

ORIGINAL ARTICLE

GESTATIONAL WEIGHT GAIN AS A PREDICTOR OF MACROSOMIA AND LOW BIRTH WEIGHT: A SYSTEMATIC REVIEW

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ABSTRACT

Objectives: To evaluate the predictive capacity of gestational weight gain recommendations regarding low birth weight (LBW) and neonatal macrosomia, proposed by the Institute of Medicine (IOM) and the Latin American Center of Perinatology (CLAP). **Materials and methods:** The bibliographic search was performed in PubMed, Embase (via Ovid), Cochrane Library, EBSCOhost, Scopus, LILACS and SciELO. Methodological quality was evaluated using QUADAS 2. **Results:** A total of 1,192 articles were identified, only 5 articles met the inclusion criteria, no study evaluated the CLAP recommendations. Sensitivity and specificity to predict LBW and macrosomia varied widely depending on which country the study took place. In the Latin American cohorts, the sensitivity for predicting LBW ranged from 62.8% to 74% and the specificity from 61.7% to 68%, while the sensitivity for predicting macrosomia was 28.8% and the specificity 43.8%. In most studies the positive predictive value was less than 25%, and the negative predictive value was more than 90%. Most studies had high risk of bias and applicability problems in patient selection. **Conclusions:** The limited methodological quality and representativeness of the studied cohorts, probable unadjusted confounding factors and modest values of sensitivity and specificity suggest the need to develop studies aimed at providing recommendations that fit the epidemiological characteristics of the Peruvian population.

Keywords: Gestational Weight Gain; Sensitivity and Specificity; infant, Low birth weight; Fetal Macrosomia (source: MeSH NLM).

INTRODUCTION

Weight gain during gestation is an important predictor of newborn outcomes⁽¹⁾. Insufficient gain increases the risk of preterm and low birth weight (LBW) births^(2,3), while excessive gain increases the risk of neonatal macrosomia⁽⁴⁾. In turn, both LBW and macrosomia increase neonatal mortality and morbidity⁽¹⁾, adverse maternal outcomes⁽²⁾, and the risk of chronic diseases during adulthood^(2,5), which means a significant economic burden on health services and society⁽⁶⁾.

During the 1970s and 1980s, a single gestational weight gain of 12.5 kg was recommended in most countries, regardless of pre-pregnancy weight and height⁽⁷⁾. In 1983, the Latin American Center for Perinatology (CLAP) of the Pan American Health Organization developed weight gain patterns when pre-pregnancy weight was unknown⁽⁸⁾. While in 1990, the Institute of Medicine (IOM) of the United States published recommendations for weight gain during pregnancy, adopted by most countries worldwide, and updated in 2009⁽¹⁾.

In Peru, the recommendations from CLAP and the IOM are commonly used because of the absence of a national pattern of weight gain during pregnancy. However, both international

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patterns present limitations that affect their diagnostic accuracy, such as the origin and age of the basic epidemiological data, the representativeness of the reference population, and methodological aspects, such as the inclusion and source of information on pre-pregnancy body mass index (BMI) data. For this reason, a systematic review was carried out to evaluate the ability of both recommendations to predict LBW and neonatal macrosomia.

MATERIALS AND METHODS

This systematic review seeks to evaluate the best diagnostic parameter for pregnancy weight gain. The study was conducted following the recommendations of the PRISMA statement⁽⁹⁾, except for the protocol's registration in a database, which is available upon request to the corresponding author.

Bibliographic search strategy

A systematic search for observational prospective or retrospective cohort and case-control studies was conducted in 7 electronic databases: PubMed, Embase (via OVID), Cochrane Library, EBSCOhost, Scopus, LILACS, and SciELO; by using a combination of the following search terms: pregnancy, gestation, pregnant women, gestational weight gain, accuracy, sensitivity, specificity, predictive value. The search for studies was limited to those published in Spanish and English, without being restricted by the publication date. The last search took place in May 3, 2019. The search strategies for each database consulted are found in the supplementary material. Additionally, a manual search was performed on Google Scholar and the reference lists of the selected studies were checked to include any relevant references.

Eligibility criteria

Studies that met the following criteria were considered: a) type of participants: apparently healthy pregnant women of any age and gestational condition (single or multiple pregnancy); b) index tests: total and/or trimester-specific gestational weight gain, as recommended by CLAP and IOM; c) standard: low birth weight and neonatal macrosomia diagnosis, according to criteria, such as low birth weight below 2,500 g, and neonatal macrosomia above 4,000 g; d) outcome measurement types: sensitivity, specificity, positive or negative predictive value.

KEY MESSAGES

Motivation for the study: The recommendations on gestational weight gain from the Institute of Medicine (IOM) and the Latin American Center for Perinatology (CLAP) are widely used; however, they have methodological limitations that could affect their ability to predict low birth weight (LBW) and macrosomia.

Main findings: The IOM recommendations showed low sensitivity and specificity in predicting LBW and macrosomia, especially in cohorts from Latin America. No studies evaluated the CLAP recommendations.

Implications: Studies with adequate methodological quality are required to establish recommendations adjusted to the epidemiological characteristics of the Peruvian population.

Study selection and data extraction

Records obtained with the search strategy were initially evaluated by reading first the titles and abstracts, and then the full text of the selected articles. The information about the study methodology, participants, intervention, control and reported outcomes was registered in a data extraction form designed in Microsoft® Excel 2010.

Results presentation

Quantitative variables are presented as averages plus standard deviation. Qualitative variables are presented as proportions. For both types of variables, and if available, the 95% confidence intervals and the values of statistical significance are presented. When sensitivity, specificity, and positive or negative predictive values were not found in the study, these data were calculated using Review Manager 5.3 (The Cochrane Collaboration, Oxford, UK).

Quality assessment of the studies

The methodological quality of each included study was evaluated using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS 2) tool (10). Two independent reviewers participated in each stage. Any disagreement was resolved by group discussion or by consensus of the authors.

RESULTS

A total of 2,601 references were identified. The systematic review included 5 studies that met the previously established selection criteria⁽¹¹⁻¹⁵⁾ (Figure 1).

Characteristics of the included studies

The studies were conducted in public health facilities located in the United States⁽¹²⁾, Brazil^(13,14), Italy⁽¹¹⁾, and China⁽¹⁵⁾. Only 4 studies used a retrospective cohort design^(12,15) and 1 used a prospective cohort design⁽¹¹⁾. The data collection period ranged from 7 months to 9 years (Table 1).

One study was conducted on adolescents with an average age of 17.6 years⁽¹³⁾, and 4 studies were conducted in adults with ages between 26.5 and 31.7 years on average^(11,12,14,15). Two studies reported a greater predominance of white pregnant women^(12,13), and 3 studies did not report the race of the study population^(11,14,15). In the 2 studies that reported the newborn sex, a similar male to female ratio was obser-

ved^(11,15). All studies evaluated the diagnostic accuracy of the gestational weight gain recommendations suggested by the IOM (Table 2).

Interventions' effect

Low birth weight

Barros⁽¹³⁾, Carvallo⁽¹⁴⁾, and Li⁽¹⁵⁾ reported that the prevalence of LBW varied between 2.2% and 10.8%. The sensitivity was 16.9% in the Chinese population⁽¹⁵⁾, and varied between 62.8% and 74% in the Brazilian population^(13,14). The specificity varied between 61.7% and 68.3% in the Brazilian population^(13,14), and it was 90.3% in the Chinese population⁽¹⁵⁾.

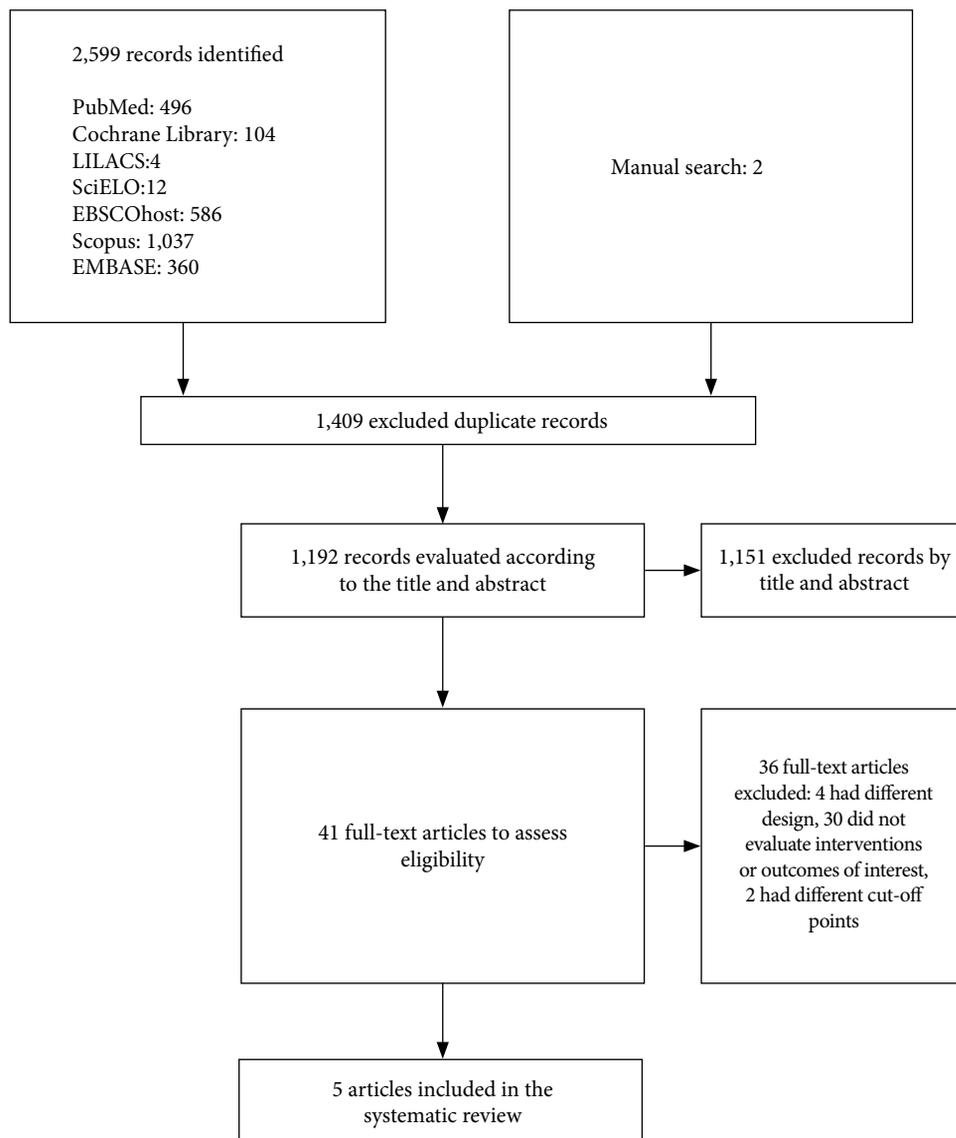


Figure 1. Study selection flowchart

The positive predictive value varied between 3.8% and 19.2%, while the negative predictive value varied between 6.1% and 98% (Table 3).

Neonatal Macrosomia

Prevalence of neonatal macrosomia varied between 4% and 15.6%. Sensitivity, between 28.8% and 76%. The specificity, between 43.8% and 72.6%. The positive predictive value, between 12.6% and 92.6%, and the negative predictive value, between 89.1% and 97.6% (Table 3). The estimates correspond to 4 studies: Alberico ⁽¹¹⁾, Asplund ⁽¹²⁾, Barros ⁽¹³⁾ and Li ⁽¹⁵⁾.

Quality evaluation

All studies presented a high risk of bias regarding patient selection and the reference test. Most studies showed a high risk of bias regarding the index, flow and time tests. As for the applicability of the studies, most of them presented high risk in the patient selection and low risk in the reference

test; the results of the index test were variable (Table 4).

DISCUSSION

Nowadays, there is a greater understanding of the interaction between maternal diet, pre-pregnancy BMI, weight gain during pregnancy, maternal comorbidities, and immediate and long-term health outcomes ⁽¹⁶⁾. However, optimal gestational weight gain has not yet been clearly defined and remains a controversial and critical issue ⁽¹⁷⁾. There are weight gain recommendations from the IOM and CLAP, which are commonly used in prenatal care. In this context, the study aimed to evaluate the recommendations for gestational weight gain proposed by the IOM and CLAP based on their ability to predict birth weight and neonatal macrosomia knowing that they have been associated with a significant increase in the risk of adverse maternal and neonatal outcomes ⁽¹⁸⁾.

The findings suggest that the country where the study takes place influences both outcomes. With respect to low

Table 1. Characteristics of the studies included

Author, year	Country	Study design	Inclusion criteria	Exclusion criteria	Data collection period	Research sites
Alberico, 2014 ⁽¹¹⁾	Italy	Prospective cohort	Pregnancies with complete records of variables of interest	Multiple pregnancy, premature birth.	18 months	Health facilities that attend low-risk births
Asplund, 2008 ⁽¹²⁾	United States	Retrospective cohort	Delivery of a live newborn baby at 37-42 gestation weeks	Gestational diabetes, multiple pregnancy, admission to prenatal care after the first trimester, premature delivery, incomplete data	7 months (June - December 2006)	Armed forces health facility
Barros, 2014 ⁽¹³⁾	Brazil	Retrospective cohort	Pregnant adolescents with information on pre- and post-pregnancy weight, height, gestational age at birth, date of last period, no chronic disease, singleton pregnancy	NR	20 months (July 1999 - March 2001)	Municipal maternity hospitals
Carvalho Padilha, 2015 ⁽¹⁴⁾	Brazil	Retrospective cohort	Pregnant women >20 years, no chronic diseases, singleton pregnancy, access to prenatal care, no dietary restrictions	NR	9 years (1999 - 2008)	Public maternity hospital
Li, 2013 ⁽¹⁵⁾	China	Retrospective cohort	Pregnancies attended in an urban health center with complete obstetric and neonatal records	Fetal death, multiple pregnancy, multiparous mothers, incomplete obstetric and neonatal records.	23 months (June 2009 - May 2011)	Maternal and Child Health Center

NR: not reported

Table 2. Characteristics of the study population

Author, year	Initial N / included N	Mean age (years) (SD)	Race	Mother's height	Weight/Pre-seasonal BMI	Gestational diseases	Tobacco/ alcohol consumption	Newborn sex
Alberico, 2014 ⁽¹¹⁾	15,255/14,109	31.7 (5.2)	NR	<165 cm: 52.9% >165 cm: 47.1%	Average weight: 62.1 kg	Gestational diabetes: 2.6%	NR	Female: 49.7% Male: 50.3%
Asplund, 2008 ⁽¹²⁾	238/186	26.5	White: 56.5% Black: 25.8%	NR	BMI: Women with normal weight newborn: 25.8 + 5.09 Women with macrosomic newborn: 25.3 + 5.43	Exclusion	NR	NR
Barros, 2014 ⁽¹³⁾	1,968/826	17.6 (1.35)	Caucasian: 50.2%	NR	BMI (WHO, 2007): According to age Low weight: 2.5% Adequate: 83.9% Overweight: 11.5% Obesity: 2.1%	Gestational diabetes: 1.3%	NR	NR
Carvalho Padilha, 2015 ⁽¹⁴⁾	NR/827	27.6 (5.2)	NR	NR	BMI (WHO, 1995): Low weight (<18.5): 10.9% Normal (18.5-24.99): 63.8% Overweight/Obesity (>25): 25.3%	NR	NR	NR
Li, 2013 ⁽¹⁵⁾	43,854/33,973	27.6	NR	NR	BMI (WOGC, 2004): Low weight (<18.5): 11.2% Normal (18.5-23.9): 64.6% Overweight (24-27.9): 18.2% Obesity (>28): 6	Gestational diabetes: 5.1% Pregnancy-induced HBP: 2.5%	Smoking <18.5: 1.2% 18.5-23.9: 1% 24-27.9: 1.2% >28: 2.2%	Female: 51.7% Male: 48.3%

HBP: high blood pressure; BMI: body mass index; NR: not reported; WHO: World Health Organization; WOGC: Working Group on Obesity in China; SD: standard deviation

birth weight, the findings were consistent, showing similar values for sensitivity and specificity among the Brazilian cohort of adult pregnant women ⁽¹⁴⁾ and adolescent pregnant women ⁽¹³⁾; different from those obtained in a Chinese cohort, which presents lower sensitivity and higher specificity ⁽¹⁵⁾. These differences were also observed in the outcome of neonatal macrosomia, where the Brazilian cohort obtained less sensitivity and specificity ⁽¹³⁾, compared with the Italian ⁽¹¹⁾, American ⁽¹²⁾, and Chinese ⁽¹⁵⁾ cohorts.

Some studies describe differences in pre-pregnancy nutritional status, weight gain during pregnancy, and the magnitude of risk of adverse gestational and neonatal outcomes around populations of different continents and ethnicities ^(19,20). In that sense, the IOM proposed the development of additional studies to investigate whether the recommendations for weight gain

during pregnancy differ according to the racial/ethnic group, suggesting that they could reflect not only the biological differences between the groups, but also the difference in their socio-economic conditions ⁽¹⁾.

On the other hand, the studies included in our review reported a higher proportion of negative predictive values, mostly above 90%, compared to the proportion of positive predictive values, mostly below 25% for both outcomes. Positive and negative predictive values indicate the probability that a diagnostic test will obtain the correct diagnosis if it turns out to be positive or negative, while sensitivity and specificity assess the probability of obtaining a positive or negative result, depending on the patient's true condition. In a scenario where this condition is previously unknown, predictive values could be relevant to support clinical decisions ^(21,22).

However, the prevalence of the disease or condition to be

Table 3. Results on diagnostic accuracy

Author, year	Prevalence of the outcome %	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)
Low birth weight					
Barros, 2014 ⁽¹³⁾	10.8	62.8	68.3	19.2	6.1
Carvalho Padilha, 2015 ⁽¹⁴⁾	4.6	74	61.7	10.4	97.5
Li, 2013 ⁽¹⁵⁾	2.2	16.9 (14.3-19.8)	90.3 (90.0-90.6)	3.8 (3.2-4.5)	98 (97.8-98.1)
Neonatal macrosomia					
Alberico, 2014 ⁽¹¹⁾	7.6	48.5 (45.5-51.6)	72.5 (71.7-73.2)	12.6 (11.6-13.7)	94.5 (94.1-95)
Asplund, 2008 ⁽¹²⁾	15.6	51.7 (32.9-70.1)	72.6 (64.8-79.3)	25.9 (15.6-39.3)	89.1 (82.0-93.7)
Barros, 2014 ⁽¹³⁾	4	28.8	43.8	92.6	97.6
Li, 2013 ⁽¹⁵⁾	9.8	76 (74.5-77.4)	44.9 (44.4-45.5)	13 (12.5-13.5)	94.5 (94.2-94.9)

95% CI: 95% confidence interval

evaluated influences the predictive values. When it is low, the negative predictive value is higher and, consequently, the positive predictive value is lower ^(21,23). In this context, this review reports higher negative predictive values, which could mean an important characteristic and would allow the presence of low birth weight and neonatal macrosomia to be ruled out with greater security and confidence in settings where both prevalences are relatively low.

The average age of the adult pregnancy cohorts included in our review ranged from 26 to 31 years. This epidemiological characteristic differs from the fecundity of Peruvian women. In Peru, the average age at the first birth is 22.3 years, and 12.6% of women between 15 and 19 years have been pregnant at some time ⁽²⁴⁾, which increases the risk of

age-related adverse obstetric and neonatal outcomes ⁽²⁵⁾. The exact origin of this relationship has not been determined. One hypothesis suggests that the older the mother, the greater the body weight before pregnancy, due to the cumulative weight increase in adulthood ⁽²⁶⁾, while in older pregnant women the influence of the natural aging process and the existence of comorbidities cannot be ruled out ⁽²⁵⁾. Similarly, it has been demonstrated that adolescent pregnancy increases the obstetric and neonatal risk related to biological and social factors ⁽²⁷⁾.

Three studies reported the characteristics of maternal body mass index before pregnancy ⁽¹³⁻¹⁵⁾. In these 3 studies, 2.5% to 11.2% of the patients presented with thinness, and 13.6% to 25.3% presented with overweight or obesity before

Table 4. Quality evaluation of the included studies according to QUADAS 2

Author, year	Risk of bias				Applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Alberico, 2014 ⁽¹¹⁾	High	High	High	Low	High	Low	Low
Asplund, 2008 ⁽¹²⁾	High	High	High	High	Low	Not clear	Low
Barros, 2014 ⁽¹³⁾	High	High	High	High	High	Low	Low
Carvalho Padilha, 2015 ⁽¹⁴⁾	High	Low	High	High	High	Not clear	Low
Li, 2013 ⁽¹⁵⁾	High	High	High	High	High	High	Low

gestation. Both conditions differ from the characteristics of women of childbearing age in Peru, where thinness measured by BMI is found in 1.6%, and excess weight (overweight or obesity) in 62.2% (24). We believe that these differences could be explained by the age of the cohorts, between 1999 and 2009. These discrepancies could influence in the accuracy of the results of our review, given that there are studies that show that pre-pregnancy thinness is associated with an increased risk of low birth weight^(28,29), while pre-pregnancy overweight and obesity is associated with an increased risk of neonatal macrosomia⁽²⁹⁾. For this reason, it is important that recommendations on weight gain during pregnancy should consider the pre-pregnancy body mass index.

Three studies included pregnant women with gestational diabetes, with an average prevalence of 1.3% to 2.6%, and 1 study excluded pregnant women with this condition. Two studies did not report controlling this variable. In all cases, this situation limits the representativeness of the results, given that the estimated prevalence of gestational diabetes affects up to 16% of pregnant women in Peru⁽³⁰⁾. Gestational diabetes triples the risk of macrosomic births, while treatment of this disease reduces the incidence of macrosomia in neonates. The proposed physiological mechanisms to explain the relationship between gestational diabetes and macrosomia are explained by fetal hyperinsulinemia, increased glucose use, and increased fetal adipose tissue⁽³¹⁾.

There is no gold standard that properly assesses the fetal development and, at the same time, provides an error-free classification of all subjects assessed, verifies all index test results, and that can be performed within a short time interval that avoids changes in the target condition⁽³²⁾. Measuring fetal growth by using ultrasound or MRI does not comply with the conditions described above^(33,34); this is why gestational weight gain is used for an approximate measure of fetal growth, it is simple to use and low cost. However, misclassification due to an imperfect standard inevitably leads to positive or negative biased accuracy.

Worldwide, it is estimated that 47% of pregnant women had a gestational weight gain higher than IOM's recommendation, and 23% had a lower gain than those recommendations⁽¹⁸⁾. In this context, it has been identified that social determinants configure a complex problem that goes beyond solely biological issues. Within this set of social determinants, parity could influence the pre-pregnancy body mass index⁽³⁵⁾; periods between pregnancies under 18 months and over 59 months could increase the risk of low birth weight⁽³⁶⁾; low educational level

increases the risk of insufficient or excessive weight gain during pregnancy⁽³⁷⁾; psychological factors, such as emotional distress or dissatisfaction with body image, influence in weight gain⁽³⁸⁾, or low levels of physical activity during pregnancy increases the risk of excessive weight gain⁽³⁹⁾. Each of these social determinants is accompanied by underlying factors that interrelate to form a complex causal model.

One systematic review reported that quantifying weight as an isolated intervention in antenatal care is not effective in reducing weight gain during pregnancy⁽⁴⁰⁾. Thus, it should be part of the interventions made by health professionals in collaboration with mothers to achieve weight gain goals, such as to monitor and provide feedback on their progress⁽⁴⁰⁾, to have standardized and evidence-based approaches⁽⁴¹⁾, to improve knowledge and beliefs about weight gain in women of childbearing age⁽⁴²⁾, to incorporate a holistic approach integrating not only the pregnant woman, but also the family or her social environment⁽⁴³⁾, to provide nutritional consultation on healthy food, oriented to calories, needed macronutrients and adequate levels of physical activity⁽⁴⁴⁾, to accompany the dietary activities with strategies of behavior change, mainly in the provision of information, motivational interviews, self-monitoring and contingent rewards⁽⁴⁵⁾, to provide prenatal care with a multidisciplinary approach^(46,47). The exact duration, frequency, intensity or an optimal environment for providing these interventions has not been determined⁽⁴⁸⁾.

One of the most important limitations of this systematic review is that the majority of the included studies were retrospective cohorts that gathered information from medical records. Some other limitations, due to the study type: difficulty in controlling confounding factors (gestational age, mother's age, socioeconomic level, pre-existing diseases, among others), often there are no variables that could narrow the analysis or that could be measured precisely; additionally, not ensuring a high percentage of participation and follow-up increases the risk of probable selection bias. For example, the included studies had between 20% and 40% of data loss, mostly related to the variables of interest. Only 1 study⁽¹³⁾ analyzed the related characteristics between the studied population and the losses, and found significant differences between both groups. The heterogeneous methodology for measuring the variables of interest may not have been adequately controlled, which increased the risk of bias.

Our review focused on the ability to predict low birth weight and neonatal macrosomia as recommended by the IOM on gestational weight gain. However, inadequate gesta-

tional weight gain is also related to maternal outcomes: the lower probability of starting or continuing breastfeeding⁽⁴⁹⁾, increased postpartum weight retention⁽⁵⁰⁾, the risk of obesity, diabetes, heart disease, endocrine disease, and psychiatric disease in later years⁽⁵¹⁾. In the newborn, it is associated with an increased risk of obesity, metabolic and cardiovascular disease in later life⁽⁵²⁾.

We did not find studies that evaluated the ability of CLAP weight gain recommendations to predict LBW and neonatal macrosomia. As for the IOM recommendations, sensitivity and specificity was low, especially in Latin American cohorts. However, the low methodological quality of the studies, the limited representativeness of the studied cohorts and the probable unadjusted confounding factors indicate that there is a need to develop studies with an adequate methodological quality to allow the establishment of recommendations that would fit the epidemiological characteristics of the Peruvian population. Likewise, it is absolutely necessary to prevent inadequate weight gain during pregnancy,

providing quality antenatal care, based on a multidisciplinary approach, with interventions supported by scientific evidence and considering the different social determinants involved in its development.

Authors' contributions: GS, KA and PV conceived the original idea for the study. AA wrote the preliminary version of the protocol, which was reviewed and approved by all the authors. AA designed the strategies and conducted the systematic search for studies. All authors participated in the selection and data extraction of the studies. AA and GS wrote the preliminary version of the manuscript, whose final version was reviewed and approved by all the authors. All authors assume responsibility for the contents of the article.

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