



## Short Communication

## Overweight and obesity in PKU: The results from 8 centres in Europe and Turkey



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## ABSTRACT

**Introduction:** In PKU there is little data comparing the prevalence of overweight and obesity in different countries. The aim of this cross sectional study was to evaluate prevalence data from different PKU treatment centres in Europe and Turkey.

**Subjects and methods:** In children, body mass index (BMI) and z scores and in adults BMI were calculated in 947 patients (783 children aged <19 years; 164 adults aged ≥19 years) with PKU from centres in Europe and Turkey (Ankara, Birmingham, Brussels, Copenhagen, Groningen, Madrid, Munich and Porto).

**Results:** In adults with PKU, 83% of centres (n = 5/6) had less overweight than the general populations but 83% (n = 5/6) had a higher rate of female obesity. In childhood, all centres reported obesity rates within or similar to local population ranges in boys but in 57% (n = 4/7) of centres a higher rate of obesity in girls. The percentage of overweight and obesity increased with age.

**Discussion:** In PKU, it is clear from a number of treatment centres that women and girls with PKU appear particularly vulnerable to excess weight gain and it is important that female weight gain is closely monitored and individual strategies introduced to prevent excess weight gain. Overall, in PKU there is a need to understand better the food patterns and activity levels of patients.

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## 1. Introduction

In phenylketonuria (PKU) there is a suggestion that overweight and obesity is 'equivalent to' or more common than in the general population [1–3]. Low phenylalanine and high energy foods are encouraged in order to promote anabolism and to prevent protein insufficiency [4]. There is some speculation that this approach may promote obesity [1] but it requires further study. There are no evidence-based studies to indicate if overweight or obesity is related to the disorder itself, the low phenylalanine diet or patient lifestyle behaviour [4].

Considering that in PKU there are a lack of studies comparing prevalence of overweight and obesity between countries, the aim of this cross sectional study was to evaluate prevalence data from 8 different treatment centres in Europe and Turkey.

## 2. Subjects and methods

This was a retrospective, cross-sectional study comparing data on BMI (collected between 2005 and 2014), using a predefined set of questions for treated patients with PKU from one Turkish and 7 European centres. The centres providing data were from Belgium (Brussels), Denmark (Copenhagen), Germany (Munich), The Netherlands (Groningen), Portugal (Porto), Spain (Madrid), Turkey (Ankara) and the United Kingdom (UK) (Birmingham). One hundred and sixty four

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**Table 1**  
Number of patients and patient demographics from 8 centres across Europe and Turkey all diagnosed by newborn screening.

PKU centres	Total	Treatment	Children (<19 years)	Adults
Ankara	411	Low phe diet n = 411	n = 397 (219 boys, 178 girls) Age range: 1.7 months–17.9 years	14 (4 males, 10 females) Median age 22.9 years (range 19–26 years)
Data collected in 2008				
All patients born ≥ 1982				
Birmingham	85	BH4 + low phe diet n = 7 Low phe diet n = 78	n = 85 (46 boys, 39 girls) Age range: 1–17 years	n/a
Data collected in 2014				
All children born ≥ 1996				
Brussels	62	BH4 + low phe diet n = 12 Low phe diet n = 50	n = 40 (20 boys, 20 girls) Age range: 1 year, 3 months–17 years, 11 months	22 (7 males, 15 females) Median age 19 years, 7 months
Data collected in 2012				
Copenhagen	85	Low phe diet n = 85	n = 85 (28 boys, 57 girls) Age range: 6–15 years	n/a
Data collected in 2011				
All children born ≥ 1995				
Groningen	78	Low phe diet n = 78 <sup>a</sup>	n = 45 (23 boys, 22 girls)	33 (16 males, 17 females)
Data collected in 2011				
Madrid	83	BH4 only n = 11 BH4 + low phe diet n = 8 Low phe diet n = 64	n = 49 (21 males, 28 females) Age range: 1 year–<19 years	34 (14 males, 20 females)
Data collected in 2012				
All patients born ≥ 1979				
Munich	32	Low phe diet n = 32	n/a	32 (12 males, 20 females)
Data collected in 2005–2006				
All patients born ≥ 1967				
Porto	111	Low phe diet n = 111	n = 82 (51 boys, 31 girls) Age range: 1 year–<19 years	29 (10 males, 19 females)
Data collected in 2010–2011.				
All patients born ≥ 1982				
Totals	947	947	783	164

<sup>a</sup> 25 patients started BH4 for only a short time pre-assessment of overweight/obesity.

adults from 6 centres (Ankara, Brussels, Groningen, Madrid, Munich and Porto) and 783 children aged <19 years from 7 centres (Ankara, Birmingham, Brussels, Copenhagen, Groningen, Madrid and Porto) were included (Table 1). This project was considered by the NHS Health Research Authority decision tool ([www.hra-decisiontools.org.uk](http://www.hra-decisiontools.org.uk)) as non-research and as such did not require ethical approval.

Eligible patients with PKU were diagnosed by newborn screening, on dietary treatment, with or without BH<sub>4</sub> (tetrahydrobiopterin, sapropterin dihydrochloride) therapy and with or without large neutral amino-acid (LNAA) supplements. Exclusion criteria included patients not on dietary treatment, on pre-conception diet, pregnant or late treated patients.

The age, gender, height and body weight for all patients <19 years of age were collected in routine hospital clinics. The WHO Anthro and AnthroPlus programmes, software programmes provided by the WHO, calculated BMI percentile and z-score. Overweight classification was as follows: for patients <5 years: BMI z score ≥ 2 and <3 SD, for patients 5–18 years: BMI z score ≥ 1 and <2 SD. Obesity classification was for patients <5 years: BMI z score ≥ 3 and for patients 5–18 years: BMI z score ≥ 2 SD [5–8]. Percentages of overweight/obesity and obesity were calculated respectively from BMI z scores and compared with local general population ranges [9].

For adult PKU patients (≥ 19 years), BMI was calculated as weight (kg) / height (m<sup>2</sup>), and classified into BMI categories according to the WHO classification; overweight (≥ 25.0–29.9 kg/m<sup>2</sup>) and obesity

(≥ 30.0 kg/m<sup>2</sup>) [10]. Subsequently, percentages of overweight/obesity and obesity were calculated.

### 3. Results

#### 3.1. Adults (Table 2)

The majority of centres (83%; n = 5 of 6) had less overweight in patients with PKU, with obesity rates being the same or less in 4 of 6 (67%) centres than the respective general populations. In 5 of 6 (83%) centres there was a higher rate of obesity in females than males and in 4 centres this was higher than the respective general population. In contrast, only in Groningen and Munich were there more obese males with PKU than the general population.

#### 3.2. Children (Table 3)

In boys in Ankara, Birmingham, and Porto there were less overweight and obesity than the respective ranges in the general populations. Although boys in Brussels, Copenhagen, Groningen and older boys in Madrid had a higher rate of combined overweight/obesity, they had a lower rate of obesity only than the general population ranges. In girls there was a higher rate of combined overweight/obesity in Brussels, and Copenhagen and more obesity only in Ankara, Birmingham, Copenhagen and Groningen than the general population ranges. In Brussels, Madrid and Porto girls, there was less obesity.

**Table 2**  
Overweight and obesity percentages in adults with PKU compared with national general population (OECD i library, updated 2013) and gender differences for 6 centres.

PKU centres	PKU population % overweight/obese BMI ≥ 25.0 kg/m <sup>2</sup>	General population % overweight/obese BMI ≥ 25.0 kg/m <sup>2</sup>	PKU population % obesity BMI ≥ 30 kg/m <sup>2</sup>	General population % obesity BMI ≥ 30 kg/m <sup>2</sup>	Gender differences			
					Overweight		Obesity	
					Male %	Female %	Male %	Female %
Ankara	28.4	33.0	14.3	16.9	25.0	20.0	0	20.0
Brussels	27.3	33.1	4.5	13.8	14.3	33.3	0	6.7
Groningen	15.2	36.8	24.2	11.4	19.0	24.0	19.0	18.0
Madrid	42.0	37.6	16.0	16.0	42.0	40.0	7.0	25.0
Munich	34.4	36.7	18.7	14.7	33.3	35.0	16.7	20
Porto	24.1	36.2	10.3	15.4	30.0	21.1	10.0	10.5

**Table 3**  
Overweight and obesity percentages in children with PKU compared with national general population (Ng et al. [9]) for 7 centres.

PKU centres	Age of children with PKU	% overweight (includes overweight and obesity) in PKU	% obesity in PKU	Boys (PKU)		Girls (PKU)		Data from global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: Ng et al. [9]			
				Overweight (includes overweight and obesity)	Obesity	Overweight (includes overweight and obesity)	Obesity	Boys		Girls	
								Overweight (includes overweight and obesity)	Obesity	Overweight (includes overweight and obesity)	Obesity
Ankara	1.7–17.9 years median age 4.6 years (n = 397)	19.8%	9.8%	18.7%	7.8%	21.3%	12.3%	20.4 (17.5–23.6)	7.1 (5.7–8.7)	19.8 (16.6–23)	5.7 (4.5–7)
Birmingham	1–3 years (n = 12)	8%	0%	21.7%	6.5%	31%	10.3%	26.1 (23.8–28.5)	7.4 (6.5–8.5)	29.2 (26.8–31.9)	8.1 (7.0–9.3)
	4–11 years (n = 45)	20%	8.9%								
	≥12 years–18 years (n = 28)	43%	11%								
Brussels	1–8 years median age 7.1 years	32.5%	2.5%	40%	5%	25%	0%	20.5 (17.7–23.6)	4.6 (3.7–5.5)	18.8 (16.0–21.8)	4.2 (3.3–5.1)
	Copenhagen	6–10 years (n = 49)	29%	6%	33%	7%	26%	9%	19.7 (16.8–23.1)	8.7 (7.1–10.7)	19.4 (15.8–23.2)
Groningen	11–15 years (n = 36)	30%	8%	27%	0%	35%	13%	18.3 (15.7–21.3)	4.1 (3.4–5)	16.1 (13.4–18.9)	3.8 (3–4.7)
	4–10 years (n = 28)	25%	4%	45%	0%	17%	17%				
Madrid	11–18 years (n = 17)	45%	17%	0%	6%	0%	0%	27.6 (23.9–31.2)	8.4 (6.7–10.2)	23.8 (20.2–27.4)	7.6 (6.0–9.3)
	≤10 years (n = 30)	3%	3%								
Porto	10–18 years (n = 19)	29%	0%	37%	0%	22%	0%	28.7 (24.9–31.8)	8.9 (7.4–10.9)	27.1 (23.4–31.4)	10.6 (8.5–12.9)
	<5 years (n = 9)	0%	0%	0%	0%	0%	0%				
	5–< 19 years (n = 73)	26%	8.2%	22.7%	9.1%	31%	6.9%				

#### 4. Discussion

This is the first multi-centre European and Turkish cross sectional study in 947 patients with PKU to report the prevalence of overweight and obesity. In adults, the majority of centres reported similar or lower rates of obesity to their general populations [10]. In children although there is less or similar rates of obesity in boys to the local general population, in girls there is a trend for a higher rate of obesity, as previously reported [2,3]. It is unknown if body composition studies would reflect the same trend and this deserves further study [11]. In parallel to the respective general populations [9,10], the percentage of overweight increased with age. In order to avoid using different criteria to assess defining overweight and obesity and to facilitate comparisons between different countries and populations, in this survey the WHO BMI z scores were used to assess overweight and obesity in children and the body mass index (weight / height<sup>2</sup>) for the adult population.

Overall, despite similar PKU treatment approaches, the prevalence of overweight and obesity did vary between treatment centres, and it commonly followed respective national trends. Blood phenylalanine control of PKU patients from this group of PKU centres, except for Porto, has been published previously [12]. Energy and protein intakes were not reported in this audit but commonly overweight and obesity result from an eclectic combination of genetic, environmental, dietary and social factors. Although in non-PKU individuals, associated non-dietary factors include maternal overweight, high birth weight and smoking in pregnancy, there is little data reported in PKU for any of these factors [4].

In conclusion, although the prevalence of overweight and obesity varied widely between countries it was mainly similar or even less than the respective general populations for adults and boys. Women and girls with PKU appear particularly vulnerable to excess weight gain and it is important that female weight gain is targeted and closely monitored from an early age with individual strategies introduced to avoid and control excess weight gain. More research is needed to identify the main risk factors associated with overweight and obesity in females with PKU. In general, there is a need to better understand the food patterns, energy and nutrient intakes and the physical activity of patients with PKU.

#### Authors' roles

All authors were involved in data collection, interpretation of data, writing and critical revision of the paper for important intellectual content and final approval of the version to be published.

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#### Conflict of interest

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