

1-h OGTT e rischio cardio-metabolico. Lo studio **CA**tanзарo **ME**tabolic **RI**sks factors (**CATAMERI**)

Giorgio Sesti

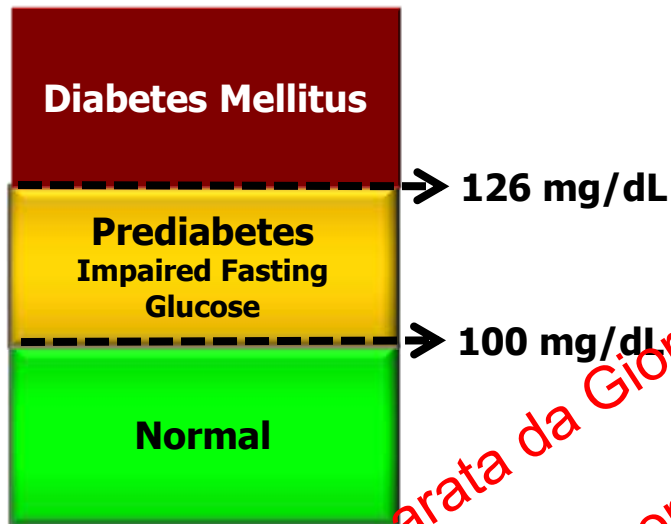


Università "Magna Graecia" di Catanzaro

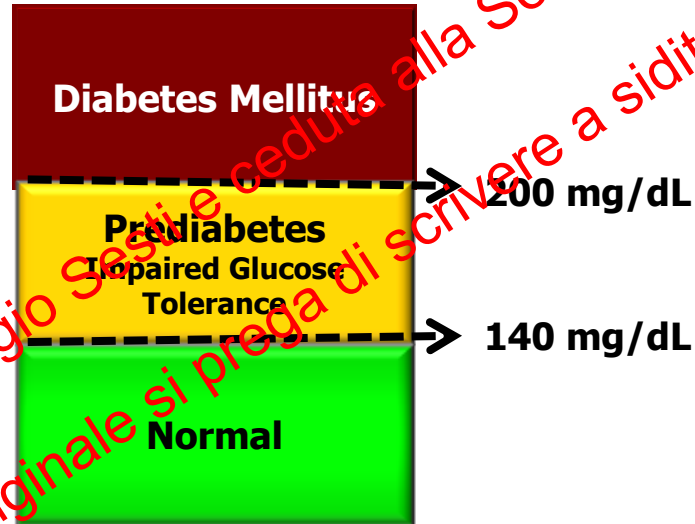


What is Prediabetes?

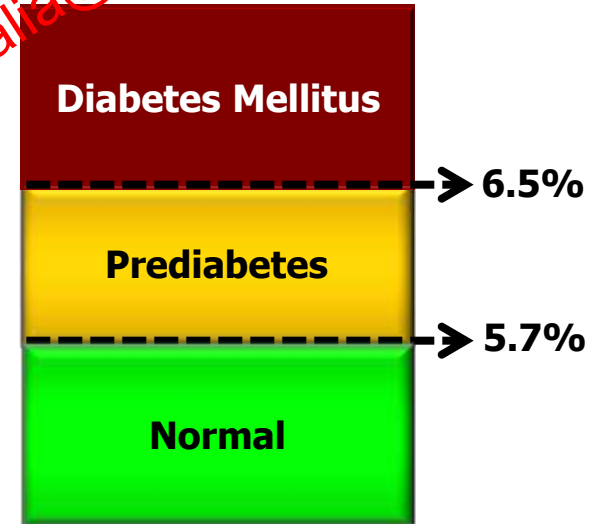
Fasting Plasma Glucose



2-hour Plasma Glucose On OGTT



Hemoglobin A1C



Any abnormality must be repeated and confirmed on a separate day

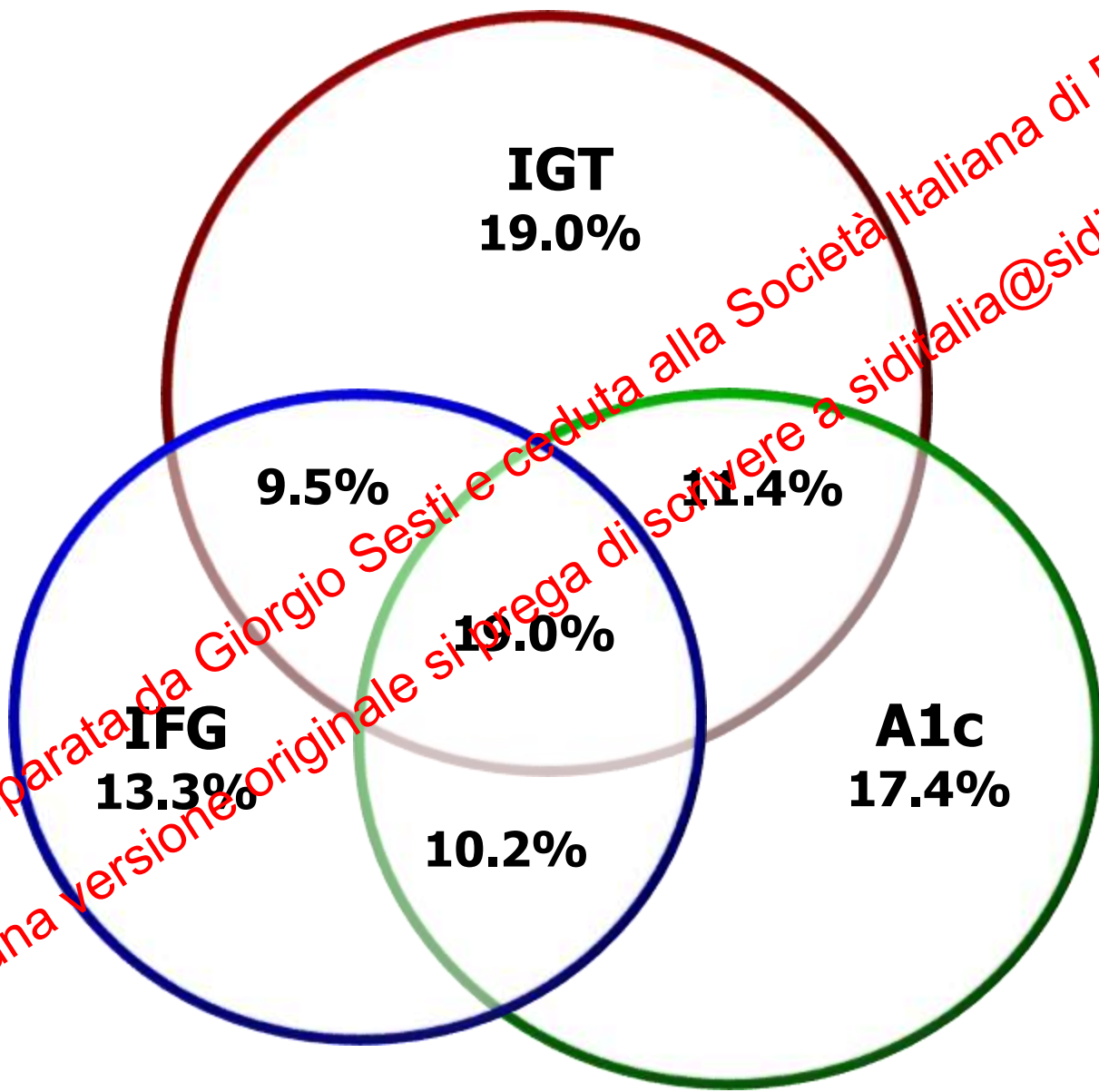
The diagnosis of diabetes can also be made based on unequivocal symptoms and a random glucose >200 mg/dL

Classification of glucose tolerance states - ADA

State	FPG (mg/dl)	2-h PG OGTT (mg/dl)	HbA1c (%)
NGT	<100	<140	<5.7
Isolated IFG	100-125	<140	<5.7
Isolated IGT	<100	140-199	<5.7
Isolated A1c	<100	<140	5.7-6.4
Combined IFG/IGT	100-125	140-199	<5.7
Combined IFG/A1c	100-125	<140	5.7-6.4
Combined IGT/A1c	<100	140-199	5.7-6.4
Combined IFG/IGT/A1c	100-125	140-199	5.7-6.4

Diapositiva preparata da Giorgio Sesti e ceduta alla Società Italiana di Diabetologia.
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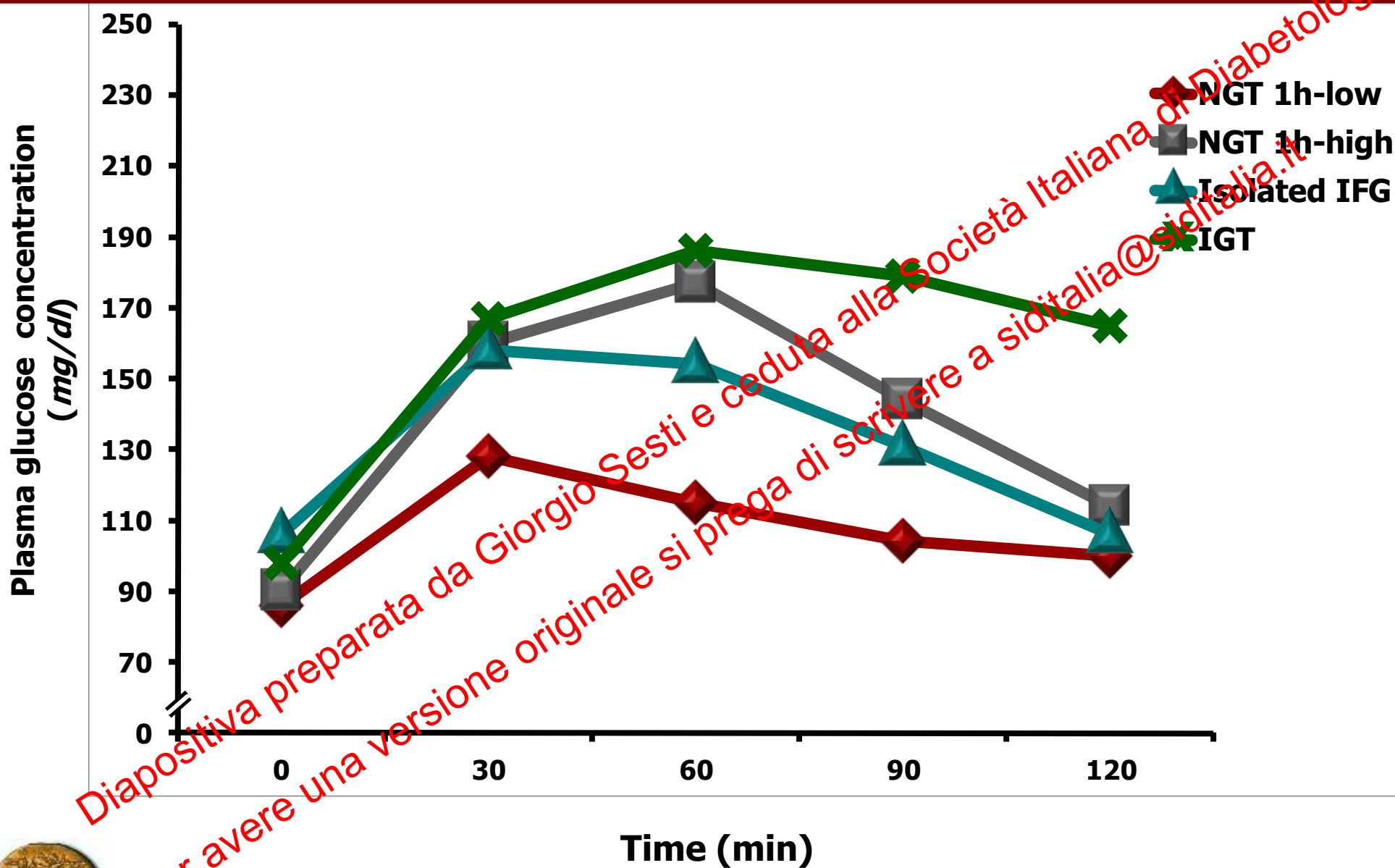
Venn diagram representing the percentage of elevated A1c, IGT, and IFG in an Italian cohort with dysglycemia (n=420)



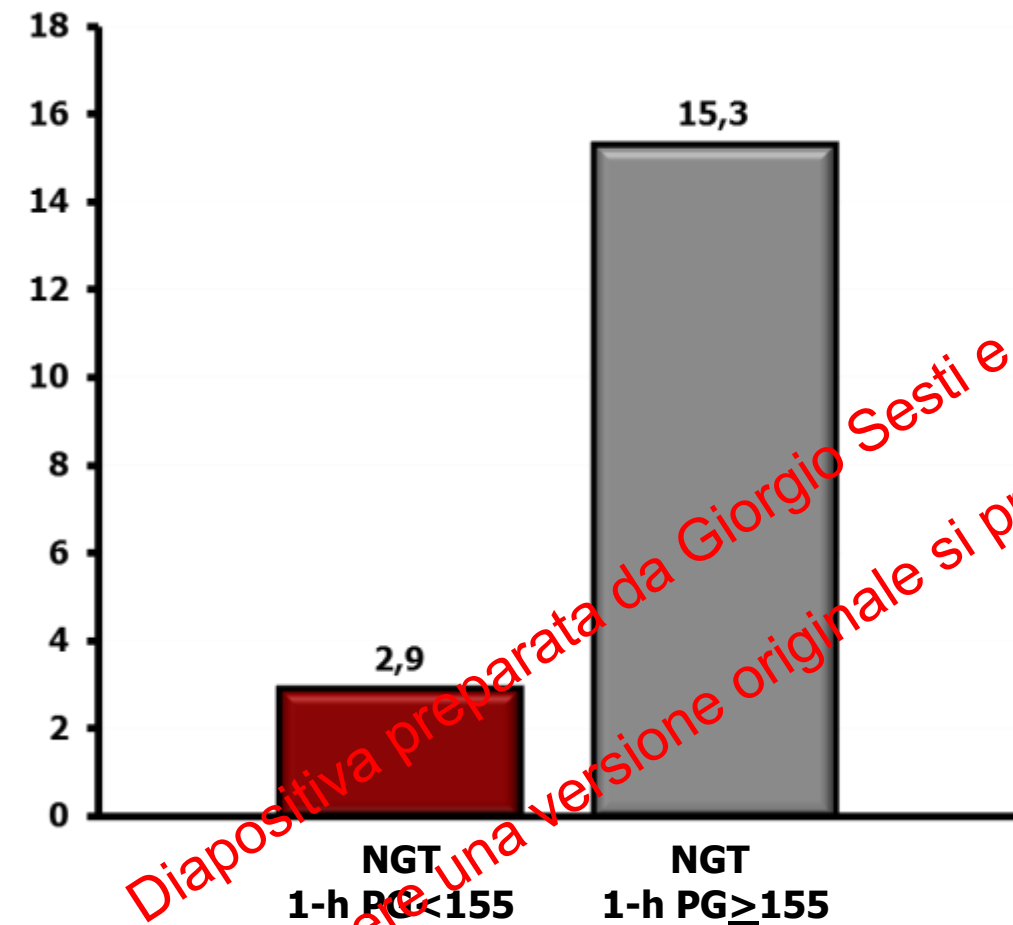
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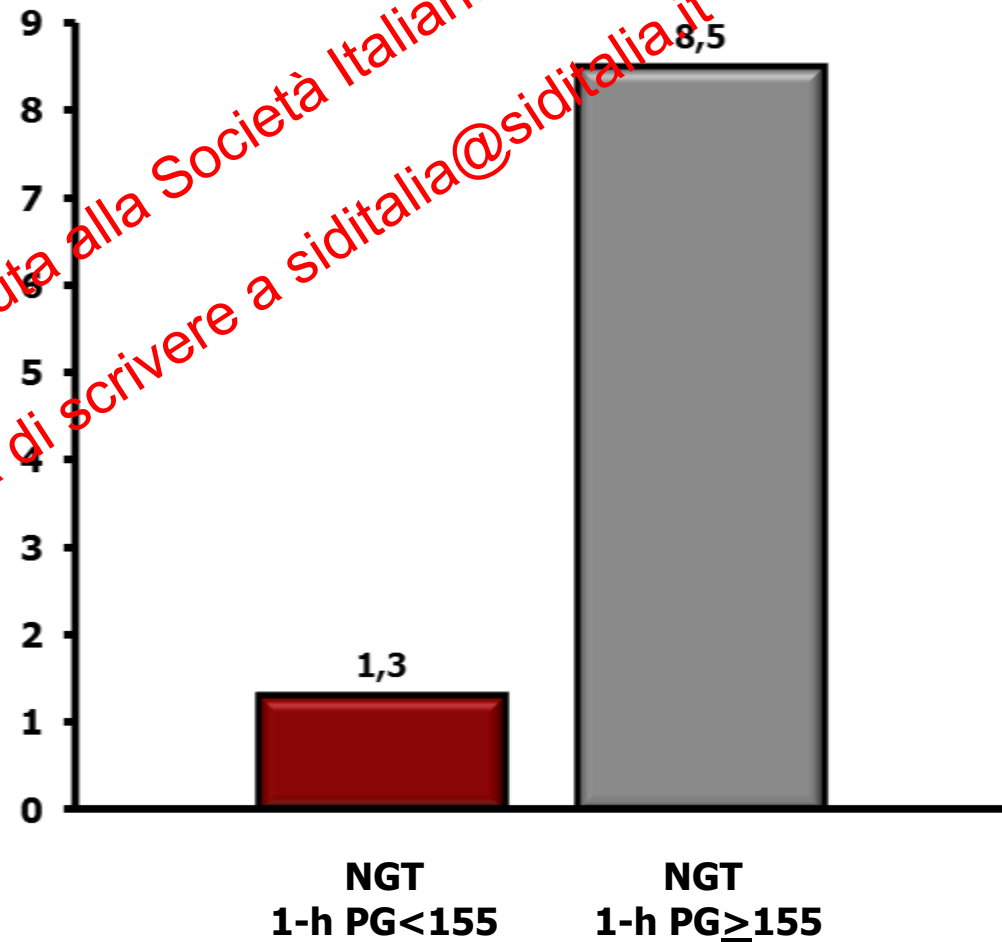
Plasma glucose levels during OGTT in subjects with NGT 1h-low, NGT 1h-high, isolated IFG and IGT



Incidence of type 2 diabetes according to 1-hour post-load plasma glucose (≥ 155 mg/dl) in the San Antonio Heart Study (n=1610)



Incidence of type 2 diabetes according to 1-hour post-load plasma glucose (≥ 155 mg/dl) in the Botnia Study (n=2442)



Area under the ROC curve for various predictive parameters for future development of T2DM

Parameter	ROC	Cutoff	Sensitivity	Specificity
Fasting plasma glucose	0.75			
Plasma glucose at 30 min	0.77			
Plasma glucose at 60 min	0.84	155	0.75	0.79
Plasma glucose at 120 min	0.79	140	0.51	0.92

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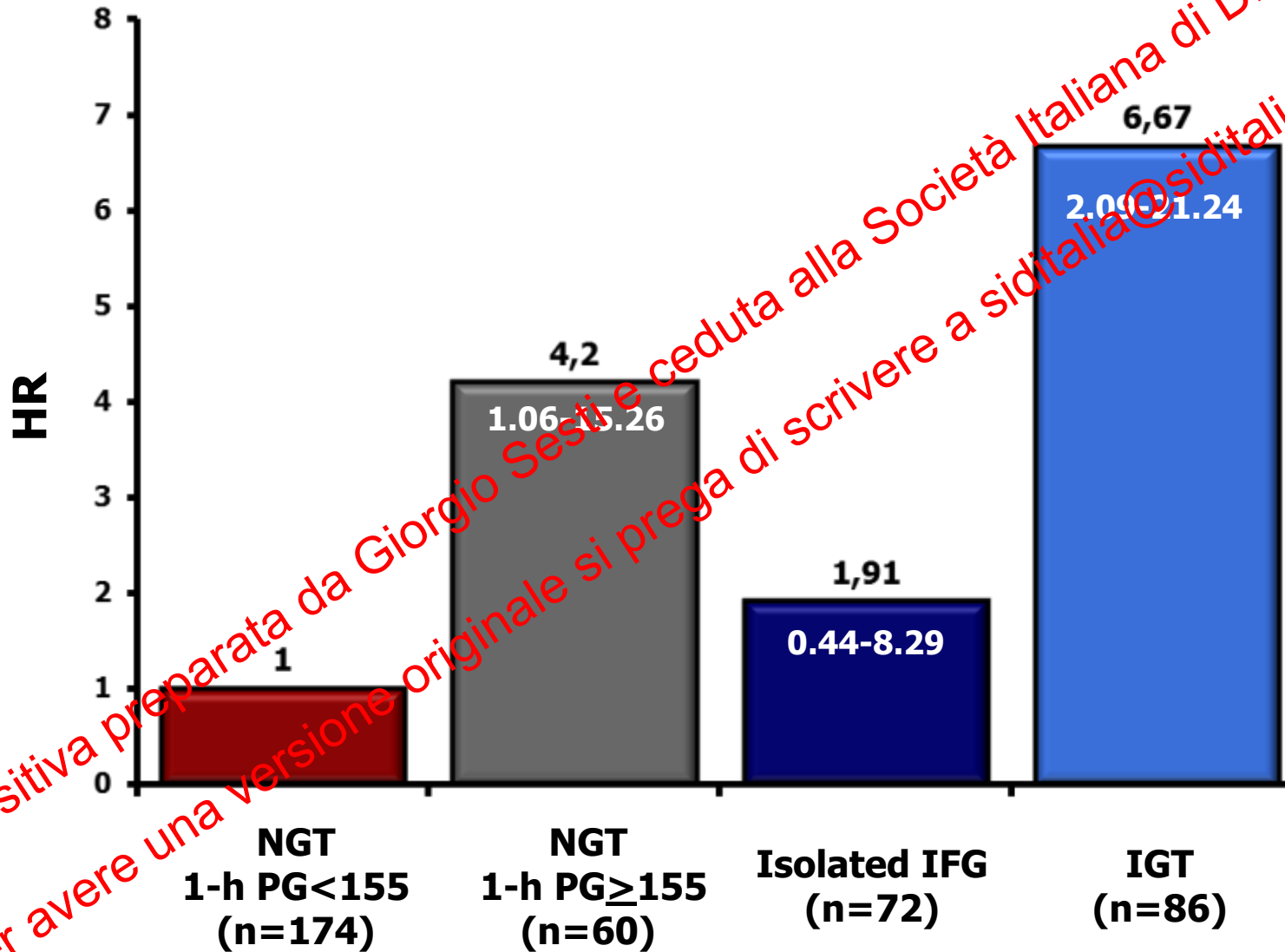
ARTICLE

Modelling of OGTT curve identifies 1 h plasma glucose level as a strong predictor of incident type 2 diabetes: results from two prospective cohorts

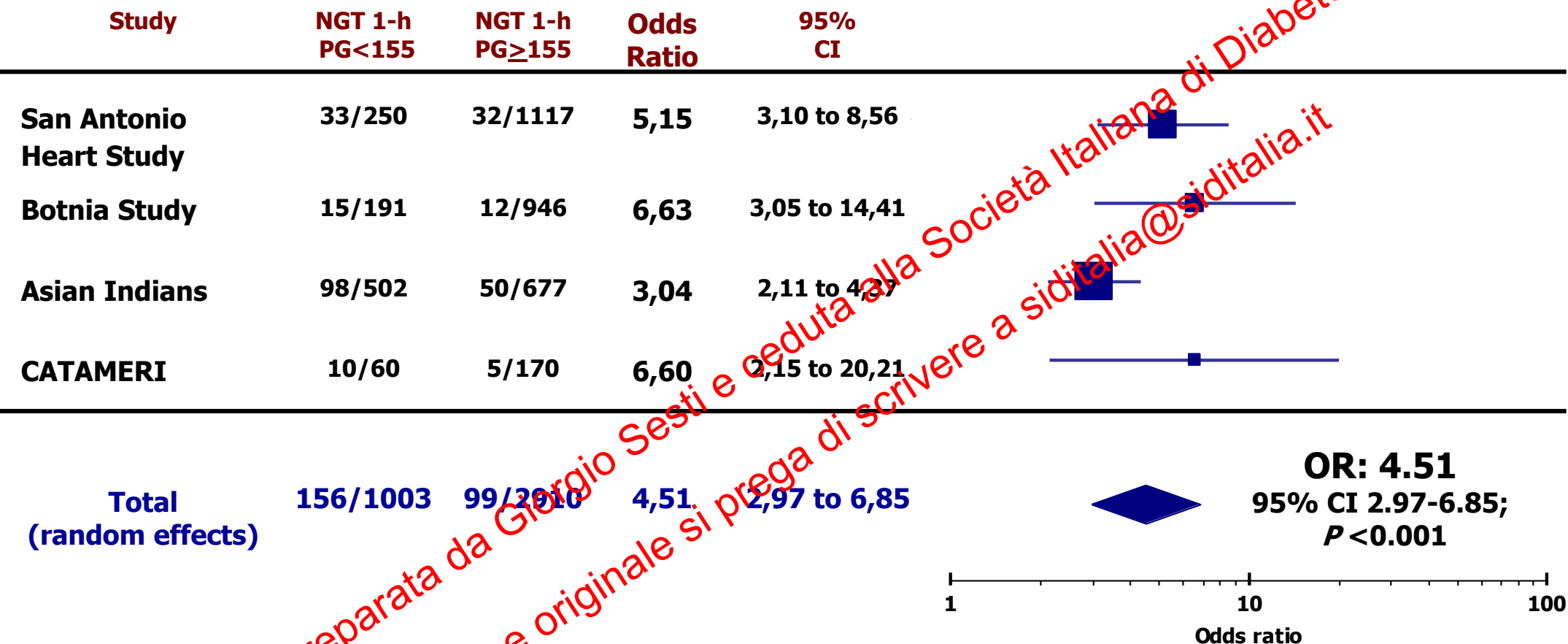
Akram Alyass • Peter Almgren • Mikael Akerlund • Jonathan Dushoff •
Bo Isomaa • Peter Nilsson • Taina Maija Tuomi • Valeriya Lyssenko •
Leif Groop • David Meier

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Cox regression analyses adjusted for age, gender and BMI at baseline comparing the risk of NGT 1h-high, isolated IFG and IGT to develop T2DM

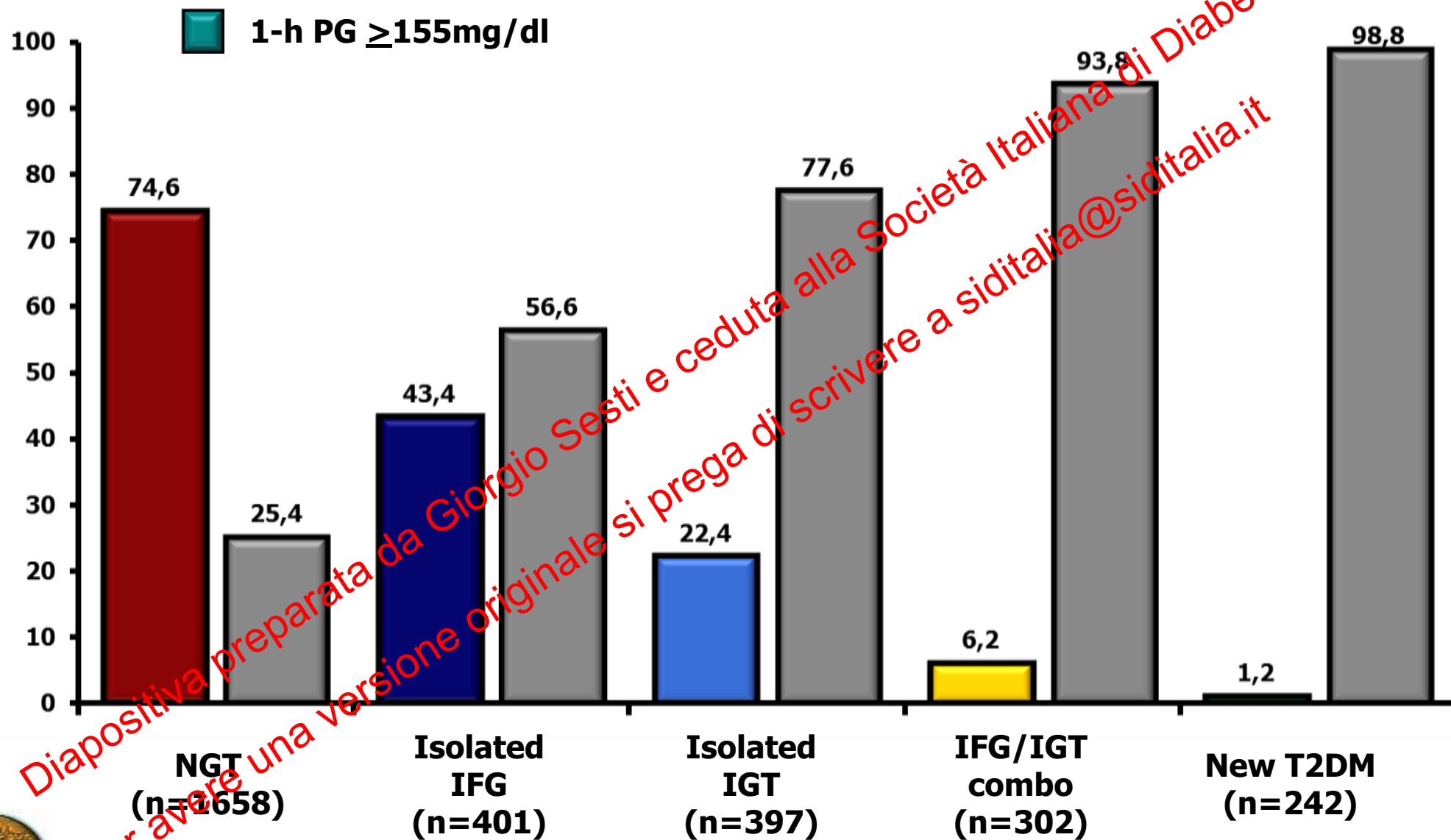


Meta-analysis of four prospective studies



Test for Heterogeneity for 4 studies:
 $P = 0,1313$, $I^2 = 46,67\%$

Proportion of subjects with 1-h PG ≥ 155 mg/dl across dysglycemic conditions. The CATAMERI study (n=3020)



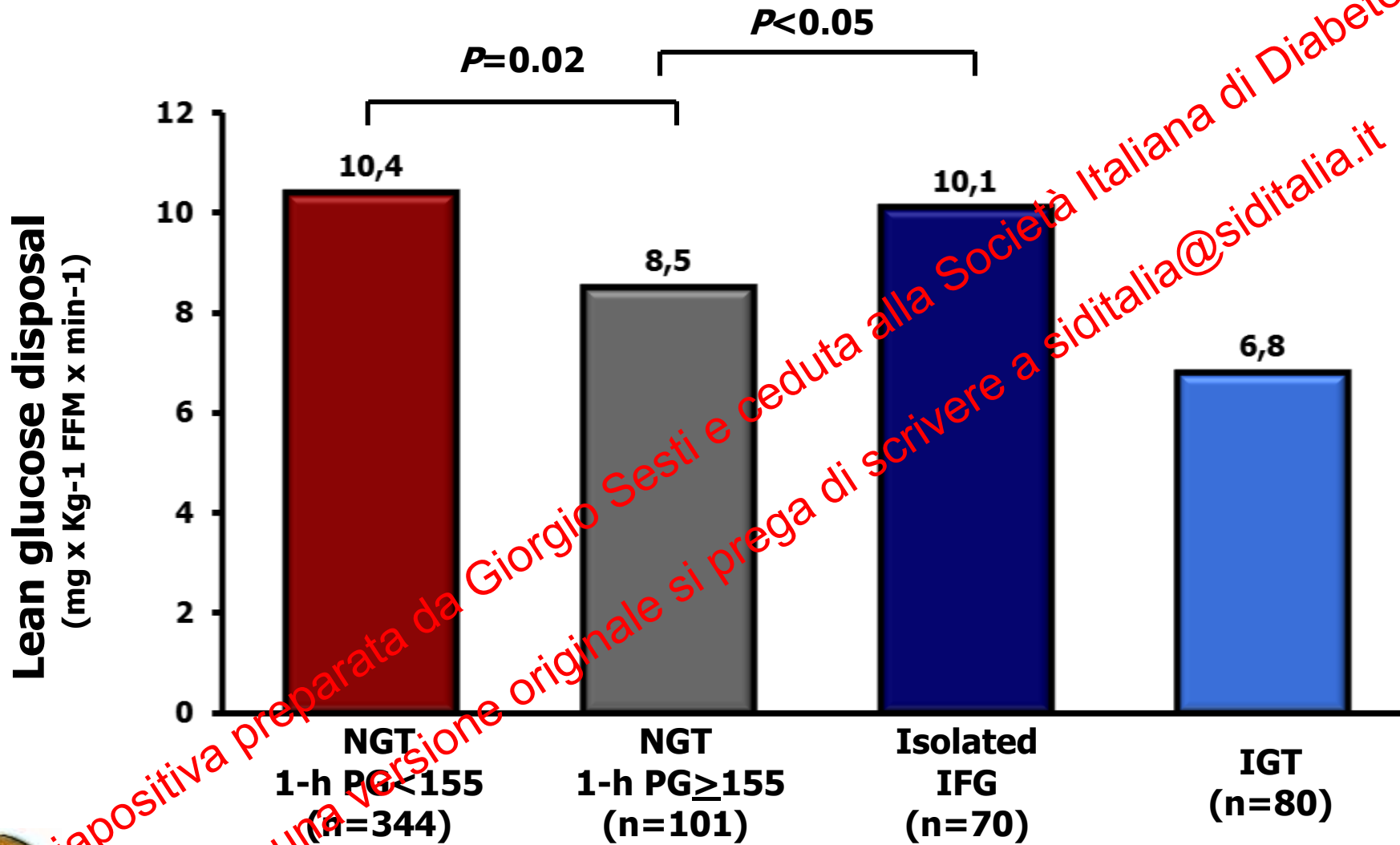
AGENDA

Clinical characteristics of NGT 1h-high individuals:

- **insulin sensitivity and β -cell function,**
- **classical and non classical CV risk factors,**
- **hepatic steatosis,**
- **CV organ damage, and risk of CVD.**

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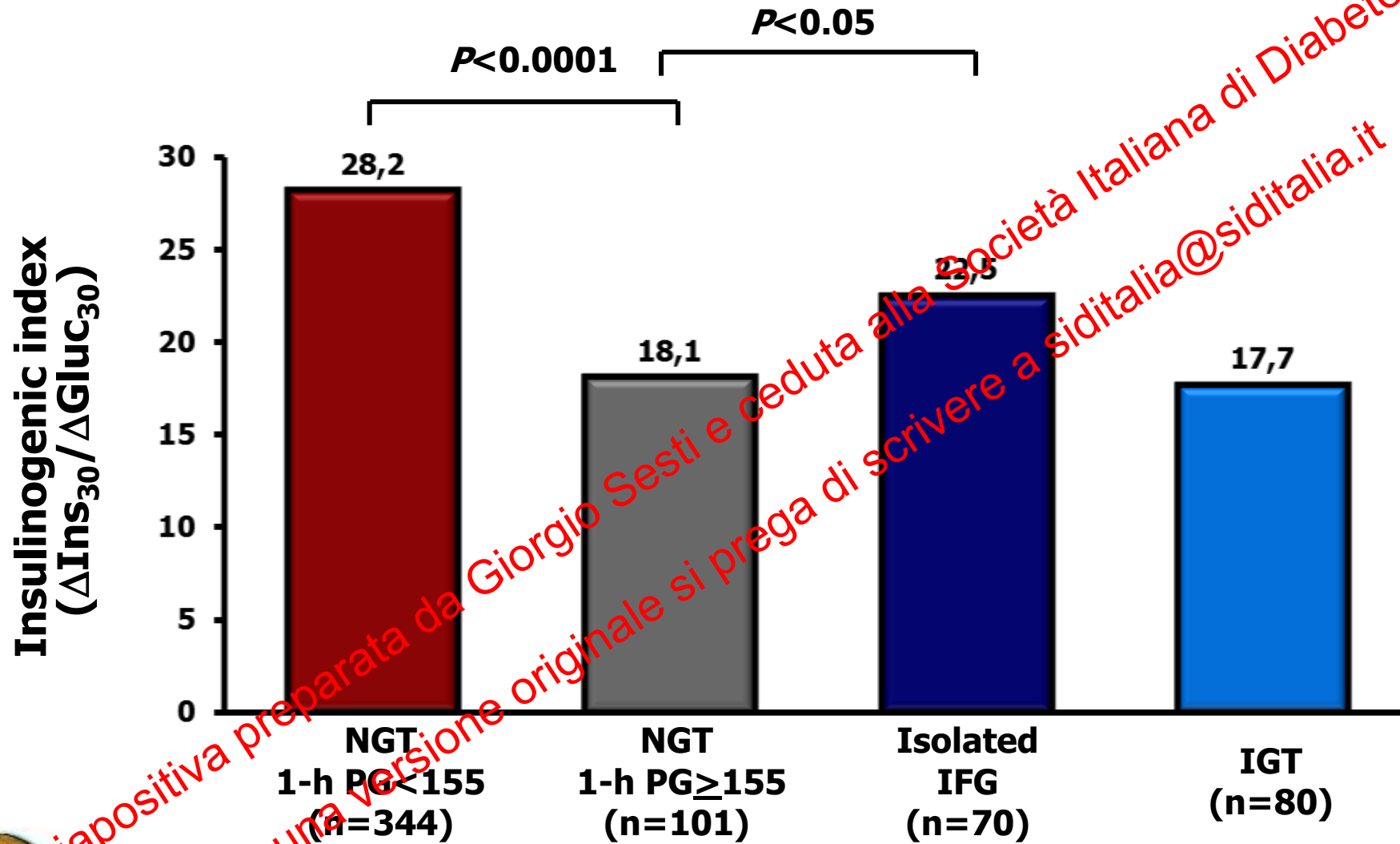
Insulin sensitivity is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl or IFG



P values refer to results after analyses with adjustment for age, gender, and BMI



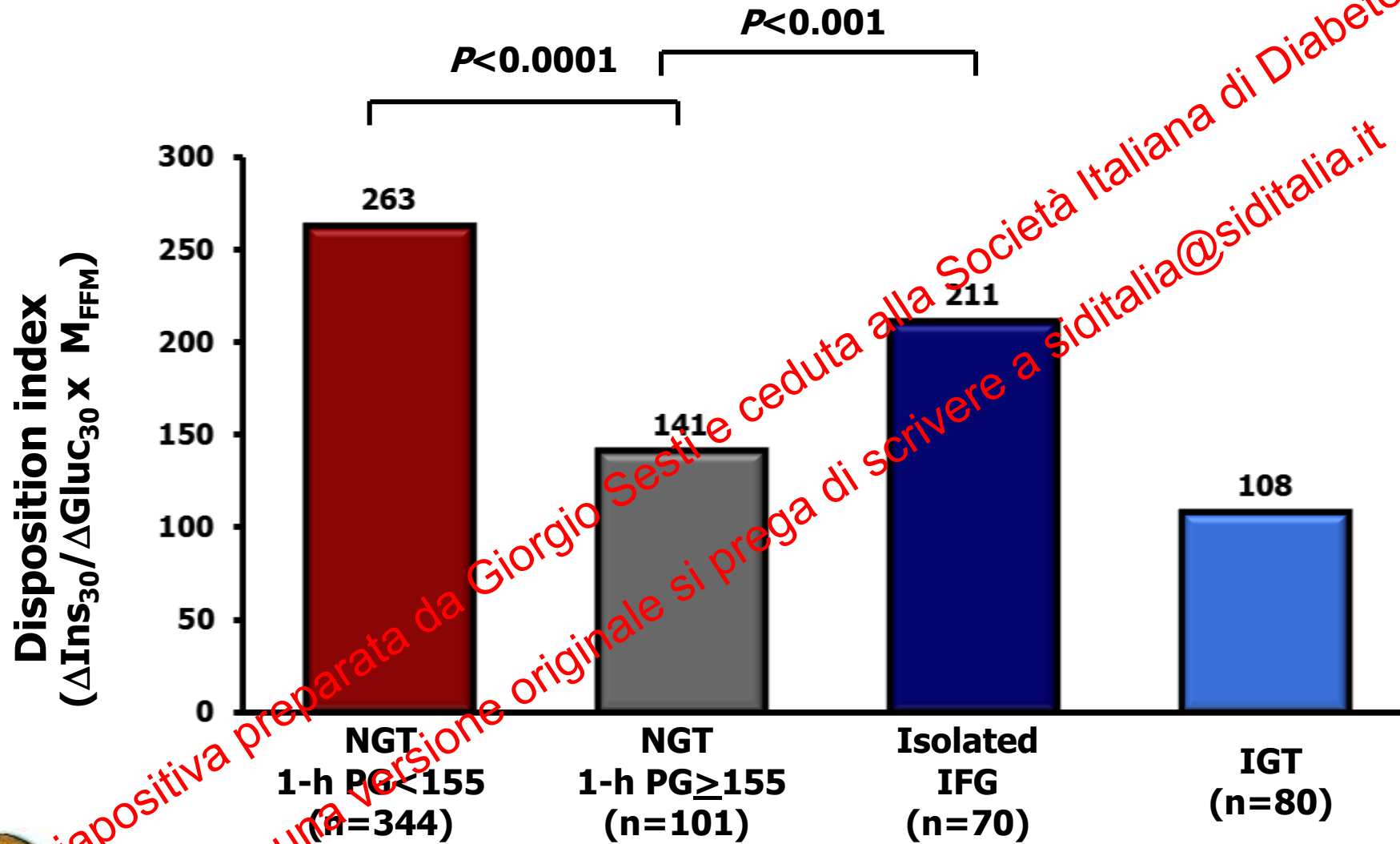
Insulin secretion is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl or IFG



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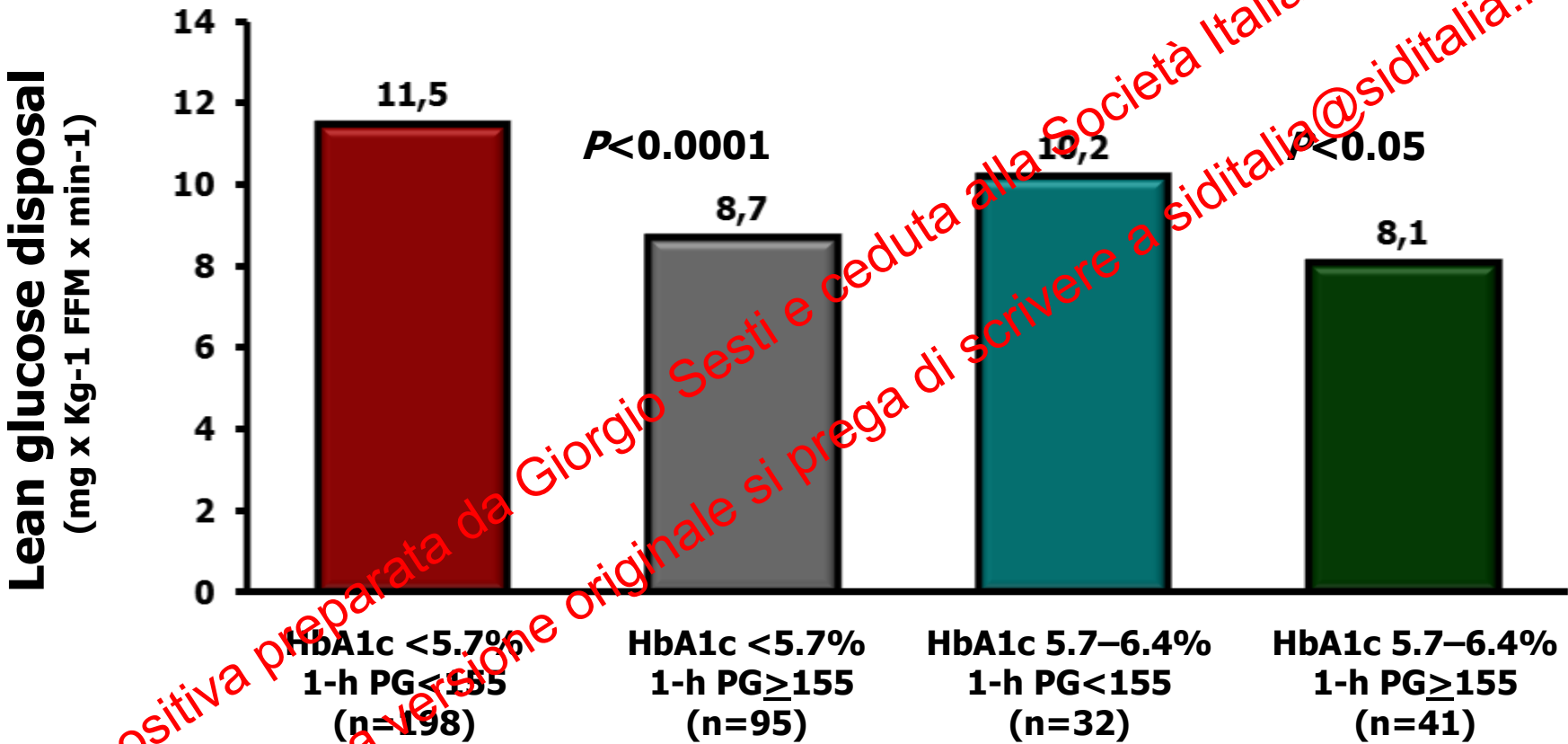
Disposition index is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl or IFG



P values refer to results after analyses with adjustment for age, gender, and BMI



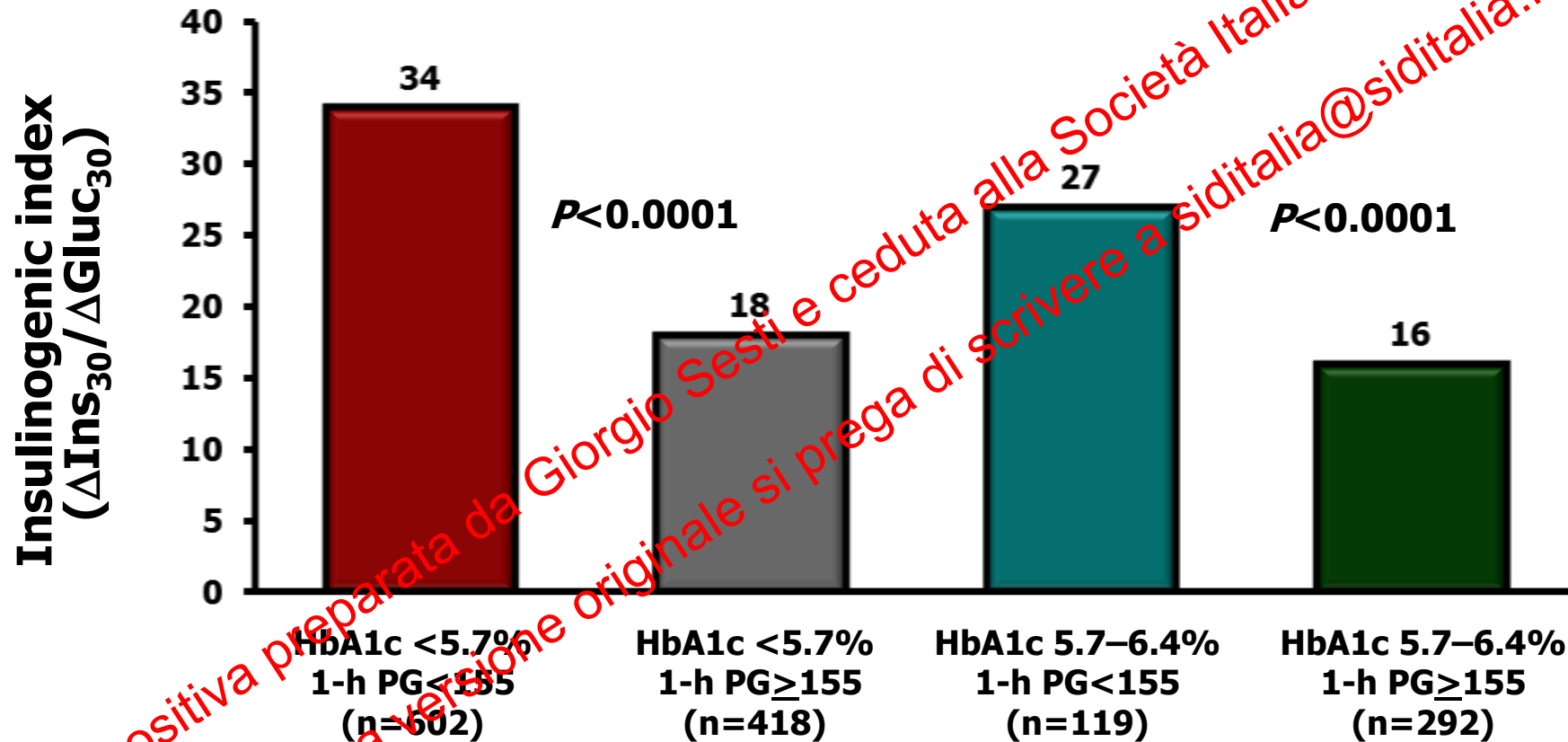
Insulin sensitivity is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG <155 mg/dl stratified by HbA1c



P values refer to results after analyses with adjustment for age, gender, and BMI

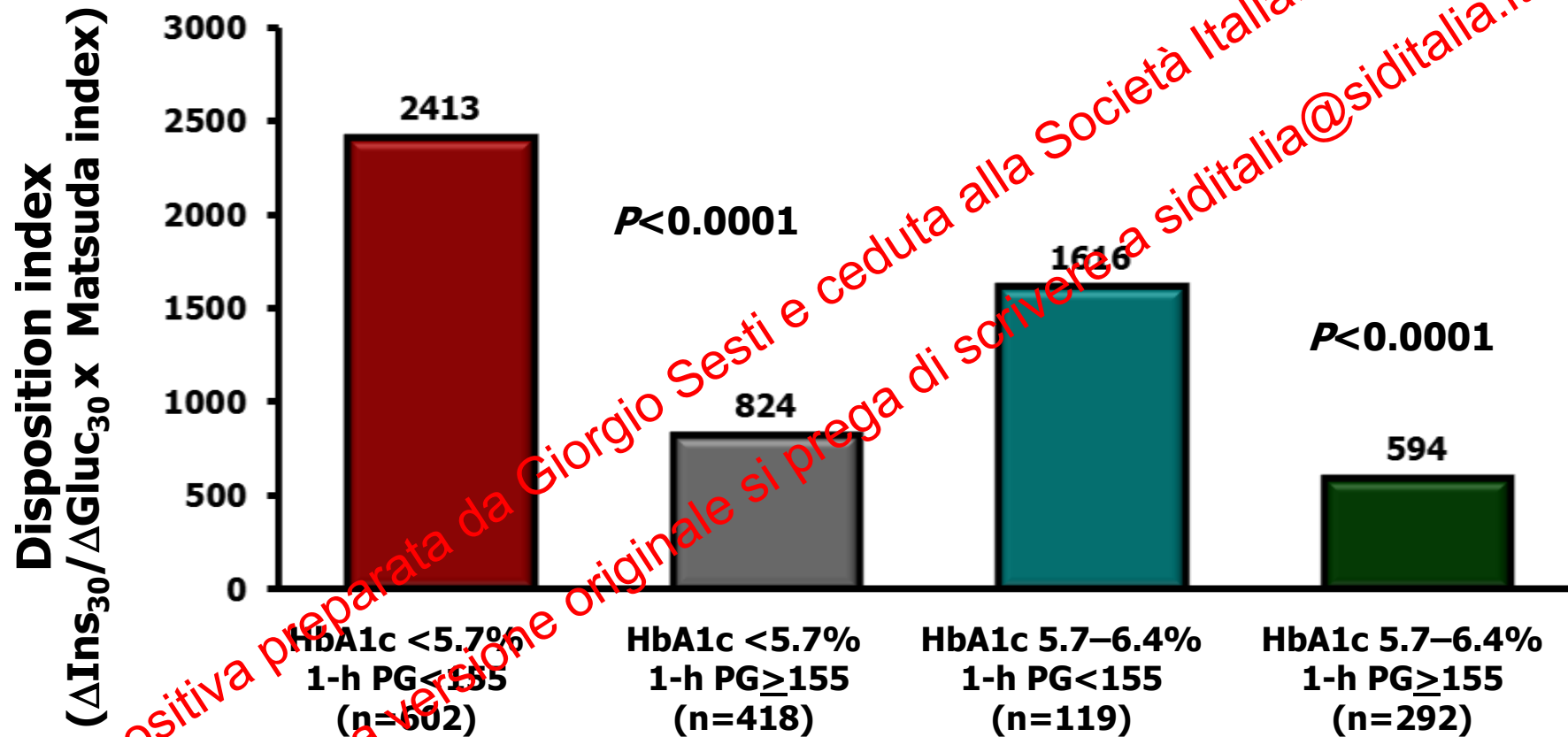


Insulin secretion is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl stratified by HbA1c



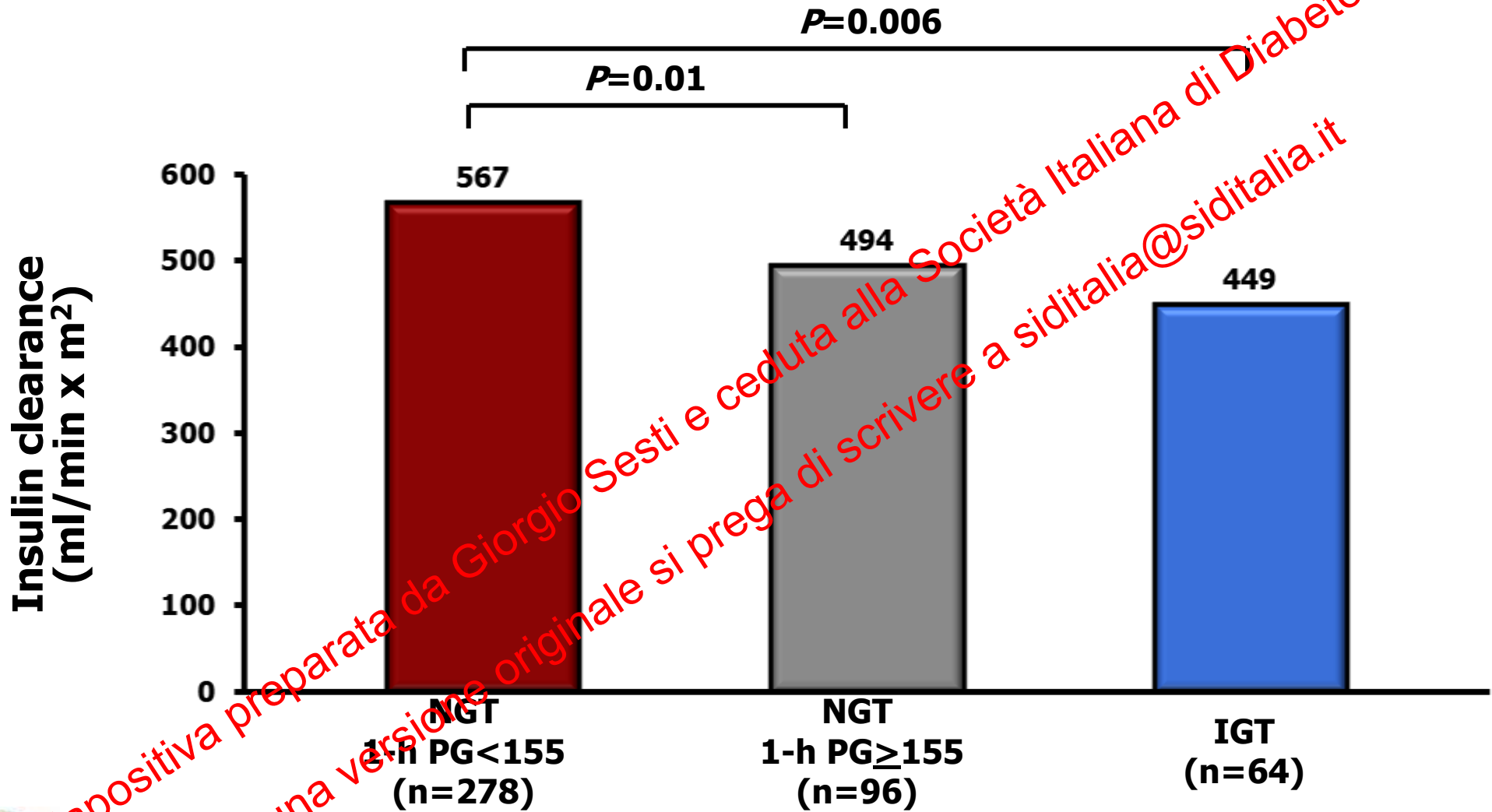
P values refer to results after analyses with adjustment for age, gender, and BMI

Disposition index is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl stratified by HbA1c



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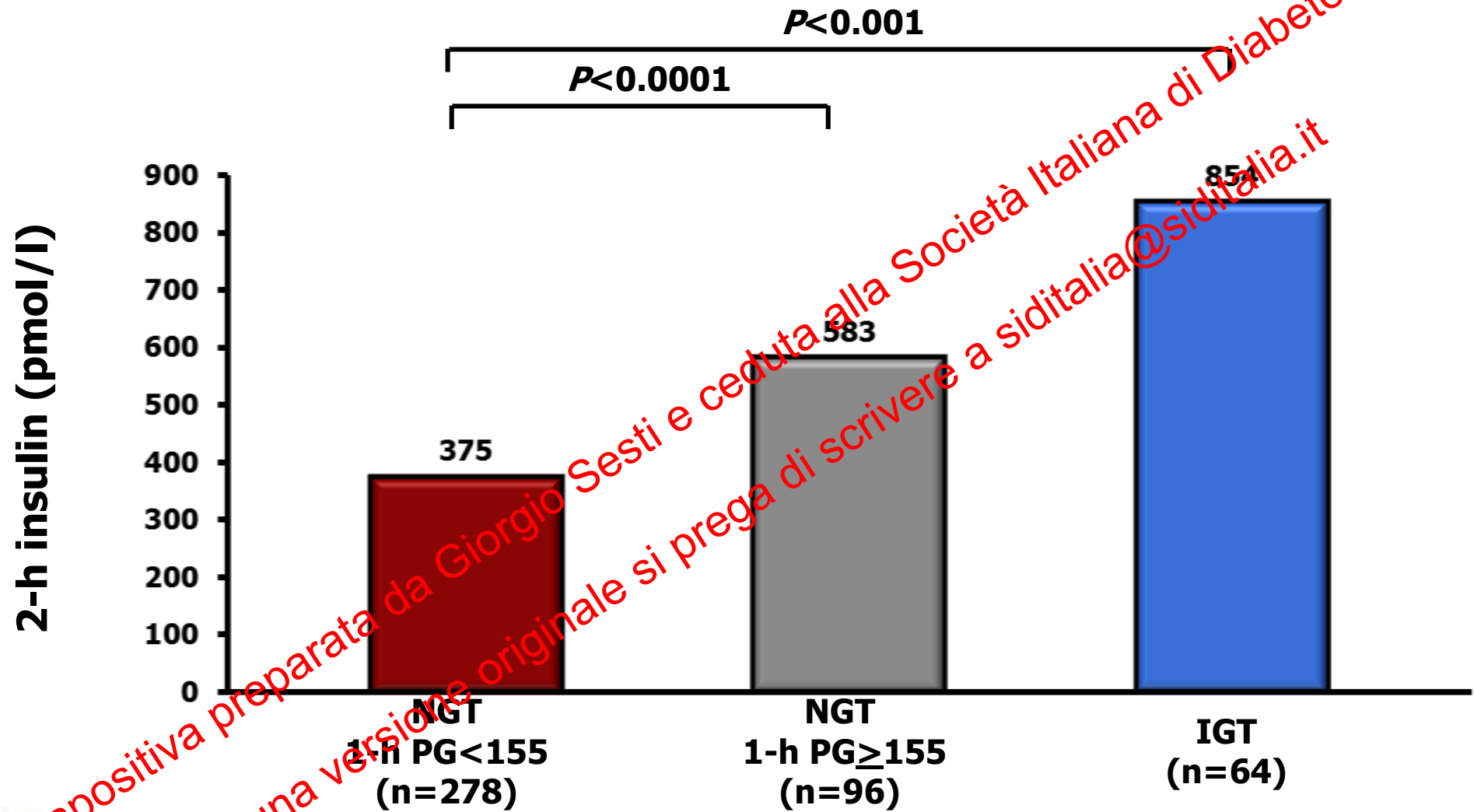
Insulin clearance is reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



P values refer to results after analyses with adjustment for age, gender, and BMI



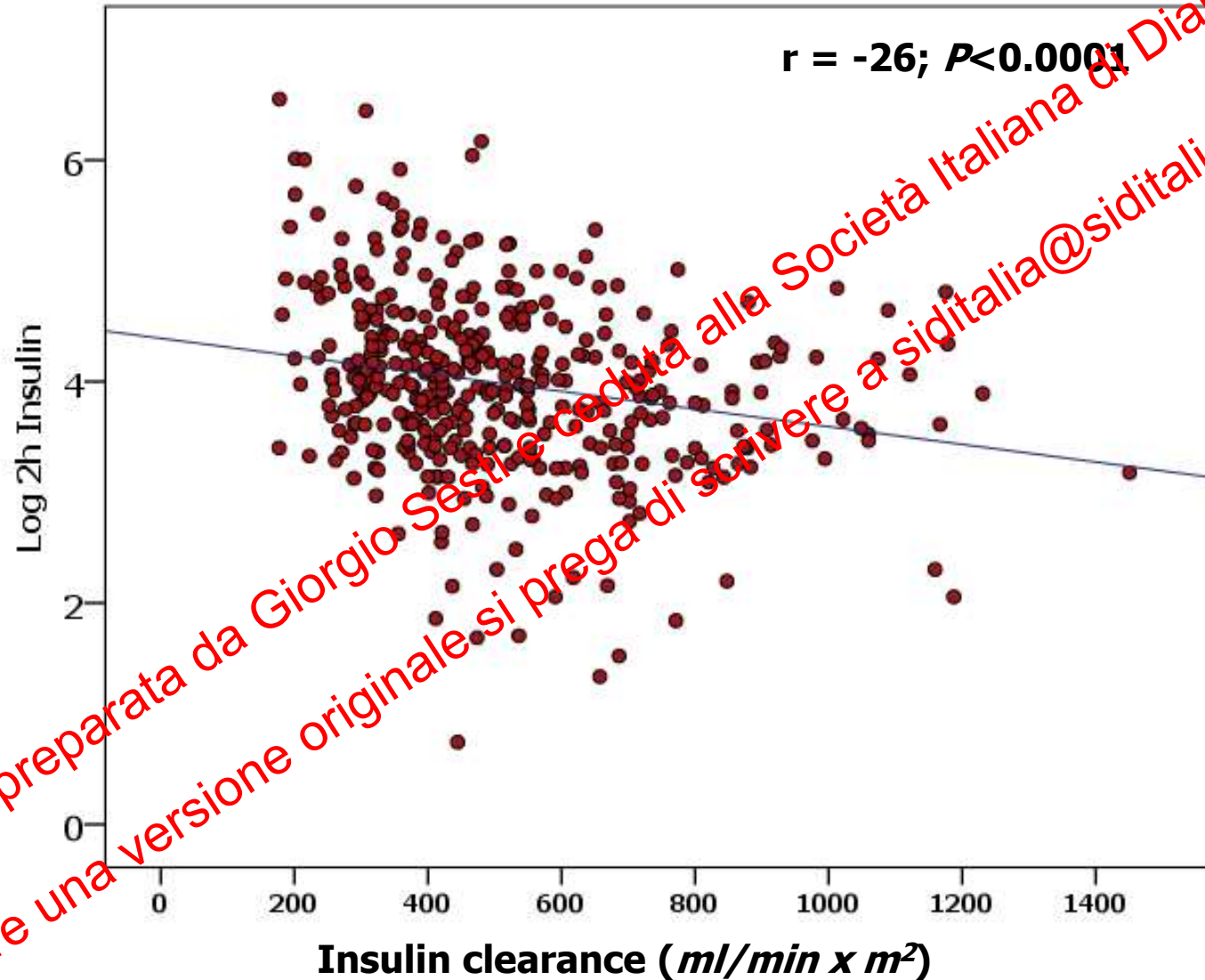
2h-Insulin levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



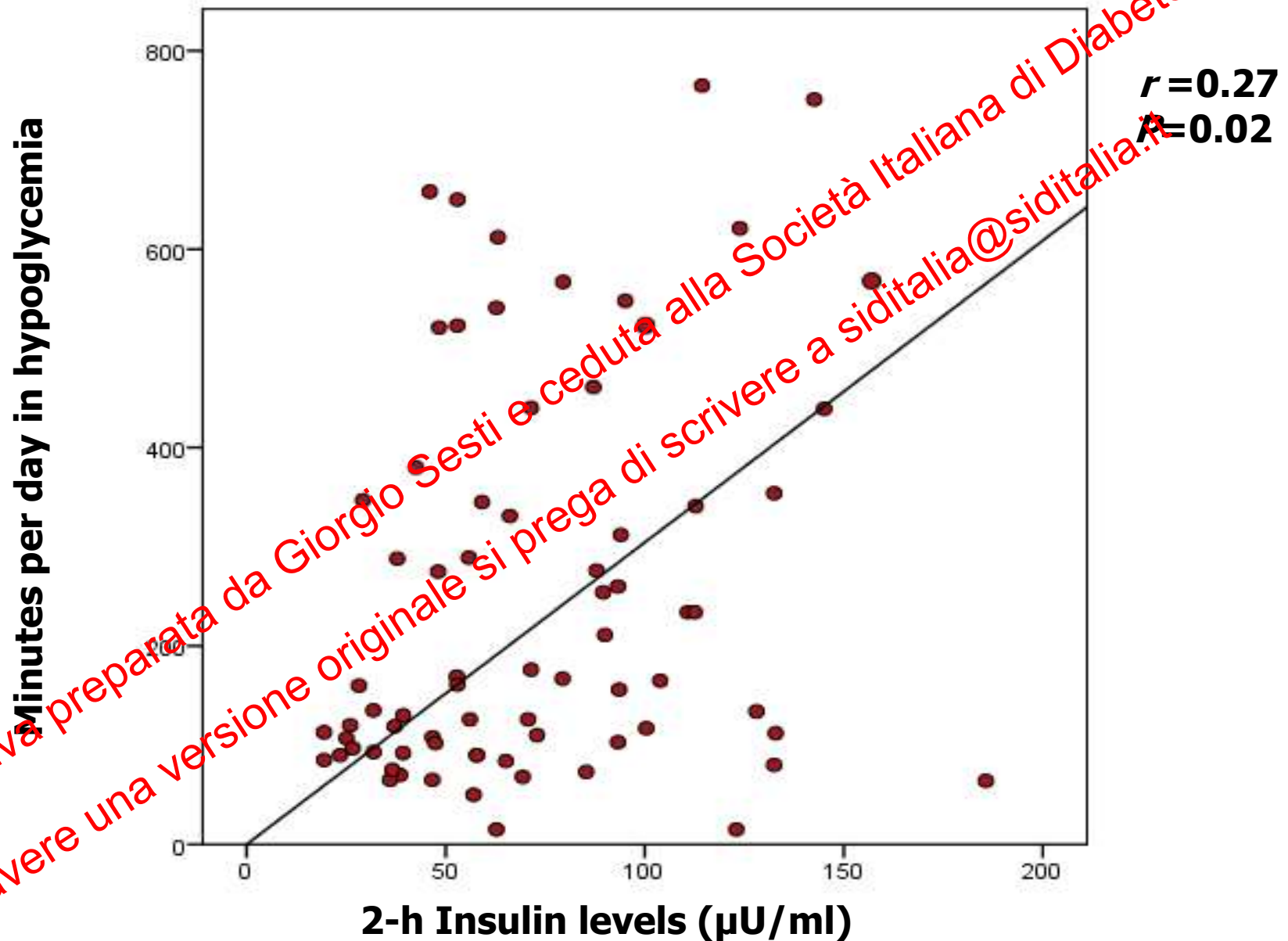
P values refer to results after analyses with adjustment for age, gender, and BMI



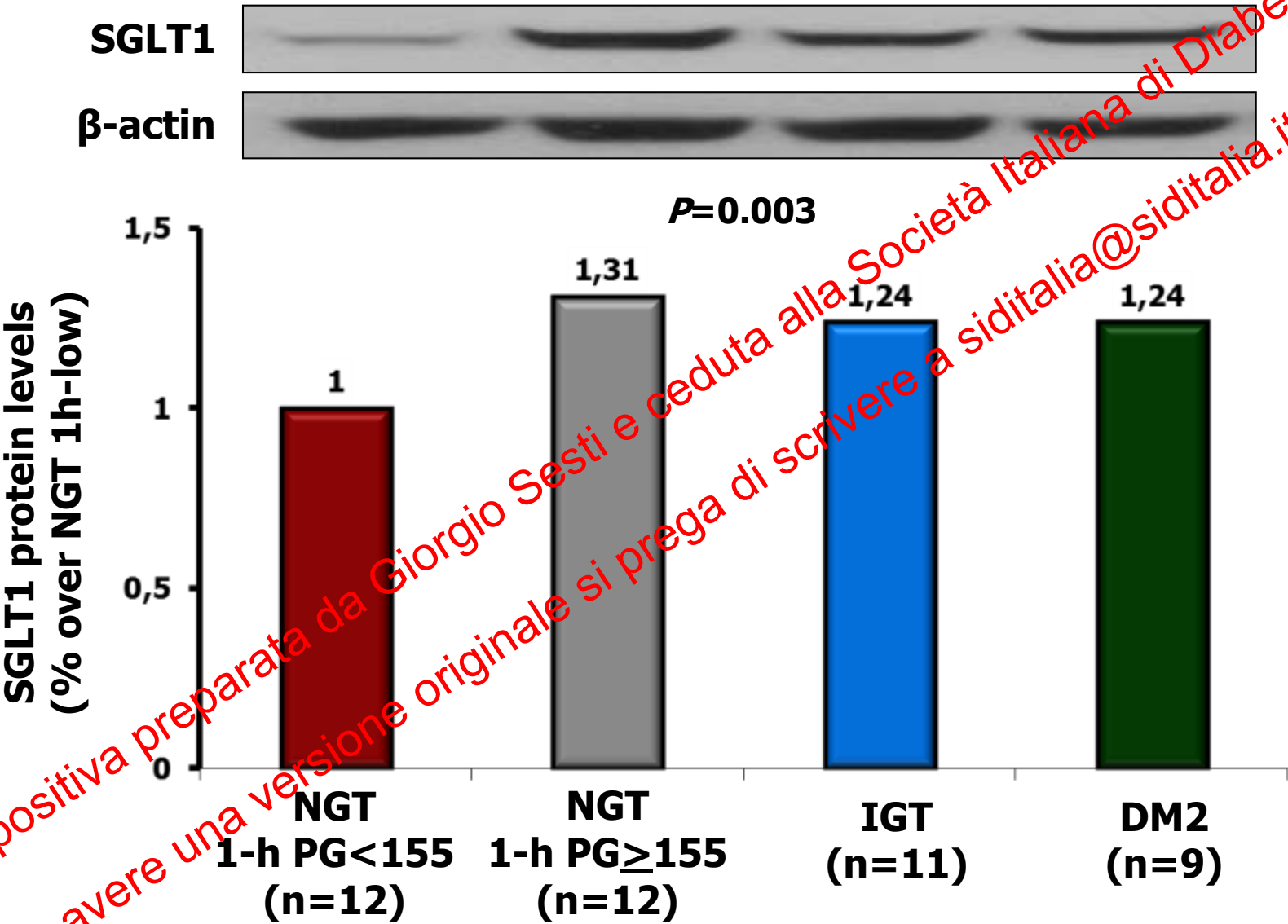
Insulin clearance correlates with 2h insulin levels



Correlation between minutes spent in hypoglycemia and 2-h post-load insulin levels

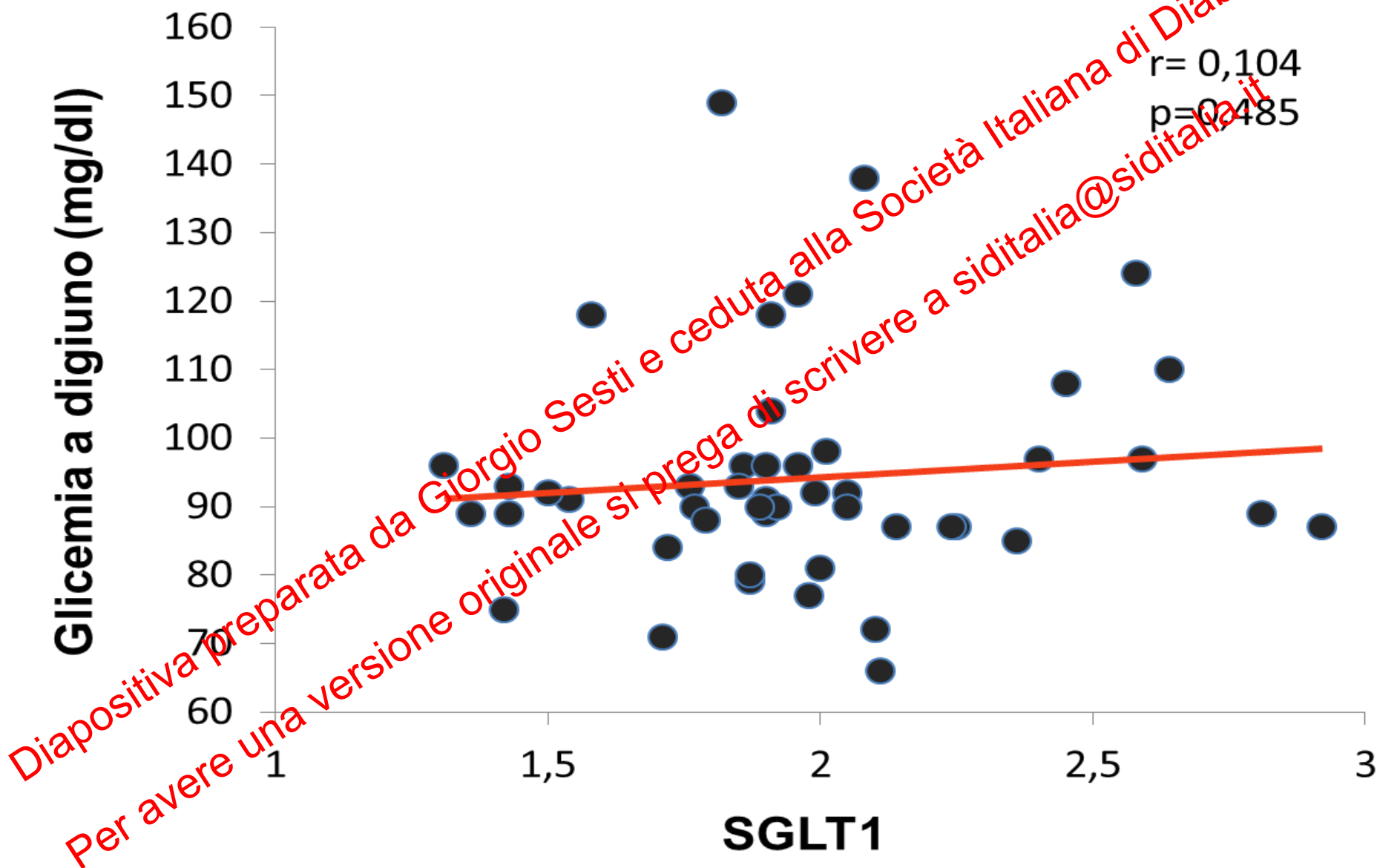


Intestinal SGLT1 protein levels are increased in subjects with post-load hyperglycemia

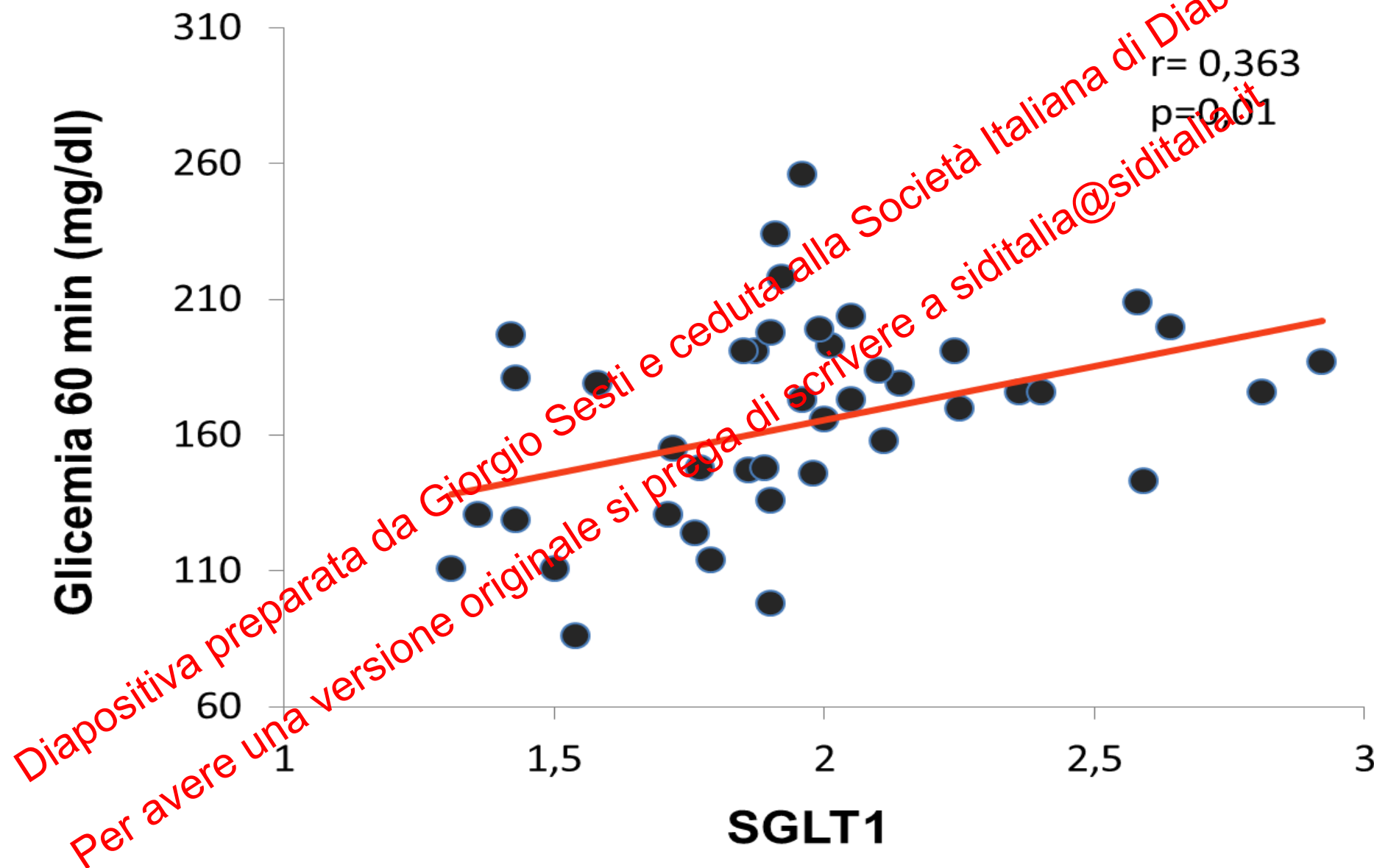


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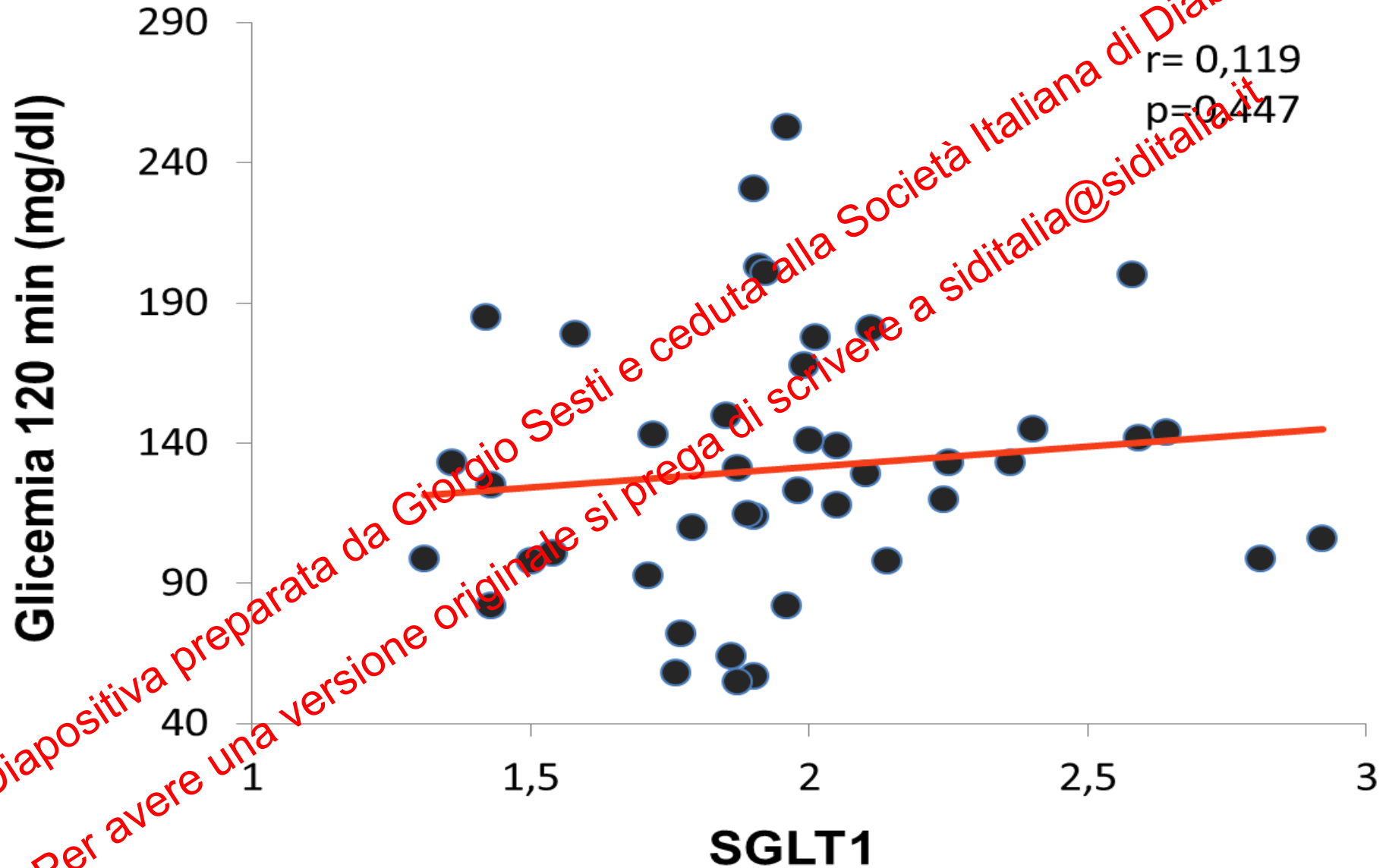
L'espressione di SGLT1 non correla con la glicemia a digiuno



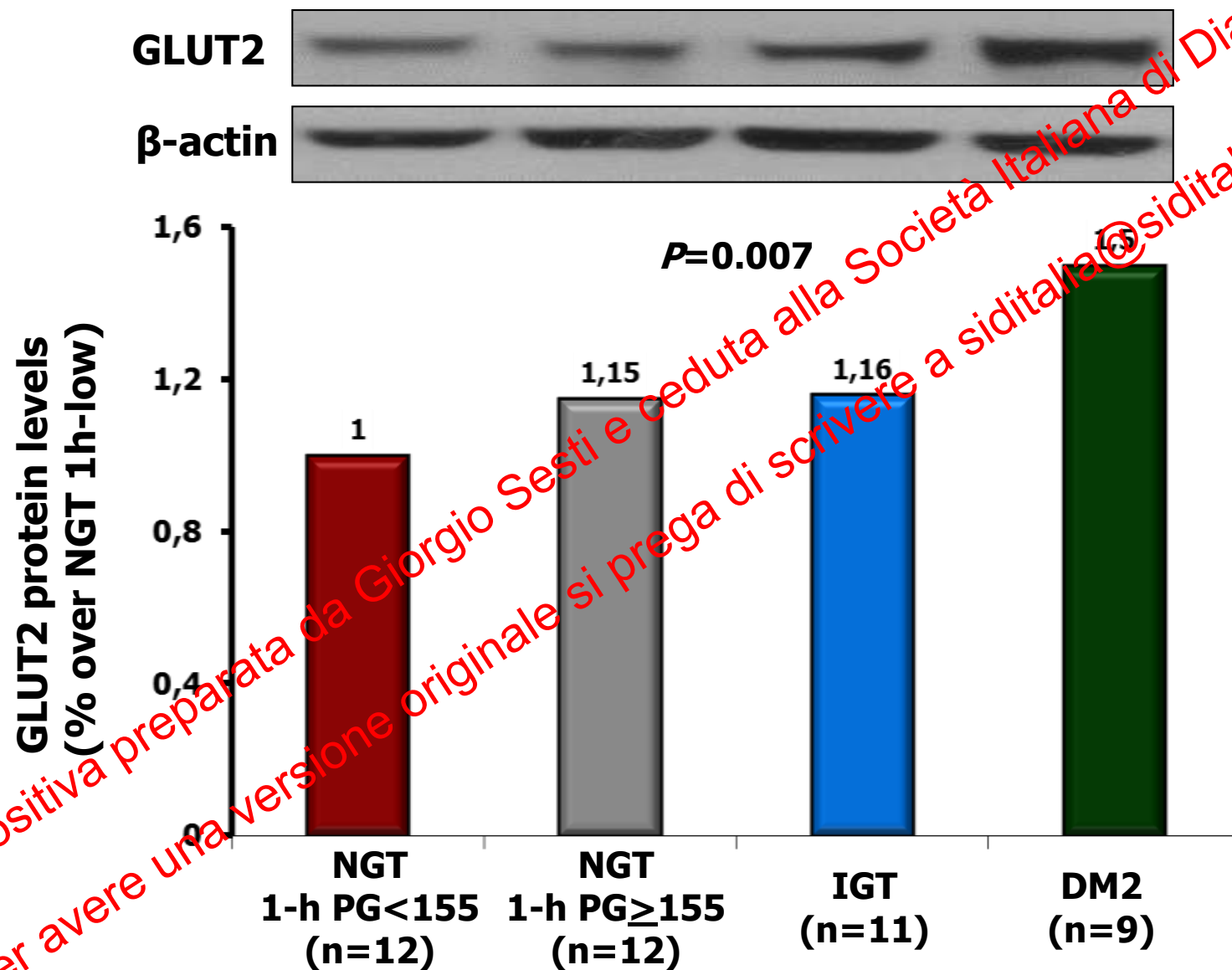
L'espressione di SGLT1 correla con la glicemia a 1 ora post-carico



L'espressione di SGLT1 non correla con la glicemia a 2 ore post-carico



Intestinal GLUT2 expression is increased in subjects with type 2 diabetes



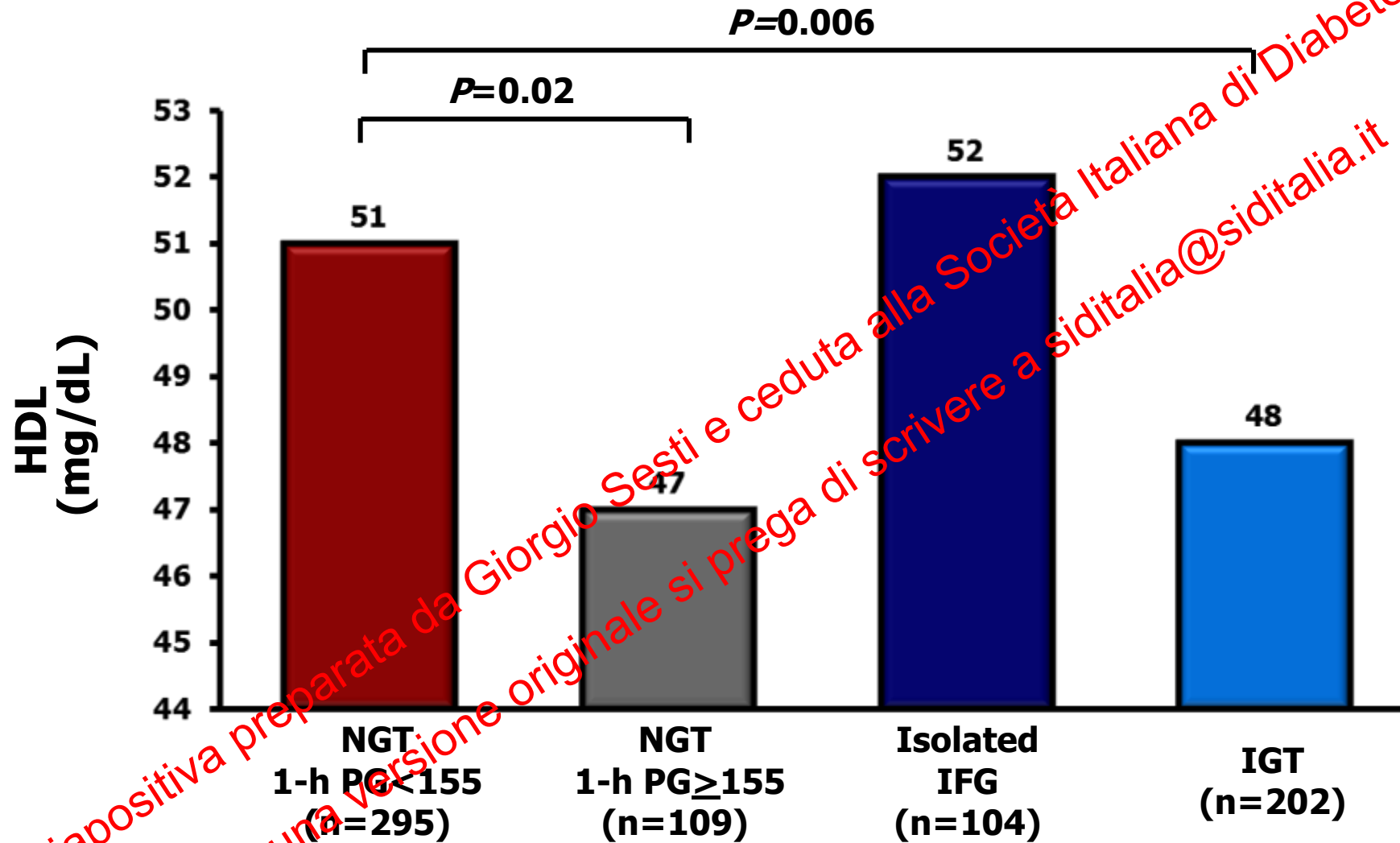
AGENDA

Clinical characteristics of NGT 1h-high individuals:

- insulin sensitivity and β -cell function,
- classical and non classical CV risk factors,
- hepatic steatosis,
- CV organ damage, and risk of CVD.

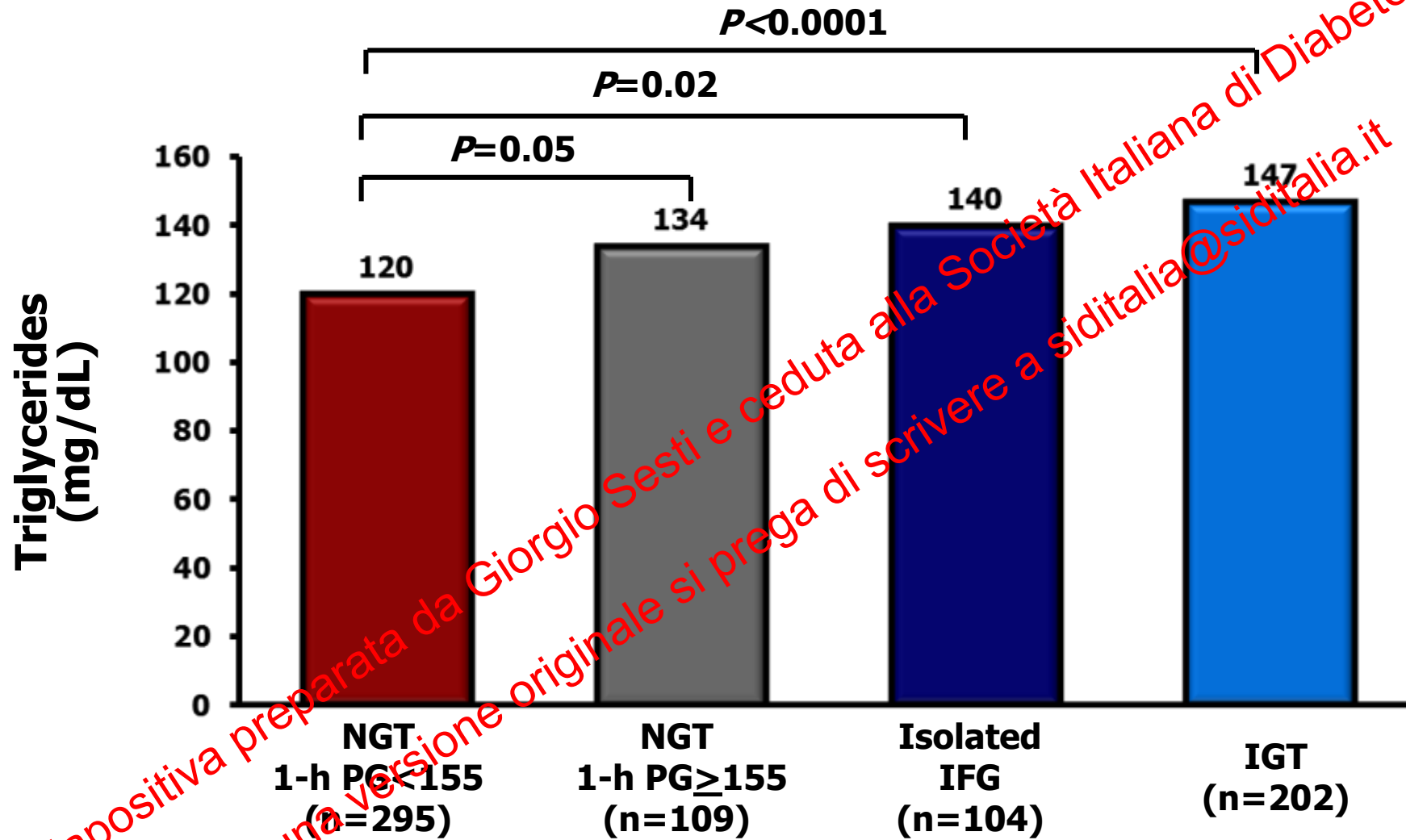
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HDL levels are reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



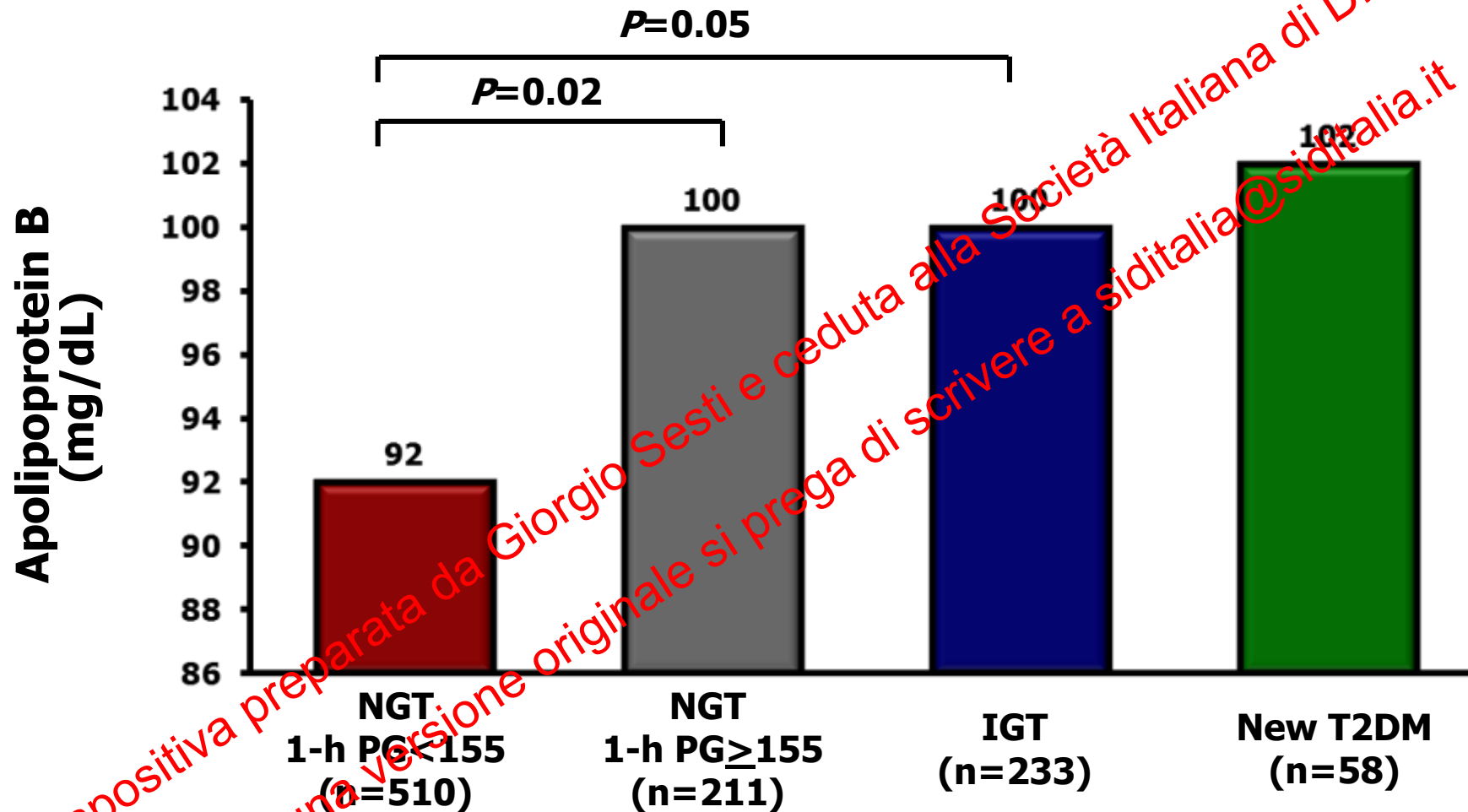
P values refer to results after analyses with adjustment for age, gender, and BMI

Triglycerides levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



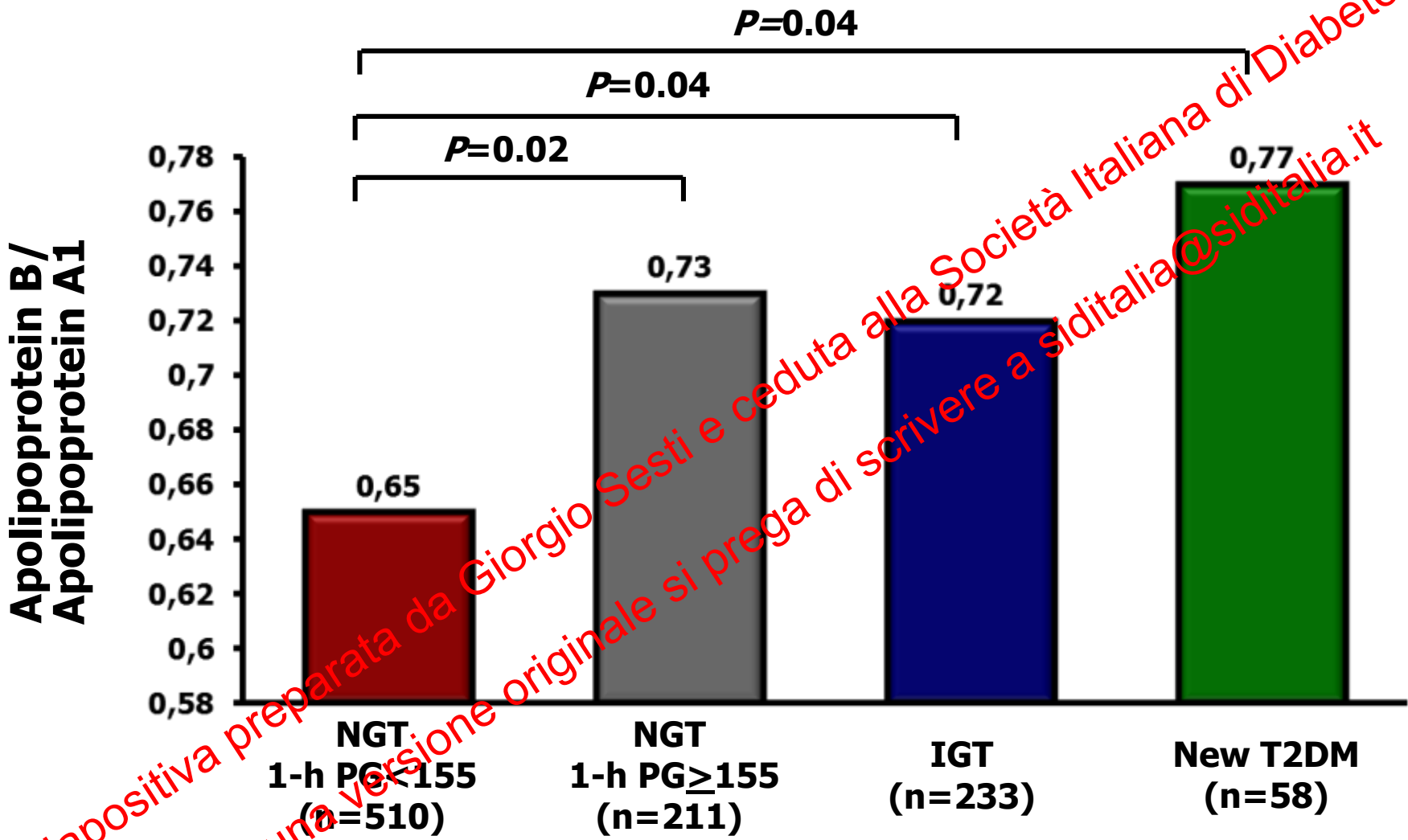
P values refer to results after analyses with adjustment for age, gender, and BMI

Apolipoprotein B levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



P values refer to results after analyses with adjustment for age, gender, and BMI

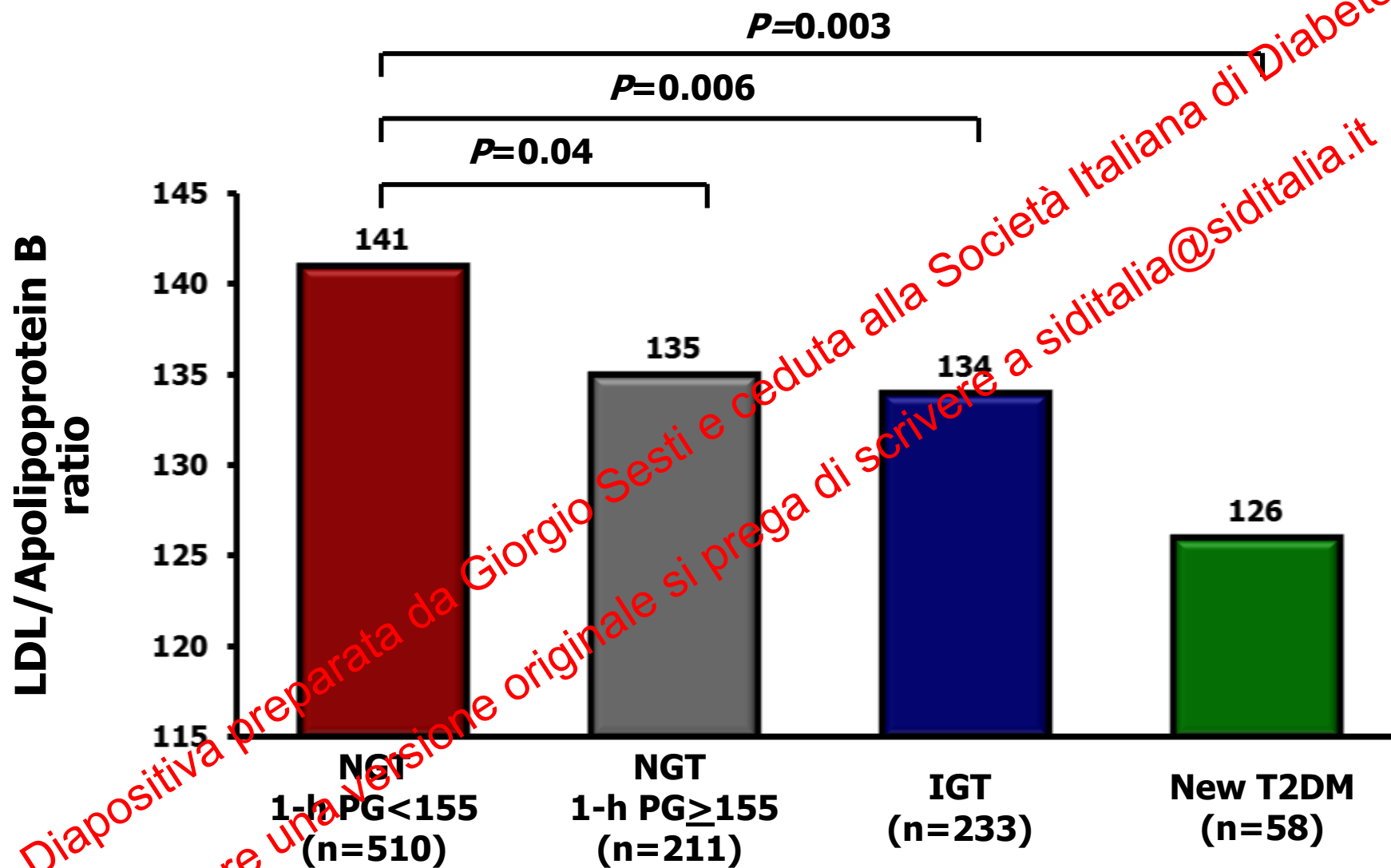
Apolipoprotein B/ Apolipoprotein A1 ratio is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



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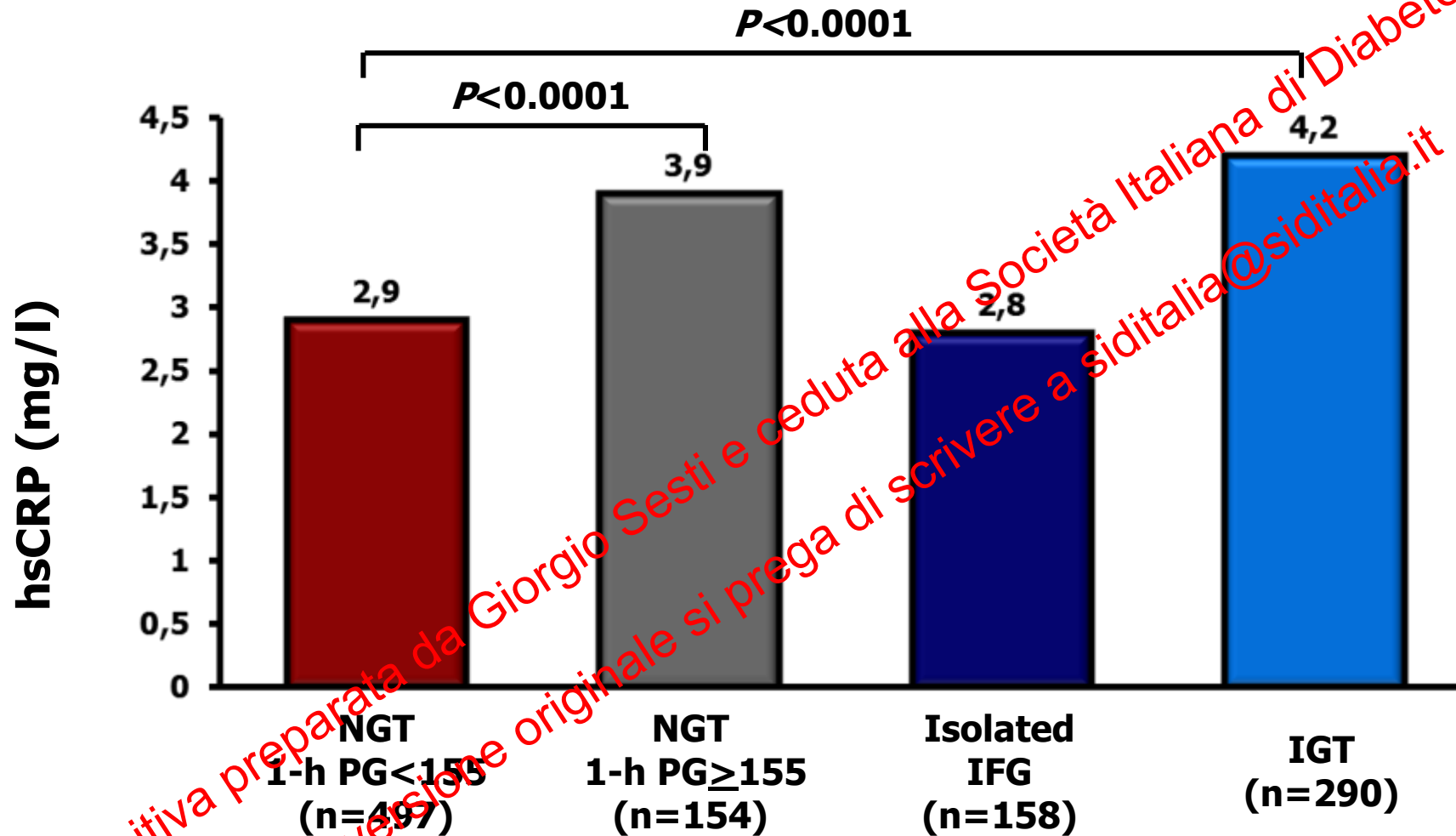
LDL cholesterol/Apolipoprotein B ratio is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



P values refer to results after analyses with adjustment for age, gender, and BMI

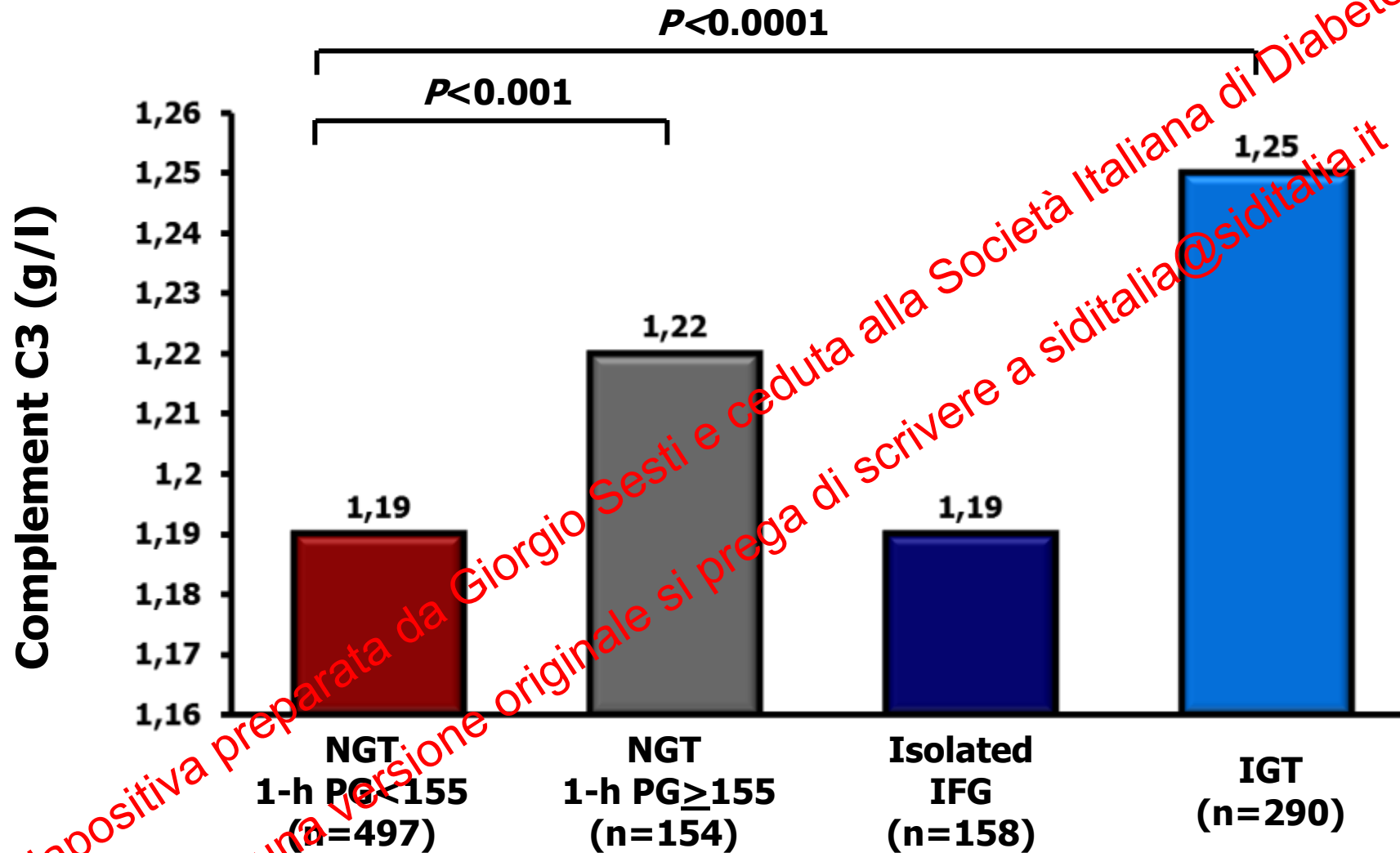


hsCRP levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the CATAMERI Study



P values refer to results after analyses with adjustment for age, gender, and BMI

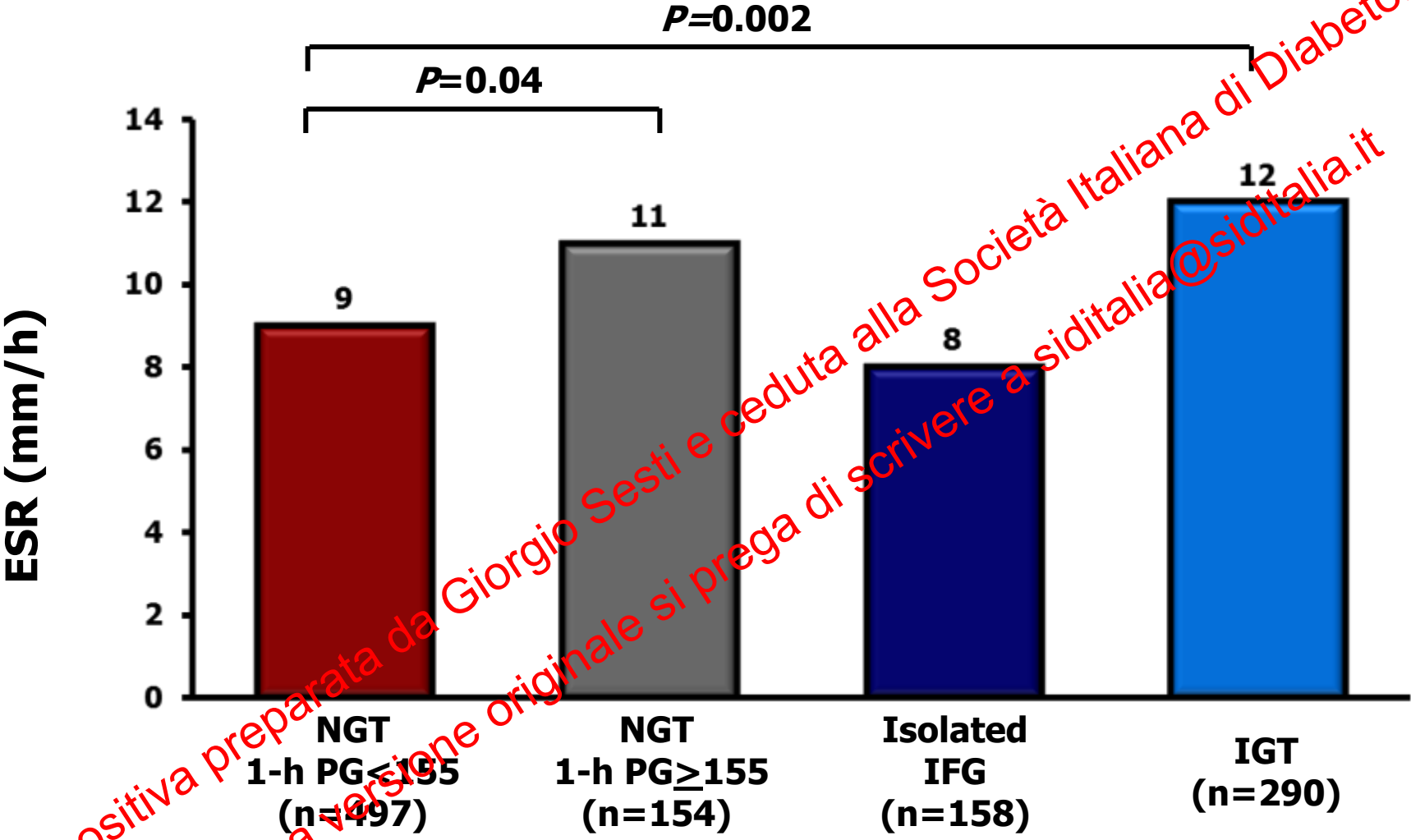
Complement C3 levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the CATAMERI study



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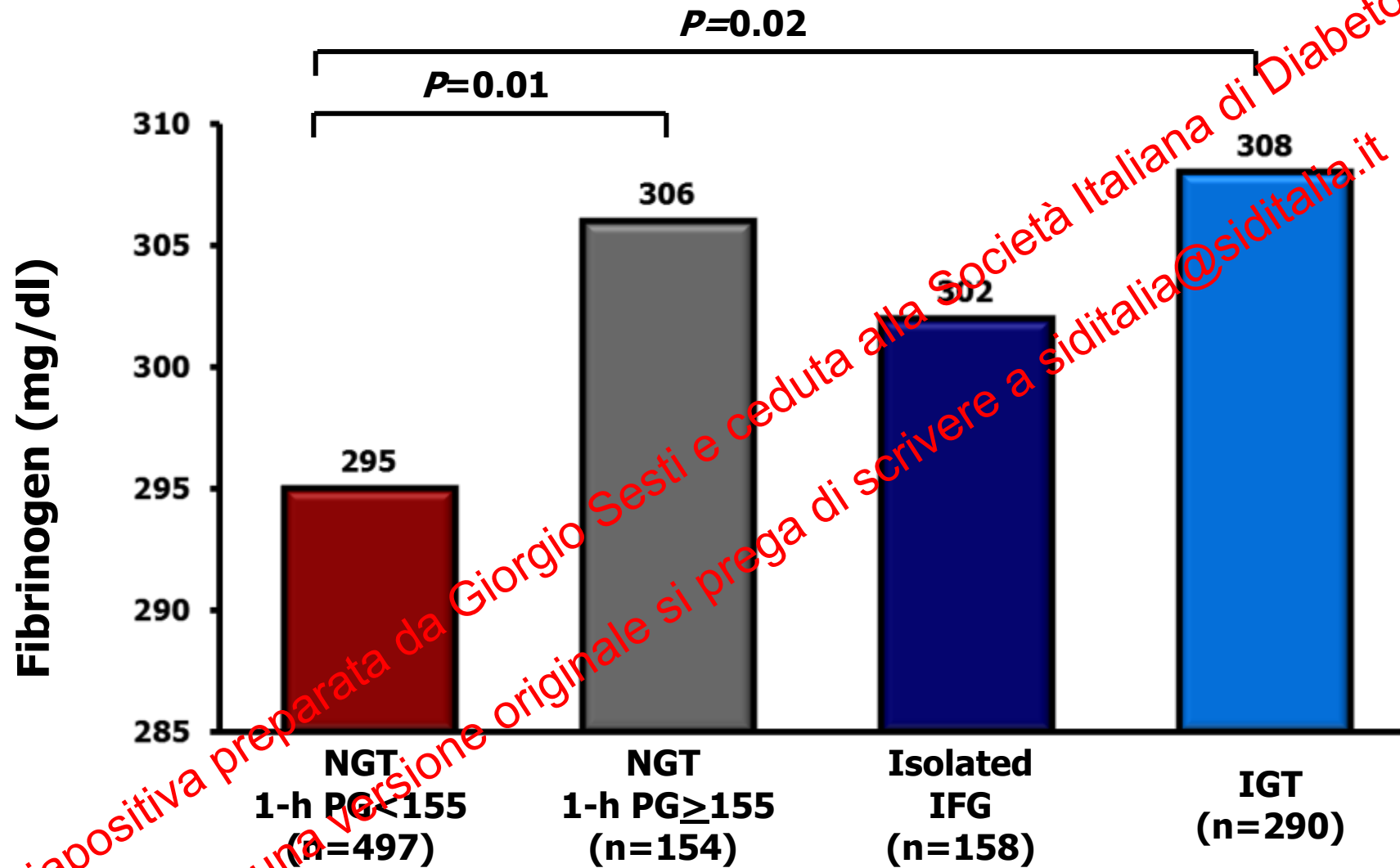


ESR levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the CATAMERI study



P values refer to results after analyses with adjustment for age, gender, and BMI

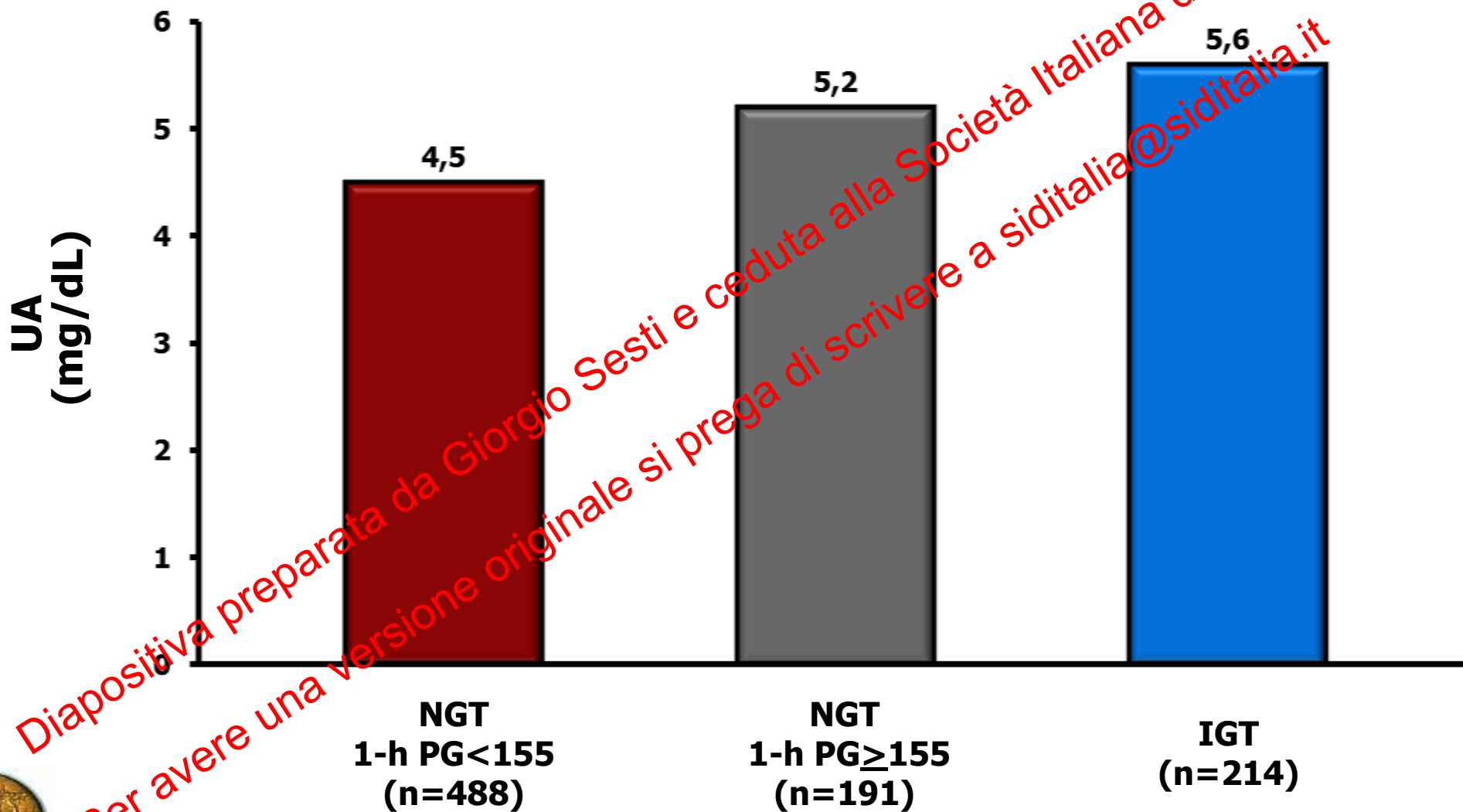
Fibrinogen levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the CATAMERI Study



P values refer to results after analyses with adjustment for age, gender, and BMI

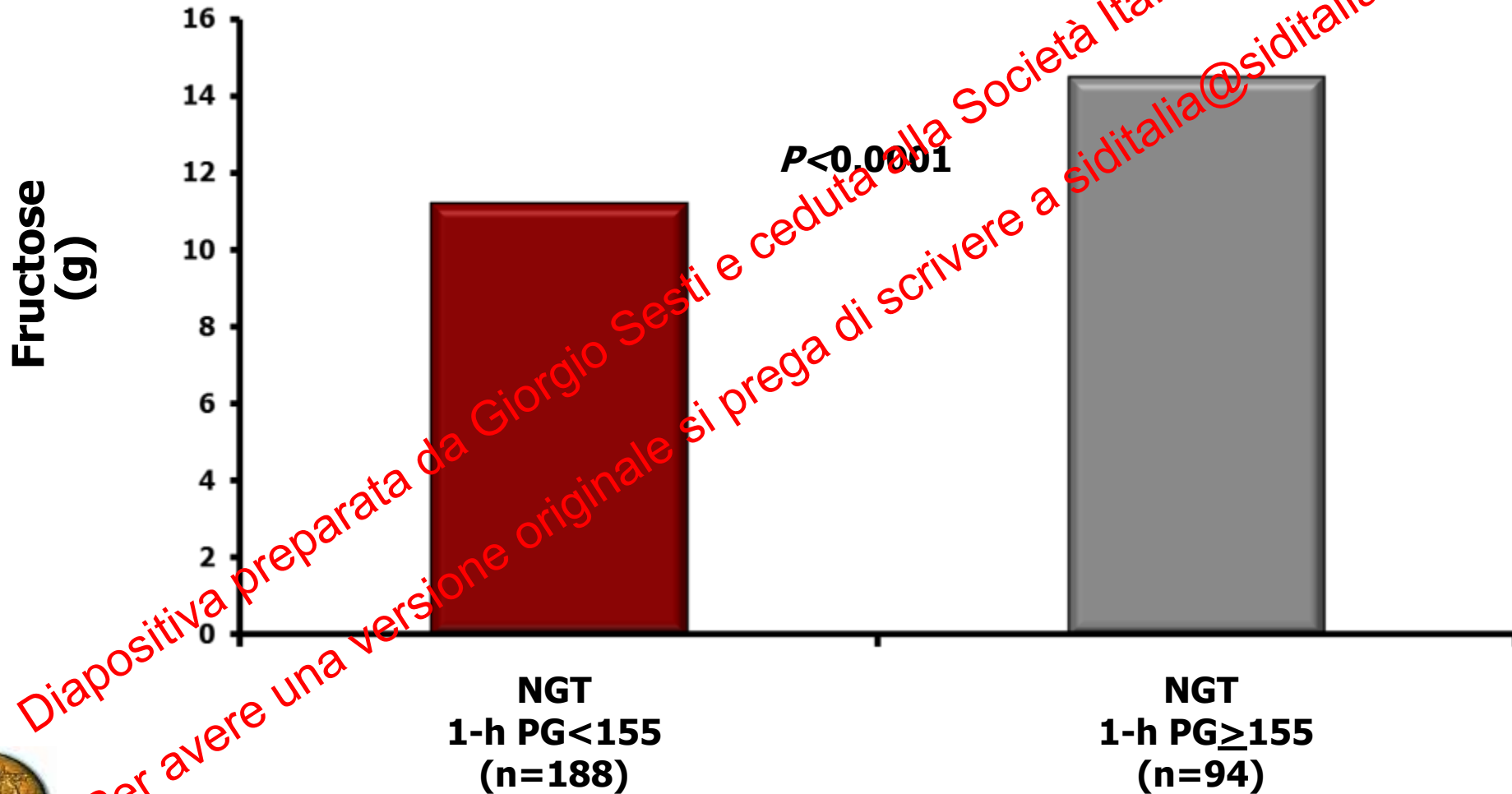
Uric acid levels are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl

$P < 0.0001$

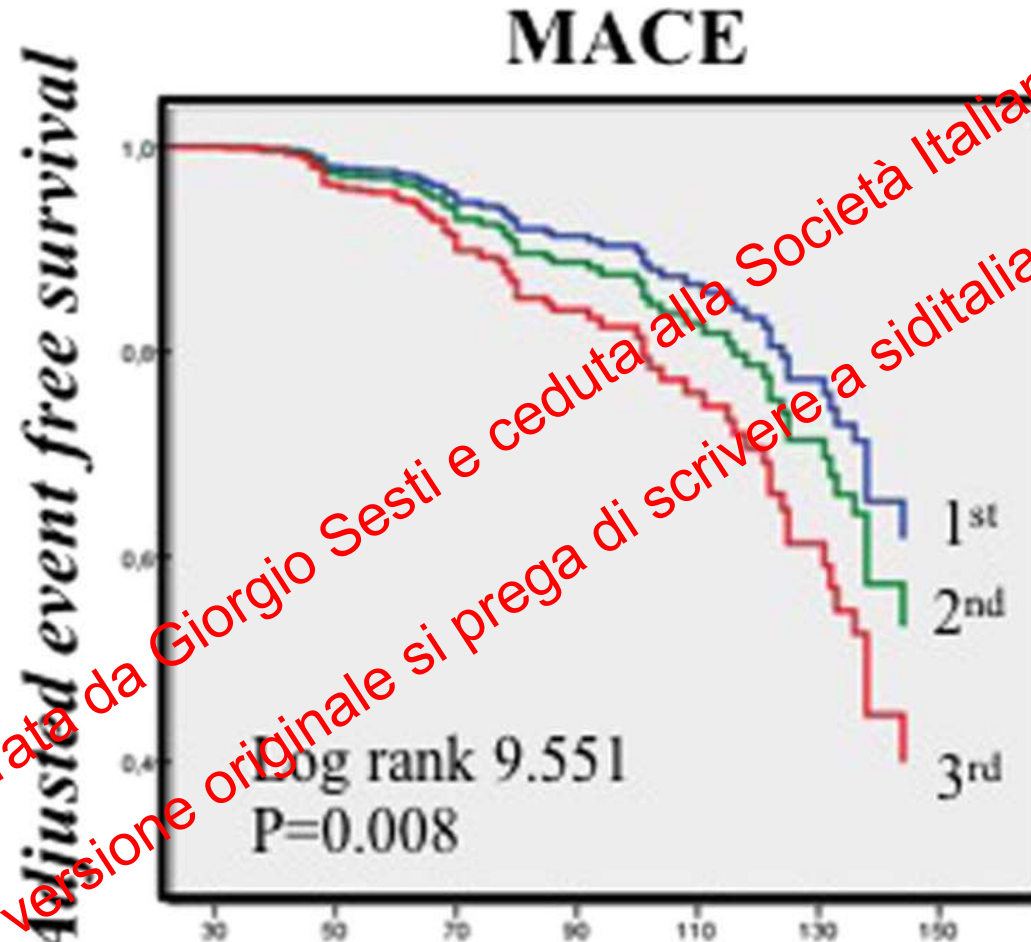


Fructose consumption is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl

Dietary intake was quantified by a semiquantitative food frequency questionnaire (FEQ) validated in the European Investigation into Cancer and Nutrition (EPIC) study.



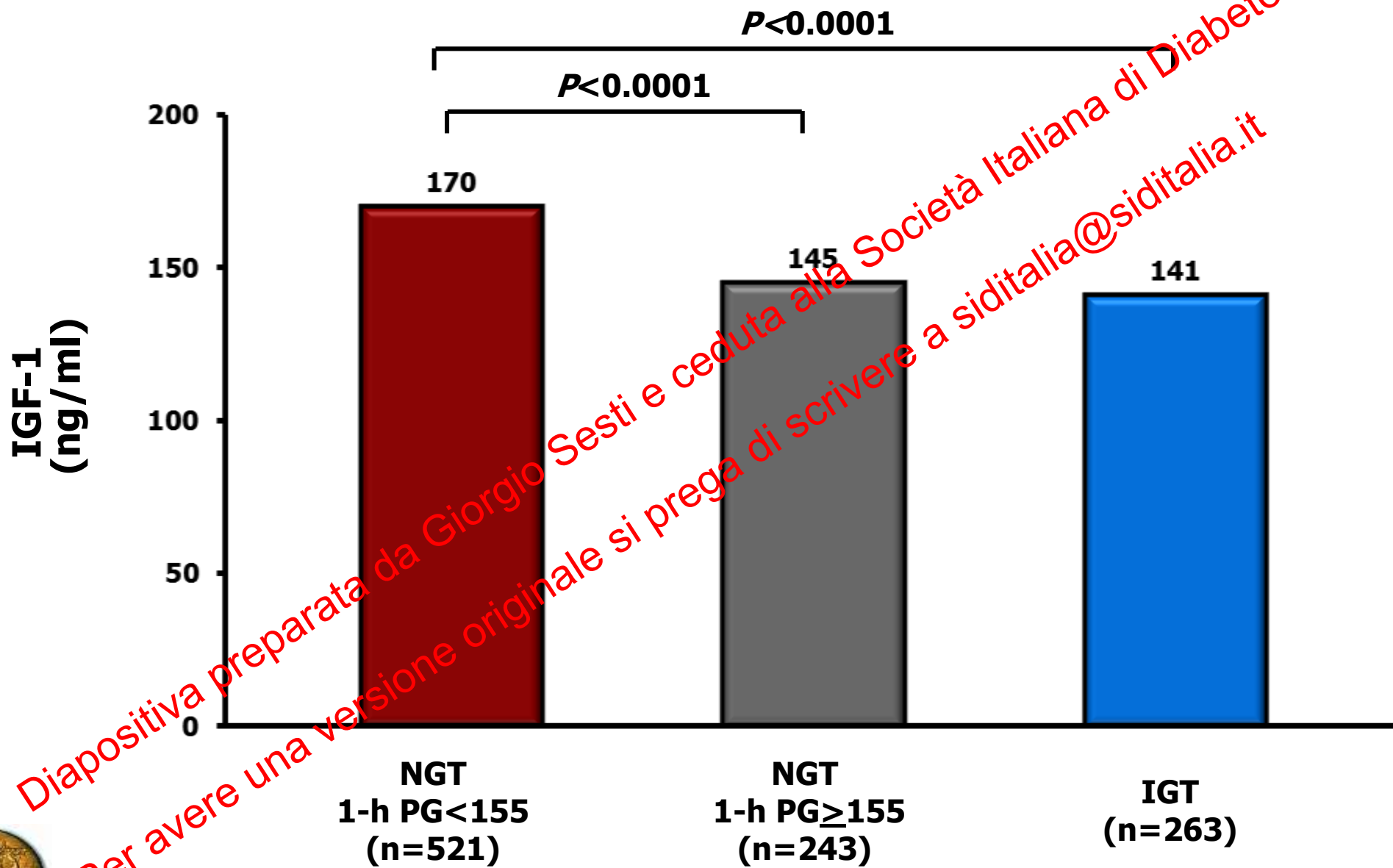
Uric acid is an independent predictor of cardiovascular events in post-menopausal women (n=645)



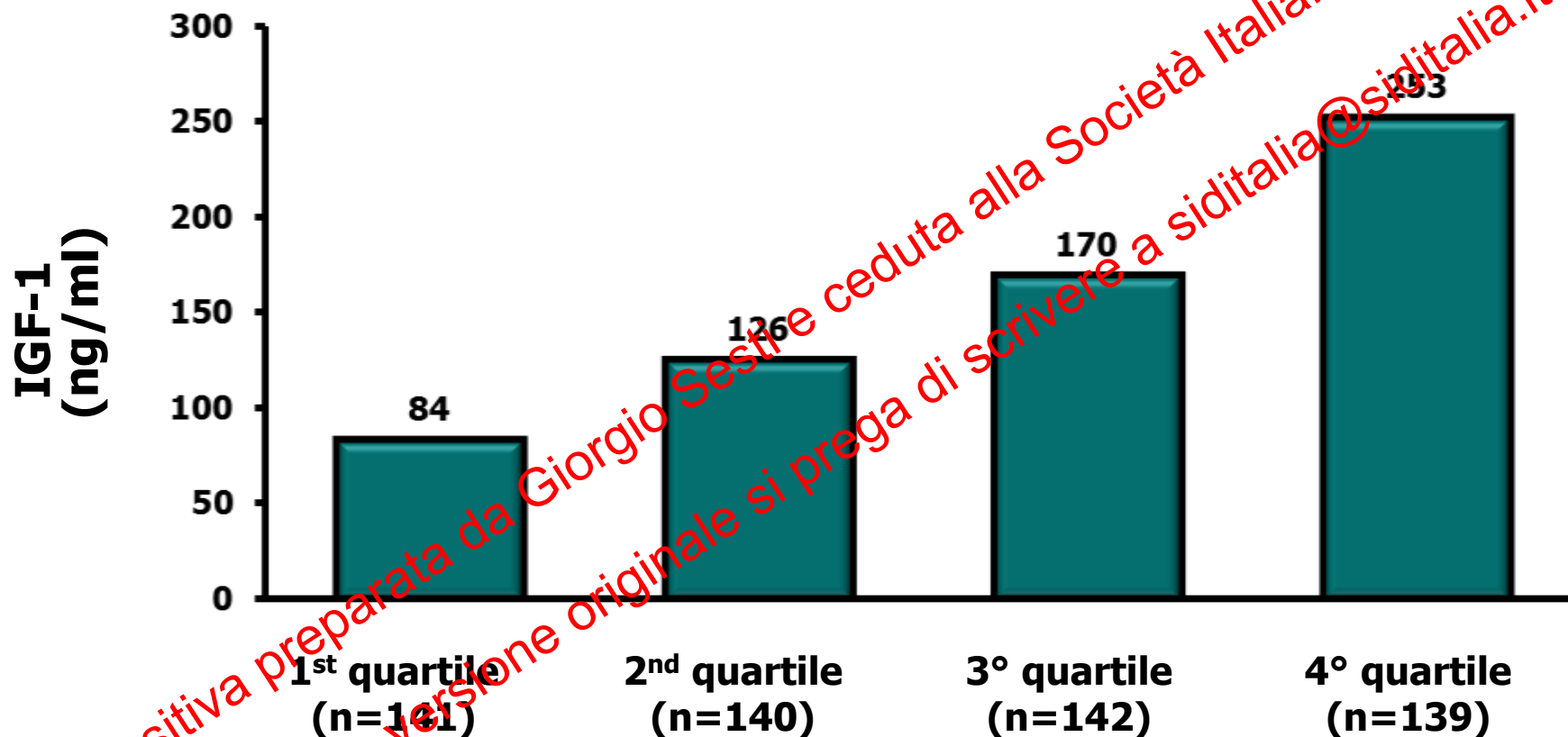
***3rd tertile vs. 1^o tertile**
HR=1.903, P=0.021

*Multivariable Cox regression model including age, smoking, LDLcholesterol, pulse pressure, fasting glucose and BMI

Plasma IGF-1 levels are reduced in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl

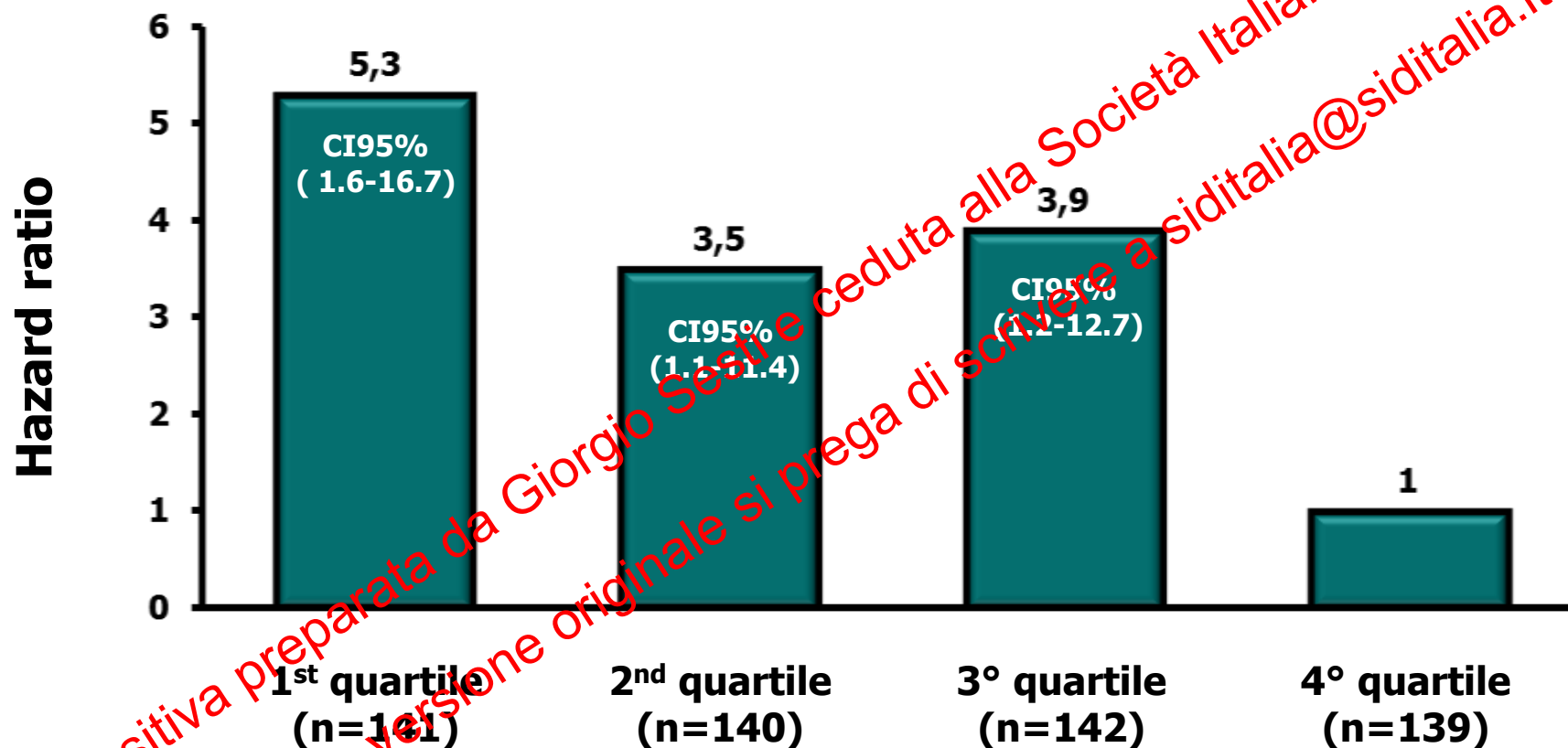


Risk of developing type-2 diabetes by baseline IGF-I concentrations for 567 nondiabetic individuals, The CATAMERI Study (mean follow-up 5,7 years)



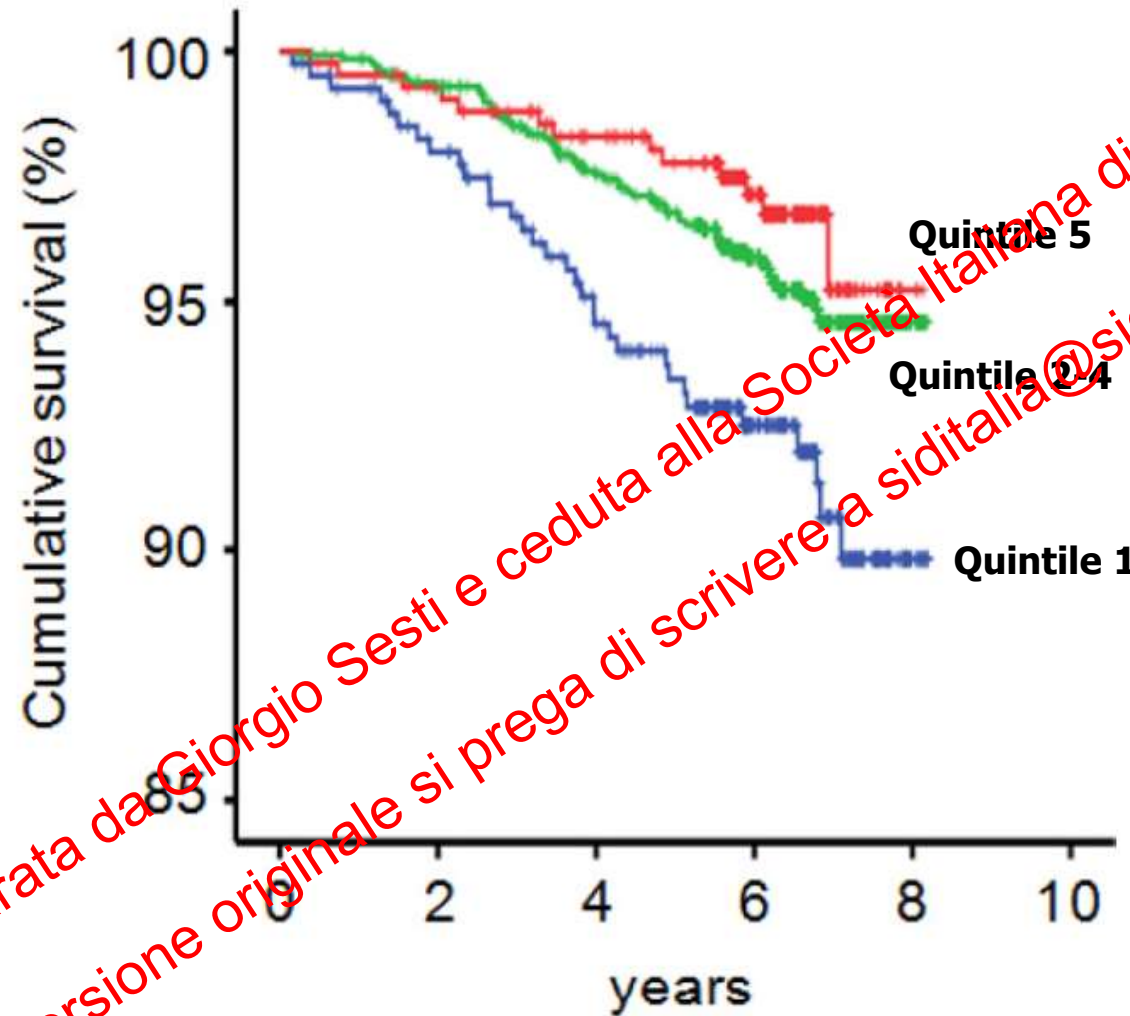
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Risk of developing type-2 diabetes by baseline IGF-I concentrations for 567 nondiabetic individuals, The CATAMERI Study (mean follow-up 5,7 years)



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Kaplan-Meier survival curves for CVD mortality by serum IGF-I concentration



No. at risk	2138	2079	1956	1349	82
Cumulative CVD deaths	0	20	57	88	102

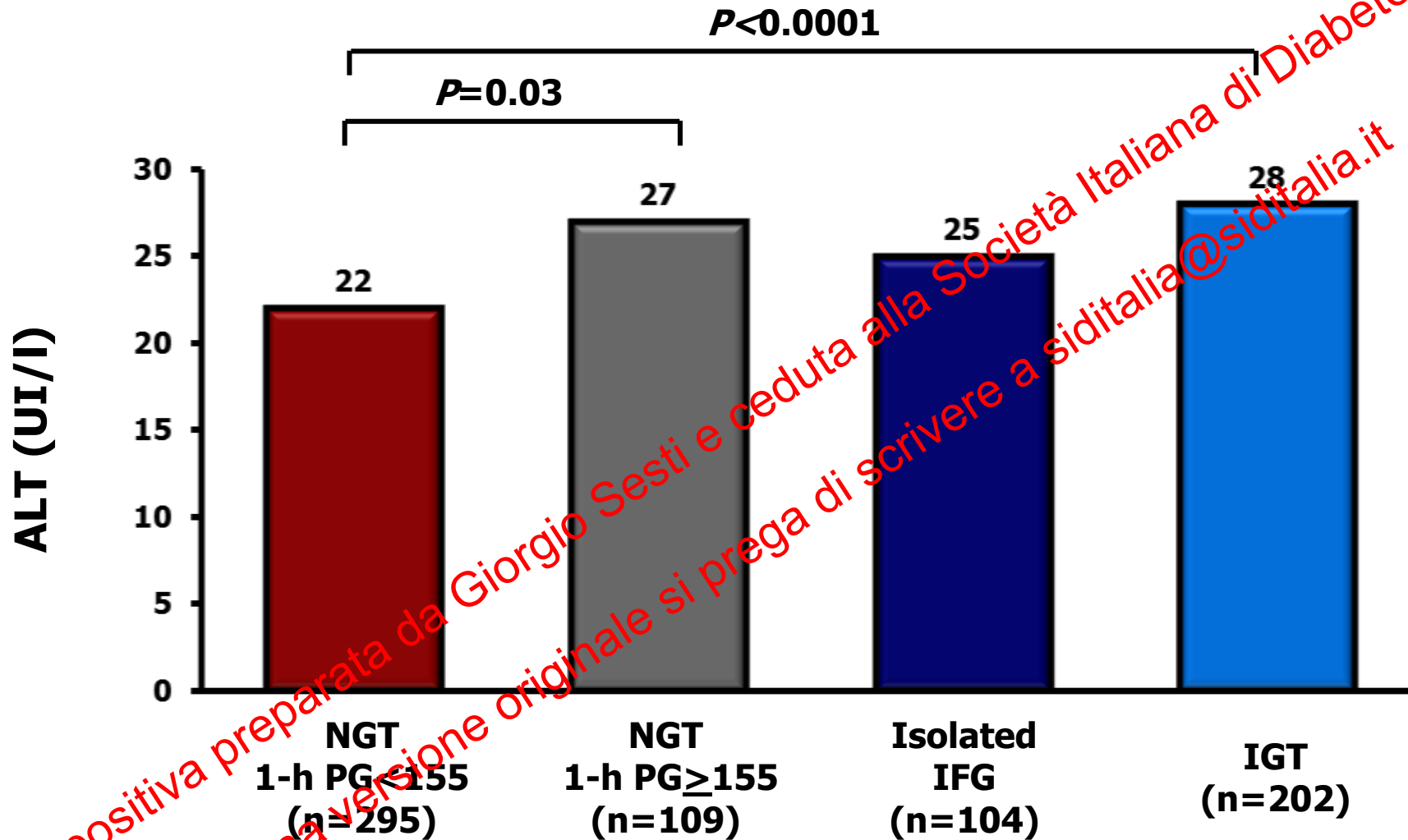
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Clinical characteristics of NGT 1h-high individuals:

- **insulin sensitivity and β -cell function,**
- **classical and non classical CV risk factors,**
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- **CV organ damage, and risk of CVD.**

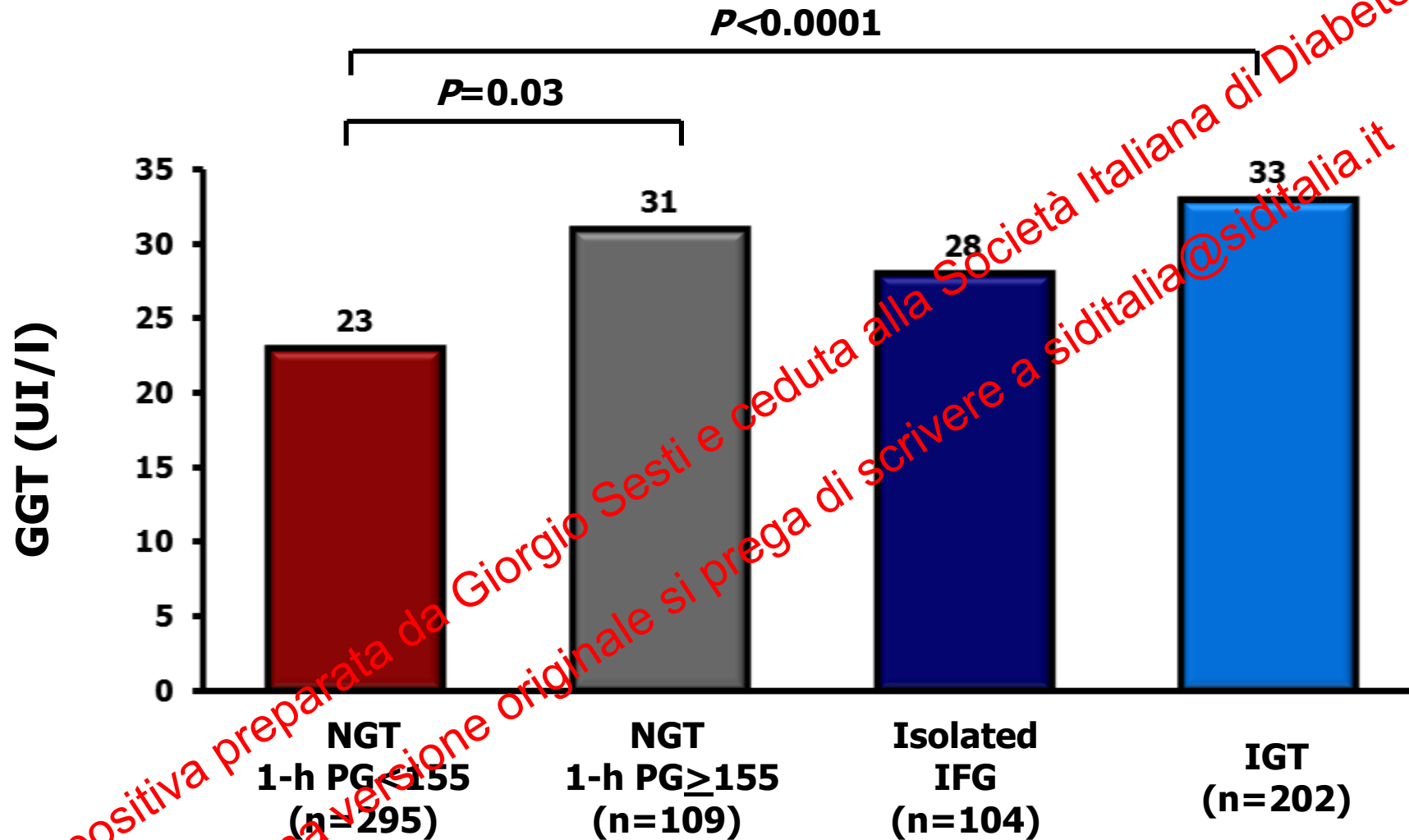
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Liver enzymes are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



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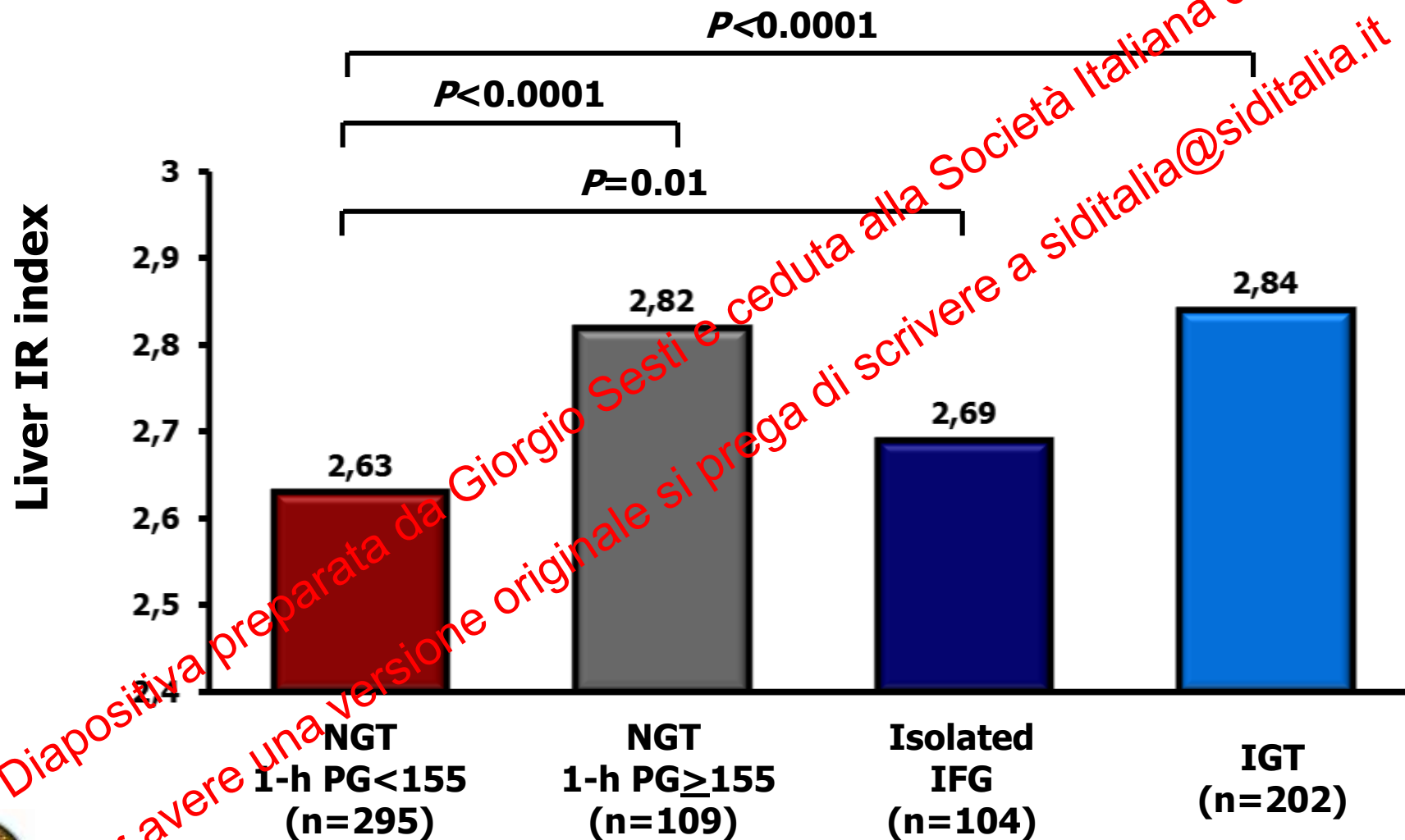
Liver enzymes are increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



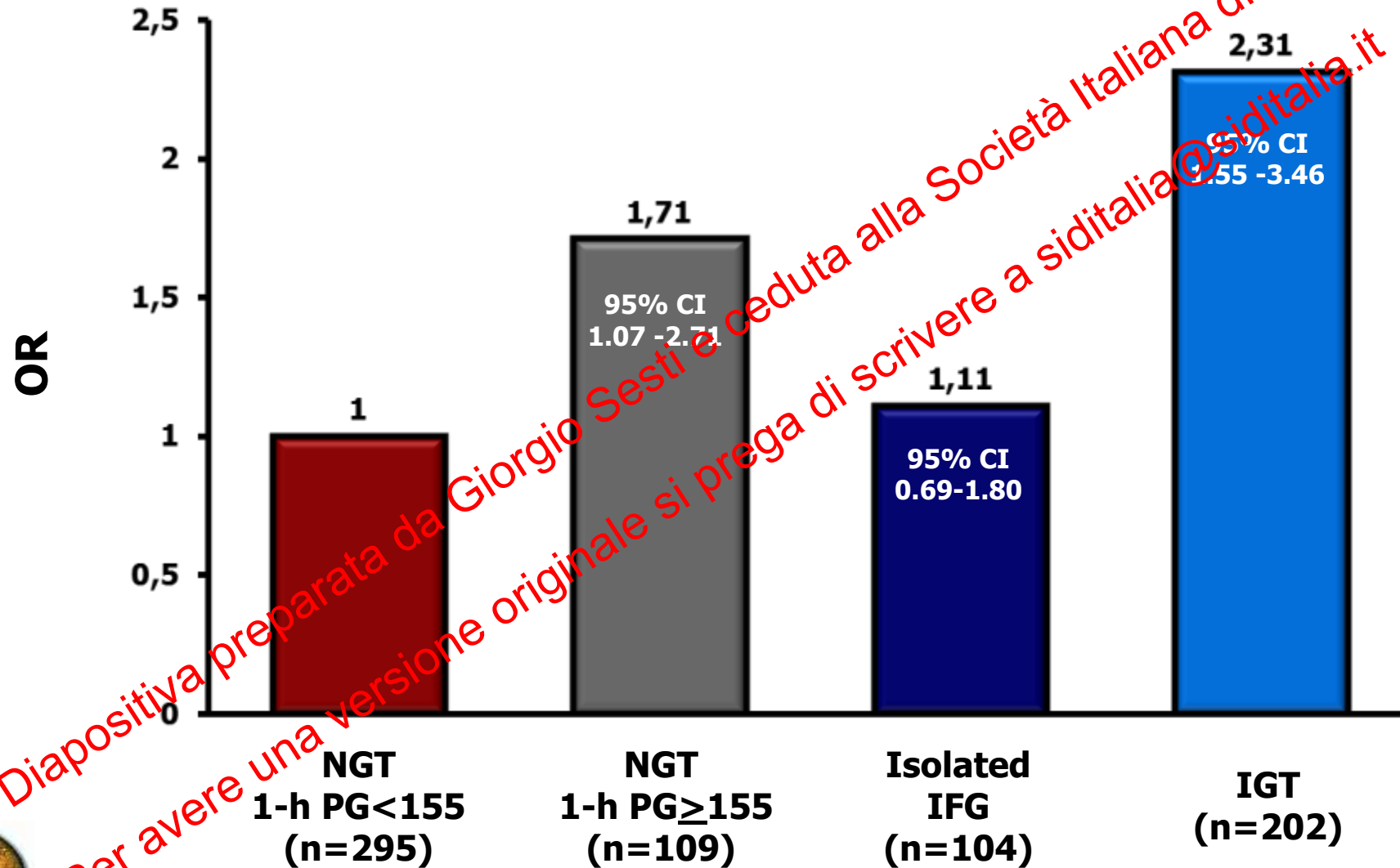
P values refer to results after analyses with adjustment for age, gender, and BMI

Liver IR index is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the CATAMERI study

The liver IR index was calculated using the formula: $-0.091 + (\log \text{insulin AUC } 0-120 \text{ min} \times 0.400) + (\log \text{fat mass \%} \times 0.346) - (\log \text{HDL Cholesterol} \times 0.408) + (\log \text{BMI} \times 0.435)$



Logistic regression analyses adjusted for age, and gender of the association between study group subjects and hepatic steatosis



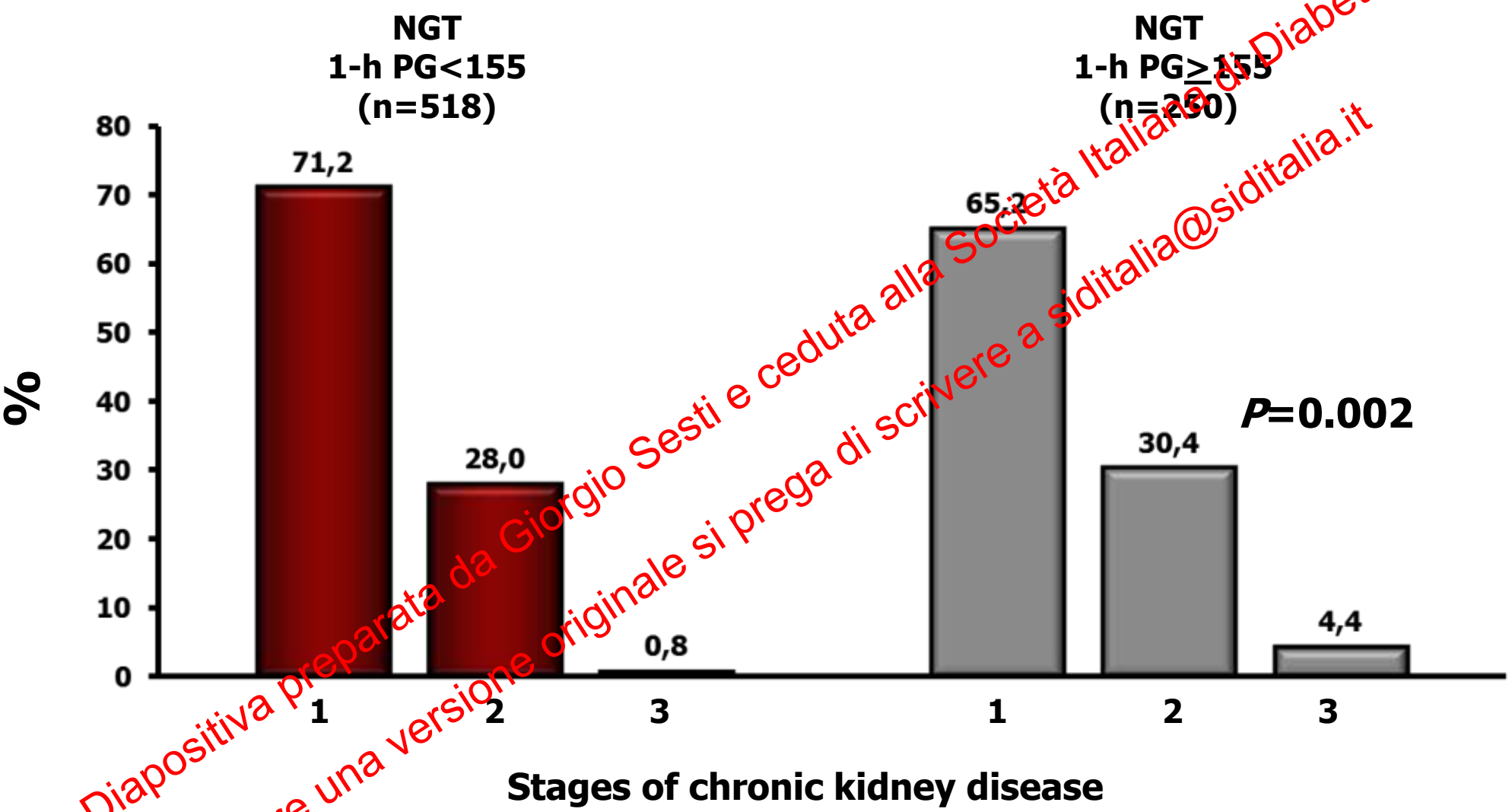
AGENDA

Clinical characteristics of NGT 1h-high individuals:

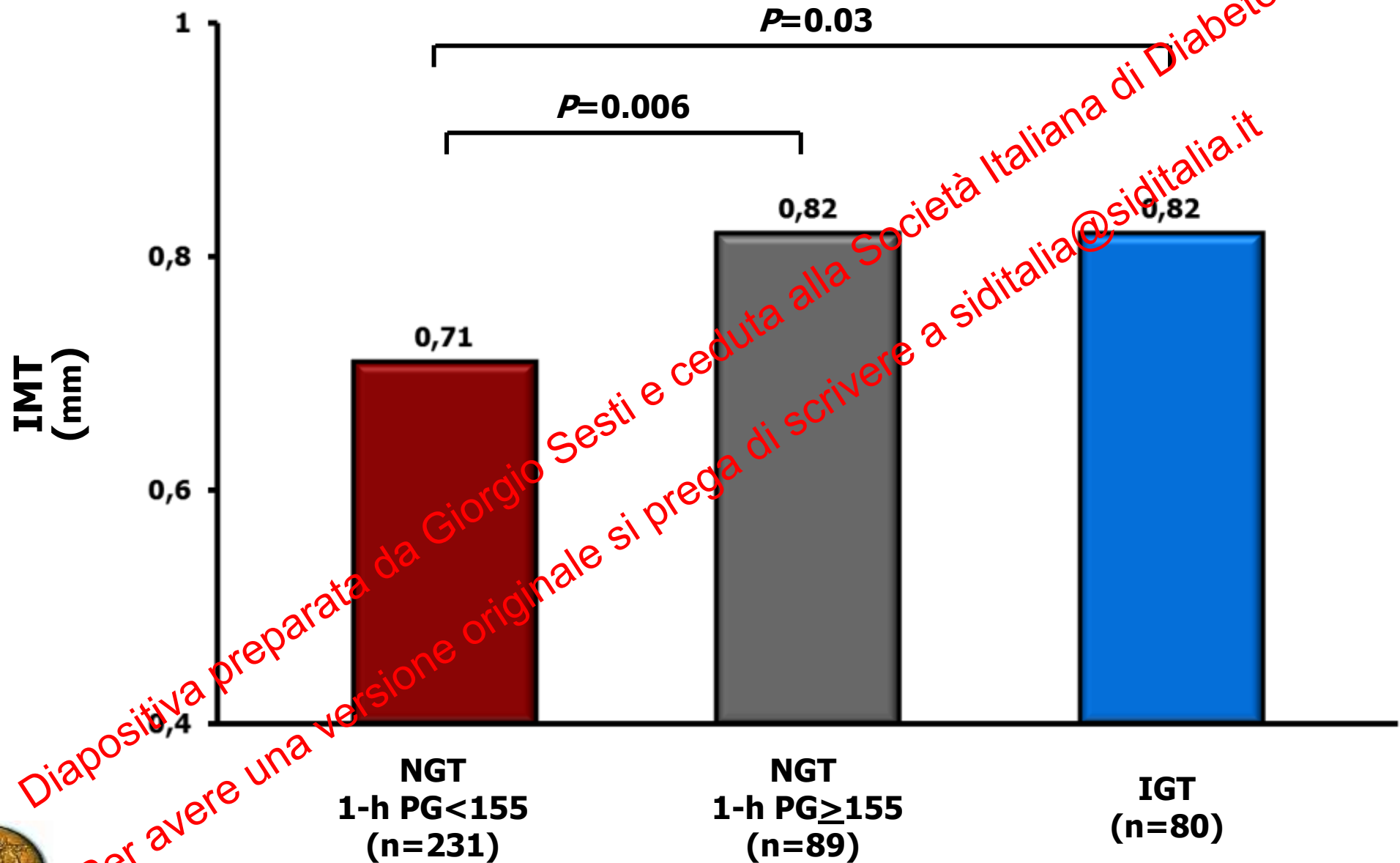
- insulin sensitivity and β -cell function,
- classical and non classical CV risk factors,
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- CV organ damage, and risk of CVD.

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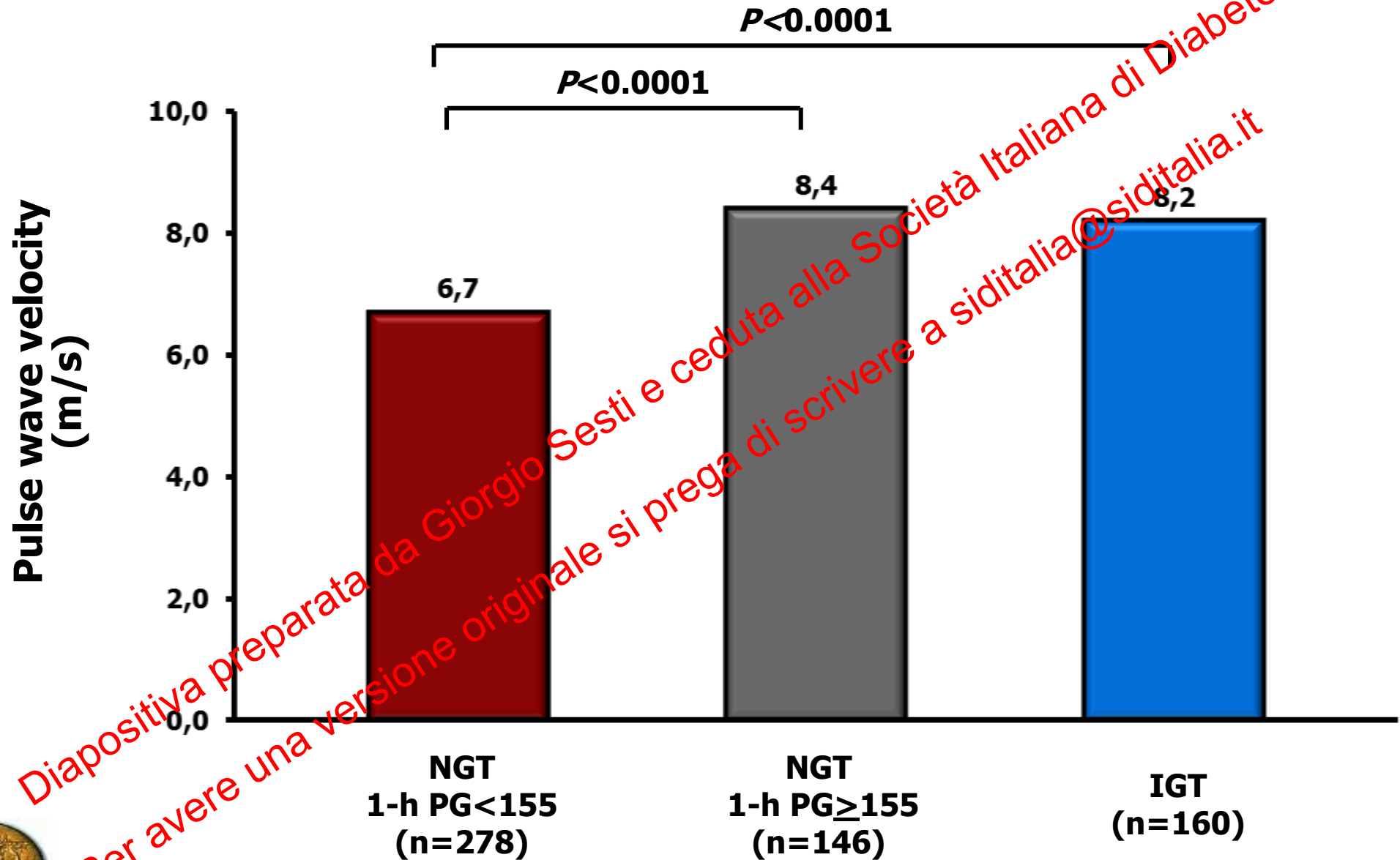
A higher proportion of NGT subjects with 1-h PG>155 mg/dl have stage 2 or stage 3 disease as compared with individuals with 1-h PG<155 mg/dl



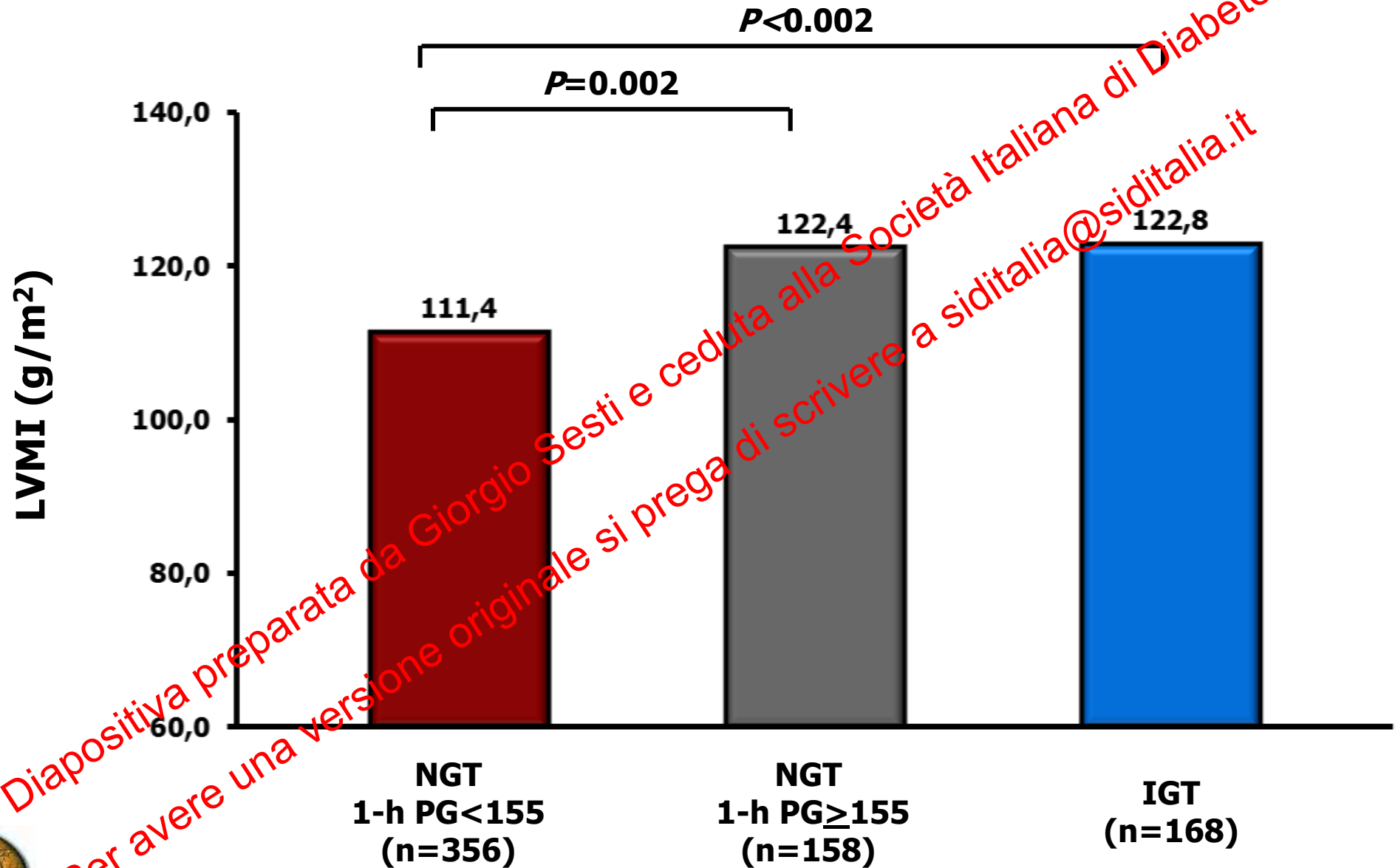
IMT is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



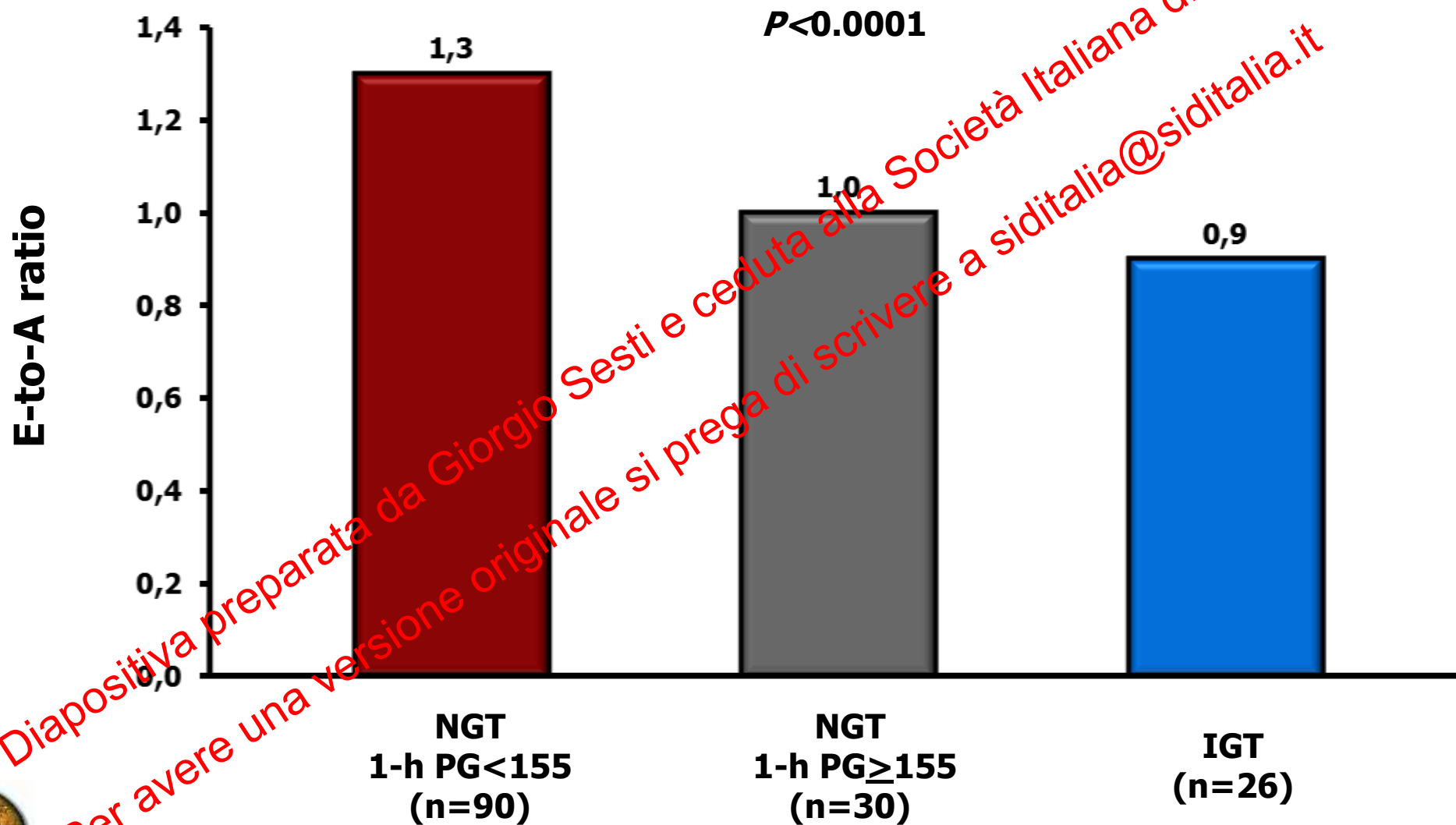
Pulse wave velocity is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



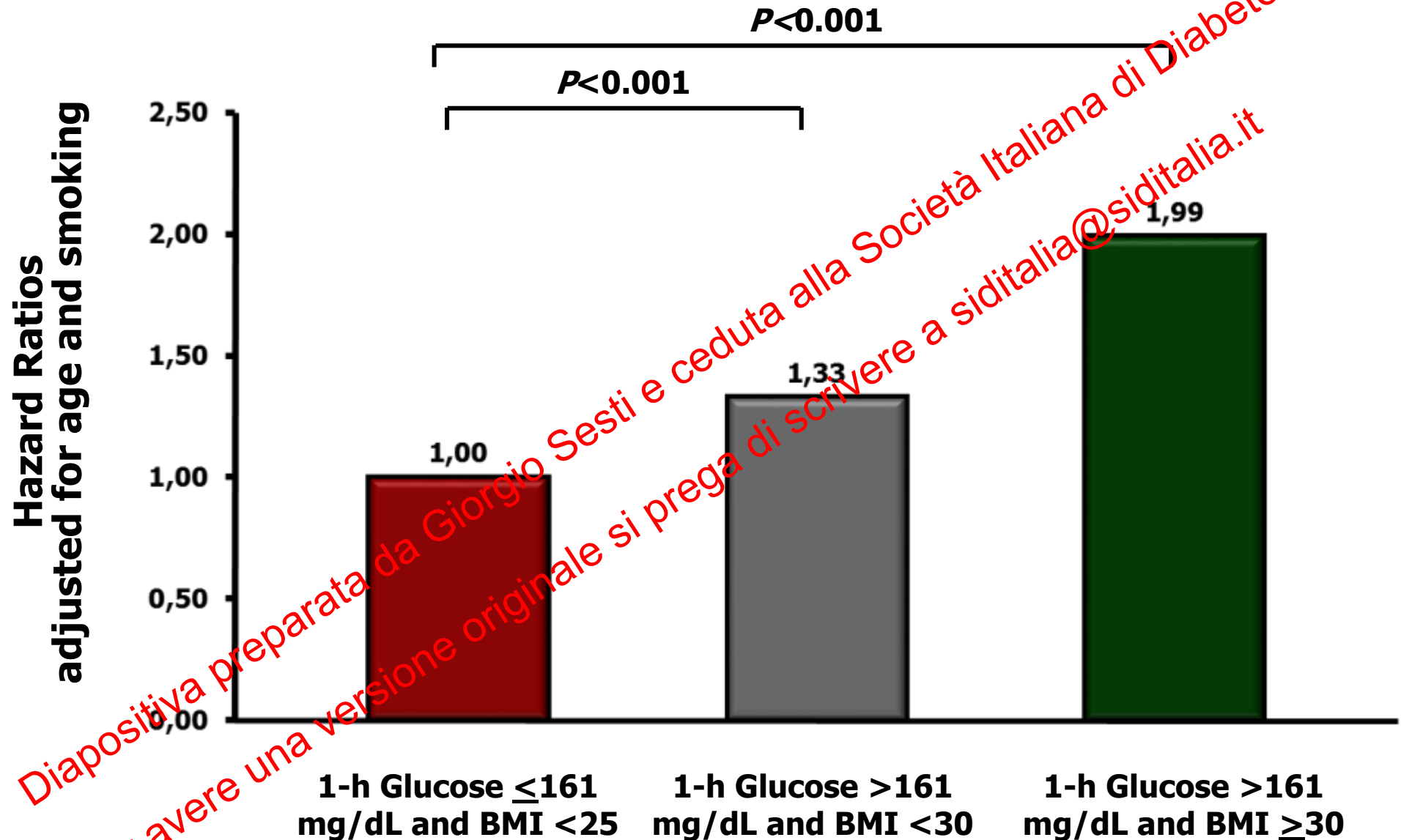
Left ventricular mass is increased in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the CATAMERI Study



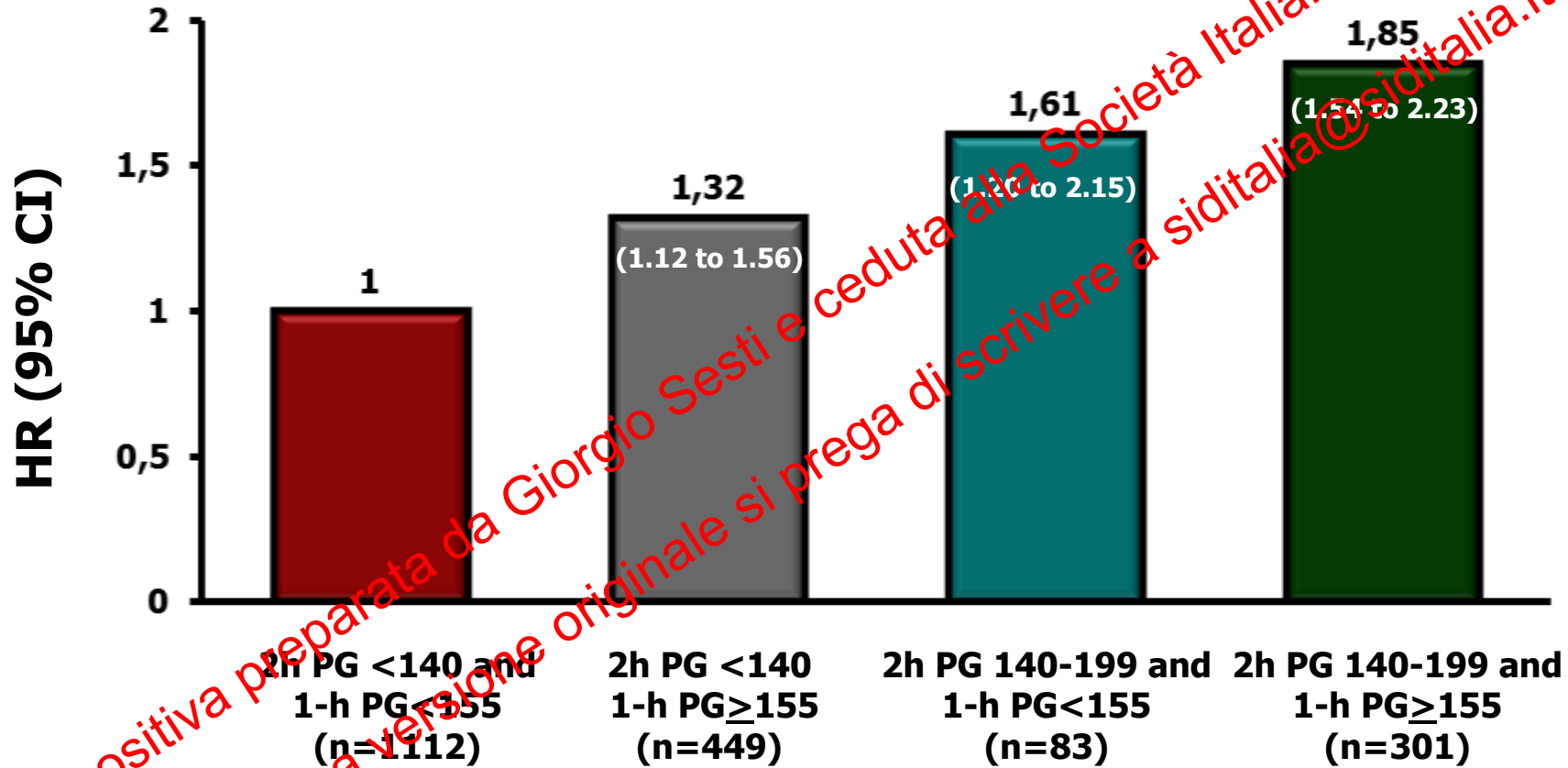
Impairment of left ventricular diastolic function in NGT subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl



Total mortality is increased in subjects with 1-h PG >161 mg/dl as compared with individuals with 1-h PG ≤161 mg/dl - the Helsinki Businessmen Study



Total mortality is increased in subjects with 1-h PG ≥ 155 mg/dl as compared with individuals with 1-h PG < 155 mg/dl - the Israel Study of Glucose Intolerance, Obesity and Hypertension (n= 1942)



P values refer to results after analyses with adjustment for sex, age, smoking, BMI, systolic and diastolic blood pressure and fasting blood glucose

Summary

- **NGT 1h-high individuals may represent an intermediate state of glucose intolerance between NGT and type 2 diabetes characterized by insulin resistance, and reduced β -cell function, the two main pathophysiological defects responsible for the development of type 2 diabetes.**
- **NGT 1h-high individuals exhibit a worse cardio-metabolic risk profile.**
- **A high level of 1hPG during OGTT may be helpful in the identification of subjects with normal glucose tolerance, but at increased risk for T2DM and CVD.**

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THANK YOU !

Now it's time for discussion.



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