

# The INTERGROWTH-21st Gestational Weight Gain Standard and Interpregnancy Weight Increase: A Population-Based Study of Successive Pregnancies

Jennifer A. Hutcheon<sup>1,2</sup>, Nuria Chapinal<sup>1</sup>, Lisa M. Bodnar<sup>3</sup>, and Lily Lee<sup>1</sup>

**Objective:** To link the INTERGROWTH-21st gestational weight gain standard with the risks of excess maternal postpartum weight retention, approximated by women's weight change between successive pregnancies.

**Methods:** A population-based retrospective cohort study of 58,534 women delivering successive pregnancies in British Columbia, Canada (2000-2015) was conducted. Pregnancy weight gain (kg) in the index pregnancy was converted into a gestational age-standardized z-score using the INTERGROWTH-21st standard. Excess interpregnancy weight gain was defined as weight increases of 5 kg, 10 kg, or obesity ( $\geq 30$  kg/m<sup>2</sup>) at the next pregnancy. Weight gain z-scores and excess interpregnancy weight change were associated using logistic regression.

**Results:** For all definitions of excess interpregnancy weight gain, risks remained low and stable below a weight gain z-score of 0 (50th percentile) but rose sharply with increasing z-scores above zero. Compared with women gaining  $-1$  to  $0$  SD (16th to 50th percentiles), women gaining  $>0$  to  $+1$  SD (51st to 84th percentiles) were 55% to 84% more likely to retain excess weight between pregnancies. Risks were three- to sixfold higher in women gaining  $>+1$  SD.

**Conclusions:** A large range of the INTERGROWTH-21st percentiles were associated with increased risks of excess interpregnancy weight gain. The standard may normalize high weight gains of women at increased risk of excess weight retention.

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## Introduction

Pregnancy may be a critical period in the prevention of obesity. Women with excessive pregnancy weight gain are more likely to have high postpartum weight retention, which in turn can lead to prepregnancy obesity in future pregnancies and long-term obesity in mothers (1-4). High pregnancy weight gain also increases the risk of childhood obesity in offspring (5,6). Nevertheless, there are concerns that inadequate pregnancy weight gain may lead to fetal growth restriction and preterm birth (7). Recommendations for gestational weight gain that balance the risks associated with inadequate and excess weight gain are therefore an important tool for optimizing the health of pregnant women and their offspring.

The international INTERGROWTH-21st weight gain chart has recently been published as a standard for weight gain in pregnancy (8). The

INTERGROWTH-21st study was a high-quality, prospective, longitudinal cohort study designed to create new standards for fetal and newborn growth (9,10). The study, which collected serial fetal growth and maternal weight gain measurements from a multiethnic cohort in eight geographically diverse international sites, including the United States, was restricted to healthy women with an ultrasound-confirmed estimate of gestational age, free from major medical, social, and environmental risk factors, and with good perinatal outcomes. As a standard, it is intended to be a prescriptive chart describing how much weight women ought to gain (as opposed to a reference chart, which describes how much weight a given population of women actually gains) (11).

Yet when selecting the population of women to derive optimal weight gain patterns from, the INTERGROWTH-21st weight gain standard did not exclude women with excess postpartum weight

<sup>1</sup> Perinatal Services British Columbia, Provincial Health Services Authority, Vancouver, British Columbia, Canada. Correspondence: Jennifer A. Hutcheon (jhutcheon@cfri.ca) <sup>2</sup> Department of Obstetrics & Gynaecology, University of British Columbia, Vancouver, Canada <sup>3</sup> Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

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retention. This is potentially a serious concern, because more than 40% of women in well-resourced settings gain excess weight during pregnancy (12-14), and pregnancy weight gain is a strong predictor of excess postpartum weight retention and long-term obesity (4). As a result, the standard may not describe how much weight women ought to gain with respect to outcomes such as maternal obesity. As clinical and public health organizations contemplate adoption of the INTERGROWTH-21st charts into routine care, an understanding of the implications of the standard's use on longer-term maternal weight status is needed.

In this study, our goal was to determine the risk of excess postpartum weight retention, as approximated by weight change between successive pregnancies, across the pregnancy weight gain ranges recommended by the INTERGROWTH-21st pregnancy weight gain standard.

## Methods

### Study population

Our study population was drawn from deliveries at or beyond 20 weeks' gestation in British Columbia, Canada, April 1, 2000, to March 31, 2015, excluding late pregnancy terminations. Abstracted maternal and neonatal medical record data were obtained from the British Columbia Perinatal Data Registry, a quality-controlled, population-based registry maintained by the provincial agency Perinatal Services British Columbia. The British Columbia Perinatal Data Registry contains records for >99% of deliveries in the province, including home births. Use of provincially standardized forms, standardized training of abstractors, and ongoing data quality checks helps to ensure the completion and validity of database variables (15). For this study, we identified women with two or more pregnancies during the study period whose index pregnancy (the woman's first pregnancy during the study period) was a singleton pregnancy starting at a normal prepregnancy BMI (18.5-24.9 kg/m<sup>2</sup> [as the INTERGROWTH-21st standard is only available for normal-weight women]). The index pregnancy was not necessarily the woman's first (nulliparous) pregnancy, as some women had their first child before the start of our study period. We used only the first two pregnancies per woman. The study was approved by the Research Ethics Board of the British Columbia Children's and Women's Hospital.

Perinatal Services British Columbia has linked successive pregnancies to individual women through an iterative matching process that considers maternal personal health number (a provincially issued identifier for all individuals in British Columbia used to access universal health care services), date of birth, first name, surname, hospital medical record number, and hospital identifier. In this iterative process, pregnancies are linked based on a series of matching criteria, starting with the most rigorous criteria before applying a less rigorous criteria set to the remaining unmatched women. This ensures, for example, that a woman whose date of birth had a typographical error in her first pregnancy would still likely be matched to successive pregnancies for which date of birth was entered correctly. Internal audits were conducted to ensure that the algorithm optimized accuracy and completion.

### Pregnancy weight and weight gain

Height and prepregnancy weight in the British Columbia Perinatal Data Registry are either measured or self-reported. Prepregnancy BMI

was calculated as height divided by weight squared, and normal weight was defined as a prepregnancy BMI of 18.5 to 24.9 kg/m<sup>2</sup>.

Total pregnancy weight gain was calculated as weight at the time of the delivery admission (or within 7 d of delivery) minus prepregnancy weight (in kilograms). Weight gain was standardized into gestational age-specific *z*-scores using the means and standard deviations (SD) in the INTERGROWTH-21st standard (8). We examined weight gain *z*-scores as a continuous variable and grouped them into categories of <-1, -1 to 0, >0 to +1, and >+1. These categories correspond to <16th percentile, 16th to 50th percentile, 51st to 84th percentile, and >84th percentile of a weight gain chart assuming a normal (Gaussian) distribution.

### Excess interpregnancy weight gain

Interpregnancy weight gain was calculated as the difference in prepregnancy weights between a woman's index and subsequent pregnancy. Excess weight gain was defined as an interpregnancy weight increase of >5 kg and >10 kg. These values correspond to approximately the top 25% and top 10% of weight gain observed in our cohort. We also examined the risk of a woman beginning her subsequent pregnancy with obesity (pregnancy BMI  $\geq$  30 kg/m<sup>2</sup>).

### Statistical analysis

Analyses were conducted using Stata® v.14 (College Station, Texas). Multivariable logistic regression was used to estimate the association between INTERGROWTH-21st weight gain *z*-score and risk of excess interpregnancy weight gain. Risk ratios and risk differences were calculated from these models through the *margins* postestimation command (16). Weight gain *z*-score was modeled as a restricted cubic spline with five knots to allow for smooth, nonlinear relationships (17). Models were adjusted for maternal age, parity, smoking in pregnancy, preexisting diabetes or hypertension in the index pregnancy, and interpregnancy interval. We did not control for gestational diabetes or hypertensive disorders of pregnancy, as we hypothesized that these events could be downstream consequences of excess pregnancy weight gain. We conducted a sensitivity analysis to adjust for prepregnancy BMI (among normal-weight women) but kept our primary analyses unadjusted for BMI, as we wished to evaluate the impact of the chart's *z*-scores as they would be used in the clinical setting.

### Missing data

Pregnancy BMI and pregnancy weight gain are known to be missing in a sizable fraction of British Columbia Perinatal Data Registry (due to missingness in the medical records) (15). Given the relatively large size, we opted against imputing our primary outcome using multiple imputation and instead compared the characteristics and pregnancy outcomes in women with missing versus nonmissing weight and weight gain data to evaluate the potential for systematic differences.

## Results

### Study population

From 2000 to 2015, there were 183,839 women in British Columbia with more than one delivery. Excluding women with twins or higher-order multiples, women with missing prepregnancy BMI, women with overweight, underweight, or obesity, and women who were missing pregnancy weight gain data in the index pregnancy left 58,534 women

**TABLE 1** Index pregnancy characteristics of 58,534 women with normal prepregnancy weight and a singleton pregnancy in British Columbia, Canada, 2000-2015, with one or more subsequent pregnancies

	INTERGROWTH pregnancy weight gain z-score			
	<-1 (<16th percentile)	-1 to 0 (16th to 50th percentile)	>0 to +1 (51st to 84th percentile)	> +1 (>84th percentile)
<i>n</i>	5,031	13,727	21,899	17,877
Maternal age (y)	28.6 ± 5.0	28.9 ± 4.8	28.7 ± 4.8	27.3 ± 5.1
Height	163 ± 7.1	163.8 ± 7.0	164.5 ± 6.9	165 ± 6.9
Prepregnancy BMI (kg/m <sup>2</sup> )	21.9 ± 1.7	21.6 ± 1.7	21.6 ± 1.7	21.8 ± 1.7
Nulliparous	4,246 (84.4)	11,971 (87.2)	19,429 (88.7)	16,090 (90.0)
Smoked during pregnancy	367 (7.3)	780 (5.7)	1,438 (6.6)	2,180 (12.2)
Pregestational diabetes	44 (0.9)	80 (0.6)	109 (0.5)	100 (0.6)
Prepregnancy hypertension	11 (0.2)	43 (0.3)	61 (0.3)	50 (0.3)
Cesarean delivery	964 (19.2)	2,940 (21.4)	5,352 (24.4)	5,172 (29.0)
Infant birth weight (g)	3,197 ± 511	3,307 ± 488	3,399 ± 499	3,496 ± 552
Preterm delivery < 37 wk	378 (7.5)	778 (5.7)	1,304 (6.0)	1,446 (8.1)
Interpregnancy interval (y)	3.1 ± 1.7	3.0 ± 1.6	3.0 ± 1.6	3.1 ± 1.8

Data are mean ± SD or *n* (%).

for analysis. As shown in the flow of participants in Supporting Information Figure S1, the most common reasons for exclusion were lack of prepregnancy BMI data ( $n = 48,081$ ) and non-normal prepregnancy BMI ( $n = 45,881$ ) in the index pregnancy. Despite the relatively large fraction of women excluded due to missing data (48,081 with missing BMI in index pregnancy + 12,052 with missing weight gain + 12,623 with missing BMI data in subsequent pregnancy out of 183,839 women = 41%), we found no meaningful differences in maternal age, infant birth weight, gestational age at delivery, preeclampsia risk, gestational diabetes risk, or prepregnancy BMI (when available) of women with missing versus available data (Supporting Information Table S1). Women with missing data were moderately more likely to smoke (10.9% vs. 8.1%) and deliver by cesarean section (26.7% vs. 24.7%).

### Maternal characteristics according to pregnancy weight gain

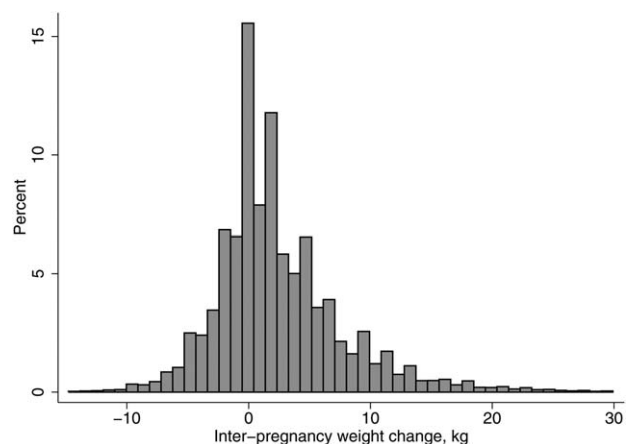
The study population had a median pregnancy weight gain z-score of 0.46 (interquartile range: 0.22-1.16), representing a shift to systematically higher values than the median (50th percentile) of the INTERGROWTH-21st chart (i.e., a z-score of 0). In the cohort, 5,031 (8.6%) gained < -1 SD, 13,727 (23.5%) gained between -1 and 0 SD, 21,899 (37.4%) gained between > 0 and +1 SD, and 17,877 (30.5%) of women gained +1 SD. Pregnancy weight gain z-score was not meaningfully different according to maternal age, prepregnancy BMI, or duration of interpregnancy interval in the index pregnancy (Table 1). In contrast, higher pregnancy weight gain was more common in women who were taller, were nulliparous, and smoked during pregnancy. High pregnancy weight gain was also linked with a higher risk of cesarean section delivery (29% vs. 19.2% in women in the highest and lowest weight gain categories, respectively) and higher infant birth weight (3,496 vs. 3,197 g, respectively).

### Excess interpregnancy weight gain

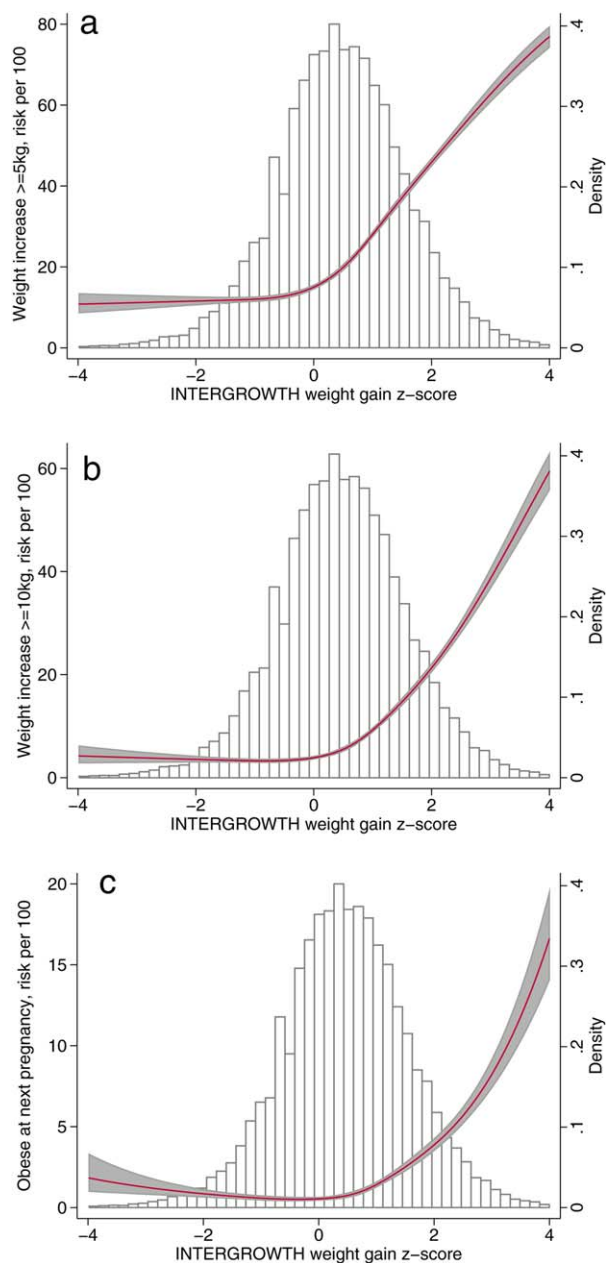
Figure 1 shows the distribution of interpregnancy weight change in the population. The median weight change was +1.4 kg (interquartile

range: -0.6 to +4.6). At the start of the subsequent pregnancy, 14,093 (24.1%) women were heavier by 5 kg or more, 5,179 (8.9%) were heavier by 10 kg or more, and 910 (1.6%) were women who developed obesity (from a normal-weight index pregnancy). In Figure 2, the risk of excess interpregnancy weight gain is shown according to pregnancy weight gain z-score classified using the INTERGROWTH-21st standard. For all three definitions of excess weight gain (Figure 2a-2c), risks remained stable across the lower half of weight gain z-scores but then rose steadily at weight gain z-scores above zero.

As expected, high weight gain z-scores (> +1) were associated with a significantly elevated risk of excess weight retention, with three- to sixfold increased risks of being 5 kg heavier, being 10 kg heavier, or developing obesity after adjusting for confounders (Table 2). However, women gaining between 0 and +1 SD (i.e., between the



**Figure 1** Interpregnancy weight change among normal-weight women in British Columbia, Canada, 2000-2015.



**Figure 2** Risk of excess interpregnancy weight gain by INTERGROWTH pregnancy weight gain z-score. Histogram bars indicate distribution of pregnancy weight gain z-scores in the cohort, and the solid line indicates predicted risk of excess weight gain with 95% confidence interval (shaded grey area) for (a) 5 kg retention, (b) 10 kg retention, and (c) obesity at next pregnancy. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

51st and 84th percentile on the standard) were also at significantly increased risk of excess weight retention, with 55%, 76%, and 84% higher risks of being 5 kg heavier, being 10 kg heavier, or developing obesity, respectively, compared with women gaining weight corresponding to  $-1$  to  $0$  z-scores. Converted to absolute terms (risk differences), these adjusted risk ratios mean that among women gaining between the 51st and 84th percentile of the standard, there will be 7.1 per 100 (95% confidence interval [CI]: 6.3, 7.9) more women who are heavier by 5 kg or more, 2.3 per 100 (95% CI: 1.9,

2.7) who are heavier by 10 kg or more, and 0.3 per 100 (95% CI: 0.2, 0.5) who develop obesity by the start of their next pregnancy compared with women gaining between the 16th and the 50th percentile. After adjustment for confounders, women gaining  $< -1$  SD had an 18% lower risk of retaining 5 kg, but risks of retaining 10 kg or developing obesity were not significantly different than the reference group. Further adjustment for prepregnancy BMI had minimal effect on estimates (data available on request). Adjusted risk ratios calculated using z-score as a continuous value are shown in Supporting Information Figure S2, in which the risk ratio estimated at each 0.5 z-score increment in relation to a z-score of 0 using the regression equation is shown. Even at a z-score of  $+0.5$ , risks were significantly elevated compared with a z-score of 0 (adjusted risk ratios of 1.4 [95% CI: 1.4, 1.5], 1.4 [95% CI: 1.3, 1.5], and 1.4 [95% CI: 1.2, 1.6] for 5 kg retention, 10 kg retention, and developing obesity, respectively).

## Discussion

### Summary

In this large, population-based cohort of successive pregnancies in British Columbia, Canada, we found that approximately half of the weight gain z-score values on the recently published INTERGROWTH-21st weight gain standard were associated with increased risks of excess maternal weight gain between pregnancies. Risks of excess weight gain remained stable below a z-score of 0 but rose steadily with increasing weight gain z-scores above 0. This finding is important because it suggests that use of the chart in clinical practice as a prescriptive standard of how much weight women with a normal prepregnancy BMI ought to gain during pregnancy could contribute to the development of obesity in mothers or excess adiposity for a subsequent pregnancy.

### Comparison with the literature

Unlike the fields of fetal growth and child growth, which have more established traditions of using weight-for-age charts (18-21), maternal weight-gain-for-gestational-age charts are more recent. Gestational weight gain charts for US, Swedish, and Malawi populations have been produced by groups including ours (22-25), but these charts were either presented as references (descriptive charts) to be used as tools to establish the unbiased association between weight gain and adverse pregnancy outcomes (22-24) or for lower-resourced settings (25) where inadequate, rather than excess, weight gain is the primary concern. The INTERGROWTH-21st chart is the first of which we are aware to provide percentiles of recommended weight gain in pregnancy for a global general obstetrical population (albeit limited to normal-weight women). Although the INTERGROWTH-21st standard does not have recommended cutoffs to define normal and abnormal weight gain, our expectation a priori was that the majority of values on a standard would be associated with good outcomes, with increased risks observed only with extreme percentiles. For example, the 85th and 95th percentiles of child growth charts are used to define overweight and obesity, respectively (26), while percentiles such as the 10th, 5th, or 3rd percentiles have conventionally been used to define small-for-gestational-age births (27). It was therefore unexpected that risk of excess weight retention began to increase at thresholds as low as 0 (50th percentile) on the INTERGROWTH-21st weight gain standard, which raises concerns about its implementation in clinical practice.

**TABLE 2** Weight status at subsequent pregnancy among women with a singleton, normal-weight index pregnancy in British Columbia, Canada, 2000-2015

	INTERGROWTH pregnancy weight gain z-score			
	<-1 (<16th percentile)	-1 to 0 (16th to 50th percentile)	>0 to +1 (51st to 84th percentile)	> +1 (>84th percentile)
<i>n</i>	5,031	13,727	21,899	17,877
Weight change at subsequent pregnancy (kg), mean $\pm$ SD	0.03 $\pm$ 5.4	1.0 $\pm$ 4.7	2.2 $\pm$ 5.2	5.1 $\pm$ 7.2
Increase of > 5 kg, <i>n</i> (%)	576 (11.5)	1,818 (13.2)	4,467 (20.4)	7,232 (40.5)
Risk ratio [95% CI]	0.86 [0.79, 0.94]	reference	1.54 [1.46, 1.62]	3.05 [2.91, 3.20]
Adjusted risk ratio [95% CI] <sup>a</sup>	0.82 [0.75, 0.89]	reference	1.55 [1.47, 1.63]	2.98 [2.83, 3.12]
Increase of > 10 kg, <i>n</i> (%)	167 (3.3)	463 (3.4)	1,304 (6.0)	3,245 (18.2)
Risk ratio [95% CI]	0.98 [0.81, 1.16]	reference	1.77 [1.58, 1.95]	5.38 [4.87, 5.89]
Adjusted risk ratio [95% CI] <sup>a</sup>	0.91 [0.75, 1.08]	reference	1.76 [1.57, 1.95]	4.94 [4.46, 5.42]
Obesity at beginning of subsequent pregnancy, <i>n</i> (%)	40 (0.8)	64 (0.5)	192 (0.9)	614 (3.4)
Risk ratio [95% CI]	1.71 [1.03, 2.38]	reference	1.88 [1.35, 2.41]	7.37 [5.48, 9.26]
Adjusted risk ratio [95% CI] <sup>a</sup>	1.58 [0.95, 2.20]	reference	1.84 [1.32, 2.37]	5.98 [4.43, 7.53]

<sup>a</sup>Adjusted for prepregnancy interval, preexisting hypertension, prepregnancy diabetes, maternal age, nulliparity, and smoking during pregnancy in the index pregnancy.

Our finding that many *z*-score values on the INTERGROWTH-21st chart were associated with an increased risk of excess postpartum weight retention is nevertheless consistent with the current Institute of Medicine recommendations for pregnancy weight gain (7). For normal-weight women, the Institute of Medicine recommends a total pregnancy weight gain of 11.5 to 16.0 kg. At 40 weeks, this corresponds to *z*-scores of  $-0.6$  to  $0.44$  on the INTERGROWTH-21st chart, or the 27th to 67th percentiles. Unlike the INTERGROWTH-21st standard, the Institute of Medicine recommendations were established by examining the association between gestational weight gain and several adverse maternal and child health outcomes, including excess postpartum weight retention and estimating the range at which risks were minimized. This may explain the narrower range of the Institute of Medicine recommendations compared with the INTERGROWTH-21st percentile. For example, the upper limit of the Institute of Medicine guidelines is 16 kg, which is considerably lower than the 90th percentile of the INTERGROWTH-21st chart (20.2 kg) or the 97th percentile of the chart (23.8 kg).

### Strengths and limitations

Strengths of this study include its use of a large, population-based cohort in a jurisdiction with universal health care and standardized documentation of clinical care. Data on index pregnancy prepregnancy BMI, weight gain, and other key variables were collected in a prospective manner in the medical records, reducing the risk of information bias. Pregnancy linkages were conducted using a rigorous iterative linkage strategy to maximize the completeness and accuracy of successive pregnancy linkages.


Nevertheless, limitations of the study should be noted. First, data on prepregnancy weight and/or weight gain were missing in a sizeable fraction of the cohort. Although this is a common concern in perinatal databases (e.g., data on interpregnancy weight change were missing in nearly 20% of a recent report from the Swedish Medical Birth

Register (28)) and the characteristics of women included in our study were reasonably similar to those excluded, we cannot rule out a potential for selection bias if the effect of weight gain on interpregnancy weight in our cohort was systematically different than those women with missing weight data. The generalizability of our cohort is further supported by the comparability of the interpregnancy weight changes observed in our cohort to those from other populations. For example, among 1,300 normal-weight women delivering at a San Francisco teaching hospital, the mean interpregnancy weight changes in the middle two quartiles were  $+2.0$  and  $+2.8$  kg (median in our cohort was  $+1.4$  kg [interquartile range  $-0.6$  to  $+4.6$ ]) (4). Among 465,836 women in Sweden, interpregnancy BMI change was found to be within  $-1$  to  $\leq 1$  kg/m<sup>2</sup> in 46% of the cohort and  $1$  to  $< 2$  kg/m<sup>2</sup> in 20% (vs. 44% and 15% in our cohort, respectively) (29). A large fraction of the prepregnancy weights in our cohort were likely self-reported at the time of the first antenatal visit. While self-reported weights are known to have measurement error (30), their use is pragmatic because it represents the information typically available to caregivers at the time of the first antenatal visit.

We used interpregnancy weight change as a proxy for postpartum weight retention, and this approach cannot distinguish between weight retained following pregnancy and new weight gain post partum. Nevertheless, research commissioned by the 2009 Institute of Medicine committee to reevaluate the pregnancy weight gain guidelines found that in all prepregnancy BMI categories and at all visits in the early postpartum period (up to 12 months after delivery), high weight gain was associated with increased postpartum weight retention (7). This increases the likelihood that our findings at a median of approximately 3 years also represent differences due to weight retention rather than postpartum weight gain. Furthermore, we did not have data available on potentially important confounders such as physical activity. As a result, firm conclusions about the causality of our associations cannot be made. However, the value of our results from a predictive

perspective (i.e., the ability to use pregnancy weight gain as a tool to identify women at increased risk of weighing more at the start of their next pregnancy) would not be affected.

## Conclusion

The INTERGROWTH-21st standard provides valuable new tools to assess growth in normal-weight pregnancy across the world in a consistent and rigorous manner. However, our finding that the pregnancy weight gain standard does not appear to describe optimal weight gain patterns with respect to maternal weight status in a subsequent pregnancy suggests that this chart should not be adopted into clinical practice as a standard. At present, the chart could be adopted as a descriptive reference in which only weight gain values below approximately the 50th percentile are recommended in order to reduce the risk of excess maternal weight gain. Future research seeking to create pregnancy weight gain standards (in the INTERGROWTH or other cohorts) should ensure that their normative values for healthy weight gain are derived from study populations that exclude women with excess postpartum weight retention. 

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