

# Prevalence of low weight and small for gestational age in Argentina: Comparison between the INTERGROWTH-21<sup>st</sup> standard and an Argentine reference

Gabriela B. Revollo, B.S.<sup>a</sup>, Jorge I. Martínez, B.S.<sup>a</sup>, Carlos Grandi, M.D.<sup>b</sup>,  
Emma L. Alfaro, M.D.<sup>a</sup> and José E. Dipierri, M.D.<sup>a</sup>

## ABSTRACT

**Introduction.** The term “low birth weight” (< 2500 g) encompasses preterm newborns and term newborns small for gestational age (SGA) (< P10). The World Health Organization defines low weight (LW) as a birth weight < P3 of weight/age. There is no consensus at an international level about which standards and/or references related to birth weight for gestational age (GA) should be used to assess SGA and LW among preterm newborns. LW and SGA prevalence was determined using the INTERGROWTH-21<sup>st</sup> standard and Urquía’s reference for the Argentine population, and agreement between the prevalence observed with both tools was analyzed.

**Population and methods.** Observational, analytical, and retrospective study based on all births occurred in 2013 as reported by the Argentine National Ministry of Health. Exclusion criteria were GA < 24<sup>+0</sup> - > 42<sup>+6</sup> weeks, twin pregnancy, and missing data on weight, GA, and sex. Prevalence was estimated by sex, region, and prematurity category for LW and SGA according to the standard and the reference. Agreement was assessed using the Kappa index.

**Results.** The prevalence of LW and SGA was higher according to the standard among preterm newborns; the contrary was observed among full-term newborns. Statistical significance varied based on GA category, sex, and region. A higher prevalence was observed in the northern regions of Argentina, and agreement among prevalence values ranged from weak to very good.

**Conclusions.** Prevalence agreement of LW and SGA observed according to the standard and the reference among preterm and full-term newborn infants was moderate, with interregional variability. Results propose new auxological perspectives in the epidemiological assessment of intrauterine growth restriction in Argentina.  
**Key words:** growth charts, intrauterine growth restriction, small for gestational age newborn, prevalence.

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- a. Institute of Ecoregions of the Andes (Instituto de Ecorregiones Andinas, INECOA), National Scientific and Technical Research Council (Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET), Universidad Nacional de Jujuy (UNJu), High-Altitude Biology Institute (Instituto de Biología de la Altura, INBIAL), San Salvador de Jujuy.
- b. School of Medicine, Universidade de São Paulo, Brazil.

## E-mail address:

Gabriela B. Revollo, B.S.:  
gabrielairevollo@gmail.com

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## INTRODUCTION

The prevalence of low birth weight (LBW, birth weight [BW] < 2500 g) is a general health indicator that demonstrates the socioeconomic and environmental circumstances of people and society.<sup>1</sup> By means of Resolution 65.6, the World Health Assembly proposed to reduce LWB by 30% in 2025.<sup>2</sup>

LBW includes small for gestational age (SGA) newborns and preterm newborns as well as overlapping cases. SGA is an indicator of intrauterine growth restriction and, together with prematurity, constitutes a risk factor for fetal, neonatal, and infant mortality, and negative consequences on health in the long term.<sup>3,4</sup>

There is no international consensus on anthropometric analysis among preterm newborns. The National Committee on Growth and Development (*Comité Nacional de Crecimiento y Desarrollo*) and the Fetoneonatal Study Committee (*Comité de Estudios Fetoneonatales*) have proposed the curves obtained by Fenton and Kim for preterm newborn infants (NBIs) follow-up.<sup>5</sup> References describe how subjects “have grown” in a specific time and place; however, standards are prescriptive and describe how subjects “should grow” in optimal conditions. Recently, weight, height, and head circumference standards for NBIs by sex and gestational age (GA) were published by the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century Project (INTERGROWTH-21<sup>st</sup>).<sup>6</sup> This was a cross-sectional,

multicenter, cross-cultural study of NBI growth, conducted using the same prescriptive approach and methodological design as in the development of the World Health Organization (WHO) Child Growth Standards currently valid in Argentina.<sup>7,8</sup> The INTERGROWTH-21<sup>st</sup> helps to conduct an anthropometric analysis of full-term and preterm NBIs born between 24<sup>+0</sup> and 42<sup>+6</sup> weeks of GA. In 2011, Urquía et al. published a BW reference for the Argentine population, which was representative of the recent Argentine population and included all births occurred between 2003 and 2007.<sup>9</sup>

The WHO defines low weight (LW) as a BW for GA < P3 according to the WHO Child Growth Standards,<sup>7</sup> which is appropriate for term NBIs for whom GA is not reliably known and for those who did not have a LBW. If GA is known accurately and NBIs present intrauterine growth restriction, it is better to use an appropriate BW for GA reference or standard. Villar et al.<sup>10</sup> define two different altered fetal growth phenotypes, which are analogous to those proposed by the WHO, to define malnutrition in NBIs: stunting and wasting. These phenotypes are defined based on length (stunting) and body mass index (wasting) measurements at birth lower than the P3 of the INTERGROWTH-21<sup>st</sup>. By extension, in this study, LW is used to describe fetal malnutrition.

The objective of this study was to determine the prevalence of LW and SGA by sex at a regional level by GA among Argentine NBIs using the INTERGROWTH-21<sup>st</sup> standard<sup>6</sup> and Urquía's reference for the Argentine population,<sup>9</sup> and to analyze agreement between the prevalence observed with each tool.

## POPULATION AND METHODS

This was an observational, analytical, and retrospective study based on all live births occurred in Argentina in 2013. Data were publicly available and obtained from the Live Birth Statistical Report (Health Statistics and Information Department of the Ministry of Health of Argentina).<sup>11</sup> Exclusion criteria were GA < 24<sup>+0</sup> - > 42<sup>+6</sup> weeks, twin pregnancy, and missing data on weight, GA, and sex.

Intrauterine growth restriction was classified based on the following indicators: LW (< P3 BW/GA) and SGA (< P10 BW/GA). To define LW and SGA, the INTERGROWTH-21<sup>st</sup> standard<sup>6</sup> and Urquía's reference for the Argentine population for BW were used.<sup>9</sup>

According to GA, NBIs were grouped into the following categories: a) extremely preterm (< 28<sup>+0</sup> weeks); b) very preterm (28<sup>+0</sup> - ≤ 31<sup>+6</sup> weeks); c) moderate to late preterm (32<sup>+0</sup> - ≤ 36<sup>+6</sup> weeks); and d) full-term (≥ 37<sup>+0</sup> weeks).<sup>12</sup>

LW and SGA prevalence was estimated by sex and GA category by census regions: 1) Northwest region of Argentina (NOA) (Jujuy, Salta, Tucumán, Santiago del Estero, Catamarca, and La Rioja); 2) Northeast region of Argentina (NEA) (Formosa, Chaco, Misiones, and Corrientes); 3) Cuyo (San Juan, San Luis, and Mendoza); 4) Central region of Argentina (Santa Fe, Córdoba, Entre Ríos, Buenos Aires, and La Pampa); 5) Autonomous City of Buenos Aires (CABA); and 6) Patagonia (Neuquén, Río Negro, Chubut, Santa Cruz, and Tierra del Fuego). The regional prevalence of LBW was also estimated.

Graphic comparisons were done between the P3 and P10 of the INTERGROWTH-21<sup>st</sup> and Urquía's reference for the Argentine population. The Kappa index was used to assess agreement between the prevalence observed according to both tools, and it was classified into poor (≤ 0.20), weak (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), and very good (> 0.80).<sup>13</sup> Prevalence differences between both sexes and according to the reference and the standard were estimated using the  $\chi^2$  test. The significance level was established at  $p < 0.001$  due to the large sample size. The SPSS IBM version 22 and MEDCALC software were used.

## RESULTS

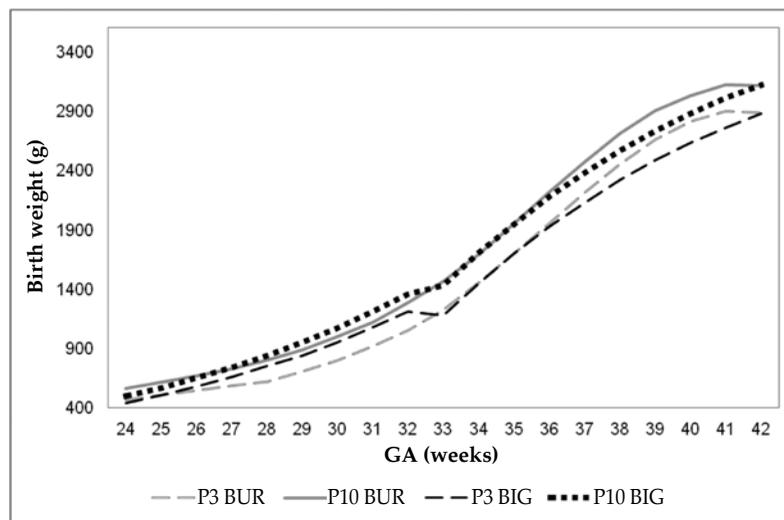
The population included 735 491 live NBIs born in Argentina in 2013. *Figure 1* and *2* show the BW P3 and P10 by sex according to the INTERGROWTH-21<sup>st</sup> standard and Urquía's reference for the Argentine population. In both boys and girls, as of 27<sup>+0</sup> - 33<sup>+6</sup> weeks, both percentiles were higher based on the INTERGROWTH-21<sup>st</sup> standard; from 33<sup>+0</sup> to 36<sup>+6</sup> weeks, the percentiles obtained with the reference and the standard practically overlapped; and as of 37<sup>+0</sup> weeks, the reference shows higher percentiles.

*Tables 1* and *2* show the prevalence of LW and SGA by sex and GA category. In both boys and girls, LW and SGA prevalence was higher according to the standard across all prematurity categories; the contrary was observed among full-term NBIs. The statistical significance of such differences was highly heterogeneous by GA category, sex, and geographic region but,

remarkably, statistically significant differences were observed in the full-term category in all regions and both sexes. In the very preterm and moderately to late preterm categories, in some regions and, exclusively in boys, prevalence agreement of LW and SGA in both, boys and girls, was very good (> 0.80), whereas in the rest of the categories and in full-term NBIs, agreement ranged from fair to good.

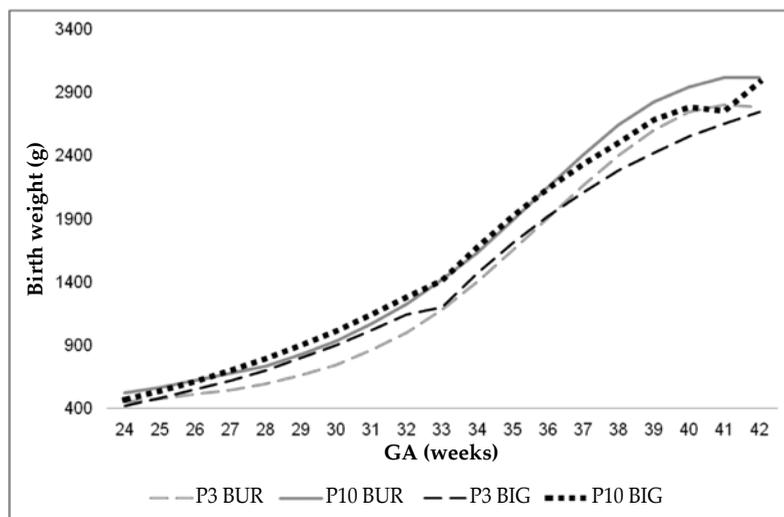
Figure 3 shows the prevalence distribution of LBW, LW, and SGA by region according to the standard and the reference, regardless of sex. Whereas LBW prevalence is similar across all regions, a higher interregional heterogeneity of LW and SGA was observed. The CABA and Patagonia regions show a lower prevalence of LW and SGA according to both the reference and the standard.

FIGURE 1: Comparison between Urquía's reference for the Argentine population and the INTERGROWTH-21<sup>st</sup> standard for the 3rd and 10th percentiles of birth weight (Argentina, 2013, boys)



GA: gestational age. P3 BUR: 3rd percentile, boys, Urquía et al. P10 BUR: 10th percentile, boys, Urquía et al. P3 BIG: 3rd percentile, boys, INTERGROWTH-21<sup>st</sup>. P10 BIG: 10th percentile, boys, INTERGROWTH-21<sup>st</sup>.

FIGURE 2: Comparison between Urquía's reference for the Argentine population and the INTERGROWTH-21<sup>st</sup> standard for the 3rd and 10th percentiles of birth weight (Argentina, 2013, girls)



GA: gestational age. P3 GUR: 3rd percentile, girls, Urquía et al. P10 GUR: 10th percentile, girls, Urquía et al. P3 GIG: 3rd percentile, girls, INTERGROWTH-21<sup>st</sup>. P10 GIG: 10th percentile, girls, INTERGROWTH-21<sup>st</sup>.

At a national level, LW prevalence was very similar among boys and girls according to the INTERGROWTH-21<sup>st</sup> standard and higher among preterm NBIs compared to Urquía's reference for the Argentine population, and statistically

significant among very preterm, moderate preterm, and full-term NBIs. Agreement was good to very good in 3 out of 4 categories.

In addition, SGA prevalence was higher according to the INTERGROWTH-21<sup>st</sup> standard

TABLE 1: Prevalence of low weight according to Urquía's reference for the Argentine population and the INTERGROWTH-21<sup>st</sup> standard by sex and gestational age category, based on Argentine regions (2013)

Region/ country	GA categories	Girls					Boys				
		Reference		Standard		Kappa	Reference		Standard		Kappa
		N	Prev.	N	Prev.		N	Prev.	N	Prev.	
NOA	EP	2	1.5	5	3.6	0.562	2	1.5	4	3.0	0.660
	VP	3	1.1	20	7.3	0.247	1	0.4	20	7.2*	0.089
	MP	126	3.4	153	4.1	0.899**	144	3.8	149	3.9	0.925**
	FT	1372	3.1	683	1.5*	0.658	1572	3.4	799	1.7*	0.666
NEA	EP	2	1.9	4	3.9	0.658	2	1.7	3	2.5	0.388
	VP	3	1.3	14	6.1*	0.339	2	0.8	14	5.6*	0.239
	MP	104	3.5	124	4.1	0.909**	100	3.3	105	3.4	0.894**
	FT	1396	4.1	745	2.2*	11.687	1435	4.0	728	2.0*	0.664
CUYO	EP	1	1.2	2	2.4*	0.661	0	SD (?)	1	1.1	ND (?)
	VP	3	2.0	8	5.3	0.532	0	SD (?)	7	4.1*	ND (?)
	MP	51	3.2	63	4.0	0.891**	46	2.9	48	3.0	0.956**
	FT	883	3.3	398	1.5*	0.613	898	3.4	456	1.7*	0.666
CENTRAL REGION	EP	9	1.6	19	3.4	0.635	17	2.5	26	3.8	0.688
	VP	24	1.8	71	5.4*	0.491	19	1.3	77	5.2*	0.383
	MP	481	3.1	592	3.8*	0.893**	590	3.4	615	3.5	0.917**
	FT	7154	3.9	4049	2.2*	0.715	7899	4.0	4429	2.2*	0.710
CABA	EP	0	ND (?)	1	1.6	ND (?)	4	4.4	5	5.6	0.883**
	VP	3	2.0	11	7.3	0.410	5	2.9	11	6.5	0.609
	MP	36	2.6	44	3.1	0.897**	47	3.1	51	3.4	0.895**
	FT	537	2.8	250	1.3*	0.629	524	2.6	223	U*	0.591
PATAGONIA	EP	2	3.3	4	6.7	0.651	1	1.3	3	3.8	0.490
	VP	1	0.8	7	5.5	0.240	5	2.7	9	4.9	0.704
	MP	26	1.8	36	2.6	0.835**	34	2.1	35	2.2	0.896**
	FT	412	2.2	195	1.0*	0.637	432	2.2	207	1.0*	0.643
TOTAL	EP	16	1.6	35	3.5	0.619	26	2.2	42	3.5	0.668
	VP	37	1.6	131	5.8*	0.426	32	1.3	138	5.5*	0.363
	MP	824	3.1	1012	3.8*	0.894**	961	3.3	1003	3.4*	0.916**
	FT	11 754	3.6	6320	1.9*	0.692	12 760	3.7	6842	2.0*	0.690

\* Statistically significant differences between the reference and the INTERGROWTH-21<sup>st</sup> standard ( $p < 0.001$ ).

\*\* Very good agreement (Kappa  $> 0.80$ ). GA: gestational age. SD: standard deviation. ND: no data.

CABA: Autonomous City of Buenos Aires. NOA: Northwest region of Argentina. NEA: Northeast region of Argentina. EP: extremely preterm. VP: very preterm. MP: moderately preterm. FT: full-term.

only among girls, while the Kappa index was good to very good across all GA categories.

## DISCUSSION

At a national level, and using the new

INTERGROWTH-21<sup>st</sup> standard for BW, a relative increase was observed in the prevalence of LW at a younger GA, which was approximately 1.2 to 3.6 times higher compared to Urquía's reference for the Argentine population. Such

TABLE 2: Prevalence of small for gestational age according to Urquía's reference for the Argentine population and the INTERGROWTH-21<sup>st</sup> standard by sex and gestational age category, based on Argentine regions (2013)

Region/ country	GA categories	Girls					Boys				
		Reference		Standard		Kappa	Reference		Standard		Kappa
		N	Prev.	N	Prev.		N	Prev.	N	Prev.	
NOA	EP	10	7.3	9	6.6	0.717	20	14.8	13	9.6	0.8
	VP	20	7.3	45	16.4*	0.572	35	12.6	46	16.6	0.8**
	MP	383	10.4	418	11.3	0.951**	436	11.4	411	10.7	0.9**
	FT	3940	8.8	1975	4.4*	0.647	4176	9.1	2255	4.9*	0.7
NEA	EP	2	1.9	11	10.7*	0.284	7	5.9	7	5.9	0.848**
	VP	14	6.1	30	13.2*	0.603	17	6.9	29	11.7	0.714
	MP	287	9.6	322	10.7	0.936**	307	10.1	296	9.7	0.925**
	FT	3624	10.7	2042	6.0*	0.697	3625	10.2	2069	5.8*	0.705
CUYO	EP	2	2.4	6	7.3	0.481	8	8.6	6	6.5	0.846**
	VP	8	5.3	16	10.7	0.641	14	8.2	17	10.0	0.894**
	MP	187	11.9	204	12.9	0.950**	182	11.4	171	10.7	0.946**
	FT	2577	9.7	1287	4.9*	0.643	2469	9.2	1311	4.9*	0.673
CENTRAL REGION	EP	38	6.7	44	7.8	0.685	84	12.2	57	8.3*	0.772
	VP	87	6.6	173	13.1*	0.637	134	9.1	188	12.7*	0.812**
	MP	1377	8.8	1490	9.5*	0.955**	1784	10.2	1738	9.9	0.930**
	FT	18 174	9.9	9828	5.3*	0.680	19 296	9.8	10 990	5.6*	0.705
CABA	EP	1	1.6	5	8.2	0.315	16	17.8	10	11.1	0.733
	VP	14	9.3	25	16.6	0.680	16	9.4	20	11.8	0.876**
	MP	145	10.3	154	10.9	0.966**	160	10.7	148	9.9	0.906**
	FT	1570	8.2	782	4.1*	0.646	1555	7.7	809	4.0*	0.667
PATAGONIA	EP	4	6.7	6	10.0	0.565	5	6.1	3	3.8	0.738
	VP	6	4.7	18	14.2*	0.462	15	8.2	26	14.1	0.701
	MP	100	7.1	112	7.9	0.939**	102	6.3	98	6.1	0.947**
	FT	1268	6.8	632	3.4*	0.649	1332	6.8	687	3.5*	0.665
TOTAL	EP	57	5.6	81	8*	0.612	140	11.6	96	8	0.775
	VP	149	6.6	307	13.6	0.620	231	9.1	326	12.9	0.809**
	MP	2479	9.2	2700	10.1	0.952**	2971	10.2	2862	9.8*	0.927**
	FT	31 153	9.5	16 546	5.1	0.672	32 453	9.4	18 121	5.2	0.696

\* Statistically significant differences between the reference and the INTERGROWTH-21<sup>st</sup> standard ( $p < 0.001$ ).

\*\* Very good agreement (Kappa > 0.80). GA: gestational age. CABA: Autonomous City of Buenos Aires.

NOA: Northwest region of Argentina. NEA: Northeast region of Argentina. EP: extremely preterm. VP: very preterm.

MP: moderately preterm. FT: full-term.



The pattern of divergence between the INTERGROWTH-21<sup>st</sup> standard and Urquía's reference for the Argentine population varies depending on GA. The BW of full-term NBIs with the INTERGROWTH-21<sup>st</sup> standard was lower than with the reference, but the difference between both curves widens among those with an older GA. It has been speculated that such divergence may be due to risk factors (gestational diabetes, maternal overweight and obesity) related to a higher birth weight and preterm birth,<sup>18</sup> which are more predominant in the Argentine population but were excluded from the INTERGROWTH-21<sup>st</sup> standard.

Among full-term NBIs, the LW category reflects body mass relative to GA and is influenced by both height and weight. Interpretation is intricate because it may be determined interchangeably or in combination with stunting and wasting. There is not much information about the prevalence of malnutrition phenotypes (wasted, LW, and stunted) among full-term NBIs, and even less among preterm ones.<sup>19</sup>

The overall and regional LW prevalence (Latin America and the Caribbean) among infants aged 0-5 months was 7% and 1%, respectively.<sup>20</sup> Although LW prevalence estimated in this study is higher than that established by the National Survey on Nutrition and Health (Encuesta Nacional de Nutrición and Salud, ENNyS) in 2004-2005,<sup>21</sup> both estimations are lower than the clinical and epidemiological significance levels (10%) proposed by the WHO.<sup>22</sup> According to the INTERGROWTH-21<sup>st</sup> standard, LW prevalence at a regional level is higher—almost twice as high—among preterm than full-term NBIs. On the contrary, according to the reference, LW prevalence tends to be higher among full-term NBIs in most regions (Figure 3).

At a national level and in all geographic regions, there was a very good agreement in the prevalence of LW and SGA between the reference and the standard in the moderately to late preterm category (Tables 1 and 2), which is consistent with the overlapping percentile curves observed in Figure 1. However, for the remaining prematurity categories, agreement was weak to moderate; for this reason, the results obtained with the standard and reference are dissimilar. This may be explained by the difference in GA estimation, the registry of stillbirths with a short GA as live births in the reference for which intrauterine growth restriction is one of the causes,<sup>23</sup> and the INTERGROWTH-21<sup>st</sup> standard's

prescriptive criterion.

Regardless of the approach or the prescriptive, maternal, and fetal criteria used in the INTERGROWTH-21<sup>st</sup> standard,<sup>6,24</sup> in order to develop growth standards for fetuses and NBIs in accordance with the guidelines of the Multicentre Growth Reference Study,<sup>25</sup> the most critical point for the development of these longitudinal growth charts is GA. In the INTERGROWTH-21<sup>st</sup> standard, GA was estimated based on the date of the last menstrual period (LMP) and confirmed by an early ultrasound (< 14<sup>+0</sup> weeks). If the difference between the ultrasound and the date of the LMP was ≤ 7 days, it was considered valid and adopted as the actual biological date. Pregnant women with a difference of > 7 days were excluded from the study. On the contrary, Urquía's reference for the Argentine population estimated GA based on the guidelines of the Live Birth Statistical Report, which used the date of the LMP with a range between 20<sup>+0</sup> and > 42<sup>+6</sup> weeks.<sup>11</sup> In Urquía's reference for the Argentine population, errors in GA classification based on the LMP were corrected using mixed-normal distribution models adjusted by altitude above sea level of the maternal place of residence weighted by the likelihood that BW corresponds to the predominant distribution.<sup>9</sup> In addition, the reference includes twin pregnancies and risk factors associated with intrauterine growth restriction and preterm birth. Due to such differences, the INTERGROWTH-21<sup>st</sup> standard includes few preterm or postterm NBIs and, therefore, few data were obtained about NBIs with the youngest GA.

Another factor that may have influenced the differences in SGA and LW prevalence between the reference and the standard is sample size. A small sample affects percentile estimation among extreme GA categories.<sup>9</sup> For the INTERGROWTH-21<sup>st</sup> standard, only 35% (n = 20 488) of pregnant women were selected based on eligibility criteria, whereas Urquía's reference for the Argentine population was based on 3 478 286 births. This is reflected in Figures 1 and 2, with the higher percentile differences between the reference and the standard in the extreme GA categories.

Percentile estimation and smoothing methods also affect the differences observed between the reference and the standard. For Urquía's reference for the Argentine population, percentiles were estimated using quantile regression, whereas for the standard, fractional polynomials were used assuming a biased t distribution; smoothing

procedures were also different.<sup>6,9</sup>

The regional prevalence of LBW showed little variation among regions, from 6.1% (Patagonia) to 7.6% (Central region), while the less developed regions of the NOA and NEA showed a prevalence similar to that of the most developed regions of the central and southern regions of Argentina. On the contrary, LW and SGA prevalence showed greater interregional variability. In 2013, the infant mortality rate (IMR) in Argentina was 10.8‰; at a regional level, IMR ranged between 12.6‰ (NOA) and 8.9‰ (Central region). The regional distribution of SGA and LW estimated according to the standard and the reference are related to the regional distribution of IMR, and higher values were observed in the northern regions of the country; this reinforces the concept that SGA newborns with a LW have higher risks of neonatal and post-neonatal mortality compared to those born with an adequate BW for GA. This risk is higher among preterm SGA newborns.<sup>14,26</sup> The use of LW and SGA for epidemiological analysis, together with other indicators, such as LBW, to assess the risk of infant death and adverse health outcomes would allow to enhance the results of the policies aimed at improving infant health.

A likely explanation of why moderate to late preterm NBIs were the only ones with a high Kappa index is their higher prevalence among preterm NBIs (87% between 2003 and 2013)<sup>11</sup> and their behavior in terms of morbidity and mortality (especially between 35 and 36 weeks), which is similar to that of early preterm NBIs (37-38 weeks).<sup>27</sup>

The main limitation of this study was the lack of data, for comparison purposes, about SGA and LW prevalence at a regional level, whereas its main strength was that it included all live births occurred in Argentina in 2013.

## CONCLUSIONS

Prevalence agreement of LW and SGA observed according to the INTERGROWTH-21<sup>st</sup> standard and Urquía's reference for the Argentine population among preterm and full-term NBIs was moderate, with interregional variability. Results propose new auxological perspectives in the epidemiological assessment of intrauterine growth restriction in Argentina. However, adopting the reference and the standard in epidemiological studies requires their validation as morbidity and mortality indicators among preterm and full-term NBIs. ■

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