

# 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](#),<sup>1</sup> [Bonita Falkner](#),<sup>2</sup> [Karen Kowal](#),<sup>1</sup> and [Judith L Ross](#)<sup>1</sup>

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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



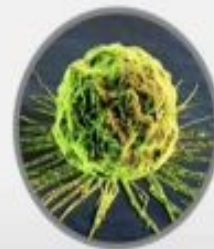
HYPERTENSION



TYPE 2 DIABETES



DEMENTIA



CANCER



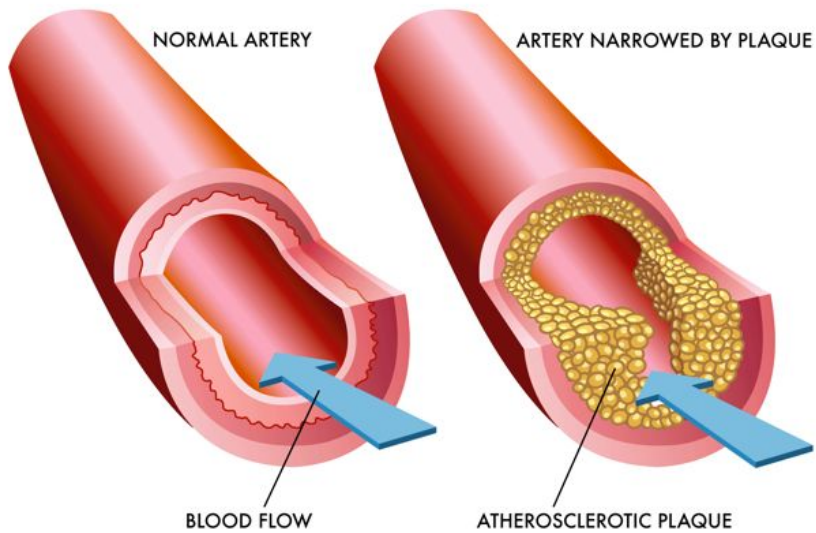
POLYCYSTIC  
OVARIAN  
SYNDROME



NON-ALCOHOLIC  
FATTY LIVER  
DISEASE

UCTVPrime

# ATHEROSCLEROSIS



Tekening: Auke Herrema

# 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?

# Physical Exam Features of Boys with Klinefelter Syndrome compared with Controls

	<b>KS (n = 89)</b>	<b>Controls (n = 34)</b>	<b>p Value</b>
<b>Mean age (years)</b>	<b>7.5 ± 2.4</b>	<b>8.1 ± 2.3</b>	<b>0.3</b>
<b>% Pubic Hair Tanner 1</b>	<b>91</b>	<b>97</b>	<b>0.1</b>
<b>Mean height (SDS)</b>	<b>0.6 ± 1.0</b>	<b>0.1 ± 1.0</b>	<b>0.02*</b>
<b>Mean weight (SDS)</b>	<b>0.6 ± 1.1</b>	<b>0.6 ± 1.2</b>	<b>0.8</b>
<b>Mean BMI (SDS)</b>	<b>0.5 ± 1.2</b>	<b>0.7 ± 1.2</b>	<b>0.4</b>
<b>% Body Fat</b>	<b>25.6 ± 9.3</b>	<b>27.8 ± 12.0</b>	<b>0.5</b>
<b>% waist circumference &gt; 7</b>	<b>49</b>	<b>56</b>	<b>0.6</b>
<b>% waist circumference &gt; 9</b>	<b>30</b>	<b>21</b>	<b>0.4</b>



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

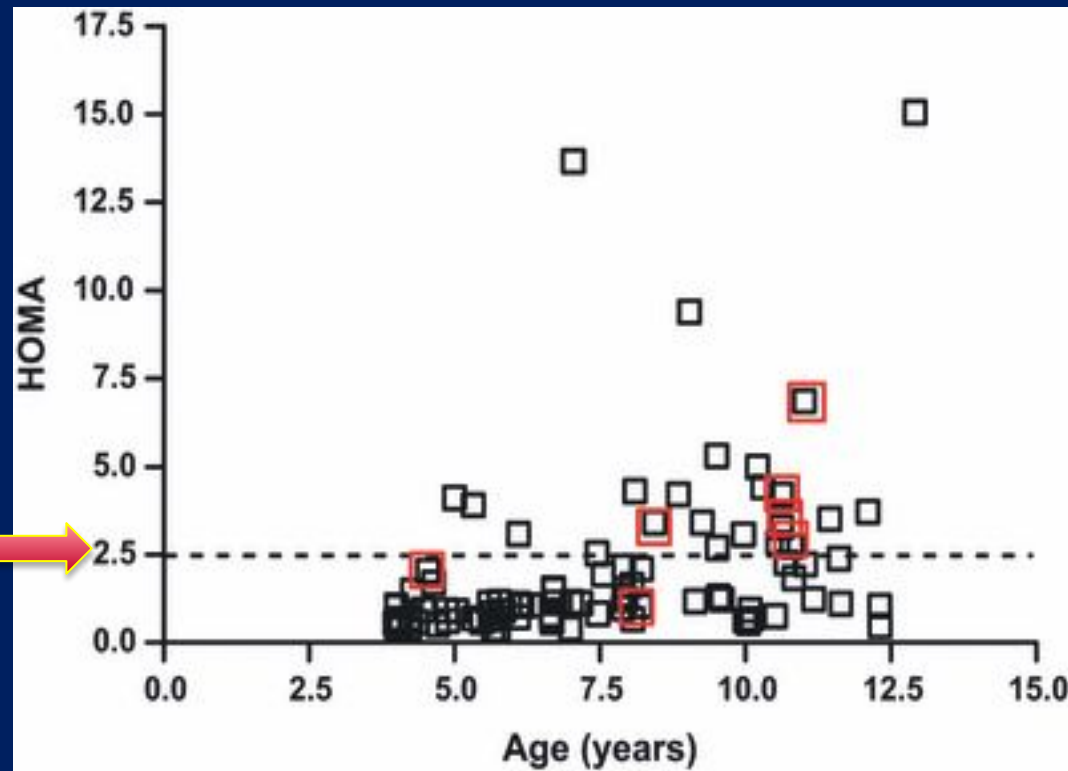
Lab and cut-off value	% who met cut-off	Mean $\pm$ SD	Mean 5-18-year-olds
Low-density lipoprotein $\geq$ 2.9 mmol/L ( $\geq$ 110 mg/dL)	37	2.7 $\pm$ 0.7 (105 $\pm$ 25 mg/dL)	2.4-2.6 (92-100 mg/dL)
T cholesterol $\geq$ 4.4 mmol/L ( $\geq$ 170 mg/dL)	40	4.3 $\pm$ 0.8 (165 $\pm$ 28 mg/dL)	4.1-4.2 (157-162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

# 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

# Insulin Resistance and Metabolic Syndrome in Prepubertal Boys with Klinefelter syndrome



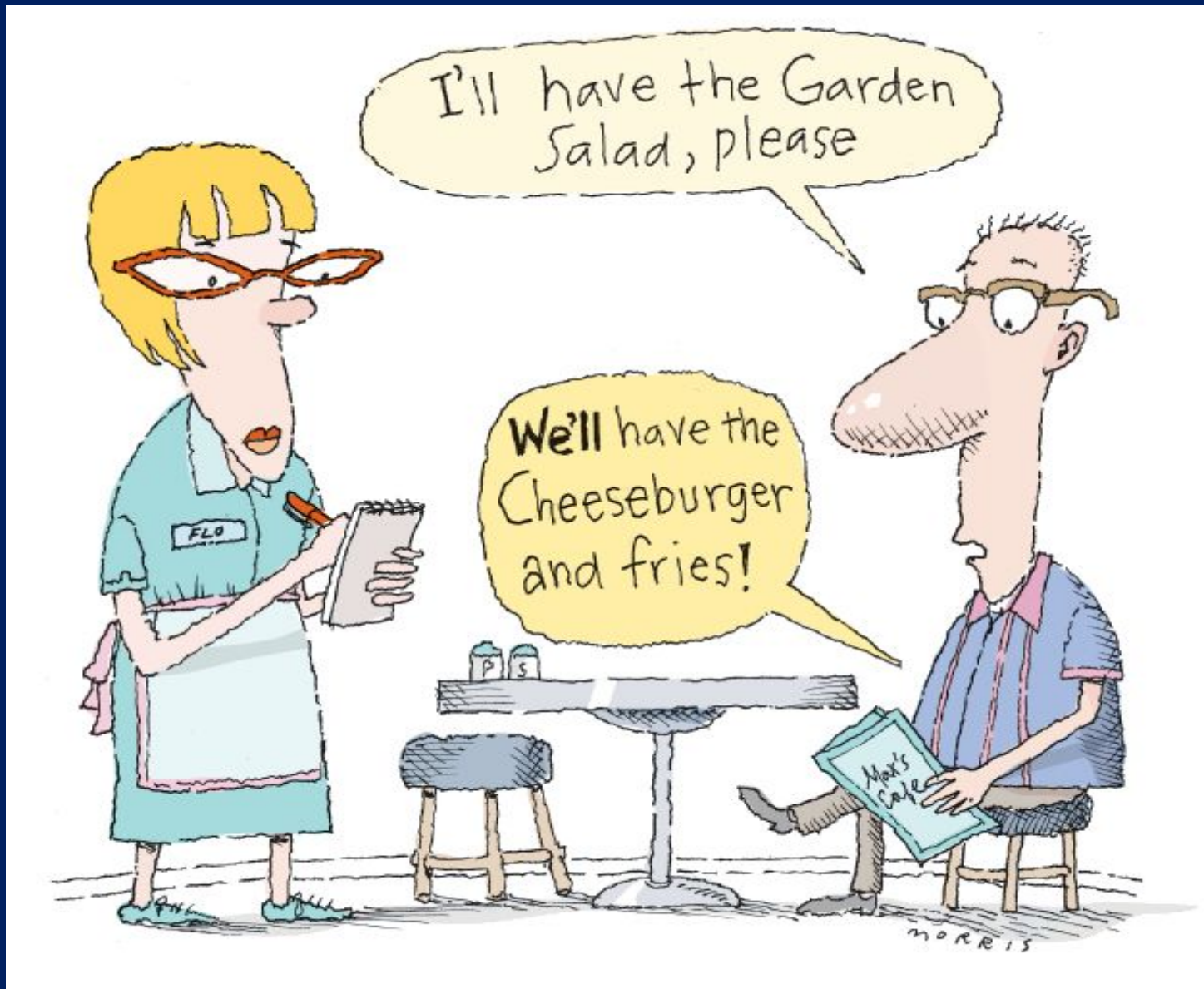
Red box  
Indicates subjects  
who fit criteria for  
metabolic  
syndrome

Insulin  
resistance

Insulin resistance:  $\text{fasting blood glucose (mmol/L) x fasting insulin (uU/mL) / 22.5}$

# 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



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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- 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,XXXYY	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%)

# Gonadal Function in Klinefelter Syndrome

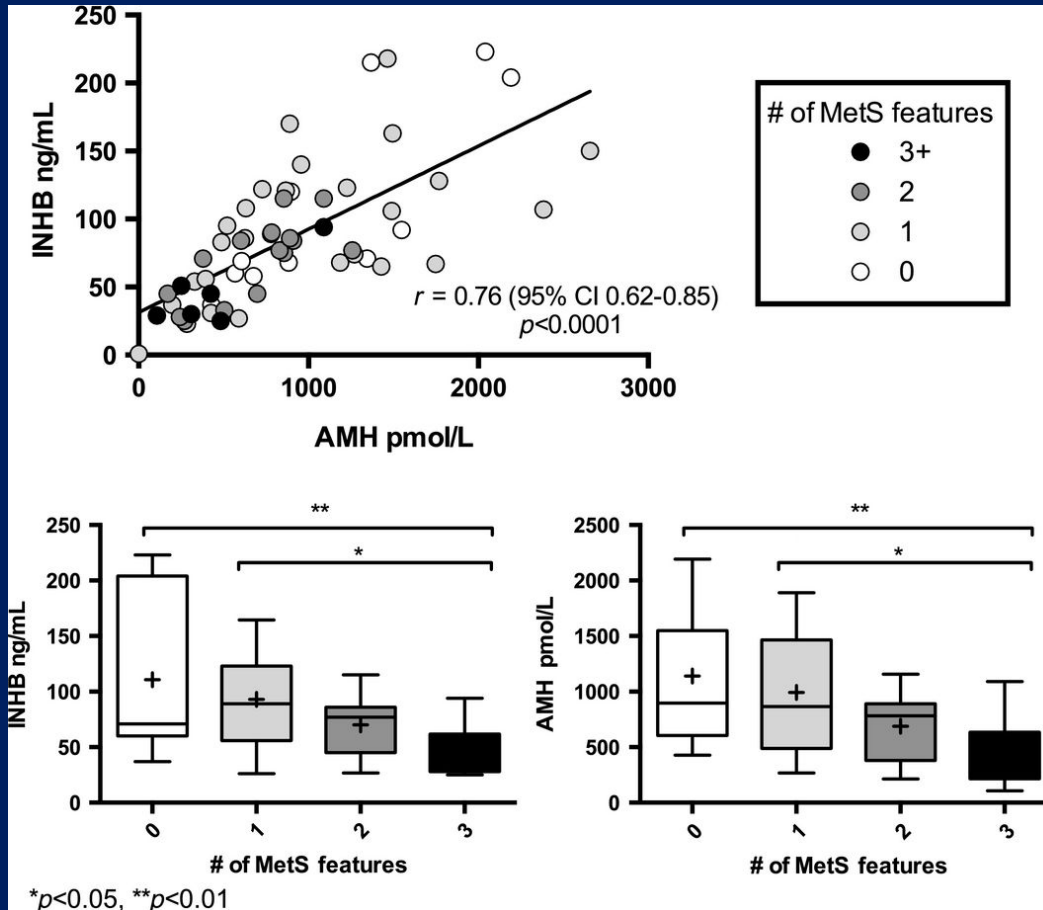
- FSH was elevated in 20% of subjects
- LH was lower than expected
- Total testosterone was below the expected range for age in nearly half the pre-pubertal participants
- Supports the hypothesis that androgen deficiency is present prior to puberty in boys KS



# 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



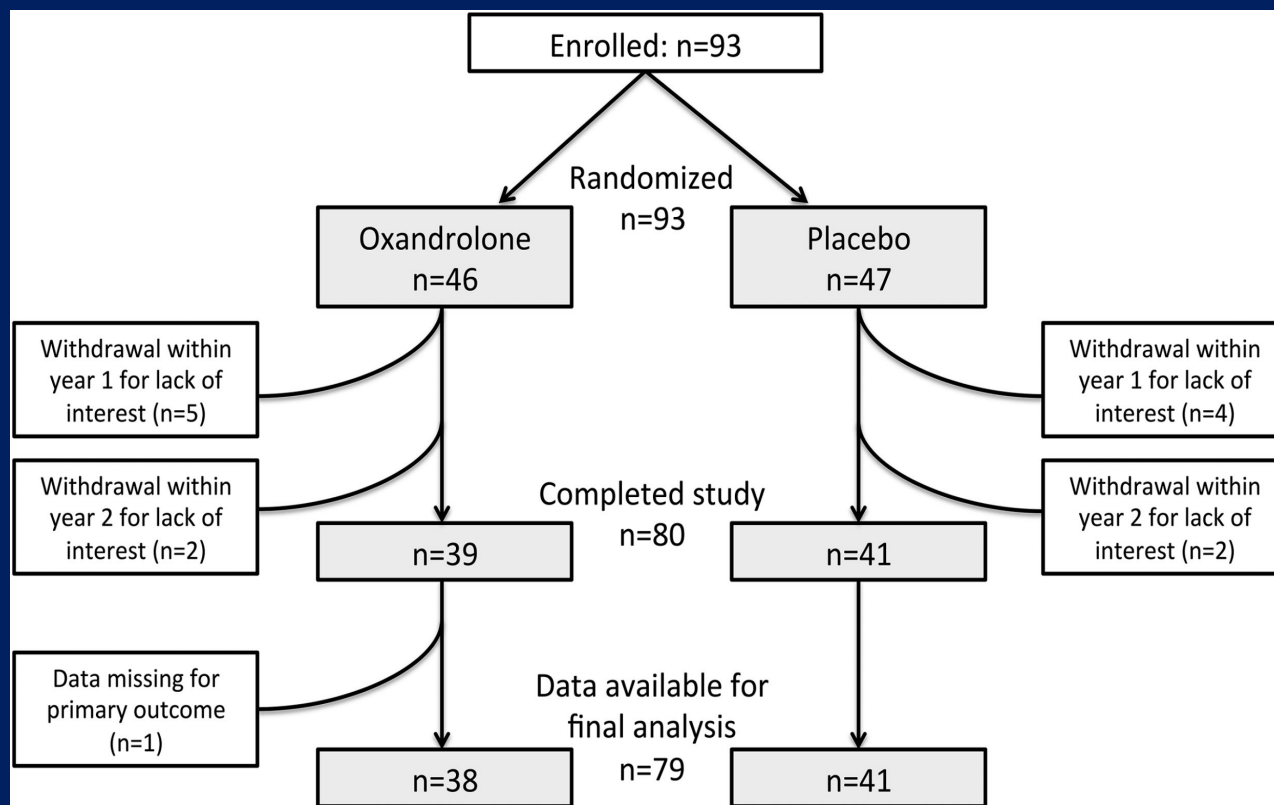
## MetS

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

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

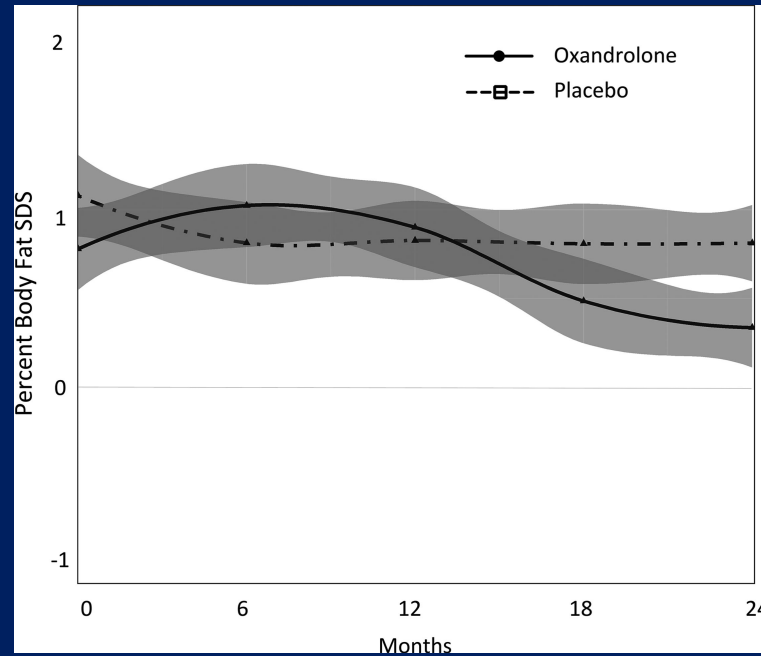
- High prevalence of cardiometabolic risk factors
  - Increased waist circumference
  - Dyslipidemia
  - Insulin resistance
  - independent of age and BMI
- Evidence of pre-pubertal gonadal dysfunction
- Pre- pubertal gonadal dysfunction is associated with increased markers of cardiometabolic risk

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



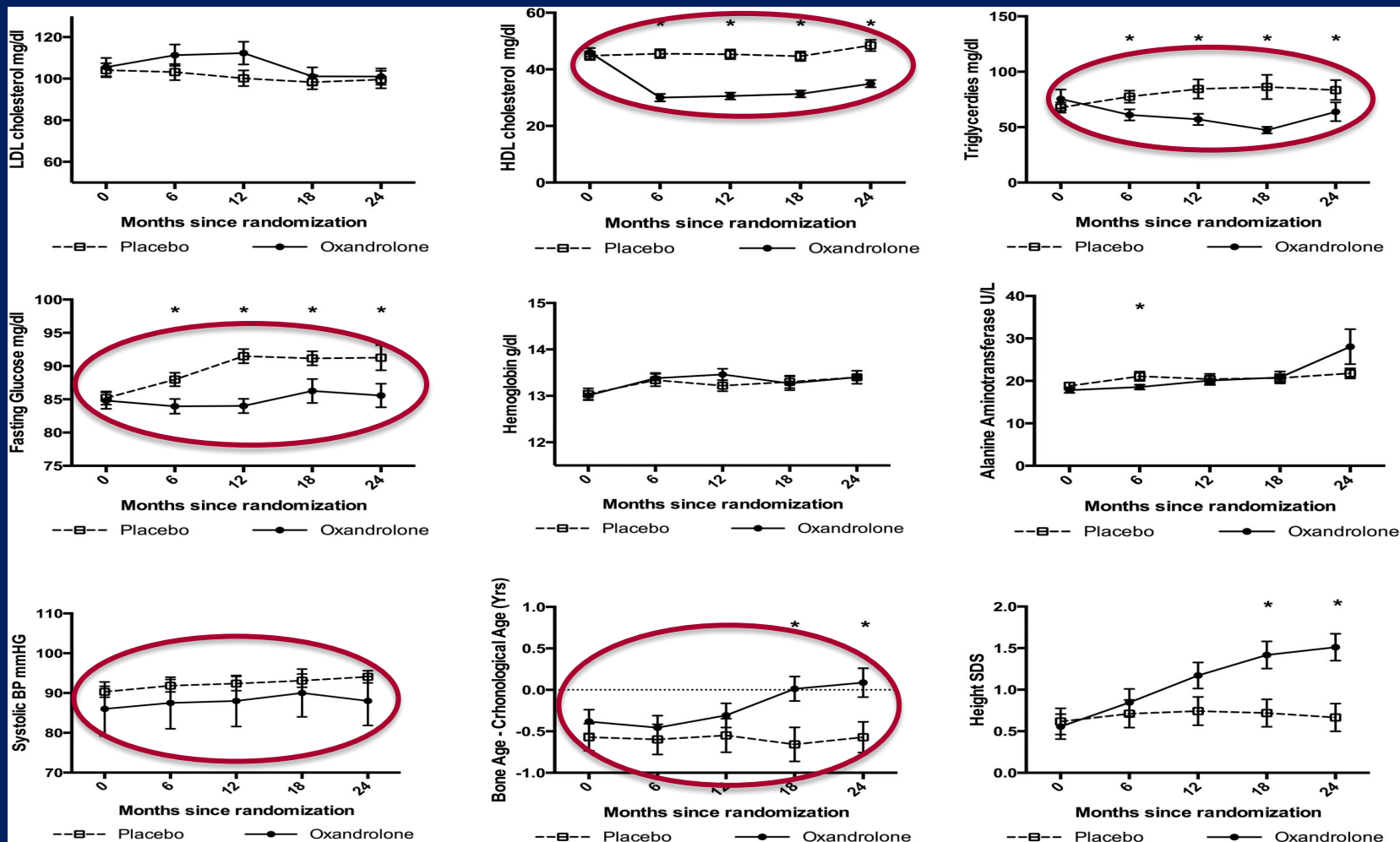
From: **Effects of Oxandrolone on Cardiometabolic Health in Boys With Klinefelter Syndrome: A Randomized Controlled Trial**

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



%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.



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 Klinefelters syndrome



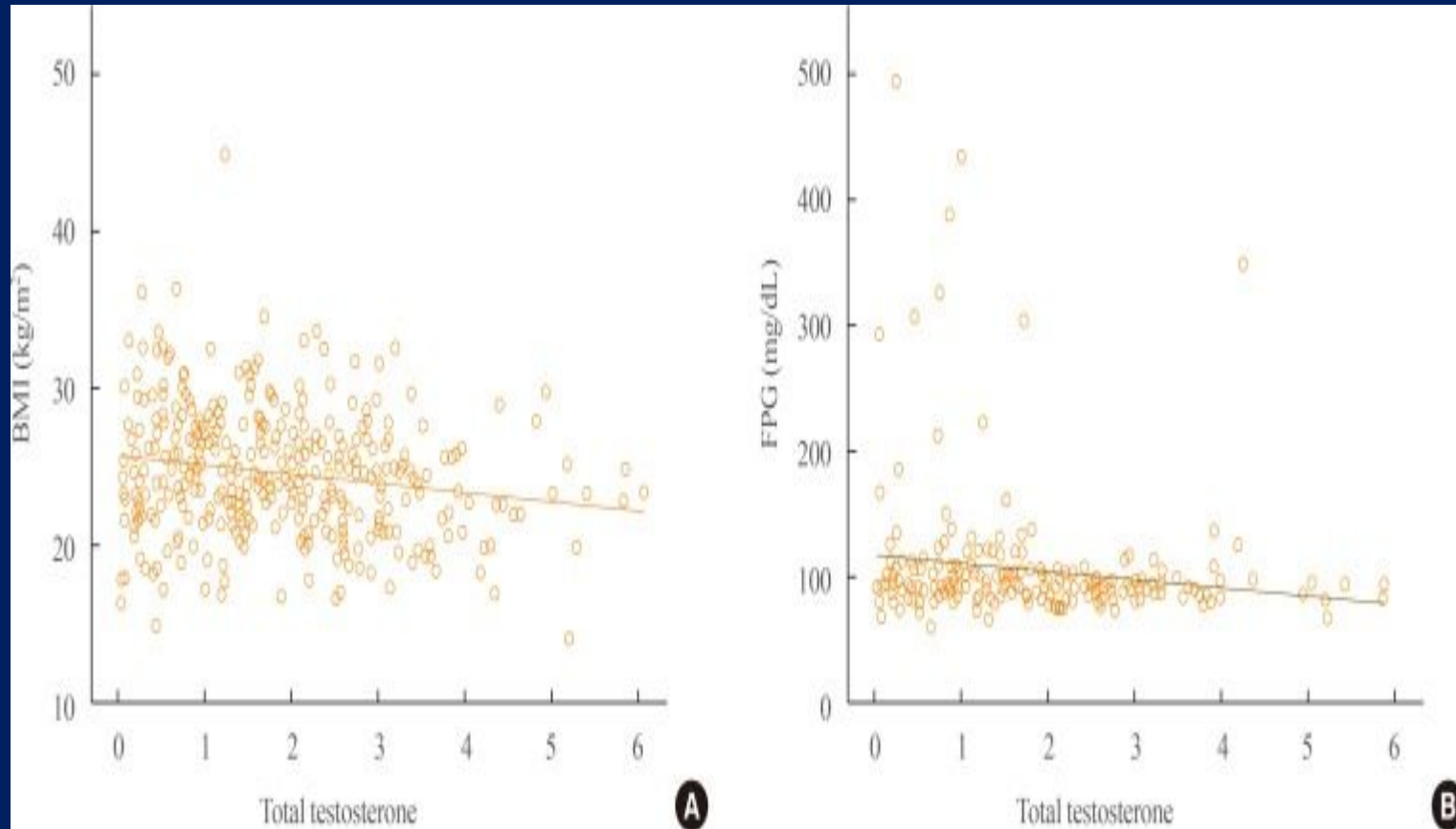
Han SJ, Kim K-S, Kim W, et al. Obesity and Hyperglycemia in Korean Men with Klinefelter Syndrome: The Korean Endocrine Society Registry. *Endocrinology and Metabolism*. 2016;31(4):598-603. doi:10.3803/EnM.2016.31.4.598.



# Comparison of Characteristics in Obese versus Nonobese Patients with Klinefelter Syndrome

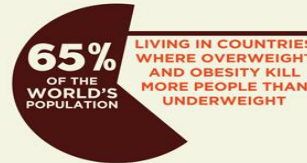
Characteristic	Total (n=376)	Nonobese (n=216)	Obese (n=160)	P value
Age, yr	32 (18–53)	32 (18–53)	32 (20–53)	0.430
Height, cm	177.0±6.5	177.1±6.3	177.0±6.9	0.904
Body weight, kg	77.5±13.8	69.2±8.8	88.8±11.1	<0.001
BMI, kg/m <sup>2</sup>	24.7±3.9	22.0±2.2	28.3±2.7	<0.001
Hypertension	57 (15.2)	27 (12.5)	30 (18.8)	0.095
Hyperglycemia <sup>a</sup>	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 <sup>b</sup>	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

**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**

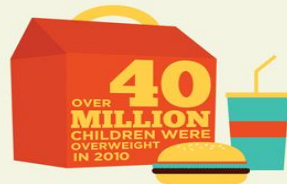


Han SJ, Kim K-S, Kim W, et al. Obesity and Hyperglycemia in Korean Men with Klinefelter Syndrome: The Korean Endocrine Society Registry. *Endocrinology and Metabolism*. 2016;31(4):598-603. doi:10.3803/EnM.2016.31.4.598.

# WORLDWIDE OBESITY: A FRIGHTENING LOOK AT THE FACTS



## CHILDREN



## ADULTS



## YOU = ?

**BMI**  $\geq 25$  = OVERWEIGHT  
**BMI**  $\geq 35$  = OBESE  
\*BMI = BODY MASS INDEX

<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

	<b>NCEP ATP III<sup>a</sup></b>	<b>IDF<sup>b</sup></b>
	<b>≥ 3 of 5 Criteria</b>	<b>Criterion 2 Plus 2 of the Other 4</b>
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).

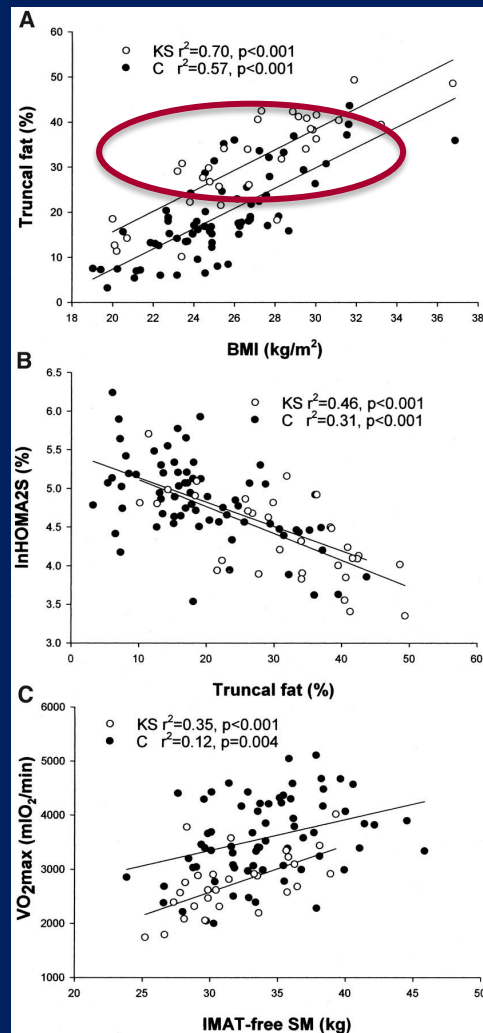


# The Metabolic Syndrome is Frequent in Klinefelter's Syndrome and Is Associated with Abdominal Obesity and Hypogonadism

**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 AND 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.

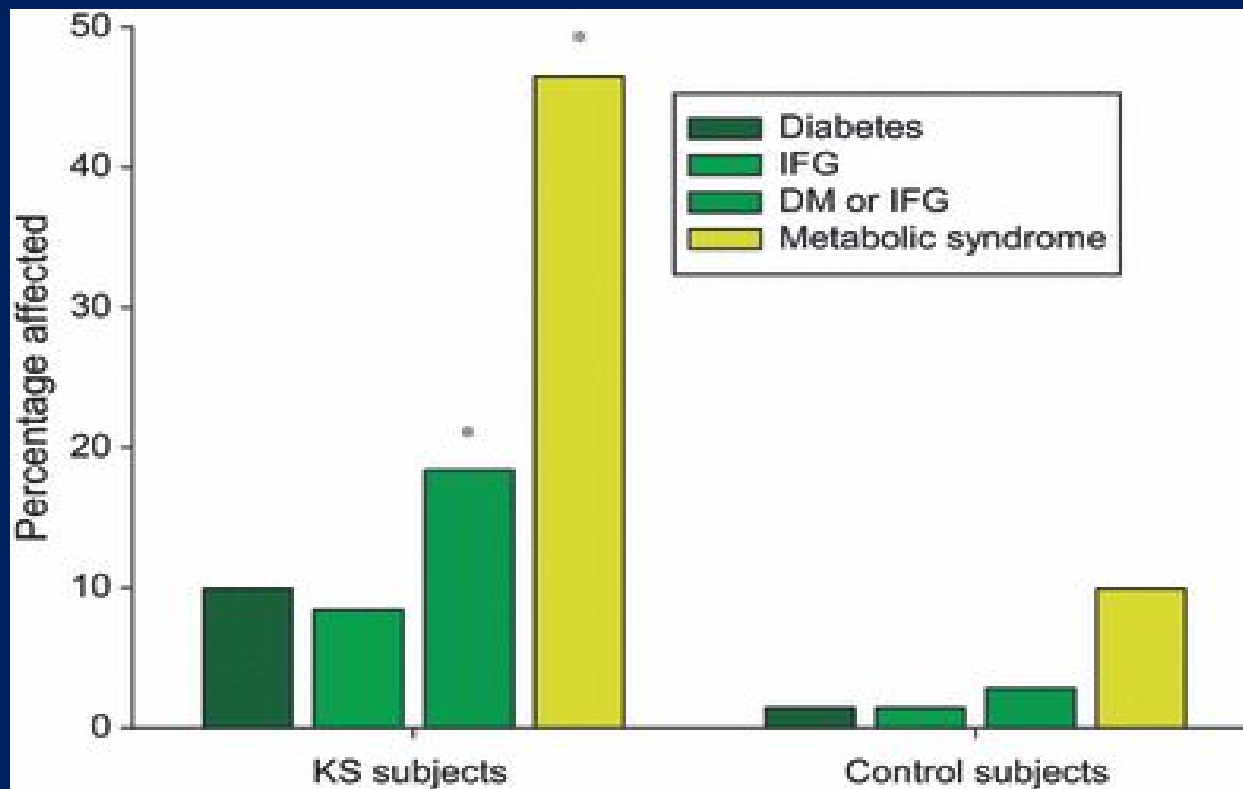
# Truncal Fat in Correlation with BMI in Klinefelter Syndrome Patients versus Controls



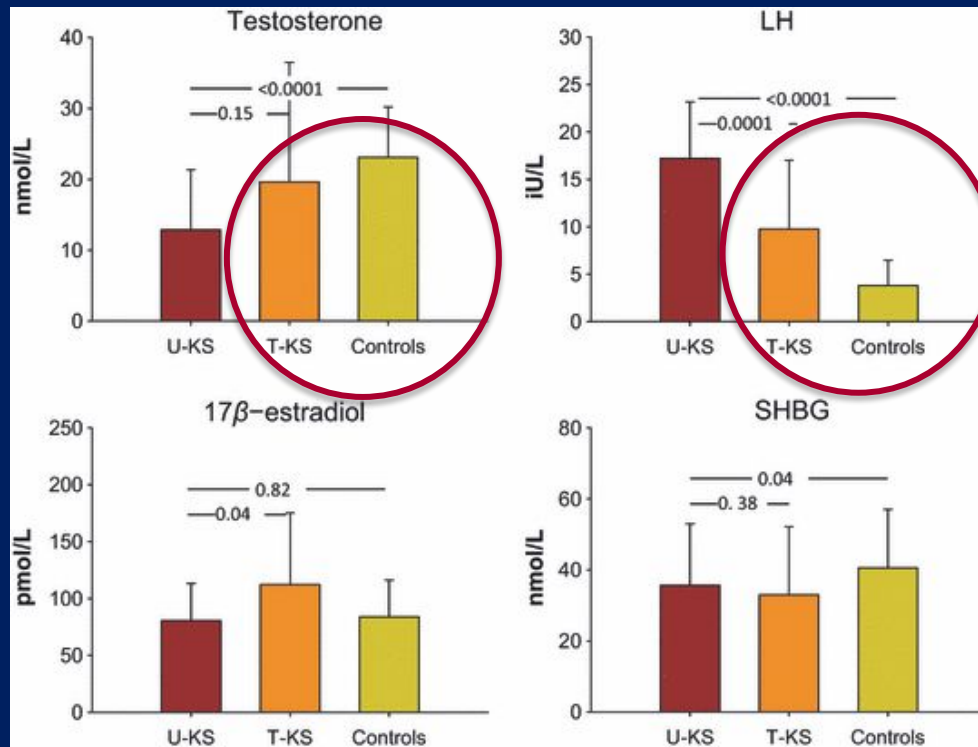
**Klinefelter's syndrome patients (KS, ○) have more Truncal Fat (~8% more) for any value of BMI than control subjects (C, ■)**



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



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



Treatment regimen offered to many men with KS is insufficient



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

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

 Author Affiliations

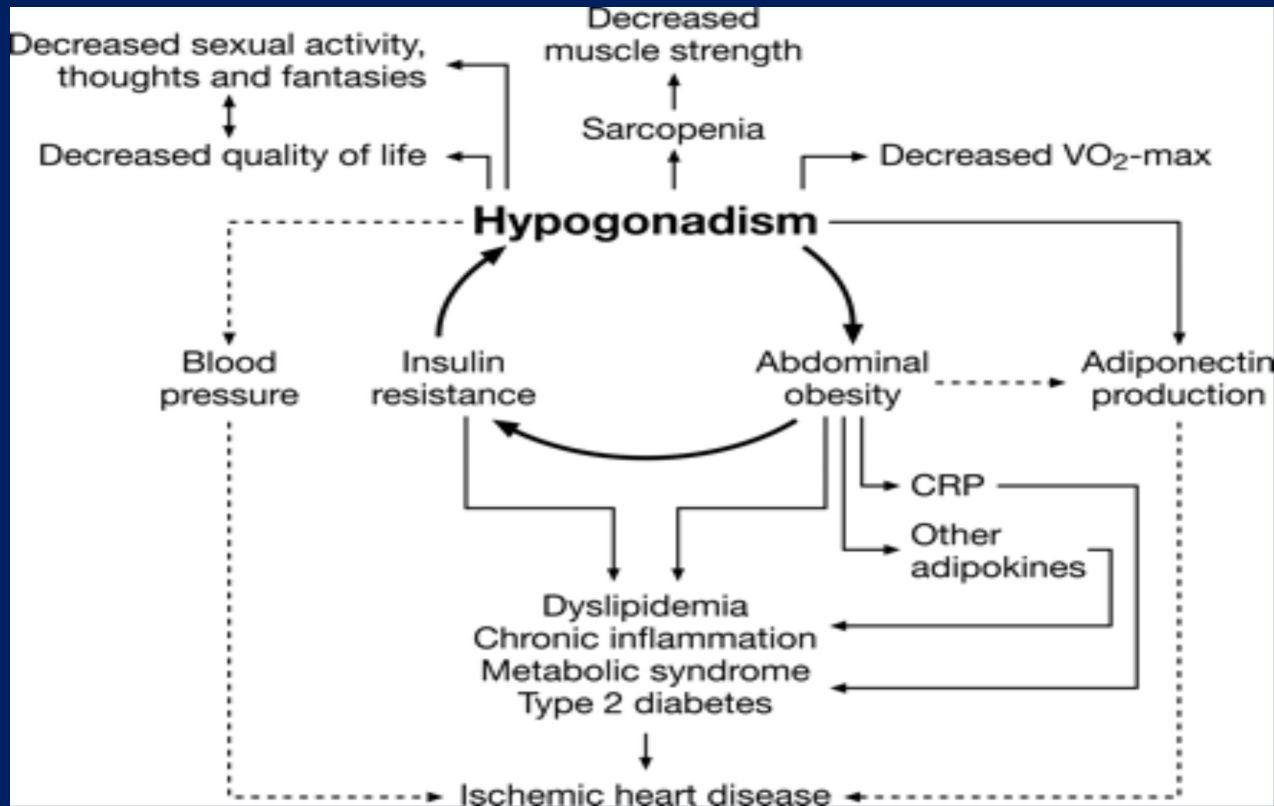
Address correspondence and reprint requests to Anders Bojesen, MD, Medical Department M, Endocrinology and Diabetes, Aarhus University Hospital, Noerrebrogade 42-44, DK-8000, Aarhus C, Denmark. E-mail: [anders.bojesen@dadlnet.dk](mailto:anders.bojesen@dadlnet.dk)

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

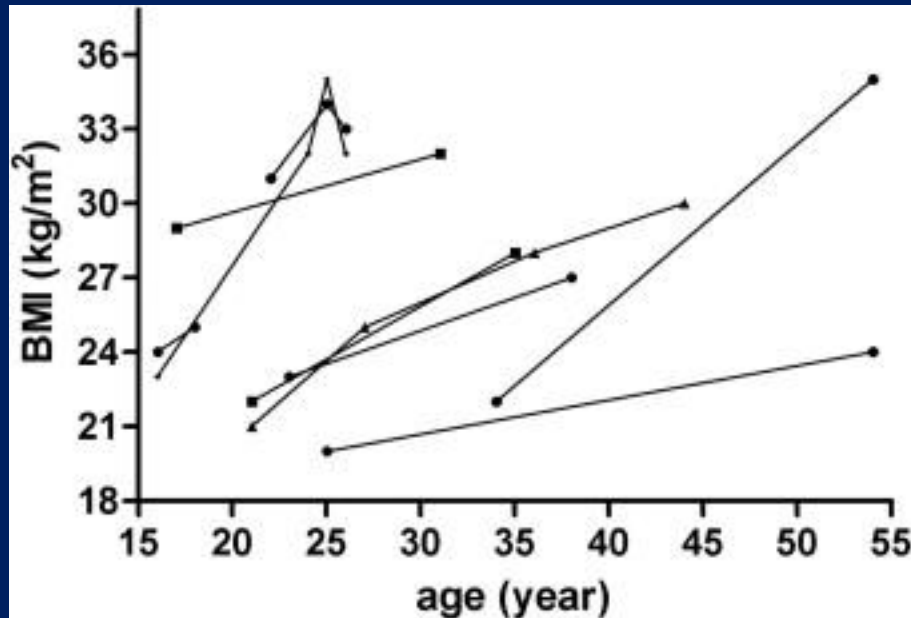
- Strongest predictor of metabolic syndrome was adiposity and truncal fat
- Almost half of Klinefelter syndrome patients fulfilled the NCEP/ATPIII criteria for metabolic syndrome
- Only 10% of the control subjects met criteria for metabolic syndrome
- CRP
  - Marker of low grade inflammation
  - Predictor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

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**

## 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	47xyy	6.6	Severe pancreatitis <coma> fatty liver	Lantus + NovoRapid
P2	23	23	173	83	47xyy/46xx	10.4	Fatty liver Severe fatty liver	Novomix 30 + metformin
P3	24	16	178	100	47xyy	11.2		Metformin
P4	29	24	185	61	48xyy	6.9	Mental retardation TG 32 mmol/L <comma> fatty liver	Refuse to take medicine
P5	30	19	167	77	46xy/47xy	9.9		Novomix 30
P6	30	33	178	68	46xy/47xy	7.7	Acute myeloid leukemia M3	Refuse to take medicine
P7	32	35	179	88	47xyy	9.1	Fatty liver	Metformin + regular insulin
P8	55	25	185	68	47xyy	6.4	TG 11 mmol/L	Metformin

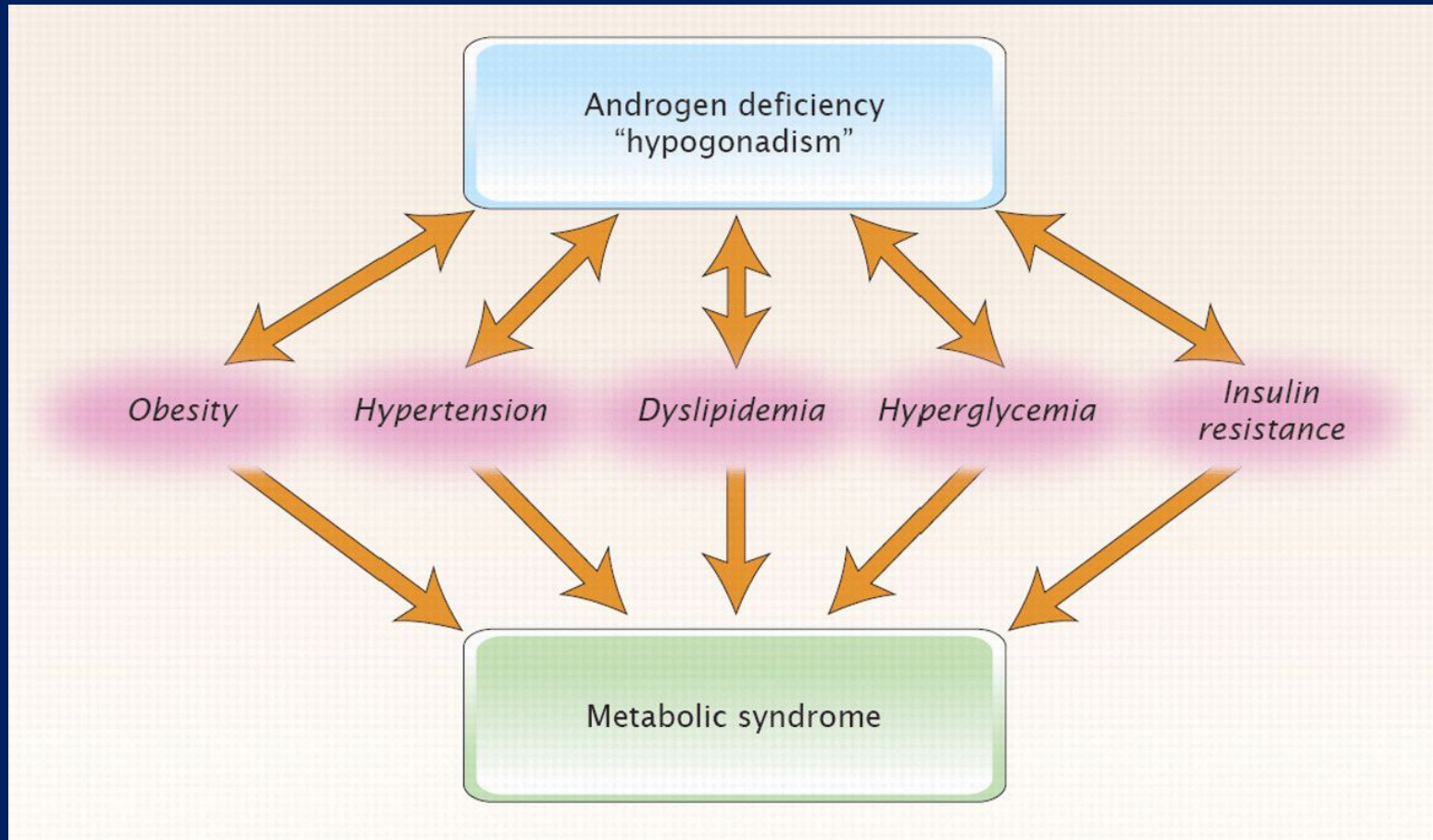
## Relationship between incidence of diabetes and karyotype.

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 <sup>a</sup>
Total	8/39	20.5

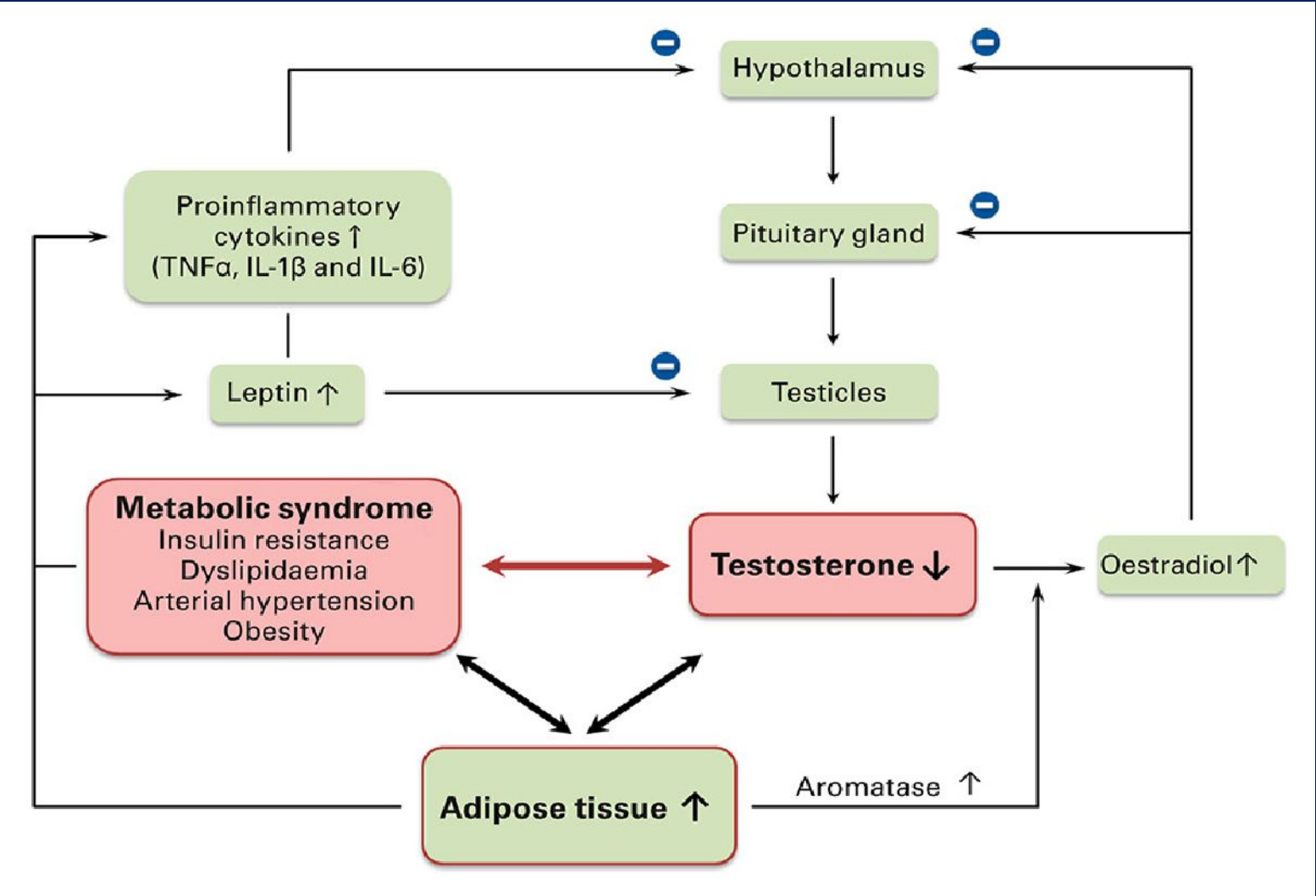
# Low Testosterone & Cardiovascular Disease Risks & Type 2 Diabetes

- 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

# The Emerging Link Between Hypogonadism and Metabolic Syndrome



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





# Low Testosterone is associated with Increased Mortality in Older Men

<b>Study design</b>	<b>n</b>	<b>Follow-up (years)</b>	<b>Mortality</b>	<b>Hazard ratio (95% CI)</b>	<b>Recent studies</b>
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)

# 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

# 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
<i>n</i>	24	32	184	220
Duration (months)	3	12	6	6/12 <sup>2</sup>
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 <sub>1c</sub>	-0.37	-0.80	ND	↔ [-0.45] <sup>‡</sup>
Total cholesterol (nmol/L)	-0.4	ND	↔	↔ [-0.13]
LDL cholesterol (nmol/L)	↔	ND	↔	↔ <sup>‡</sup>
HDL cholesterol (nmol/L)	↔	↑ <sup>§</sup>	↔	-0.049 <sup>‡</sup>
Triglycerides	↔	↓	↔	↔
Lipoprotein a	ND	ND	ND	↓
BMI	↔	↔	↔	↔
Waist circumference	↓	↓	↓	↔
% Body fat	ND	ND	ND	↔
Blood pressure	↔	↓ <sup>¶</sup>		



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

Victoria K Shanmugam, Katina C Tsagaris, Christopher E Attinger

## Key Points

- ❖ a 38-year-old male was evaluated for bilateral lower extremity ulcers that had been present for 4 years
- ❖ 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



**Figure 1.** Appearance of right leg at presentation.



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

# 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

# 8 Habits of Healthy Kids<sup>®</sup>

## Healthy kids:



Spend at least 1 hour a day being physically active

Spend less than 2 hours a day watching TV and playing video and computer games



Eat at least a total of 5 fruits and vegetables everyday

Snack on healthy foods and less junk food and sweets



Drink or eat at least 3 low fat dairy foods a day

Drink at least 2 glasses or bottles of water a day instead of soda



Eat less fast food and make healthier fast food choices

Eat smaller amounts - bigger is not better





# eXemplarY Kids Clinic



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