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# **“Patrones de cambio de peso durante el primer año posparto y su asociación con riesgo cardiometabólico entre los 6 y 7 años posparto”**

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DEDICATORIAS

Para mi familia, Rigoberto, Ángeles, Denise, Angie, Alma y Luis,

por inspirarme y apoyarme de forma incondicional.

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## 1. Introducción

En México el 76% de las mujeres adultas tienen sobrepeso u obesidad. La tendencia de aumento de estos padecimientos es alarmante ya que, en menos de 3 décadas, el sobrepeso y obesidad se incrementaron en 42% y 290%, respectivamente, en las mujeres de 20-49 años (1). El exceso de peso aumenta el riesgo de diabetes mellitus tipo 2 (DM2) y enfermedades cardiovasculares (2,3), padecimientos que actualmente se encuentran entre las principales causas de mortalidad entre mujeres mexicanas (4). Estas cifras resaltan la importancia de identificar y controlar factores de riesgo para sobrepeso y obesidad en las mujeres.

Se ha propuesto que el efecto acumulado de cada embarazo por el que atraviesa una mujer a lo largo de su vida reproductiva, es un factor contribuyente al aumento en la prevalencia de sobrepeso u obesidad y enfermedades metabólicas (3,5,6). A la fecha, distintos estudios sustentan esta hipótesis. Por un lado, haber tenido hijos, en comparación con ser nulípara, se asocia con mayor riego de obesidad y DM2 (5,7). Estas asociaciones son respaldadas por el hallazgo de que tener un hijo, se asocia con aumentos significativos de peso, circunferencia de cintura (CC) y grasa visceral en los años posteriores al parto (8,9). Esta mayor adiposidad asociada al embarazo, puede ser el resultado de retención o ganancia de peso en el posparto (10).

Durante el embarazo, la ganancia de peso materna promueve el adecuado crecimiento y desarrollo del feto (11). En las primeras 6 semanas después del parto, existe una disminución de peso que consiste en la pérdida fetal, de la placenta, líquido amniótico y otros componentes, diferentes al tejido adiposo, acumulados durante la gestación. La pérdida de peso que ocurre posterior a las 6 semanas involucra pérdida del tejido adiposo

(12). A pesar de que, de forma fisiológica, la tendencia de cambio de peso en la mujer es regresar al estado pregestacional durante los primeros 12 meses posparto (13), un gran número de mujeres no lo logra.

Al primer año posparto, las mujeres pesan en promedio de 0.8 a 2.6 kg más, en comparación con su peso pregestacional (14–18). La mayoría de los estudios asumen que el peso observado en el posparto corresponde a peso retenido del embarazo. Debido a esto, la retención de peso posparto (RPP) es el patrón de cambio de peso más reportado en la literatura. En la mayoría de los estudios, la RPP se define como la diferencia del peso en algún momento específico del posparto, usualmente 12 meses, y el peso pregestacional (15–17,19). Esta definición no permite diferenciar otros patrones de cambio de peso que las mujeres también experimentan como son la ganancia de peso posparto (GPP) y la retención + ganancia de peso (RPP+GPP) (20). Estos patrones de cambio de peso han sido escasamente estudiados debido a la falta de mediciones repetidas de peso durante el primer año posparto.

Es importante distinguir la RPP, GPP y RPP+GPP ya que sus efectos en la salud metabólica de la mujer pueden ser diferentes. Se ha sugerido que el exceso de grasa retenido al primer año posparto tiene una localización central y que es grasa no subcutánea, principalmente de tipo visceral (21). Dado que la grasa visceral se asocia con resistencia a la insulina y alteraciones en factores de riesgo cardiovascular (22,23), la RPP y la RPP+GPP podrían conferirle mayor riesgo metabólico a la mujer.

Distintos estudios han evaluado la asociación de características o comportamientos maternos con la RPP. El índice de masa corporal (IMC) pregestacional, se asocia inversamente con la RPP (16,24). Esta asociación inversa se puede deber a que las mujeres con IMC pregestacional elevado presentan, en promedio, menor ganancia de peso gestacional (GPG) (16). La GPG es el principal predictor de la RPP (25). Ganar peso en exceso durante el embarazo, independientemente del IMC pregestacional, incrementa el riesgo de retener ≥5 kg a los 12 meses posparto (16). Por otro lado, distintos estudios muestran que la práctica de la lactancia materna disminuye el riesgo de RPP (18,26), sin embargo, una revisión sistemática con meta-análisis reciente concluyó que la evidencia disponible no es suficiente para apoyar esta asociación (27). Debido a que la GPP y la RPP+GPP han sido poco estudiados, existe poca información sobre sus predictores. Tener un IMC pregestacional elevado y distintas características del estilo de vida (patrones de dieta, actividad física y tiempo en actividades sedentarias) se han asociado con GPP (10,13,15,20,28). En México, contamos con información limitada sobre los patrones de cambio de peso que las mujeres experimentan después del embarazo, ya que la mayoría de estos estudios han sido realizados en mujeres blancas de países desarrollados como Estados Unidos, Canadá, y Dinamarca.

No regresar al peso pregestacional después del embarazo tiene implicaciones en el corto y largo plazo. Las mujeres que no regresan a su peso pregestacional durante el primer año posparto desarrollan un perfil cardiometabólico deletéreo que consiste en mayor presión arterial, resistencia a la insulina, colesterol de baja densidad (LDL por sus siglas en inglés) y apolipoproteína B, así como niveles más bajos de adiponectina (20). También estas mujeres tienen mayor posibilidad de cambiar de categoría de IMC, al primer año posparto, por ejemplo, de peso normal a sobrepeso (17).

Escasos estudios han evaluado los efectos de los patrones de cambio de peso posparto en la salud de la mujer en el largo plazo. La retención de peso a los 6 meses y la ganancia de peso entre los 6 y 18 meses posparto se asocian con aumento en el peso y en la CC a los 7 años posparto (10). Un estudio identificó que el peso a los 12 meses posparto es uno de los principales predictores del desarrollo de sobrepeso u obesidad 15 años después del embarazo (29). Por otro lado, la evidencia sobre la posible asociación de los patrones de cambio de peso posparto con alteraciones metabólicas es indirecta y proviene de estudios que utilizan la GPG como exposición. Se ha observado que las mujeres que tienen GPG excesiva, tienen mayor IMC, CC y presión arterial sistólica (PAS) 16 años después del parto, así como mayor riesgo de DM2 a los 21 años posparto (30,31). A pesar de que estos resultados pueden ser explicados por el cambio de peso posparto, por ejemplo por la RPP, estas asociaciones no han sido evaluadas de forma directa.

En la presente tesis, caracterizamos el cambio de peso posparto en mujeres mexicanas participantes en la cohorte *PROGRESS* (Programming Research in Obesity, Growth, Environment and Social Stressors), en 4 patrones mutualmente excluyentes: regreso al peso pregestacional, RPP, GPP y RPP+GPP. Evaluamos la asociación de características maternas modificables como el IMC pregestacional, la GPG y la lactancia materna con los patrones de cambio de peso posparto. En un segundo análisis determinamos la asociación de los patrones de cambio de peso con el IMC, CC y distintos factores de riesgo cardiovascular 6 años después del parto. Este estudio aporta la primera evidencia de la asociación entre el cambio de peso posparto y distintos factores de riesgo cardiovascular años después del embarazo.

## 2. Objetivos

### 2.1 Objetivo general 1

- Evaluar la asociación del IMC pregestacional, la ganancia de peso gestacional y la lactancia materna con los patrones de cambio de peso, regreso al peso pregestacional, retención de peso posparto, ganancia de peso posparto, retención + ganancia de peso posparto, a los 12 meses posparto.

***Objetivos específicos***

- Caracterizar los patrones de cambio de peso a los 12 meses posparto.
- Determinar cómo se asocian el IMC pregestacional, la ganancia de peso gestacional y la lactancia materna con los patrones de cambio de peso caracterizados.

### 2.2 Objetivo general 2

- Evaluar la asociación de los patrones de cambio de peso a los 12 meses posparto con factores de riesgo cardiometabólico entre los 6 y 7 años posparto.

***Objetivos específicos***

- Evaluar la asociación de los patrones de cambio de peso con el IMC, la presión arterial, glucosa, insulina, perfil de lípidos y circunferencia de cintura entre los 6 y 7 años posparto.

## 3. Resumen

Con esta tesis nos planteamos evaluar la asociación del IMC pregestacional, la GPG y la lactancia materna con 4 patrones de cambio de peso mutuamente excluyentes a los 12 meses posparto, los cuales fueron: regreso al peso pregestational, retención de peso posparto, ganancia de peso posparto, retención + ganancia de peso posparto. En un segundo análisis, evaluamos la asociación de estos patrones de cambio de peso con factores de riesgo cardiometabólico entre los 6 y 7 años posparto. Los mapas conceptuales de los estudios se muestran en los **anexos 1 y 2.**

Para cumplir nuestros objetivos, realizamos dos análisis secundarios utilizando datos de la cohorte de nacimientos *PROGRESS.* La cohorte *PROGRESS* inició en la ciudad de México en el año 2007 reclutando mujeres embarazadas entre julio de ese año y febrero del 2011. El reclutamiento y la primera visita de las madres participantes se llevaron a cabo en el 2º trimestre de embarazo. Posteriormente se realizaron visitas durante el 3° trimestre de embarazo, el parto, primer y sexto mes posparto, y cada 6 meses hasta los 2 años (12, 18 y 24 meses posparto). En una segunda fase, se realizó un seguimiento a los 48 meses y a los 72 meses posparto. Las mujeres incluidas eran derechohabientes del Instituto Mexicano del Seguro Social y cumplieron con los siguientes criterios de inclusión: tener entre 18 y 45 años de edad, embarazo de producto único entre las semanas de gestación 12 y 24, no padecer problemas renales o cardiacos, tener acceso a una línea de teléfono, planear vivir en la ciudad de México en los siguientes 3 años y no utilizar ningún tipo de esteroide o medicamentos antiepilépticos. Se excluyeron a las mujeres con historial de infertilidad, diabetes, psicosis, consumo $\geq 1$ bebida alcohólica por día, uso de drogas y uso habitual de medicamentos (por prescripción médica o no) y medicina tradicional (32,33).

Los objetivos de *PROGRESS*, en sus dos fases, fueron los siguientes:

- Evaluar el efecto de la exposición a manganeso, arsénico y plomo durante el embarazo y los primeros años de vida, en el neurodesarrollo durante los primeros 2 años de vida.
- Evaluar el efecto del estrés materno prenatal y postnatal en el neurodesarrollo durante los primeros 3 años de vida.
- Evaluar el efecto de la exposición a plomo y a anemia por deficiencia de hierro en el neurodesarrollo durante los primeros 3 años de vida.
- Evaluar la interacción del estrés prenatal y metales pesados en el neurodesarrollo.

Los procedimientos de la cohorte, en sus 2 fases, fueron aprobada por los Comités de Ética, Bioseguridad e Investigación del Instituto Nacional de Salud Pública, así como los comités de ética de la Escuela de Salud Pública de Harvard, y la Escuela Icahn de medicina de Mount Sinai.

En *PROGRESS*, 948 mujeres fueron reclutadas y continuaron activas en el estudio hasta la visita del parto. En el primer análisis incluimos a mujeres con un recién nacido vivo, sin malformaciones congénitas y que tenían pesos disponibles para caracterizar su patrón de cambio de peso durante el primer año posparto. Excluimos a aquellas que se embarazaron nuevamente durante este primer año. La muestra final fueron 500 mujeres. Para el segundo análisis, partimos de la muestra del estudio uno y excluimos a aquellas que no tenían información de adiposidad y desenlaces metabólicos a los 6 años posparto (visita de los 72 meses). También excluimos a las mujeres que en la visita de los 6 años posparto estaban embarazadas o que habían dado a luz en los 12 meses anteriores a la visita. La muestra final fueron 361 mujeres. En ninguno de los dos estudios se encontraron diferencias importantes entre las mujeres analizadas y no analizadas.

El primer artículo titulado “Predictors of patterns of weight change one year after delivery in a cohort of Mexican women”, utilizamos información recabada durante el embarazo (2° y 3° trimestre), y los meses posparto 1, 6 y 12. El desenlace de interés fueron los patrones de cambio de peso al primer año posparto, los cuales caracterizamos utilizando el peso pregestacional y los pesos medidos en los meses posparto 1, 6, 12. Los criterios considerados para esta clasificación fueron los siguientes:

- *Regreso al peso pregestacional:* se incluyeron mujeres que al primer año posparto habían recuperado su peso pregestacional (margen de <500 g), o que pesaban menos en comparación con este.
- *Retención de peso posparto*: incluyó mujeres que presentaron una tendencia a perder peso durante el primer año posparto, pero que en ninguna etapa recuperaron su peso pregestacional.
- *Ganancia de peso posparto*: incluyó mujeres que recuperaron su peso pregestacional durante los primeros 6 meses posparto, y que posteriormente re-incrementaron peso.
- *Retención y ganancia de peso posparto*: incluyó mujeres que no recuperaron su peso pregestacional durante los primeros 6 meses posparto, y que en promedio, mostraron una tendencia a incrementar peso.

En todos los casos, se tomó en cuenta un margen de 500 g para considerar que un mujer regresó a su peso pregestacional. Esta clasificación se basó inicialmente en la propuesta por Kew y cols. (20), pero se adaptó de acuerdo a los resultados iniciales del análisis exploratorio.

Una vez que caracterizamos los patrones de cambio de peso, evaluamos su asociación con el IMC pregestational, la GPG y la lactancia materna al mes posparto, utilizando modelos de regresión logística multinomial. Los modelos estuvieron ajustados por variables confusoras incluyendo la edad materna, estado civil, educación, paridad, nivel socioeconómico (NSE), así como tabaquismo, actividad física y actividades sedentarias en el embarazo, entre otras. El IMC pregestacional (kg/m$^2$) se clasificó siguiendo los criterios de la OMS (34). La GPG se definió como la diferencia entre el peso medido en el 3° trimestre del embarazo y el peso pregestacional. La adecuación de la GPG se estableció para cada mujer de acuerdo a su IMC pregestacional y a las semanas de gestación en las que se midió el peso del 3° trimestre del embarazo (insuficiente, adecuada, excesiva) (11,35). La lactancia materna al primer mes posparto se clasificó de acuerdo los criterios de la OMS (36). El **anexo 3 y 4** muestran las recomendaciones de GPG de acuerdo al IMC pregestacional y la clasificación de la lactancia materna, respectivamente.

Encontramos que la mayoría de las mujeres (57%) regresaron a su peso pregestacional al primer año posparto, 8% tuvo RPP, 14% GPP y 21% RPP+GPP. En modelos logísticos multinomiales, el sobrepeso y la obesidad pregestacional, en comparación con tener peso normal, se asociaron con mayor riesgo de GPP (sobrepeso: RRR 2.5 [95% CI: 1.3, 4.8]; obesidad: RRR 2.2 [1.0, 4.7]), pero no de RPP o RPP+GPP. Tener GPG excesiva durante el embarazo, en comparación con adecuada, se asoció con mayor riesgo de RPP (RRR 3.3 [1.6, 6.9]) y RPP+GPP (RRR 2.4 [1.4, 4.2]). Lactar de forma exclusiva al primer mes posparto se asoció con menor riesgo de RPP (RRR 0.3 [0.1, 0.9]).

Este primer análisis aporta evidencia valiosa sobre el cambio de peso que experimentan las mujeres después del embarazo y sobre factores potencialmente modificables asociados al cambio de peso. Dichos factores pueden ser el objeto de intervenciones o políticas públicas enfocadas a mejorar la salud de la mujer durante sus años reproductivos.

Distintos estudios han mostrado que el peso ganado durante el embarazo, se asocia con el IMC, CC y algunos factores de riesgo cardiovascular, años después del embarazo (30,37,38). Uno de los mecanismos propuestos para explicar esta asociación es el cambio de peso posparto, en específico la RPP (30,39). A pesar de esto, ningún estudio ha explorado de forma directa la asociación de los patrones de cambio de peso durante el primer año posparto con factores de riesgo cardiovascular años después del embarazo. Este fue el objetivo de nuestro segundo análisis. En este análisis, incluimos factores clásicos de riesgo metabólico como son el IMC, CC, glucosa, resistencia a la insulina (índice de HOMA), PAS, presión arterial diastólica (PAD), triglicéridos, colesterol total, colesterol de alta densidad (HDL por sus siglas en inglés) y LDL. Dada la relación que existe entre los factores de riesgo metabólico, nuestro primer paso fue realizar un análisis de componentes principales para agrupar desenlaces de acuerdo a sus correlaciones. Con este abordaje redujimos los desenlaces a 3 grupos: 1) IMC, CC, glucosa, índice de HOMA, triglicéridos y HDL; 2) PAS y PAD; 3) colesterol total y LDL. Realizamos un modelaje basado en análisis de senderos (path analysis), el cual nos permitió considerar la relación temporal entre las variables, además de explorar la asociación directa de los patrones de cambio de peso con los desenlaces y la indirecta a través de la adiposidad (IMC) a los 6 años posparto. Construimos tres grandes modelos, uno para cada grupo de desenlaces, considerando variables confusoras pre-exposición (edad, paridad, escolaridad, estado civil, NSE, IMC pregestacional, GPG, lactancia materna, tiempo en actividades sedentarias, tabaquismo, diagnóstico de desórdenes hipertensivos del embarazo, haber tenido un bebé grande para la edad gestacional), y variables post-exposición potencialmente asociadas con los desenlaces (energía consumida por día, porciones de bebidas azucaradas por día, tabaquismo, consumo de medicamentos a los 6 años posparto).

La RPP+GPP al primer año posparto, en comparación con regresar al peso pregestacional, se asoció con mayor IMC ($\beta$ 2.30 kg/m$^2$, 95% CI [1.67, 2.93]), CC (3.38 cm [1.14, 5.62]) e índice de HOMA (0.21 unidades [0.04, 0.39]). La RPP y la GPP se asociaron con mayor IMC y CC a los 6 años posparto (RPP: 1.80 kg/m$^2$ [0.80, 2.79], 3.15 cm [-0.35, 6.65]; GPP: 1.22 kg/m$^2$ [0.53, 1.92] y 3.32 cm [0.85, 5.78]). No se observaron asociaciones directas significativas entre los patrones de cambio de peso y los factores de riesgo metabólico, con excepción de la ya mencionada para el índice de HOMA. La RPP+GPP, la RPP y la GPP tuvieron asociaciones indirectas, a través del IMC a los 6 años posparto, con todos los factores de riesgo metabólico, excepto con el colesterol total y LDL.

Este estudio aporta evidencia importante sobre el efecto de no regresar al peso pregestacional en la salud metabólica de la mujer años después del embarazo.

## 4. Artículo 1

**Target journal:** Public Health Nutrition

**Title:** Predictors of patterns of weight change one year after delivery in a cohort of Mexican women

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**Short title:** Predictors of postpartum weight change

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**Conflict of interest.** The authors declare that they have no competing interests.

**Authorship:** DCSC conceptualized and designed the study, carried out the statistical analysis, interpretation of the data, and drafted the manuscript. MMTR, BTV, and RLR participated in the conceptualization and design of the study, interpretation of the data and critically reviewed the manuscript. EO helped in the interpretation of the data and critically reviewed the manuscript. ROW, ACP, MLPZ, AAB, ACJ, MAO, and IRS critically reviewed the manuscript.

**Ethical standards disclosure:** "This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Committees on Ethics, Biosafety, and Research at the Mexican National Institute of Public Health, as well as the Institutional Review Boards of the participating institutions. Written informed consent was obtained from all subjects/patients."

**Abstract**

**Objective.** The long-term increase in weight associated with pregnancy may result from postpartum weight retention (i.e. retention of gestational weight), postpartum weight gain (i.e. weight gained within the postpartum), or retention + gain. Most of the literature focuses on weight retention, and few studies have described postpartum weight gain, or retention + gain, and their predictors.

**Design.** In a secondary analysis, we characterized maternal weight change one year after delivery into 1) return to pregestational weight, 2) postpartum weight retention, 3) weight gain, or 4) retention + gain, and evaluated their associations with pregestational BMI, gestational weight gain (GWG) and breastfeeding at one month, using multinomial logistic regression.

**Setting.** *Programming Research in Obesity, Growth, Environment and Social Stressors* pregnancy cohort in Mexico City.

**Subjects**. Mothers (n=500)

**Results.** Most (57%) women returned to their pregestational weight; 8% experienced retention, 14% gain, and 21% retention + gain. Compared to normal weight, pregestational overweight (Relative risk ratio (RRR) 2.5, 95% CI [1.3, 4.8]) and obesity (RRR 2.2 [1.0, 4.7]) were associated with a higher risk of weight gain. Exclusive breastfeeding, compared to no breastfeeding, was associated with a lower risk of retention (RRR 0.3 [0.1, 0.9]). Women with excessive GWG, compared to adequate, had higher risk of retention (RRR 3.3 [1.6, 6.9]) and retention + gain (RRR 2.4 [1.4, 4.2]).

**Conclusions.** Women with excessive GWG, pregestational overweight or obesity, and who do not breastfeed, represent high-risk groups for adverse weight patterns after pregnancy. Future interventions should target these high-risk women for obesity prevention.


**Keywords:** postpartum weight change, pregestational BMI, gestational weight gain, breastfeeding, postpartum weight retention

## Introduction

Overweight and obesity have increased at alarming rates worldwide and currently afflict 76% of adult women in Mexico [1], highlighting the importance of identifying risk factors for excess weight in this population. Pregnancy and childbearing are risk factors for weight gain in women in developed countries [2,3]. In this context, having a child has been associated with a weight increase of 0.9 to 6.0 kg over the subsequent 10 years [3].

Weight increase associated with pregnancy may be the result of postpartum weight retention (PPWR) or postpartum weight gain (PPWG) [4–8]. Most of the published research included a single postpartum weight and has characterized all weight change as PPWR (i.e. retention of gestational weight). PPWR is usually defined as the difference from weight at a specific time, typically 12 months, and pregestational weight [9–12]. When evaluated at 12 months, mean PPWR has ranged from 0.8 to 2.6 kg [9–11]. Some studies have described that women also experience PPWG (i.e. weight gain that occurs entirely in the postpartum period) [4,7,13], or a combination of postpartum weight retention and gain (PPWR+WG) (i.e. retention of gestational weight, followed by postpartum weight gain) [4,14]. The occurrence of PPWG or PPWR+WG may be overlooked when using the traditional definition of PPWR [7]. Therefore, a different approach needs to be considered to distinguish the different patterns of weight change that women experience postpartum. Moreover, it is important to characterize patterns of postpartum weight change, because their implications for women´s health may be different. There is evidence that excess fat retained after pregnancy is preferentially centrally localized [15,16], therefore, PPWR or PPWR+WG may increase women's risk of metabolic diseases [17].

Different factors may predispose women to experience weight gain versus retention after delivery. Gestational weight gain (GWG) is a consistent and strong predictor of PPWR [18,19]. Pregestational body mass index (BMI) has shown an inverse association with PPWR [10,18], and a positive association with PPWG [7]. In some studies, exclusive breastfeeding has been associated with lower weight retention [20], but other studies have failed to show this association [21,22]. No studies have looked at predictors PPWR+WG within the first year after delivery. Furthermore, most of the literature has focused on primarily white women living in the United States (US), Western Europe or Australia. Little is known about predictors and patterns of weight change in other settings, including Mexico. The objective of this study was to evaluate the associations of pregestational BMI, GWG, and breastfeeding with four mutually exclusive patterns of weight change during the first year postpartum: PPWR, PPWG, PPWR+WG, and return to pregestational weight.

## Methods

### ***Study population***

This was a secondary analysis of 948 mothers participating in the prospective birth cohort *Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS).* A full description of the cohort is provided elsewhere [23,24]. Briefly, *PROGRESS* is an ongoing prospective cohort study initiated in Mexico City in 2007. Between July 2007 and February 2011, women with a singleton pregnancy who received health insurance and prenatal care through the Mexican Social Security System were invited to participate. They had to be at least 18 years old, less than 22 weeks pregnant, free of renal or heart diseases, not users of steroids or anti-epileptic drugs, have access to a telephone line, and plan to live in Mexico City for the next three years. Women were excluded if they had a history of infertility, diabetes or psychosis, consumed ≥1 alcoholic drink a day, or used drugs or any prescription, herbal or over-the-counter medications regularly.

For the present analysis, we used information collected by in-person interviews during the second and third trimesters of pregnancy, and at 1, 6 and 12 months postpartum. In this analysis, women who delivered a live newborn, free of congenital malformations were included (n=937). Out of the 937 women, only 515 had weights available to determine their pattern of postpartum weight change, which was the outcome of interest. Out of the 515 women, those who became pregnant again during the first year postpartum were excluded (n=14). We further excluded one woman who underwent weight-loss surgery before pregnancy, due to her extreme weight loss during and after pregnancy. The final sample consisted of 500 women, who were comparable in demographic and anthropometric characteristics (e.g. pregestational BMI, GWG), smoking history, lifestyle behaviors (e.g. physical activity and sedentary activities) and breastfeeding practices to the 448 women not included in the analysis. The only exception was gestational age at delivery, which was slightly higher in the analytic sample (38.4 vs. 38.1 weeks).

### ***Exposures: Predictors of patterns of postpartum weight change***

#### ***Pregestational BMI***

Trained personnel measured women´s height at the first study visit following standardized procedures [25]. All participants self-reported their pregestational weight at the initial visit. However, self-reported weight is less reliable in this setting where few women are regularly weighed. Considering this, we used an estimated pregestational weight obtained from a linear mixed-effects model. The model used weights measured in pregnancy (second and third trimesters) that were available for most women, as well as clinical weight measurements in the 6 months prior to pregnancy through the early pregnancy period that were recovered from Mexican Social Security System clinical records. The model also included days of gestation at the time of weight collection, maternal height, age, socioeconomic status (SES), education, parity, and self-reported pregestational weight.

Model performance was assessed with 10-fold cross-validation, which was based on an evaluation of how well the model predictions at the last menstrual period agreed with weights measured at the Mexican Social Security System clinics for a subset of women (n=87). These weights were measured within +/-20 days of the last menstrual period. The predictive accuracy assessed by the root mean square error was 3.2 kg. In a *post hoc* analysis, the model´s predictions were compared to those obtained by a model recently proposed by Thomas et al. [26], obtaining similar results (data not shown).

We calculated pregestational BMI as estimated pregestational weight divided by height squared, and classified women as underweight, normal weight, overweight or obese following the World Health Organization (WHO) criteria [27]. Underweight women were combined with the normal weight category due to the small sample size (n=3).

***Gestational weight gain***

Study personnel measured women´s weight at the third trimester of pregnancy [25]. GWG was calculated as the difference between third-trimester weight and pregestational weight. It was corrected by the length of gestation following the procedure described by Perichart-Perera et al. [28]. We classified women as having adequate, insufficient or excessive GWG for their gestational age following the US Institute of Medicine (IOM) guidelines, which have been previously used in a Mexican population [28,29].

***Breastfeeding practices***

At the first month postpartum visit, women reported whether they were breastfeeding or not, and the exclusivity of breastfeeding (i.e. only breast milk or not). They also reported on the introduction of formula, medications and other types of milk, fluids, and foods. With this information, we classified breastfeeding as exclusive (i.e. only breast milk), predominant (i.e. breast milk and certain liquids such as water and water-based drinks, but excluding non-human milk), partial (i.e. breast milk and any food or liquid, including non-human milk) [30].

***Outcome: Patterns of postpartum weight change***

In every visit, study personnel measured weights with a digital scale following standardized procedures [25]. We categorized postpartum weight change into four mutually exclusive patterns using weights at 1, 6 and 12 months postpartum, as well as predicted pregestational weight. We focused on the first year postpartum because weight changes associated with pregnancy are more likely to occur during this time [5], and also to be consistent with published research [11,12]. *Return to pregestational weight* at any postpartum time point was defined as a weight no more than 500 g higher than the predicted pregestational weight. The following definitions were applied for this classification:

- *Return to pregestational weight:* Women who returned to their pregestational weight at 12 months postpartum. Includes women who lost weight compared to the pregestational state.
- *Postpartum weight retention (PPWR):* Women who, on average, lost weight through 12 months postpartum without ever reaching their pregestational weight.
- *Postpartum weight gain (PPWG):* Women who reached their pregestational weight at any point during the first 6 months postpartum and gained weight after that.
- *Postpartum weight retention and weight gain (PPWR+WG):* Women who did not return to their pregestational weight during the first 6 months and, on average, gained weight through 12 months postpartum.

We imputed weight at 12 months for 100 women with missing weight at this time point using a multiple regression model. For this procedure, we used the information from the subsample of women (n=345) with weights available at both 12 and 18 months postpartum. This subsample was statistically comparable in demographic and anthropometric characteristics to the imputed set (n=100) and the overall cohort. Weights at 12 and 18 months were logarithmically transformed to maximize their linear association, as suggested by the Box-Cox family of transformations [31]. A basic model included weight at 18 months as the only independent variable and explained 96% of the variability of weight at 12 months. However, we included additional covariates to improve the model explanatory capacity and to increase precision in the model estimates, namely age, marital status, and pregestational BMI. The final model achieved goodness of fit. To predict weight on the original scale, we used the exponential function.

***Covariates***

At the first study visit, women reported their age, parity (primiparous or multiparous), marital status (single/separated or married/cohabitating) and education (basic: elementary and secondary school, middle: high school, and college: at least college). Women were classified into six SES categories (A/B (highest), C+, C, D+, D, E) using a validated questionnaire that included 13 items on household assets and conditions (i.e. housing quality, services, material goods), and head of household education [32]. For the present analysis, the six categories were collapsed into three: high (A/B, C+, and C), middle (D+) and low (D, E). Gestational age at delivery was calculated from the child’s birth date and the self-reported last menstrual period date. We used the Capurro method, which is based on the newborn´s physical characteristics, as a secondary method to estimate gestational age. In cases where the two methods differed by >3 weeks, we used the Capurro method-derived gestational age [33].

Women provided information on smoking history, physical activity, and sedentary activities via questionnaire at the first study visit. Women were categorized as never smokers, smokers around pregnancy and former smokers (i.e. quit at least one year before pregnancy). Women reported leisure-time exercise as days per week and time per day invested in activities such as walking, running, swimming and aerobics, among others. Because of the high prevalence of women who did not engage in any leisure-time activity (87%), we dichotomized this variable as physically active or not. Women also reported time spent reading or watching TV during weekdays and weekends. We computed average hours per day spent in these sedentary activities and categorized them as $<2$ h/day or $\geq 2$ h/day.

***Statistical analysis***

We described participant characteristics by the pattern of postpartum weight change using mean (SD) for numeric variables and percentages for categorical variables. The statistical significance of the associations was evaluated with multinomial logistic regression models.

To evaluate the associations of pregestational BMI, GWG and breastfeeding (each categorized) with patterns of postpartum weight change (dependent variable), we fit multinomial logistic regression models. The reference group was women who returned to their pregestational weight at 12 months postpartum. We first included each predictor individually in separate models to assess their independent effects on patterns of postpartum weight change. All the models were adjusted for relevant confounders selected after a thorough literature review, including maternal age, marital status, education, parity, and SES. The models including GWG as the main predictor were further adjusted for pregestational BMI, smoking history, physical activity, and sedentary activities in pregnancy. The models for breastfeeding were additionally adjusted by pregestational BMI, adequacy of GWG, smoking history, gestational age at delivery and complications of pregnancy including preeclampsia, gestational hypertension, and gestational diabetes. The Hosmer-Lemeshow test was performed to assess the goodness-of-fit of the models [(34)]. For comparison, we performed the same analysis (i.e. association between pregestational BMI, GWG and breastfeeding with patterns of postpartum weight change) excluding women with imputed weight at 12 months. The results did not differ substantially, therefore, only the results on the full dataset are presented.

In a sensitivity analysis, we used a modified definition of patterns of postpartum weight change considering a 0 g instead of the 500 g margin as a threshold to return to pregestational weight. Additionally, to compare our proposed classification of patterns of weight change with an outcome commonly reported in the literature [(7,11,35)], we evaluated the association of pregestational BMI, GWG and breastfeeding at one month with the odds of substantial postpartum weight retention using logistic regression models. Women were classified as having substantial postpartum weight retention if the difference between their weight at 12 months and their pregestational weight was ≥4.5 kg.

We performed all the analyses in STATA 15 (StataCorp LP, College Station, Texas).

## Results

Women were 27 years on average, the majority had basic education only (42%), were married or cohabitating (82%), had low SES (53%) and were multiparous (64%) **(Table 1)**. Pregestational overweight affected 41% and obesity 18% of the women. Mean (SD) gestational weight gain was 7.4 (3.1) kg, and adequate gestational weight gain (47%) was more common than insufficient (26%) and excessive (27%) gain. The majority (53%) practiced partial breastfeeding at one month postpartum, and 28% practiced exclusive breastfeeding.

Most women returned to their pregestational weight by 12 months postpartum (57%), while 8% had PPWR, 14% PPWG, and 21% PPWR+WG. Marital status, parity, pregestational BMI and GWG, differed between patterns of postpartum weight change (Table 1). Mean (SD) weight change at 12 months postpartum for all women was 0.2 (4.6) kg with a range of -14.7 kg to 18.2 kg. Women who returned to their pregestational weight lost on average 2.8 (2.7) kg by 12 months postpartum, those who retained increased 2.9 (2.1) kg, and women who gained also increased 2.9 (1.8) kg. Women classified as PPWR+WG experienced the highest weight increase from pregestational to 12 months postpartum with a mean of 5.8 kg (3.6). As shown in **Figure 1**, weight trajectories from before pregnancy to 12 months postpartum also differed between the four patterns of postpartum weight change.

**Tables 2-4** present the association of each predictor with patterns of postpartum weight change. In the age-adjusted model **(Table 2)**, pregestational overweight and obesity, compared to normal weight, were each associated with a higher risk of PPWG (overweight: relative risk ratio (RRR) 2.5 [95% CI: 1.3, 4.8]; obesity: RRR 2.2 [1.0, 4.7]). They were not associated with PPWR or PPWR+WG, although, obesity showed a protective tendency for PPWR, but the 95% CI included the null value. These results persisted after adjustment for parity and sociodemographic covariates (Model 2).

Excessive GWG, in comparison to adequate GWG, was associated with a higher risk of PPWR (RRR 3.3 [1.6, 6.9]) and PPWR+WG (RRR 2.4 [1.4, 4.2]). On the other hand, insufficient GWG was associated with a lower risk of PPWR+WG (RRR 0.4 [0.2, 0.9]) **(Table 3).** These associations became somewhat stronger after adjustment for pregestational BMI, sociodemographic characteristics and lifestyle behaviors during pregnancy (Model 2). GWG was not associated with PPWG in any of the models.

In the age-adjusted model, partial and exclusive breastfeeding at one month, compared to no breastfeeding, appeared to be protective for PPWR but not for PPWG or PPWR+WG **(Table 4)**. Predominant breastfeeding was not associated with any of the patterns of postpartum weight change. After adjustment for covariates (Model 2), the association of partial breastfeeding with PPWR persisted, but the 95% CI included the null (RRR 0.4 [0.1, 1.1]). On the other hand, the association between exclusive breastfeeding and lower risk of PPWR became stronger, and confidence intervals excluded the null (RRR 0.3 [0.1, 0.9]).

In a sensitivity analysis using a modified definition of the outcome, we observed similar associations between pregestational BMI, GWG, and patterns of postpartum weight change (**Supplementary Table 1)**. In this supplementary analysis, exclusive breastfeeding at one month, compared to no breastfeeding, was not associated with a lower risk of PPWR (RRR 0.5 [0.2, 1.4]). We also wanted to assess how our proposed classification of patterns of postpartum weight change compared with the widely used definition of substantial postpartum weight retention (i.e. retaining ≥4.5 kg at 12 months postpartum). In our sample, 17% of women experienced substantial postpartum weight retention (**Supplementary Table 2**). Of these women, 13%, 17%, and 70% would be classified as PPWR, PPWG, and PPWR+WG, respectively, according to our classification. In age-adjusted and fully adjusted models, pregestational BMI and breastfeeding at one month were not associated with the odds of retaining ≥4.5 kg. On the other hand, insufficient GWG, compared to adequate GWG, was associated with lower odds of substantial postpartum weight retention (RRR 0.4 [0.2, 0.9]) and excessive GWG with higher odds of this outcome (RRR 3.3 [1.8, 6.0]).

## Discussion

Weight increases associated with pregnancy may be the result of retaining gestational weight, gaining weight postpartum or both. These patterns of weight change are associated with potentially modifiable factors. In this study, pregestational overweight and obesity were associated with a higher risk of PPWG during the first year postpartum, whereas excessive GWG was associated with a higher risk of PPWR and PPWR+WG. Exclusive breastfeeding at one month postpartum decreased the risk of PPWR.

In our study, 21% of women experienced PPWR+WG the first year after delivery, while 14% experienced PPWG and 8% PPWR. To date, most of the studies have lumped all women who do not return to their pregestational weight as having PPWR. None of these studies have differentiated weight gain women may have also experienced [(9,11,36–39)]. Some studies have shown that PPWG occurs in the late postpartum (≥12 or ≥18 months) [(5,7,8,40)]. We build on these results by showing that a considerable proportion of women gains weight, either alone or combined with retention, within the first 12 months after delivery. To the best of our knowledge, only one study has characterized different patterns of weight change the first year after delivery, using repeated weight assessments [(4)]. In this study of 305 Canadian women, 15% were heavier at 3 months postpartum, compared to their pregestational weight, and gained weight from 3 to 12 months. Sixty-six percent were heavier at 3 months and lost weight from 3 to 12 months. However, on average, they were still heavier compared to their pregestational weight by 12 months. Another 11% were lighter at 3 months, compared to their pregestational weight, and re-gained from 3 to 12 months [(4)]. The three groups described in this study are comparable to our patterns of PPWR+WG, PPWR, and PPWG, respectively.

In our study, pregestational obesity showed a protective tendency for PPWR at one year. In different studies including a recent meta-analysis, a higher pregestational BMI was associated with lower weight retention [(10,18,41)]. We also found that women with pregestational overweight and obesity, compared to normal weight, had a higher risk of PPWG**.** Similar to our cohort, in the study of Kew et al., the women who regained weight after having reached their pregestational weight had the highest BMI before pregnancy [(4)]. Lipsky et al., in a study of 413 American women, found that women with overweight and obesity, compared to normal weight, had increased odds of gaining ≥2.25 kg from 1 to 2 years postpartum (overweight OR 2.4 [1.3, 4.4]; obese OR 3.0 [1.6, 5.6]) [(7)]. Gunderson et al. also showed that women with overweight and obesity were more likely to gain ≥2 kg from 6 weeks to a median of 2 years postpartum [(13)]. The reason why women with pregestational overweight or obesity are more likely to gain weight postpartum is unclear. However, it is possible that behavioral factors associated with weight gain, such as lower physical activity, longer time in sedentary activities and unhealthy dietary patterns are more prevalent among these groups of women [(40,42)].

We found that excessive GWG was associated with an increased risk of PPWR and PPWR+WG, while insufficient GWG was associated with a lower risk of PPWR+WG. Higher GWG has been consistently associated with PPWR [(10,11,18,19,37,41,43)], although none of these studies have made the distinction between retention alone versus retention and gain. In a recent meta-analysis, GWG below recommendations, compared to within recommendations, was associated with lower weight retention (−2.1 kg [−2.4, −1.9 kg]), and GWG above the IOM with higher weight retention (3.2 kg [2.8, 3.6 kg]) (18). An analysis of postpartum weight trajectories in Norwegian women found that excessive GWG was associated with two weight trajectories characterized by high initial weight retention (six months), followed by either weight loss or sustained weight gain through three years postpartum. Insufficient GWG was associated with a lower risk of these trajectories (14). A recent study showed that excess GWG represents mostly gains in maternal fat (44). This additional fat mass may persist beyond delivery and explain the increased risk of PPWR or PPWR+WG observed in our study.

In the present study, exclusive breastfeeding at one month was associated with a decreased risk of PPWR. Martin et al., in a study of Australian women, did not find any association between the type of breastfeeding at three months and weight retention at 12 months (39). Consistent with our findings, López-Olmedo et al., in a group of Mexican women, found that those who breastfed exclusively until the third month postpartum had greater weight loss in comparison to those non-breastfeeding (45). One recent meta-analysis did not find an association between breastfeeding and postpartum weight change (21). Methodological differences between studies including different exposure times or definitions of breastfeeding, and lack of adjustment by relevant covariates might explain the inconsistency in findings.

Our study has several implications. First, we proposed a different approach to characterize postpartum weight trajectories in women. Although some authors have suggested using the term *postpartum weight retention* within a limited period following delivery, for example, 12 to 18 months (5,7), we have shown that women also gain weight during this time. In fact, when we classified women as having substantial postpartum weight retention (i.e. retaining ≥4.5 kg at 12 months), we showed that only 13% experienced PPWR, whereas 17% had PPWG and 70% had PPWR+WG. Second, our approach allowed us to identify specific modifiable factors associated with each of the patterns of postpartum weight change, some of which were not identified using the traditional definition of substantial postpartum weight retention. Focused interventions during the first year postpartum could target women with excessive GWG and pregestational overweight or obesity. Third, weight change during the first year postpartum can have longlasting effects on women's weight [6,46], and therefore chronic disease risk [47–49]. Nevertheless, the long-term health consequences of each of the patterns of postpartum weight change are unknown. However, in our study, women who experienced PPWR+WG increased more weight (5.8 kg) which, if maintained, could increase their risk of weight-related sequelae such as type 2 diabetes and coronary heart disease [47–49]. More research in this subject is warranted.

Our findings should be evaluated considering the strengths and limitations of the study. Generalizability may be limited because our population consisted primarily of women of low SES living in Mexico City. Also, only 53% of the original cohort had information available for this analysis but analyzed and non-analyzed women were not substantially different. The potential for confounding was minimized by adjusting for relevant covariates for each of the associations studied. However, we did not have information on diet, which likely plays a role in the variability of postpartum weight change [50–52]. We categorized breastfeeding practices according to the WHO [30] and adjusted by pregestational BMI, GWG, and parity, which are important confounders of the association between breastfeeding and postpartum weight change [22]. Studying breastfeeding at one month postpartum may be seen as a limitation. However, by doing this we were certain that the exposure (i.e. breastfeeding) preceded the outcome of interest (i.e. patterns of weight change). A strength of this study is that most weights used for the analysis were objectively measured by trained personnel. One exception was weight at 12 months that was imputed for a subset of women. However, the results excluding this subset of women were comparable to those of the main analysis including imputed and non-imputed weights. Self-reported pregestational weight is highly subject to error in this population and misreport can be substantial [26]. In the absence of measured pregestational weight, using an estimated pregestational weight rigorously validated, instead of self-reported, might be a strength of this analysis.

## Conclusions

Our findings suggest that while most women return to their pregestational weight one year after delivery, an important subset experiences retention of gestational weight, weight gain or both, which may increase their long-term obesity risk. To minimize any negative effect of pregnancy on women´s weight, we need to improve our understanding of the factors associated with maternal weight change after delivery. Since the postpartum is a time when women are usually motivated to adopt lifestyle changes, it may represent the ideal period to intervene to optimize maternal weight. For some women, this time also represents the preconception period for a subsequent pregnancy. Future postpartum interventions should target high-risk groups for unfavorable weight change patterns such as women with excessive GWG, pregestational overweight or obesity, and who do not breastfeed.

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**Table 1. Participant characteristics according to patterns of postpartum weight change in 500 women participating in the PROGRESS cohort**

| | | Patterns of postpartum weight change | | | | |
|---|---|---|---|---|---|---|
| | **All women n=500** | **Return to pregestational weight** | **PPWR** | **PPWG** | **PPWR + WG** | |
| | | **n=286 (57.2%)** | **n=40 (8%)** | **n=70 (14%)** | **n=104 (20.8%)** | |
| **Characteristic** | | **Mean (SD) or percent** | | | | **p *** |
| **<u>Pre-pregnancy</u>** | | | | | | |
| **Maternal age (years)** | 27.2 ( 5.5) | 27.3 (5.4) | 26.4 (4.3) | 27.7 (6.3) | 26.8 (5.4) | 0.582 |
| **Education** | | | | | | 0.518 |
| Basic | 42.2% | 40.9% | 57.5% | 40.0% | 41.4% | |
| Middle | 35.2% | 36.4% | 30.0% | 34.3% | 34.6% | |
| College | 22.6% | 22.7% | 12.5% | 25.7% | 24.0% | |
| **Marital status** | | | | | | *0.047* |
| Married/ cohabitating | 82.0% | 85.7% | 85.0% | 74.3% | 76.0% | |
| **SES** | | | | | | 0.181 |
| Low | 52.6% | 51.8% | 55.0% | 44.3% | 59.6% | |
| Medium | 22.4% | 21.0% | 22.5% | 24.3% | 25.0% | |
| High | 25.0% | 27.3% | 22.5% | 31.4% | 15.4% | |
| **Parity** | | | | | | *0.002* |
| Multiparous | 64.0% | 69.6% | 72.5% | 55.7% | 51.0% | |
| **Pregestational BMI** | | | | | | *0.033* |
| Normal weight | 41.0% | 43.4% | 55.0% | 24.3% | 40.4% | |
| Overweight | 40.6% | 37.8% | 35.0% | 52.9% | 42.3% | |
| Obese | 18.4% | 18.9% | 10.0% | 22.9% | 17.3% | |
| **<u>Pregnancy</u>** | | | | | | |
| **Gestational age at delivery (weeks)** | 38.4 ( 1.6) | 38.3 (1.6) | 38.4 (1.7) | 38.2 (1.5) | 38.7 (1.7) | 0.203 |
| **Smoking history** | | | | | | 0.104 |
| Smokers around pregnancy | 24.4% | 23.4% | 35.0% | 24.3% | 23.1% | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Former smokers | 8.8% | 8.7% | 5.0% | 2.9% | 14.4% | |
| Never smokers | 66.8% | 67.8% | 60.0% | 72.9% | 62.5% | |
| **Physical activity** | | | | | | 0.272 |
| No | 87.2% | 85.3% | 95.0% | 88.6% | 88.5% | |
| **Time in sedentary activities (reading, watching TV)** | | | | | | 0.153 |
| ≥2 hours/day | 55.8 | 51.8 | 65.0 | 57.1 | 62.5 | |
| **GWG ł** | 7.4 (3.1) | 6.7 (3.0) | 10.5 (2.7) | 6.4 (2.5) | 8.7 (2.5) | *<0.001* |
| **Adequacy of GWG ł** | | | | | | *<0.001* |
| Insufficient | 26.1% | 32.8% | 0.0% | 32.8% | 13.0% | |
| Adequate | 46.8% | 48.4% | 43.2% | 45.3% | 44.6% | |
| Excessive | 27.2% | 18.8% | 56.8% | 21.9% | 42.4% | |
| **Postpartum** | | | | | | |
| **Type of breastfeeding at one month ł** | | | | | | 0.645 |
| No breastfeeding | 13.3% | 11.2% | 22.5% | 9.2% | 17.3% | |
| Partial | 53.3% | 54.2% | 45.0% | 55.4% | 52.9% | |
| Predominant | 5.5% | 5.6% | 7.5% | 6.2% | 3.9% | |
| Exclusive | 28.0% | 28.9% | 25.0% | 29.2% | 26.0% | |

PPWR, postpartum weight retention; PPWG, postpartum weight gain; PPWR+WG, postpartum weight retention + weight gain; SES, socioeconomic status; BMI, body mass index, GWG, gestational weight gain.
* p-value for the association between maternal characteristics and patterns of postpartum weight change using single multinomial logistic regression models.
ł GWG and adequacy of GWG: n= 449 (n=256 return to preg. weight, n=37 for PPWR, n=64 for PPWG and n=92 for PPWR+WG); type of breastfeeding at one month: n=458 (n=249 return to preg. weight, n=40 for PPWR, n=65 for PPWG and n=104 for PPWR+WG).

**Table 2. Association of pregestational BMI with patterns of postpartum weight change**

| ***Reference group: return to pregestational weight*** | | PPWR | | | PPWG | | | PPWR+WG | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | **Model 1** | | | | | |
| **Pregestational BMI** | **n** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| **Normal weight** | 205 | | *Reference* | | | *Reference* | | | *Reference* | |
| **Overweight** | 203 | 0.77 | 0.37, 1.61 | *0.491* | 2.53 | 1.33, 4.81 | ***0.005*** | 1.26 | 0.76, 2.09 | *0.370* |
| **Obese** | 92 | 0.44 | 0.14, 1.37 | *0.158* | 2.19 | 1.02, 4.71 | ***0.045*** | 1.04 | 0.54, 1.99 | *0.911* |
| | | | | | **Model 2** | | | | | |
| | **n** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| **Normal weight** | 205 | | *Reference* | | | *Reference* | | | *Reference* | |
| **Overweight** | 203 | 0.81 | 0.39, 1.70 | *0.583* | 2.49 | 1.30, 4.77 | ***0.006*** | 1.27 | 0.75, 2.13 | *0.373* |
| **Obese** | 92 | 0.42 | 0.13, 1.29 | *0.129* | 2.19 | 1.00, 4.79 | ***0.049*** | 1.03 | 0.53, 2.00 | *0.940* |

Results from multinomial logistic models. PPWR, postpartum weight retention; PPWG, postpartum weight gain; PPWR+WG, postpartum weight retention + weight gain; BMI, body mass index; RRR, relative risk ratio; CI, confidence interval.
Model 1: adjusted for age.
Model 2: adjusted for age, marital status, education, parity, and socioeconomic level.

**Table 3. Association of gestational weight gain with patterns of postpartum weight change**

| ***Reference group: return to pregestational weight*** | | **PPWR** | | | **PPWG** | | | **PPWR+WG** | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Adequacy of GWG** | | | | | **Model 1** | | | | | |
| | **n** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| **Insufficient ł** | 117 | -- | -- | -- | 1.08 | 0.58, 2.02 | *0.814* | 0.43 | 0.21, 0.87 | ***0.018*** |
| **Adequate** | 210 | | *Reference* | | | *Reference* | | | *Reference* | |
| **Excessive** | 122 | 3.32 | 1.59, 6.92 | ***0.001*** | 1.29 | 0.62, 2.65 | *0.496* | 2.43 | 1.40, 4.23 | ***0.002*** |
| | | | | | **Model 2** | | | | | |
| | **n** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| **Insufficient ł** | 117 | -- | -- | -- | 1.30 | 0.67, 2.53 | *0.439* | 0.42 | 0.20, 0.88 | ***0.021*** |
| **Adequate** | 210 | | *Reference* | | | *Reference* | | | *Reference* | |
| **Excessive** | 122 | 6.16 | 2.62, 14.50 | <***0.001*** | 0.97 | 0.45, 2.10 | *0.937* | 3.04 | 1.62, 5.69 | ***0.001*** |

Results from multinomial logistic models. PPWR, postpartum weight retention; PPWG, postpartum weight gain; PPWR+WG, postpartum weight retention + weight gain; GWG, gestational weight gain; RRR, relative risk ratio; CI, confidence interval.
ł n=0 for insufficient GWG and postpartum weight retention.
Model 1: adjusted for age.
Model 2: adjusted for age, marital status, education, parity, socioeconomic level, pregestational BMI, smoking history, physical activity, and sedentary activities in pregnancy.

**Table 4. Association of breastfeeding with patterns of postpartum weight change**

| ***Reference group: return to pregestational weight*** | | **PPWR** | | | **PPWG** | | | **PPWR+WG** | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Type of breastfeeding at 1 month** | | | | | **Model 1** | | | | | |
| | **n** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| **No breastfeeding** | 61 | | *Reference* | | | *Reference* | | | *Reference* | |
| **Partial** | 244 | 0.43 | 0.17, 1.05 | *0.063* | 1.24 | 0.47, 3.22 | *0.665* | 0.64 | 0.33, 1.26 | *0.197* |
| **Predominant** | 25 | 0.65 | 0.15, 2.81 | *0.567* | 1.34 | 0.33, 5.56 | *0.683* | 0.44 | 0.12, 1.55 | *0.200* |
| **Exclusive** | 128 | 0.44 | 0.16, 1.19 | *0.104* | 1.23 | 0.45, 3.40 | *0.690* | 0.59 | 0.28, 1.23 | *0.156* |
| | | | | | **Model 2** | | | | | |
| | **n** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| **No breastfeeding** | 55 | | *Reference* | | | *Reference* | | | *Reference* | |
| **Partial** | 222 | 0.38 | 0.13, 1.09 | *0.071* | 1.23 | 0.44, 3.38 | *0.693* | 0.61 | 0.28, 1.33 | *0.214* |
| **Predominant** | 22 | 0.76 | 0.12, 4.61 | *0.761* | 2.18 | 0.47, 10.02 | *0.316* | 0.51 | 0.12, 2.19 | *0.367* |
| **Exclusive** | 114 | 0.27 | 0.08, 0.91 | ***0.035*** | 1.57 | 0.52, 4.72 | *0.419* | 0.69 | 0.29, 1.69 | *0.421* |

Results from multinomial logistic models. PPWR, postpartum weight retention; PPWG, postpartum weight gain; PPWR+WG, postpartum weight retention + weight gain; RRR, relative risk ratio; CI, confidence interval.
Model 1: adjusted for age.
Model 2: adjusted for age, marital status, education, parity, socioeconomic level, pregestational BMI, adequacy of GWG, smoking history, gestational age at delivery and complications of pregnancy (i.e., preeclampsia, gestational hypertension, and gestational diabetes).

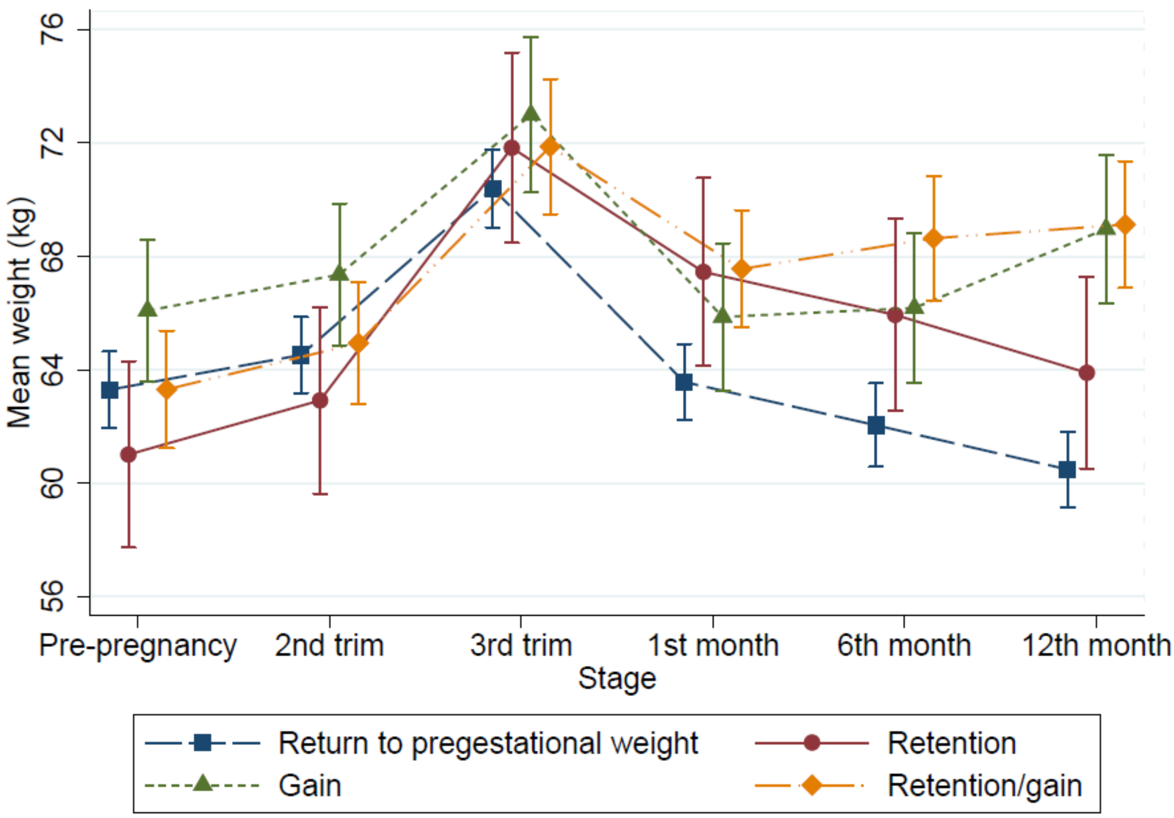


**Figure 1.** Weight changes from pre-pregnancy to 12 months postpartum by patterns of weight change. The graph displays the mean weight in kg and 95% CI at each time point within each category.

## 5. Artículo 2

**Target journal:** American Journal of Clinical Nutrition

**Title:**

Maternal patterns of weight change one year after delivery are associated with cardiometabolic risk factors at six years postpartum in Mexican women

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None.

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**Short running head:**

Postpartum weight change and cardiometabolic risk

**Abbreviations:**

DBP: diastolic blood pressure

FFQ: food frequency questionnaire

GWG: gestational weight gain

HDL-c: high-density lipoprotein cholesterol

HDP: hypertensive disorders of pregnancy

HOMA-IR: homeostatic model assessment for insulin resistance

*LDL-c: l*ow-density lipoprotein cholesterol

LGA: large for gestational age

LMP: last menstrual period

PROGRESS: Programming Research in Obesity, Growth, Environment and Social Stressors

PPWG: postpartum weight gain

PPWR: postpartum weight retention

PPWR+WG: postpartum weight retention + gain

SBP: systolic blood pressure

SES: socioeconomic status

SSBs: sugar-sweetened beverages

TG: *triglycerides*

Total-c: total cholesterol

WC: waist circumference

**Abstract**

**Background.** Pregnancy is a contributor to the obesity epidemic in women, probably through postpartum weight retention (PPWR), weight gain (PPWG), or a combination of both (PPWR+WG). Evidence suggests that weight retained after pregnancy consist of visceral fat, therefore, PPWR and PPWR+WG may be associated with long-term metabolic dysfunction in women. **Objective.** To evaluate the associations between patterns of weight change one year after delivery and cardiometabolic risk factors at six years postpartum. **Design.** Secondary analysis of 361 women from the prospective cohort *PROGRESS.* Using principal component analysis, we grouped cardiometabolic risk factors into 1) body mass index (BMI), waist circumference (WC), homeostatic model assessment for insulin resistance (HOMA-IR), high-density lipoprotein cholesterol (HDL-c), triglycerides (TG), glucose; 2) systolic (SBP) and diastolic blood pressure (DBP); 3) low-density lipoprotein cholesterol and total cholesterol. Using path analysis we studied direct associations (patterns of weight change-outcomes), and indirect associations through BMI at six years postpartum. **Results.** Around 60% of women returned to their pregestational weight (reference) by one year, 6.6% experienced PPWR, 13.9% PPWG, and 19.9% PPWR+WG. Women with PPWR+WG, vs. the reference, had higher BMI and WC at six years (2.30 kg/m$^2$, 95% CI [1.67, 2.93]; 3.38 cm [1.14, 5.62]). This was also observed in women with PPWR (1.80 kg/m$^2$ [0.80, 2.79]; 3.15 cm [-0.35, 6.65]) and PPWG (1.22 kg/m$^2$ [0.53, 1.92]; 3.32 cm [0.85, 5.78]). PPWR+WG had a direct association with HOMA-IR (0.21 units [0.04, 0.39]). The three patterns of weight change, vs. the reference, had significant indirect associations with HOMA-IR, glucose, TG, HDL-c, SBP, and DBP through BMI at six years. **Conclusions:** Women with PPWR+WG, compared to those who recover their pregestational weight postpartum, are at high-risk for obesity and insulin resistance.

Interventions targeting women the first year postpartum may have implications for their long-term risk of obesity and cardiovascular disease.

**Keywords**

Postpartum weight change, postpartum weight retention, postpartum weight gain, adiposity, cardiovascular risk, PROGRESS cohort

## Introduction

In Mexico, the prevalence of obesity among women from 20 to 49 years of age increased by almost 300% over the past three decades (1). Pregnancy-related weight changes are possible contributors to the obesity epidemic in reproductive-aged women (2,3). Parous, compared to nulliparous women, experience a significant increment in weight and waist circumference in the years following delivery (4). The increased adiposity following pregnancy may put women at higher risk of obesity and metabolic dysfunction.

According to studies conducted in high-income countries, less than 50% of women return to their pregestational weight one year after delivery (5–7). Postpartum weight retention (PPWR) (i.e. weight retained from pregnancy) is a common problem with disparate consequences on women´s weight. On average women retain from 0.8 to 2.6 kg at one year postpartum (5,8,9), but up to 27% retain ≥4.5 kg (5). In addition, few studies have shown that some women experience postpartum weight gain (PPWG) (i.e. weight gain that originates entirely during the postpartum period), or a combination of PPWR and PPWG (PPWR+WG) (10–12).

During pregnancy, fat is gained in peripheral and central sites, however, after delivery, peripheral fat is preferentially mobilized (13,14). This change in fat distribution favors the accumulation of central adipose tissue, from which a large part represents visceral fat (14). Therefore, it has been suggested that weight retained after pregnancy consists of visceral fat, which may be especially harmful to women´s health. Hence, it is possible that PPWR, either alone or combined with PPWG, increases the risk of metabolic dysfunction in women.

The literature supporting the association between patterns of postpartum weight change and cardiometabolic risk factors is scarce. Different studies have shown associations between excessive gestational weight gain (GWG) and BMI, weight change from pre-pregnancy, waist circumference (WC) and systolic blood pressure (SBP), 8 to 16 years after delivery (15,16). Excessive GWG has also been associated with increased odds of overweight or obesity, and central adiposity (15,16). Given that GWG is strongly associated with PPWR (17), it has been argued that the latter is partly responsible for some of these associations (15,16). In addition, there is evidence suggesting that PPWR at six months and weight gain from 6 to 18 months are strongly associated with weight and BMI-adjusted WC, 7 years after delivery (11). Altogether, there is evidence to support an association between PPWR, and other patterns of postpartum weight change, with long-term adiposity and cardiometabolic outcomes, however, to the best of our knowledge, no other studies have evaluated these associations. Using data from a prospective cohort study, we aimed to evaluate the associations between four mutually exclusive patterns of weight change one year after delivery (return to pregestational weight, PPWR, PPWG, and PPWR+WG) and cardiometabolic risk factors at six years postpartum.

## Subject and methods

### *Study design and participants*

This was a secondary analysis of 948 mothers participating in the Mexico City-based prospective cohort *Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS).* Between 2007 and 2011, *PROGRESS* enrolled women who were ≥18 years old, in the second trimester of a singleton pregnancy (<22 weeks), and who received health insurance and prenatal care through the Mexican Social Security System. The eligibility criteria and a description of the cohort have been published elsewhere (18,19).

Out of the 948 participating women, 515 had information to characterize their pattern of postpartum weight change (**Supplemental figure 1)**. After excluding women who became pregnant within the first year postpartum (n=14), and one woman with an extreme weight loss during pregnancy and after delivery, the sample with information on the exposure was 500. Out of these women, 391 had information on adiposity and cardiometabolic outcomes at six years postpartum (72 months' visit). Of these 391 women, 101 became pregnant again between one and six years postpartum. During pregnancy, women experience physiological changes in adiposity, insulin resistance, glucose tolerance and lipoprotein metabolism (20), and some of these alterations remain for several months after delivery (21,22). Considering this, we excluded women who at the six-year postpartum visit were pregnant (n=9) or who had given birth within the 12 months prior to the visit (n=21). The analytic sample included 361 women, who were comparable to those non-analyzed (n=587) in terms of demographics, anthropometric characteristics, lifestyle behaviors and patterns of postpartum weight change. The only exceptions were the age at enrollment (27.5 vs. 26.7 years), marital status (16.1% vs. 21.3% single), and smoking during pregnancy (69.8% vs. 61.3% never smokers).

The Committees on Ethics, Biosafety, and Research at the Mexican National Institute of Public Health, as well as the Institutional Review Boards of the participating institutions approved the cohort procedures. At enrollment and also at the six-year visit, women provided written informed consent after all the study procedures were explained to them.

***Measurements***

This analysis was focused on information obtained by in-person interviews at the second and third trimester of pregnancy and at 1, 6, 12 and 72 months postpartum. A description of the measurements is presented below.

***<u>Exposure: patterns of postpartum weight change</u>***

We categorized postpartum weight change into four mutually exclusive patterns using pregestational weight and weights measured at 1, 6, and 12 months postpartum. For this classification, the following definitions were used:

- *Return to pregestational weight:* Women who returned to their pregestational weight at 12 months postpartum. This group included women who lost weight compared to the pregestational state.
- *Postpartum weight retention (PPWR):* Women who, on average, lost weight through 12 months postpartum without ever reaching their pregestational weight.
- *Postpartum weight gain (PPWG):* Women who reached their pregestational weight at any point during the first six months postpartum and gained weight thereafter.
- *Postpartum weight retention and weight gain (PPWR+WG):* Women who did not return to their pregestational weight during the first six months and, on average, gained weight through 12 months postpartum.

Return to pregestational weight at any postpartum time point was defined as a weight no more than 500 g higher than pregestational weight. Pregestational weight was estimated from a prediction model as described in the covariates section. For a subset of women, we used imputed weight at 12 months as previously reported (Soria-Contreras et al., 2019, unpublished manuscript).

***<u>Outcomes: cardiometabolic risk factors</u>***

At six years postpartum, trained nurses measured women´s WC and weight (digital scale). WC was measured above the iliac crest to the nearest 0.1 cm with a fiberglass tape. These measurements were taken in duplicate, following standardized procedures (23). In case of differences ±0.2 kg for weight or ±0.5 cm for waist circumference, they took an additional measurement. The average of the measurements was used for analysis. Height was measured at the first study visit following standardized procedures (23). We calculated BMI at six years postpartum as weight divided by height squared. Nurses recorded SBP and diastolic blood pressure (DBP) two times, three minutes apart, with an ambulatory blood pressure monitor (Spacelabs 90217). The average was used for analysis.

Nurses collected fasting blood samples from which plasma glucose, total cholesterol (total-c) and triglycerides (TG) were assayed by enzymatic procedures using an automated analyzer (DiaSys Respons®910). High-density lipoprotein cholesterol (HDL-c) was assayed by an immunoprecipitation-based method (Immuno FS, DiaSys Respons®910). Insulin was determined by a solid-phase, enzyme-labeled chemiluminescent immunometric assay (Siemens IMMULITE 1000). We calculated insulin resistance with the homeostatic model assessment (HOMA-IR=fasting insulin [uU/mL] x fasting glucose [mmol/L]/22.5), and low-density lipoprotein cholesterol (LDL-c) with the Friedewald equation (24).

***<u>Covariates</u>***

At enrollment, women reported their age, parity, marital status and education (basic: elementary and secondary school, middle: high school, and college: at least college). Using a validated questionnaire (25), women provided information on household assets, conditions (i.e. housing quality, services, material goods), and head of household education. With this information, they were classified into six socioeconomic status (SES) categories (A/B (highest), C+, C, D+, D, E). For this analysis, we collapsed the categories into three: high (A/B, C+, and C), middle (D+) and low (D, E). Women also provided information on smoking habits, and time spent in sedentary activities such as reading and television viewing.

We derived mean pregnancy SBP and DBP as the average of second and third trimesters' readings of SBP and DBP, respectively. Women were classified as being diagnosed with a hypertensive disorder of pregnancy (HDP) (preeclampsia and gestational hypertension) using information collected from the medical record. Gestational age at delivery was calculated from the child's birth date and the self-reported last menstrual period (LMP). The Capurro method was used as a secondary method to estimate gestational age. In cases where the two methods differed by >3 weeks, the Capurro method-derived gestational age was preferred (26). Newborn´s size for gestational age was determined by calculating the birth weight for gestational age and sex z-score, using the reference data of the International Fetal and Newborn Growth Consortium for the 21st Century (27). A birth weight z-score >90$^{th}$ percentile was considered large for gestational age (LGA).

Women self-reported their pregestational weight at the first study visit (second trimester). However, given that this indicator tends to be misreported (28), we used an estimated pregestational weight obtained from a linear mixed-effects model. The model used measured weights during pregnancy (second and third trimester), as well as clinical weight measurements in the 6 months prior to pregnancy through the early pregnancy period that were recovered from clinical records. It also included days of gestation at the time of weight collection, maternal height, age, SES, education, parity, and self-reported pregestational weight. Model´s predictions of weight at the LMP were validated against weights objectively measured at the Mexican Social Security System clinics for a subset of women (measured within +/-20 days of the LMP, n=87). The predictive accuracy assessed by the root mean square error was 3.2 kg. In a *post hoc* analysis, we compared model´s predictions with those obtained from a model recently proposed by Thomas et al. (28). A Bland-Altman plot showed good agreement between the two methods (data not shown). Also, the correlation between the two predictions was high (r=0.99), while the average difference was low (0.16±1.72 kg).

We calculated pregestational BMI as kg/m$^2$ and GWG as the difference between weight measured in the third trimester of pregnancy and estimated pregestational weight. Women were classified as having adequate, insufficient or excessive GWG for their gestational age following the United States Institute of Medicine guidelines (29,30). Using information reported via questionnaire at one month postpartum, we classified women as breastfeeding (any type) or not.

At six years postpartum, women reported information on current smoking (yes or no), current use of medications for diabetes (metformin and/or insulin) or hypertension (yes/no), and pregnancies occurred between one and six years postpartum. Women filled-in a semi-quantitative food frequency questionnaire (FFQ) that queried the consumption of 109 food items over the past week. The FFQ was validated and used in the 2006 Mexican Health and Nutrition Survey (31). From the FFQ, we derived total energy intake (kcal) and servings of sugar-sweetened beverages (SSBs) per day. We considered SSBs as the sum of ml consumed of regular soda, fruit drinks, fruit or flavored water with sugar, coffee or tea with added sugar. Total ml per day were divided by 355 ml to represent a standard serving. We focused on SSBs because of their excessive contribution to caloric intake in Mexican adults and their consistent association with the metabolic syndrome (32,33).

***Statistical analysis***

All the outcomes were modeled as continuous, with logarithmic transformations for glucose, HOMA-IR, HDL-c, TG, total-c, and LDL-c. Given the complex patterns of associations among the outcomes, we simplified the analysis by reducing the number of variables using a principal component approach. We identified three possible, non-correlated groups that explained 67% of the total variance. Group 1 included BMI, WC, glucose, HOMA-IR, HDL-c, and TG; group 2 included SBP and DBP, and group 3 total-c and LDL-c.

We used a path analysis approach to evaluate the associations between the patterns of postpartum weight change and each group of outcome variables. One of the advantages of path analysis is that direct and indirect associations among variables can be tested (34). In our analysis, we evaluated direct associations between the patterns of postpartum weight change and each outcome, and indirect associations mediated through BMI at six years for glucose, HOMA-IR, HDL-c, TG, SBP, DBP, and total-c and LDL-c.

For each outcome group, we constructed a complete initial model that included covariates derived from the literature**.** In all the outcome groups we included potential baseline and pregnancy-related covariates such as sociodemographic information, pregestational BMI, GWG, breastfeeding, time in sedentary activities and smoking during pregnancy. We also included the diagnosis of HDP because they have been associated with postpartum cardiovascular risk factors (35). In the three groups, some post-exposure covariates were included because they may act as mediator-outcome confounders (i.e. associated with BMI and outcomes at six years) or because they may be associated with the outcomes. These included pregnancy during follow up, smoking, energy intake and servings of SSBs at six years postpartum. The model for group 1 additionally included having had a newborn LGA (study pregnancy), which has been associated with postpartum adiposity, glucose, insulin and TG (35), and use of medications for diabetes at six years. The model for group 2 additionally included mean SBP and DBP during pregnancy and use of medications for hypertension at six years postpartum. A reduced model for each group of outcomes was achieved by eliminating all associations with a significance level >0.20. The robustness and fit of the reduced model were tested against the initial model, using the likelihood ratio test and Akaike's Information Criterion.

WC and BMI are both associated with cardiovascular mortality in the general population (36,37) and were strongly correlated (r=0.84) in our study. We did not choose WC as a mediator for our primary analysis because of its lower precision, especially when measured above the iliac crest (38,39). However, in a sensitivity analysis we evaluated the indirect associations between the patterns of postpartum weight change and cardiometabolic risk factors substituting BMI at six years by WC as mediator. The results were comparable with those presented in our main analysis and are thus not described in further detail (see **Supplemental table 1**).

We performed all analyses using Stata 15 (StataCorp LP, College Station, Texas).

## Results

At baseline, women were on average 27 years, most of them were married (83.9%), low SES (54.3%), multiparous (66.5%), had basic education only (42.7%) and had never been smokers (69.8%) **(Table 1)**. Women were on average overweight (26.5 kg/m$^2$) before pregnancy, had adequate weight gain during pregnancy (46.9%) and were breastfeeding at one month (85.8%). At one year postpartum, 59.6% had returned to their pregestational weight, while 6.6% experienced PPWR, 13.9% PPWG, and 19.9% PPWR+WG. Marital status, parity and GWG differed by the pattern of postpartum weight change ($p<0.05$).

**Supplemental figure 2** displays the average BMI by pattern of postpartum weight change from 12 to 72 months. On average women showed a trend to increase BMI from 12 to 72 months, with some variability by pattern of postpartum weight change. Women who returned to their pregestational weight by one year postpartum, showed the greatest increase in BMI from 12 to

72 months (1.9 kg/m$^2$), while those with PPWG and PPWR+WG experienced the lowest increase (~ 1 kg/m$^2$). Despite this, women who returned to their pregestational weight had the lowest increase in BMI from pre-pregnancy to 72 months with a mean of 0.6 kg/m$^2$; those with PPWR+WG had the highest increase from pre-pregnancy with a mean of 3.3 kg/m$^2$.

**Supplemental figure 3,** displays the initial model for all the outcome groups. **Figure 1 to 3** show the final adjusted path models for outcome group 1, 2 and 3. The gray arrows represent paths ($p<0.20$) between covariates, and patterns of weight change and cardiometabolic outcomes, which were not or primary interest. The black arrows (continuous and doted, $p<0.05$ and $0.05 \leq p<0.10$, respectively) represent the paths central to our research objective (i.e. patterns of postpartum weight change and outcomes at six years). **Table 2** shows the associations between the patterns of postpartum weight change and outcome group 1. For BMI and WC only direct associations are presented, whereas for glucose, TG, HOMA-IR, and HDL-c, direct and indirect associations are shown. Compared to the reference group, women who experienced PPWR+WG had the greatest BMI at six years ($\beta$ 2.30 kg/m$^2$, 95% CI [1.67, 2.93]), followed by women with PPWR (1.80 kg/m$^2$ [0.80, 2.79]), and PPWG (1.22 kg/m$^2$ [0.53, 1.92]). For WC, the increase was similar for the three groups with 3.38 cm [1.14, 5.62], 3.32 cm [0.85, 5.78] and 3.15 cm [-0.35, 6.65], for PPWR+WG, PPWG and PPWR, respectively. However, for PPWR the 95% CI for WC included the null value.

Women with PPWR+WG had a higher HOMA-IR (0.21 units [0.04, 0.39]), which translate to 23% higher insulin resistance compared to women who returned to their pregestational weight by one year postpartum (Table 2). For women with PPWR and PPWG, the direct pathways were not significant. The indirect associations, mediated by BMI at six years, were significant for all the patterns of postpartum weight change and corresponded to 20%, 15% and 11% higher insulin resistance for PPWR+WG, PPWR, and PPWG, respectively. PPWR and PPWG showed tendencies of direct associations with HDL-c. The three patterns of postpartum weight change had significant associations with HDL-c mediated through BMI. These associations were similar in magnitude and corresponded to a 3% lower HDL-c for PPWR+WG and PPWR, and 2% lower for PPWG, compared to the reference group. We did not find direct associations between the patterns of weight change with glucose and TG, but indirect associations were identified. Compared to the reference group, women with PPWR+WG had higher concentrations of glucose (3%) and TG (15%). The same was observed for women with PPWR (+2% glucose, +12% TG) and PPWG (+1% glucose, +8% TG).

**Table 3** shows the direct and indirect associations between the patterns of postpartum weight change and outcome groups 2 and 3. For SBP and DBP, only the indirect pathways, mediated through BMI, were significant. Women with PPWR+WG had the highest SBP (1.11 mm Hg [0.53, 1.70]) and DBP (0.61 mm Hg [0.16, 1.06]), followed by women with PPWR (SBP, 0.90 mm Hg [0.26, 1.54]; DBP, 0.50 mm Hg [0.06, 0.93]) and PPWG (SBP, 0.62 mm Hg [0.18, 1.07]; DBP, 0.34 mm Hg [0.04, 0.65]). For LDL-c and total-c we did not find significant direct nor indirect pathways.

## Discussion

This study provides the first evidence on the effect of postpartum weight change patterns in relation to long-term adiposity and cardiovascular risk. In this cohort of Mexican women, those who experienced PPWR+WG at one year postpartum, compared to women who returned to their pregestational weight, had the greatest BMI, WC, and insulin resistance six years after delivery. The three patterns of postpartum weight change, PPWR+WG, PPWR, and PPWG, were associated with HOMA-IR, HDL-c, TG, glucose, SBP, and DBP through BMI at six years.

PPWR+WG, PPWR, and PPWG one year after delivery, compared to the reference group, were associated with increased BMI and WC at six years postpartum, with stronger associations for PPWR+WG and PPWR, especially for BMI. The association between PPWR and WC was strong but not highly significant probably because of the small sample in this group (n=24). The findings for PPWR+WG and PPWR are supported by previous research that showed associations between excessive GWG and long-term adiposity outcomes (15,16,40,41). McClure et al., in a study of American women showed that excessive GWG, compared to adequate, was associated with a 4.9% higher BMI, and a 3.2 cm higher WC at an average of eight years postpartum (16). Although our results are not directly comparable, we could argue that the pattern of postpartum weight change, in specific PPWR+WG or PPWR, might be the potential link between excessive GWG and long-term adiposity. In fact, we previously showed an increased risk of PPWR+WG and PPWR one year after delivery in women with excessive GWG (Soria-Contreras et al., 2019, unpublished manuscript). This mechanistic explanation is further supported by findings from 23,701 women within the Danish National Birth Cohort, which showed that GWG was associated with maternal weight at seven years postpartum primarily through PPWR. In this study, 1-kg of weight retained at six months corresponded to a 0.48 kg increase in weight and to a 0.03 cm higher BMI-adjusted WC at seven years postpartum, independently of GWG (11). In our previous analysis, pregestational overweight and obesity increased the risk of PPWG (Soria-Contreras et al., 2019, unpublished manuscript). Behavioral factors associated with long-term weight gain such lack of physical activity, longer time in sedentary activities and poor diet quality are more prevalent among women with overweight or obesity (42–44). Therefore, the association between PPWG and long-term adiposity may be the result of pre-existing unhealthy behaviors and weight-control challenges in these women.

In our study, we did not find significant direct associations between any of the patterns of weight change with glucose, TG, SBP, DBP, total-c, and LDL-c. PPWR+WG had a direct and significant association with HOMA-IR at six years postpartum. Previous studies have failed to show associations between HOMA-IR and total, trimester-specific (41) or excessive GWG (16). One possible explanation for these inconsistencies is that GWG reflects increases in different components not particularly related to metabolic risk, including placental and fetal weight, as well as fat-free mass and fat mass (30). On the other hand, PPWR+WG might reflect primarily increases in fat mass, including visceral adipose tissue, which is associated with insulin resistance (45). It is not surprising that only women with PPWR+WG had higher insulin resistance since they experienced the highest weight (7.7 kg) and BMI (3.3 $kg/m^2$) increase from pre-pregnancy to six years postpartum. According to one study of non-pregnant French women and men, weight gain over six years was associated with worsening in all metabolic syndrome components especially WC and insulin. Women who gained 6 to 8 kg increased their WC by 8% and their insulin concentrations by ~30%, compared to those who maintained their weight stable (±2 kg) (46).

PPWR and PPWG had marginally significant direct associations with low HDL-c ($0.05 \leq p < 0.10$). For PPWR+WG the association was on the same direction but the 95% CI was wider ($0.10 \leq p < 0.20$). In a recent study among Latina women in the US, each additional live birth was associated with increased odds of both abdominal obesity and low HDL-c (OR 1.1, 95% CI 1.0–1.2) (47). It has been postulated that an increase in adiposity, in specific visceral adipose tissue, following pregnancy may in part be responsible for the associations between childbearing and low HDL-c (47–49), however, this has not been confirmed. This would explain why in our study women in any of the three patterns of postpartum weight change, had similar WC at six years postpartum, as well as lower HDL-c. However, the fact that PPWR+WG had the strongest association with BMI and WC, and the weakest association with HDL-c deserves further investigation.

PPWR+WG, PPWR, and PPWG had significant indirect associations with glucose, TG, HOMA-IR, HDL-c, SBP and DBP through BMI at six years postpartum. These are expected findings given that a higher BMI is associated with higher levels of all the components of the metabolic syndrome, and lower concentrations of HDL-c (50,51). Overall, the associations were stronger for PPWR+WG, followed by PPWR and PPWG, which reflects the stronger association of PPWR+WG with BMI at six years.

Our findings build on previous work by showing that, independently of GWG, PPWR+WG, PPWR, and PPWG are associated with long-term adiposity, which may put women at higher risk of cardiovascular disease. We also showed that PPWR+WG was more common among women than PPWR and PPWG. Women who experienced PPWR+WG had the worst cardiometabolic profile at six years postpartum, characterized by increased BMI, WC and insulin resistance. Increased adiposity and insulin resistance are central components of the metabolic syndrome, therefore, women with PPWR+WG may be a higher risk group for developing this syndrome.

This work has some limitations and strengths that must be considered. Our population was primarily low SES women living in Mexico City, which limits the generalizability of our findings. In this analysis, we used information collected throughout more than six years of follow-up. During this time, some women were lost to follow-up or had some missing information, therefore, only 38% of women participating in *PROGRESS* had enough information to be included in the present analysis. However, included women were not substantially different from those excluded. As in most studies, confounding cannot be completely ruled out. We minimized this possibility by adjusting our path models for relevant covariates, but some important information was missing. For example, we did not have information on the maternal glucose tolerance status or the diagnosis of gestational diabetes during the *PROGRESS* pregnancy, or in any subsequent pregnancy. Instead, we adjusted by the newborn´s size for gestational age at the study pregnancy because of the strong, positive correlation between maternal glucose concentrations during pregnancy and infant birth weight (52). We had information on medication intake at six years but not on the diagnosis of diabetes or any chronic disease. Therefore, we cannot rule out the possibility of residual confounding on these variables potentially associated with maternal outcomes at six years. Another limitation is that measured pregestational weight was not available in *PROGRESS*. Instead of using self-reported pregestational weight that was available for all women, we used an estimated pregestational weight from a prediction model. Self-reported pregestational weight tends to be misreported but, even with some degree error, is accurate for some populations (28). However, this is not the case for women participating in *PROGRESS* who, according to a recent study, may be less likely to know their pregestational weight and have high ranges of misreport (-39.2 to 25.7 kg) (28). Given the absence of measured pregestational weight, we would argue that using the predicted weight, instead of self-reported, is less subject to error in our population.

Our study has some strengths worth mentioning. Our cohort had extensive information on potential confounders and the majority of the anthropometric measures were objectively measured by trained personnel. Additionally, we used a statistical approach that allowed us to examine the direct effect of the patterns of postpartum weight change on outcomes, but also an indirect effect mediated through adiposity at six years postpartum. With this approach, we were also able to consider the temporal and complex relations between the study variables.

In conclusion, our results suggest that women who do not recover their pregestational weight during the first year postpartum have increased adiposity years after delivery and are at increased cardiovascular risk. Women who experience PPWR+WG after pregnancy are a high-risk group for obesity, insulin resistance, and metabolic syndrome. Interventions and public health policies targeting women the first year after delivery may have important implications for their long-term risk of obesity and cardiovascular disease.

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**Conflict of interest**

The authors declare that they have no competing interests.

**Authors' contributions**

DCSC, MMTR, BTV, and RLR designed the research; MLPZ and ACP conducted research (data collection); ACJ provided essential databases for the research; DCSC, performed the statistical analysis and wrote the manuscript; MMTR, BTV, and RLR, ACP, MLPZ, AAB, ACJ, EC, ALD, ROW, EO provided input to interpret the results; DCSC, MMTR, BTV, and RLR had primary responsibility for final content. All authors read and approved the final manuscript.

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**Table 1.** Participant characteristics according to patterns of postpartum weight change in women participating in the PROGRESS cohort

| | *PATTERNS OF POSTPARTUM WEIGHT CHANGE* | | | | | |
|---|---|---|---|---|---|---|
| | All women n=361 | Return to pregestational weight n=215 (59.6%) | PPWR n=24 (6.6%) | PPWG n=50 (13.9%) | PPWR+WG n=72 (19.9%) | P [1] |
| *Pre-pregnancy characteristics* | | | | | | |
| Maternal age, years (mean ± SD**)** | 27.5 ± 5.6 | 27.6 ± 5.6 | 26.9 ± 4.3 | 27.6 ± 6.4 | 27.4 ± 5.4 | 0.94 |
| Pregestational BMI, kg/m$^2$ (mean ± SD**)** | 26.5 ± 4.2 | 26.3 ± 4.2 | 25 ± 3.4 | 27.7 ± 4.2 | 26.5 ± 4.3 | 0.08 |
| | | | **N (%)** | | | |
| Education | | | | | | 0.10 |
| *Basic* | 154 (42.7) | 87 (40.5) | 17 (70.8) | 21 (42.0) | 29 (40.3) | |
| *Middle* | 126 (34.9) | 77 (35.8) | 6 (25.0) | 18 (36.0) | 25 (34.7) | |
| *College* | 81 (22.4) | 51 (23.7) | 1 (4.2) | 11 (22.0) | 18 (25.0) | |
| Marital status | | | | | | 0.02 |
| *Single* | 58 (16.1) | 26 (12.1) | 2 (8.3) | 14 (28.0) | 16 (22.2) | |
| *Married* | 303 (83.9) | 189 (87.9) | 22 (91.7) | 36 (72.0) | 56 (77.8) | |
| SES | | | | | | 0.13 |
| *High* | 86 (23.8) | 59 (27.4) | 4 (16.7) | 14 (28.0) | 9 (12.5) | |
| *Medium* | 79 (21.9) | 44 (20.5) | 6 (25.0) | 13 (26.0) | 16 (22.2) | |
| *Low* | 196 (54.3) | 112 (52.1) | 14 (58.3) | 23 (46.0) | 47 (65.3) | |
| Parity | | | | | | 0.01 |
| *Primiparous* | 121 (33.5) | 60 (27.9) | 6 (25.0) | 21 (42.0) | 34 (47.2) | |
| *Multiparous* | 240 (66.5) | 155 (72.1) | 18 (75.0) | 29 (58.0) | 38 (52.8) | |
| *Pregnancy characteristics* | | | | | | |
| Smoking | | | | | | 0.38 |
| *Never smokers* | 252 (69.8) | 152 (70.7) | 15 (62.5) | 36 (72.0) | 49 (68.1) | |
| *Smokers around pregnancy* | 78 (21.6) | 44 (20.5) | 7 (29.2) | 13 (26.0) | 14 (19.4) | |
| *Former smokers* | 31 (8.6) | 19 (8.8) | 2 (8.3) | 1 (2.0) | 9 (12.5) | |
| Sedentary activities [2] | | | | | | 0.50 |
| *<2 hours/day* | 161 (44.6) | 102 (47.4) | 11 (45.8) | 21 (42.0) | 27 (37.5) | |
| *≥2 hours/day* | 200 (55.4) | 113 (52.6) | 13 (54.2) | 29 (58.0) | 45 (62.5) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adequacy of GWG | | | | | | <0.001 |
| *Insufficient* | 85 (26.2) | 61 (32.1) | 0 (0.0) | 17 (35.4) | 7 (10.9) | |
| *Adequate* | 152 (46.9) | 90 (47.4) | 10 (45.5) | 22 (45.8) | 30 (46.9) | |
| *Excessive* | 87 (26.9) | 39 (20.5) | 12 (54.5) | 9 (18.8) | 27 (42.2) | |
| Newborn LGA | 29 (8.0) | 19 (8.8) | 1 (4.2) | 6 (12.0) | 3 (4.2) | 0.33 |
| Diagnosis of HDP | 24 (6.7) | 15 (7.0) | 1 (4.2) | 5 (10.0) | 3 (4.2) | 0.59 |
| *Postpartum characteristics* | | | | | | |
| Any breastfeeding at 1 month | | | | | | 0.32 |
| *Yes* | 302 (85.8) | 178 (86.4) | 20 (83.3) | 46 (92.0) | 58 (80.6) | |
| *No* | 50 (14.2) | 28 (13.6) | 4 (16.7) | 4 (8.0) | 14 (19.4) | |

[1] P value from multinomial logistic regression.
[2] Includes time reading and watching television.
GWG, gestational weight gain; HDP, hypertensive disorders of pregnancy (preeclampsia and gestational hypertension); LGA, large for gestational age; PPWG, postpartum weight gain; PPWR, postpartum weight retention; PPWR+WG, postpartum weight retention + weight gain; SES, socioeconomic status.

**Table 2.** Path coefficients and 95% CI for the association between patterns of weight change one year after delivery with adiposity and selected cardiometabolic outcomes at six years postpartum

| | Direct associations | | | Indirect associations | | |
|---|---|---|---|---|---|---|
| ***Outcome group 1*** | ***β*** | **95% CI** | ***P*** | ***β*** | **95% CI** | ***P*** |
| ***Body mass index (kg/m²) 1*** | | | | | | |
| ***PPWR*** | 1.80 | 0.80, 2.79 | *<0.001* | | | |
| ***PPWG*** | 1.22 | 0.53, 1.92 | *0.001* | | | |
| ***PPWR+WG*** | 2.30 | 1.67, 2.93 | *<0.001* | | | |
| ***Waist circumference (cm) 1*** | | | | | | |
| ***PPWR*** | 3.15 | -0.35, 6.65 | *0.078* | | | |
| ***PPWG*** | 3.32 | 0.85, 5.78 | *0.008* | | | |
| ***PPWR+WG*** | 3.38 | 1.14, 5.62 | *0.003* | | | |
| ***Log glucose*** | | | | | | |
| ***PPWR*** | -0.03 | -0.09, 0.02 | *0.274* | 0.02 | 0.004, 0.04 | *0.012* |
| ***PPWG*** | 0.002 | -0.04, 0.04 | *0.937* | 0.01 | 0.003, 0.02 | *0.013* |
| ***PPWR+WG*** | -0.03 | -0.06, 0.01 | *0.158* | 0.03 | 0.01, 0.04 | *0.002* |
| ***Log triglycerides*** | | | | | | |
| ***PPWR*** | 0.05 | -0.17, 0.26 | *0.675* | 0.11 | 0.04, 0.18 | *0.003* |
| ***PPWG*** | -0.08 | -0.23, 0.06 | *0.262* | 0.08 | 0.03, 0.13 | *0.003* |
| ***PPWR+WG*** | -0.07 | -0.21, 0.07 | *0.333* | 0.14 | 0.08, 0.20 | *<0.001* |
| ***Log HOMA-IR*** | | | | | | |
| ***PPWR*** | -0.18 | -0.45, 0.08 | *0.174* | 0.14 | 0.05, 0.24 | *0.003* |
| ***PPWG*** | 0.15 | -0.03, 0.33 | *0.104* | 0.10 | 0.03, 0.16 | *0.003* |
| ***PPWR+WG*** | 0.21 | 0.04, 0.39 | *0.018* | 0.18 | 0.10, 0.26 | *<0.001* |
| ***Log HDL-c*** | | | | | | |
| ***PPWR*** | -0.10 | -0.20, 0.01 | *0.084* | -0.03 | -0.04, -0.01 | *0.004* |
| ***PPWG*** | -0.07 | -0.15, 0.003 | *0.058* | -0.02 | -0.03, -0.01 | *0.004* |
| ***PPWR+WG*** | -0.05 | -0.12, 0.02 | *0.188* | -0.03 | -0.05, -0.02 | *<0.001* |

Reference group: return to pregestational weight.

*1* For BMI and WC at six years only direct associations were tested.

HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; PPWG, postpartum weight gain; PPWR, postpartum weight retention; PPWR+WG, postpartum weight retention + weight gain.

**Table 3.** Path coefficients and 95% CI for the association between patterns of weight change one year after delivery with SBP, DBP, total-c, and LDL-c at six years postpartum

| | *Direct associations* | | | *Indirect associations* | | |
|---|---|---|---|---|---|---|
| ***Outcomes*** | ***β*** | **95% CI** | ***P*** | ***β*** | **95% CI** | ***P*** |
| ***Group 2*** | | | | | | |
| ***SBP (mm Hg)*** | | | | | | |
| ***PPWR*** | 1.22 | -2.86, 5.31 | *0.557* | 0.90 | 0.26, 1.54 | *0.006* |
| ***PPWG*** | 0.44 | -2.47, 3.36 | *0.766* | 0.62 | 0.18, 1.07 | *0.006* |
| ***PPWR+WG*** | 1.09 | -1.62, 3.80 | *0.430* | 1.11 | 0.53, 1.70 | *<0.001* |
| ***DBP (mm Hg)*** | | | | | | |
| ***PPWR*** | 1.65 | -1.83, 5.13 | *0.354* | 0.50 | 0.06, 0.93 | *0.025* |
| ***PPWG*** | -0.90 | -3.42, 1.61 | *0.480* | 0.34 | 0.04, 0.65 | *0.027* |
| ***PPWR+WG*** | 0.71 | -1.57, 3.00 | *0.541* | 0.61 | 0.16, 1.06 | *0.008* |
| ***Group 3*** | | | | | | |
| ***Log total-c*** | | | | | | |
| ***PPWR*** | -0.02 | -0.09, 0.06 | *0.649* | 0.01 | -0.003, 0.02 | *0.136* |
| ***PPWG*** | -0.02 | -0.07, 0.04 | *0.574* | 0.01 | -0.002, 0.01 | *0.137* |
| ***PPWR+WG*** | -0.01 | -0.06, 0.05 | *0.841* | 0.01 | -0.003, 0.03 | *0.110* |
| ***Log LDL-c*** | | | | | | |
| ***PPWR*** | -0.003 | -0.13, 0.13 | *0.966* | -0.01 | -0.02, 0.01 | *0.402* |
| ***PPWG*** | -0.05 | -0.14, 0.04 | *0.286* | -0.004 | -0.01, 0.005 | *0.402* |
| ***PPWR+WG*** | 0.03 | -0.06, 0.11 | *0.513* | -0.01 | -0.02, 0.01 | *0.392* |

Reference group: return to pregestational weight.
DBP, diastolic blood pressure; LDL-c, low-density lipoprotein cholesterol; PPWG, postpartum weight gain; PPWR, postpartum weight retention; PPWR+WG, postpartum weight retention + weight gain; SBP, systolic blood pressure; Total-c, total cholesterol.

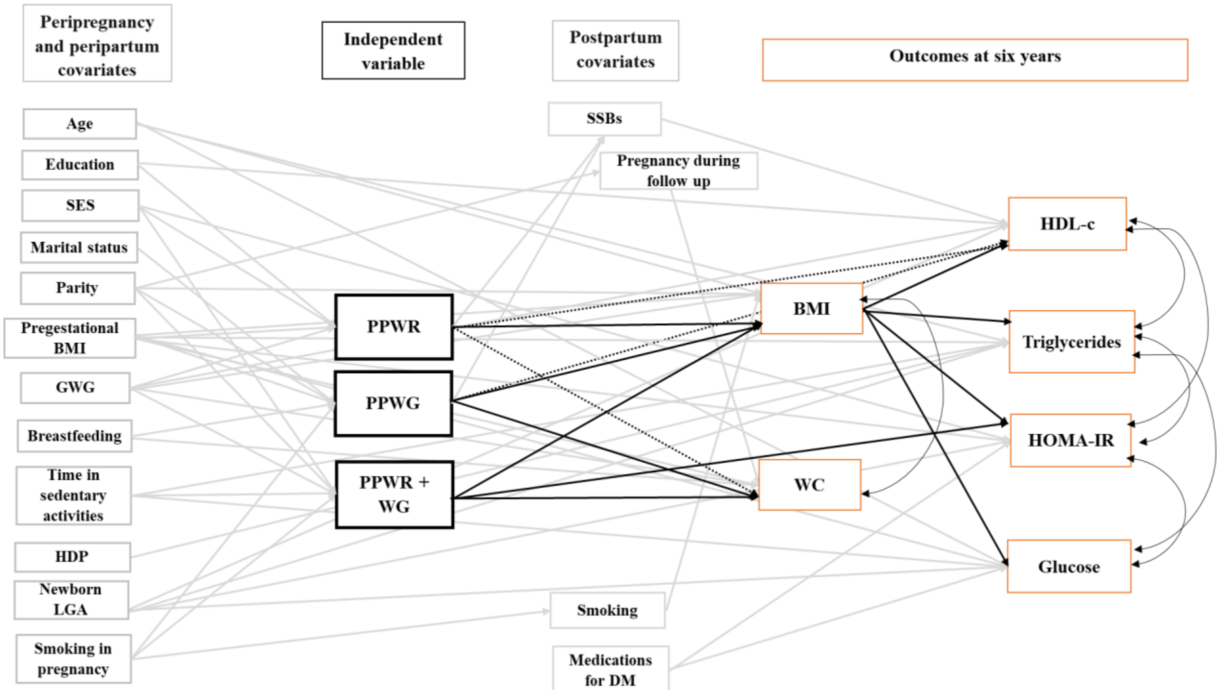


**Figure 1.** Final path model of the association between patterns of weight change one year after delivery and outcome group 1 at six years postpartum. The figure displays direct associations between patterns of postpartum weight change and outcome group 1, and indirect associations mediated through BMI. The reference group was women who returned to their pregestational weight by one year postpartum. Arrows represent pathways among variables. The black arrows represent paths relevant to our study objectives. A continuous black arrow indicates a statistically significant association ($p<0.05$); a doted black arrow represents a tendency of association ($0.05\leq p<0.10$).

BMI, body mass index; DM, diabetes mellitus; GWG, gestational weight gain; HDL-c, high-density lipoprotein cholesterol; HDP, hypertensive disorders of pregnancy; HOMA-IR, homeostatic model assessment of insulin resistance; LGA, large for gestational age; PPWG, postpartum weight gain; PPWR, postpartum weight retention PPWR+WG, postpartum weight retention + weight gain; SES, socioeconomic status; SSBs, servings of sugar-sweetened beverages; WC, waist circumference.

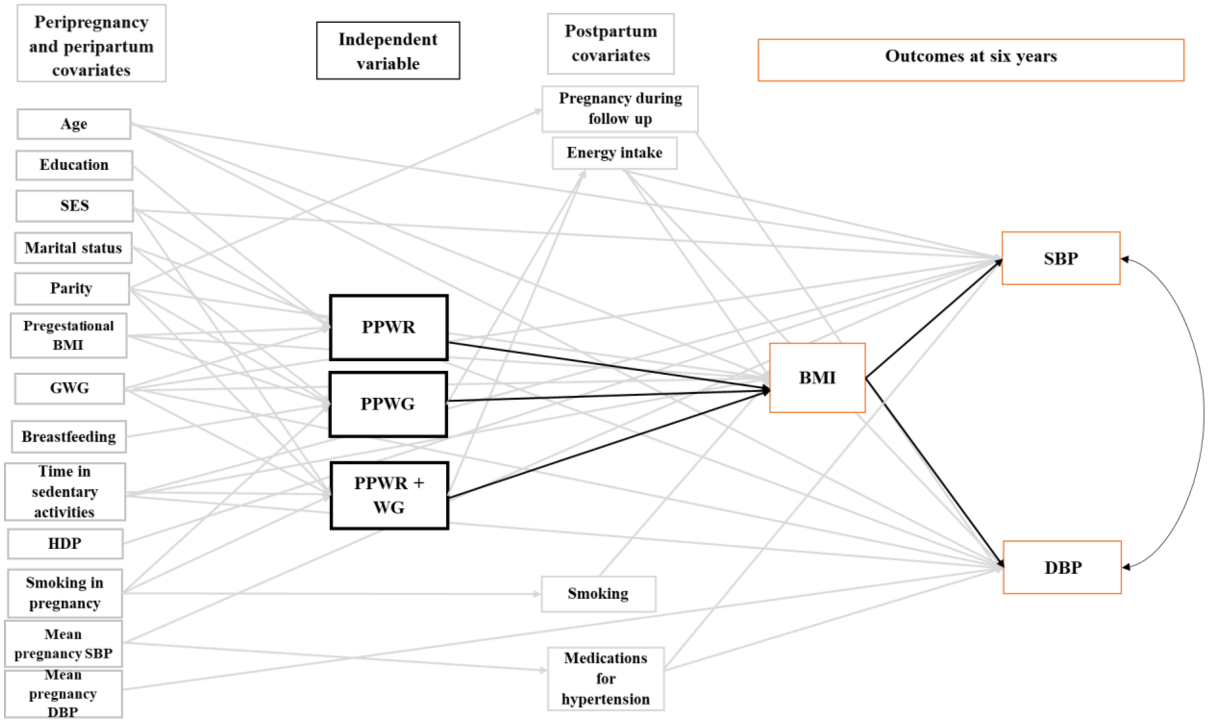


**Figure 2.** Final path model of the association between patterns of weight change one year after delivery and outcome group 2 at six years postpartum. The reference group was women who returned to their pregestational weight by one year postpartum. Arrows represent pathways among variables. The black arrows represent paths relevant to our study objectives. A continuous black arrow indicates a statistically significant association ($p<0.05$). For these outcomes, only indirect associations (mediated through BMI) were identified.

BMI, body mass index; DBP, diastolic blood pressure; GWG, gestational weight gain; HDP, hypertensive disorders of pregnancy; PPWG, postpartum weight gain; PPWR, postpartum weight retention PPWR+WG, postpartum weight retention + weight gain; SES, socioeconomic status; SBP, systolic blood pressure.

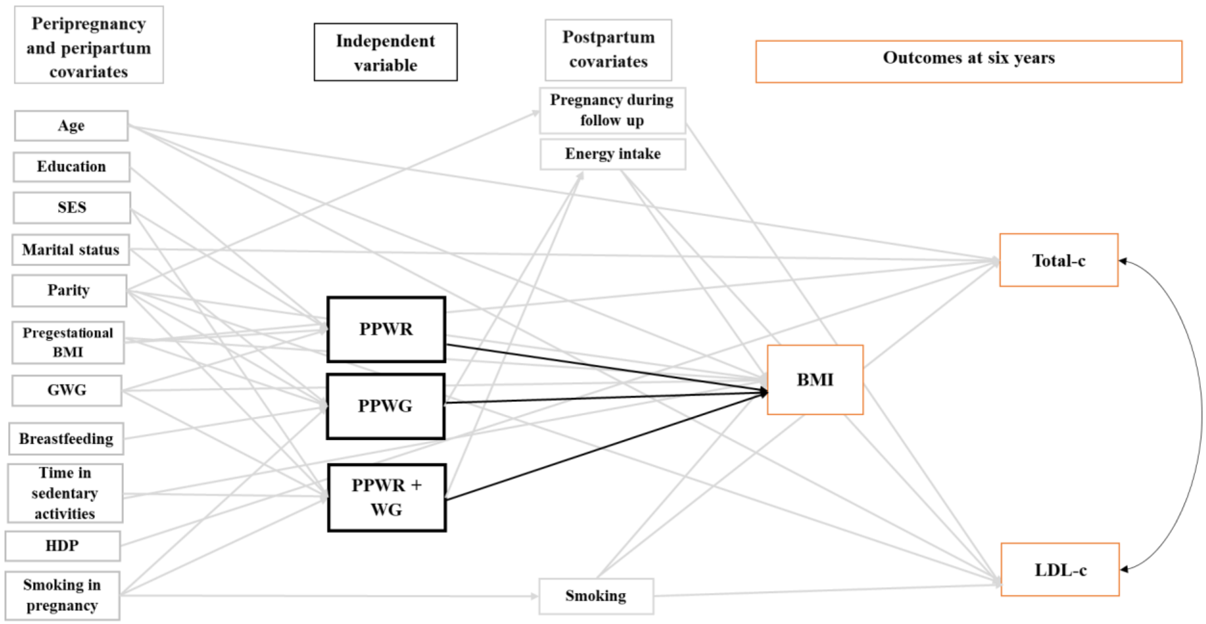


**Figure 3.** Final path model of the association between patterns of weight change one year after delivery and outcome group 3 at six years postpartum. The reference group was women who returned to their pregestational weight by one year postpartum. Arrows represent pathways among variables. The black arrows represent paths relevant to our study objectives. A continuous black arrow indicates a statistically significant association ($p<0.05$). For these outcomes, neither direct nor indirect associations were identified. BMI, body mass index; GWG, gestational weight gain; HDP, hypertensive disorders of pregnancy; LDL-c, low-density lipoprotein cholesterol; PPWG, postpartum weight gain; PPWR, postpartum weight retention PPWR+WG, postpartum weight retention + weight gain; SES, socioeconomic status; total-c, total cholesterol.

## 6. Discusión

En el primer estudio identificamos 4 patrones de cambio de peso durante el primer año posparto, y factores prenatales y perinatales asociados con ellos. La mayoría de las mujeres (57%) regresaron a su peso pregestacional al primer año posparto, 21% tuvieron RPP+GPP, 14% GPP y 8% RPP. En estudios realizados en los Estados Unidos se ha reportado que del 25 al 37% de las mujeres regresan a su peso pregestacional al primer año posparto (17,40). Diferencias en la población de estudio podrían explicar la inconsistencia en los resultados. Por ejemplo, en el estudio de Endres y cols., el 46% de las mujeres eran Áfrico-Americanas, las cuales retienen más peso en comparación con las mujeres blancas e hispanas (40,41). La mayoría de los estudios considera que el peso en exceso al primer año posparto, en comparación con el pregestacional, corresponde a retención de peso (14,17–19,40). Estos estudios no han diferenciado la ganancia de peso que las mujeres experimentan. En nuestro estudio mostramos que gran proporción de mujeres experimenta ganancia de peso durante el primer año posparto ya sea sola (i.e. GPP) o combinada con retención (i.e. RPP+GPP).

Con respecto a los predictores de los patrones de cambio de peso, encontramos que el sobrepeso y la obesidad pregestacional aumentaron el riesgo de GPP al primer año, lo cual es consistente con lo que otros estudios han mostrado en mujeres de Estados Unidos y Canadá (15,20,28). Nuestros hallazgos de mayor riesgo de RPP o RPP+GPP en las mujeres con GPG excesiva, son consistentes con los resultados de diversos estudios y meta-análisis (24,42–44). Sin embargo, ninguno de estos estudios ha diferenciado la RPP+GPP de la retención. En nuestro estudio observamos menor riesgo de RPP en las mujeres que lactaron de forma exclusiva hasta el primer mes posparto. Otro estudio en mujeres Mexicanas reportó mayor pérdida de peso en las mujeres que lactaron de forma exclusiva hasta los 3 meses posparto (45). En general el efecto de la lactancia materna en el cambio de peso posparto es inconsistente (27,46,47), lo cual se puede deber a diferencias metodológicas entre los estudios como diferentes tiempos de exposición o definiciones de lactancia materna, y a la falta de ajuste por variables confusoras clave como son el IMC pregestacional, la GPG y la paridad (46).

En diversos estudios, la GPG se ha asociado con mayor adiposidad años después del parto (30,37,38). Nuestro segundo análisis, extiende estos resultados al mostrar que el cambio de peso posparto caracterizado como patrones de RPP+GPP, RPP y GPP, se asocian con mayor IMC y CC a los 6 años posparto, independientemente de la GPG. Un estudio en 23,701 mujeres Danesas encontró que cada 1 kg de peso retenido a los 6 meses posparto correspondía a un aumento de 0.48 kg de peso y 0.03 cm de CC a los 7 años posparto, de forma independiente a la GPG (10). La mayoría de los estudios con los que podemos comparar nuestros resultados utilizan a la GPG excesiva como exposición (30,37–39). En nuestro estudio, las mujeres con GPG excesiva tuvieron mayor riesgo de RPP y RPP+GPP. Considerando esto, podemos argumentar que son los patrones de cambio de peso posparto, RPP y RPP+GPP, los que explican las asociaciones previamente reportadas.

Con respecto a los desenlaces metabólicos, solamente observamos asociaciones directas significativas entre la RPP+GPP y el índice de HOMA, el cual refleja mayor resistencia a la insulina en este grupo de mujeres. Estudios utilizando la GPG excesiva como exposición no han encontrado asociaciones significativas con este índice (38,39). Las mujeres con RPP+GPP son las que más aumentaron peso (7.7 kg) e IMC (3.3 kg/$m^2$) de la etapa pregestacional hasta los 6 años posparto. Un estudio en mujeres Francesas no embarazadas encontró que aquellas que ganaron entre 6 y 8 kg en un lapso de 6 años aumentaron de forma considerable su CC y niveles de insulina, en comparación con las que mantuvieron su peso estable (50). Es posible que la magnitud del cambio en la adiposidad de las mujeres con RPP+GPP explique estos resultados. Otro hallazgo importante es la asociación indirecta, a través del IMC a los 6 años posparto, de la RPP+GPP, RPP y GPP con el índice de HOMA, glucosa, triglicéridos, HDL, PAS y PAD. Estos hallazgos refuerzan el papel central de la adiposidad en el riesgo metabólico (51,52).

Nuestros resultados deben ser evaluados considerando las limitaciones y fortalezas de los 2 estudios. Una limitación es que solamente el 53% y 38% del total de las mujeres participantes en *PROGRESS* fueron incluidas en el primer y segundo análisis, respectivamente. A pesar de esto, en ningún análisis encontramos evidencia de diferencias sustanciales entre las mujeres analizadas y no analizadas. Por otro lado, la generalizabilidad de los resultados a otras poblaciones puede estar limitada ya que estudiamos a mujeres predominantemente de bajo NSE, habitantes de la Ciudad de México. Imputamos el peso a los 12 meses posparto en un grupo de 100 mujeres, el cuál fue un insumo para nuestra clasificación de patrones de cambio de peso. Existe la posibilidad de que la imputación de pesos afectara las asociaciones observadas. Sin embargo, al replicar el primer análisis excluyendo a las mujeres con peso imputado no observamos diferencias importantes en los resultados. Otra limitación es que no contamos con información del peso pregestacional medido. Recientemente se reportó que el peso pregestacional auto-reportado en las mujeres de *PROGRESS* presenta un error considerable que potencialmente podría sesgar nuestros resultados (53). Considerando esto, utilizamos un peso pregestacional predicho, el cuál fue validado de forma rigurosa en la cohorte.

Algunas fortalezas merecen ser mencionadas. Ambos análisis tuvieron un diseño prospectivo lo que nos permitió asegurar que las exposiciones de interés precedieron los desenlaces. La riqueza de datos en la cohorte *PROGRESS* nos permitió ajustar cada análisis por las variables confusoras más relevantes identificadas en la revisión de literatura. Para el segundo análisis, utilizamos un abordaje estadístico (path analysis) que nos permitió considerar la correlación existente entre las variables de desenlace, y que nos permitió explorar el papel de la adiposidad como elemento central para el desarrollo de alteraciones metabólicas.

## 7. Conclusiones

Los resultados derivados de ésta tesis proporcionan evidencia del efecto que tiene el embarazo en el aumento de peso y el desarrollo de alteraciones metabólicas a largo plazo en mujeres Mexicanas. El primer estudio reveló la existencia de distintos patrones de cambio de peso durante el primer año posparto, y de factores modificables asociados a ellos. El segundo estudio representa la primera evidencia a nivel mundial del efecto que tiene no regresar al peso pregestacional al primer año posparto en la adiposidad y factores de riesgo metabólicos en la mujer, años después del embarazo. Además, mostramos que el patrón de cambio de peso más común, que representa una combinación de retención de peso gestacional y ganancia de peso en el posparto, se asocia con mayor adiposidad y alteraciones metabólicas a los 6 años posparto.

Nuestros resultados enfatizan la importancia del primer año posparto como una ventana de oportunidad para mitigar el efecto del embarazo en el aumento de peso y el riesgo de enfermedades en la mujer. El posparto representa un momento oportuno para intervenir ya que las mujeres suelen ser más receptivas a recibir información sobre cambios en el estilo de vida, además de estar más motivadas para adoptar estos cambios. Para muchas mujeres el posparto representa la etapa preconcepcional de un siguiente embarazo. Optimizar el peso materno en esta etapa puede tener una influencia positiva en los desenlaces maternos y neonatales en un embarazo subsecuente. En otros países, las intervenciones en el posparto han mostrado ser eficaces para promover la pérdida de peso en el posparto (54). De acuerdo a nuestros resultados, intervenciones enfocadas en grupos de alto riesgo como las mujeres con GPG excesiva, sobrepeso y obesidad pregestacional, y que no lactan pueden disminuir el riesgo de patrones de cambio de peso poco favorables y tener implicaciones en la salud de la mujer a largo plazo.

Los resultados de esta tesis pueden servir como insumo para modificar los esquemas de atención de la mujer después del parto y para generar guías de atención durante el posparto. Actualmente en México, la NOM-007-SSA2-2016, para la atención de la mujer durante el embarazo, parto y puerperio, y de la persona recién nacida, recomienda que las mamás reciban 2 consultas durante los primeros 42 días posparto (55). De acuerdo a la NOM-007, con esto finaliza el seguimiento de la mujer posterior al parto. Idealmente, debemos migrar hacia modelos donde se brinde atención multidisciplinaria a la mujer durante el embarazo y se extienda, al menos, durante todo el primer año posparto.

## 8. Abreviaciones

CC: circunferencia de cintura

DM2: diabetes mellitus tipo 2

GPG: ganancia de peso gestacional

GPP: ganancia de peso posparto

HDL: colesterol de alta densidad

IMC: índice de masa corporal

LDL: colesterol de baja densidad

NSE: nivel socioeconómico

PAD: presión arterial diastólica

PAS: presión arterial sistólica

PROGRESS: Programming Research in Obesity, Growth, Environment and Social Stressors

RPP: retención de peso posparto

RPP+GPP: retención + ganancia de peso posparto

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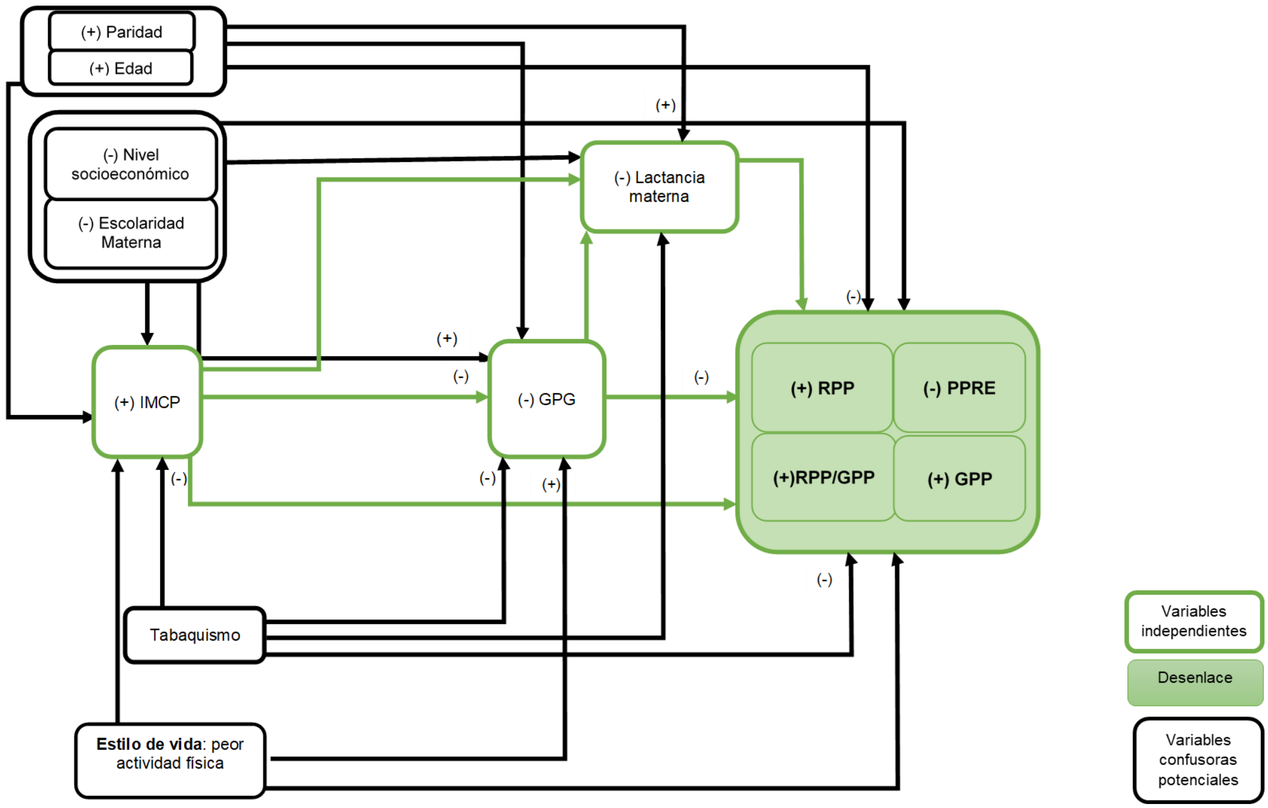
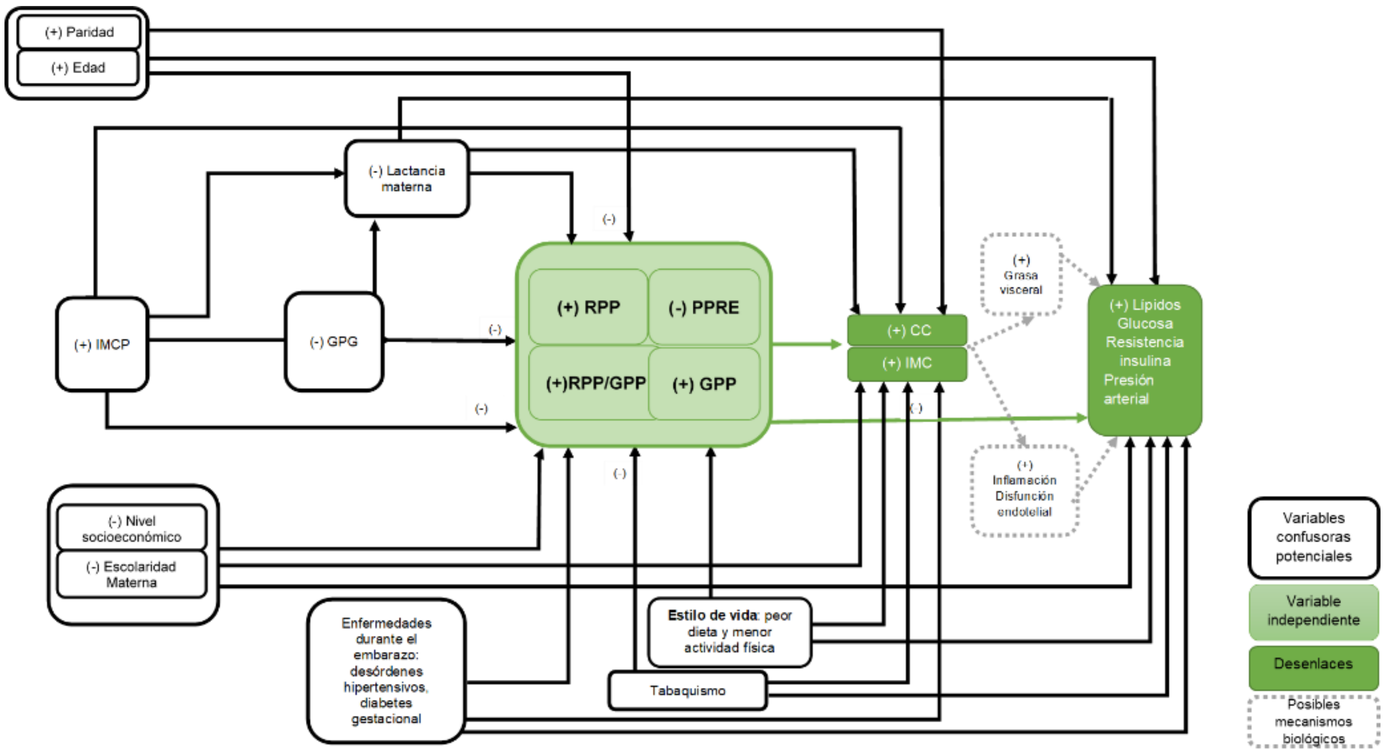
## 2. Anexos

### Anexo 1. Mapa conceptual de la asociación entre el IMC pregestacional, la GPG y la lactancia materna con los patrones de cambio de peso al primer año posparto



**Anexo 2. Mapa conceptual de la asociación entre los patrones de cambio de peso al primer año posparto y factores de riesgo cardiometabólico a los 6 años posparto**




**Anexo 3. GPG recomendada de acuerdo al IMC pregestacional**

| | **IMC** (34) | **GPG total recomendada** (11) |
|---|---|---|
| | | **Rango** |
| Bajo peso | <18.5 kg/m$^2$ | 12.5-18 kg |
| Peso normal | 18.5-24.9 kg/m$^2$ | 11.5-16 kg |
| Sobrepeso | ≥25 kg/m$^2$ | 7-11.5 kg |
| Obesidad | ≥30 kg/m$^2$ | 5-9 kg |
| **IMC: índice de masa corporal, GPG: ganancia de peso gestacional** | | |
| ***Se considera adecuado un aumento de 0.5-2 kg totales durante el 1° trimestre** | | |

**Anexo 4. Clasificación de la lactancia materna al primer mes posparto**

| **Tipo de lactancia materna** (36) | **Incluye** | **No incluye** |
|---|---|---|
| ***No lactancia materna** | -Otro tipo de leche<br>-Agua/té<br>-Bebidas (jugo, atole, refresco)<br>-Alimentos sólidos | -Leche materna |
| ***Parcial*** | -Otro tipo de leche<br>-Bebidas (jugo, atole, refresco)<br>- Agua/té<br>-Alimentos sólidos<br>+<br>-Leche materna | |
| ***Predominante*** | -Leche materna<br>-Agua/té | -Otro tipo de leche<br>-Bebidas (jugo, atole, refresco)<br>-Alimentos sólidos |
| ***Exclusiva*** | -Leche materna | -Otro tipo de leche<br>-Agua/té<br>-Bebidas (jugo, atole, refresco)<br>-Alimentos sólidos |
| *Alimentación con fórmula en el 100% de los casos. | | |

**Anexo 5. Material suplementario artículo 1**

**Supplementary table 1. Association of pregestational BMI, GWG and breastfeeding with patterns of postpartum weight change using a different definition of the outcome***

| ***Reference group: return to pregestational weight*** | | **PPWR** | | | **PPWG** | | | **PPWR+WG** | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | **Model** | | | | | |
| **Pregestational BMI** | **n ƚ** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| ***Normal weight*** | 202 | | *Reference* | | | *Reference* | | | *Reference* | |
| ***Overweight*** | 196 | 0.66 | 0.33, 1.32 | *0.244* | 2.28 | 1.17, 4.42 | ***0.015*** | 1.31 | 0.79, 2.18 | *0.290* |
| ***Obese*** | 90 | 0.43 | 0.17, 1.13 | *0.089* | 1.84 | 0.82, 4.14 | *0.142* | 1.06 | 0.56, 2.01 | *0.867* |
| **Adequacy of GWG** | **n ƚ** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| ***Insufficient*** | 115 | 0.17 | 0.05, 0.59 | ***0.006*** | 1.26 | 0.63, 2.53 | *0.517* | 0.51 | 0.26, 1.00 | ***0.051*** |
| ***Adequate*** | 203 | | *Reference* | | | *Reference* | | | *Reference* | |
| ***Excessive*** | 122 | 4.33 | 1.96, 9.56 | ***<0.001*** | 0.77 | 0.33, 1.78 | *0.541* | 2.79 | 1.52, 5.12 | ***0.001*** |
| **Type of breastfeeding at one month** | **n ƚ** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** | **RRR** | **95% CI** | ***p*** |
| ***No breastfeeding*** | 55 | | *Reference* | | | *Reference* | | | *Reference* | |
| ***Partial*** | 218 | 0.60 | 0.23, 1.59 | *0.303* | 1.46 | 0.49, 4.36 | *0.498* | 0.67 | 0.31, 1.42 | *0.296* |
| ***Predominant*** | 22 | 0.82 | 0.15, 4.37 | *0.819* | 1.80 | 0.34, 9.62 | *0.494* | 0.61 | 0.16, 2.33 | *0.474* |
| ***Exclusive*** | 114 | 0.47 | 0.15, 1.43 | *0.182* | 1.60 | 0.49, 5.25 | *0.436* | 0.77 | 0.33, 1.78 | *0.540* |

Results from multinomial logistic models. PPWR, postpartum weight retention; PPWG, postpartum weight gain; PPWR+WG, postpartum weight retention + weight gain; BMI, body mass index; RRR, relative risk ratio; CI, confidence interval; GWG, gestational weight gain.
*This definition does not consider the 500 g margin as a threshold to return to pregestational weight.
Distribution of patterns as follows: Return to pregestational weight: n=255 (52.3%); PPWR: n=51 (10.5%); PPWG: n=65 (13.3%); PPWR+WG: n=117 (n=24%).
ƚ Total sample may be <500 due to missing values.

Model: adjusted for age, marital status, education, parity, and socioeconomic status. For adequacy of GWG, the model was further adjusted for pregestational BMI, smoking history, physical activity, and sedentary activities in pregnancy. For type of breastfeeding, the model was additionally adjusted for pregestational BMI, adequacy of GWG, smoking history, gestational age at delivery and complications of pregnancy (including preeclampsia, gestational hypertension, and gestational diabetes).

**Supplementary table 2. Adjusted odds ratios of retaining at least 4.5 kg at 12 months postpartum**

| | Odds of retaining ≥4.5 kg at 12 months postpartum | | | | | |
|---|---|---|---|---|---|---|
| | Model 1 | | | Model 2 | | |
| **Pregestational BMI** | **OR** | **95% CI** | ***p*** | **OR** | **95% CI** | ***p*** |
| ***Normal weight*** | | *Reference* | | | *Reference* | |
| ***Overweight*** | 1.19 | 0.70, 2.04 | *0.521* | 1.16 | 0.67, 1.99 | *0.603* |
| ***Obese*** | 1.31 | 0.68, 2.53 | *0.426* | 1.31 | 0.66, .57 | *0.437* |
| **Adequacy of GWG** | **OR** | **95% CI** | ***p*** | **OR** | **95% CI** | ***p*** |
| ***Insufficient*** | *0.40* | 0.17, 0.94 | ***0.035*** | *0.39* | 0.16, 0.94 | ***0.036*** |
| ***Adequate*** | | *Reference* | | | *Reference* | |
| ***Excessive*** | 2.92 | 1.68, 5.06 | ***<0.001*** | 3.31 | 1.81, 6.05 | ***<0.001*** |
| **Type of breastfeeding at one month** | **OR** | **95% CI** | ***p*** | **OR** | **95% CI** | ***p*** |
| ***No breastfeeding*** | | *Reference* | | | *Reference* | |
| ***Partial*** | 1.00 | 0.50, 1.98 | *0.990* | 1.35 | 0.61, 2.99 | *0.465* |
| ***Predominant*** | 0.69 | 0.20, 2.38 | *0.561* | 1.29 | 0.32, 5.25 | *0.720* |
| ***Exclusive*** | 0.53 | 0.24, 1.19 | *0.124* | 0.86 | 0.34, 2.20 | *0.757* |

Results from logistic regression models. BMI, body mass index; OR, odds ratio; CI, confidence interval; GWG, gestational weight gain.

n=84 (16.8%) retained ≥4.5 kg postpartum out of n=500 women.

Model 1: adjusted for age.

Model 2: adjusted for age, marital status, education, parity, and socioeconomic status. For adequacy of GWG, the model was further adjusted for pregestational BMI, smoking history, physical activity, and sedentary activities in pregnancy. For type of breastfeeding, the model was additionally adjusted for pregestational BMI, adequacy of GWG, smoking history, gestational age at delivery and complications of pregnancy (including preeclampsia, gestational hypertension, and gestational diabetes).

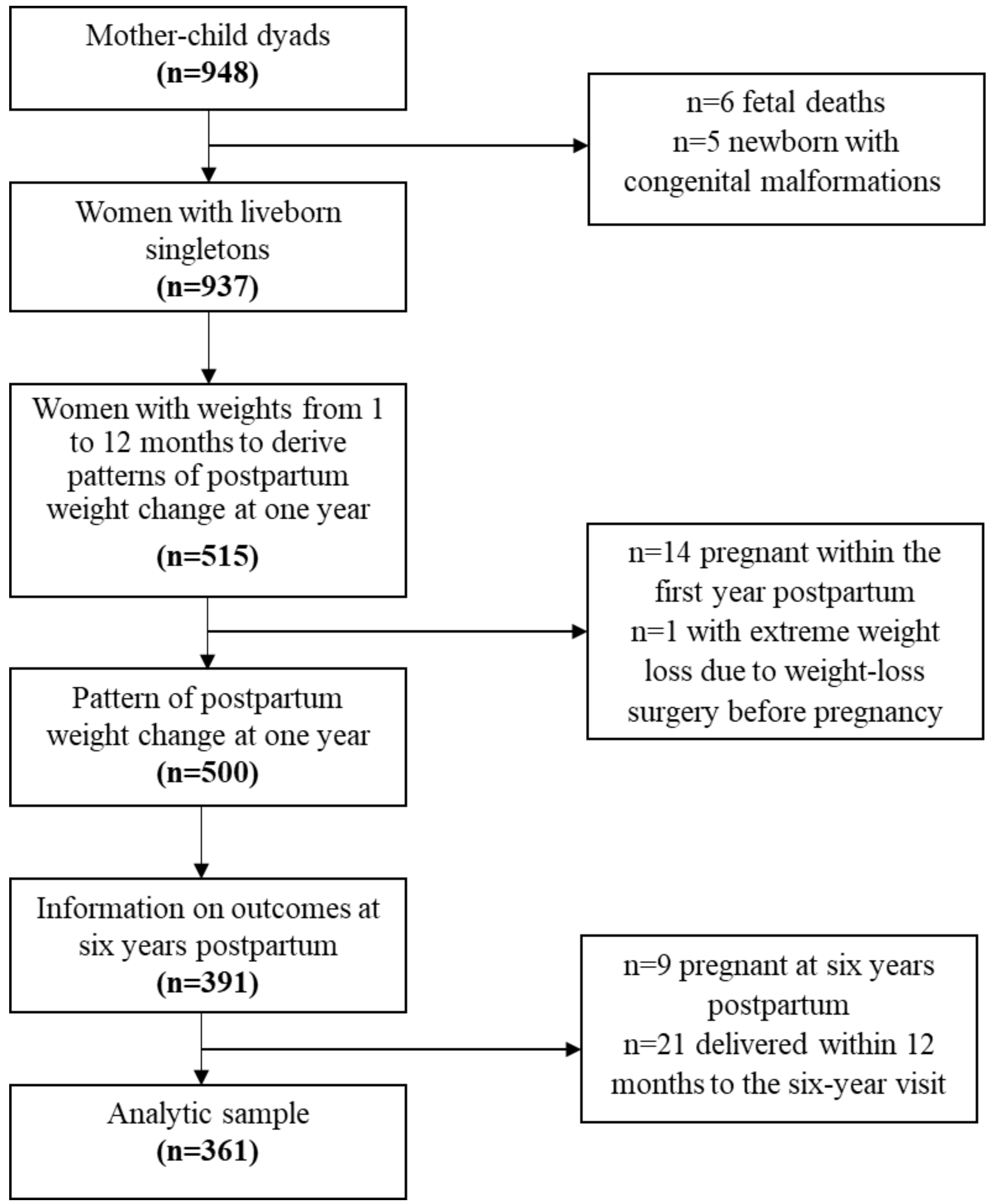
**Anexo 6. Material suplementario artículo 2**

**Supplemental table 1.** Path coefficients and 95% CI for the association between patterns of weight change one year after delivery and cardiometabolic risk factors at six years postpartum [1]

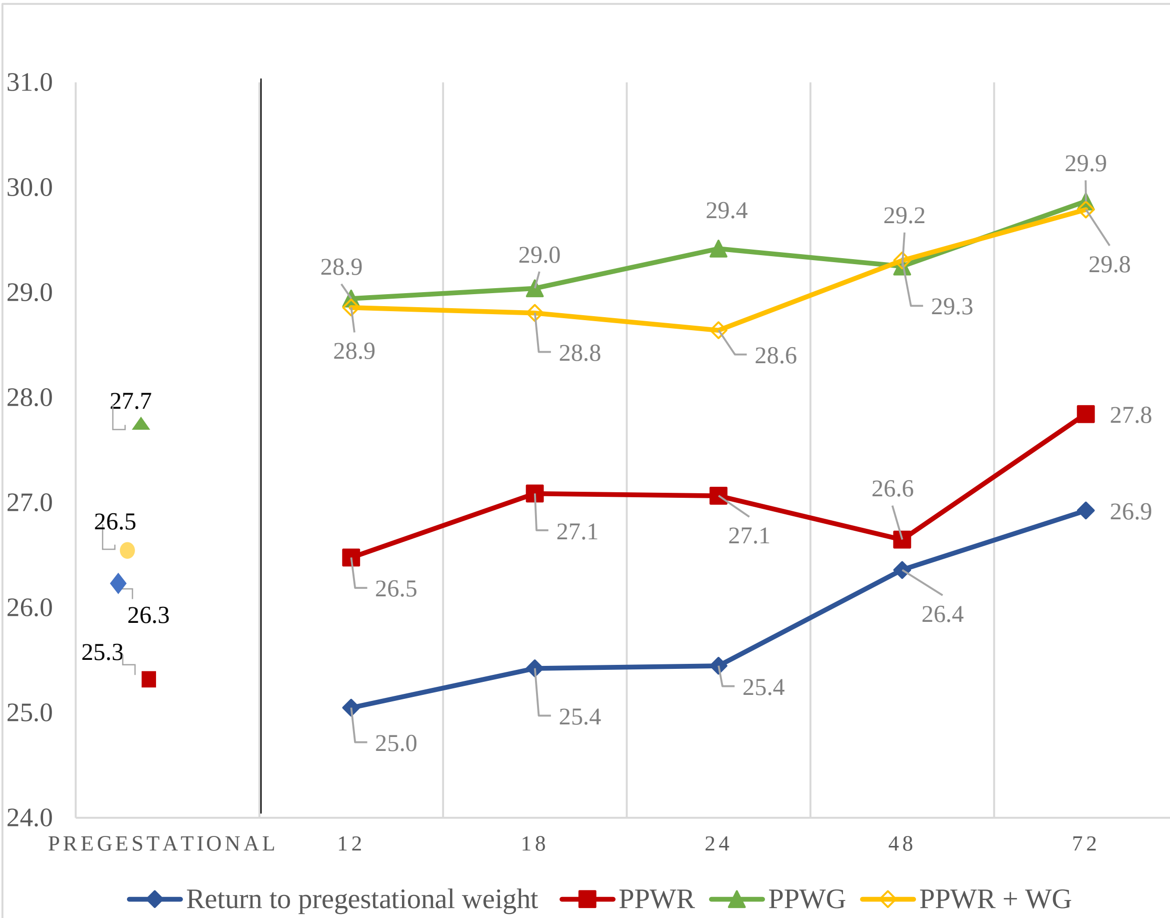
| | Direct associations | | | Indirect associations | | |
|---|---|---|---|---|---|---|
| ***Outcomes*** | ***β*** | **95% CI** | ***p*** | ***β*** | **95% CI** | ***p*** |
| ***Group 1*** | | | | | | |
| **Log glucose** | | | | | | |
| ***PPWR*** | -0.02 | -0.08 , 0.05 | *0.628* | 0.01 | -0.002 , 0.02 | *0.104* |
| ***PPWG*** | -0.01 | -0.06 , 0.03 | *0.528* | 0.01 | 0.001 , 0.02 | *0.025* |
| ***PPWR+WG*** | -0.02 | -0.07 , 0.02 | *0.227* | 0.01 | 0.002 , 0.02 | *0.015* |
| **Log triglycerides** | | | | | | |
| ***PPWR*** | 0.13 | -0.08 , 0.33 | *0.224* | 0.04 | -0.01 , 0.09 | *0.093* |
| ***PPWG*** | -0.03 | -0.18 , 0.12 | *0.673* | 0.04 | 0.01 , 0.08 | *0.017* |
| ***PPWR+WG*** | 0.05 | -0.09 , 0.18 | *0.477* | 0.04 | 0.01 , 0.07 | *0.009* |
| **Log HOMA-IR** | | | | | | |
| ***PPWR*** | -0.08 | -0.33 , 0.17 | *0.534* | 0.09 | -0.01 , 0.20 | *0.082* |
| ***PPWG*** | 0.12 | -0.06 , 0.30 | *0.196* | 0.10 | 0.02 , 0.17 | *0.011* |
| ***PPWR+WG*** | 0.26 | 0.09 , 0.42 | *0.002* | 0.10 | 0.03 , 0.17 | *0.004* |
| **Log HDL-c** | | | | | | |
| ***PPWR*** | -0.12 | -0.23 , -0.01 | *0.028* | -0.02 | -0.04 , 0.003 | *0.101* |
| ***PPWG*** | -0.08 | -0.16 , -0.004 | *0.040* | -0.02 | -0.03 , -0.002 | *0.023* |
| ***PPWR+WG*** | -0.06 | -0.13 , 0.01 | *0.081* | -0.02 | -0.03 , -0.004 | *0.013* |
| ***Group 2*** | | | | | | |
| ***SBP (mm Hg)*** | | | | | | |
| ***PPWR*** | 2.46 | -1.72 , 6.65 | *0.249* | 0.14 | -0.30 , 0.59 | 0.530 |
| ***PPWG*** | 0.94 | -2.08 , 3.95 | *0.542* | 0.15 | -0.31 , 0.61 | 0.515 |
| ***PPWR+WG*** | 2.21 | -0.57 , 5.00 | *0.119* | 0.15 | -0.29 , 0.58 | 0.514 |
| ***DBP (mm Hg)*** | | | | | | |
| ***PPWR*** | 3.07 | -0.42 , 6.57 | *0.085* | -0.28 | -0.74 , 0.19 | *0.245* |
| ***PPWG*** | -0.51 | -3.05 , 2.03 | *0.693* | -0.30 | -0.73 , 0.14 | *0.180* |
| ***PPWR+WG*** | 1.68 | -0.63 , 3.98 | *0.155* | -0.28 | -0.69 , 0.13 | 0.175 |
| ***Group 3*** | | | | | | |
| ***Log total-c*** | | | | | | |
| ***PPWR*** | -0.02 | -0.10 , 0.05 | *0.578* | 0.004 | -0.004 , 0.01 | 0.295 |
| ***PPWG*** | -0.01 | -0.07 , 0.04 | *0.665* | 0.004 | -0.003 , 0.01 | 0.241 |
| ***PPWR+WG*** | 0.004 | -0.04 , 0.05 | *0.861* | 0.004 | -0.003 , 0.01 | 0.237 |
| ***Log LDL-c*** | | | | | | |
| ***PPWR*** | -0.01 | -0.14 , 0.11 | *0.834* | -0.002 | -0.01 , 0.01 | 0.691 |
| ***PPWG*** | -0.06 | -0.15 , 0.04 | *0.226* | -0.002 | -0.01 , 0.01 | 0.687 |

| | | | | | | |
|---|---|---|---|---|---|---|
| ***PPWR+WG*** | 0.02 | -0.06 , 0.10 | *0.621* | -0.002 | -0.01 , 0.01 | *0.686* |

Reference group: return to pregestational weight.
[1] Indirect paths are mediated through waist circumference at six years instead of BMI.
DBP, diastolic blood pressure; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-c, low-density lipoprotein cholesterol; PPWG, postpartum weight gain; PPWR, postpartum weight retention; PPWR+WG, postpartum weight retention + weight gain; SBP, systolic blood pressure; Total-c, total cholesterol.

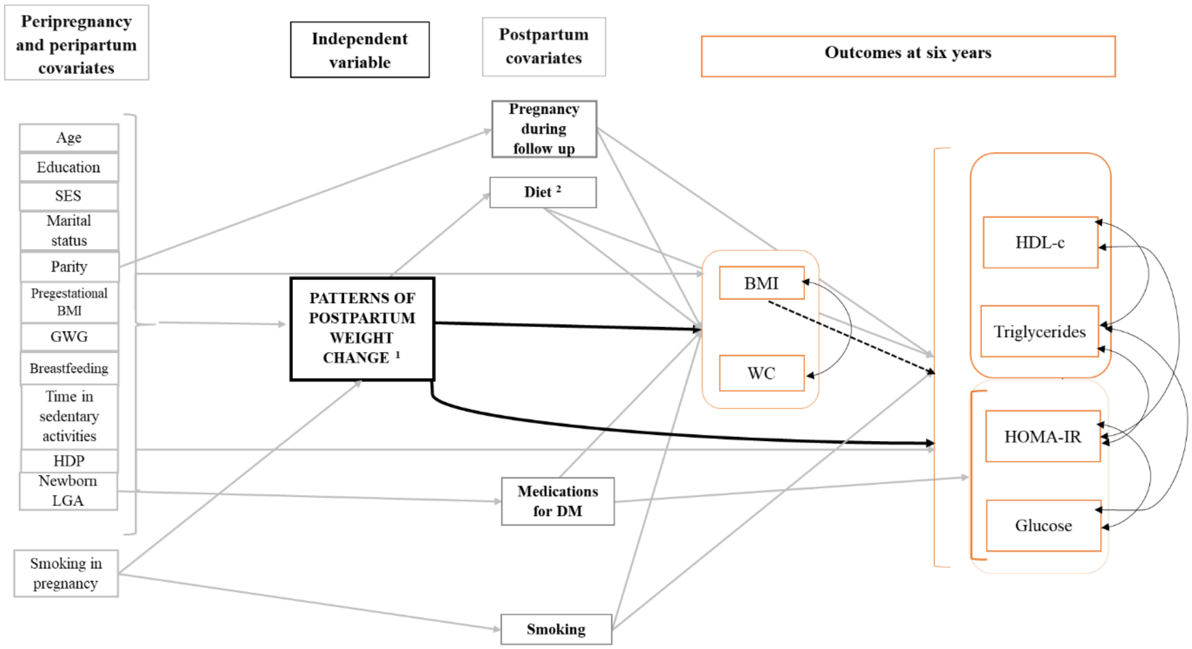



**Supplemental figure 1.** Flowchart of the study population

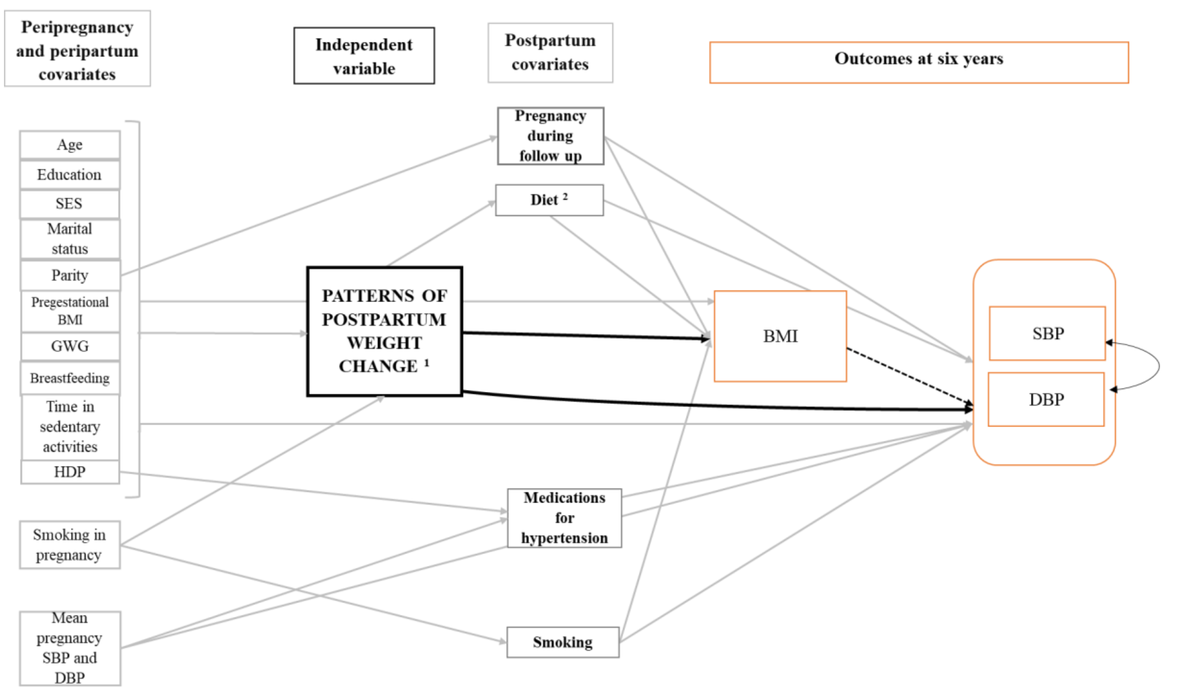



**Supplemental figure 2.** BMI by patterns of weight change from 12 to 72 months postpartum. The figure displays the mean BMI (kg/m$^2$) by patterns of weight change and postpartum month. The pregestational BMI in each group is included as a reference. PPWG, postpartum weight gain; PPWR, postpartum weight retention; PPWR+WG, postpartum weight retention + weight gain.

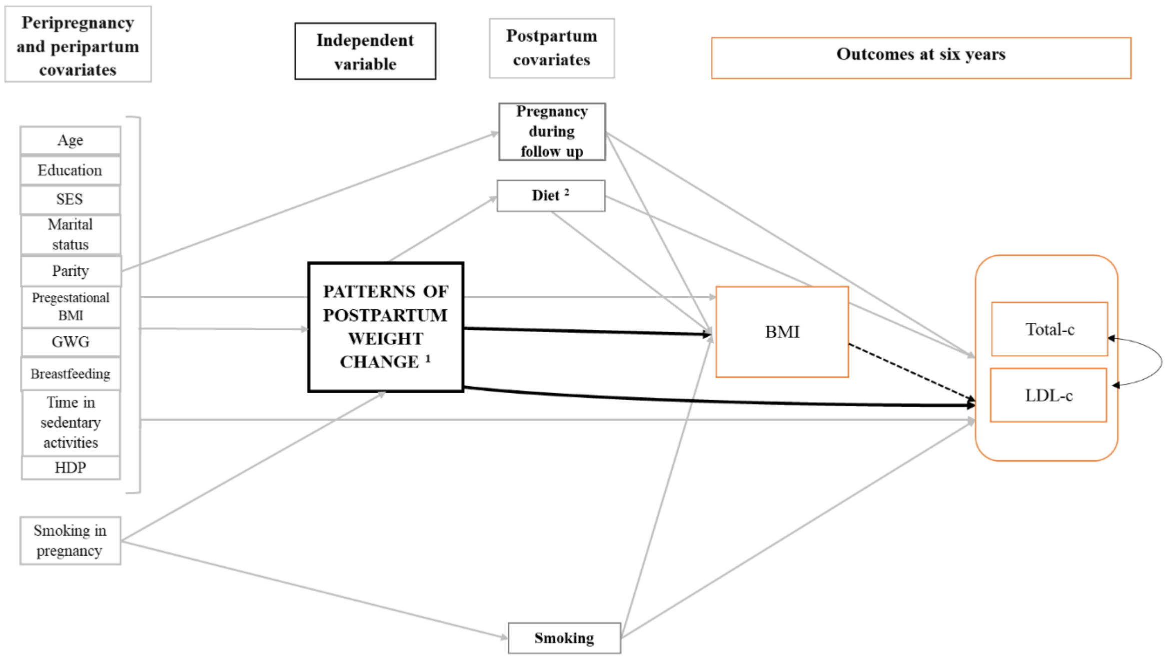
**A**


Peripregnancy and peripartum covariates
Independent variable
Postpartum covariates
Outcomes at six years
Age
Education
SES
Marital status
Parity
Pregestational BMI
GWG
Breastfeeding
Time in sedentary activities
HDP
Newborn LGA
Smoking in pregnancy
Pregnancy during follow up
Diet ²
PATTERNS OF POSTPARTUM WEIGHT CHANGE ¹
Medications for DM
Smoking
BMI
WC
HDL-c
Triglycerides
HOMA-IR
Glucose

**B**


Peripregnancy and peripartum covariates
Independent variable
Postpartum covariates
Outcomes at six years
Age
Education
SES
Marital status
Parity
Pregestational BMI
GWG
Breastfeeding
Time in sedentary activities
HDP
Smoking in pregnancy
Mean pregnancy SBP and DBP
Pregnancy during follow up
Diet ²
PATTERNS OF POSTPARTUM WEIGHT CHANGE ¹
Medications for hypertension
Smoking
BMI
SBP
DBP

**C**




**Supplemental figure 3.** Initial path models of the association between patterns of weight change one year after delivery and cardiometabolic risk factors at six years postpartum. **Figure A** highlights the possible paths between the patterns of postpartum weight change and outcome group 1; **figure B** focuses on outcome group 2; **figure C** refers to outcome group 3. Arrows represent pathways among variables. The black arrows represent paths relevant to our study objectives. A continuous black arrow indicates a possible direct association between the patterns of postpartum weight change and outcomes; a doted black arrow highlights a possible indirect association between patterns of weight change and outcomes, mediated through BMI at six years.

[1] Patterns of postpartum weight change included: return to pregestational weight (reference group), postpartum weight retention, postpartum weight gain, postpartum weight retention + weight gain.

[2] Diet includes energy intake per day (kcal), and servings of sugar-sweetened beverages per day at six years.

BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; GWG, gestational weight gain; HDL-c, high-density lipoprotein cholesterol; HDP, hypertensive disorders of pregnancy; HOMA-IR, homeostatic model assessment of insulin resistance;

LDL-c, low-density lipoprotein cholesterol; LGA, large for gestational age; SBP, systolic blood pressure; SES, socioeconomic status; total-c, total cholesterol; WC, waist circumference.