



Uppsala Longitudinal Study of Childhood Obesity (ULSCO)

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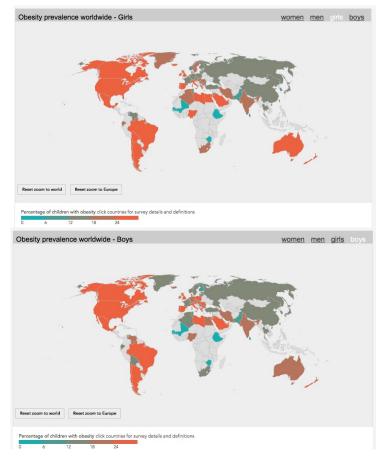
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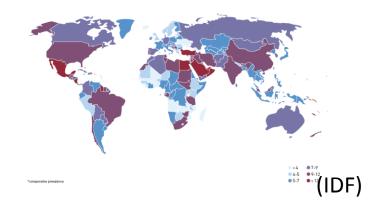
Urgency

Childhood obesity

 Obesity-related complications; CVD, T2DM, T1DM



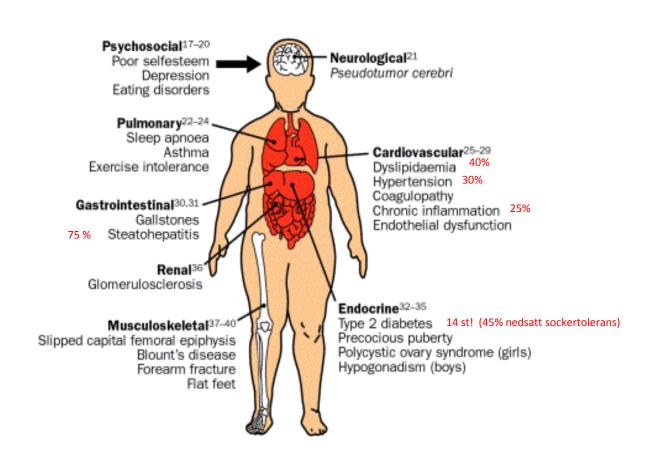
(World Obesity Federation)





Barnfetma och dess komplikationer har ökat epidemiskt i Europa (ref EU, WHO)

Barn med fetma i Uppsala har följande komplikationer





Uppsala Longitudinal Study of Childhood Obesity (ULSCO)

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Uppsala Longitudinal Study of Childhood Obesity: Protocol Description

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Longitudinal work



FIGURE 1

Time chart of visits by subjects at the pediatric obesity clinic and specified times when assessments and examinations are conducted within the ULSCO cohort. Red arrowheads indicate a potential new treatment strategy and/or research focus.





Procedures and assessments



Sensormedics Vmax-system ®



Inbody S20 ®



Harpenden kaliper ®





Procedures and assessments



Accelerometer



6-minute-walk-test



Biobank – for 1 subject

			FFA Ir	FFA Ins, C-peptid		
		1	2	3	4	
<u>Fasted</u>	1 EDTA	250	250	250	600	
(-15, -5)	1 P800	250	250	400		
			GLP-1			

During OGTT from every timepoint

(min 5, 10, 15, 30, 60, 90, 120, 150, 180):

1 EDTA	250	250	800
1 P800	250	250	400



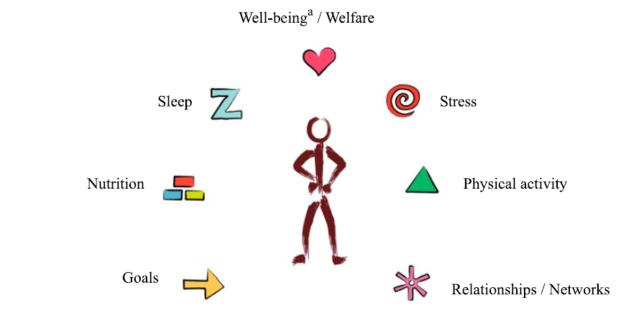


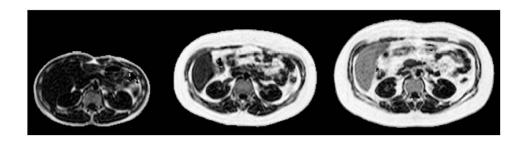
FIGURE 2

Areas covered by the ULSCO cohort questionnaires that address factors contributing to development of obesity. ^aIncludes determining the psychological and psychiatric status of the subject.



Procedures and assessments

- Obese, overweight and normal weight children, 5-18 years; regional referral center
- Longitudinal, annual visits
- Patient history (T2DM heredity)
- Questionnaires (food, physical activity)
- Procedures
 - Anthropometry, MRI
 - OGTT
 - Clamps
 - Indirect calorimetry
- Blood analysis
 - Glucose
 - Insulin, glucagon, GLP-1
 - Free fatty acids (FFAs), palmitate
- Genetic analysis
- Treatment: life-style, metformin
- Tissue repository, biobank (whole blood, plasma)

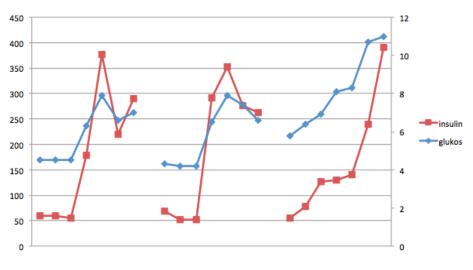


ULSCO

- Cohort
 - Obese: 690
 - Obese, second visit: 135
 - Normal weight, first visit: 110
- Glucose tolerance
 - Obese, NGT: 35%
 - Obese, IFG: 20%
 - Obese, IGT: 41%
 - Obese, T2DM: 4%

Obese 15-year-old girl)

First visit 2009







THEME [HEALTH.2011.2.4.3-2] [Development of novel treatment strategies based on knowledge of cellular dysfunction]

Grant agreement for: Collaborative project

Annex I - "Description of Work"

Project acronym: Beta-JUDO

Project full title: " Beta-cell function in juvenile diabetes and obesity "

Grant agreement no: 279153 Version date: 2012-01-30



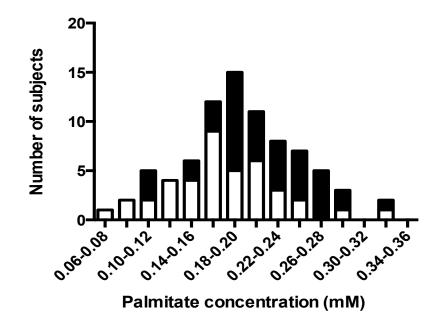


Obese children and FFAs

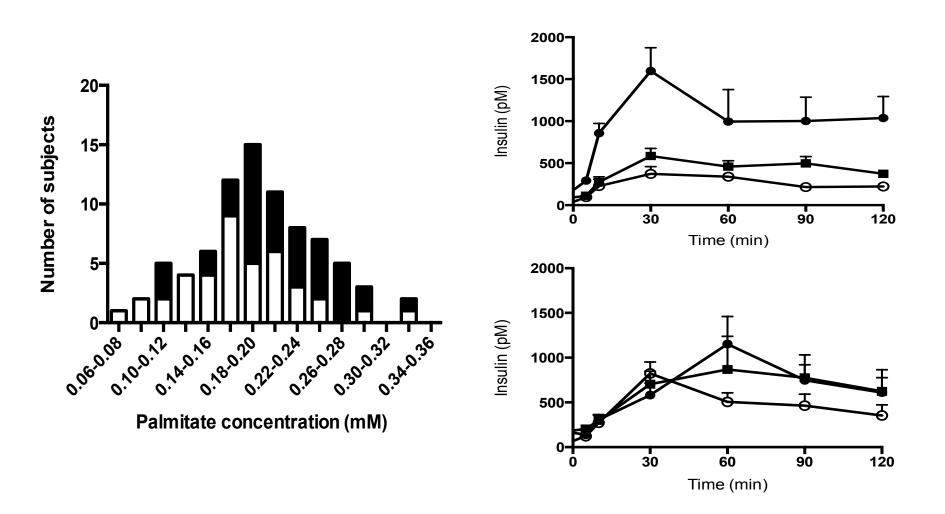
Table 3 FFA levels of study population

FFA				
Palmitoleic acid	1.25±0.10 (0.24–3.83)			
Palmitic acid	5.46 ± 0.19 (2.61–8.66)			
Linoleic acid	2.41 ± 0.16 (0.30–5.64)			
Oleic acid	8.96 ± 0.43 (3.10–18.05)			
Stearic acid	2.17+0.12 (0.29-4.10)			

Results are given as mean \pm SEM (in milligram per deciliter) and range



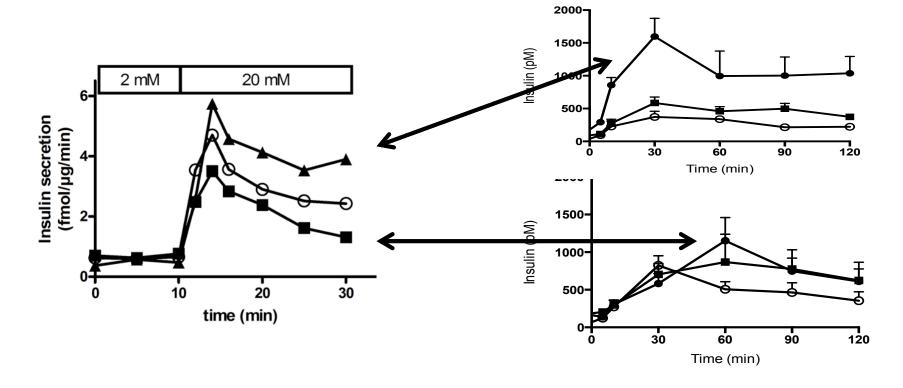
Obese children and palmitate



(Staaf et al, Pediatric Res, 2016)

Obese children, islets and palmitate

- Human islets exposed to high palmitate
- Obese children with high palmitate



(Staaf et al, Pediatric Res, 2016)

Hypothesis

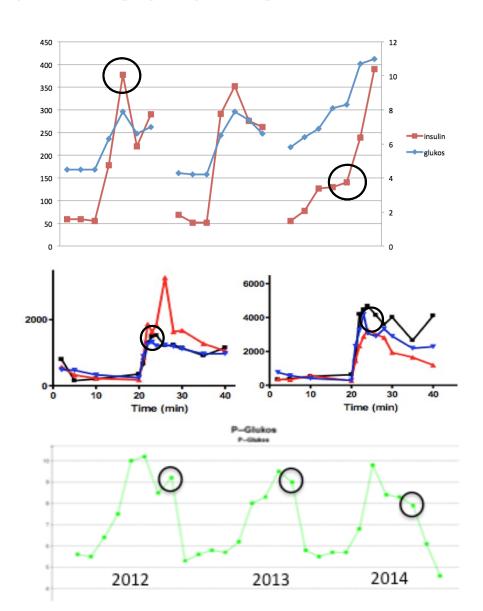
- Insulin hypersecretion:
 - early factor promoting and preceding lipid accumulation, insulin resistance and glucose intolerance (FP7 project "Beta-JUDO")

Translational medicine

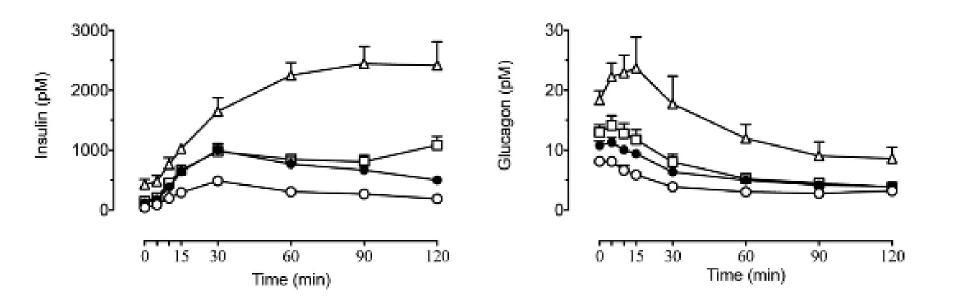
 15-year old girl developing T2DM

 Human islets high FFAs fail (red), recover with GLP-1 (blue)

 17-year old boy glucose intolerant, improving with metformin



Glucagon and insulin in ULSCO



Acknowledgements

- European Commission, FP7 project "Beta-JUDO" (2012-2016)
- Uppsala Health Summit: "Ending Childhood Obesity" (ECHO) (October 2016)
- European Commission, H2020 project "ECHO-zones" (decision Dec 2017)
- Swedish Diabetes Association (2012-2017)
- Regional Clinical Research Council (2012-2017)
- Swedish MRC (2010-2014)
- Network: Finland, Norway, Iceland, Austria, Spain, South Africa, Qatar, New Zeeland, Sri Lanka, USA, WHO



Tack!