The Metabolic Syndrome
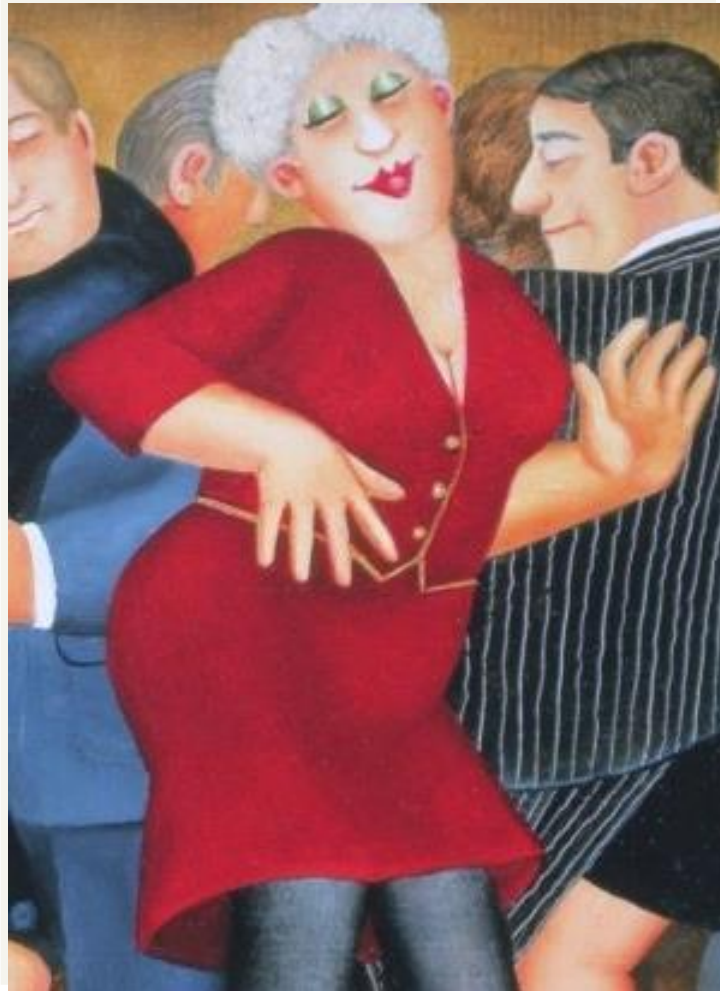
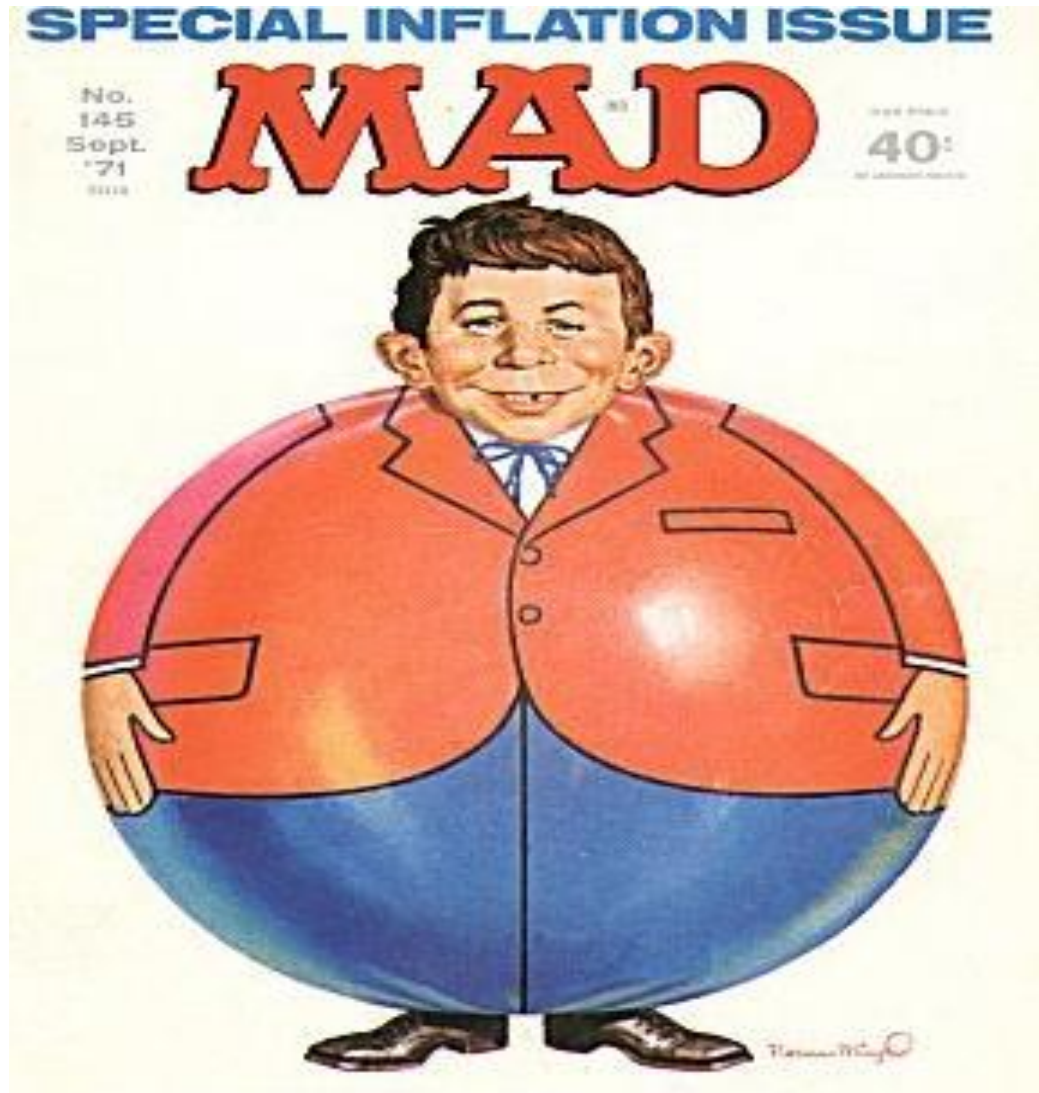**Prof Orit Pinhas-Hamiel**
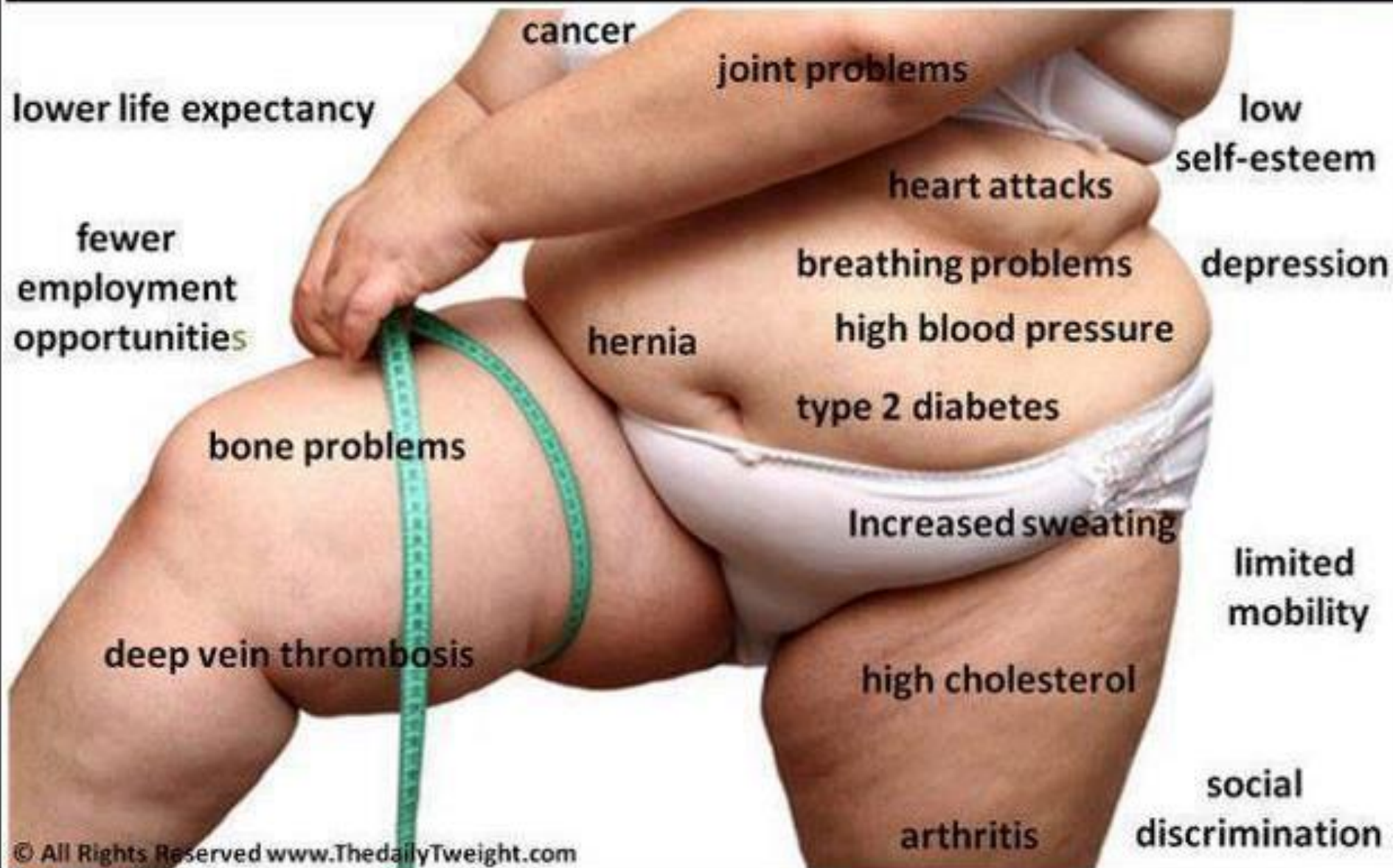
Pediatric Endocrine & Diabetes Unit
Safra Children's Hospital
Sheba Medical Center
Tel-Aviv University
Israel

What Me Worry?

Negative Effects of Obesity on Health

cancer

joint problems

lower life expectancy

low self-esteem

heart attacks

fewer employment opportunities

breathing problems

depression

hernia

high blood pressure

type 2 diabetes

bone problems

Increased sweating

limited mobility

deep vein thrombosis

high cholesterol

social discrimination

arthritis

The Jolly Fat...

The Metabolically Healthy Obese (MHO)

- A unique subset of obese individuals that appear to be protected from development of metabolic disturbances associated with obesity

- They have large quantities of fat mass, but demonstrate remarkably favorable cardiovascular risk profiles

The Normal Weight Metabolically Obese (NWMO)

- NWMO persons are a subgroup of individuals who have normal weight and BMI,
  but display a cluster of obesity-related abnormalities

Metabolic Syndrome
(Insulin Resistance Syndrome, Syndrome X)

- A clustering of cardiovascular risk factors that substantially increases the risk of
  - Cardiovascular disease
  - Type 2 diabetes
  - Cancer
  - Mortality

Metabolic Syndrome - Definition

n *National Cholesterol Education Program's Adult Treatment Panel III report* (**NCEP – ATPIII)**

 > 3 must be present

n Central obesity

n Triglycerides > 150 mg/dl

n HDL < 40 mg/dl in men, < 50 mg/dl in women

n Blood pressure > 130/80 mm/H

n Fasting glucose > 100 mg/dl

Metabolic Syndrome - Definition

- **WHO – 1999**

  - **Impaired glucose tolerance (2 hour > 140)**
  - **diabetes mellitus (fasting plasma > 126, 2 hour > 200)**
  - **insulin resistance (highest quartile fasting insulin or HOMA score)**

  - **PLUS at least 2**
    - **Blood pressure > 140/90 or on antihypertensive medication**
    - **Triglyceride > 150 or HDL < 40 men, < 50 women**
    - **Central or general obesity – BMI > 30 or WHR > 0.9 men, 0.85 women**
    - **Microalbuminuria (> 20 mcg/min or albumin:creatinine > 30)**

Metabolic Syndrome in children – Modified ATPIII

Criterion	Adults	Adolescents
Triglyceride	≥150	≥ 110
HDL	Males <40 Females < 50	≤ 40
Obesity	WC Males > 102 Females > 88	BMI or WC ≥ 90th
Glucose	Fasting ≥ 100 2 hour ≥ 140	Fasting ≥ 100 2 hour ≥ 140
Blood pressure	≥ 130/85	≥ 90th

Cook et al, Arch Pediatr Adolesc Med 157:821, 2003

Central Obesity

Central Obesity

Labels on diagram: Bottom of ribs, Umbilicus, Waist, Iliac crest, Greater Trochanter, Hips
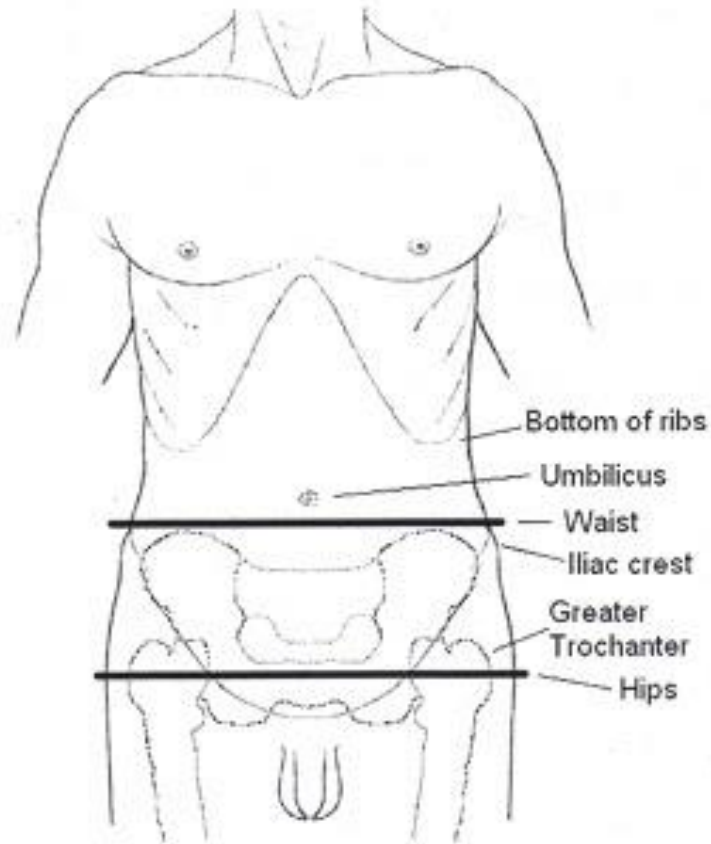
Waist Measurement	At Increased Risk	At High Risk
Men	>94 cm	>102 cm
Women	>80 cm	>88 cm

Waist Circumference

|	Percentile for boys					Percentile for girls				
	10th	25th	50th	75th	90th	10th	25th	50th	75th	90th
Intercept	39.7	41.3	43.0	43.6	44.0	40.7	41.7	43.2	44.7	46.1
Slope	1.7	1.9	2.0	2.6	3.4	1.6	1.7	2.0	2.4	3.1
Age (y)										
2	43.2	45.0	47.1	48.8	50.8	43.8	45.0	47.1	49.5	52.2
3	44.9	46.9	49.1	51.3	54.2	45.4	46.7	49.1	51.9	55.3
4	46.6	48.7	51.1	53.9	57.6	46.9	48.4	51.1	54.3	58.3
5	48.4	50.6	53.2	56.4	61.0	48.5	50.1	53.0	56.7	61.4
6	50.1	52.4	55.2	59.0	64.4	50.1	51.8	55.0	59.1	64.4
7	51.8	54.3	57.2	61.5	67.8	51.6	53.5	56.9	61.5	67.5
8	53.5	56.1	59.3	64.1	71.2	53.2	55.2	58.9	63.9	70.5
9	55.3	58.0	61.3	66.6	74.6	54.8	56.9	60.8	66.3	73.6
10	57.0	59.8	63.3	69.2	78.0	56.3	58.6	62.8	68.7	76.6
11	58.7	61.7	65.4	71.7	81.4	57.9	60.3	64.8	71.1	79.7
12	60.5	63.5	67.4	74.3	84.8	59.5	62.0	66.7	73.5	82.7
13	62.2	65.4	69.5	76.8	88.2	61.0	63.7	68.7	75.9	85.8
14	63.9	67.2	71.5	79.4	91.6	62.6	65.4	70.6	78.3	88.8
15	65.6	69.1	73.5	81.9	95.0	64.2	67.1	72.6	80.7	91.9
16	67.4	70.9	75.6	84.5	98.4	65.7	68.8	74.6	83.1	94.9
17	69.1	72.8	77.6	87.0	101.8	67.3	70.5	76.5	85.5	98.0
18	70.8	74.6	79.6	89.6	105.2	68.9	72.2	78.5	87.9	101.0

Fernández JR 2004 Oct;145

Central Obesity

- Abdominal obesity is associated with multiple cardiometabolic risk factors, including: dyslipidemia, elevated blood glucose, type 2 diabetes and inflammation – all factors leading to the development of cardiovascular disease

- Overall, 86% of abdominally obese patients had at least one other cardiometabolic risk factor (NHANES data on file).

Turkoglu C *et al*, 2003).

Glucose Metabolism / Diabetes

Prediabetes
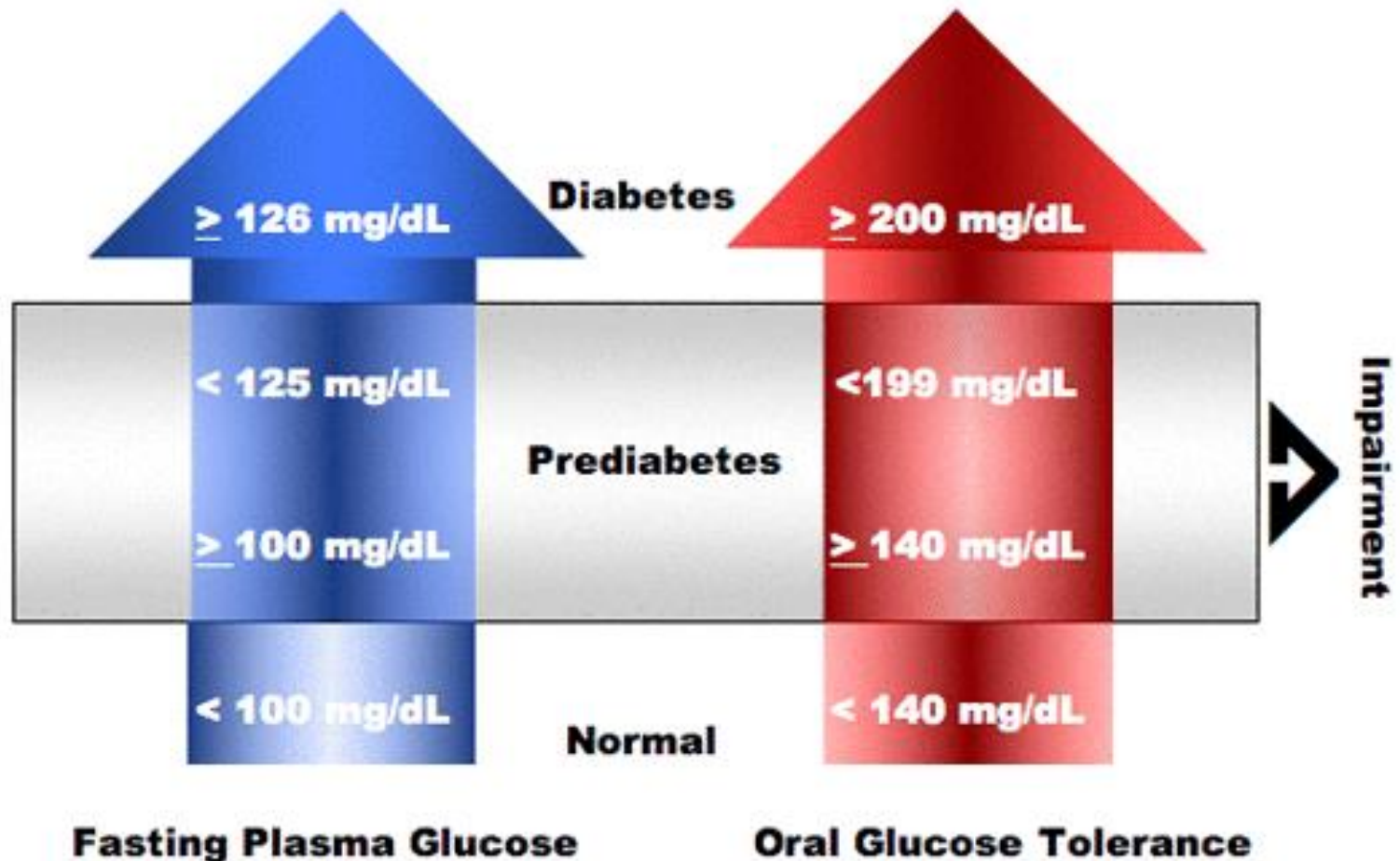
- Prediabetes is characterized by higher than normal blood glucose levels, either impaired fasting glucose or impaired glucose tolerance not yet high enough to be classified as diabetes

Hypertension

Hypertension

- A systolic blood pressure **(SBP) >139 mmHg** and/or

- A diastolic **(DBP) >89 mmHg.**

- Based on the average of **two or more** properly measured, seated BP readings.

- On each of **two or more** office visits

Table 1. Classification and management of blood pressure for adults*

| BP CLASSIFICATION	SBP* MMHG	DBP* MMHG	LIFESTYLE MODIFICATION	INITIAL DRUG THERAPY	
				WITHOUT COMPELLING INDICATION	WITH COMPELLING INDICATIONS (SEE TABLE 8)
NORMAL	<120	and <80	Encourage		
PREHYPERTENSION	120–139	or 80–89	Yes	No antihypertensive drug indicated.	Drug(s) for compelling indications.[‡]
STAGE 1 HYPERTENSION	140–159	or 90–99	Yes	Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.	Drug(s) for the compelling indications.[‡] Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.
STAGE 2 HYPERTENSION	≥160	or ≥100	Yes	Two-drug combination for most[†] (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).	

Dyslipidemia

Triglycerides

Triglycerides

- Elevated triglyceride levels, are stronger risk factors for heart disease in women than in men

NORMAL ARTERY

ARTERY NARROWED BY PLAQUE

BLOOD FLOW

ATHEROSCLEROTIC PLAQUE
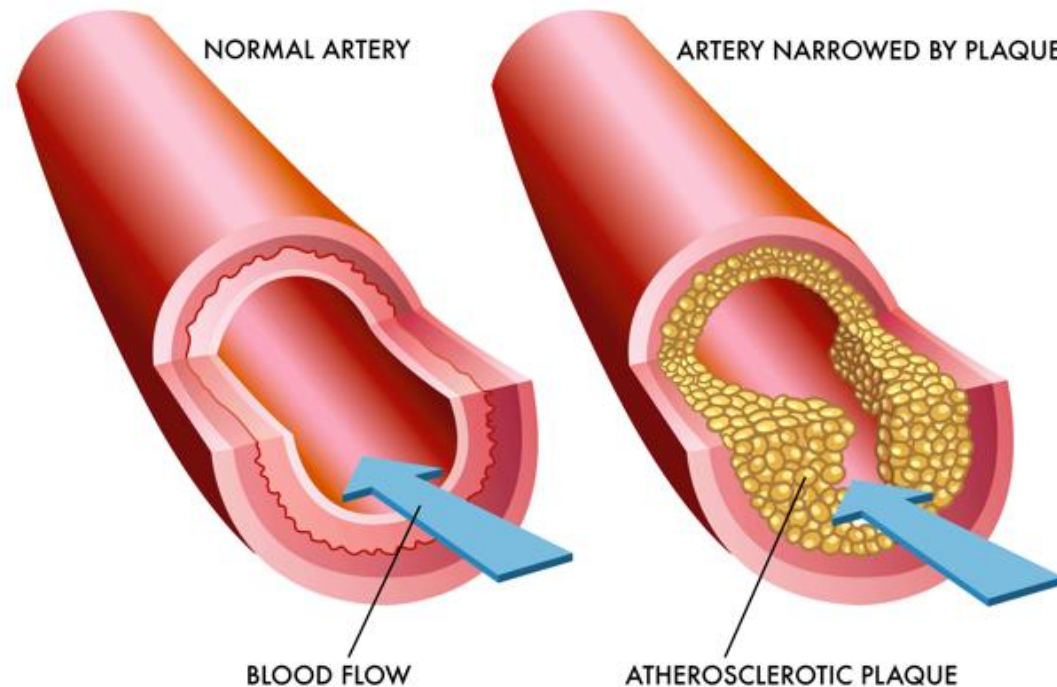
- Diets high in refined carbohydrates, with carbohydrates accounting for more than 60% of the total energy intake, can increase triglyceride levels

- There is evidence that carbohydrate consumption causing a **high glycemic index** can cause insulin overproduction and increase triglyceride levels
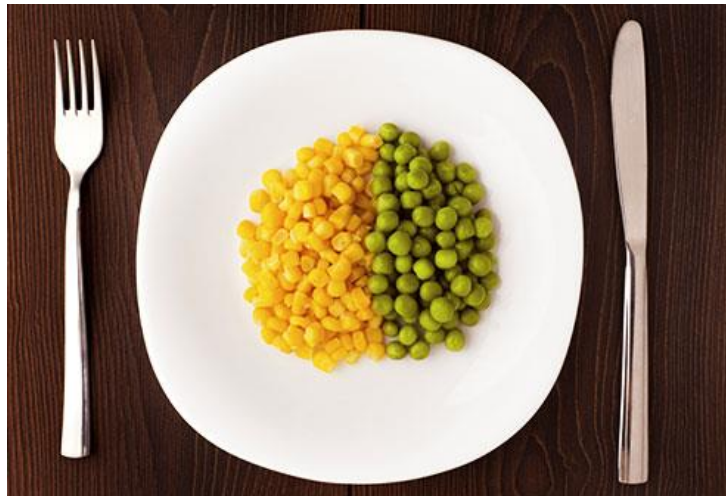
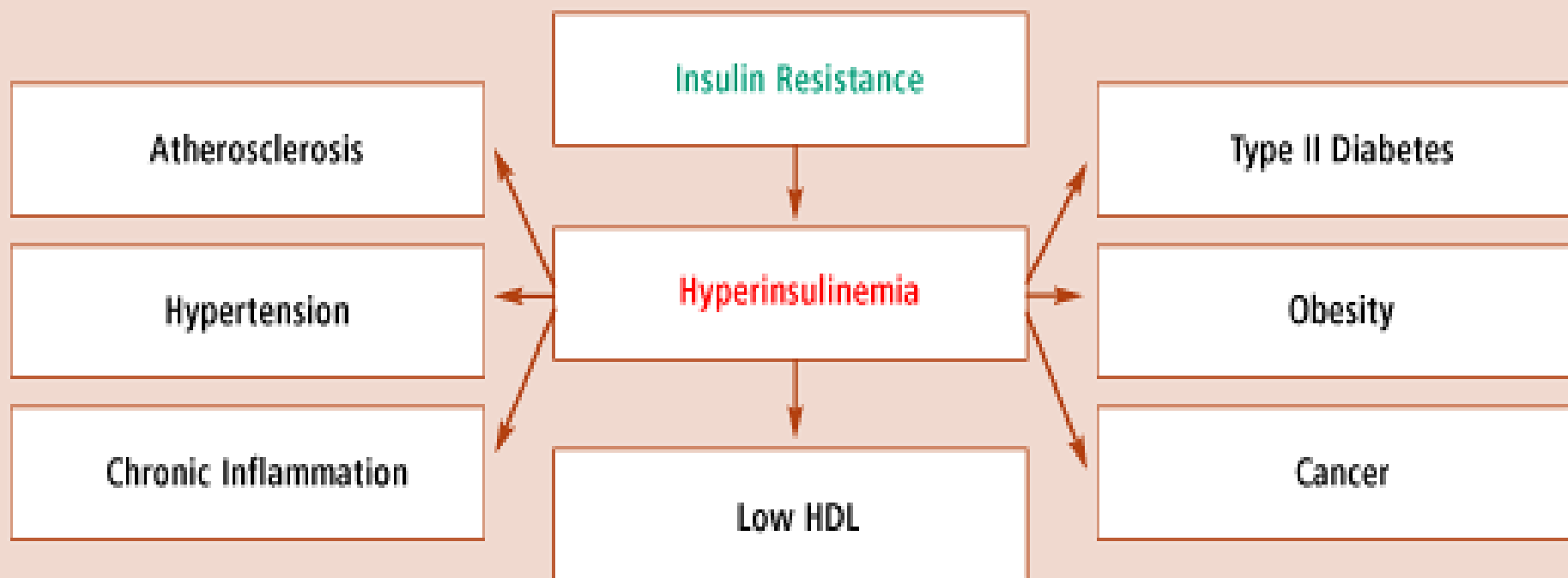- Heavy alcohol consumption can elevate triglycerides levels

HDL

HDL

- Low HDL is an independent risk factor for CVD

- In contrast, high HDL levels are associated with longevity and are protective against the development of atherosclerotic disease

- In the Framingham Study, risk for CVD increases sharply as HDL below 40 mg/dL

Insulin Resistance

Acanthosis Nigricans

Prevalence of the Metabolic Syndrome

- Depends on
  - ethnicity and sex
  - the prevalence increases with age
  - the prevalence increases with BMI
  - underlying disease

Metabolic status	BMI											
	≤18.5 kg/m^2			18.6–23.9 kg/m^2			24.0–27.9 kg/m^2			≥28.0 kg/m^2		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Individual component												
High blood pressure	57.4	56.3	56.8	67.3	64.7	65.8	72.8	75.3	74.3	88.0	82.6	84.6
Hyperglycemia	21.3	32.4	28.0	40.9	44.7	43.1	57.4	54.6	55.8	64.1	61.4	62.4
Hypertriglyceridemia	4.3	11.3	8.5	12.1	25.8	20.1	26.9	36.1	32.3	31.5	43.7	39.4
Low HDL cholesterol	4.3	16.9	11.9	7.8	27.8	19.4	18.8	40.4	31.4	25.5	41.9	36.1
Central obesity	2.1	8.5	5.9	12.5	44.8	31.4	61.1	91.9	79.0	97.8	100	99.2
Metabolic syndrome	0	1.6	0.9	7.5	24.4	17.3	38.9	64.8	53.9	71.7	76.0	74.5
Numbers of components												
≥1	68.1	77.5	73.7	79.2	88.5	84.6	94.7	98.4	96.9	100	100	100
≥2	17.0	35.2	28.0	42.4	68.5	57.8	77.0	90.1	84.6	96.2	95.2	95.6
≥3	4.3	9.9	7.6	13.3	33.4	25.0	46.4	65.8	57.6	72.8	76.0	74.9
≥4	0	2.8	1.7	4.3	14.6	10.3	16.6	33.4	26.4	29.9	43.4	38.6
5	0	0	0	0	2.5	1.5	2.4	10.7	7.2	8.2	15.0	12.5

Prevalence of Overweight, Obesity and Metabolic Syndrome Components in Multiple Sclerosis Patients with Significant Disability

Moran Livne

European Journal of Neurology

AIM

- To determine the prevalence of overweight and obesity, as assessed by BMI and cardiometabolic risk factors, in a cohort of adult patients with long duration of MS and significant disability

- We hypothesized that MS patients may be at increased risk to be heavier and to have components of the MetS, compared with the general population.

Obesity in MS

- Obesity may be increased among MS patients secondary to the deleterious effects of the disease:
  - These effects include frequent high dose steroid treatments
  - Decreased mobility and physical activity due to motor disability.

Methods

- The Sheba MS Center data registry was queried to identify patients according to the following:
  - diagnosis of MS according to Macdonald criteria
  - age 40 to 65 years
  - disease duration >10 years
  - neurological disability according to the Expended Disability Status Scale (EDSS) score ≥3.0

Demographic & clinical data accessed from database

- Gender, age, disease duration and EDSS

- Number of high dose steroid treatments
- The use of the following medications:
  - Antidepressants
  - Hypertension treatment
  - Oral anti diabetic medications

- Weight, height, **waist circumference**, and blood pressure are measured within the last three months

- Laboratory data, including fasting glucose, triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) levels

- Prevalence rates of overweight and obesity in Israel were obtained from the first Israeli National Health and Nutrition Survey (MABAT)

Results

- The study population comprised 130 MS patients, 72.3 % females

- mean±SD age 55.8±6.0 years

- disease duration 18.2±10.1 years

- EDSS 5.5±1.0

Results

- **Obesity** was present in
  - **18.5%** of disabled MS patients compared with
  - **28.3**% in the general population (p<0.001)

- **Overweight** was present in
  - **34.6%** of disabled MS patients compared with
  - **45.0%** in the general population (p<0.001)

- Overall, **46.9%** of MS patients were with normal weight compared to **27%** in the age matched general population.

Rates of Obesity & Overweight

	MS men patients	General population:
Obesity	8.1%	24.9%
Overweight	45.9%	50.7 %

	MS women	General population
Obesity	22.6%	33.1%
Overweight	30.1%	38.7 %

* (p<0.001)

Within the MS population the prevalence of obesity was higher for females than for males, while the prevalence of overweight was lower for females than for males, similar to the trend observed in the general population

The MetS among MS Individuals

- 39 MS patients (**30%**) had the MetS

The MetS among MS Individuals

- There are no data on the prevalence of MetS in the general Israeli population

- Data of same age groups from other countries showed that **21-37** % of the general population have the MetS, according to the ATP III criteria

- Thus, our findings show similar rates of the MetS, despite lower rate of overweight and obesity.

The MetS among MS Individuals

- 39 MS patients (**30%**) had the MetS
- MS patients with the MetS compared with those without MetS were significantly
  - older   (59.1±5.8 vs. 54.3±5.5 years, p<0.0001)
  - heavier (BMI 29.6±7. vs. 25.1±4.7 3 kg/m^2, p=0.001)

- no difference in
  - disease duration (17.7±9.9 vs. 18.5±10.2 years, p=0.6) or in
  - the number of steroid courses (6.5±10.1 vs. 6.4±8.2)

Components of the MetS

- 56.1% of disabled MS patients had **central obesity** by waist circumference
- 27.7 % were treated for hypertension
- 17.7% had elevated blood pressure
- 10% had type 2 diabetes mellitus
- 35.5% had fasting hyperglycemia
- 31.3% had treated dyslipidemia
- 26.1% had elevated TG level
- 28% had low HDL-C

Central Obesity in MS

- **56%** of MS patients had waist circumference consistent with abdominal obesity

- Abdominal obesity is a major risk factor for coronary heart disease and type 2 diabetes

- Indeed, patients with MS have been reported to have a 2.4 fold increased rate of deaths related to CVD than people without MS

Central Obesity in MS

- The paradox between lower prevalence of obesity & overweight but increased waist circumference suggests that the lower BMI is misleading as an indication of health

- This finding is supported by previous observations of lower ratios of muscle to fat in MS patients and individuals with other disabilities

Hypertension

- **28%** of the study population is treated for hypertension, corresponding to the reported prevalence in the general Israeli population

- Consistent with the finding of the NARCOMS study, in which 30% of patients with MS reported hypertension

Type 2 Diabetes

- 10% of MS patients are diagnosed with T2DM, similar to the prevalence of 11.7% of the Israeli population ages 45-64 years

Dyslipidemia

- There are limited data on the prevalence of dyslipidemia in the general population in this age group in Israel, we could not assess the prevalence of MS patients compared with the general population

- Nevertheless as an adverse lipid profile was found to be associated with disability and progression in disability in subjects with MS

In Summary

- Increased waist circumference & other cardiovascular risk factors were found to be particularly prevalent among adult disabled MS patients, despite reduced rates of obesity and overweight

- This suggests that the lower BMI in this population is misleading in its association with health risk

- Our findings highlight the importance of guiding clinicians to follow waist circumference as a marker for potential cardiovascular risk among normal weight individuals with MS.

Overweight, Obesity and the Metabolic Syndrome in Type 1 Diabetes

Kaidar Kfir

Type 1 Diabetes Mellitus

- Type 1 diabetes mellitus (T1DM) is one of the most prevalent chronic diseases of childhood, with a distinct risk factor for CVD

- Onset of atherosclerotic changes has been shown to appear early in T1DM patients

- Overweight and obesity have been found to be highly prevalent among children with T1DM and to be associated with cardiometabolic risk

*Snell-Bergeon JK, Nadeau K (2012). J Cardiovasc Transl Res 5: 446-462
* Jarvisalo MJ, Raitakari M, Toikka JO, et al. (2004). Circulation 109: 1750-1755
* Liu LL, Lawrence JM, Davis C, et al. (2010) y. Pediatr Diabetes 11: 4-11

Aims

- Determine the prevalence of overweight and obesity among children, adolescents & young adults with type 1 diabetes (T1DM) compared to the general population

- Assess the prevalence of the metabolic syndrome (MetS) and its components

Methods

➢ Patients aged 5 to 30 years, diagnosed with T1DM and followed in the National Juvenile Diabetes Clinic, Maccabi Health Care Services, Raanana

➢ Definition of obesity and overweight by Centers for Disease Control and Prevention (CDC):

- <u>Overweight</u>: $85^{th} \leq$ BMI $< 95^{th}$ percentile (1.036<Standard deviation score<1.645), or $25 \leq$ BMI $<$ 30 kg/m2

- <u>Obesity</u>: BMI $\geq 95^{th}$ percentile (SDSs $\geq$1.645), or BMI $\geq$ 30 kg/m2

Methods

Criteria for the metabolic syndrome:

- two or more of the following criteria:
    - BMI above the 97th percentile (z score, 2.0 or more)
    - Triglyceride level above the 95th percentile
    - HDL cholesterol level below the 5th percentile
    - Elevated blood pressures, defined as systolic and /or diastolic blood pressure above the 95th percentile for age and sex

* Weiss R, Dziura J, Burgert TS, et al. (2004) . N Engl J Med 350: 2362-2374
* Daniels SR, Greer FR (2008) Pediatrics 122: 198-208
* (1996) Update on the 1987 Task Force Report on High Blood Pressure in   Pediatrics 98: 649-658

Methods

Data obtained by chart review, 2012 - 2013:
- Gender
- Age of onset of diabetes
- Disease duration
- Weight, height, BMI percentiles, and BMI Z score
- Blood pressure
- Mode of diabetes treatment (pump or multiple daily injections (MDI)
- HbA1c level
- Triglycerides and HDL-C levels

Additional diseases:
- Hyper or hypothyroidism
- Celiac
- ADHD
- Medications:
  - Antidepressant
  - Hypertension treatment [angiotensin-converting enzyme (ACE) inhibitors / angiotensin receptor blockers (ARB)]
  - Ritalin

Methods

➢ males and females separately

➢ age groups:

- 6 to <12 years (children)
- 12 to <15 (younger adolescents)
- 15 to <18 (older adolescents)
- 18 to <25 (young adults)
- and 25 to <34 (older adults)

➢ Databases:

➢ the 1st Israeli national health and nutrition survey (MABAT) for ages 12-15, 15-18 and adults aged 25-34 years

➢ data from nominees for military service in the Israel Defense Forces (IDF)

➢ Survey of Israeli schoolchildren aged 6-12 years

[*] Nitzan Kaluski D, et al (2009) . Public Health Nutr 12: 774-782
[*] Keinan-Boker L, (2005) Isr Med Assoc J 7: 219-223
[*Levin A, (2010) Weight disorders and associated morbidity among young adults in Israel 1990-2003. Pediatr Int 52: 347-352
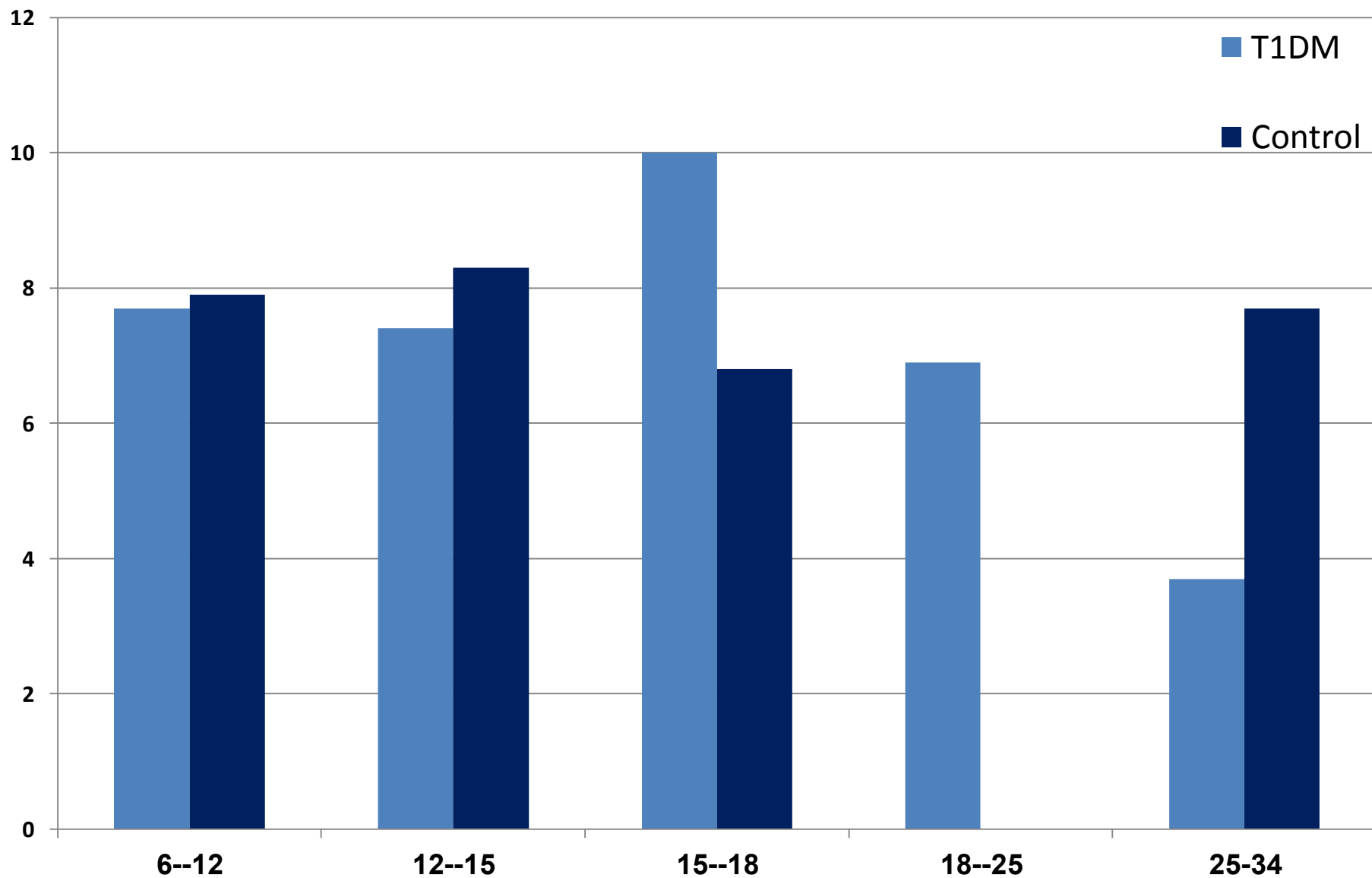[* Huerta M, et al (2006) : 1990-2000. Acta Paediatr 95: 444-449
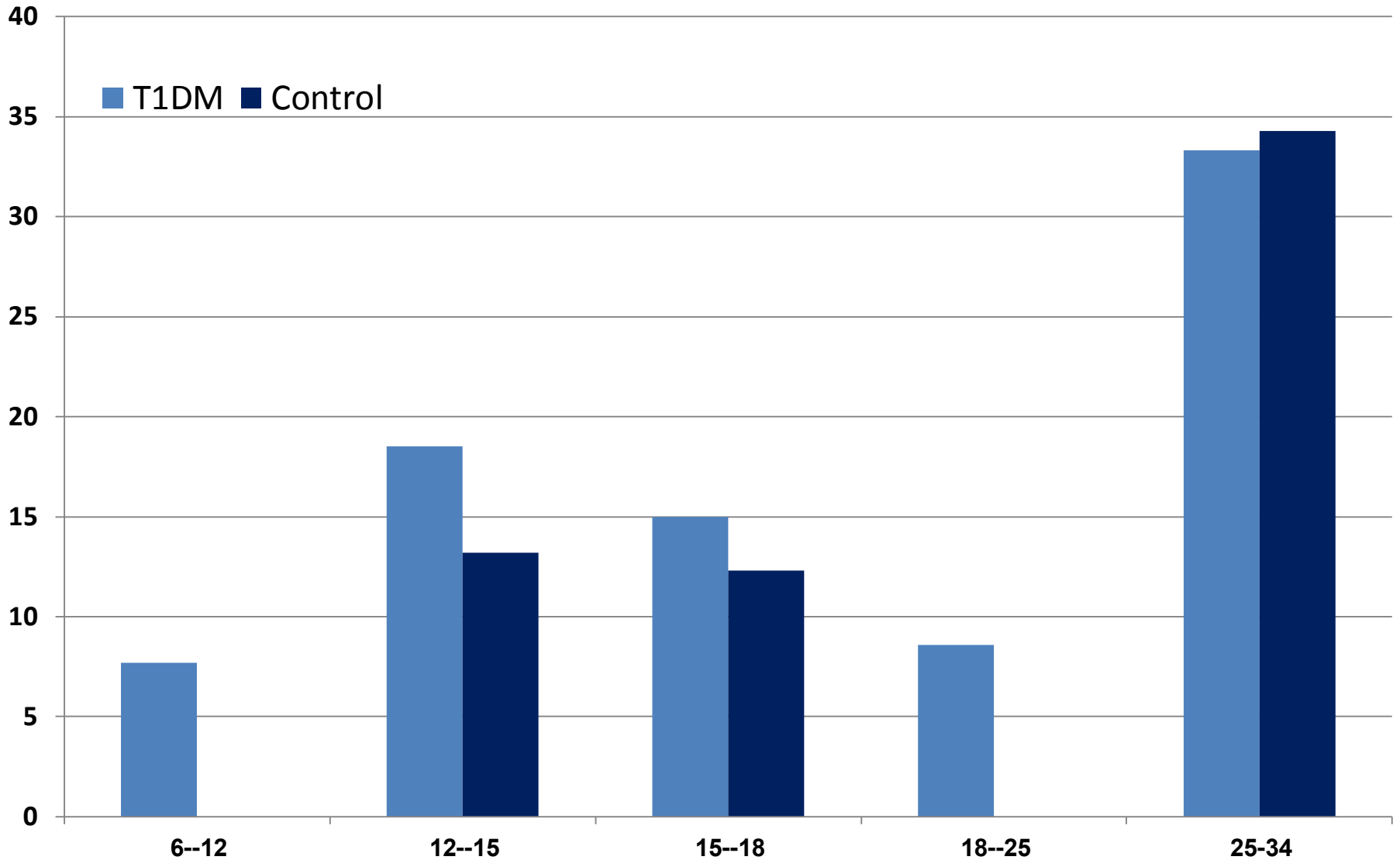[*] Greenberg L, (2007) . Int J Eat Disord 40: 51-58

Results : The study population

- 326 patients: 168 (51%) females; 158 (49%) males

- **Age**: mean   18.5±6.0 years
      median: 18.3 years (IQR 13.8-23.2)

- **Diabetes duration**:
  mean: 8.7±5.0 years (range 1.0-24.9)
  median : 7.5 years (IQR 4.9-11.6)

- **HbA1c level**: 8.1±1.3 %
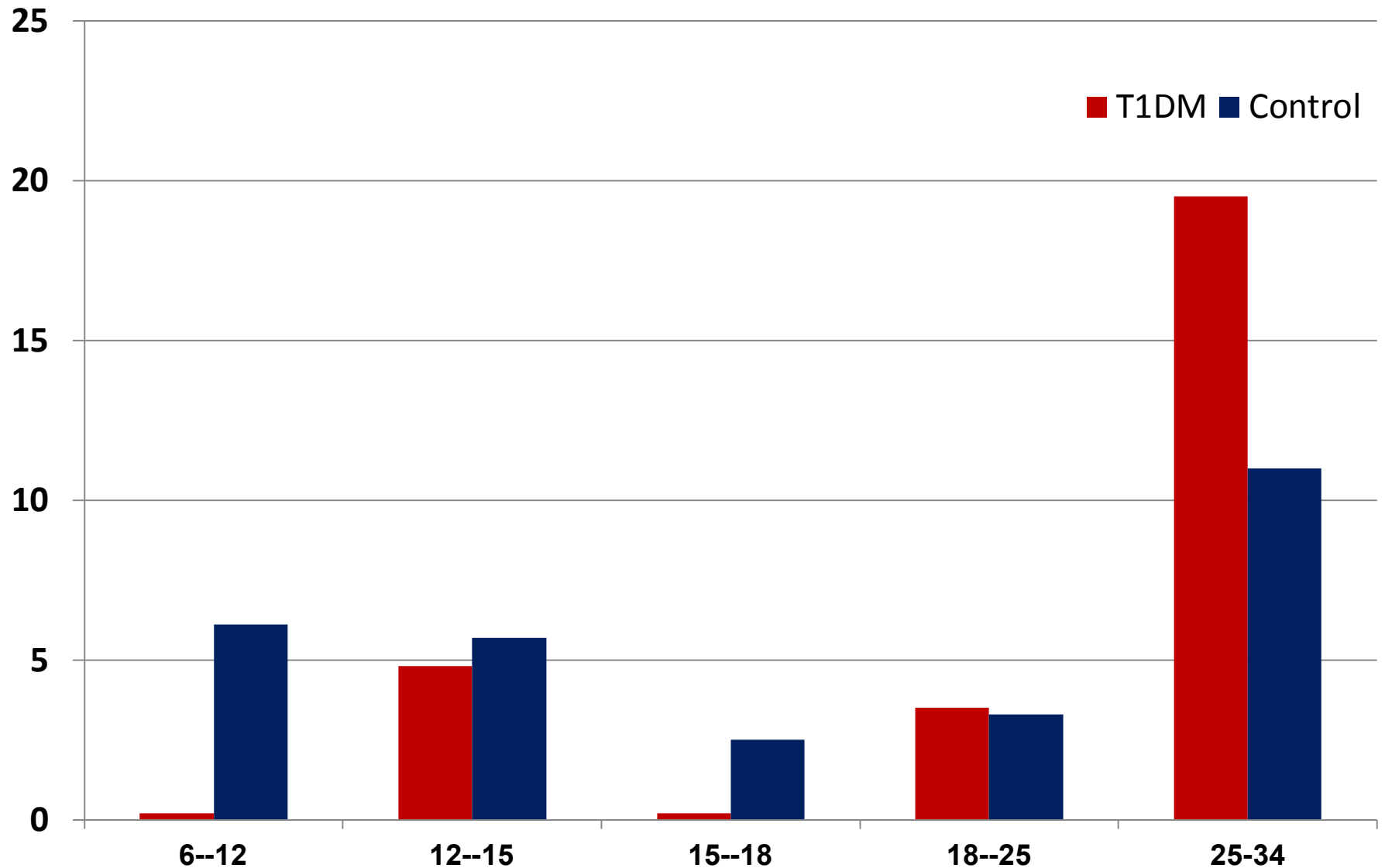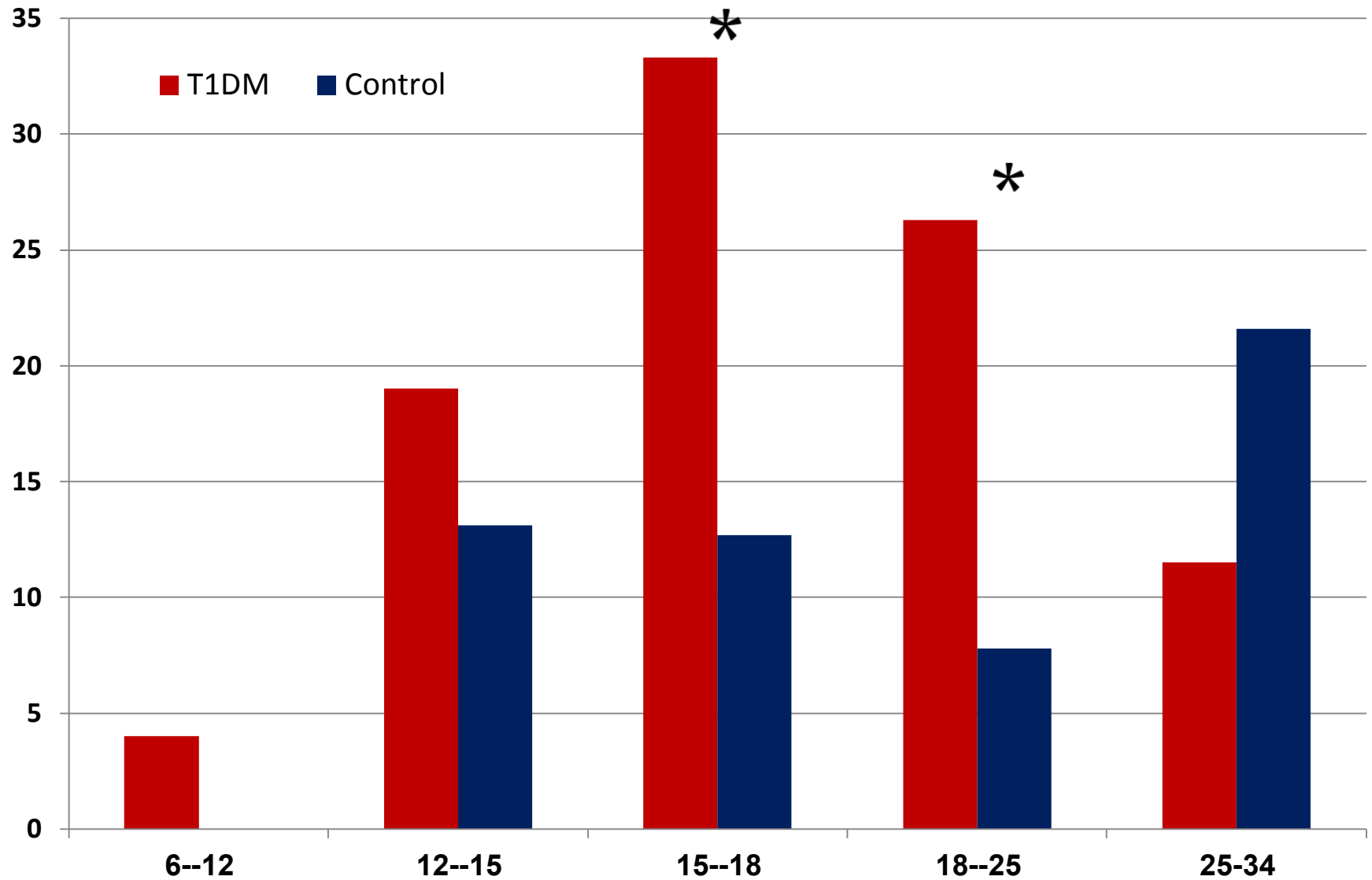
Obesity - **males**

Overweight - **males**

Obesity - **Females**

OVERWEIGHT - FEMALES

In summary

- The prevalence of overweight among older adolescents (15-18 years) & young adults (18-25 years) with T1DM was significantly higher than that of the general Israeli population

- There were no obese T1DM females in the 15-18 year   age group

- No association was found between the patients characteristics and the different weight groups

Metabolic Syndrome in Type 1 Diabetes

- **7%** of all patients met the modified criteria for MetS

- The mean±SD HbA1c level of patients with MetS was 8.6±1.9 compared with those without the syndrome 8.0±1.3, p=0.14.

Prevalence of Metabolic Syndrome & its Parameters in T1DM

P value	Obesity %	Overweight %	Normal weight %	N	
0.0004	**35.3**	**8.1**	**4.9**	**23**	**Metabolic syndrome**
<0.0001					**Hypertension**
	52.9	**22.6**	**13.6**	56	*Abnormal*
	11.8	**3.2**	**3.3**	12	*ACEi\ARB Treatment*
0.04	**17.7**	**9.7**	**4.5**	20	**low HDL**
0.5	17.6	8.1	11.7	37	high triglycerides
0.003	11.8	0	0	2	BMI- Z score ≥2
0.1	18.8	16.1	8.2	33	low non HDL
0.04					**LDL**
	23.5	40.3	30.3	103	*High*
	23.5	9.7	5.7	24	*Statin Treatment*

Summary and Conclusions

- Overweight but not obesity was more prevalent in females with T1DM.

- MetS , hypertension and low HDL-C were more prevalent among overweight and obese individuals with T1DM than among normal weight individuals with T1DM

- These findings are important, as MetS and its components,

- mainly microalbuminuria, have been shown to predict

- coronary artery disease, renal failure and diabetesrelated

- death in T1DM patients

Thanks for Your Attention

Newsweek

THE AUSTRALIANS ARE COMING • BEIJING BACKLASH

Fat World

We're Eating More Junk And Getting Less Exercise.

Obesity Is The Globe's Newest Epidemic.

TIME

The Obesity Epidemic in America