



Quarte  
**Giornate  
Romane**  
PEDIATRIA  
ON LINE

10 - 12 OTTOBRE 2019  
Auditorium Aragonarium - Roma



# Il pediatra di famiglia ed il bambino con malattia cronica

## Le malattie endocrine Gianpaolo De Filippo

ASSISTANCE PUBLIQUE  HÔPITAUX DE PARIS

Centre de référence  
des maladies endocriniennes  
de la croissance et du développement



European  
Reference  
Networks

centre de référence  
maladies rares

Hôpital universitaire  
mère-enfant  
Robert-Debré

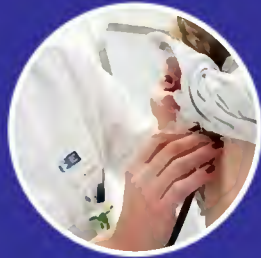


**L educazione terapeutica**, come definito dall'OMS, dovrebbe permettere al paziente di acquisire e mantenere le capacità e le competenze che lo aiutano a vivere in maniera ottimale con la sua malattia

1. Elaborare una diagnosi educativa
2. Definire un programma personalizzato
3. Pianificare e realizzare le sedute
4. Realizzare una valutazione delle competenze acquisite



Paziente



Pediatria  
di famiglia



Ospedale



# Patologie endocrine croniche

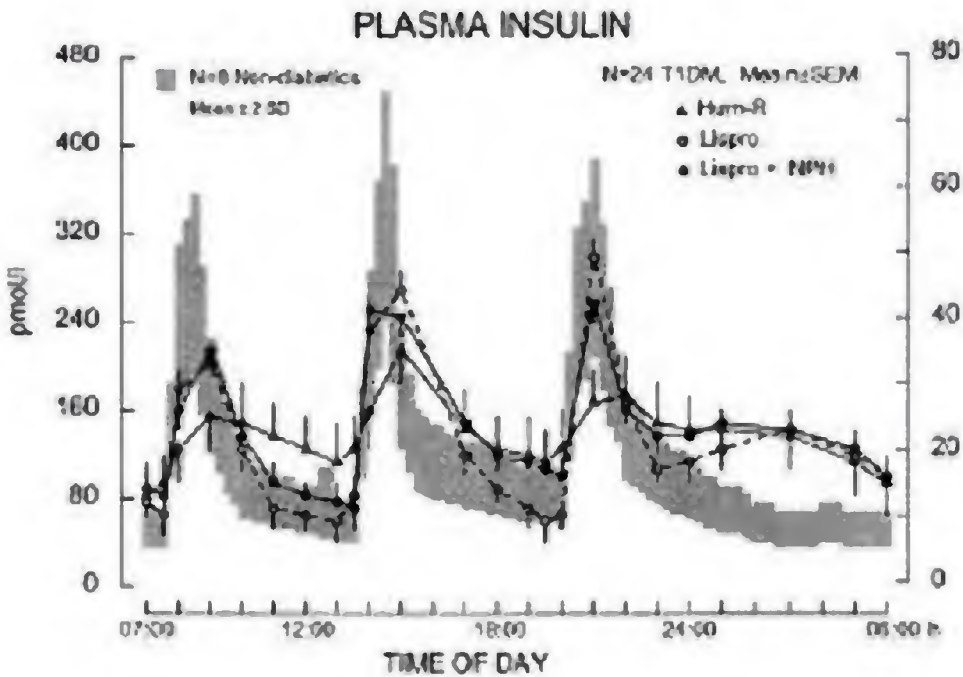
- Diabete mellito
- Insufficienza surrenalica

Obesità – sindrome metabolica

- Ipotiroidismo congenito
- Tiroidite di Hashimoto
- Ipogonadismo
- Deficit di ormone della crescita



# Diabete di tipo 1



Insulina aspart per via s.c.: picco 1-3 ore, durata d'azione 3-5 ore

Insulina Glargine: durata d'azione 24 ore

Insulina aspart per via s.c. tramite microinfusore : < 5 minuti



**Presentation**

97% overweight or obese



Symptomatic at presentation



Symptoms of hyperglycaemia in 67%

DKA in 6-11%  
HSS in 2%

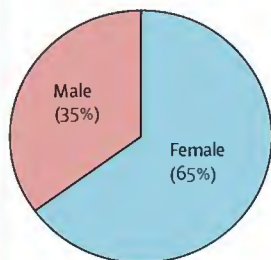
86% with acanthosis nigricans



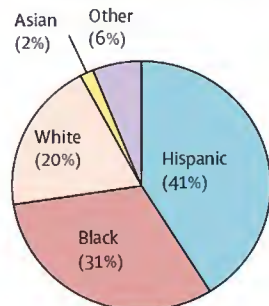
**Characteristics**

65-70% are female in all cohorts; ethnic minorities are predominantly affected, although ethnic groups vary by country

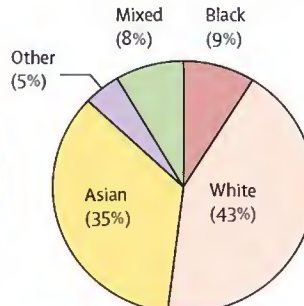
Sex



Ethnicity (TODAY cohort, USA)



Ethnicity (NPDA cohort, USA)



Family history of type 2 diabetes in 90%

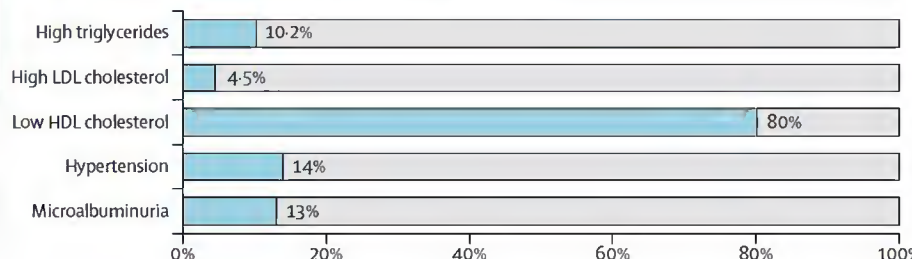


Type 2 diabetes in nuclear family (60%)

Type 2 diabetes in grandparents (30%)

**Complications at diagnosis**

Complications are common at diagnosis in adolescent type 2 diabetes



**Europa**

Prevalenza  
0,04/1000

Incidenza annuale  
1,52/100,000

**Stati Uniti**  
0,46/1000  
5,089/100.000

*Insitut de veille sanitaire 2002*

*Viner et al. 2017*

*Hannon & Arslanian, 2019*

## Characteristics of Type 2 Diabetes in Youth and Adults

Characteristic	Youth in TODAY	Adults
Obesity	Common Poor response to intensive lifestyle change program	Common Lifestyle change programs more effective in older adults
Pancreatic beta cell function	20–35% decline per year	7–11% decline per year
Initial therapeutic response to metformin monotherapy	Poor durability of glycemic control in approximately half of youth	Durability of glycemic control better in older adults
Microalbuminuria	6.3% at baseline 16.6% by 4 years Long-term data unavailable	38% of UKPDS participants after 15 yrs <sup>34</sup> ; Diabetic nephropathy occurs in 20–40% of adults with type 2 diabetes and is the leading cause of kidney failure in the US <sup>53</sup>
Hypertension	11.6% at baseline 33.8 % over 3.9 years Long-term data unavailable	Common (67% of adults with diabetes <sup>53</sup> )
Dyslipidemia	Triglyceride $\geq 150$ mg/dL or LLM: 23.3% at 3 yrs LDL-chol $< 100$ mg/dL: 55.9% at 3 yrs; LDL-chol $\geq 130$ mg/dL or LLM: 10.7% at 3 yrs Long-term data unavailable	Triglyceride $\geq 150$ mg/dL: $> 50\%$ of adults <sup>54</sup> LDL-chol $< 100$ mg/dL: less than 1/3 of men and 20% of women <sup>54</sup>
Retinopathy	13.7% at 2.8 yrs diabetes duration	12.6% in adults 3 yrs after diagnosis of diabetes
Depressive symptoms	15%	17.6% <sup>55</sup>

### TODAY\* Study

699 partecipanti

10-17 anni

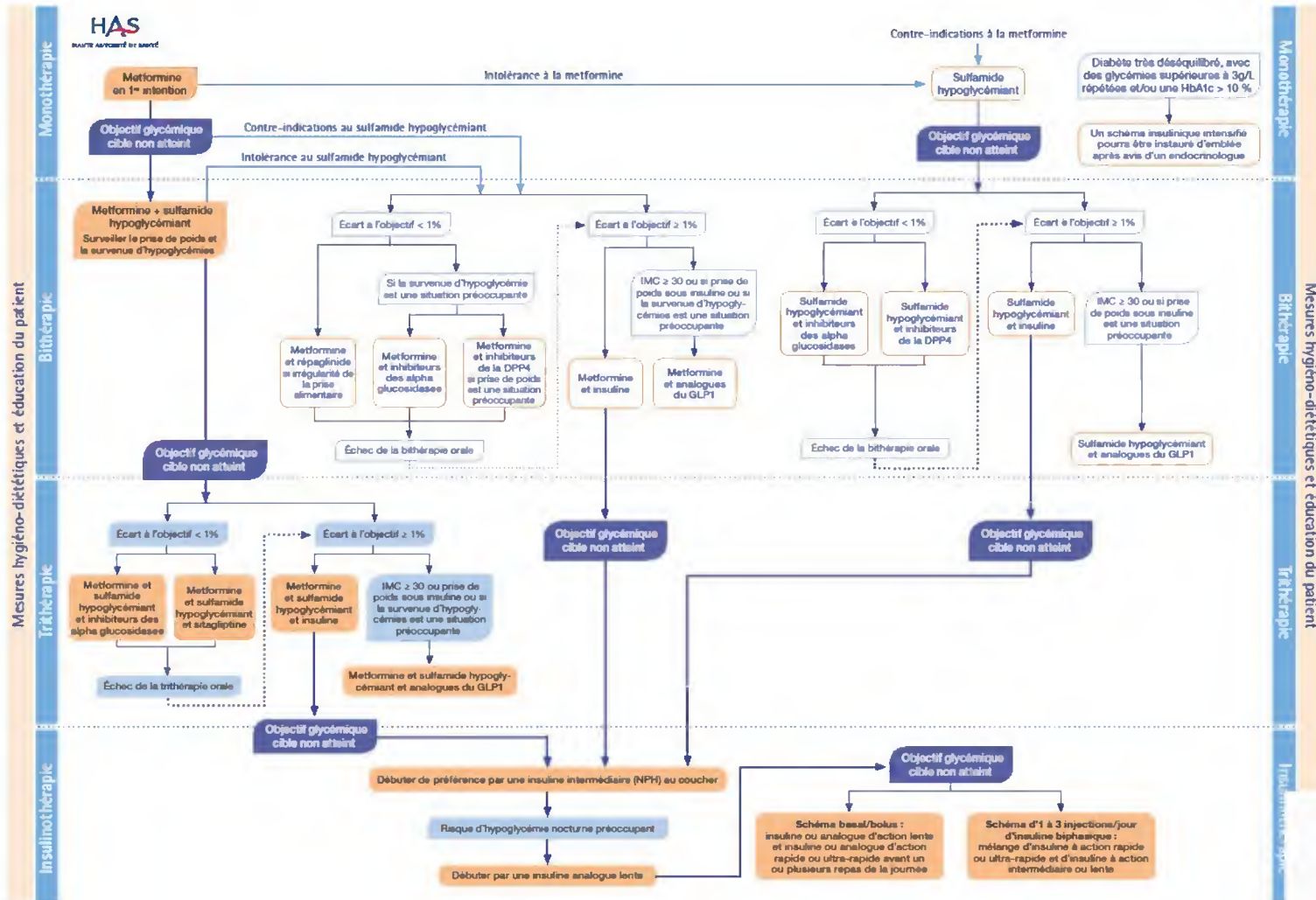
T2D diagnosticato secondo i criteri ADA

Durata della malattia  $\leq 2$  years

\*Treatment Options of Diabetes in Adolescents and Youth



# I bambini (e gli adolescenti) non sono degli adulti in miniatura



## Treatment Guidelines for Type 2 Diabetes

	Youth	Adults
<u>Lifestyle change</u>		
Diet	6–12 years of age: 900–1200 kcal/day 13–18 years of age: ≥1200 kcal/day Increase fruits and vegetables Limit sugary drinks Limit high fat foods, snacks and fast food Consider short-term (10 wks) supervised protein-sparing modified fast if body weight > 120% ideal body weight and there is need for rapid weight loss for a serious medical condition	Individualize Saturated fat <7%; low trans fat. For weight loss: low carbohydrate, low-fat low-calorie or Mediterranean diet Reduce protein if renal disease present (0.8–1.0 gm/kg/day)
Physical activity	Moderate-rigorous ≥ 60 min/day Nonacademic screen time <2 hrs/day	Moderate intensity aerobic ≥ 150 min/wk over ≥3 days/wk Resistance training ≥ 2days/wk
Smoking cessation	Recommended	Recommended
Education (including preconception counseling)	Recommended	Recommended
<u>Glycemic Control</u>		
<u>Medications</u>		
Metformin	Initial therapy. Inexpensive, effective, weight neutral; cau cause diarrhea, abdominal discomfort, anorexia, nausea; effective in half of youth in the TODAY trial	Initial therapy. Inexpensive, effective, weight neutral; cau cause diarrhea, abdominal discomfort, anorexia, nausea; rare lactic acidosis
Sulfonylureas (glyburide, glipizide, glimepiride)	Not approved	Inexpensive, can cause hypoglycemia and weight gain
Meglitinides (repaglinide, nateglinide)	Not approved	Medium cost, short-acting, can cause hypoglycemia and weight gain
DPP-4 inhibitors (sitagliptin, saxagliptin, linagliptin, alogliptin)	Not approved	Expensive, weight neutral, risk of pancreatitis
GLP-1 receptor agonists (exenatide, liraglutide)	Not approved	Injectable, expensive, associated with weight loss, gastrointestinal side effects, risk of pancreatitis
Thiazolidinediones (pioglitazone, rosiglitazone)	Not approved	Rarely used because of adverse effects: weight gain, heart failure, edema, fracture, bladder cancer risk (pioglitazone) and possible increased CVD risk (rosiglitazone)
Alpha glucosidase inhibitors (acarbose, miglitol)	Not approved	Medium cost, moderate efficacy, gastrointestinal side effects
SGLT2 inhibitors (canagliflozin)	Not approved	Expensive, no hypoglycemia; weight loss possible. Risks: genital mycotic and urinary tract infections, hypotension, impaired renal function, hyperkalemia, increased LDL-cholesterol
Insulin	Initial therapy with marked hyperglycemia; main adverse effect is hypoglycemia	Initial therapy with marked hyperglycemia; main adverse effect is hypoglycemia

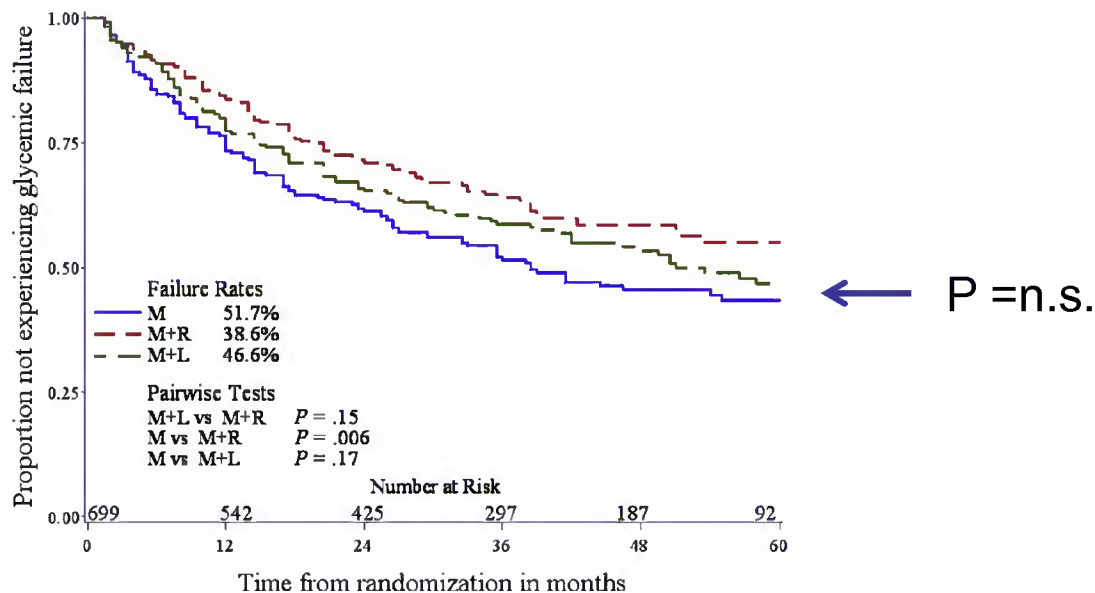




# Intervento dietetico

**Table 1.** Classification of diets based on carbohydrate content (modified from Liebman, 2014 [26]).

Carbohydrate Diet Classification	Amount of Carbohydrate	Example of Dietary Pattern
Typical/high-carbohydrate diets	45%–65% of total calories	Low-fat diet, STOP/Traffic light diet, Standard-protein diet, lower-GI diet
Moderately restricted carbohydrate diets	26%–44% of total calories	Intermittent fasting diet, increased-protein diet
Low-carbohydrate diets	51–130 g/day (or approximately 16%–26% of calories of a 2000 calorie diet)	Low-carbohydrate diet, Paleo style diet
Very low-carbohydrate diets [27–29]	Typically 20–50 g/day or 5%–15% of total calories	Very low-carbohydrate diet, very low-energy diet, Atkins diet



# Obiettivi della terapia iniziale

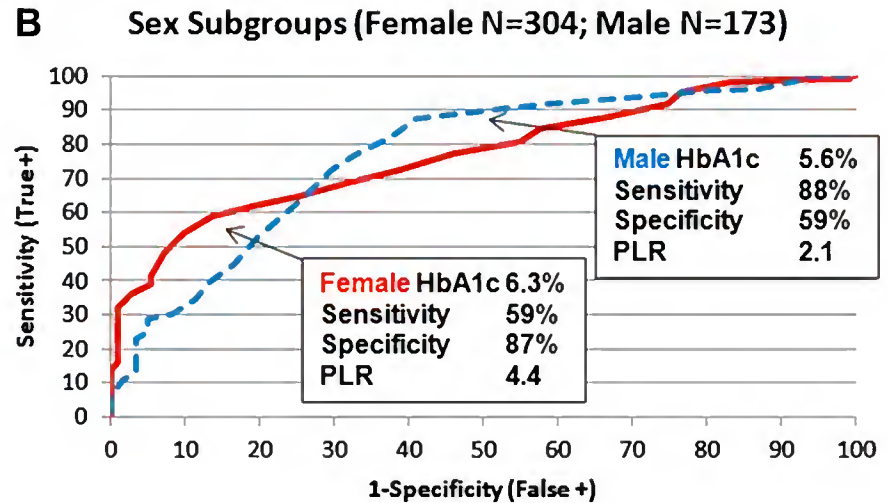
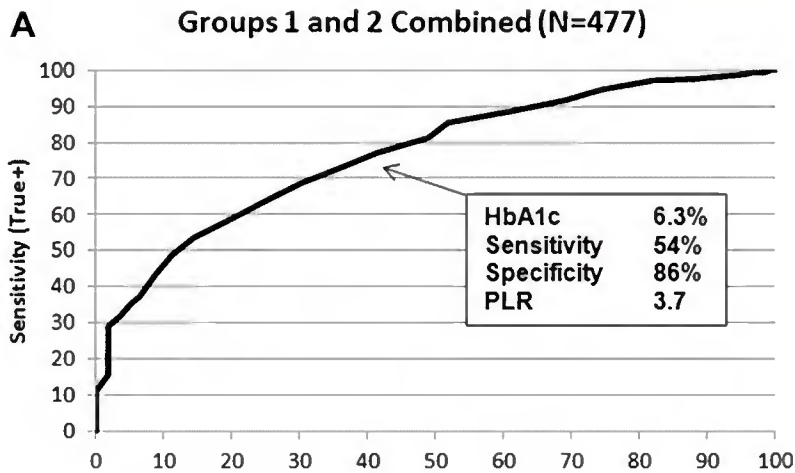
- Ottenere un valore di HbA1c inferiore a 7 %
- In alcune situazioni: 6,5 %

Se il risultato non è ottenuto in 4 (o 6) mesi:  
insulinoterapia basale

Se il risultato non è ottenuto (dose di insulina fino a 1,5 U/kg/die), considerare i boli preprandiali



# Fattori predittivi dell'efficacia terapeutica



Zitler P et al. Diab Care 2016


Received: 2 June 2018 | Revised: 13 July 2018 | Accepted: 16 August 2018

DOI: 10.1111/pedi.12761

WILEY 

ORIGINAL ARTICLE

## Treatment adherence and BMI reduction are key predictors of HbA1c 1 year after diagnosis of childhood type 2 diabetes in the United Kingdom

Toby P. Candler<sup>1,6</sup>  | Osama Mahmoud<sup>2,3</sup> | Richard M. Lynn<sup>4</sup> | Abdalmonen A. Majbar<sup>1</sup> | Timothy G. Barrett<sup>5</sup> | Julian P. H. Shield<sup>1</sup>



# Insufficienza surrenalica acuta

Primitiva (70%)

SAG

Addison (AI, ALD)

Centrale

Terapia cortisonica  
prolungata

Deficit ACTH (isolato,  
panipopituitarismo)



# Corticoterapia e rischio di ISA

- Grande variabilità individuale
- Terapia prolungata (non meno di 10 giorni)
- > 6 mesi per i cortisonici inalatori
- Fluticasone > Beclometasone,  
Budesonide
- Terapia sospesa da meno di 10 settimane

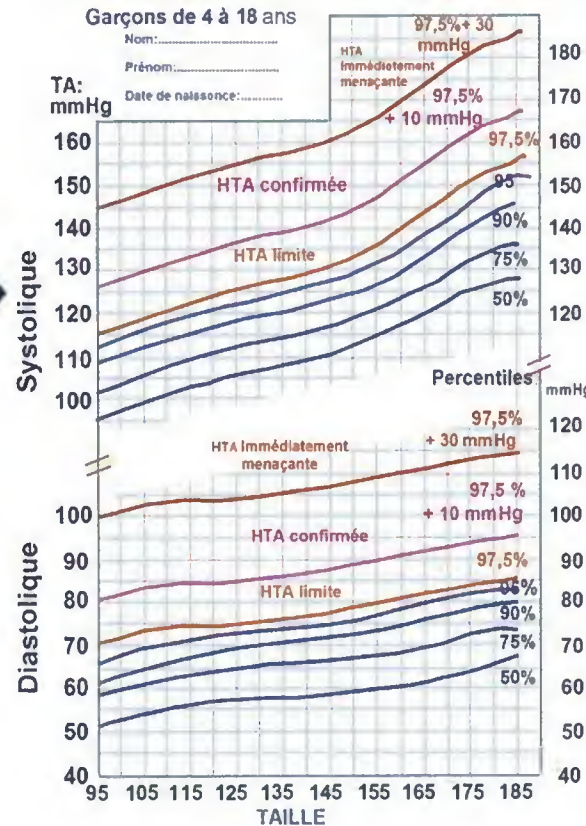
# Criteri di allarme

- Vomito (più di due episodi in meno di 4 ore)
- Diarrea
- Dolori addominali intensi
  
- Disidratazione, ipoglicemia, ipotensione, tachicardia

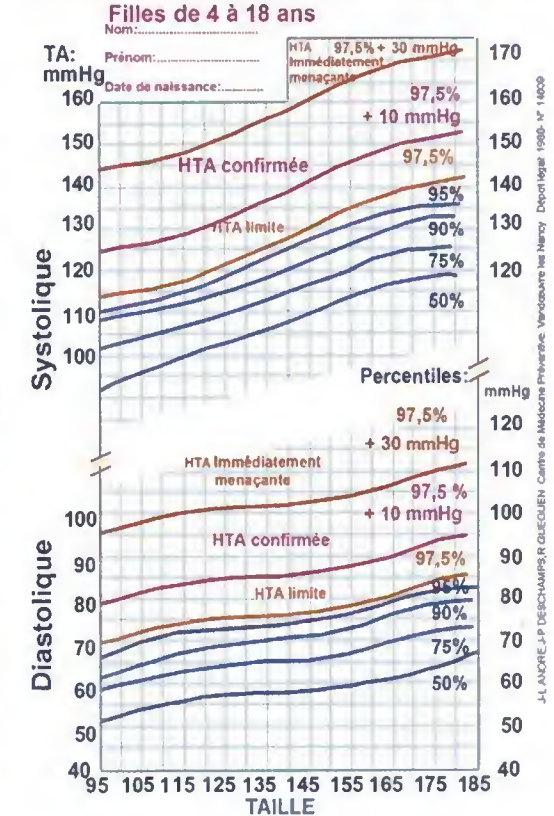
# L'ipertensione arteriosa in pediatria



Tension artérielle en fonction de la taille:



Tension artérielle en fonction de la taille:



ORIGINAL ARTICLE

# Blood pressure reference values for European non-overweight school children: The IDEFICS study

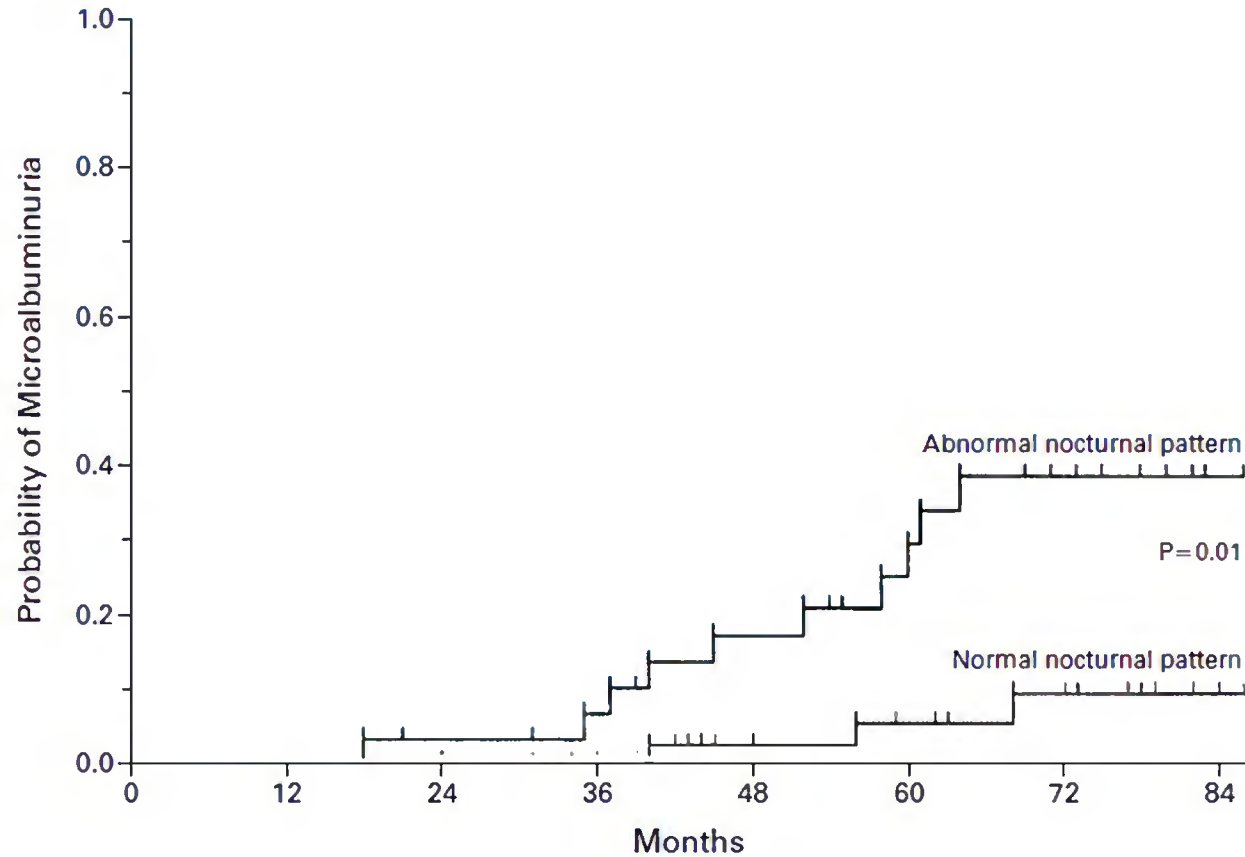
G Barba<sup>1,4</sup>, C Buck<sup>2</sup>, K Bammann<sup>2,3</sup>, C Hadjigeorgiou<sup>4</sup>, A Hebestreit<sup>2</sup>, S Märlid<sup>5</sup>, D Molnár<sup>6</sup>, P Russo<sup>1</sup>, T Veidebaum<sup>7</sup>, K Vyncke<sup>8</sup>, W Ahrens<sup>2,9</sup> and LA Moreno<sup>10</sup> on behalf of the IDEFICS consortium

**Table 2.** Percentiles of systolic BP (mm Hg) in non-overweight children calculated with GAMLSS

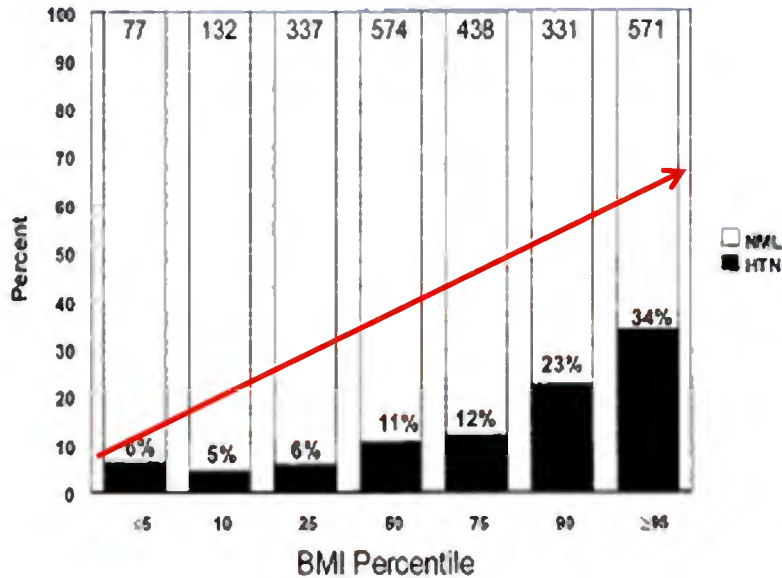
Age (years)	Ht (cm)	Percentiles for girls							Age (years)	Ht (cm)	Percentiles for boys										
		1	3	10	25	50	75	90			97	99	1	3	10	25	50	75	90	97	99
2–<3 (n=200)	85	76.1	78.6	82.1	85.0	90.7	96.0	101.5	108.0	113.7	2–<3 (n=224)	85	74.5	77.7	81.9	86.0	90.6	95.6	100.5	106.0	110.8
	87	76.6	79.1	82.7	86.6	91.3	96.6	102.2	108.7	114.4		88	75.2	78.4	82.6	86.8	91.5	96.5	101.4	107.0	111.8
	89	77.1	79.6	83.2	87.1	91.9	97.3	102.9	109.4	115.2		91	75.9	79.2	83.4	87.6	92.3	97.4	102.4	108.0	112.9
	92	77.8	80.4	84.0	88.0	92.8	98.2	103.9	110.5	116.3		93	76.3	79.6	83.9	88.1	92.9	98.0	103.0	108.7	113.6
	94	78.3	80.9	84.6	88.5	93.4	98.8	104.5	111.2	117.0		96	77.0	80.4	84.7	88.9	93.8	98.9	103.9	109.7	114.6
	97	79.1	81.7	85.4	89.4	94.2	99.8	105.5	112.2	118.1		98	77.5	80.9	85.2	89.5	94.3	99.5	104.6	110.3	115.3
100	79.8	82.4	86.2	90.2	95.1	100.7	106.5	113.3	119.2	101	78.2	81.6	85.9	90.3	95.2	100.4	105.5	111.3	116.3		
3–<4 (n=960)	92	77.3	80.0	83.7	87.7	92.5	97.9	103.4	109.7	115.2	3–<4 (n=1016)	92	76.0	79.3	83.6	87.8	92.5	97.6	102.6	108.2	113.1
	95	78.0	80.7	84.5	88.5	93.4	98.8	104.4	110.8	116.3		95	76.7	80.0	84.3	88.6	93.4	98.5	103.5	109.2	114.1
	97	78.5	81.2	85.0	89.1	94.0	99.4	105.0	111.5	117.0		98	77.4	80.8	85.1	89.4	94.2	99.4	104.5	110.2	115.2
	100	79.3	82.0	85.8	89.9	94.9	100.4	106.0	112.5	118.1		101	78.1	81.5	85.8	90.2	95.1	100.3	105.4	111.2	116.2
	102	79.8	82.5	86.4	90.5	95.4	101.0	106.7	113.2	118.8		103	78.6	82.0	86.4	90.7	95.6	100.9	106.0	111.9	116.9
	105	80.5	83.3	87.2	91.3	96.3	101.9	107.7	114.3	119.9		106	79.3	82.7	87.1	91.5	96.5	101.7	107.0	112.9	117.9
108	81.3	84.1	88.0	92.2	97.2	102.9	108.7	115.3	121.1	109	80.0	83.4	87.9	92.3	97.3	102.6	107.9	113.9	119.0		
4–<5 (n=1196)	98	78.2	81.0	84.9	89.1	94.0	99.4	104.9	111.1	116.3	4–<5 (n=1290)	99	77.6	80.9	85.2	89.5	94.4	99.6	104.7	110.4	115.4
	101	79.0	81.8	85.7	89.9	94.9	100.4	105.9	112.1	117.4		102	78.3	81.7	86.0	90.4	95.3	100.4	105.6	111.4	116.4
	104	79.7	82.6	86.5	90.7	95.8	101.3	106.9	113.2	118.5		105	79.0	82.4	86.8	91.2	96.1	101.3	106.6	112.4	117.5
	107	80.5	83.3	87.3	91.6	96.6	102.2	107.9	114.2	119.6		108	79.7	83.1	87.5	92.0	96.9	102.2	107.5	113.4	118.5
	110	81.2	84.1	88.1	92.4	97.5	103.2	108.9	115.2	120.7		111	80.4	83.8	88.3	92.7	97.6	102.9	108.4	114.2	119.1
	113	81.9	84.9	88.9	93.3	98.4	104.1	109.9	116.3	121.8		114	81.1	84.6	89.1	93.6	98.6	104.0	109.4	115.4	120.6
116	82.7	85.6	89.7	94.1	99.3	105.0	110.8	117.4	122.9	117	81.8	85.3	89.8	94.4	99.5	104.9	110.3	116.4	121.6		
5–<6 (n=1002)	104	79.2	82.1	86.2	90.4	95.5	101.0	106.4	112.4	117.5	5–<6 (n=1121)	105	78.9	82.3	86.7	91.1	96.0	101.2	106.4	112.3	117.4
	108	80.2	83.1	87.2	91.6	96.7	102.2	107.7	113.8	119.0		108	79.6	83.0	87.5	91.9	96.8	102.1	107.4	113.3	118.4
	111	80.9	83.9	88.0	92.4	97.6	103.1	108.7	114.9	120.0		111	80.3	83.7	88.2	92.7	97.7	103.0	108.3	114.3	119.4
	114	81.6	84.7	88.8	93.2	98.4	104.1	109.7	115.9	121.1		115	81.2	84.7	89.2	93.7	98.8	104.2	109.6	115.6	120.8
	117	82.4	85.4	89.5	94.1	99.3	105.0	110.7	116.9	122.1		118	81.9	85.4	90.0	94.5	99.6	105.0	110.4	116.4	121.6
	120	83.1	86.2	90.4	94.9	100.2	106.0	111.7	118.0	123.3		121	82.6	86.2	90.8	95.4	100.5	106.0	111.5	117.6	122.9
123	83.8	87.0	91.2	95.8	101.1	106.9	112.7	119.1	124.4	125	83.5	87.1	91.8	96.4	101.7	107.2	112.7	118.9	124.3		
6–<7 (n=1398)	110	80.1	83.2	87.4	91.8	97.0	102.5	107.9	113.8	118.7	6–<7 (n=1390)	111	80.2	83.7	88.1	92.6	97.6	102.9	108.2	114.2	119.3
	113	80.8	83.9	88.2	92.7	97.9	103.4	108.9	114.9	119.8		115	81.1	84.6	89.2	93.7	98.7	104.1	109.5	115.5	120.7
	117	81.8	85.0	89.3	93.8	99.1	104.7	110.2	116.3	121.2		118	81.8	85.4	89.9	94.5	99.6	105.0	110.4	116.5	121.7
	120	82.5	85.7	90.1	94.6	99.9	105.6	111.2	117.3	122.3		121	82.5	86.1	90.7	95.3	100.4	105.9	111.3	117.5	122.8
	123	83.3	86.5	90.9	95.5	100.8	106.6	112.2	118.4	123.4		125	83.5	87.1	91.7	96.3	101.6	107.1	112.6	118.8	124.1
	127	84.2	87.5	91.9	96.6	102.0	107.8	113.5	119.7	124.9		128	84.2	87.8	92.5	97.1	102.4	108.0	113.5	119.8	125.2
130	85.0	88.3	92.7	97.4	102.9	108.8	114.5	120.8	126.0	132	85.1	88.7	93.5	98.2	103.5	109.2	114.8	121.1	126.6		
7–<8 (n=1945)	115	80.7	84.0	88.4	92.9	98.2	103.7	109.1	114.9	119.6	7–<8 (n=1854)	117	81.5	85.0	89.6	94.1	99.2	104.6	110.0	116.0	121.3
	119	81.7	85.0	89.4	94.1	99.4	105.0	110.4	116.3	121.0		120	82.2	85.8	90.3	94.9	100.0	105.5	110.9	117.0	122.3
	123	82.6	86.0	90.5	95.2	100.5	106.2	111.7	117.7	122.5		124	83.1	86.7	91.4	96.0	101.2	106.7	112.2	118.4	123.7
	126	83.4	86.7	91.3	96.0	101.4	107.2	112.7	118.7	123.6		127	83.8	87.5	92.1	96.8	102.0	107.6	113.1	119.3	124.7
	131	84.3	87.8	92.4	97.1	102.6	108.4	114.0	120.1	125.0		131	84.8	88.4	93.1	97.8	103.2	108.8	114.4	120.7	126.1
	133	85.1	88.5	93.2	98.0	103.5	109.4	115.0	121.1	126.1		134	85.5	89.1	93.9	98.6	104.0	109.7	115.3	121.7	127.1
137	86.1	89.5	94.2	99.1	104.7	110.6	116.3	122.5	127.5	138	86.4	90.1	94.9	99.7	105.1	110.9	116.6	123.0	128.5		
8–<9 (n=1287)	120	81.3	84.7	89.3	94.0	99.4	105.0	110.3	116.0	120.5	8–<9 (n=1239)	122	82.6	86.2	90.8	95.3	100.5	105.0	110.4	116.6	122.9
	124	82.3	85.7	90.4	95.2	100.6	106.2	111.6	117.3	121.9		126	83.5	87.1	91.8	96.4	101.6	107.2	112.7	118.9	124.2
	128	83.2	86.8	91.5	96.3	101.8	107.5	112.9	118.7	123.4		129	84.2	87.9	92.5	97.2	102.5	108.1	113.6	119.9	125.3
	132	84.2	87.8	92.5	97.4	102.9	108.7	114.2	120.1	124.8		133	85.2	88.8	93.6	98.3	103.6	109.3	114.9	121.2	126.7
	136	85.2	88.8	93.6	98.5	104.1	110.0	115.5	121.5	126.2		137	86.1	89.8	94.6	99.4	104.7	110.5	116.1	122.5	128.0
	139	85.9	89.5	94.4	99.3	105.0	110.9	116.5	122.5	127.3		140	86.9	90.7	95.6	100.4	105.4	111.4	117.1	123.4	129.1
143	86.9	90.5	95.5	100.5	106.2	112.2	117.8	123.9	128.8	144	87.7	91.5	96.4	101.2	106.7	112.5	118.3	124.9	130.5		
9–<10 (n=299)	125	81.9	85.5	90.3	95.1	100.6	106.2	111.5	117.0	121.4	9–<10 (n=286)	127	83.7	87.3	92.0	96.6	101.8	107.4	112.9	119.1	124.5
	130	83.1	86.7	91.6	96.5	102.1	107.8	113.1	118.8	124.2		131	84.6	88.3	93.0	97.7	103.0	108.6	114.2	120.4	125.9
	134	84.0	87.7	92.7	97.7	103.2	109.0	114.4	120.1	124.6		134	85.3	89.0	93.7	98.5	103.8	109.5	115.1	121.4	126.9
	138	85.0	88.7	93.7	98.8	104.4	110.3	115.7	121.5	126.1		138	86.2	90.0							



# Rischio di progressione verso una microalbuminuria



# Screening dell'ipertensione arteriosa negli obesi



## Bogalusa heart study

Hypertension systolique x 4,5  
Hypertension diastolique x 2,5

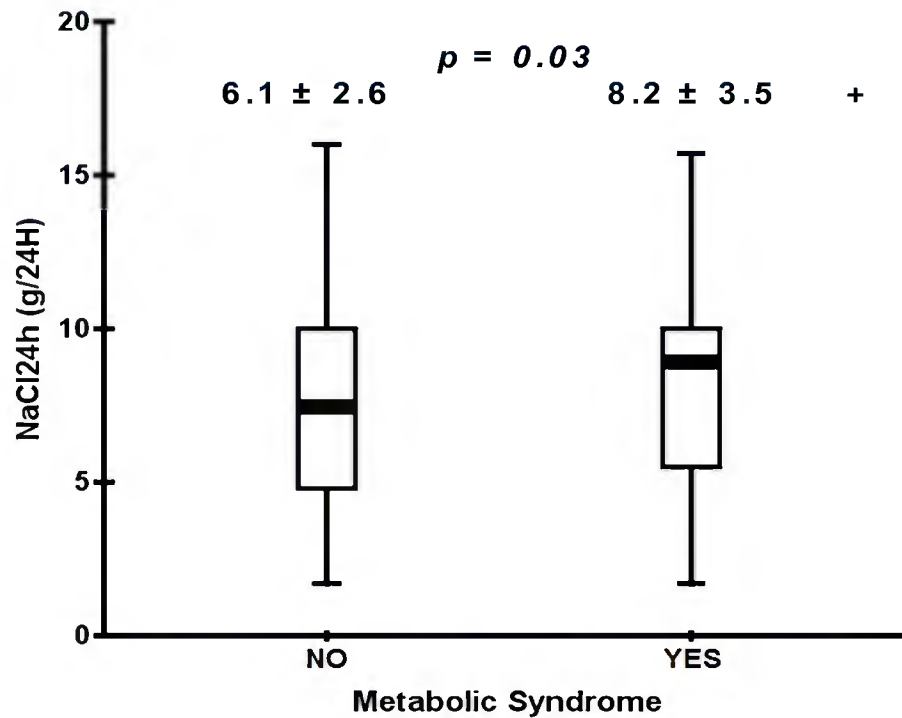
En cas de surpoids/obésité

Pediatrics 1999

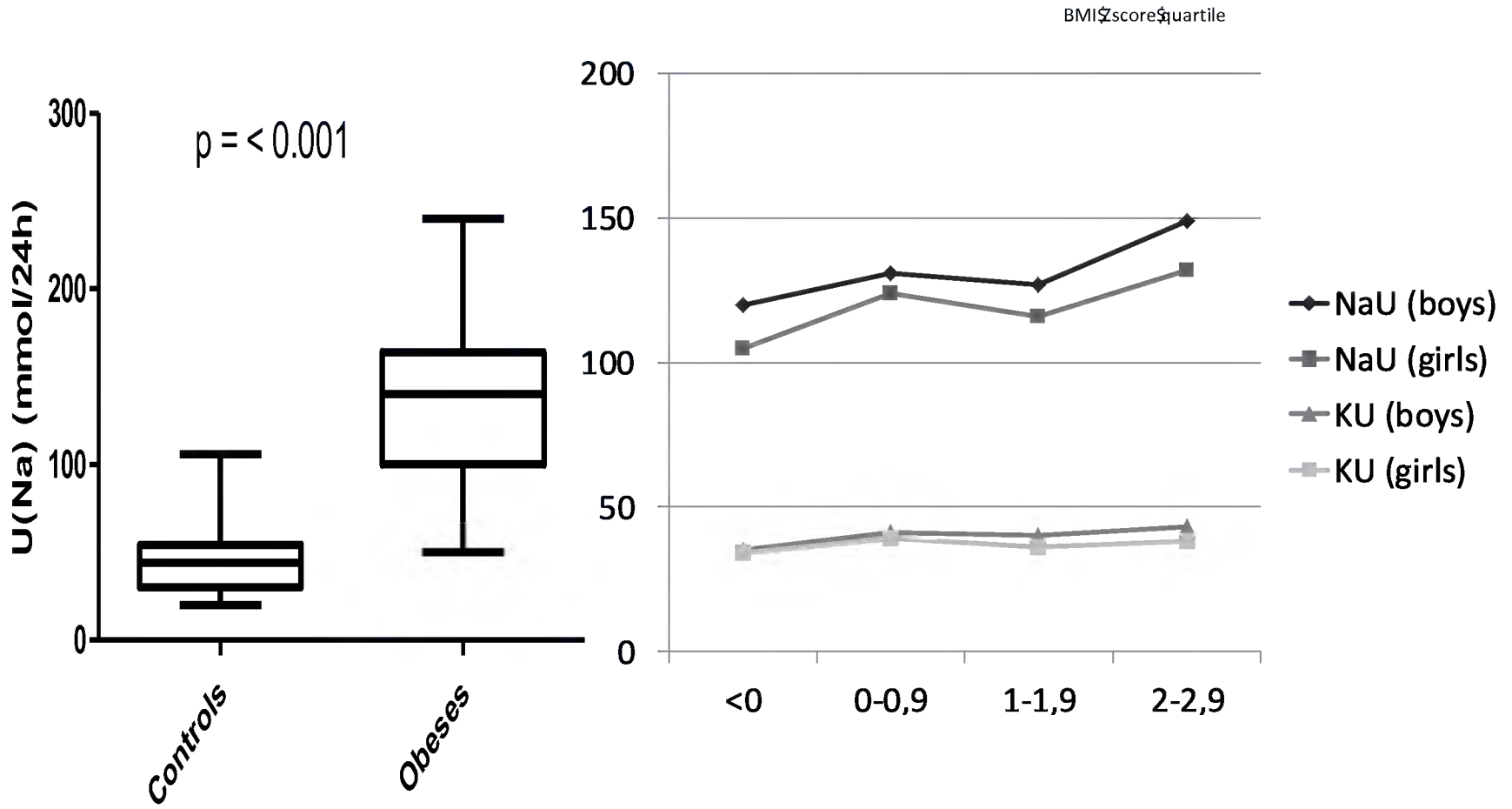
Sorof JM et al. J Pediatr 2002



# Consumo di sale e sindrome metabolica



# Consumo di sale ed IMC

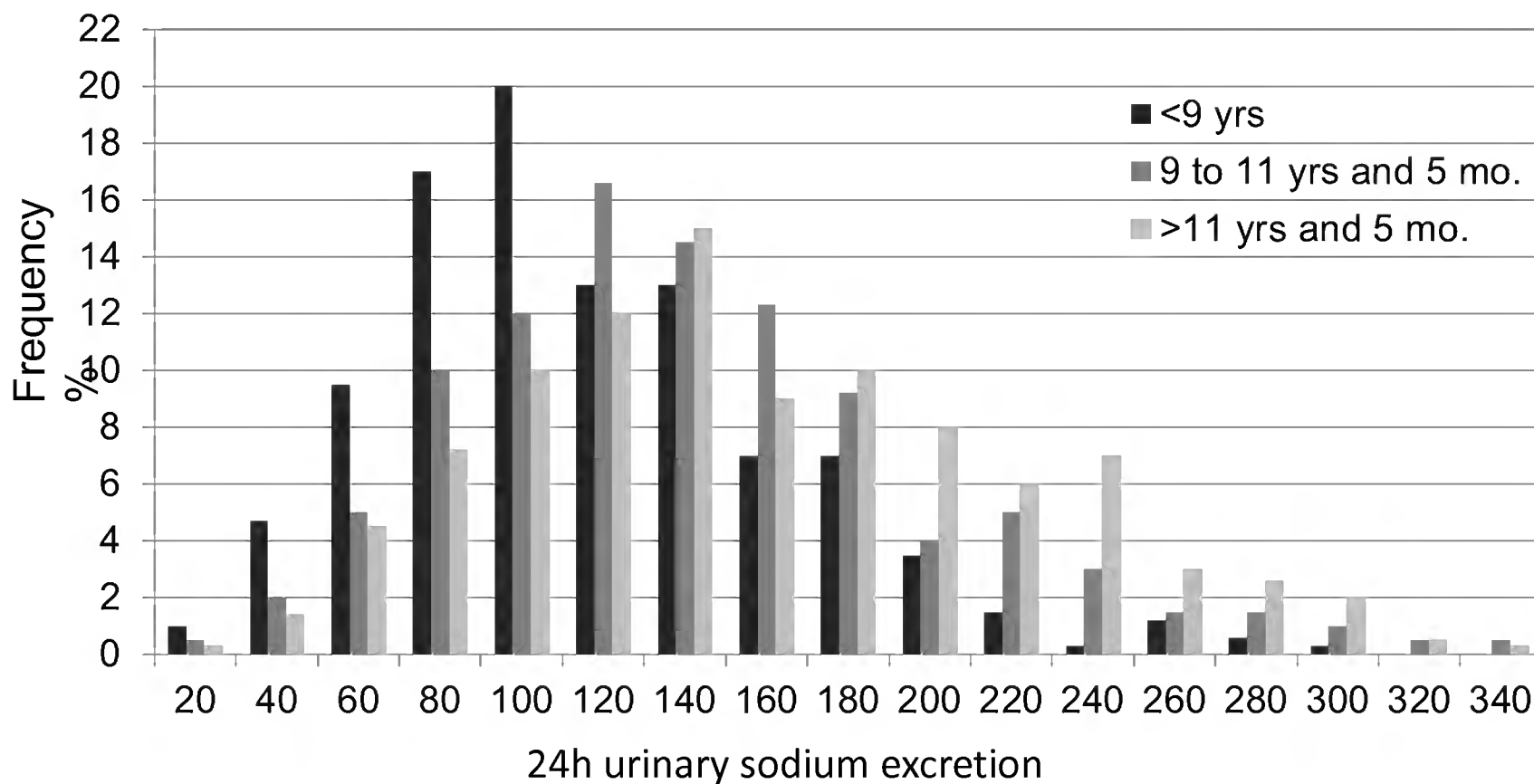


De Filippo G. et al. 2012

Campanozzi A. et al. 2013

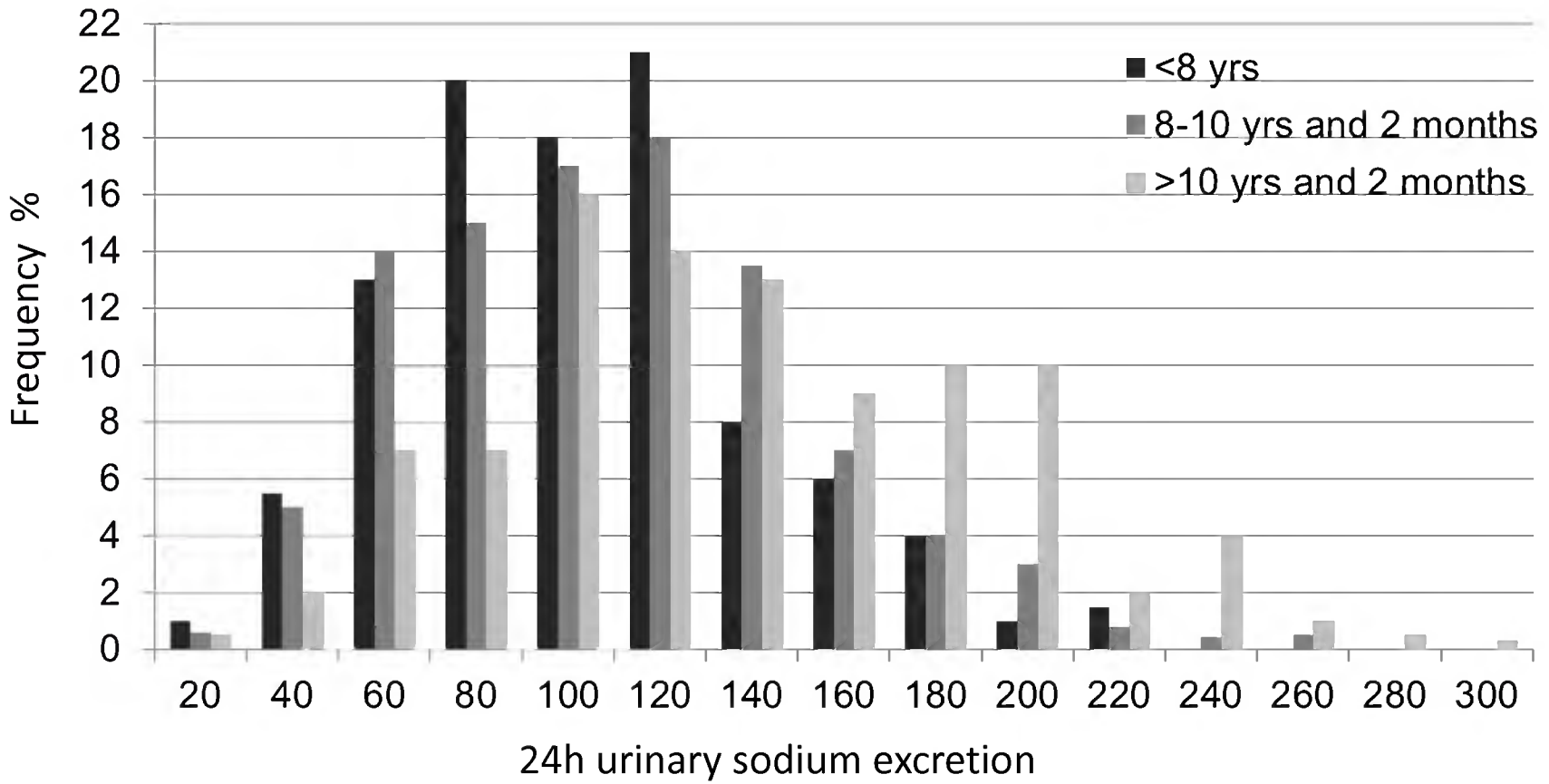
# Boys

Age Category	N	24h UNa (mean and 95% C.I.)	% above the age-specific Adequate Intake*
I. <9 yrs	303	108 (102-114)	91%
II. 9-11yrs and 5 months	228	134 (126-142)	96%
III. > 11 yrs and 5 months	235	151 (142-159)	91%

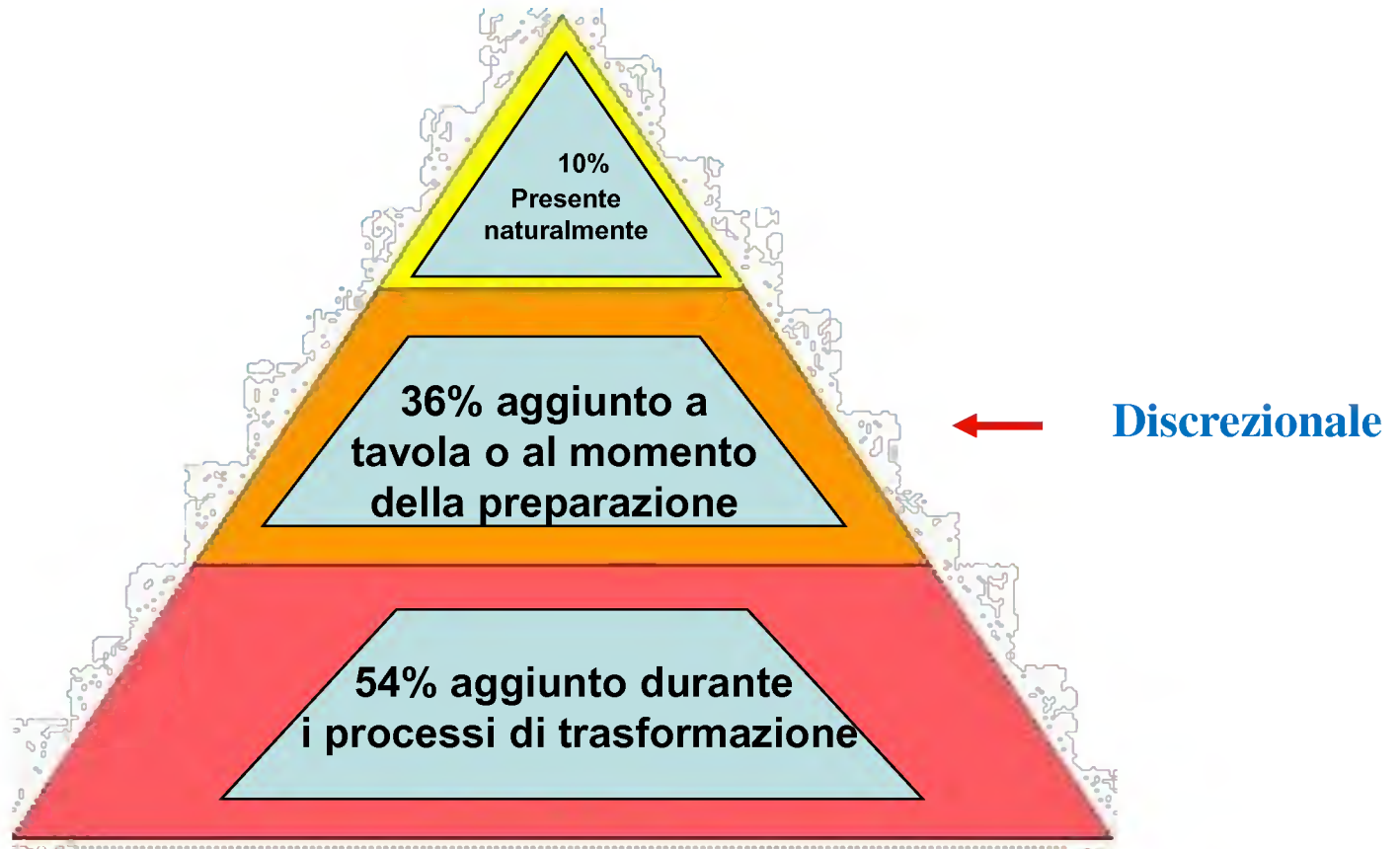


# Girls

Age category	N	24h UNa (mean and 95% C.I.)	% above the age-specific Adequate Intake*
I. <8 yrs	162	94 (88-101)	89%
II. 8-10yrs and 2 months	180	102 (95-109)	88%
III. >10 yrs and 2 months	316	136 (129-143)	89%



# Apporto di sale con l'alimentazione



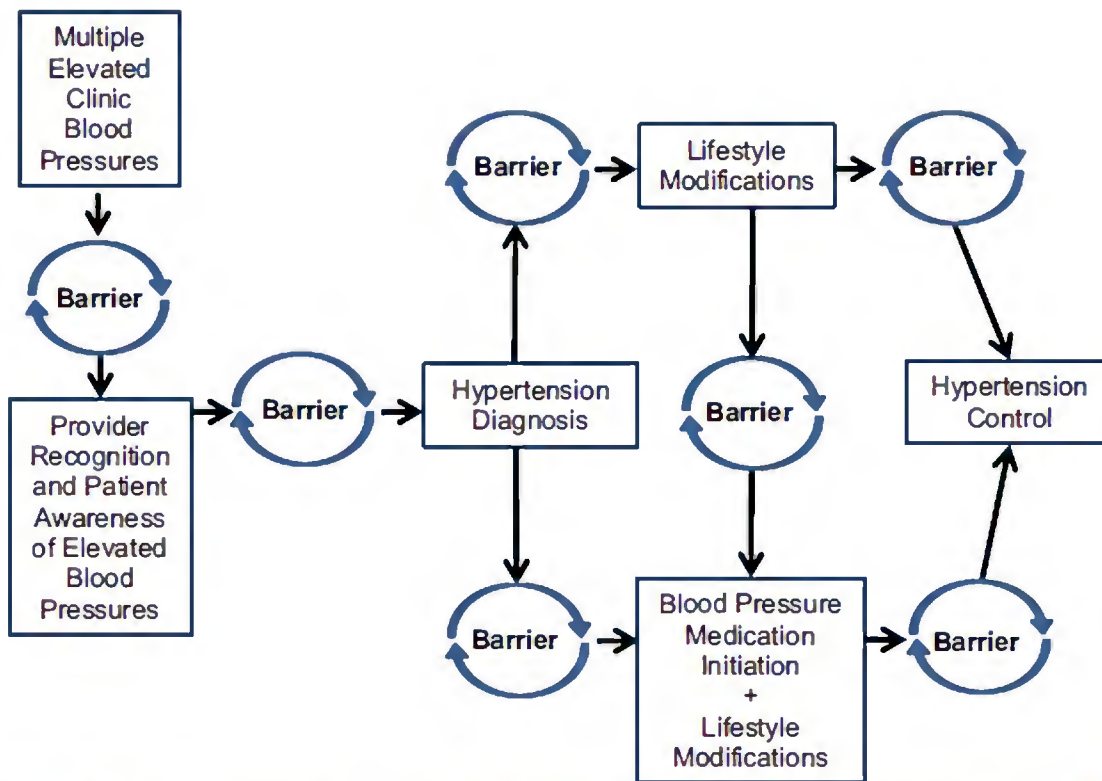
RESEARCH ARTICLE

Open Access



# “They’re younger... it’s harder.” Primary providers’ perspectives on hypertension management in young adults: a multicenter qualitative study

Heather M. Johnson<sup>1,2\*</sup>, Ryan C. Warner<sup>3</sup>, Christie M. Bartels<sup>2,4</sup> and Jamie N. LaMantia<sup>1,2</sup>



**Fig. 1** “Barrier points” to deliver hypertension care to young adults. This figure summarizes the most common emergent themes during the 60-min one-on-one Family Practice/Family Medicine provider interviews about barriers and challenges to diagnosis, treat, and control hypertension in young adults





# CONCLUSIONI

La gestione di un bambino con patologia cronica endocrinologica è un lavoro

- Di équipe
- Quotidiano
- Di continuo apprendimento bidirezionale

