SID Società Italiana di Diabetologia

AMD 1974 ANNO DI FONDAZIONE ASSOCIAZIONE MEDICI DIABETOLOGI

III Congresso Congiunto

Prediabete e rischio cardiovascolare



29-30 Novembre 2018

Antonino Di Pino

Il Dr. Antonino Di Pino dichiara di **NON** aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

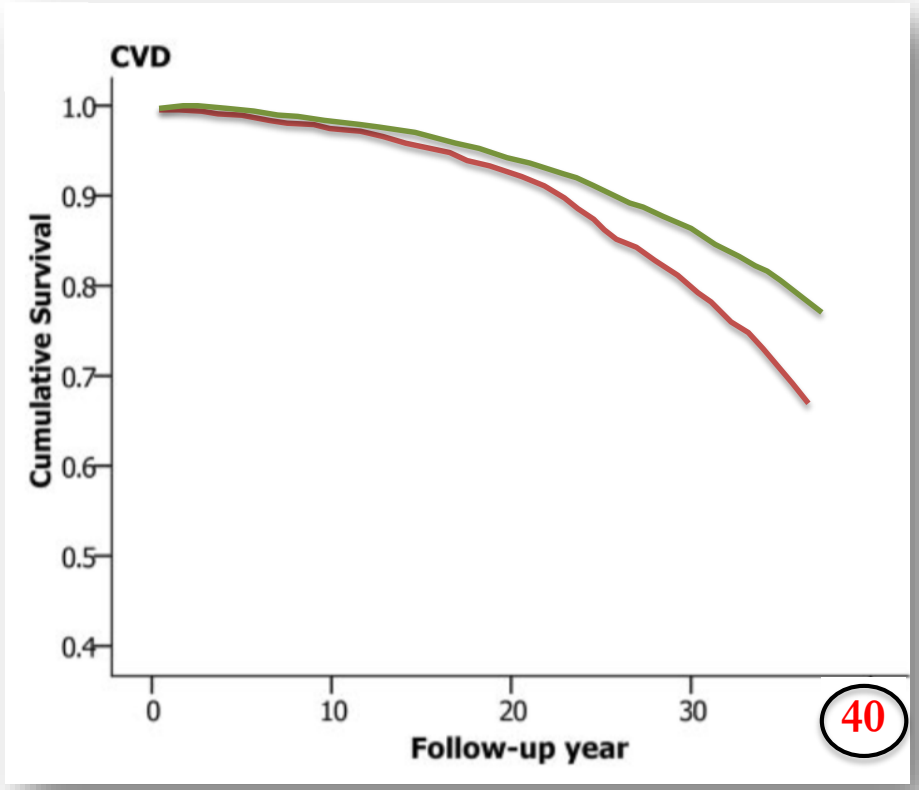
Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

PREDIABETE E RISCHIO CARDIOVASCOLARE





PREDIABETE E RISCHIO CARDIOVASCOLARE





Ning F et al. DECODE study group, Diabetes Care 2010

Prediabete e Rischio Cardiovascolare

1. Danno Cardiovascolare Subclinico

Come identificare i soggetti



2. Studi di Intervento



Stile di vita

Intervento Farmacologico in Prevenzione Primaria

Intervento Farmacologico in Prevenzione Secondaria

I Prediabetici hanno un Danno Miocardico Subclinico

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ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.10.875

Hyperglycemia and the Heart

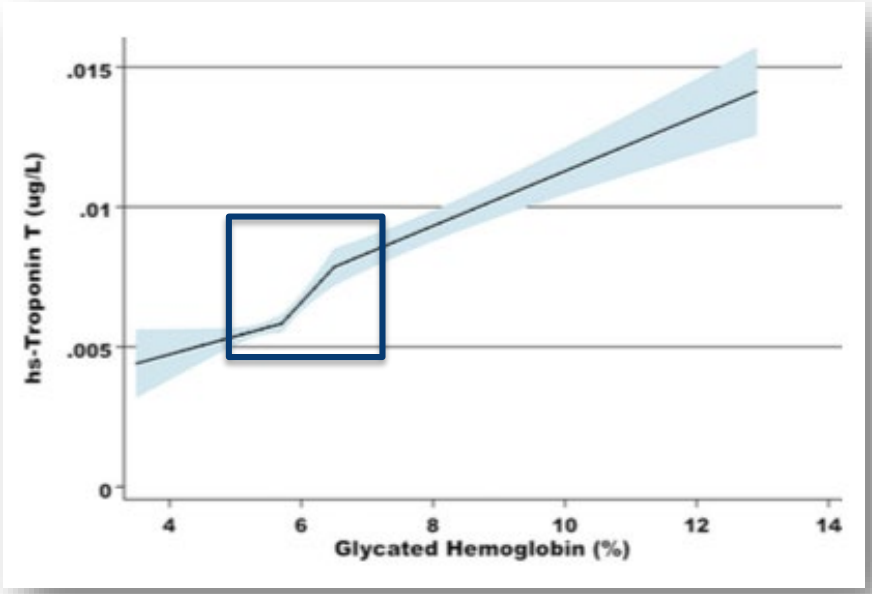
Chronic Hyperglycemia and Subclinical Myocardial Injury

Jonathan Rubin, MD,* Kunihiro Matsushita, MD, PhD,* Christie M. Ballantyne, MD,†
Ron Hoogeveen, PhD,† Josef Coresh, MD, PhD,* Elizabeth Selvin, PhD, MPH*

Baltimore, Maryland; and Houston, Texas



HS Troponin



Rubin J JACC 2012

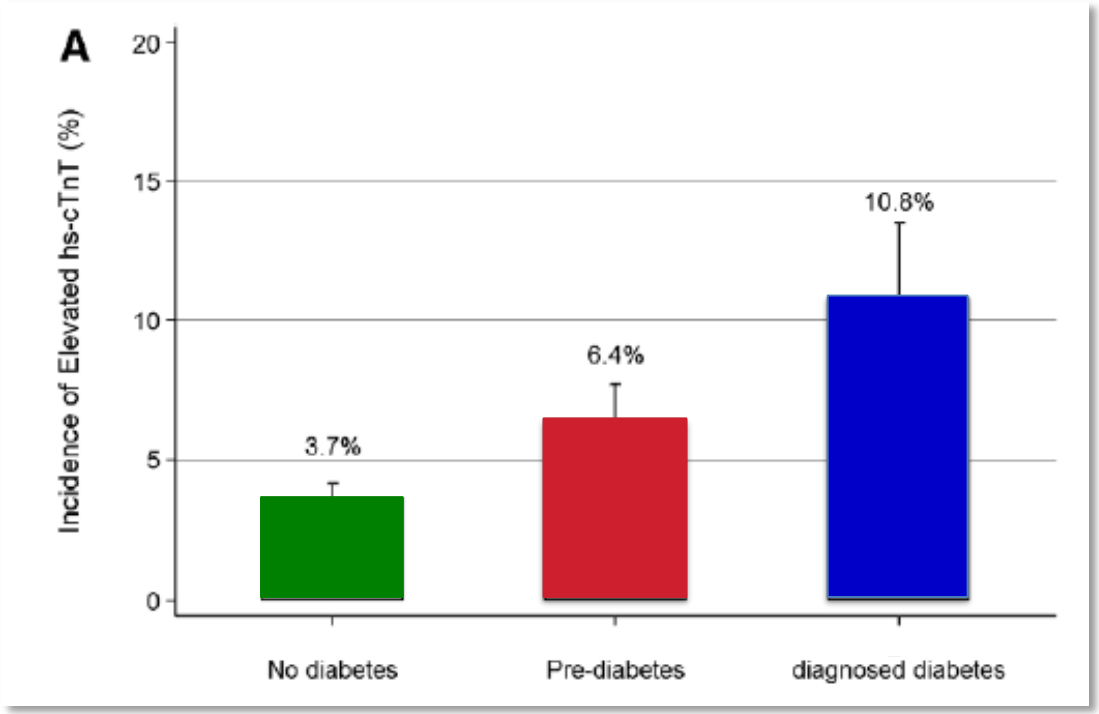
I Prediabetici hanno un Danno Miocardico Subclinico

Epidemiology and Prevention

Diabetes Mellitus, Prediabetes, and Incidence of Subclinical Myocardial Damage

Elizabeth Selvin, PhD, MPH; Mariana Lazo, MD, PhD, ScM; Yuan Chen, MS; Lu Shen, BS; Jonathan Rubin, MD, MHS; John W. McEvoy, MB, BCh, BAO, MRCPI; Ron C. Hoogeveen, PhD; A. Richey Sharrett, MD, DrPH; Christie M. Ballantyne, MD; Josef Coresh, MD, PhD, MHS

Il Prediabetico Svilupperà più Facilmente Danno d'Organo Subclinico



Selvin E. Circulation 2015

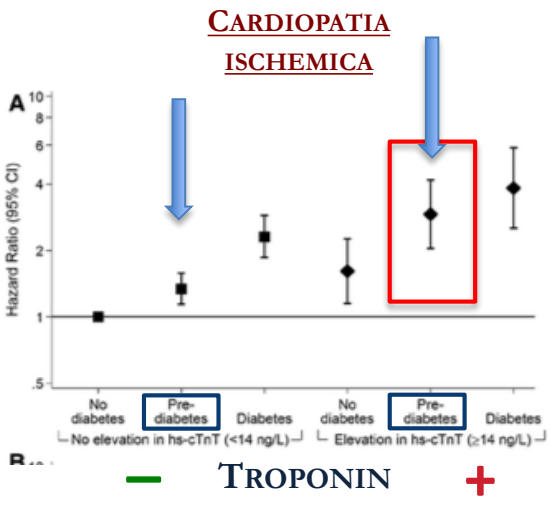
I Prediabetici hanno un Danno Miocardico Subclinico

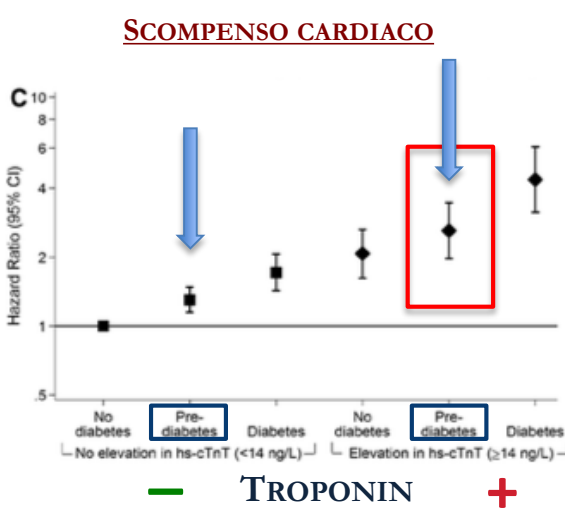
Epidemiology and Prevention

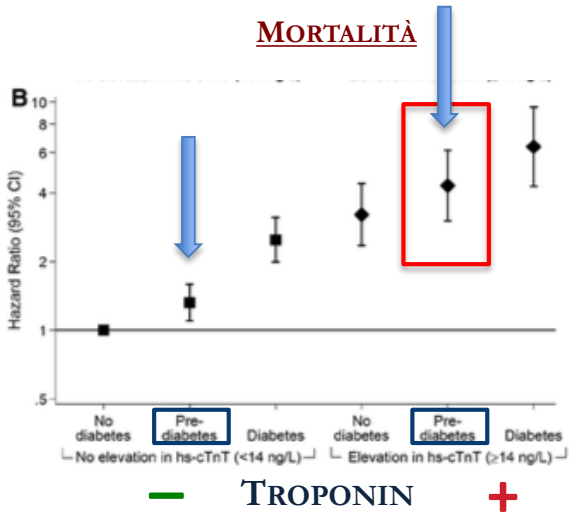
Diabetes Mellitus, Prediabetes, and Incidence of Subclinical Myocardial Damage

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Il Prediabetico Sviluppa Cardiopatia Ischemica Gradualmente e Eventi Cardiovascolari





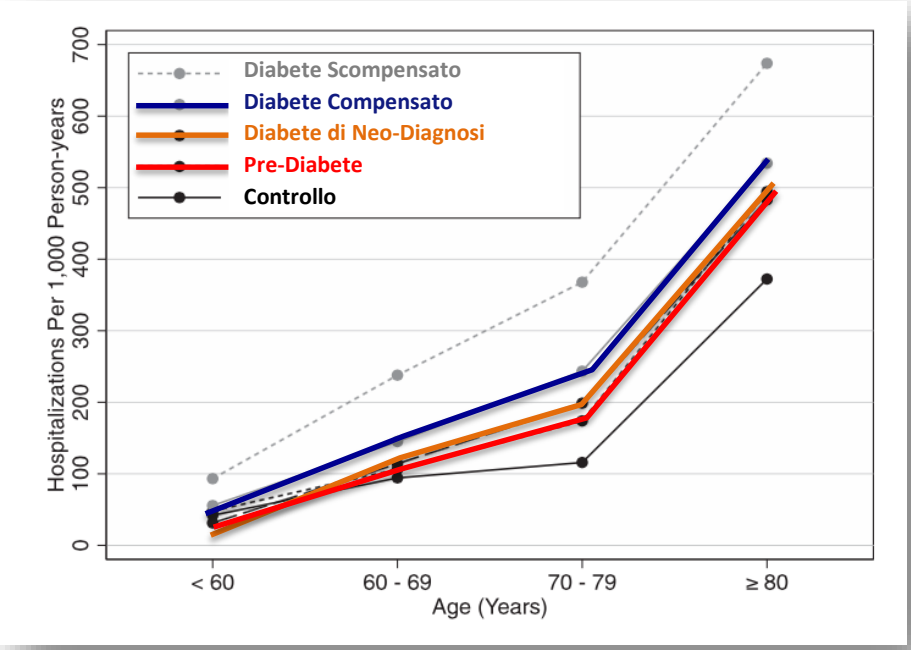


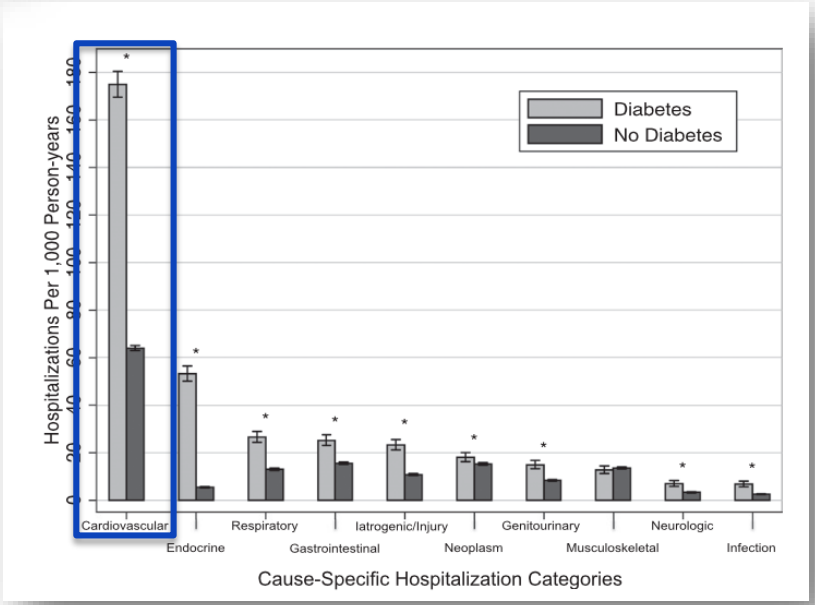
Selvin E. Circulation 2015

Diabetes and Prediabetes and Risk of Hospitalization: The Atherosclerosis Risk in Communities (ARIC) Study

Andrea L.C. Schneider,[1,2] Rita R. Kalyani,[3] Sherita Golden,[1,3] Sally C. Stearns,[4] Lisa Wruck,[5] Hsin Chieh Yeh,[1,3] Josef Coresh,[1,3] and Elizabeth Selvin[1,3]

Diabetes Care 2016;39:772–779 | DOI: 10.2337/dc15-1335





Schneider A Diabetes Care 2016

Prediabete e Rischio Cardiovascolare

1. Danno Cardiovascolare Subclinico

Come identificare i soggetti



2. Studi di intervento



- **Stile di vita**
- **Intervento Farmacologico in Prevenzione Primaria**
- **Intervento Farmacologico in Prevenzione Secondaria**

Categories at Increased Risk of Diabetes

Table 1 Diagnostic criteria for categories at increased risk of diabetes

Category	Marker	Diagnostic range
IFG	Fasting plasma glycemia	⩾ 5.6 mmol/L (100 mg/dL) < 6.9 mmol/L (126 mg/dL)
IGT	2-h post-load glycemia	⩾ 7.8 mmol/L (140 mg/dL) < 11 mmol/L (200 mg/dL)
HbA_{1c}-prediabetes	HbA_{1c}	⩾ 39 mmol/mol (5.7%) < 47 mmol/mol (6.5%)

IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance; HbA_{1c}: Glycated haemoglobin.

Classsification and diagnosis of diabetes, Diabetes Care 2015

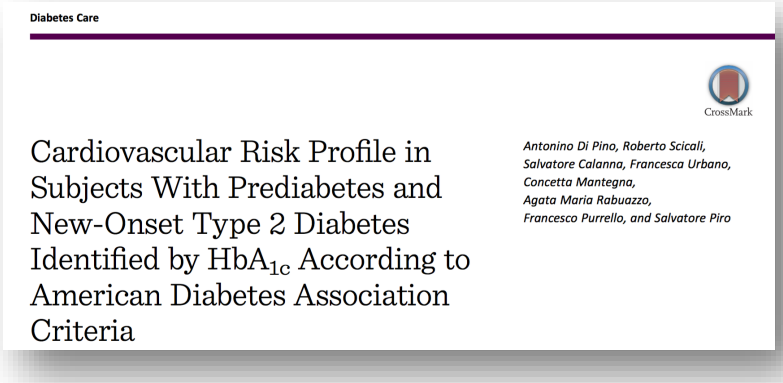
OBJECTIVE

TO EVALUATE CARDIOVASCULAR RISK PROFILE OF SUBJECTS WITH HbA_{1C} PRE-DIABETES

HbA_{1C}

5.7-6.4%





272 Patients Without Hystory of Overt Cardiovascular Disease

Control

NFG/NGT and

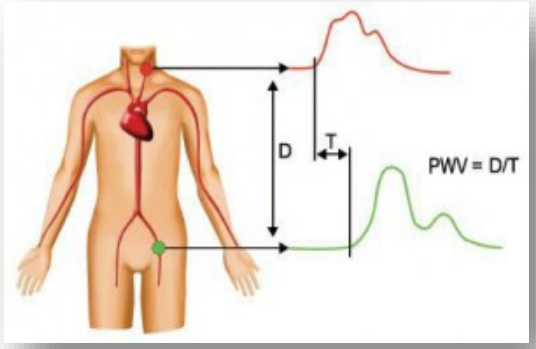
HbA_{1c}<5.7% (n=99)

Pre-Diabetes

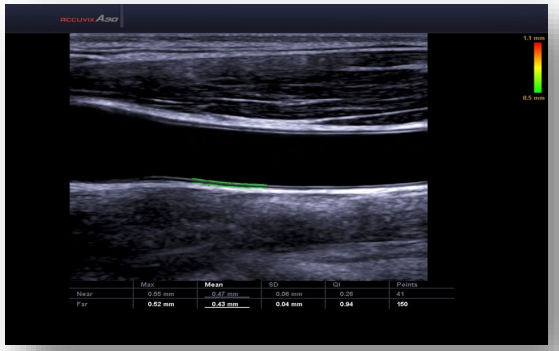
HbA_{1C} 5.7-6.4% (n=220)

New Onset Type 2 Diabetes (n=61)

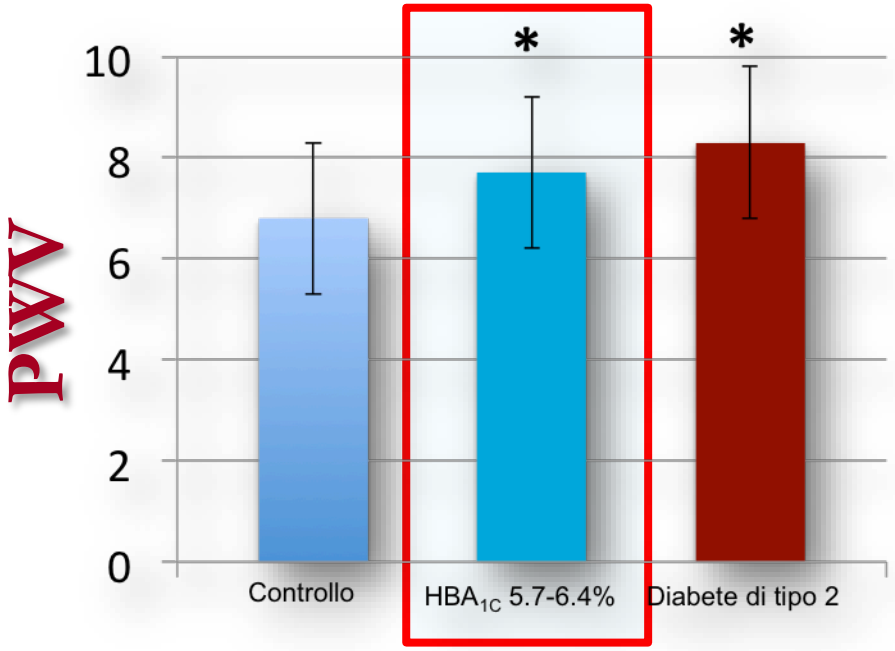
PWV

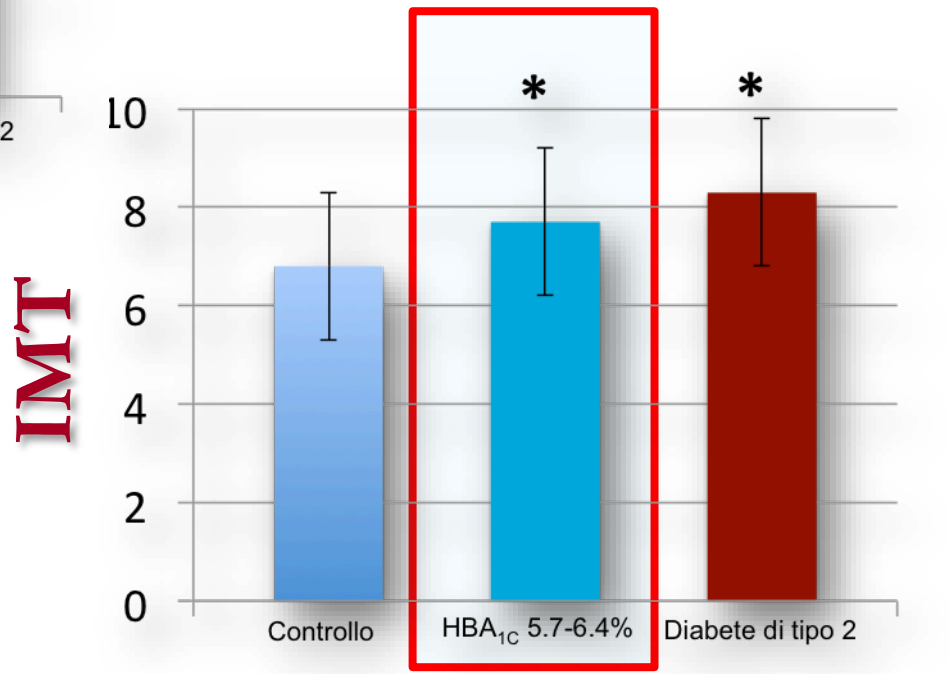


IMT



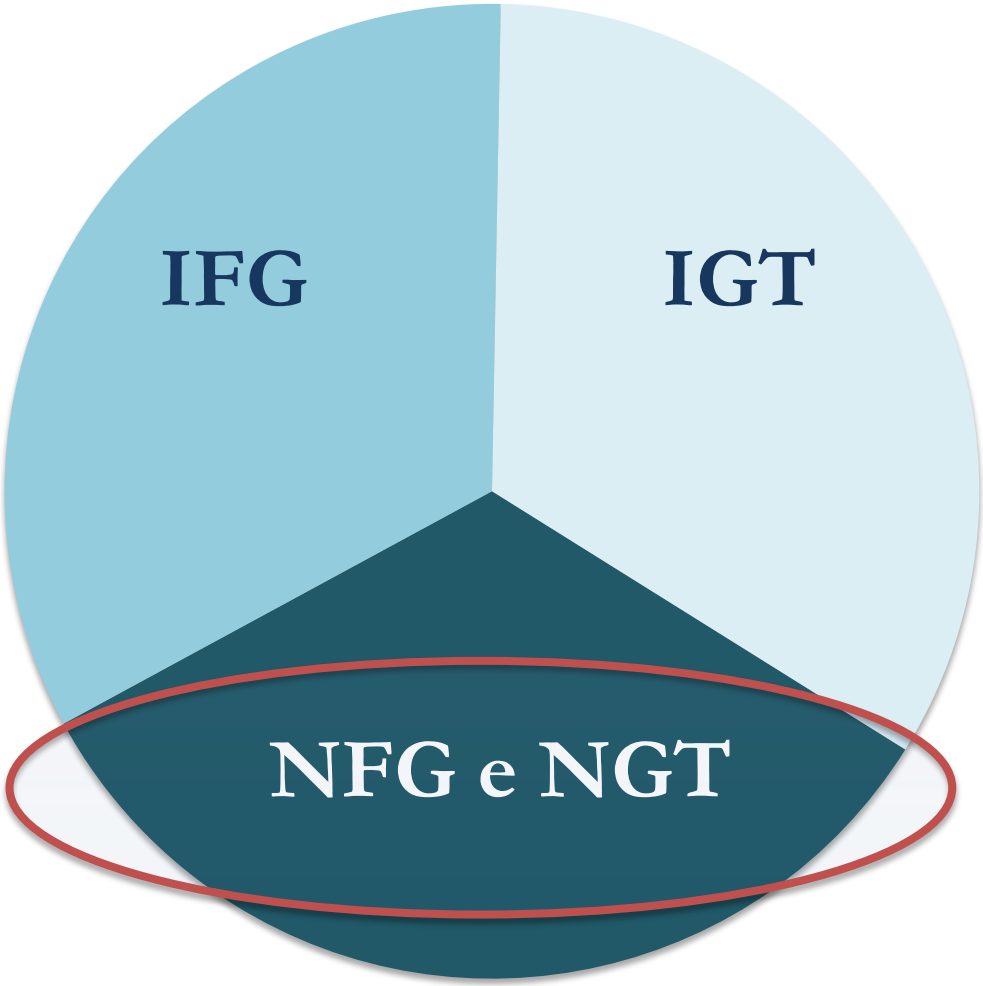
RESULTS



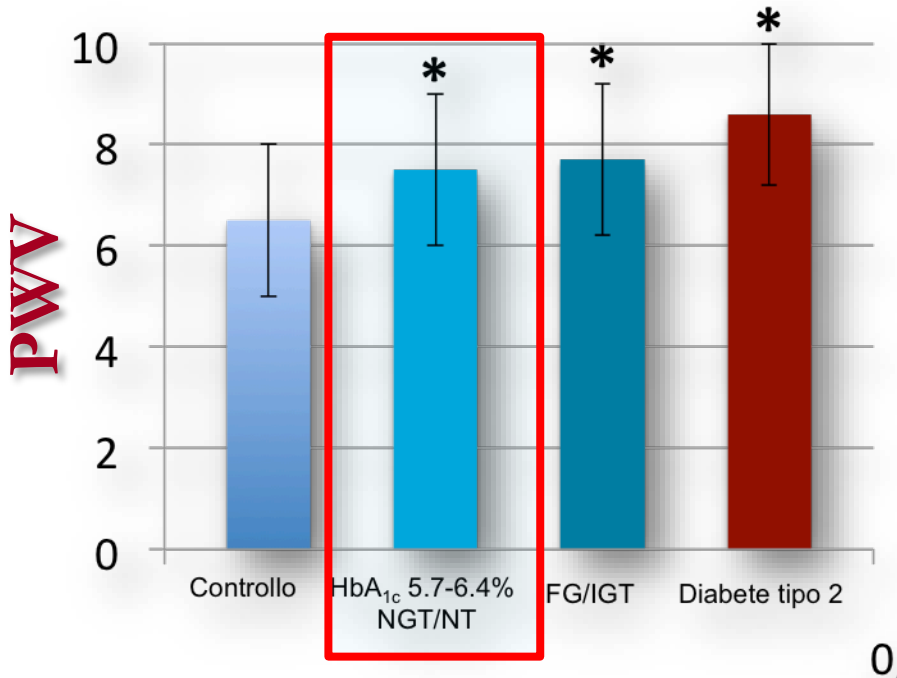


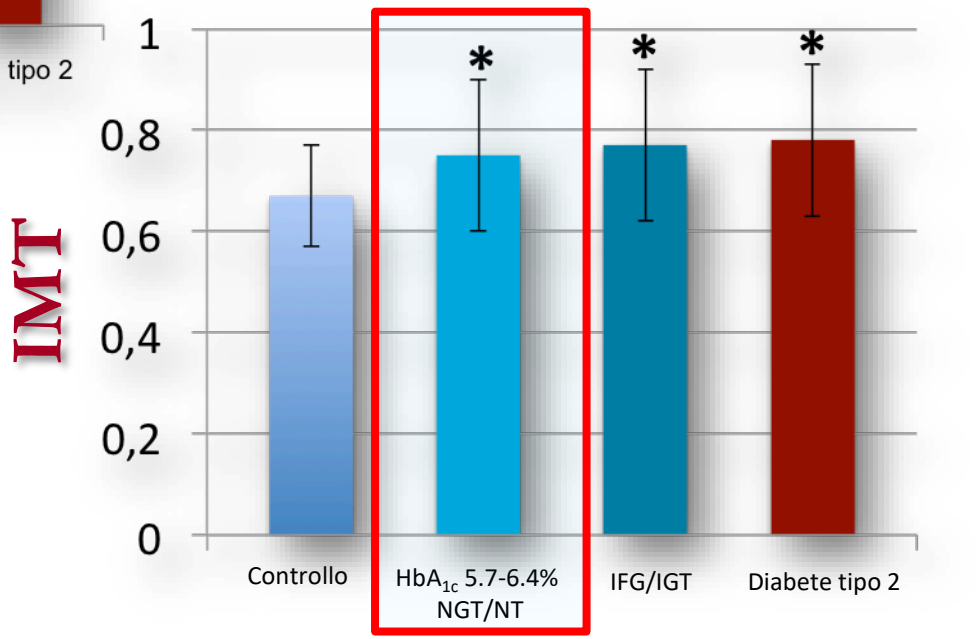
*$P<0.05$ vs Controls

HbA_{1C} 5.7-6.4%



RESULTS

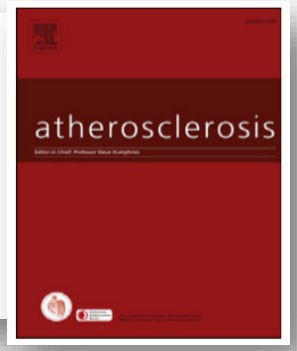




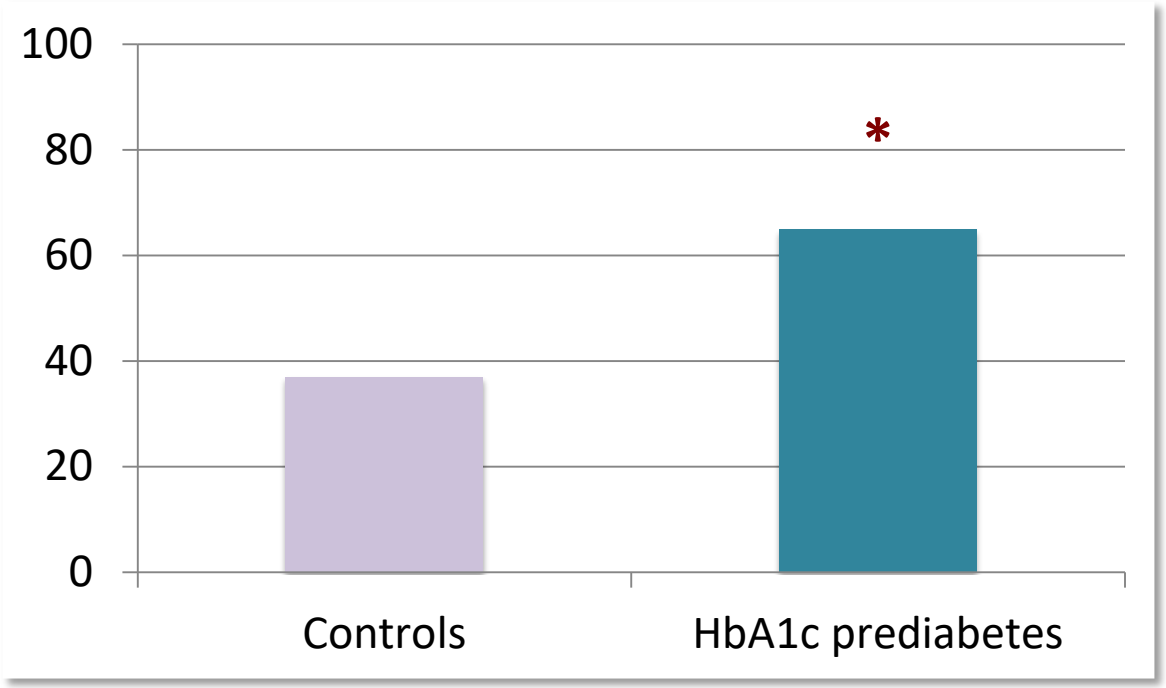
****P*<0.05 vs Controls**

HbA1c increase is associated with higher coronary and peripheral atherosclerotic burden in non diabetic patients

Roberto Scicali [a, b], Philippe Giral [b, d], Antonio Gallo [b, c], Antonino Di Pino [a], Agata Maria Rabuazzo [a], Francesco Purrello [a], Philippe Cluzel [c, e], Alban Redheuil [c, e], Eric Bruckert [b, d], David Rosenbaum [b, c, *]



PREVALENCE OF CAC > 0



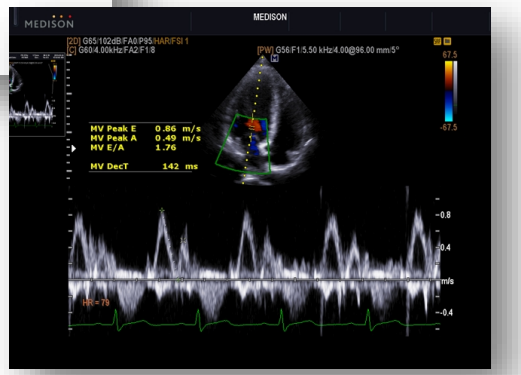
*vs Controls P<0.05

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

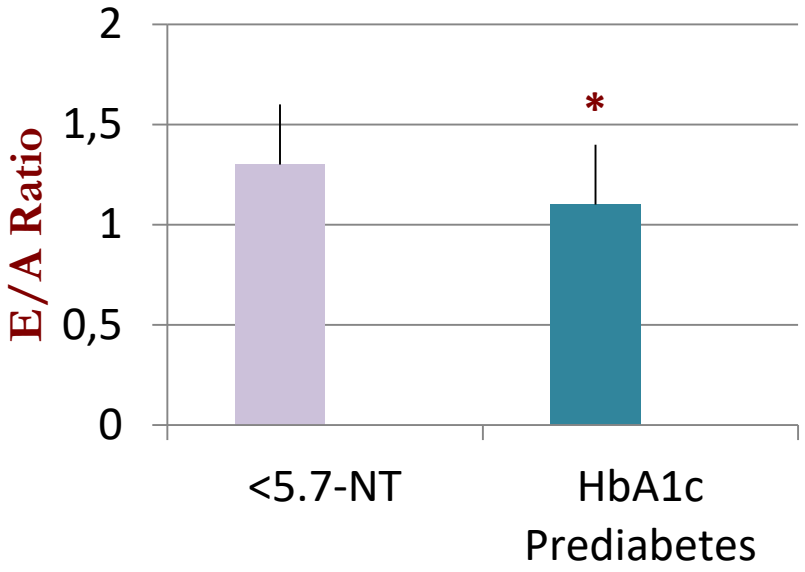
HbA_{1c} identifies subjects with prediabetes and subclinical left ventricular diastolic dysfunction

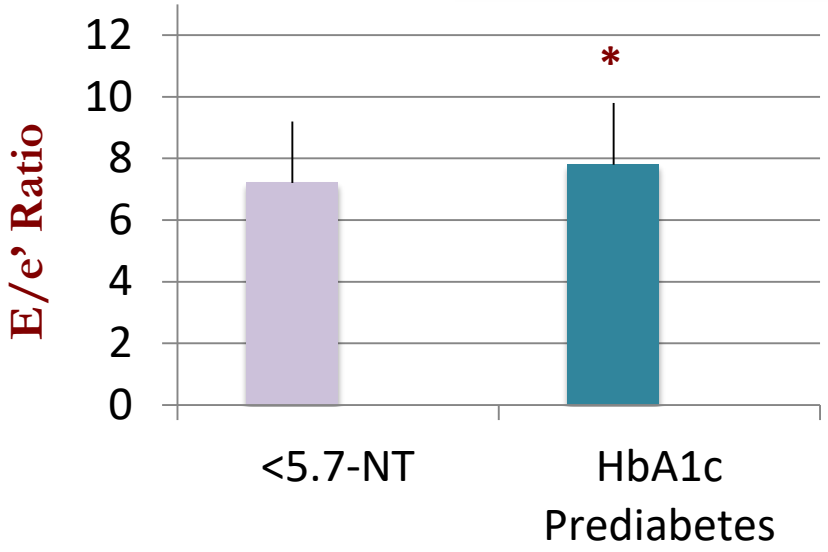
Antonino Di Pino, Sarah Mangiafico, Francesca Urbano, Roberto Scicali, Salvatore Scandura, Veronica D'Agate, Salvatore Piro, Corrado Tamburino, Francesco Purrello, Agata Maria Rabuazzo





VALUTAZIONE ECOCARDIOGRAFICA



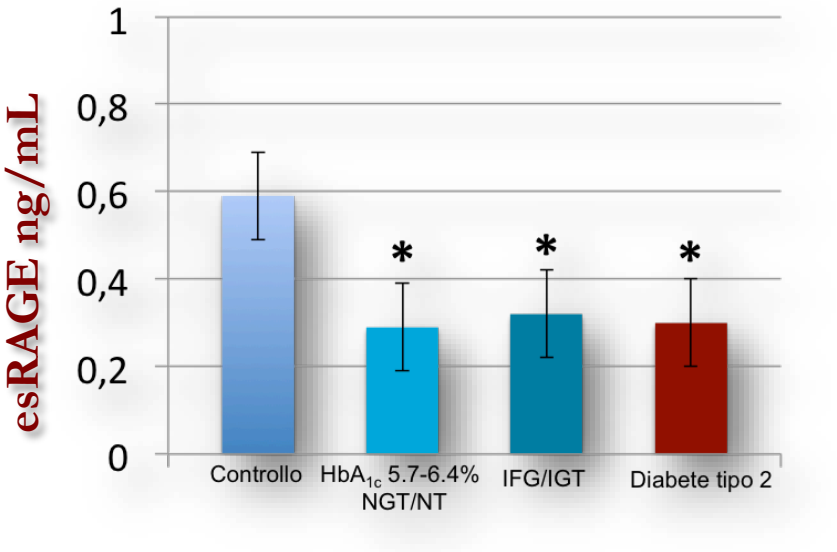


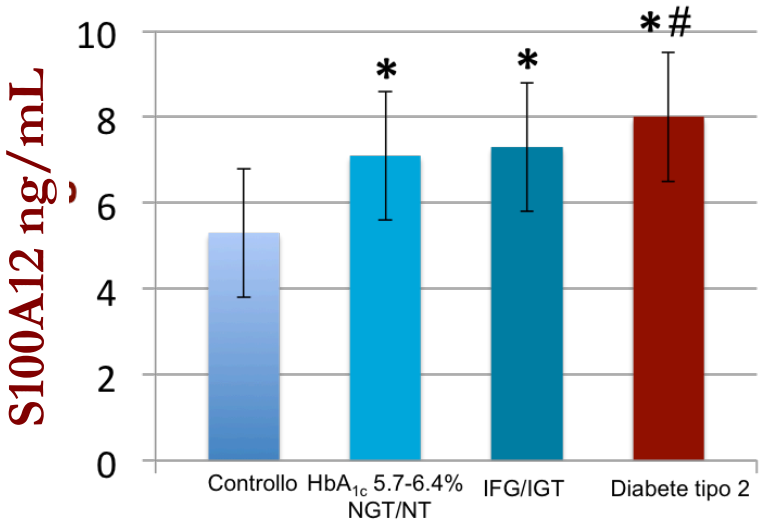
*vs Controls P<0.05

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Low Endogenous Secretory Receptor for Advanced Glycation End-Products Levels Are Associated With Inflammation and Carotid Atherosclerosis in Prediabetes

Antonino Di Pino, Francesca Urbano, Rose Maria Zagami, Agnese Filippello, Stefania Di Mauro, Salvatore Piro, Francesco Purrello, and Agata Maria Rabuazzo





*$P<0.05$ vs Controls

Subjects with HbA_{1C} Pre-Diabetes Show



Subclinical alterations of markers of cardiovascular risk (PWV, IMT, CAC)

Subclinical alterations of markers of diastolic function

Alterations of markers of glycation and inflammation

These Data Support The Utilization of HbA_{1C} For Pre-Diabetes Diagnosis

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glycated Hemoglobin, Diabetes, and Cardiovascular Risk in Nondiabetic Adults

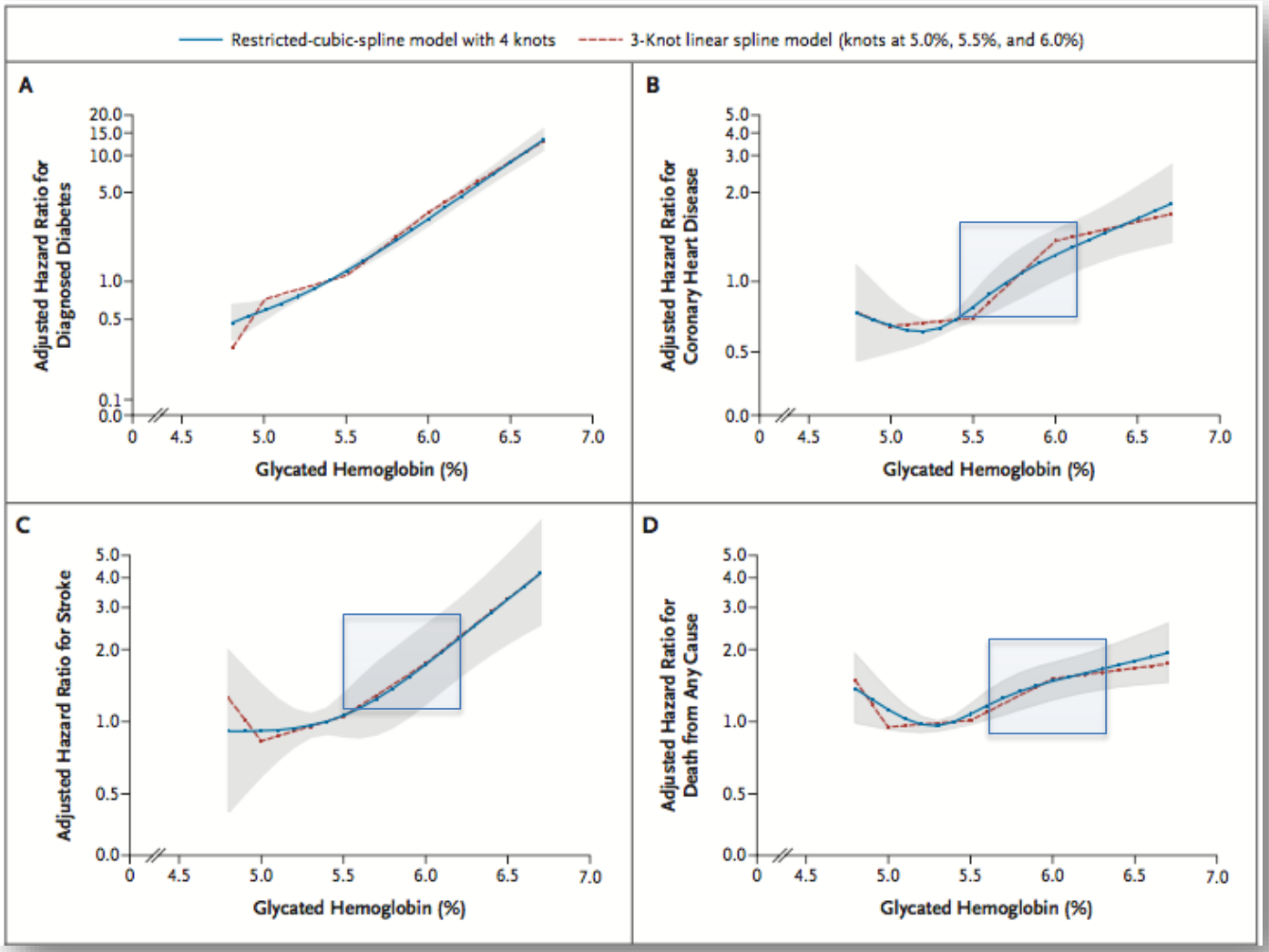
Elizabeth Selvin, Ph.D., M.P.H., Michael W. Steffes, M.D., Ph.D., Hong Zhu, B.S., Kunihiro Matsushita, M.D., Ph.D., Lynne Wagenknecht, Dr.P.H., James Pankow, Ph.D., M.P.H., Josef Coresh, M.D., Ph.D., and Frederick L. Brancati, M.D., M.H.S.

HbA_{1C} *VS* FASTING GLUCOSE

Association Between Glycated Hemoglobin and Adverse Outcomes

Diabetes

P < 0.001



Coronary Heart Desease

P < 0.001

Stroke

P < 0.001

Death from Any Cause

P < 0.001

Selvin NEJM 2010

Association Between Fasting Glucose and Adverse Outcomes

Coronary Heart Desease

Stroke

Death from Any Cause

Coronary heart disease			
Fasting glucose category — hazard ratio (95% CI)			
<100 mg/dl (reference)	1.00	1.00	1.00
100 to <126 mg/dl	1.19 (1.05–1.35)	1.03 (0.91–1.18)	1.01 (0.88–1.14)
≥126 mg/dl	1.80 (1.46–2.22)	1.29 (1.04–1.61)	1.00 (0.77–1.30)
P value for trend	<0.001	0.09	0.97
Fasting glucose — hazard ratio (95% CI) per 10 mg/dl increase	1.058 (1.034–1.082)	1.013 (0.986–1.041)	0.913 (0.877–0.950)
C statistic	0.6761	0.7329	0.7383
Ischemic stroke			
Fasting glucose category — hazard ratio (95% CI)			
<100 mg/dl (reference)	1.00	1.00	1.00
100 to <126 mg/dl	1.06 (0.84–1.34)	0.97 (0.76–1.23)	0.93 (0.73–1.18)
≥126 mg/dl	2.33 (1.68–3.24)	1.89 (1.33–2.69)	1.30 (0.85–1.98)
P value for trend	<0.001	0.02	0.63
Fasting glucose — hazard ratio (95% CI) per 10 mg/dl increase	1.089 (1.057–1.121)	1.068 (1.034–1.104)	0.950 (0.893–1.012)
C statistic	0.7109	0.7506	0.7594
Death from any cause			
Fasting glucose category — hazard ratio (95% CI)			
<100 mg/dl (reference)	1.00	1.00	1.00
100 to <126 mg/dl	1.11 (0.99–1.24)	1.07 (0.96–1.21)	1.06 (0.94–1.19)
≥126 mg/dl	1.42 (1.17–1.73)	1.31 (1.07–1.61)	1.16 (0.91–1.47)
P value for trend	0.001	0.03	0.20
Fasting glucose — hazard ratio (95% CI) per 10 mg/dl increase	1.035 (1.012–1.058)	1.021 (0.997–1.045)	0.980 (0.945–1.018)
C statistic	0.6865	0.7313	0.7314

Prediabete e Rischio Cardiovascolare

1. Danno Cardiovascolare Subclinico

Come identificare i soggetti



2. Studi di Intervento



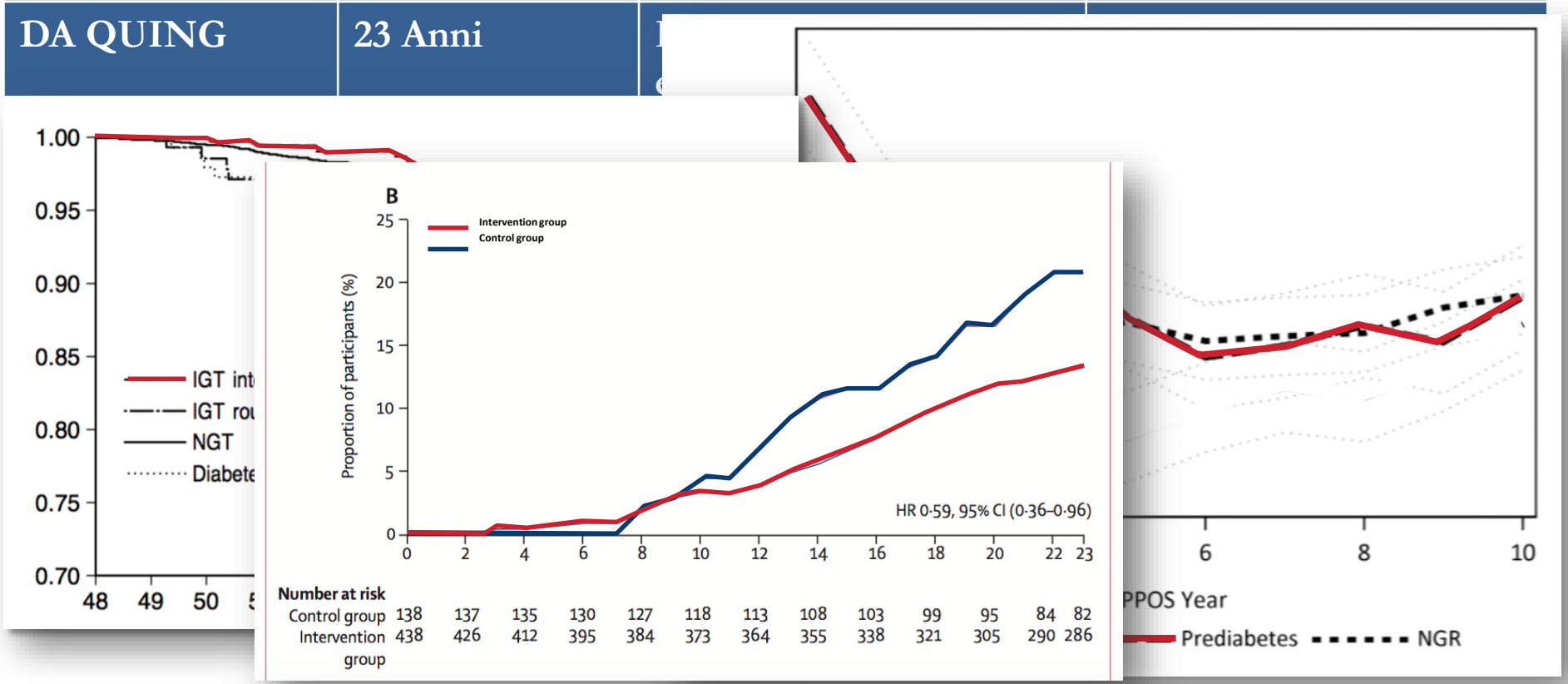
Stile di vita

Intervento Farmacologico in Prevenzione Primaria

Intervento Farmacologico in Prevenzione Secondaria

PRE-DIABETE E RISCHIO CV – STUDI D'INTERVENTO
STILE DI VITA

STUDIO	Follow Up	Risultato	Limiti
DPPOS	10 Anni	Riduzione score	Utilizzo score di rischio Farmaci
MALMO	12 Anni	Riduzione mortalità	Non Randomizzato
DA QUING	23 Anni		



STUDI D'INTERVENTO FARMACOLOGICO

PREVENZIONE PRIMARIA

JAMA

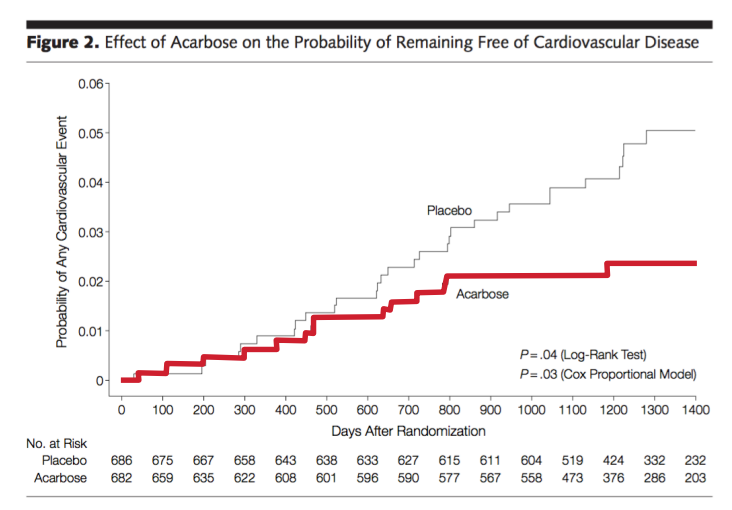
Acarbose Treatment and the Risk of Cardiovascular Disease and Hypertension in Patients With Impaired Glucose Tolerance
The STOP-NIDDM Trial

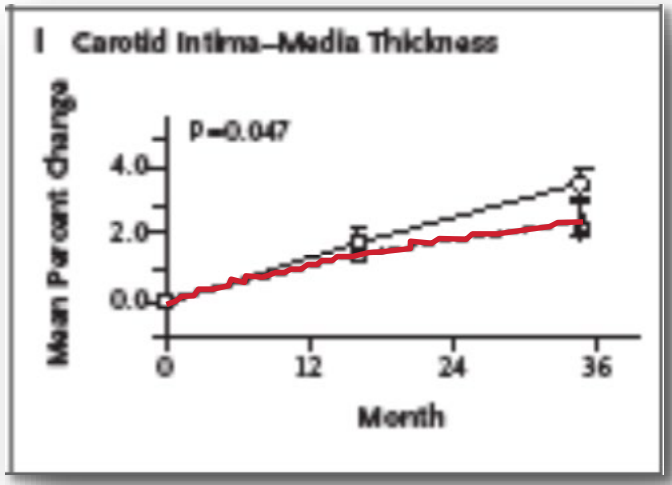
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pioglitazone for Diabetes Prevention in Impaired Glucose Tolerance

Ralph A. DeFronzo, M.D., Devjit Tripathy, M.D., Ph.D., Dawn C. Schwenke, Ph.D., MaryAnn Banerji, M.D., George A. Bray, M.D., Thomas A. Buchanan, M.D., Stephen C. Clement, M.D., Robert R. Henry, M.D., Howard N. Hodis, M.D., Abbas E. Kitabchi, M.D., Ph.D., Wendy J. Mack, Ph.D., Sunder Mudaliar, M.D., Robert E. Ratner, M.D., Ken Williams, M.Sc., Frankie B. Stentz, Ph.D., Nicolas Musi, M.D., and Peter D. Reaven, M.D., for the ACT NOW Study





STUDI D'INTERVENTO FARMACOLOGICO

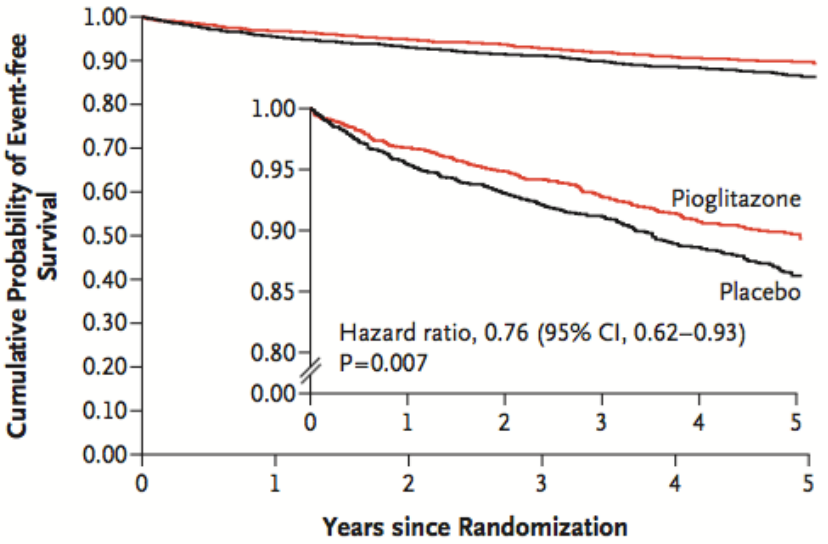
PREVENZIONE SECONDARIA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pioglitazone after Ischemic Stroke or Transient Ischemic Attack

W.N. Kernan, C.M. Viscoli, K.L. Furie, L.H. Young, S.E. Inzucchi, M. Gorman, P.D. Guarino, A.M. Lovejoy, P.N. Peduzzi, R. Conwit, L.M. Brass,* G.G. Schwartz, H.P. Adams, Jr., L. Berger, A. Carolei, W. Clark, B. Coull, G.A. Ford, D. Kleindorfer, J.R. O'Leary, M.W. Parsons, P. Ringleb, S. Sen, J.D. Spence, D. Tanne, D. Wang, and T.R. Winder, for the IRIS Trial Investigators†



No. at Risk						
Pioglitazone	1939	1793	1701	1491	1196	481
Placebo	1937	1778	1690	1476	1182	459

Other adverse event			
Bone fracture¶	133 (6.9)	94 (4.9)	0.008
Heart failure¶	29 (1.5)	32 (1.7)	0.70
Weight gain			
>4.5 kg	1013 (52.2)	653 (33.7)	<0.001
>13.6 kg	221 (11.4)	88 (4.5)	<0.001
Edema‖	691 (35.6)	483 (24.9)	<0.001
Shortness of breath	342 (17.6)	292 (15.1)	0.03
Alanine aminotransferase >ULN	26 (1.3)	59 (3.0)	<0.001
Macular edema	3 (0.2)	2 (0.1)	0.66

Conclusioni

I Soggetti con Prediabete Presentano un Aumentato Rischio Cardiovascolare.

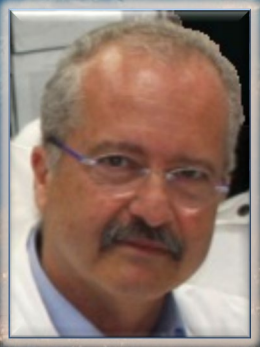
L'HbA_{1C} Rappresenta Un Ottimo Metodo Per Identificare Non Solo Soggetti Ad Elevato Rischio Di Diabete Ma Anche A Rischio Di Complicanze Macrovascolari.

L'intervento Sullo Stile Di Vita Ad Oggi È un Metodo sicuro Per Ridurre Le Complicanze Macrovascolari

…grazie



Prof.ssa Agata M. Rabuazzo



Prof. Francesco Purrello



Agnese Filippello



Salvatore Piro



Stefania Di Mauro



Alessandra Scamporrino



Francesca Urbano



Roberto Scicali