



Review

Malnutrition in pediatric hospital patients: Current issues

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ABSTRACT

Malnutrition in hospitalized children is still very prevalent, especially in children with underlying disease and clinical conditions. The purpose of this review is to describe current issues that have to be taken into account when interpreting prevalence data. Weight-for-height and height-for-age standard deviation scores are used for classification for acute and chronic malnutrition, respectively. Body mass index for age can also be used for the definition of acute malnutrition but has a few advantages in the general pediatric population. The new World Health Organization child-growth charts can be used as reference but there is a risk of over- and underestimation of malnutrition rates compared with country-specific growth references. For children with specific medical conditions and syndromes, specific growth references should be used for appropriate interpretation of nutritional status. New screening tools are available to identify children at risk for developing malnutrition during admission. Because of the diversity of medical conditions and syndromes in hospitalized children, assessment of nutritional status and interpretation of anthropometric data need a tailored approach.

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Introduction

From the early 1980s it has been known that the prevalence of acute and chronic malnutrition of children admitted to the hospital is high depending on the criteria used [1]. The prevalence of malnutrition is also dependent on the used reference growth curves and the use of specific growth curves for specific conditions and premature infants. Most commonly, for wasting or acute malnutrition, weight-for-height (WFH) standard deviation (SD) scores are used, and for chronic malnutrition, height-for-age (HFA) SD scores are used, but the body mass index (BMI) is also used to describe malnutrition. Although actual nutritional status can be expressed in SD scores, there is still discussion about the definition of faltering growth or failure to thrive. Furthermore, there is a need for screening for the risk of malnutrition in hospitalized children and several tools have been developed. In this review, current issues about these topics are described.

Definition of malnutrition

Malnutrition can be defined as a state of nutrition in which a deficiency or an excess of energy, protein, and other nutrients

causes measurable adverse effects on tissue and body form and function and on clinical outcome.

Growth is the best indicator of nutritional status and using growth curves remains the simplest way for assessing nutritional status in children. Assessment of growth involves accurate measurements of weight and height.

The reported prevalence of acute malnutrition over the previous 10 y in hospitalized children in Germany, France, UK, and USA has varied from 6% to 14%, whereas in Turkey a prevalence of malnutrition of up to 40% has been reported [2–6]. Very recently, a national survey in 41 hospitals in the Netherlands showed that 19% of children had acute and/or chronic malnutrition at admission [7].

BMI to describe malnutrition

Various definitions are used to describe the prevalence of malnutrition. To compare prevalence data appropriately, using equivalent criteria for defining malnutrition has been proposed [1]. Most commonly, for wasting or acute malnutrition, WFH SD scores are used, and for chronic malnutrition, HFA SD scores are used. The likelihood of malnutrition is defined using a cutoff point of -2 SD. One criterion that is currently used more frequently is the BMI. The BMI is a simple and reproducible index that reflects body composition and function. Since the 1960s, BMI has been

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used to assess obesity in adults. However, there are no valid BMI cutoffs for assessing malnutrition in adolescents or children. In 2007 an international survey was done (including almost 200 000 children) to determine cutoffs to define thinness in children and adolescents based on BMI at 18 y of age [8]. The cutoff value of BMI at age 18 y was chosen because this coincided with the World Health Organization (WHO) adult cutoff value. The WHO defines thinness grades 1, 2, and 3 as BMIs below 18.5, 17, and 16 kg/m², respectively. The BMI cutoff of 17 kg/m² is not only the WHO definition of thinness grade 2, it is also near to the SD score -2 . Thus, the WHO classification provides a bridge between child and adult in that a young person with a BMI of 17 kg/m² at age 18 y is a borderline thin adult (grade 2) and a borderline thin child (-2 SD). For this reason, Cole et al. [8] proposed using the cutoff of 17 kg/m² plus the other two WHO cutoffs of 18.5 and 16 kg/m² as the basis for their classification. Cutoff values for BMI for underweight in younger children were determined by first calculating the percentage of 18-y-olds with a BMI lower than 18.5 kg/m², followed by a calculation of the BMI of younger subjects who were within the same percentage. Considering these calculations, i.e., a BMI of -2 SD for a 2-y-old boy is approximately 14 kg/m² and that for an 8-y-old boy is 13.5 kg/m². For general screening of acute malnutrition in a mixed population of children who are admitted to the hospital, there will be only a slight difference using the SD score for BMI or WFH. The benefit of simply classifying the calculated BMI into a thinness category in adults does not apply for children because the cutoff levels depend on the age of the child.

Failure to thrive

Failure to thrive (FTT) describes the problem of inadequate growth in early childhood [9]. These children do not achieve a normal or expected rate of growth. This may result in delayed physical and intellectual development. However, it is not clear whether there is a threshold for the association between poor growth and intellectual impairment. For many years, there has been ambiguity and inconsistency in the precise definition and use of FTT [10].

In 2007, Olsen et al. [11] compared seven clinically used anthropometric criteria for FTT. In five of these seven criteria, actual nutritional status using weight and height of the child was determined. In two of the seven criteria, a deceleration of weight in time was used to define malnutrition, e.g., 1) weight deceleration crossing more than two major centile lines and 2) conditional weight gain is equal to the lowest 5%, adjusted for regression toward the mean from birth until weight within the given age group.

Olsen et al. [11] applied these seven criteria to a birth cohort of 6090 Danish infants and compared two age groups, 2 to 6 and 6 to 11 mo of life. A poor concurrence was found among all seven criteria. Moreover, the sensitivity and positive predictive value of a single criterion to detect children with undernutrition were low. Olsen et al. concluded that, for identifying nutritional growth delay in the general population, no single measurement on its own seems to be adequate.

Dynamic definitions that assess weight velocity and change over time are regarded by most researchers as preferable to attain values, but there is limited consensus as to which dynamic definitions to use [12]. A well-established criterion for identification of FTT in children until 2 y of age is a decrease across two centile channels or a decrease beneath the second centile on standardized growth charts for at least 3 mo (to exclude weight loss secondary to an acute illness) [13].

Table 1

Criteria for failure to thrive and immediate nutritional intervention

Inadequate growth or weight gain for >1 mo in a child <2 y of age
Weight loss or no weight gain for >3 mo in a child >2 y of age
Change in weight/age > -1 SD in 3 mo for children <1 y of age on growth charts
Change in weight/height > -1 SD in 3 mo for children ≥ 1 y of age on growth charts
Decrease in height velocity 0.5–1 SD/y at <4 y of age and 0.25 SD/y at >4 y of age
Decrease in height velocity >2 cm from preceding year during early/mid puberty

Ideally, the definition of FTT should be based on a decline in nutritional status that has to be related to clinical endpoints. Emond et al. [14] defined weight faltering as those infants with a conditional weight gain below the fifth centile and showed that weight faltering from birth to 8 wk was associated with persisting deficits in IQ at 8 y. Eskedal et al. [15] showed that a decrease in WFA during the first months after surgery for congenital heart defects of more than 0.67 z-score, corresponding to a downward percentile crossing through at least one of the displayed percentile lines on standard growth charts, is strongly related to late mortality in children operated on for congenital heart defects. In contrast, long-term surviving children showed a mean increase in weight z-scores after the final operation.

Table 1 presents a summary for proposed criteria for FTT in relation to weight and/or height loss. In children fulfilling these criteria, immediate nutritional evaluation and intervention are necessary.

Use of WHO growth charts

The most established way to describe malnutrition is the use of SD scores, with the reference population defined as according to reference charts from a specific country. In 2006 the new WHO child-growth charts were established on the basis of a longitudinal study conducted in children living in different countries and different continents [16]. These WHO growth charts are based on data from the Multicenter Growth reference study (1997–2003) involving 8500 children from Brazil, Ghana, India, Norway, and the USA. The included children had non-smoking mothers, infants received breast-feeding according WHO recommendations, and were selected in four countries from a higher social class (except USA and Norway).

The goal of developing the WHO growth charts was to construct standards for length/HFA, weight-for-length/height, and BMI for age. There are, however, concerns about the use of the new charts because of the risk of underestimation or overestimation of the prevalence of under- and overweight in specific countries. In 2009 the new WHO standards were compared with the new national growth curves of Belgian and Norwegian children [17,18]. There were significant deviations in the proportion of children outside normal limits of the WHO standards. This was true for all children, including those who were exclusively breast-fed. In general, the number of Belgian and Norwegian children below the -2 SD lines of the WHO standards was lower, and those above $+2$ SD higher than expected. The growth pattern of breast-fed children of non-smoking mothers was in both countries more like the local national growth references than the WHO standards.

It can be concluded from the cited references that prevalence rates of under- and overweight in countries that adopt the new

WHO charts will be different from previous data and this might have consequences for clinical decision-making.

Use of target height

Stunting or chronic malnutrition is defined if a SD score is lower than -2 . In a general population, this means that 2.3% of healthy children have a short stature. Therefore, determination of genetic height potential, based on parental heights, might be helpful in the evaluation of growth in children. Various mathematical formulas have been proposed for target height, expressed in centimeters or SD score units [19]. In some formulas the target height is modified assuming a secular trend across generations. In recent decades, however, the secular trend of increasing height seems to have stopped in several European countries, whereas it has continued in other countries, which means that correction for secular trend is not necessary for all countries [20].

A high prevalence of chronic malnutrition is found in children with a chronic cardiac or renal disease or in children after cancer treatment who received total body irradiation before stem cell transplantation [1,21]. In these groups of children, target height can be useful to distinguish the influence of disease on normal growth.

Malnutrition in preterm neonates and use of specific growth charts

Preterm infants are sensitive to changes in nutritional status, and growth failure during a hospital stay is common. For many years, to determine the growth of prematurely born infants, the intrauterine growth curves of Usher and McLean [22] were used for calculation of SD scores for weight and length up to a postconceptual age of 41 wk. These reference data were derived from preterm infants born from 1959 to 1963 in Canada and were revised regularly in different countries (USA, Sweden, Norway, and Israel) [23–26]. In 2001 a new and improved population-based Canadian reference for birth weight for gestational age was published [27]. Large-for-gestational age cutoffs (90th percentile) at young gestational age were considerably lower than those of existing references, whereas small-for-gestational age cutoffs (10th percentile) after term were higher. In 2008 Davidson et al. [28] reported a hospital-based growth reference for preterm and term singletons in Israel based on a population born from 1991 to 2005. The developed

growth references differed markedly from the Canadian counterparts because the Israeli neonates were consistently smaller.

It might be concluded that existing fetal growth references have the same methodologic problems such as errors in reported gestational age, implausible birth weight for gestational age, and insufficient sample size at a young gestational age.

One should be aware that the generalizability of “standard” growth references is questionable and prevalence data for malnutrition may be different.

After discharge from the hospital, follow-up of weight and height can be done with standard growth charts but these should be corrected in accordance to gestational age. There is general agreement that correction has to be done until a postnatal age of 2 y.

Use of growth charts for specific groups

Malnutrition has been reported to be highly prevalent in children with an underlying disease. Compared with data from 20 to 30 y ago, the prevalence rate of malnutrition has been reported to be lower, especially in children with CF and malignancies, but in children with chronic inflammatory diseases such as chronic kidney disease, acute and chronic malnutrition remain very prevalent [1]. Furthermore, in children with neurologic disorders, attention should be focused on appropriate methods of nutritional assessment to obtain a reliable picture of their nutritional status.

Currently, there are several specific growth references for specific groups of children, including those with syndromal disorders. These growth references will enable a more appropriate assessment of nutritional status [29]. Table 2 presents growth charts and references for several specific medical conditions.

Screening tools to identify children at risk of malnutrition

Currently, there is no consensus on the ideal method to determine which children on admission are at risk to develop malnutrition during a hospital stay. Such a screening tool is basically different from measuring actual nutritional status with weight and height. There are four screening tools available in the literature. Secker and Jeejeebhoy (2007) [30] and Sermet-Gaudelus et al. (2000) [31] developed the Pediatric Nutritional Risk Score and the Subjective Global Nutritional Assessment, respectively. These identify children at risk of malnutrition during hospitalization. Sermet-Gaudelus et al. evaluated in

Table 2
Growth chart references for several specific medical conditions and syndromes

Medical condition	Year	Type of chart	Reference
Duchenne muscular dystrophy	1988	WFA	35
	1993	WFA	36
Cerebral palsy		WFA, HFA, BMI for age	http://www.lifeexpectancy.org/articles/GrowthCharts.shtml
Down's syndrome	2003	WFA, HFA, BMI for age	37
	1996	HFA	38*
Prader-Willi syndrome	2000	WFA, HFA, BMI	39*
Silver-Russel syndrome	1993	HFA	40*
Turner's syndrome	1993	BMI for age, WFA, WFH	41*
		HFA, height velocity for age	42*
Noonan's syndrome	1988	HFA	43*
Achondroplasia	1978	HFA	44*
Idiopathic short stature	1996	HFA	45*

BMI, body mass index; HFA, height for age; WFA, weight for age; WFH, weight for height

* See also www.growthanalyser.org.

Table 3
Interpretation of prevalence rates of malnutrition: issues to account for

Used classification system: SD criteria or percentiles
Used definition to describe acute and chronic malnutrition
Used reference data general population: World Health Organization references, country-specific references, or ethnicity-specific references
Used reference data for specific medical conditions and syndromes
Body mass index prevalence data close to weight-for-age prevalence data
Used reference data for prematurely born infants
Correction for prematurity until postnatal age 2 y
Use of target height based on parental height for determination of genetic height potential
Used definition for faltering growth or failure to thrive: decrease in centile lines or decrease in SD scores

a group of children with mixed diagnoses various clinical factors within 48 h of admission and multivariate analysis indicated that a food intake less than 50%, pain, and a group of specific pathologic conditions were associated with a weight loss greater than 2%. Secker and Jeejeebhoy evaluated prospectively the preoperative nutritional status of children having major thoracic or abdominal surgery. Their instrument consisted of a nutrition-related physical examination and gathered information on the child's recent and current height and weight history, parental heights, dietary intake, frequency and duration of gastrointestinal symptoms, current functional capacity, and recent changes. These items together led to a classification of well-nourished, moderately malnourished, or severely malnourished. Within these three groups, significantly different mean values for various anthropometric measurements complications and length of hospital stay were found. However, the tools of Sermet-Gaudelus et al. and Secker and Jeejeebhoy are considered too complicated and time-consuming to use in daily clinical practice.

A simpler tool was developed by McCarthy et al. [32], the STAMP tool, which is a combination of measurements of weight and height, with two additional questions on disease risk and intake. By now only a description of this tool is available and no studies have been performed using this tool.

Gerasimidis et al. [33] developed the Paediatric Yorkhill Malnutrition Score, which is a four-stage evaluation based on four questions considering the BMI value, recent weight loss, decreased intake the previous week, and expected affected nutrition by the admission/condition for the next week. The validity of this tool was assessed by comparison with a full dietetic assessment as a golden standard for nutritional assessment (dietary history, anthropometric measurements, nutrition-associated physical examination, ability to maintain age-appropriate energy levels, and review of medical notes). Children were classified as having low, medium, or high malnutrition risk. Of the 247 children studied (1–16 y old), the nurse-rated Paediatric Yorkhill Malnutrition Score identified 59% of those rated at high risk by full dietetic assessment. Of those rated at high risk by the nursing Paediatric Yorkhill Malnutrition Score, 47% were confirmed as having high risk on full assessment.

Hulst et al. [34] developed a simple tool of assessing nutritional risk. This tool, STRONG_{kids}, was tested during a nationwide survey in the Netherlands. It consists of four key items, i.e., risk of disease, intake, weight loss, and Subjective Global Assessment. The four questions in this tool can be completed just after admission and are not time-consuming. With this tool, the risk can immediately be calculated. The survey in the Netherlands showed that in 98% of the 424 children included, the tool was successfully applied. Using this tool, a significant relation was found between having a "high-risk" score, a negative SD score in

WFH, and a prolonged hospital stay. It was concluded that use of the STRONG_{kids} tool helps to raise the clinician's awareness of the importance of nutritional status in children and enables the clinician to refer children at risk for early dietary intervention.

Conclusion

Because of the diversity of medical conditions and syndromes in hospitalized children, assessment of nutritional status and interpretation of anthropometric data need a tailored approach. Table 3 presents a summary of issues that have to be taken into account for the interpretation of prevalence data of malnutrition.

References

- [1] Joosten KF, Hulst JM. Prevalence of malnutrition in pediatric hospital patients. *Curr Opin Pediatr* 2008;20:590–6.
- [2] Dogan Y, Erkan T, Yalvac S, Altay S, Cokugras FC, Aydin A, et al. Nutritional status of patients hospitalized in pediatric clinic. *Turk J Gastroenterol* 2005;16:212–6.
- [3] Hendricks KM, Duggan C, Gallagher L, Carlin AC, Richardson DS, Collier SB, et al. Malnutrition in hospitalized pediatric patients. Current prevalence. *Arch Pediatr Adolesc Med* 1995;149:1118–22.
- [4] Marteletti O, Caldari D, Guimber D, Mention K, Michaud L, Gottrand F. [Malnutrition screening in hospitalized children: influence of the hospital unit on its management]. *Arch Pediatr* 2005;12:1226–31.
- [5] Moy R, Smallman S, Booth I. Malnutrition in a UK children's hospital. *J Hum Nutr Diet* 1990;3:93–100.
- [6] Pawellek I, Dokoupil K, Koletzko B. Prevalence of malnutrition in paediatric hospital patients. *Clin Nutr* 2008;27:72–6.
- [7] Joosten KF, Zwart H, Hop WC, Hulst JM. National malnutrition screening days in hospitalized children in the Netherlands. *Arch Dis Child* 2010;95:141–5.
- [8] Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ* 2007;335:194.
- [9] Olsen EM. Failure to thrive: still a problem of definition. *Clin Pediatr (Phila)* 2006;45:1–6.
- [10] Wilcox WD, Nieburg P, Miller DS. Failure to thrive. A continuing problem of definition. *Clin Pediatr (Phila)* 1989;28:391–4.
- [11] Olsen EM, Petersen J, Skovgaard AM, Weile B, Jorgensen T, Wright CM. Failure to thrive: the prevalence and concurrence of anthropometric criteria in a general infant population. *Arch Dis Child* 2007;92:109–14.
- [12] Spencer NJ. Failure to think about failure to thrive. *Arch Dis Child* 2007;92:95–6.
- [13] O'Brien LM, Heycock EG, Hanna M, Jones PW, Cox JL. Postnatal depression and faltering growth: a community study. *Pediatrics* 2004;113:1242–7.
- [14] Emond AM, Blair PS, Emmett PM, Drewett RF. Weight faltering in infancy and IQ levels at 8 years in the Avon Longitudinal Study of Parents and Children. *Pediatrics* 2007;120:e1051–8.
- [15] Eskedal LT, Hagemo PS, Seem E, Eskild A, Vcancarova M, Seiler S, et al. Impaired weight gain predicts risk of late death after surgery for congenital heart defects. *Arch Dis Child* 2008;93:495–501.
- [16] WHO Multicentre Growth Reference Study Group. WHO child growth standards based on length/height, weight and age. *Acta Paediatr* 2006;450:1–101.
- [17] Juliusson PB, Roelants M, Hoppenbrouwers K, Hauspie R, Bjercknes R. Growth of Belgian and Norwegian children compared to the WHO growth standards: prevalence below –2 and above +2 standard deviations and the effect of breastfeeding. *Arch Dis Child*; 2010. Epub ahead of print.
- [18] Roelants M, Hauspie R, Hoppenbrouwers K. Breastfeeding, growth and growth standards: performance of the WHO growth standards for monitoring growth of Belgian children. *Ann Hum Biol* 2010;37:2–9.
- [19] Hermanussen M, Cole J. The calculation of target height reconsidered. *Horm Res* 2003;59:180–3.
- [20] Larnkaer A, Attrup Schroder S, Schmidt IM, Horby Jorgensen M, Fleischer Michaelsen K. Secular change in adult stature has come to a halt in northern Europe and Italy. *Acta Paediatr* 2006;95:754–5.
- [21] Chemaitilly W, Boulad F, Heller G, Kernan NA, Small TN, O'Reilly RJ, et al. Final height in pediatric patients after hyperfractionated total body irradiation and stem cell transplantation. *Bone Marrow Transplant* 2007;40:29–35.
- [22] Usher R, McLean F. Intrauterine growth of live-born Caucasian infants at sea level: standards obtained from measurements in 7 dimensions of infants born between 25 and 44 weeks of gestation. *J Pediatr* 1969;74:901–10.
- [23] Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. *Obstet Gynecol* 1996;87:163–8.

- [24] Dollberg S, Haklai Z, Mimouni FB, Gorfein I, Gordon ES. Birth weight standards in the live-born population in Israel. *Isr Med Assoc J* 2005;7:311–4.
- [25] Niklasson A, Ericson A, Fryer JG, Karlberg J, Lawrence C, Karlberg P. An update of the Swedish reference standards for weight, length and head circumference at birth for given gestational age (1977–1981). *Acta Paediatr Scand* 1991;80:756–62.
- [26] Skjaerven R, Gjessing HK, Bakkeiteig LS. Birthweight by gestational age in Norway. *Acta Obstet Gynecol Scand* 2000;79:440–9.
- [27] Kramer MS, Platt RW, Wen SW, Joseph KS, Allen A, Abrahamowicz M, et al. A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics* 2001;108:E35.
- [28] Davidson S, Sokolover N, Erlich A, Litwin A, Linder N, Sirota L. New and improved Israeli reference of birth weight, birth length, and head circumference by gestational age: a hospital-based study. *Isr Med Assoc J* 2008;10:130–4.
- [29] Zemel BS, Riley EM, Stallings VA. Evaluation of methodology for nutritional assessment in children: anthropometry, body composition, and energy expenditure. *Annu Rev Nutr* 1997;17:211–35.
- [30] Secker DJ, Jeejeebhoy KN. Subjective Global Nutritional Assessment for children. *Am J Clin Nutr* 2007;85:1083–9.
- [31] Sermet-Gaudelus I, Poisson-Salomon AS, Colomb V, Brusset MC, Mosser F, Berrier F, et al. Simple pediatric nutritional risk score to identify children at risk of malnutrition. *Am J Clin Nutr* 2000;72:64–70.
- [32] McCarthy H, McNulty H, Dixon M, Eaton-Evans MJ. Screening for nutrition risk in children: the validation of a new tool. *J Hum Nutr Diet* 2008;21:395–6.
- [33] Gerasimidis K, Keane O, Macleod I, Flynn DM, Wright CM. A four-stage evaluation of the Paediatric Yorkhill Malnutrition Score in a tertiary paediatric hospital and a district general hospital. *Br J Nutr* 2010;19:1–6.
- [34] Hulst JM, Zwart H, Hop WC, Joosten KF. Dutch national survey to test the STRONG(kids) nutritional risk screening tool in hospitalized children. *Clin Nutr* 2010;29:106–11.
- [35] Griffiths RD, Edwards RH. A new chart for weight control in Duchenne muscular dystrophy. *Arch Dis Child* 1988;63:1256–8.
- [36] Willig TN, Carlier L, Legrand M, Riviere H, Navarro J. Nutritional assessment in Duchenne muscular dystrophy. *Dev Med Child Neurol* 1993;35:1074–82.
- [37] Myrelid A, Gustafsson J, Ollars B, Anneren G. Growth charts for Down's syndrome from birth to 18 years of age. *Arch Dis Child* 2002;87:97–103.
- [38] Cremers MJ, van der Tweel I, Boersma B, Wit JM, Zonderland M. Growth curves of Dutch children with Down's syndrome. *J Intellect Disabil Res* 1996;40:412–20.
- [39] Hauffa BP, Schlippe G, Roos M, Gillessen-Kaesbach G, Gasser T. Spontaneous growth in German children and adolescents with genetically confirmed Prader-Willi syndrome. *Acta Paediatr* 2000;89:1302–11.
- [40] Wollmann HA, Kirchner T, Enders H, Preece MA, Ranke MB. Growth and symptoms in Silver-Russell syndrome: review on the basis of 386 patients. *Eur J Pediatr* 1995;154:958–68.
- [41] Rongen-Westerlaken C, Corel L, van den Broeck J, Massa G, Karlberg J, Albertsson-Wikland K, et al. Reference values for height, height velocity and weight in Turner's syndrome. Swedish Study Group for GH treatment. *Acta Paediatr* 1997;86:937–42.
- [42] Karlberg J, Glander L, Albertsson-Wikland K. Distinctions between short- and long-term human growth studies. *Acta Paediatr* 1993;82:631–4.
- [43] Ranke MB, Heidemann P, Knupfer C, Enders H, Schmaltz AA, Bierich JR. Noonan syndrome: growth and clinical manifestations in 144 cases. *Eur J Pediatr* 1988;148:220–7.
- [44] Horton WA, Rotter JJ, Rimoin DL, Scott CI, Hall JG. Standard growth curves for achondroplasia. *J Pediatr* 1978;93:435–8.
- [45] Rekers-Mombarg LT, Wit JM, Massa GG, Ranke MB, Buckler JM, Butenandt O, et al. Spontaneous growth in idiopathic short stature. European Study Group. *Arch Dis Child* 1996;75:175–80.