

## Perinatal mortality in three population-based cohorts from Southern Brazil: trends and differences

Mortalidade perinatal em três coortes de base populacional no Sul do Brasil: tendências e diferenças

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### Abstract

*Trends in perinatal mortality were studied in the city of Pelotas, Southern Brazil, using three population-based cohort studies carried out in 1982, 1993 and 2004. The objective of the present study was to analyze trends and differences in perinatal mortality during the 1982-2004 period. All hospital deliveries and perinatal deaths were monitored through daily visits to maternity wards. Cause of death was determined using information from hospital records and by interviewing physicians. Perinatal mortality fell by 43% in the two decades, with a greater reduction between 1982 and 1993. Intrapartum fetal deaths decreased by 72% and deaths from asphyxia fell from 4.5 per thousand in 1982 to 1.4 per thousand in 2004. In conclusion, reductions in perinatal mortality were also seen across all birth weight categories between 1982 and 1993, but the same was not true for the 1993 to 2004 period, when mortality increased in several categories above 2,000g.*

*Perinatal Mortality; Child Health; Cohort Studies*

### Introduction

Perinatal mortality, which includes both late fetal deaths and early neonatal deaths, is an important indicator of the status of maternal/child health, the conditions of obstetric care and the level of economic development of a community <sup>1</sup>. The perinatal mortality rate reflects both the characteristics of reproductive health and the quality of antenatal care, delivery, and newborn care <sup>2</sup>.

At the global level, an estimated 7.5 million perinatal deaths take place each year, most of which are in developing countries <sup>3,4</sup>. Even though comparisons between different countries are limited by the heterogeneity of the criteria used for defining perinatal death and by the quality of the information available<sup>5</sup>, large differences in mortality rates exist between different countries, ranging from less than 10 per 1,000 in most developed countries to up to 60 per 1,000 in certain regions of Asia and Africa <sup>3,4</sup>.

The causes and determinants of perinatal mortality vary between different regions. It is therefore important to analyze these factors in order to improve preventive measures. Complications during delivery such as obstructed labor and fetal malpresentation are frequent causes of perinatal death in settings where obstetric care is lacking <sup>6</sup>. In developing countries, it is estimated that asphyxia during labor and delivery leads to approximately seven deaths per thousand births, whereas in developed countries this proportion

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is less than one per 1,000<sup>3</sup>. In Brazil, the major causes of perinatal mortality are intrauterine and intrapartum asphyxia and low birth weight/preterm births. In contrast, the main causes of death in developed countries are extreme preterm births and congenital malformations<sup>7,8</sup>.

The decline in perinatal mortality registered in most countries over the last decades has been considered as an indicator of improved population health, reflecting advances in the quality of antenatal and perinatal care<sup>9</sup>. In Brazil, the perinatal mortality rate fell from about 30 to 20 deaths per 1,000 births during the 1990s<sup>10</sup>. However, reductions in perinatal mortality have been slower and more difficult to achieve than reductions in infant mortality, and levels have stagnated in recent years<sup>11</sup>, a fact that has been reported elsewhere<sup>7</sup>.

Tracing the evolution of maternal/child health indicators is essential for evaluating the impact of social and economic changes, as well as the availability and quality of healthcare in a community. Nevertheless, the study of such trends is made complicated by under-reporting and the lack of a standardized definition of cause of death. In Brazil, the SINASC (Information System on Live Births) and the SIM (Mortality Information System) are used as sources of data for research. However, several researchers have detected both under-reporting and a lack of agreement between these two databases<sup>5,12</sup>.

In the city of Pelotas, Southern Brazil, three cohort studies using similar methodologies were carried out in 1982, 1993, and 2004, providing a unique opportunity to study trends in this field. The present work is a follow-up to the article published by Menezes et al.<sup>13</sup>, which compared data from the 1982 and 1993 cohorts. We aim to analyze trends and differences in perinatal mortality in the city of Pelotas between 1982 and 2004 with the aim of evaluating obstetric and neonatal care, and proposing appropriate preventive measures.

## Methods

In 1982, 1993, and 2004, all births that took place in the city of Pelotas were included in cohort studies that used similar methodologies<sup>14</sup>. The city's maternity wards were visited on a daily basis and mothers were interviewed soon after delivery. Mothers provided information on socioeconomic and demographic conditions, reproductive health and healthcare during pregnancy and delivery. In the present article, we describe only the methods used in the perinatal mortality sub-study.

Perinatal mortality surveillance included regular visits to maternity wards and to intensive and intermediate care centers. In addition, regular visits were made to cemeteries, state death registry offices and the Municipal Health Secretariat in order to monitor deaths that occurred outside of hospitals.

In order to compare the three cohorts, we used the definition of perinatal death applied to the 1982 and 1993 cohorts, namely the sum of fetal deaths that occurred after the 28<sup>th</sup> week of pregnancy (or fetuses larger than 1,000g when the gestational age was unknown) and early neonatal deaths that occurred during the first week of life. Outcomes studied included the perinatal mortality rate (number of perinatal deaths per 1,000 live births and stillbirths) and its two components: the fetal mortality rate (number of fetal deaths per 1,000 births) and the early neonatal mortality rate (number of deaths in the first week of life per 1,000 live births).

In order to determine the underlying cause of death and the time of its occurrence (antepartum vs. intrapartum), we interviewed the obstetrician responsible for each delivery. For early neonatal deaths, we interviewed the child's pediatrician or reviewed patient charts in the case of hospitalized children.

Two pediatricians independently evaluated the information available on each death to determine the underlying cause of death. In case of disagreement between the two referees, a third referee provided a final diagnosis. Causes of death were grouped according to the classification proposed by Wigglesworth<sup>15</sup>, in which deaths fall into five categories: antepartum fetal deaths, congenital malformations, immaturity, asphyxia, and other causes of fetal or early neonatal death.

Independent variables investigated included sex, birth weight, gestational age, intrauterine growth retardation, family income, and method of delivery.

Fetuses and newborns were weighed by maternity staff at the time of birth using regularly calibrated pediatric scales. Children weighing less than 2,500g were considered as low birth weight.

In 1982, the gestational age was calculated based on the date of the mother's last period. Children whose birth weight was incompatible with normal standards for that age<sup>16,17</sup> were considered as unknown gestational age. In 1993 and 2004, we also used the Dubowitz score<sup>18</sup> to evaluate newborn maturity, and in each case a reasonable estimate was made based on birth weight, length, and head circumference. In 2004, ultrasound exams carried out early in pregnancy

were available for a large number of births, and were included in the algorithm used to calculate gestational age. Newborns with gestational age below 37 full weeks were classified as preterm. The presence of intrauterine growth retardation was established by comparing values obtained with those of the Williams curve<sup>19</sup>. We classified as small for gestational age children with a weight below percentile 10 for their gestational age and sex. Remaining children were classified as adequate for gestational age.

Family income was determined based on the family's earnings, as a multiple of the minimum wage, in the month prior to the child's birth. Income was categorized in two different ways: across five categories,  $\leq 1.0$ , 1.1-3.0, 3.1-6.0, 6.1-10.0 and  $> 10.0$  times the minimum wage; and across two categories,  $\leq 3$  times and  $> 3$  times the minimum wage.

We used the chi-squared test to determine associations between independent variables and mortality rates. Whenever possible, the linear trend test was used. All analyses were carried out using the Stata Statistical Software: Release 9.2. (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 we obtained verbal consent from mothers to participate in the study. In 2004, written consent was also requested.

## Results

The number of births decreased by 29% in the period under study, from 6,011 in 1982 to 5,304

in 1993 and 4,287 in 2004. The number of births in each cohort according to the variables studied has been described previously<sup>14,20</sup>.

Perinatal mortality fell by 43% in the period. The most important reduction occurred between 1982 and 1993 (31%), with a smaller reduction (16%) between 1993 and 2004 (Table 1). From 1982 to 1993 fetal mortality decreased by 35% and early neonatal mortality by 29%. In the 1993 to 2004 period, these reductions were 9% and 23%, respectively.

The definition of late fetal death changed substantially in the period under study. The ninth revision of the International Classification of Diseases (ICD-9)<sup>21</sup> included fetal deaths after the 28<sup>th</sup> week or of children weighing more than 1,000g. In ICD-10<sup>22</sup>, which was adopted in Brazil in 1996, the perinatal period begins in the 22<sup>nd</sup> week of pregnancy or when the baby reaches 500g. By the more recent definition, the perinatal mortality rate in 2004 would have been 21.5 per 1,000, compared to 18.5 per 1,000 under the old definition. We did not collect information on fetal deaths that occurred between the 22<sup>nd</sup> and 27<sup>th</sup> weeks of the gestational period in the earlier cohorts; therefore we were unable to use the current definition in the present article. All results from here on will be expressed in terms of the older definition.

Antepartum fetal deaths decreased from 13.1 per 1,000 births in 1982 to 6.0 per 1,000 in 1993, but increased to 8.4 per 1,000 in 2004. On the other hand, the intrapartum fetal rate, which had increased between 1982 and 1993 (from 2.5 to 3.6 per 1,000 births, respectively), decreased to 0.7 per 1,000 in 2004 (Table 1).

Table 1

Perinatal mortality in Pelotas, Southern Brazil, 1982, 1993, and 2004.

Indicators	1982	1993	2004
Number of births	6,011	5,304	4,287
Fetal deaths			
Number	97	55	41
Rate per 1,000	16.1	10.5	9.6
Antepartum deaths, rate per 1,000	13.1	6.0	8.4
Intrapartum deaths, rate per 1,000	2.5	3.6	0.7
Time of death unknown	0.5	0.9	0.5
Early neonatal deaths			
Number	97	62	38
Rate per 1,000	16.4	11.7	9.0
Perinatal deaths			
Number	194	117	79
Rate per 1,000	32.2	22.1	18.5

Table 2 presents the causes of perinatal deaths according to the Wigglesworth classification<sup>15</sup>. As previously mentioned, antepartum fetal mortality, which had declined between 1982 and 1993, increased between 1993 and 2004. The same occurred for immaturity deaths, which fell by 47% between 1982 and 1993 and subsequently increased by 45% in the 1993 to 2004 period. Rates of congenital malformation remained more or less constant, whereas deaths due to asphyxia fell by 69% between 1982 and 2004.

There were no differences in fetal mortality between the sexes in any of the three cohorts. In 1993, early neonatal and perinatal mortality rates were significantly lower among girls, but such a difference was not found in 2004 (Table 3).

Table 4 presents the perinatal, fetal, and early neonatal mortality rates for 1982, 1993, and 2004 according to birth weight categories. For fetal mortality, reductions were found among babies smaller than 1,000g between 1993 and 2004 and among newborns heavier than 3,000g between 1982 and 2004. However, fetal mortality rates for the remaining birth weight categories increased between 1993 and 2004, although

they did not reach 1982 levels. For early neonatal mortality, on the other hand, there was a reduction in rates in the 1,000-1,999g, 2,500-3,499g, and  $\geq 4,000$ g categories. Rates in the  $< 1,000$ g and 2,000-2,499g categories remained stable at 1993 levels. Early neonatal mortality in children born weighing 3,500-3,999g increased to levels higher than those of 1982; however, the absolute number of deaths in this category is very low ( $n = 4$  in 1982,  $n = 1$  in 1993 and  $n = 4$  in 2004). Overall, reductions of perinatal mortality were observed in all birth weight categories between 1982 and 1993. However, this did not happen in the 1993-2004 period, where perinatal mortality increased in several birth weight categories above 2,000g.

Table 5 presents the rates of perinatal, fetal, and early neonatal mortality in 1982, 1993, and 2004 according to birth weight and gestational age. The improvements seen in mortality coefficients between 1982 and 1993 were not sustained in the following period. In all three cohorts, pre-term children with adequate weight for gestational age showed higher rates of fetal, neonatal, and perinatal mortality when compared to term

Table 2

Perinatal mortality rates (per 1,000 live births) according to the Wigglesworth classification. Pelotas, Southern Brazil, 1982, 1993, and 2004.

Causes	Number of deaths			Percentage of all deaths			Mortality rate (per thousand)			p *
	1982	1993	2004	1982	1993	2004	1982	1993	2004	
Antepartum stillbirth	79	29	32	41%	25%	40%	13.1	6.0	8.4	0.4
Malformations	14	13	9	7%	11%	11%	2.3	2.5	2.0	0.2
Immaturity	45	21	26	23%	17%	33%	7.3	3.9	5.7	0.2
Asphyxia	27	44	6	14%	38%	8%	4.5	8.3	1.4	0.08
Other causes	29	10	6	15%	8%	8%	5.0	1.4	1.0	0.05
All causes	194	117	79	100%	100%	100%	32.3	22.1	18.5	-

\*  $\chi^2$  for linear trend (for the perinatal mortality rate).

Table 3

Fetal, early neonatal, and perinatal mortality rates (per 1,000 total births). Pelotas, Southern Brazil, 1982, 1993, and 2004.

Variable	Fetal			Early neonatal			Perinatal		
	1982	1993	2004	1982	1993	2004	1982	1993	2004
Sex									
Male	15.9	8.8	8.1	16.5	15.1	11.4	32.1	23.8	19.4
Female	16.1	7.4	9.7	15.3	8.2	6.4	31.1	15.6	16.1
p *	0.9	0.6	0.6	0.7	0.03	0.09	0.8	0.04	0.4

\*  $\chi^2$  test.

Table 4

Fetal, early neonatal, and perinatal mortality rates (per 1,000 total births) by birth weight. Pelotas, Southern Brazil, 1982, 1993, and 2004.

Birthweight (g)	Fetal			Early neonatal			Perinatal		
	1982	1993	2004	1982	1993	2004	1982	1993	2004
< 1,000	*	238	161	952	588	654	952	714	710
1,000-1,499	306	118	167	488	500	229	645	559	357
1,500-1,999	128	22.2	68.2	64.2	136	36.6	184	156	102
2,000-2,499	42.4	10.5	31.0	55.4	10.6	10.7	95.4	21.1	41.4
2,500-2,999	9.9	0.8	5.7	7.1	3.8	1.9	17.0	4.6	7.6
3,000-3,499	6.2	3.4	1.8	4.9	2.0	0.6	11.1	5.3	2.4
3,500-3,999	6.3	1.8	1.1	2.8	0.9	4.4	9.1	2.8	5.5
≥ 4,000	19.8	3.6	0.0	2.8	3.6	0.0	22.7	7.1	0.0
p **	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
< 2,500	87.1	28.6	59.9	127	80.2	73.1	203	107	129
≥ 2,500	8.1	2.3	2.6	4.8	2.3	1.8	12.9	4.6	4.5
p **	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
All	16.1	10.5	9.6	16.4	11.7	9.0	32.2	22.1	18.4

\* Fetal deaths weighing less than 1,000g were excluded from the study;

\*\*  $\chi^2$  test.

Table 5

Fetal, early neonatal, and perinatal mortality rates (per 1,000 total births) by birth weight and gestational age (date of mother's last period). Pelotas, Southern Brazil, 1982, 1993, and 2004.

Birth weight and gestational age	Fetal			Early neonatal			Perinatal			Deaths/Births		
	1982	1993	2004	1982	1993	2004	1982	1993	2004	1982	1993	2004
Small for gestational age	41	4	21	20	10	10	61	14	31	44/723	7/489	16/516
Adequate for gestational age												
Preterm	59	7	28	75	50	43	129	57	70	35/271	31/542	40/574
Term	6	-	2	4	1	2	11	1	3	40/3,742	4/4139	10/3,159
p *	< 0.001	< 0.003	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	-	-	-

\*  $\chi^2$  test.

babies and babies with intrauterine growth retardation (small for gestational age).

Table 6 presents mortality rates by method of delivery. Early neonatal mortality was higher among babies delivered by caesarian section than among those delivered vaginally in 1982 ( $p = 0.04$ ). In the 1993 and 2004 cohorts there was no difference in terms of this outcome.

Figure 1 shows the relationship between perinatal mortality and family income. In these two decades, there was a reduction in perinatal mortality rates across almost all income categories. In 1982, children from families earning less than the minimum wage showed perina-

tal mortality rates that were 4 times higher than in children from families earning more than 10 times the minimum wage. In 1993, this difference increased to about 7-fold, returning to 4-fold in 2004. In absolute terms, the difference between the extreme income groups ( $\leq 1$  vs.  $> 10$  times the minimum wage) fell from 34 deaths per thousand (46 minus 12) in 1982 to 17 per thousand (22 minus 5) in 2004.

Figure 2 shows the relationship between perinatal mortality and family income analyzed together with birth weight in each cohort. In low birth weight children from families earning  $\leq 3$  times the minimum wage there was a 34% re-

Table 6

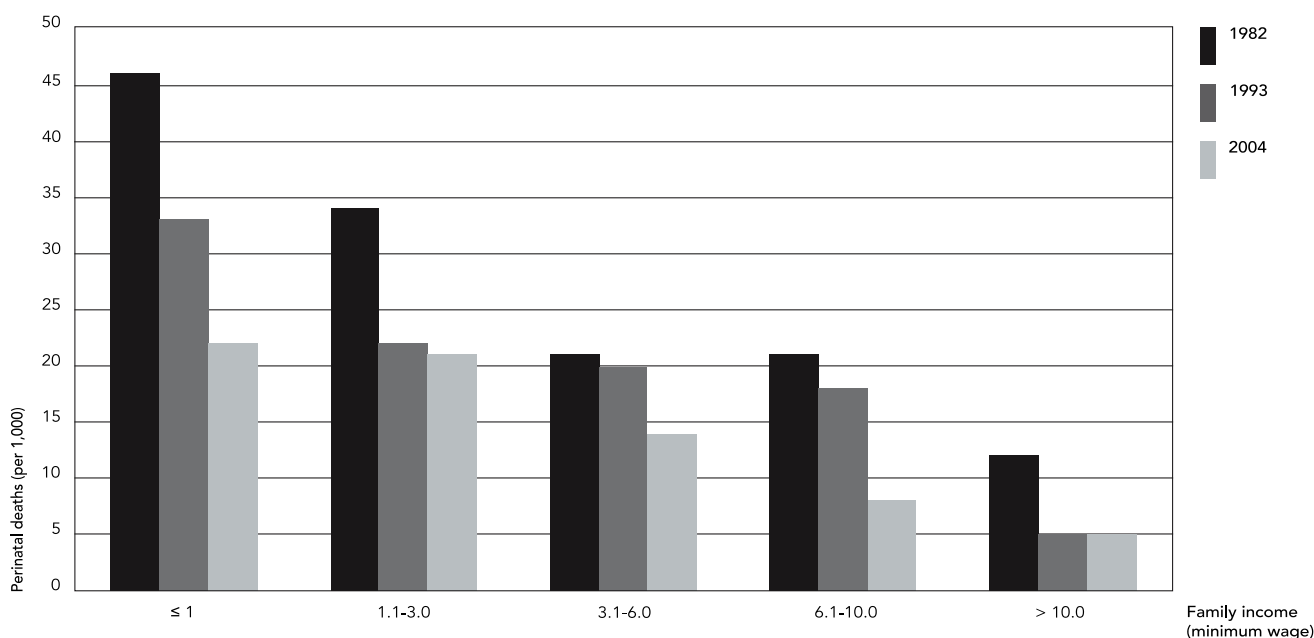
Fetal, early neonatal, and perinatal mortality rates (per 1,000 total births) according to method of delivery Pelotas, Southern Brazil, 1982, 1993, and 2004.

Variables	Fetal			Early neonatal			Perinatal		
	1982	1993	2004	1982	1993	2004	1982	1993	2004
Method of delivery									
Vaginal	16.0	10.0	11.1	14.0	11.2	10.4	29.8	21.2	21.4
c-section	16.2	11.1	7.7	22.6	13.1	7.3	38.5	24.1	15.0
p *	0.9	0.7	0.3	0.04	0.7	0.3	0.1	0.6	0.1

\*  $\chi^2$  test.

Figure 1

Perinatal mortality by family income. Pelotas, Southern Brazil, 1982, 1993, and 2004.



duction in perinatal mortality between 1982 and 2004. However, low birth weight children from families earning > 3 times the minimum wage showed a 68% decrease between 1982 and 1993 followed by a marked increase – close to 200% – between 1993 and 2004. In 2004, perinatal mortality rates among children born weighing  $\geq 2,500$ g from families who earned > 3 times the minimum wage were 2.5 times lower than lower income children, a difference almost entirely due to lower fetal mortality (Figure 3).

## Discussion

The present study describes the trends in perinatal mortality in the city of Pelotas across a 22-year period, with the advantage of using population-based data. The methods used for monitoring deaths and for cross referencing using several sources meant that under reporting was virtually eliminated<sup>5</sup>. Mortality records in Pelotas improved substantially during the two decades of our study<sup>23,24,25</sup>; the official perinatal mortality

Figure 2

Perinatal mortality by income and birthweight. Pelotas, Southern Brazil, 1982, 1993, and 2004.

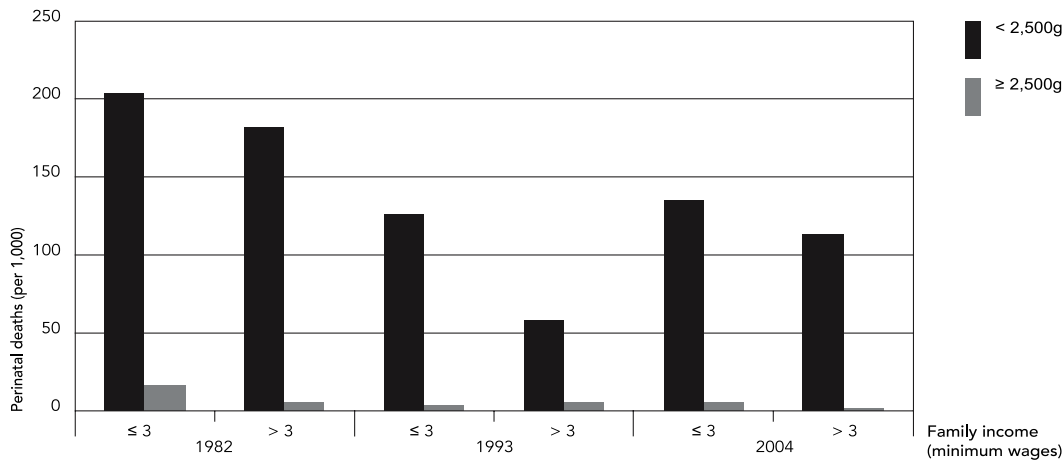
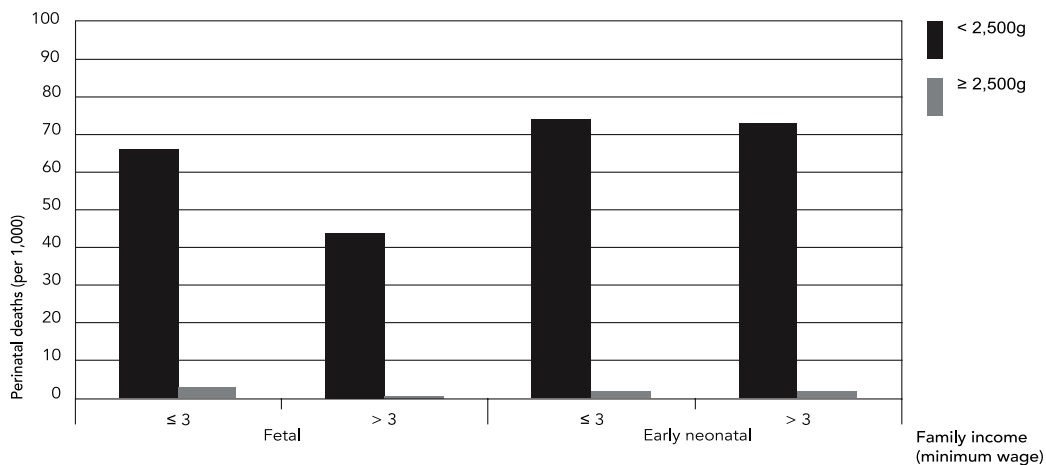


Figure 3

Fetal mortality (per 1,000 total births) and early neonatal mortality (per 1,000 live births) by income and birth weight. Pelotas, Southern Brazil, 2004.



rate in 2004 was 21.8 per 1,000 for the municipality as a whole <sup>26</sup>, which was very similar to that found in our study.

The city's mortality rate for 2004 places Pelotas in an intermediate position both globally and within Brazil. Rates in Pelotas were higher

than those of the states of Rio Grande do Sul, (17.3 per 1,000) and São Paulo (19.2) <sup>11</sup>. Worldwide perinatal mortality in 2002 was estimated at 47 deaths per 1,000 births, with a marked difference between more and less developed regions <sup>3</sup>.

There was an overall reduction in perinatal mortality in the period under study. This reduction was more pronounced between 1982 and 1993 than between 1993 and 2004. When analyzing such a reduction, potential changes in both maternal and healthcare-related conditions must be taken into consideration. As discussed in another article in this Supplement<sup>14</sup>, important changes took place in Pelotas in the last two decades. The city witnessed an economic decline caused by recession and a reduction in industrial activity; however, there was a marked expansion of the healthcare system, especially with regard to primary healthcare, with improvements in coverage of antenatal care, delivery services, and newborn care. Certain maternal variables, especially those relating to schooling and smoking during pregnancy, also improved during the period<sup>27</sup>. Neonatal intensive care units were established and expanded and human resources training in the field of neonatal care has increased, especially over the last ten years. Increased access to surfactant and antenatal corticoids and advancements in the field of assisted ventilation also played a role in the decrease in early neonatal mortality, especially among newborns in the 1,000-1,999g weight range.

Although still more common than in developed countries<sup>28</sup>, intrapartum fetal deaths decreased in the period, probably due to improvements in obstetric care, which is reflected in the reduction of perinatal deaths due to asphyxia. The significant increase in deaths related to immaturity between 1993 and 2004 is associated with the increase in the rate of preterm deliveries, from 6.3% in 1982 to 11.4% in 1993 and 14.7%

in 2004, as reported in another publication in this supplement<sup>20</sup>. Excessive numbers of caesarian sections<sup>29,30</sup> may be contributing simultaneously to a reduction in intrapartum mortality – given that vaginal deliveries are becoming less and less common – and to an increase in preterm deliveries.

An important finding regarding the 1982 and 1993 cohorts, reported previously<sup>13</sup>, was the persistence of differences between social groups, despite the decrease in rates in almost all categories of family income. Also noteworthy was the increase, in 2004, of perinatal mortality rates among low birth weight children from families earning more than 3 times the minimum wage, which may be related to the increase in preterm births among this group, in which five of every six births are by caesarian section<sup>31</sup>.

The decrease in perinatal mortality is related to the expansion of antenatal care, delivery services, and newborn care. In the United States, the regionalization of services is considered to be an equally important factor in reducing mortalities as that of technological developments<sup>32</sup>. In Pelotas, the reduction observed in the 1982-1993 period was much higher than that seen between 1993 and 2004, which indicates a deceleration similar to that seen in infant mortality rates<sup>33</sup>. It is cause for concern that such deceleration is occurring at levels much higher than those of developed countries. A more accessible and efficient healthcare system that places an emphasis on equity and the prevention of large numbers of unnecessary interventions may contribute towards a reduction in the current perinatal mortality rates.



## Resumo

*Foram estudadas as tendências de mortalidade perinatal no município de Pelotas, Rio Grande do Sul, utilizando três coortes de base populacional, de 1982, 1993 e 2004. O estudo teve como objetivo analisar as tendências e diferenças na mortalidade perinatal no período de 1982 a 2004. Todos os partos hospitalares e óbitos perinatais foram monitorados através de visitas diárias às maternidades. A causa de óbito era determinada através dos prontuários hospitalares e entrevistas com médicos. A mortalidade perinatal diminuiu em 43% ao longo das duas décadas, com a maior redução entre 1982 e 1993. Óbitos fetais intra-parto diminuíram em 72%, e óbitos por asfixia caíram de 4,5 por mil em 1982 para 1,4 por mil em 2004. Em conclusão, houve reduções na mortalidade perinatal em todas as categorias de peso ao nascer entre 1982 e 1993, mas o mesmo não foi observado durante o período de 1993 a 2004, quando a mortalidade aumentou em várias categorias acima de 2000g.*

*Mortalidade Perinatal; Saúde da Criança; Estudos de Coortes*

## Contributors

A. Matijasevich designed the research question, conducted the analyses and wrote the first draft of the article. C. G. Victora, I. S. Santos, A. J. D. Barros, A. M. B. Menezes and F. C. Barros contributed to the analyses and assisted with the editing of the article. E. P. Albernaz and I. K. Timm contributed to data collection and analyses.

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Submitted on 29/Mar/2007

Final version resubmitted on 07/Nov/2007

Approved on 09/Jan/2008