

## Preterm births, low birth weight, and intrauterine growth restriction in three birth cohorts in Southern Brazil: 1982, 1993 and 2004

Prematuridade, baixo peso ao nascer e restrição do crescimento intrauterino em três coortes de nascimentos no Sul do Brasil: 1982, 1993 e 2004

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### Abstract

*Three birth cohort studies from 1982, 1993 and 2004, in Pelotas, Southern Brazil provided the data for this study of trends in preterm births, low birth weight, and intrauterine growth restriction. We found a slight increase in the period in the low birth weight prevalence from 9% to 10%. Intrauterine growth restriction decreased from 14.8% in 1982 to 9.4% in 1993, and subsequently increased to 12% in 2004, whereas preterm births increased markedly, from 6.3% in 1982 to 14.7% in 2004. This striking increment could not be explained by changes in maternal characteristics, as mothers in 2004 were heavier, smoked less during pregnancy and attended antenatal clinics more often and earlier than those of previous cohorts. However, pregnancy interruptions due either to caesarean sections or to inductions significantly increased. Caesareans increased from 28% in 1982 to 45% in 2004, and inductions were 2.5% in 1982 but 11.1% in 2004. The increase in preterms could be partially explained by the growing number of pregnancy interruptions, but there must be other causes since this increase was also observed among babies born by non-induced vaginal deliveries.*

*Low Birth Weight Infant; Fetal Growth Retardation; Premature Infant; Cohort Studies*

### Introduction

Low birth weight children (<2,500g) are at greater risk of morbidity and mortality during the first year of life <sup>1</sup>, and those that survive show a higher incidence of neurocognitive disorders <sup>2</sup>. In addition, growth patterns during fetal life and in the first years after birth may have permanent consequences, affecting the risk of chronic diseases such as arterial hypertension, myocardial infarction, and diabetes in adult life <sup>3,4</sup>.

Birth weight is determined by both fetal growth and duration of pregnancy. It is estimated that roughly 40% of the variation in fetal growth may be attributed to genetic factors, among which maternal and fetal genotypes play the most important role, with a small additional contribution of the child's sex. The remaining 60% of this variation is determined by maternal environmental factors. Certain exposures – such as age, parity, and smoking – have been studied extensively, whereas others – accounting for about 30% of this variance – remain unknown <sup>5</sup>.

Major factors associated with intra-uterine growth restriction include unfavorable maternal anthropometric conditions (low pre-pregnancy weight, low stature, and low body mass index) and smoking during pregnancy. Major determinants of preterm birth include genital tract infections, pregnancy-induced hypertension, and low body mass index <sup>6</sup>.

Pelotas, a medium-sized city with a current population of 340,000 inhabitants, is located in Rio Grande do Sul, the southernmost State of Brazil. In 1982, 1993, and 2004, three birth cohort studies were conducted in the city; these studies included all hospital deliveries that occurred during these three years. Considering that less than 1% of deliveries in the city occurred outside hospitals<sup>7</sup>, this study has a solid populational basis. The perinatal data from these cohorts allowed for an analysis of trends in birth weight, preterm delivery, and intra-uterine growth restriction. The present article describes these trends and analyzes the potential reasons for the differences observed over the period covered by the studies.

## Methods

In 1982, 1993, and 2004, all hospital-born children in the city of Pelotas were followed within three cohort studies using similar methods<sup>7</sup>. Maternity wards were visited on a daily basis, and all women who gave birth were interviewed within a few hours of delivery. Subjects provided information on socioeconomic and demographic conditions, reproductive health, and health care during gestation and delivery.

In the three cohorts, newborns were weighed by maternity staff at the time of birth using regularly calibrated pediatric scales. With regard to birth weight, gestational age, and intra-uterine growth, newborns were classified as follows: low birth weight – live births weighing under 2,500g; preterm birth – live births with gestational age below 37 weeks. In 1982, gestational age was calculated based on the date of last menstrual period, and children whose birth weight was incompatible with standards for that age were considered to be of unknown gestational age. In 1993 and 2004, we used the algorithm proposed by the National Center for Health Statistics (NCHS)<sup>8</sup>, using an estimated age based on the last menstrual period whenever it was consistent with birth weight, length, and head circumference, based on the normal curves for these parameters for each week of gestational age<sup>9</sup>. In case the last menstrual period-based gestational age was unknown or inconsistent, we adopted the clinical maturity estimate based on the Dubowitz method<sup>10</sup>, which was performed on all newborns. For intrauterine growth restriction, we included children with birth weight lower than percentile 10 for their gestational age and sex, in accordance with the standard population of the curve proposed by Williams et al.<sup>11</sup>. For calculating prevalence of preterm delivery and intra-

uterine growth restriction, we excluded from the denominator newborns whose gestational age was unknown.

As an indicator of socioeconomic status, we used family income, measured in multiples of the minimum wage (MW), that was earned in the month preceding the child's birth. This variable was categorized into five groups:  $\leq 1.0$ , 1.1-3.0, 3.1-6.0, 6.1-10.0, and  $> 10.0$  MW. We also analyzed birth weight and gestational age according to type of delivery, which was classified as vaginal (induced or non-induced) or caesarian section.

We used the chi-squared test to evaluate associations between independent variables and the above described dependent variables. Whenever possible, linear trend tests were used. In some analyses, the relative risks of certain outcomes were analyzed, comparing different family income groups. All analyses were carried out using the Stata statistical package (Stata Corp., College Station, USA).

The study protocol was approved by the Medical Ethics Committee of the Federal University of Pelotas. In 1982 and 1993, mothers provided oral informed consent for participation in the study. In 2004, written consent was also obtained.

## Results

The number of live births in Pelotas hospitals was 5,914 in 1982, 5,249 in 1993, and 4,231 in 2004. Mean birth weight was 3,187g (SD = 565g), 3,157g (SD = 549g), and 3,150g (SD = 567g), respectively. Table 1 shows the distribution of birth weight in 500g intervals for the three cohorts. Prevalence of very low birth weight (below 1,500g) was 1.1% in 1982, falling to 0.9% in 1993, and rising to 1.4% in 2004.

Table 2 shows that the prevalence of low birth weight increased from 9% in 1982 to 9.8% in 1993 and 10% in 2004. Intra-uterine growth restriction, which had fallen markedly between 1982 and 1993, increased again in 2004, affecting 12% of newborns. Finally, the prevalence of preterm births, which had almost doubled between 1982 and 1993 – from 6.3% to 11.4%, increased further to 14.7% in 2004.

The distribution of preterm births according to gestational age groups in the three studies is presented in Table 3. As shown in the table, the increases seen between 1982 and 1993 and between 1993 and 2004 occurred in all preterm subgroups. Especially noteworthy is the increase in preterms below the age of 32 weeks, which accounted for 1.9% of births in 2004. The table also shows the proportion of newborns whose gestational age was considered as unknown in each of

Table 1

Distribution of birth weight among live births. Pelotas, Southern Brazil, 1982, 1993, and 2004.

Birth weight (g)	1982		1993		2004	
	n	%	n	%	n	%
< 1,000	22	0.4	18	0.3	26	0.6
1,000-1,499	43	0.7	30	0.6	35	0.8
1,500-1,999	109	1.8	88	1.7	82	1.9
2,000-2,499	361	6.1	376	7.2	281	6.6
2,500-2,999	1,392	23.6	1,310	25.0	1,043	24.7
3,000-3,499	2,219	37.6	2,049	39.2	1,651	39.1
3,500-3,999	1,418	24.0	1,080	20.6	912	21.6
≥ 4,000	345	5.8	280	5.4	198	4.7
Not weighed	5		18		3	
<b>Total</b>	<b>5,914</b>	<b>100.0</b>	<b>5,249</b>	<b>100.0</b>	<b>4,231</b>	<b>100.0</b>

Table 2

Evolution of the characteristics of children in the three cohorts. Pelotas, Southern Brazil, 1982, 1993, and 2004.

Variables	1982	1993	2004	p *
Low birth weight (%)	9.0	9.8	10.0	0.08
Intra-uterine growth restriction (%)	14.8	9.4	12.0	< 0.001
Preterm birth (%)	6.3	11.4	14.7	< 0.001
Total live births with known gestational age **	4,669	5,171	4,225	-

\*  $\chi^2$  linear trend;

\*\* n for low birth weight is the same as in Table 1.

Table 3

Prevalence of preterm births according to gestational age category, and proportion of cases of unknown gestational age. Pelotas, Southern Brazil, 1982, 1993, and 2004.

Gestational age group (weeks)	1982	1993	2004	p *
< 32	0.6	0.8	1.9	< 0.001
32-33	0.5	1.5	1.6	< 0.001
34-36	5.2	9.1	11.2	< 0.001
Unknown gestational age	21.0	1.5	0.3	< 0.001
Total live births of known gestational age	4,669	5,171	4,225	-

\*  $\chi^2$  linear trend.

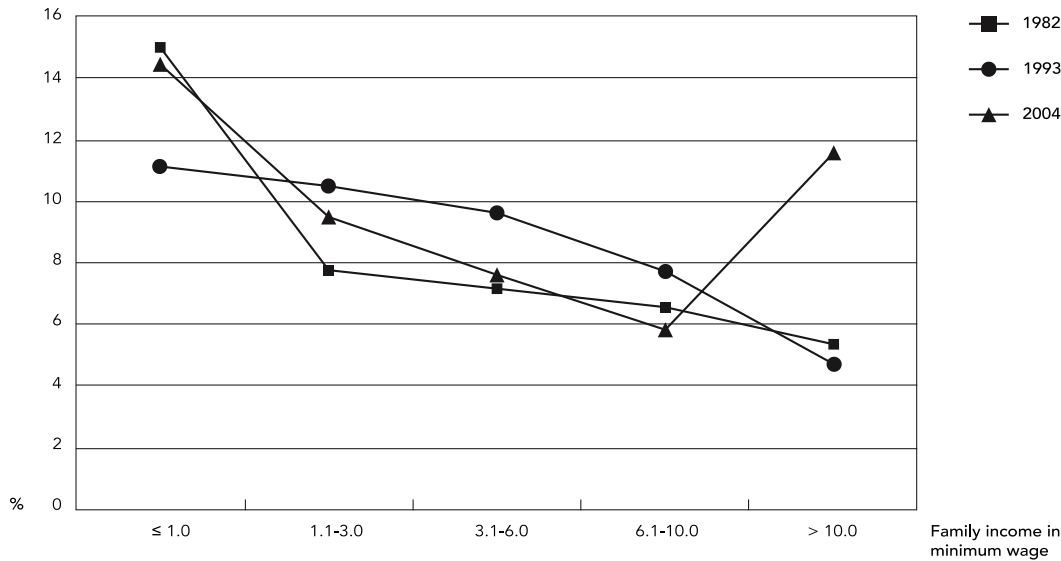
the perinatal studies. This proportion was 21% in 1982, 1.5% in 1993, and 0.3% in 2004.

Figure 1 shows the prevalence of low birth weight in the three cohorts for each of the five income groups, given in monthly MW (MW/month). According to this analysis, in 1982 and

1993 there was a marked trend towards a reduced prevalence of low birthweight as family income increased. In 1982, lower income families ( $\leq 1$  MW/month) were 2.8 times more likely to have a low-birth weight child than families earning more than 10 MW/month. In 1993, the same compari-

Figure 1

Prevalence of low birth weight according to family income. Pelotas, Southern Brazil, 1982, 1993, and 2004.



son showed 2.4 times greater risk. However, this scenario changed in 2004, when although a trend showing a reduction in low birth weight as family income increased was seen up to the 6.1-10 MW group, the highest income group now showed increased risk, with 11.6% of all babies being in the low birth weight group.

Figure 2 shows the prevalence of intra-uterine growth restriction, also according to family income strata. There is a clear inverse relation between family income and intra-uterine growth restriction, in spite of a slight increase in the >10 MW/month group when compared with the 6.1-10 MW/month group. On the other hand, the prevalence of intra-uterine growth restriction increased between 1993 and 2004, and this is evident across all family income groups, with the exception of the 6.1-10 MW/month group, where prevalence remained stable.

Figure 3 shows that the progressive increase in preterm births occurred across all income groups studied. In 2004, the proportion of preterm births among poorer mothers reached 19.8%. Preterm births almost tripled also among higher income families, from 5.7% in 1982 to 13.5% in 2004.

The proportion of preterms among low birth weight babies also increased markedly – from 42.5% in 1982 to 60% in 1993 and 67.3% in 2004.

This increase occurred in all family income groups (data not shown in the figure).

Figure 4 shows the distribution of the several subgroups defined by the presence or absence of low birth weight, preterm birth, and intra-uterine growth restriction in the three cohorts. The totals for these indicators are not exactly the same as those of previous tables because the number of excluded cases differed as a result of missing information on birth weight or sex. Of particular note is the fact that the increase in the prevalence of preterm births between 1993 and 2004 occurred mostly among children born weighing > 2,500g and without intra-uterine growth restriction, which correspond to more than half the entire group, as well as in small preterms with or without intra-uterine growth restriction.

Table 4 presents the prevalence of preterm births according to method of delivery – vaginal or caesarian section – in the three cohorts. This analysis shows that the increase in preterm deliveries in 2004 occurred among both caesarian section babies and babies born by non-induced vaginal delivery.

Figure 2

Prevalence of intra-uterine growth restriction according to family income. Pelotas, Southern Brazil, 1982, 1993, and 2004.

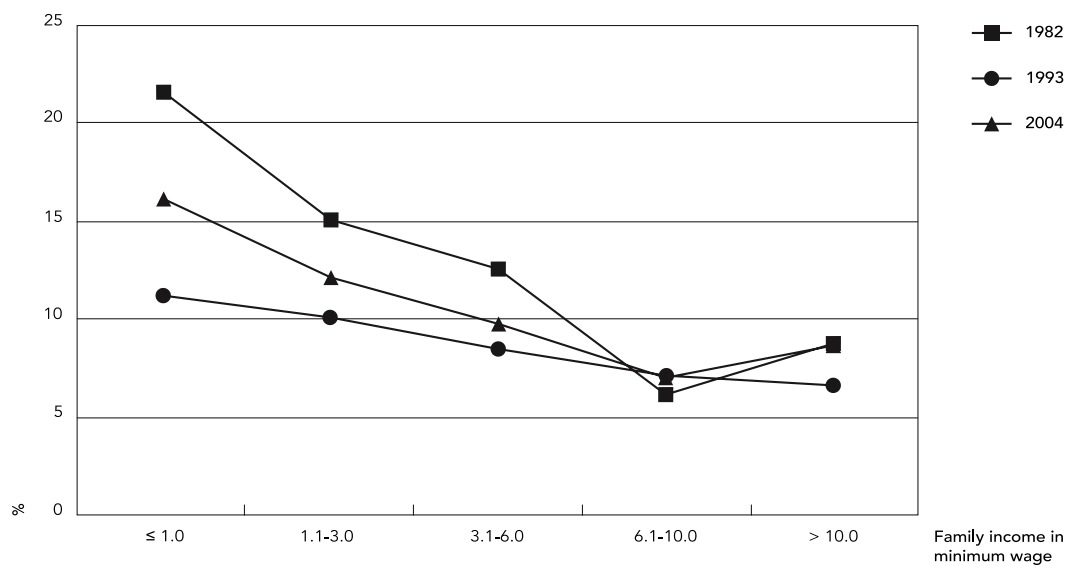


Figure 3

Prevalence of preterm birth according to family income. Pelotas, Southern Brazil, 1982, 1993, and 2004.

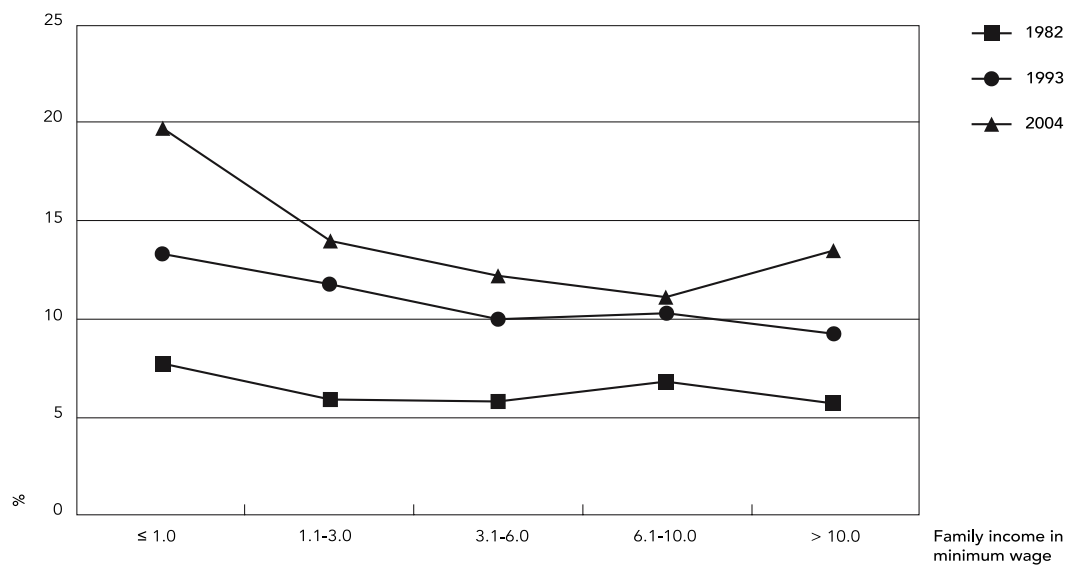
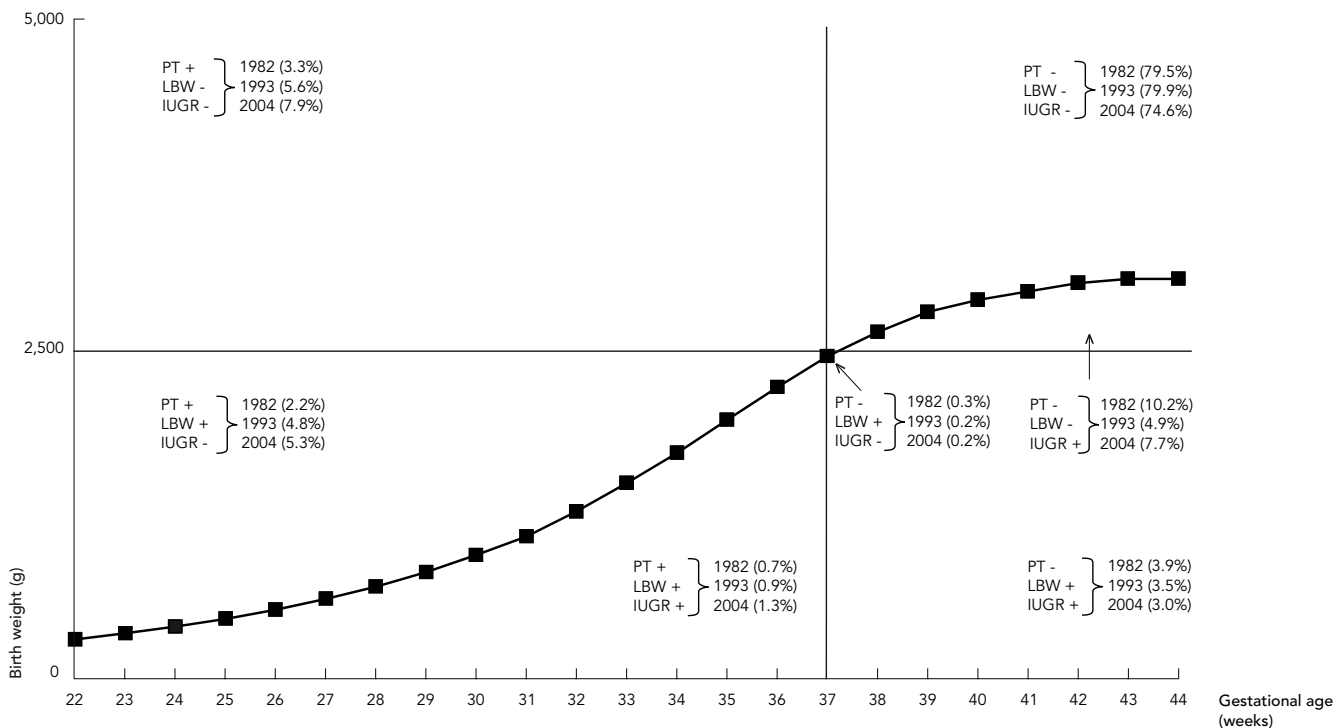


Figure 4

Distribution of the studied population according to low birth weight (LBW), intra-uterine growth restriction (IUGR), and preterm birth (PT). Pelotas, Southern Brazil, 1982, 1993, and 2004.



## Discussion

The three population-based perinatal studies carried out in Pelotas in 1982, 1993, and 2004 analyzed more than 99% of births that occurred in the city in these three years. This database, which allows for an evaluation of the evolution of perinatal health in the city across a 22-year period, is a rich source of epidemiologic information.

In this period, we detected significant changes in indicators associated with maternal health, including a reduction in fertility and increases in child spacing and schooling<sup>12</sup>. As other articles in this supplement show, the proportion of mothers of African descent increased markedly across the period, from 18% in 1982 to 27% in 2004. Coverage of antenatal care improved, mean pre-pregnancy weight and weight gain during pregnancy both increased, and the prevalence of

smoking during pregnancy fell significantly<sup>12,13</sup>. On the other hand, mothers were on average one centimeter shorter in 2004 than in 1993. We also detected a slight increase in the proportion of adolescent mothers and a significant increase in the proportion of primiparas<sup>12</sup>.

The most striking finding regarding newborn health indicators is the marked increase in preterm births, from 6.3% in 1982 to 11.4% in 1993, and then 14.7% in 2004. Although there have been reports in the literature of increases in preterm and low birth weight births in other countries<sup>14</sup>, as well as in Brazil<sup>15,16,17</sup>, we were unable to find any description of an increase in prevalence of preterms that was as marked as that described in the present study. Recent data from the Brazilian Ministry of Health's Information System on Live Births (SINASC) show that, for the country as a whole, preterm births decreased between 2000

Table 4

Prevalence of preterm deliveries according to method of delivery. Pelotas, Southern Brazil, 1982, 1993, and 2004.

Cohort (n)	Preterm deliveries (%)		
	Vaginal induced	Vaginal non-induced	Caesarian section
1982 (n = 4,674)	6.2	7.1	6.4
1993 (n = 5,171)	11.8	11.8	11.2
2004 (n = 4,225)	9.9	14.7	15.3
p *	< 0.001	< 0.001	< 0.001

\* Test for linear trend between cohorts.

and 2004 from 6.9% to 6.5%. However, the quality of the information on gestational age found in SINASC has been called into question<sup>18</sup>.

Since the method used to estimate gestational age in 1982 was different from that employed in 1993 and 2004, temporal trends in preterm delivery should be considered with caution. In 1982, only the date of last period was used for determining gestational age, and newborns with ages considered as incompatible with birth weight (21% of the total) were classified as of unknown gestational age, and were excluded from the denominator in prevalence calculations. It is probable, therefore, that the prevalence of preterms in 1982 was underestimated, for it is highly likely that at least some children of unknown gestational age belonged to the preterm group – the prevalence of low birth weight among children of unknown gestational age was 16.3%, compared to 48% among children with gestational age below 37 weeks. If we assume that roughly 20% of babies of unknown gestational age were preterms, the estimated prevalence of preterm birth for 1982 would have been 8.5%. For both 1993 and 2004, however, the same evaluation method was used for measuring gestational age, ensuring the compatibility of estimates. In these two studies, the maturity of all newborns was assessed using the Dubowitz method, and when estimated gestational age based on date of last menstrual period was unknown or inconsistent with birth weight, length, and head perimeter curves, and the Dubowitz method provided a more reliable estimate, we used the latter to measure the child's gestational age. The proportion of cases of unknown gestational age thus fell to 1.5% in 1993 and 0.3% in 2004.

A factor that may have contributed to the progressive increase in preterm births across the three cohorts was the increase in pregnancy interruption, both through caesarian sections and

induced labor. As discussed in another article in this Supplement<sup>13</sup> the proportion of c-section deliveries, which was already extremely high in 1982 (28%)<sup>19</sup>, increased to 31% in 1993, and reached 45% in 2004, with a rate of 36% among mothers delivering through the Unified National Health System (SUS) and 84% among mothers delivering privately<sup>20</sup>. As to labor induction, although information on this procedure is self-reported by mothers and thus not entirely reliable, this practice increased from 2.5% in 1982 to 11.1% in 2004<sup>19</sup>. One of the reasons for these excess interventions may have been the excessive reliance on technology: in 2004, 96.5% of pregnant women underwent ultrasound exams, and one-third of these had three or more such exams performed. Other more simple routine antenatal care procedures were less frequent – including vaginal examinations, which were not performed on 39% of women, or anti-tetanus vaccinations, which were not given to 24% of women not previously immunized. When we compare the difference between gestational age based on ultrasonographic examination in the first 20 weeks of pregnancy with that based on the date of the mother's last period, for children born between weeks 32 and 36 of the gestational period, when analyzed together with anthropometric data, ultrasound exams overestimate gestational age by a mean 1.5 weeks (SD = 2.6); this difference was 1.8% for pregnant women in the public sector, and 0.7% among women seen privately<sup>20</sup>.

It is possible, therefore, that there may have been cases in which misestimation of gestational age by ultrasonography led to an early interruption of the pregnancy. Thus, the excessive medicalization seen in Pelotas – which includes induction of labor, c-sections, and imprecise ultrasound exams – may have had a negative effect on the duration of pregnancy and birth weight, helping to neutralize the improvements result-

ing from the better health status of women and greater coverage of healthcare services.

Since the increase in the number of preterms between 1993 and 2004 was also seen among babies born through non-induced vaginal deliveries, the preterm epidemic is likely to have had two distinct causes – excessive interruption of pregnancy without medical justification, especially among higher income mothers, and another unidentified cause acting upon poorer women. Potential determinants among the latter include infections (urinary, gynecological<sup>6</sup>, and even periodontal<sup>21</sup>), capable of producing systemic inflammatory reactions. Another potential cause of preterm delivery is emotional stress, which manifests itself especially among ethnic/racial minorities<sup>22</sup>. The possibility of a multiplier effect between some of these factors

can also not be discarded<sup>23</sup>. Further investigation will be required to elucidate the causes of these preterm births, so that preventive measures may be adopted.

The increase in prevalence of intra-uterine growth restriction observed between 1993 and 2004, especially among lower-income women, is also a point of concern, given the potential short and long-term consequences associated with this condition. As demonstrated by our previous studies of the 1982 cohort<sup>24</sup>, children born small for their gestational age show greater morbidity and mortality in early life, and may have a higher risk of chronic-degenerative disease in adulthood<sup>25</sup>. The causes for such an increase need also be investigated, so that preventive action can be taken.

## Resumo

*Três coortes de nascimentos, de 1982, 1993 e 2004, em Pelotas, Rio Grande do Sul, permitiram o estudo de tendências em nascimentos prematuros, de baixo peso ao nascer e de restrição do crescimento intrauterino. O estudo mostrou, durante o período, um pequeno aumento na prevalência de baixo peso ao nascer, de 9% para 10%. A restrição do crescimento intrauterino diminuiu, de 14,8% em 1982 para 9,4% em 1993, e aumentou novamente para 12% em 2004, enquanto a proporção de nascimentos prematuros aumentou de maneira marcante, de 6,3% em 1982 para 14,7% em 2004. Não foi possível explicar esse aumento através de mudanças nas características maternas, já que as mães em 2004 apresentavam peso corporal mais alto, fumavam menos durante a gestação e mostravam mais consultas pré-natais e iniciam o atendimento pré-natal mais precocemente, quando comparadas às mães das coortes anteriores. Entretanto, houve um aumento significativo nas interrupções da gravidez, seja por cesariana ou indução. A taxa de cesarianas aumentou de 28% em 1982 para 45% em 2004, e de parto induzido de 2,5% em 1982 para 11,1% em 2004. O aumento nos nascimentos prematuros pode ser explicado parcialmente pelo número crescente de interrupções, mas devem existir outras causas, já que esse aumento foi observado também entre crianças que nasceram de partos vaginais não-induzidos.*

*Recém-Nascido de Baixo Peso; Retardo do Crescimento Fetal; Prematuro; Estudos de Coortes*

## Contributors

F. C. Barros participated in the three cohort studies, analyzed the data and wrote the article. C. G. Victora participated in the three cohort studies, analyzed the data and was involved in discussions about the article. A. Matijasevich, I. S. Santos, B. L. Horta, M. F. Silveira and A. J. D. Barros participated in at least one of the cohort studies and were actively involved in the data analysis and writing of the article.



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