

# Long-term impact of infantile short bowel syndrome on nutritional status and growth

Joanne F. Olieman<sup>1,2</sup>, Corine Penning<sup>1,3</sup>, Marjolein Spoel<sup>1</sup>, Hanneke IJsselstijn<sup>1</sup>, Thelma L. van den Hoonaard<sup>1</sup>, Johanna C. Escher<sup>4</sup>, Nikolaas M. A. Bax<sup>1</sup> and Dick Tibboel<sup>1\*</sup>

<sup>1</sup>Department of Pediatric Surgery, Erasmus Medical Center, Sophia Children's Hospital, SK 3286, PO Box 2060, 3000 CB Rotterdam, The Netherlands

 $^2$ Department of Dietetics, Erasmus Medical Center, Dr Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands

 $^3$ Department of Intellectual Disability Medicine/General Practice, Erasmus Medical Center, Dr Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands

<sup>4</sup>Department of Pediatric Gastroenterology, Erasmus Medical Center, Sophia Children's Hospital, SK 3286, PO Box 2060, 3000 CB Rotterdam, The Netherlands

(Submitted 6 January 2011 - Final revision received 15 July 2011 - Accepted 16 July 2011 - First published online 15 September 2011)

#### **Abstract**

Short-term bowel adaptation has been documented, but data on long-term effects are scarce. The aim of the present study was to evaluate the long-term consequences of infantile short bowel syndrome (SBS). A cross-sectional assessment (2005-7) of growth, nutritional status, defecation pattern and health status in individuals with a history of infantile SBS, born between 1975 and 2002, were performed. Data were compared with reference values of healthy controls and presented as means and standard deviations or median and ranges. A total of forty subjects (sixteen male and twenty-four female; mean age 14·8 (sp 6·8) years) had received parenteral nutrition during a median of 110 (range 43-2345) d, following small bowel resection. The mean standard deviation scores (SDS) for weight for height and target height (TH) of the children were normal; mean SDS for height for age was -0.9 (sp. 1.3). The median BMI adults was 19.9 (range 17-26) kg/m<sup>2</sup>; mean SDS for height for age was -1.0 (range -2.5 to 1.5). Height in general was significantly shorter than TH, and 53% of children and 78% of adults were below TH range. Most subjects had normal body fat percentage (%BF). SDS for total body bone mineral density were generally normal. The SDS for bone mineral content (BMC) of the children were -1.0 (sp. 1.1). Mean energy intake was 91% of the estimated average requirements. The frequencies of defecation and bowel complaints of the subjects were significantly higher than in healthy controls. In conclusion, infantile SBS results in shorter stature than was expected from their calculated TH. BMC was lower than reference values, but the subjects had normal weight for height and %BF.

Key words: Short bowel syndrome: Growth: Body composition: Nutrition



Short bowel syndrome (SBS) is a condition characterised by an increased intestinal transit time, leading to diarrhoea and malabsorption of nutrients and, potentially, growth retardation. The most frequent underlying diagnoses in neonates are necrotising enterocolitis, volvulus, intestinal atresia and gastroschisis<sup>(1,2)</sup>.

Bowel adaptation starts shortly after bowel resection and may last 1-2 years, during which nutrient absorption is relatively inadequate(3).

Improved care has led to increased survival rates of infants with SBS, but little information is available on the long-term impact of infantile SBS on growth and physical development. Short stature has been reported<sup>(4)</sup>, as well as delayed onset of puberty<sup>(5)</sup>. The latter, however, is generally associated with chronic malabsorption, and with growth delay and the pubertal growth spurt<sup>(6)</sup>. Chronic illness with malabsorption also has a negative effect on bone maturation, as documented in children with inflammatory bowel disease<sup>(7,8)</sup>.

The aim of the present cross-sectional study was to evaluate the long-term effects of infantile SBS on growth, nutritional status, defecation pattern and food intake.

Abbreviations: %BF, percentage body fat; BMC, bone mineral content; BMD, bone mineral density; BMDls, bone mineral density of the lumbar spine; BMDtb, bone mineral density of the total body; DEXA, dual-energy X-ray absorptiometry; LBM, lean body mass; PN, parenteral nutrition; SBS, short bowel syndrome; SDS, standard deviation score; TH, target height.

\*Corresponding author: D. Tibboel, fax +31 10 7036288, email d.tibboel@erasmusmc.nl



#### Methods

#### **Population**

Children with SBS were identified from the medical databases and charts of the hospital, as reported elsewhere (9). All surviving children or adults with infantile SBS (aged ≤1 year) treated in their first year of life in the Erasmus Medical Center, Sophia Children's Hospital between January 1975 and January 2003 were asked to participate. Patients with psychomotor retardation due to additional anomalies were excluded, because most measurements cannot reliably be performed. Patients who were still parenteral nutrition (PN) dependent at the time of measurement are excluded in order to reduce the heterogeneity of the present study group.

#### Definition of short bowel syndrome

The definition of SBS used in the present study was the one formulated by the Dutch Committee on Intestinal Failure:

- (1) greater than 70% resection of the small bowel<sup>(2,10)</sup>;
- (2) PN needed for longer than 42d after bowel resection<sup>(11–14)</sup>;
- (3) residual small bowel length, distal to the ligament of Treitz, (50 cm for a premature neonate (gestational age 27-36 weeks) and <75 cm for a term neonate<sup>(15,16)</sup>.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Erasmus Medical Center Ethical Review Board. Subjects and parents received written information on the study design, and written informed consent from the parents for subjects younger than 18 years and separately from subjects older than 12 years of age were obtained.

## Study design

In the present single-centre, cross-sectional study, all diagnostic measurements concerning subjects' growth, nutritional and dietary status were performed during a single outpatient visit in the period from November 2005 to August 2007. Measurements were taken by a dietitian (nutritional assessment and dietary intake), physician (general health examination) or nuclear laboratory technician (dual-energy X-ray absorptiometry (DEXA) scan).

## Clinical characteristics during the first year of life

Demographic data such as date of birth, sex, underlying diagnosis leading to SBS, gestational age and birth weight were collected retrospectively. Surgical reports were searched for the presence of the ileocaecal valve and the remaining small bowel length, measured distally to the ligament of Treitz. Percentage of remaining small bowel length was calculated from predicted bowel length for gestational age<sup>(15)</sup>. Number of operations in the first year of SBS was counted. The number of central venous catheter (re)placements, as a consequence of occlusion, thrombosis or sepsis, was also recorded. Length of stay and PN duration were derived from data for the entire follow-up period (>1 year) until October 2007.

Dates of start and end of minimal enteral feeding (9,17) and enteral nutrition were collected. Type of nutrition was classified as breastfeeding, polymeric or semi-elemental. The numbers of interruptions of enteral nutrition, necessitated by inadequate passage through the gastrointestinal tract, were counted.

Detailed information on growth and nutrition in the first year of life of these patients has been published elsewhere<sup>(9)</sup>.

#### Measurements

Subjects were asked not to eat or drink within 2h before measurement and to refrain from strenuous exercise on this day.

# Height and weight

Body weight was recorded to the nearest 0.1 kg using an electrical scale (Seca Alpha 770, Hamburg, Germany). Height was measured to the nearest 0.1 cm using a stadiometer (Stanley Mabo, London, UK). The height of the patients was measured in the outpatient clinic, if possible, or by their general practitioners. The target height (TH) of the subjects was calculated as ((father's height  $\pm$  13)/2) + 4·5 cm. TH range was defined as TH standard deviation score (SDS)  $(1.3 \pm SDS)$ . In adults, the BMI was calculated using weight  $(kg)/ height (m)^2$ .

## Skinfolds

Skinfold thickness in the biceps, triceps, subscapular and supra-iliac region was measured three times (18) to the nearest 0.1 mm using a Harpenden calliper (John Bull, British Indicators Ltd, Burgess Hill, West Sussex, UK) on the non-dominant side of the body, and the mean value was calculated. Body fat percentage (%BF) was calculated from the sum of four skinfold measurements in  $children^{(19)}$  and in  $adults^{(20)}$ using group-specific equations. Skinfold measurement is a cost-effective and non-invasive nutritional assessment method with reasonable accuracy<sup>(21)</sup>.

# Dual-energy X-ray absorptiometry

Total body DEXA was performed using a Lunar-Prodigy (GE Healthcare, Waukesha, WI, USA) scanner in order to determine bone mineral density (BMD, g/cm<sup>2</sup>) of the lumbar spine (ls) and total body (tb). Total body DEXA also measured bone mineral content (BMC, g) and lean body mass (LBM, g), with %BF given for total tissue mass. Many studies found DEXA to be a good reference method for nutritional assessment, due to its high correspondence with outcome of isotope dilution techniques (21-23).

The values of BMDls, BMDtb, BMC, LBM and %BF (measured with DEXA) of the children were compared to Dutch reference data, depending on age and sex<sup>(24)</sup>, and expressed in SDS. Adult values of BMDls and BMDtb were





compared to reference values delivered by the manufacturer and expressed in SDS.

Furthermore, measurements of skinfolds were compared to measurements of DEXA in children to examine the interrelationship.

#### Dietary intake

Before the outpatient visit, subjects were asked to record quantities of foods and beverages consumed during a weekend day and on two week days. During the outpatient visit, a trained dietitian cross-checked the records and asked the subjects to specify entries, if necessary, and add missing items or amounts. The dietary intakes were compared to the recommended daily allowances for children and adults, and when appropriate, to the estimated average requirements, depending on age and sex<sup>(25,26)</sup>.

#### Defecation pattern

Defecation pattern was determined by a self-developed questionnaire based on the symptom checklist of Poley et al. (27). It comprised stool frequency, self-estimated quantity of stool of the subjects, the Bristol stool form scale (28) and applicable symptoms from the Rome II criteria (29), such as bowel cramps, flatulence and bloating. As control data were not available, the questionnaire was additionally filled out by age- and sex-matched healthy controls, recruited through schools and the university in Rotterdam.

#### Current health status and Tanner stages

General medical, neurological and pubertal development (30) was examined by a physician. For patients in puberty, delay in puberty was determined by comparing Tanner stage and age with reference data of Dutch children (31). Blood pressure (expressed in mmHg) and heart rate (beats per min) were measured once by Dinamap Procare (GE Healthcare). Values were compared to the reference data<sup>(32)</sup>.

#### Statistical analysis

Group size was not based on a formal power analysis. The incidence of SBS in the Netherlands is unknown, but from clinical experience, it is judged to be relatively low. We therefore aimed at including all patients with SBS admitted to our hospital between 1975 and 2003. Descriptive statistics (frequencies, mean, median, standard deviations and range) were calculated. The patients were stratified in two age groups, namely, 5-18 years (children) and over 18-year-old patients (adults), and differentiated by sex.

Kruskal-Wallis tests and  $\chi^2$  tests served to identify differences between the study group and all eligible patients. Cystic fibrosis itself might be associated with impaired growth; therefore, data for the whole study group were compared by appropriate tests to data for a subgroup excluding patients with cystic fibrosis.

Values of weight, height, TH and skinfolds were compared to national standards (33-36) and expressed in SDS, depending on sex, age and race (Growth Analyser version 3; Dutch Growth Foundation, Rotterdam, the Netherlands).

Bland-Altman plots were used to assess the agreement between outcomes of skinfold measurements and DEXA<sup>(37)</sup>. One-sample t tests were performed to compare the mean SDS values with normal values. Means were compared using paired t tests. When data were not normally distributed, median values were compared using the Wilcoxon rank test or  $\chi^2$  test. The level of significance was set at 0.05.

#### **Results**

Of the seventy-two eligible subjects, thirty-two did not participate in the present study because either they did not give informed consent  $(n \ 15)$  or they could not be located  $(n \ 17)$ ; Fig. 1). Kruskal–Wallis tests and  $\chi^2$  tests identified no differences in underlying diagnoses, sex, age, percentages of premature birth or length of remaining bowel between the groups 'included', 'no informed consent' and 'not located' (data not shown).

Thus, forty subjects (sixteen males and twenty-four females), with a mean age of 14·8 (SD 6·8) years, participated in the present study. Underlying diagnoses were normally distributed and are shown in Table 1. Other diagnoses were long-segment Hirschsprung disease  $(n \ 1)$  and ischaemic small bowel of unknown origin (n 1). The mean residual bowel length was 70.8 cm, which corresponds with 26.5% of the small bowel remaining. PN had been given for a median period of 110 (range 43-2345) d and all subjects were weaned off PN by the time of measurement. The clinical characteristics representing the first year of life are presented in Table 1.

#### Growth

Weight and height are presented in Table 2. The mean age of the children (twelve males and nineteen females) was 11.8 (SD 4·2) years. Their mean weight for age and height for age were significantly lower than reference values (P=0.005 and P=0.001, respectively). Mean weight for height and mean TH were normal. Mean height for age was significantly (P=0.000)lower than TH. In total, 53% were below their TH range.

Owing to the small number of adults, the results are presented as median (range). Median age of the adults (four males and five females) was 24.9 (range 21.8-29.7) years. Median BMI and weight for height were normal. Median height for age was significantly lower than TH (Z = -2.68,P=0.008). In total, 78% were below their TH range.

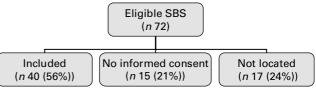


Fig. 1. Flow chart study. SBS, short bowel syndrome.



1492 J. F. Olieman et al.

Table 1. Clinical characteristics of the first year of life (n 40)

(Numbers, percentages, mean values and standard deviations, medians, minimum and maximum values)

	n	%
Underlying first diagnosis of SBS		
Small bowel atresia	14	35
NEC	8	20
Volvulus and/or malrotation  Meconium peritonitis with CF	6 4	15 10
Gastroschisis*	3	7.5
Meconium peritonitis no CF	3	7·5
Others	2	5
Sex		
Male	16	40
Female	24	60
Number of prematures (GA ≤ 36 weeks)	23	58
GA (weeks)		- 0
Mean		5.3
SD Birth weight (a)	2	1.2
Birth weight (g)  Mean	2	270
SD		898
Birth weight (SDS)		,,,,
Mean	_	0.7
SD		1.5
LOS first admission (d)		
Median	1	37
Min-max	13-	-552
Number of hospital admittances in the first year of SBS		
Median		1
Min-max	Ü	-8
Age initial date SBS (date surgery leading to SBS) (d)  Median		3
Min-max	0-	-270
Length residual small bowel (cm) (n 28)	Ü	2,0
Mean	7	0-8
SD	2	3.5
SB remaining (%)		
Mean	2	6-5
SD		8
Presence of ICV		
Yes	33	83
No Number of operations (ex-central lines)	7	17
Median		3
Min-max	1	-7
Duration of PN (d)		•
Median	1	10
Min-max	43-	-2345
Number of central catheters used in 1 year		
Median		2
Min-max	0	-8
Start of MEF (d)		
Median		11
Min-max	3-	-74
Start of EN (d)  Median		26
Min-max		-110
Type of EN	0	110
Breast milk	4	10
Semi-elemental	28	72
Polymeric	7	18
Number of interruptions of EN		
Median		3
Min-max	0	-8

SBS, short bowel syndrome; NEC, necrotising enterocolitis; CF, cystic fibrosis; GA, gestational age; SDS, standard deviation score, LOS, length of stay; min, minimum; max, maximum; SB, small bowel; ICV, ileocaecal valve; PN, parenteral nutrition; MEF, minimal enteral feeding; EN, enteral nutrition.

#### **Body composition**

For children, the mean of the sum of four skinfolds was -0.9 (sp 1.0) SDS. Their mean BMC (-1.0 (sp 1.1) SDS) and mean LBM (-1.2 (sp 1.0) SDS) were significantly lower than reference values (P=0.000). Only the mean BMDIs (-0.47 (sp 1.2) SDS) was significantly lower than reference values (P=0.036).

In adults, BMDls and BMDtb did not differ significantly from reference values. SDS of BMC, LBM and %BF of adults could not be calculated for lack of appropriate reference values. Table 3 reports the bone composition of all patients, as measured by DEXA.

%BF calculated from DEXA and skinfold measurements are shown in Table 4. In three of the four adult males and five of the eleven male children had %BF below 10%, indicating malnutrition. All the females, but one, had normal (15–25 %BF).

The limits of agreement of %BF for the two methods in children are shown in Fig. 2. Skinfolds underestimated %BF with  $4\cdot1$  (95% CI  $1\cdot97$ ,  $6\cdot23$ ). Paired-sample t tests showed significant differences in means between %BF measured by skinfolds and %BF measured by DEXA (P=0·001).

## Dietary intake

Dietary intakes are shown in Table 5. Mean energy intake was 8823 (sp 2433) kJ (2107 (sp 581) kcal), which is 91 (sp 28)% of the estimated average requirements. In all, seventeen subjects (45%) had a energy intake more than 10% below estimated average requirements and six (17%) had a energy intake more than 10% above estimated average requirements. A total of four subjects (10%) were using enteral supplements (i.e. tube feeding). A total of nineteen (50%) had a dietary calcium intake more than 10% below recommended daily allowances.

#### Defecation pattern

The results of the questionnaire are presented in Table 6. Stool frequency for all subjects (median 2 (range 0.3-7) per d) was significantly higher than that in the healthy population (median 1 (range 0.3-5); P=0.000). A total of 35% reported abnormal stool form (type 1, 6 and 7 of Bristol stool form scale) v. 2% of the healthy population. Subjects self-estimated stool quantity was significantly higher (P=0.014) than that for the normal population, and they also reported significantly more complaints such as bowel cramps, bloating and flatulence (P<0.05).

## Current health status and Tanner stages

Most children had Tanner stages corresponding with their age. One girl was in early puberty (age 9 years, Tanner stage 2) and two girls had delayed puberty (15 and 17 years old and both in Tanner stage 3). Most subjects had normal heart rates and blood pressure (data not shown). Standard neurological examination by the physician revealed no neurological problems.



<sup>\*</sup> A patient lost more bowels at the age of 11 years as result of strangulation and underwent a Bianchi procedure at the age of 12 years and was measured at 16 years.



Table 2. Weight and height

(Mean values and standard deviations, medians, minimum and maximum values)

	Children (n 31)		Adults (n 9)	
	Mean	SD	Median	Min-max
Age (years)	11.8	4.2	24.9	21.8-29.7
Sex				
Female				
n	19			5
%	61			56
M				
n	12			4
%	39			
Weight for age (SDS)	− 0.7*	1.2	_	_
BMI	_	_	19.9	17 to 26
Weight for height (SDS)	0.1	1.0	-0.5	-2⋅1 to 1⋅5
Height for age (SDS)†	-0.9‡	1.3	<b>−1.0</b>	-2.5 to 2.0
TH (SDS)†	0.3	1.1	0.5	-0.8 to 2.3

Min, minimum; max, maximum; SDS, standard deviations score; TH, target height.

Measurement results for the whole group did not differ from those for the subpopulation excluding subjects with cystic fibrosis (data not shown). Subjects with cystic fibrosis were in the same range as those with other underlying diagnoses.

#### Discussion

Increasing concern about morbidity following infantile bowel resection has resulted in intestinal rehabilitation programmes in different institutions (38–43). However, multidisciplinary data on long-term outcomes in patients with infantile SBS are still scarce. The present study was conducted to add to the knowledge on nutritional status and growth parameters after infantile SBS. More than half of the children and three-quarters of adults had not reached their TH range. Weight in general was normal for height and most subjects had normal %BF. LBM and BMC evaluated by DEXA were significantly below reference values in children.

Recently, we reported that the SDS for weight for age in the first year of life of these subjects were subnormal and had even declined significantly in the second- and third-quarterly terms<sup>(9)</sup>. From the results of the present study, it can be concluded that weight for age seems to revert to normal in the long run. SDS for height for age had also improved over the years, but were still significantly below reference values and TH. In contrast, Goulet et al. (44) reported that the final height in fifty-seven children after 16 years follow-up generally was not different from their TH. As a possible explanation, Goulet et al. used Tanner's formula (1970) for the calculation of TH, which typically yields height values 4.5 cm shorter than those resulting from the calculation method that we used (Dutch growth study, 1997). Some other studies also found short stature (defined as < 50th percentile of height for age) in 60-90% of children with SBS after weaning from PN<sup>(45-47)</sup>. In contrast, several studies reported normal

Table 3. Bone composition measured by dual-energy X-ray absorptiometry

(Mean values and standard deviations, medians, minimum and maximum values)

	Children	Children (n 31)		Adults (n 9)	
	Mean	SD	Median	Min-max	
BMDtb (SDS) BMDls (SDS) %BF (SDS) LBM (SDS) BMC (SDS)	- 0.04 - 0.47* 0.36 - 1.21* - 1.0*	1·4 1·2 0·73 1·2 1·1	- 0·1 0·0	- 1.0 to 1.8 - 1.5 to 2.5	

Min, minimum; max, maximum; BMDtb, bone mineral density of total body; SDS, standard deviation scores; BMDls, bone mineral density of lumbar spine; %BF, percentage body fat; LBM, lean body mass; BMC, bone mineral content.

growth for most subjects<sup>(48–50)</sup>. The conflicting data seem to arise from differences in reference populations, definitions of short stature and moments of measurement.

The children in the present study showed reduced bone mineralisation only in the lumbar spine, which seems to suggest that only the trabecular bone, which is predominant in the lumbar spine, was affected<sup>(51)</sup>. In contrast to children, the BMDls for the adults was normal. Leonberg et al. (50) also found subnormal BMC values, i.e. in four out of nine children with SBS. These values were established by single-photon absorptiometry in the forearm using other reference values<sup>(52)</sup> than that used by us. Dellert et al.<sup>(53)</sup> did not find subnormal BMC after adjusting the values for weight and height, but did when adjusting for age. It is not easy to compare results, as these researchers used another type of DEXA (Hologic) and studied two age-, sex- and race-matched controls per subject. Moreover, these controls were significantly heavier and taller than the children with SBS<sup>(53)</sup> - a finding most probably explained by either malabsorption or prolonged inadequate dietary intake in the subjects (54). The differences in BMC when control subjects and patients with SBS

**Table 4.** Body composition (Mean values and standard deviations, medians, minimum and maximum values)

Body fat (%)	Sum of four skinfolds	DEXA
Children		
Male ( <i>n</i> 11)		
Mean	11.8	12.6
SD	2.5	6.1
Min-max	8.9-17.3	7.0-30.0
Female ( <i>n</i> 17)		
Mean	15⋅5	23.0
SD	2.6	7.7
Min-max	11.9-21.6	12-4-40-2
Adults		
Male (n 4)		
Median	4.2	7.7
Min-max	3.3-16.1	5.7-36.1
Female (n 5)		
Median	20.7	26.0
Min-max	16-6-23-0	24.5-34.5

DEXA, dual-energy X-ray absorptiometry; min, minumum; max, maximum.

<sup>\*</sup> Mean values were significantly lower than reference value (P=0.005).

<sup>†</sup> Mean values were significant different between height and TH in children (P=0.000) and in adults (P=0.008).

<sup>‡</sup> Mean values were significantly lower than reference value (P=0.001).

 $<sup>^{\</sup>star}$  Mean values were significantly lower than the reference values (P<0.05).

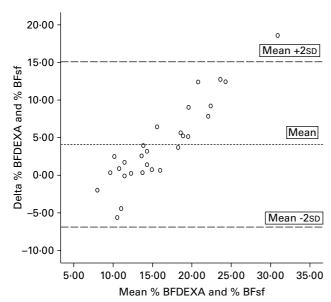


Fig. 2. Bland-Altman plot percentage of body fat (%BF) skinfolds (sf) and dual-energy X-ray absorptiometry (DEXA).

were matched for age are an indication for some sort of nutrient deficiency<sup>(54)</sup>. This is also seen in patients with inflammatory bowel disease<sup>(7)</sup>. Vitamin D deficiency impairs Ca absorption and may explain low mineral content. Miyasaka et al. (55) showed that some adolescents with SBS, who had poor growth, were vitamin D deficient and needed extra nutritional supplementation during puberty. Differences in BMC may reflect differences in either bone size or bone density<sup>(56)</sup>. Ahmed et al. (56) suggested that children with inflammatory bowel disease often have small bones for age, as result of growth retardation. When they interpreted DEXA data adjusted for bone size, bone mass was generally found to be adequate (56). It seems, therefore, that low BMC values in the present study can partially be explained by the short stature of the subjects with its inherent small bones.

Haderslev et al. (57) found that PN-independent adults (mean age 50.6 years), who had undergone bowel resection a mean 11 years ago, had lower weight and mainly lower %BF compared to reference values. This holds true for only nine (22%) of the subjects in the present study. Most of the children and female adults had normal weight for height and %BF. Two other studies also found normal weight for height and %BF(49,50)

The present study showed wide limits of agreement between outcomes of DEXA and skinfold thickness measurements, which indicates that these methods are not interchangeable. This finding is consistent with prior studies<sup>(58-61)</sup>. Skinfold thickness measurements are based on two assumptions. First, the thickness of subcutaneous adipose tissue reflects a constant proportion of total body fat; second, the sites selected for measurement represent the average thickness of subcutaneous adipose tissue<sup>(62)</sup>. Moreover, body composition measured by skinfold thickness is based on a two-compartment model: fat-free mass and fat mass. DEXA is based on a three-compartment model: BMC, LBM and fat mass. The predictive equations used to calculate the body composition in the present study were developed and validated in healthy individuals, which might explain the wide levels of agreement. We have to realise that the degree to which subcutaneous adipose tissue reflects total body fat mass may change with age, sex, race and disease (60,63,64) It would seem, therefore, that DEXA is to be preferred.

The mean reported dietary intake of the subjects was lower than their average estimated intake. Dietary intake is difficult to measure and it is easily under or overrated<sup>(65)</sup>. Protein intake was high compared to the recommended daily allowances, but similar when compared to a Dutch food

Table 5. Dietary intake (Mean values and standard deviations, medians, minimum and maximum values)

	Total group (n 38)			Children (n 29)		Adults (n 9)	
Dietary assessment	Mean	SD	Min-max	Mean	SD	Median	Min-max
Energy							
kJ	8823	2433	4430-15301	8848	1080	7559	5066-14932
kcal	2107	581	1058-3654	2113	258	1805	1210-3566
% EAR	91	28	42-160	95	26	65	49-146
Protein (g/d)							
g/d	73	20	44-126	72	19	68	44-123
% RDA	193	76	71-339	212	76	128	71-202
Fat							
en%	34	5	23-45	35	5	31	26-41
% RDA	85	13	59-112	87	13	79	66-103
Carbohydrate							
en%	51	7	34-65	51	6	50	34-60
%RDA	124	18	85-162	124	16	124	85-151
Ca (%AI)							
Median	91		98		80		
Min-max	34-221		53-221		34-142		
Vitamin D (%AI)							
Median	96		92		116		
Min-max	28-1340		28-1340		40-160		

Min, minimum; max, maximum; EAR, estimated average requirements; RDA, recommended daily allowance; AI, adequate intake.





Table 6. Defecation pattern (Numbers, percentages, mean values and standard deviations)

	Subjects (n 40)	Healthy controls (n 322)	Р
Age (years)			
Mean	14.8	12.9	
SD	6.8	5⋅1	
Sex			
Male	16	135	
Female	24	187	
Bristol stool form scale (%)			0.00
Type 1	0	1	
Type 2	8	4	
Type 3	37	63	
Type 4	15	28	
Type 5	5	3	
Type 6	32	1	
Type 7	3	0	
Aspect of stool (%)			0.00
Normal	63	95	
Contains mucus	15	0	
Contains blood	0	1	
Contains undigested material	15	2	
Different	7	2	
Quantity stool per movement (%)			0.01
<50 g	10	17	
100-200 g	73	79	
> 500 g	17	4	
Bowel cramps (%)			0.00
Never	3	17	
Sometimes	45	63	
Often	35	16	
Always	18	4	
Flatulence (%)			0.04
Never	7	21	
Sometimes	53	52	
Often	33	20	
Always	7	8	
Bloating (%)	•	-	0.00
Never	28	58	2 30
Sometimes	59	35	
Often	10	6	
Always	3	1	

consumption survey<sup>(66)</sup>. Moreover, 50% of the patients had a dietary Ca intake 10% below the recommended daily allowances. These results might be skewed, because oral supplementation of Ca supplements (i.e. calcium carbonate) was not taken into account. Assuming that the dietary records truly reflected dietary intake over the previous years, the lower dietary intake might explain the shorter stature and lower values of BMC of the subjects.

Several studies<sup>(28,67–70)</sup> showed that the Bristol stool scale form is correlated with whole-gut transit time and can be used to monitor change in intestinal function.

The subjects in the present study reported a higher frequency of stools than that reported by healthy aged-matched controls and 35 % had abnormal stools, which might indicate malabsorption and can partly explain lower BMC values. Moreover, they appeared to have complaints such as bowel cramps, bloating and flatulence significantly more often. The questionnaire was designed to ask what their normal bowel habits were, and we realise that this does not describe the bowel habits and changes over time. It does reveal, however, that SBS is associated with intestinal bowel dysfunction in the longer term.

The present study has limitations in its cross-sectional design, which causes age differences, in the absence of a functional test to determine the actual absorptive function of the bowel, in the absence of a hand X-ray to determine bone age and in the absence of measurement of vitamin D status. Moreover, subjects were identified from medical records and eligible patients could have been missed. Finally, the group is heterogeneous with respect to underlying diagnosis and remaining bowel lengths, which nevertheless is inherent to SBS.

On the other hand, the present study covered a long period, from 5 to 30 years after infantile SBS. This enabled us to describe the natural history of SBS into adulthood. As another strength, we used a unique combination of parameters to determine a broad spectrum of long-term effects in a relatively large group of patients.

## Conclusion

Subjects in the present study had shorter stature, low BMC, but normal weight for height and %BF. This might be explained by the low energy intake and intestinal bowel dysfunction





reported. These results show that continuing follow-up into adulthood is important even after subjects have reached nutritional autonomy. This way, low energy intake and intestinal bowel dysfunction might be identified early, enabling prevention of short stature by targeted nutritional management. Measurement of body composition is an essential aspect of providing optimal nutritional management and should preferably be done by DEXA.

## Acknowledgements

The authors thank Jopie Sluimer (Erasmus Medical Center, Rotterdam, the Netherlands) for performing DEXA scans and Ko Hagoort (Erasmus Medical Center, Rotterdam, the Netherlands) for editing. J. F. O., J. C. E., H. I., T. L. v. d. H. and D. T. designed the study; J. F. O. and M. S. performed the experiments; J. F. O. and C. P. carried out data analysis; J. F. O. and C. P. prepared the manuscript; C. P., M. S., H. I., T. L. v. d. H., J. C. E., N. M. A. B. and D. T. carried out critical reviews of the manuscript. All the authors approved the final version of the manuscript. The authors state that the present study did not receive any funding. The authors declare no conflict of interest.

#### References

- 1. Sigalet DL (2001) Short bowel syndrome in infants and children: an overview. Semin Pediatr Surg 10, 49-55.
- Koffeman GI, van Gemert WG, George EK, et al. (2003) Classification, epidemiology and aetiology. Best Pract Res Clin Gastroenterol 17, 879-893.
- Goulet O, Ruemmele F, Lacaille F, et al. (2004) Irreversible intestinal failure. J Pediatr Gastroenterol Nutr 38, 250-269.
- Vanderhoof JA & Young RJ (2003) Enteral and parenteral nutrition in the care of patients with short-bowel syndrome. Best Pract Res Clin Gastroenterol 17, 997-1015.
- Delemarre-van de Waal HA, van Coeverden SC & Engelbregt MT (2002) Factors affecting onset of puberty. Horm Res 57, Suppl. 2, 15-18.
- Pozo J & Argente J (2002) Delayed puberty in chronic illness. Best Pract Res Clin Endocrinol Metab 16, 73-90.
- Boot AM, Bouquet J, Krenning EP, et al. (1998) Bone mineral density and nutritional status in children with chronic inflammatory bowel disease. Gut 42, 188-194.
- Cowan FJ, Warner JT, Dunstan FD, et al. (1997) Inflammatory bowel disease and predisposition to osteopenia. Arch Dis Child 76, 325-329.
- Olieman JF, Tibboel D & Penning C (2008) Growth and nutritional aspects of infantile short bowel syndrome for the past 2 decades. J Pediatr Surg 43, 2061-2069
- Teitelbaum DH, Drongowski R & Spivak D (1996) Rapid development of hyperbilirubinemia in infants with the short bowel syndrome as a correlate to mortality: possible indication for early small bowel transplantation. Transplant Proc 28, 2699-2700.
- Wales PW, de Silva N, Kim JH, et al. (2005) Neonatal short 11. bowel syndrome: a cohort study. J Pediatr Surg 40, 755–762.
- Quiros-Tejeira RE, Ament ME, Reyen L, et al. (2004) Longterm parenteral nutritional support and intestinal adaptation in children with short bowel syndrome: a 25-year experience. J Pediatr 145, 157–163.
- Sondheimer JM, Asturias E & Cadnapaphornchai M (1998) Infection and cholestasis in neonates with intestinal

- resection and long-term parenteral nutrition. J Pediatr Gastroenterol Nutr 27, 131-137.
- 14. Kaufman SS, Loseke CA, Lupo JV, et al. (1997) Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. J Pediatr 131, 356-361.
- 15. Touloukian RJ & Smith GJ (1983) Normal intestinal length in preterm infants. J Pediatr Surg 18, 720-723.
- Heij HA, Meijers-IJsselstijn H, Olieman JF, et al. (2005) Dutch National Protocol Short Bowel Syndrome. Dutch National Committee of Intestinal Failure.
- Tyson JE & Kennedy KA (1997) Minimal enteral feeding for promoting feeding tolerance and preventing morbidity in parenterally fed infants. The Cochrane Database of Systematic Reviews 1997 issue 2, CD000504.
- Gerver WJ & de Bruin R (1996) Body composition in children based on anthropometric data. A presentation of normal values. Eur J Pediatr 155, 870–876.
- Deurenberg P, Pieters JJ & Hautvast JG (1990) The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. Br J Nutr 63, 293-303.
- Durnin JV & Womersley J (1974) Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 vears. Br I Nutr 32, 77-97.
- Lohman TG (1986) Applicability of body composition techniques and constants for children and youths. Exerc Sport Sci Rev 14, 325-357.
- 22. Pintauro SJ, Nagy TR, Duthie CM, et al. (1996) Crosscalibration of fat and lean measurements by dual-energy X-ray absorptiometry to pig carcass analysis in the pediatric body weight range. Am J Clin Nutr 63, 293-298.
- Uszko-Lencer NH, Bothmer F, van Pol PE, et al. (2006) Measuring body composition in chronic heart failure: a comparison of methods. Eur J Heart Fail 8, 208-214.
- van der Sluis IM, de Ridder MA, Boot AM, et al. (2002) Reference data for bone density and body composition measured with dual energy X-ray absorptiometry in white children and young adults. Arch Dis Child 87, 341-347, discussion 341-347.
- Health Council (2000) Voedingsnormen: calcium, vitamine D, thiamine, riboflavine, niacine, pantotheenzuur en biotine (Nutrition Requirements: Calcium, Vitamin D, Thiamin, Riboflavin, Niacin, Vitamin B<sub>5</sub> and Biotin, publication no. 2000/2012). The Hague: Gezondheidsraad (Health Council).
- Health Council (2001) Voedingsnormen: energie, eiwitten, vetten en verteerbare koolhydraten (Nutrition Requirements: Energy, Protein, Fat and Digestible Carbobydrates, publication no. 2001/2019R. The Hague: Gezondheidsraad (Health Council).
- 27. Poley M, Stolk E, Tibboel D, et al. (2004) Short term and long term health related quality of life after congenital anorectal malformations and congenital diaphragmatic hernia. Arch Dis Child 89, 836-841.
- Heaton KW, Radvan J, Cripps H, et al. (1992) Defecation frequency and timing, and stool form in the general population: a prospective study. Gut 33, 818-824.
- Caplan A, Walker L & Rasquin A (2005) Development and preliminary validation of the questionnaire on pediatric gastrointestinal symptoms to assess functional gastrointestinal disorders in children and adolescents. J Pediatr Gastroenterol Nutr 41, 296-304.
- Tanner J (1962) Growth at Adolescence, 2nd ed. Oxford: Blackwell.
- Roede M & Van Wieringen J (1985) Growth diagrams 1980. T Soc Gez Suppl. 63, 1-34.



https://doi.org/10.1017/S0007114511004582 Published online by Cambridge University Press

- National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (2004) The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 114, 555-576.
- Fredriks AM, van Buuren S, Burgmeijer RJ, et al. (2000) Continuing positive secular growth change in The Netherlands 1955-1997. Pediatr Res 47, 316-323.
- 34. Fredriks AM, van Buuren S, Jeurissen SE, et al. (2003) Height, weight, body mass index and pubertal development reference values for children of Turkish origin in the Netherlands. Eur J Pediatr 162, 788-793.
- Fredriks AM, van Buuren S, Jeurissen SE, et al. (2004) Height, weight, body mass index and pubertal development references for children of Moroccan origin in The Netherlands. Acta Paediatr 93, 817–824.
- Gerver WJM & de Bruin R (2001) Paediatric Morphometrics, a Reference Manual, 2nd ed. Maastricht: University Press
- Bland JM & Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1, 307-310.
- Torres C, Sudan D, Vanderhoof J, et al. (2007) Role of an intestinal rehabilitation program in the treatment of advanced intestinal failure. J Pediatr Gastroenterol Nutr 45, 204–212.
- Fishbein TM, Schiano T, LeLeiko N, et al. (2002) An integrated approach to intestinal failure: results of a new program with total parenteral nutrition, bowel rehabilitation, and transplantation. J Gastrointest Surg 6, 554–562.
- Nucci A, Burns RC, Armah T, et al. (2008) Interdisciplinary management of pediatric intestinal failure: a 10-year review of rehabilitation and transplantation. J Gastrointest Surg 12, 429–435, discussion 435–426.
- 41. Modi BP, Langer M, Ching YA, et al. (2008) Improved survival in a multidisciplinary short bowel syndrome program. J Pediatr Surg 43, 20-24.
- 42. Diamond IR, de Silva N, Pencharz PB, et al. (2007) Neonatal short bowel syndrome outcomes after the establishment of the first Canadian multidisciplinary intestinal rehabilitation program: preliminary experience. J Pediatr Surg 42, 806–811.
- Sudan D, Dibaise J, Torres C, et al. (2005) A multidisciplinary approach to the treatment of intestinal failure. J Gastrointest Surg 9, 165-177.
- Goulet O, Baglin-Gobet S, Talbotec C, et al. (2005) Outcome and long-term growth after extensive small bowel resection in the neonatal period: a survey of 87 children. Eur J Pediatr Surg 15, 95-101.
- Barksdale EM Jr., Koehler AN, Yaworski JA, et al. (1999) Insulinlike growth factor 1 and insulinlike growth factor 3: indices of intestinal failure in children. J Pediatr Surg 34, 655-661, discussion 661-652.
- Galea MH, Holliday H, Carachi R, et al. (1992) Short-bowel syndrome: a collective review. J Pediatr Surg 27, 592-596.
- Gonzalez HF, Perez NB, Malpeli A, et al. (2005) Nutrition and immunological status in long-term follow up of children with short bowel syndrome. JPEN J Parenter Enteral Nutr 29, 186–191.
- Weber TR, Tracy T Jr & Connors RH (1991) Short-bowel syndrome in children. Quality of life in an era of improved survival. Arch Surg 126, 841-846.
- Wu J, Tang Q, Feng Y, et al. (2007) Nutrition assessment in children with short bowel syndrome weaned off parenteral nutrition: a long-term follow-up study. J Pediatr Surg 42, 1372 - 1376.
- Leonberg BL, Chuang E, Eicher P, et al. (1998) Long-term growth and development in children after home parental nutrition. J Pediatr 132, 461-466.

- Martin TJ, Ng KW & Nicholson GC (1988) Cell biology of bone. Baillieres Clin Endocrinol Metab 2, 1-29.
- 52. Mazess RB & Cameron JR (1972) Growth of bone in school children: comparison of radiographic morphometry and photon absorptiometry. Growth 36, 77-92.
- Dellert SF, Farrell MK, Specker BL, et al. (1998) Bone mineral content in children with short bowel syndrome after discontinuation of parental nutrition. J Pediatr 132, 516-519.
- 54. Ament ME (1998) Bone mineral content in patients with short bowel syndrome: the impact of parenteral nutrition. I Pediatr 132, 386-388.
- 55. Miyasaka EA, Brown PI, Kadoura S, et al. (2010) The adolescent child with short bowel syndrome: new onset of failure to thrive and need for increased nutritional supplementation. J Pediatr Surg 45, 1280-1286.
- 56. Ahmed SF, Horrocks IA, Patterson T, et al. (2004) Bone mineral assessment by dual energy X-ray absorptiometry in children with inflammatory bowel disease: evaluation by age or bone area. J Pediatr Gastroenterol Nutr 38, 276-280.
- Haderslev KV, Jeppesen PB, Sorensen HA, et al. (2003) Body composition measured by dual-energy X-ray absorptiometry in patients who have undergone small-intestinal resection. Am J Clin Nutr 78, 78-83.
- 58. Haderslev KV & Staun M (2000) Comparison of dual-energy X-ray absorptiometry to four other methods to determine body composition in underweight patients with chronic gastrointestinal disease. *Metabolism* **49**, 360–366.
- 59. Elberg J, McDuffie JR, Sebring NG, et al. (2004) Comparison of methods to assess change in children's body composition. Am J Clin Nutr 80, 64-69.
- 60. King S, Wilson J, Kotsimbos T, et al. (2005) Body composition assessment in adults with cystic fibrosis: comparison of dual-energy X-ray absorptiometry with skinfolds and bioelectrical impedance analysis. Nutrition 21, 1087-1094.
- 61. de Meer K, Gulmans VA, Westerterp KR, et al. (1999) Skinfold measurements in children with cystic fibrosis: monitoring fatfree mass and exercise effects. Eur J Pediatr 158, 800-806.
- 62. Lukaski HC (1987) Methods for the assessment of human body composition: traditional and new. Am J Clin Nutr 46, 537-556
- Brodie D, Moscrip V & Hutcheon R (1998) Body composition measurement: a review of hydrodensitometry, anthropometry, and impedance methods. Nutrition 14, 296-310.
- 64. Deurenberg P (2003) Validation of body composition methods and assumptions. Br J Nutr 90, 485-486.
- Cade J, Thompson R, Burley V, et al. (2002) Development, validation and utilisation of food-frequency questionnaires a review. Public Health Nutr 5, 567–587.
- 66. Centre of Nutrition (1998) Zo eet Nederland; resultaten voedselconsumptiepeiling 1998 (Eating Pattern The Netherlands; Results Food Consumption Survey 1998). The Hague: Voedingscentrum (Centre of Nutrition).
- 67. Davies GJ, Crowder M, Reid B, et al. (1986) Bowel function measurements of individuals with different eating patterns. Gut 27, 164-169.
- 68. Lewis SJ & Heaton KW (1997) Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 32,
- 69. Heaton KW, Ghosh S & Braddon FE (1991) How bad are the symptoms and bowel dysfunction of patients with the irritable bowel syndrome? A prospective, controlled study with emphasis on stool form. Gut 32, 73-79.
- 70. Heaton KW & O'Donnell LJ (1994) An office guide to wholegut transit time. Patients' recollection of their stool form. J Clin Gastroenterol 19, 28-30.

