Metabolic Syndrome in 47 XXY

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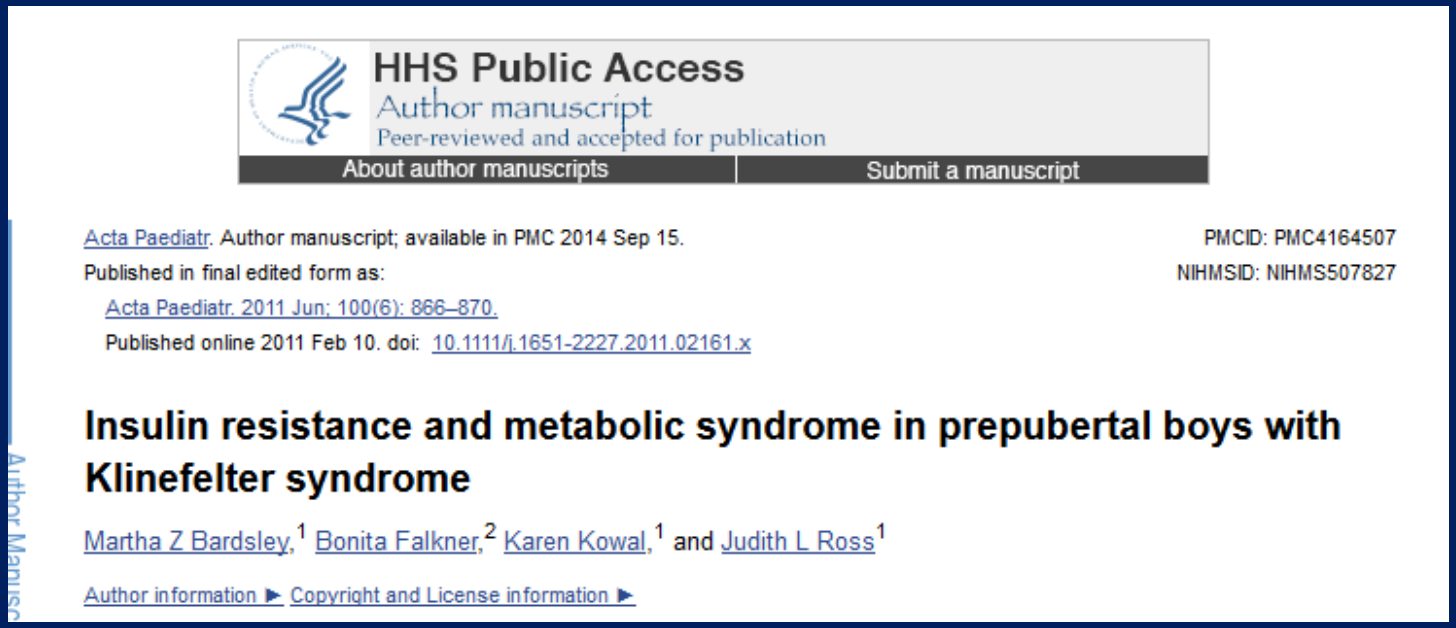
Learning Objectives

- Review the data on body composition, insulin resistance and metabolic syndrome in relation to hypogonadism in those with XXY
- Review the data on treatment with testosterone and impact on body composition, insulin resistance and metabolic syndrome in those with XXY versus 46 XY men
- Review the relationship among 47 XXY and the cardiovascular system and risk for thrombosis



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Insulin resistance and metabolic syndrome in prepubertal boys with Klinefelter syndrome

Martha Z Bardsley,[1] Bonita Falkner,[2] Karen Kowal,[1] and Judith L Ross[1]

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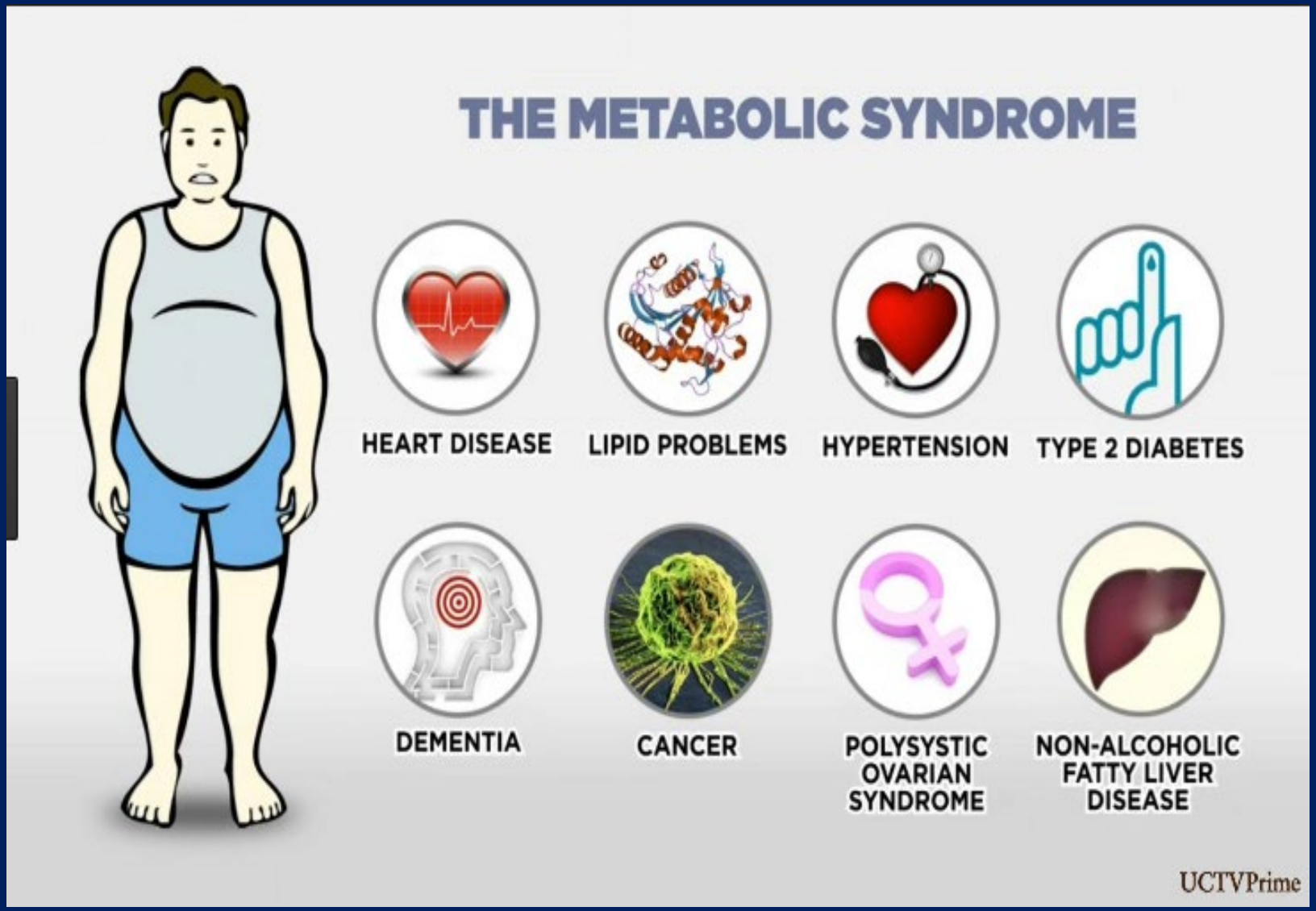
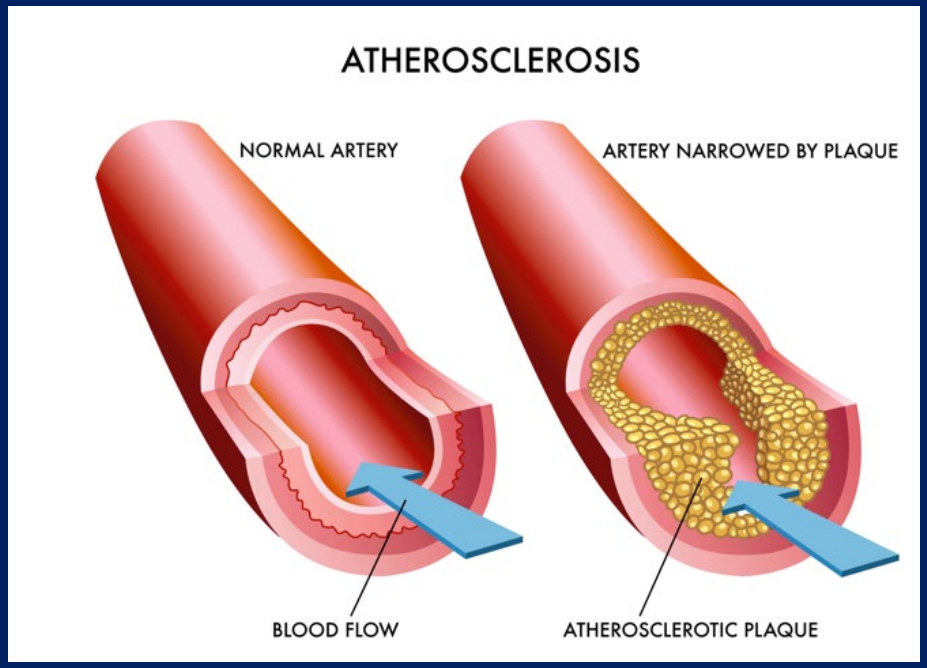
- Aim: To investigate risk factors for metabolic syndrome in prepubertal boys with Klinefelter Syndrome


THE METABOLIC SYNDROME
HEART DISEASE
LIPID PROBLEMS
HYPERTENSION
TYPE 2 DIABETES
DEMENTIA
CANCER
POLYSYSTIC OVARIAN SYNDROME
NON-ALCOHOLIC FATTY LIVER DISEASE
UCTVPrime



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Insulin resistance and metabolic syndrome in prepubertal boys with Klinefelter Syndrome (KS)

- It is unclear what factors increase the risk for insulin resistance and diabetes in adult men with KS
  - Does this risk begin during childhood
  - Does increased total body fat/waist circumference precede the hypogonadal state?
  - Does the hypogonadal state predispose to increased total body fat?

Bardley et al. Acta Paediatrica, 2011, pp 866-870

Physical Exam Features of Boys with Klinefelter Syndrome compared with Controls

	KS (n = 89)	Controls (n = 34)	p Value
Mean age (years)	7.5 ± 2.4	8.1 ± 2.3	0.3
% Pubic Hair Tanner 1	91	97	0.1
Mean height (SDS)	0.6 ± 1.0	0.1 ± 1.0	0.02*
Mean weight (SDS)	0.6 ± 1.1	0.6 ± 1.2	0.8
Mean BMI (SDS)	0.5 ± 1.2	0.7 ± 1.2	0.4
% Body Fat	25.6 ± 9.3	27.8 ± 12.0	0.5
% waist circumference > 75 ‰	49	56	0.6
% waist circumference > 90 ‰	30	21	0.4

Bardley et al. Acta Paediatrica, 2011, pp 866-870

Fasting Lipid and Glucose Values in Boys with Klinefelter Syndrome Compared with Normative Data

Lab and cut-off value	% who met cut-off	Mean ± SD	Mean 5–18-year-olds
Low-density lipoprotein ≥ 2.9 mmol/L (≥110 mg/dL)	37	2.7 ± 0.7 (105 ± 25 mg/dL)	2.4–2.6 (92–100 mg/dL)
T cholesterol ≥ 4.4 mmol/L (≥170 mg/dL)	40	4.3 ± 0.8 (165 ± 28 mg/dL)	4.1–4.2 (157–162 mg/dL)
Triglycerides ≥ 1.1 mmol/L (≥100 mg/dL)	15	0.8 ± 0.5 (71 ± 46 mg/dL)	0.60–0.90 (53–80 mg/dL)
High-density lipoprotein < 1.3 mmol/L (<50 mg/dL)	65	1.2 ± 0.3 (46 ± 10 mg/dL)	1.2–1.4 (48–55 mg/dL)
Glucose ≥ 6.1 mmol/L (≥110 mg/dL)	1	4.7 ± 0.4 (85 ± 8 mg/dL)	3.3–5.8 (60–105 mg/dL

Bardley et al. Acta Paediatrica, 2011, pp 866-870

Boys with Klinefelter Syndrome Meeting Criteria for Metabolic Syndrome

No. criteria met	n (%)	Which criteria (n)
3 (diagnosis metabolic syndrome)	7 (8)	HDL, WC, Trig (7)
2	32 (36)	HDL, WC (26) HDL, Trig (5) WC, Trig (1)
1	30 (34)	HDL (20) WC (10) TG (0)

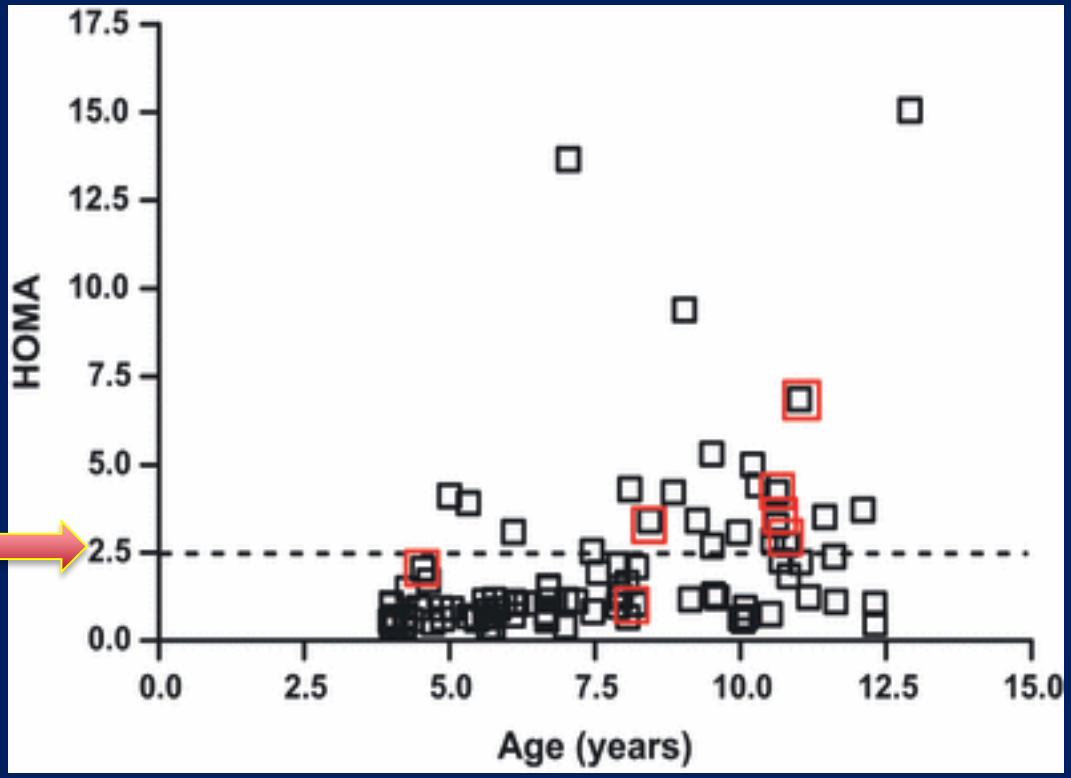
Metabolic syndrome was defined as > 3 of the following: fasting TG > 100; HDL < 50 mg/dl, WC > 75 % for age, systolic/diastolic BP > 90 percentile and FBG > 100 mg/dl

Bardley et al. Acta Paediatrica, 2011, pp 866-870

Insulin Resistance and Metabolic Syndrome in Prepubertal Boys with Klinefelter syndrome

Red box Indicates subjects who fit criteria for metabolic syndrome

Insulin resistance



Insulin resistance: fasting blood glucose (mmol/L x fasting insulin (uU/mL)/ 22.5

Bardley et al. Acta Paediatrica, 2011, pp 866-870

Insulin resistance and metabolic syndrome in prepubertal boys with Klinefelter Syndrome (KS)

- In a large cohort of prepubertal boys as young as 4-12 years with KS
  - 24% had insulin resistance
  - 7% had metabolic syndrome
  - The boys with KS had decreased activity levels compared with age-matched controls

  - Boys were all prepubertal but yet appeared to have increased waist circumference and increased risk for metabolic syndrome

  - Suggests that increased total body fat mass/ waist circumference precedes the hypogonadal state or that subtle hypogonadism early in life has later effects on total body fat mass

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Original Article

Gonadal function is associated with cardiometabolic health in pre-pubertal boys with Klinefelter syndrome

S. Davis ✉, N. Lahlou, M. Bardsley, M.-C. Temple, K. Kowal, L. Pyle, P. Zeitler, J. Ross

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November 2016
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- Aim: to assess the relationship of gonadal and cardiometabolic function in pre-pubertal children with Klinefelter Syndrome

Subject Characteristics (*n* = 93)

Karyotype	
47,XXY	88 (95%)
47,XXY/46,XY	2 (2%)
48,XXYY	1 (1%)
48,XXXY	1 (1%)
46,XX+SRYtrans	1 (1%)
Race/Ethnicity	
Caucasian	67 (72%)
African American	12 (13%)
Hispanic	8 (9%)
Asian/Pacific Islander	5 (5%)
Other	1 (1%)
Diagnosis ascertainment	
Prenatal	58 (62%)
Birth – 2 years	6 (6%)
2–12 years	29 (31%)

Andrology, 2016, 4, 1169-1177

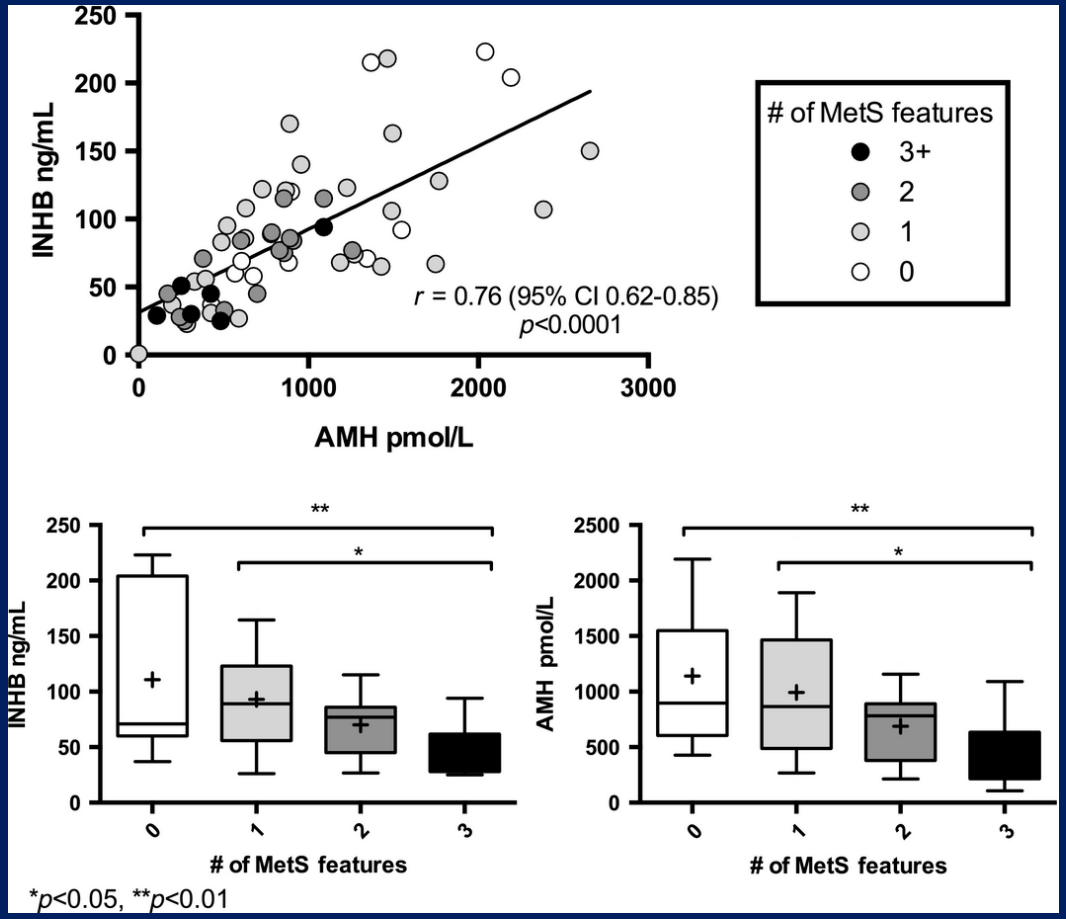
Gonadal Function in Klinefelter Syndrome

- FSH was elevated in 20% of subjects
- LH was lower than expected
- Total testosterone was below the expected range for age in nearly half the pre-pubertal participants
- Supports the hypothesis that androgen deficiency is present prior to puberty in boys KS

Gonadal Function in Klinefelter Syndrome

- -AMHB and INHB are products of Sertoli Cells and are both excellent markers for gonadal function in pre-pubertal boys
- INHB is reflective of Sertoli cell mass
  - Largely independent of gonadotropin stimulation in the prepubertal period
- AMH
  - Regulation of AMH in normal prepubertal boys is complex
  - Production and secretion requires both FSH stimulation and functioning of Sertoli cells and low intratesticular testosterone concentrations

Gonadal Function is Associated with Cardiometabolic Health in Pre-Pubertal Boys with Klinefelter Syndrome



MetS

- waist circumference
- fasting lipid panel
- fasting blood glucose
- blood pressure

Andrology, 2016, 4, 1169-1177

Gonadal Function is Associated with Cardiometabolic Health in Pre-Pubertal Boys with Klinefelter Syndrome

- High prevalence of cardiometabolic risk factors
  - Increased waist circumference
  - Dyslipidemia
  - Insulin resistance
  - independent of age and BMI
- Evidence of pre-pubertal gonadal dysfunction
- Pre- pubertal gonadal dysfunction is associated with increased markers of cardiometabolic risk

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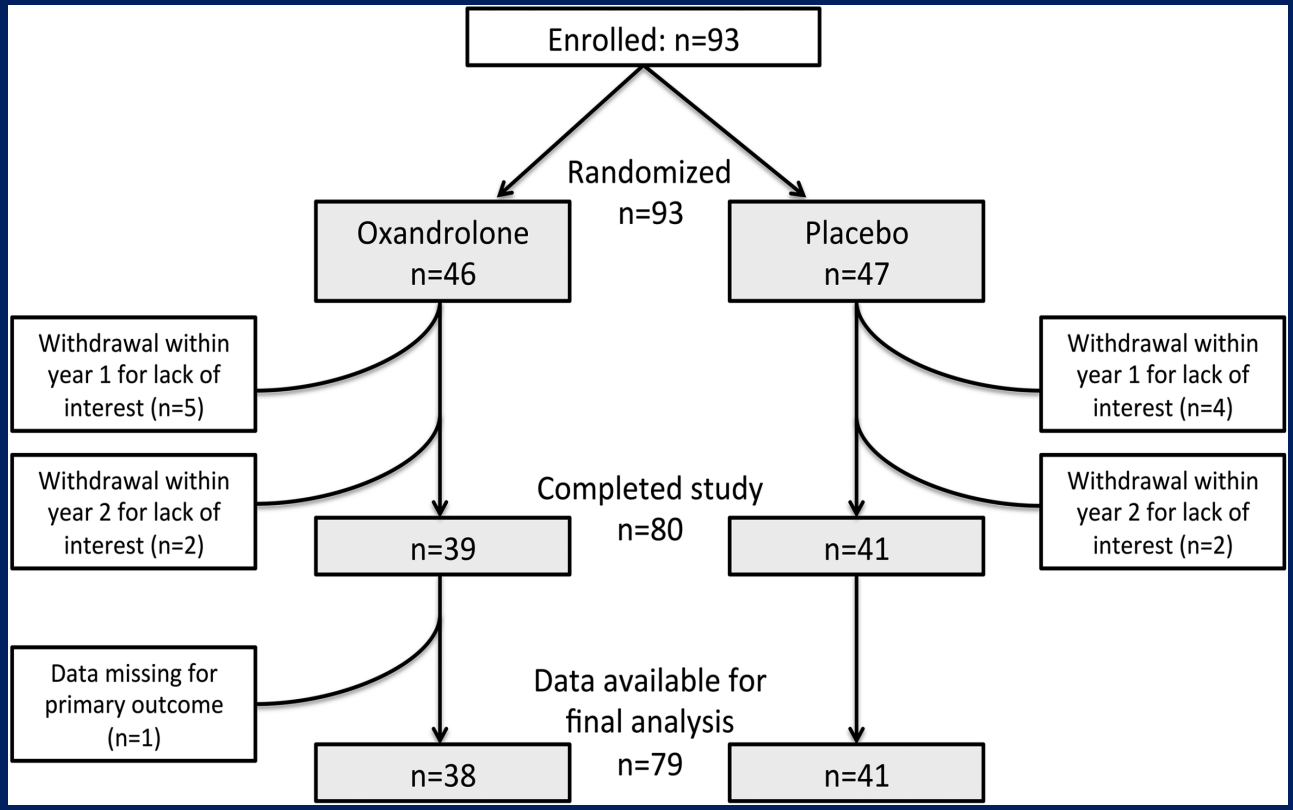
Effects of Oxandrolone on Cardiometabolic Health in Boys With Klinefelter Syndrome: A Randomized Controlled Trial



J Clin Endocrinol Metab. 2016;102(1):176-184. doi:10.1210/jc.2016-2904

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From: **Effects of Oxandrolone on Cardiometabolic Health in Boys With Klinefelter Syndrome: A Randomized Controlled Trial**

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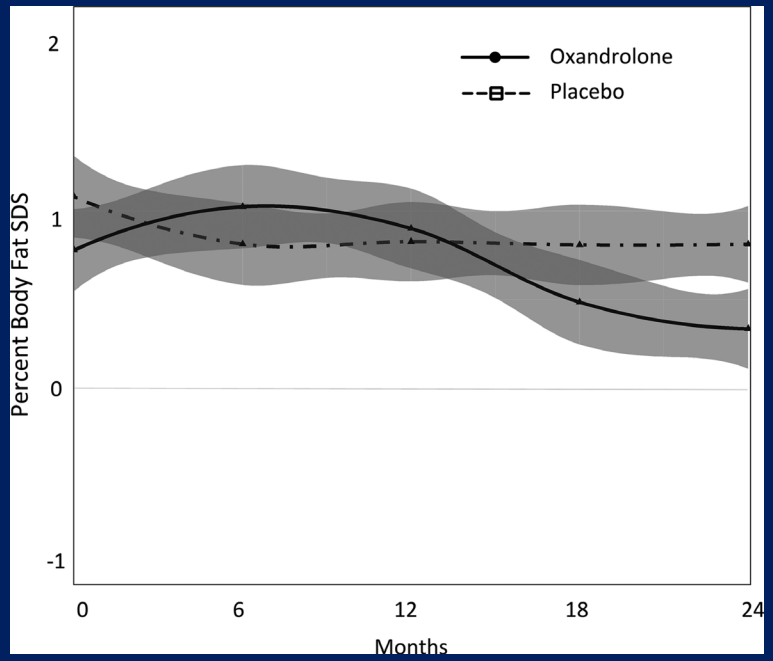
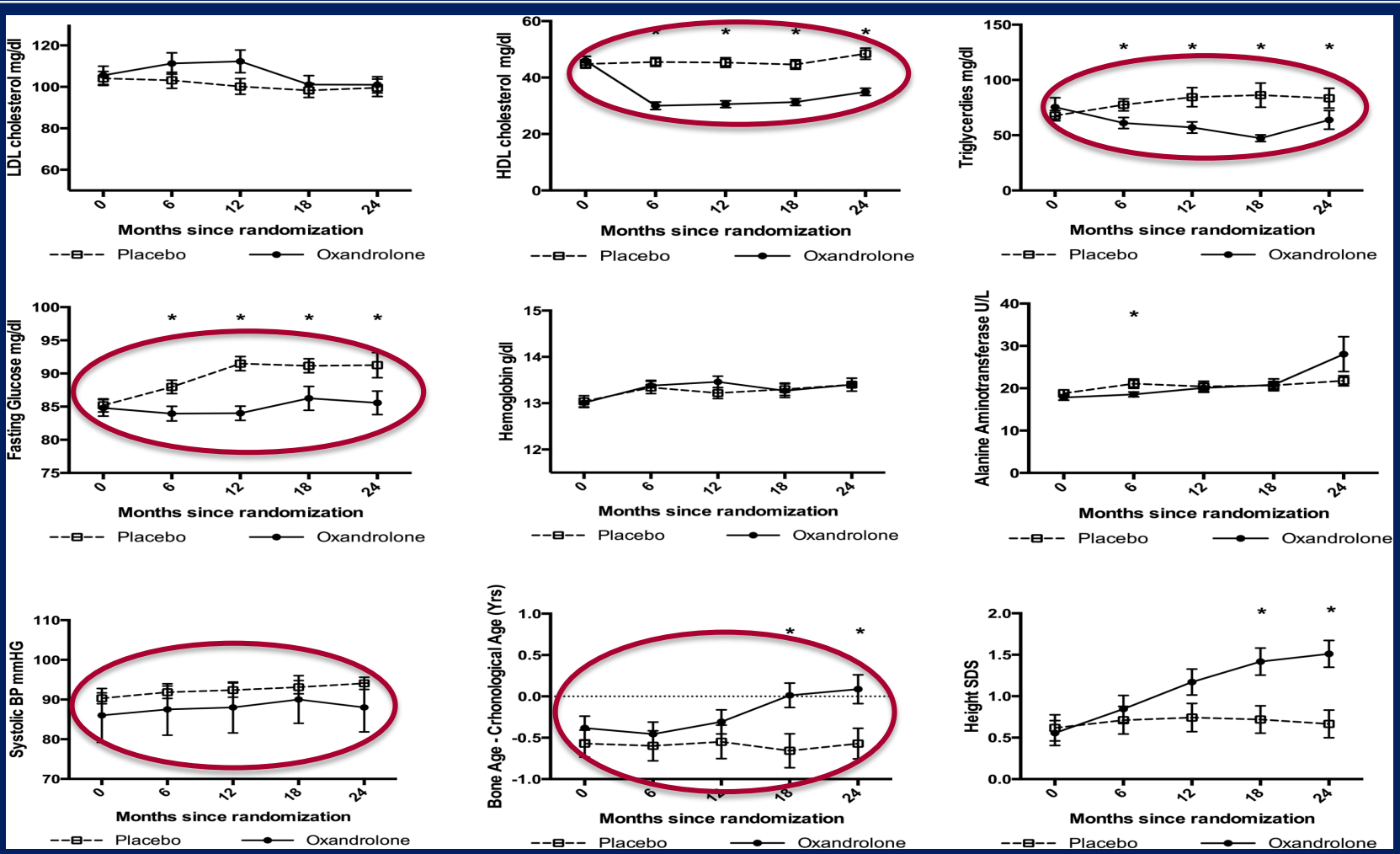


%BF SDS loess curves over the 2-year study period for those treated with Ox (solid line) and placebo (dashed line). The shaded gray curves represent the standard error.

From: **Effects of Oxandrolone on Cardiometabolic Health in Boys With Klinefelter Syndrome: A Randomized Controlled Trial**



Ox (solid black line) compared with placebo (dashed). Asterisk represents a significant difference between Ox and placebo groups at that time point with an alpha of 0.05.

J Clin Endocrinol Metab. 2016;102(1):176-184.

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From: **Klinefelter's syndrome, type 2 diabetes and the metabolic syndrome: the impact of body composition**

Mol Hum Reprod. 2010;16(6):396-401. doi:10.1093/molehr/gaq016

A KS patient with a rather atypical phenotype. Note the relatively large muscle mass, normal masculine body hair distribution, beard and baldness, but also the typical abdominal obesity. This patient was diagnosed at the age of 35 years, because of infertility. Height 181 cm, weight 94 kg, karyotype 47,XXY.

Karyotyping of Patients with Klinfelters syndrome

Karyotype	Number of patients (%)
47 XXY	354 (94.1)
46 XY/47 XXY	13 (3.5)
46 XY/47 XXY/48 XXXY	3 (0.8)
48 XXXY	2
48 XXYY	1
46 XY/46 XX/47 XXY	1
47 XX, inv (Y)	1
47 XXY/48 XXXY	1

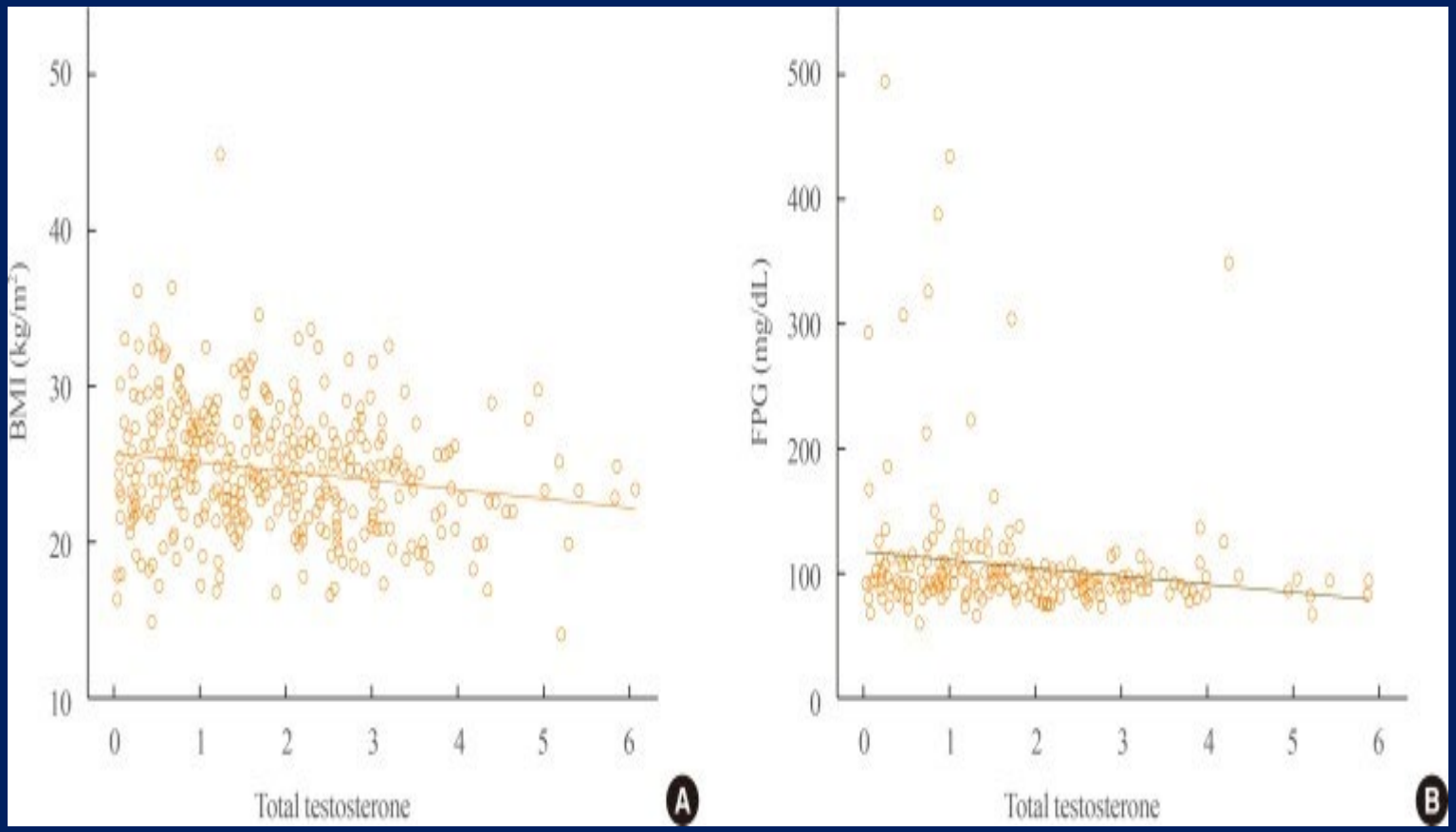
Han SJ, Kim K-S, Kim W, et al. Obesity and Hyperglycemia in Korean Men with Klinefelter Syndrome: The Korean Endocrine Society Registry. *Endocrinology and Metabolism*. 2016;31(4):598-603. doi:10.3803/EnM.2016.31.4.598.

Comparison of Characteristics in Obese versus Nonobese Patients with Klinefelter Syndrome

Characteristic	Total (*n*=376)	Nonobese (*n*=216)	Obese (*n*=160)	*P* value
Age, yr	32 (18–53)	32 (18–53)	32 (20–53)	0.430
Height, cm	177.0±6.5	177.1±6.3	177.0±6.9	0.904
Body weight, kg	77.5±13.8	69.2±8.8	88.8±11.1	<0.001
BMI, kg/m^2	24.7±3.9	22.0±2.2	28.3±2.7	<0.001
Hypertension	57 (15.2)	27 (12.5)	30 (18.8)	0.095
Hyperglycemia[a]	85 (38.8)	38 (31.4)	47 (48.0)	0.012
Prediabetes	57 (26.0)	24 (19.8)	33 (33.7)	
Diabetes	28 (12.8)	14 (11.6)	14 (14.3)	
Dyslipidemia[b]	72 (19.1)	34 (27.2)	38 (38.0)	0.084
Testosterone, ng/mL	1.83±1.24	1.97±1.33	1.64±1.09	0.008
LH, mIU/mL	17.8±8.4	19.0±8.9	16.3±7.5	0.003
FSH, mIU/mL	37.4±15.5	42.5±15.8	30.9±12.4	<0.001

Han SJ, Kim K-S, Kim W, et al. Obesity and Hyperglycemia in Korean Men with Klinefelter Syndrome: The Korean Endocrine Society Registry. *Endocrinology and Metabolism.* 2016;31(4):598-603. doi:10.3803/EnM.2016.31.4.598.

Correlation among serum testosterone, body mass index (BMI), and fasting plasma glucose (FPG). (A) The association between testosterone and BMI. (B) The association between testosterone and FPG



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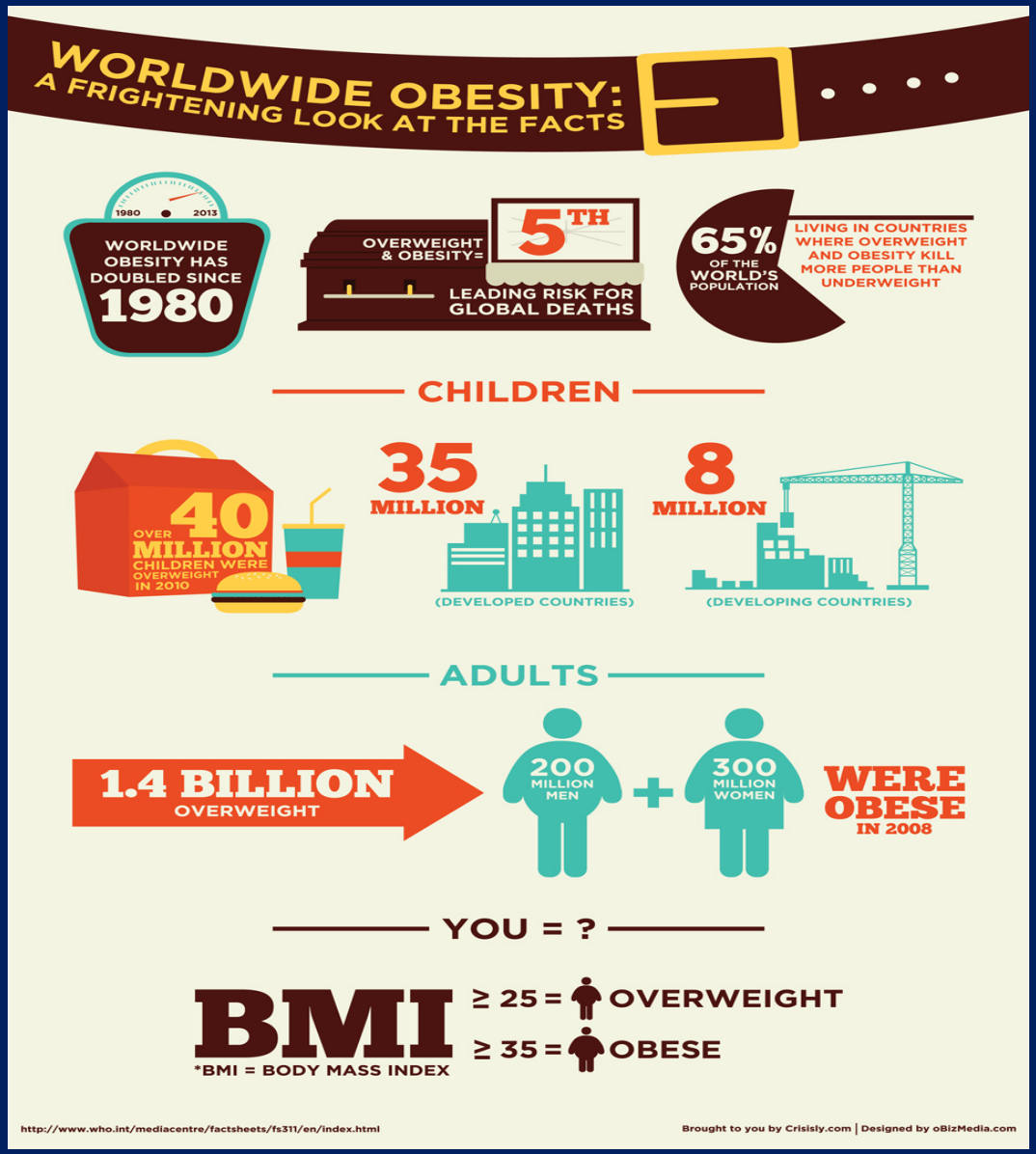
WORLDWIDE OBESITY:
A FRIGHTENING LOOK AT THE FACTS
1980
2013
WORLDWIDE OBESITY HAS DOUBLED SINCE 1980
OVERWEIGHT & OBESITY=
5TH
LEADING RISK FOR GLOBAL DEATHS
65%
OF THE WORLD'S POPULATION
LIVING IN COUNTRIES WHERE OVERWEIGHT AND OBESITY KILL MORE PEOPLE THAN UNDERWEIGHT
CHILDREN
OVER 40 MILLION CHILDREN WERE OVERWEIGHT IN 2010
35 MILLION
(DEVELOPED COUNTRIES)
8 MILLION
(DEVELOPING COUNTRIES)
ADULTS
1.4 BILLION
OVERWEIGHT
200 MILLION MEN
+
300 MILLION WOMEN
WERE OBESE IN 2008
YOU = ?
BMI
*BMI = BODY MASS INDEX
≥ 25 = OVERWEIGHT
≥ 35 = OBESE
http://www.who.int/mediacentre/factsheets/fs311/en/index.html
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The Various Components of the NCEP ATP III and IDF Definitions of the Metabolic Syndrome in Men

	NCEP ATP III[a] ≥ 3 of 5 Criteria	IDF[b] Criterion 2 Plus 2 of the Other 4
1. Hyperinsulinemia, hyperglycemia	FBS ≥ 110 mg/dL (≥6.1 nmol/L) or T2DM	FBS ≥ 100 mg/dL or T2DM
2. Increased body size	WC ≥ 102 cm	WC ≥ 94 cm
3. Triglyceride	≥150 mg/dL (≥2.3 mmol/L)	≥150 mg/dL (≥2.3 mmol/L)
4. HDL cholesterol	<40 mg/dL (<1.03 mmol/L)	<40 mg/dL (<1.03 mmol/L)
5. Blood pressure	BP ≥ 130/85 mm Hg, or HTN on Rx	Systolic BP ≥ 130 mm Hg, diastolic BP ≥ 85 mm Hg, or HTN on Rx

1.Abbreviations: BP, blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; HTN, hypertension, IDF, International Diabetes Federation; NCEP ATP III, National Cholesterol Education Program—Adult Treatment Panel III; Rx, prescription; T2DM, type 2 diabetes mellitus; WC, waist circumference.
2.a Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2001).
3.b Balkau and Charles (1999).

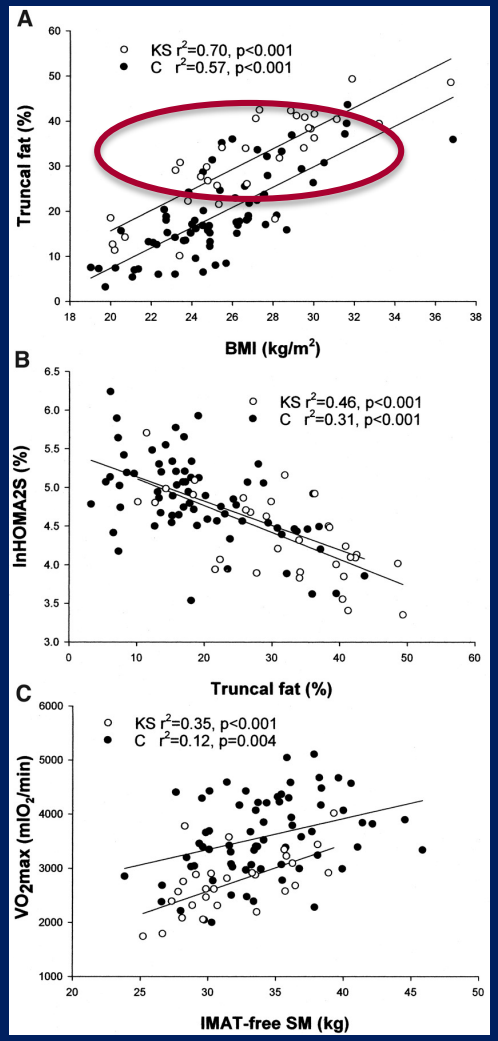
The Metabolic Syndrome is Frequent in Klinefelter's Syndrome and Is Associated with Abdominal Obesity and Hypogondism

OBJECTIVE—Klinefelter's syndrome is associated with an increased prevalence of diabetes, but the pathogenesis is unknown. Accordingly, the aim of this study was to investigate measures of insulin sensitivity, the metabolic syndrome, and sex hormones in patients with Klinefelter's syndrome and an age-matched control group.

RESEARCH DESIGN AN METHODS—In a cross-sectional study, we examined 71 patients with Klinefelter's syndrome, of whom 35 received testosterone treatment, and 71 control subjects. Body composition was evaluated using dual-energy X-ray absorptiometry scans. Fasting blood samples were analyzed for sex hormones, plasma glucose, insulin, C-reactive protein (CRP), and adipocytokines. We analyzed differences between patients with untreated Klinefelter's syndrome and control subjects and subsequently analyzed differences between testosterone-treated and untreated Klinefelter's syndrome patients.

Diabetes Care 29: 1591-1598, 2006

Truncal Fat in Correlation with BMI in Klinefelter Syndrome Patients versus Controls

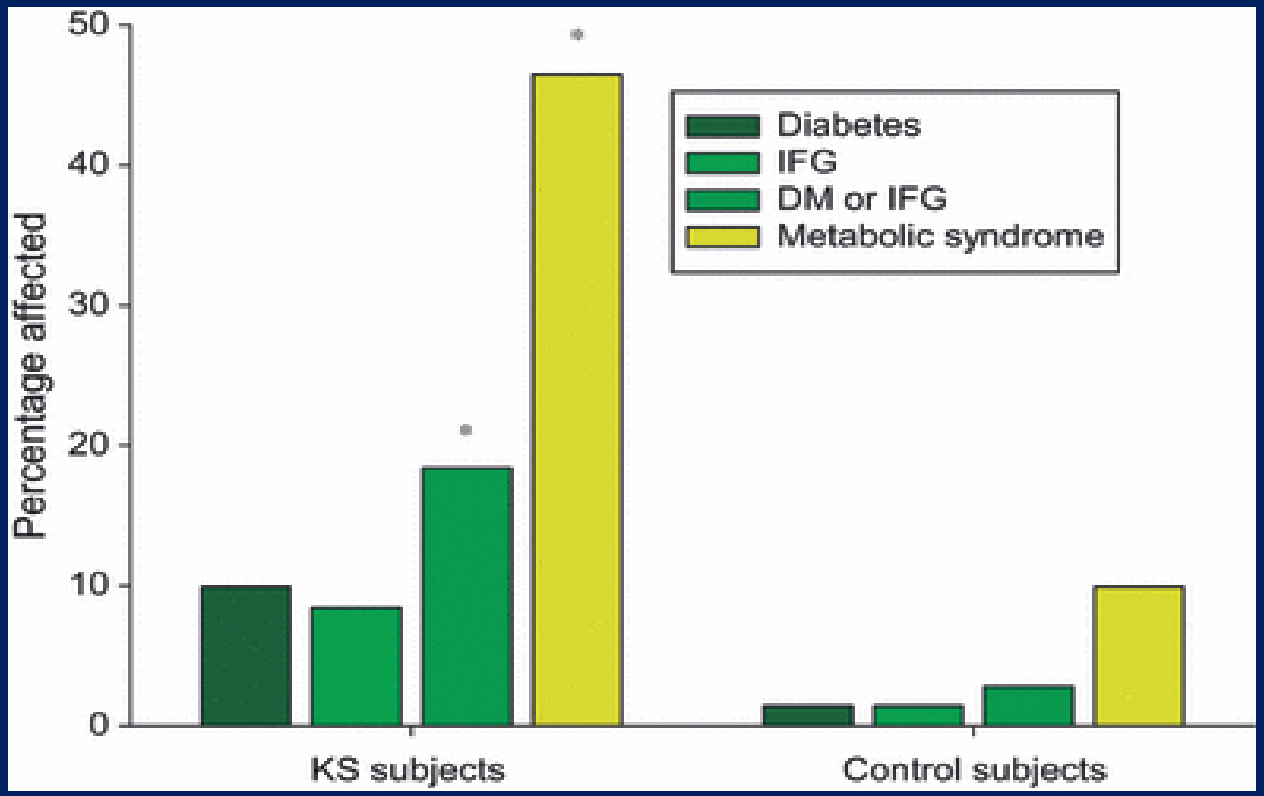


Klinefelter's syndrome patients (KS, ○) have more Truncal Fat (~8% more) for any value of BMI than control subjects (C, •)

American Diabetes Association.

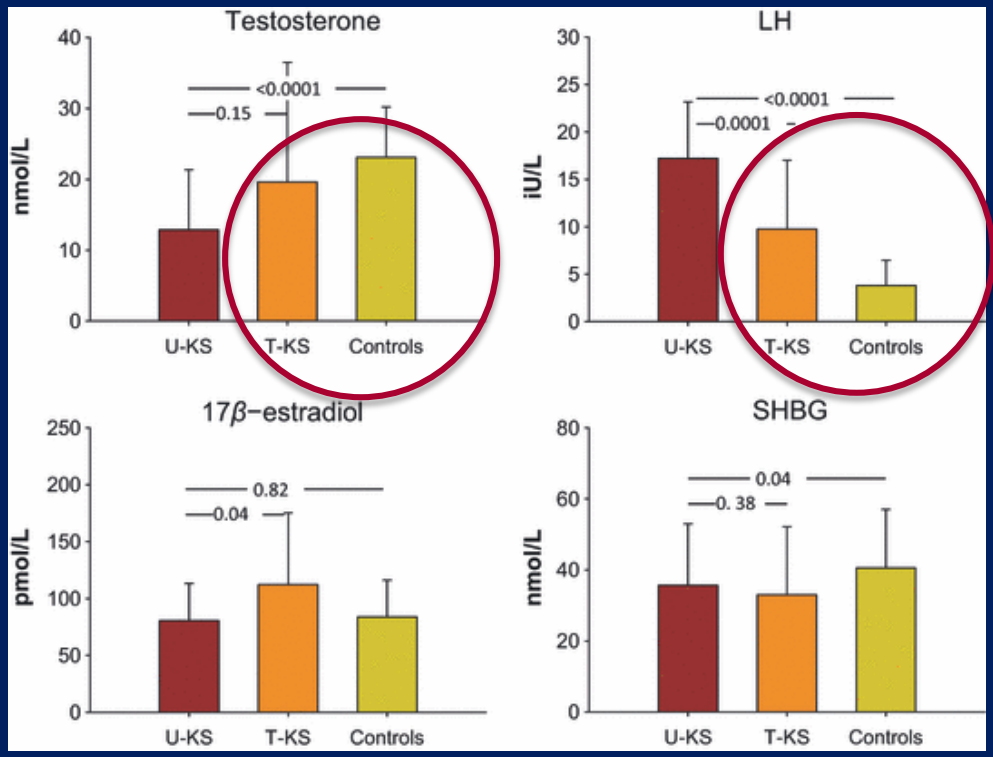
Anders Bojesen et al. Dia Care 2006;29:1591-1598

Body Composition, Metabolic Syndrome and Type 2 Diabetes in Klinefelter Syndrome



Acta Paediatrica pages 871-877, 16 MAR 2011 DOI: 10.1111/j.1651-2227.2011.02233.x

Body Composition, Metabolic Syndrome and Type 2 Diabetes in Klinefelter Syndrome



Treatment regimen offered to many men with KS is insufficient

Acta Paediatrica_pages 871-877, 16 MAR 2011 DOI: 10.1111/j.1651-2227.2011.02233.x

The Metabolic Syndrome Is Frequent in Klinefelter's Syndrome and Is Associated With Abdominal Obesity and Hypogonadism

Anders Bojesen, MD, PHD[1,2], Kurt Kristensen, MD, PHD[3], Niels H. Birkebaek, MD, PHD[3], Jens Fedder, MD, PHD[4], Leif Mosekilde, MD, DMSCI[5], Paul Bennett, MD[6], Peter Laurberg, MD, DMSCI[7], Jan Frystyk, MD, DMSCI[1], Allan Flyvbjerg, MD, DMSCI[1], Jens S. Christiansen, MD, DMSCI[1] **and** Claus H. Gravholt, MD, DMSCI[1]

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Address correspondence and reprint requests to Anders Bojesen, MD, Medical Department M, Endocrinology and Diabetes, Aarhus University Hospital, Noerrebrogade 42-44, DK-8000, Aarhus C, Denmark. E-mail: anders.bojesen@dadlnet.dk

Diabetes Care 2006 Jul; 29(7): 1591-1598. https://doi.org/10.2337/dc06-0145

- Strongest predictor of metabolic syndrome was adiposity and truncal fat
- Almost half of Klinefelter syndrome patients fulfilled the NCEP/ATPIII criteria for metabolic syndrome
- Only 10% of the control subjects met criteria for metabolic syndrome
- CRP
  - Marker of low grade inflammation
  - Predictor of cardiovascular disease
  - significantly increased in Klinefelter Syndrome patients

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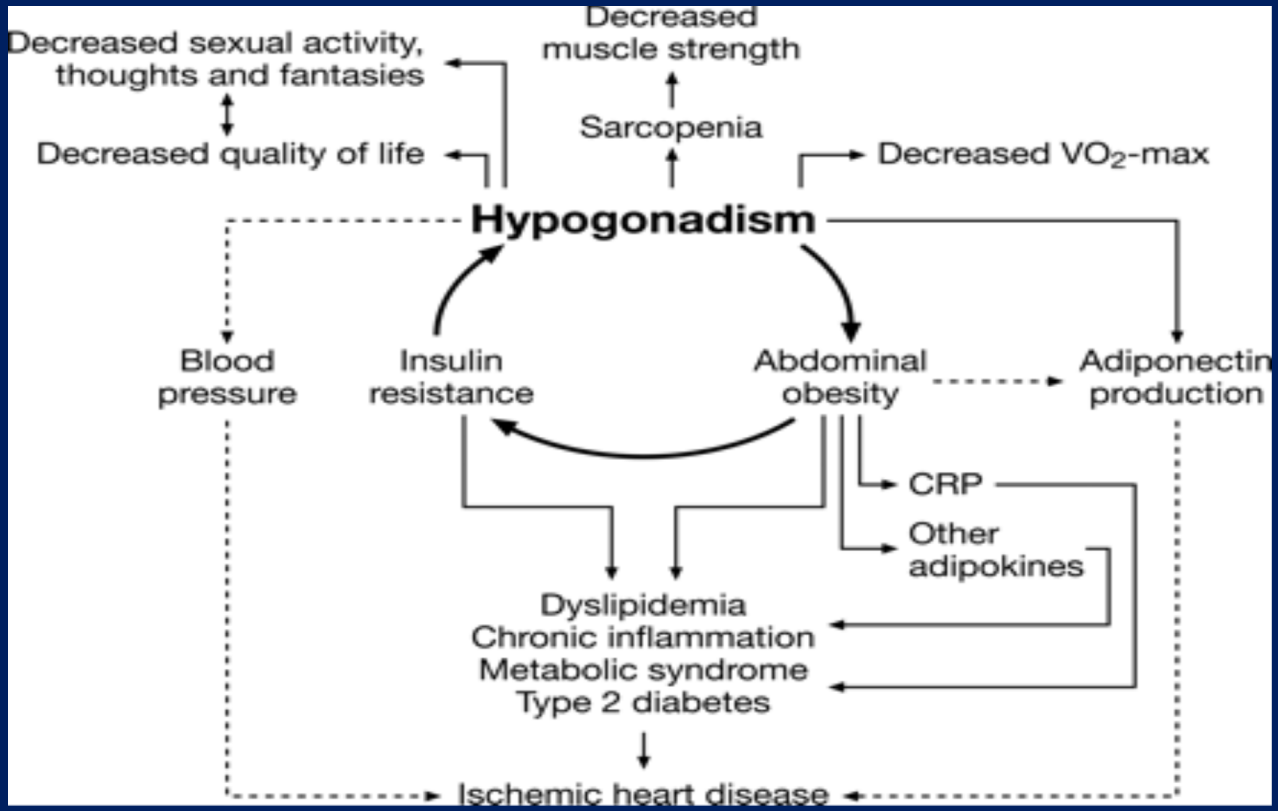
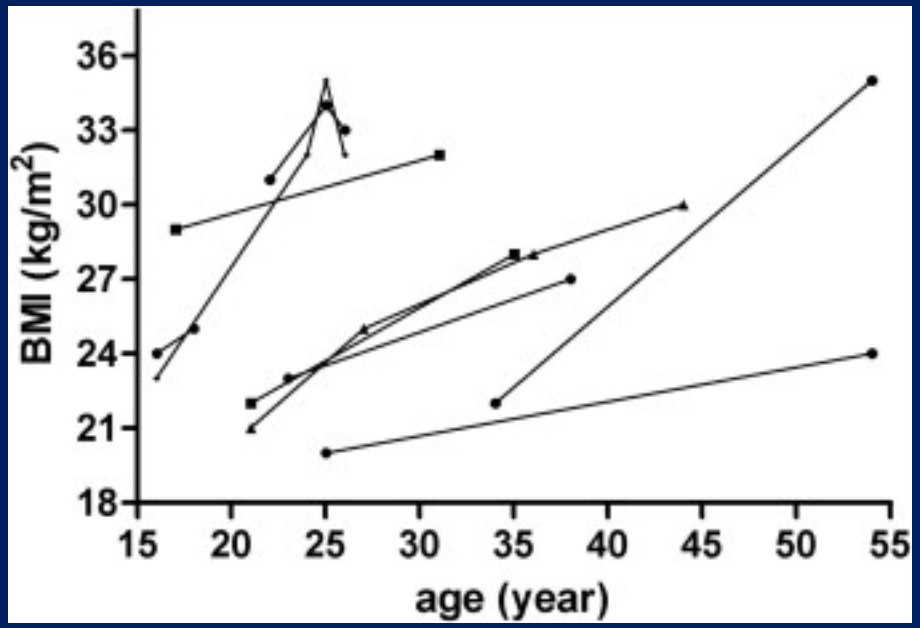
From: **Klinefelter's syndrome, type 2 diabetes and the metabolic syndrome: the impact of body composition**

Mol Hum Reprod. 2010;16(6):396-401. doi:10.1093/molehr/gaq016



Prevalence and Risk Factors of Diabetes in Patients with Klinefelter Syndrome: a Longitudinal Observational Study



In the Klinefelter patient group the BMI dramatically increased in nine patients during follow-up

Fertility and Sterility, Volume 98, Issue 5, 2012, 1331–1335

Basic line data and clinical features in patients with KS and diabetes (n = 8).

Patient no.	Age at diagnosis of diabetes (y)	Starting T therapy (y)	Height (cm)	Weight (kg)	Karyotype	HbA1c (%)	Comorbidities	Therapeutic regimens for diabetes
P1	20	20	180	65	47xxy	6.6	Severe pancreatitis<comma> fatty liver	Lantus + NovoRapid
P2	23	23	173	83	47xxy/46xx	10.4	Fatty liver	Novomix 30 + metformin
P3	24	16	178	100	47xxy	11.2	Severe fatty liver	Metformin
P4	29	24	185	61	48xxxy	6.9	Mental retardation	Refuse to take medicine
P5	30	19	167	77	46xy/47xxy	9.9	TG 32 mmol/L<comma> fatty liver	Novomix 30
P6	30	33	178	68	46xy/47xxy	7.7	Acute myeloid leukemia M3	Refuse to take medicine
P7	32	35	179	88	47xxy	9.1	Fatty liver	Metformin + regular insulin
P8	55	25	185	68	47xxy	6.4	TG 11 mmol/L	Metformin

Fertility and Sterility, Volume 98, Issue 5, 2012, 1331–1335

Relationship between incidence of diabetes and karyotype.

Karyotype	No. of patients (diabetes/total patients)	Incidence of diabetes mellitus (%)
Classic karyotype (47,XXY)	4/32	12.5
Atypical karyotype (46XY/47XXY chimera and others)	4/7	57.1[a]
Total	8/39	20.5

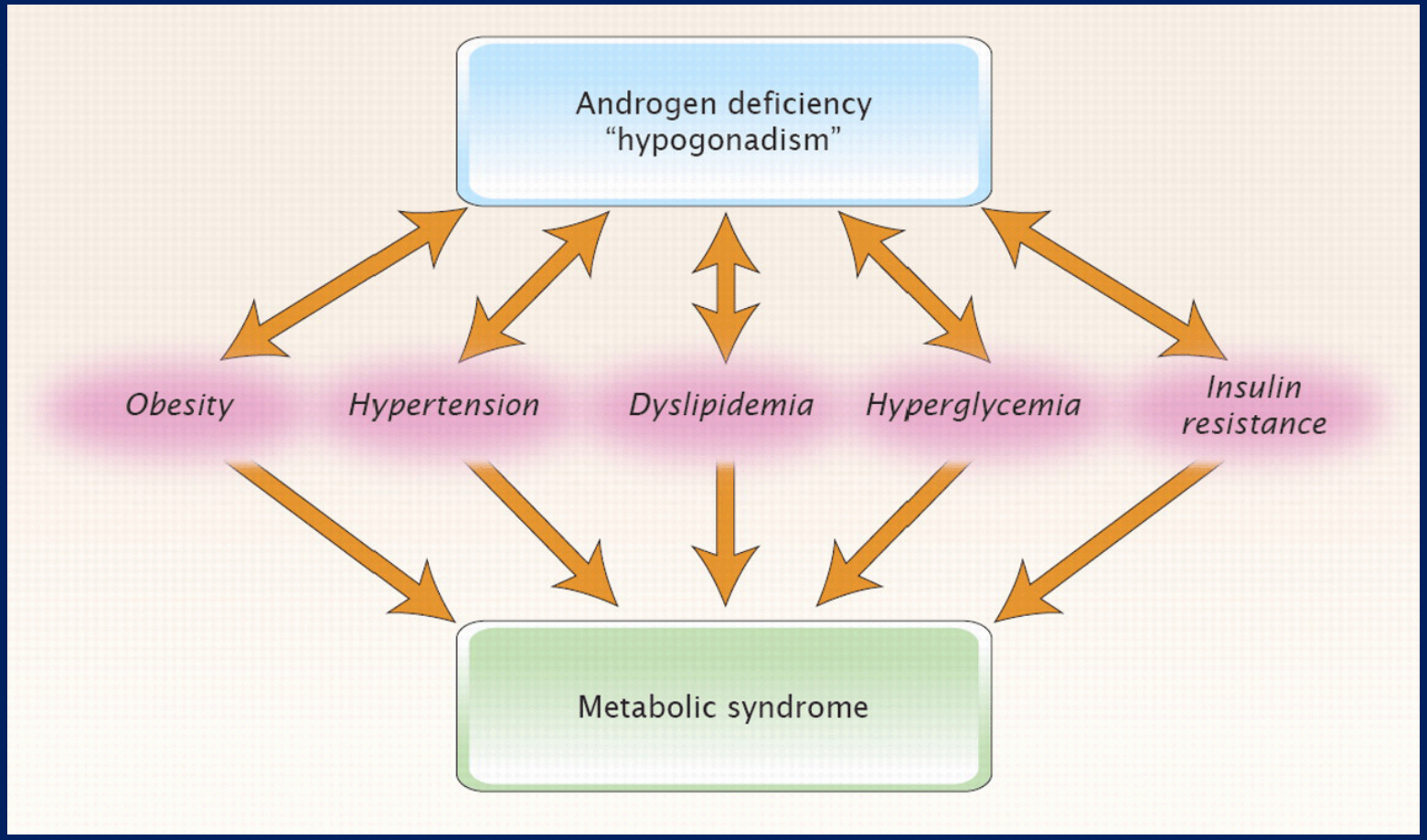
Fertility and Sterility, Volume 98, Issue 5, 2012, 1331–1335

Low Testosterone & Cardiovascular Disease Risks & Type 2 Diabetes

- Increasing evidence from multiple studies that low serum testosterone is associated
  - Atherosclerosis
  - Cardiovascular disease
  - Metabolic syndrome
  - High prevalence of low testosterone levels in men with diabetes
    - Relationship is so strong in some studies that it stated that low testosterone levels predicted future diabetes
  - The more medical problems a man has, more stress on his body, the lower his testosterone will be

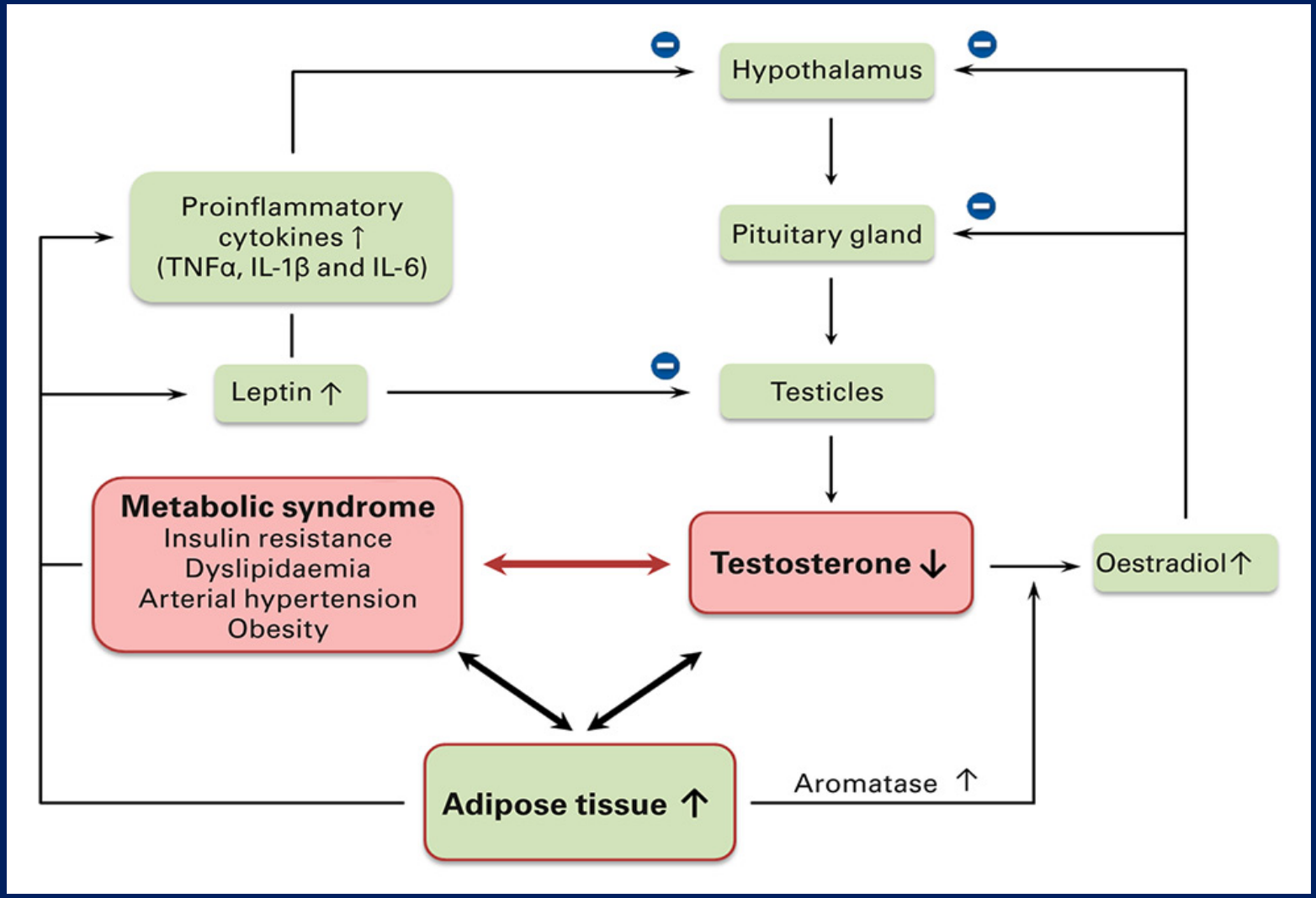
Blouin K et al. Metabolism. 2005; 54:1034-1040
Kaplan et al. J Urol. 2006;176:1524-1528

The Emerging Link Between Hypogonadism and Metabolic Syndrome



Journal of Andrology pages 370-376, 2 JAN 2013 DOI: 10.2164/jandrol.108.006015

Pathophysiological interplay between adverse metabolic parameters, adipose tissue and testosterone deficiency



Swiss Med Wkly. 2016; 146

Low Testosterone is associated with Increased Mortality in Older Men

Study design	*n*	Follow-up (years)	Mortality	Hazard ratio (95% CI)	Recent studies
Retrospective	858	8	All-cause	1.88 (1.34–2.63)*	Shores et al. (42)
Prospective	794	20	All-cause and CVD	1.40 (1.14–1.71)* 1.38 (1.02–1.85)*	Laughlin et al. (45)
Prospective	2,314	10	All-cause and CVD	2.29 (1.60–3.26)*	Khaw et al. (43)
Prospective	1,954	7.2	All-cause and CVD	2.32 (1.38–3.89)*	Haring et al. (44)
Prospective	930	6.9	All-cause and CVD in men with CVD	2.27 (1.45–3.60)*	Malkin et al. (46)

Diabetes care, volume 43, 2011

Testosterone Replacement in Hypogonadal Men with Metabolic Syndrome or Type 2 Diabetes

- Testosterone replacement:
  - promotes insulin sensitivity in hypogonadal men with and without type 2 diabetes
  - Several studies report decrease in HbA1c levels in men with diabetes
  - Reduces body fat mass and waist circumference
  - Significant fall in total cholesterol and in some LDL
  - No change in triglycerides
  - HDL may fall, rise or remain unchanged
  - Lipoprotein a
    - Has the strongest positive correlation with premature coronary heart disease than any other component of the lipid profile
    - Found to fall significantly after testosterone treatment of men with metabolic syndrome or type 2 diabetes

Jones et al. Atherosclerosis 2009; 207: 318-327

Randomized trials of Testosterone Replacement in Hypogonadal Men with Metabolic Syndrome or Type 2 Diabetes

Study	Kapoor et al. (55)	Heufelder et al. (56)	Kalinchenko et al. (57)	Jones et al.* (37)
Subjects	Type 2 diabetes	New type 2 diabetes/metabolic syndrome	Type 2 diabetes/metabolic syndrome	Type 2 diabetes/metabolic syndrome
Study design	RCT-c	NRCT	RCT-p	RCT-p
n	24	32	184	220
Duration (months)	3	12	6	6/12*
Medications for diabetes	Diet, oral, insulin	Naive	Diet, oral	Diet, oral
Baseline serum testosterone (nmol/L)	≤8.6	≤10.5	≤6.7	≤10.2
Testosterone formulation	TES injections (200 mg/2 weeks)	Testosterone gel (50 mg/day)	TU depot injections	Testosterone gel (40–80 mg/day)
Treatment effects (changes)				
HOMA-IR	−1.7	−0.9	−1.49	−0.54
Fasting glucose (nmol/L)	−1.6	−0.3 (AS)	↔	−0.42 (AS)
Fasting insulin (mIU/mL)	↔	↓	↔	↓(AS)
HbA_{1c}	−0.37	−0.80	ND	↔ [−0.45]‡
Total cholesterol (nmol/L)	−0.4	ND	↔	↔ [−0.13]
LDL cholesterol (nmol/L)	↔	ND	↔	↔‡
HDL cholesterol (nmol/L)	↔	↑§	↔	−0.049‡
Triglycerides	↔	↓	↔	↔
Lipoprotein a	ND	ND	ND	↓
BMI	↔	↔	↔	↔
Waist circumference	↓	↓	↓	↔
% Body fat	ND	ND	ND	↔
Blood pressure	↔	↓		

Diabetes care, volume 43, 2011

Key Points

- a 38-year-old male was evaluated for bilateral lower extremity ulcers that had been present for 4years
- Type 2 diabetes for 3 years
- Treatment with local wound care, including silver sulfadiazine cream and compression therapy had been ineffective
- On examination, the patient was noted to have gynaecomastia and bilateral small testes approximately 10 ml each (normal 12–25 ml)
- Heterozygous for the 4G/5G plasminogen activator inhibitor (PAI)-1 mutation
- Androgen replacement therapy was initiated with topical testosterone gel 50 mg applied to non lesional skin daily
- Therapy resulted in 75% reduction in ulcer size

Leg ulcers associated with Klinefelter's syndrome: a case report and review of the literature

Victoria K Shanmugam, Katina C Tsagaris, Christopher E Attinger

Figure 1. Appearance of right leg at presentation.

Figure 2. Appearance of right leg after commencing androgen replacement therapy with testosterone gel.

Metabolism
Volume 95, June 2019, Pages 21-26

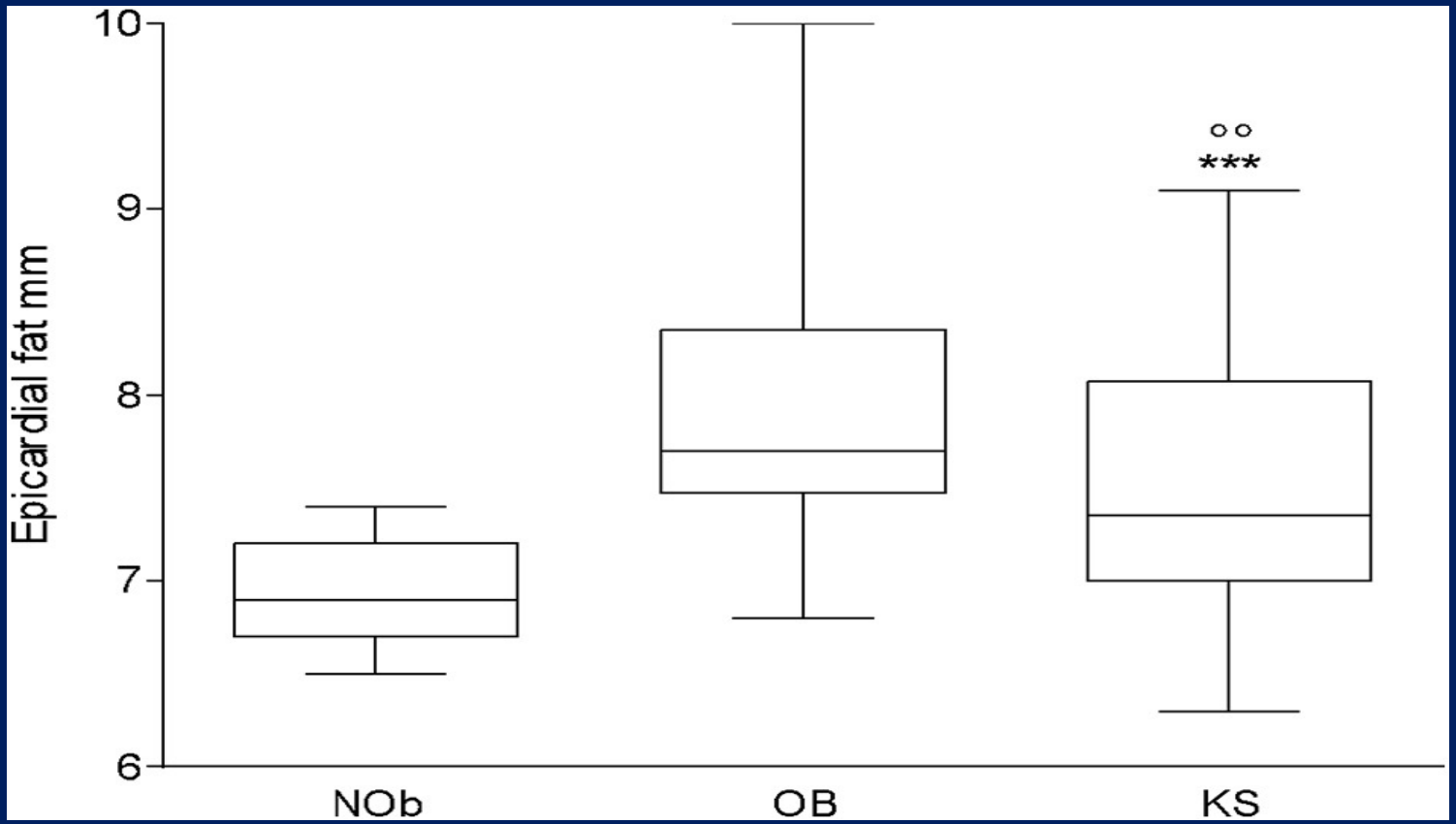
Clinical Science

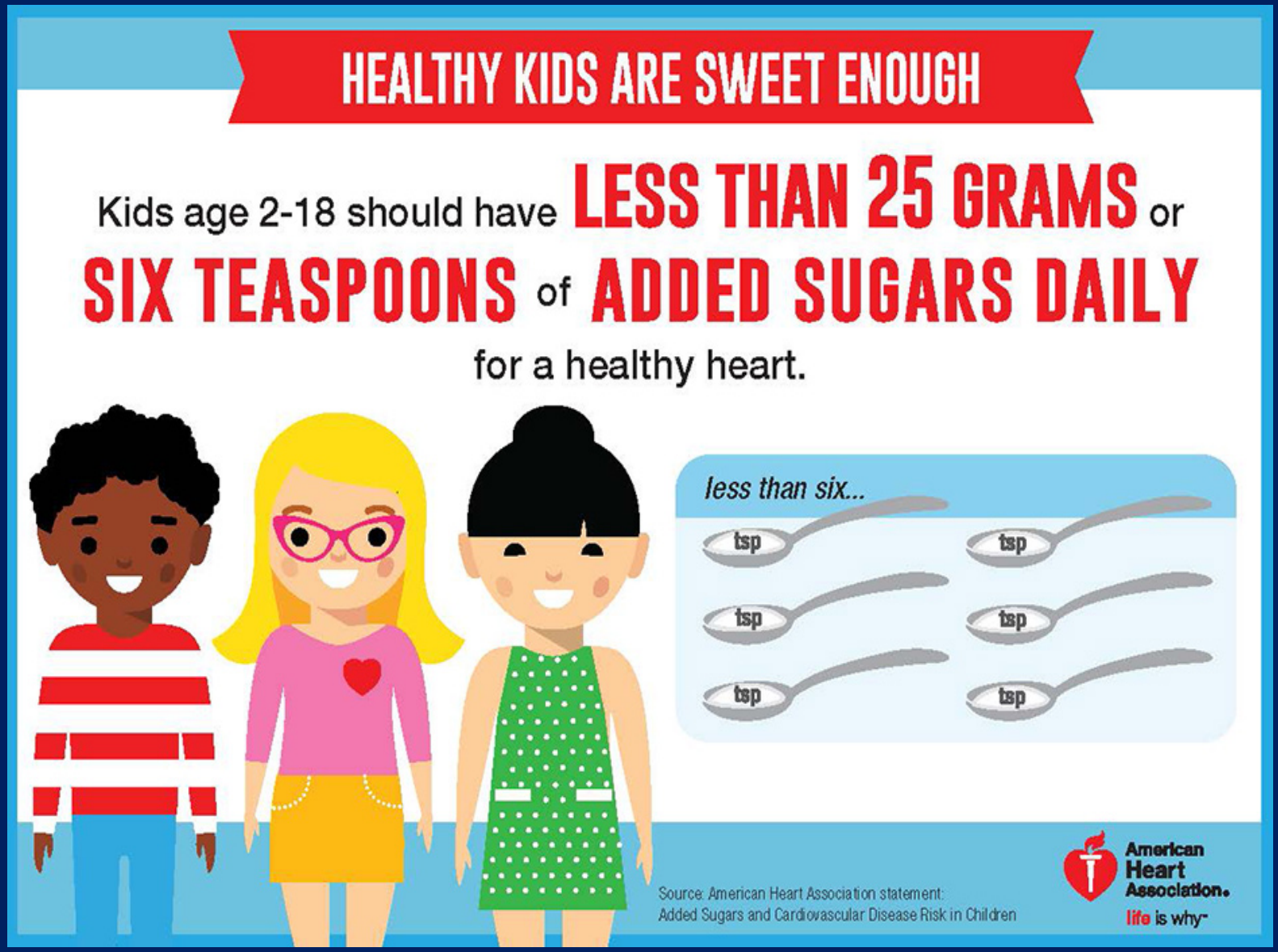
Epicardial fat: the role of testosterone and lipid metabolism in a cohort of patients with Klinefelter syndrome

S. Granato [a, b], G. Barbaro [b], M.R. Di Giorgio [b], F.M. Rossi [b], C. Marzano [b], F. Impronta [b], M. Spaziani [a, b], A. Anzuini [b], A. Lenzi [b], A.F. Radicioni [a, b]

Show more

https://doi.org/10.1016/j.metabol.2019.03.002



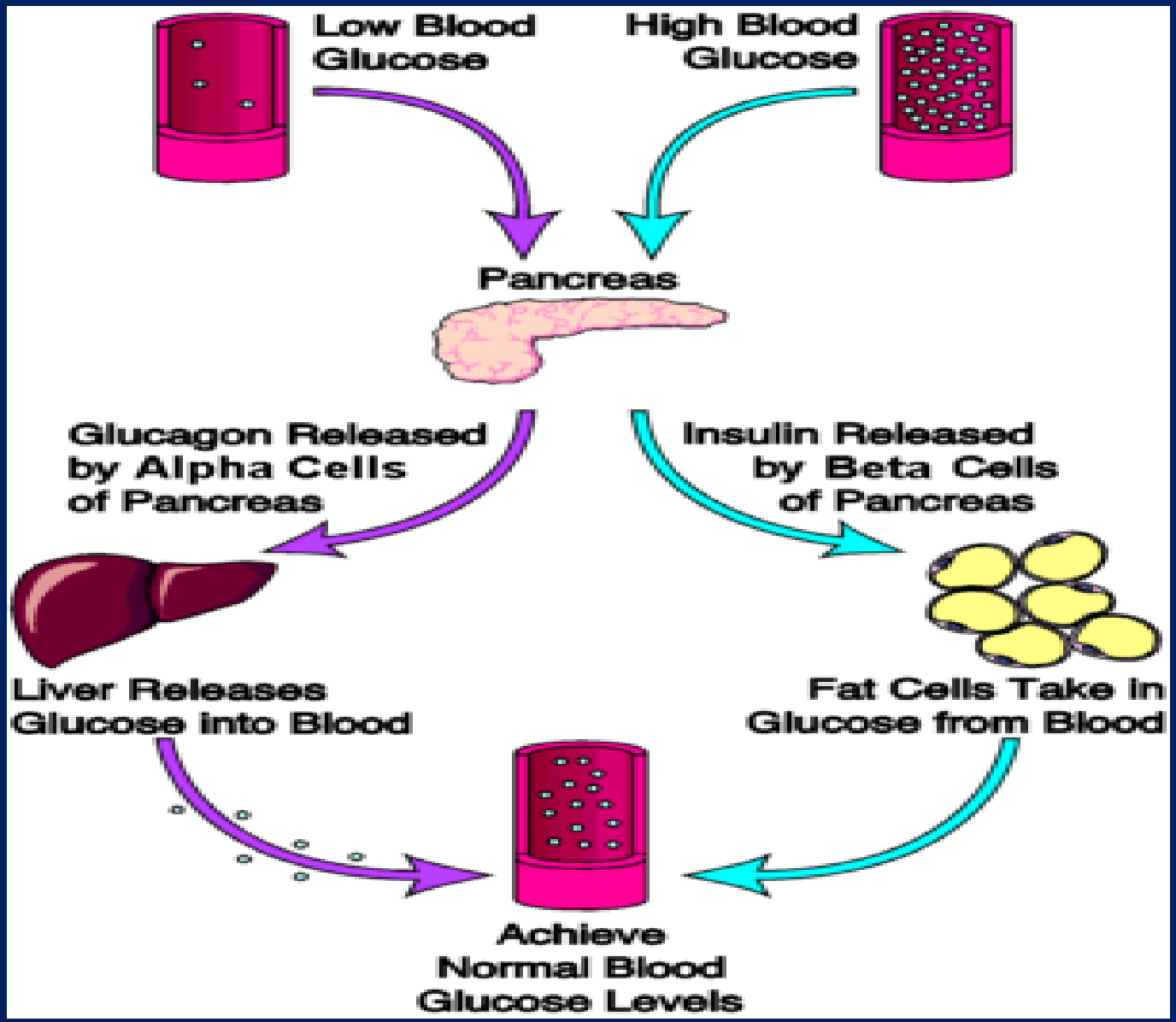

HEALTHY KIDS ARE SWEET ENOUGH
Kids age 2-18 should have LESS THAN 25 GRAMS or
SIX TEASPOONS of ADDED SUGARS DAILY
for a healthy heart.
less than six...
tsp
tsp
tsp
tsp
tsp
tsp
Source: American Heart Association statement:
Added Sugars and Cardiovascular Disease Risk in Children
American Heart Association.
life is why

https://www.healthfitnessrevolution.com/burning-calories-20-oz-soda-requires-quite-long-walk/

foodexercise1-itok=hvCrqreP.jpg

https://www.healthfitnessrevolution.com/burning-calories-20-oz-soda-requires-quite-long-walk/


The number of kilometres you need to RUN to BURN these off...
= 1.87 KM
You can't
= 5.97 KM
= 11.99 KM
out RUN
=3.66 KM
= 10.47 KM
a bad DIET.
=2.21 KM

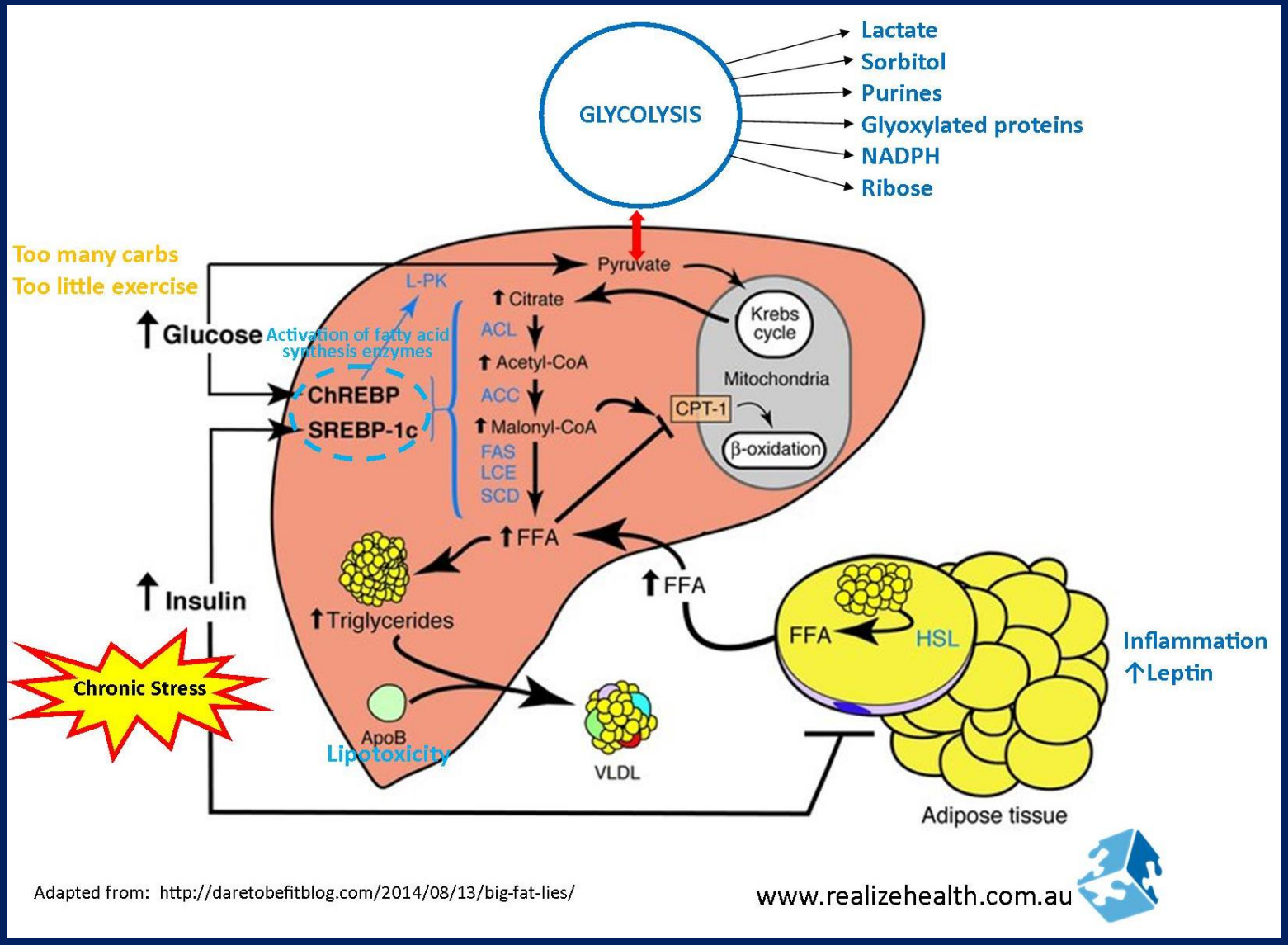


https://www.endocrineweb.com/conditions/diabetes/normal-regulation-blood-glucose

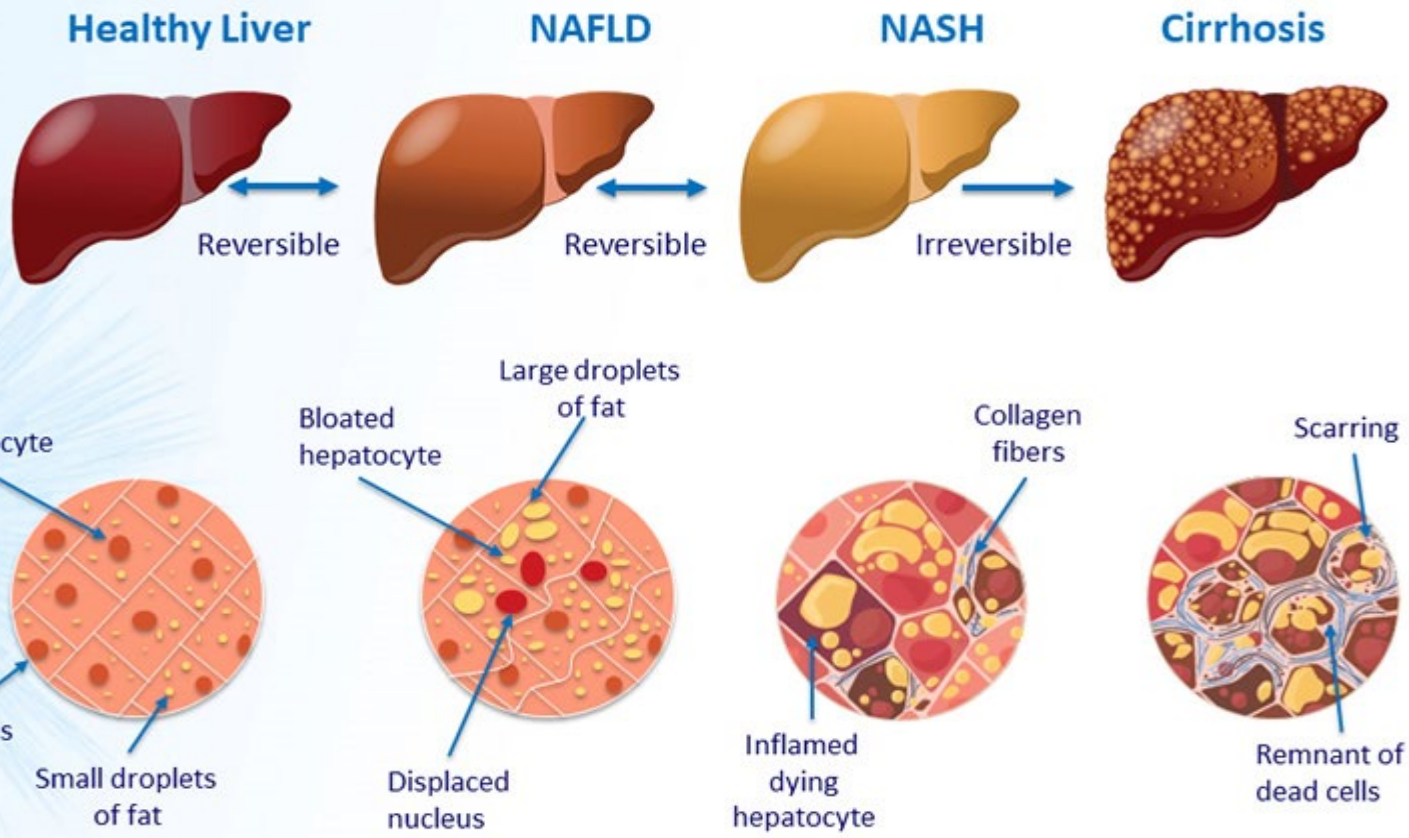
Caloric Density

400 Calories of Oil | 400 Calories of Beef | 400 Calories of Vegetables

Stretch receptors are located throughout the stomach. When they are triggered by food, they send signals to your brain to tell you to stop eating. With high fiber, whole plant foods, you can eat the most quantity for the least amount of calories.


GLYCOLYSIS
Lactate
Sorbitol
Purines
Glyoxylated proteins
NADPH
Ribose
Too many carbs
Too little exercise
Glucose
Pyruvate
L-PK
Citrate
ACL
Acetyl-CoA
ACC
Malonyl-CoA
FAS
LCE
SCD
Activation of fatty acid synthesis enzymes
ChREBP
SREBP-1c
Krebs cycle
Mitochondria
CPT-1
β-oxidation
FFA
Insulin
Triglycerides
Chronic Stress
ApoB
Lipotoxicity
VLDL
FFA
FFA
HSL
Inflammation
↑Leptin
Adipose tissue
Adapted from: http://daretobefitblog.com/2014/08/13/big-fat-lies/
www.realizehealth.com.au

NAFLD: progression of disease



http://www.slowcontrol.com/en/the-science-of-eating-slowly-and-its-benefits-on-health/nafld-or-fatty-liver-disease/

Jackienenwgent.com


POSITIVE THINKING
EAT BETTER
FEEL GOOD
EXERCISE


thank you!

Summary

- Testosterone deficiency is a predictor of abdominal obesity and metabolic syndrome
- Testosterone may play a central role in metabolic syndrome and type 2 diabetes by
  - Increasing skeletal muscle mass
  - Decreasing abdominal obesity and free fatty acids
- Testosterone treatment in patients with KS does not fully correct the unfavorable body composition
- Increased body fat mass is already present before puberty in boys with KS which suggests that both genetic abnormalities and testosterone deficiency influence fat in patients with KS
- Future studies are required to better understand
  - the effects of testosterone on cardiovascular health
  - Shed light on pathophysiology of bidirectional interplay between testosterone and metabolic syndrome

eXemplarY Kids Clinic

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