



## UvA-DARE (Digital Academic Repository)

### Nutrition and growth in European children with end-stage renal disease

Bonthuis, M.

**Publication date**

2014

**Document Version**

Final published version

[Link to publication](#)

**Citation for published version (APA):**

Bonthuis, M. (2014). *Nutrition and growth in European children with end-stage renal disease*. [Thesis, fully internal, Universiteit van Amsterdam].

**General rights**

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

**Disclaimer/Complaints regulations**

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

# 6

## UNDERWEIGHT, OVERWEIGHT AND OBESITY IN PAEDIATRIC DIALYSIS AND RENAL TRANSPLANT PATIENTS

**Marjolein Bonthuis**, Karlijn J van Stralen, Enrico Verrina, Jaap W Groothoff, Ángel Alonso Melgar, Alberto Edefonti, Michael Fisbach, Patricia Mendes, Elena A Molchanova, Dušan Paripović, Amira Peco-Antic, Nikoleta Printza, Lesley Rees, Jacek Rubik, Constantinos J Stefanidis, Manish D Sinha, Ilona Zagożdżon, Kitty J Jager, Franz Schaefer

**Neprol Dial Transplant 2013 Nov; 28 Suppl 4: iv195-iv204**

**Background:** The prevalence of childhood overweight is rising worldwide, but in children on renal replacement therapy (RRT) a poor nutritional status is still the primary concern. We aimed to study the prevalence of and factors associated with underweight and overweight/obesity in the European paediatric RRT population. Moreover, we assessed the evolution of body mass index (BMI) after the start of RRT.

**Methods:** We included 4474 patients younger than 16 years from 25 countries of whom BMI data, obtained between 1995 and 2010, were available within the ESPN/ERA-EDTA Registry. Prevalence estimates for under- and overweight/obesity were calculated using age and sex-specific criteria of the World Health Organisation (0-1 year olds) and the International Obesity Task Force cut-offs (2-15 year olds).

**Results:** The prevalence of underweight was 3.5%, whereas 20.8% of the patients were overweight and 12.5% obese. Risk factors for being underweight were receiving dialysis treatment and infant age. Among transplanted recipients a very short stature (OR: 1.64, 95% CI: 1.40-1.92) and glucocorticoid treatment (OR: 1.23, 95% CI: 1.03-1.47) were associated with a higher risk of being overweight/obese. BMI increased post-transplant, and a lower BMI and a higher age at start of RRT were associated with greater BMI changes during RRT treatment.

**Conclusions:** Overweight and obesity, rather than underweight, are highly prevalent in European children on RRT. Short stature among graft recipients had a strong association with overweight, while underweight appears to be only a problem in infants. Our findings suggest that nutritional management in children receiving RRT should focus as much at the prevention and treatment of overweight as on preventing malnutrition.

## INTRODUCTION

Nutritional therapy is a key aspect of the management of paediatric end-stage renal disease (ESRD) [1] since nutrition has a major impact on linear growth and development [2]. Traditionally, nutritional therapy predominantly focused on the prevention of protein-energy malnutrition [3]. To date, much less attention has been paid to the potential impact of the global epidemic of childhood obesity [4], on the weight distribution in children with ESRD [5–8].

Both a low and a high Body Mass Index (BMI) are associated with an increased mortality risk in children with ESRD [9] and obesity might adversely affect short-term graft function after renal transplantation [10]. Previous clinical studies focused on either protein-energy malnutrition among paediatric dialysis patients, which were found in 5% to 65% of the patients depending on the definition [8,11–13], or on overweight and obesity following renal transplantation [5,10,14,15]. The prevalence of an abnormal nutritional status in ESRD patients in Europe remains poorly documented.

Furthermore, in healthy children large regional differences in the prevalence of overweight and obesity have been reported across Europe [16–19]. Such differences may also exist for the paediatric ESRD population. Our study sought to describe the prevalence of, and factors associated with, an abnormal nutritional status defined by a low BMI (underweight) or a high BMI (overweight/obese) in European children with ESRD. In addition we studied the evolution of BMI after start of renal replacement therapy (RRT), including the effect of changes in treatment modality.

## METHODS

### Subjects

Data on paediatric patients were collected within the framework of the European Society for Paediatric Nephrology/European Renal Association and European Dialysis and Transplant Association (ESPN/ERA-EDTA) Registry and included amongst others, date of birth, sex, treatment modality at start of renal replacement therapy (RRT), and any subsequent changes in treatment modality. Patients from the following countries were included: Belarus, Belgium, Croatia, Czech Republic, Estonia, Finland, France, Greece, Hungary, Iceland, Italy, Lithuania, FYR Macedonia, the Netherlands, Norway, Poland, Portugal, Russia, Serbia, Slovakia, Slovenia, Spain, Switzerland, Turkey, and the United Kingdom. For the present study, we included patients younger than 16 years for whom data on height and weight were available for the period of January 1995 to December 2010.

### **Height and Body Mass Index assessment**

The BMI was calculated as weight/height<sup>2</sup> and expressed to chronological age for 0-1 year old children and to height-age (the age of a child with a given height growing at the 50<sup>th</sup> height percentile) for 2-15 year old children, by using either recent national or European growth charts for height [20]. For 0-1 year old children BMI was categorised according to age- and sex specific criteria of the World Health Organisation (WHO): underweight (BMI SDS  $\leq -2$  SDS), normal weight ( $-2 < \text{BMI SDS} \leq +2$ ), overweight ( $+2 < \text{BMI SDS} \leq +3$ ), and obesity (BMI SDS  $> +3$ ) [21–23]. For 2-15 year olds we used cut-off values from the International Obesity Task Force (IOTF) [24,25] to categorise their BMI. These age and sex-specific cut-off values are based on centile curves passing through adult health related cut-off points for underweight (BMI of 17 kg/m<sup>2</sup>), overweight (BMI of 25 kg/m<sup>2</sup>), and obesity (BMI of 30 kg/m<sup>2</sup>) at the age of 18 years. To study changes in BMI within 6-18 months after commencing RRT we expressed BMI as the percent difference from the median BMI (BMI%) [26] according to WHO growth charts [21–23,27]. In this way a BMI% of zero corresponds to the median BMI for age and sex from a healthy reference population.

### **Statistical analyses**

There were large differences in the number of BMI measurements per patient. Since measurements within the same patient are correlated, we used multinomial logistic generalised estimating equations (GEE) analyses to estimate prevalence estimates of underweight, overweight and obesity as well as to analyse predictors of being underweight and overweight/obese. In this study, we modelled the probability of either being underweight or overweight/obese compared to being normal weight. When comparing countries in the risk for being overweight or obese we selected only those countries which provided data for at least 80 patients. To study factors associated with changes in BMI% from the start of RRT we used linear mixed models. All statistical analyses were carried out using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).  $P < 0.05$  was considered statistically significant.

## RESULTS

### Patient characteristics

Patient characteristics are shown in Table 1. For 4474 patients at least one BMI measurement was available. The median number of measurements per patient was 3 with a range of 1-27 measurements, resulting in a total number of 16,432 measurements. At the time of BMI determination, most patients (46.4%) were adolescents (12-15 years), 48.6% of the patients were living with functioning graft, while 34.2% received peritoneal dialysis (PD) and 17.2% haemodialysis (HD) treatment. The most common cause of renal failure was congenital anomalies of the kidney and the urinary tract (CAKUT) (41.3%), and 59.5% of the patients were male.

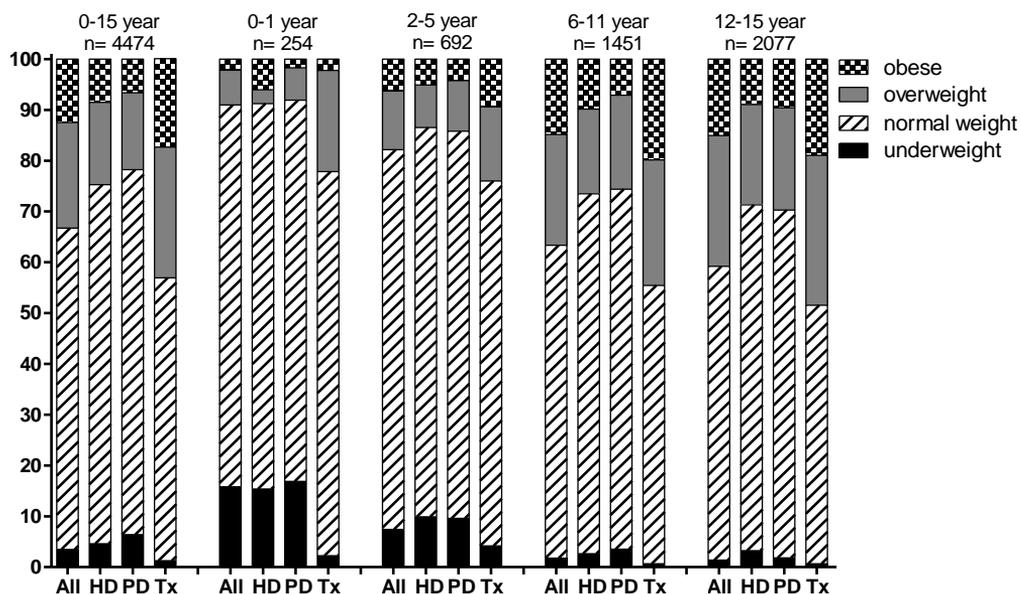
**Table 1.** Characteristics of patients included in the study

		Patients N=4474
Age at start of RRT (%)	0-1 years	954 (21.3)
	2-5 years	965 (21.6)
	6-11 years	1574 (35.2)
	12-15 years	981 (21.9)
Age at BMI measurement (%)	0-1 years	254 (5.7)
	2-5 years	692 (15.5)
	6-11 years	1451 (32.4)
	12-15 years	2077 (46.4)
Gender (male) (%)		2663 (59.5)
Treatment at start of RRT (%)	HD	1139 (25.5)
	PD	2467 (55.1)
	Tx	726 (16.2)
	Unknown/Missing	142 (3.2)
Current treatment (%)	HD	770 (17.2)
	PD	1529 (34.2)
	Tx	2175 (48.6)
	Unknown/Missing	142 (3.2)
Primary renal disease	Glomerulonephritis	637 (14.2)
	CAKUT	1848 (41.3)
	Cystic Kidneys	489 (10.9)
	Hereditary	368 (8.2)
	Nephropathy	
	Ischemic Renal Failure	101 (2.3)
	HUS	205 (4.6)
	Metabolic Disorders	154 (3.5)
	Vasculitis	80 (1.8)
	Miscellaneous	232 (5.2)
	Unknown/Missing	360 (8.0)

Abbreviations: RRT, renal replacement therapy; HD, haemodialysis; PD, peritoneal dialysis; Tx, renal transplant; CAKUT, congenital anomalies of the kidney and the urinary tract; HUS, haemolytic-uremic syndrome.

**Prevalence of underweight, overweight and obesity**

The prevalence of underweight in the total cohort was 3.5 %, while 20.8% of the patients were overweight and 12.5% obese. Of the 0-1 year old patients 15.8% were underweight, and 9.0% were overweight or obese. Among the 12-15 year old patients only 1.4% were underweight, while 40.8% were overweight or obese. Among dialysis patients the prevalence of underweight was higher (4.6% in HD patients, 6.4% in PD patients) than among transplanted patients (1.3%), while for overweight and obesity the reverse was true. Percentages of patients being underweight, normal weight, overweight, and obese stratified by age and treatment modality are depicted in Figure 1. In the countries (Finland, Italy, Spain, Switzerland, United Kingdom) with BMI data on the entire follow-up period (1995-2010), the prevalence of underweight, overweight, and obesity did not change over time.



**Figure 1.** Prevalence estimates for underweight, normal weight, overweight, and obesity stratified by treatment modality and age category

### Predictors of being underweight

We found that in both dialysis patients and allograft recipients a younger age was associated with a significantly increased risk of being underweight (Table 2). Among dialysis patients a short stature (height SDS < -1.88) was associated with a significantly lower risk of being underweight compared to children with a height SDS above -1.88 (OR: 0.66, 95% CI: 0.49-0.88) (Table 2).

Children who received dialysis treatment for less than one year or those who were transplanted pre-emptively were slightly more likely to be underweight than children who spent 1-3 years on dialysis or who received a renal transplant 1-3 years ago (OR<sub>dialysis</sub>: 1.20, 95% CI: 0.92-1.20; OR<sub>transplant</sub>: 1.56, 95% CI: 1.00-1.59). Gender and the type of dialysis were not associated with the risk of being underweight (Table 2).

**Table 2.** Odds ratios (OR) for being underweight compared to being normal weight stratified by treatment

	Dialysis patients OR (95% CI)	Transplanted patients OR (95% CI)
<b>Age group (years)<sup>1</sup></b>		
0-1	1.48 (1.10-1.98)	#
2-5	1.00	1.00
6-11	0.32 (0.23-0.44)	0.21 (0.12-0.38)
12-15	0.23 (0.16-0.32)	0.19 (0.10-0.34)
<b>Gender<sup>2</sup></b>		
Male	1.00	1.00
Female	1.10 (0.83-1.46)	0.91 (0.52-1.59)
<b>Height SDS<sup>3</sup></b>		
< -3 SDS	0.86 (0.62-1.19)	0.88 (0.43-1.80)
-3 < -1.88 SDS	0.66 (0.49-0.88)	0.79 (0.41-1.80)
≥ -1.88 SDS	1.00	1.00
<b>Time on current treatment (years)<sup>4</sup></b>		
< 1	1.20 (0.92-1.58)	1.56 (1.00-2.44)
1 < 3	1.00	1.00
≥ 3	0.79 (0.56-1.12)	0.78 (0.45-1.37)
<b>Type of dialysis<sup>5</sup></b>		
PD	1.00	
HD	1.02 (0.72-1.43)	
<b>Steroid use among Tx recipients<sup>6</sup></b>		
Non user		1.00
User		0.28 (0.16-0.49)

<sup>1</sup>Adjusted OR for country, gender; <sup>2</sup>Adjusted OR for country; <sup>3</sup>Adjusted OR for country, age, gender, time on RRT; <sup>4</sup>Adjusted for country, age, gender; <sup>5</sup>Adjusted OR for country, age, gender; <sup>6</sup>Adjusted for country, age at transplant and time since transplant.

# Number of patients in this category was too low to obtain an effect estimate.

**Predictors of being overweight or obese**

Predictors of being overweight/obese stratified by treatment are depicted in Table 3. Both among dialysis patients and patients with a functioning graft, children aged 6-11 years as well as adolescents had a significantly higher risk of being overweight compared to children aged 2-5 years.

Also a longer duration of either dialysis or transplantation was associated with a higher risk of being overweight. Among the transplanted patients, children with a very short stature (height SDS < -3) showed an increased risk of being overweight compared to children with a height SDS  $\geq$  -1.88 (OR: 1.64, 95% CI: 1.40-1.92), and this relation was already seen among children with moderate growth retardation, i.e. a height SDS between -3 and -1.88 SDS (OR: 1.16, 95% CI: 1.04-1.30) (Table 3). Adjustment for steroid therapy or growth hormone therapy did not change these results. Finally, among transplanted children, steroid use was associated with a 23% increased risk for being overweight (steroid use vs. no steroid use: OR 1.23, 95% CI: 1.03-1.47) (Table 3).

**Table 3.** Odds Ratios (OR) for being overweight/obese compared to being normal weight stratified by treatment

	Dialysis patients	Transplanted patients
	OR (95 % CI)	OR (95% CI)
<b>Age group (years)<sup>1</sup></b>		
0-1	0.58 (0.42-0.68)	#
2-5	1.00	1.00
6-11	1.99 (1.46-2.73)	1.98 (1.70-2.31)
12-15	2.37 (1.93-2.90)	2.30 (1.95-2.71)
<b>Gender<sup>2</sup></b>		
Male	1.00	1.00
Female	1.00 (0.84-1.20)	1.17 (1.01-1.37)
<b>Height SDS<sup>3</sup></b>		
< -3 SDS	1.12 (0.94-1.33)	1.64 (1.40-1.92)
-3 < -1.88 SDS	0.99 (0.86-1.14)	1.16 (1.04-1.30)
$\geq$ -1.88 SDS	1.00	1.00
<b>Time on current treatment (years)<sup>4</sup></b>		
< 1	0.73 (0.64-0.97)	0.98 (0.88-1.08)
1 < 3	1.00	1.00
$\geq$ 3	1.23 (1.06-1.42)	1.00 (0.90-1.11)
<b>Type of dialysis<sup>5</sup></b>		
PD	1.00	
HD	1.01 (0.85-1.21)	
<b>Steroid use among Tx recipients<sup>6</sup></b>		
Non user		1.00
User		1.23 (1.03-1.47)

<sup>1</sup>Adjusted OR for country, gender; <sup>2</sup>Adjusted OR for country; <sup>3</sup>Adjusted OR for country, age, gender, time on RRT; <sup>4</sup>Adjusted for country, age, gender; <sup>5</sup>Adjusted OR for country, age, gender; <sup>6</sup>Adjusted for country, age at transplant and time since transplant. # Number of patients in this category was too low to obtain an effect estimate.

**BMI change from start of renal replacement therapy**

For 1564 patients (35.0%) BMI data were available at the start of RRT and during follow-up. At the start of RRT 6.1% of the patients were underweight, while 11.8% were overweight and 6.3% obese.

Factors associated with the change in BMI% after the start of RRT are shown in Table 4. Both among dialysis patients and graft recipients the BMI% at the start of RRT was negatively associated with the change in BMI%. In other words, a lower BMI% at the start of RRT was associated with greater increases in BMI% during RRT treatment. Higher age at start of RRT, and a longer time on dialysis or a longer time with a functioning graft were positively associated with change in BMI%. Furthermore, among transplanted patients the change in BMI% was lower among those who were transplanted pre-emptively compared to those who started with PD treatment.

**Table 4.** Factors associated with change in BMI percent after the start of RRT stratified by treatment

	Dialysis patients		Transplanted patients	
	Mean change in BMI%	P-value	Mean change in BMI%	P-value
<b>BMI% at start RRT</b>				
Per % increase	-0.32	< 0.0001	-0.55	< 0.0001
<b>Age at start RRT (years)</b>				
0-1	-0.65	0.03	6.30	0.002
2-5	1.19	Reference	10.74	Reference
6-11	4.33	0.0001	16.17	< 0.0001
12-15	3.05	0.02	12.16	0.26
<b>Gender</b>				
Male	2.63	Reference	12.21	Reference
Female	1.88	0.16	13.94	0.05
<b>Treatment at start RRT</b>				
PD	2.39	Reference	13.53	Reference
HD	2.11	0.64	13.55	0.99
Tx	2.44	0.99	11.30	0.02
<b>Time on current treatment (years)</b>				
< 1	1.38	0.0001	11.67	0.0002
1 < 3	4.54	Reference	13.02	Reference
≥ 3	5.59	0.01	15.03	< 0.0001

Abbreviations: BMI, body mass index; RRT, renal replacement therapy; PD, peritoneal dialysis; HD, haemodialysis; Tx, renal transplant;

<sup>1</sup>Adjusted for country, gender, age at start of RRT, treatment at start of RRT, time on treatment;

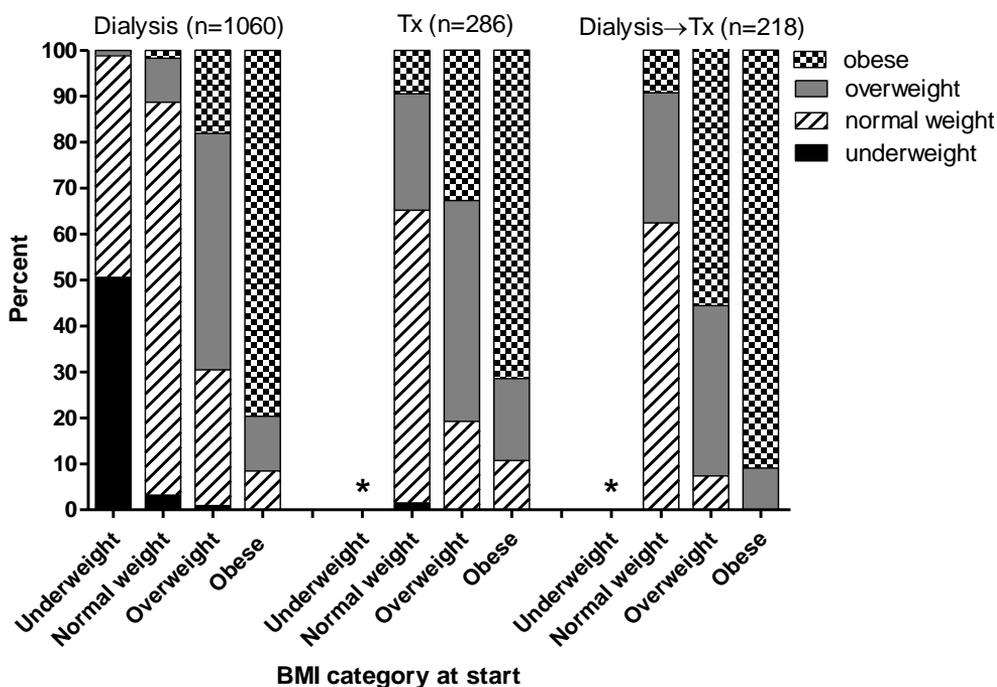
<sup>2</sup>Adjusted for country, BMI percent at start of RRT, gender, time on treatment;

<sup>3</sup>Adjusted for country, BMI percent at start of RRT, time on treatment;

<sup>4</sup>Adjusted for country, BMI percent at start of RRT, gender, age at start of RRT, time on treatment;

<sup>5</sup>Adjusted for country, BMI percent at start of RRT, gender, age at of start RRT, treatment at start of RRT.

Within 6 to 18 months after start of RRT, the mean BMI% of patients who remained on dialysis increased slightly by 1.9% (95% CI: 1.1-2.6%). In 79% of the children who remained on dialysis during the 18 months of follow-up, BMI did not change substantially from commencement of dialysis (Figure 2). However, in 50% of patients who were underweight at dialysis initiation, BMI increased into the normal range within the 6-18 month follow-up period. The BMI% significantly increased by 8.5% (95% CI: 6.7-10.3%;  $P<0.0001$ ) in patients with a pre-emptive transplant, and by 10.9% (95% CI: 9.2-12.6%;  $P<0.0001$ ) in children receiving a transplant after a dialysis period of less than 18 months. After the 6-18 month follow-up period more children were overweight and obese than at the start of RRT (Figure 2).



**Figure 2.** Distribution of changes in BMI category between start of renal replacement therapy and 6 to 18 months of follow-up

Patients were grouped by treatment modality: patients who were on dialysis treatment, patients who received a pre-emptive transplant, and patients who started on dialysis, but received a transplant during 6 to 18 months of follow-up.

\* Very few patients were underweight at the start of RRT in the group of pre-emptive transplantation, as well as in the group who switched from dialysis to transplantation.

Tx=Transplantation.

### Country differences in prevalence of overweight and obesity

We found a significant variation in the prevalence of overweight and obesity across countries both within the general paediatric [16,17,19] and paediatric RRT population (Table 5). Overweight and obesity were most prevalent in Spanish (34.5%), British (27.4%) and Finnish children (23.5%) on dialysis, resulting in a significantly higher risk for being overweight compared to Dutch dialysis patients, in whom the prevalence of overweight was only 17.2%. Transplanted patients from the United Kingdom (52.5%) and Spain (39.9%) also showed the highest prevalence of overweight and obesity (Table 5), whereas the overweight and obesity risk did not differ between transplant recipients from the Netherlands, Finland, Poland and Russia. These country differences in overweight/obesity were largely similar to differences in the general population (Table 5).

**Table 5.** Country as a predictor of being overweight/obese compared to being normal weight stratified by treatment

Country	Prevalence of overweight and obesity in general paediatric population <sup>1</sup>	Dialysis	Transplantation
		OR (95 % CI) <sup>2</sup>	OR (95% CI) <sup>3</sup>
Finland	15.6	2.28 (1.13-4.62)	0.93 (0.59-1.47)
Italy	13.3-36.0	0.94 (0.52-1.68)	#
The Netherlands	8.2-14.1	1.00	1.00
Poland	10.7-30.0	0.94 (0.50-1.79)	1.19 (0.74-1.91)
Russia	9.0-10.0	0.85 (0.44-1.64)	0.85 (0.53-1.34)
Spain	17.3-34.0	2.73 (1.55-4.79)	1.70 (1.09-2.66)
United Kingdom	11.9-21.9	2.21 (1.24-3.95)	2.61 (1.79-3.80)

Abbreviations: OR, odds ratio; CI, confidence interval.

<sup>1</sup>In Finland this prevalence was found in children aged 11-15 years [17]; In Italy the prevalence was 13.3-22.2% in children aged 0-4 years [16], 18.3% in children aged 11-15 years [17], and 36.0% in 9 year old children [19]; In the Netherlands the prevalence was 8.2% among 11-15 year old children [17], 11.0-12.0% in children aged 7-17 years [19], and 14.1% in 1-4 year old children [16]; In Poland the prevalence varied from 10.7% in children aged 11-15 years [17], and 12.0-18.0% in children aged 7-17 years [19], to 17.1-30.0% in 1-4 year old children [16]; In Russia the prevalence was 9.0-10.0% in children aged 7-17 years [17,19]; In Spain the prevalence varied from 17.3% among 11-15 year old children [17], and 21.0-34.0% among 7-17 year old children [19], to 29.7-33.2% among 0-4 year old children [16]; In the UK prevalence rates varied from 11.9% among children aged 11-15 years [17], and 19.8-21.9% among children aged 2-4 years [16], to 20.0-21.0% in children aged 7-17 years [19].

<sup>2</sup>Adjusted OR for age, gender, dialysis type;

<sup>3</sup>Adjusted OR for age and gender.

# Number of patients in this category was too low to obtain an effect estimate.

## DISCUSSION

In this analysis of the European paediatric ESRD population over the past 15 years, we found a considerably higher global prevalence of overweight (20.8%) and obesity (12.5%) than of underweight (3.5%). Only in the infant group, a substantial fraction of patients was affected by underweight (15.8%), in keeping with considerable clinical difficulties in helping children with ESRD to thrive [1]. Our prevalence figures for overweight and obesity were slightly lower than estimates in the North American paediatric ESRD population [5], in keeping with findings from the International Paediatric Peritoneal Dialysis Network registry [8]. The high prevalence of overweight and obesity mirrors the distribution observed in recent studies in the general childhood population in Europe [17–19].

We also for the first time describe remarkable country-to-country differences in prevalence estimates for being overweight or obese in children on RRT. Globally overweight and obesity were most prevalent in Spain and the United Kingdom, partly reflecting the situation observed among healthy children, where overweight and obesity is particularly common in the Mediterranean region [16,18,19] and among children from the British islands [16]. Potential differences in nutritional and growth management across countries might also contribute to this variation [8]. The Finnish children displayed a high prevalence of overweight and obesity while on dialysis, but not following transplantation. This finding may reflect a particularly efficient enforcement of nutritional targets in dialyzed infants, an age group which is likely overrepresented in the Finnish cohort due to the high incidence of congenital nephrotic syndrome in this country. After transplantation, which largely reflects the post-infantile period, Finnish children with ESRD appear to adopt the relatively low obesity prevalence typical for this country.

In general, transplantation apparently increased the risk of overweight and obesity in the paediatric ESRD population. A lower BMI% and older age at the start of RRT, as well as a longer duration of dialysis or a longer time with a functioning graft were associated with greater changes in BMI% from the start of RRT. The BMI% of children who were transplanted pre-emptively or who received a transplant within 1.5 years after starting RRT increased substantially, whereas smaller changes were seen in children who commenced, or remained on, dialysis. These findings are in keeping with results of the North American Paediatric Renal Trials and Cooperative Study [5]. Increased caloric intake [2] and glucocorticoid-based immunosuppression are well known factors associated with post-transplant weight gain [2,10,14,15]. Indeed we found a 23% higher risk of overweight in graft recipients receiving steroids as compared to patients on steroid-free protocols.

Surprisingly, we found an inverse association between height SDS and being overweight or obese in renal graft recipients. Short stature is related to obesity in healthy adults [28,29], whereas in healthy children height and BMI are positively correlated [28,30]. In our study this

association might be a consequence of glucocorticoid therapy, which is associated with both impaired growth as well as with weight gain [31]. Some patients may demonstrate a particular sensitivity to glucocorticoids by growth failure and excessive weight gain. Whilst statistical adjustment for the use of steroids did not remove this association, this might be explained by confounding by indication, i.e. glucocorticoid therapy is most likely to be discontinued or avoided in patients with a short stature and/or in those who are overweight. The very limited available glucocorticoid dosing information did not allow studying the role of steroid therapy in more detail. Furthermore, the association also tended to be present in dialyzed infants, in keeping with previous smaller studies reporting that children who were obese at the time of transplant had a shorter stature compared to non-obese children [6,10]. A likely explanation for this finding is that in poorly growing infants on enteral nutrition, the energy intake tends to be forced up to supraphysiological levels, leading to overweight and obesity with very limited effect on length gain. In addition, nutritional supplementation was found to improve weight but not height gain [32], suggesting that protein-energy wasting, a concept characterized by maladaptive metabolic responses to caloric intake and growth retardation [33], might have contributed to the observed association between short stature and overweight. Moreover, the association between short stature and being overweight might, at least partly, be attributable to the expression of BMI relative to height-age instead of chronological age. Data on BMI in children showed that during mid childhood expressing BMI relative to height-age better reflected adiposity in children with a short stature than BMI according to chronological age. This situation changes after completing of sexual maturation; at this stage, BMI for chronological age appears to give more valid estimates of adiposity than height-related BMI. This accounts for both children with chronic kidney disease [34] as for healthy children (Bonthuis et al, unpublished data). We therefore only included patients younger than 16 years of age, since data on pubertal development were not reported in the registry.

Predictors for being underweight were younger age, as well as receiving dialysis treatment compared to having a functioning graft. A higher risk of being underweight in young children compared to older children was also found in a study in PD patients [12] and might be due to a poor caloric intake and vomiting, which occur frequently in young children with chronic kidney disease [1].

A limitation of this study is a potential overestimation of BMI within the paediatric dialysis population due to the presence of fluid overload [35]. However, since fluid overload is a well-known phenomenon [3], and because we requested data on dry body weight, it is not very likely that a large overestimation of BMI occurred. On the other hand, to capture underestimation of the BMI as a result of growth retardation and delayed maturity, we expressed the BMI relative to height-age instead of normalizing to chronological age for children aged 2-16 years.

A major strength of our study is the inclusion of a large number of patients with repeated measurements from several different European countries as well as the inclusion of both dialysis and transplanted patients, whereas most others studied dialysis [8,12] and transplant patients [5–7,10,14,15,36] separately. Furthermore, we included data on infants, whereas most other studies restricted their analyses to children older than 2 years of age, as normative BMI values for infants became available only recently [21–23].

### **CONCLUSION**

In European children on RRT the prevalence of overweight and obesity outweighs the prevalence of underweight; only in infants underweight is still a common problem. Overweight and obesity were predominately observed in patients from Spain and the United Kingdom. The BMI increases substantially post-transplant, and short stature has a strong association with overweight and obesity. As both a low and a high BMI are associated with increased mortality risk, nutritional therapy for paediatric ESRD patients should not be limited to the prevention of protein-energy malnutrition but should encompass weight management in general.

## Reference List

1. Foster BJ, McCauley L, Mak RH (2011). Nutrition in infants and very young children with chronic kidney disease. *Pediatr Nephrol* 27(9): 1427-1439.
2. Rees L, Shaw V (2007). Nutrition in children with CRF and on dialysis. *Pediatr Nephrol* 22: 1689-1702.
3. National Kidney Foundation (2009). KDOQI clinical practice guideline for nutrition in children with CKD: 2008 Update. *American Journal of Kidney Diseases* 53: S1-S124.
4. Lobstein T, Baur L, Uauy R (2004). Obesity in children and young people: a crisis in public health. *Obes Rev* 5 Suppl 1: 4-104.
5. Foster BJ, Martz K, Gowrishankar M, et al. (2010). Weight and height changes and factors associated with greater weight and height gains after pediatric renal transplantation: a NAPRTCS study. *Transplantation* 89: 1103-1112.
6. Hanevold CD, Ho PL, Talley L, et al. (2005). Obesity and renal transplant outcome: a report of the North American Pediatric Renal Transplant Cooperative Study. *Pediatrics* 115: 352-356.
7. Omolaja A, Stolfi A, Mitsnefes M (2005). Pediatric obesity at renal transplantation: a single center experience. *Pediatr Transplant* 9: 770-772.
8. Rees L, Azocar M, Borzych D, et al. (2011). Growth in Very Young Children Undergoing Chronic Peritoneal Dialysis. *J Am Soc Nephrol* 22(12): 2303-2312.
9. Wong CS, Gipson DS, Gillen DL, et al. (2000). Anthropometric measures and risk of death in children with end-stage renal disease. *Am J Kidney Dis* 36: 811-819.
10. Mitsnefes MM, Khoury P, McEnery PT (2002). Body mass index and allograft function in pediatric renal transplantation. *Pediatr Nephrol* 17: 535-539.
11. Edefonti A, Picca M, Damiani B, et al. (2001). Prevalence of malnutrition assessed by bioimpedance analysis and anthropometry in children on peritoneal dialysis. *Perit Dial Int* 21: 172-179.
12. Edefonti A, Paglialonga F, Picca M, et al. (2006). A prospective multicentre study of the nutritional status in children on chronic peritoneal dialysis. *Nephrol Dial Transplant* 21: 1946-1951.
13. Sylvestre LC, Fonseca KP, Stinghen AE, et al. (2007). The malnutrition and inflammation axis in pediatric patients with chronic kidney disease. *Pediatr Nephrol* 22: 864-873.
14. Denburg MR, Pradhan M, Shults J, et al. (2010). Longitudinal relations between obesity and hypertension following pediatric renal transplantation. *Pediatr Nephrol* 25: 2129-2139.
15. Vester U, Schaefer A, Kranz B, et al. (2005). Development of growth and body mass index after pediatric renal transplantation. *Pediatr Transplant* 9: 445-449.
16. Cattaneo A, Monasta L, Stamatakis E, et al. (2010). Overweight and obesity in infants and pre-school children in the European Union: a review of existing data. *Obes Rev* 11: 389-398.
17. Haug E, Rasmussen M, Samdal O, et al. (2009). Overweight in school-aged children and its relationship with demographic and lifestyle factors: results from the WHO-Collaborative Health Behaviour in School-aged Children (HBSC) study. *Int J Public Health* 54 Suppl 2: 167-179.
18. Lissau I, Overpeck MD, Ruan WJ, et al. (2004). Body mass index and overweight in adolescents in 13 European countries, Israel, and the United States. *Arch Pediatr Adolesc Med* 158: 27-33.
19. Lobstein T, Frelut ML (2003). Prevalence of overweight among children in Europe. *Obes Rev* 4: 195-200.
20. Bonthuis M, van Stralen KJ, Verrina E, et al. (2012). Use of national and international growth charts for studying height in European children: development of up-to-date European height-for-age charts. *PLoS One* 7: e42506.
21. de Onis M, Garza C, Victoria CG, et al. (2004). The WHO Multicentre Growth Reference Study (MGRS): rationale, planning, and implementation. *Food Nutr Bull* 25: S89.
22. WHO Multicentre Growth Reference Study Group (2006). Assessment of differences in linear growth among populations in the WHO Multicentre Growth Reference Study. *Acta Paediatr Suppl* 450: 56-65.
23. World Health Organization (2006). WHO child growth standards: height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age; methods and development. Geneva: World Health Organization .

24. Cole TJ, Bellizzi MC, Flegal KM, et al. (2000). Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 320: 1240-1243.
25. Cole TJ, Flegal KM, Nicholls D, et al. (2007). Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ* 335: 194.
26. Cole TJ, Faith MS, Pietrobelli A, et al. (2005). What is the best measure of adiposity change in growing children: BMI, BMI %, BMI z-score or BMI centile? *Eur J Clin Nutr* 59: 419-425.
27. de Onis M, Onyango AW, Borghi E, et al. (2007). Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ* 85: 660-667.
28. Bosy-Westphal A, Plachta-Danielzik S, Dorhofer RP, et al. (2009). Short stature and obesity: positive association in adults but inverse association in children and adolescents. *Br J Nutr* 102: 453-461.
29. Sichieri R, Dos Santos BF, Moura EC (2010). Relationship between short stature and obesity in Brazil: a multilevel analysis. *Br J Nutr* 103: 1534-1538.
30. Freedman DS, Thornton JC, Mei Z, et al. (2004). Height and adiposity among children. *Obes Res* 12: 846-853.
31. Schacke H, Docke WD, Asadullah K (2002). Mechanisms involved in the side effects of glucocorticoids. *Pharmacol Ther* 96: 23-43.
32. Rashid R, Neill E, Smith W, et al. (2006). Body composition and nutritional intake in children with chronic kidney disease. *Pediatr Nephrol* 21: 1730-1738.
33. Mak RH, Cheung WW, Zhan JY, et al. (2012). Cachexia and protein-energy wasting in children with chronic kidney disease. *Pediatr Nephrol* 27: 173-181.
34. Gao T, Leonard MB, Zemel B, et al. (2012). Interpretation of Body Mass Index in Children with CKD. *Clin J Am Soc Nephrol* 7: 558-564.
35. Foster BJ, Leonard MB (2004). Measuring nutritional status in children with chronic kidney disease. *Am J Clin Nutr* 80: 801-814.
36. Ramirez-Cortes G, Fuentes-Velasco Y, Garcia-Roca P, et al. (2009). Prevalence of metabolic syndrome and obesity in renal transplanted Mexican children. *Pediatr Transplant* 13: 579-584.