

Slaap-gerelateerde ademhalingsstoornissen bij obese kinderen en adolescenten

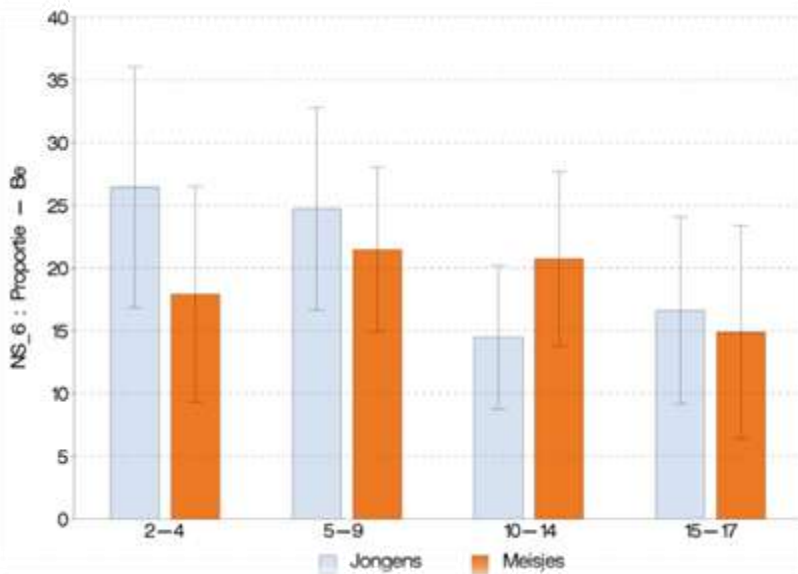
Dr. Annelies Van Eyck

Dr. Kim van Hoorenbeeck, Dr. Luc Bruyndoncx, Prof. dr. Stijn Verhulst

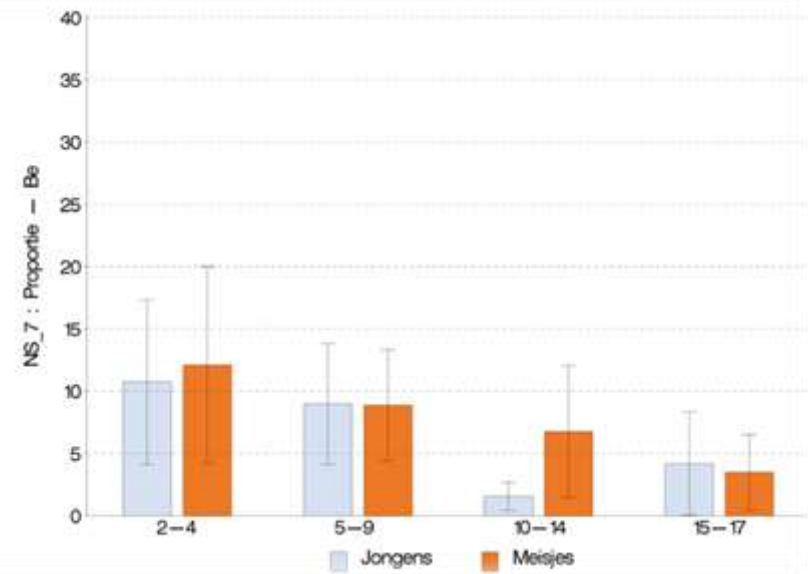
Multisystem Interventions in Childhood Obesity and Sleep Apnea

Childhood obesity: prevalence

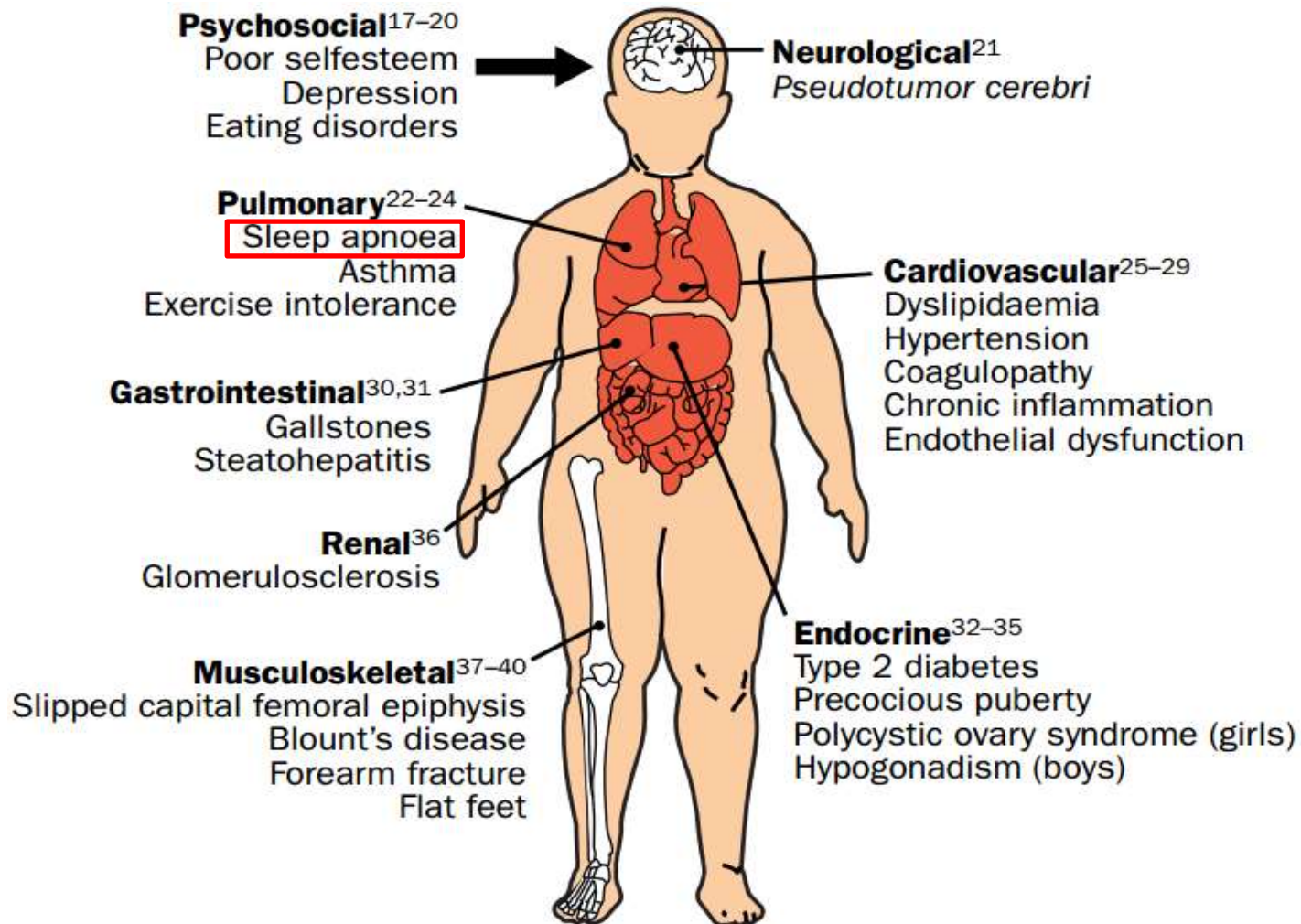
OVERWEIGHT



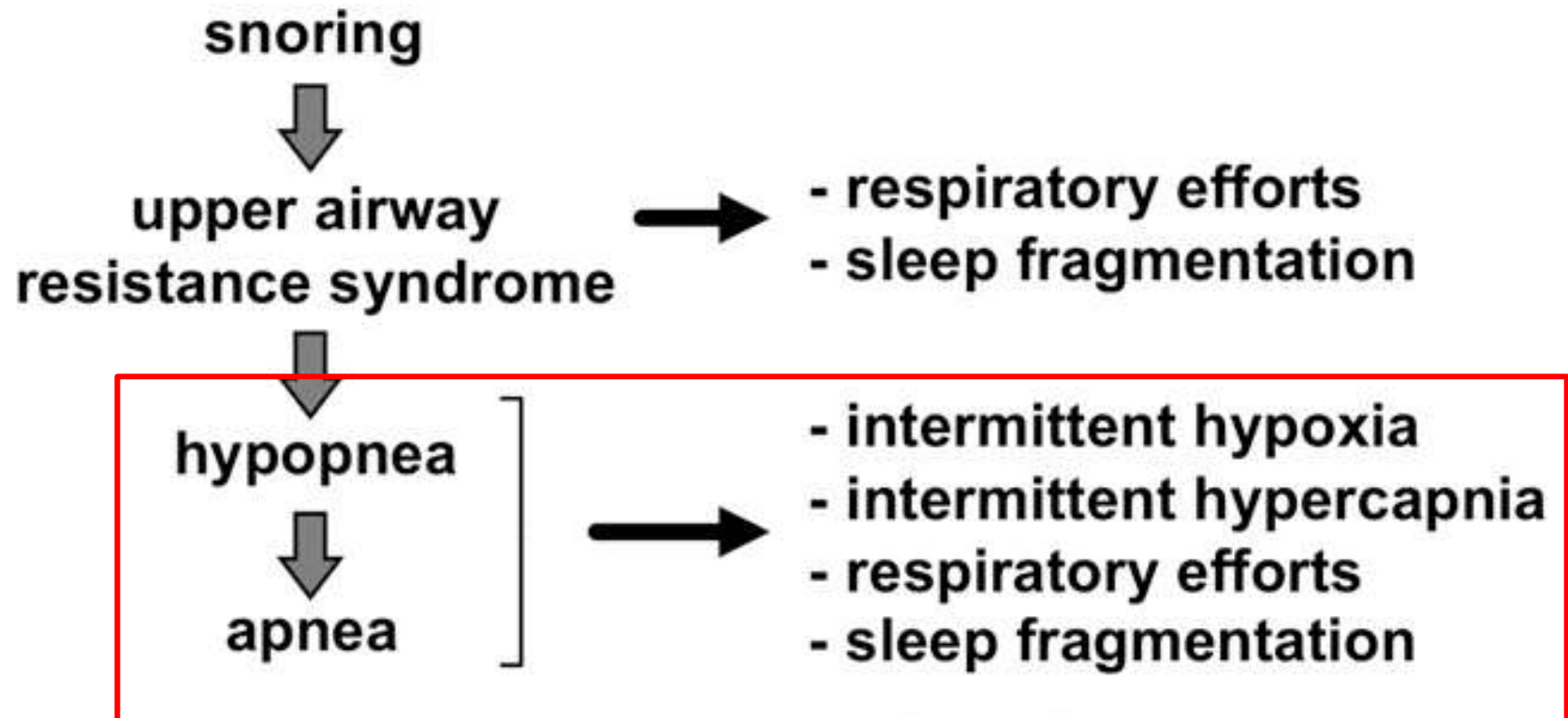
OBESE



Childhood obesity: complications



Obstructive sleep-disordered breathing



Epidemiology SDB in childhood

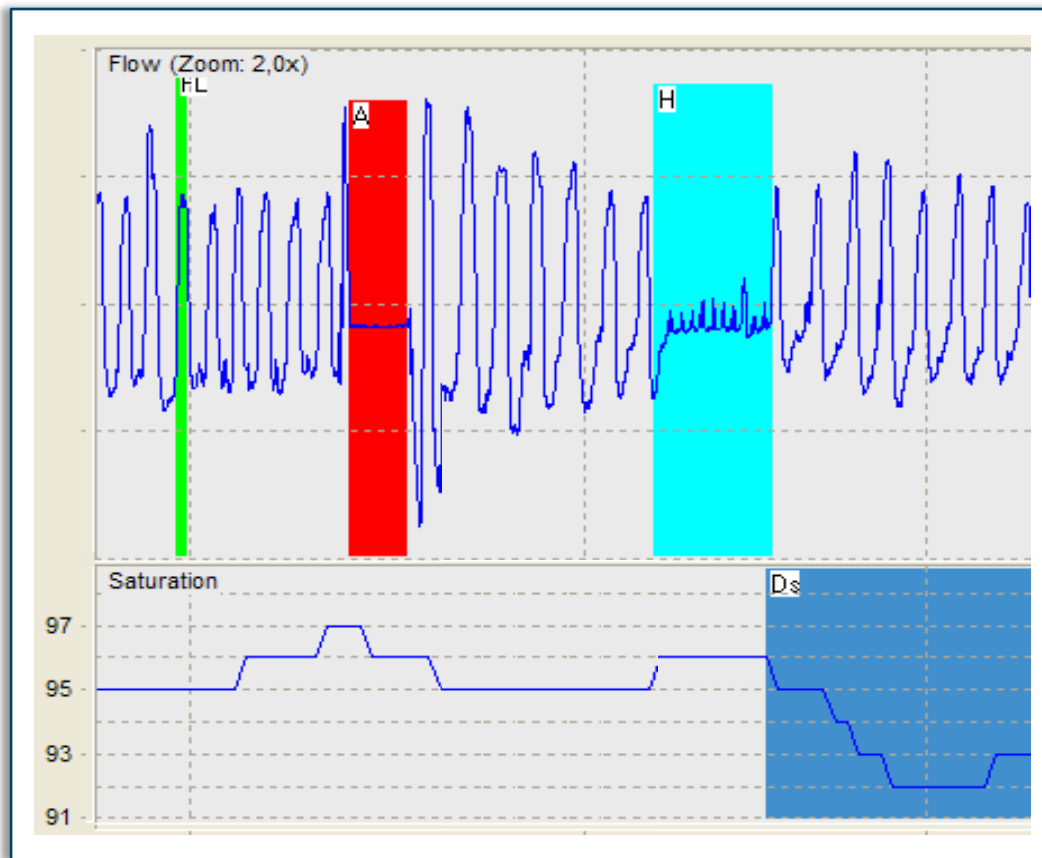
- Prevalence general pediatric population: 2-3% ⁽¹⁾
- Prevalence obese children: ⁽²⁾

Refs.	Subject characteristics	Obesity	OSAS	Prevalence of OSAS (%)
Mallory et al. ²¹	45 subjects, mean age of 10.3 years (SD=4.4), average ideal body weight was 208% (SD=42.2); all had a history suggesting abnormal breathing during sleep, referred to a sleep clinic	Ideal body weight >150%	AHI>5	24
Silvestri et al. ²²	32 subjects, mean age of 8.6 years (SD=3.3), average ideal body weight was 196% (SD=45%); all had a history suggesting abnormal breathing during sleep	Weight >95th percentile or ideal body weight >120% or BMI >90th percentile	Occurrence of ≥1 obstructive apnea	59
Marcus et al. ²⁴	22 subjects, mean age of 10 years (SD=5), average ideal body weight was 184% (SD=36%); none presented with sleep or respiratory complaints, referred to routine patient care	Ideal body weight >120%	OAI>1, and/or desaturation and/or hypercapnia	36
Chay et al. ²³	60 subjects; recruited from a pediatric obesity clinic	Ideal body weight ≥180%	AHI>5	13
Wing et al. ²⁶	46 subjects; mean age of 10.8 years (SD=2.3), average BMI was 27.4 kg/m ² (SD=5.1); recruited from a pediatric obesity clinic	Ideal body weight ≥120%	OAI≥1	26.1
Verhulst et al. ²⁵	64 subjects; mean age of 11.2 years (SD=2.6), average BMI z-score was 2.3 (SD=0.5); recruited from a pediatric obesity clinic	International Obesity Task ²⁸	OAI≥1 and/or obstructive AHI≥2	19

(1) Marcus, C. L. (2001). "Sleep-disordered breathing in children." Am J Respir Crit Care Med **164**: 16-30.

(2) Verhulst, S. L., et al. (2008). "The prevalence, anatomical correlates and treatment of sleep-disordered breathing in obese children and adolescents." Sleep Med Rev **12**(5): 339-346.

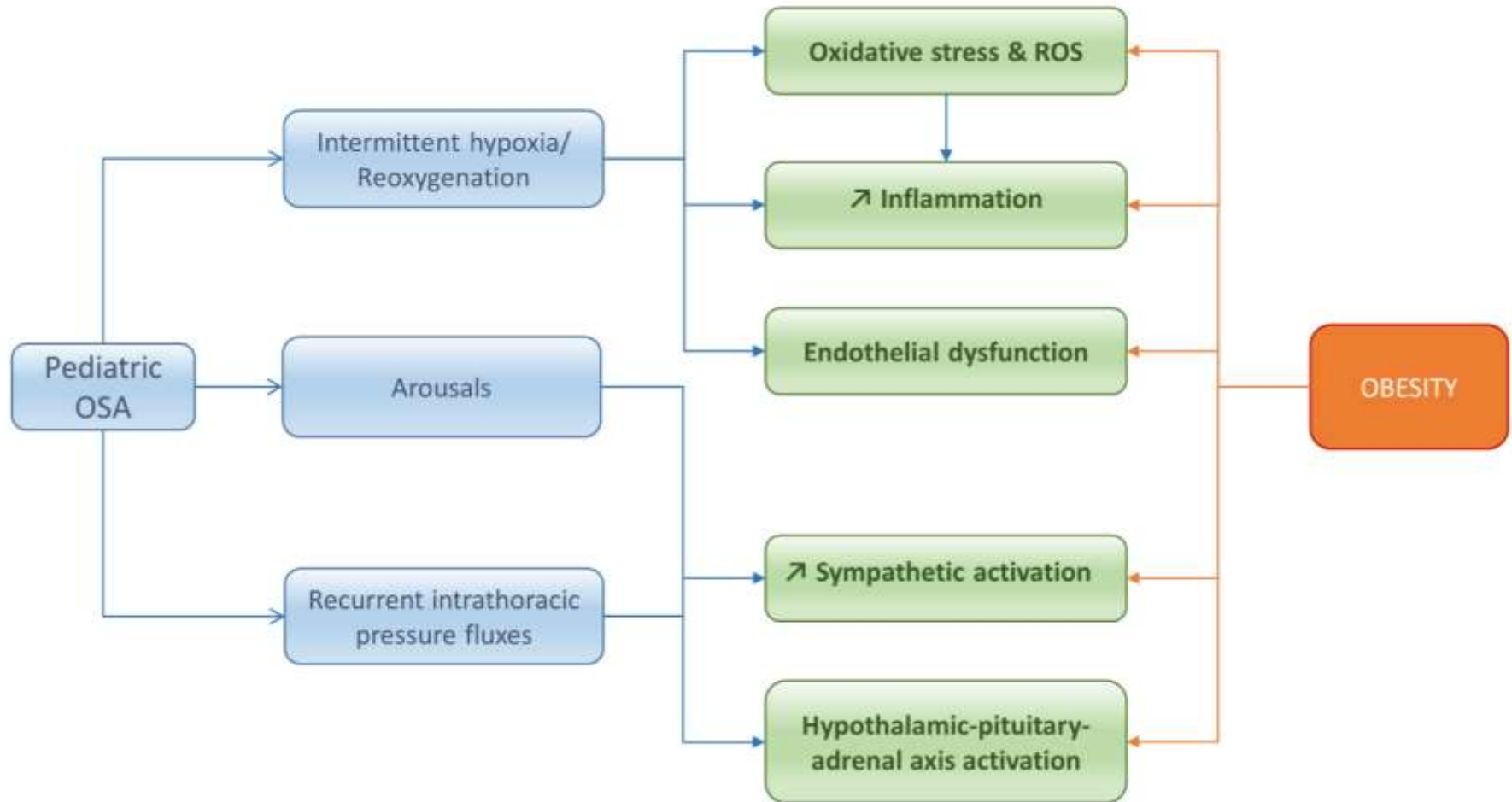
Sleep-disordered breathing: diagnosis



Complications of OSA in childhood

- Cardiovascular complications:
 - Impaired endothelial function
 - ↗ Diastolic blood pressure
 - ↘ Left ventricular function
 - ...
- Metabolic complications:
 - Metabolic syndrome
 - NAFLD
 - ...

Hypothesized mechanism that link OSA with its associated complications



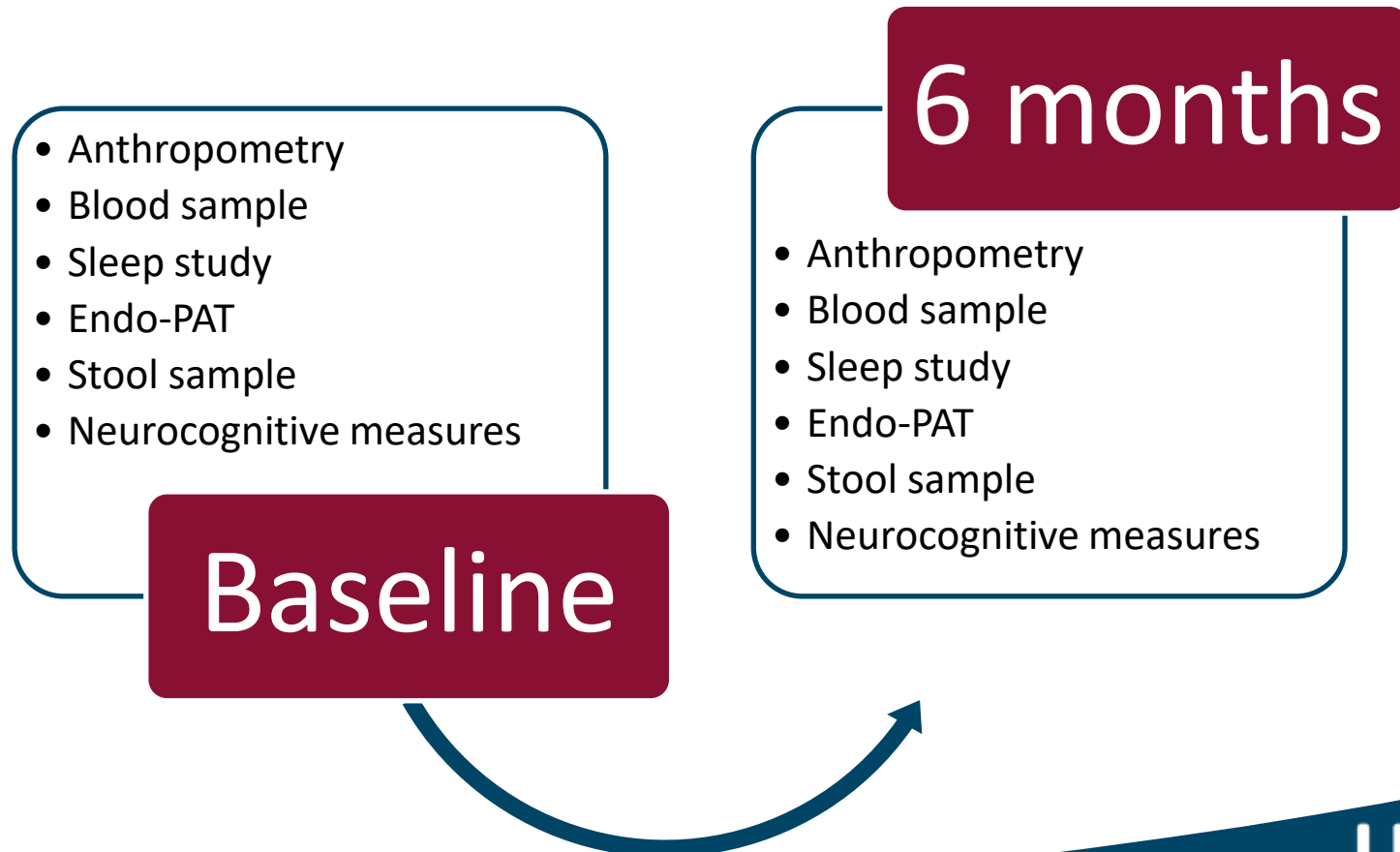
Treatment of OSA in childhood

- Classic first-line treatment: adenotonsillectomy
 - Successful in less than 50% of obese children
 - Often weight gain and reoccurrence of OSA in obese children
- Weight loss more effective as treatment for OSA in obese children
 - Beneficial effects on metabolic dysregulation and cardiovascular risk factors
 - Previous studies: success rate of 62-78%



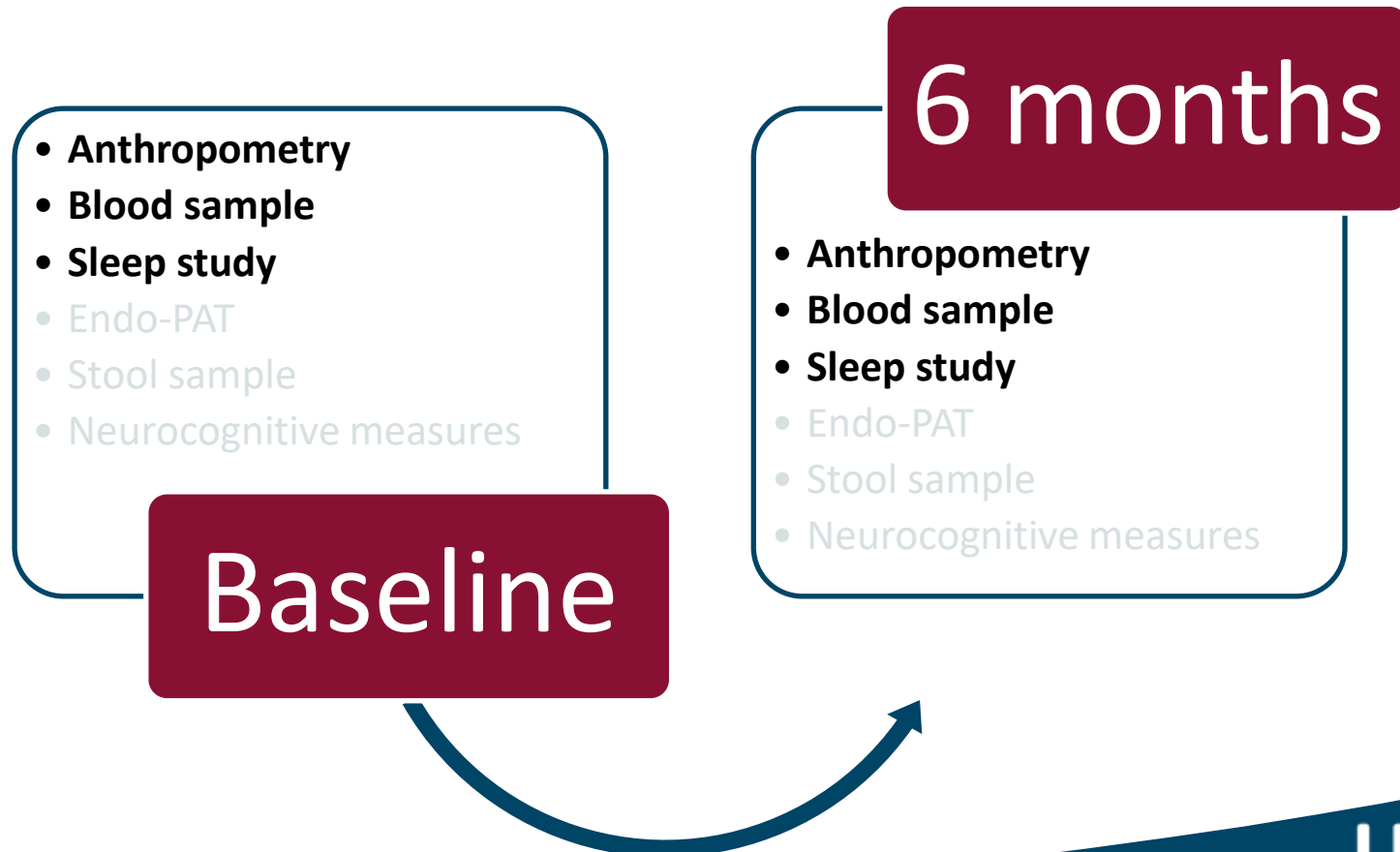
Study design

- Prospective intervention study at “Zeepreventorium”
 - **Intervention:** In-patient weight loss treatment program
 - **Study design:** baseline visit and follow-up after 4-6 months weight loss treatment



Study design

- Prospective intervention study at “Zeepreventorium”
 - **Intervention:** In-patient weight loss treatment program
 - **Study design:** baseline visit and follow-up after 4-6 months weight loss treatment



Results

	Baseline	6 months follow-up
N	62	54
Gender (male/female)	20/42	15/39
Age (years)	15,8 ± 1,8	16,3 ± 1,8
Height (m)	1,684 ± 0,096	1,700 ± 0,094
Weight (kg)	112,6 ± 24,0	91,5 ± 19,7
BMI z-score	2,9 ± 0,4	2,1 ± 0,6
SDB diagnosis (%)	39,30%	5,60%

- Drop-out rate of **13%**
- Mean weight loss of **21,1 kg**, which corresponds with a drop in BMI z-score of **0,8**
- Of the **24** patients with SDB at baseline, only **3** patients still had an abnormal sleep study after 6 months of weight loss

Results

	Baseline	6 months follow-up	p
Leukocytes (*10 ⁹ /l)	7,3 (3,1-14,0)	7,1 (4,8-12,7)	0,02
hs-CRP (mg/l)	4,2 (0,3-26,5)	1,4 (0,3-16,0)	<0,001
Uric acid (mg/dl)	7,0 ± 1,1	5,2 ± 0,9	<0,001
Glucose (mg/dl)	88 (73-117)	88 (71-99)	0,7
AST (U/L)	24 (13-67)	18 (11-33)	<0,001
ALT (U/L)	23 (10-120)	15 (9-54)	<0,001
Triglycerides (mg/dl)	110 ± 41	89 ± 30	<0,001
Total cholesterol (mg/dl)	168 ± 30	140 ± 29	<0,001
HDL (mg/dl)	42 (31-92)	47 (31-77)	0,07
LDL (mg/dl)	100 ± 24	70 (37-124)	<0,001
TSH (mU/L)	2,53 (0,89-22,66)	2,86 (1,15-8,67)	0,6
fT4 (pmol/L)	15,26 ± 2,09	15,38 ± 1,70	0,3
Insulin (pmol/L)	148,5 (42,4-489,7)	99,3 (37,1-483,1)	<0,001

Results

	Baseline	6 months follow-up	p
Leukocytes (*10 ⁹ /l)	7,3 (3,1-14,0)	7,1 (4,8-12,7)	0,02
hs-CRP (mg/l)	4,2 (0,3-26,5)	1,4 (0,3-16,0)	<0,001
Uric acid (mg/dl)	7,0 ± 1,1	5,2 ± 0,9	<0,001
Glucose (mg/dl)	88 (73-117)	88 (71-99)	0,7
AST (U/L)	24 (13-67)	18 (11-33)	<0,001
ALT (U/L)	23 (10-120)	15 (9-54)	<0,001
Triglycerides (mg/dl)	110 ± 41	89 ± 30	<0,001
Total cholesterol (mg/dl)	168 ± 30	140 ± 29	<0,001
HDL (mg/dl)	42 (31-92)	47 (31-77)	0,07
LDL (mg/dl)	100 ± 24	70 (37-124)	<0,001
TSH (mU/L)	2,53 (0,89-22,66)	2,86 (1,15-8,67)	0,6
fT4 (pmol/L)	15,26 ± 2,09	15,38 ± 1,70	0,3
Insulin (pmol/L)	148,5 (42,4-489,7)	99,3 (37,1-483,1)	<0,001

Results: baseline

	No SDB	SDB	p
N	37	24	
Gender (male/female)	28/9	14/10	0,2
Age (years)	15,7 ± 1,9	15,8 ± 1,5	0,7
Height (m)	1,671 ± 0,110	1,702 ± 0,067	0,2
Weight (kg)	102,3 ± 19,5	128,3 ± 22,4	<0,001
BMI z-score	2,7 ± 0,4	3,1 ± 0,4	<0,001
Waist circumference (cm)	116 ± 13	132 ± 12	<0,001
Waist-to-hip ratio	0,96 ± 0,07	1,01 ± 0,06	0,004
Fat mass (%)	43,2 (27,3-60,8)	49,0 (40,6-71,3)	<0,001
ODI (events/hour)	0,8 (0,3-1,9)	3,8 (2,1-21,7)	<0,001
AHI (events/hour)	2,2 (0,2-7,1)	4,1 (1,8-11,9)	<0,001
<SaO ₂ > (%)	97 (95-98)	96 (94-97)	0,002
SaO ₂ nadir (%)	91 (81-95)	89 (78-92)	<0,001

Results: baseline

	No SDB	SDB	p
Leukocytes (*10 ⁹ /l)	7,0 (3,1-11,2)	7,5 (4,1-14,0)	0,9
hs-CRP (mg/l)	3,6 (0,3-26,5)	5,6 (0,8-18,2)	0,5
Uric acid (mg/dl)	6,8 ± 1,0	7,3 ± 1,3	0,2
Glucose (mg/dl)	88 (73-117)	88 (79-97)	0,9
AST (U/L)	22 (13-61)	27 (15-67)	0,03
ALT (U/L)	22 (10-56)	26 (13-120)	0,1
Triglycerides (mg/dl)	108 ± 42	113 ± 41	0,6
Total cholesterol (mg/dl)	170 ± 32	166 ± 28	0,6
HDL (mg/dl)	47 (31-92)	40 (32-72)	0,003
LDL (mg/dl)	98 ± 24	102 ± 24	0,5
TSH (mU/L)	2,51 (1,18-5,16)	2,62 (1,06-22,66)	0,2
fT4 (pmol/L)	15,30 ± 1,93	15,15 ± 2,39	0,7
Insulin (pmol/L)	128,4 (42,4-276,8)	194,2 (67,3-489,7)	0,002

Results: baseline

	No SDB	SDB	p
Leukocytes (*10 ⁹ /l)	7,0 (3,1-11,2)	7,5 (4,1-14,0)	0,9
hs-CRP (mg/l)	3,6 (0,3-26,5)	5,6 (0,8-18,2)	0,5
Uric acid (mg/dl)	6,8 ± 1,0	7,3 ± 1,3	0,2
Glucose (mg/dl)	88 (73-117)	88 (79-97)	0,9
AST (U/L)	22 (13-61)	27 (15-67)	0,03
ALT (U/L)	22 (10-56)	26 (13-120)	0,1
Triglycerides (mg/dl)	108 ± 42	113 ± 41	0,6
Total cholesterol (mg/dl)	170 ± 32	166 ± 28	0,6
HDL (mg/dl)	47 (31-92)	40 (32-72)	0,003
LDL (mg/dl)	98 ± 24	102 ± 24	0,5
TSH (mU/L)	2,51 (1,18-5,16)	2,62 (1,06-22,66)	0,2
fT4 (pmol/L)	15,30 ± 1,93	15,15 ± 2,39	0,7
Insulin (pmol/L)	128,4 (42,4-276,8)	194,2 (67,3-489,7)	0,002

Results: 6 month follow-up

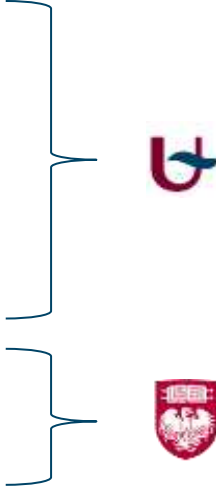
- Of the 24 patients with SDB at baseline:
 - 20 patients received a second sleep study
 - 17 patients had a normalized sleep study
 - 3 patients still had residual sleep apnea
- Success rate of **85%** for treating sleep apnea in obese adolescents with conventional weight loss management strategies.



Conclusion

- 6 months of weight loss therapy has a **positive effect** on **measures of metabolic dysregulation**.
- Success rate of **85%** for treating sleep apnea in obese adolescents with conventional weight loss management strategies.
- SDB is associated with a **more severe** degree of (abdominal) obesity.
- Adolescents with SDB have **increased AST and insulin** levels, and **decreased HDL-cholesterol** levels.

To do

- Analysis blood samples:

- Leptin
 - Adiponectin
 - IL-6
 - TNF alpha
 - Ghrelin
 - GLP-1
- 

- Analysis Endo-PAT data 
- Microbiome studies on stool sample 
- Collect data STROOP test (neurocognitive measures) 