



# V Convegno Nazionale

Centro Studi e Ricerche Fondazione AMD - onlus  
La ricerca di AMD e l'innovazione in diabetologia

▶▶▶ FIRENZE 18-20 novembre 2010



## Il target terapeutico e il dogma del 7%

Edoardo Mannucci

*Agenzia Diabetologia*

*Azienda Ospedaliero-Universitaria Careggi, Firenze*



## Tabella 9

### Obiettivi glicemici in diabetici adulti di tipo 1 e 2

HbA<sub>1c</sub> < 7,0%\* (< 6,5% in singoli pazienti)

Glicemia a digiuno e pre-prandiale 70-130 mg/dl

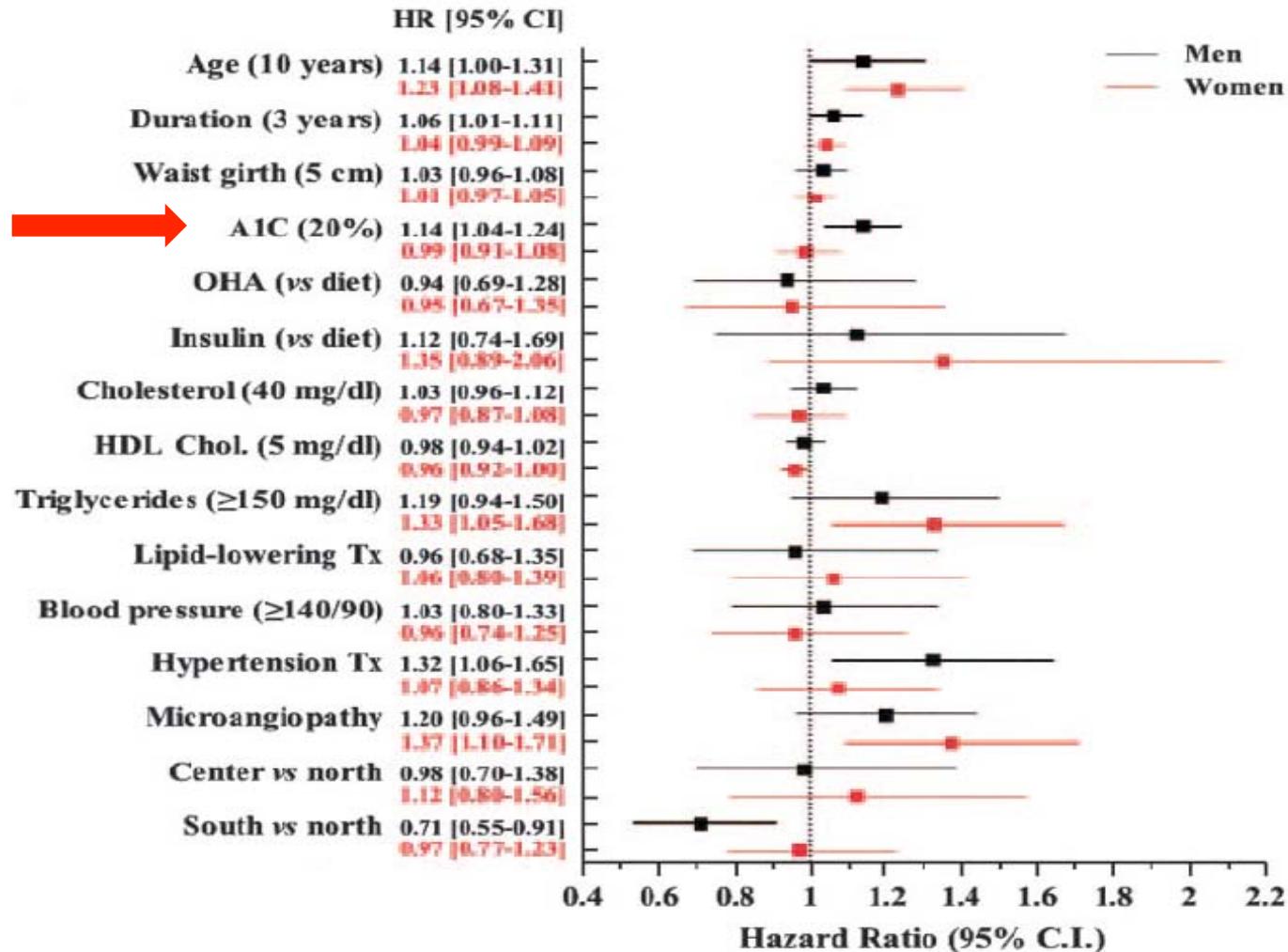
Glicemia post-prandiale<sup>§</sup> < 180 mg/dl<sup>§#</sup>

# Incidence of Coronary Heart Disease in Type 2 Diabetic Men and Women

Impact of microvascular complications, treatment, and geographic location

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 CARLO GIORDA, MD<sup>2</sup>  
 MARINA MAGGINI, PHD<sup>3</sup>  
 EDOARDO MANNUCCI, MD<sup>4</sup>  
 ROBERTO RASCHETTI, PHD<sup>3</sup>  
 FLAVIA LOMBARDO, PHD<sup>3</sup>  
 STEFANIA SPILA-ALEGIANI, PHD<sup>3</sup>  
 SALVATORE TURCO, MD<sup>5</sup>  
 MARIO VELUSSI, MD<sup>6</sup>  
 ELE FERRANNINI, MD<sup>7</sup>

*Diabetes Care* 30:1241–1247, 2007



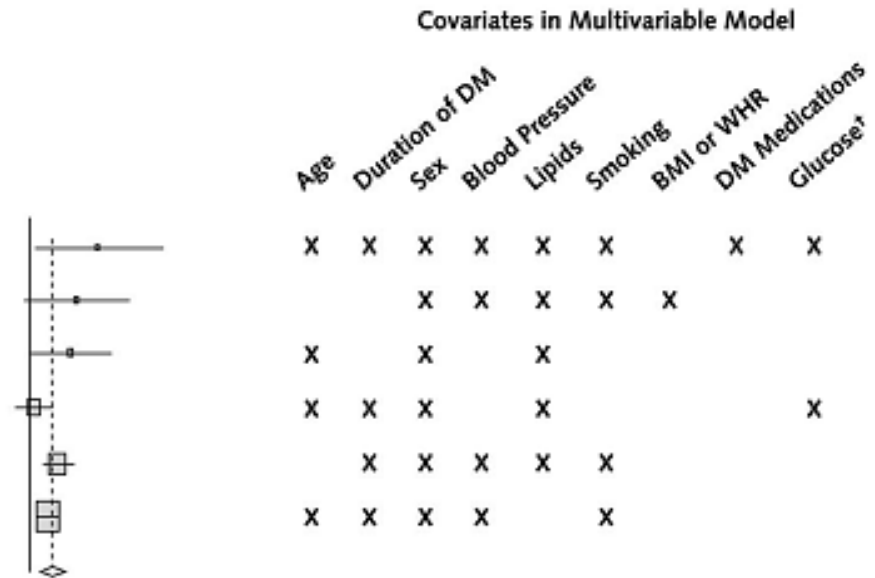
# Meta-Analysis: Glycosylated Hemoglobin and Cardiovascular Disease in Diabetes Mellitus

ARTICLE

Elizabeth Selvin, MPH; Spyridon Marinopoulos, MD, MBA; Gail Berkenblit, MD, PhD; Tejal Rami, MPH; Frederick L. Brancati, MD, MHS; Neil R. Powe, MD, MPH, MBA; and Sherita Hill Golden, MD, MHS

## Type 2 diabetes

Study, Year (Reference)	Events/Persons, n/n*	RR (95% CI)
<b>Coronary heart disease (fatal and nonfatal)</b>		
Florkowski et al., 1998 (24)	92/422	1.43 (1.02–2.00)
Kuusisto et al., 1994 (36)	33/229	1.29 (0.98–1.70)
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Lehto et al., 1997 (32)	256/1059	1.03 (0.96–1.15)
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Moss et al., 1994 (44)	241/1194	1.10 (1.04–1.17)
<b>Pooled</b>	<b>1248/6684</b>	<b>1.13 (1.06–1.20)</b>



➤ **1.13 (1.06 – 1.20)**

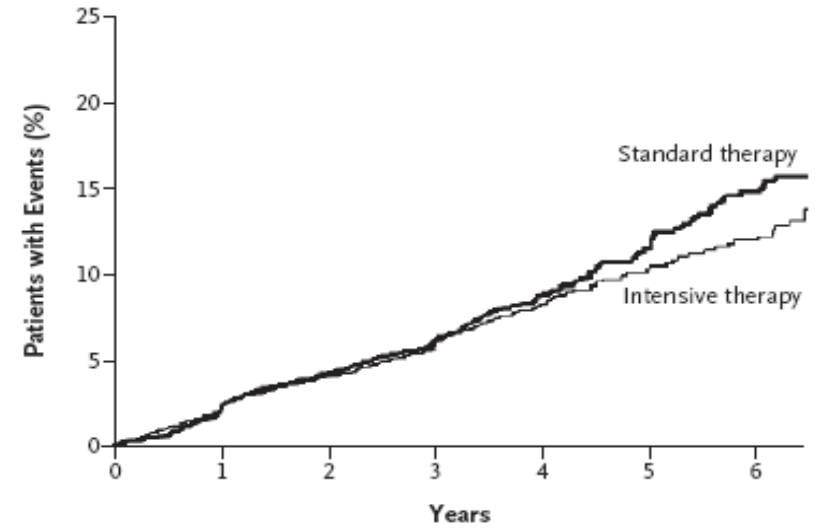
## Effects of Intensive Glucose Lowering in Type 2 Diabetes

The Action to Control Cardiovascular Risk in Diabetes Study Group\*

### ACCORD

N Engl J Med 2008;358:2545-59.

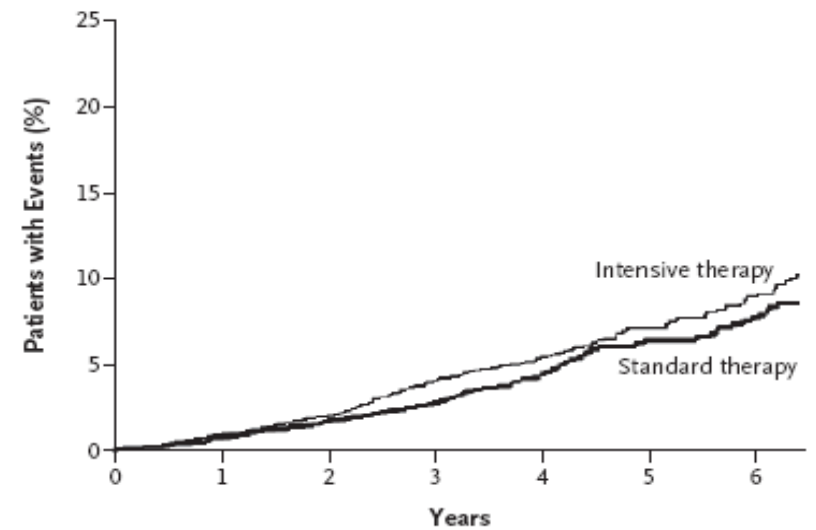
#### A Primary Outcome



#### No. at Risk

Intensive therapy	5128	4843	4390	2839	1337	475	448
Standard therapy	5123	4827	4262	2702	1186	440	395

#### B Death from Any Cause



#### No. at Risk

Intensive therapy	5128	4972	4803	3250	1748	523	506
Standard therapy	5123	4971	4700	3180	1642	499	480

# Survival as a function of HbA<sub>1c</sub> in people with type 2 diabetes: a retrospective cohort study

Craig J Currie, John R Peters, Aodán Tynan, Marc Evans, Robert J Heine, Oswaldo L Bracco, Tony Zagar, Chris D Poole

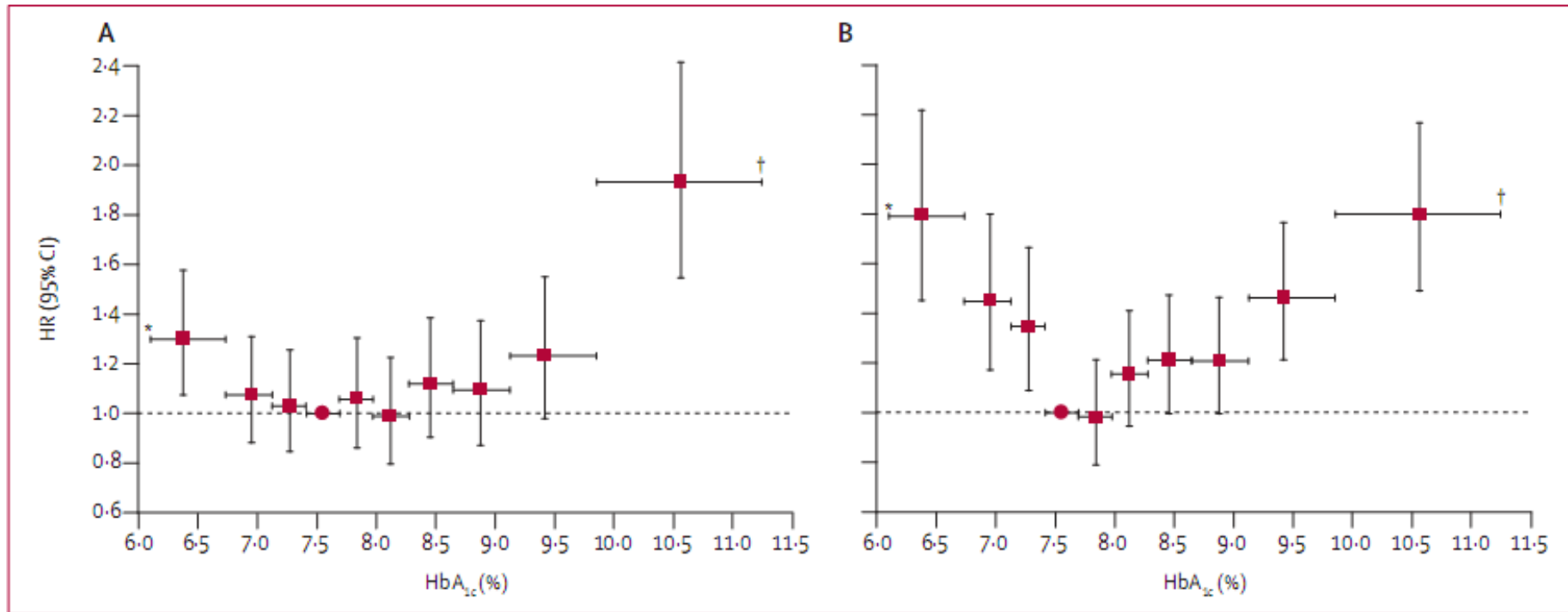


Figure 1: Adjusted hazard ratios for all-cause mortality by HbA<sub>1c</sub> deciles in people given oral combination and insulin-based therapies

Cox proportional hazards models were used, with the HbA<sub>1c</sub> base case scenario. Vertical error bars show 95% CIs, horizontal bars show HbA<sub>1c</sub> range. Red circle=reference decile. \*Truncated at lower quartile. †Truncated at upper quartile. Metformin plus sulphonylureas (A); and insulin-based regimens (B).



# Glycated Hemoglobin, Diabetes, and Cardiovascular Risk in Nondiabetic Adults

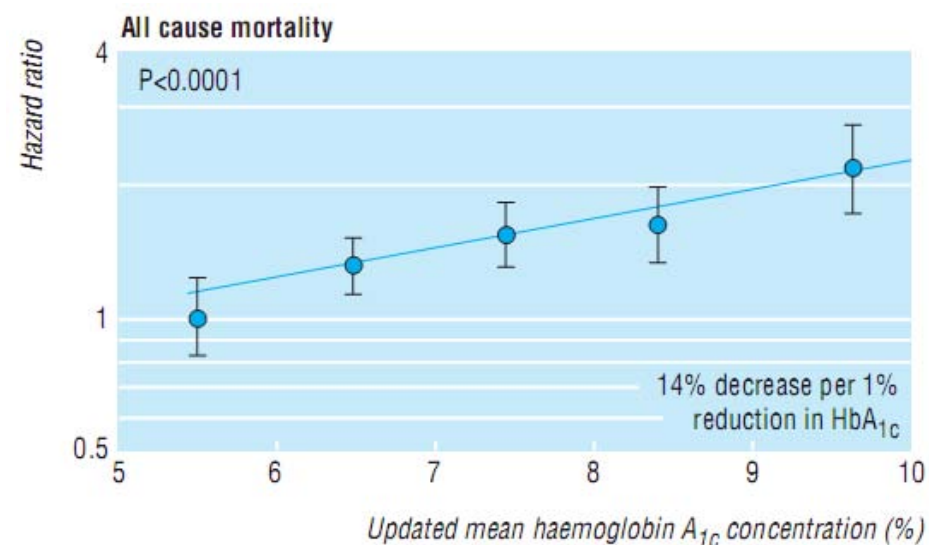
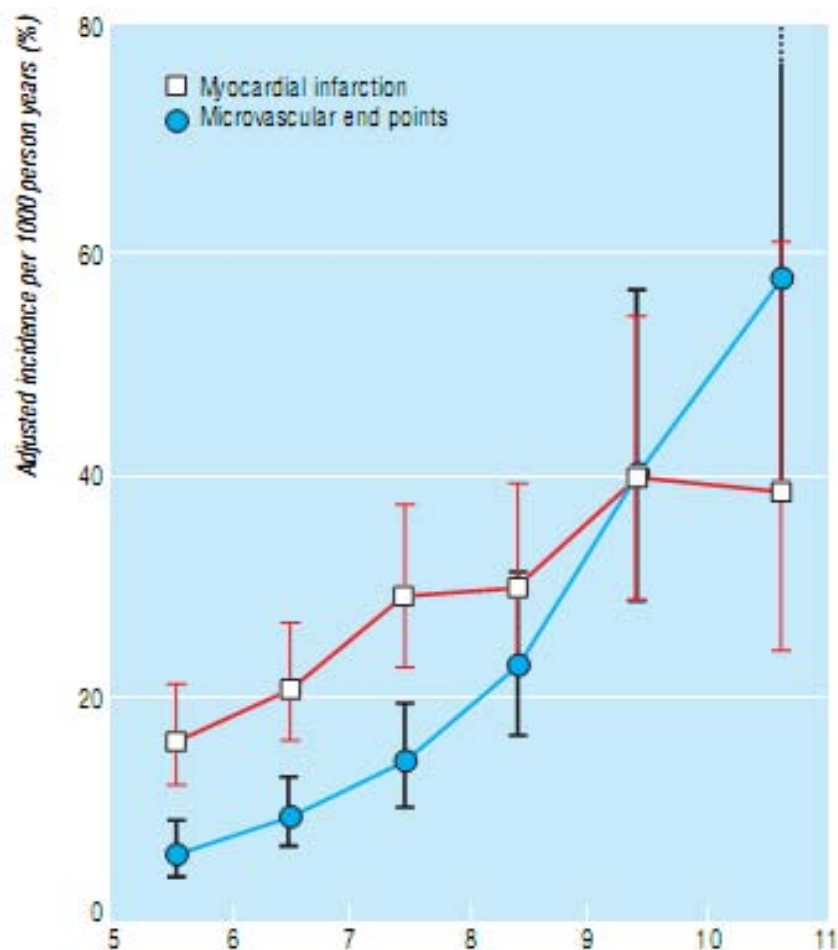
Elizabeth Selvin, Ph.D., M.P.H., Michael W. Steffes, M.D., Ph.D., Hong Zhu, B.S.,  
 Kunihiro Matsushita, M.D., Ph.D., Lynne Wagenknecht, Dr.P.H.,  
 James Pankow, Ph.D., M.P.H., Josef Coresh, M.D., Ph.D.,  
 and Frederick L. Brancati, M.D., M.H.S.

**Table 2. (Continued.)**

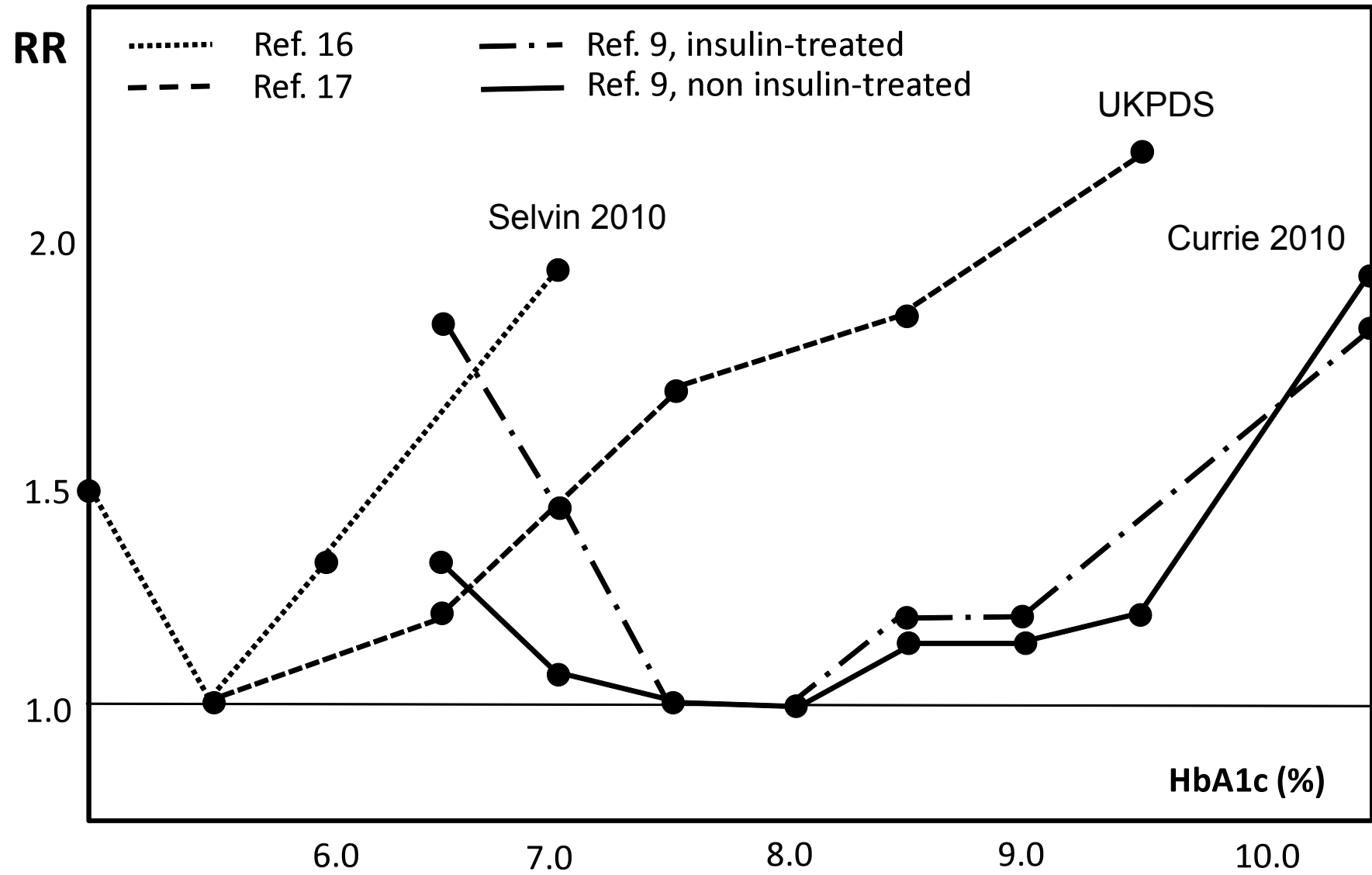
Outcome	Model 1a	Model 2a	Model 3a
<b>Death from any cause</b>			
Glycated hemoglobin category — hazard ratio (95% CI)			
<5.0%	1.43 (1.17–1.74)	1.48 (1.21–1.82)	1.48 (1.21–1.81)
5.0 to <5.5% (reference)	1.00	1.00	1.00
5.5 to <6.0%	1.34 (1.18–1.52)	1.18 (1.04–1.35)	1.19 (1.05–1.35)
6.0 to <6.5%	1.92 (1.63–2.27)	1.59 (1.34–1.89)	1.61 (1.35–1.91)
≥6.5%	1.92 (1.54–2.40)	1.65 (1.31–2.08)	1.71 (1.30–2.25)
P value for trend <sup>§</sup>	—	—	—
Glycated hemoglobin value — hazard ratio (95% CI)	1.21 (1.13–1.28)	1.12 (1.05–1.21)	1.18 (1.05–1.32)
C statistic	0.6885	0.7316	0.7314

# Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study

Irene M Stratton, Amanda I Adler, H Andrew W Neil, David R Matthews, Susan E Manley, Carole A Cull, David Hadden, Robert C Turner, Rury R Holman on behalf of the UK Prospective Diabetes Study Group







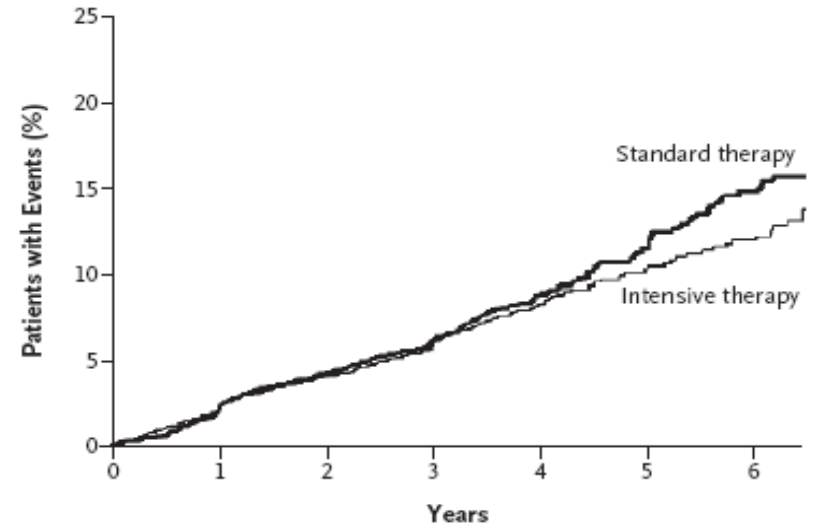
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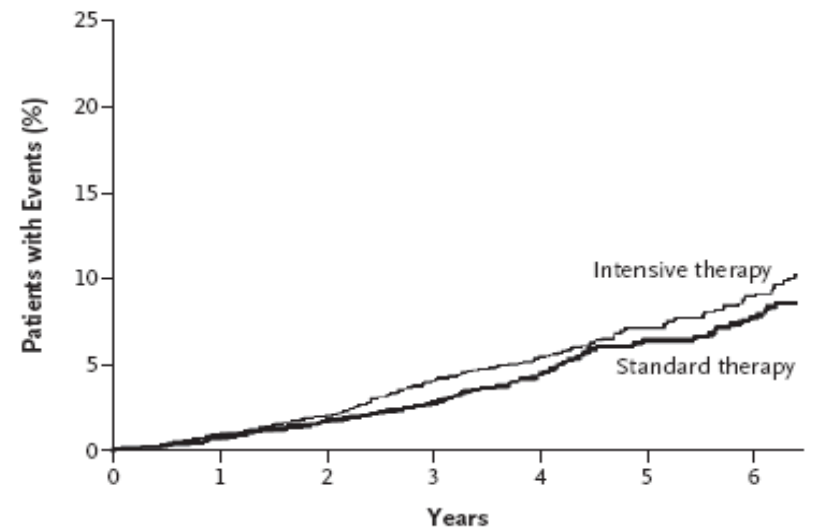
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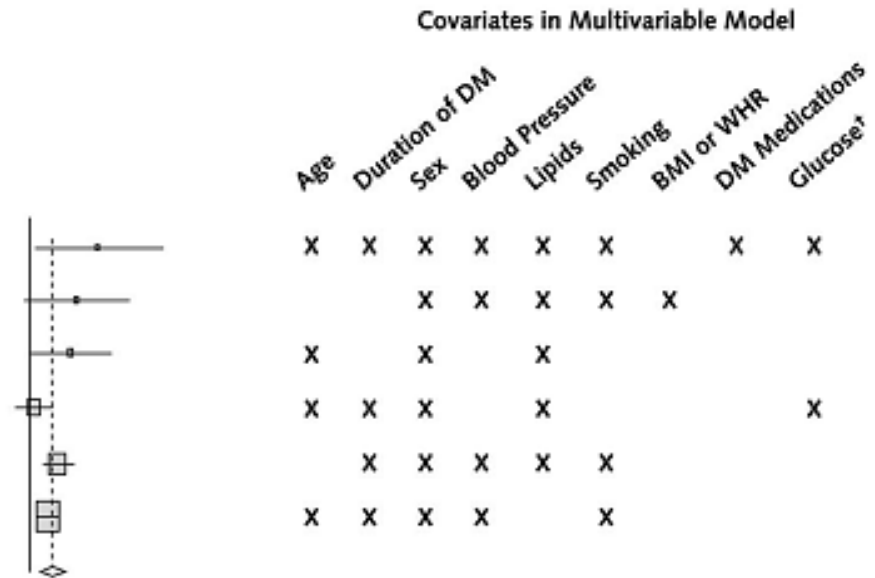
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**Rischio cardiovascolare**

2,6  
2,4  
2,2  
2  
1,8  
1,6  
1,4  
1,2  
1  
0,8

4

5

6

7

8

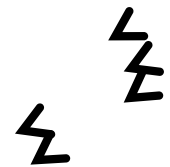
9

10

**HbA1c**

**ACCORD**  
7.5 vs 6.4

**VADT**  
8.4 vs 6.9



**UKPDS**  
7.0 vs 7.9

**PROACTIVE**  
7.0 vs 7.6

**ADVANCE**  
7.3 vs 6.5

# Prevention of cardiovascular disease through glycemic control in type 2 diabetes: A meta-analysis of randomized clinical trials

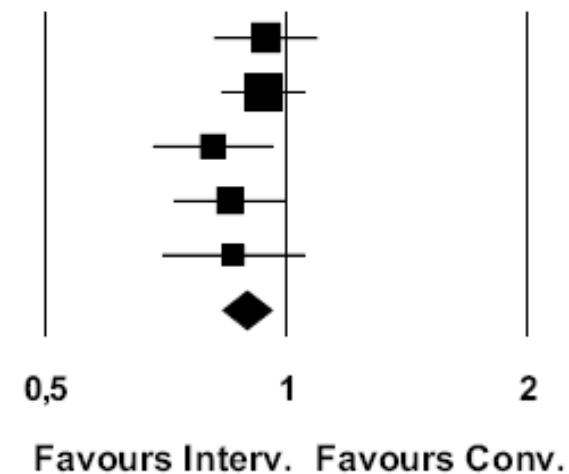
E. Mannucci\*, M. Monami, C. Lamanna, F. Gori, N. Marchionni

Weighted mean reduction of HbA1c: about 1.0%

## A Cardiovascular events

<u>Study name</u>	<u>Statistics for each study</u>				
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
ACCORD	0,944	0,811	1,098	-0,746	0,455
ADVANCE	0,937	0,830	1,059	-1,035	0,301
PROACTIVE	0,811	0,681	0,966	-2,346	0,019
UKPDS 33+34	0,852	0,723	1,003	-1,920	0,055
VADT	0,860	0,700	1,058	-1,425	0,154
<b>OVERALL</b>	<b>0,893</b>	<b>0,832</b>	<b>0,957</b>	<b>-3,182</b>	<b>0,001</b>

### Odds ratio and 95% CI



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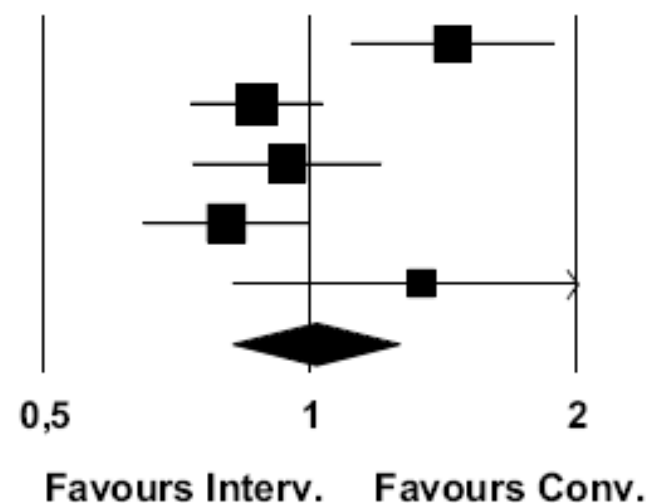
## F Cardiovascular mortality

### Study name

### Statistics for each study

### Odds ratio and 95% CI

	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
ACCORD	1,447	1,108	1,888	2,718	0,007
ADVANCE	0,869	0,731	1,033	-1,589	0,112
PROACTIVE	0,941	0,734	1,206	-0,480	0,631
UKPDS 33+34	0,805	0,647	1,001	-1,950	0,051
VADT	1,335	0,816	2,184	1,150	0,250
<b>OVERALL</b>	<b>1,012</b>	<b>0,815</b>	<b>1,257</b>	<b>0,110</b>	<b>0,912</b>





**Rischio di morte cardiovascolare**

2,4  
2,2  
2  
1,8  
1,6  
1,4  
1,2  
1  
0,8

4

5

6

7

8

9

10

**HbA1c**

**ACCORD**  
7.5 vs 6.4

**PROACTIVE**  
7.0 vs 7.6

**ADVANCE**  
7.3 vs 6.5

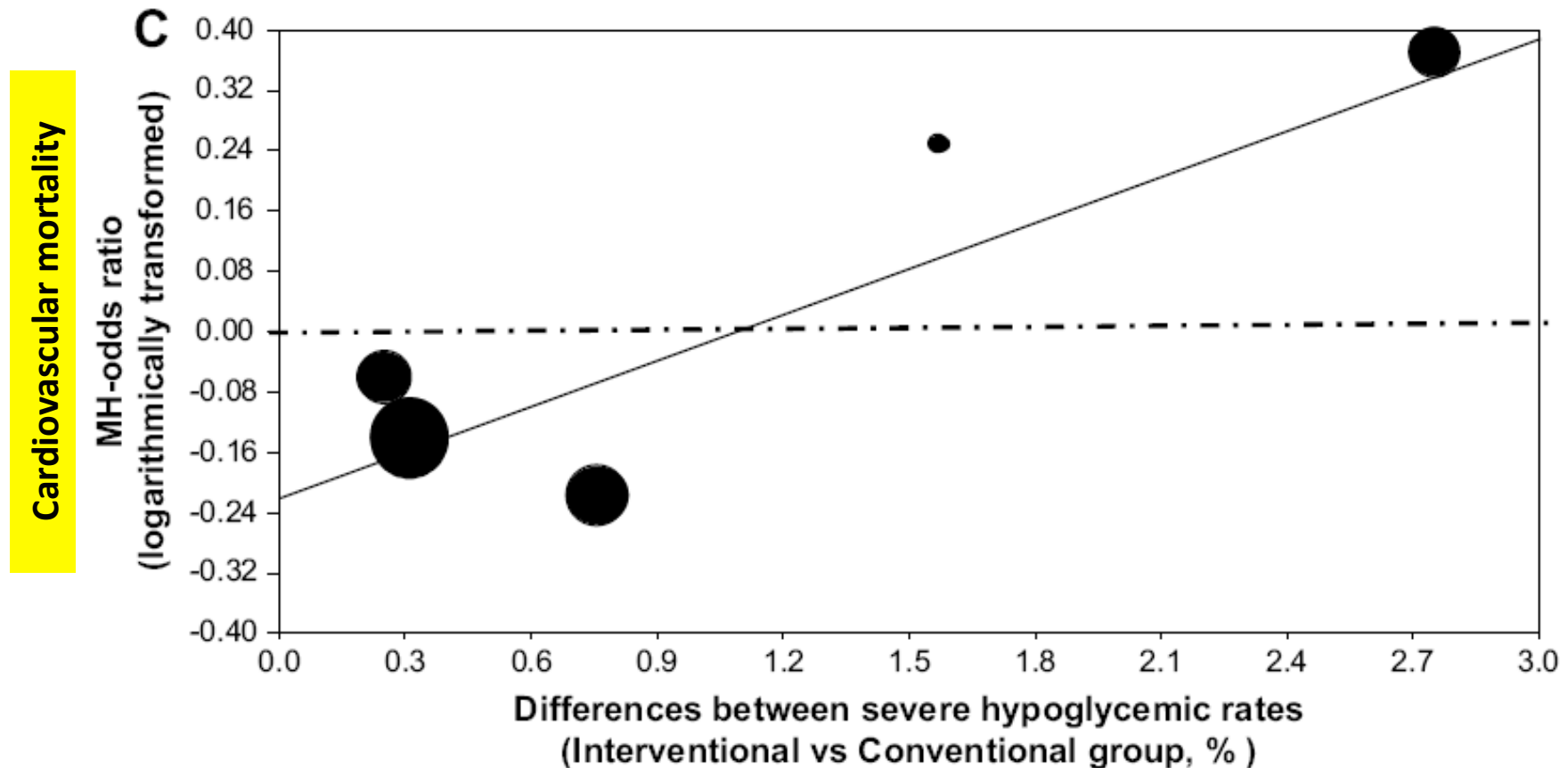
**VADT**  
8.4 vs 6.9

**UKPDS**  
7.0 vs 7.9



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*In trials in which the reduction of HbA1c was obtained with a higher incidence of hypoglycaemia, CV MORTALITY is increased*

