



Trattamento della cardiopatia ischemica del paziente diabetico

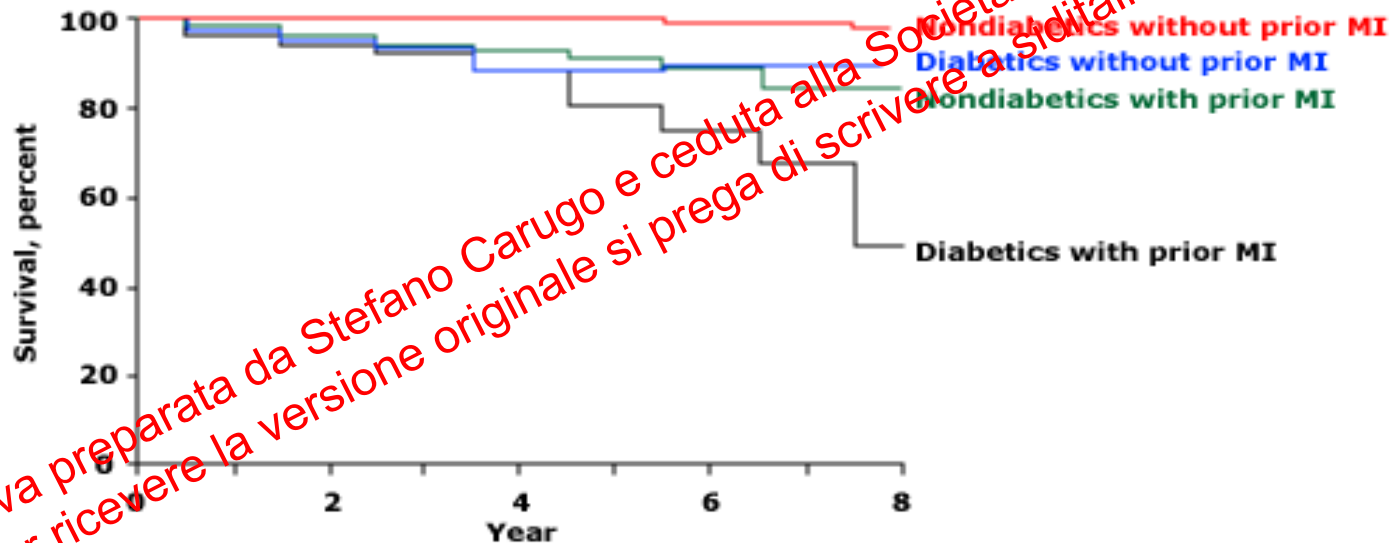
Milano 7 Luglio 2017

Prof. Stefano Carugo

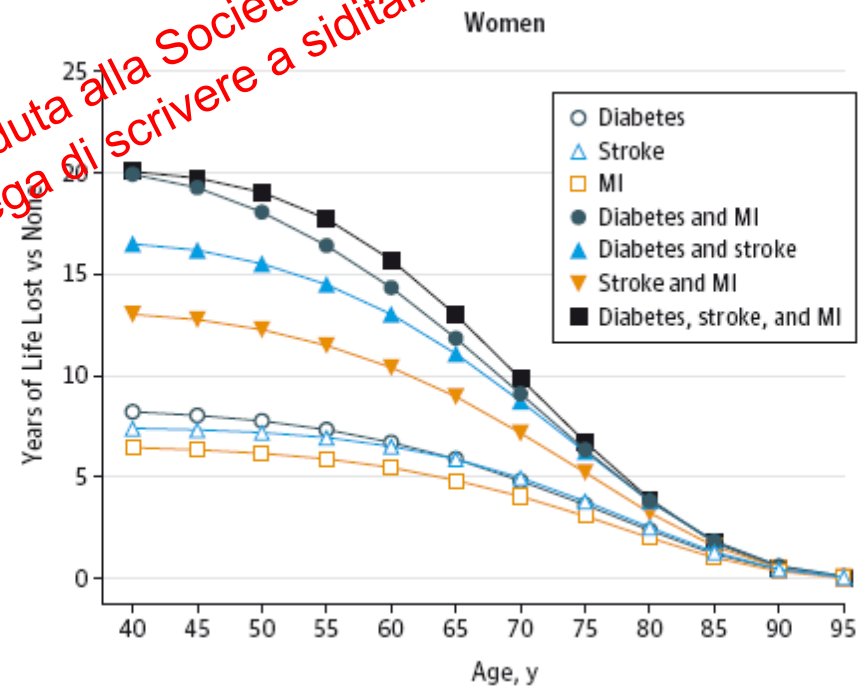
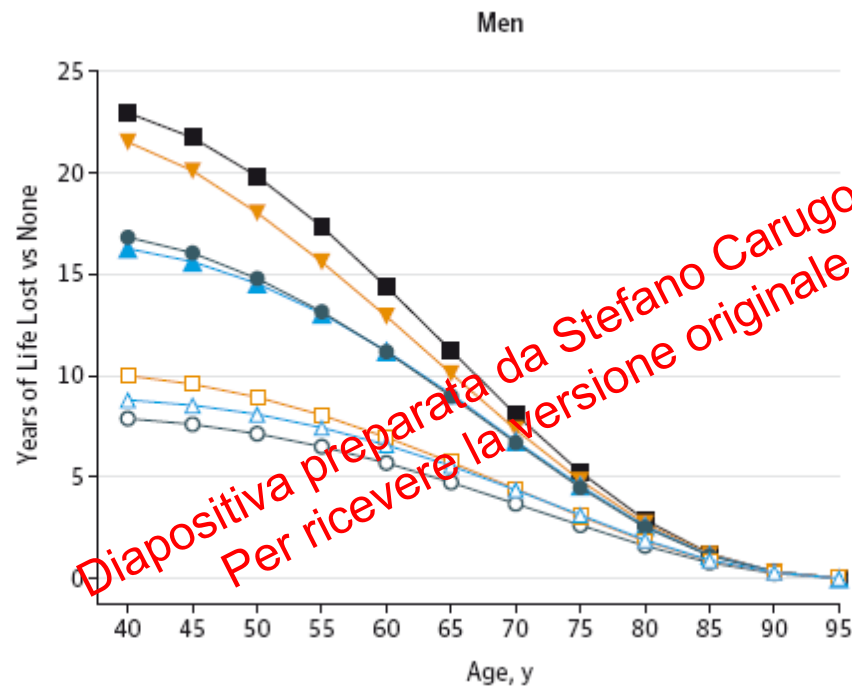
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Diabetes increases coronary mortality with and without a prior MI



Modeling of Years of Life Lost by Disease Status of Participants at Baseline Compared With Those Free of Diabetes, Stroke, and Myocardial Infarction (MI)



Glycaemic continuum and cardiovascular disease

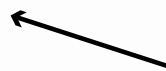
Frank diabetes

High blood glucose



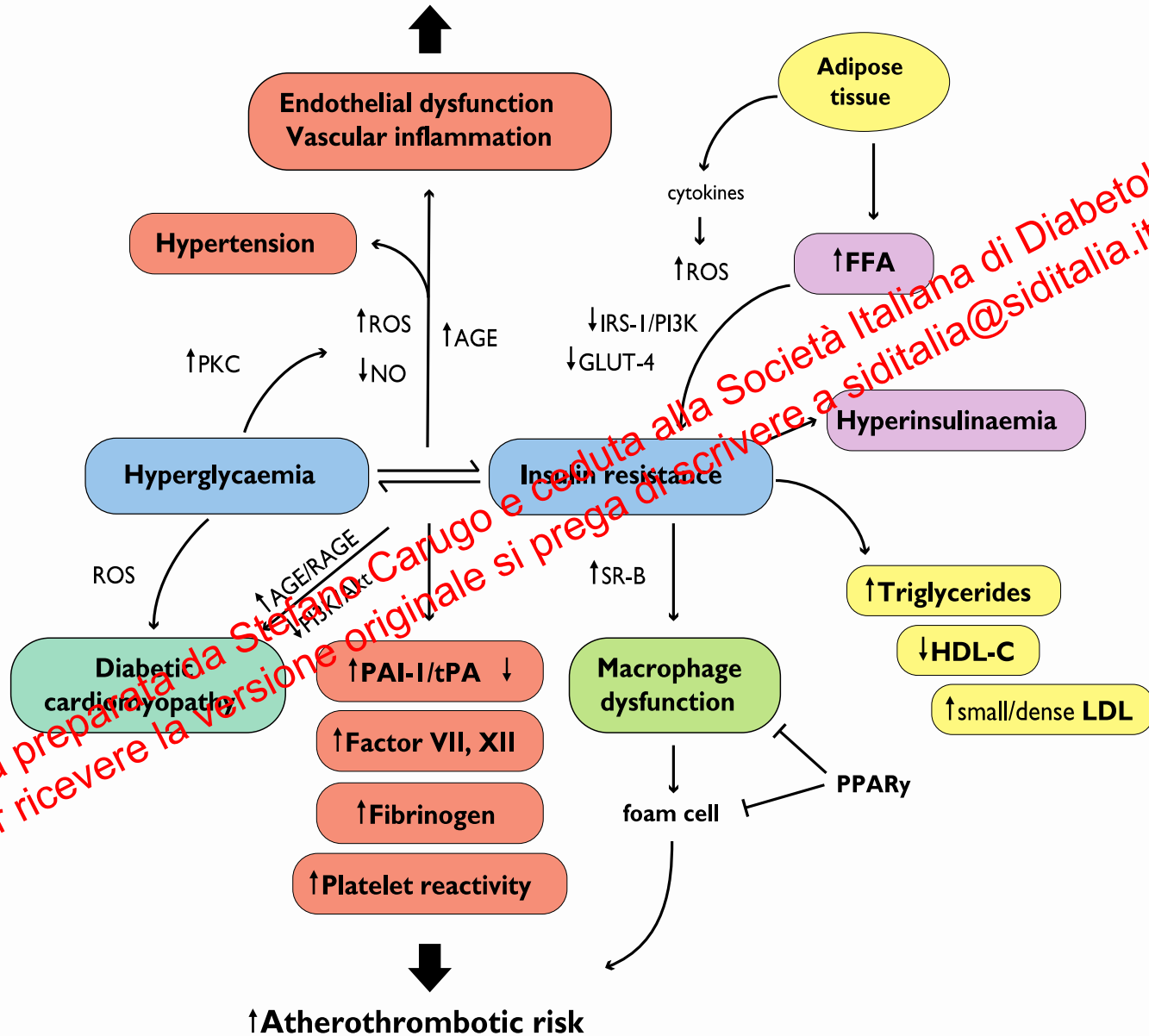
Microvascular complications

Macrovascular complications



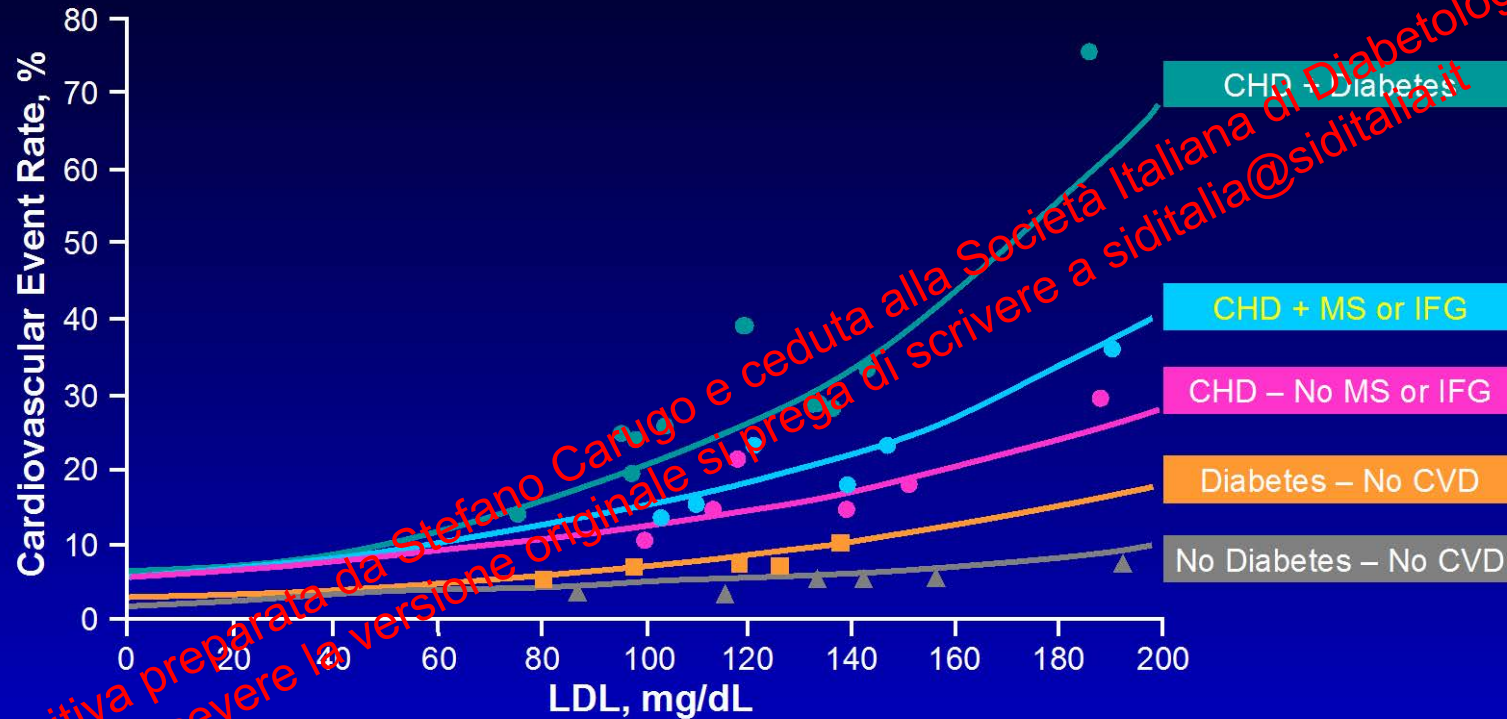
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↑Atherothrombotic risk



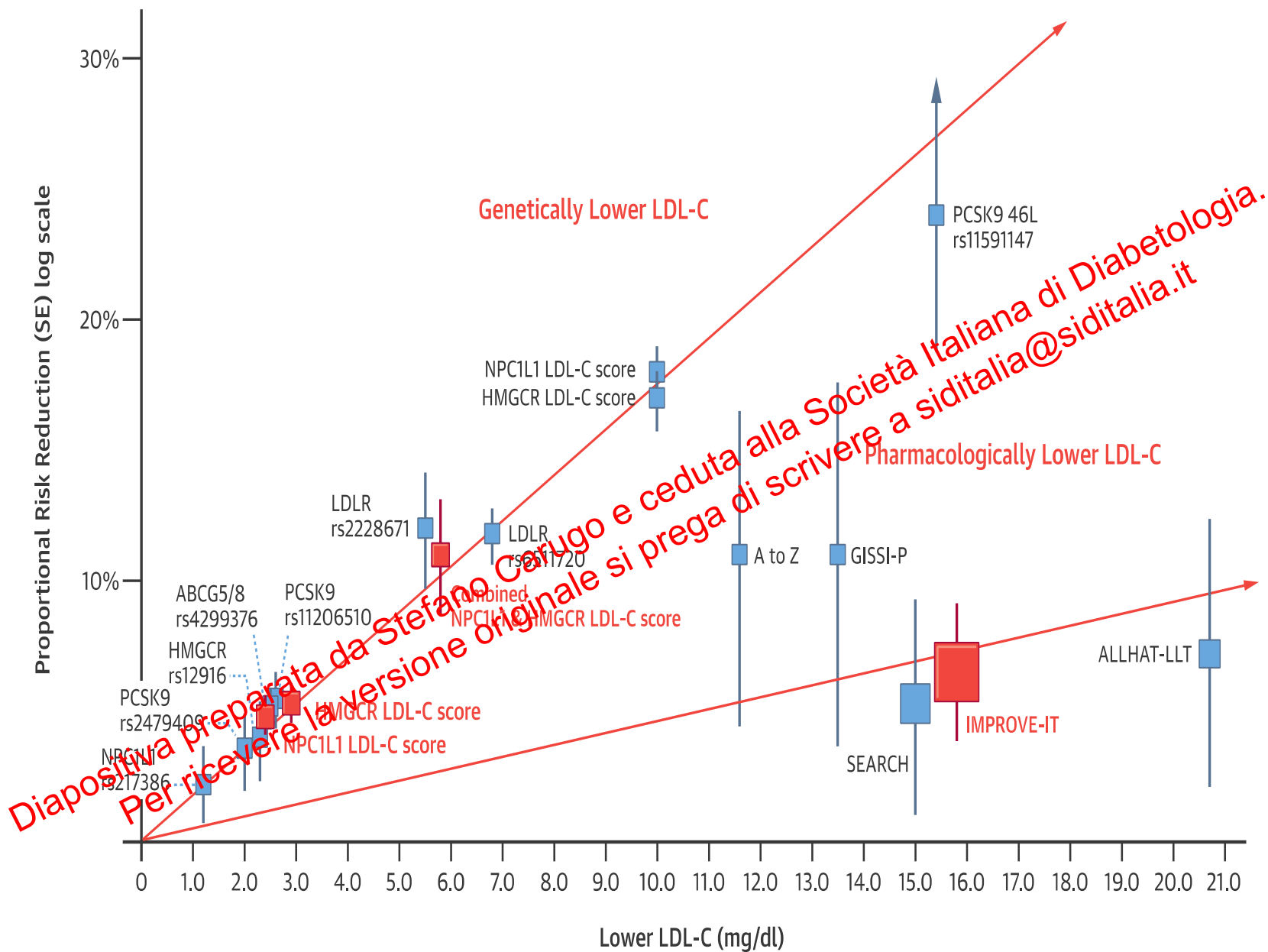
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Risk Pattern for Subsequent CV Events Over a Range of LDL-C Values¹



CV = cardiovascular; CHD = coronary heart disease; MS = metabolic syndrome; IFG = impaired fasting glucose; CVD = CV disease.

1. Robinson JG et al. *Am J Cardiol*. 2006;98:1405-1408.

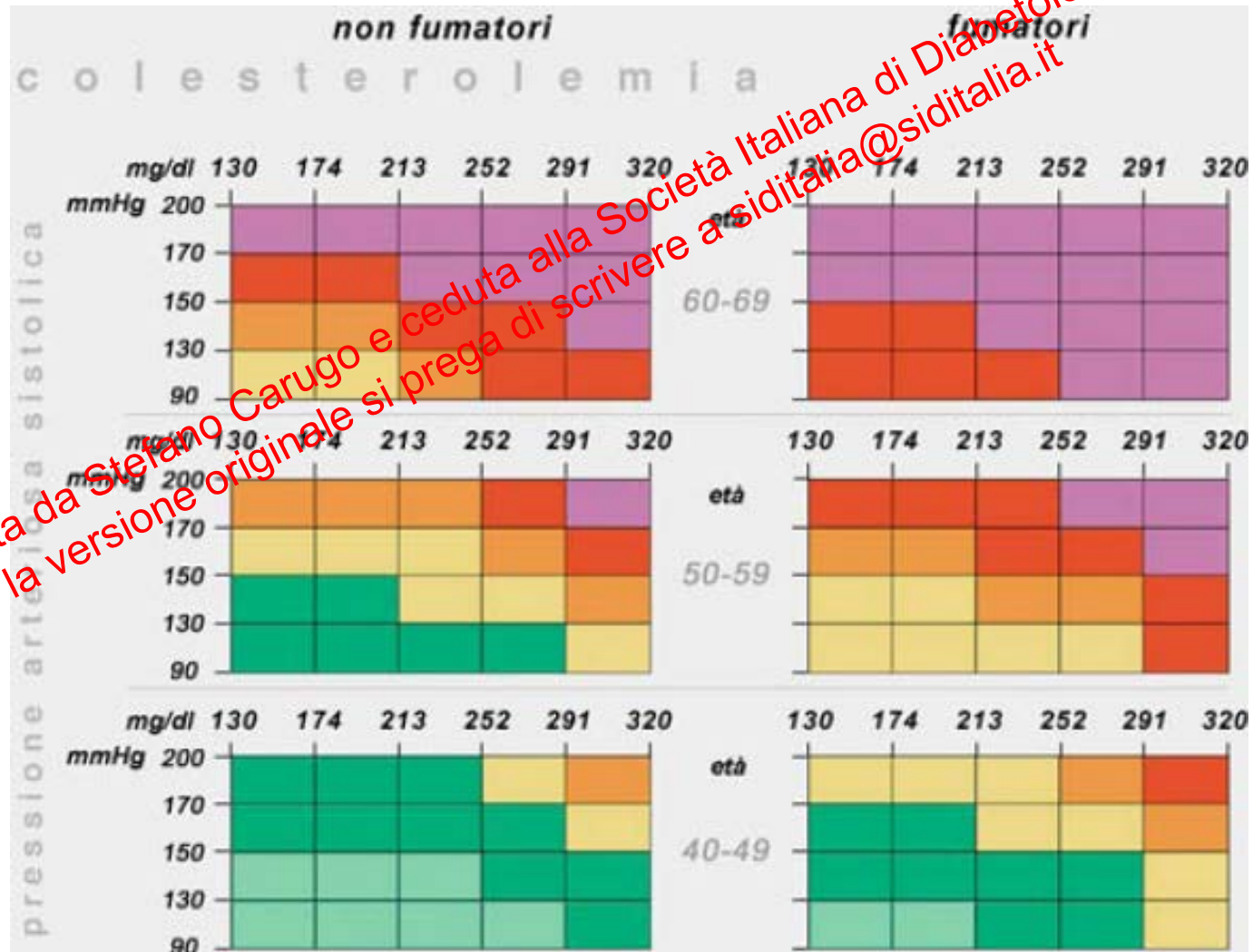


Carte del rischio cardiovascolare

Uomini diabetici



livello di rischio a 10 anni		
rischio MCV	VI	oltre 30%
rischio MCV	V	20% - 30%
rischio MCV	IV	15% - 20%
rischio MCV	III	10% - 15%
rischio MCV	II	5% - 10%
rischio MCV	I	meno 5%

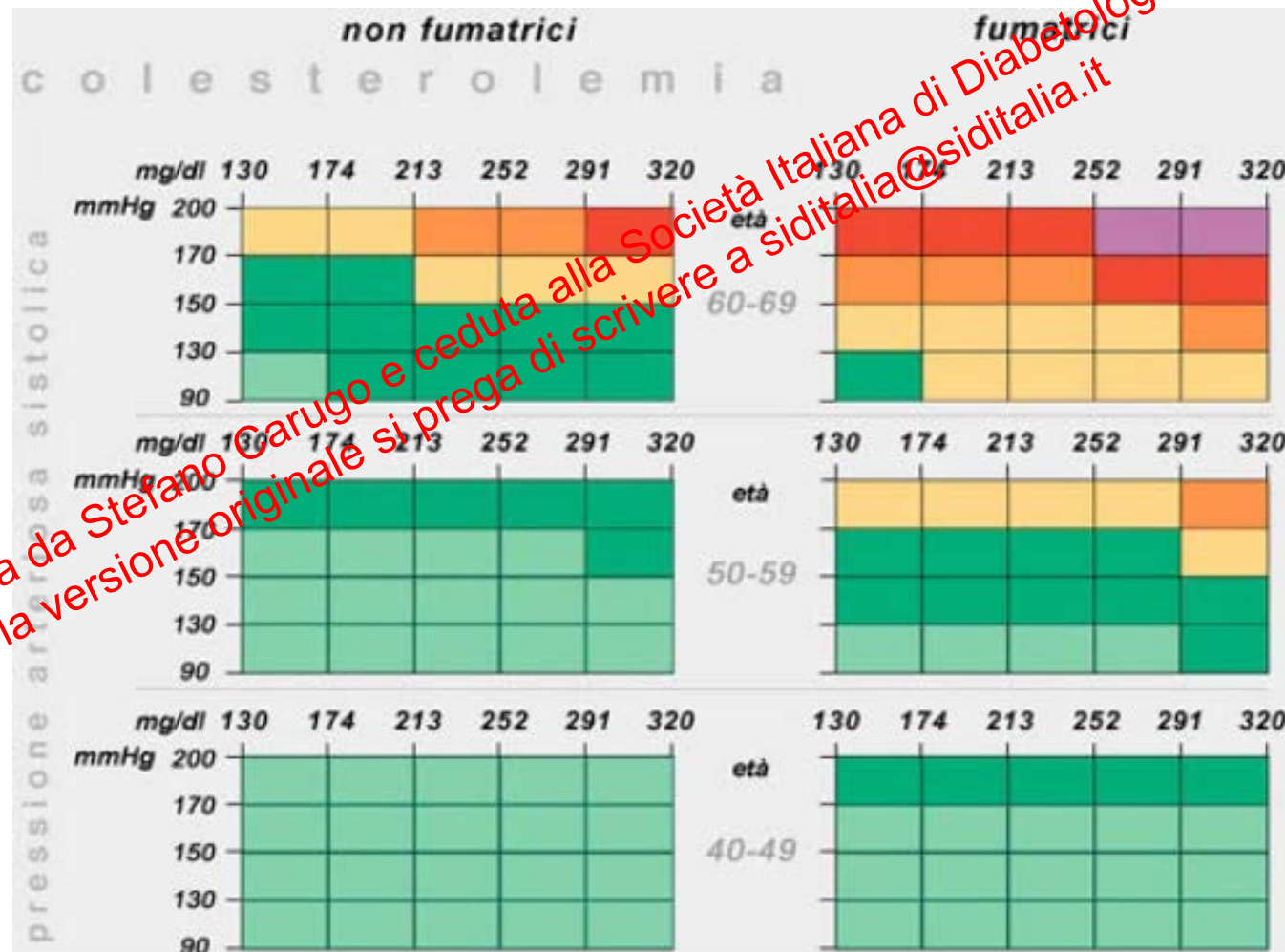


Carte del rischio cardiovascolare

Donne diabetiche



livello di rischio a 10 anni		
rischio MCV I	meno	5%
rischio MCV II	5% - 10%	
rischio MCV III	10% - 15%	
rischio MCV IV	15% - 20%	
rischio MCV V	20% - 30%	
rischio MCV VI	oltre	30%



Macrophages infiltration

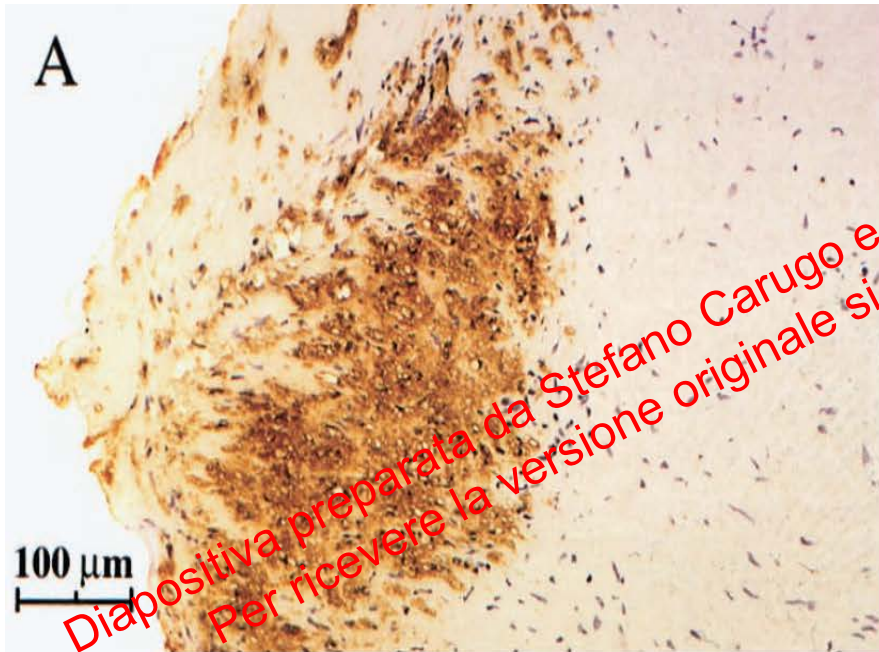
(From coronary atherectomy)

Coronary Composition and Macrophage Infiltration in Atherectomy Specimens From Patients With Diabetes Mellitus

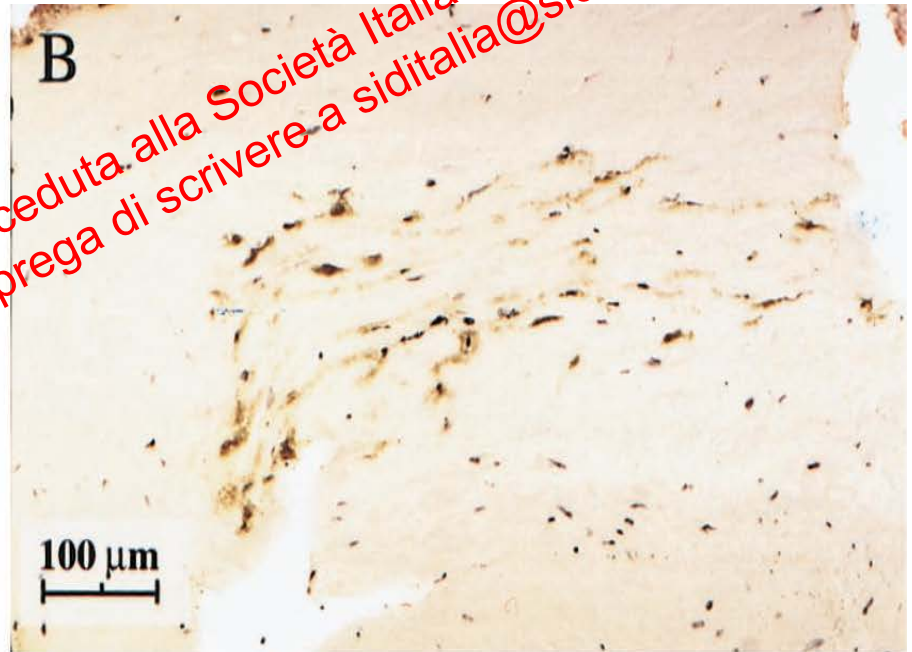
Pedro R. Moreno, MD, Alvaro M. Murcia, MD, Igor F. Palacios, MD, Alhadi N. Leon, Victor H. Benatti, MD, Valentin Foster, MD, PhD, John J. Pasterkamp, MD, PhD

Background—Lipid-rich, inflamed atherosclerotic lesions are associated with increased risk of cardiovascular thrombotic events, which are the most important causes of death in patients with diabetes mellitus. The purpose of this study was to quantify lipid composition and macrophage infiltration in the coronary lesions of patients with and without diabetes mellitus.

Methods and Results—A total of 77 coronary atherectomy specimens from 39 patients with diabetes mellitus were examined and compared with 43 atherectomy specimens from 22 patients without diabetes. Plaque composition was characterized by histologic staining. Macrophage infiltration was quantified by immunohistochemistry. Clinical and demographic data were similar in both groups. The percentage of lipid-rich atheroma was larger in specimens from patients with diabetes (22.1%) than in specimens from patients without diabetes (2.1%; $P=0.01$), and the percentage of lipid area occupied by macrophages was larger in specimens from patients with diabetes (22.2%) than in specimens from patients without diabetes (2.1%; $P=0.001$). The percentage of thrombus was also higher in specimens from patients with diabetes (45%) versus patients without diabetes (35%; $P=0.04$). Plaque macrophage infiltration was higher in specimens from patients with diabetes (45%) versus patients without diabetes (35%; $P=0.04$). These findings suggest that atherectomy lesions from diabetic patients treated with insulin have a higher content of lipid-rich atheroma, macrophage infiltration, and thrombus than lesions from patients without diabetes. These differences suggest an increased vulnerability to thrombotic events in patients with diabetes mellitus. (Circulation. 2000;102:2180-2184.)

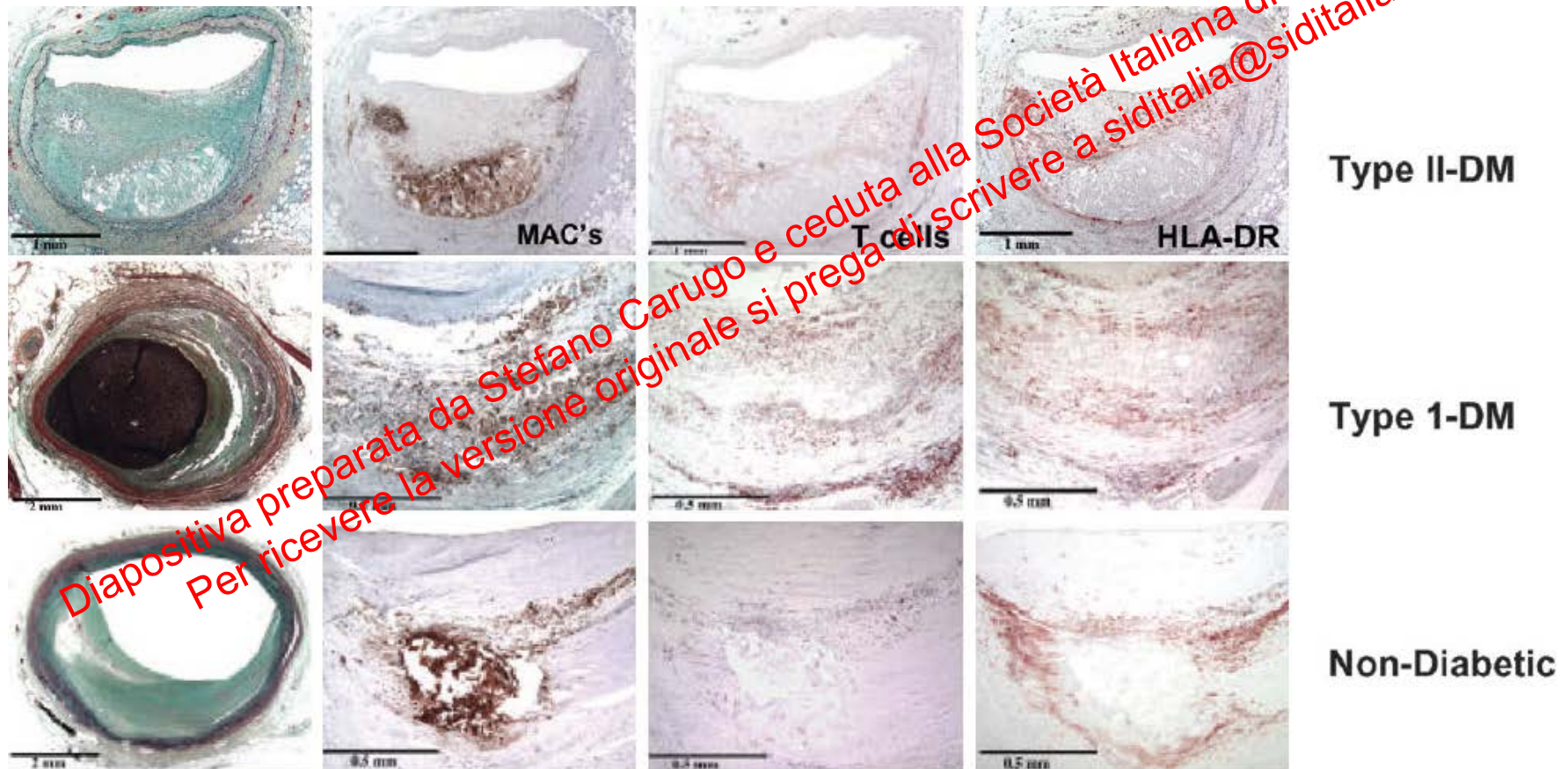


Diabetes mellitus

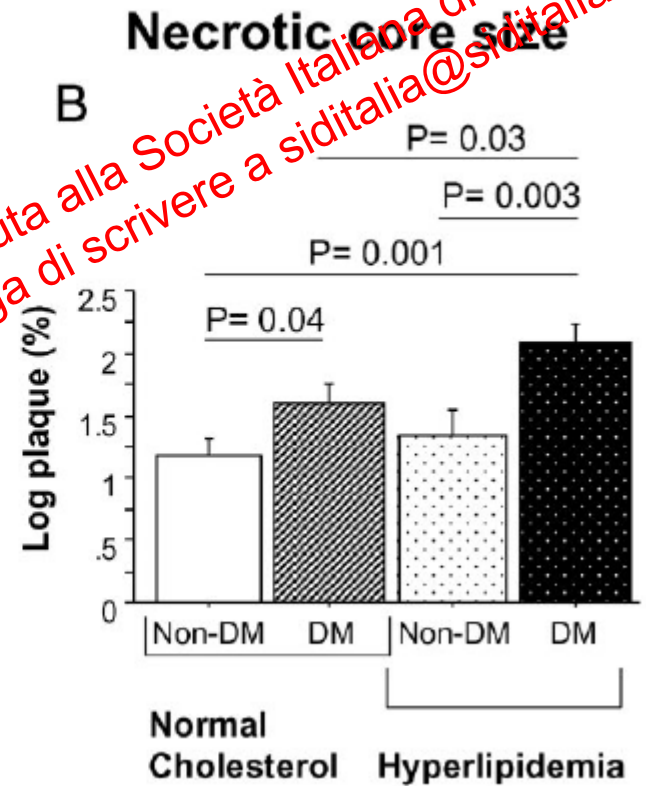
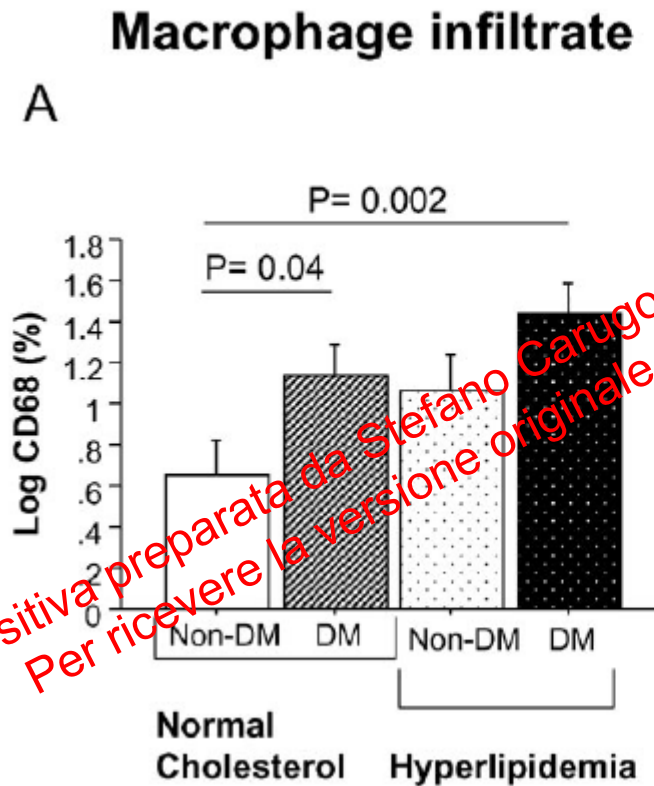


Non Diabetes mellitus

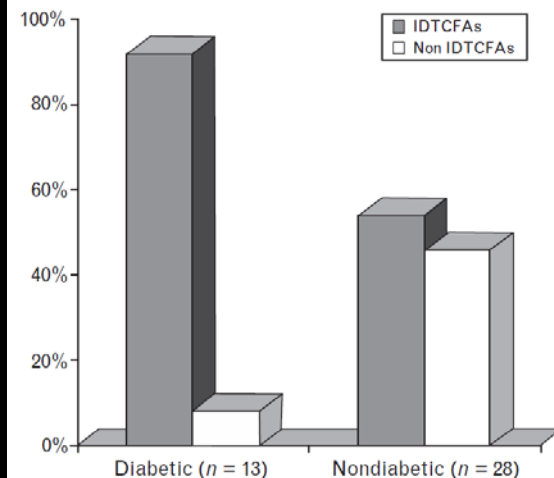
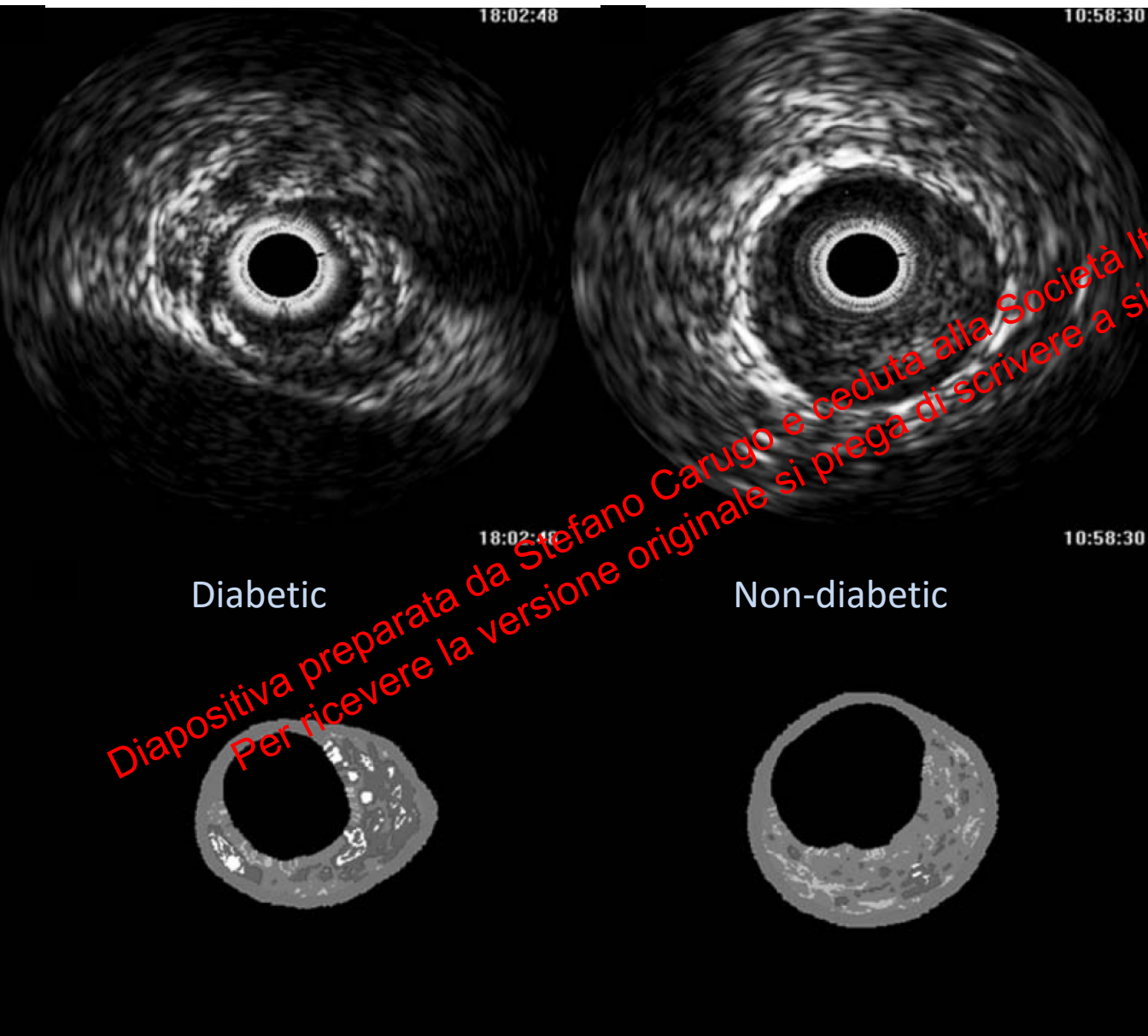
Inflammation in coronary arteries in diabetic and non-diabetic patients



Macrophages infiltrates and necrotic core size



IVUS-VH in diabetic and non diabetic patients



Il rischio cardiovascolare nel diabete

- Dal raffronto tra pazienti diabetici e non diabetici con angina instabile si osserva:

- una placca ulcerata nel 94% *vs* il 60%,
- trombi intracoronarici nel 94% *vs* il 55%,
- maggiore prevalenza di malattia bi- e trivasale.

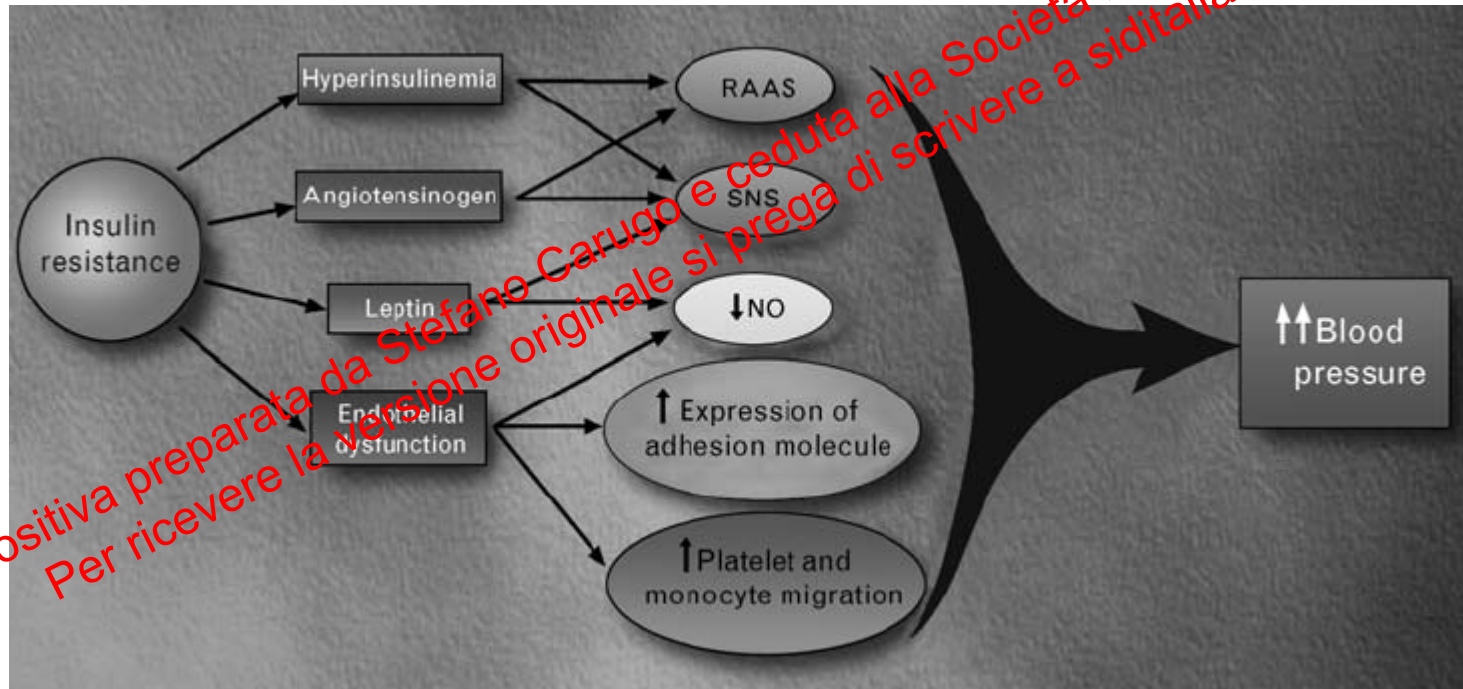


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**La soglia di percezione del dolore anginoso
risulta **più alta**
a causa della neuropatia autonoma che
coinvolge l'innervazione sensitiva del cuore**

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Ruolo della resistenza all'insulina nel determinare incremento pressorio



POSITION PAPER

Gestione multidisciplinare del paziente con sindrome coronarica acuta e diabete mellito: dalla terapia antitrombotica al trattamento dell'iperglicemia

Roberta Rossini¹, Antonino Cimino², Stefano De Servi³, Niccolò Grieco⁴, Corrado Lettieri⁵, Antonio Mafrici⁶, Giuseppe Musumeci¹, Gianluca Perseghin⁷, Carlo Sponzilli⁸, Roberto Trevisan⁹, Luigi Oltrona Visconti³, a nome della Sezione Lombarda dell'Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO), della Società Italiana di Cardiologia Invasiva (GISE), dell'Associazione Medici Diabetologi (AMD) e della Società Italiana di Diabetologia (SID)

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Documento di posizione “SCA-Diabete”



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dr. Antonio Mafrici, Milano

CARDIOLOGI INTERVENTISTI:

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dr. Corrado Cattieri, Mantova
dr. Stefano De Servi, Legnano
dr. Carlo Sponzilli, Milano

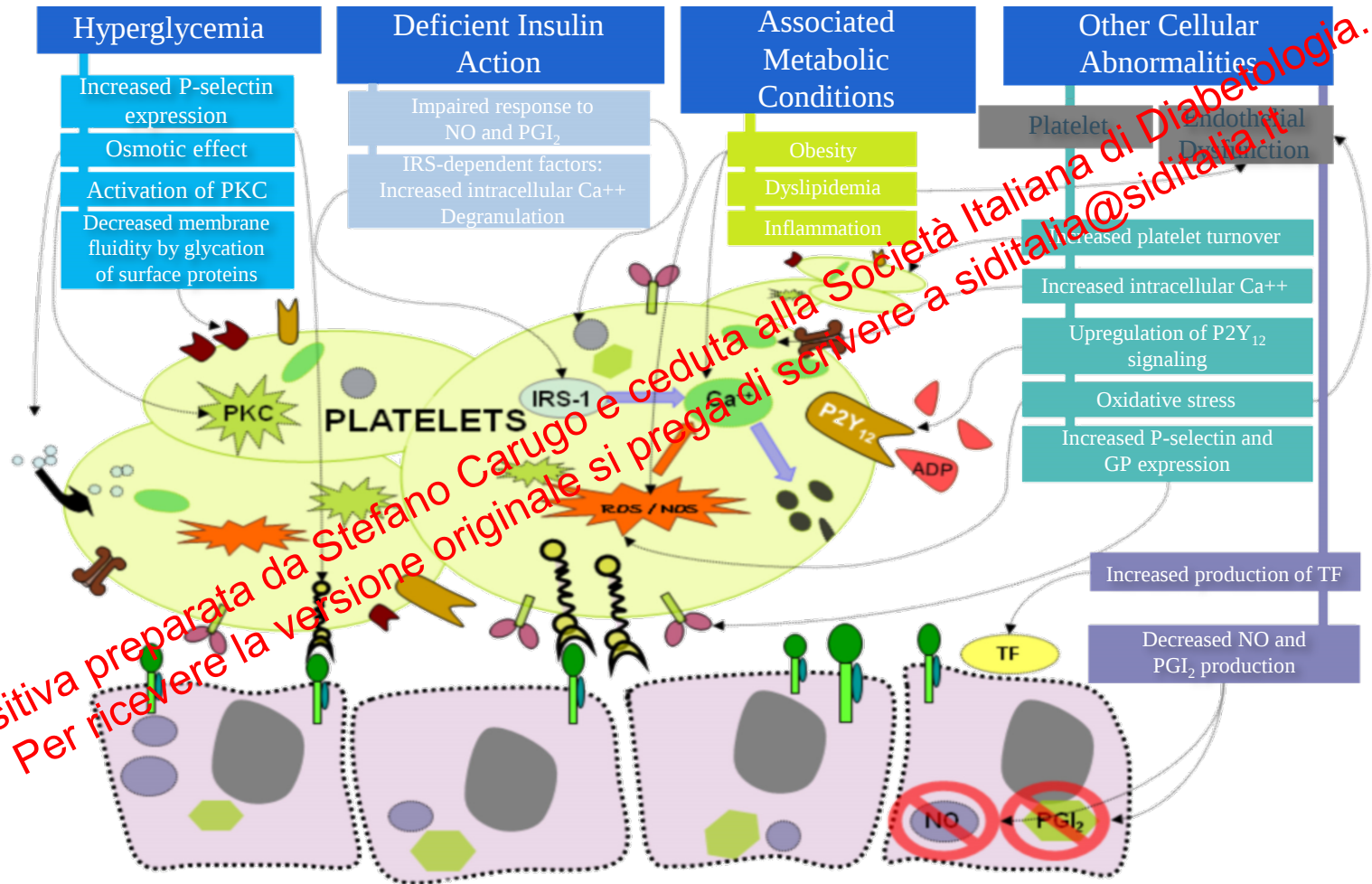
DIABETOLOGI:

dr. Roberto Trevisan, Bergamo
dr. Emanuele Perseghin, Monza
dr. Antonio Cimino, Brescia

**Aumentare il grado di
appropriatezza secondo uno
standard di qualità**

GISE Lombardia, ANMCO Lombardia, LombardIMA, SID Lombardia, AMD Lombardia

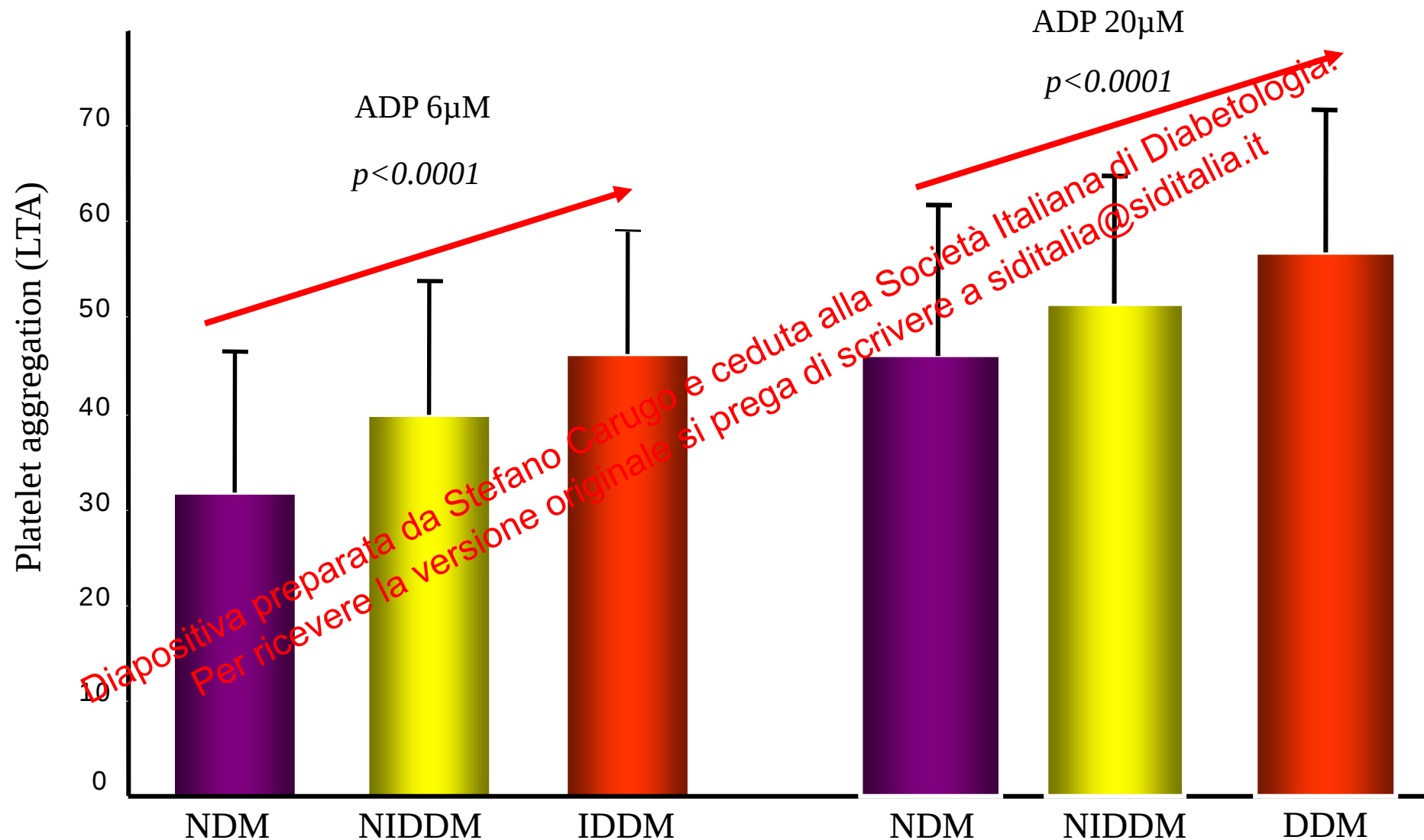
Mechanisms Involved in Platelet Dysfunction in Diabetes Mellitus



ACP=adenosine diphosphate; GP=glycoprotein; IRS-1=insulin receptor substrate-1; NO=nitric oxide; PGI₂=prostacyclin; PKC= protein kinase C; TF=tissue factor.

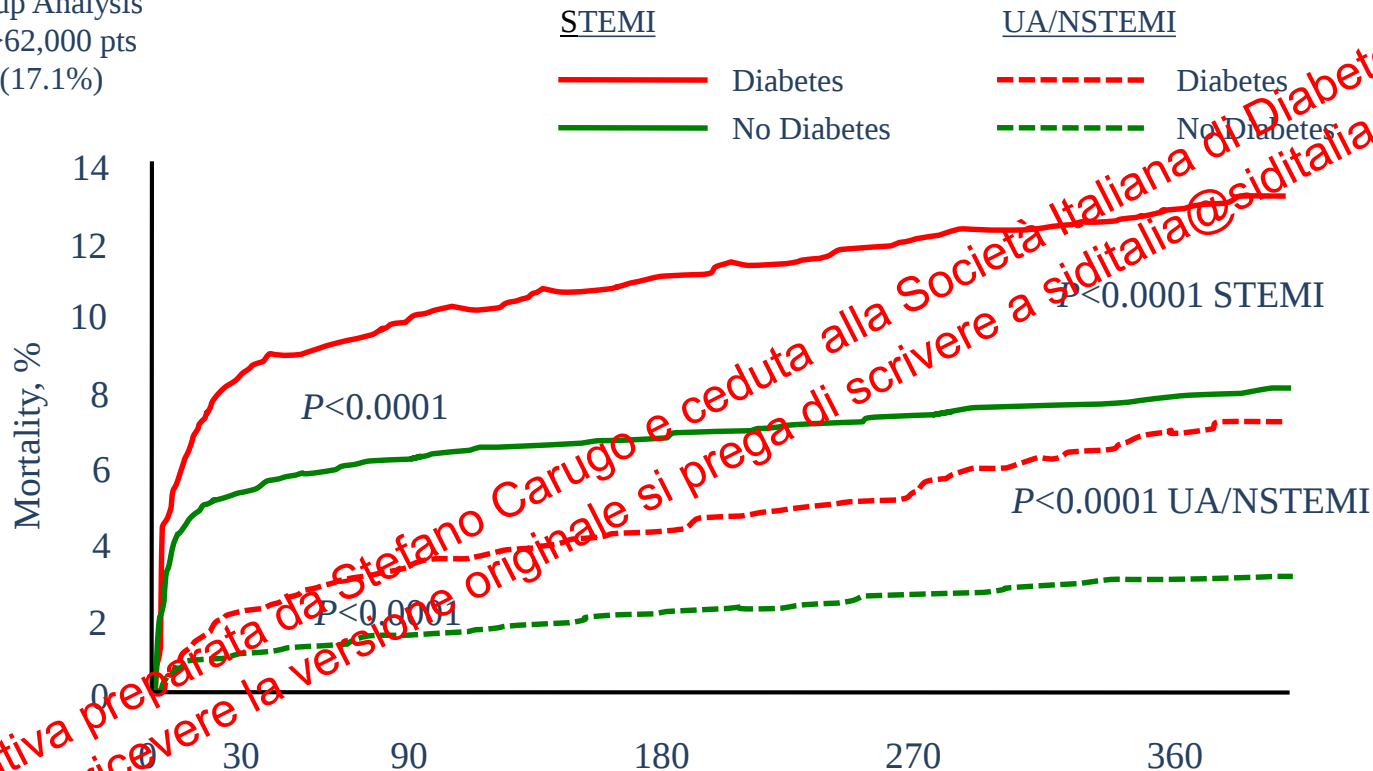
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Platelet Function According to Hypoglycemic Treatment



Cumulative Incidence of All-Cause Mortality Through 1 Year After ACS

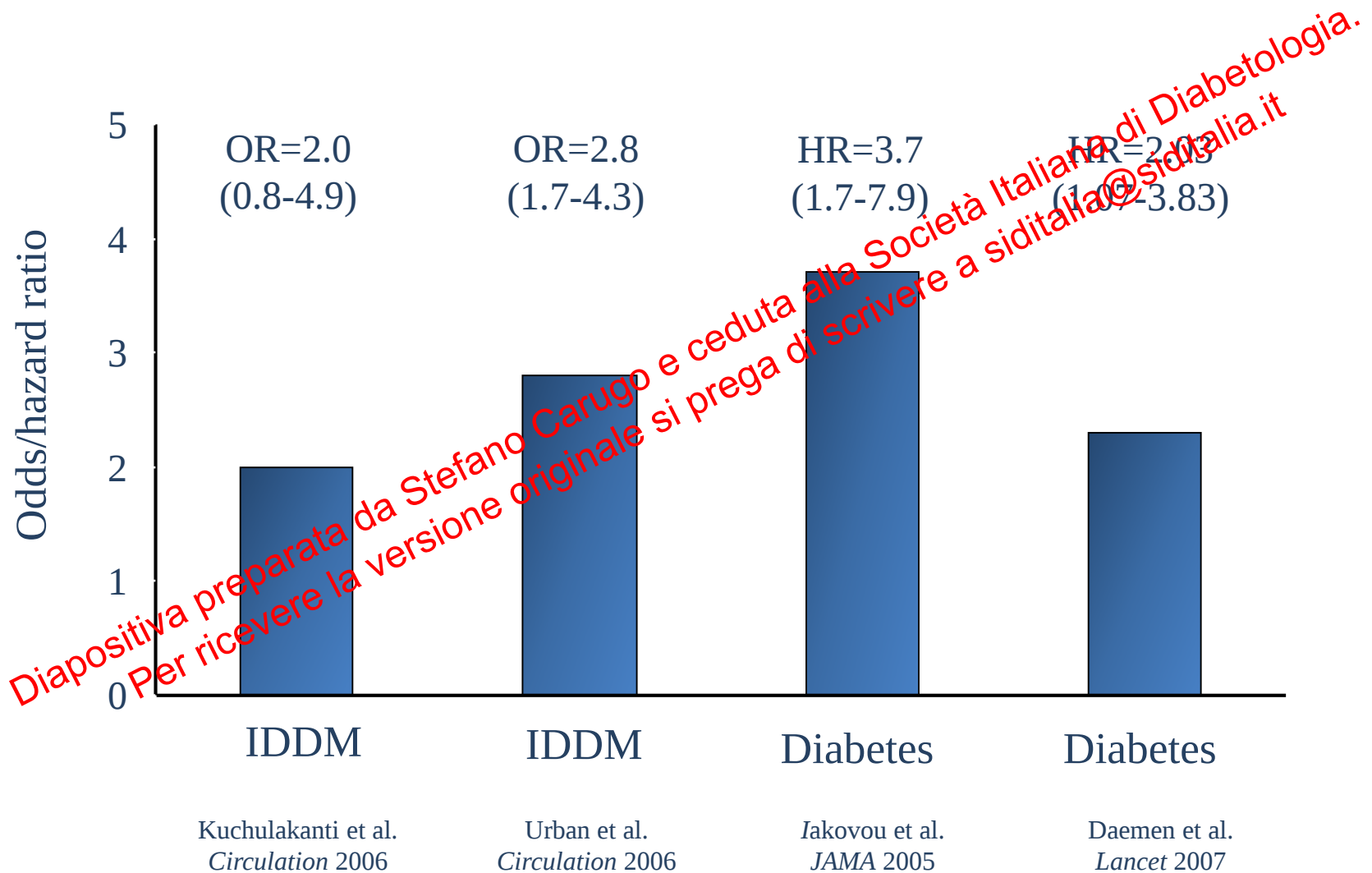
Diabetes Subgroup Analysis
11 TIMI Trials, >62,000 pts
10,613 diabetics (17.1%)



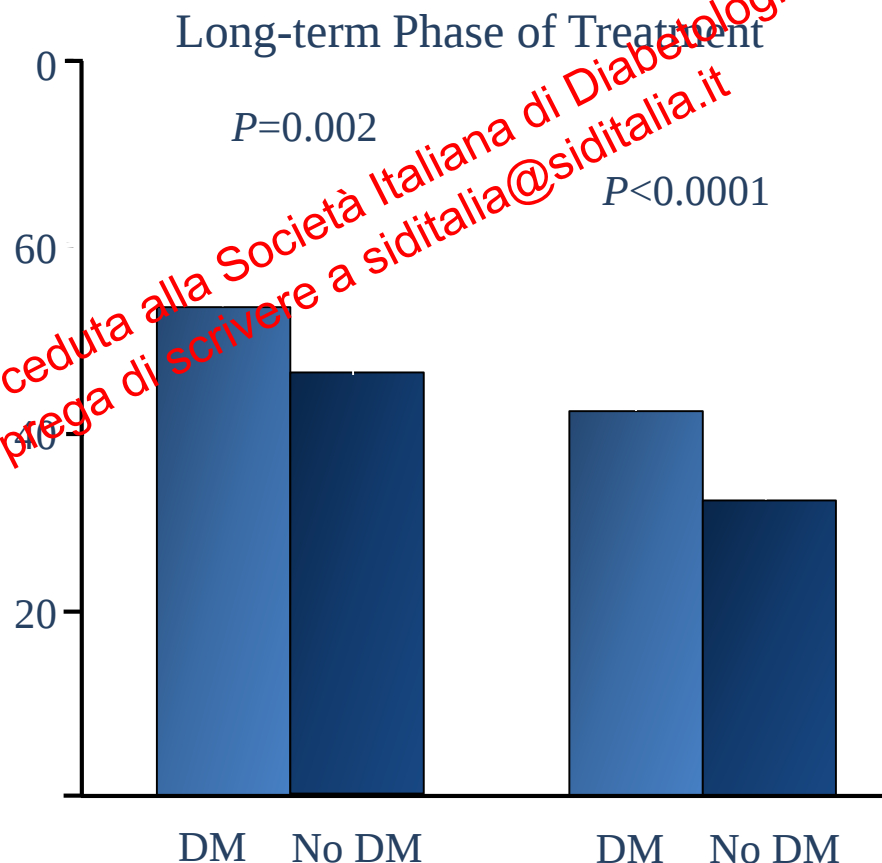
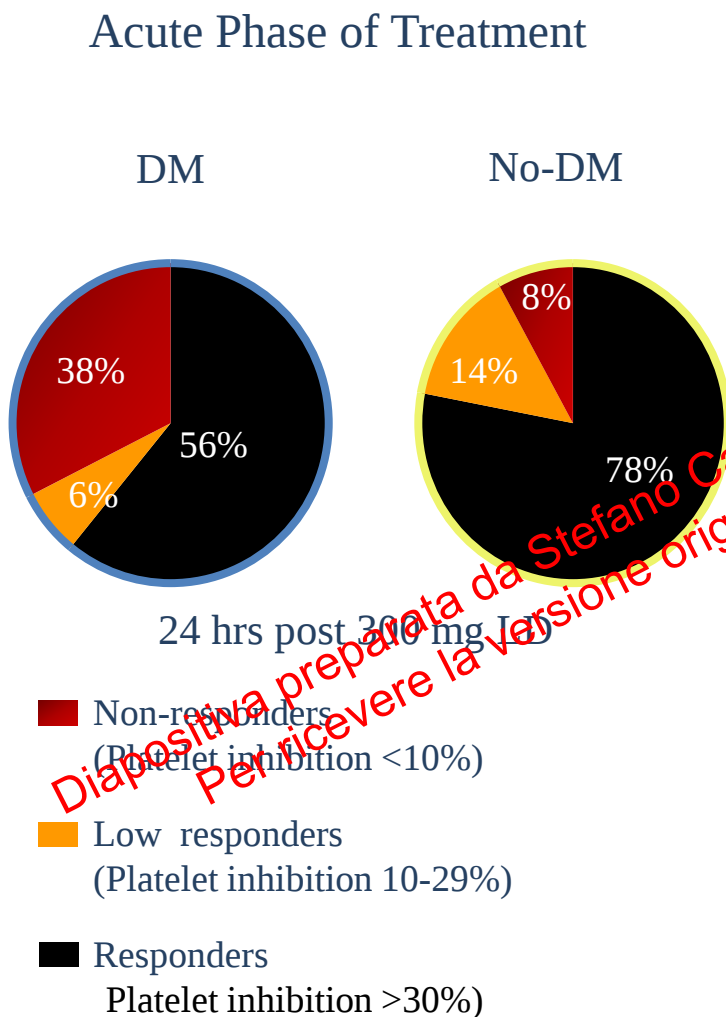
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STEMI						
Diabetes	7156	6508	2947	2653	2118	1610
No diabetes	39421	37136	16685	15274	12276	9351
UA/NSTEMI						
Diabetes	3457	3313	2923	2339	1317	924
No diabetes	12002	11658	10505	8191	5141	4008

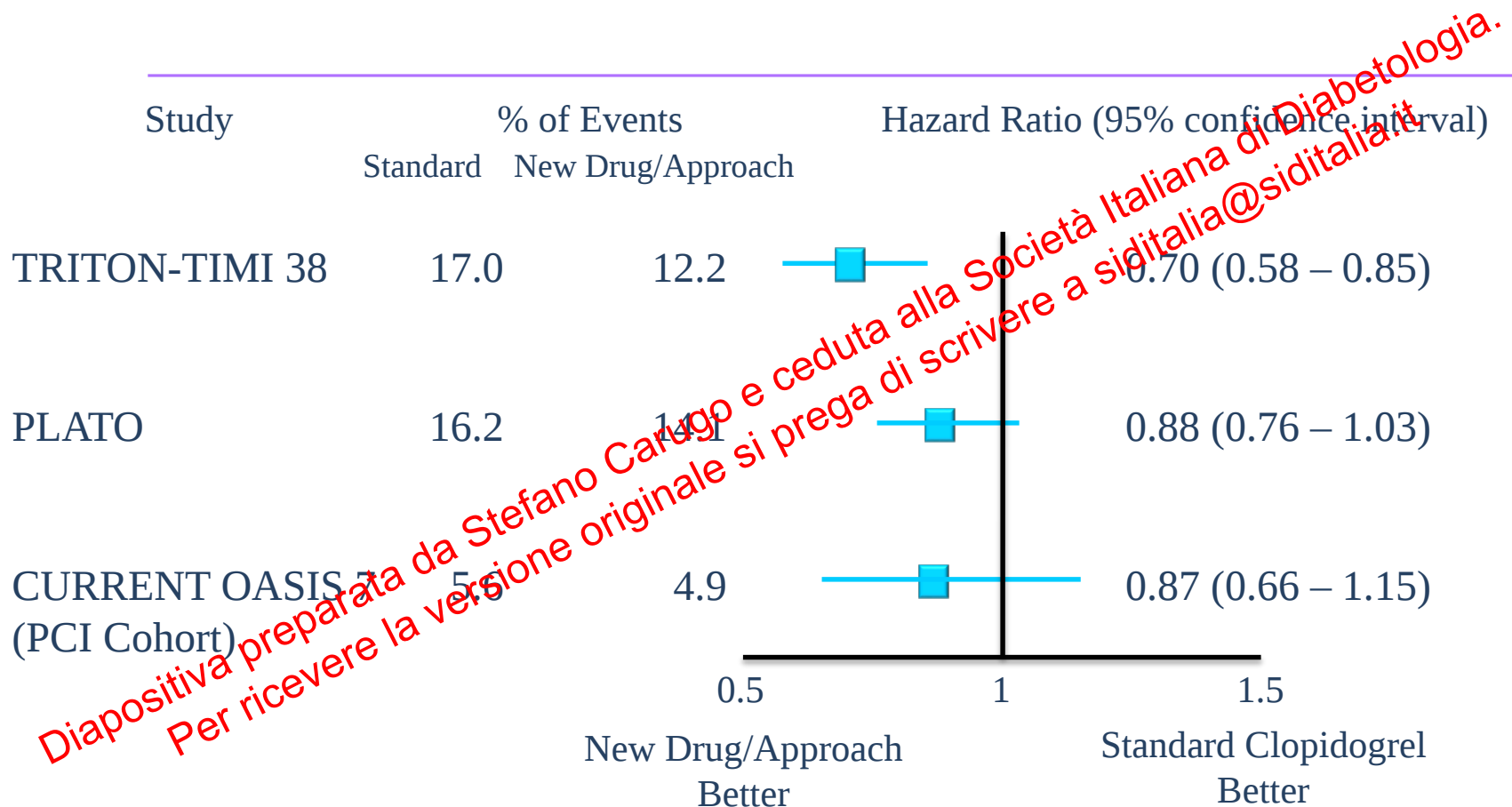
Diabetes as Predictor of Stent Thrombosis at 1 Year in the Era of DES



Influence of Diabetes Mellitus on Clopidogrel-induced Antiplatelet Effects



Efficacy of New Drugs/Approaches in Reducing Adverse Outcomes in Diabetes Mellitus From Large-Scale Clinical Trials

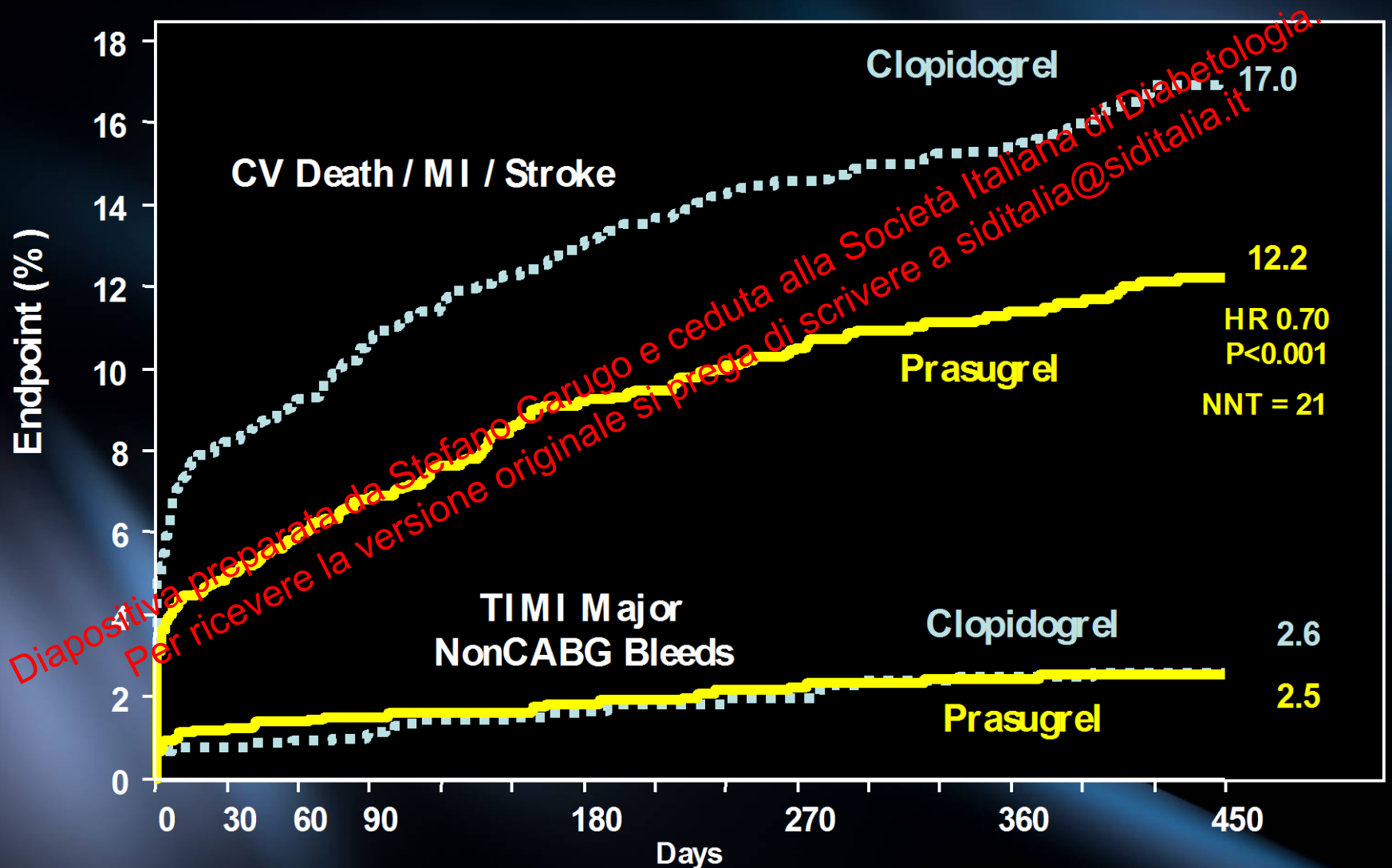


for Interventions; PCI=percutaneous intervention; PLATO= A Study of Platelet Inhibition and Patient Outcomes; TRITON-TIMI= Trial To Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel Thrombolysis in Myocardial Infarction.

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Diabetic Subgroup

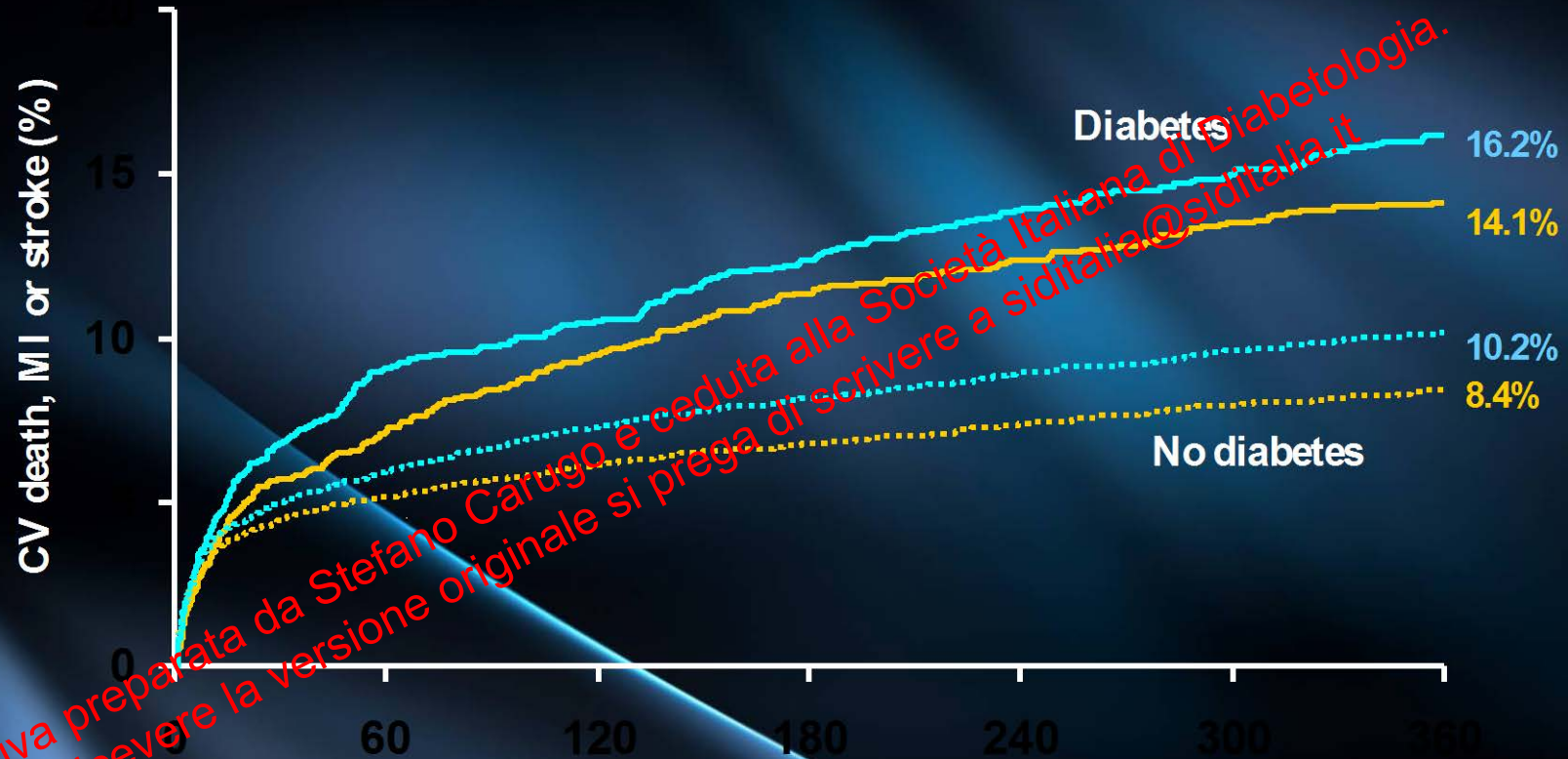
N=3146



Diabetes N=4662

Primary endpoint

Diabetes



No diabetes

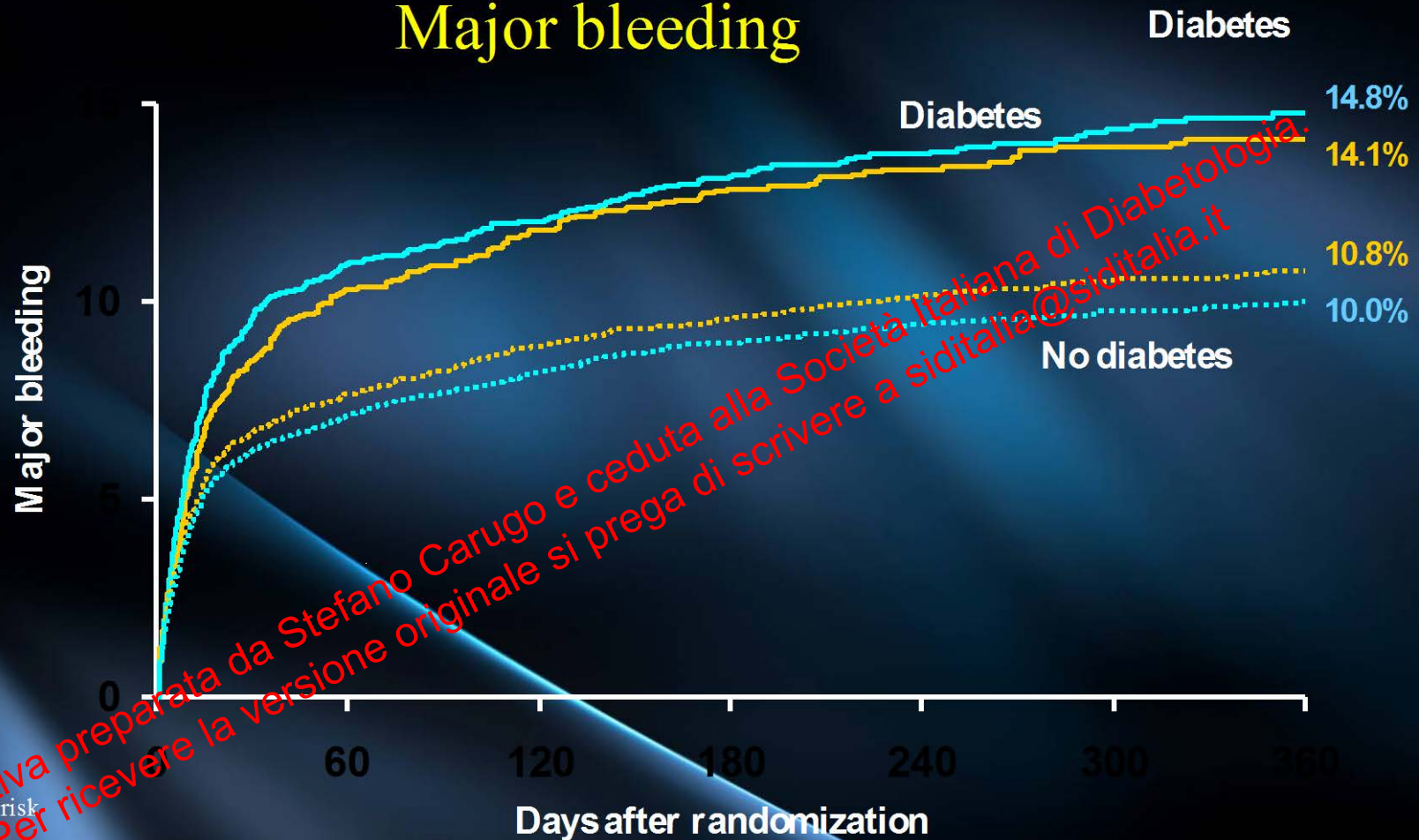
Days after randomization

Number at risk
Diabetes

—	Ticagrelor	6999	6507	6407	6252	5143	3955	3191
—	Clopidogrel	6952	6434	6318	6153	5044	3869	3097
.....	No diabetes							
.....	Ticagrelor	2326	2113	2045	1959	1593	1199	953
.....	Clopidogrel	2336	2084	2041	1968	1604	1225	975

Diabetes N=4662

Major bleeding



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Recommendations for antiplatelet therapy in patients with diabetes

Antiplatelet therapy in patients with diabetes		
Recommendations	Class ^a	Level ^b
Antiplatelet therapy with aspirin in DM-patients at low CVD risk is not recommended.	III	A
Antiplatelet therapy for primary prevention may be considered in high risk patients with DM on an individual basis.	IIb	C
Aspirin at a dose of 75–160 mg/day is recommended as secondary prevention in DM.	I	A
A P2Y ₁₂ receptor blocker is recommended in patients with DM and ACS for 1 year and in those subjected to PCI (duration depending on stent type). In patients with PCI for ACS preferably prasugrel or ticagrelor should be given.	I	A
Clopidogrel is recommended as an alternative antiplatelet therapy in case of aspirin intolerance.	I	B

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Algoritmo delle SCA

Primary

- Relevant rise or fall in troponin^a
- Dynamic ST- or T-wave changes (symptomatic or silent)

Secondary

- Diabetes mellitus
- Renal insufficiency (eGFR < 60 mL/min/1.73 m²)
- Reduced LV function (ejection fraction $< 40\%$)
- Early post-infarction angina
- Recent PCI
- Prior CABG
- Intermediate to high GRACE risk score (Table 5)

No CAD

no/elective

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At Admission (in-hospital/to 6 months)

At Discharge (to 6 months)

Age

80-89

HR

70-89

SBP

140-159

Creat.

1.2-1.59

CHF

1 (no CHF)

☐ Cardiac arrest at admission

☐ ST-segment deviation

☒ Elevated cardiac enzymes/markers

Probability of

Death

Death or MI

In-hospital

150

168

To 6 months

136

168

SI Units

Reset

Display Risk

LG ESC 2016 NSTEMI

Nei Pazienti diabetici

An early invasive strategy is recommended.

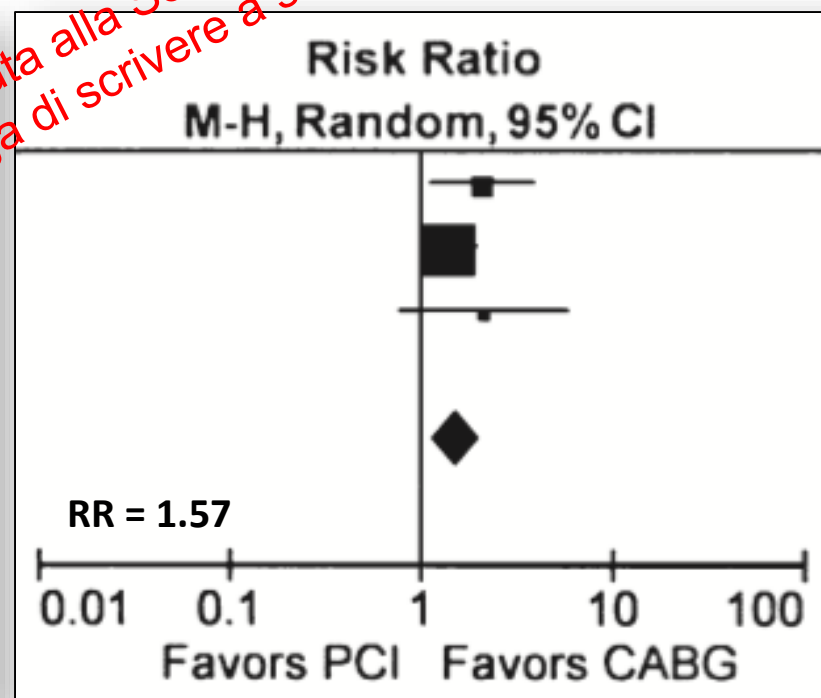
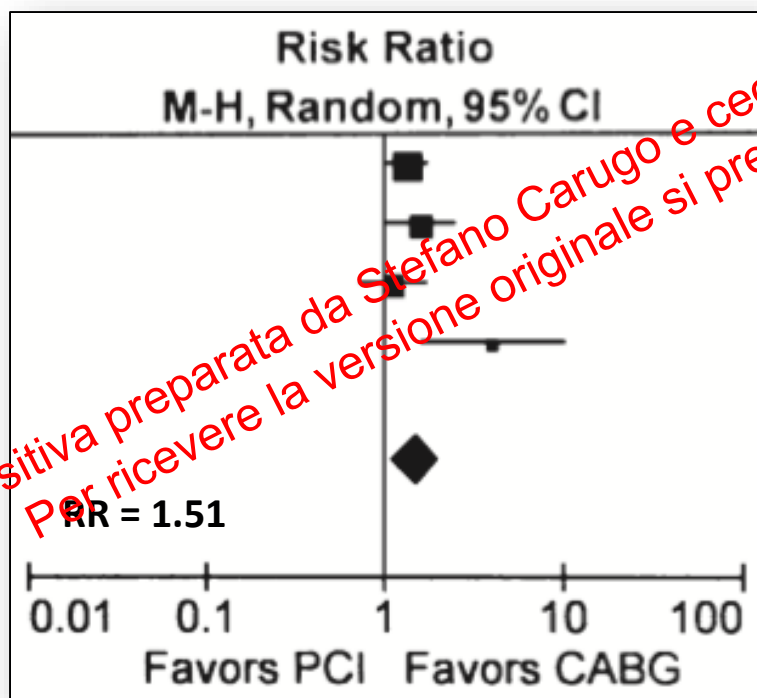
I

A

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CABG vs PCI in diabetics with MVD: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data (3052 pts)

Total and Cardiovascular Death



SCA e Diabete :i 4 “must”!

1. Il paziente diabetico richiede l'impiego di una terapia antiaggregante ad hoc

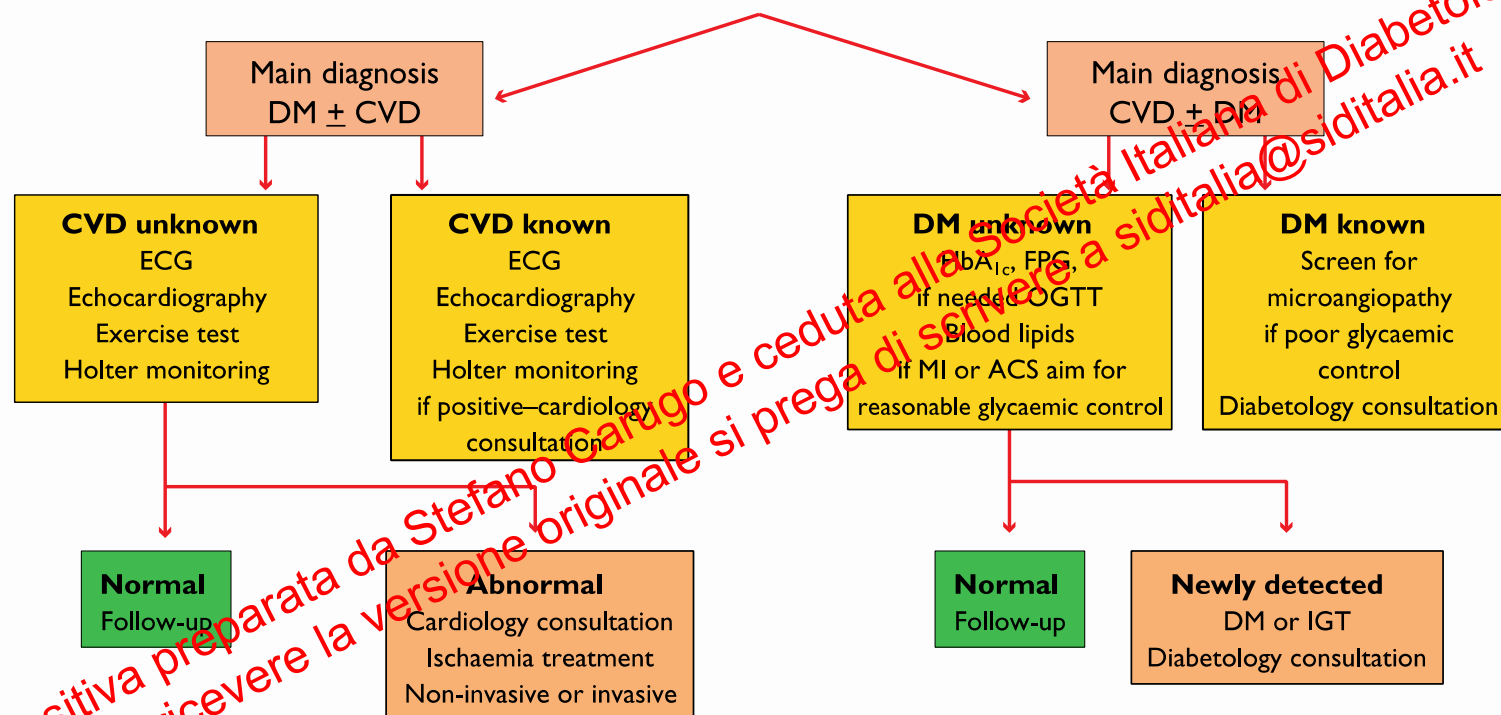
2- Considerare una strategia early invasive

3- Scelta individualizzata della strategia di rivascularizzazione (chirurgica vs percutanea)

4- Trattamento aggressivo delle dislipidemie

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Cardiovascular disease (CVD) and Diabetes mellitus (DM)



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Conclusions

- Platelets from patients with diabetes mellitus are dysfunctional:
 - ✓ increased platelet reactivity
 - ✓ reduced responsiveness to antiplatelet agents
- Increased platelet reactivity and reduced responsiveness to standard dual antiplatelet treatment regimens (aspirin plus clopidogrel) are associated with atherothrombotic risk.
- Potent antithrombotic strategy
- Potent antidiyslipidemia treatment
- Best revascularization option should be decided on a patient basis
- Early invasive approach is recommended



Grazie per l'attenzione



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