications to the model in order to achieve convergence.

The interpretation of some of the SITAR estimates in the context of gestational weight gain is unclear. For example, the absolute amount parameter allows for different starting values, which has limited interpretability for weight gain, since all women should have 0 kg weight gain at conception. This parameter is partially capturing measurement error in self-reported pre-pregnancy weight, which produces estimated weight gains at conception above (or below) zero. Age at peak velocity may have limited interpretability in this setting where growth spurts or peak inflections in the weight gain curve are less pronounced than in other types of growth curves (such as pediatric growth during puberty). This is especially true for obese class 2 and 3 women, whose weight gain curves have been estimated to be more linear.²³ Finally, patterns of weight gain during gestation can be quite variable, especially among women with higher BMI. While most women will primarily gain weight over the course of pregnancy, some women will have little or no gains, and others will lose weight. In these cases, the population-average trajectory may be less informative.

We found that characteristics of the population-average trajectory were quite sensitive to model specifications. When we compared the trajectories from the best-fitting model to the model containing only absolute amount and acceleration parameters, we were surprised by the difference in the estimated ages at peak velocity, especially in obese women. Given that gestational weight gain does not exhibit stark inflection points, age at peak velocity may be more sensitive to the model choice.

Although we have outlined many potential challenges of the SITAR model when applied to gestational weight gain, we nevertheless believe that the SITAR parameters may capture important aspects regarding the timing and acceleration of gain that are missed in studies of total weight gain at delivery. Based on our findings, researchers may opt to fit a small selection of the best-fitting SITAR models that we explored and choose one of these models to derive individual-specific random effects. Models of a maternal, infant, or child health outcome can then be created, including a reduced model that includes total weight gain as the only covariate and a full model that also includes the three SITAR parameters (i.e., woman-specific random effect estimates for the absolute amount, timing, and acceleration). The R^2 values can be compared and a likelihood ratio test performed to examine how parameterizing total weight gain according to absolute amount, timing, and acceleration

better explains the variation in the outcome of interest. Such investigations will be informative in determining when the trajectory of gain is important for clinical decision making and policy decisions.

With some modifications, the SITAR model can be applied to serial pregnancy weight gain measurements to characterize patterns of weight gain. Future investigations can incorporate SITAR-derived exposures to determine the independent contribution of weight gain timing and acceleration to adverse health outcomes, above and beyond total weight gain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Illustration of shifts to the SITAR population-average gestational weight gain curve
 Each panel illustrates how the random effects in the SITAR model (dashed curves) allow the shape of each woman's weight gain curve to vary from the population average curve (solid black curves). For example, a woman who underestimated her pre-pregnancy weight would have a curve shifted upward according to the value of the absolute amount parameter (a). A woman who gains weight later in gestation would have a curve shifted rightward according to the value of the timing parameter (b), and a woman who gains weight at a faster pace would have a curve with a steeper slope than the average (c). To best fit each woman's weight gain trajectory, the population average curve can be modified in all three ways combined and the last panel illustrates the net effect of the preceding individual shifts.

Figure 2. Population-averaged weight gain trajectory (solid black curve) and individual maternal weight gain trajectories (coloured thin curves) in women with normal pre-pregnancy BMI delivering at Magee-Womens Hospital, Pittsburgh, PA, 1998–2010, after accounting for absolute amount, timing, and/or acceleration of weight gain using the SITAR growth model
 Amount + Timing + Acceleration model: includes random effects for all parameters and fixed effects for amount and timing.

Figure 3. Population-average gestational weight gain trajectories (solid black curve) and accelerations (dashed curve) from the best-fitting model according to pre-pregnancy BMI category, in women delivering non-anomalous infants at the Magee-Women's Hospital in Pittsburgh, Pennsylvania, 1998 to 2010

APV = age at peak velocity, PV = peak velocity.

These models have random effects for all parameters but do not include a fixed effect for the acceleration parameter (normal and obese women) or timing parameter (overweight women).

Table 1

Comparison of SITAR models applied to serial weight gain measurements in women delivering non-anomalous infants at the Magee-Women's Hospital in Pittsburgh, Pennsylvania, 1998 to 2010.

Parameters with random effects ¹	AIC	BIC	% variance explained by random effects	Modeling technique to achieve convergence
Normal weight				
Absolute amount	65,953	66,013.9	82.21%	None
Timing	61,388.8	61,457.4	87.31%	None
Acceleration rate	62,040.1	62,108.7	86.7%	None
Absolute amount + timing	56,890.9	56,959.5	92.7%	-Reduced number of spline knots to 3
Absolute amount + acceleration	53,937.1	54,005.7	94.4%	-Reduced number of spline knots to 3
Timing + acceleration	56,501.5	56,577.7	92.4%	-Reduced number of spline knots to 3 -Log-transformed the outcome
Absolute amount, timing, acceleration	51,591.8	51,683.3	95.9%	-Reduced number of spline knots to 3 -Excluded acceleration fixed effect
Overweight				
Absolute amount	50,345.2	50,403.2	83.79%	None
Timing	47,562.4	47,627.8	88.02%	None
Acceleration rate	48,850.6	48,915.9	86.33%	None
Absolute amount + timing	42,633.0	42,698.3	94.5%	-Reduced number of spline knots to 3
Absolute amount+ acceleration	40,467.1	40,532.4	95.8%	-Reduced number of spline knots to 3
Timing + acceleration	42,818.0	42,890.6	94.3%	-Reduced number of spline knots to 3 -Log-transformed the outcome
Absolute amount, timing, acceleration	40,133.1	40,220.1	96.8%	-Reduced number of spline knots to 3 -Excluded timing fixed effect
Obese				
Absolute amount	47,305.5	47,362.9	85.34%	None
Timing	45,070.7	45,135.2	88.82%	None
Acceleration rate	47,098.1	47,148.3	86.2%	-Reduced number of spline knots to 3
Absolute amount + timing	40,020.6	40,085.2	95.2%	-Reduced number of spline knots to 3
Absolute amount + acceleration	38,858.2	38,922.8	95.9%	-Reduced number of spline knots to 3
Timing + acceleration	Did not converge	NA	NA	NA
Absolute amount, timing, acceleration ²	37,487.5	37,573.6	96.9%	-Reduced number of spline knots to 3 -Excluded acceleration fixed effect

¹ All models included both fixed and random effects for the parameters listed in this column, unless otherwise specified in the final column. All models also include a fixed effect for the absolute amount parameter. For example, the row labeled "Timing + acceleration" included fixed and random effects for timing and acceleration, as well as a fixed effect for absolute amount.

² This model also converged after excluding the timing fixed effect (rather than the acceleration fixed effect). In this case, the AIC was 38,180.3, the BIC was 38,266.4, and the % variance explained was 97.0%.