

Pediatric Endocrinology **In Premature Infants**

**The optimal nutritional balance
needed for preventing metabolic
syndrome while achieving
optimal development for
preterm infants**

Dr. Iris Morag Prof. Orit Hamiel

Dr. Orly Stern Sarit Atia

Dr. Tzipi Strauss

Student: Mor Frisch



About the study

Longitudinal case control study

- **Inclusion criteria:** Preterm twins born at SMC between 2008-2015
- **Cases:** SGA twin ($<10^{\text{th}}\%$)
- **Controls:** AGA twin ($10^{\text{th}}-90^{\text{th}}\%$)

We chose twins in order to control genetic and life style variables

- **Exclusion:** Death prior to discharge, CNS & genetic abnormalities

Building the database

**We identified 1300
pairs of twins born at
Sheba Medical Center
between 2008-2015**



**97 sets of AGA/SGA
twins qualified for the
study**



**Twins that reached
the age of 5 will be
included in the
study**



What's next?

The aims of the study

- **To check for early signs of metabolic syndrome at the age of 5-8 years among the small babies (SGAs)**



The metabolic syndrome

Metabolic syndrome is a clustering of at least three of five of the following medical conditions:

- **abdominal (central) obesity**
- **elevated blood pressure**
- **elevated fasting plasma glucose**
- **high serum triglycerides**
- **low HDL**

Metabolic syndrome is associated with the risk of developing cardiovascular disease and diabetes.

What's next?

The aims of the study



- **To study the risk and additional risk factors for early markers of metabolic syndrome among the above population**
- **To check if the twins still show a difference in their percentiles today at 5-8 years**

What's next?

The aims of the study



- **To study weight changes over time**
- **If there are early signs, we want to be aware of them and therefore prevent or postpone the development of diabetes**

What's next?

The aims of the study

- **To evaluate neurodevelopment among SGA preterm infants and its correlation to early nutrition and growth**



Building the database

We created a chart that
includes more than 50(!)
different demographic &
clinical parameters in
analyzed risk factors

Building the database

	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AO		
	Study_Subj_Identifier	Study_Identifier	Family_Identifier	Sex_of_mother	Private_name_of_the_mother	Date_of_Birth	Twin 1/2	Mother's_age_at_Birth	spontaneous_DVT	Number_of_pregnancies (G)	Number_of_Children_present to this (P)	reason of birth	Antibiotic_delivery_start_date	steroids_delivery_start_date	Magnesium_delivery_start_date	VAG_CS	Apge_1 (min/score)	Apge_5 (min/score)	body_temperature_at_birth	CRP 22 at birth	Diabetes_during_pregnancy	Diabetes_1_year	Diabetes_2_year	Diabetes_3_year	Delivery_week	Delivery_day	Delivery_weight_kg	Head_circumference	Weight_at_25_weeks	head_circumference_25_weeks	minimal_weight	days_to_birth_weight	days_of_liveline	age in the beginning of per OS	Age(days)_at_milestone_100g	Age(days)_at_milestone_140g	NGC
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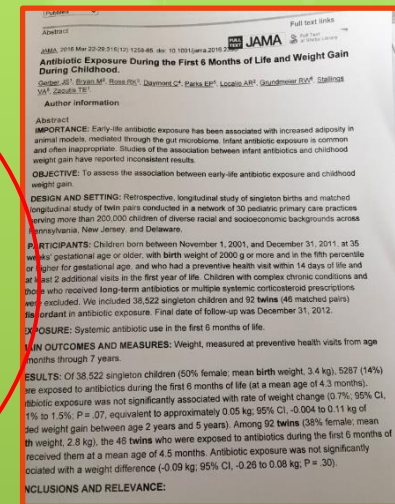
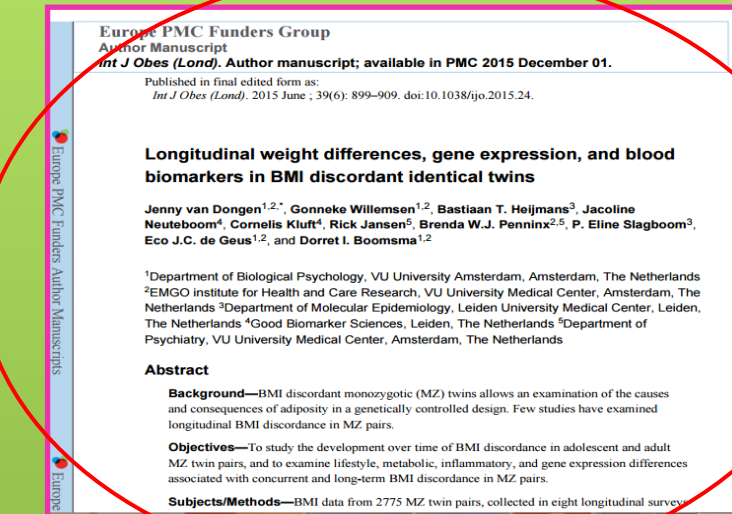
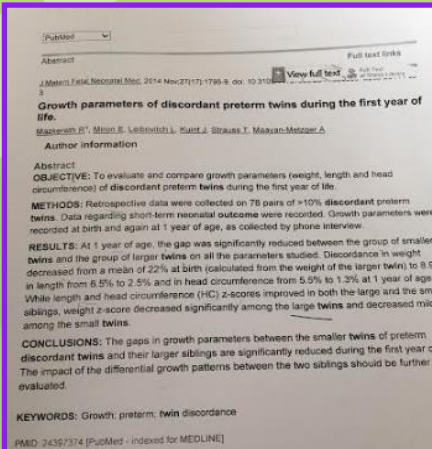
Building the database

About the chart :

- **Maternal demographic data** – e.g. mother's age at birth
- **Pregnancy data** – e.g. types of birth (vaginal\CS); spontaneous pregnancy or IVF
- **Hospitalization data**
- **Feeding data** - e.g. percentage of breast milk; number of days to regain birth weight
- **Infant demographic data** and clinical course during the NICU stay or initial hospitalization
- Etc...

Reading similar articles in Pubmed

In order to find what is already known
and what we can innovate



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ORIGINAL
ARTICLES

Girls and Boys Born before 28 Weeks Gestation: Risks of Cognitive, Behavioral, and Neurologic Outcomes at Age 10 Years

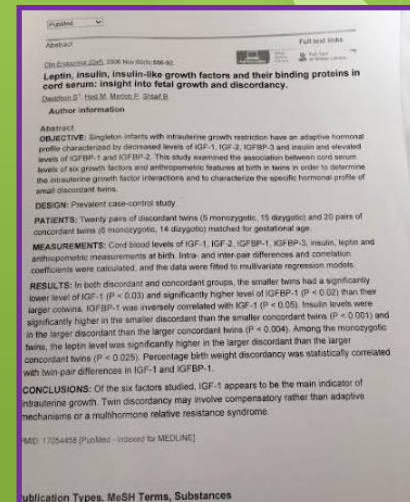
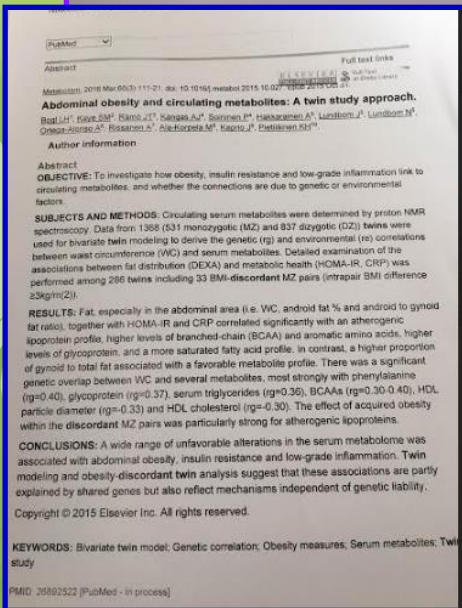
Karl C. K. Kuban, MD, SMEpi¹, Robert M. Joseph, PhD², Thomas M. O'Shea, MD³, Elizabeth N. Alred, MS^{4,5}, Timothy Heeren, PhD⁶, Laurie Douglass, MD¹, Carl E. Stafstrom, MD, PhD⁷, Hernan Jara, PhD⁸, Jean A. Frazier, MD⁹, Deborah Hirtz, MD¹⁰, and Alan Leviton, MD^{4,5}, on behalf of the Extremely Low Gestational Age Newborn (ELGAN) Study Investigators*

Objectives To compare the prevalence of cognitive, neurologic, and behavioral outcomes at 10 years of age in 428 girls and 446 boys who were born extremely preterm.

Study design A total of 889 of 966 eligible children previously enrolled in the multicenter Extremely Low Gestational Age Newborns Study from 2002-2004 were evaluated at 10 years of age. Children underwent a neuropsychological battery and testing for autism spectrum disorder (ASD), and parents reported on their child's behavior, development, and seizures.

Results Of the children, 28% of boys and 21% of girls exhibited moderate to severe impairment on summary measures of cognitive abilities. Boys had a higher prevalence of impairment than girls in nearly all measures of cognition, were more than twice as likely to have microcephaly (15% in boys, 8% in girls), and require more often assistive devices to ambulate (6% in boys, 4% in girls). In contrast, boys and girls had comparable risk for a history of seizure (identified in 10% of the cohort) or epilepsy (identified in 7% of the cohort). The boy-to-girl ratio of ASD (9% in boys, 5% in girls) was lower than expected compared with the overall US autism population.

Conclusions In this contemporary cohort of children born extremely premature and evaluated at school age,



Reading similar articles in Pubmed

**In order to find what is already known
and what we can innovate**

**We did not find anything similar to our
idea**

- **The most similar study was a monozygotic twins study in Leiden. They took 2775 pairs of twins and followed up on them over 20 years**

Reading similar articles in Pubmed

**In order to find what is already known
and what we can innovate**

Their goals were:

- 1. Checking the incidence of discordancy –
changes in BMI over 20 years**
- 2. Periodic evaluation of the following:
inflammatory, metabolic and other
biomarkers (glucose, insulin, total cholesterol,
LDL, triglycerides, CRP, IL-6, sIL-6R) in the
cohort of the monozygotic twins**

What's next?

Recruitment of the participants of the study

Invite the twins during their summer vacation

- **Running blood tests – checking blood markers of the metabolic syndrome (glucose, insulin, total cholesterol, LDL, triglycerides, CRP, IL-6, sIL-6R, and GGT, a lower level of HDL)**
- **Height evaluation**
- **Weight evaluation**
- **BMI**
- **Cognitive test**
- **Psychological test**
- **Parents background questionnaire**
- **Nutritional assessment**

Recruitment of the participants of the study



*** Invite the twins during their summer vacation and other school vacations during the year**

How does a day in the research look like?



Dr. Iris Morag

- **Running blood tests** –
checking blood markers of the
metabolic syndrome (glucose,
insulin, total cholesterol, LDL,
triglycerides, CRP, IL-6, sIL-6R,
and GGT, a lower level of HDL)



- **Height evaluation**
- **Weight evaluation**
- **BMI**



- **Nutritional assessment**



Sarit Atia
Dietitian

- **Cognitive test**
Gabriel Mandel



- **Endocrine Evaluation**
- **Parents background questionnaire**



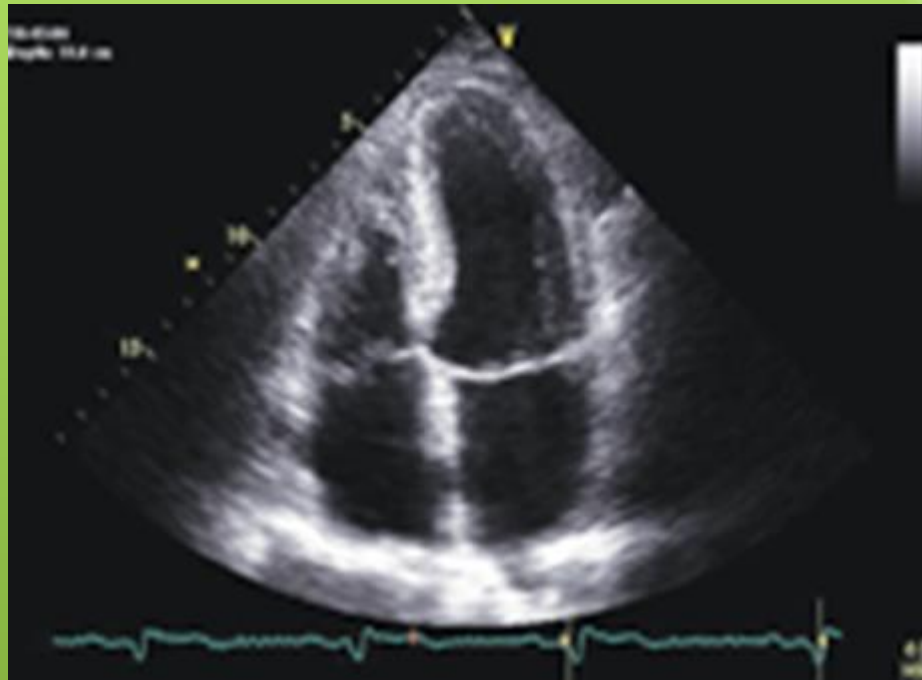
Prof. Orit Hamiel

- **Visceral fat and adipose tissue**



Dr. Orly Stern

- **Cardiac Echo**
Dr. Sharon Borik



What's next

- **Recruit more twins (hopefully)**
- **Analyzing the data**



Thank You





**To Dr. Iris Morag
on her acceptance to a
special research program in
Stanford, USA for a year!!!**



Stanford
University