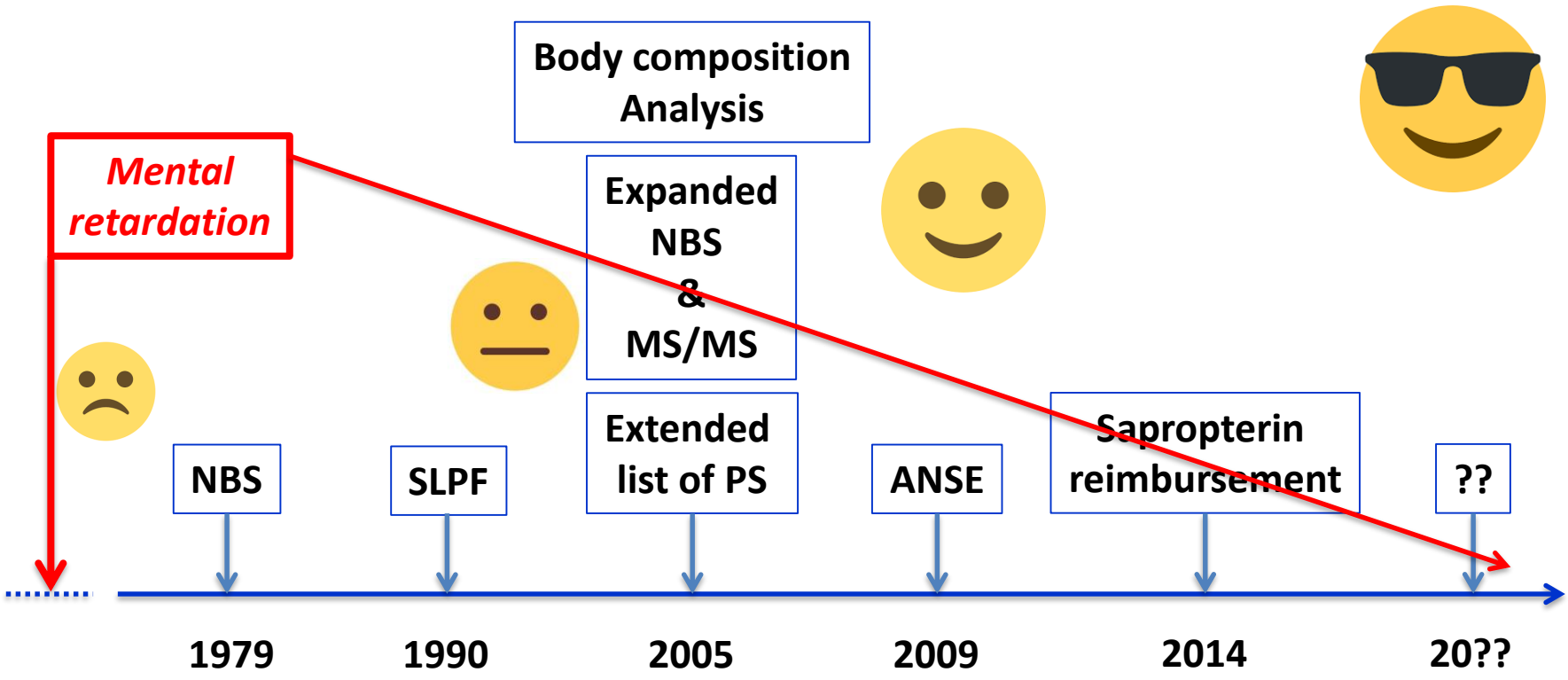
Nutritional management in patients with Phenylketonuria

Júlio César Rocha

Reference Centre Inborn Metabolic Diseases - Porto, Portugal

Zalau, Romania
29th June 2018

The '*PKU Journey*'



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Agenda

1. **Introduction**
2. Current management practices
3. Nutritional status
4. Medical treatment
5. Conclusion

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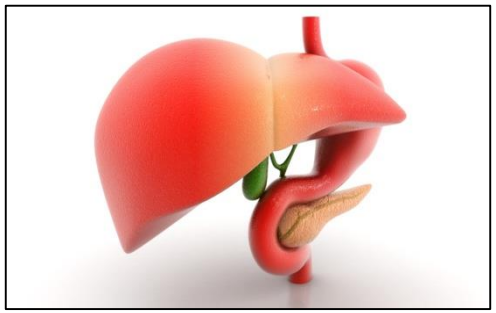
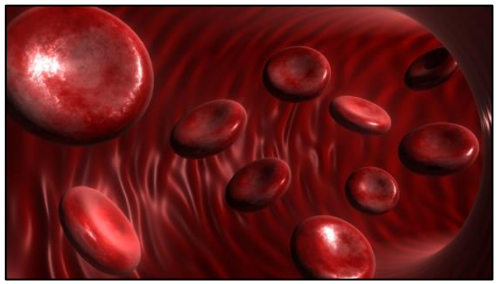
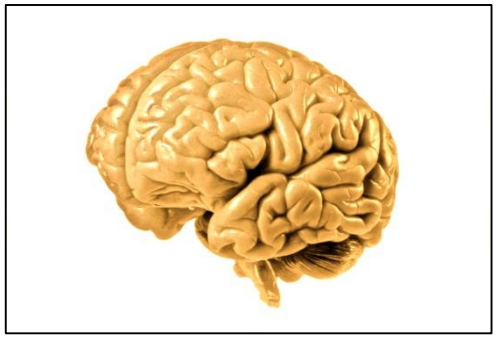






"There is no doubt that the early identification of PKU and prompt and continuous intervention prevents mental retardation in most patients."

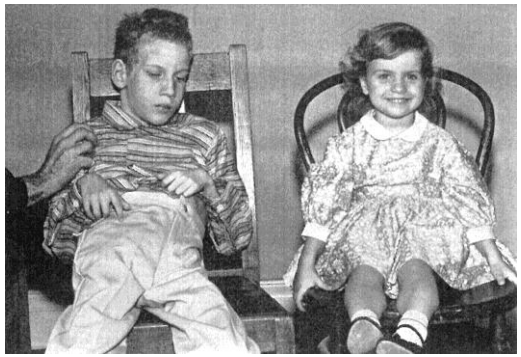
Nenad Blau

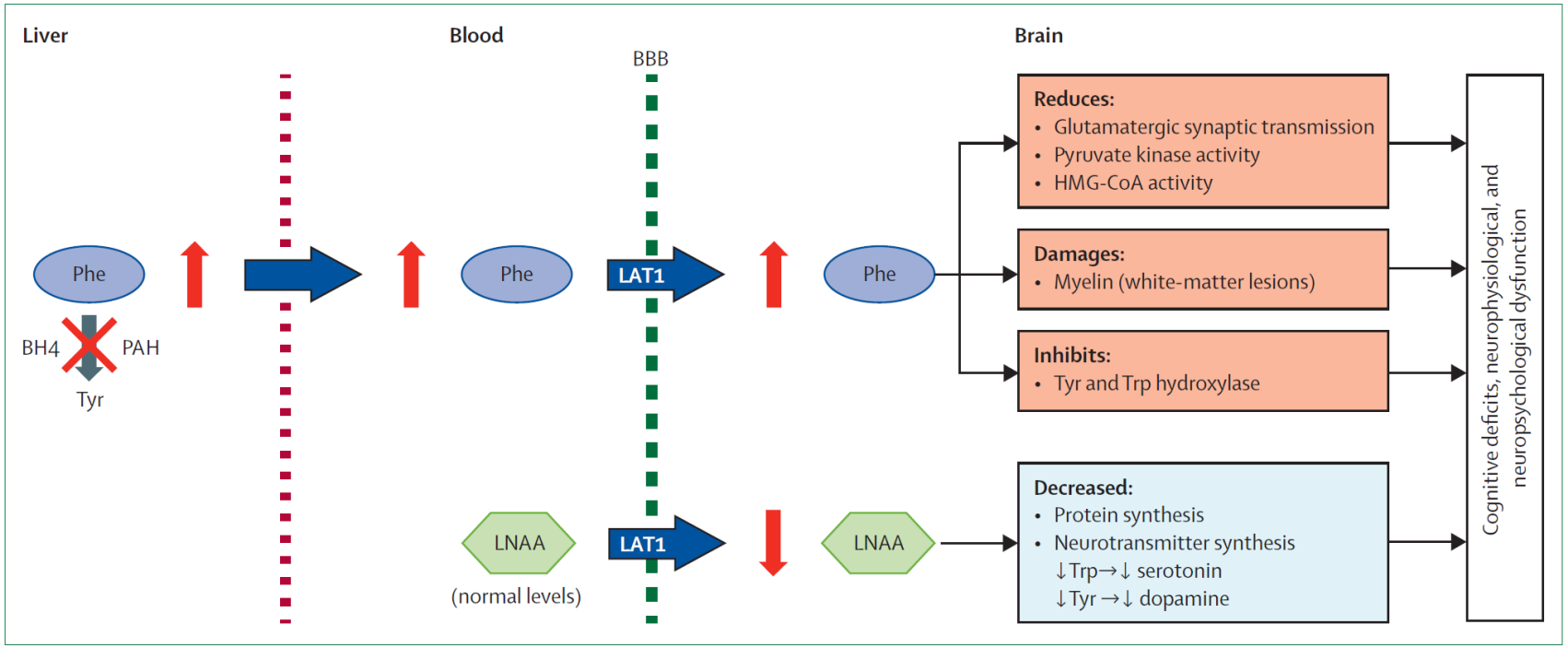
Anita MacDonald

Francjan van Spronsen

In Editorial

Molecular Genetics and Metabolism, 2011 (S1)





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Portuguese Association of PKU and Allied Disorders

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Pediatric Health, Medicine and Therapeutics

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REVIEW

Dietary intervention in the management of phenylketonuria: current perspectives

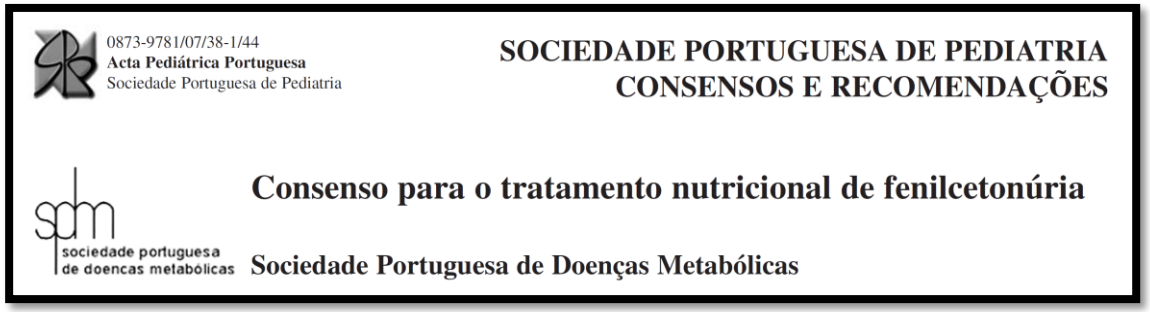
Júlio César Rocha[1-3]
Anita MacDonald[4]

Pediatric Health, Medicine and Therapeutics 2016:7 155–163

- Diet construction – dilemmas
- Nutritional challenges: feeding issues and nutritional imbalance
- Role of special dietary products
- Measurement of nutritional status
- Alternative treatments
- Glycomacropeptide
- Large neutral amino acids
- Sapropterin
- Phenylalanine ammonia lyase enzyme substitution therapy

PKU treatment approach in Portugal

- Treatment for life
- Keep patients under follow-up
- Focus on blood [Phe] management but also in other health status markers
- **Sapropterin as a possibility to optimize nutritional treatment:**
  - **To reduce dietary restrictions and dependence on medical and SLPF;**
  - **To clearly observe a significant clinical impact.**



Acta Pediatr Port 2007;38(1):44-54

- **Full reimbursement of:**
  - **PS**
  - **SLPF**
  - **Sapropterin**
  - **GMP**
  - **LNAA**

ORIGINAL ARTICLE

Protein substitutes for phenylketonuria in Europe: access and nutritional composition

MJ Pena[1], MF de Almeida[1,2], E van Dam[3], K Ahring[4], A Bélanger-Quintana[5], K Dokoupil[6], H Gokmen-Ozel[7], AM Lammardo[8], A MacDonald[9], M Robert[10] and JC Rocha[1,11,12]

BACKGROUND/OBJECTIVES: Protein substitutes (PS) are an essential component in the dietary management of phenylketonuria (PKU). PS are available as phenylalanine-free amino-acid mixtures (AAM), glycomacropeptide-based PS (GMP) and large neutral amino acids (LNAA). There is a lack of information regarding their availability in different countries and comparison of their nutritional composition is limited. The objectives of this study were to identify the number of PS available in different European countries and Turkey and to compare their nutritional composition.

SUBJECTS/METHODS: Members of the European Nutritionist Expert Panel on PKU (ENEP) (Portugal, Spain, Belgium, Italy, Germany, Netherlands, United Kingdom, Denmark and Turkey) provided data on PS available in each country. The nutritional composition of PS available in Portugal was analyzed.

RESULTS: The number of PS available in each country varied from 30 (Turkey) to 105 (Germany), with a median of 64. GMP was available only in Portugal, whereas LNAA was an option in Portugal, Italy, Turkey and Denmark. Some PS were designed for weaning. Many PS did not contain added fat and fiber. GMP contained the highest carbohydrate (CHO) and energy content as well as higher LNAA content compared with AAM. Only one AAM contained added fructo-oligosaccharides and galacto-oligosaccharides. AAM designed for the first year of life had the highest CHO, fat and LNAA contribution. Liquid AAM had lower CHO and fat contents compared with powdered AAM, but contained higher LNAA.

CONCLUSIONS: There was widely dissimilar numbers of PS available in different countries. Nutritional composition of different PS was variable and should be considered before prescription.

European Journal of Clinical Nutrition advance online publication, 27 April 2016; doi:10.1038/ejcn.2016.54

Pena *et al. Orphanet Journal of Rare Diseases* (2015) 10:162
DOI 10.1186/s13023-015-0378-7

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Special low protein foods for phenylketonuria: availability in Europe and an examination of their nutritional profile

Maria João Pena[1], Manuela Ferreira Almeida[1,2], Esther van Dam[3], Kirsten Ahring[4], Amaya Bélanger-Quintana[5], Katharina Dokoupil[6], Hulya Gokmen-Ozel[7], Anna Maria Lammardo[8], Anita MacDonald[9], Martine Robert[10] and Júlio César Rocha[1,11,12*]

Table 2 Nutritional composition of SLPF available in Portugal, according to sub-groups

SLPF	Usual portion	Phe (mg)	Protein (g)	Fat (g)	CHO (g)	Energy (Kcal)
Baby Cereals	30 g	48 [4–70]	1.3 [0.2–1.8]	10.0 [0.5–14.8]	83.0 [77.1–95.0]	415 [381–449]
Bread	50 g	29 [10–65]	0.8 [0.5–1.3]	5.8 [3.7–10.0]	61.3 [50.0–82.3]	305 [236–412]
Breakfast Cereals	30 g	13 [5–31]	0.5 [0.2–1.0]	1.1 [0.7–1.9]	92.2 [90.5–93.6]	381 [370–387]
Cakes/Mix Cakes/Pancake Mix	50 g	11 [4–30]	0.4 [0.2–0.9]	5.2 [0.2–15.2]	77.6 [58.0–88.2]	362 [341–372]
Chocolate/Energy Bars/Jelly	unit	41 [10–90]	1.2 [0.2–2.5]	18.5 [1.0–33.6]	67.6 [42.6–93.3]	441 [377–548]
Cookies	unit	14 [2–34]	0.4 [0.1–0.8]	19.1 [1.5–49.4]	75.1 [48.3–87.7]	478 [395–639]
Flour	*variable*	13 [10–15]	0.3 [0.3–0.4]	0.8 [0.4–1.1]	86.6 [82.8–89.6]	357 [344–372]
Ice Cream	unit	27 [14–43]	0.7 [0.3–1.1]	4.5 [3.3–5.2]	85.6 [82.0–88.9]	386 [376–394]
Milk replacers	200 mL	6 [0.0–10]	0.2 [0.0–0.4]	2.7 [2.0–3.8]	6.1 [4.8–8.1]	49 [40–66]
Pasta	40 g	12 [11–13]	0.4 [0.2–0.5]	0.8 [0.6–1.2]	86.2 [85.4–87.4]	355 [348–363]
Rice	40 g	13	0.4	0.8	88.9	365
Savoury Foods	unit	26 [0–90]	0.7 [0.0–2.1]	16.2 [0.0–39.5]	40.5 [0.0–88.4]	323 [0–577]

CHO = Carbohydrate; Phe = Phenylalanine; SLPF = Special low protein foods
Nutritional composition data is presented in mean [range] per 100 g / 100 mL of each SLPF sub-group

Pena MJ, *et al*. Orphanet J Rare Dis. 2015 Dec 22;10(1):162.

Our routine nutritional status evaluation protocol

Annual Nutritional Status Evaluation (ANSE)

Procedures sequence:

1st. Anthropometric evaluation

2nd. Body composition analysis

3rd. Blood pressure determination

4th. Blood sample collection

5th. Nutrition appointment: - food and nutrition data collection
- nutritional adjustments

Combined with neuropsychological tests!

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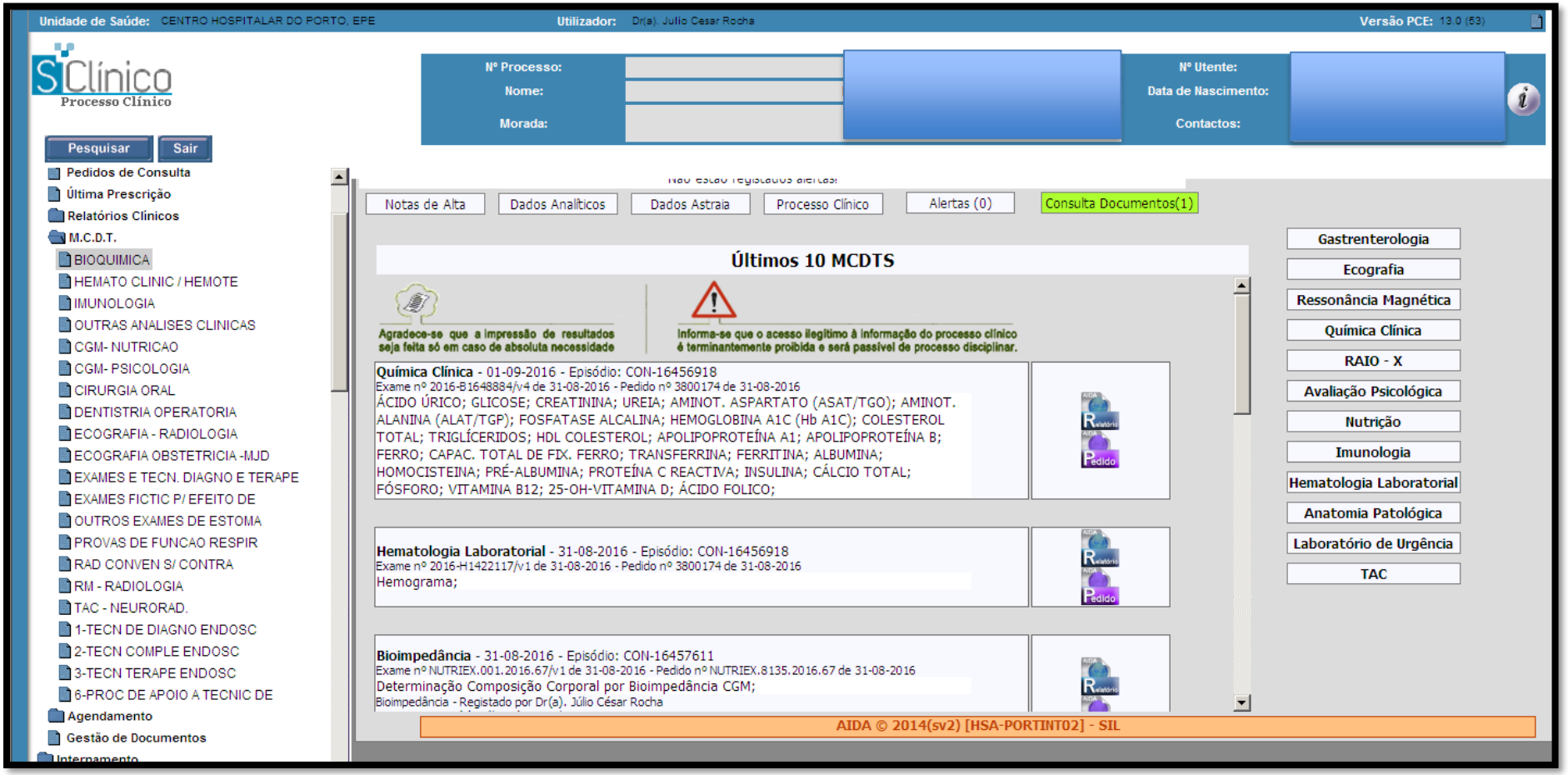
Clinical assistance to our patients



- **Biochemistry**
- **Haematology**
- **Body composition**

All results available to all team members!

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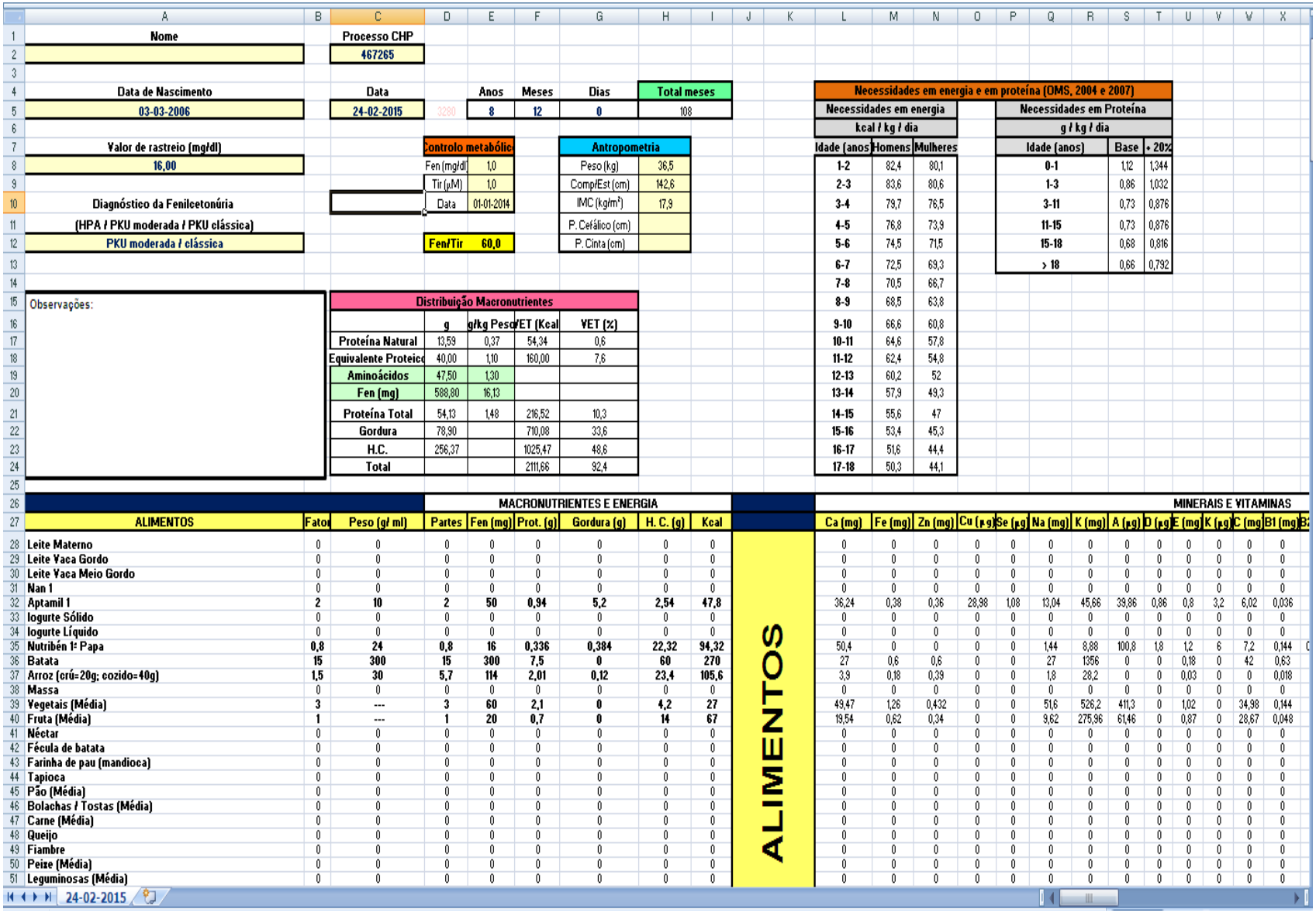
Our strategy to determine nutritional intake



Nome	Processo CHP
	467265

Data de Nascimento	Data	Anos	Meses	Dias	Total meses
03-03-2006	24-02-2015	8	12	0	108

Valor de rastreio (mg/dl)
16,00

Diagnóstico da Fenilcetonúria
(HPA / PKU moderada / PKU clássica)
PKU moderada / clássica

Controlo metabólico	
Fen (mg/dl)	1,0
Tir (µM)	1,0
Data	01-01-2014
Fen/Tir	60,0

Antropometria	
Peso (kg)	36,5
Compr/Est (cm)	142,6
IMC (kg/m²)	17,9
P. Cefálico (cm)	
P. Cinta (cm)	

Observações:

Distribuição Macronutrientes	g	g/kg Peso	VET (Kcal	VET (%)
Proteína Natural	13,59	0,37	54,34	0,6
Equivalente Proteic	40,00	1,10	160,00	7,6
Aminoácidos	47,50	1,30		
Fen (mg)	588,80	16,13		
Proteína Total	54,13	1,48	216,52	10,3
Gordura	78,90		710,08	33,6
H.C.	256,37		1025,47	48,6
Total			2111,66	92,4

Necessidades em energia e em proteína (OMS, 2004 e 2007)

Necessidades em energia kcal / kg / dia		
Idade (anos	Homens	Mulheres
1-2	82,4	80,1
2-3	83,6	80,6
3-4	79,7	76,5
4-5	76,8	73,9
5-6	74,5	71,5
6-7	72,5	69,3
7-8	70,5	66,7
8-9	68,5	63,8
9-10	66,6	60,8
10-11	64,6	57,8
11-12	62,4	54,8
12-13	60,2	52
13-14	57,9	49,3
14-15	55,6	47
15-16	53,4	45,3
16-17	51,6	44,4
17-18	50,3	44,1

Necessidades em Proteína g / kg / dia		
Idade (anos)	Base	+ 20%
0-1	1,12	1,344
1-3	0,86	1,032
3-11	0,73	0,876
11-15	0,73	0,876
15-18	0,68	0,816
> 18	0,66	0,792

ALIMENTOS	Fator	Peso (g/ ml)	MACRONUTRIENTES E ENERGIA Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal	MINERAIS E VITAMINAS Ca (mg)	Fe (mg)	Zn (mg)	Cu (µg)	Se (µg)	Na (mg)	K (mg)	A (µg)	D (µg)	E (mg)	K (µg)	C (mg)	B1 (mg)
Leite Materno	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Leite Vaca Gordo	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Leite Vaca Meio Gordo	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nan 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Aptamil 1	2	10	2	50	0,94	5,2	2,54	47,8	36,24	0,38	0,36	28,98	1,08	13,04	45,66	39,86	0,86	0,8	3,2	6,02	0,036
Iogurte Sólido	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Iogurte Líquido	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nutribén 1ª Papa	0,8	24	0,8	16	0,336	0,384	22,32	94,32	50,4	0	0	0	0	1,44	8,88	100,8	1,8	1,2	6	7,2	0,144
Batata	15	300	15	300	7,5	0	60	270	27	0,6	0,6	0	0	27	1356	0	0	0,18	0	42	0,63
Arroz (crú=20g; cozido=40g)	1,5	30	5,7	114	2,01	0,12	23,4	105,6	3,9	0,18	0,39	0	0	1,8	28,2	0	0	0,03	0	0	0,018
Massa	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vegetais (Média)	3	---	3	60	2,1	0	4,2	27	49,47	1,26	0,432	0	0	51,6	526,2	411,3	0	1,02	0	34,98	0,144
Fruta (Média)	1	---	1	20	0,7	0	14	67	19,54	0,62	0,34	0	0	9,62	275,96	61,46	0	0,87	0	28,67	0,048
Néctar	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fécula de batata	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Farinha de pau (mandioca)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tapioca	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pão (Média)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bolachas / Tostas (Média)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Carne (Média)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Queijo	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fiambre	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Peixe (Média)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Leguminosas (Média)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

24-02-2015

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CINTESIS Health. Research.

Our strategy to determine nutritional intake

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X
58		Fator	Peso (g/ ml)	Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal			Ca (mg)	Fe (mg)	Zn (mg)	Cu (µg)	Se (µg)	Na (mg)	K (mg)	A (µg)	D (µg)	E (mg)	K (µg)	C (mg)	B1 (mg)
59	MISTURAS DE AA ISENTAS DE FEN + GMP + LNAA	Fator	Peso (g/ ml) / Porçã	Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal	aa (g)		Ca (mg)	Fe (mg)	Zn (mg)	Cu (µg)	Se (µg)	Na (mg)	K (mg)	A (µg)	D (µg)	E (mg)	K (µg)	C (mg)	B1 (mg)
60	PKU 1 (1 med=5g)	0	0	0	0	0	0	0	0	0	MISTURAS DE AA ISENTAS DE FEN + GMP + LNAA	0	0	0	0	0	0	0	0	0	0	0	0	0
61	PKU 2 Prima (1 med=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
62	PKU 2 Secunda (1 med=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
63	PKU 3 Advanta (1 med=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
64	PKU Anamix Infant (1 med=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
65	PKU Anamix Junior (1 saqueta=29g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
66	Phlexy - 10 Drink Mix (1 saqueta=20g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
67	PKU Lophex LQ 10 (1 bolsa = 62,5 mL)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
68	PKU Lophex LQ 20 (1 bolsa = 125 mL)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
69	PhenylAde (1 med=40g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
70	PKU express 15 (1 saqueta=25g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
71	PKU cooler 10 (1 bolsa=87ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
72	PKU cooler 15 (1 bolsa=130ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
73	PKU cooler 20 (1 bolsa=174ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
74	PKU air 15 (1 bolsa =130ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
75	PKU air 20 (1 bolsa=174ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
76	Fleet PKU 1 (1 med=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
77	Fleet PKU Star (1 med=7,5g)	25	125	0	0	40	18,75	50,75	527,5	47,5		1292,5	17,5	11,75	1375	46,25	347,5	785	777,5	11,75	13,75	42,5	105	1,25
78	Fleet PKU Plus (1 med=7,5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
79	Fleet PKU Avant (1 med=7,5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
80	Fleet PKU Gold (10 cápsulas=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
81	XPHE Mix Infant LCP (1 med=5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
82	XPHE ENERGY K (Kid) (1 saqueta=16,5g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
83	XPHE ENERGY J (Junior) (1 saqueta=33g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
84	XPHE ENERGY A (Advance) (1 saqueta=33g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
85	XPHE JUMP 10 (1 bolsa=63ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
86	XPHE JUMP 20 (1 bolsa=125ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
87	Camino PRO BETTERMILK (1 saqueta=49g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
88	Camino PRO SWIRL (1 saqueta=77g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
89	Camino PRO COMPLETE Manteig. Amendoim (1 barra=54g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
90	Camino PRO COMPLETE Mistura Frutos (1 barra=54g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
91	Camino PRO RESTORE (1 garrafa=500ml)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
92	NeoPhe (1 comprimido=685mg)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
93	Tyrosine 1000 aa suplement (1 saqueta=4g)	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
94	Outro	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0
95	Total Parcial 2			0,00	0,00	40,00	18,75	50,75	527,50	47,50		1292,50	17,50	11,75	1375,00	46,25	347,50	785,00	777,50	11,75	13,75	42,50	###	1,25
96		Fator	Peso (g/ ml) / Porçã	Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal	aa (g)		Ca (mg)	Fe (mg)	Zn (mg)	Cu (µg)	Se (µg)	Na (mg)	K (mg)	A (µg)	D (µg)	E (mg)	K (µg)	C (mg)	B1 (mg)
97	SUPLEMENTOS ENERGÉTICOS	Fator	Peso (g/ ml)	Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal			Ca (mg)	Fe (mg)	Zn (mg)	Cu (µg)	Se (µg)	Na (mg)	K (mg)	A (µg)	D (µg)	E (mg)	K (µg)	C (mg)	B1 (mg)
98	Energivit	0	0	0	0	0	0	0	0		SUPLEMENTOS ENERGÉTICOS	0	0	0	0	0	0	0	0	0	0	0	0	0
99	PFD1	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
100	KcaLIP	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
101	Fantomalt (Maltodextrina)	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
102	MCT oil	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
103	Docomega (1 saqueta=4g)	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
104	Kegomega (1 saqueta=4g)	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
105	DHA Basic (1ml)	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
106	DHA Richoil (1 pérola)	0	---	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
107	Outro	0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0
108	Total Parcial 3			0,00	0,00	0,00	0,00	0,00	0,00			0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00

Rocha JC, 2018

CINTESIS Health. Research.

Our strategy to determine nutritional intake

ALIMENTOS ESPECIAIS HIPOPROTEICOS	Fator	Peso (g/ ml) / Porção	Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal	Ca (mg)	Fe (mg)	Zn (mg)	Cu (µg)	Se (µg)	Na (mg)	K (mg)	A (µg)	D (µg)	E (mg)	K (µg)	C (mg)	B1 (
BOLACHAS A (A: | V.E.T., Gord., H.C.), B e C (C: | V.E.T., Gord., H.C.)																					
A-Bolachas tipo Água e Sal (Loprofin) - 150g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Bolachas tipo Maria (Taranis) - 120g	0,5	3	0,014	0,275	0,015	0,52	2,365	14,2	0	0	0	0	0	0,485	0,24	0	0	0	0	0	0
A-Bolachas com Pepitas de Chocolate (Taranis) - 100g	0,5	3,125	0,0265	0,53	0,015	0,565	2,5	15,125	0,6245	0	0	0	0	0,53	1,125	0	0	0	0	0	0
A-Tostadas (Harifen) - 200g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Bolachas Baunilha (Loprofin) - 100g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Bolachas Baunilha / Chocolate (Loprofin) - 100g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Bolachas de Manteiga (Bezgluten) - 150g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Bolachas de Manteiga e Canela (Bezgluten) - 150g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Wafers de Morango (Bezgluten) - 70g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Biscoitos Ovais (Harifen) - 125g	0,5	5,7	0,029	0,58	0,02	0,355	4,65	22,5	10,25	0,235	0	0	0	10,25	1,425	0	0	0	0	0	0,0
B-Bolachas com Chocolate Branco (Harifen) - 150g	0,5	5,75	0,06	1,215	0,015	1,02	4,36	26,8	0	0	0	0	0	0	0	0	0	0	0	0	0
C-Bolachas de Noz (Taranis) - 135g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C-Bolachas de Côco (Bezgluten) - 190g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C-Barritas de Morango (Harifen) - 125g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MASSAS / ARROZ (essenciais)																					
A-Massas Loprofin - 250g, 500g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Massas Bezgluten - 250g, 400g	1	40	0,212	4,24	0,08	0,24	34,16	139,28	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Massas Harifen - 500g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Arroz (Harifen) - 500g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FARINHAS (essenciais)																					
A-Farinha Loprofin - 500g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Farinha Taranis - 1000g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Farinha Harifen- 500g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SUBS. LEITE A (A: com cálcio) e B (B: sem cálcio, Prozero rico em H.C.)																					
A-Subs. Leite pacote Dália Taranis - 200ml	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Subs. Leite pacote Harifen - 200ml (sabor a baunilha)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Subs. Leite pacote Matilde Loprofin - 200ml	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Subs. Leite pacote Prozero Vitaflo - 250ml	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PÃES A e B (B: | V.E.T., Gord.)																					
A-Pão caseiro (800g pão=1 saqueta farinha 500g + 30g vaqueiro + 10g sal + 10g fermento padeiro; 80g fatia)	0,8	64	0,528	10,616	0,24	2,856	34,656	160,58	0,232	0,5648	0,044	0	0	381,784	11,488	14,4	0,005	0	0	0	0,0
A-Pão de forma fatiado (Loprofin) - 400g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Pão de forma fatiado (Bezgluten) - 300g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Pão cacete fatiado (Bezgluten) - 350g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Tostas (Valpiform) - 250g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Pãezinhos pequenos (Taranis) - 180g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Pão Ciabatta (Bezgluten) - 140g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Pão ralado (Bezgluten) - 400g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Pão em Baguete (Hammermühle) - 250g / unidade	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Bases de Pizza (Hammermühle) - 125g / unidade	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PAPAS A (A: | Prot., Gord.) e B																					
A-Papa Pêra (Milupa) - 300g	0,1	3	0,105	2,1	0,054	0,444	2,313	13,47	5,4	0,15	0,009	0,9	0,09	0,36	1,2	9,6	0,18	0,063	0,18	1,26	0,0
A-Papa Banana Maçã (Milupa) - 300g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Papa Baunilha / Papa Frutos Silvestres (Taranis) - 400g	0,1	3	0,006	0,119	0,006	0,015	2,85	11,43	0,204	0	0	0	0	2,514	0,27	0	0	0	0	0	0
CEREAIS																					
A-Cereais Loops (Loprofin) - 375g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Cereais Morango (Loprofin) - 375g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Corn-Flakes Especiais (Milupa) - 375g	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Cereais Chocolate (Milupa) - 250g	0,5	15	0,2325	4,65	0,15	0,285	13,71	58,05	0	0,315	0	0	0	9,75	16,5	0	0,165	0	1,245	0	0
SALGADOS																					

ESPECIAIS HIPOPROTEICOS

Rocha JC, 2018

Produtos Dietéticos Hipoproteicos

PRESCRIÇÃO NUTRICIONAL

centro hospitalar do Porto

Nome: _____

Processo _____

Doenças Hereditárias do Metabolismo

CONSULTA DE NUTRIÇÃO

PKU 2015

Descrição	Unidades	Acerto	
A-Bolachas tipo Água e Sal (Loprofin) - 150g	3		BOLACHAS
A-Bolachas tipo Maria (Taranis) - 120g	3		
A-Bolachas com Pepitas de Chocolate (Taranis) - 100g	4		
A-Tostadas (Harifen) - 200g	0		
B-Bolachas Baunilha (Loprofin) - 100g	0		
B-Bolachas Baunilha / Chocolate (Loprofin) - 100g	0		
B-Bolachas de Manteiga (Bezgluten) - 150g	0		
B-Bolachas de Manteiga e Canela (Bezgluten) - 150g	0		
B-Wafers de Morango (Bezgluten) - 70g	0		
B-Biscoitos Ovais (Harifen) - 125g	0		
B-Bolachas com Chocolate Branco (Harifen) - 150g	0		
C-Bolachas de Noz (Taranis) - 135g	0		
C-Bolachas de Côco (Bezgluten) - 190g	0		
C-Barritas de Morango (Harifen) - 125g	0		
A-Massas Loprofin - 250g, 500g	0		MASSAS ARROZ
A-Massas Bezgluten - 250g, 400g	0		
A-Massas Harifen - 500g	0		
A-Arroz (Harifen) - 500g	0		
A-Farinha Loprofin - 500g	0		FARINHAS
A-Farinha Taranis - 1000g	0		
A-Farinha Harifen- 500g	0		
A-Subs. Leite pacote Dália Taranis - 200ml	0		SUB. LEITE
A-Subs. Leite pacote Harifen - 200ml (sabor a baunilha)	0		
B-Subs. Leite pacote Matilde Loprofin - 200ml	0		
B-Subs. Leite pacote Prozero Vitaflo - 250ml	0		
A-Pão caseiro (800g pão=1 saqueta farinha 500g)	0		PÃO
A-Pão de forma fatiado (Loprofin) - 400g	0		
A-Pão de forma fatiado (Bezgluten) - 300g	0		
A-Pão cacete fatiado (Bezgluten) - 350g			
A-Tostas (Valpiform) - 250g	3		
B-Pãezinhos pequenos (Taranis) - 180g			
B-Pão Ciabatta (Bezgluten) - 140g	0		
B-Pão ralado (Bezgluten) - 400g	0		
B-Pão em Baguete (Hammermühle) - 250g / unidade	0		
B-Bases de Pizza (Hammermühle) - 125g / unidade	0		

Tempo prescrição (dias) 60

2 months!

Rocha JC, 2018

CINTESIS Health.Research.

A-Papa Pêra (Milupa) - 300g	0		PAPAS
A-Papa Banana Maçã (Milupa) - 300g	0		
B-Papa Baunilha / Frutos Silvestres (Taranis) - 400g	0		
A-Cereais Loops (Loprofin) - 375g	0		CEREAIS
A-Cereais Morango (Loprofin) - 375g	0		
A-Corn-Flakes Especiais (Milupa) - 375g	0		
A-Cereais Chocolate (Milupa) - 250g	0		
B-Preparado para hamburger (Taranis) - 248g	3		SALGADOS
B-Substituto de clara de ovo (Loprofin) - 100g	0		
B-Substituto de ovo (Bezgluten) - 200g	0		
B-Substituto de queijo fatiado (Taranis) - 120g	0		
C-Aperitivos com Sal (Bezgluten) - 70g	0		
C-Aperitivos com Ervas Aromáticas (Bezgluten) - 70g	0		
B-Bombons Choquitos (Taranis) - 260g	0		CHOCOLATES/ BARRA/GELATINA
B-Chocolate Vita-Bite (Taranis) - 175g	0		
B-Barra Energética Frutos Silvestres (Milupa) - 75g	0		
B-Creme Avelãs (Taranis) - 230g	0		
B-Gelatina Baunilha Chocolate (Taranis) - 95g (5x19g)	0		
B-Gelado Mix Baunilha (Loprofin) - 150g pó / saqueta	0		GELADOS
B-Gelado Mix Morango (Loprofin) - 150g pó / saqueta	0		
B-Gelado Mix Chocolate (Loprofin) - 150g pó / saqueta	0		
B-Bolo Chocolate (Loprofin) - 500g / saqueta	0		BOLOS E PREPARADOS / MISTURA PANQUECAS
B-Bolo Limão (Loprofin) - 500g / saqueta	0		
B-Preparado Bolo Simples (Taranis) - 300g / saqueta	0		
B-Mini Bolos Limão (Taranis) - 6x40g	0		
B-Mini Bolos Pêra (Taranis) - 6x40g	0		
B-Mistura para Panquecas (Bezgluten) - 500g	0		
B-Panqueca	0		
Outro			

Data: 20-01-2016

O Nutricionista,

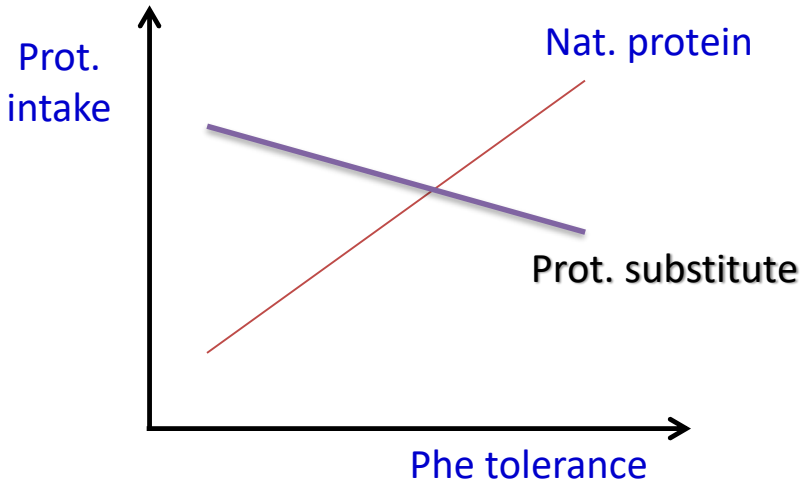
_____

N.º Mec: _____

SLPF			1,01	20,19	0,48	4,19	29,21	166,94	
	Fator	Peso (g/ ml) / Porção	Partes	Fen (mg)	Prot. (g)	Gordura (g)	H. C. (g)	Kcal	aa (g)
TOTAL			32,71	653,19	70,58	45,19	186,01	1477,94	66,00

Phenylketonuria classification

- **Hyperphenylalaninemia**
  - $[Phe]_{blood}$ between 3 mg/dL and 6 mg/dL
- **Mild PKU**
  - $[Phe]_{blood}$ between 6 mg/dL and 20 mg/dL
- **Classical PKU**
  - $[Phe]_{blood}$ > 20 mg/dL



Rocha JC, *et al. Acta Pediatr Port. 38(1):44-54, 2007*

Treatment implementation (± 10th day of life)

- $[Phe]_{blood}$ > 20 mg/dL:
  - Stop phe intake (breastfeeding or infant formula) up to 48h
  - Gradual phe reintroduction: 60-80 mg / day
  - Protein substitute + energy (CHO + lipids)

- $[Phe]_{blood}$ < 20 mg/dL:
  - Reduce phe intake (breastfeeding or infant formula)
  - Protein substitute + energy (CHO + lipids)

Rocha JC, 2018

Is breastfeeding possible?

All the known advantages plus:

- Low phe content!
- LCPUFAS content!

However… it is difficult to measure!!!

- based on weight, estimation of total daily fluid intake **(3.200 kg x 170 mL/kg = 544 mL/day)**
- estimation of the volume of each breastfeed **(544 mL / 8 = 68 mL)**
- duration time of each breastfeed **68 mL = 20 minutes**
- minutes «» volume «» **phe content**

Rocha JC, 2018

Infant formula

- Availability of complete amino acid profile.
- LCPUFAS enriched.
- Protein content.
- Exact phe content throughout 1st year of life!
- Possibility to prepare the mixture together with protein substitute and energy sources.

Rocha JC, 2018

Practical schemes – an example

AA + Energy

+

Phe

8 equal meals a day
OR
6 equal meals a day +
2 breastfeeds during night

AA + Energy + Phe

8 equal meals a day

Rocha JC, 2018

1st year of life – a case report

- Male
- Date of birth
- Mild PKU (R261Q/R261Q)

- NBS [Phe] (7th day of life): 11.7 mg/dL

Rocha JC, 2018

1st appointment (13 d)

- [Phe] (13d): 10.2 mg/dL

- Weight = 3000 g (P10)
- Length = 49.5 cm (P10)
- HC = 35 cm (P10-25)

- Breastfeeding – 7x / day
- Blood sample – DHPR + amino acids
- Urine sample – Pterins + amino acids

Diet prescription (160 mg Phe):

- **15 g of AAM** + energy supplements
- 7 meals
  - 2x only breast milk
  - 5x – bottle-feed + breastfeed (limited)

Rocha JC, 2018

Age: 1 month

- Weight = 3500 g (P5-10)
- Length = 53.5 cm (P25-50)
- HC = 37 cm (P25)

Blood Phe (mg/dL):
0.9
0.3
0.7

Diet prescription (240 mg Phe):

- **7.5 g de AAM (↓)**
- 7 meals
  - 3x only breast milk
  - 4x bottle-feed + breastfeed (free)

Rocha JC, 2018

Age: 3 months 24 d

- Weight = 6120 g (P25-50)
- Length = 63.5 cm (P50-75)
- HC = 42.2 cm (P50-75)

Phe challenge! →

Blood Phe (mg/dL):

2.2
1.4
8.9
6.6
3.8
2.8
1.5
....
3.3

Diet prescription (340 mg Phe):

- **20 g of AAM (↑)**
- free breast milk
- weaning: 30 g of cereals

Rocha JC, 2018

Age: 5 m 17 d

- Weight = 7290 g (P25-50)
- Length = 67.3 cm (P50-75)
- HC = 44.4 cm (P75)

Blood Phe (mg/dL):

3.3
2.2
4.1
1.8

Diet prescription (420 mg Phe):

- **25 of AAM (↑)**
- vegetables soup (4 phe exchanges = 80 mg) + fruit (1 PE)
- 3 x breast milk + bottle-feed
- cereals together with protein substitute

Rocha JC, 2018

Age: 8 m 16 d

- Weight = 8580 g (P25-50)
- Length = 72 cm (P50-75)
- HC = 46.3 cm (P75-90)

Blood Phe (mg/dL):

3.2
1.1
1.4
…
0.6
3.2
2.5
2.8

Diet prescription (284 mg Phe):

- **35 g AAM (↑)** + 20 g **infant formula**
  - 2 bottle-fed
  - 1 with cereals
- 5 Phe exchanges (vegetables soup + fruit)
- 3 more Phe exchanges »» solid meal

Rocha JC, 2018

Age: 12 m

- Weight = 9780 g (P25-50)
- Length = 76.5 cm (P50-75)
- HC = 47 cm (P50-75)

Blood Phe (mg/dL):

1.9
1.7
2.1
...
7.8
...
2.2
2.9
1.7

Diet prescription (334 mg Phe):

- **25 g AAM + 30 g (↑) infant formula (3 meals / day)**
- total: 8 Phe exchanges
- introduction of special low protein foods

Rocha JC, 2018

Age: 19 m

- Weight = 12.400 kg (P50-75)
- Length = 86.3 cm (P75-90)
- HC = 49.6 cm (P90)

Blood Phe (mg/dL):

...
5.5
4.5
4.0
3.8
5.3
5.9
3.7
3.3

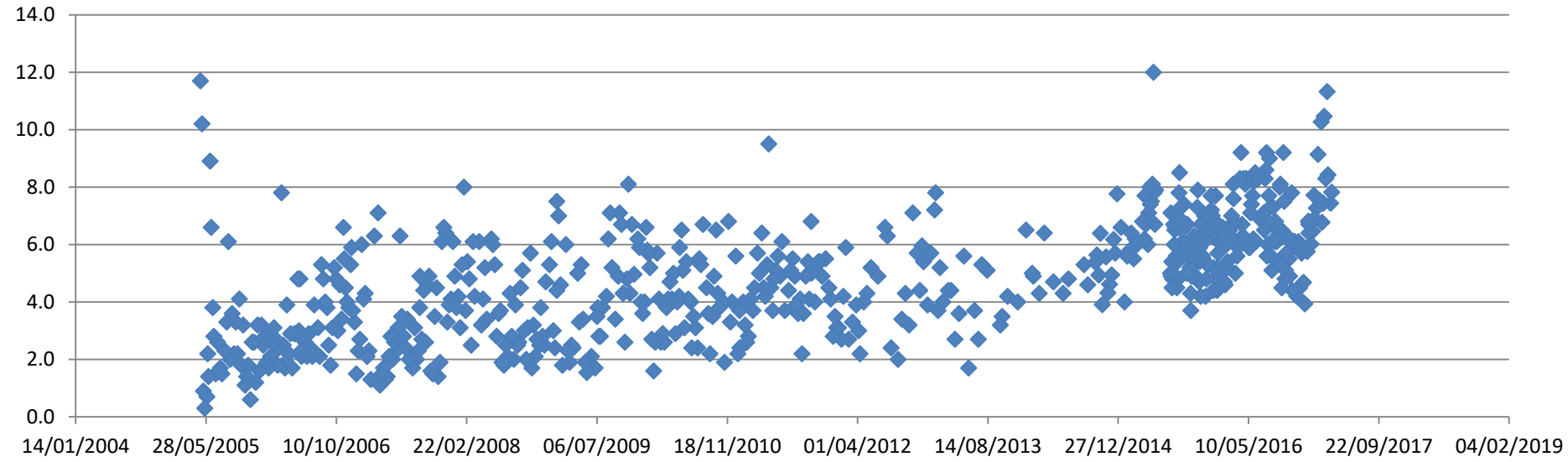
Diet prescription (309 mg Phe) »» 24.9 mg phe/kg/dia

- **30 g (↑) AAM + 25 g (↓) infant formula**
- total: 8 Phe exchanges

Rocha JC, 2018

Longitudinal metabolic control

Blood Phe (mg/dL)



Rocha JC, 2018

Nutritional intake in February 2014

Nutritional intake				
	g	g/kg	Energy (Kcal)	Energy (%)
Natural protein	11,98	0,34	47,92	0,7
Protein equivalent	40,00	1,13	160,00	8,8
Amino acids	48,00	1,35		
Phe (mg)	506,92	14,28		
Total protein	54,13	1,52	216,50	11,9
Fat	69,68		627,12	34,3
Carbohydrate	243,52		974,10	53,3
Total energy intake			1826,07	99,5

Nutritional intake in February 2015

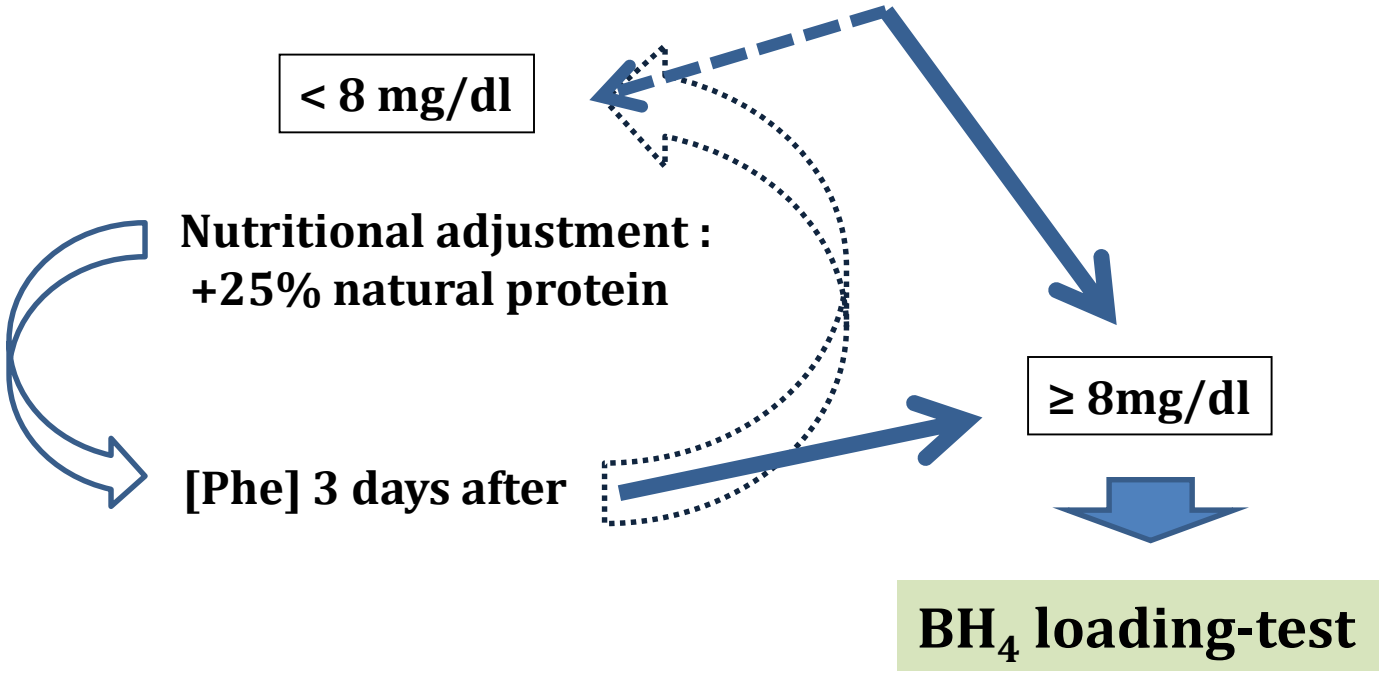
Nutritional intake				
	g	g/kg	Energy (Kcal)	Energy (%)
Natural protein	24,15	0,59	96,59	1,0
Protein equivalent	38,00	0,93	152,00	6,3
Amino acids	45,60	1,11		
Phe (mg)	1121,56	27,36		
Total protein	64,55	1,57	258,20	10,6
Fat	71,20		640,77	26,4
Carbohydrate	377,39		1509,58	62,2
Total energy intake			2426,89	99,2

Rocha JC, 2018

BH4-loading test adopted by SPDM, 2014

- HPA / PKU
- Under phe restricted diet
- Age ≥ 4 years

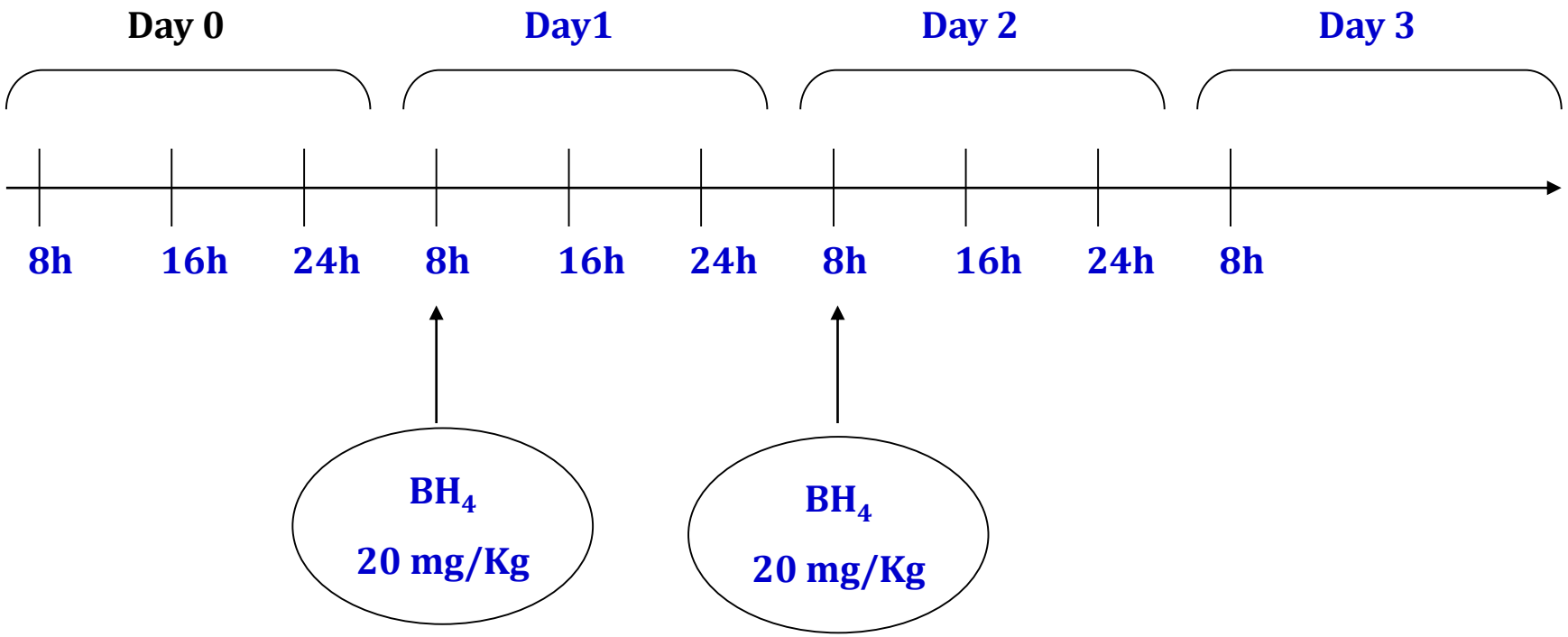
Median of blood [Phe] in the previous year



SPDM – Sociedade Portuguesa de Doenças Metabólicas.

Rocha JC, 2018

BH4-loading test adopted by SPDM, 2014

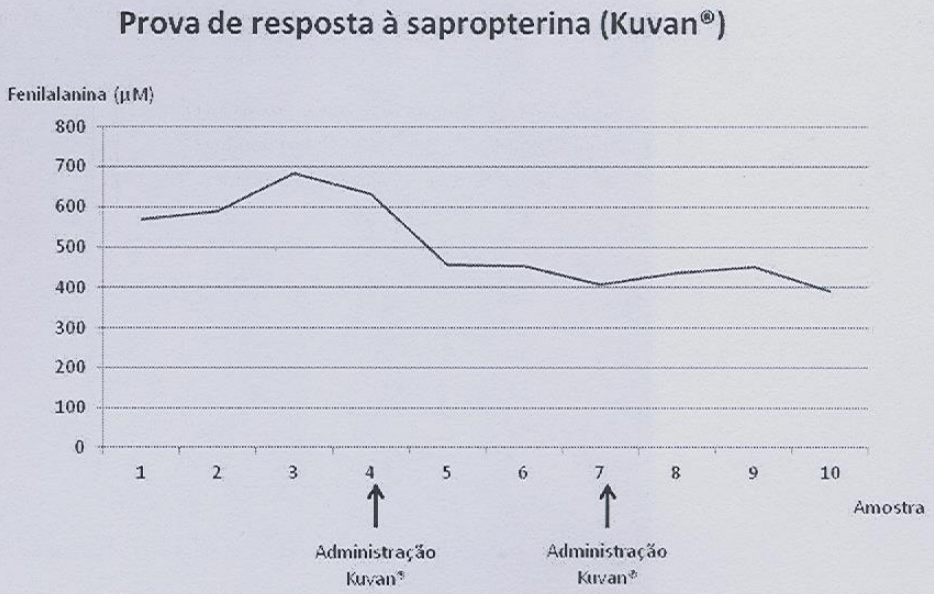


SPDM – Sociedade Portuguesa de Doenças Metabólicas.

Rocha JC, 2018

BH_4 loading test: May 2015

	Amostra	Resultado
1 -	(Véspera - 8h)	568 µM (9,4 mg/dL)
2 -	(Véspera - 16h)	591 µM (9,7 mg/dL)
3 -	(Véspera - 24h)	685 µM (11,3 mg/dL)
4 -	(Dia 1 - 8h)	632 µM (10,4 mg/dL)
5 -	(Dia 1 - 16h)	458 µM (7,6 mg/dL)
6 -	(Dia 1 - 24h)	453 µM (7,5 mg/dL)
7 -	(Dia 2 - 8h)	407 µM (6,7 mg/dL)
8 -	(Dia 2 - 16h)	438 µM (7,2 mg/dL)
9 -	(Dia 2 - 24h)	450 µM (7,4 mg/dL)
10 -	(Dia 3 - 8h)	390 µM (6,4 mg/dL)



Rocha JC, 2018

Nutritional intake in February 2016 (BH4: 20 mg/kg)

Nutritional intake				
	g	g/kg	Energy (Kcal)	Energy (%)
Natural protein	35,98	0,83	143,92	1,8
Protein equivalent	38,00	0,87	152,00	7,8
Amino acids	45,60	1,05		
Phe (mg)	1766,34	40,61		
Total protein	73,98	1,70	295,92	15,2
Fat	61,30		551,70	28,4
Carbohydrate	266,22		1064,88	54,7
Total energy intake			1945,52	98,3

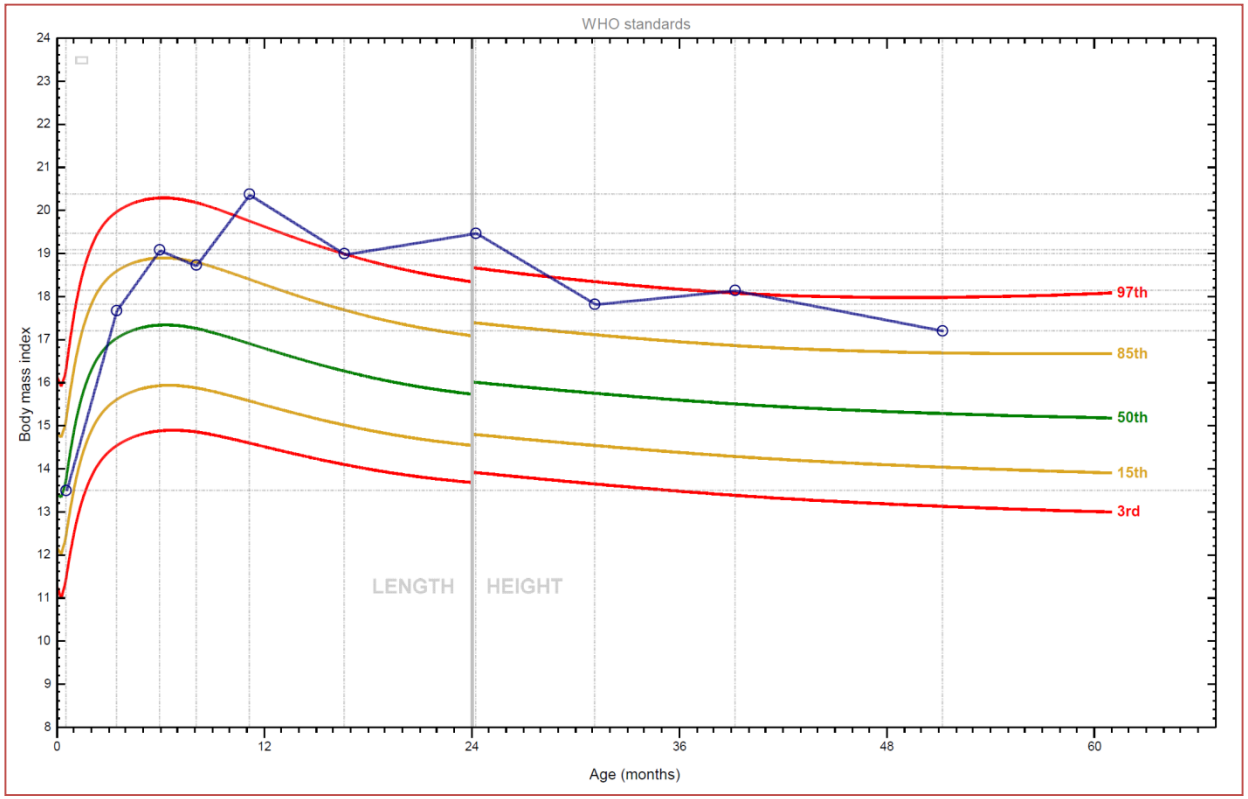
Nutritional intake in February 2017 (BH4: 10 mg/kg)

Nutritional intake				
	g	g/kg	Energy (Kcal)	Energy (%)
Natural protein	31,03	0,62	124,12	1,5
Protein equivalent	38,00	0,76	152,00	7,6
Amino acids	45,60	0,91		
Phe (mg)	1518,84	30,38		
Total protein	69,03	1,38	276,12	13,8
Fat	66,90		602,10	30,0
Carbohydrate	273,87		1095,48	54,6
Total energy intake			2007,02	98,3

Rocha JC, 2018

Infancy

- Danger of tasting not-allowed foods
- BMI rebound; perform BIA when possible - usually after 3 y of age
- Phe levels not a usual problem at this time
- Check the amount of low protein foods ingestion



Rocha JC, 2018

Adolescence: nutritional and lifestyle issues

- **Physical activity**
- **BIA / BMI check**

- **Frequent advices regarding compliance**
  - **What are the real consequences of non-compliance?**
  - **Only increased Phe levels as a major consequence?**
  - **The importance of analysing together the full blood analysis!**

- **Waist circumference monitoring – where is body fat located? Obesity does not represent always the same risk!!**
- **To show the evolution of body composition…**

Rocha JC, 2018

Late adolescence / young adult: case report

- Young female with PKU, **18y 10m**
- Beginning of treatment at 18th day of life

- $[Phe]_{blood}$ at NBS: **21 mg/dL**
- $[Phe]_{blood}$ when treatment began: **27.4 mg/dL**

- Genotype: **R270K / IVS10-11 G>A**

Rocha JC, 2018

Nutrition appointment: 9th September 2009

- Body weight: 51 kg; Height: 1.63 m; BMI: 19.2 kg/m^2; WC: 80.7 cm
- Body fat: 25.3% (12.9 kg)
- Blood pressure: 105/51 mm Hg

- **Natural protein intake:** 11.7 g (potatoes, fruits, vegetables)
- **Protein substitute:**

  not taking despite last prescription in April 2009: 1.05 g aa/kg bw
- **Total energy intake:** 1800 kcal/day
- **Not taking any vitamin and mineral supplements, despite prescription**

Blood analytical results: 9th September 2009

	Result	Normal range
Haemoglobin (g/L)	133	120-170
Red cells (x10^{12}/L)	4.14	4.0-5.0
Hematocrit (L/L)	0.388	0.370-0.490
MCV (fL)	93.7	87.0-103.0
Blood iron (µg/dL)	145	37-145
Ferritin (ng/mL)	35	6-159
Transferrin (mg/dL)	269	200-360
Iron binding capacity (µg/dL)	327	112-346
Folic acid (µg/L)	1.9	3.0-17.0
Vitamin B_{12} (pmol/L)	120	128-648
Vitamin B_6 (nmol/L)	63.5	20-101

	Result	Normal range
Prealbumin (mg/dL)	28.1	>20 (adults)
Albumin (g/L)	39	35-52
Retinol Bindong Protein (mg/dL)	5.9	3.0-6.0
Zinc (µg/dL)	202.2	50-141
Erythrocyte DHA (%)	2.23	3.1-8.5
C-reactive protein (mg/L)	0.8	0-5
Phenylalanine (mg/dL)	17.8	2-8
Tyrosine (µmol/L)	33	25-60
Total homocysteine (µmol/L)	116.6	4.2-14.6

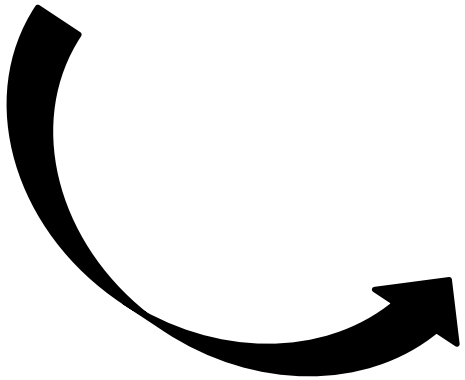
Rocha JC, 2018

Treatment outcome: December 2009

Treatment during 2 months:

Oral vitamin B_{12} (cianocobalamin) tablets:
1mg / day

Folic acid tablets:
2.5mg / day

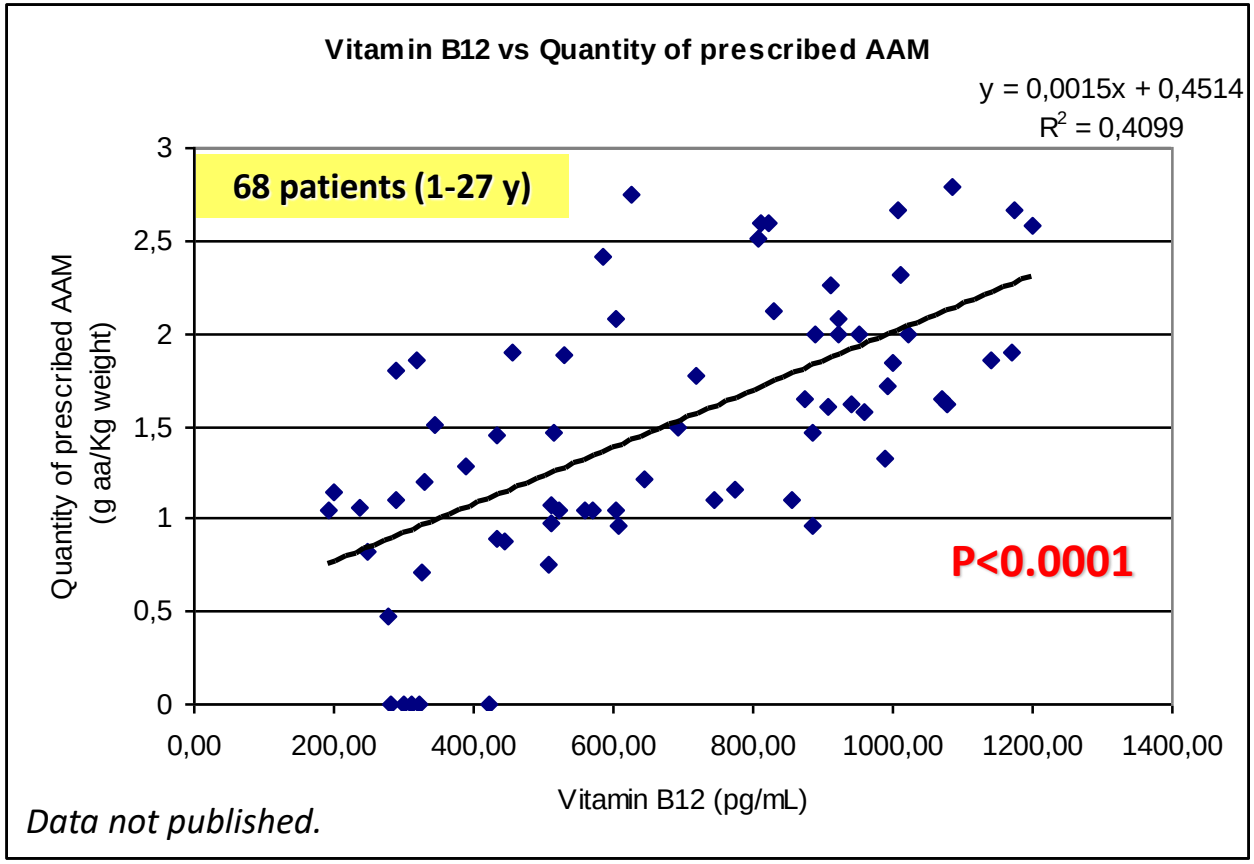


Blood	Result	Normal range
Total homocysteine (μmol/L)	7.0	4.2-14.6
Phenylalanine (mg/dL)	**16.8**	2-8
Tyrosine (μmol/L)	**24**	25-60
Folic acid (μg/L)	**20.0**	3.0-17.0
Vitamin B_{12} (pmol/L)	359	128-648

Urine – organic acids
Increased amounts of:
Phenyllactate
3-hydroxy-phenyllactate
2-hydroxy-phenyllactate

Rocha JC, 2018

Vitamin B12 levels: the importance of compliance



Data not published.

↓ B_{12}, B_6 and Folate
Bad AAM compliance
+
Option for low protein foods

Megaloblastic anemia

↑ [homocysteine]

Feillet F and Agostoni C. *J Inherit Metab Dis*, 2010

Rocha JC, 2018

Molecular Genetics and Metabolism Reports 13 (2017) 105–110

Case Report

Dietary management of maternal phenylketonuria with glycomacropeptide and amino acids supplements: A case report

A. Pinto[a], M.F. Almeida[a,b,c], A. Cunha[c], C. Carmona[a,b,c], S. Rocha[c], A. Guimas[c], R. Ribeiro[c], C.R. Mota[d], E. Martins[b,c], A. MacDonald[e], J.C. Rocha[a,c,f,g,*]

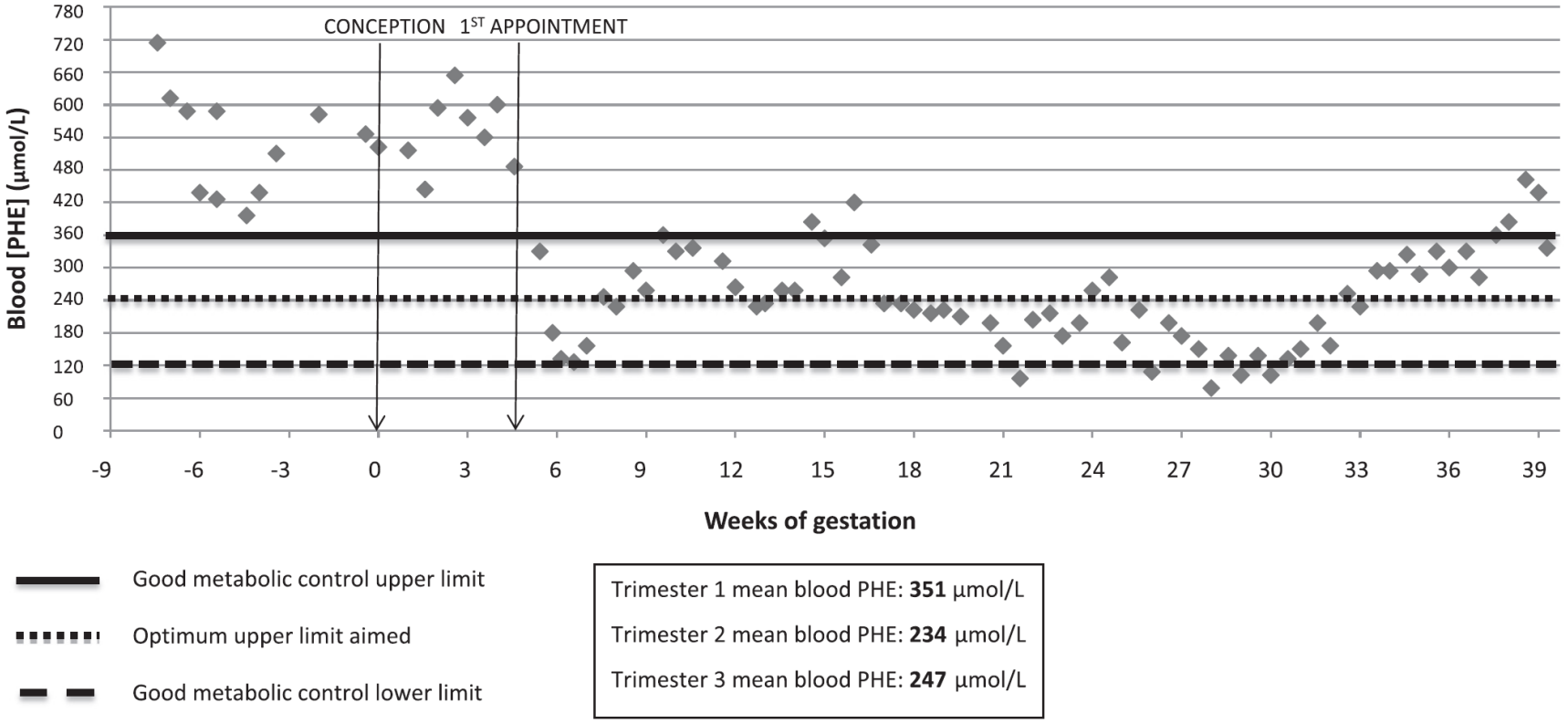


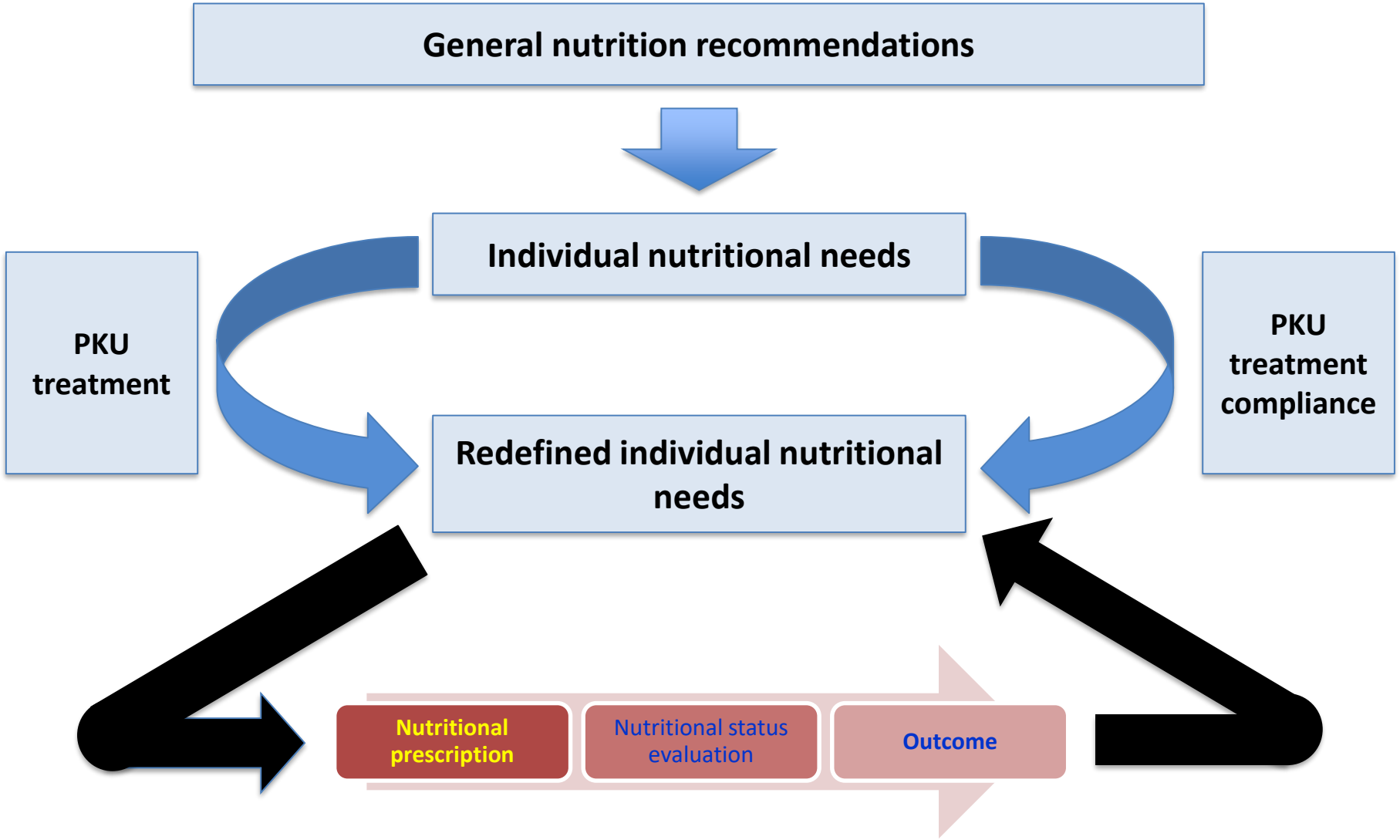
Fig. 2. Blood PHE concentrations (µmol/L) during pregnancy.

Agenda

1. **Introduction**
2. **Current management practices**
3. **Nutritional status**
4. Medical treatment
5. Conclusion

Rocha JC, 2018

Dietary management in PKU



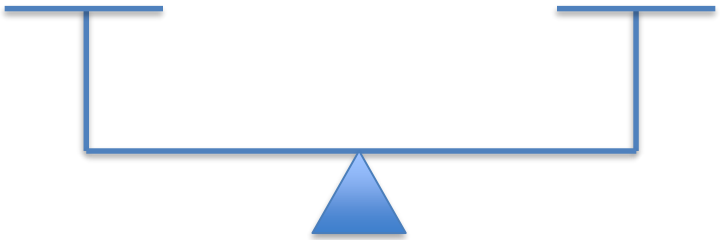
Rocha JC, 2018

Nutritional status in patients with PKU

Micronutrients bioavailability?

How disease affects nutrient needs?

Special low protein foods 'without ' micronutrients!



If Phe tolerance optimized?

Micronutrient intake is mainly defined by PS prescription!

What is the impact of other treatment options / strategies, e.g., LNAA, GMP or sapropterin?

PS – protein substitute
SLPF – special low protein food
LNAA – large neutral amino acids
GMP – glycomacropeptide

Rocha JC and MacDonald A. Dietary intervention in the management of phenylketonuria: current perspectives. Journal of Pediatric Health, Medicine and Therapeutics. 2016:7 155–163

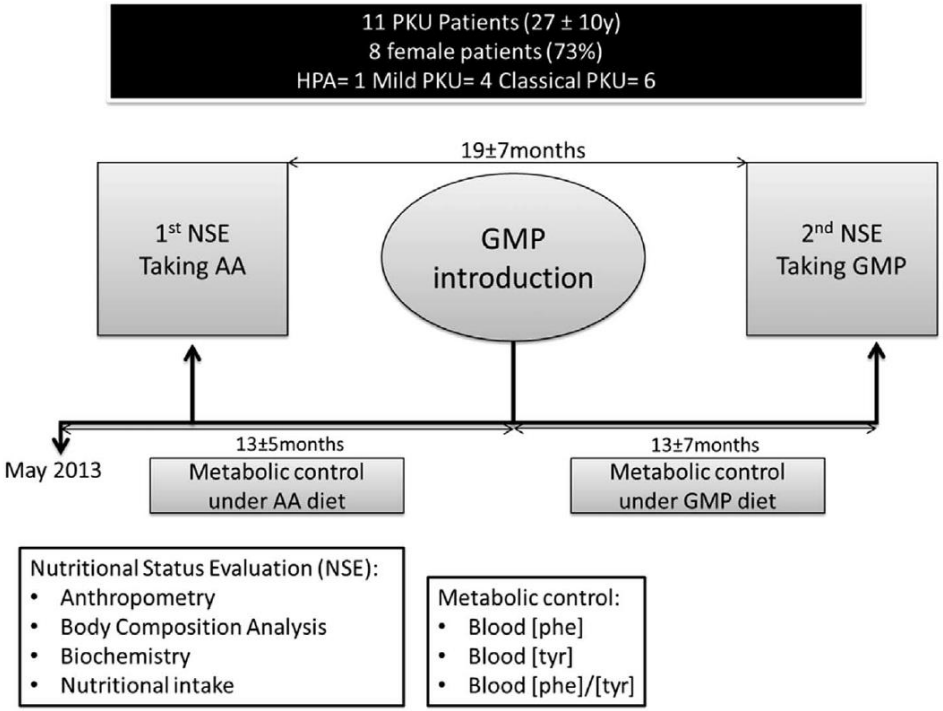
European Journal of Clinical Nutrition (2017), 1–5

www.nature.com/ejcn

ORIGINAL ARTICLE

Nutritional status in patients with phenylketonuria using glycomacropeptide as their major protein source

A Pinto[1], MF Almeida[1,2], PC Ramos[1], S Rocha[3], A Guimas[3], R Ribeiro[3], E Martins[3], A Bandeira[3], A MacDonald[4] and JC Rocha[1,5,6]



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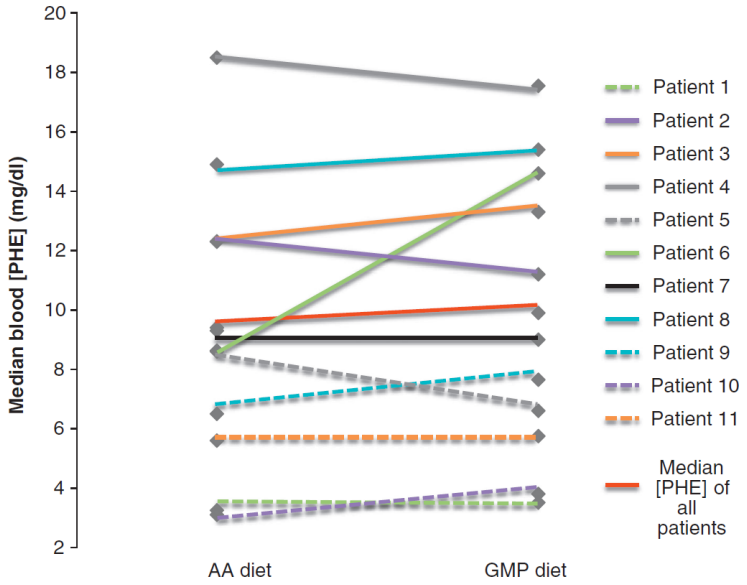

Figure 2. Blood [PHE] of patients with PKU taking AA vs GMP. AA, L-amino acid supplements; GMP, glycomacropeptide-based protein substitute; PHE, phenylalanine; PKU, phenylketonuria.

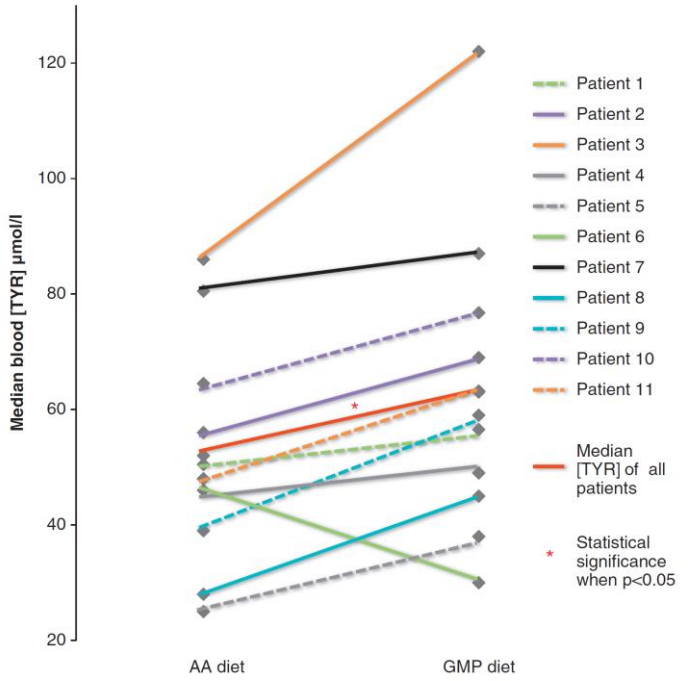

Figure 3. Blood [TYR] of patients with PKU taking AA vs GMP. AA, L-amino acid supplements; GMP, glycomacropeptide-based protein substitute; PKU, phenylketonuria; TYR, tyrosine.

Table 2. Nutritional intake, metabolic control, anthropometry and body composition of patients with PKU taking AA vs GMP

Nutritional intake	*AA diet*	*GMP diet*	P
Natural protein intake (g/kg/day)	0.47 ± 0.27	0.59 ± 0.49	0.241
Protein substitute (g/kg/day)	0.85 (0.73–1.08)	0.75 (0.61–0.99)	0.182
PHE intake (mg/day)	1269 ± 847	1575 ± 1217	0.425
TYR intake from protein substitute (g/day)	5.18 ± 1.77	4.37 ± 1.68	0.259
PHE intake from protein substitute (mg/day)	0	33.8 ± 11.7	—
Leucine intake from protein substitute (g/day)	6.02 ± 1.73	6.94 ± 2.10	0.282
Protein (%)	13.8 ± 2.3	14.4 ± 3.1	0.384
Fat (%)	26.9 ± 5.0	28.2 ± 2.9	0.317
Carbohydrate (%)	57.0 (52.1–60.1)	58.4 (54.8–58.9)	0.594
Energy (kcal)	2277 ± 551	2222 ± 421	0.690
Metabolic control			
Median blood (PHE) (mg/dl)	8.6 (5.6–12.3)	9.0 (5.8–14.6)	0.594
s.d. blood (PHE) (mg/dl)	2.3 ± 0.8	2.2 ± 1.1	0.563
Median blood (TYR) (μmol/l)	52.0 ± 19.2	63.2 ± 25.6	**0.033**
s.d. blood (TYR) (μmol/l)	19.3 ± 13.9	18.3 ± 9.3	0.812
Median blood (PHE)/(TYR)	10.4 (7.1–23.0)	7.5 (5.6–20.3)	**0.041**
Anthropometry and body composition			
Weight (kg)	60.4 ± 15.2	62.1 ± 15.1	0.112
Height (cm)	161.0 (154.5–163.3)	161.0 (154.5–165.0)	0.317
WC (cm) ($n = 10$)	86.2 ± 15.5	87.5 ± 14.7	0.481
BMI (kg/m^2)	24.0 ± 6.0	24.4 ± 6.5	0.367
Body fat (kg) ($n = 9$)	17.3 ± 13.5	19.6 ± 14.4	0.099
Body fat (%) ($n = 9$)	25.5 ± 16.1	28.6 ± 15.0	0.174
Lean mass (%) ($n = 9$)	74.5 ± 16.1	71.4 ± 15.0	0.174
Phase angle ($n = 9$)	6.8 ± 0.7	6.7 ± 0.7	0.684

Pinto A, *et al*. Nutritional status in patients with phenylketonuria using glycomacropeptide as their major protein source. European Journal of Clinical Nutrition. 2017 71(10):1230-1234.

Rocha JC, 2018

CINTESIS Health. Research.

Table 4. Blood pressure and biochemical data of patients with PKU taking AA vs GMP

	AA diet	*GMP diet*	P
Systolic blood pressure (mm Hg) ($n = 10$)	115.5 ± 8.5	114.5 ± 13.4	0.724
Diastolic blood pressure (mm Hg) ($n = 10$)	62.3 ± 14.1	58.3 ± 8.6	0.423
Heart rate (beats per minute) ($n = 10$)	71.1 ± 7.1	75.0 ± 12.7	0.298
Uric acid (mg/dl)	4.0 ± 0.8	4.0 ± 1.0	0.881
Glucose (mg/dl)	78.2 ± 6.8	75.8 ± 5.4	0.296
Creatinine (mg/dl)	0.7 ± 0.1	0.7 ± 0.1	0.666
Urea (mg/dl)	20.5 ± 7.6	24.8 ± 5.3	0.050
Haemoglobin A1C (%) ($n = 10$)	5.1 ± 0.4	5.0 ± 0.3	**0.011**
Total cholesterol (mg/dl)	165 ± 37	160 ± 38	0.613
Triglycerides (mg/dl)	84 ± 27	89 ± 47	0.587
HDL (mg/dl)	55 ± 14	51 ± 9	0.143
LDL (mg/dl)	93 ± 32	91 ± 34	0.789
VLDL (mg/dl)	17 ± 6	18 ± 10	0.574
ApoA1 (mg/dl) ($n = 10$)	153 ± 25	144 ± 23	0.184
ApoB (mg/dl) ($n = 10$)	82 ± 22	88 ± 23	0.199

Pinto A, *et al*. Nutritional status in patients with phenylketonuria using glycomacropeptide as their major protein source. **European Journal of Clinical Nutrition**. 2017 71(10):1230-1234.

Rocha JC, 2018

CINTESIS Health. Research.

Table 4. Blood pressure and biochemical data of patients with PKU taking AA vs GMP

	AA diet	*GMP diet*	P
Transferrin (mg/dl)	271 ± 43	262 ± 39	0.520
Ferritin (ng/ml)	56 [43–81]	59 [36–69]	0.262
Albumin (g/dl)	4.69 ± 0.33	4.69 ± 0.21	0.971
Homocysteine (μmol/l) ($n = 8$)	8.44 ± 1.51	7.84 ± 1.14	0.411
Prealbumin (mg/dl)	249 ± 28	245 ± 53	0.770
C-reactive protein (mg/dl) ($n = 10$)	1.95 ± 2.18	2.12 ± 1.76	0.757
Insulin (μU/ml) ($n = 8$)	9.65 ± 3.77	12.38 ± 6.65	0.080
Calcium (mmol/l)	2.37 ± 0.12	2.34 ± 0.09	0.279
Phosphorus (mmol/l)	1.07 ± 0.24	0.99 ± 0.15	0.202
Zinc (μmol/l)	13.16 ± 3.44	12.38 ± 1.86	0.510
Vit. B_{12} (pg/ml)	641 ± 340	665 ± 389	0.672
Vit. D (nmol/l)	77 ± 26	72 ± 27	0.274
Folic acid (ng/ml)	13.4 ± 3.9	14.9 ± 4.7	0.395
Haemoglobin (g/dl) ($n = 8$)	14.2 ± 1.2	13.8 ± 0.7	0.159

Pinto A, *et al*. Nutritional status in patients with phenylketonuria using glycomacropeptide as their major protein source. European Journal of Clinical Nutrition. 2017 71(10):1230-1234.

Agenda

1. Introduction
2. Current management practices
3. Nutritional status
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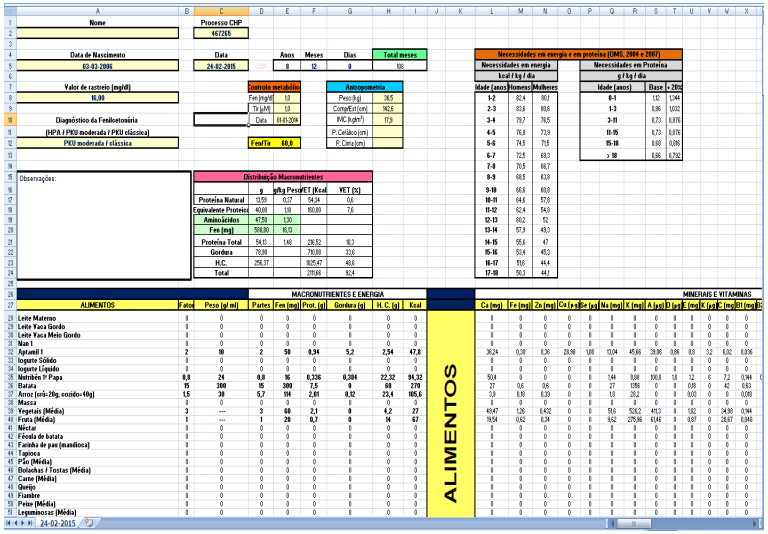
Do we really know the real patient's ingestion?



Evidence of underestimated natural protein tolerance in patients with Phenylketonuria

Rocha JC[1,2,3], Pinto A[1], Ramos PC[1], Rocha S[4], Guimas A[4], Ribeiro R[4], Martins E[4,5], Bandeira A[4], van Spronsen FJ[6], Almeida MF[1,5]

[1] Centro de Genética Médica JM, CHP EPE, Porto, Portugal; [2] Faculdade de Ciências da Saúde, UFP, Porto, Portugal; [3] Center for Health Technology and Services Research (CINTESIS); [4] Unid Doen Heredit Metab, CHP, EPE, Porto, Portugal; [5] UMIB/ICBAS/UP, Porto, Portugal; [6] Beatrix Children's Hospital, UMCG, Groningen, The Netherlands.

Poster presentation at the SSIEM 2015 in Lyon

J Inherit Metab Dis (2015) 38 (Suppl 1):S92–S93.

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[1] Centro de Genética Médica JM, CHP EPE, Porto, Portugal; [2] Faculdade de Ciências da Saúde, UFP, Porto, Portugal; [3] Center for Health Technology and Services Research (CINTESIS); [4] Unid Doen Heredit Metab, CHP, EPE, Porto, Portugal; [5] UMIB/ICBAS/UP, Porto, Portugal; [6] Beatrix Children's Hospital, UMCG, Groningen, The Netherlands.

Dietary intake in the two different nutrition appointments.

	First appointment	Second appointment	
Natural protein intake (g/kg)	0.84 [0.46-1.50]	0.92 [0.53-1.65]	p=0.002
Protein equivalent from protein substitute (g/kg)	0.77 [0.49-1.10]	0.75 [0.36-1.00]	p<0.001

NP intake increased in:

- 72.7% of patients with hyperphenylalaninemia (HPA);
- 61.3% of patients with mild PKU;
- 57% of patients with classical PKU.

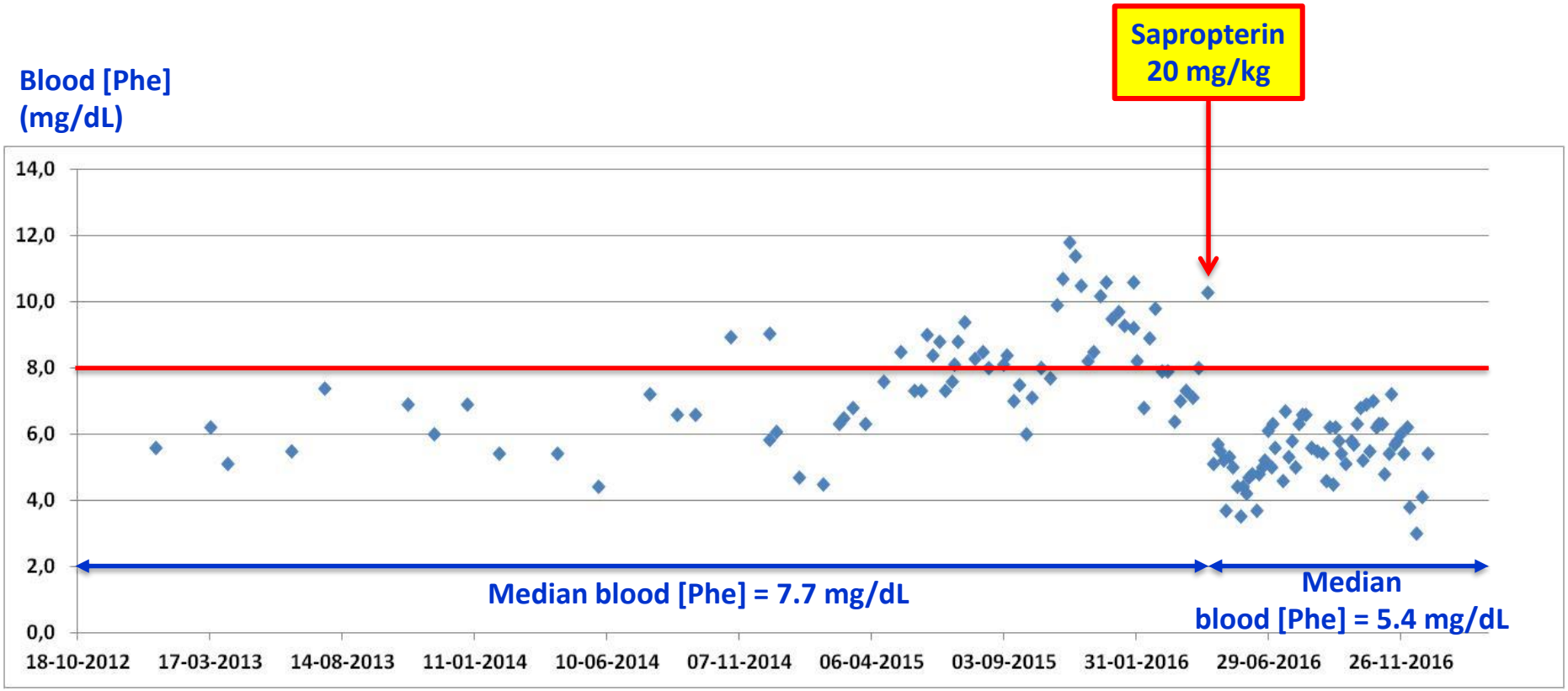
Rocha JC, 2018

Metabolic control and sapropterin

	Diet treatment	Diet treatment + sapropterin treatment	Sapropterin treatment
Metabolic control	**Within** target range	**To keep within target range**	**To keep within target range**
	Out of target range	**To optimize towards target range**	**To optimize towards target range**

Rocha JC, 2018

Metabolic control before and after sapropterin



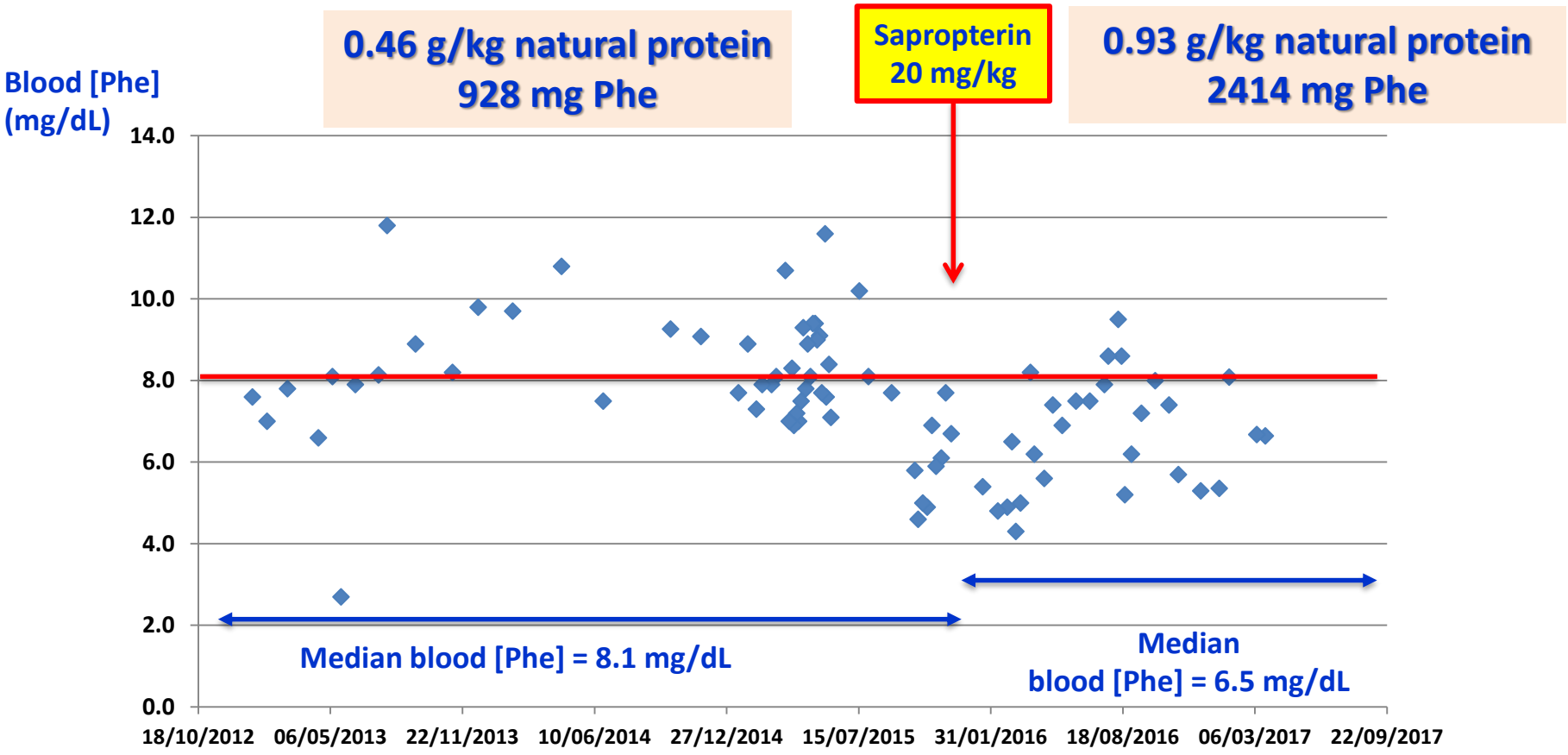
- 29 year old male
- Loading test response: **64% decrease**
- **R408W / Y414C**

Standard deviation:
Before sapropterin: 1.7 mg/dl
After sapropterin: 0.9 mg/dl

% of blood Phe measurements in target range:
Before sapropterin: 53 %
After sapropterin: 100%

Rocha JC, 2018

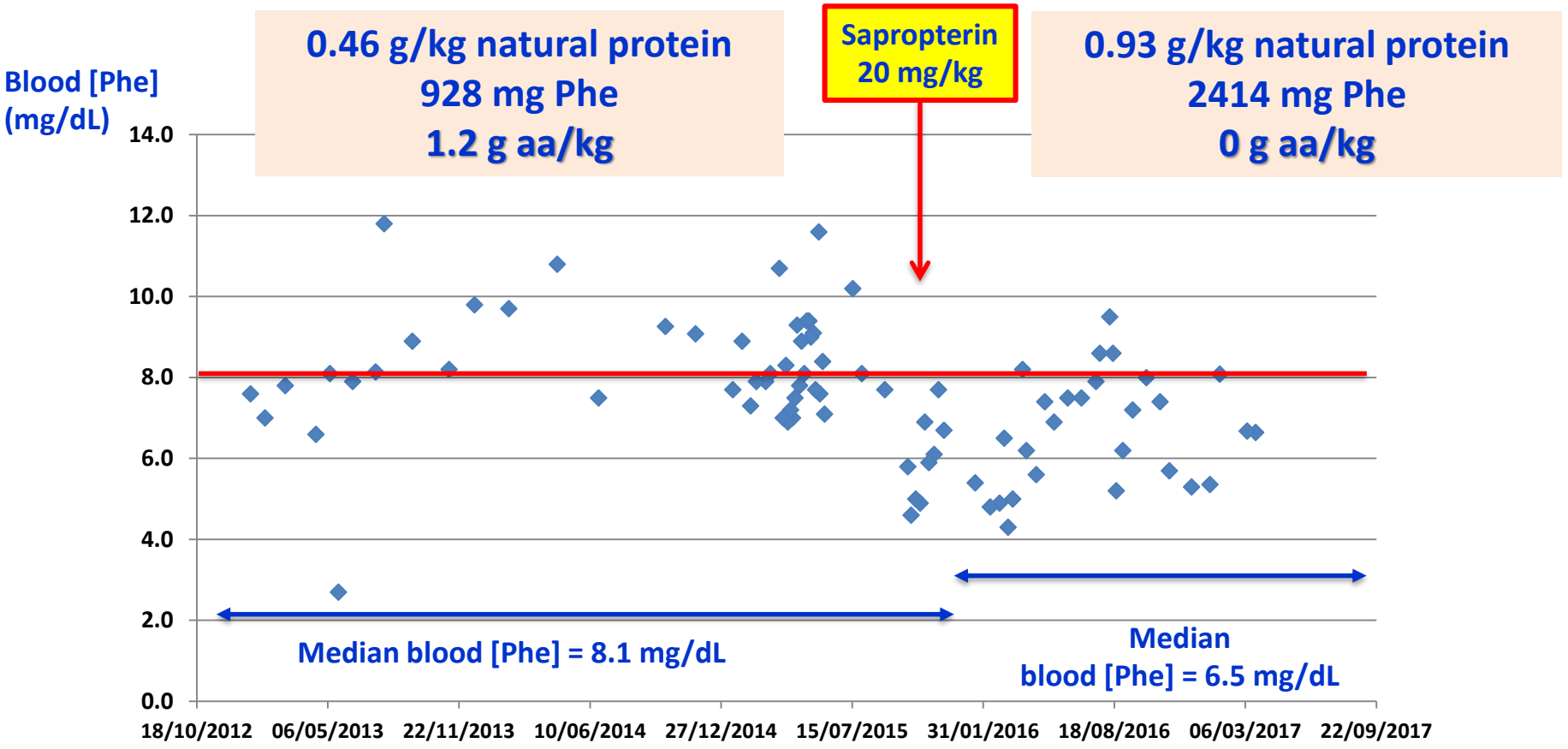
Protein intake before and after sapropterin



- 19 year old female
- Loading test response: **67% decrease**
- **R261Q / V388M**

Rocha JC, 2018

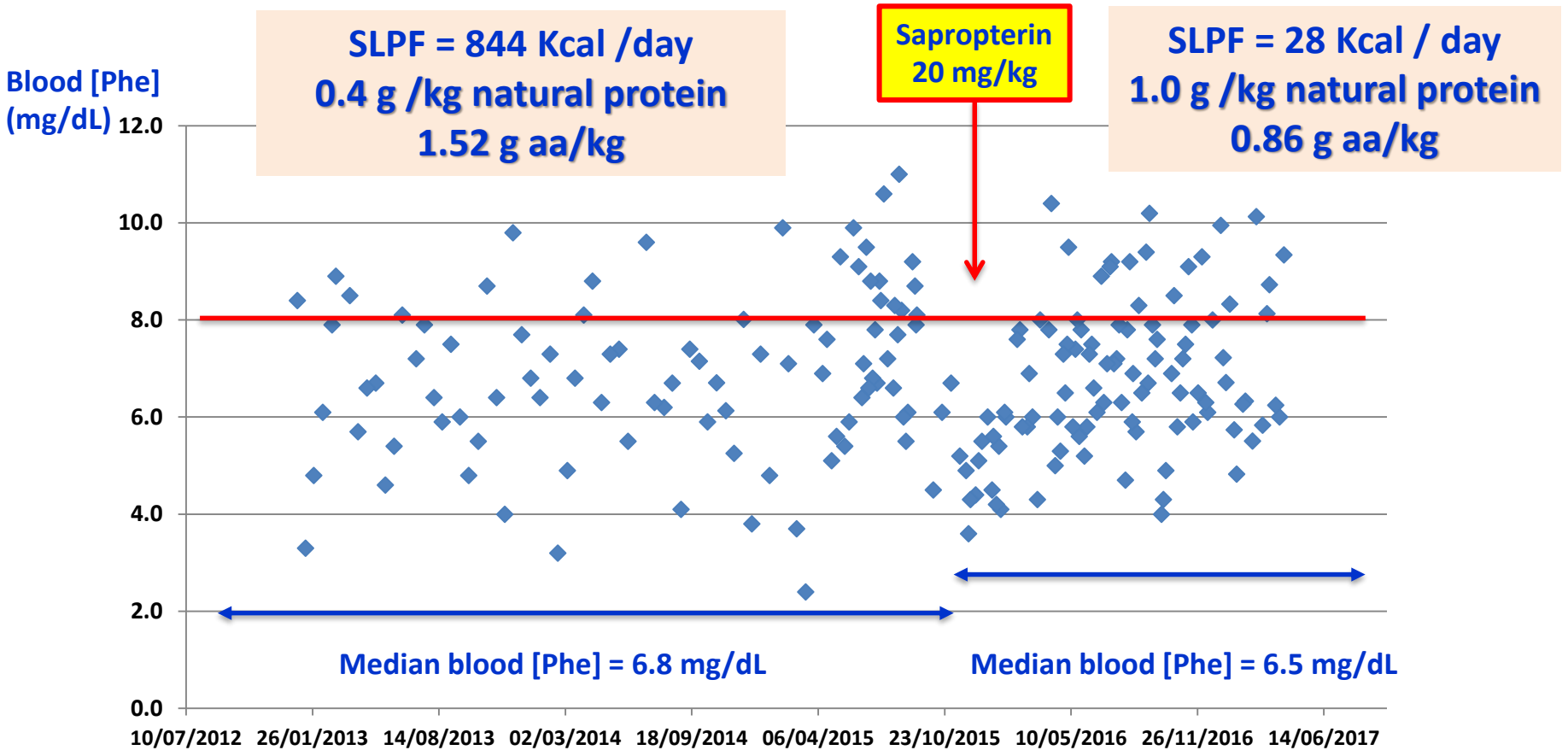
Protein substitute before and after sapropterin



- 19 year old female
- Loading test response: **67% decrease**
- **R261Q / V388M**

Rocha JC, 2018

SLPF intake before and after sapropterin



- 15 year old female
- Loading test response: **40% decrease**
- **R261Q / R261Q**

Rocha JC, 2018

Transition to a new food pattern in PKU…

Pediatric Health, Medicine and Therapeutics

Dovepress

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REVIEW

Dietary intervention in the management of phenylketonuria: current perspectives

Júlio César Rocha[1-3]
Anita MacDonald[4]

Pediatric Health, Medicine and Therapeutics 2016:7 155–163

New treatments – new needs!

Rocha JC, 2018

Obesity should be prevented!

Review Article

Annals of Nutrition & Metabolism

Ann Nutr Metab 2016;68:60–65
DOI: 10.1159/000442304

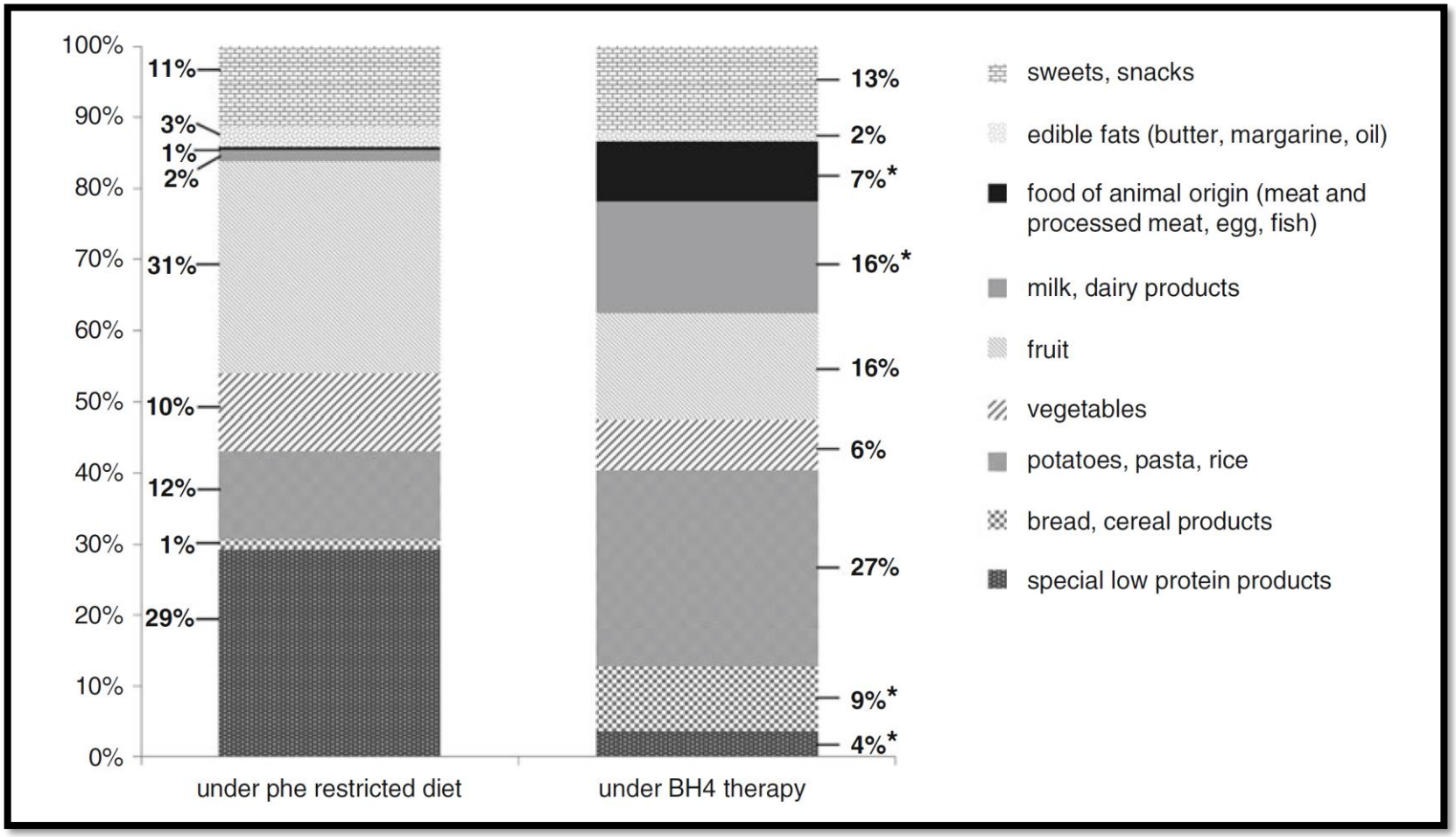
Received: August 3, 2015
Accepted after revision: November 5, 2015
Published online: November 25, 2015

Weight Management in Phenylketonuria: What Should Be Monitored?

Julio César Rocha[a–c] Margreet van Rijn[d] Esther van Dam[d] Kirsten Ahring[e]
Amaya Bélanger-Quintana[f] Katharina Dokoupil[g] Hulya Gokmen Ozel[h]
Anna Maria Lammardo[i] Martine Robert[j] Carina Heidenborg[k]
Anita MacDonald[l]

Rocha JC, 2018

Nutritional Changes and Micronutrient Supply in Patients with Phenylketonuria Under Therapy with Tetrahydrobiopterin (BH4).



Thiele AG, *et al*. JIMD Rep, 2013; 9:31-40

Rocha JC, 2018

Nutritional status in PKU

The major source of micronutrients is from supplemented Phe-free L-amino acids and if the intake of Phe-free L-amino acid supplements is suboptimal, this will increase the risk of micronutrient deficiency (e.g. iron, zinc, selenium and vitamin B12).

van Wegberg AM, *et al*. The complete European guidelines on phenylketonuria: diagnosis and treatment. Orphanet Journal of Rare Diseases. 2017:12(1):162

British Journal of Nutrition (2011), page 1 of 8
doi:10.1017/S0007114511000298

Review Article

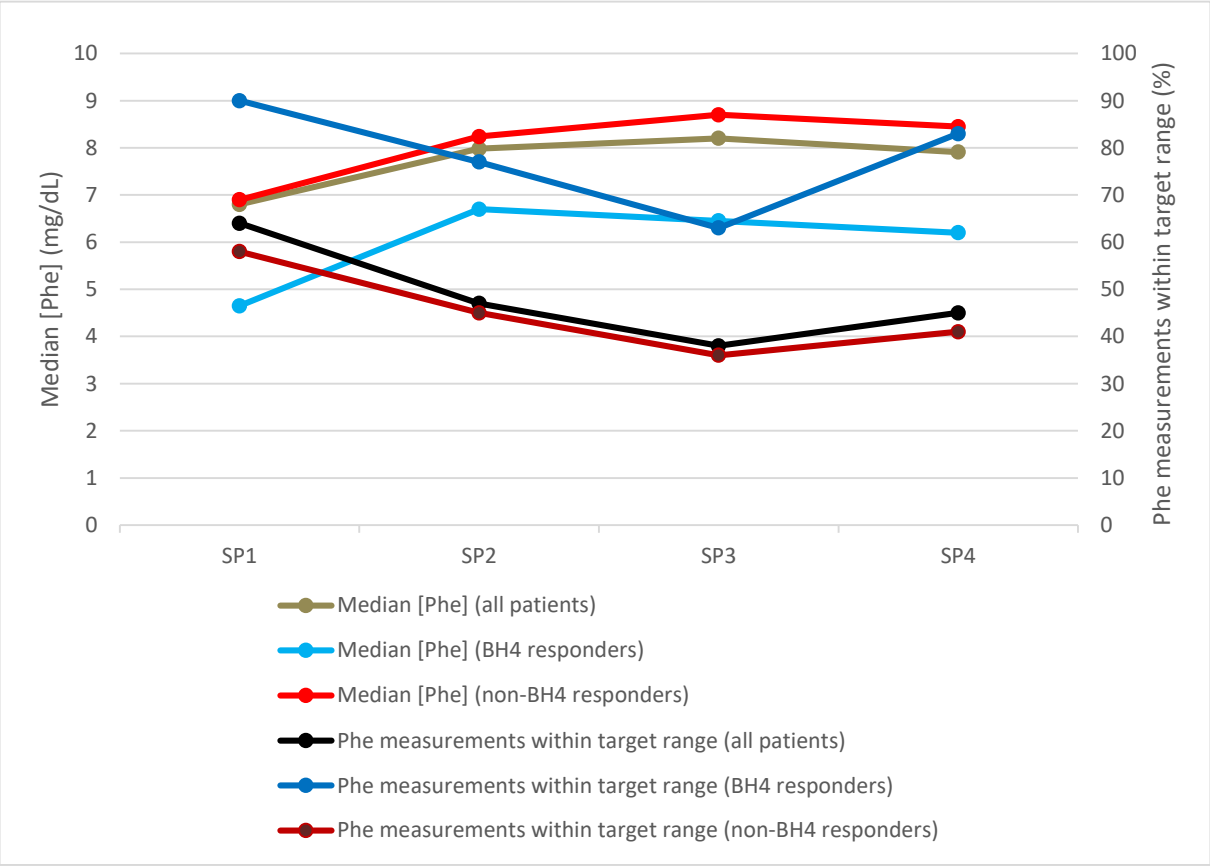
Adjusting diet with sapropterin in phenylketonuria: what factors should be considered?

Anita MacDonald[1]*, Kirsten Ahring[2], Katharina Dokoupil[3], Hulya Gokmen-Ozel[4], Anna Maria Lammardo[5], Kristina Motzfeldt[6], Martine Robert[7], Júlio César Rocha[8], Margreet van Rijn[9] and Amaya Bélanger-Quintana[10]

EPG 2017 recommendation:

To double natural protein intake!
But what about its quality?
Distribution through the day?
Other nutritional prescription?

What about metabolic control in BH4 non responders?



Sousa Barbosa C, *et al*. Metabolic control in patients with phenylketonuria pre- and post-sapropterin loading test. Journal of Inborn Errors of Metabolism and Screening. 2018. *Accepted manuscript*.

Agenda

1. Introduction
2. Current management practices
3. Nutritional status
4. Medical treatment
5. Conclusion

Conclusion

- Phenylketonuria treatment is one of the medicine's success story

- Nutritional status evaluation is crucial for the dietary management in PKU

- A precise and detailed food history is essential to understand nutritional intake in PKU

- We need to carefully identify patient's individual needs

- Long-term follow-up is crucial to understand the real impact of new therapies

Rocha JC, 2018

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Doutor Ricardo Jorge

CINTESIS Health.Research.

Thank you very much for inviting me to come to Romania!