VENDREDI 6 DÉCEMBRE 2013

14ème Journée sur l'Assistance Médicale à la Procréation de l'Hôpital Américain de Paris

Président d'Honneur: Pr Israël NISAND

Metabolic Syndrome and Male Infertility

Mario Maggi Sexual Medicine & Andrology
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Metabolic syndrome

Increased cardiovascular risk

↑ glycaemia

↓ HDL

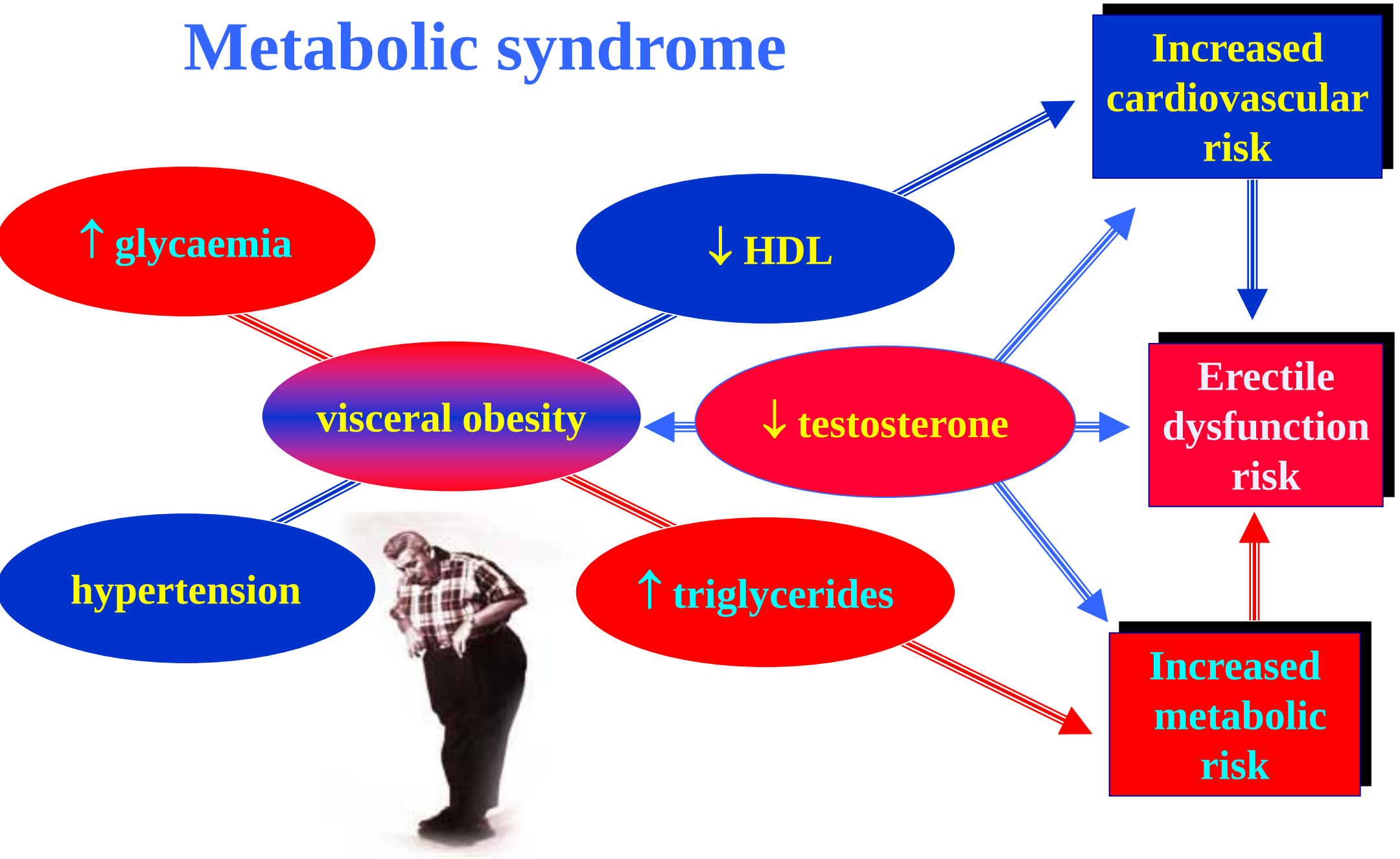
visceral obesity

hypertension

↑ triglycerides

Increased metabolic risk

Metabolic syndrome



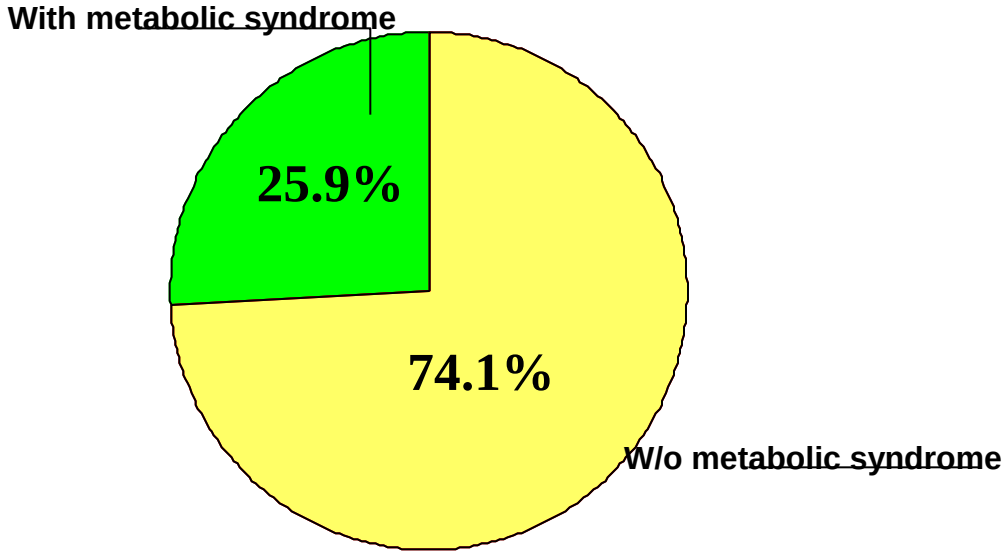
Different definitions of metabolic syndrome

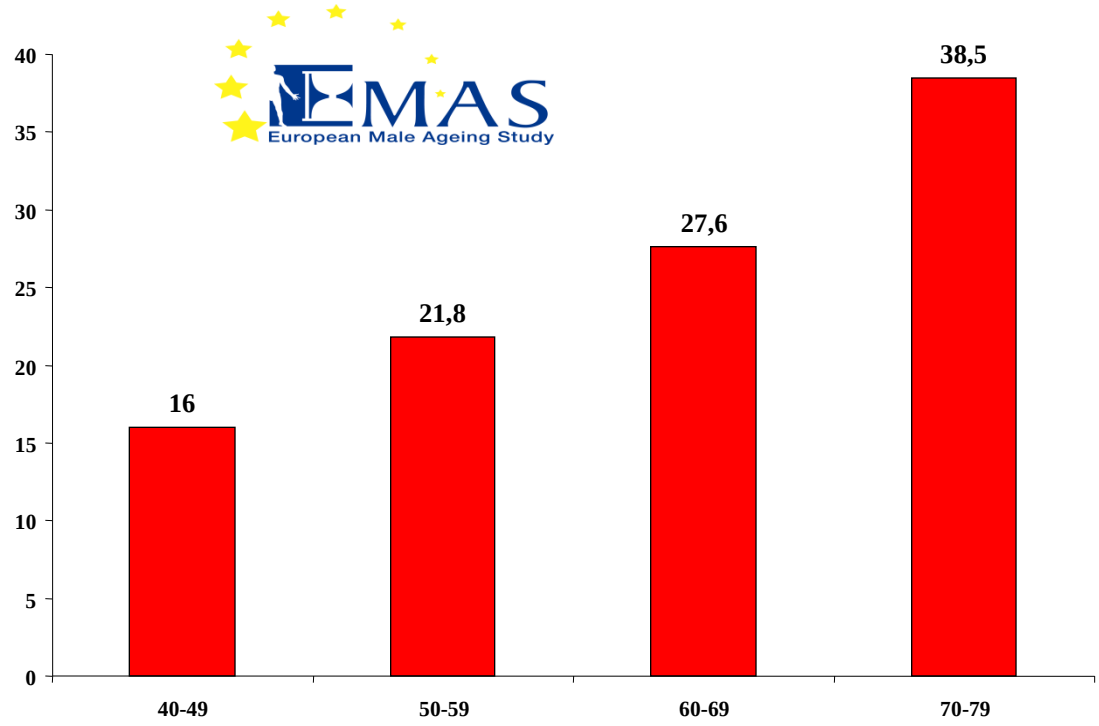
Table 2
Comparisons of definitions of metabolic syndrome: National Cholesterol Education Program-Third Adult Treatment Panel (NCEP-ATPIII), International Diabetes Federation (IDF), American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) and common definition by IDF and AHA/NHLBI. In blue are shared factors among different definitions.

NCEP-ATPIII	IDF	AHA/NHLBI	IDF&AHA/NHLBI
3 or more of the following • Central obesity (waist circumference >102 cm) • Hypertriglyceridaemia: triglycerides ≥150 mg/dl (1.7 mmol/L) or treatment • Low HDL-cholesterol: <40 mg/dl (1.03 mmol/L) or treatment • Hypertension: blood pressure ≥130/85 mmHg or treatment • Fasting plasma glucose: ≥110 mg/dl (6.1 mmol/L) or diabetes	Central obesity (waist circumference ≥94 cm) and 2 or more of the following • Hypertriglyceridaemia: triglycerides ≥150 mg/dl (1.7 mmol/L) or treatment • Low HDL-cholesterol: <40 mg/dl (1.03 mmol/L) or treatment • Hypertension: blood pressure ≥130/85 mmHg or treatment • Fasting plasma glucose: ≥100 mg/dl (5.6 mmol/L) or diabetes	3 or more of the following • Central obesity (waist circumference >102 cm) • Hypertriglyceridaemia: triglycerides ≥150 mg/dl (1.7 mmol/L) or treatment • Low HDL-cholesterol: <40 mg/dl (1.03 mmol/L) or treatment • Hypertension: blood pressure ≥130/85 or treatment • Fasting plasma glucose: ≥100 mg/dl (5.6 mmol/L) or treatment	3 or more of the following • Central obesity (population- and country-specific definitions) • Hypertriglyceridaemia: triglycerides ≥150 mg/dl (1.7 mmol/L) or treatment • Low HDL-cholesterol: <40 mg/dl (1.03 mmol/L) or treatment • Hypertension: blood pressure ≥130/85 mmHg or treatment • Fasting plasma glucose: ≥100 mg/dl (5.6 mmol/L) or treatment

Corona et al., Best Pract Res Clin Endocrinol Metab. 2011 25:337-53

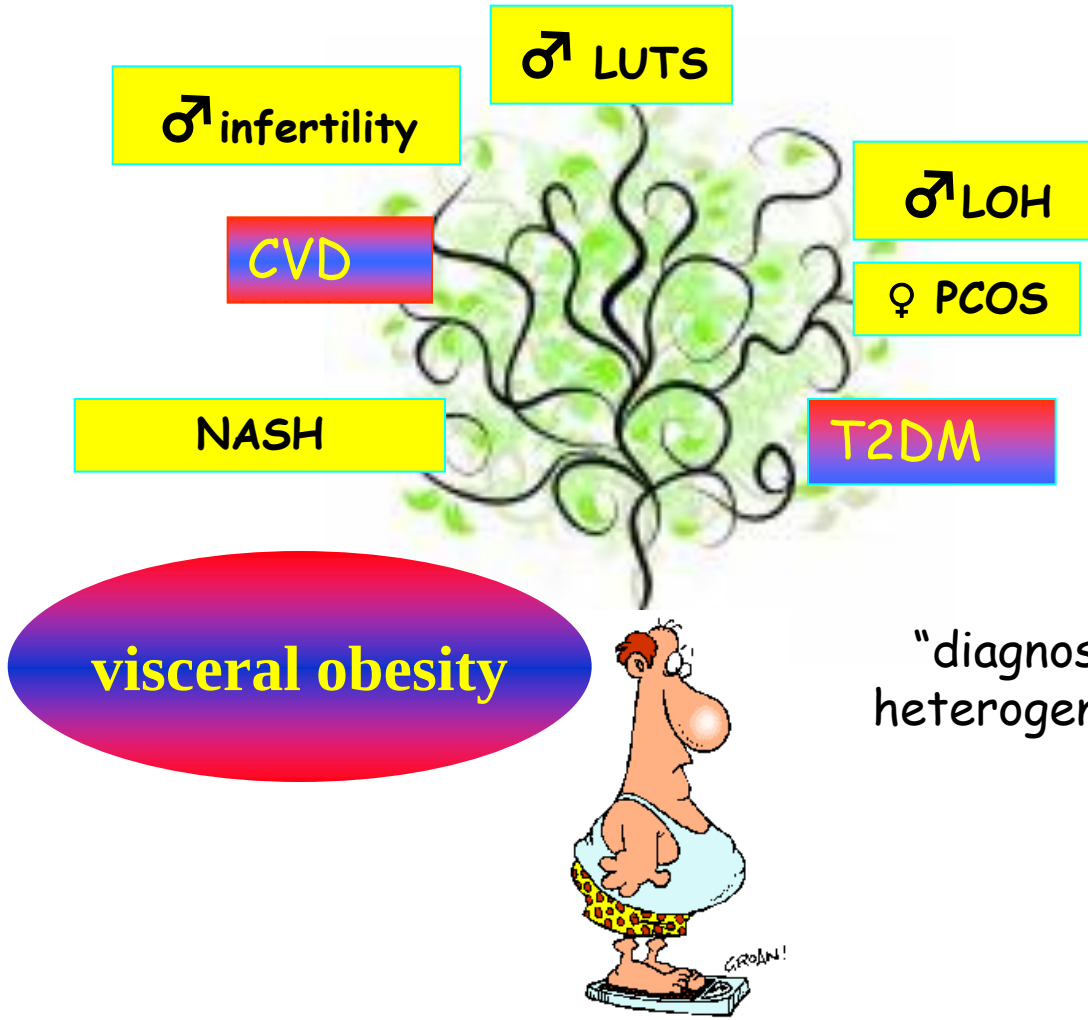
Prevalence of metabolic syndrome (NCEP-ATPIII) in Florence general population, random series of 431 community-dwelling men (EMAS), studied at the University of Florence, Florence, Italy





Corona et al., 2010 J Sex Med 7:1362-80

Metabolic syndrome:



"diagnostic category with a very heterogeneous clinical ramification"

Metabolic syndrome:

♂ infertility

visceral obesity

"diagnostic category with a very heterogeneous clinical ramification"

Journal of Andrology, Vol. 29, No. 3, May/June 2008

The Metabolic Syndrome and Male Infertility

Review

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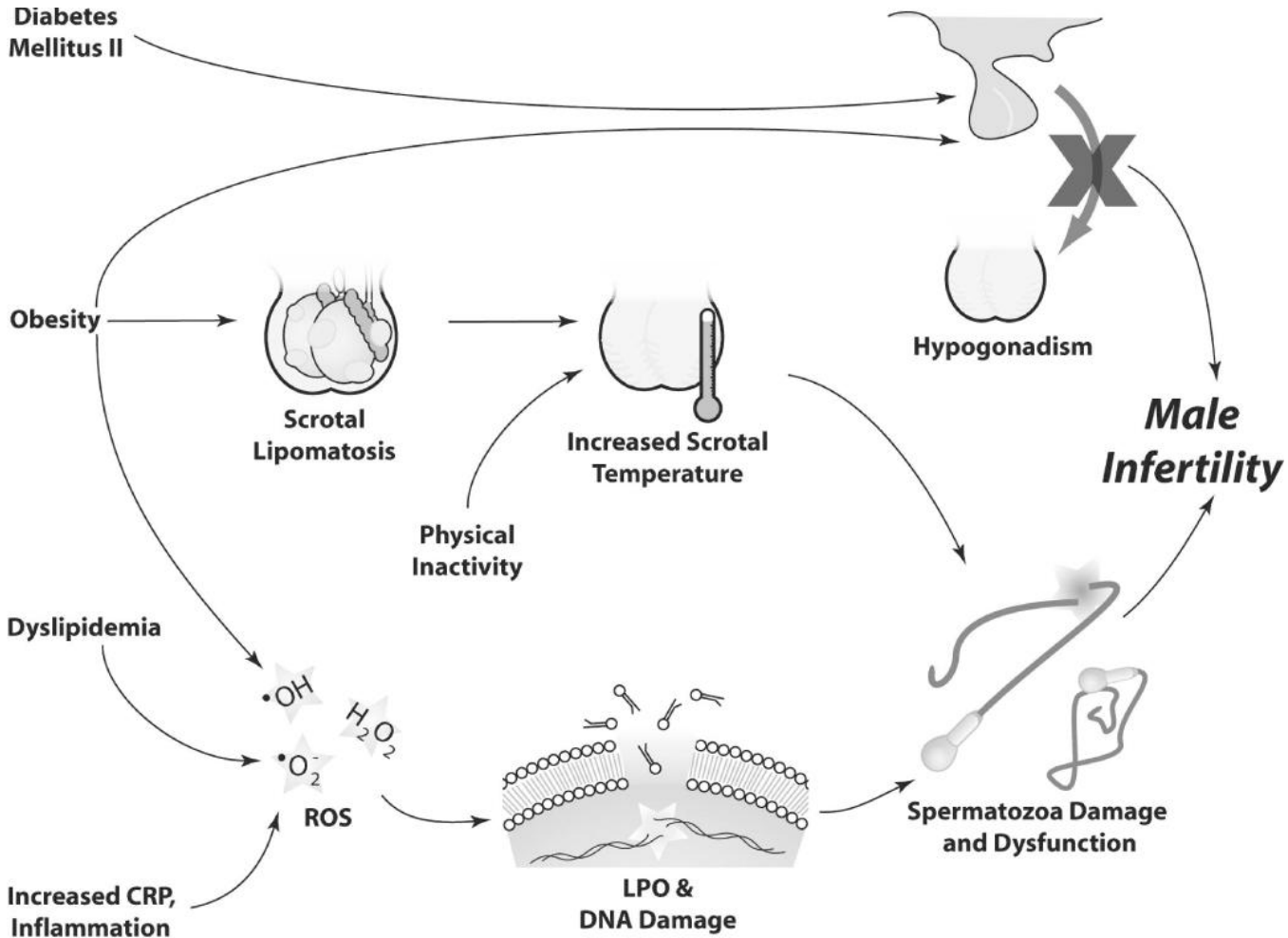

Human Reproduction Update Advance Access published May 4, 2011
Human Reproduction Update, Vol.0, No.0 pp. 1–17, 2011
doi:10.1093/humupd/dmr017
human reproduction update

Table I Summary of studies that have investigated semen parameters in overweight and obese men compared with normal-weight men with a BMI of >18.5 and <24.99 (↑, increased; ↓, decreased; NI, not clearly indicated in reference).

Semen parameters	Overweight BMI >25 <29.99 (kg/m^2)	Number of subjects	Obese BMI >30 (kg/m^2)	Number of subjects
Semen volume (normal)	Jensen *et al.* (2004)	299	Strain *et al.* (1982)	21
	Chavarro *et al.* (2010)	233	Chavarro *et al.* (2010)	127
	Ramlau-Hansen *et al.* (2010)	63	Ramlau-Hansen *et al.* (2010)	21
Sperm concentration↓	Jensen *et al.* (2004)	299	Koloszár *et al.* (2005)	58
	Magnusdottir *et al.* (2005)	25	Hammoud *et al.* (2008)	128
	Fejes *et al.* (2006)	81	Roth *et al.* (2008)	1
	Hanafy *et al.* (2007)	50	Stewart *et al.* (2009)	35
	Qin *et al.* (2007)	241	Chavarro *et al.* (2010)	19
	Hammoud *et al.* (2008)	168	Hofny *et al.* (2010)	80
	Chavarro *et al.* (2010)	35	Wegner *et al.* (2010)	36
Sperm concentration (normal)	Koloszár *et al.* (2005)	91	Strain *et al.* (1982)	21
	Magnusdottir *et al.* (2005)	47	Aggerholm *et al.* (2008)	163
	Hanafy *et al.* (2007)	30	Chavarro *et al.* (2010)	108
	Aggerholm *et al.* (2008)	773	Hofny *et al.* (2010)	42
	Chavarro *et al.* (2010)	198	Ramlau-Hansen *et al.* (2010)	21
	Ramlau-Hansen *et al.* (2010)	63		
Sperm motility↓	Magnusdottir *et al.* (2005)	25	Kort *et al.* (2006)	NI
	Kort *et al.* (2006)	NI	Hammoud *et al.* (2008)	128
	Hammoud *et al.* (2008)	168	Chavarro *et al.* (2010)	55
	Chavarro *et al.* (2010)	105	Hofny *et al.* (2010)	80
			Wegner *et al.* (2010)	35
Sperm motility (normal)	Jensen *et al.* (2004)	299	Strain *et al.* (1982)	21
	Magnusdottir *et al.* (2005)	47	Aggerholm *et al.* (2008)	163
	Aggerholm *et al.* (2008)	773	Chavarro *et al.* (2010)	72
	Chavarro *et al.* (2010)	128	Hofny *et al.* (2010)	42
	Ramlau-Hansen *et al.* (2010)	63	Ramlau-Hansen *et al.* (2010)	21
Abnormal sperm morphology↑	Qin *et al.* (2007)	241	Hammoud *et al.* (2008)	128
	Chavarro *et al.* (2010)	57	Stewart *et al.* (2009)	17
			Chavarro *et al.* (2010)	29
			Hofny *et al.* (2010)	80
			Wegner *et al.* (2010)	19
No abnormal sperm morphology	Jensen *et al.* (2004)	299	Chavarro *et al.* (2010)	98
	Hammoud *et al.* (2008)	168	Hofny *et al.* (2010)	42
	Chavarro *et al.* (2010)	176	Ramlau-Hansen *et al.* (2010)	21
	Ramlau-Hansen *et al.* (2010)	63		
Sperm DNA integrity↓	Kort *et al.* (2006)	NI	Kort *et al.* (2006)	NI
			Chavarro *et al.* (2010)	127

Functional relationship between obesity and male reproduction: from humans to animal models

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Submitted on November 11, 2010; resubmitted on January 26, 2011; accepted on April 1, 2011

Published data on the relation between overweight/obesity, semen parameters, endocrine status and human male fertility. Most overweight/obese men do not experience significant fertility problems, despite the presence of reduced testosterone alongside normal gonadotrophin levels.

Human Reproduction Update, Vol.16, No.3 pp. 293–311, 2010
Advanced Access publication on November 4, 2009 doi:10.1093/humupd/dmp047

human reproduction update

The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis

A.A. MacDonald[1], G.P. Herbison[2], M. Showell[3], and C.M. Farquhar[4,5]

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Five studies were suitable for pooling and the meta-analysis found no evidence for a relationship between BMI and sperm concentration or total sperm count. Overall review of all studies similarly revealed little evidence for a relationship with semen parameters and increased BMI.

Table III Data extracted from all studies for use in meta-analysis

	BMI Category	Aggerholm et al. (2008)	Jensen et al. (2004)	Qin et al. (2007)	Koloszár et al. (2005)	Fejes et al. (2006)
Study population	Total	1989	1558	990	274	42
	<20	67	217	42[a]	29	25
	20–25	986	1042	*690*[b]	96	
	25–30	773	299	241	91	17
	>30	171		17	58	
Mean sperm concentration (M/ml)	Total					
	<20	82		*45.2 ± 4.74*[a]	38 ± 14	11.2
	20–25	74		*69.1 ± 1.35*[b]	39 ± 14	
	25–30	70		76.2 ± 3.35	37 ± 14	8.1
	>30	80		70.6 ± 10.35	29 ± 12	
Median sperm concentration (M/mL)	Total		44 [21–79]			
	<20	67 [25 102]	40 [17, 75]			
	20–25	55 [9,99]	46 [23, 84]			
	25–30	53 [27,90]	39 [20, 69]			
	>30	65 [33 114]				
Mean total sperm count (M)	Total					
	<20	256		*117.8 ± 14.25*[a]		
	20–25	231		*175.3 ± 4.63*[b]		
	25–30	216		196.6 ± 9.51		
	>30	265		149.5 ± 25.47		
Median total sperm count (M)	Total		128 [55, 246]			
	<20	165 [86, 351]	105 [47, 240]			
	20–25	161 [77, 309]	138 [59, 259]			
	25–30	153 [67, 286]	116 [46, 213]			
	>30	156 [75, 317]				
Mean semen volume (mL)	Total					4.3 ± 0.7
	<20	3.1	3.0 ± 1.5	2.8 ± 0.20[a]		
	20–25	3.2	3.2 ± 1.4	2.5 ± 0.04[b]		
	25–30	3.2	3.2 ± 1.6	2.5 ± 0.07		
	>30	3.2		2.5 ± 0.29		
Average sperm motility (%)	Total					
	<20	42	63.7 ± 14.5	*74.5 ± 1.58*[a]		
	20–25	41	65.4 ± 12.4	*70.2 ± 0.45*[b]		
	25–30	48	65.5 ± 12.5	69.1 ± 0.87		
	>30	54		72.4 ± 2.83		

Note: Median values = median [25th, 75th percentiles]; Mean values = mean ± SD.
Data in *italics* is part of an unconventional BMI category (not as reported in BMI category column).
[a]Underweight BMI category of <18.5.
[b]Normal weight BMI category of 18.5–25.

Table IV Regression coefficients from meta-analysis

Semen Parameter	Number of studies used	Number of data entries used	Regression coefficient	95% Confidence Interval
Mean sperm concentration	4	14	−0.02	−8.24, 8.18
Median sperm concentration	2	7	1.57	−7.39, 10.53
Mean total sperm count	2	8	12.43	−164.95, 189.81
Median total sperm count	2	7	2.09	−35.79, 39.97
Semen volume	3	11	0.05	−0.05, 0.15
Average sperm motility	3	11	−1.07	−7.39, 5.25

Human Reproduction Update, Vol.19, No.3 pp. 221–231, 2013
Advanced Access publication on December 12, 2012 doi:10.1093/humupd/dms050

human reproduction update

BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis

N. Sermondade[1,2], C. Faure[1,2], L. Fezeu[2], A.G. Shayeb[3], J.P. Bonde[4], T.K. Jensen[5], M. Van Wely[6], J. Cao[7], A.C. Martini[8], M. Eskandar[9], J.E. Chavarro[10,11], S. Koloszar[12], J.M. Twigt[13], C.H. Ramlau-Hansen[14], E. Borges Jr[15], F. Lotti[16], R.P.M. Steegers-Theunissen[13], B. Zorn[17], A.J. Polotsky[18], S. La Vignera[19], B. Eskenazi[20], K. Tremellen[21], E.V. Magnusdottir[22], I. Fejes[23], S. Hercberg[2,24], R. Lévy[1,2†], and S. Czernichow[25,26,*†]

A total of 21 studies: 13 077 men

- ✓ **Obese: 1.28 (1.06-1.55)**
- ✓ **Morbidly obese: 2.04 (1.59-2.62)**

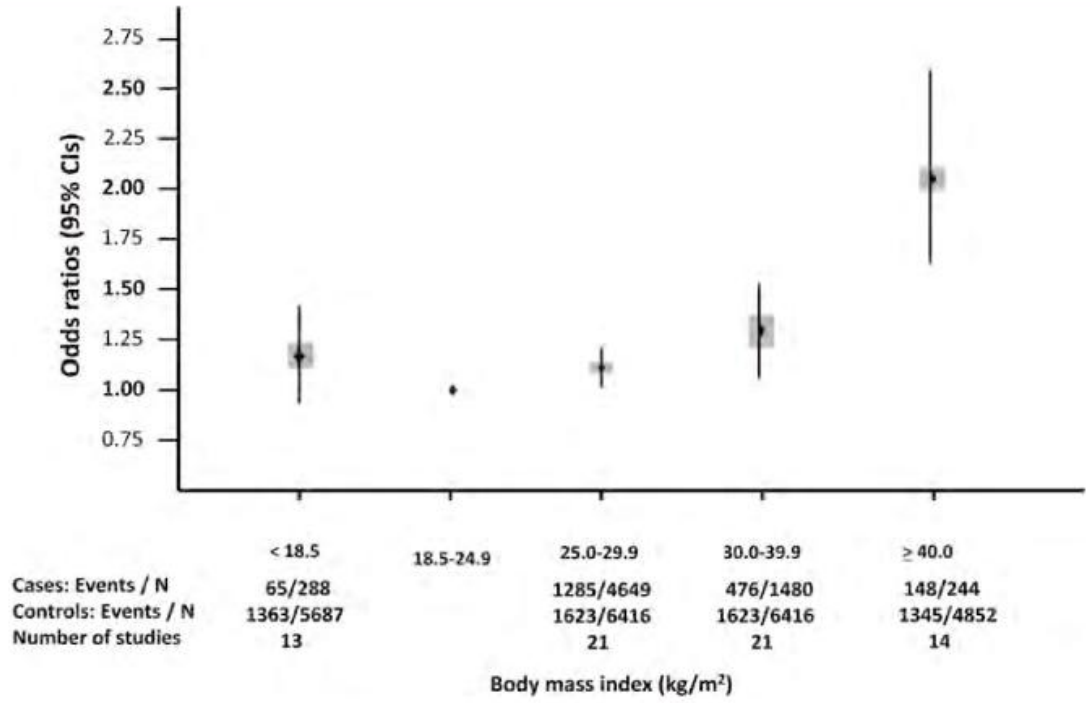

Figure 2 Association between BMI and abnormal TCS (oligozoospermia or azoospermia) according to categories of BMI.

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ANDROLOGY

ORIGINAL ARTICLE

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Seminal, ultrasound and psychobiological parameters correlate with metabolic syndrome in male members of infertile couples

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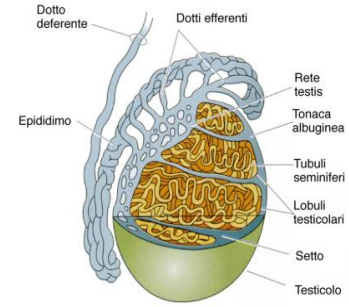
*Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence, Florence, Italy, and †Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, Italy

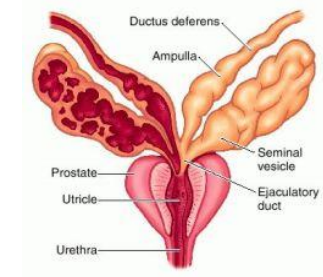


Asian Journal of Andrology (2014) 16, (???–???)

www.asiaandro.com; www.ajandrology.com

Metabolic syndrome and prostate abnormalities in male subjects of infertile couples

Francesco Lotti[1], Giovanni Corona[1,2], Linda Vignozzi[1], Matteo Rossi[1], Elisa Maseroli[1], Sarah Cipriani[1], Mauro Gacci[3], Gianni Forti[1], Mario Maggi[1]



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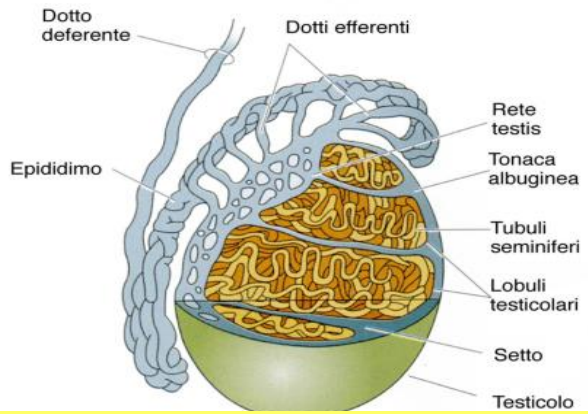
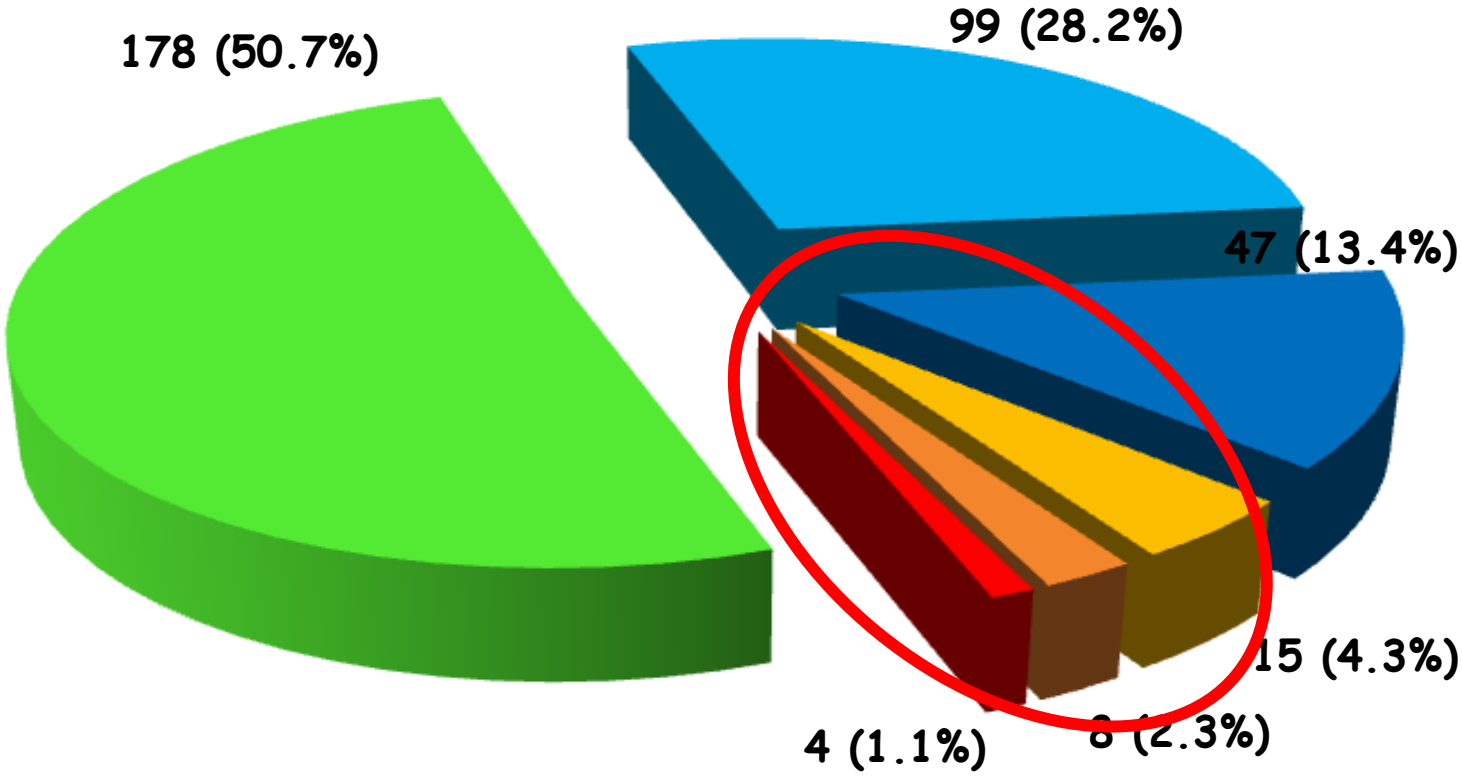


Lotti et al., Andrology. 2013 Mar;1(2):245-50

N = 351

(Mean age 36.0± 8.0 years)

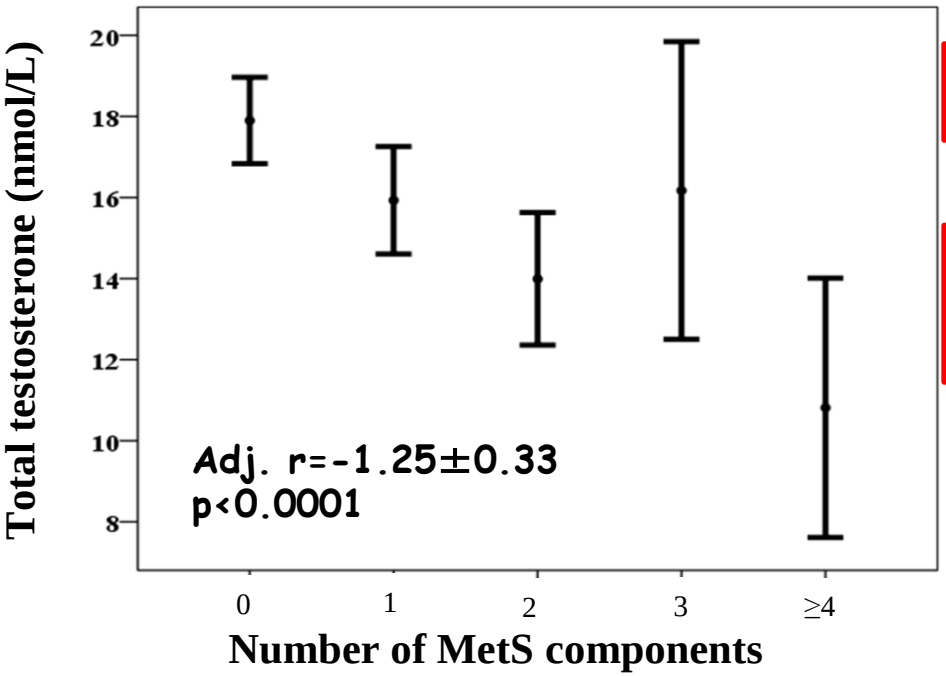


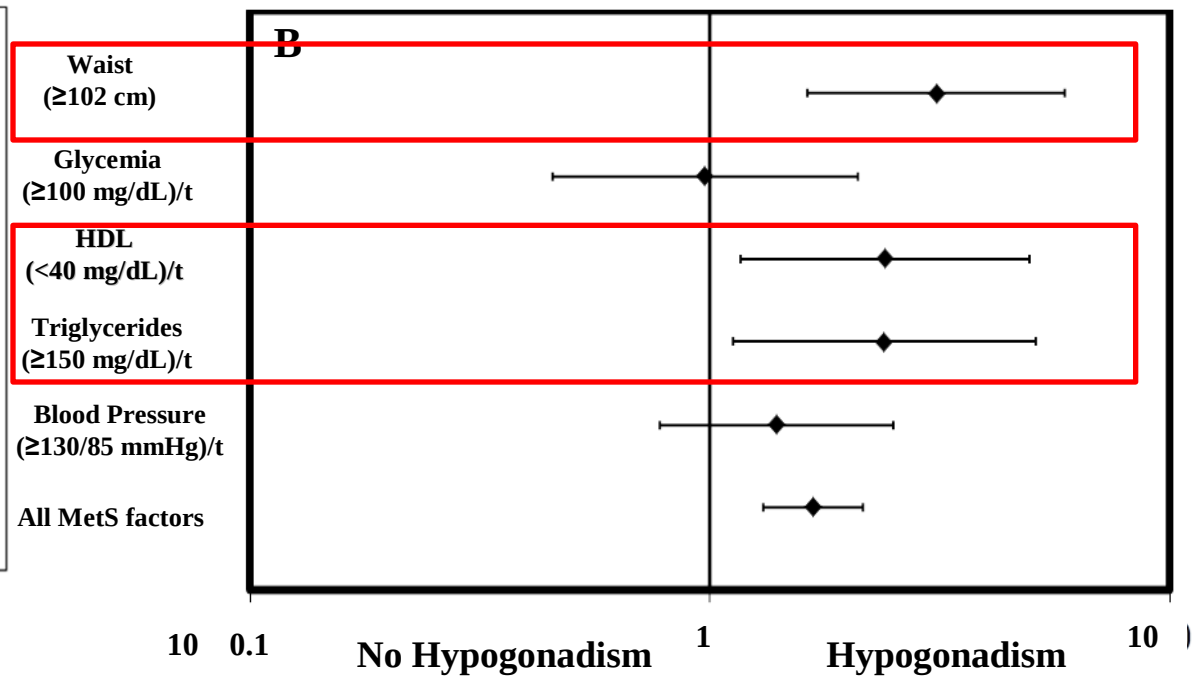
Metabolic Syndrome
27 (7.7%)

Metabolic Syndrome (IDF&AHA/NHLBI):
≥ 3 components

- Waist (≥102 cm)
- Glycemia (≥5.6 mmol/L)/t
- HDL (<1.03 mmol/L)/t
- Triglycerides (≥1.7 mmol/L)/t
- Blood Pressure (≥130/85 mmHg)/t

Testosterone levels according to # of MetS factors (IDF&AHA/NHLBI) and their relative age-adjusted hazard ratio (95% CI) for MetS and hypogonadsim (TT < 12 nmol/L) in male subjects consulting for couple infertility at the University of Florence (n=351), Florence, Italy

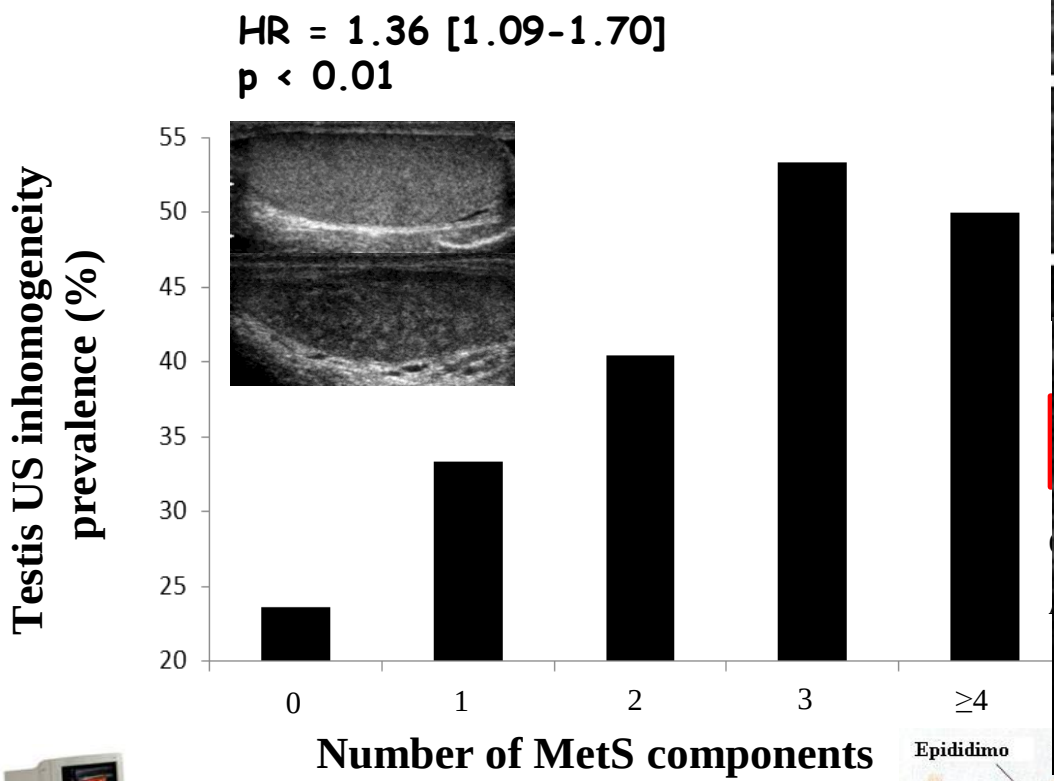


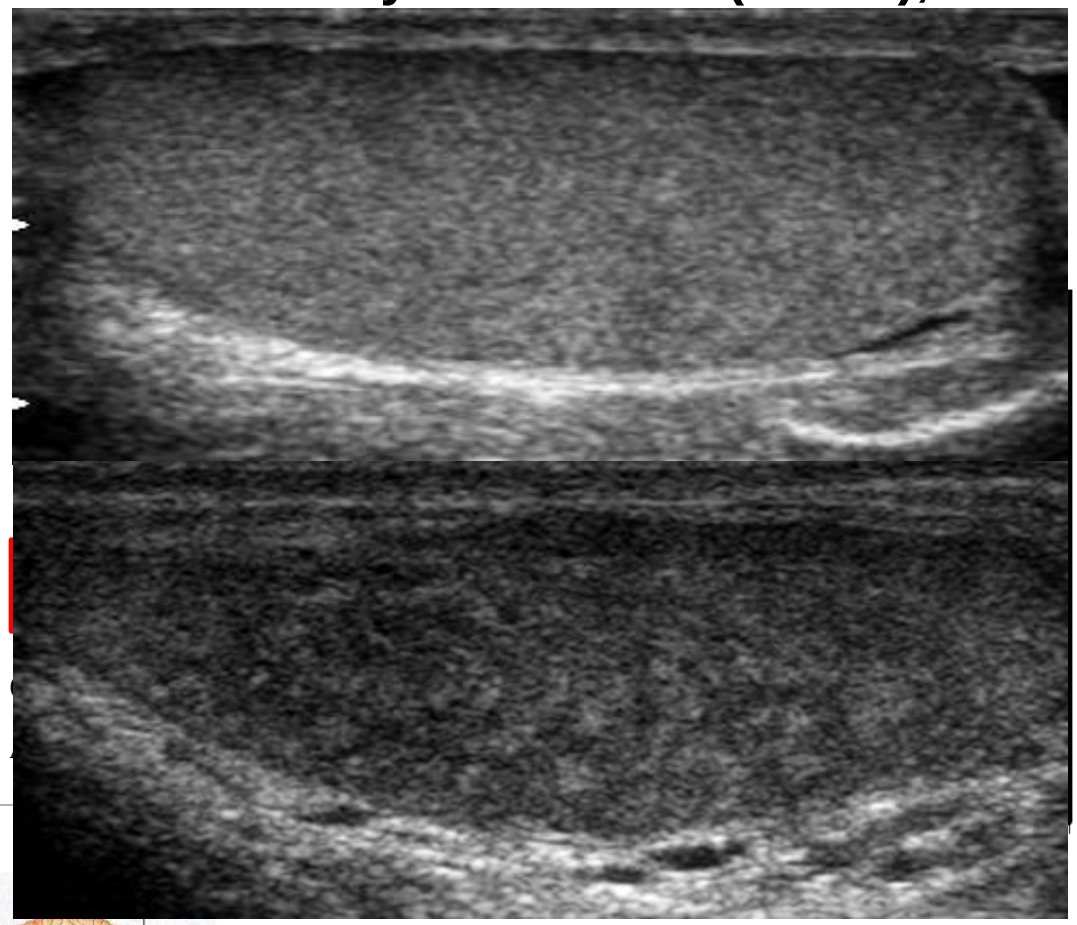


Adj. for age

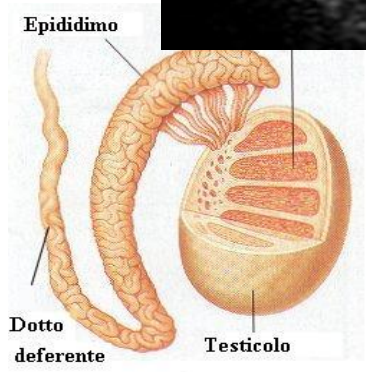
Lotti et al., Andrology. 2013 Mar;1(2):245-50

Prevalence of *testis US inhomogeneity* according to # of MetS factors (IDF&AHA/NHLBI) and their relative age-adjusted hazard ratio (95% CI) in male subjects consulting for couple infertility at the University of Florence (n=351), Florence, Italy





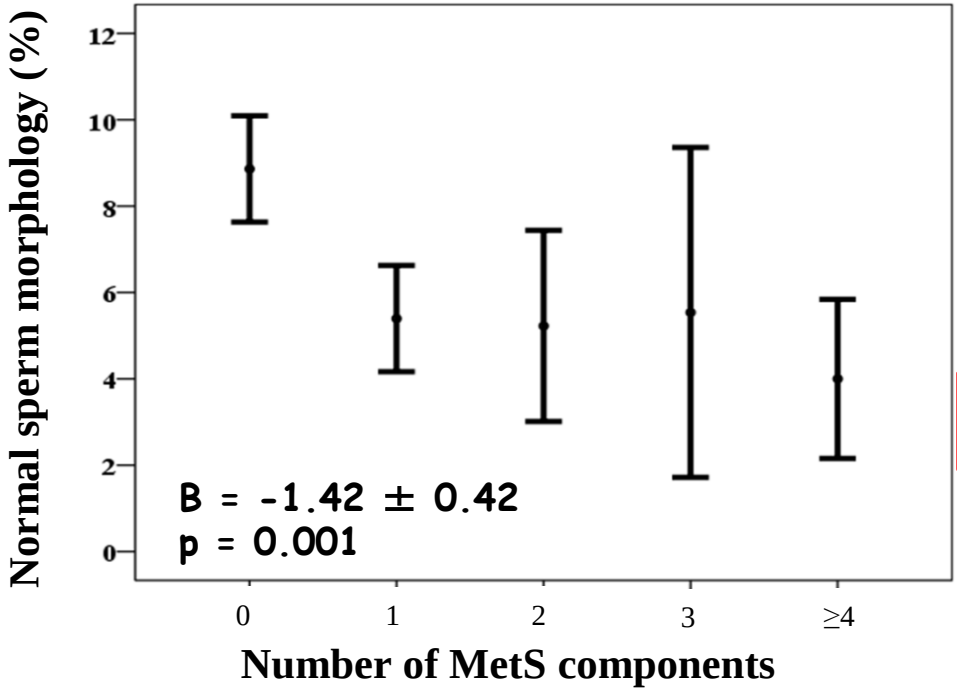
Adj. for age



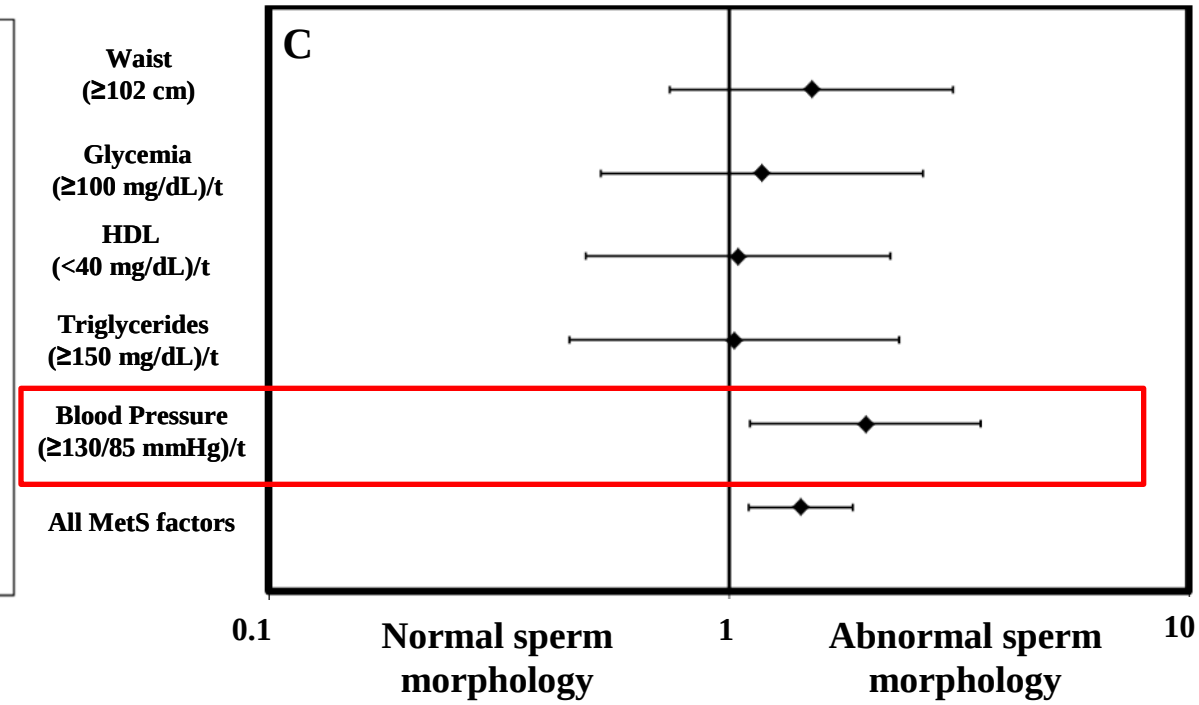
Final take-home messages for MetS and male infertility:

- **MetS (↑ waist, dyslipidaemia) is associated with LOH & testis inhomogeneity**

Normal sperm morphology according to # of MetS factors (IDF&AHA/NHLBI) and their relative age and T-adjusted hazard ratio (95% CI) in male subjects consulting for couple infertility at the University of Florence (n=351), Florence, Italy



Adj. for age
total testosterone

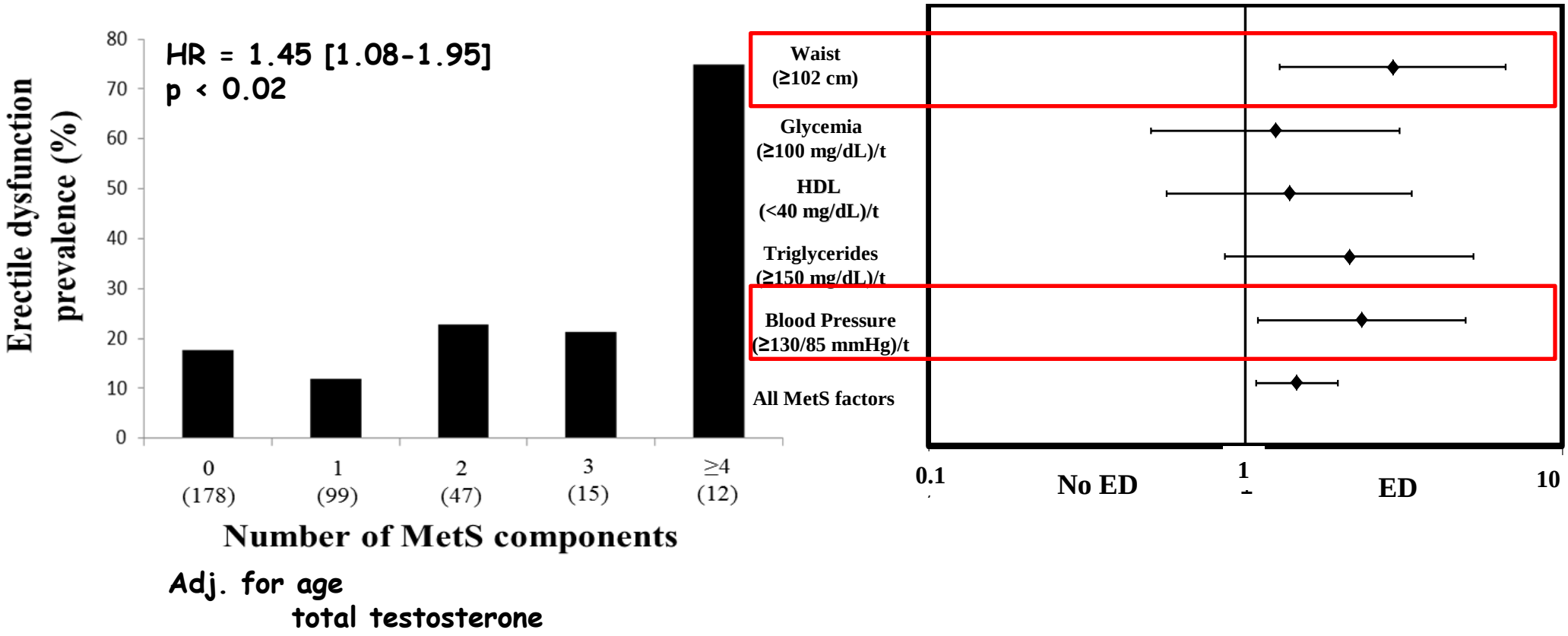


(> 4%, WHO 2010)

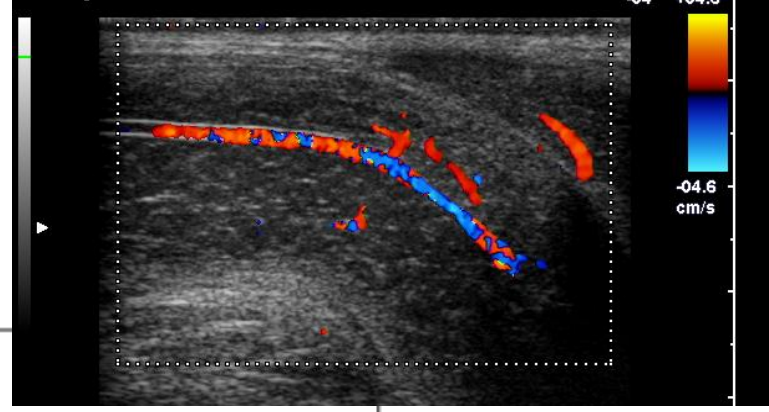
Final take-home messages for MetS and male infertility:

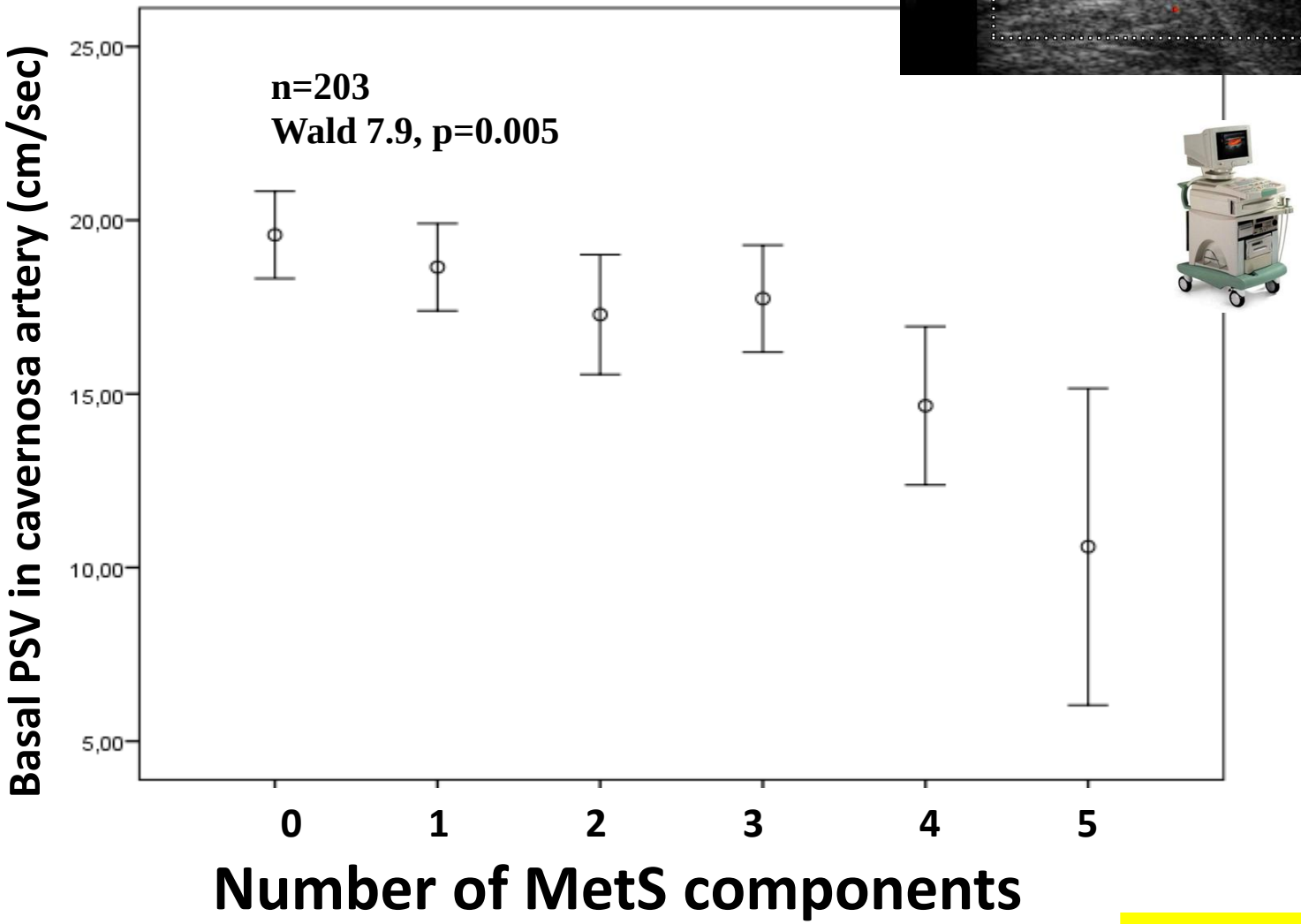
- **MetS (↑ waist, dyslipidaemia) is associated with LOH & testis inhomogeneity**
- **MetS (↑ BP) is associated with abnormal sperm morphology**

Erectile Dysfunction (IIEF-15-EFD score < 26) according to # of MetS factors (IDF&AHA/NHLBI) and their relative age and T-adjusted hazard ratio (95% CI) in male subjects consulting for couple infertility at the University of Florence (n=351), Florence, Italy



Penile Basal peak systolic velocity according to # of MetS factors (IDF&AHA/NHLBI) in male subjects consulting for couple infertility at the University of Florence (n=203), Florence, Italy





Adjusted for:
-age
-total testosterone

Lotti et al., unpublished

Final take-home messages for MetS and male infertility:

- **MetS (↑ waist, dyslipidaemia) is associated with LOH & testis inhomogeneity**
- **MetS (↑ BP) is associated with abnormal sperm morphology**
- **MetS (↑ waist, ↑ BP) is associated with arteriogenic ED**

Case-control (1:3 ratio) analysis

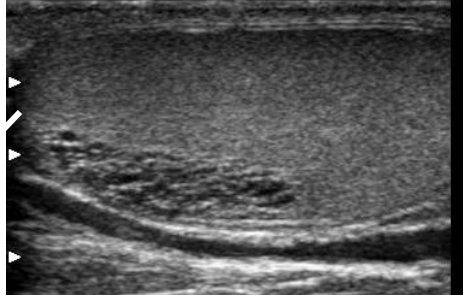
Table 4 Comparisons between subjects with metabolic syndrome (MetS) and 1 : 3 ratio matched controls (matched for age, body mass index, total testosterone, smoking habit, alcohol consumption, past or present cryptorchidism, leucocytospermia, current positive urine and/or semen cultures). Comparison between subjects with ≥4 MetS components and three MetS components

	Case patients (with 3 MetS factors, $n = 15$)	Controls (matched 1:3, $n = 45$)	p	Case patients (with ≥4 MetS factors, $n = 12$)	Controls (matched 1:3, $n = 36$)	p	Patients with ≥4 vs. 3 MetS factors, p
Age	39.9 ± 8.5	39.3 ± 7.2	0.815	48.5 ± 10.9	41.5 ± 10.1	0.055	**0.035**
Total testosterone (nmol/L)	16.1 ± 6.6	16.8 ± 5.4	0.735	10.8 ± 5.0	13.5 ± 4.8	0.137	**0.027**
BMI (kg/m^2)	29.5 ± 4.7	27.6 ± 4.6	0.181	34.5 ± 6.0	30.8 ± 5.0	0.071	**0.030**
Current smoker, %	21.4	47.4	0.118	9.1	28.6	0.194	0.404
Current alcohol consumption, %	28.6	18.9	0.454	11.1	16.0	0.723	0.322
Past or present cryptorchidism	26.7	25	0.898	0	9.4	0.272	0.053
Leucocytospermia, %	20	7.5	0.185	0	6.9	0.418	0.151
Current positive urine and/or semen cultures, %	0	6.8	0.299	12.5	3.2	0.289	0.161
Sperm concentration, × 10^6/mL	10 [3.5–27]	42 [5–120]	0.126	29 [4–60]	31 [3.4–62]	0.685	0.585
Spermatozoa per ejaculate, × 10^6/mL	43 [10.9–68]	74 [21–245]	0.114	56 [12–111]	103 [11–244]	0.183	0.659
Sperm progressive motility, %	42.1 ± 19.2	42.3 ± 18.6	0.975	35.0 ± 13.9	36.9 ± 17.8	0.741	0.305
Sperm morphology, % normal forms	3 [1.5–6.5]	12 [6–18]	**0.001**	4 [2–6]	9 [3.8–16]	**0.036**	0.973
Testis inhomogeneityat ultrasound, %	53.3	20	**0.015**	50.0	10.7	**0.006**	0.863
ED prevalence(IIEF-15-EFD < 26) , %	21.3	26.3	0.746	75.0	29.4	**0.016**	**0.006**

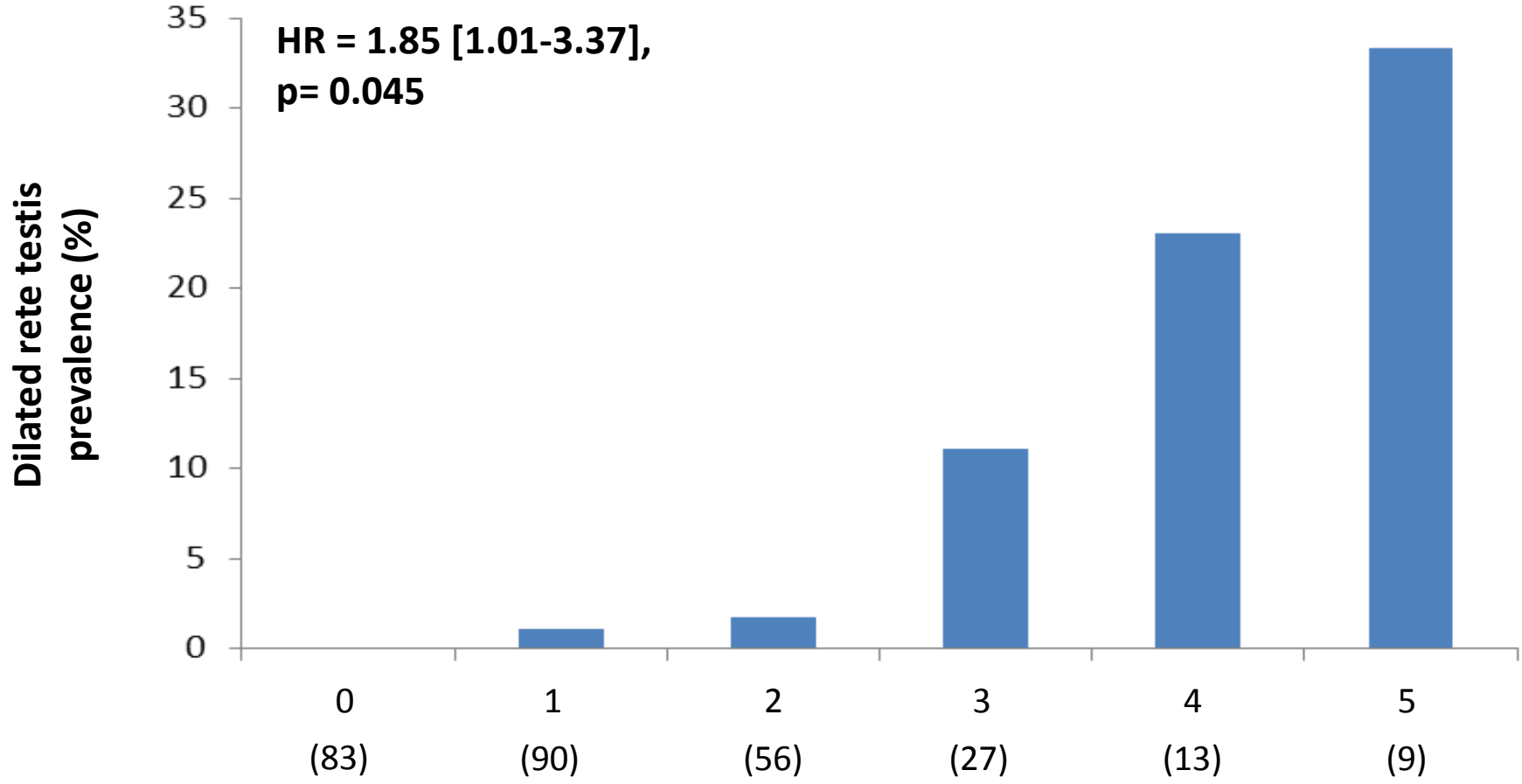
Data were expressed as mean ± standard deviation when normally distributed, median (quartiles) when not normally distributed, and as percentages when categorical. BMI: body mass index, ED: erectile dysfunction, IIEF-15-EFD: International Index of Sexual Function-15 erectile function domain. Associations with a p-value <0.05 were considered as significant, and reported in bold.

Lotti et al., Andrology. 2013 Mar;1(2):245-50

Dilated rete testis and MetS



N = 278 males of infertile couples
without genetic abnormalities

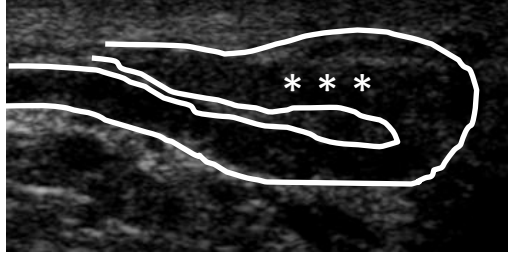


Number of MetS components

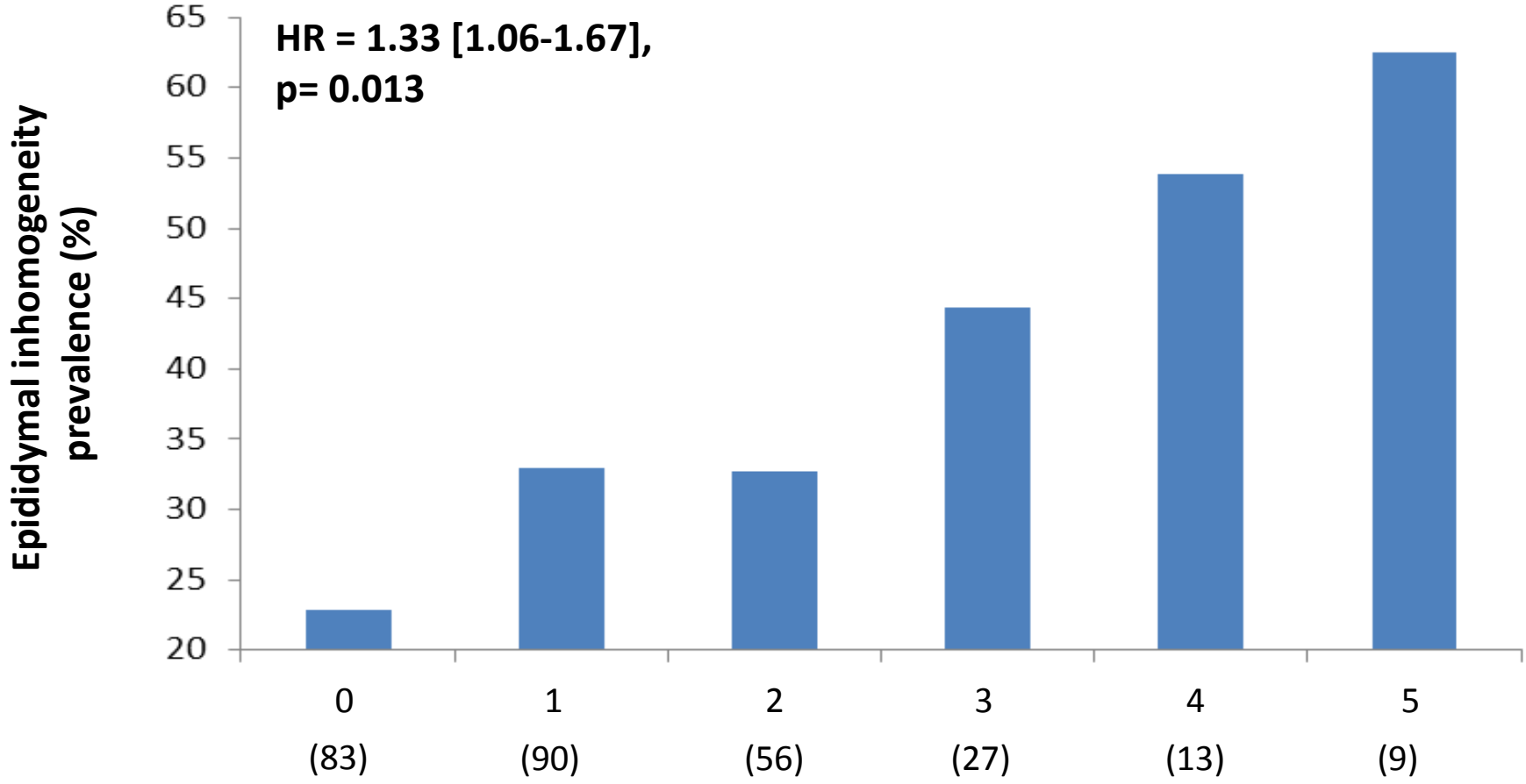
Adjusted for:
-age
-total testosterone

Lotti et al., unpublished

Epididymal inhomogeneity and MetS



N = 278 males of infertile couples
without genetic abnormalities



Number of MetS components

Adjusted for:
-age
-total testosterone

Lotti et al., unpublished

Final take-home messages for MetS and male infertility:

- **MetS (↑ waist, dyslipidaemia) is associated with LOH & testis inhomogeneity**
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- **MetS is associated with epididymal inhomogeneity and rete testis dilation**

Brit. J. Psychiat. (1966), 112, 917–923

A Short Clinical Diagnostic Self-rating Scale for Psychoneurotic Patients

The Middlesex Hospital Questionnaire (M.H.Q.)

By SIDNEY CROWN and A. H. CRISP

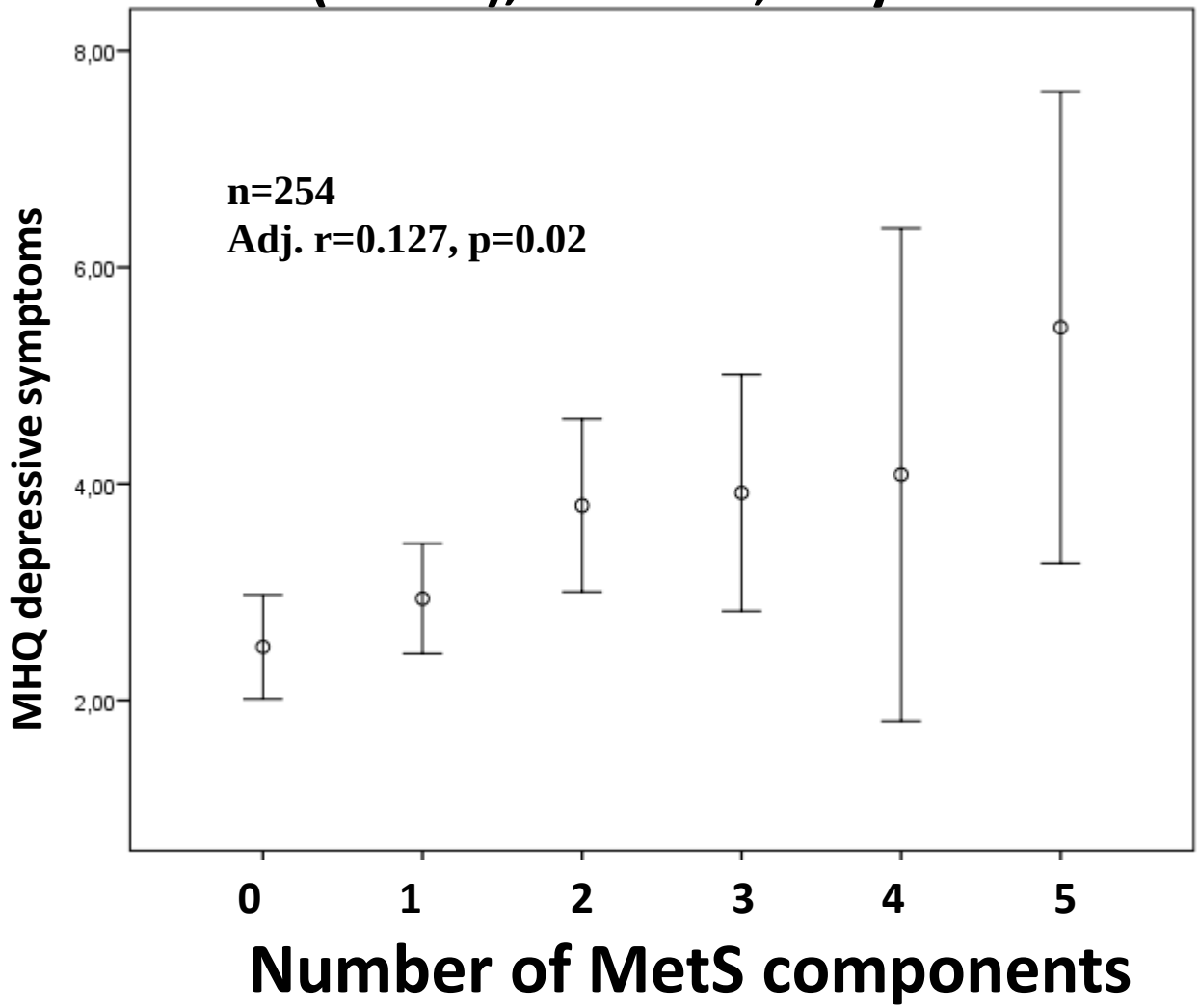
Association between Mets and:

	MetS		No MetS	
Somatized anxiety symptoms (MHQ-S):	2.96 ± 2.82	vs.	1.86 ± 2.27	p = 0.022
Depression symptoms (MHQ-D):	4.58 ± 2.85	vs.	3.00 ± 2.52	p = 0.011

Adjusted for - age

Lotti et al., Andrology. 2013 Mar;1(2):245-50

Depressive symptoms (MHQ-D) according to # of MetS factors (IDF&AHA/NHLBI) in male subjects consulting for couple infertility at the University of Florence (n=254), Florence, Italy



Adjusted for:
- age
- total testosterone
- Total MHQ score

Lotti et al., Andrology. 2013 Mar;1(2):245-50

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- MetS is associated with epididymal inhomogeneity and rete testis dilation
- MetS is associated with depressive symptoms

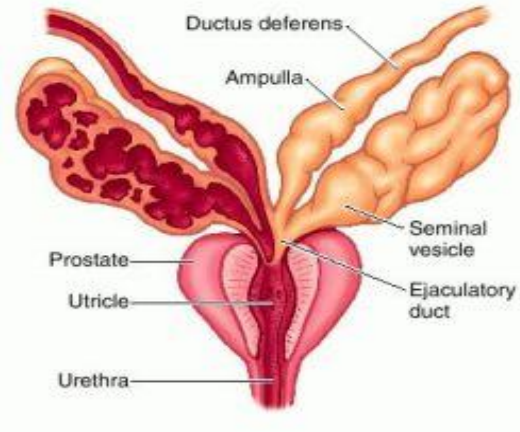
Asian Journal of Andrology (2014) 16, (???–???)

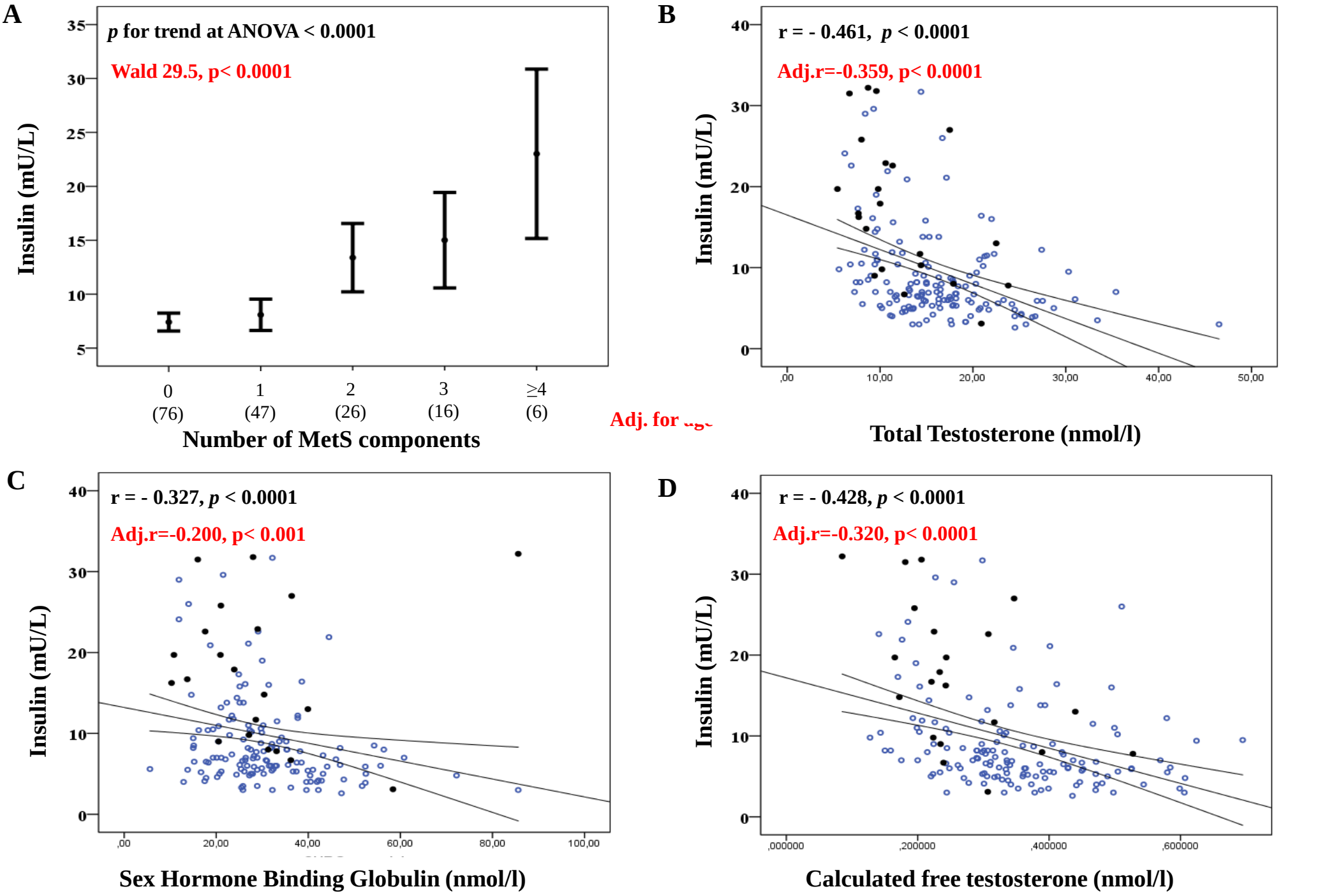
www.asiaandro.com; www.ajandrology.com

Metabolic syndrome and prostate abnormalities in male subjects of infertile couples

Francesco Lotti[1], Giovanni Corona[1,2], Linda Vignozzi[1], Matteo Rossi[1], Elisa Maseroli[1], Sarah Cipriani[1], Mauro Gacci[3], Gianni Forti[1], Mario Maggi[1]

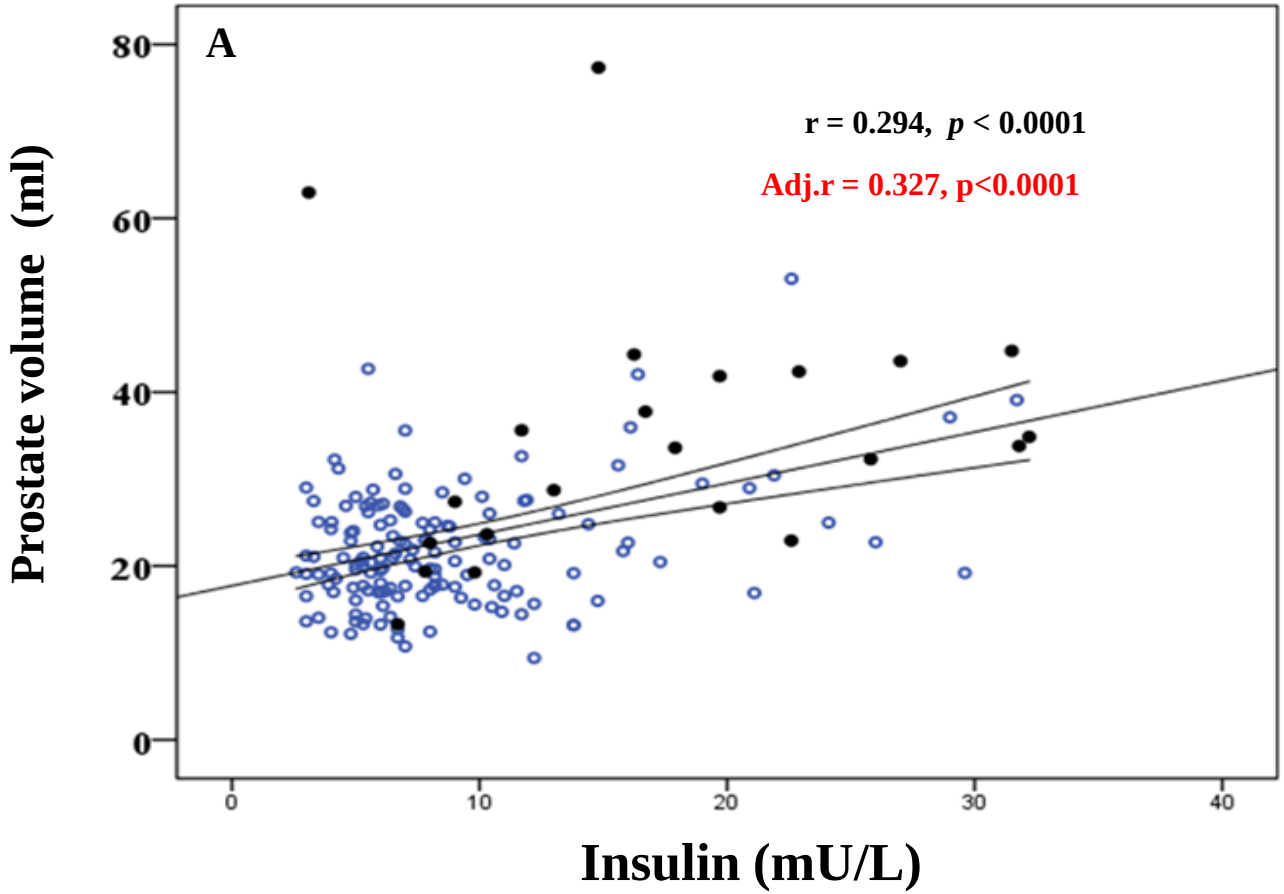
Age=36.5±8.3 years




A
p for trend at ANOVA < 0.0001
Wald 29.5, p< 0.0001
Insulin (mU/L)
35
30
25
20
15
10
5
0 (76)
1 (47)
2 (26)
3 (16)
≥4 (6)
Number of MetS components
B
r = - 0.461, p < 0.0001
Adj.r=-0.359, p< 0.0001
Insulin (mU/L)
40
30
20
10
0
,00
10,00
20,00
30,00
40,00
50,00
Total Testosterone (nmol/l)
Adj. for
C
r = - 0.327, p < 0.0001
Adj.r=-0.200, p< 0.001
Insulin (mU/L)
40
30
20
10
0
,00
20,00
40,00
60,00
80,00
100,00
Sex Hormone Binding Globulin (nmol/l)
D
r = - 0.428, p < 0.0001
Adj.r=-0.320, p< 0.0001
Insulin (mU/L)
40
30
20
10
0
,000000
,200000
,400000
,600000
Calculated free testosterone (nmol/l)

Association between insulin and prostate volume in a consecutive series of infertile subjects (n=171) at the University of Florence, Florence, Italy

Age=36.5±8.3 years

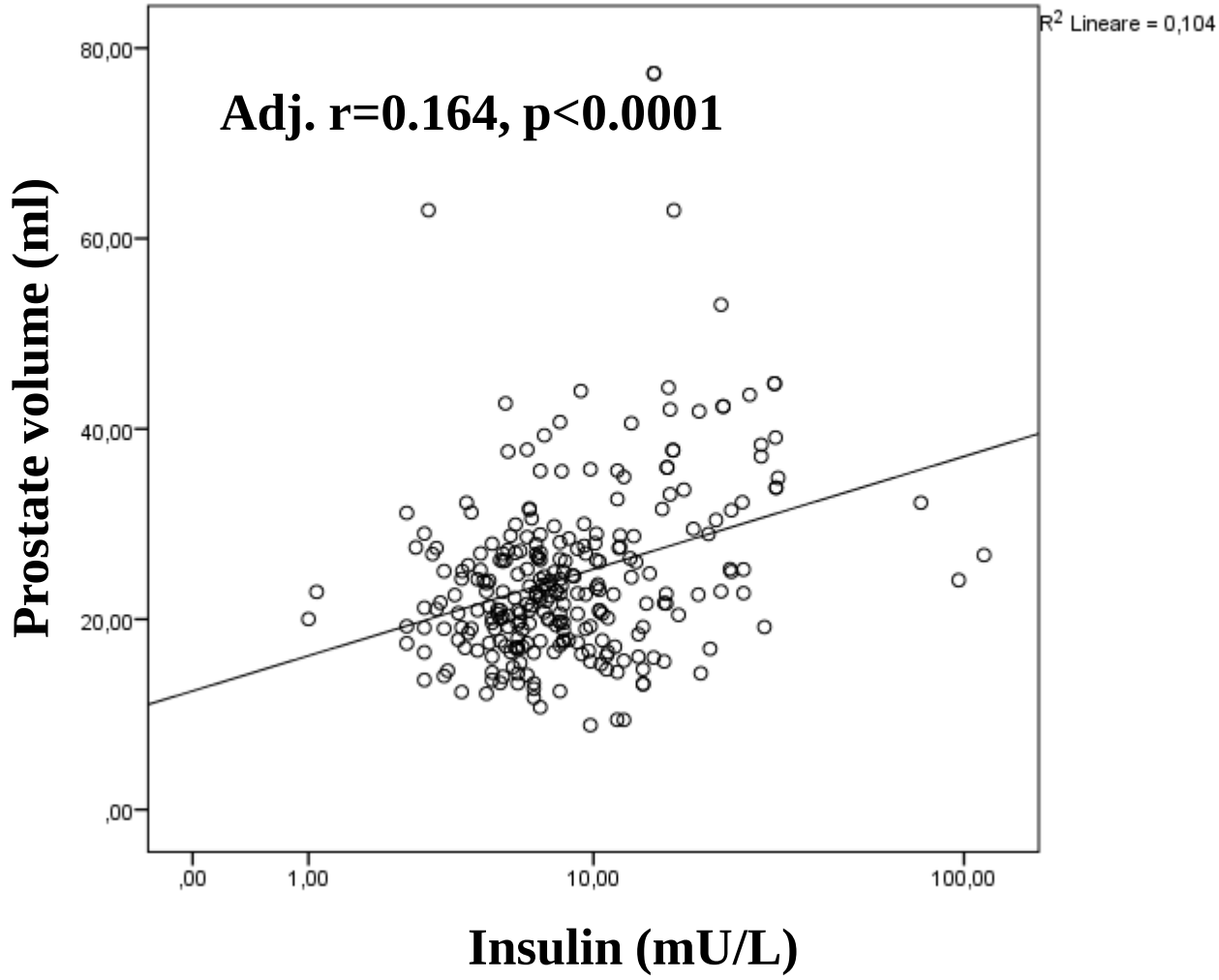


Adjusted for:

- age
- testosterone

Lotti et al., AJA, in press

Association between insulin and prostate volume in a consecutive series of infertile subjects (n=267) at the University of Florence, Florence, Italy



Adjusted for:

- age
- testosterone

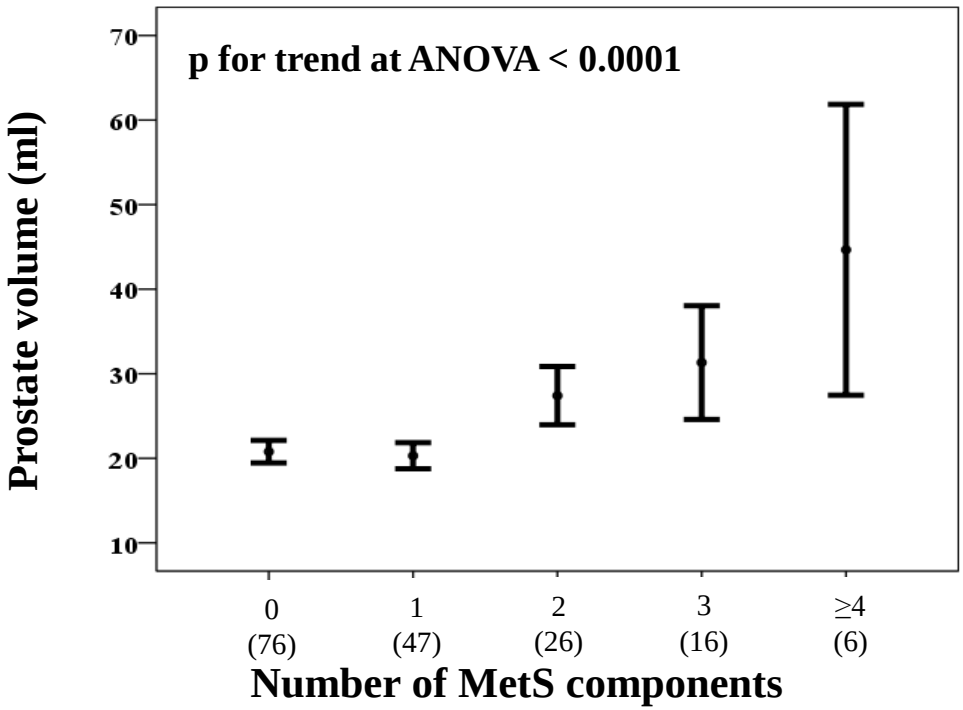
Lotti et al., unpublished

Association between # of MetS components and prostate volume in a consecutive series of infertile subjects (n=171) at the University of Florence, Florence, Italy

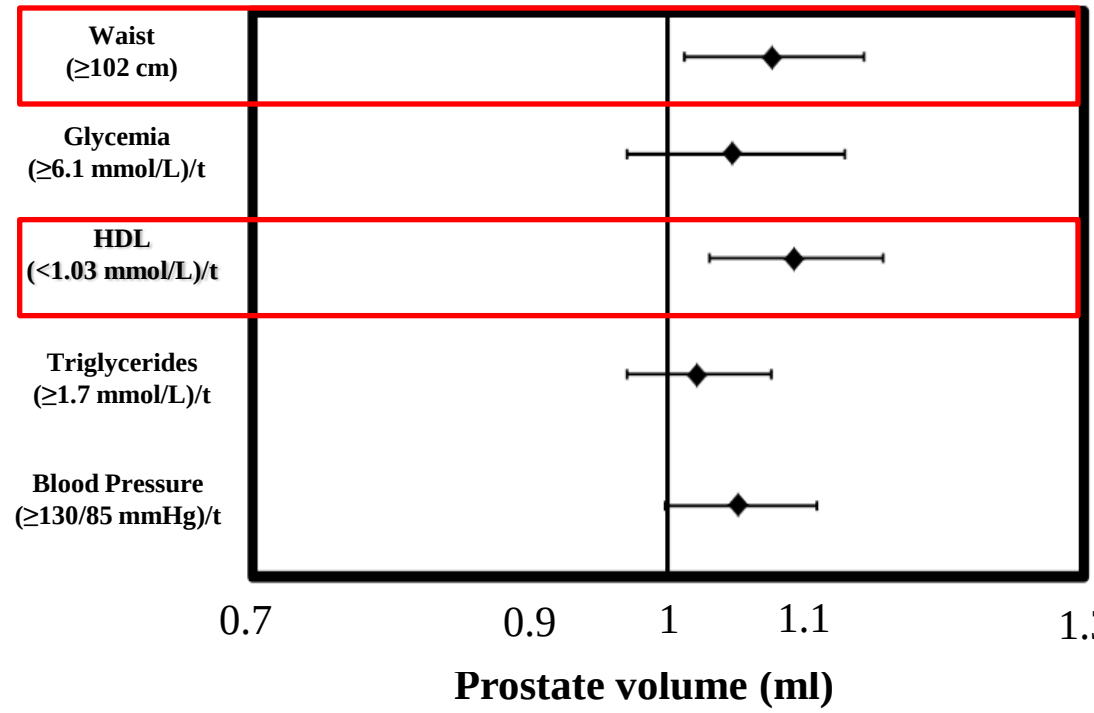
Adjusted for:

- age
- insulin
- testosterone

Age=36.5±8.3 years

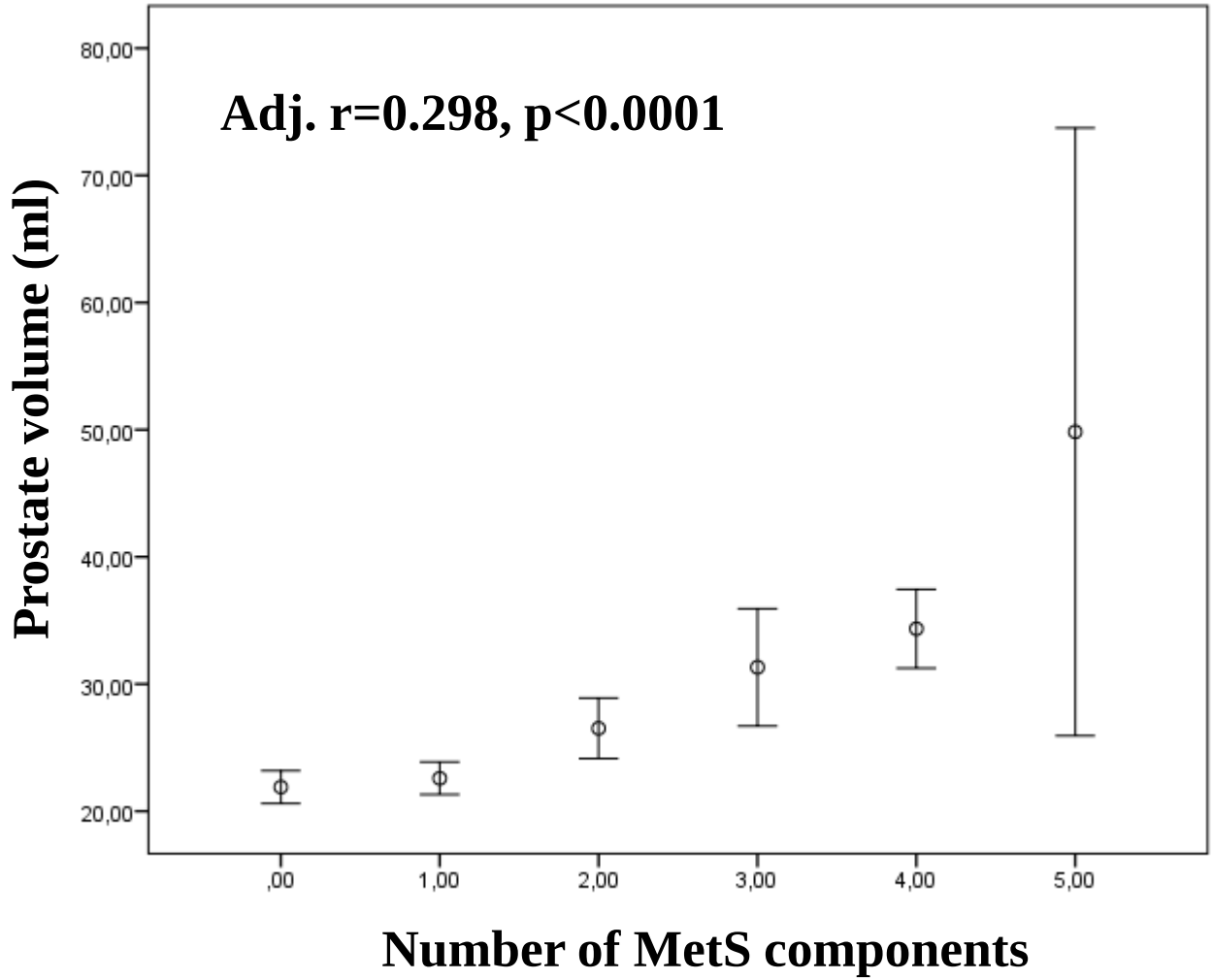


HR for increased prostate volume



Lotti et al., AJA, in press

Association between # of MetS components and prostate volume in a consecutive series of infertile subjects (n=270) at the University of Florence, Florence, Italy

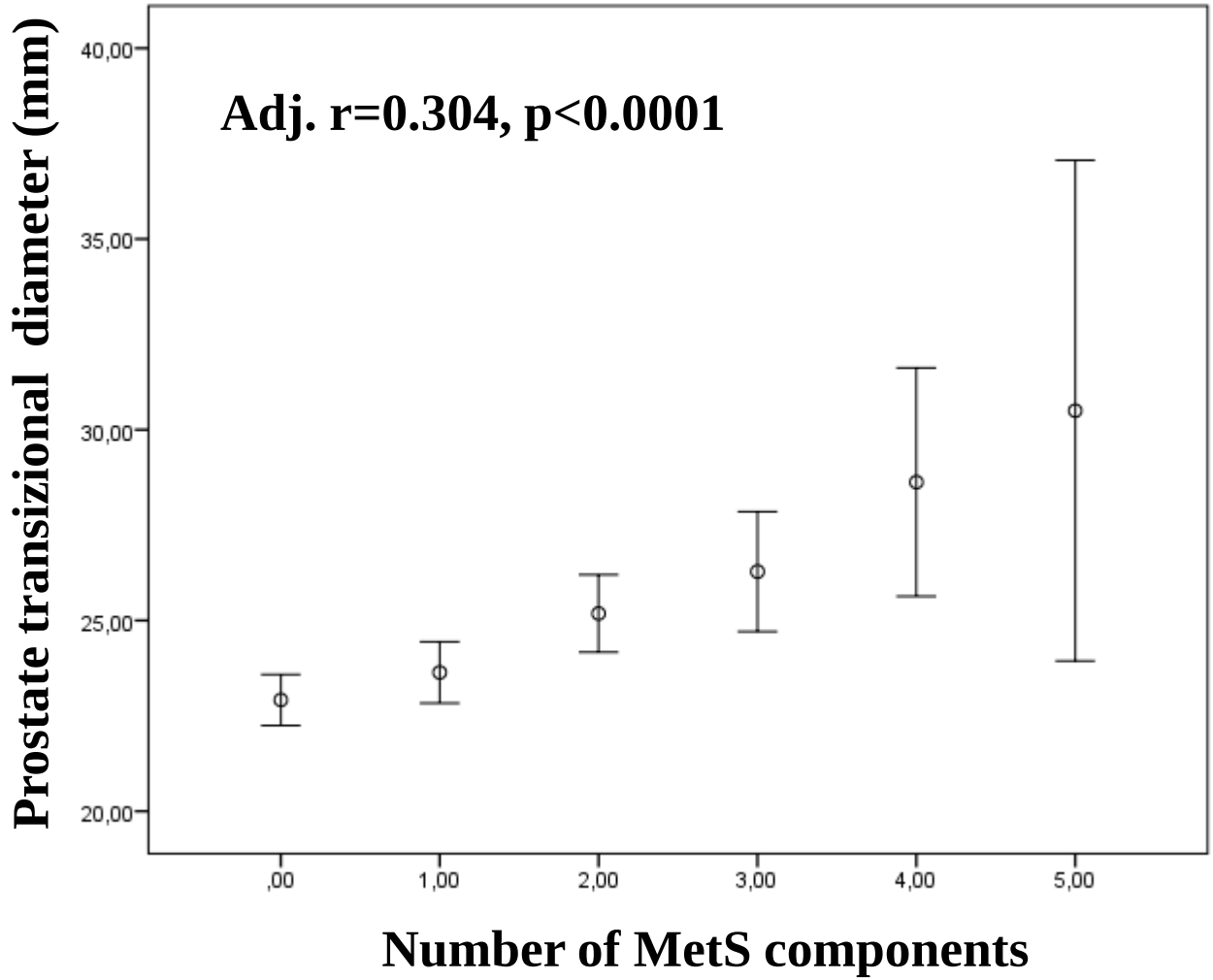


Adjusted for:

- age
- testosterone

Lotti et al., unpublished

Association between # of MetS components and prostate transizional diameter in a consecutive series of infertile subjects (n=270) at the University of Florence, Florence, Italy



Adjusted for:

- age
- testosterone

Lotti et al., unpublished

Final take-home messages for MetS and male infertility:

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- **MetS (↑ BP) is associated with abnormal sperm morphology**
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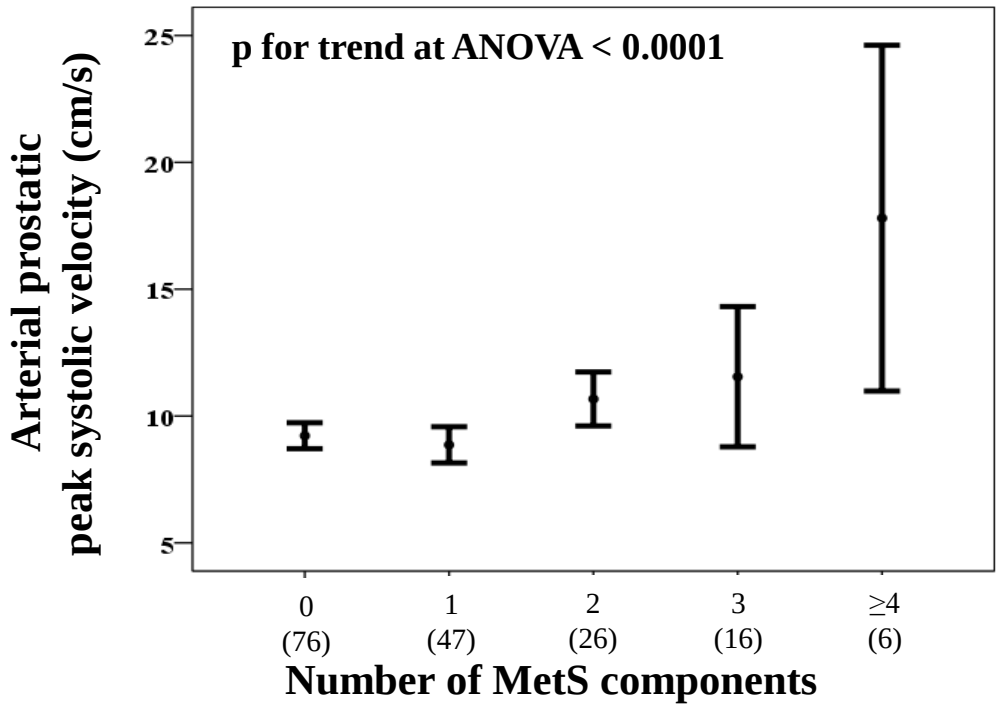
- **MetS is associated with epididymal inhomogeneity and rete testis dilation**
- **MetS is associated with depressive symptoms**
- **MetS (↑ waist, dyslipidaemia) is associated with ↑ insulin and BPE**

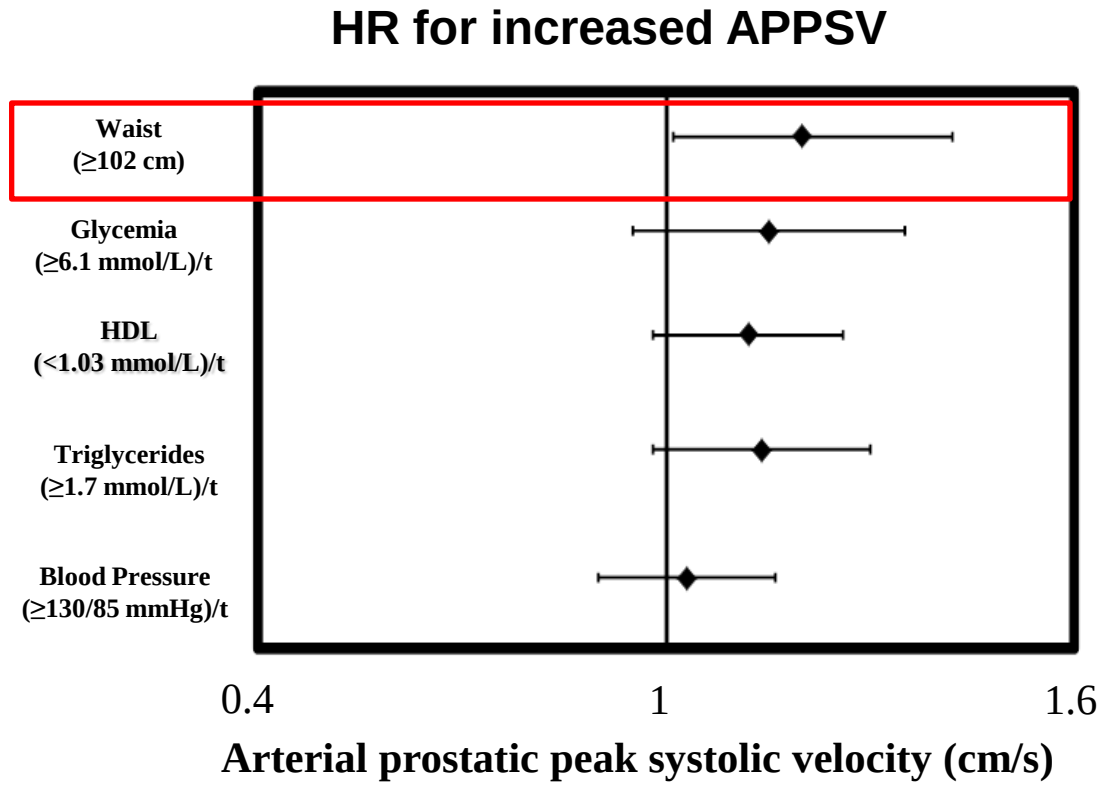
Association between # of MetS components and arterial prostatic peak systolic velocity in a consecutive series of infertile subjects (n=171) at the University of Florence, Florence, Italy

Adjusted for:

- age
- insulin
- testosterone

Age=36.5±8.3 years





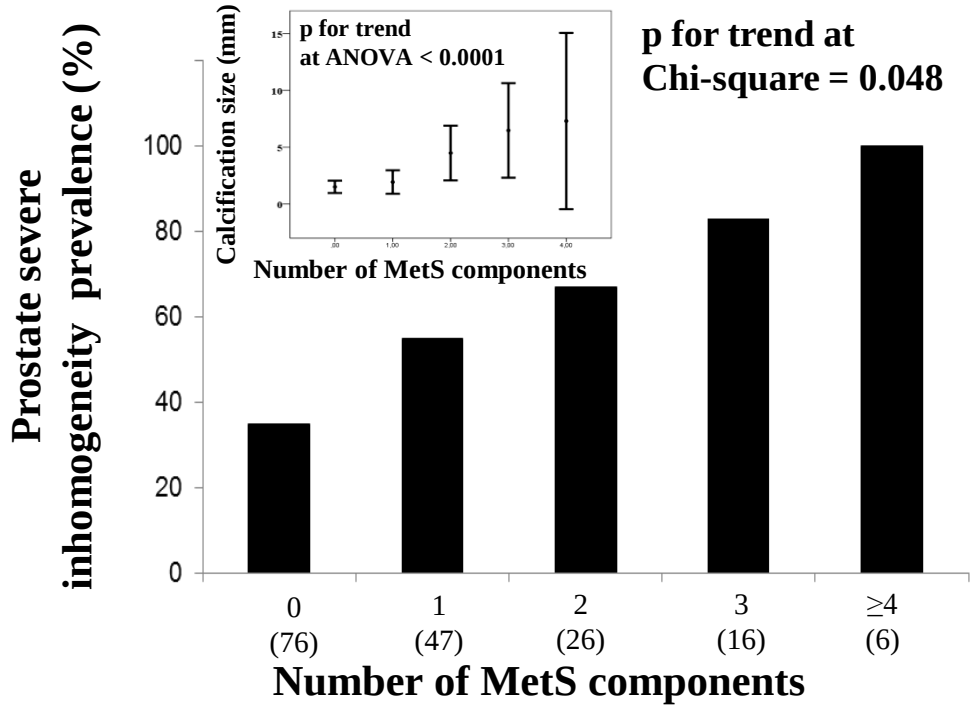
Lotti et al., AJA, in press

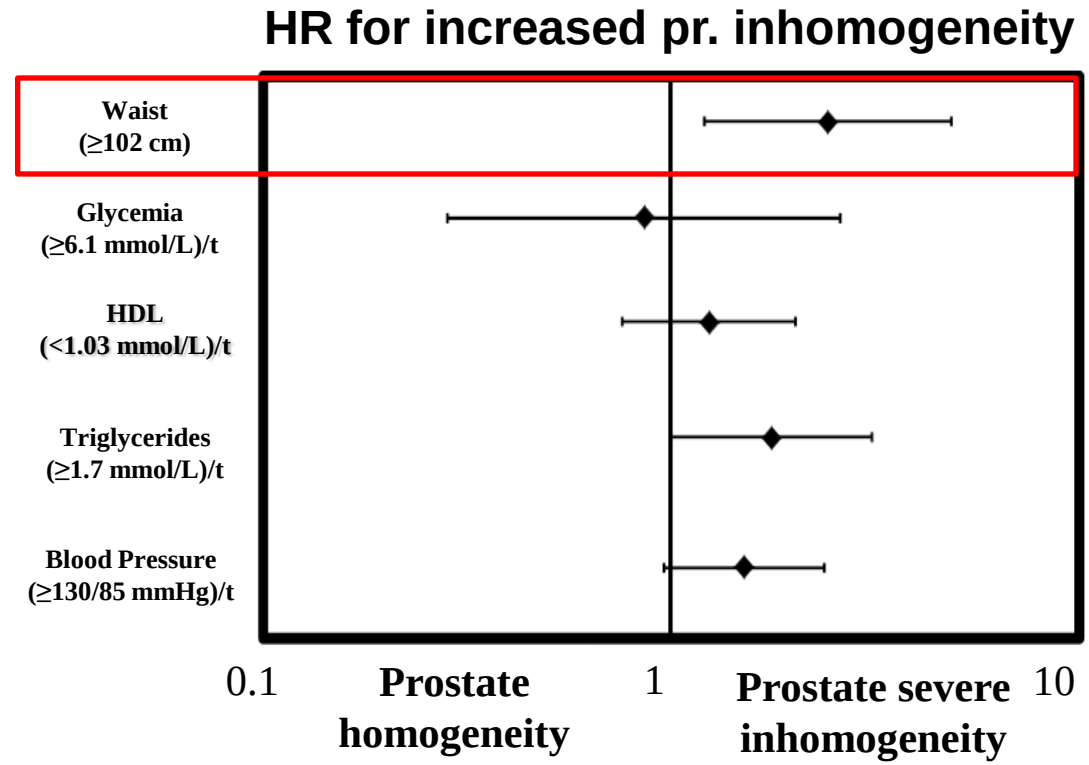
Association between # of MetS components and prostate severe inhomogeneity prevalence in a consecutive series of infertile subjects (n=171) at the University of Florence, Florence, Italy

Adjusted for:

- age
- insulin
- testosterone

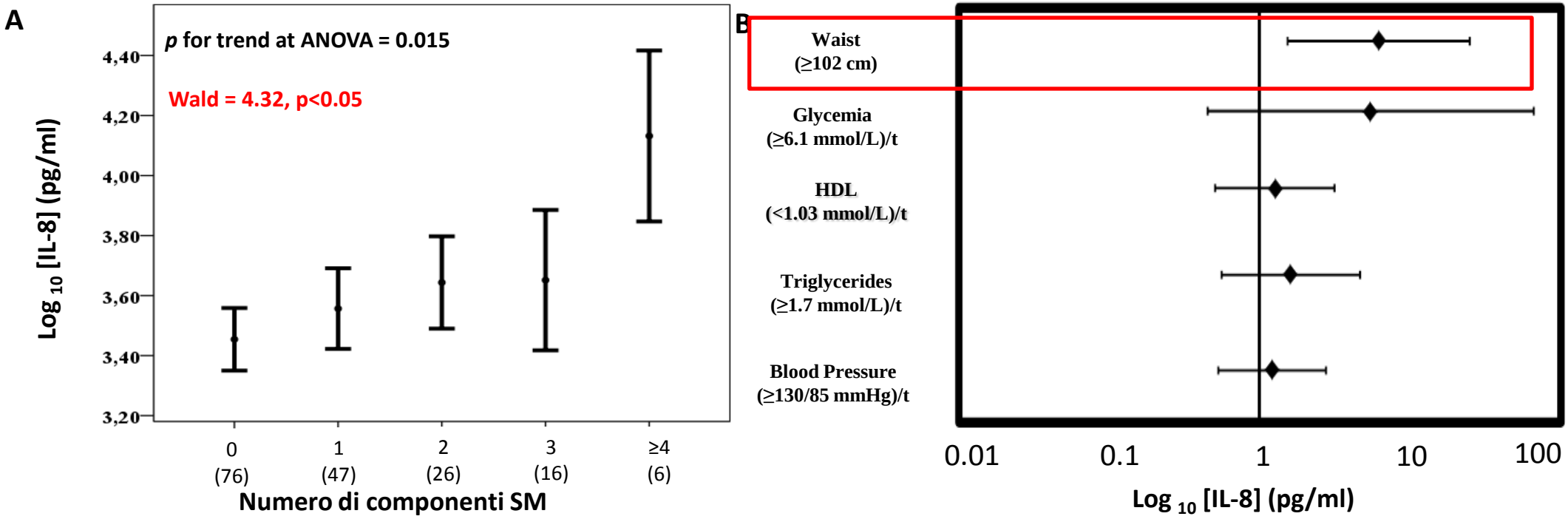
Age=36.5±8.3 years





Lotti et al., AJA, in press

Association between # of MetS components and seminal IL-8 in a consecutive series of infertile subjects (n=171) at the University of Florence, Florence, Italy



Lotti et al., AJA, in press

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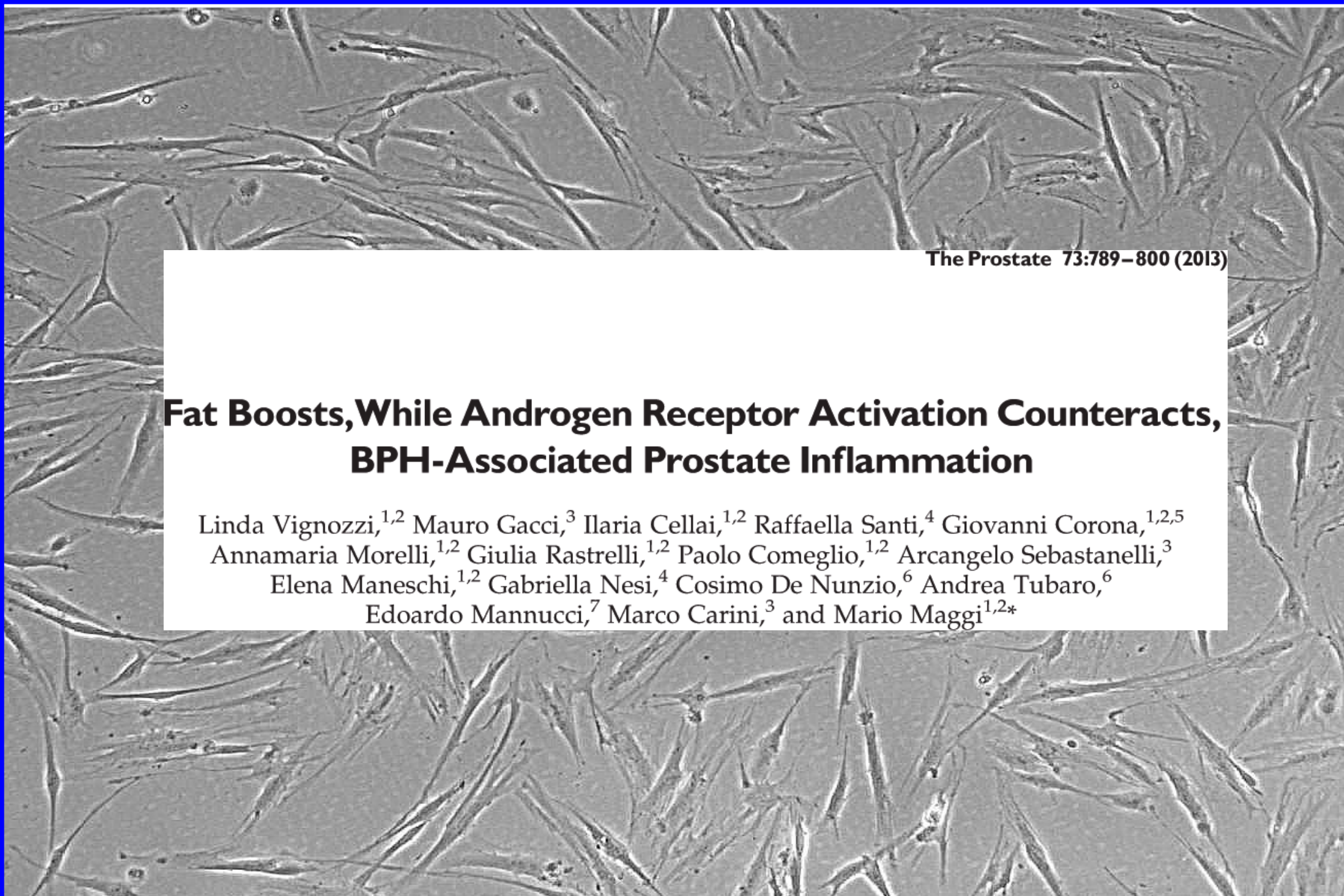
- **MetS is associated with epididymal inhomogeneity and rete testis dilation**
- **MetS is associated with depressive symptoms**
- **MetS (↑ waist, dyslipidaemia) is associated with ↑ insulin and BPE**
- **MetS (↑ waist) is associated with prostate inflammation**

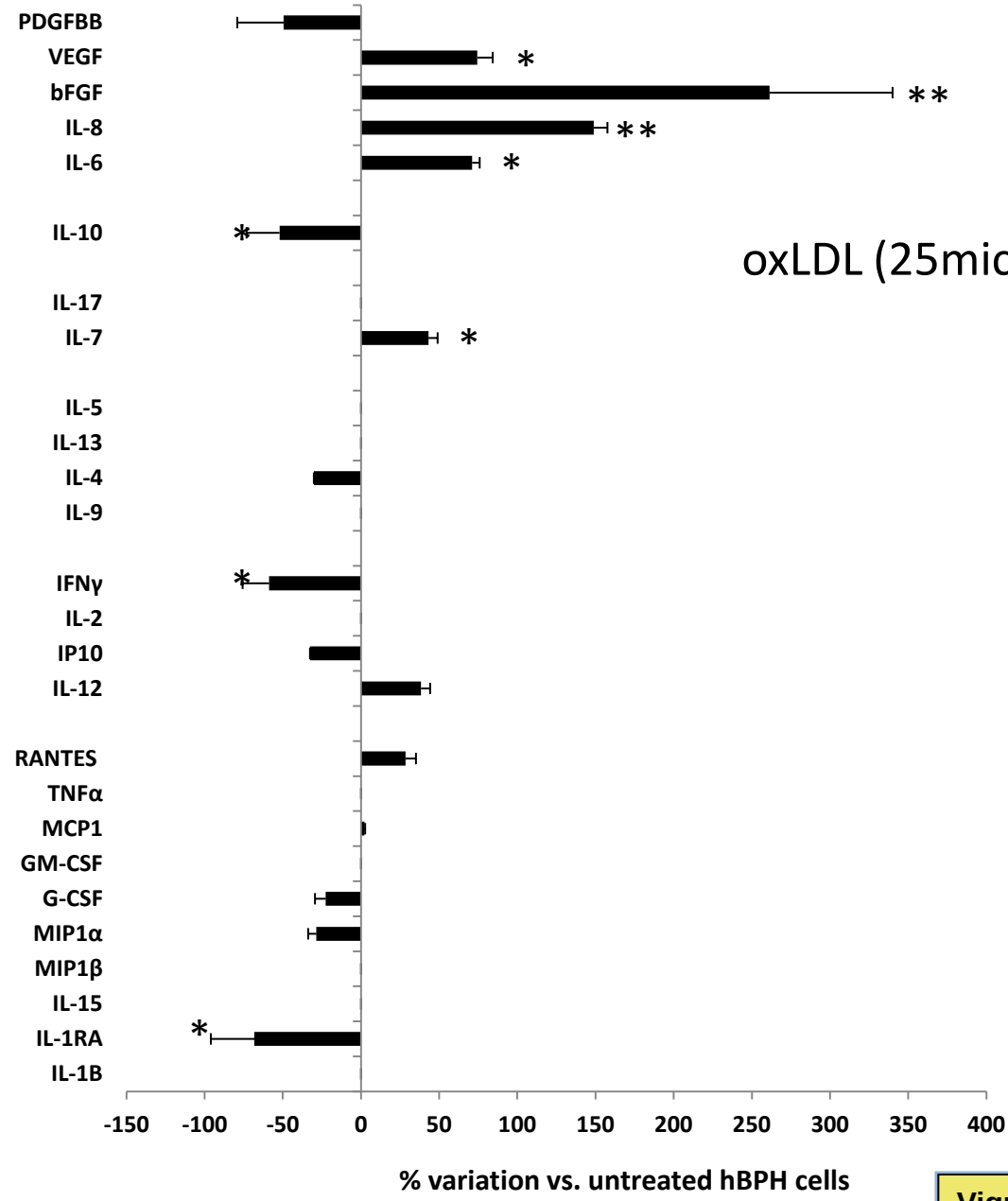


The Prostate 73:789–800 (2013)

Fat Boosts, While Androgen Receptor Activation Counteracts, BPH-Associated Prostate Inflammation

Linda Vignozzi,[1,2] Mauro Gacci,[3] Ilaria Cellai,[1,2] Raffaella Santi,[4] Giovanni Corona,[1,2,5] Annamaria Morelli,[1,2] Giulia Rastrelli,[1,2] Paolo Comeglio,[1,2] Arcangelo Sebastanelli,[3] Elena Maneschi,[1,2] Gabriella Nesi,[4] Cosimo De Nunzio,[6] Andrea Tubaro,[6] Edoardo Mannucci,[7] Marco Carini,[3] and Mario Maggi[1,2*]

Effect of oxLDL on cytokines/chemokines/growth factors secretion by hBPH cells

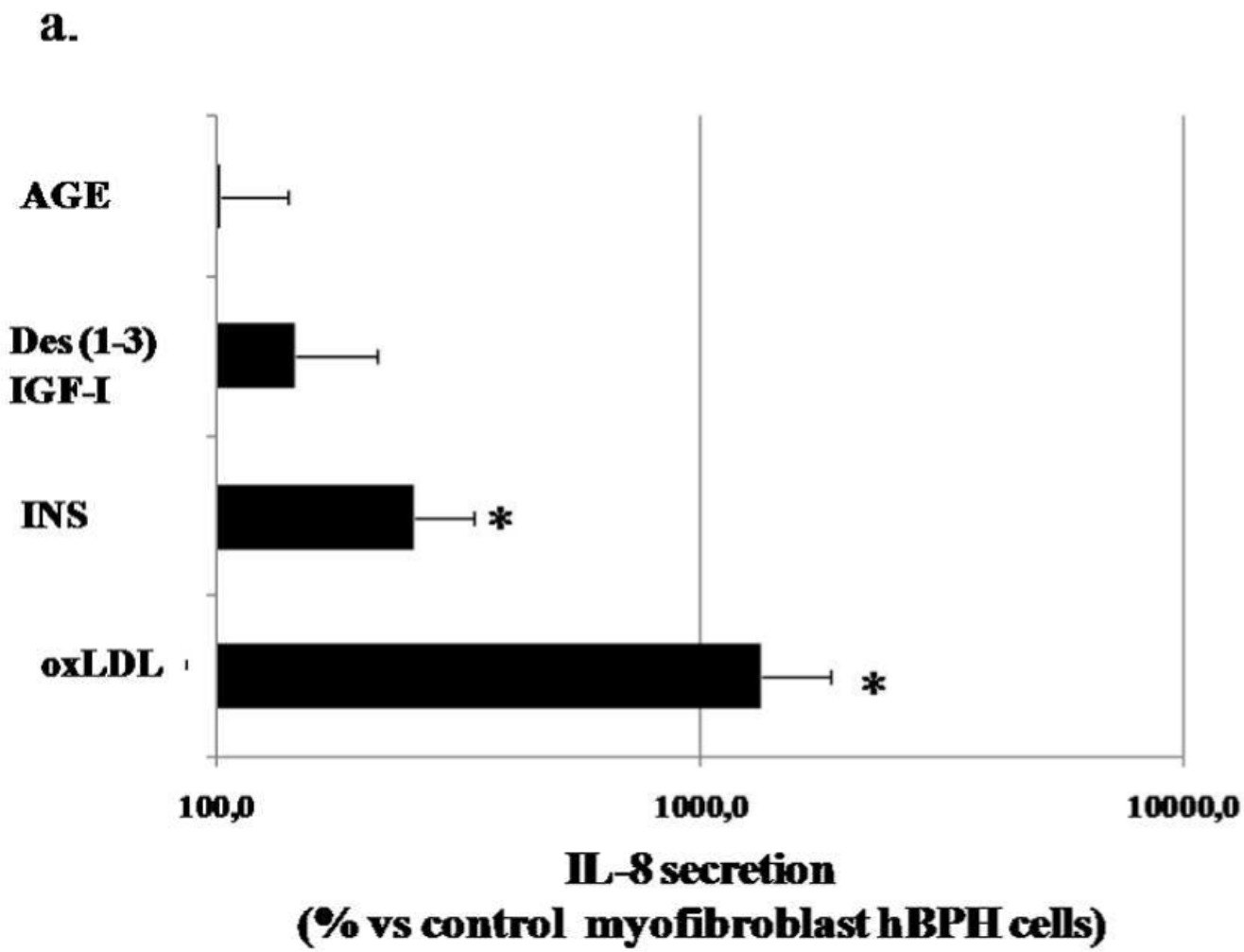


oxLDL (25microgr/mL for 24 hours)

*p<0.05; **p<0.01

Vignozzi et al., Prostate. 2013 Jun;73(8):789-800.

Effect of different metabolic stimuli on IL-8 secretion by hBPH cells



Vignozzi et al., Prostate. 2013 Jun;73(8):789-800.

Association between # of MetS components and prostatic symptoms in a consecutive series of infertile subjects (n=171) at the University of Florence, Florence, Italy

Adjusted for:

- age
- insulin
- testosterone

Age=36.5±8.3 years

No association was found between MetS and prostate-related symptoms, as captured by both NIH-CPSI and IPSS

Lotti et al., AJA, in press

ISSN: 2047-2919

ORIGINAL ARTICLE

Correspondence:
Mario Maggi, Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence, Viale Pieraccini 6, Florence 50139, Italy. E-mail: m.maggi@dfc.unifi.it

Keywords:
male infertility, National Institutes of Health-Chronic Prostatitis Symptom Index, prostatitis-like symptoms, scrotal and transrectal colour-Doppler ultrasound, seminal and laboratory parameters

Received: 23-Jul-2013
Revised: 10-Oct-2013
Accepted: 11-Oct-2013

Seminal, clinical and colour-Doppler ultrasound correlations of prostatitis-like symptoms in males of infertile couples

[1]F. Lotti, [1,2]G. Corona, [3]N. Mondaini, [1]E. Maseroli, [1]M. Rossi, [1]E. Filimberti, [4]I. Noci, [1]G. Forti and [1]M. Maggi

[1]Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence, Florence, [2]Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, [3]Santa Maria Annunziata Hospital, and [4]Department of Obstetrics and Gynecology, University of Florence, Florence, Italy

Table 3 Univariate correlations between the National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) total and subdomain scores and semen parameters

	NIH-CPSI total score	NIH-CPSI pain subdomain score	NIH-CPSI void subdomain score	NIH-CPSI QoL subdomain score
Semen pH	$r = 0.048$, $p = 0.340$	$r = 0.017$, $p = 0.730$	$r = 0.087$, $p = 0.081$	$r = 0.033$, $p = 0.509$
Semen volume (mL)	$r = 0.039$, $p = 0.440$	$r = 0.032$, $p = 0.525$	$r = 0.055$, $p = 0.253$	$r = -0.021$, $p = 0.682$
Sperm concentration (10^6/mL)	$r = 0.046$, $p = 0.355$	$r = 0.031$, $p = 0.536$	$r = 0.002$, $p = 0.967$	$r = -0.095$, $p = 0.057$
Spermatozoa per ejaculate (10^6/mL)	$r = 0.050$, $p = 0.322$	$r = 0.038$, $p = 0.445$	$r = 0.007$, $p = 0.886$	$r = 0.084$, $p = 0.093$
Sperm progressive motility (%)	$r = 0.079$, $p = 0.156$	$r = 0.071$, $p = 0.201$	$r = 0.019$, $p = 0.734$	$r = 0.101$, $p = 0.069$
Sperm morphology (%) normal forms	$r = -0.038$, $p = 0.492$	$r = -0.008$, $p = 0.888$	$r = -0.068$, $p = 0.223$	$r = -0.017$, $p = 0.762$
Leucocytospermia	RR = 1.02 [0.97–1.07], $p = 0.423$	RR = 1.06 [0.96–1.17], $p = 0.228$	RR = 0.91 [0.71–1.17], $p = 0.475$	RR = 1.25 [1.02–1.53], $p = 0.033$

QoL, quality of life.

Lotti et al., Andrology. 2013 Nov 28. doi: 10.1111/j.2047-2927.2013.00156.x. [Epub ahead of print]

Table 4 Comparisons between patients with prostatitis-like symptoms (PLS) and age-, waist-, total testosterone (TT)-matched PLS-free patients (1 : 3 ratio)

	PLS patients (n = 39)	Age-, waist-, TT-matched PLS-free patients (1 : 3 ratio, n = 117)	p
Age	38.8 ± 8.8	38.0 ± 6.9	0.609
Waist	93.1 ± 7.6	92.7 ± 6.3	0.778
Total testosterone (nmol/L)	16.9 ± 5.9	16.1 ± 5.4	0.495
Semen parameters			
Sexual abstinence (days)	4.5 ± 2.9	4.3 ± 2.2	0.177
pH	7.5 ± 0.3	7.5 ± 0.3	0.294
Semen volume	3.4 [2.0–4.5]	4.0 [4.0–5.0]	0.982
Sperm concentration (10^6/mL)	18.0 [0.6–56.0]	11.0 [1.5–51.0]	0.763
Spermatozoa per ejaculate (10^6/mL)	36.0 [2.8–171.5]	35.0 [3.6–138.4]	0.897
Sperm progressive motility (%)	39.1 ± 17.5	32.7 ± 20.5	0.116
Sperm morphology (%) normal forms	5.0 [3.0–12.0]	5.0 [2.0–10.0]	0.343
Leucocytospermia (%)	10.2	2.6	**0.044**
Current positive urine and/or seminal culture (%)	28.2	2.6	**<0.0001**
sIL-8 (ng/mL)	5.03 [2.06–11.36]	2.02 [1.16–3.92]	**<0.0001**
PSA (ng/mL)	0.99 ± 0.83	0.76 ± 0.36	0.074
Colour-Doppler ultrasound parameters			
Prostate volume (mL)	20.7 ± 5.3	21.3 ± 6.3	0.534
Prostate moderate-severe non-homogeneity (%)	66.6	17.2	**<0.0001**
Prostate hypoechoic texture (%)	69.1	6.0	**<0.0001**
Prostate hyperaemia (%)	69.1	9.5	**<0.0001**
Arterial prostatic peak systolic velocity (cm/sec)	11.7 ± 1.7	8.2 ± 2.7	**<0.0001**
Ejaculatory duct calcifications (%)	17.9	6.9	**0.042**
SV volume before ejaculation (mL)	9.2 [5.2–19.2]	6.7 [4.4–11.3]	**0.013**
SV volume after ejaculation (mL)	5.9 [3.6–11.1]	4.8 [2.7–7.3]	**0.037**
SV areas of endocapsulation after ejaculation (%)	41.0	8.6	**<0.0001**
SV wall thickening and septa (%)	20.5	1.7	**<0.0001**
Epididymal inhomogeneous tail (%)	53.8	22.4	**<0.0001**
Epididymal hyperechoic tail (%)	33.3	12.0	**0.006**
Epididymal hyperaemia (%)	15.4	2.6	**0.003**
Epididymal tail size (mm)	4.7 ± 1.5	4.1 ± 1.2	**0.028**
Hydrocele (%)	25.6	8.6	**0.006**

A p value < 0.05 was considered as significant.
Data are expressed as mean ± standard deviation or as median (quartiles) when appropriate, and as percentages when categorical. sIL8, seminal interleukin 8; SV, seminal vesicles.

Lotti et al., Andrology. 2013 Nov 28. doi: 10.1111/j.2047-2927.2013.00156.x. [Epub ahead of print]

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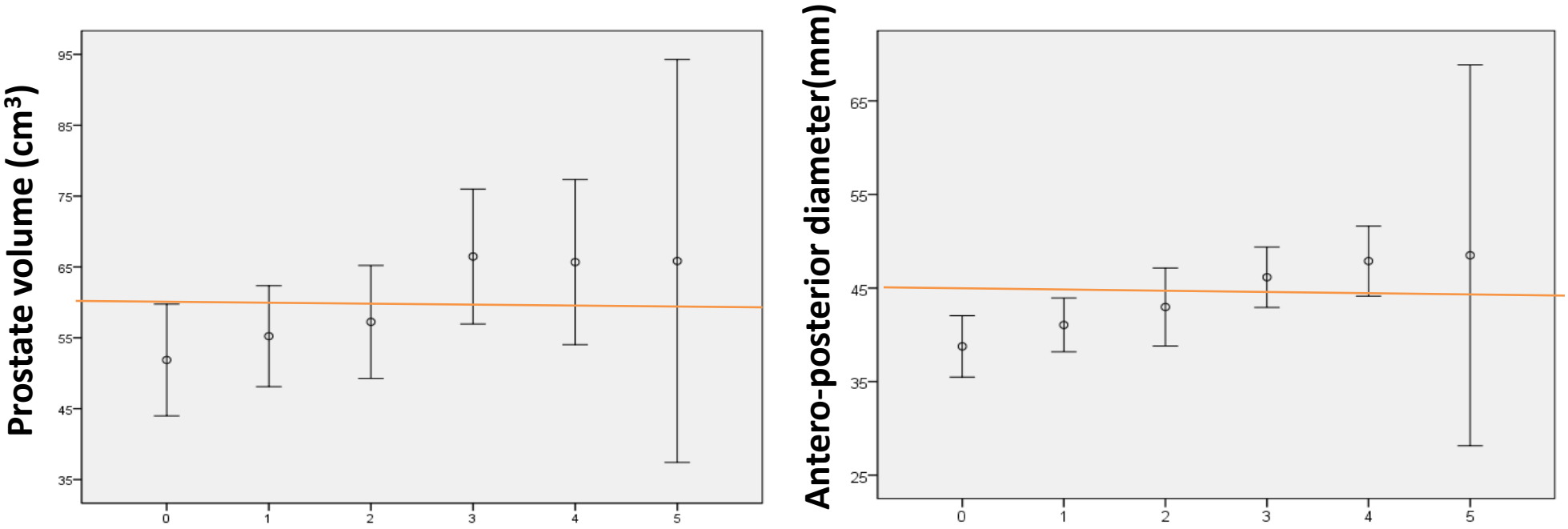
- **MetS (↑ waist, dyslipidaemia) is associated with ↑ insulin and BPE**
- **MetS (↑ waist) is associated with prostate inflammation**
- **Prostatitis-like symptoms are not associated with semen abnormalities**

Association of increasing MetS factors and sonographic prostate volume

Multi-center restrospective study in BPH patients (n=244, mean age=68±7.5)



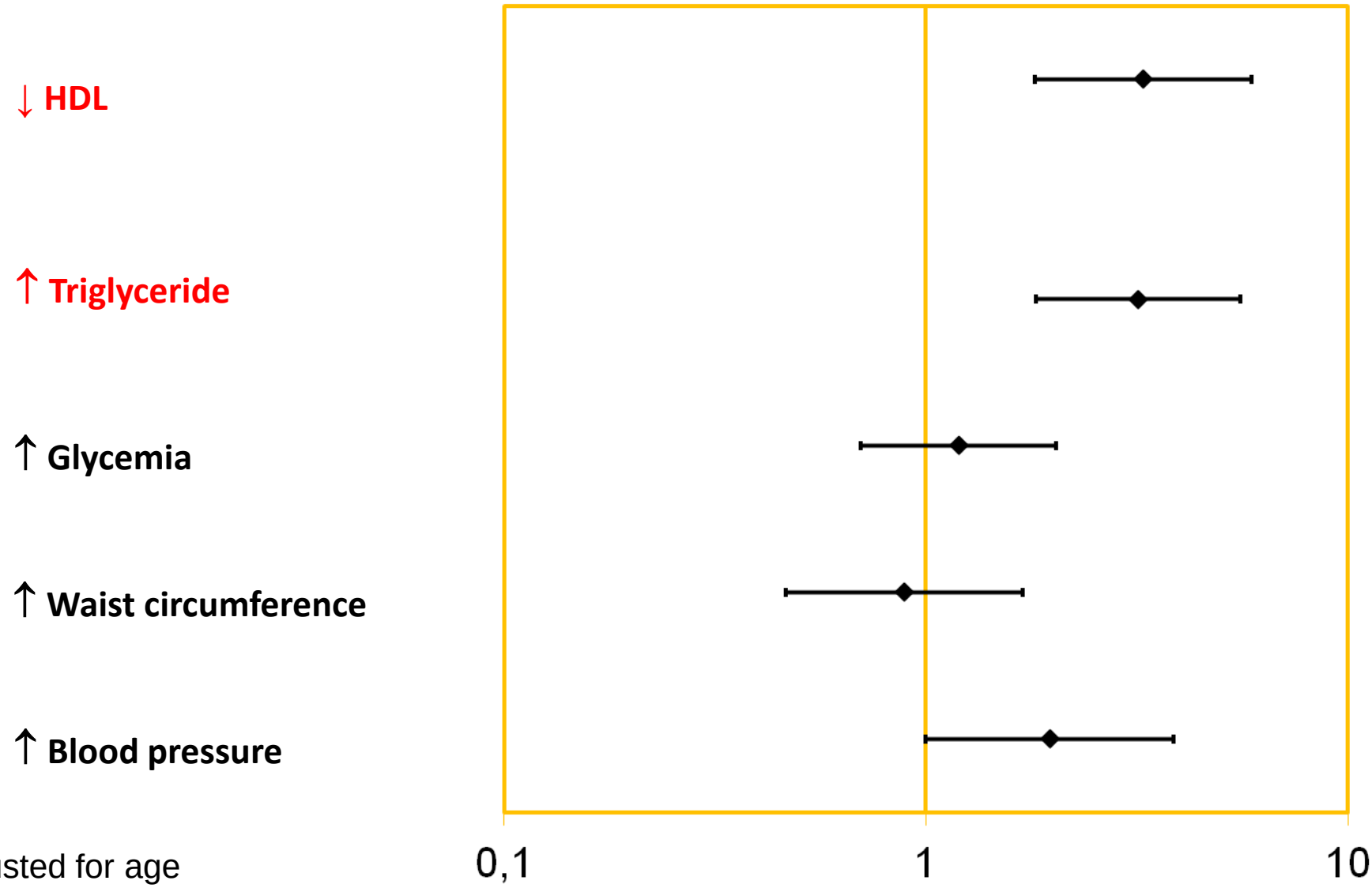
 # MetS components

(American Heart Association/National Heart, Lung and Blood Institute; AHA/NHLBI)

Gacci et al, Prostate Cancer Prostatic Dis. 2013 Mar;16(1):101-6

Age-adjusted Hazard Ratio for prostate volume > 60 cm^3 as a function of MetS factors

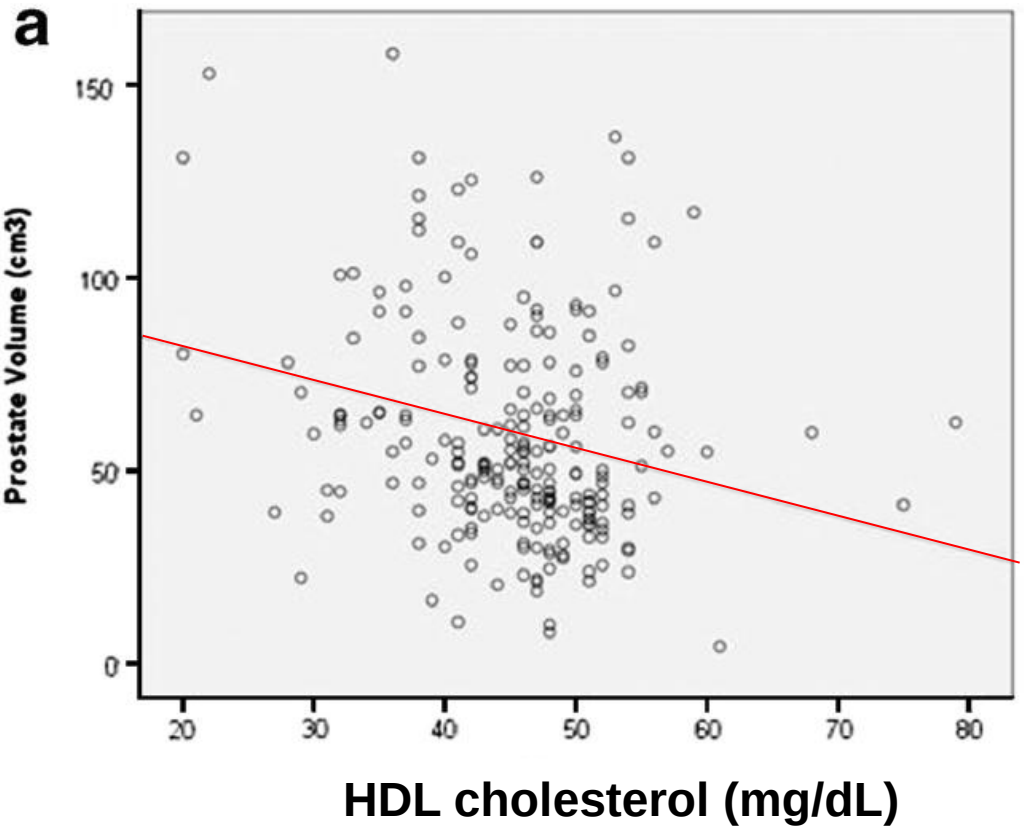
Multi-center restrospective study in BPH patients (n=244, mean age=68±7.5)

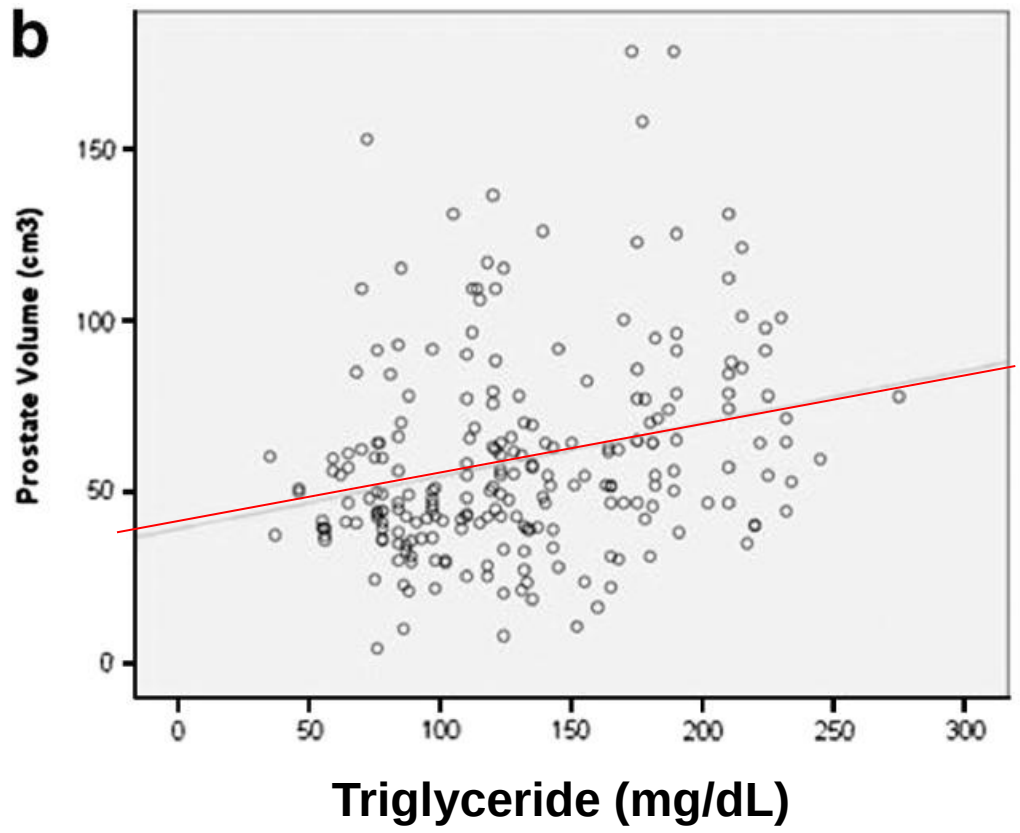


Gacci et al, Prostate Cancer Prostatic Dis. 2013 Mar;16(1):101-6

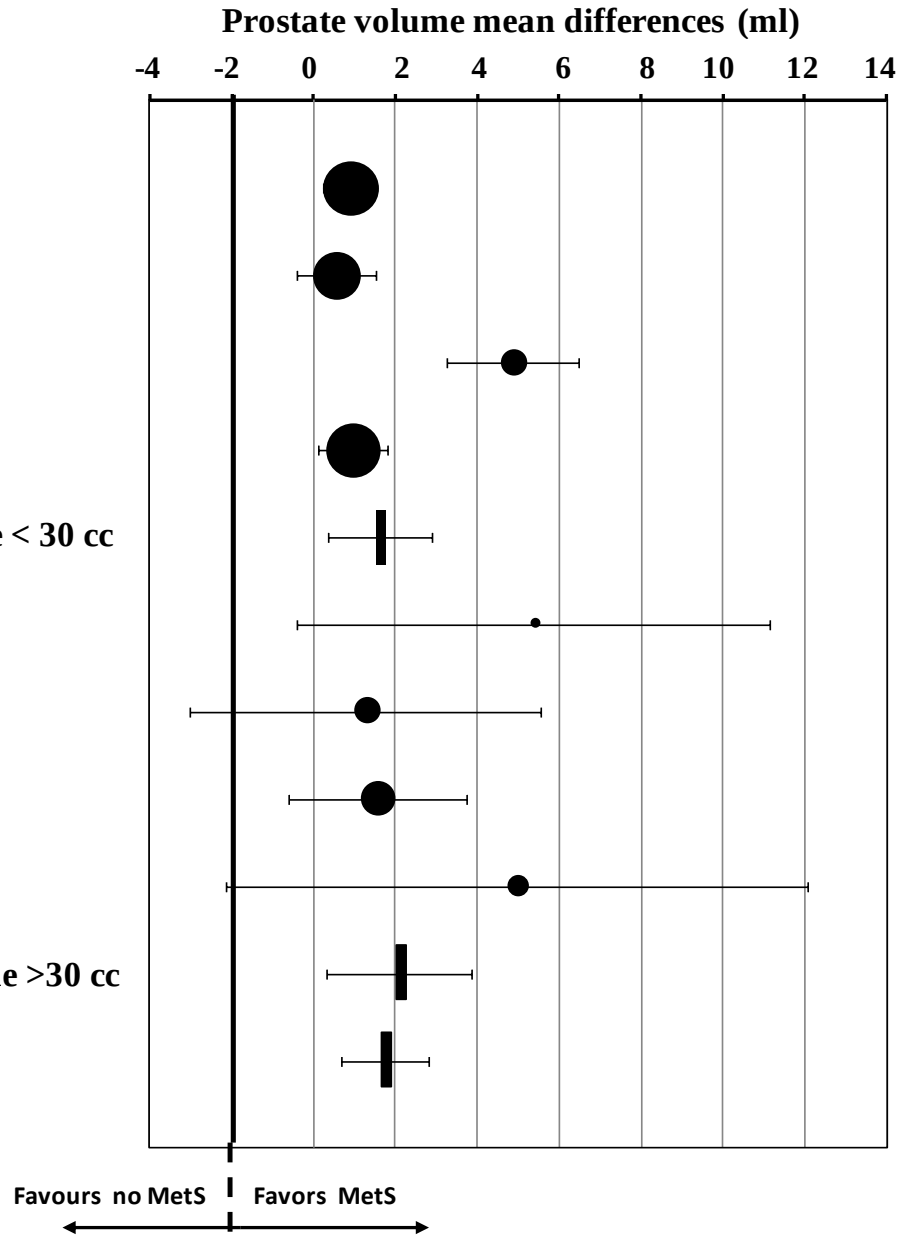
Association between dyslipidaemia and sonographic prostate volume

Multi-center restrospective study in BPH patients (n=244, mean age=68±7.5)





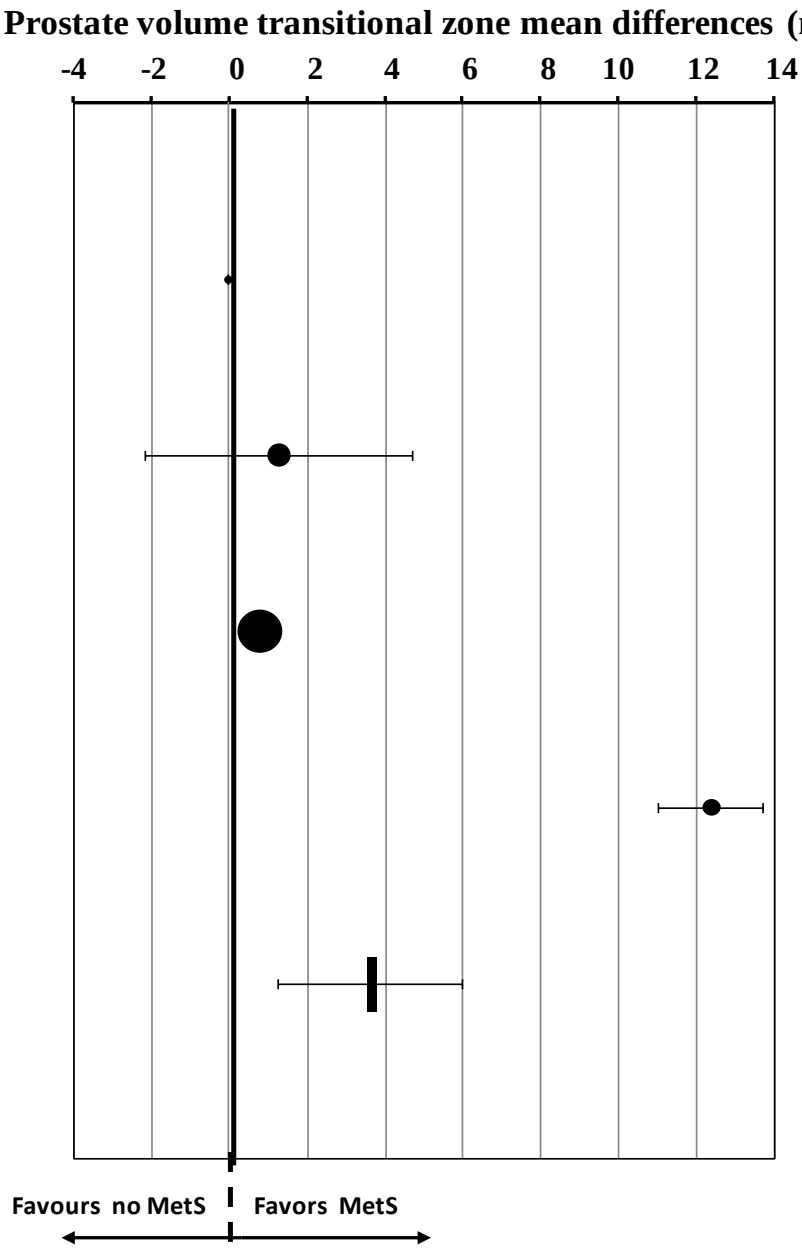
RANDOM-EFFECTS POOLED MEAN DIFFERENCE OF TOTAL PROSTATE VOLUME BETWEEN MetS CASES AND CONTROLS



Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Jeong et al., 2011	0,90	0,28	1,52	0,00
Yim et al, 2011	0,60	-0,37	1,57	0,22
Byun et al., 2012	4,90	3,29	6,51	0,00
Park et al., 2013	1,00	0,16	1,84	0,02
Oveall mean prostate volume < 30 cc	1,66	0,38	2,94	0,01
Ozden et al, 2007	5,40	-0,36	11,16	0,07
Park et al, 2008	1,30	-2,99	5,59	0,55
Yang et al, 2012	1,60	-0,58	3,78	0,15
Gacci et al., 2013	5,00	-2,09	12,09	0,17
Overall mean prostate volume >30 cc	2,13	0,34	3,91	0,02
Overall	1,80	0,74	2,87	0,00

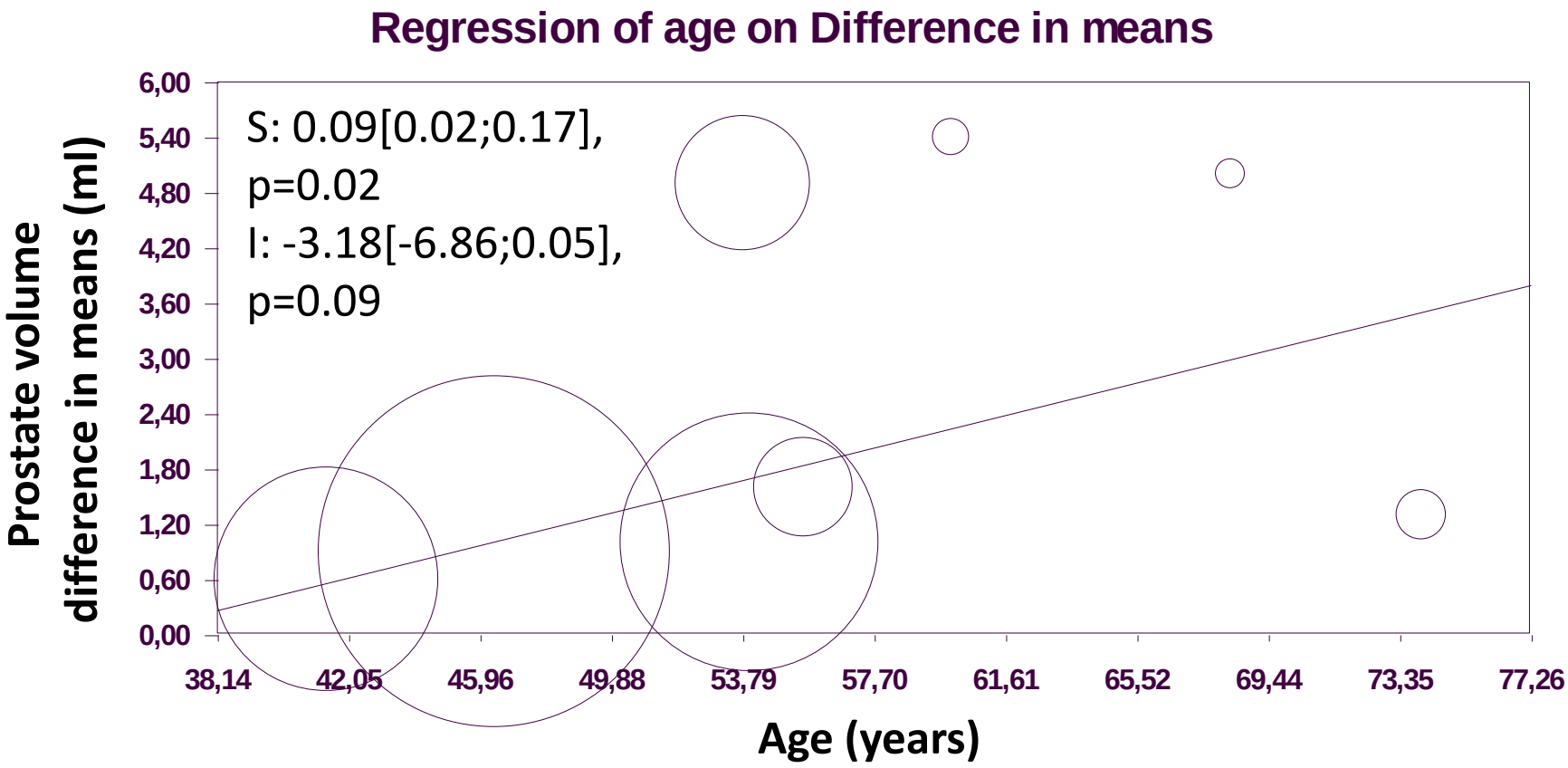
Gacci & Corona et al., 2013 submitted

RANDOM-EFFECTS POOLED MEAN DIFFERENCE OF PROSTATE VOLUME (TRANSITIONAL ZONE) BETWEEN MetS CASES AND CONTROLS

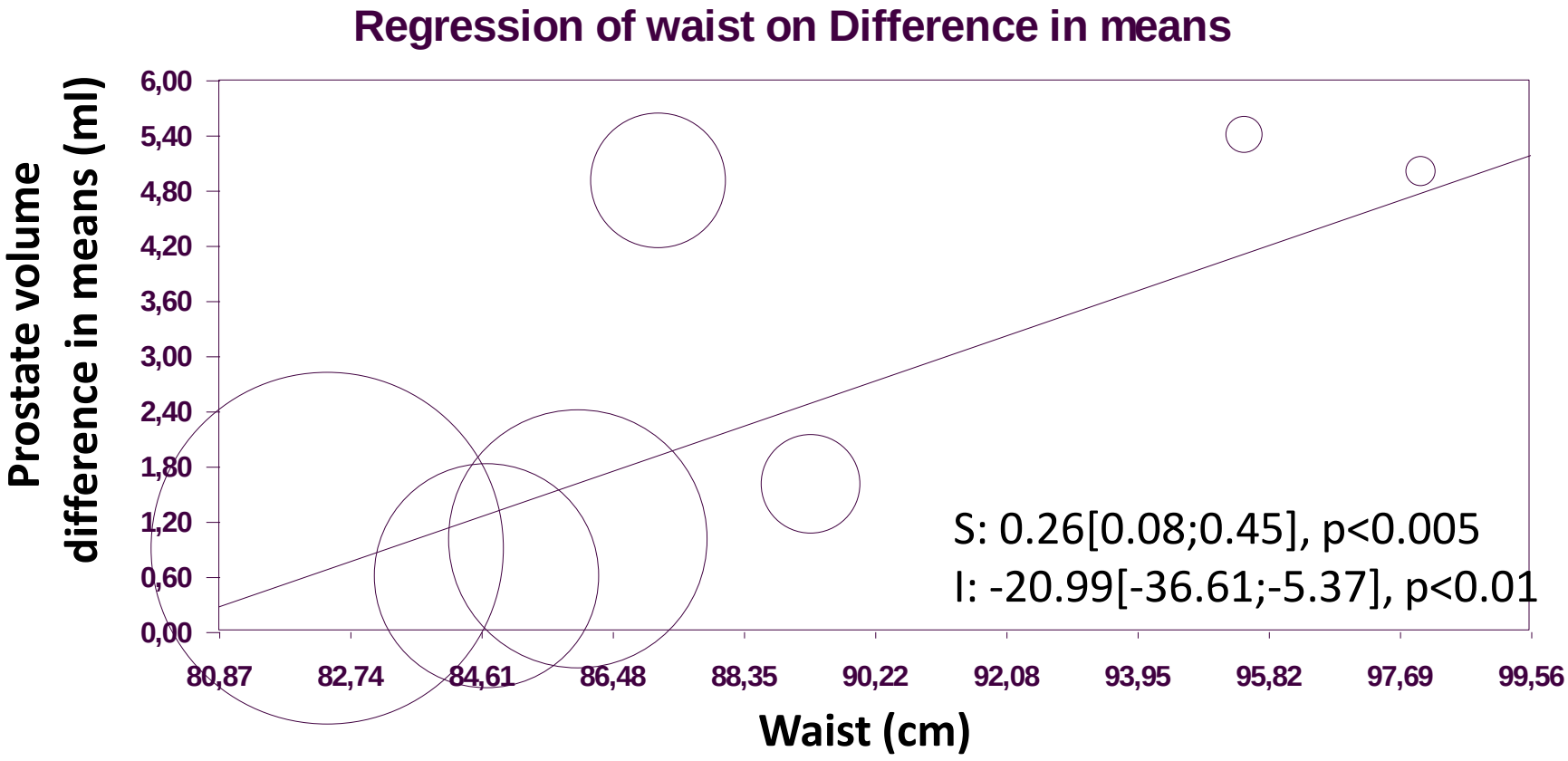


Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Ozden et al, 2007	0,00	0,00	0,00	0,05
Park et al, 2008	1,30	-2,13	4,73	0,46
Jeong et al, 2011	0,80	0,45	1,15	0,00
Gacci et al, 2013	12,40	11,06	13,74	0,00
Overall	3,67	1,31	6,03	0,00

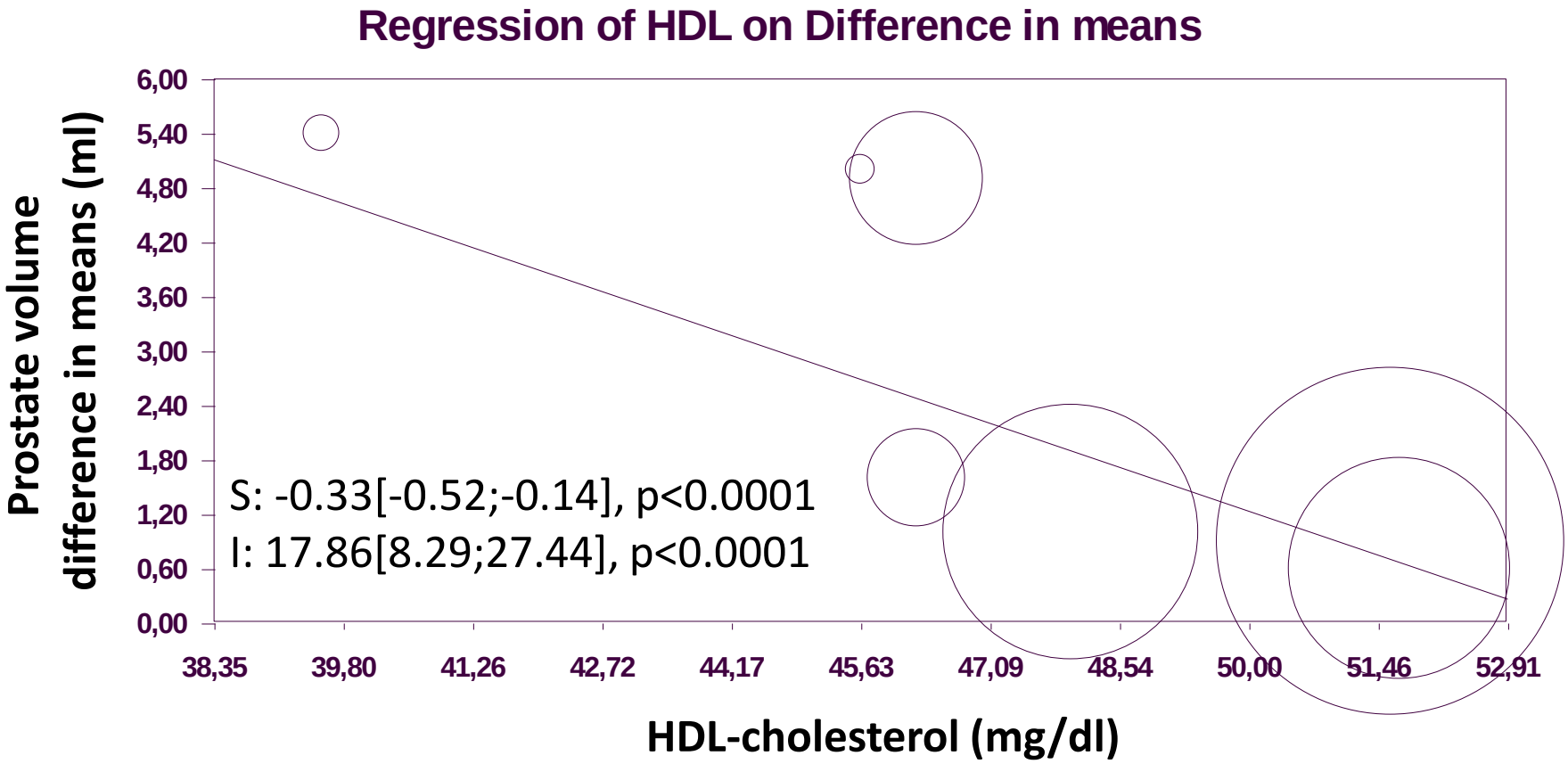
Gacci & Corona et al., 2013 submitted



Gacci & Corona et al., 2013 submitted



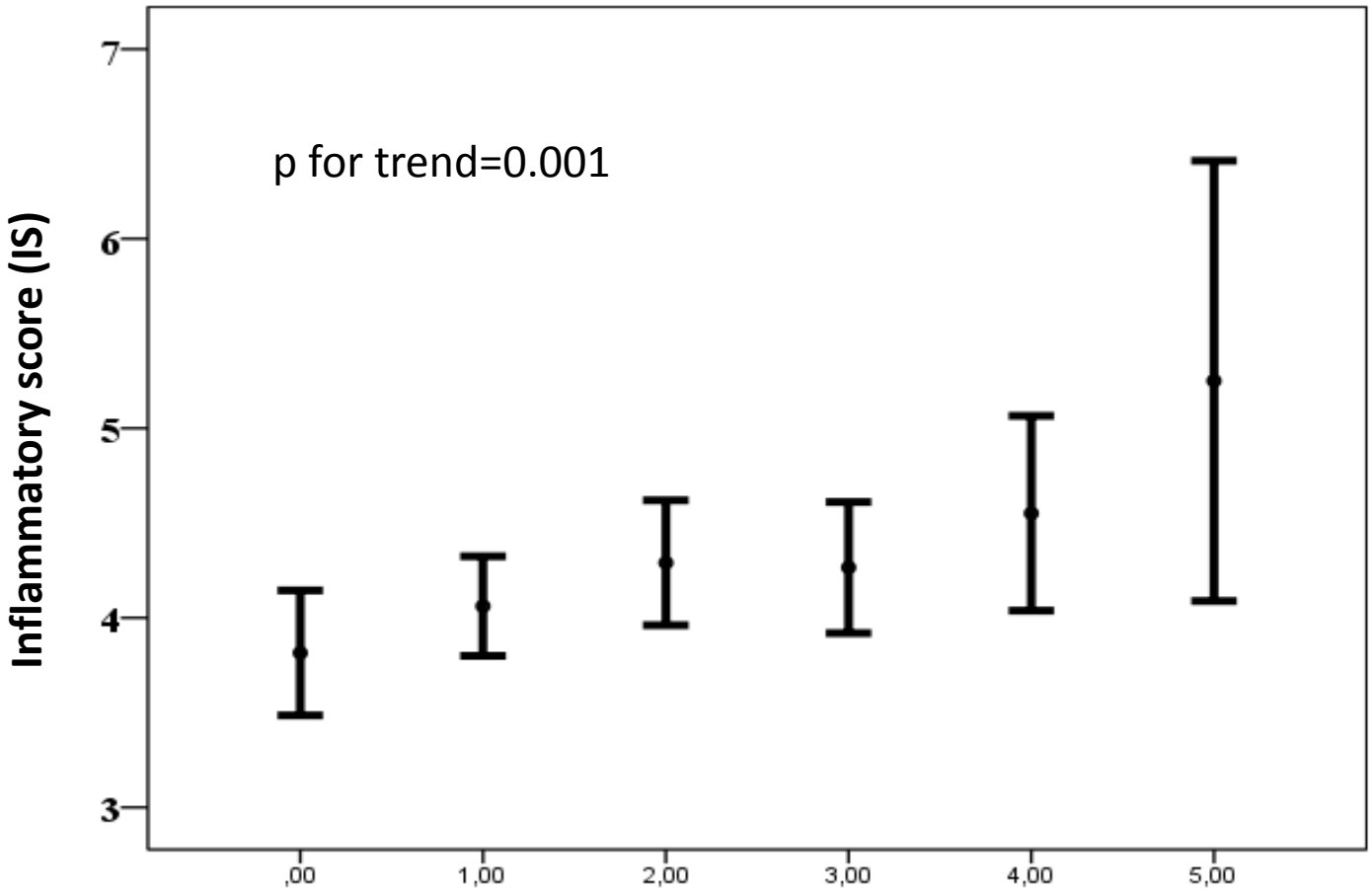
Gacci & Corona et al., 2013 submitted



Gacci & Corona et al., 2013 submitted

Association of increasing MetS factors and prostate inflammatory score

Multi-center restrospective study in BPH patients (n=244, mean age=68±7.5)

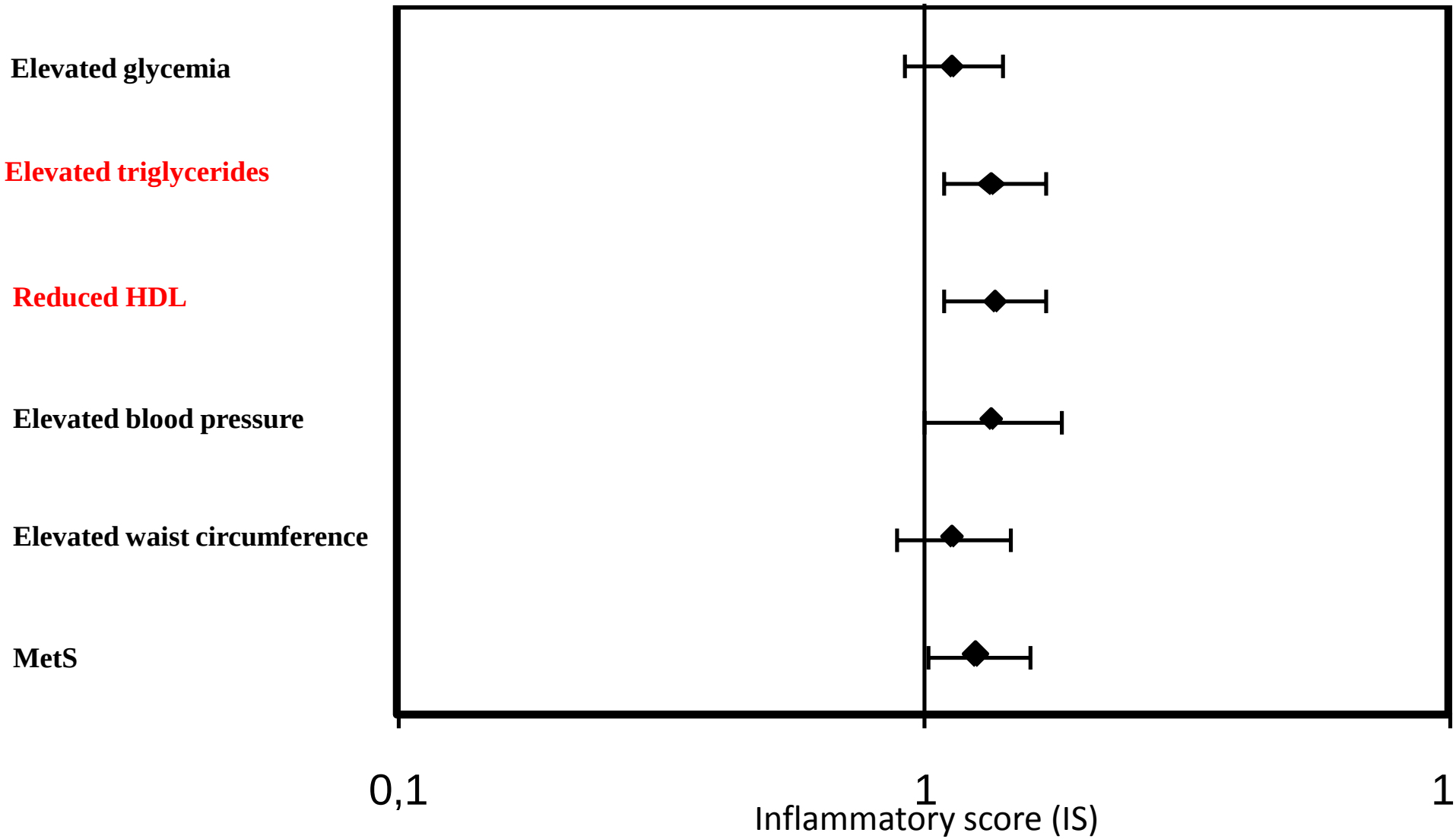


(American Heart Association/National Heart, Lung and Blood Institute; AHA/NHLBI)

Vignozzi et al., Prostate 73: 789–800, 2013

Age-adjusted Hazard Ratio for prostate inflammatory score as a function of MetS factors

Multi-center restrospective study in BPH patients (n=244, mean age=68±7.5)

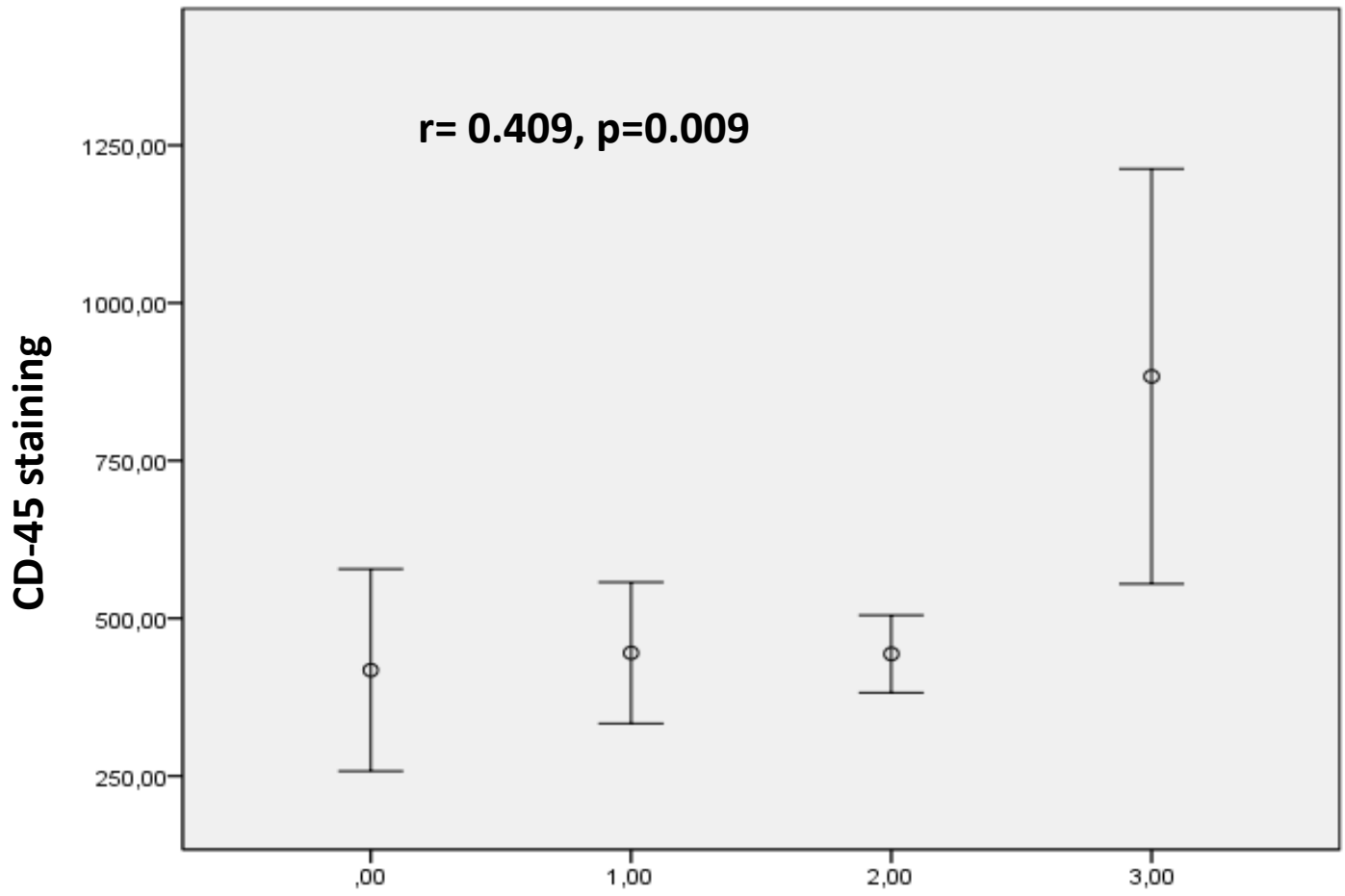


Adjusted for age

Vignozzi et al., Prostate 73: 789–800, 2013

Association of increasing MetS factors and prostate CD-45 staining

Restrospective study in BPH patients from FILUVA[1] (n=42, mean age=70±7)

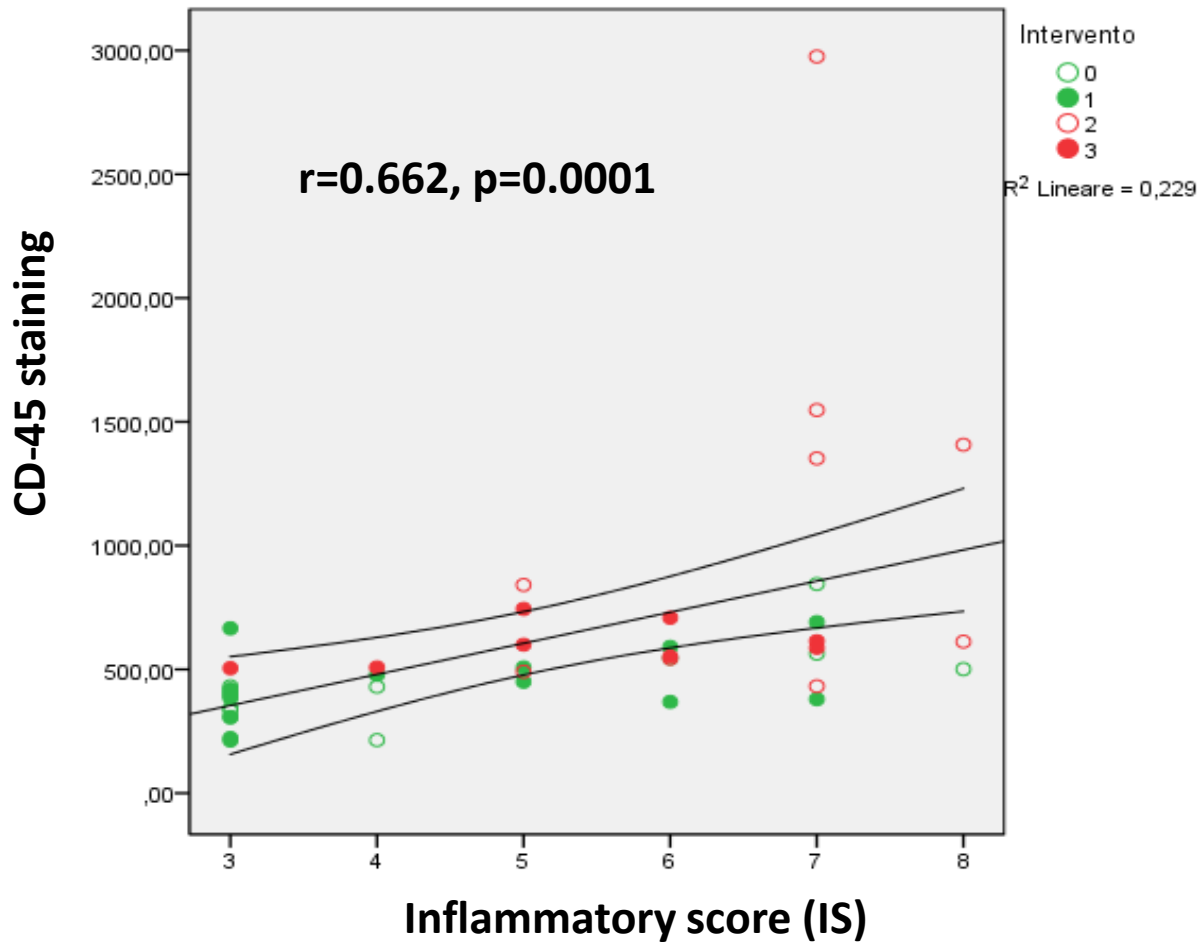


(American Heart Association/National Heart, Lung and Blood Institute; AHA/NHLBI)

Vignozzi et al., Prostate. 2013 Sep;73(13):1391-402.

Association between inflammation score and prostate CD-45 staining

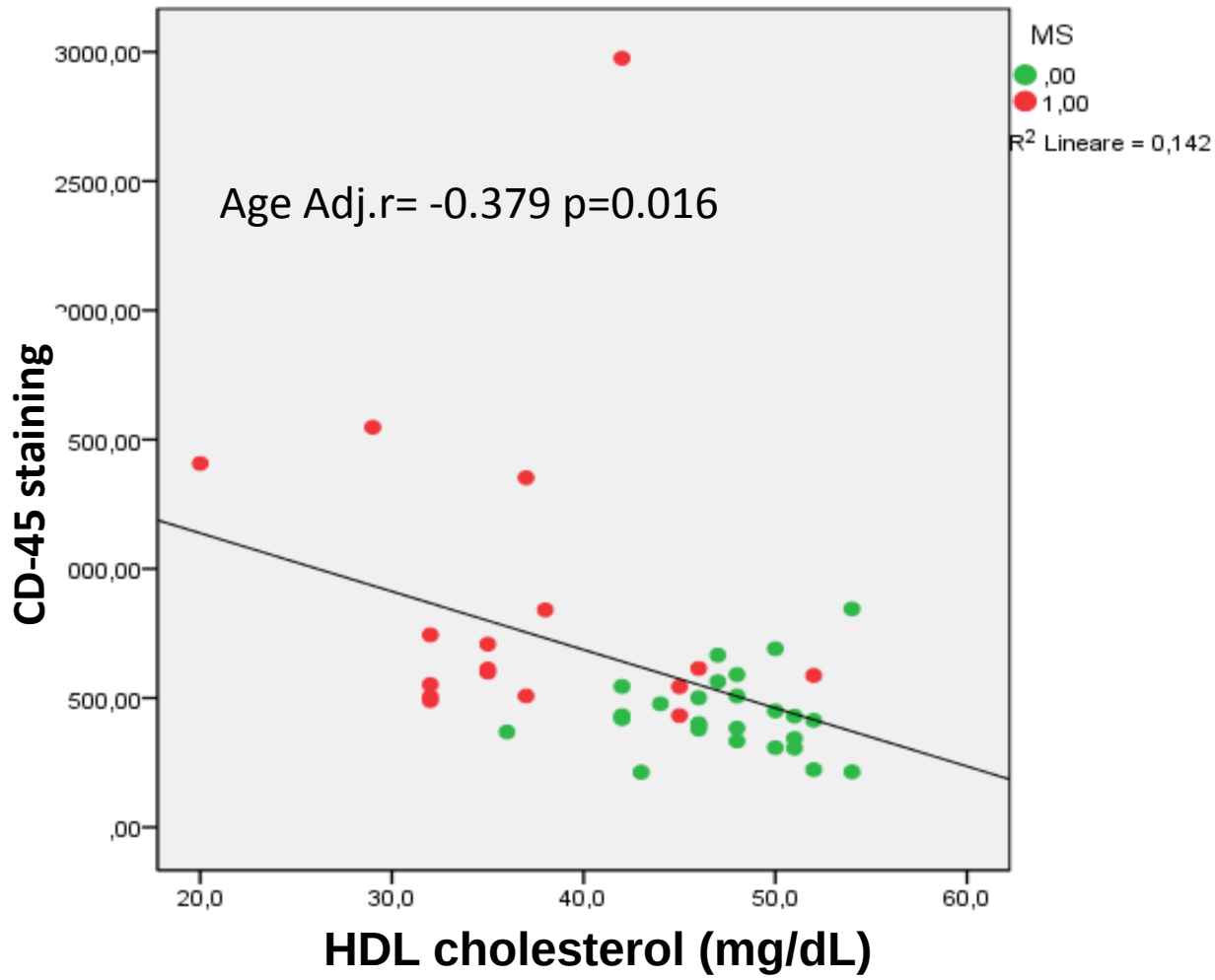
Restrospective study in BPH patients from FILUVA[1] (n=42, mean age=70±7)



Vignozzi et al., Prostate. 2013 Sep;73(13):1391-402.

Association between dyslipidaemia and prostate CD-45

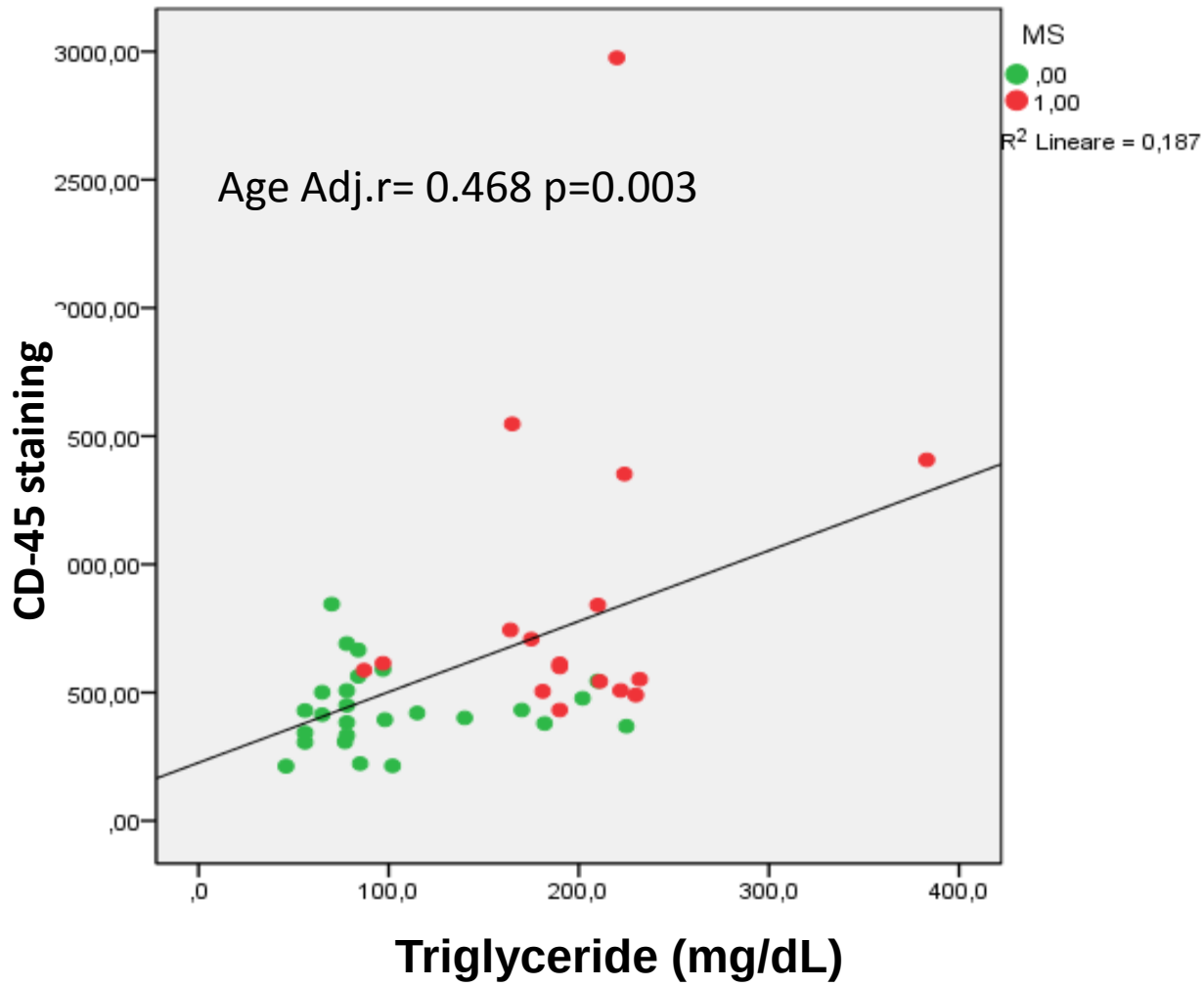
Restrospective study in BPH patients from FILUVA[1] (n=42, mean age=70±7)



Vignozzi et al., Prostate. 2013 Sep;73(13):1391-402.

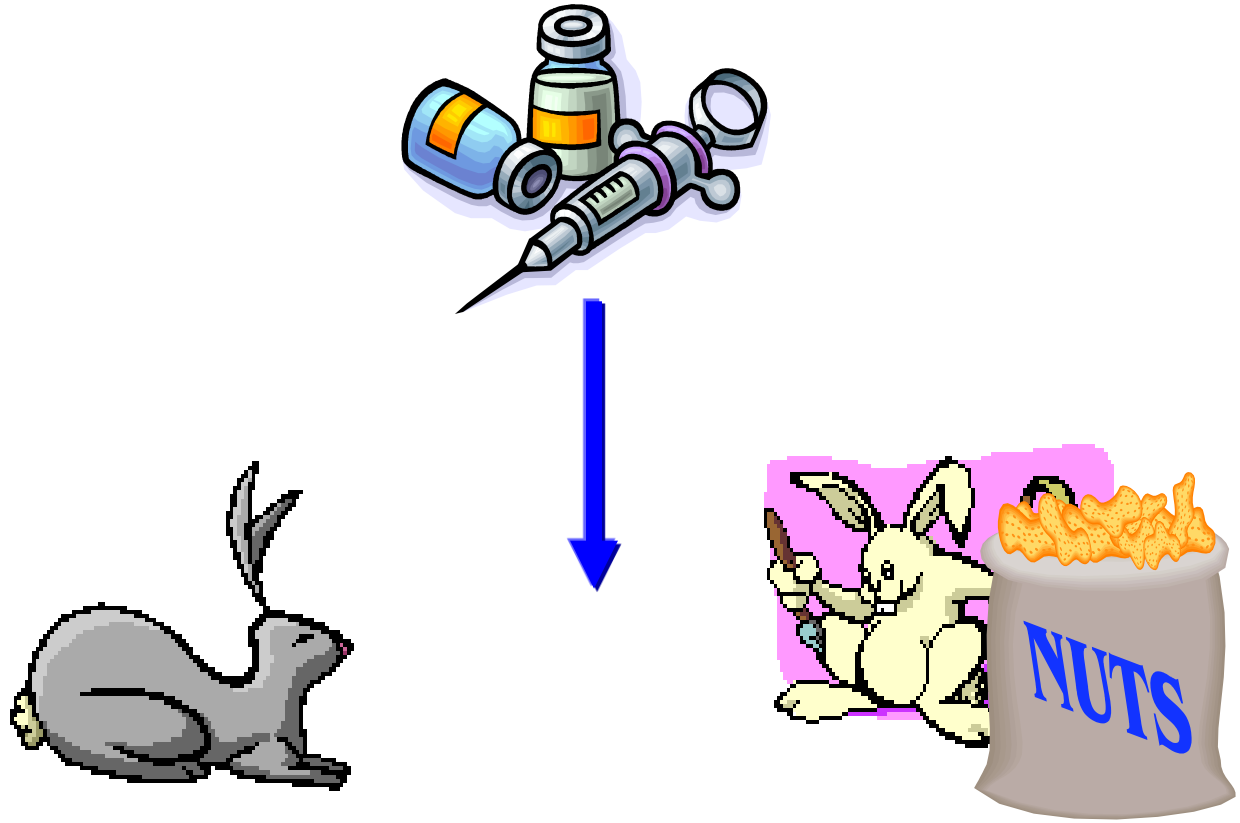
Association between dyslipidaemia and prostate CD-45

Restrospective study in BPH patients from FILUVA[1] (n=42, mean age=70±7)



Vignozzi et al., Prostate. 2013 Sep;73(13):1391-402.

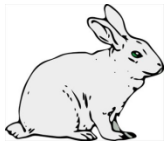
Pre-clinical studies on metabolic syndrome: The Florence experience



hypogonadism

infertility

Metabolic syndrome



0 — 3 — 6 — 9 — 12 weeks

MetS

- ✓Hyperglycaemia
- ✓Reduced glucose tolerance (OGTT)
- ✓Hypercholesterolemia
- ✓Hypertriglyceridemia
- ✓Hypertension
- ✓Increased visceral fat mass
- ✓ Overactivity of RhoA/ROCK

- •Standard diet: control
- •High fat diet: HFD

0.5% cholesterol
and 4% peanuts oil

Filippi et al., J Sex Med 2009, 6(12):3274-88
Vignozzi et al., J Sex Med. 2011 Jan;8(1):57-77
Vignozzi et al., J Endocrinol. 2012 Jan;212(1):71-84.

1: Morelli A, Sarchielli E, Comeglio P, Filippi S, Vignozzi L, Marini M, Rastrelli G, Maneschi E, Cellai I, Persani L, Adorini L, Vannelli GB, Maggi M. Metabolic syndrome induces inflammation and impairs gonadotropin-releasing hormone neurons in the preoptic area of the hypothalamus in rabbits. Mol Cell Endocrinol. 2013 Sep 21. doi:pii: S0303-7207(13)00408-5. 10.1016/j.mce.2013.09.017. [Epub ahead of print] PubMed PMID: 24064031.

2: Comeglio P, Morelli A, Cellai I, Vignozzi L, Sarchielli E, Filippi S, Maneschi E, Corcetto F, Corno C, Gacci M, Vannelli GB, Maggi M. Opposite effects of tamoxifen on metabolic syndrome-induced bladder and prostate alterations: A role for GPR30/GPER? Prostate. 2013 Aug 26. doi: 10.1002/pros.22723. [Epub ahead of print] PubMed PMID: 24037776.

3: Maneschi E, Vignozzi L, Morelli A, Mello T, Filippi S, Cellai I, Comeglio P, Sarchielli E, Calcagno A, Mazzanti B, Vettor R, Vannelli GB, Adorini L, Maggi M. FXR activation normalizes insulin sensitivity in visceral preadipocytes of a rabbit model of MetS. J Endocrinol. 2013 Jul 6;218(2):215-31. doi: 10.1530/JOE-13-0109. Print 2013. PubMed PMID: 23750014.

4: Maneschi E, Morelli A, Filippi S, Cellai I, Comeglio P, Mazzanti B, Mello T, Calcagno A, Sarchielli E, Vignozzi L, Saad F, Vettor R, Vannelli GB, Maggi M. Testosterone treatment improves metabolic syndrome-induced adipose tissue derangements. J Endocrinol. 2012 Dec;215(3):347-62. doi: 10.1530/JOE-12-0333. Epub 2012 Oct 8. PubMed PMID: 23045189.

5: Morelli A, Comeglio P, Filippi S, Sarchielli E, Vignozzi L, Maneschi E, Cellai I, Gacci M, Lenzi A, Vannelli GB, Maggi M. Mechanism of action of phosphodiesterase type 5 inhibition in metabolic syndrome-associated prostate alterations: an experimental study in the rabbit. Prostate. 2013 Mar;73(4):428-41. doi: 10.1002/pros.22584. Epub 2012 Sep 19. PubMed PMID: 22996758.

6: Morelli A, Comeglio P, Filippi S, Sarchielli E, Cellai I, Vignozzi L, Yehiely-Cohen R, Maneschi E, Gacci M, Carini M, Adorini L, Vannelli GB, Maggi M. Testosterone and farnesoid X receptor agonist INT-747 counteract high fat diet-induced bladder alterations in a rabbit model of metabolic syndrome. J Steroid Biochem Mol Biol. 2012 Oct;132(1-2):80-92. doi: 10.1016/j.jsbmb.2012.02.007. Epub 2012 Mar 8. PubMed PMID: 22406511.

7: Vignozzi L, Morelli A, Sarchielli E, Comeglio P, Filippi S, Cellai I, Maneschi E, Serni S, Gacci M, Carini M, Piccinni MP, Saad F, Adorini L, Vannelli GB, Maggi M. Testosterone protects from metabolic syndrome-associated prostate inflammation: an experimental study in rabbit. J Endocrinol. 2012 Jan;212(1):71-84. doi: 10.1530/JOE-11-0289. Epub 2011 Oct 18. PubMed PMID: 22010203.

8: Corona G, Rastrelli G, Morelli A, Vignozzi L, Mannucci E, Maggi M. Hypogonadism and metabolic syndrome. J Endocrinol Invest. 2011 Jul-Aug;34(7):557-67. doi: 10.3275/7806. Epub 2011 Jun 27. Review. PubMed PMID: 21720206.

9: Mallidis C, Czerwiec A, Filippi S, O'Neill J, Maggi M, McClure N. Spermatogenic and sperm quality differences in an experimental model of metabolic syndrome and hypogonadal hypogonadism. Reproduction. 2011 Jul;142(1):63-71. doi: 10.1530/REP-10-0472. Epub 2011 Apr 4. PubMed PMID: 21464116.

10: Morelli A, Vignozzi L, Maggi M, Adorini L. Farnesoid X receptor activation improves erectile dysfunction in models of metabolic syndrome and diabetes. Biochim Biophys Acta. 2011 Aug;1812(8):859-66. doi: 10.1016/j.bbadis.2010.10.013. Epub 2010 Nov 5. Review. PubMed PMID: 21056655.

11: Vignozzi L, Morelli A, Filippi S, Comeglio P, Chavalmane AK, Marchetta M, Toce M, Yehiely-Cohen R, Vannelli GB, Adorini L, Maggi M. Farnesoid X receptor activation improves erectile function in animal models of metabolic syndrome and diabetes. J Sex Med. 2011 Jan;8(1):57-77. doi: 10.1111/j.1743-6109.2010.02073.x. Epub 2010 Oct 18. PubMed PMID: 20955313.

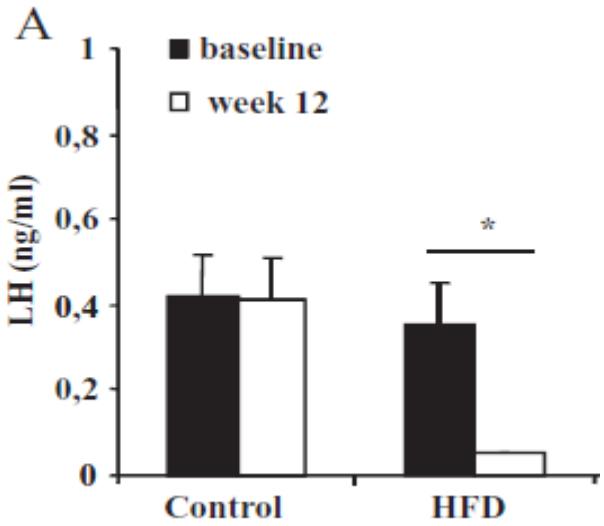
12: Filippi S, Vignozzi L, Morelli A, Chavalmane AK, Sarchielli E, Fibbi B, Saad F, Sandner P, Ruggiano P, Vannelli GB, Mannucci E, Maggi M. Testosterone partially ameliorates metabolic profile and erectile responsiveness to PDE5 inhibitors in an animal model of male metabolic syndrome. J Sex Med. 2009 Dec;6(12):3274-88. doi: 10.1111/j.1743-6109.2009.01467.x. Epub 2009 Sep 1. PubMed PMID: 19732305.

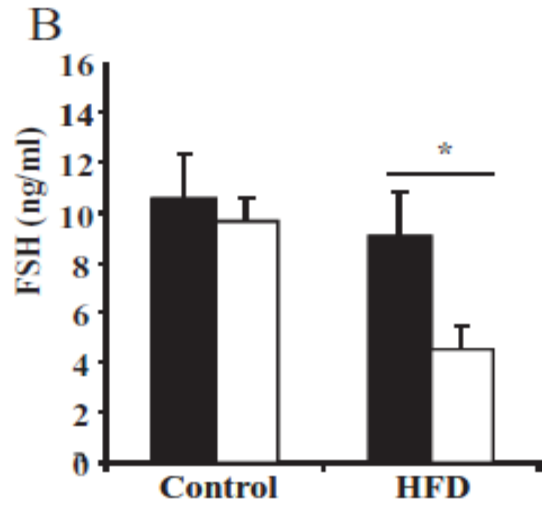
Animal model of MetS and Hypogonadism

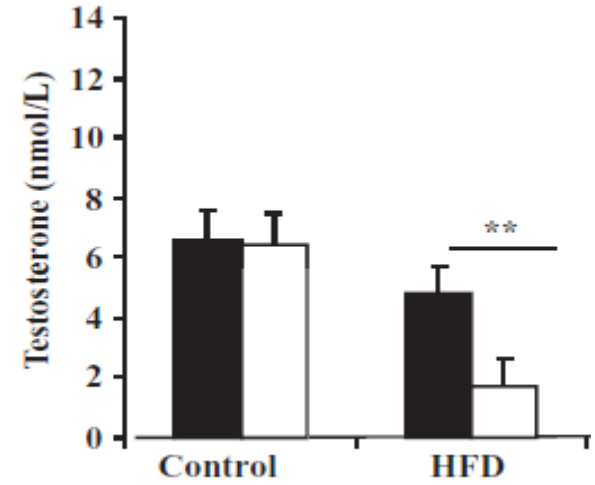
- Regular diet: RD (control)
- High fat diet: HFD

Hypogonadotropic hypogonadism

- ↓ testosterone, ↓ FSH and LH
- ↓ prostate, seminal vesicles weight
- ↓ testis weight







Filippi S et al., J Sex Med 2009, 6(12):3274-88

Molecular and Cellular Endocrinology 382 (2014) 107–119

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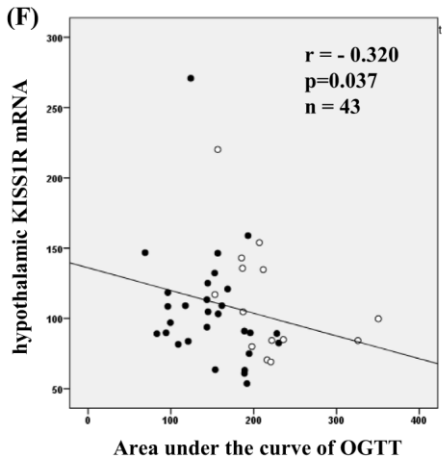
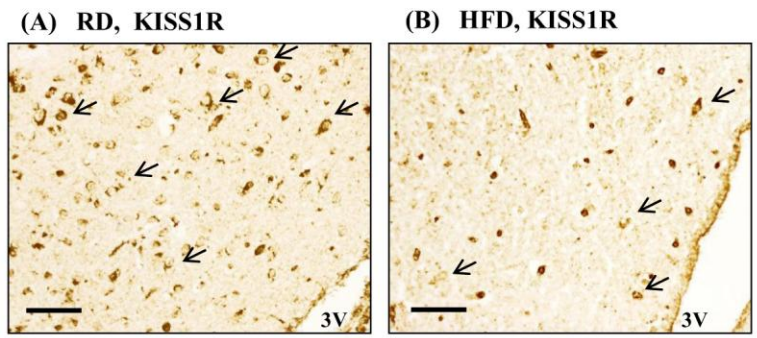
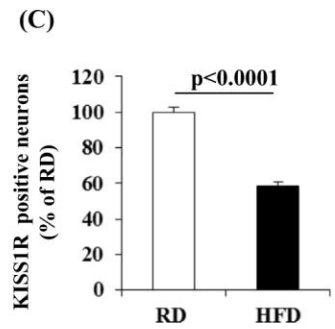
Metabolic syndrome induces inflammation and impairs gonadotropin-releasing hormone neurons in the preoptic area of the hypothalamus in rabbits

Annamaria Morelli [a], Erica Sarchielli [a], Paolo Comeglio [b], Sandra Filippi [c], Linda Vignozzi [b], Mirca Marini [a], Giulia Rastrelli [b], Elena Maneschi [b], Ilaria Cellai [b], Luca Persani [d,f], Luciano Adorini [e], Gabriella B. Vannelli [a], Mario Maggi [b,f,g,*]

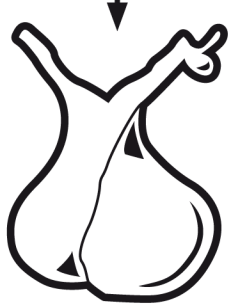






↓GnRH

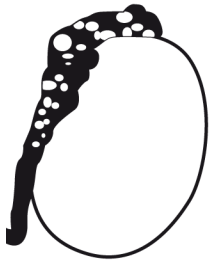
↓Kiss1R



pituitary

↑Glucose

↓LH, FSH

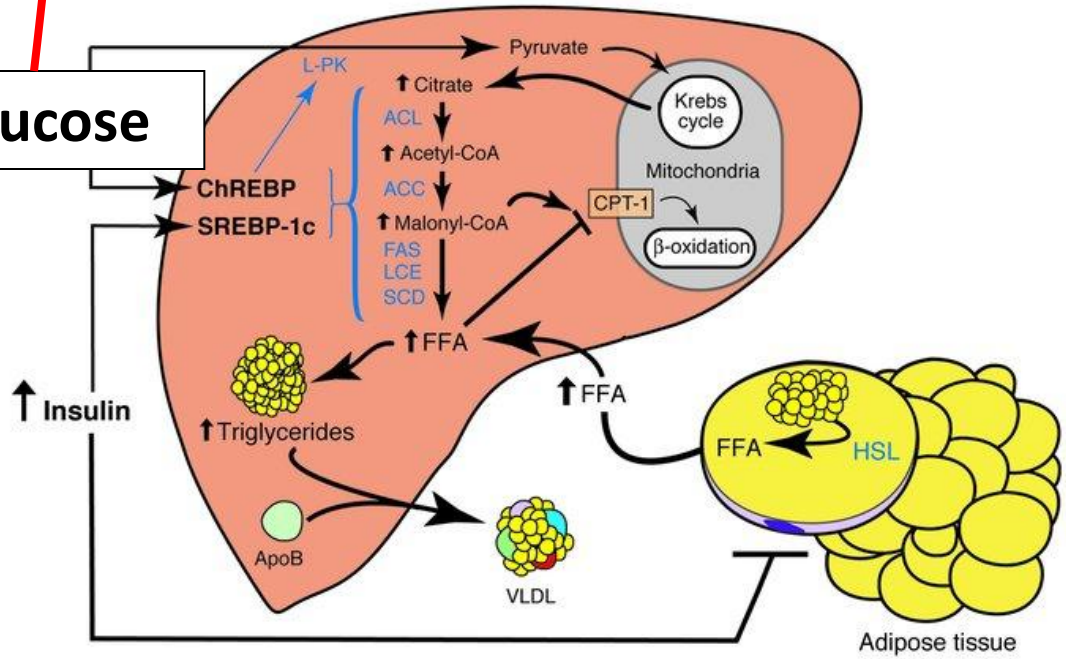


testis

↓ testosterone

In the hypothalamus MetS is associated with:

- **inflammation**
- **decreased expression of GnRH-related genes**



Testosterone protects from metabolic syndrome-associated prostate inflammation: an experimental study in rabbit

Linda Vignozzi[1], Annamaria Morelli[1], Erica Sarchielli[3], Paolo Comeglio[1], Sandra Filippi[4], Ilaria Cellai[1], Elena Maneschi[1], Sergio Serni[5], Mauro Gacci[5], Marco Carini[5], Marie-Pierre Piccinni[6], Farid Saad[7,8], Luciano Adorini[9], Gabriella B Vannelli[3] and Mario Maggi[1,2]

[1]Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence, Viale Pieraccini 6, Florence 50139, Italy
[2]CIRMAR (Centro Interuniversitario di Ricerca sulle basi molecolari della Malattie della Riproduzione), Milan, Italy
[3]Department of Anatomy, Histology and Forensic Medicine, [4]Interdepartmental Laboratory of Functional and Cellular Pharmacology of Reproduction, [5]Department of Urology and [6]Immunoallergology Unit, Department of Internal Medicine, Center of Excellence for Research, Transfer and High Education DENOTHE, University of Florence, Florence, Italy
[7]Scientific Affairs Men's Healthcare, Bayer Pharma AG, Berlin, Germany
[8]Gulf Medical University, Ajman, United Arab Emirates
[9]Intercept Pharmaceuticals Italia Srl. Via Togliatti, 06073 Corciano, Perugia, Italy

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Testosterone and farnesoid X receptor agonist INT-747 counteract high fat diet-induced bladder alterations in a rabbit model of metabolic syndrome

Q1 Annamaria Morelli[a], Paolo Comeglio[a], Sandra Filippi[b], Erica Sarchielli[c], Ilaria Cellai[a], Linda Vignozzi[a], Ravit Yehiely-Cohen[a], Elena Maneschi[a], Mauro Gacci[d], Marco Carini[d], Luciano Adorini[e], Gabriella B. Vannelli[c], Mario Maggi[a,*]

[a] Department of Clinical Physiopathology, University of Florence, Florence, Italy
[b] Interdepartmental Laboratory of Functional and Cellular Pharmacology of Reproduction, Depts. of Pharmacology and Clinical Physiopathology, University of Florence, Florence, Italy
[c] Department of Anatomy, Histology and Forensic Medicine, University of Florence, Florence, Italy
[d] Department of Urology, University of Florence, Florence, Italy
[e] Intercept Pharmaceuticals. New York. NY 10013. USA

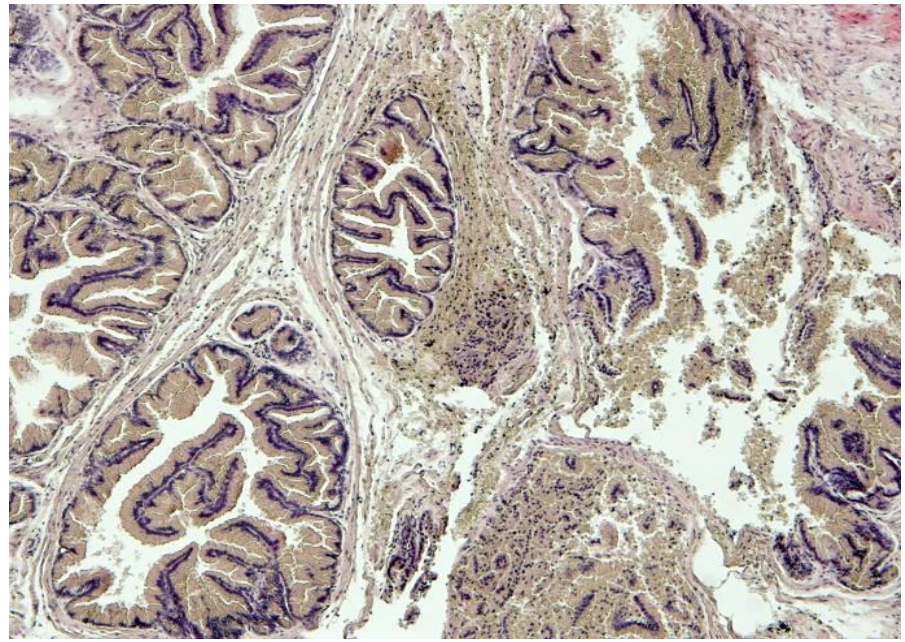
The Prostate 73:428–441 (2013)

Mechanism of Action of PhosphodiesteraseType 5 Inhibition in Metabolic Syndrome-Associated Prostate Alterations: An Experimental Study in the Rabbit

Annamaria Morelli,[1] Paolo Comeglio,[1] Sandra Filippi,[2] Erica Sarchielli,[3] Linda Vignozzi,[1] Elena Maneschi,[1] Ilaria Cellai,[1] Mauro Gacci,[4] Andrea Lenzi,[5] Gabriella B. Vannelli,[3] and Mario Maggi[1]*

In prostate & bladder MetS is associated with:

- inflammation
- fibrosis
- hypoxia



Testosterone Partially Ameliorates Metabolic Profile and Erectile Responsiveness to PDE5 Inhibitors in an Animal Model of Male Metabolic Syndrome

Sandra Filippi, PhD,* Linda Vignozzi, MD, PhD,† Annamaria Morelli, PhD,†
Aravinda K. Chavalmane, PhD,† Erica Sarchielli, PhD,‡ Benedetta Fibbi, MD, PhD,† Farid Saad, MD,§
Peter Sandner, MD,¶ Peggy Ruggiano, MD,† Gabriella B. Vannelli, MD,‡ Edoardo Mannucci, MD,** and
Mario Maggi, MD†,††

REPRODUCTION
RESEARCH

Spermatogenic and sperm quality differences in an experimental model of metabolic syndrome and hypogonadal hypogonadism

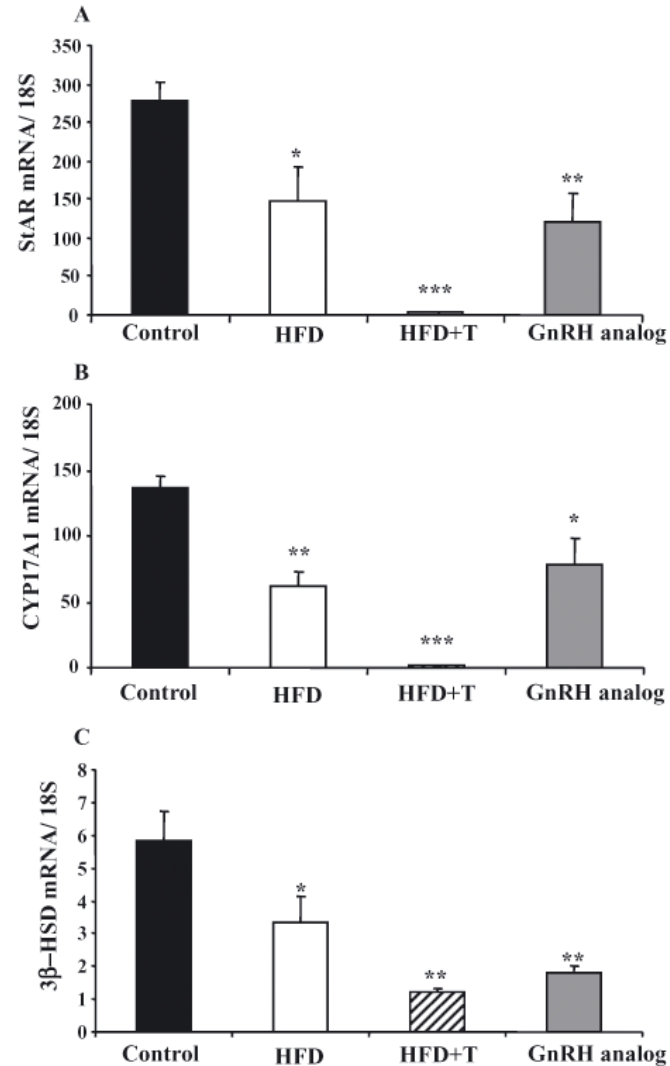
Con Mallidis[1,2], Agnieszka Czerwiec[2], Sandra Filippi[3], Jason O'Neill[2], Mario Maggi[3] and Neil McClure[2]

[1]Centre of Reproductive Medicine and Andrology, University of Münster, Domagkstrasse 11, D-48149 Munster, Germany, [2]Department of Obstetrics and Gynaecology, Queen's University Belfast, Belfast, BT12 6BJ, UK and [3]Andrology and Sexual Medicine Unit, Department of Clinical Physiopathology, University of Florence, Florence 50139, Italy

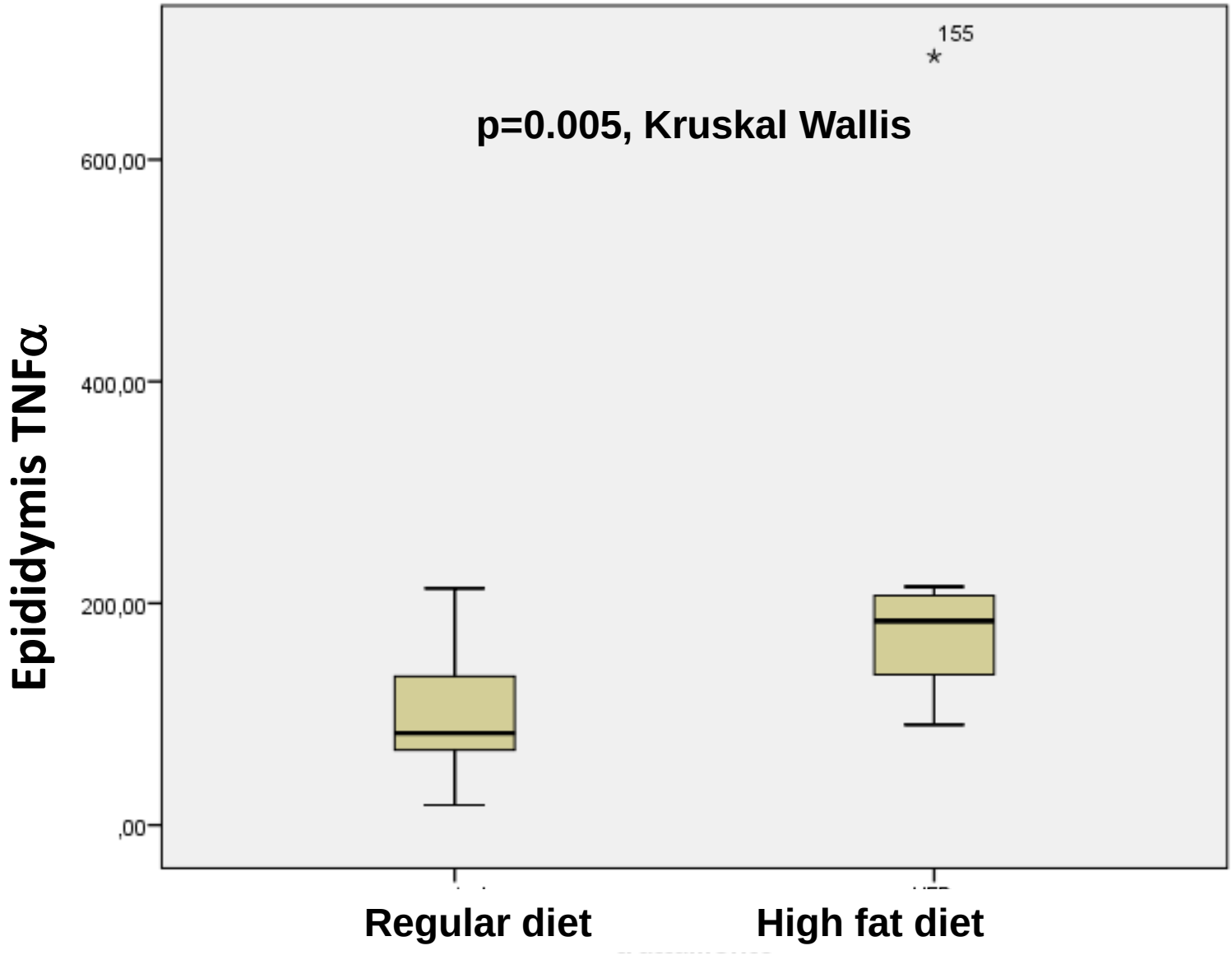
Correspondence should be addressed to C Mallidis at Centre of Reproductive Medicine and Andrology, University of Münster; Email: con.mallidis@ukmuenster.de

In the testis MetS is associated with:

- **Decreased steroidogenic enzymes**
- **No major changes in testicular histology**

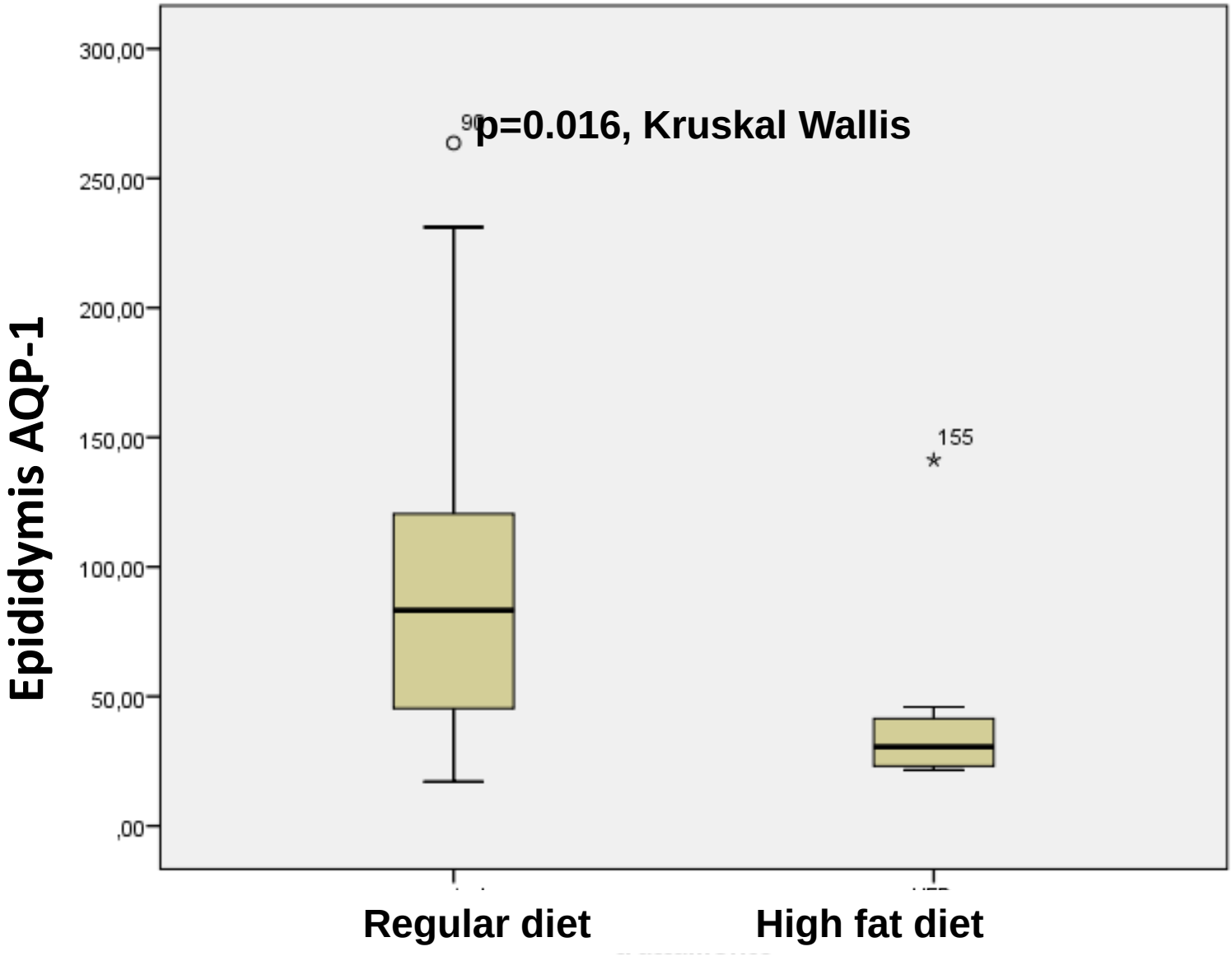


Effect of high fat diet on epididymal TNFα gene expression in MetS rabbits



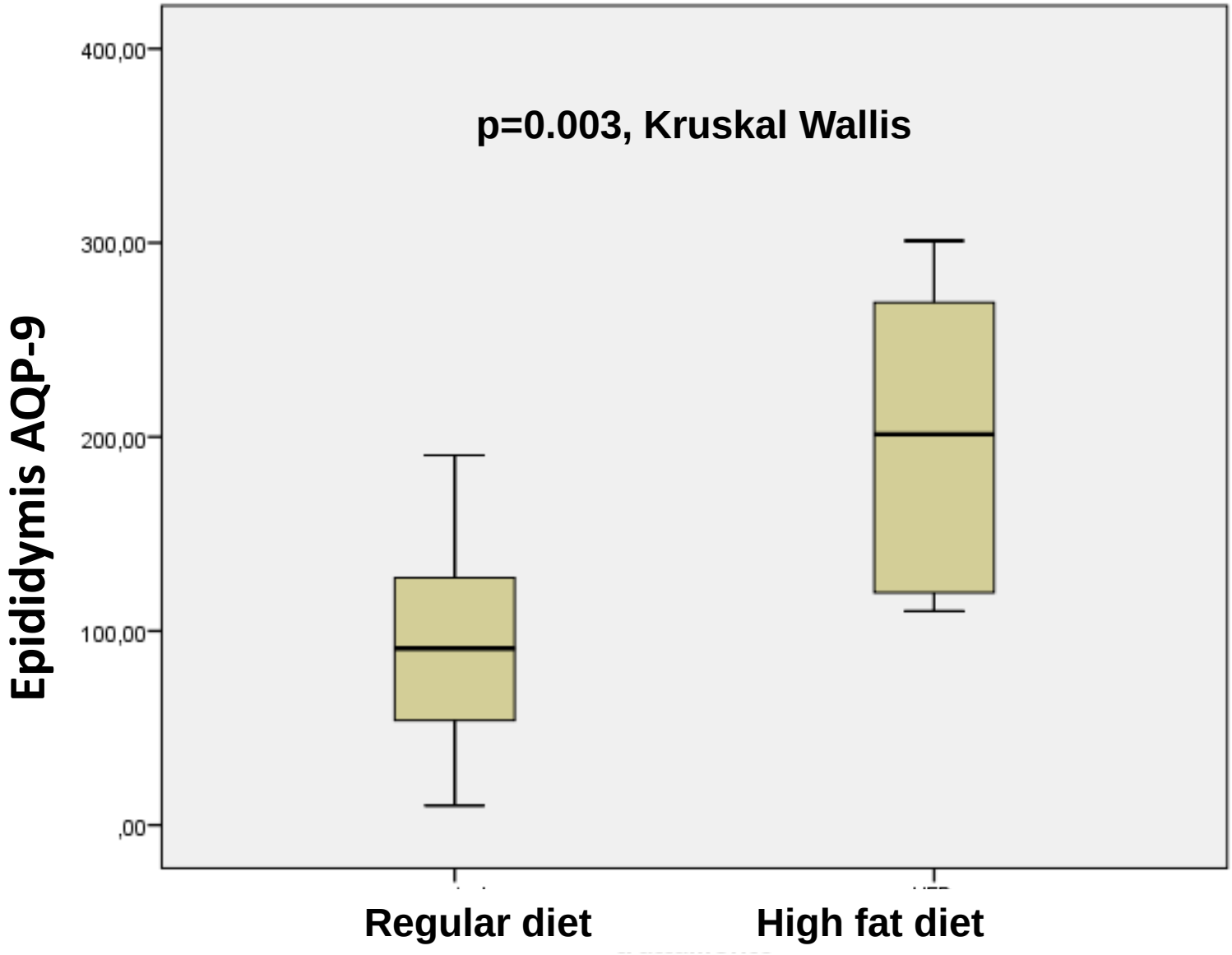
Marchiani et al., unpublished

Effect of high fat diet on epididymal aquaporin 1 gene expression in MetS rabbits



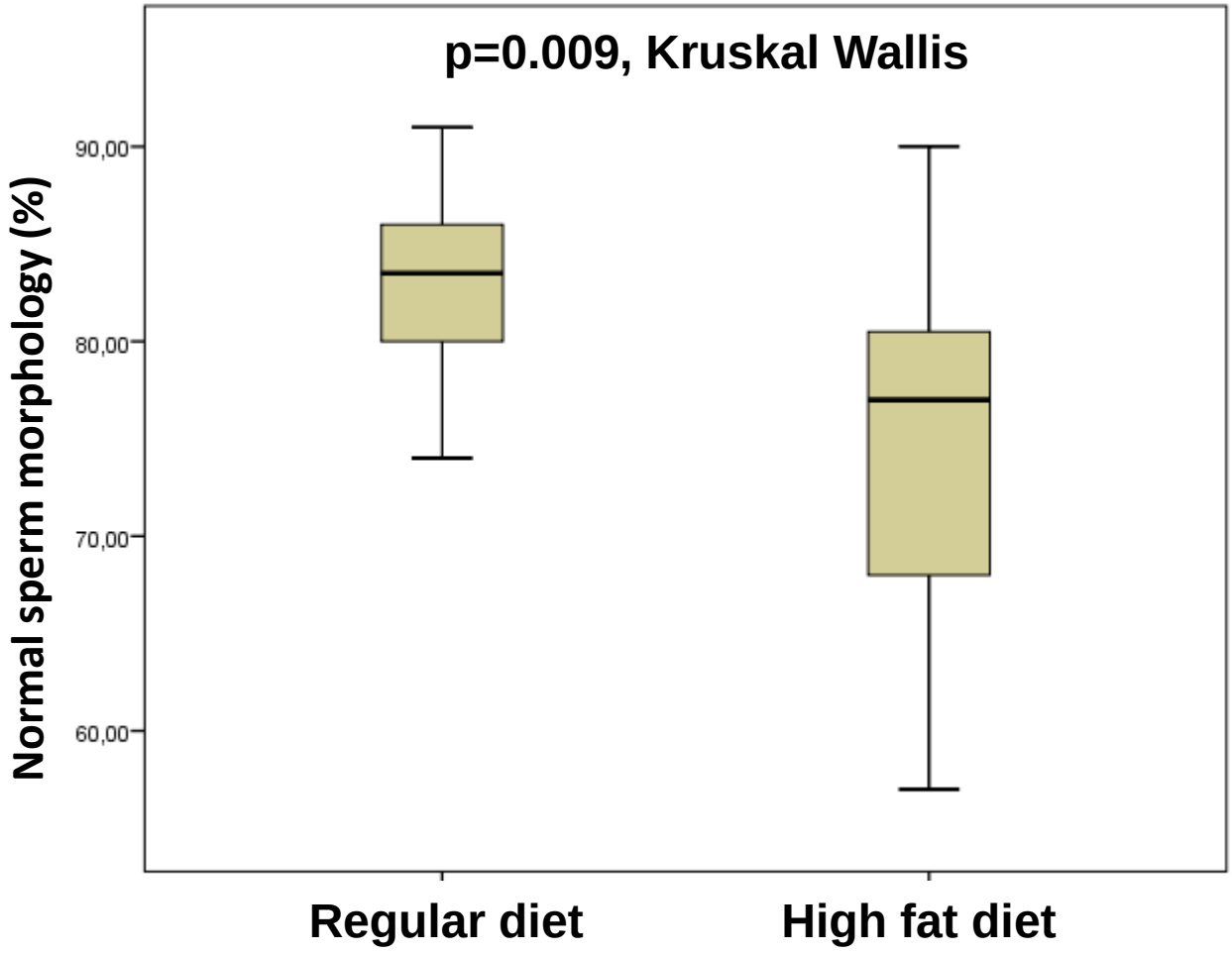
Marchiani et al., unpublished

Effect of high fat diet on epididymal aquaporin 9 gene expression in MetS rabbits



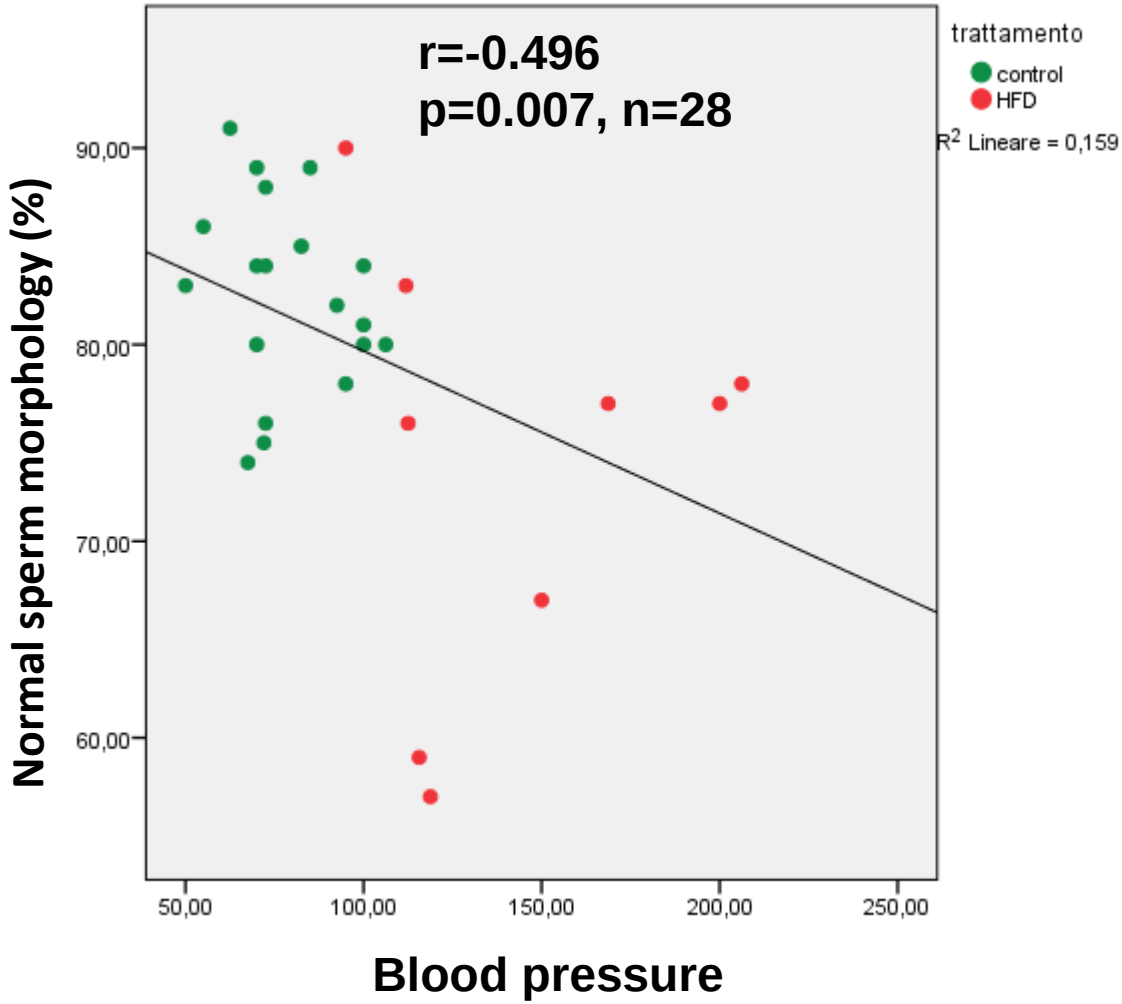
Marchiani et al., unpublished

Effect of high fat diet on epididymal sperm morphology in MetS rabbits



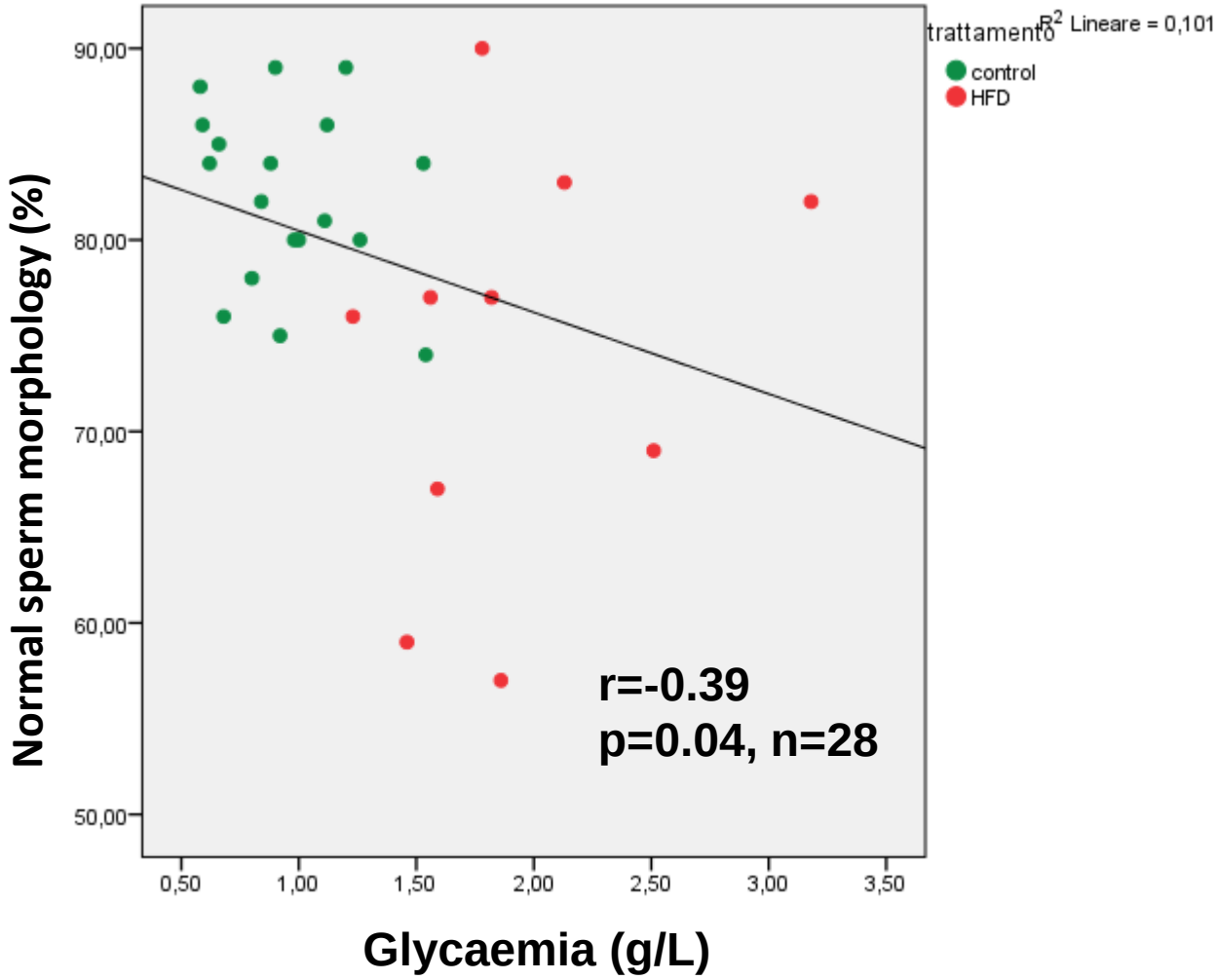
Marchiani et al., unpublished

Effect of high fat diet on epididymal sperm morphology in MetS rabbits



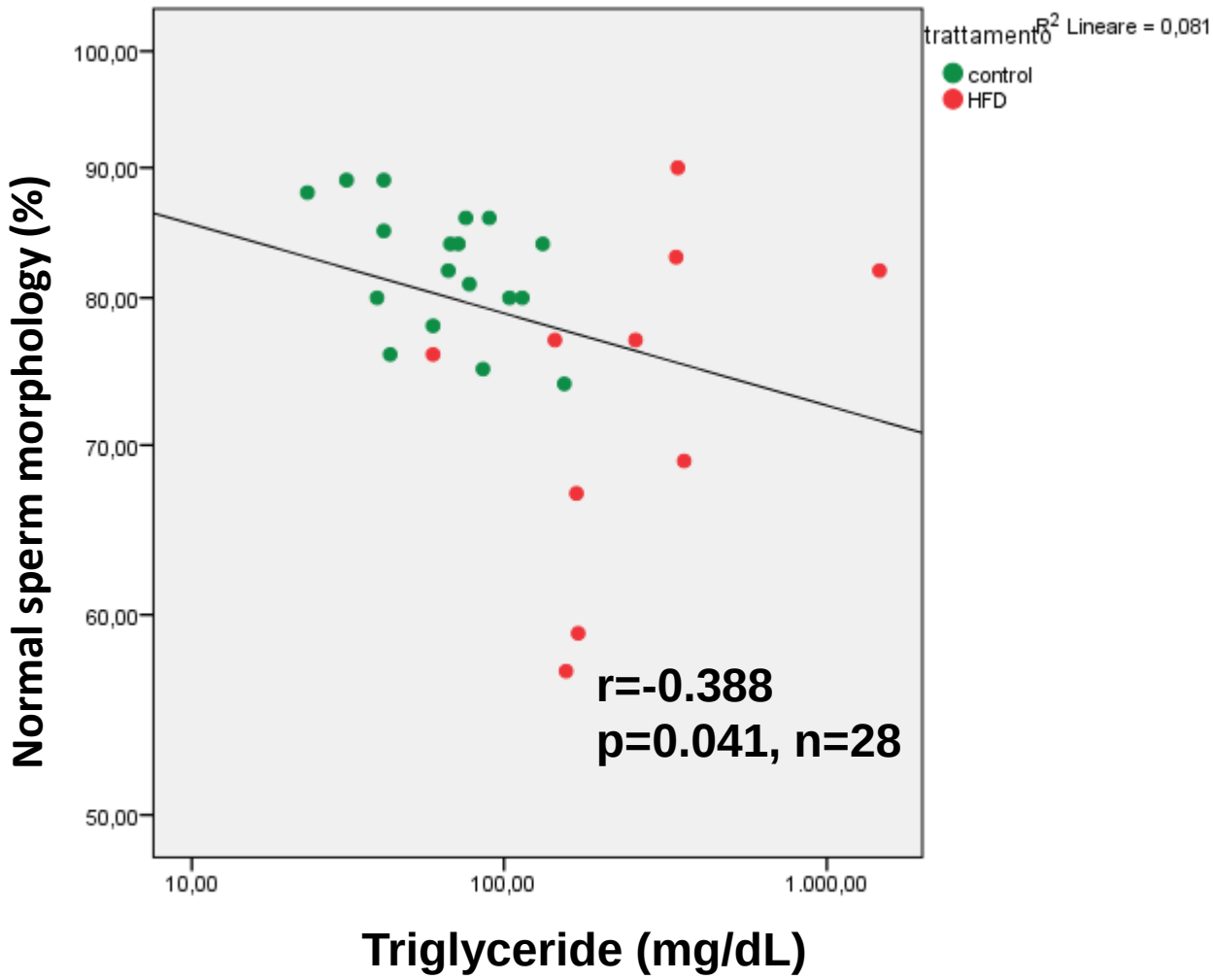
Marchiani et al., unpublished

Effect of high fat diet on epididymal sperm morphology in MetS rabbits



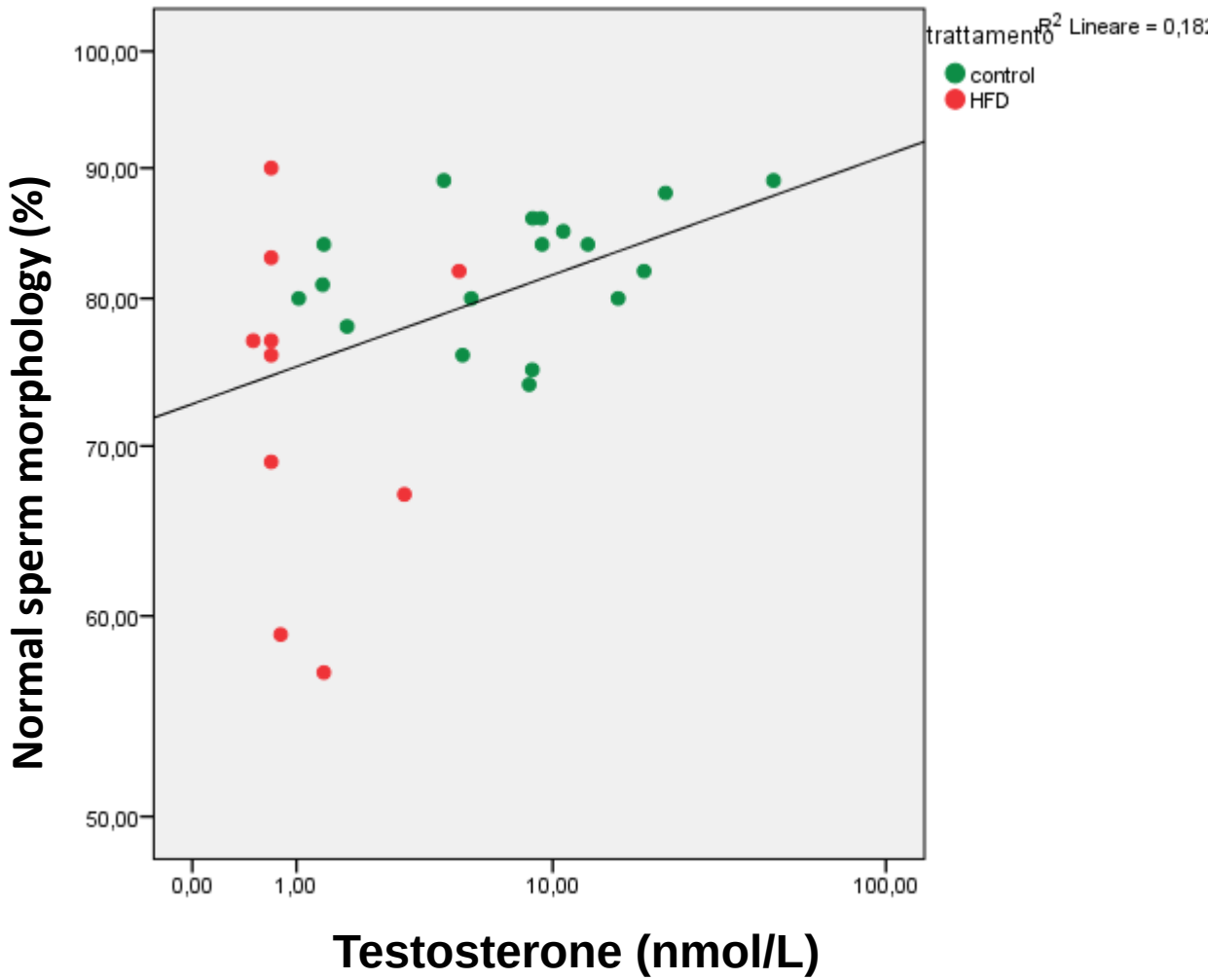
Marchiani et al., unpublished

Effect of high fat diet on epididymal sperm morphology in MetS rabbits

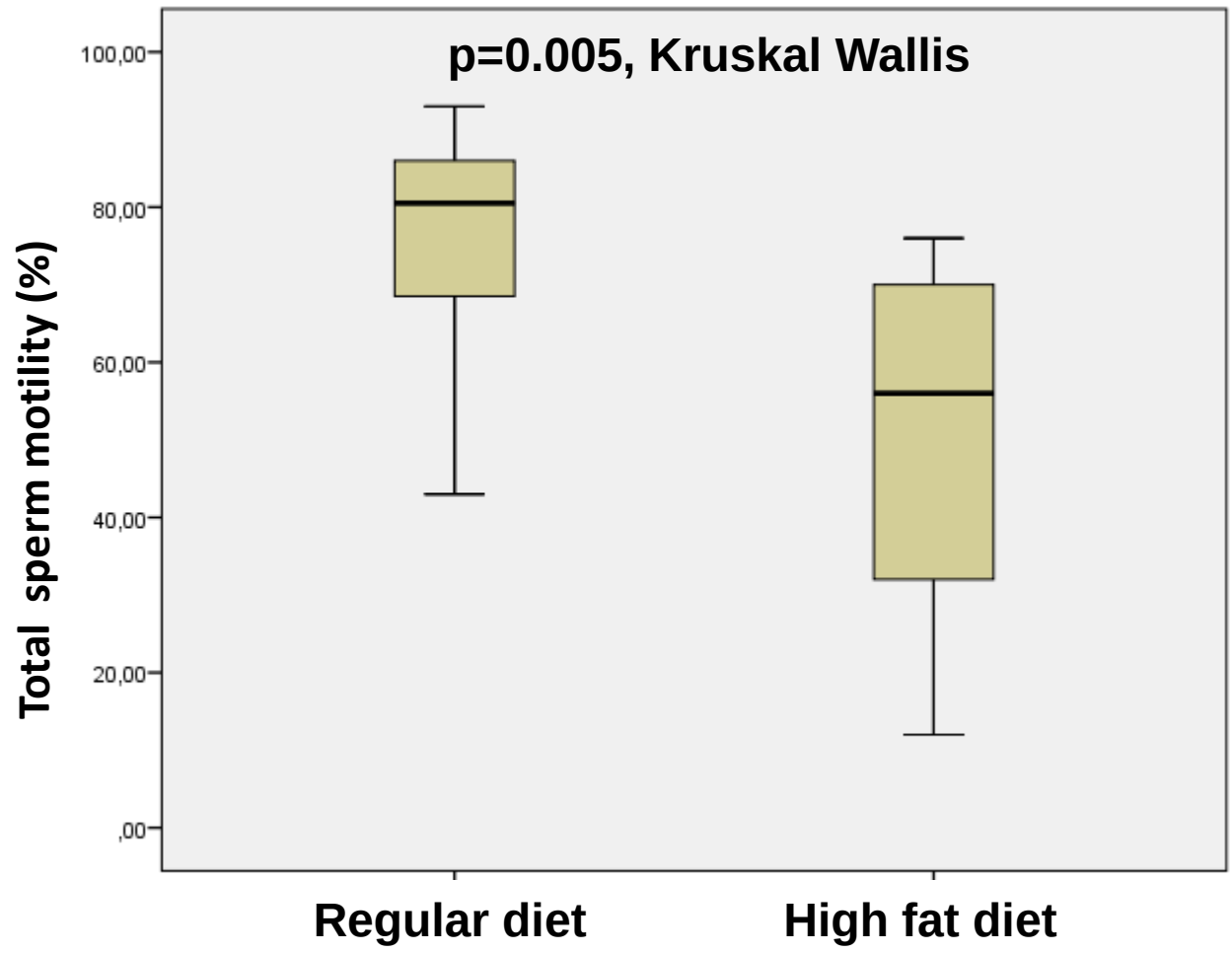


Marchiani et al., unpublished

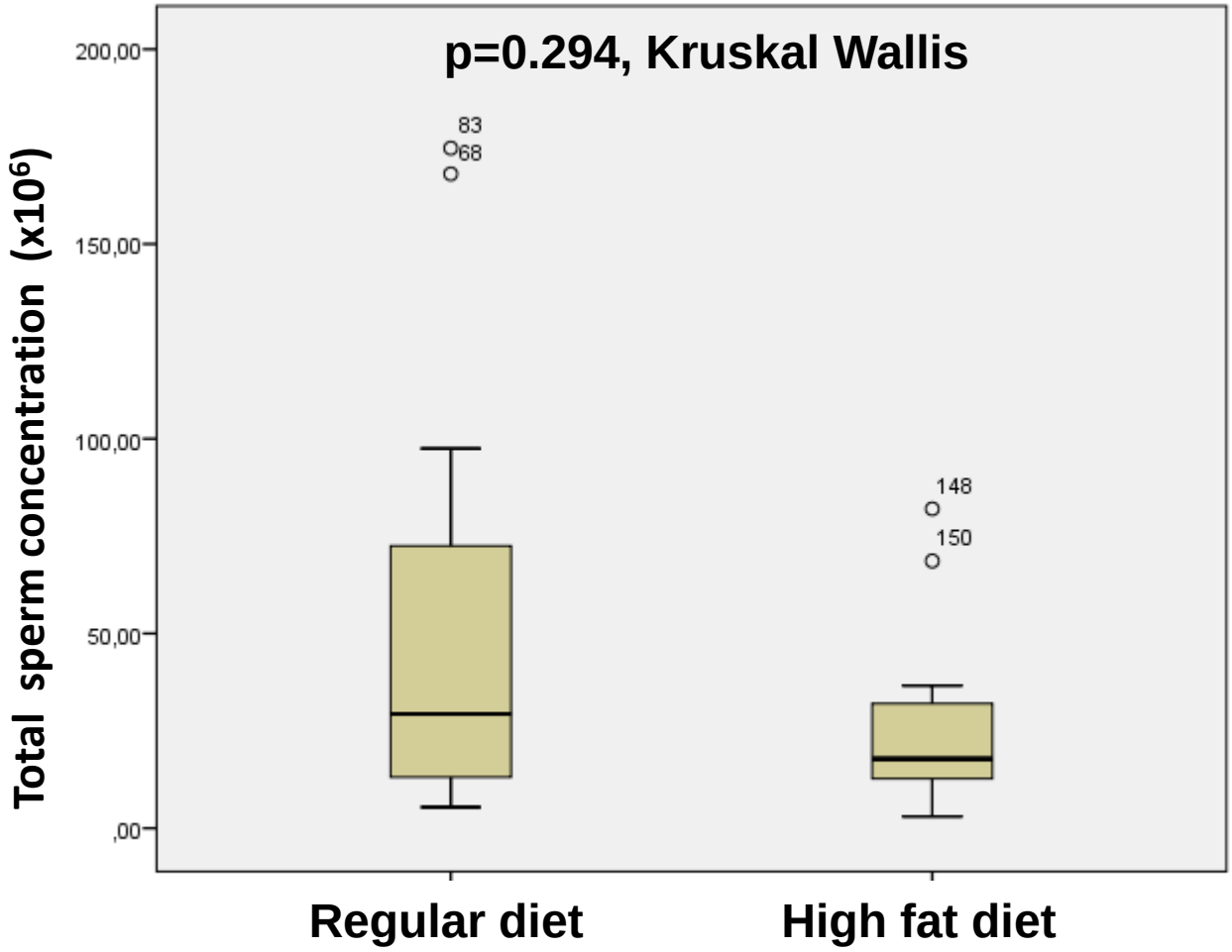
Effect of high fat diet on epididymal sperm morphology in MetS rabbits



Effect of high fat diet on epididymal sperm motility in MetS rabbits



Effect of high fat diet on epididymal sperm concentration in MetS rabbits



Marchiani et al., unpublished

Final take-home messages for MetS and male infertility:

- **MetS (↑ waist, dyslipidaemia) is associated with LOH & testis inhomogeneity**
- **MetS (↑ BP) is associated with abnormal sperm morphology**
- **MetS (↑ waist, ↑ BP) is associated with arteriogenic ED**
- **MetS is associated with epididymal inhomogeneity and rete testis dilation**
- **MetS is associated with depressive symptoms**
- **MetS (↑ waist, dyslipidaemia) is associated with ↑ insulin and BPE**
- **MetS (↑ waist) is associated with prostate inflammation**
- **Prostatitis-like symptoms are not associated with semen abnormalities**

MetS is associated with marginal changes of reproductive functions

Aknowledgements

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