

# Testosterone Deficiency and Hypogonadism in Aging Male Patients with Chronic Disease

A Comparison of HIV Infected Persons, Type 2 Diabetes and Control Patients:

Results from the HYPE Substudy of the German 50/2010 Cohort Study

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## Background

Testosterone deficiency (TD) and hypogonadism (HG) are more prevalent in chronically ill persons. Both are of growing relevance in HIV positive patients (HIV+), mainly due to their increasing life-expectancy and their various co-morbidities. This is the first comparison of aging HIV+ males to type 2 diabetes patients (DM2) and control patients without any severe chronic or malignant disease.

## Methods

HYPE is a cross-sectional substudy of the German 50/2010 cohort study, comparing aging HIV+ with DM2 and control patients, the latter without any severe chronic or malignant disease, all male and aged  $\geq 50$  years.

Objectives were to compare TD and HG (using the Aging Male Symptoms Scale [AMS]) in the three groups and to identify factors abetting hypogonadism.

Total testosterone (tT), sexual hormone binding protein (SHBG), luteinizing hormone (LH), and albumin were measured in a central laboratory; free testosterone (fT) was calculated using Vermeulen's formula (1999). TD was defined as tT  $< 3.5$  ng/ml ( $< 12$  nmol/l) and/or fT  $< 65$  pg/ml ( $< 225$  pmol/l). HG was defined as TD in combination with an AMS score  $\geq 37$  (moderate to severe impairment).

To evaluate factors independently associated with TD or HG multivariate logistic regression analyses were performed. Variables of interest were HIV infection, DM2, BMI  $> 30$  kg/m<sup>2</sup>, age  $> 60$  years,  $\geq 2$  co-morbidities, physical activity ( $\geq 2$  times weekly), alcohol use ( $\geq 2$  times weekly), smoking and specific co-medication (i.e. neuroleptics, antiepileptics, steroids, opiates). Patients with HCV infection and documented testosterone substitution were excluded.

## Results

### Study population

322 patients were eligible for analysis (87 HIV+ [98% on ART], 118 DM2, 117 controls). Median age was 58, 61, and 59 years (range: 52-81y, 51-86y, and 52-88y). BMI  $> 30$  kg/m<sup>2</sup> was observed in 10% of HIV+, 46% of DM2, and 21% of controls.

Table 1. Patient characteristics

	HIV+ (N=87)	DM2 (N=118)	Controls (N=117)	P-value
Age $> 60$ years [%]	39	64	46	0.001
BMI $> 30$ kg/m <sup>2</sup> [%]	10	46	21	$< 0.001$
$\geq 2$ co-morbidities [%]	57	73	56	0.016
Physical activity ( $\geq 2$ x/week) [%]	35	26	41	0.058
Alcohol use ( $\geq 2$ x/week) [%]	9	18	22	0.062
Smoking [%]	28	18	19	0.186
Specific co-medication [%]	6	2	2	0.148

### Acknowledgment

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### Participating centers: The 50/2010 HYPE Study Group

Dr. Baumann, Neuss; Dres. Baumgarten/Dupke/Carganico, Berlin; Dres. Brust/Schuster/Ploeger/Hensel, Mannheim; Dres. Denger/Sammler, Friedrichsthal; Dr. Dix, Konstanz; Dres. Friese/Cseke, Giessen; Dres. Gippert/Hartmann/Quaing, Muenster; Dr. Gospodinov, Saarbruecken; Dr. Haberl, Frankfurt; Dres. Hanhoff/Fussen, Geilenkirchen; Dres. Klausen/Hintsche, Berlin; Dres. Hoffmann/Hansen, Hamburg; Dres. Jaegel-Guedes/Jaeger, Munich; Dr. Karwat, Munich; Dr. Knecht/Klauke, Frankfurt; Dres. Koeppel/Kreckel, Berlin; Dres. Kuhlmann/Holm/Heiken, Hannover; Dr. Lauenroth-Mai, Berlin; Dr. Mauruschat, Wuppertal; Dres. Mayr/Schmidt, Berlin; Dr. Meurer, Munich; Dres. Mosthaf/Procaccianti/Zutavern-Bechtold, Karlsruhe; Dres. Pauli/Becker, Munich; Dres. Plettenberg/Stoehr, ifi, Hamburg; Dres. Rausch/Freiwald, Berlin; Dres. Reith/Gottstein, Duesseldorf; Dr. Schappert, Mainz; Dr. Schlote, Berlin; Dr. Schoelzel, Troisdorf; Dres. Schranz/Fischer, Berlin; Dr. Schuler, Berlin; Dr. Stuendel, Berlin; Dr. Ulmer/Frietsch/Mueller, Stuttgart; Dr. Usadel, Freiburg; Dr. Wuensche, Berlin; Dr. Zebhauser, Munich.

## Prevalence of testosterone deficiency (TD) and hypogonadism (HG)

The comparisons of hormone levels (tT, fT and SHBG) between study groups are shown in figures 1a - 1c (box plot presentations incl. the 25th, 50th (median) and 75th percentiles).

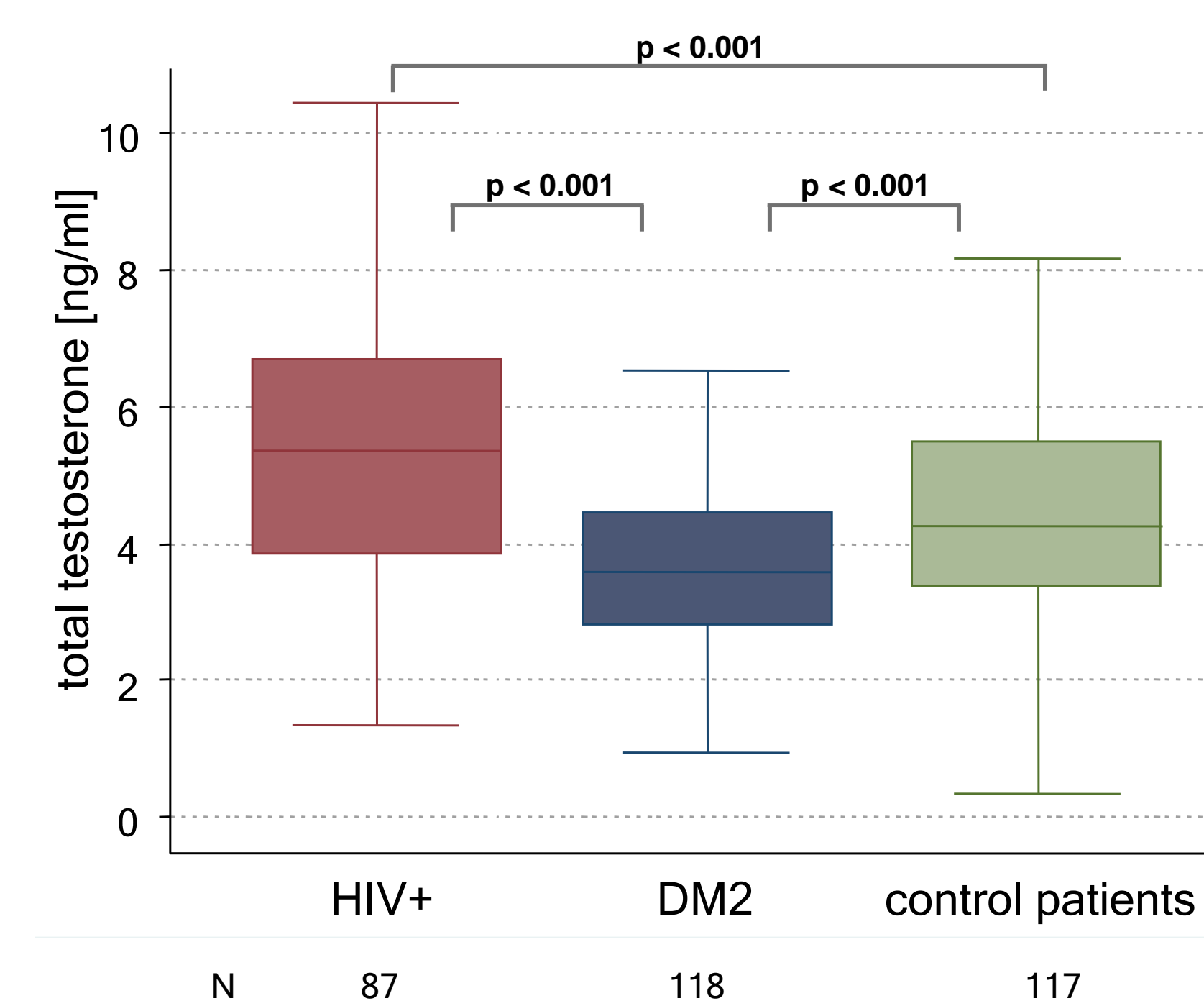


Figure 1a.

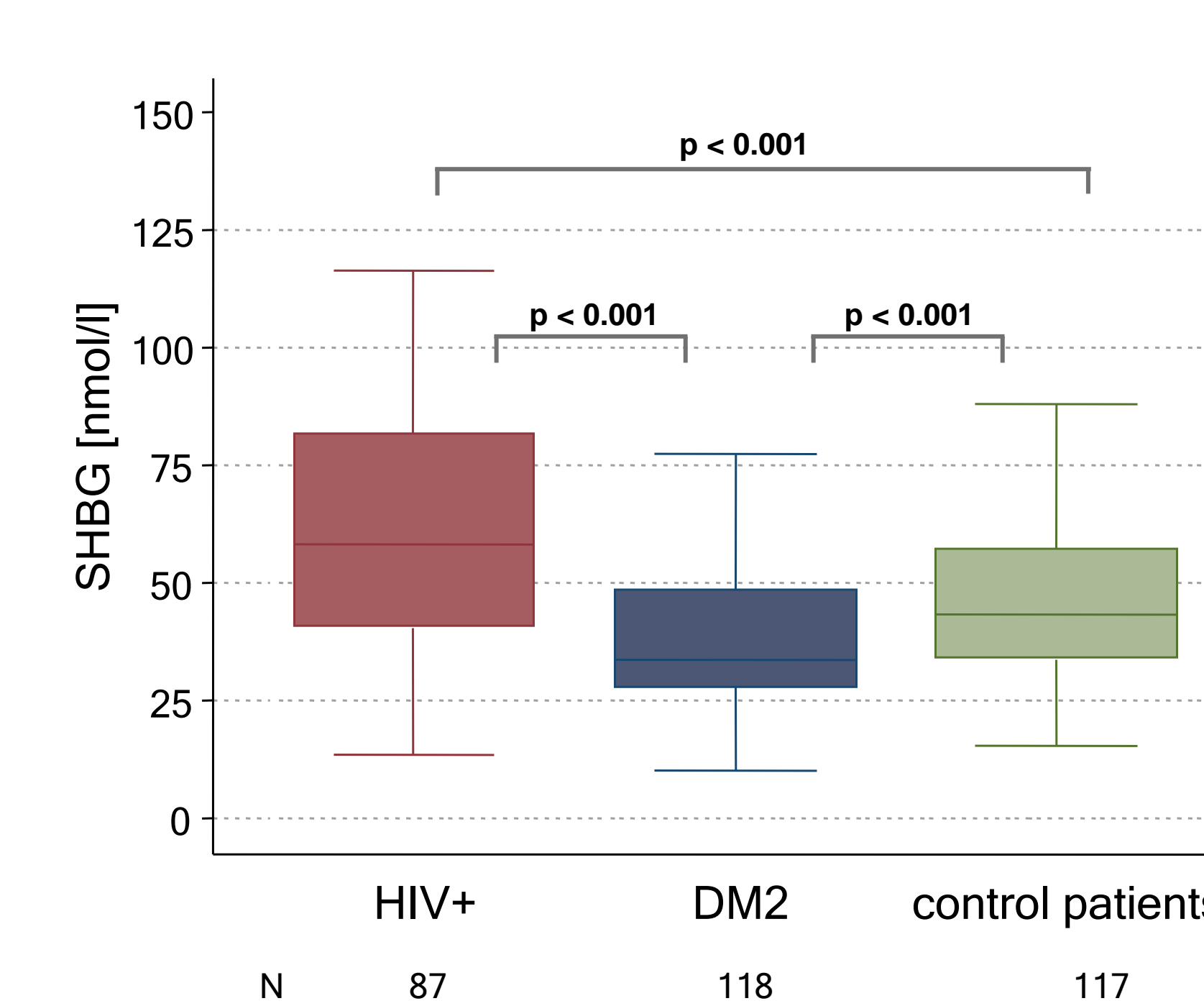


Figure 1b.

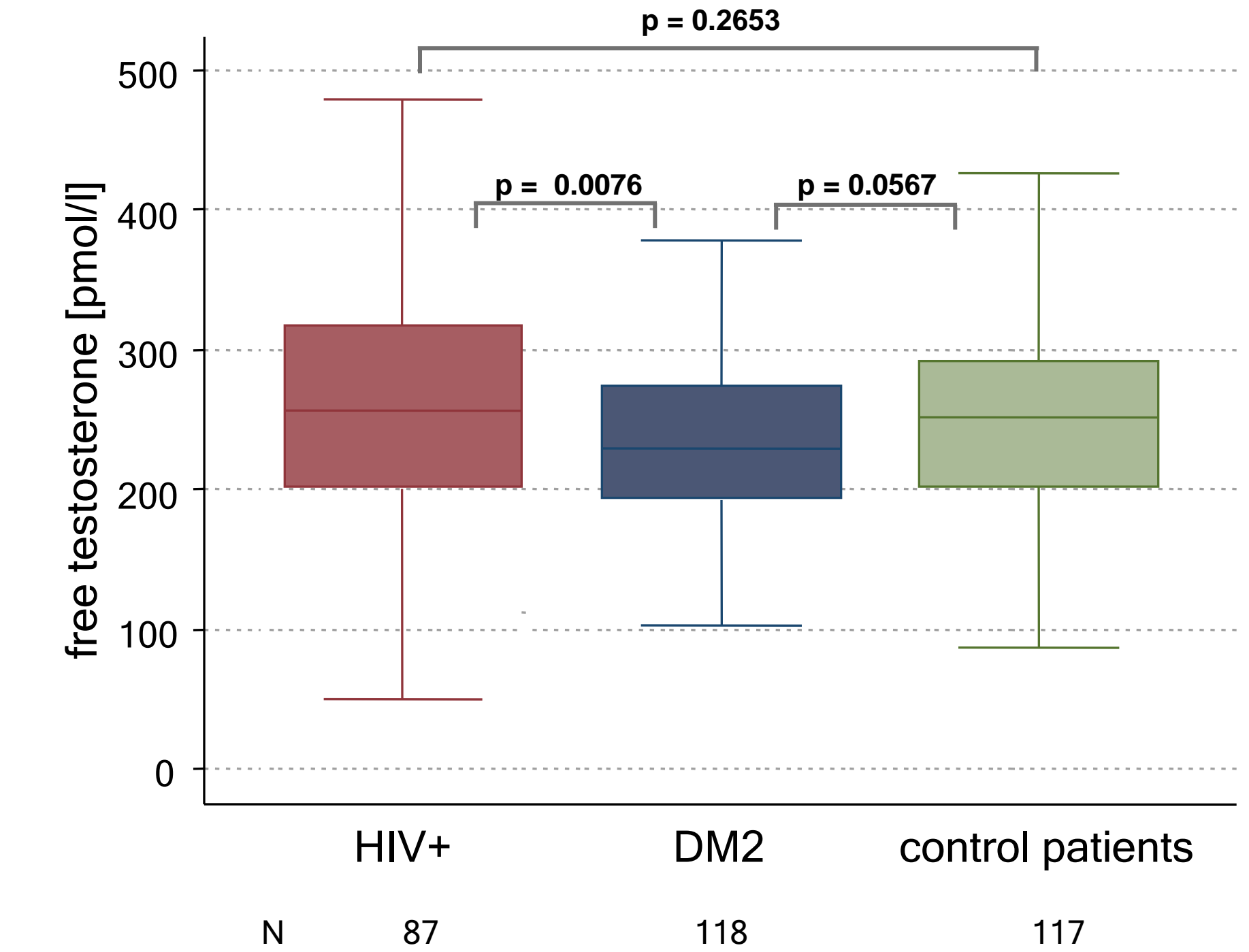


Figure 1c.

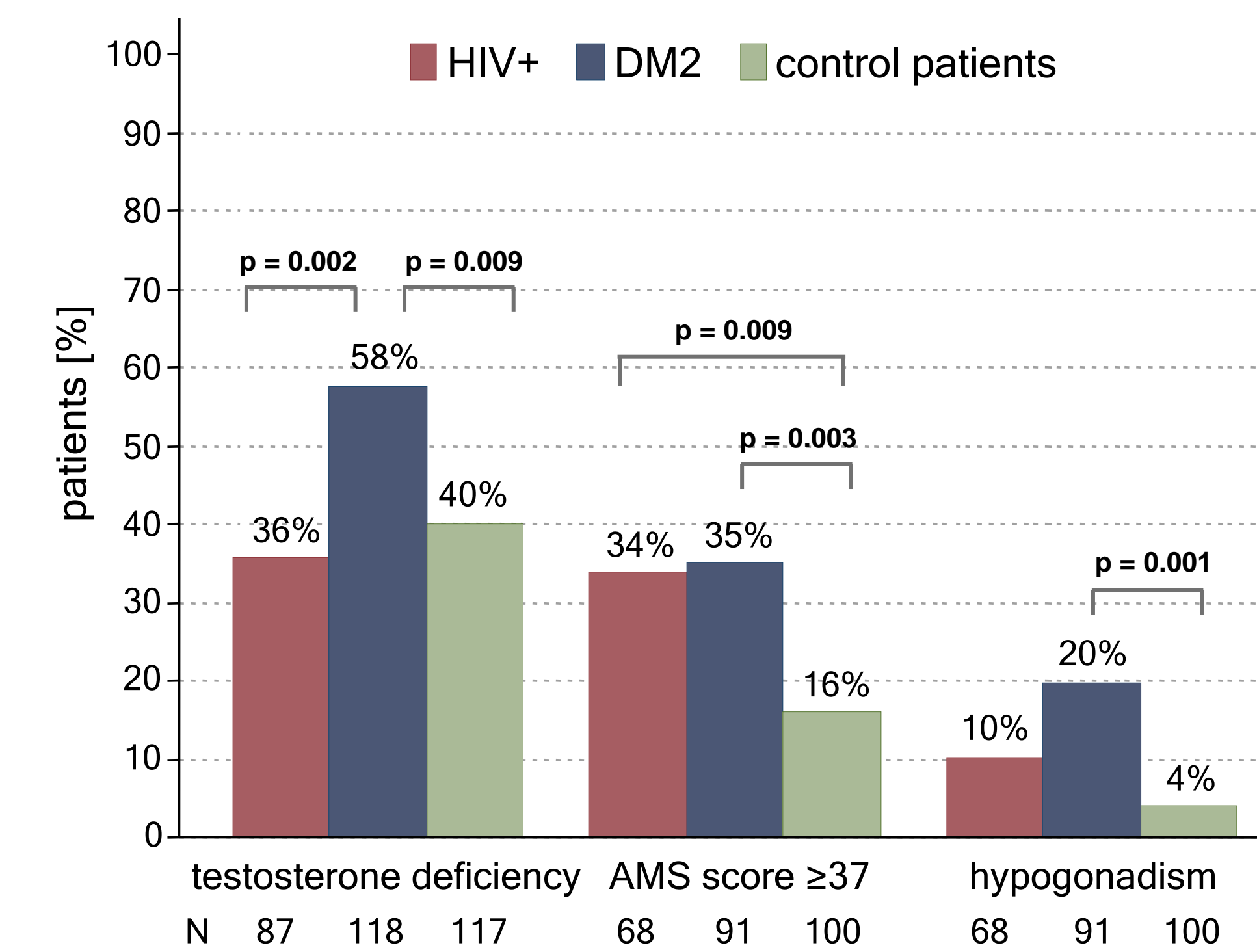


Figure 2. Prevalence of TD, high symptom scores (AMS score  $\geq 37$ ) and HG in HIV+, DM2 and control patients. Only p-levels  $< 0.05$  for pairwise comparisons are shown in the figure.

## Factors associated with testosterone deficiency (TD) and hypogonadism (HG)

Table 2. Univariate analyses

	Presence of TD	P-value	Presence of HG	P-value
HIV+ vs control patients	35.6% vs 40.2%	0.561	10.3% vs 4.0%	0.122
DM2 vs control patients	57.6% vs 40.2%	0.009	19.8% vs 4.0%	0.001
Age $> 60$ vs $\leq 60$ years	51.5% vs 39.0%	0.026	13.7% vs 8.6%	0.189
BMI $> 30$ vs $\leq 30$ kg/m <sup>2</sup>	64.3% vs 39.2%	$< 0.001$	18.6% vs 7.8%	0.022
Co-morbidities $\geq 2$ vs $< 2$	48.5% vs 40.0%	0.165	13.8% vs 7.0%	0.107
Physical activity $\geq 2$ x vs $< 2$ x/week	41.4% vs 48.1%	0.279	11.0% vs 11.0%	1.000
Alcohol use $\geq 2$ x vs $< 2$ x/week	44.4% vs 45.3%	1.000	8.9% vs 11.7%	0.796
Smoking yes vs no	37.3% vs 47.5%	0.168	7.7% vs 12.1%	0.467
Specific co-medication yes vs no	22.2% vs 46.0%	0.191	28.6% vs 10.7%	0.178

### Multivariate analyses

#### Testosterone deficiency

Factors independently associated with TD were age  $> 60$  years (OR 1.8, 95% CI 1.1-3.0) and a high BMI (OR 2.7, 95% CI 1.5-4.8).

#### Hypogonadism

The factor independently associated with HG was DM2 (OR 4.0, 95% CI 1.2-13.0); there was a trend for high BMI (OR 2.6, 95% CI 0.9-5.7,  $p = 0.09$ ) and only a marginal trend for HIV infection (OR 2.9, 95% CI 0.8-10.8,  $p = 0.12$ ).

## Conclusions

In this cohort, testosterone deficiency in treated aging HIV+ males was similar to control patients. However, a high BMI, a risk factor for TD, was more common in controls. HIV infection was associated with a higher AMS score, suggesting TD in HIV+ may be more often symptomatic than in HIV negative patients. The highest prevalence of both TD and HG was seen in DM2 patients. Higher age and a high BMI seem to contribute more markedly to TD and HG than treated HIV infection.