Limitations of Growth Charts Derived from Longitudinal Studies: The Euro-Growth Study

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Length and weight for age (1–12 months) charts are presented for the longitudinal Euro-Growth Study. "Weight-for-length", another widely used growth chart, presents a problem from a methodological point of view. Target length values (53–77 cm) are not observed in all infants, leading to truncated age distributions at most target lengths. It was demonstrated that the age at which the target length was reached (Fig. 8) had a significant influence on weight especially at a smaller length. This implies that the weight-for-length charts are biased. This phenomenon is due to the longitudinal measurement schedule at prechosen ages and not at prechosen lengths, which is impossible. To obtain the desired length-corrected weight standards, it is advocated to construct age-related body mass indices.

Key words: Longitudinal growth standards, weight-for-length, age-for-length, survival regression, mid-parent height

Introduction

The question concerning how far early nutrition influences child growth is still controversial. Several reports indicate short-term effects but the long-term outcome is not known. Therefore, the Euro-Growth Project was initiated to study longitudinally the influence of infant nutrition on growth up to 5 years of age (4).

The first step in the evaluation of nutritional status of European infants was the construction of adequate growth curves (cq. standards). Anthropometric measurements for infants and children are generally presented as percentile curves indicating weight-for-age, length-for-age and weight-for-length. A problem is that weight-for-length curves differ from length cq.-weight-for-age curves in a methodological respect. Only standards for age reflect the clinical conditions that the observations are done at prechosen ages. In constructing weight-for-length curves, it is impossible to measure weight at prechosen target lengths. Therefore, the problem in constructing weight-for-length curves on longitudinal data is that infants may reach the target lengths outside the studied age range. This implies that the sample of infants observed at the aimed target lengths may be over- or underrepresented by early/late maturers, probably leading to biased weight-for-length curves. This study discusses the magnitude of such a bias and a way to deal with this problem.

Material and Methods

The Euro-Growth Project is a longitudinal, observational, multicenter study using strictly standardized methodology. Per study center a cohort of newborn infants (intended sample size of 100) had to be enrolled. In total, 22 centers from 12 European countries agreed to participate. Normal healthy Caucasian infants, whose parents were able to communicate with the center and indicated a willingness to comply with the prescribed protocol, were enrolled before the age of 30 days. Maternal exclusion criteria were: conditions suspected for effects on intrauterine growth (e.g., insulin-dependent diabetes or epilepsy). Infantile exclusion criteria were: gestational age < 37 weeks or unknown, birth weight < 2500 g, congenital malformations, inherited metabolic disease, neonatal disease requiring hospitalization for > 7 days, chronic disease, twins, father unknown and no follow-up visit. In order to avoid seasonal influences on growth and food intake, the infants had to be enrolled during a period of at least 1 year.

Data collection was done at the target ages of 1, 2, 3, 4, 5, 6, 9 and 12 months within narrow age bands and is still going on up to the age of 5 years. For measurements of weight and length, the procedures described by Guo et al. (1) were followed, explained in a video tape to obtain standardized measurements. During each visit, dietary intake was assessed by a semiquantitative dietary recall method. Weight and length at birth, number of siblings, maternal and infant health state, parents age, and length and weight were assessed during the first visit. Questions ragarding socioeconomic parameters, lifestyle factors and diseases of the infant were posed at each visit. The data were entered using EPI info (WHO, public domain) and sent to the central data management unit in Nijmegen,

Country	Center	Infants
Austria	Vienna	118
	Salzburg	54
Croatia	Zagreb	100
France	Toulouse	83
	Nancy	79
	Reims	84
Germany	Dortmund	80
	Rostock	142
Greece	Athens	131
Hungary	East/West	218
Ireland	Dublin	114
Italy	Naples	131
Portugal	Porto	100
Scotland	Glasgow	127
Spain	Barcelona	97
	Bilbao	100
	Granada	96
	Madrid-1	87
	Madrid-2	81
	Santiago	105
Sweden	Umea	120
Total	22	2247

Table 1 Sample sizes in the Euro-Growth study.

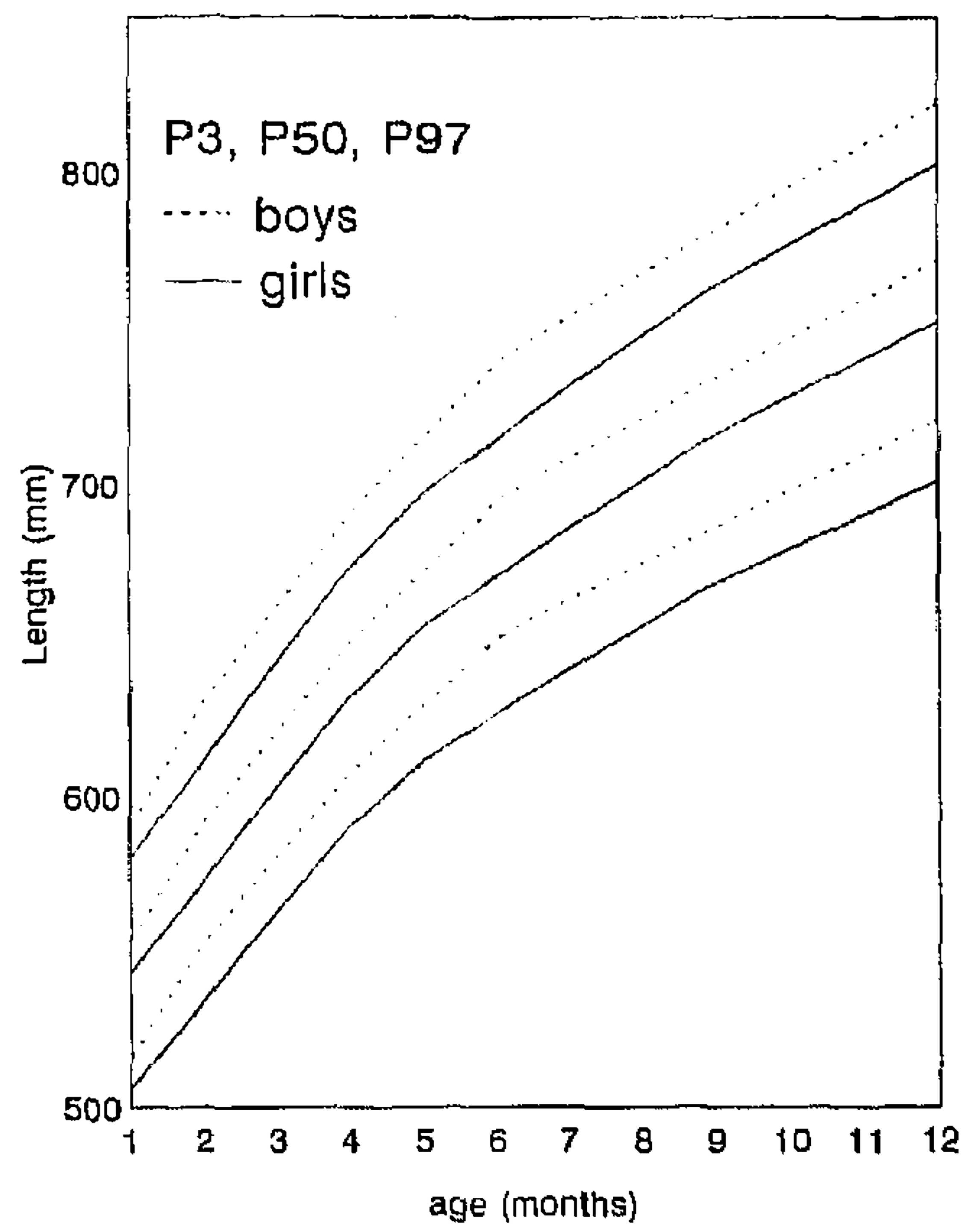

Fig. 1 Length for age in the Euro-Growth study. The standard (P3, P50, P97) is based on 2247 × 8 measurements (minus some dropouts).

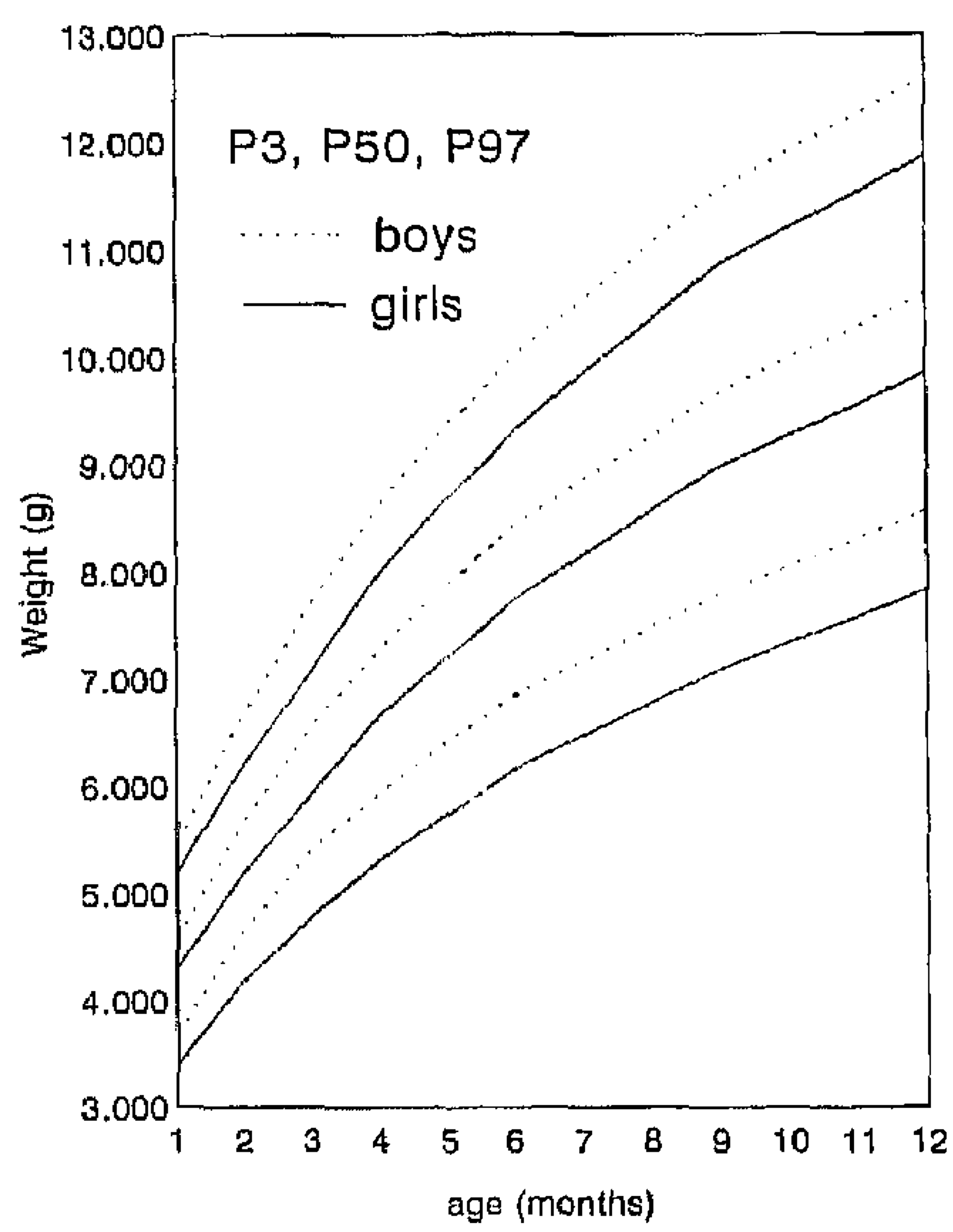

Fig. 2 Weight-for-age in the Euro-Growth Study. The standard (P3, P50, P97) is based on approximately 18 000 observations.

where data quality programs (3) were applied for correcting data errors.

In total, 2346 infants were reported at the central data management unit in Nijmegen. Inspection of their data revealed that 99 infants did not fulfil the inclusion criteria (mainly due to low birth weight or no follow-up) leading to a cohort of 2247 infants (Table **1**), equally distributed over boys and girls.

In a multicultural setup, as was the case in the Euro-Growth Study, a uniform invitation protocol for parents was not really feasible. In 13 centers only parents assumed to be able or willing to participate in the study were invited, probably selected on their social background, their interest in health problems and the travel distance to the research center. In nine centers a random sample from the clinic population was invited to participate, leading to nonparticipation, probably related to the same type of selection. A nonparticipation study based on 18 centers including 1877 participants and 1798 nonparticipants showed that the length and weight of mothers, degree of urbanization, and gender and birth weight of the infants in general were not associated with participation, while the age of the participating mothers and their educational level was higher compared to nonparticipating mothers. This general tendency was not uniform in all centers; A few centers showed an overrepresentation of lower educated mothers. A consequence of these findings must be that such selection variables have to be entered as covariables in future analyses.

Results

Sex-specific percentile curves describing length- and weight-for-age in the Euro-Growth Study (n = 2247) obtained by connecting corresponding percentiles at the target ages are presented in Figs. **1** and **2**.

In trying to construct weight-for-length curves (at integer target lengths) the problem was that many of the infants were not observed at all target lengths, in the considered age range of 1 – 12 months. At low target length values the rapidly growing infants were absent, while the slowly growing infants were absent at large target lengths. This phenomenon is best demonstrated on the cumulative age-for-length distributions as presented in Figs. **3** and **4**. The age axis ranges from 1 to 12 months, according to observed age range, and the target lengths are chosen widely (53 – 77 cm). The ages at target lengths were obtained by linear interpolation in the individual longitudinal curves. The figure shows clearly that the age distributions for both small and large length values are truncated. Only a narrow length range (60 – 67 cm) is present in all 2247 infants. The information of the cumulative age for length distributions is also shown in condensed format in Fig. **5**, the length-for-age standard. Again this figure shows the truncation of the age distributions in the extreme length values. This truncation implies that the sample of infants at extreme target length values is not complete, probably leading to selection bias in the weight-for-length curve.

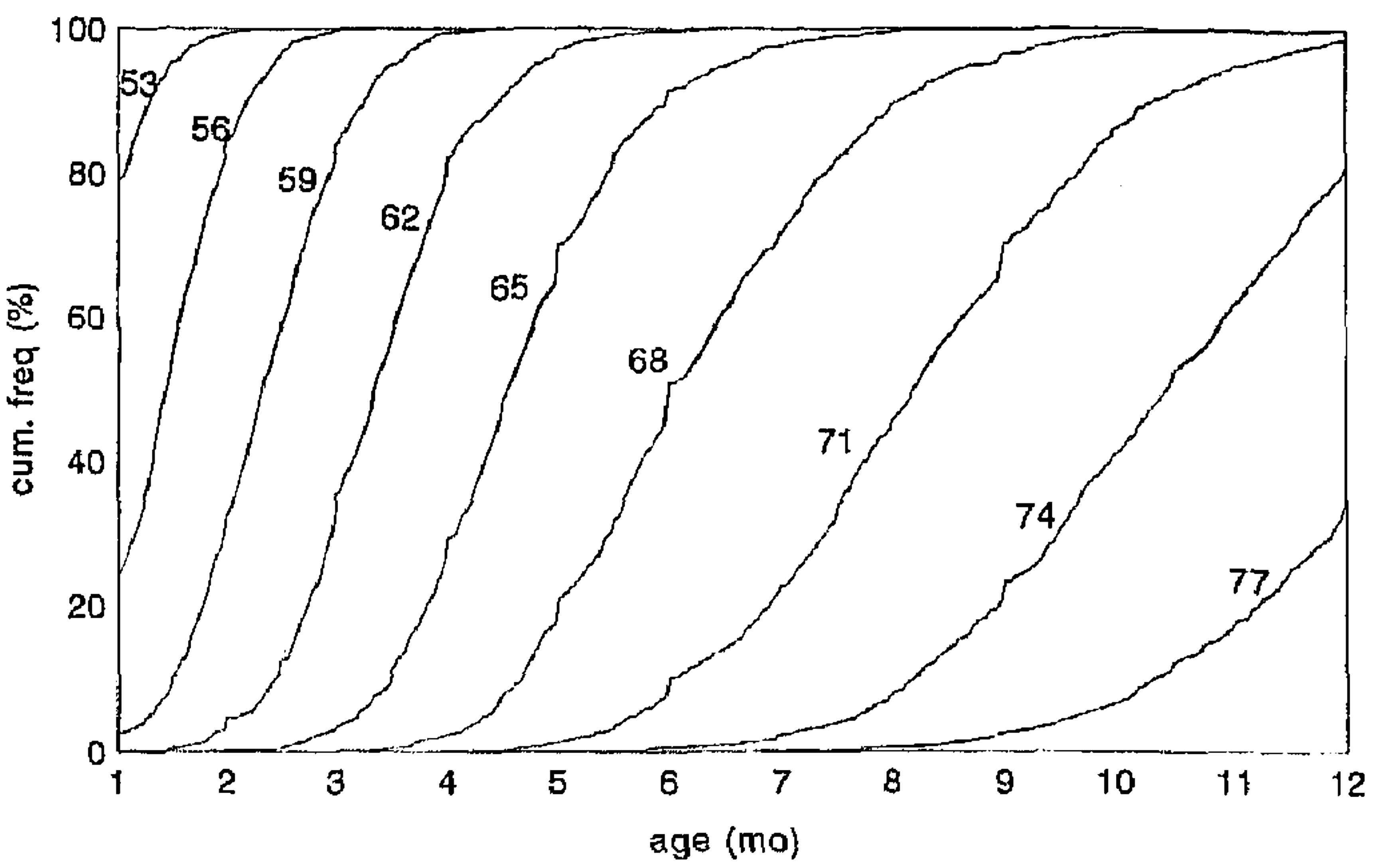

Fig. 3 Cumulative age distributions for the specified target lengths (53–77 cm) as reached by boys.

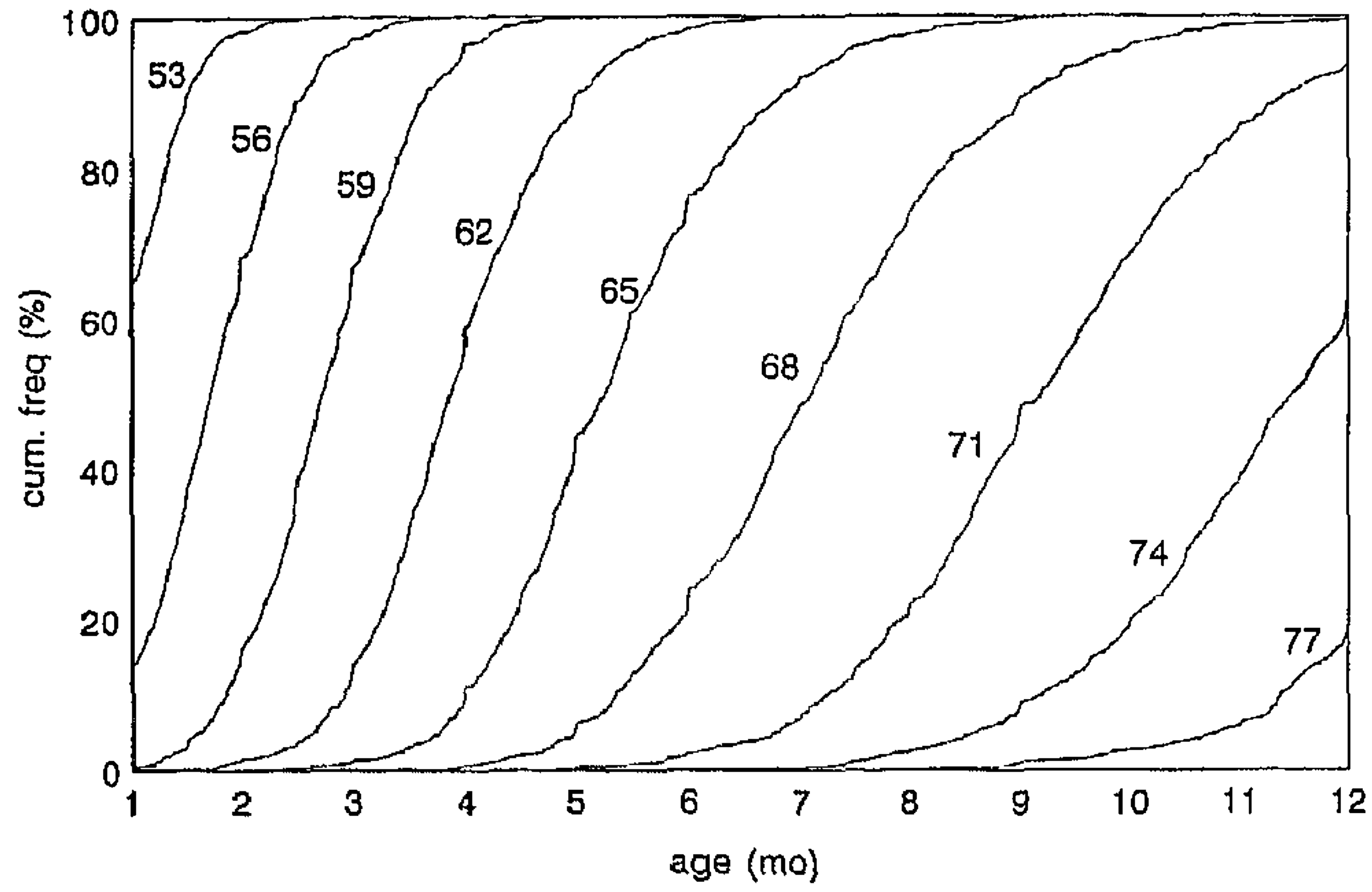

Fig. 4 Cumulative age distributions for the specified target lengths (53–77 cm) as reached by girls.

The age-for-length distribution is the key for the selectiveness in the weight-for-length distribution and needs, therefore, further analyses. Due to the truncation of the age distribution at target lengths, we have to deal with the phenomenon of "censored data". In the presence of censored data classic statistical techniques cannot be applied, since the exact value of a censored observation is unknown. Censored values may not be considered as random missings, since it is known that the value is outside the scope of the study. Statistical methods dealing with censored data are known as "survival" analysis. In this field, Cox regression, a distribution-free method assuming proportional hazards, is often applied. Anthropometric data, however, are known to be symmetrically distributed, often according to the normal distribution. Also in the situation of age-for-length the age distributions at the different target lengths follow approximately the normal distribution (see Figs. **3** and **4**). An opportunity to work with normal distributions in the presence of censored data is found in the SAS procedure "LIFEREG".

The LIFEREG procedure was applied to explain age-for-length from gender, mid-parent height and its interaction. At all considered target lengths the influence of gender and mid-parent height was significant, while the interaction of gender with mid-parent height (mean value of father's and mother's height) was not significant. This implies that these influences can be described by two separate curves (Figs. **6** and **7**).

Fig. **6** presents the influence of gender on the age-for-length. At a small target length (e.g., 55 cm) the sex difference is only small, i.e., 0.3 months (10 days). This means that boys, on the average, reached the length of 55 cm 10 days before girls. The length of 73 cm is reached by boys 1 month before girls on the average.

Fig. **7** shows the influence of mid-parent height on age-for-length. The regression coefficients are negative, indicating that infants of taller parents have smaller ages-for-length, i.e., are growing faster. The interpretation of the curve is the following: At a length of 55 cm the regression coefficient is −1 day/cm. For two couples of parents differing 1 cm in mid-parent height the difference between their infants in reaching 55 cm is 1 day. If the difference in mid-parent height is 5 cm the difference between the infants will be 5 days in reaching 55 cm. The regression coefficient at length 73 cm is −3.7 days/cm. If the difference in mid-parent height is e.g. 5 cm, the infant of the tallest couple will reach the length of 73 cm on the average 5 × 3.7 = 18 days before the infant of the shortest couple.

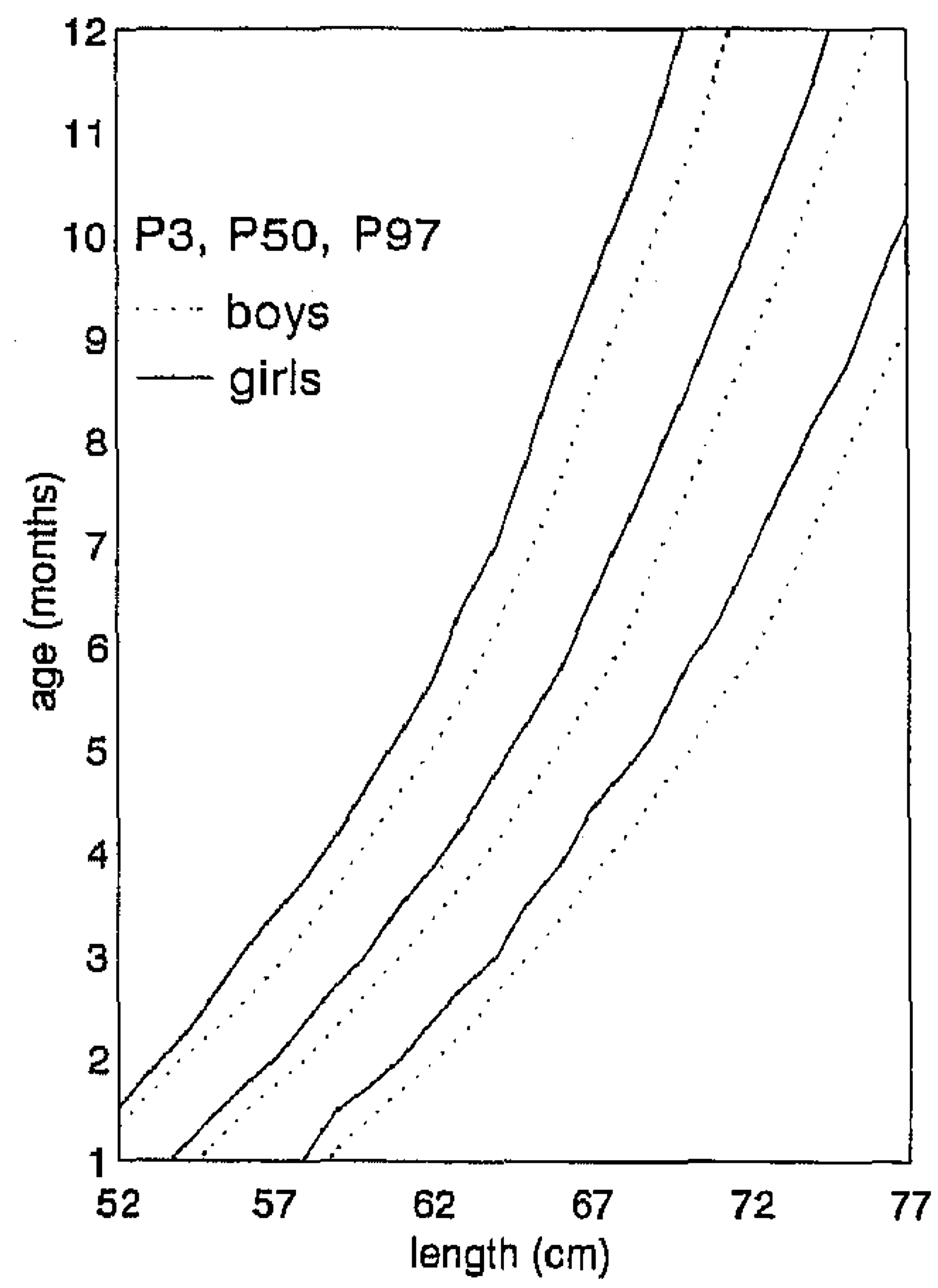

Fig. 5 Age-for-length standards (P3, P50, P97) in boys and girls as found in the Euro-Growth study.

Further classic regression analyses per target length show that the age at which the target length is reached has a significant influence on weight (Fig. **8**). The older the infant is when reaching the target length, the heavier the infant is. For the length of 55 cm, the weight effect is 6% per month later (SE 0.5%). This effect was shown to be independent of gender (nonsignificant interaction). Example: If one boy (or girl) is 2 weeks ahead of another boy (or girl, respectively) in reaching a length of 55 cm, its weight will be 3% lower (± 100 g on the average).

At a length of 73 cm this age-for-length effect on weight has almost disappeared; only a difference of 0.3% per month remains. This is in the magnitude of 30 g/month later. Due to these age-for-length effects it may be concluded that the weight-for-length distributions are biased at early infancy and are consequently not presented here.

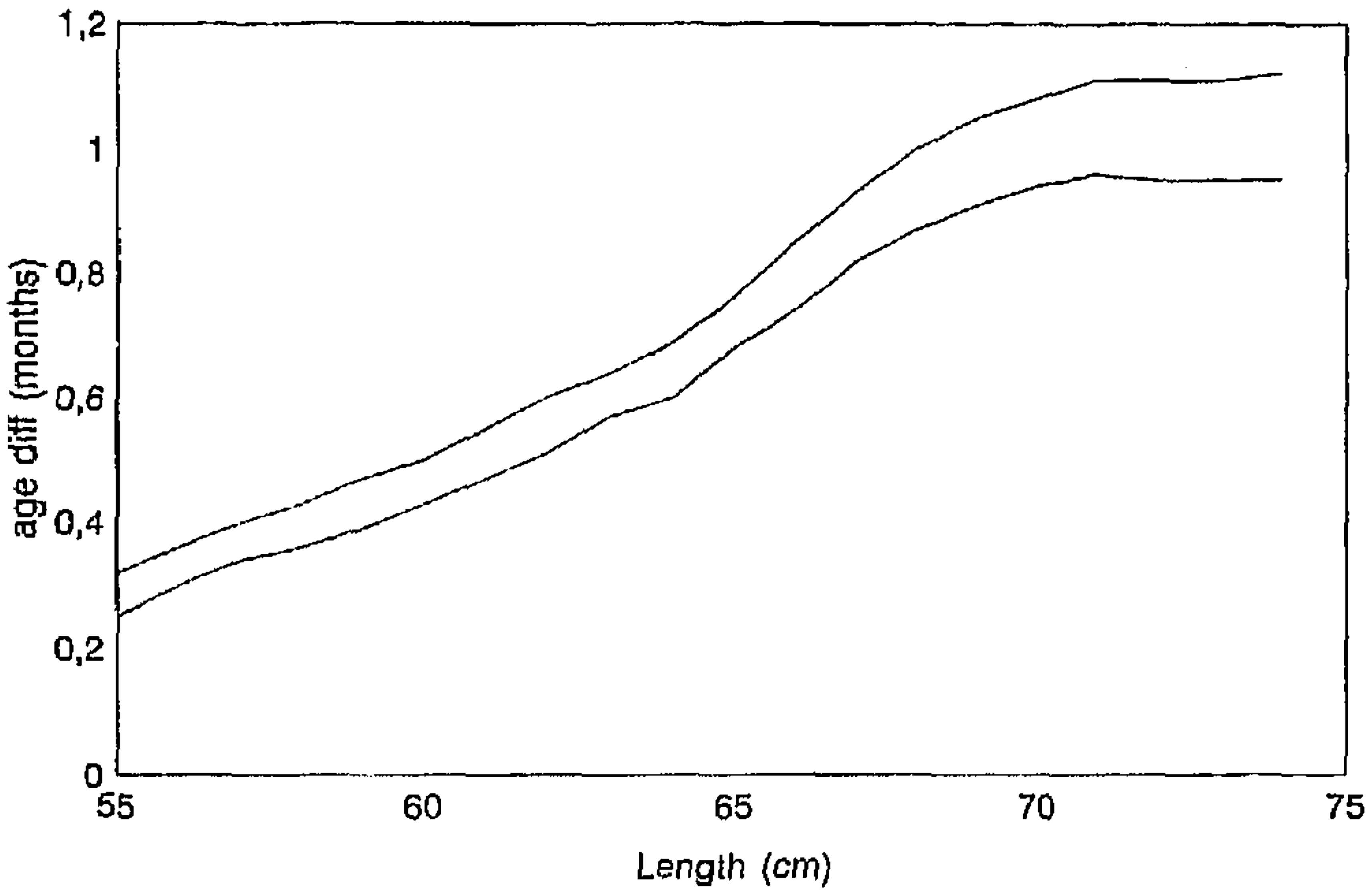

Fig. 6 Sex differences in age-for-length. The band presents the sex effect estimates (±SE) obtained by LIFEREG. The positive values indicate that boys are ahead of girls.

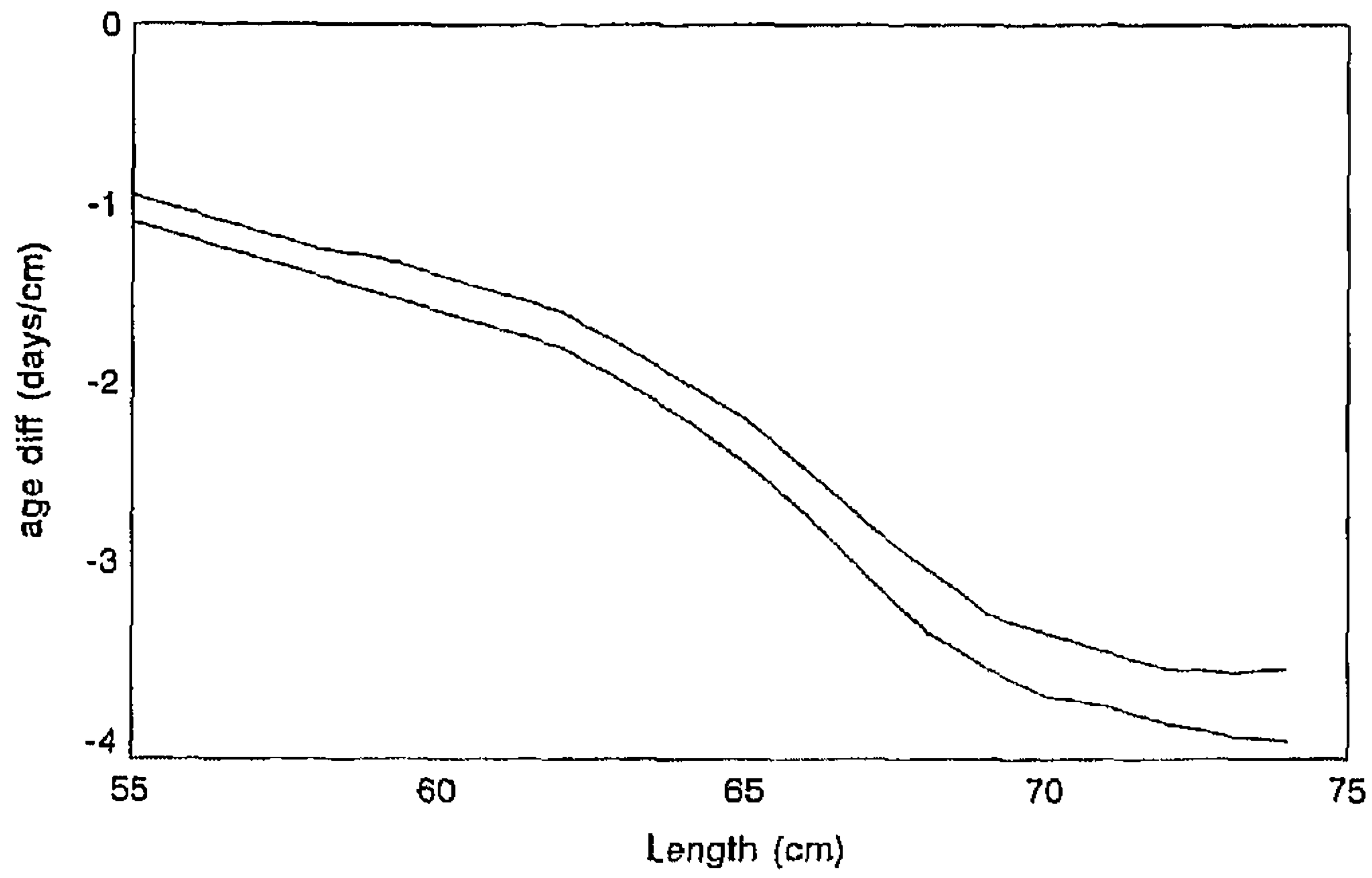

Fig. 7 Influence of mid-parent height on age-for-length. The band represents the regression coefficients (±SE) from LIFEREG. The regression coefficients (expressed in days of age gain per cm mid-parent height) are equal for boys and girls. The negative values indicate that taller parents have infants reaching the indicated length at younger ages.

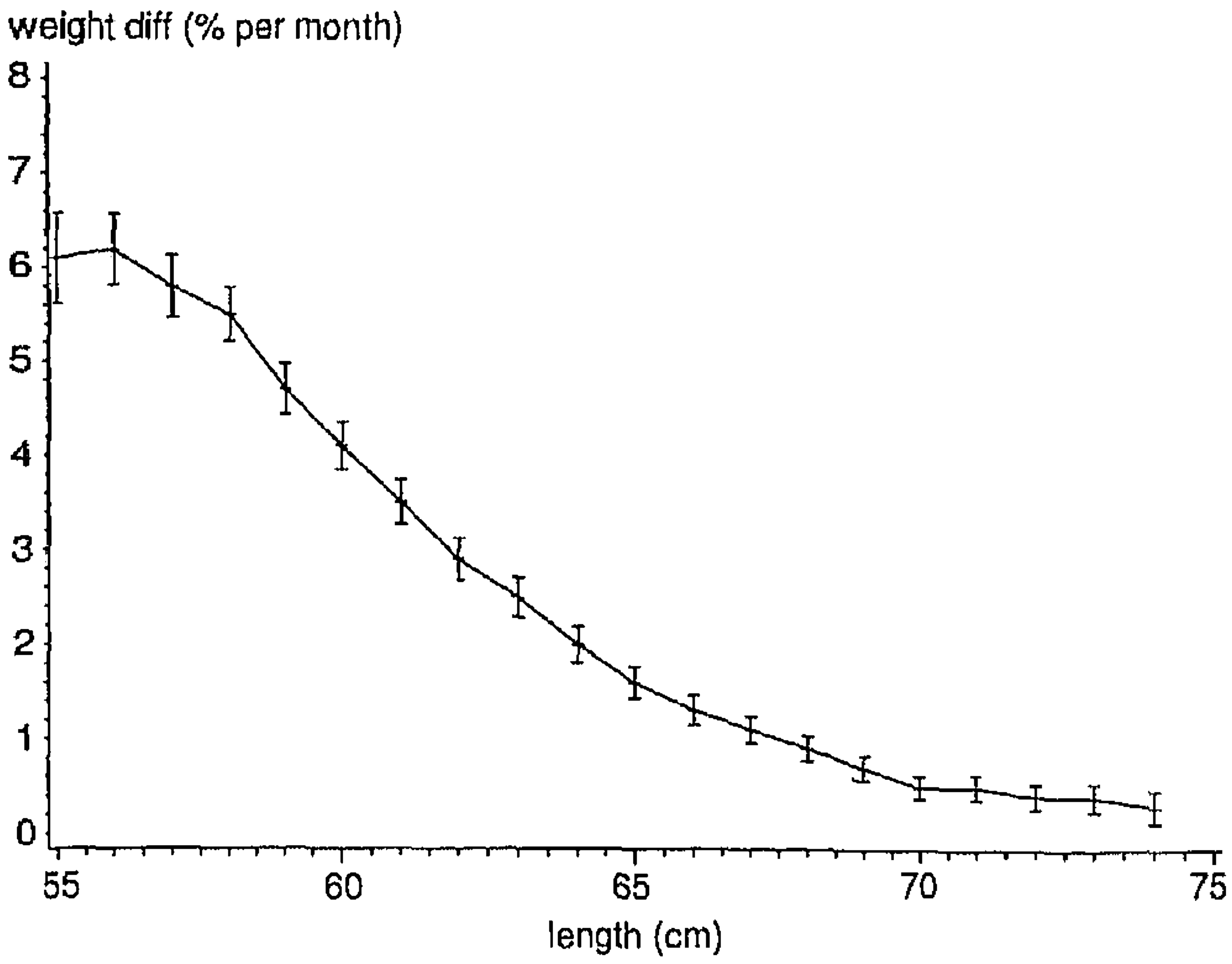

Fig. 8 Regression coefficients (±SE) for the influence of age on weight at different target lengths. The positive values indicate that weight is higher in older infants at equal length (especially at lower length values).

Discussion and Conclusions

A multicenter longitudinal approach was selected to collect European-wide data on infant growth. Such growth data are necessary because anthropometric indices are widely used as the principal criteria for assessing dietary and growth adequacy in infancy.

This study has shown that weight-for-length charts which are widely used (WHO working group) can be highly biased. The age-for-length distributions determine the selectiveness in the weight-for-length distributions and deserve more attention than normally received.

Because the age distributions are truncated, censored data need to be analyzed, in this situation by using the SAS procedure LIFEREG, showing that sex and mid-parent height influence age-for-length.

Due to the truncation of the age distributions, the weight-for-length charts are not valid, especially at shorter lengths. The problem of age- and length-corrected weights may be solved by constructing age-based, body mass index-like charts which are more in concordance with the nature of the longitudinal design.

References

[1] Guo S., Roche A. F., Fomon S. J.: Reference data on gains in weight and length during the first two years of life. *J Pediatr* 119: 355–62, 1991.

[2] Roede M. J., van Wieringen J. G.: Growth Diagrams 1980. *TSG* (Suppl.) 1985.

[3] SAS Institute Inc., SAS/STAT User's Guide, Version 6, Fourth Edition, Vol. 2, Cary, NC, U. S. A., SAS Institute Inc., 1989.

[4] Van't Hof M. A., The Euro-Growth Study Group: The Euro-Growth Study. Vth International Workgroup. Maternal and Extrauterine Nutritional Factors. Madrid, Ergon S. A., 1996, pp 281–90.

[5] WHO Working Group on Infant Growth, Nutrition Unit. Evaluation of infant growth: The use and interpretation of anthropometry in infants. *Bull WHO* 73: 165–74, 1995.

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