Comparison of Three Standards for Evaluating Fetal Growth[1]

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Three birth weight standards were applied to 1986 live births and neonatal deaths in Santiago, Chile, in order to ascertain how useful the 10th, 25th, 75th, and 90th percentile birth weights determined by these standards would be for selecting infants at high risk of neonatal death. This article reports the results of that study.

A study by Lubchenco et al. (*1*) that described intrauterine growth of a United States population in Denver, Colorado, strongly stimulated the use of growth charts for measuring the adequacy of birth weight. Since then various local studies have been published that, on the basis of the distribution of weight for each gestational age, classify births with weights lower than those of a certain cutoff percentile as "small for gestational age" (SGA); such births are deemed to involve cases of retarded growth unless another examination shows the opposite (*2*). Birth weights between the extreme percentiles, possibly the 10th and 90th or the 25th and 75th, are considered adequate for gestational age (AGA), while those above the 90th or 75th are considered large for gestational age (LGA).

Different available intrauterine growth curves set markedly different birth weight values corresponding to the inclusion limits. In consequence, depending on the curve used, the same child may be classified as belonging in different categories. This problem is particularly important in classifying SGA children, because several authors have shown that death rates are considerably higher among SGA children than among AGA ones for each gestational age at birth; these mortality differences have been described as more marked among term babies than among preterm ones (*3–13*).

The study described here grew out of a need cited by several authors (*4, 7*) for developing a means by which fetal growth standards could be used to predict mortality risk, a subject which should be studied in different populations.

The limits based on the percentiles noted above may be varied—according to the resources available for overseeing and intervening in the groups with greatest need with different diagnostic and therapeutic measures—by increasing or reducing the population deemed at risk of SGA or LGA (*14*). In view of this situation, we propose that before defining the cutoff point, the fetal growth standard to be employed should be selected according to its diagnostic reliability and predictive capacity (*15, 16*). For this purpose the likelihood of some specific harm

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(such as neonatal death) can be studied in portions of a population deemed to be SGA or LGA according to different standards.

When the distribution of birth weights by gestational age was studied in 97.75% of the live births in Chile in 1986 (*17*), the birth weight values of the 10th, 25th, and 50th percentiles were found to be greater than those of the Denver standard (*1*), similar to those of the Aberdeen standard (*18*), and less than those of a contemporary clinical survey conducted in Santiago (*19*). These findings suggested the possibility of choosing one of these various standards for clinical use based on neonatal death risk criteria.

The goal of the present study was to compare the three standards for appraising fetal growth just mentioned by studying their diagnostic reliability and predictive capacity in relation to neonatal deaths and survivals in Chile in 1986.

MATERIALS AND METHODS

The study was carried out using birth weight and gestational age data obtained by the Civil Registry Service for all live births in the country in 1986. Data on birth weight, gestational age at birth, sex, and parity were available for 254,878 live births (98.3% of a total of 259,347) and 2,335 neonatal deaths (86.3% of a total of 2,705).

More than 98% of all births in Chile occur in hospitals. Gestational age is determined from the date of the mother's last period; when that date is not recorded by the pregnant woman or when the date reported does not agree with her clinical examination, it is estimated from ultrasound examination (the country's 26 health services have ultrasound equipment) or postnatal examination by a pediatrician or both.

Public and private hospitals are required to report a birth's most significant events on the birth certificate, which family members take to the Civil Registry for legal registration. Local Civil Registry offices are generally located in the maternity services of the hospitals themselves, which facilitates the registration process. Birth registration has been further encouraged by making it a requirement for collecting financial social security benefits (including a family allotment for the insured and a single family subsidy when coverage is lacking) and for obtaining maternity leave in the case of working mothers.

Infant death certificates, which are required for burial, are routinely filled out by physicians—except in the 1% of cases where infant deaths occur without medical attention and are reported by witnesses.

Although neonatal mortality by gestational age in preterm births seems to be more significant than mortality by birth weight, precise gestational age is difficult to determine from the pediatric point of view in neonates who are quite immature (*20*). Despite this difficulty, infants deemed to have less than 26 weeks of gestational age at birth were excluded from this study.

More than 20 years ago the Inter-American Investigation of Mortality in Childhood found underregistration of neonatal deaths in Chile, especially in newborns weighing less than 1,000 g (*21*). Present estimates indicate that such underregistration seems to be extremely slight because of the great attention it receives. In this context, the latest PAHO report on health conditions in the Americas, on the basis of data from the Latin American Demographic Center, shows Chile to be the Latin American country with the lowest underregistration of all deaths (1.2% in the period 1980–85) (*22*).

The study reported here compared fetal growth standards found for populations in Denver, Colorado, U.S.A. (*1*), Aberdeen, Scotland (*18*), and Santiago,

Chile (*19*). The Denver standard, based on 5,635 cases broken down by sex, is widely known in our country. The Aberdeen standard, based on 46,703 births, includes corrections for parity and the child's sex. The Santiago standard, based on 11,543 births, also takes the effects of sex and parity into account. This latter standard was derived from a middle-class population delivering babies at the maternity clinic of the Catholic University's Faculty of Medicine.

The standards compared give different values for a particular birth weight percentile at each gestational age. Table 1 shows the birth weight values that each standard gives for the 10th, 25th, 75th, and 90th percentiles at week 40. As can be seen, the Santiago standard is the least strict for diagnosing SGA newborns, since the values of the 10th and 25th percentiles are the highest and so include a greater number of babies. The Denver standard is the most strict, while the Aberdeen standard falls between them. A comparison of other gestational age weeks shows differences of similar magnitude.

With respect to LGA, diagnosed using the 75th and 90th percentiles, the strictness of the three standards at week 40 are the reverse of those noted above. However, the birth weights cited by the Denver and Aberdeen standards for 75th and 90th percentile preterm newborns (not shown in Table 1) are higher than those cited by the Santiago standard.

The quantitative differences between these three intrauterine growth curves appear to reflect the presence or absence of environmental or maternal factors capable of stimulating or retarding fetal growth (*15*). Since the Santiago standard excludes a large number of such factors (*19*), its comparison with the other standards shows that the birth weight values of the 10th and 25th percentiles increase throughout the range of gestational age, but that the birth weight values of the 75th and 90th percentiles decrease relative to the other standards with respect to preterm births.

The Santiago and Aberdeen standards, in contrast to the Denver standard, do not include birth weight data for gesta-

Table 1. Birth weights (in grams) of the 10th, 25th, 75th, and 90th percentiles cited by the Denver, Aberdeen, and Santiago standards for newborns in the indicated gender and parity groups who were delivered at the gestational age of 40 weeks.

Standard, gender, and parity	Birth weights (g) of the indicated percentiles			
	10	25	75	90
Denver				
Males	2,700	2,995	3,610	3,880
Females	2,630	2,905	3,440	3,720
Aberdeen				
Males, primipara	2,870	3,130	3,710	3,980
Males, multipara	2,950	3,220	3,860	4,170
Females, primipara	2,730	3,000	3,540	3,790
Females, multipara	2,810	3,080	3,690	3,990
Santiago				
Males, primipara	3,027	3,252	3,783	4,044
Males, multipara	3,152	3,377	3,908	4,169
Females, primipara	2,897	3,122	3,653	3,914
Females, multipara	3,022	3,247	3,778	4,039

tional ages 24–25 weeks and 24–31 weeks, respectively. For this reason, to observe the effects of gestational age on mortality risk, the data were separated into three gestational age groupings: 26–31, 32–37, and 38–42 weeks. In analyzing the last two groupings the three standards were compared, while in analyzing the first grouping only the Denver and Santiago standards were compared.

From the 1986 Santiago totals of 254,878 live births and 2,335 neonatal deaths for which complete information was available, certain groups were excluded because of their gestational age at delivery. Specifically, 330 newborns (0.13% of the total) had a gestational age of 25 weeks or less at birth, and 269 (0.1% of the total) had a gestational age of 43 or 44 weeks. Also, 247 neonatal deaths (10.6% of the total) occurred among infants with a gestational age of 25 weeks or less at birth, and eight neonatal deaths (0.3% of the total) occurred among infants with a gestational age of over 42 weeks at birth. All four of these groups were excluded from the study. Thus, 254,279 live births and 2,080 neonatal deaths were analyzed.

The three standards were compared using the 10th, 25th, 75th, and 90th percentiles as cutoff points, the first two cutoff points being used to diagnose SGA and the last two to diagnose LGA. No other cutoff points were used, since none appeared in two of the three original publications (*18, 19*).

For each of the three standards it was necessary to determine the SGA and LGA infants among all the live births and among the neonatal deaths (those dying at less than 28 days of age) by gestational age group. This was done using the procedures of the SAS computational programs package (*23*) and an IBM 4361 computer at the University of Chile.

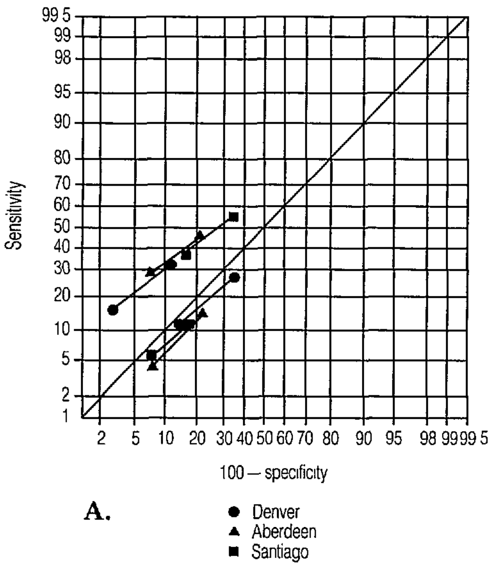
The reliability with which the various fetal growth standards could be used to detect high mortality risk was appraised using sensitivity and specificity values (*24*). The most reliable indicator is that which identifies groups yielding the highest sensitivity and specificity values. (When the sum of the sensitivity and specificity values is 100 or less it means that the indicator has not succeeded in selecting those affected better than mere randomness—*25*.)

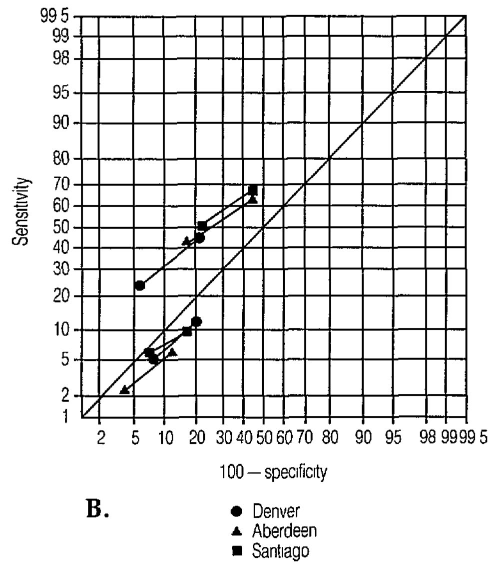
Sensitivity and specificity were derived and assessed in combination through comparative analysis of operating characteristics (relative operating characteristics (ROC) analysis), which is useful for projecting the diagnostic reliability of these indicators onto a single chart (*26, 27*). There is always an inverse relationship between sensitivity and specificity; however, by plotting sensitivity on one axis and 100 minus specificity on the other, ROC analysis provides graphic expression of the relationship between the two in a positive sense (see Figure 1). In this way the probability of true positives is expressed in relation to the probability of false positives; and as long as the former increase, so do the latter. The merits of different cutoff points can thus be weighed in terms of the relative probability of selecting true versus false positives.

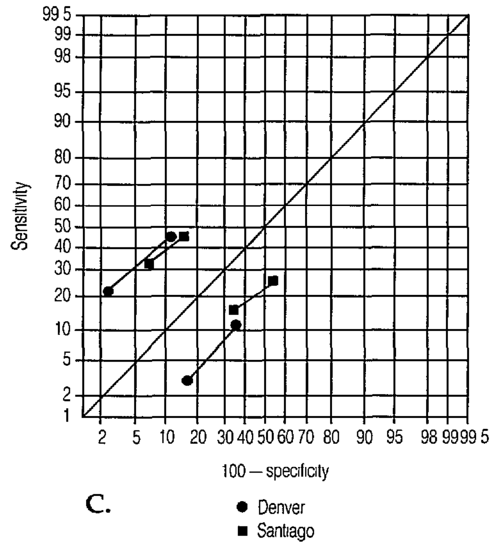
The diagonal line that divides the chart into equal lower and upper areas is called the "line of indifference" because along it the sum of sensitivity plus specificity equals 100. The entire area below this line corresponds to points where sensitivity plus specificity equal less than 100, and where the indicator involved does not discriminate better than chance. Conversely, the ROC line or curve furthest above the line of indifference recommends itself as being, relatively speaking, the best of the various indicators being compared in terms of sensitivity and specificity.

To study predictive capacity, it is necessary to recall that the SGA and LGA populations identified by the three stand-

Figure 1. Relative operating characteristics (ROC) analysis of SGA and LGA populations identified by the Denver, Aberdeen, and Santiago standards in the groups with 38–42 weeks of gestational age (Figure 1-A), 32–37 weeks of gestational age (Figure 1-B), and 26–31 weeks of gestational age (Figure 1-C).







ards presented different prevalences of health deficits; therefore, predictive capacity cannot be derived from sensitivity and specificity (*24*). In contrast to sensitivity or specificity, which queries the validity of a diagnosis in cases where damage is or is not already present, predictive capacity refers to the presence of damage in the (SGA or LGA) study subjects that places them at high risk (*24*).

RESULTS

Table 2 shows live births and neonatal deaths among study infants classified as SGA or LGA according to the Denver, Aberdeen, and Santiago standards. In all three gestational age groups, the number of SGA live births was greatest when the Santiago standard was applied and lowest when the Denver standard was applied. With respect to LGA live births the situation was more mixed, with the Denver standard detecting the largest numbers in the 32–37 and 38–42 week groups and the Santiago standard detecting the largest numbers in the 26–31 week group.

The numbers of SGA neonatal deaths

Table 2. The numbers of neonatal deaths (ND) and live births (LB) occurring among those portions of the 1986 Santiago study population with birth weights below the 10th and 25th percentile cutoffs and above the 75th and 90th percentile cutoffs of the Denver, Aberdeen, and Santiago standards, by gestational age at birth groupings.

Standards and percentiles	Numbers of neonatal deaths (ND) and live births (LB), by weeks of gestational age					
	38–42 weeks		32–37 weeks		26–31 weeks	
	ND	LB	ND	LB	ND	LB
Denver						
Percentile 10	131	7,282	181	2,003	156	188
Percentile 25	252	27,717	351	6,728	351	528
Percentile 75	205	82,161	88	5,943	83	598
Percentile 90	82	35,078	38	2,172	26	282
Aberdeen						
Percentile 10	202	17,185	295	5,398	—	—
Percentile 25	328	51,915	453	12,701	—	—
Percentile 75	108	46,090	42	3,215	—	—
Percentile 90	35	15,674	18	1,149	—	—
Santiago						
Percentile 10	274	40,448	345	7,177	218	305
Percentile 25	403	79,834	451	13,502	304	487
Percentile 75	86	37,683	70	4,339	184	882
Percentile 90	30	13,369	38	1,996	97	570

were greatest when the Santiago standard was applied to the gestational age groups of 38–42 and 32–37 weeks, and also when the Santiago standard's 10th percentile cutoff was applied to the 26–31 week group. When the 25th percentile cutoff was employed, the Denver standard was found to detect the largest number of SGA neonatal deaths in the 26–31 week group. Regarding LGA neonatal deaths, again the situation was more mixed: The Santiago standard detected the largest numbers in the 26–31 week group; the Denver standard detected the largest numbers in the 38–42 week group and also in the 32–37 week group when the 75th percentile cutoff was used; and the Santiago and Denver standards detected equal numbers (more than the Aberdeen standard) in the 32–37 week group when the 90th percentile cutoff was employed.

Table 3 shows sensitivity and specificity values. In general the Santiago standard exhibited the greatest sensitivity for SGA, followed by the Aberdeen standard. However, the situation was generally reversed with regard to specificity, with the Denver standard being most specific, followed by the Aberdeen standard, the Santiago standard coming last. Regarding LGA diagnosis, the Denver standard appeared as sensitive or more sensitive than the Santiago standard in assessing the 38–42 and 32–37 week groups, while the Santiago standard was the most sensitive in assessing the 26–31 week group. The Aberdeen standard, the least sensitive, exhibited the greatest specificity in assessing the two gestational age groups to which it was applied.

Figures 1–3 display a combined ROC analysis of sensitivity and specificity (100 minus specificity) for the three different gestational age groups. The results indicate on the one hand that none of the applied standards succeeded in distinguishing an LGA population at high risk

Table 3. The sensitivity and specificity with which neonatal deaths were detected by the SGA and LGA groupings derived by applying the Denver, Aberdeen, and Santiago standards, by gestational age group.

Standards and percentiles	Weeks of gestational age					
	38–42		32–37		26–31	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Denver						
Percentile 10	16.5	96.8	23.7	93.7	20.9	97.7
Percentile 25	31.7	87.6	46.1	78.0	47.0	87.2
Percentile 75	25.7	63.1	11.5	79.8	11.1	62.6
Percentile 90	10.3	84.3	5.0	92.6	3.5	81.4
Aberdeen						
Percentile 10	27.4	92.3	42.4	82.2	—	—
Percentile 25	44.6	76.6	65.1	57.2	—	—
Percentile 75	14.6	79.2	6.0	88.9	—	—
Percentile 90	4.8	92.9	2.6	96.0	—	—
Santiago						
Percentile 10	37.2	81.8	49.6	76.1	32.6	93.5
Percentile 25	54.8	64.0	64.8	54.4	45.4	86.4
Percentile 75	11.7	82.9	10.1	85.1	27.5	48.2
Percentile 90	5.7	92.9	5.5	93.2	14.5	64.9

of neonatal death, because the charted values fall below the line of indifference. On the other, they indicate that the three standards can distinguish SGA populations at relatively high risk of neonatal mortality, because all the SGA lines are somewhat above the line of indifference—and indeed are about the same distance above it in most cases.

Regarding predictive capacity, Table 4 shows that positive SGA predictive values were clearly low except in the 26–31 week group. Likewise, positive LGA predictive values were clearly low for all three gestational age groups. Negative predictive values were quite high in all cases (regarding both SGA and LGA), except in the 26–31 week group.

DISCUSSION AND CONCLUSIONS

In evaluating the diagnostic power of SGA as defined by the three standards with respect to neonatal death, we found that the differences between the three standards were not very marked, making selection of the most adequate standard difficult. Moreover, relative to what we observed regarding another health problem (deficient infantile growth—*28*), we found that the ROC lines (see Figures 1–3) were not far above the line of indifference; the reason for this probably lies in a lack of concordance between the selected percentiles and the real risks of neonatal death. In addition, we found that the diagnostic power of LGA as defined by the three standards was nonexistent, indicating an even greater lack of concordance between the selected percentiles and real risks of neonatal death.

The positive predictive values of SGA as defined by the three standards were generally very low (see Table 4), because of the low incidence of neonatal deaths. The exception was SGA among the 26–31 week group, where the incidence of neonatal deaths was much higher. The low incidence of neonatal deaths with a diagnosis of LGA also explains why the positive predictive values of LGA were

Table 4. Positive (+) and negative (−) predictive values of the SGA and LGA groupings derived by applying the Denver, Aberdeen, and Santiago standards, by gestational age group.

Standards and percentiles	Weeks of gestational age					
	38–42		32–37		26–31	
	PV(+)	PV(−)	PV(+)	PV(−)	PV(+)	PV(−)
Denver						
Percentile 10	1.8	99.7	9.0	97.9	83.0	69.5
Percentile 25	0.9	99.7	5.2	98.2	66.5	75.2
Percentile 75	0.2	99.6	1.5	97.2	13.8	56.5
Percentile 90	0.2	99.6	1.7	97.4	9.2	60.9
Aberdeen						
Percentile 10	1.2	99.7	5.5	98.3	—	—
Percentile 25	0.6	99.8	3.6	98.5	—	—
Percentile 75	0.2	99.6	1.3	97.5	—	—
Percentile 90	0.2	99.6	1.6	97.6	—	—
Santiago						
Percentile 10	0.7	99.7	4.8	98.4	71.5	73.6
Percentile 25	0.5	99.8	3.3	98.4	62.4	76.1
Percentile 75	0.2	99.6	1.6	97.5	20.9	57.2
Percentile 90	0.2	99.7	1.9	97.6	17.0	60.4

very low. Conversely, all the negative predictive values for both SGA and LGA were very high, in accord with the high proportion of survivors, except in the 26–31 week group where survivors were fewer. Overall, it is to be expected that a better definition of the populations at risk would improve predictive capacity.

An important conclusion of this study is that the limits defining the risk of neonatal death do not closely correspond to the SGA or LGA percentiles selected according to the three standards involved. This has been pointed out previously in a study working with data from the United Kingdom (*29*). The basic reason for this weak correlation between the newborn's well-being and the percentile birth weights defined by the various standards seems to lie in the fact that the so-called standards of fetal growth have been constructed by relating birth weight to gestational age, ascribing to it certain limits of normality with a measure of statistical distribution, without validating its diagnostic reliability and capacity for predicting injury to health.

Wilcox has noted the importance of studying the combined behavior of birth weight and gestational age in seeking to construct fetal growth standards correctly, the reason for this being that the true direction of cause and effect is unknown (*6*). Hoffman et al. also propose this kind of analysis for understanding the combined effect of birth weight and gestational age on infant survival (*30*), as does Falkner in stressing that perinatal outcome is the key aim in judging the adequacy of prenatal growth (*31*).

It is to be expected that better determination of the probabilities of death or functional injury, derived from adequate measurement of the combined effect of birth weight and gestational age, will result in fetal growth standards with greater diagnostic reliability and predictive capacity than those compared in this study.

In this vein, it should be noted that the first study to use the approach described here was conducted by Lubchenco et al. with data from the city of Denver (*4*). The neonatal risks detected were considered "essential for orienting perinatal care."

The results of that study, based on neonatal mortality data determined by birth weight and gestational age at birth in Denver for the period 1958–1969, together with the results of a later study also from Denver for the period 1974–1980 (7), were used extensively in clinical practice. Still, progress in perinatal care since then has produced quite a marked decrease in the risks of neonatal death, which in turn has created a need to explore the use of new curves where the risks of death are better adjusted to the present reality of a given population.

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Video on Foster Care for Children with HIV/AIDS

An 18-minute video called *With Loving Arms,* produced by the Child Welfare League of America, portrays three different foster care situations in which the children have HIV/AIDS, focusing on the needs of both these children and their foster parents. Viewers are reminded that a consistent primary care giver is essential in the life of any child, with or without AIDS. Babies who are abandoned in the hospital can suffer extreme emotional deprivation, which can adversely affect their immune system. This interrelationship between the immune system and stress may account for the fact that children with AIDS placed in foster day-care settings are living longer than expected.

With Loving Arms is accompanied by a discussion guide. It is intended for community-based AIDS organizations, policy making and advocacy groups, child welfare administrators, practitioners, and anyone working with HIV-infected children. For further information, contact the Child Welfare League of America, 440 First Street, N.W., Suite 310, Washington, D.C. 20001-2085; telephone (202) 638-2952.

Source: Holmes, E., With loving arms, *Canadian AIDS News* V(1):13, Nov/Dec 1991.