ACADEMIA LATINOAMERICANA
DE MEDICINA DEL ADULTO MAYOR
ALMA

Consecuencias del “legado glucémico” en el abordaje diagnóstico y terapéutico de las complicaciones

D. en C. Enrique Díaz de León González

UMAE 25

Instituto Mexicano del Seguro Social

Universidad de Monterrey

Agenda

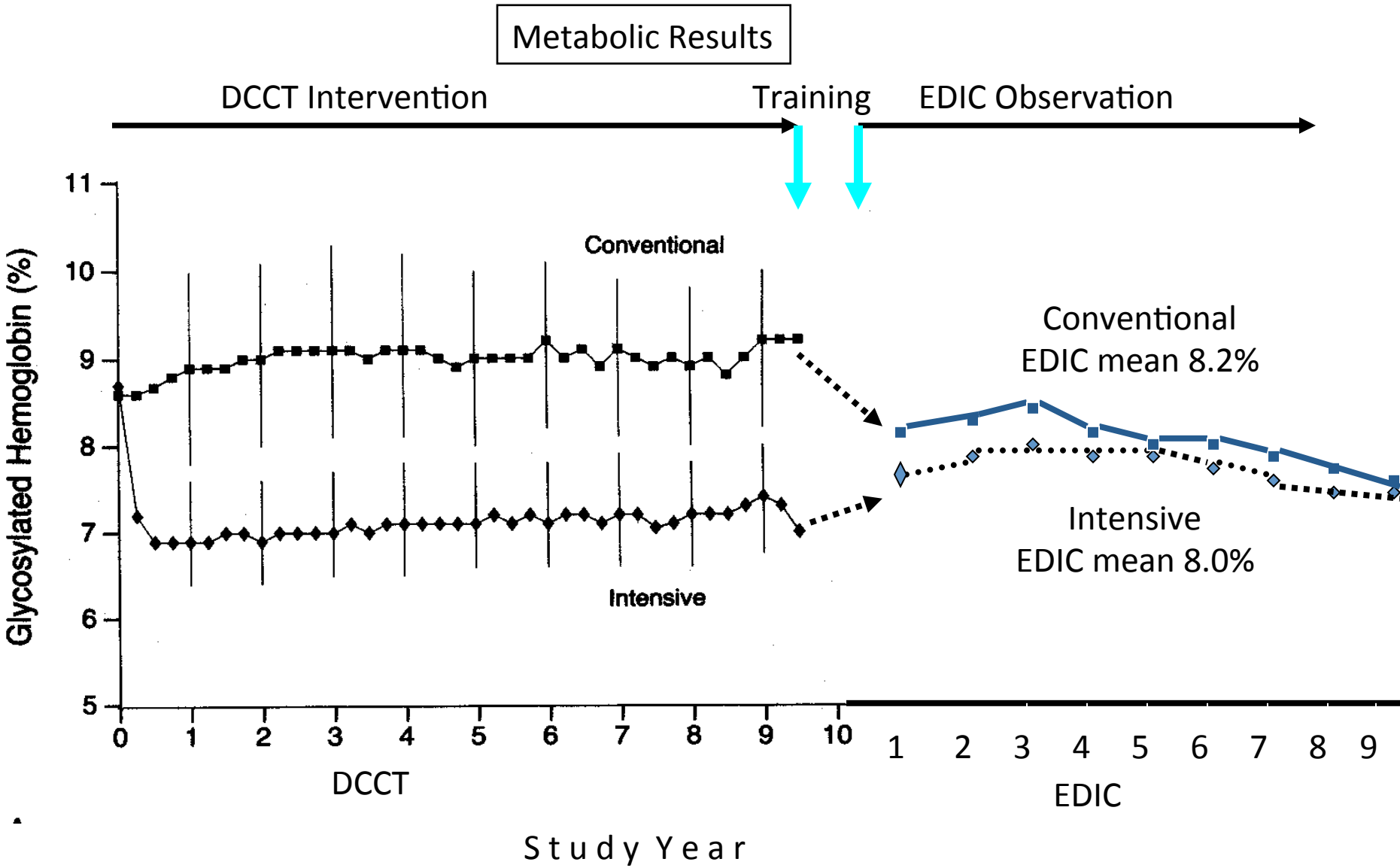
- Estudios que demostraron el legado glucémico
- Definición y concepto
- Impacto en el abordaje diagnóstico y tratamiento de las complicaciones

DCCT/EDIC

Intensive Diabetes Treatment and Cardiovascular Disease in Patients with Type 1 Diabetes

The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group*

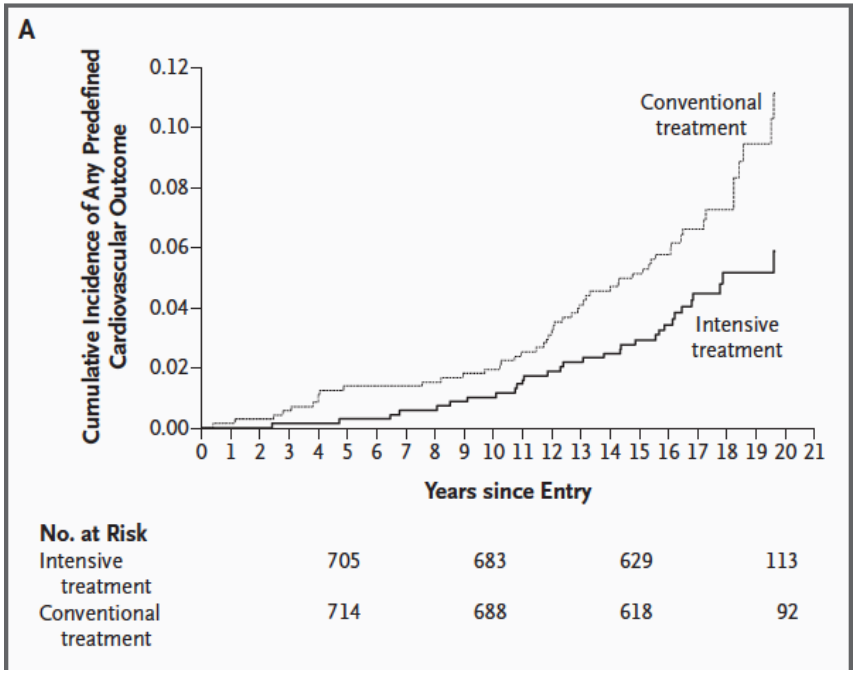
DCCT/EDIC; Memory effect

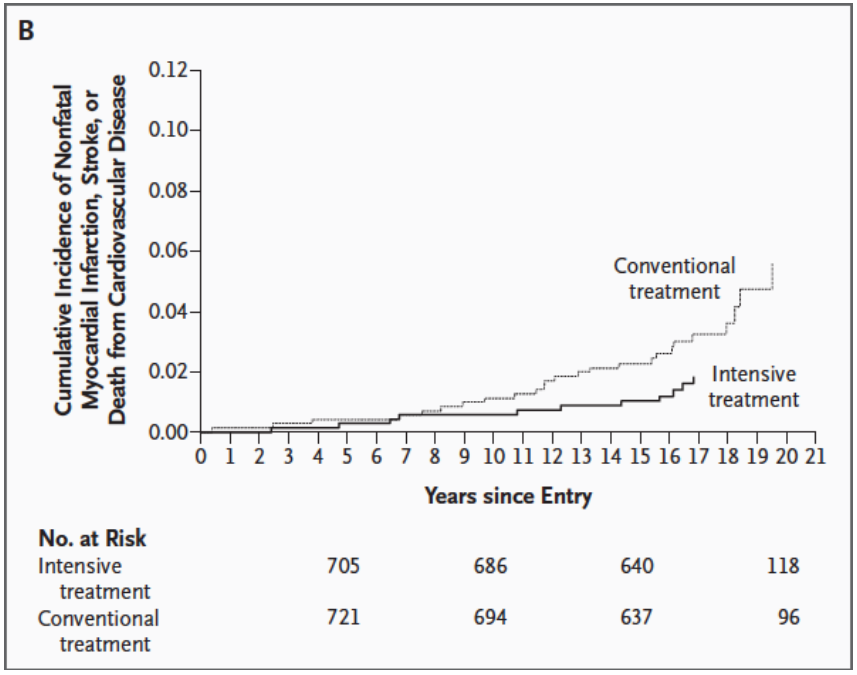


DCCT/EDIC Study Research Group, *NEJM* 2005

Eventos CV

Infarto de miocardio no fatal, EVC y muerte CV



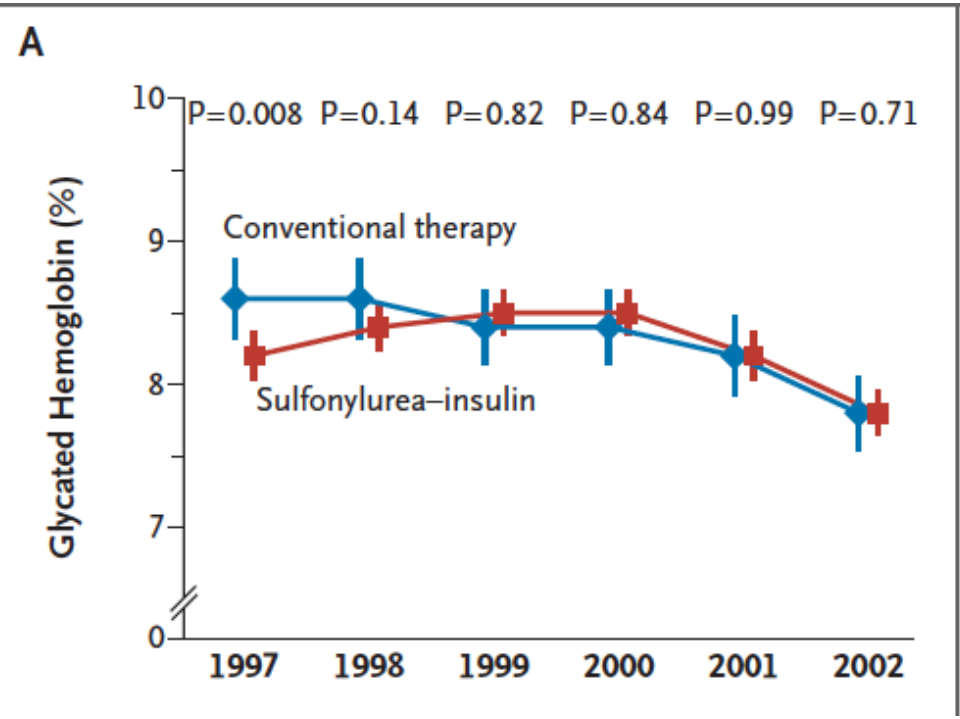


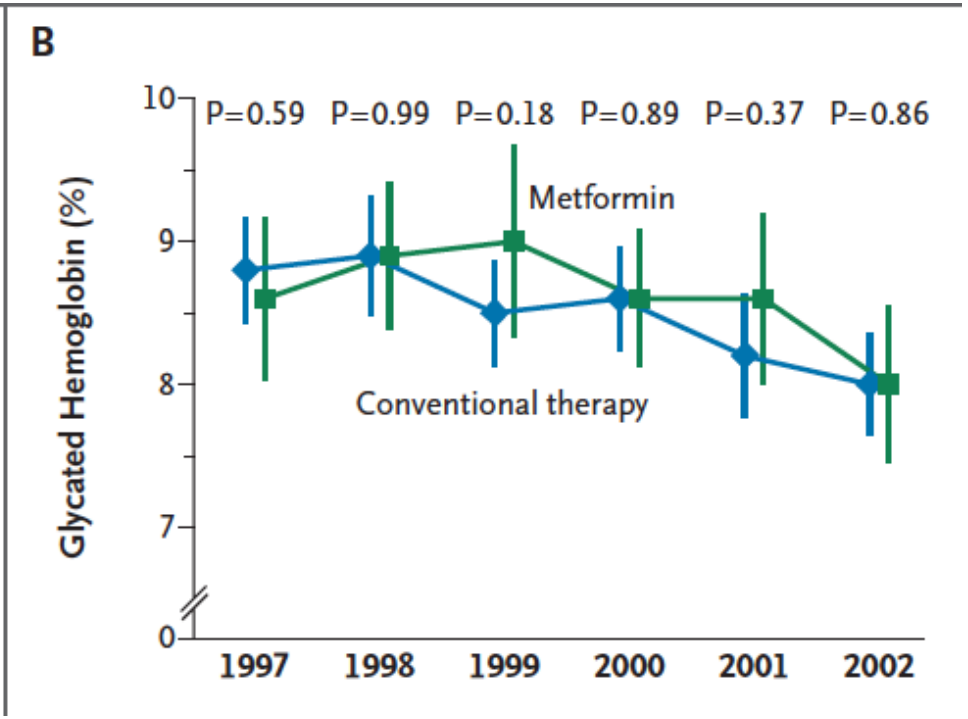
DCCT/EDIC Study Research Group, *NEJM* 2005

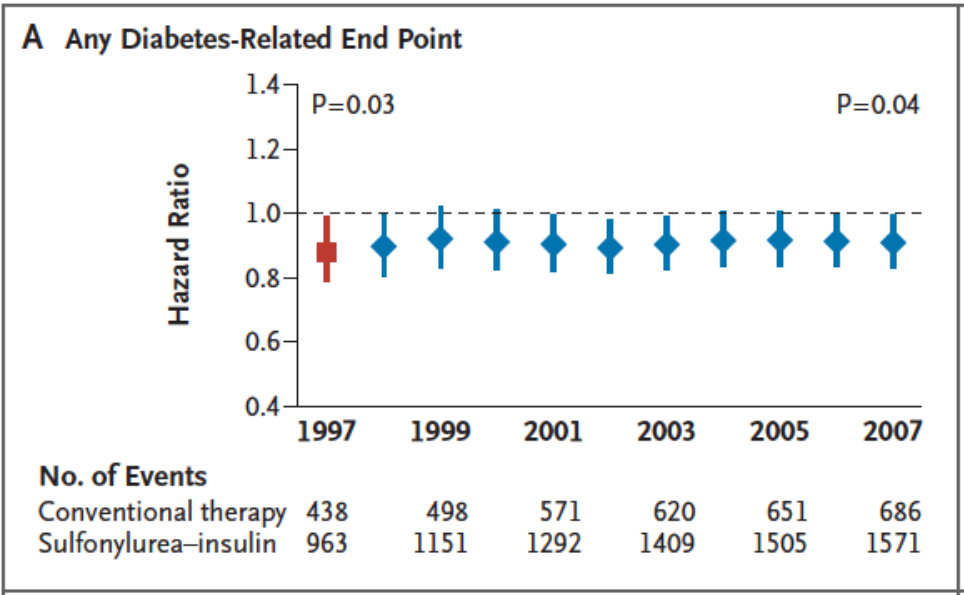
10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

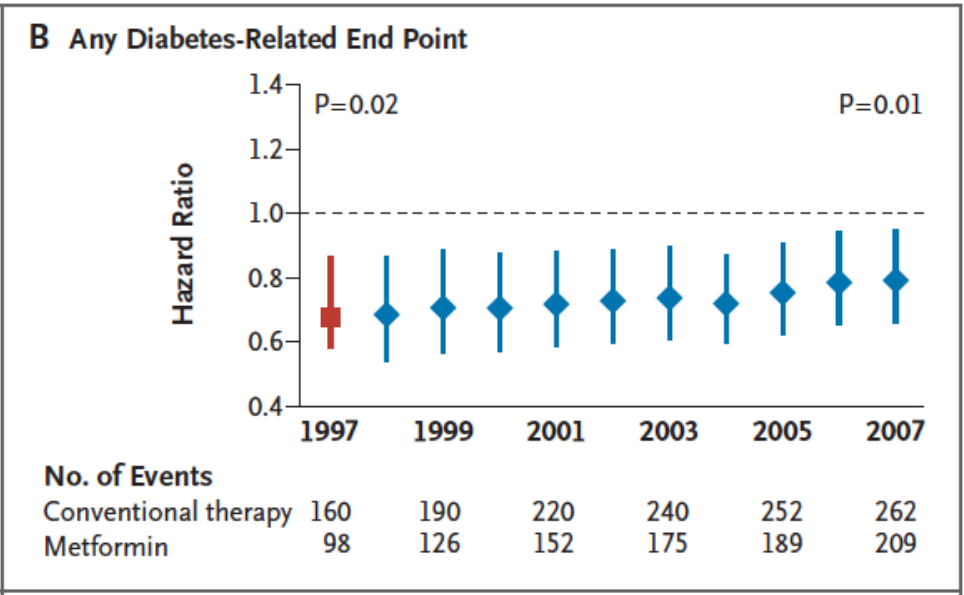
Rury R. Holman, F.R.C.P., Sanjoy K. Paul, Ph.D., M. Angelyn Bethel, M.D., David R. Matthews, F.R.C.P., and H. Andrew W. Neil, F.R.C.P.

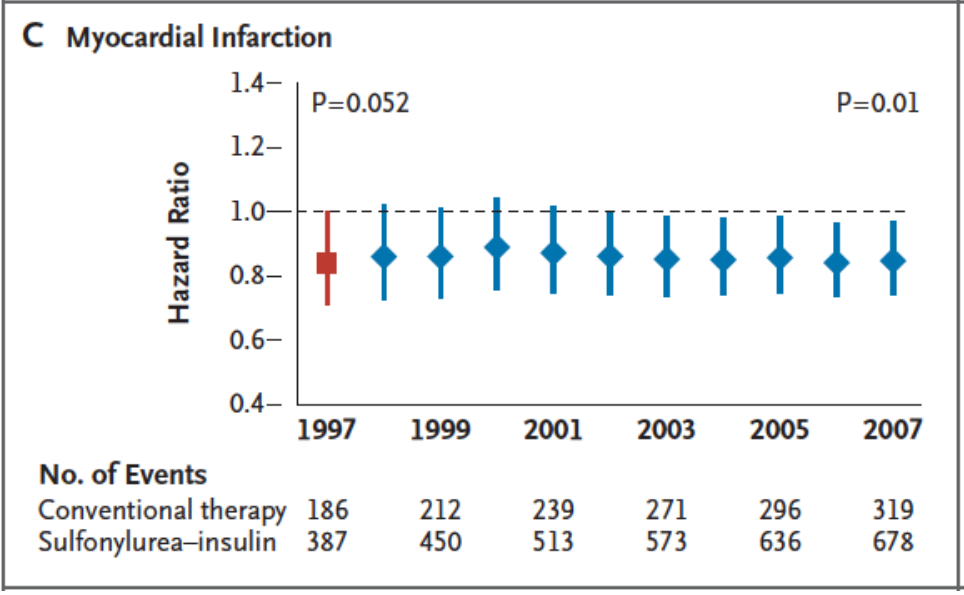
N ENGL J MED 359;15 WWW.NEJM.ORG OCTOBER 9, 2008

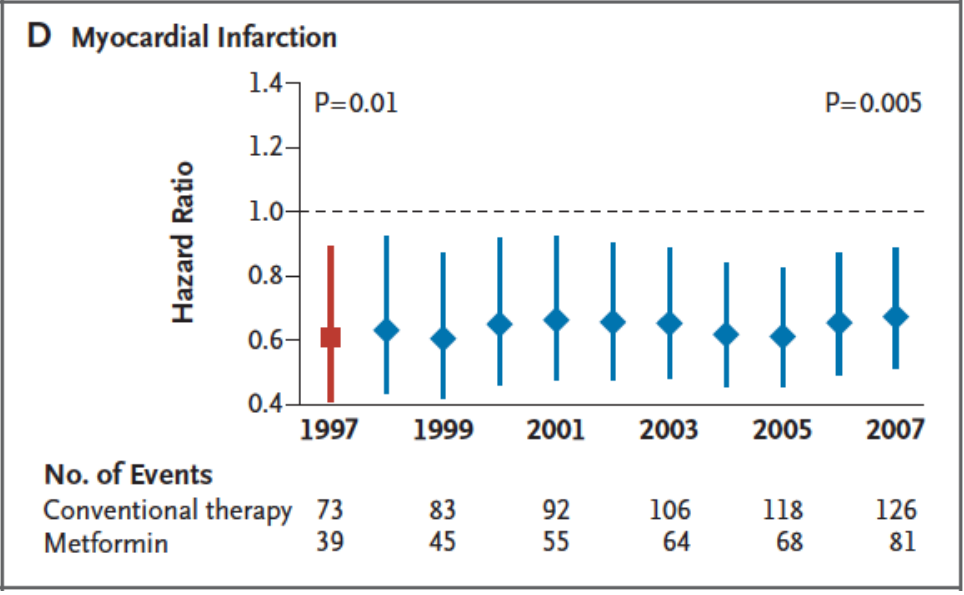

A
Glycated Hemoglobin (%)
10
9
8
7
0
P=0.008
P=0.14
P=0.82
P=0.84
P=0.99
P=0.71
Conventional therapy
Sulfonylurea–insulin
1997
1998
1999
2000
2001
2002


B
Glycated Hemoglobin (%)
10
9
8
7
0
P=0.59
P=0.99
P=0.18
P=0.89
P=0.37
P=0.86
Metformin
Conventional therapy
1997
1998
1999
2000
2001
2002

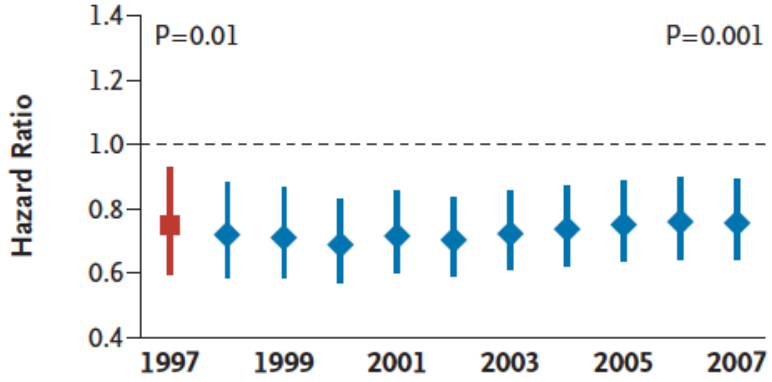

A Any Diabetes-Related End Point
Hazard Ratio
1.4
1.2
1.0
0.8
0.6
0.4
P=0.03
P=0.04
1997
1999
2001
2003
2005
2007
No. of Events
Conventional therapy 438 498 571 620 651 686
Sulfonylurea–insulin 963 1151 1292 1409 1505 1571


B Any Diabetes-Related End Point
Hazard Ratio
1.4
1.2
1.0
0.8
0.6
0.4
P=0.02
P=0.01
1997
1999
2001
2003
2005
2007
No. of Events
Conventional therapy 160 190 220 240 252 262
Metformin 98 126 152 175 189 209


C Myocardial Infarction
Hazard Ratio
1.4
1.2
1.0
0.8
0.6
0.4
P=0.052
P=0.01
1997
1999
2001
2003
2005
2007
No. of Events
Conventional therapy 186 212 239 271 296 319
Sulfonylurea–insulin 387 450 513 573 636 678

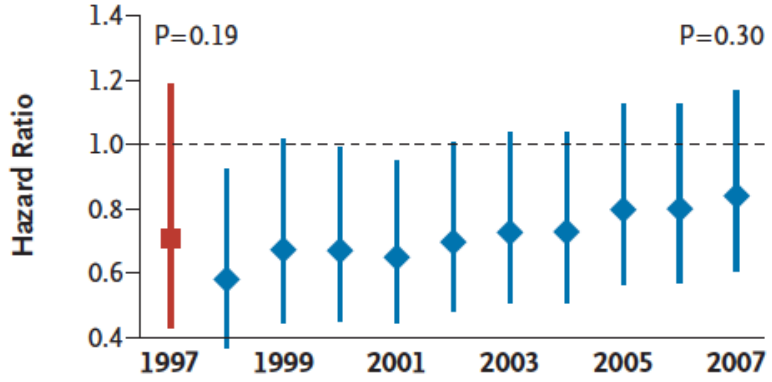

D Myocardial Infarction
Hazard Ratio
1.4
1.2
1.0
0.8
0.6
0.4
P=0.01
P=0.005
1997
1999
2001
2003
2005
2007
No. of Events
Conventional therapy 73 83 92 106 118 126
Metformin 39 45 55 64 68 81

E Microvascular Disease



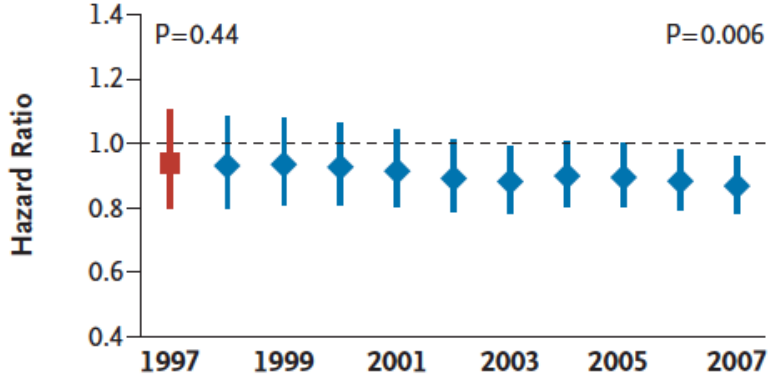
No. of Events						
Conventional therapy	121	155	187	205	212	222
Sulfonylurea–insulin	225	277	338	378	406	429

F Microvascular Disease



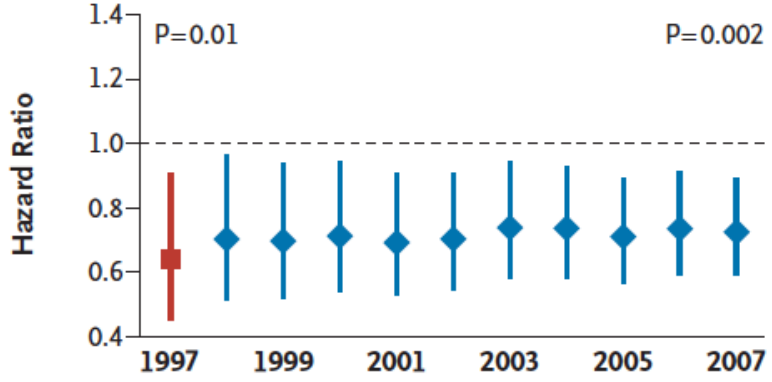
No. of Events						
Conventional therapy	38	58	70	73	74	78
Metformin	24	37	44	52	58	66

G Death from Any Cause



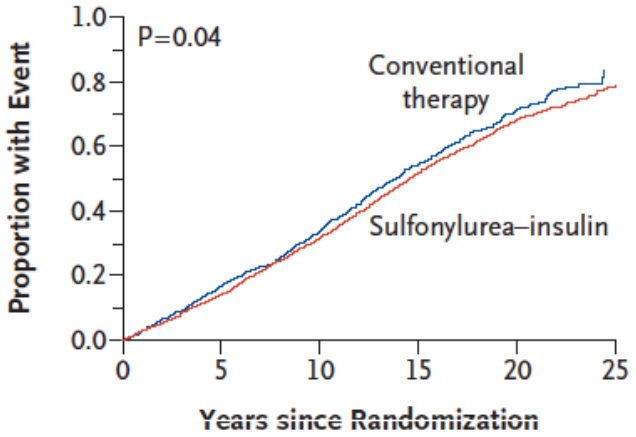
No. of Events						
Conventional therapy	213	267	330	400	460	537
Sulfonylurea–insulin	489	610	737	868	1028	1163

H Death from Any Cause



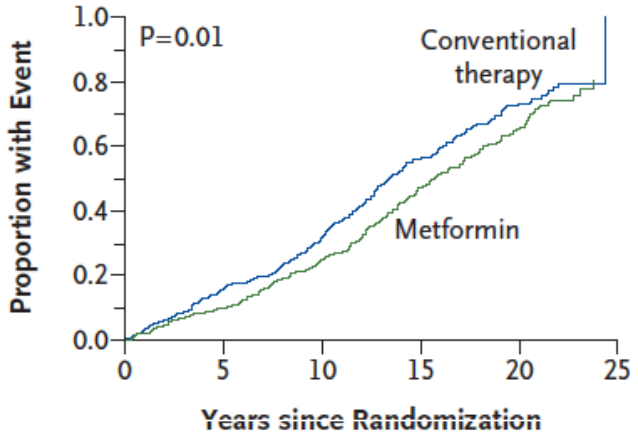
No. of Events						
Conventional therapy	89	113	136	160	183	217
Metformin	50	70	86	110	123	152

A Any Diabetes-Related End Point



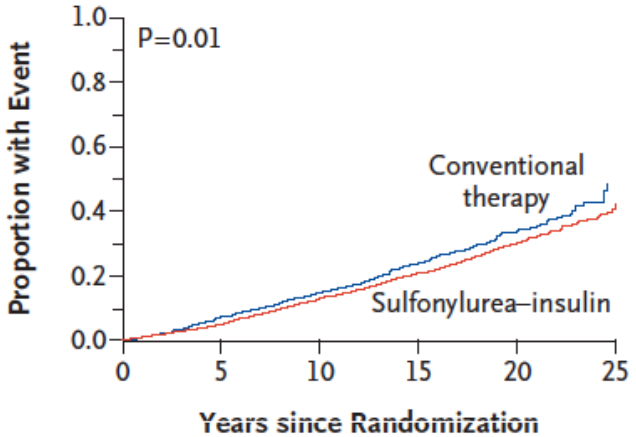
No. at Risk						
Conventional therapy	1138	913	679	370	104	5
Sulfonylurea–insulin	2729	2270	1692	933	277	32

B Any Diabetes-Related End Point



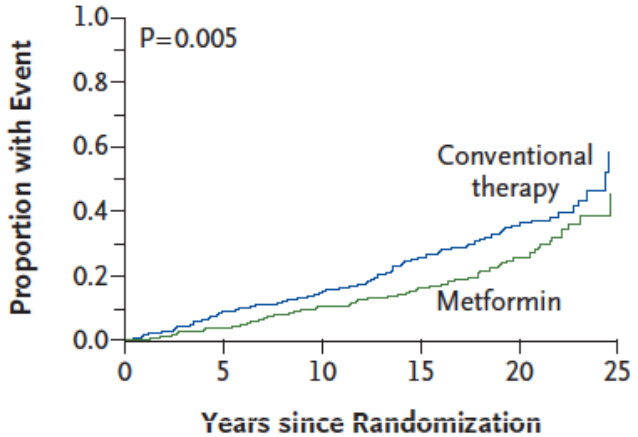
No. at Risk						
Conventional therapy	411	333	255	132	45	2
Metformin	342	300	236	144	62	7

C Myocardial Infarction



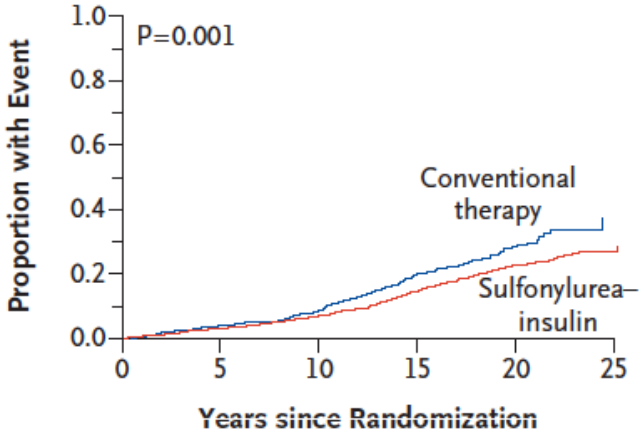
No. at Risk						
Conventional therapy	1138	1013	857	578	221	20
Sulfonylurea–insulin	2729	2488	2097	1459	577	66

D Myocardial Infarction



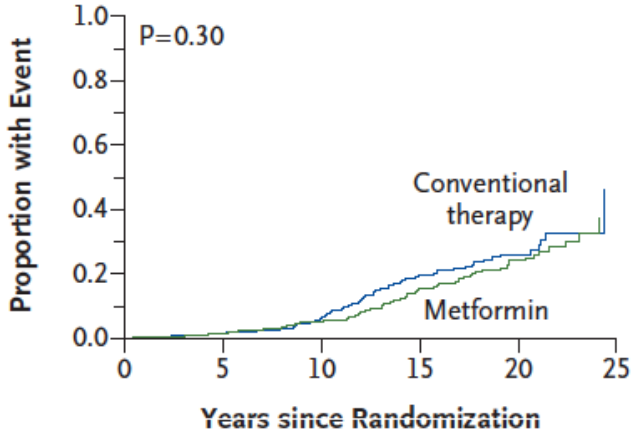
No. at Risk						
Conventional therapy	411	360	311	213	95	4
Metformin	342	317	274	214	106	16

E Microvascular Disease



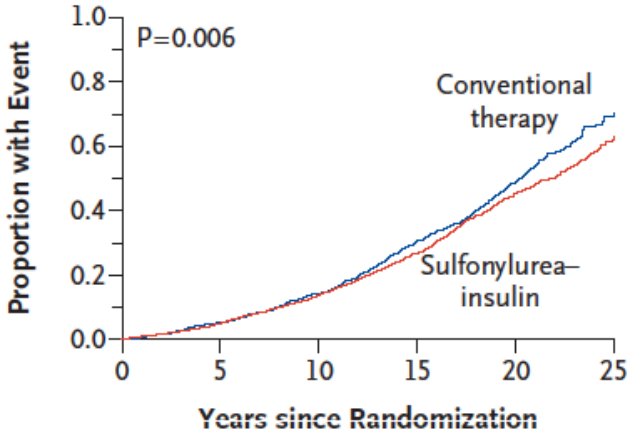
No. at Risk						
Conventional therapy	1138	1018	844	508	172	13
Sulfonylurea–insulin	2729	2465	2076	1368	488	53

F Microvascular Disease



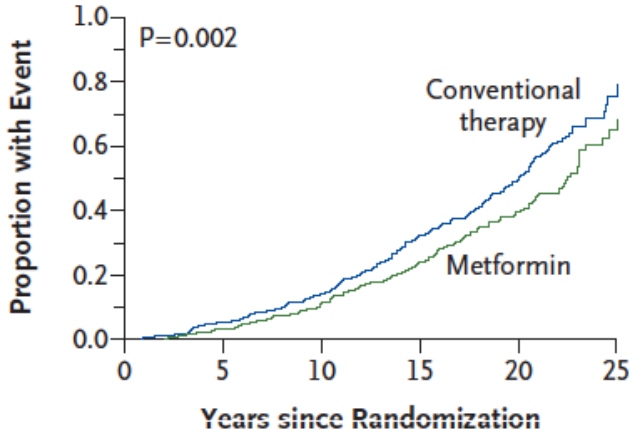
No. at Risk						
Conventional therapy	411	377	316	186	72	2
Metformin	342	319	278	197	92	16

G Death from Any Cause



No. at Risk						
Conventional therapy	1138	1066	939	665	270	28
Sulfonylurea–insulin	2729	2573	2276	1675	680	83

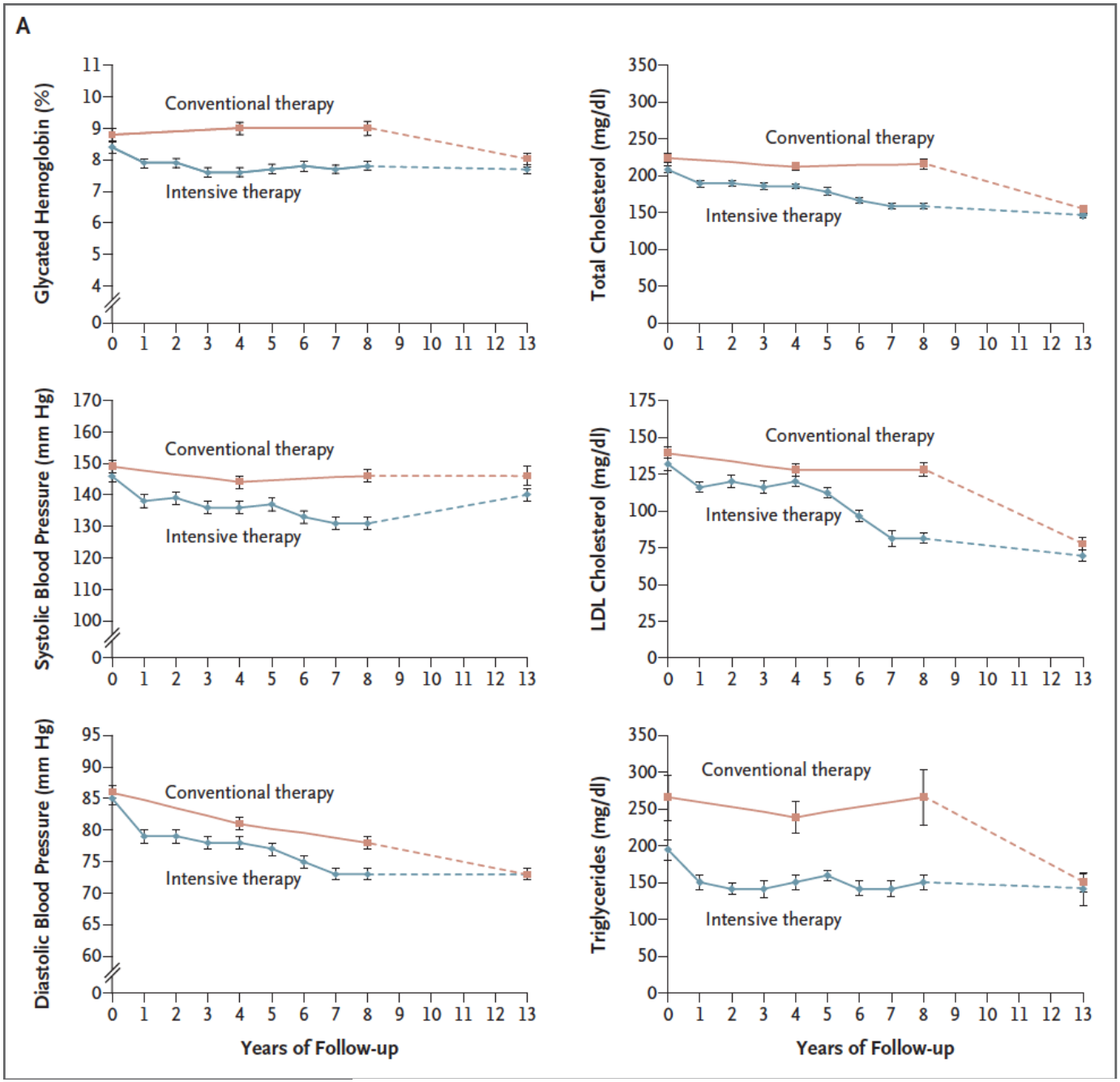
H Death from Any Cause



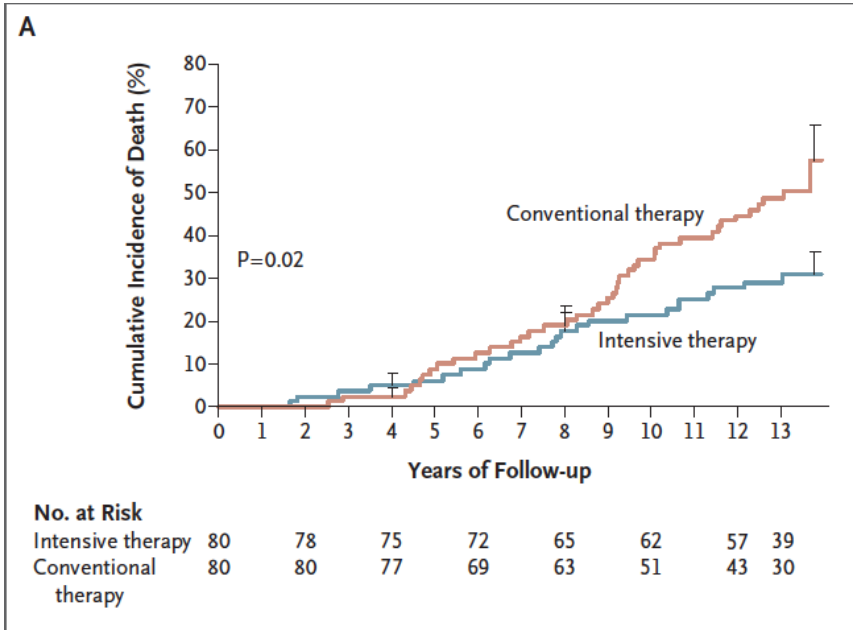
No. at Risk						
Conventional therapy	411	387	345	246	116	7
Metformin	342	328	296	239	124	11

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

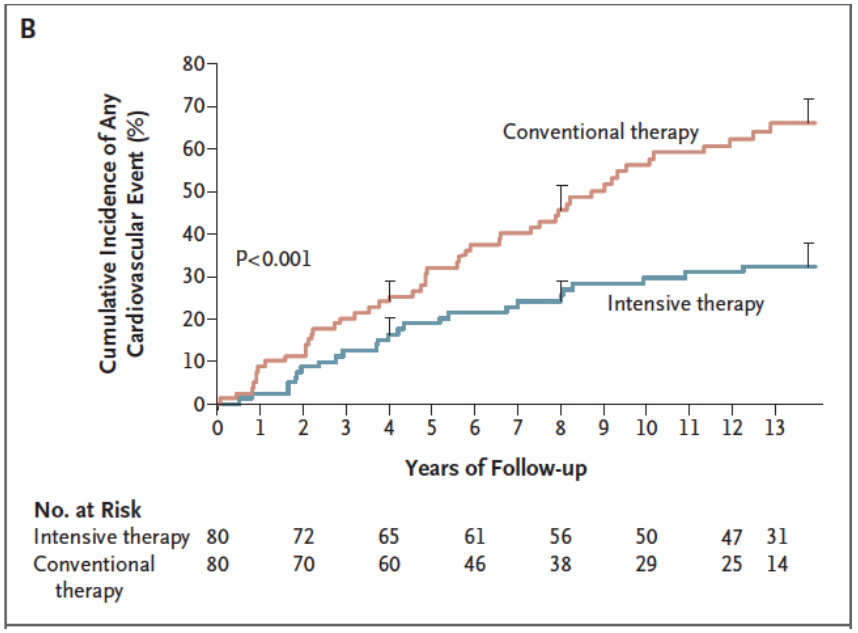
Peter Gæde, M.D., D.M.Sc., Henrik Lund-Andersen, M.D., D.M.Sc., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.


A
Glycated Hemoglobin (%)
Conventional therapy
Intensive therapy
Total Cholesterol (mg/dl)
Conventional therapy
Intensive therapy
Systolic Blood Pressure (mm Hg)
Conventional therapy
Intensive therapy
LDL Cholesterol (mg/dl)
Conventional therapy
Intensive therapy
Diastolic Blood Pressure (mm Hg)
Conventional therapy
Intensive therapy
Triglycerides (mg/dl)
Conventional therapy
Intensive therapy
Years of Follow-up
Years of Follow-up

Muerte



Eventos cardiovasculares



Long-Term Effects of Intensive Glucose Lowering on Cardiovascular Outcomes

ACCORD

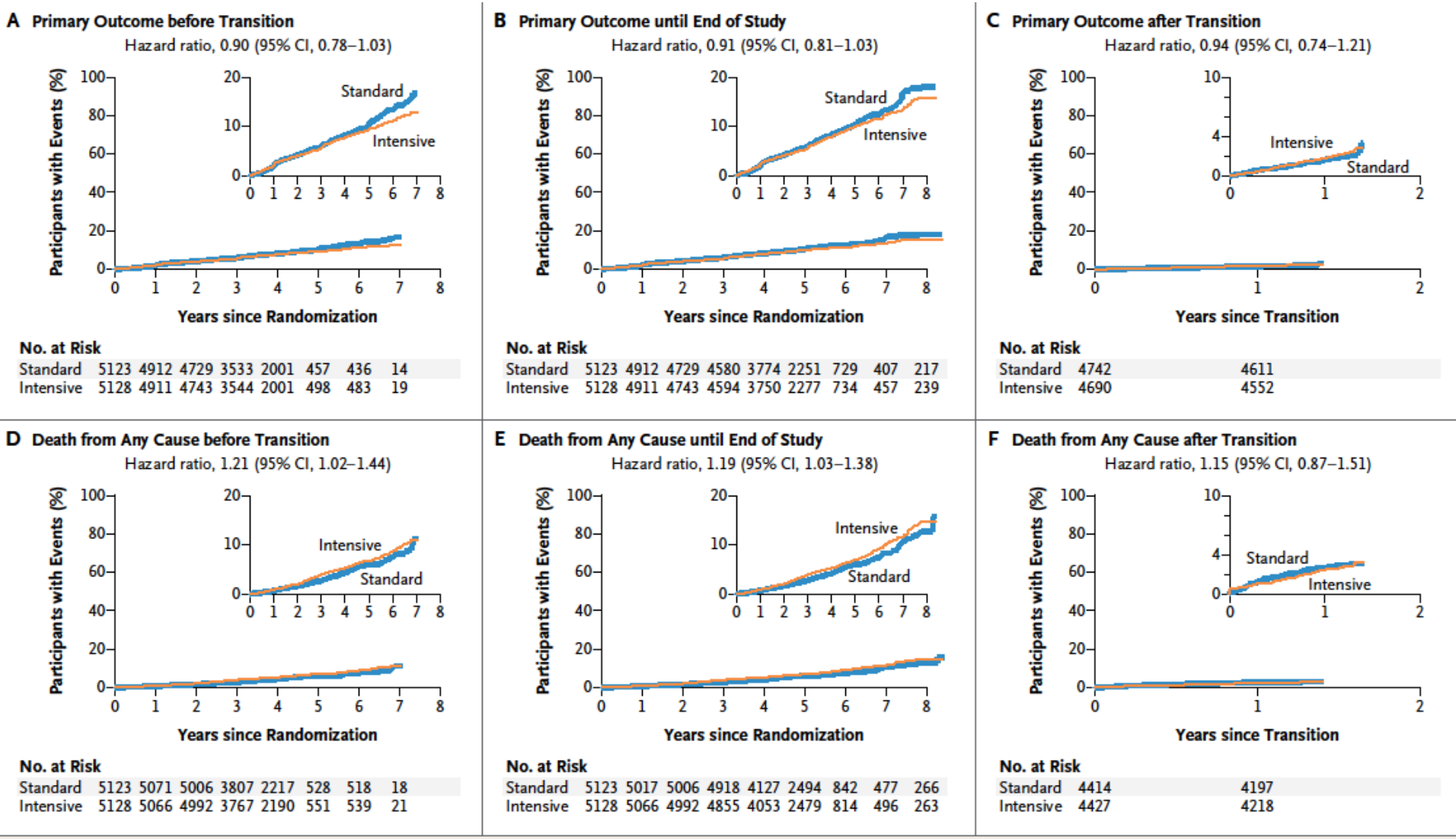


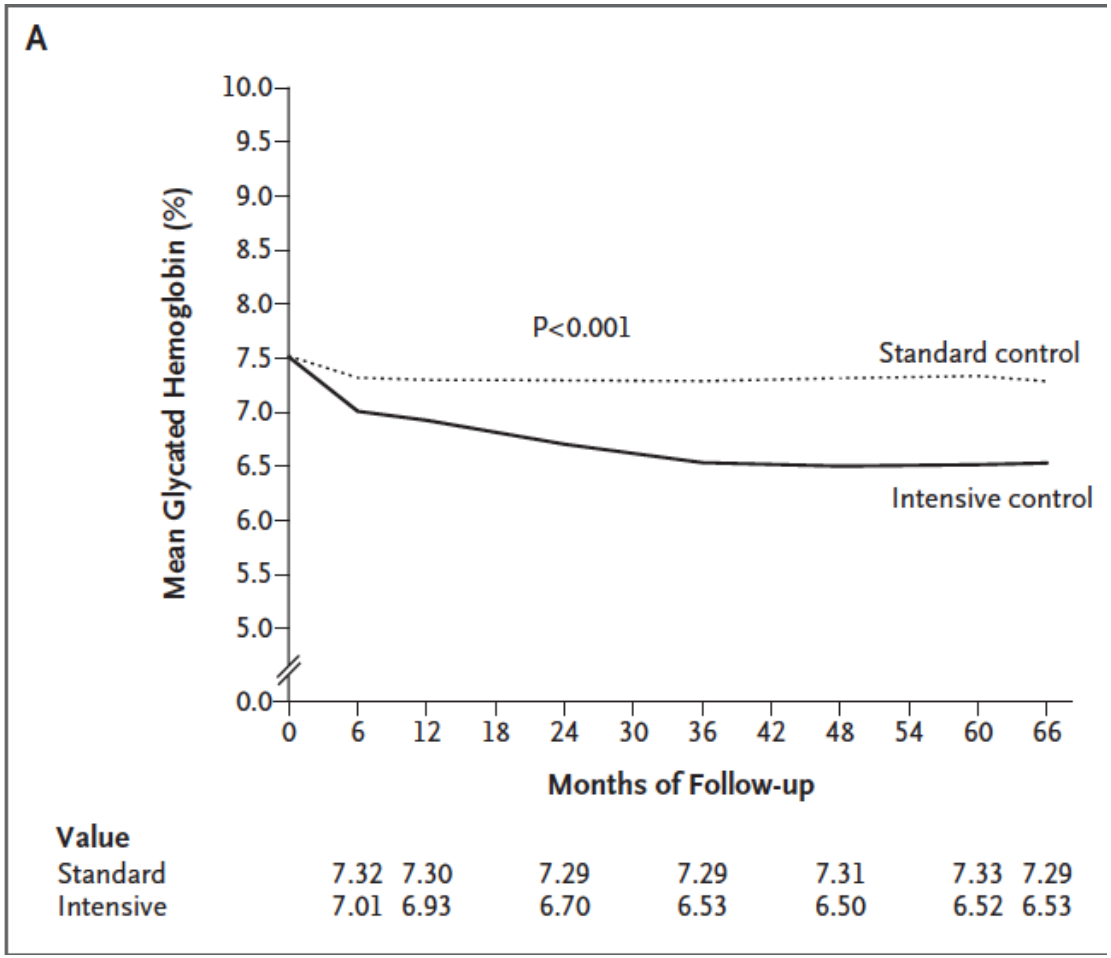
Figure 1. Kaplan–Meier Curves for the Primary Outcome and Death from Any Cause.

The primary outcome was a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. Panels A and D show the incidence rates from randomization until the time of transition, Panels B and E show the rates from randomization until the end of the trial, and Panels C and F show the rates for the post-transition period. Plots for the post-transition period (Panels C and F) are included for descriptive purposes only; they cannot be used to infer any effect of the intensive therapy in this period.

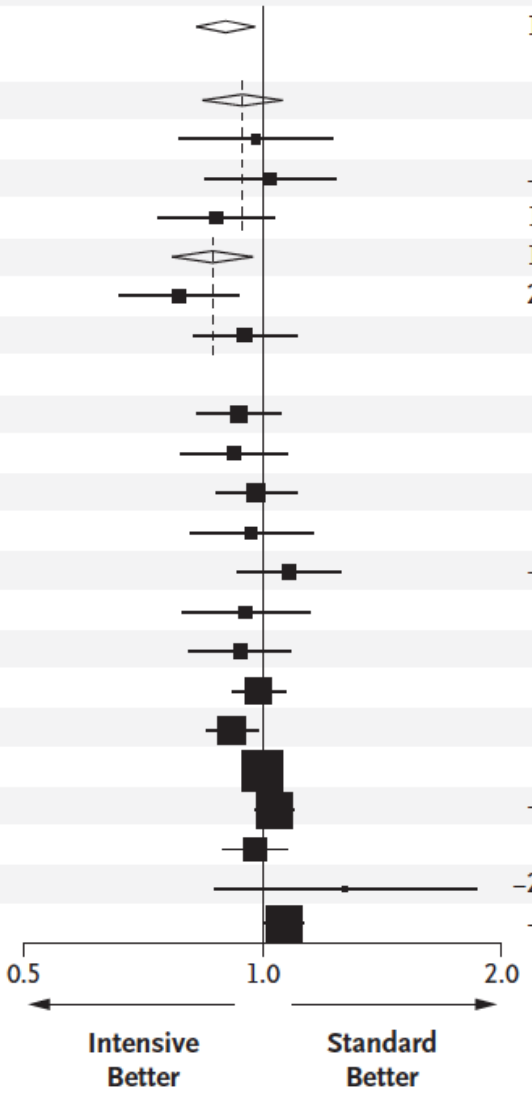
Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

The ADVANCE Collaborative Group*

N Engl J Med 2008;358:2560-72.


A
Mean Glycated Hemoglobin (%)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
0.0
P<0.001
Standard control
Intensive control
0
6
12
18
24
30
36
42
48
54
60
66
Months of Follow-up
Value
Standard 7.32 7.30 7.29 7.29 7.31 7.33 7.29
Intensive 7.01 6.93 6.70 6.53 6.50 6.52 6.53

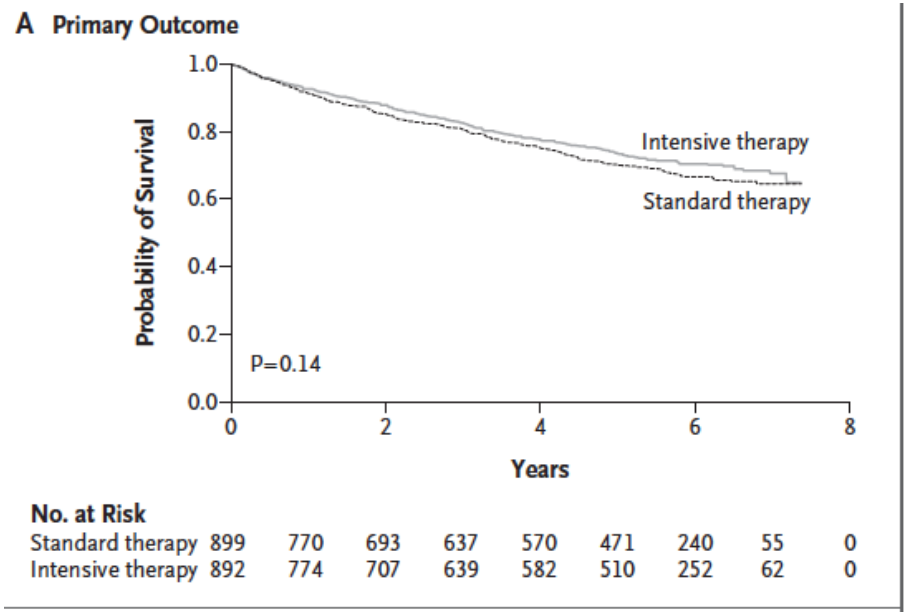
Subgroup	Intensive Control (N=5571)	Standard Control (N=5569)	Hazard Ratio (95% CI)	Relative Risk Reduction (95% CI)
	number of patients (percent)			*percent*
Primary End Points				
Combined major macrovascular and microvascular events	1009 (18.1)	1116 (20.0)		10 (2 to 18)
Major macrovascular events	557 (10.0)	590 (10.6)		6 (–6 to 16)
Nonfatal MI	153 (2.7)	156 (2.8)		2 (–23 to 22)
Nonfatal stroke	214 (3.8)	209 (3.8)		–2 (–24 to 15)
Death from cardiovascular causes	253 (4.5)	289 (5.2)		12 (–4 to 26)
Major microvascular events	526 (9.4)	605 (10.9)		14 (3 to 23)
New or worsening nephropathy	230 (4.1)	292 (5.2)		21 (7 to 34)
New or worsening retinopathy	332 (6.0)	349 (6.3)		5 (–10 to 18)
Secondary End Points				
Death from any cause	498 (8.9)	533 (9.6)		7 (–6 to 17)
Major coronary events	310 (5.6)	337 (6.1)		8 (–7 to 21)
All coronary events	560 (10.1)	572 (10.3)		2 (–10 to 13)
Major cerebrovascular events	238 (4.3)	246 (4.4)		3 (–16 to 19)
All cerebrovascular events	352 (6.3)	327 (5.9)		–8 (–26 to 7)
Heart failure	220 (3.9)	231 (4.1)		5 (–14 to 21)
Peripheral vascular events	343 (6.2)	366 (6.6)		6 (–9 to 19)
All cardiovascular events	1232 (22.1)	1249 (22.4)		1 (–7 to 9)
New-onset microalbuminuria	1318 (23.7)	1434 (25.7)		9 (2 to 5)
Visual deterioration	3033 (54.4)	3015 (54.1)		0 (–5 to 5)
New or worsening neuropathy	2353 (42.2)	2311 (41.5)		–4 (–10 to 2)
Cognitive decline	895 (16.1)	911 (16.4)		2 (–7 to 11)
Dementia	61 (1.1)	48 (0.9)		–27 (–86 to 13)
Hospitalization	2501 (44.9)	2381 (42.8)		–7 (–13 to –1)

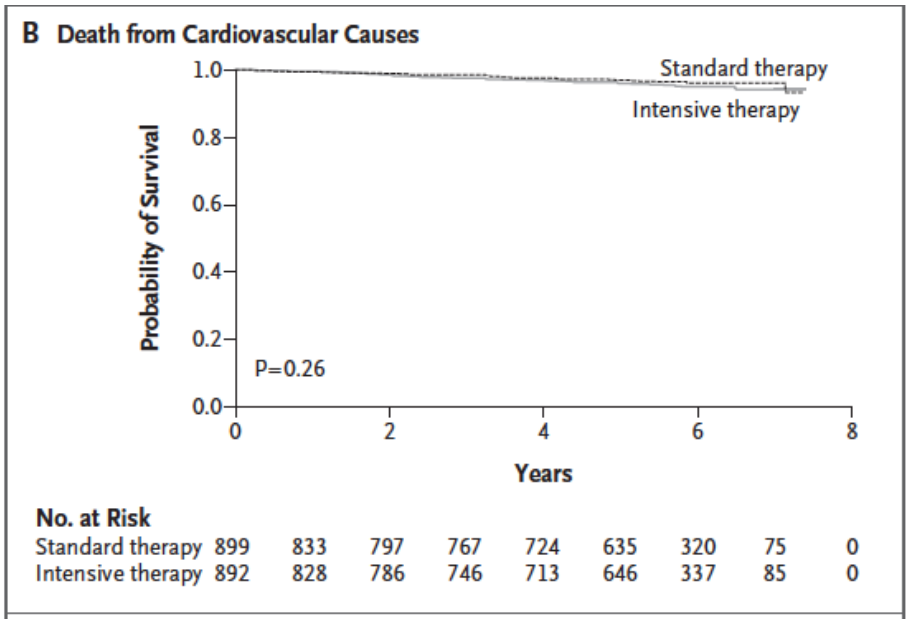


Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

William Duckworth, M.D., Carlos Abraira, M.D., Thomas Moritz, M.S., Domenic Reda, Ph.D., Nicholas Emanuele, M.D., Peter D. Reaven, M.D., Franklin J. Zieve, M.D., Ph.D., Jennifer Marks, M.D., Stephen N. Davis, M.D., Rodney Hayward, M.D., Stuart R. Warren, J.D., Pharm.D., Steven Goldman, M.D., Madeline McCarren, Ph.D., M.P.H., Mary Ellen Vitek, William G. Henderson, Ph.D., and Grant D. Huang, M.P.H., Ph.D., for the VADT Investigators*

N Engl J Med 2009;360:129-39.





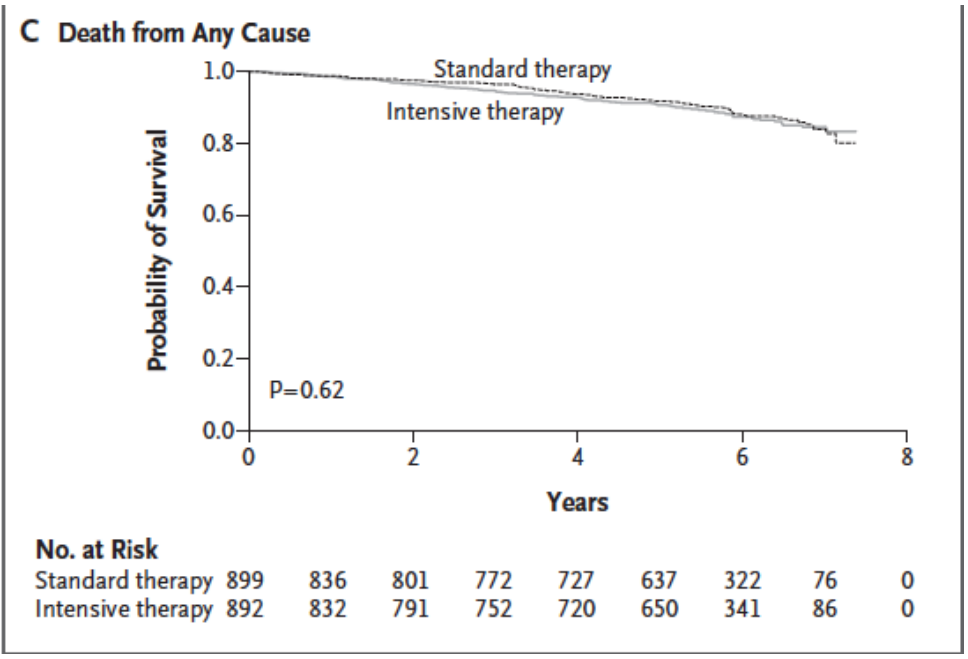


Table 2. Hypoglycemic Episodes.*

Variable	Standard Therapy (N=899)	Intensive Therapy (N=892)
	no./100 patient-yr	
Episodes with impaired consciousness	3	9
Episodes with complete loss of consciousness	1	3
Nocturnal episodes	44	152
Total episodes		
With symptoms	383	1333
Without symptoms	49	233
Relieved by food or sugar intake	421	1516
Measurement of blood glucose during episode	348	1392
With documented blood glucose <50 mg/dl (2.8 mmol/liter)	52	203

* P<0.001 for all differences between the two groups.

CONCLUSION DE LOS ESTUDIOS

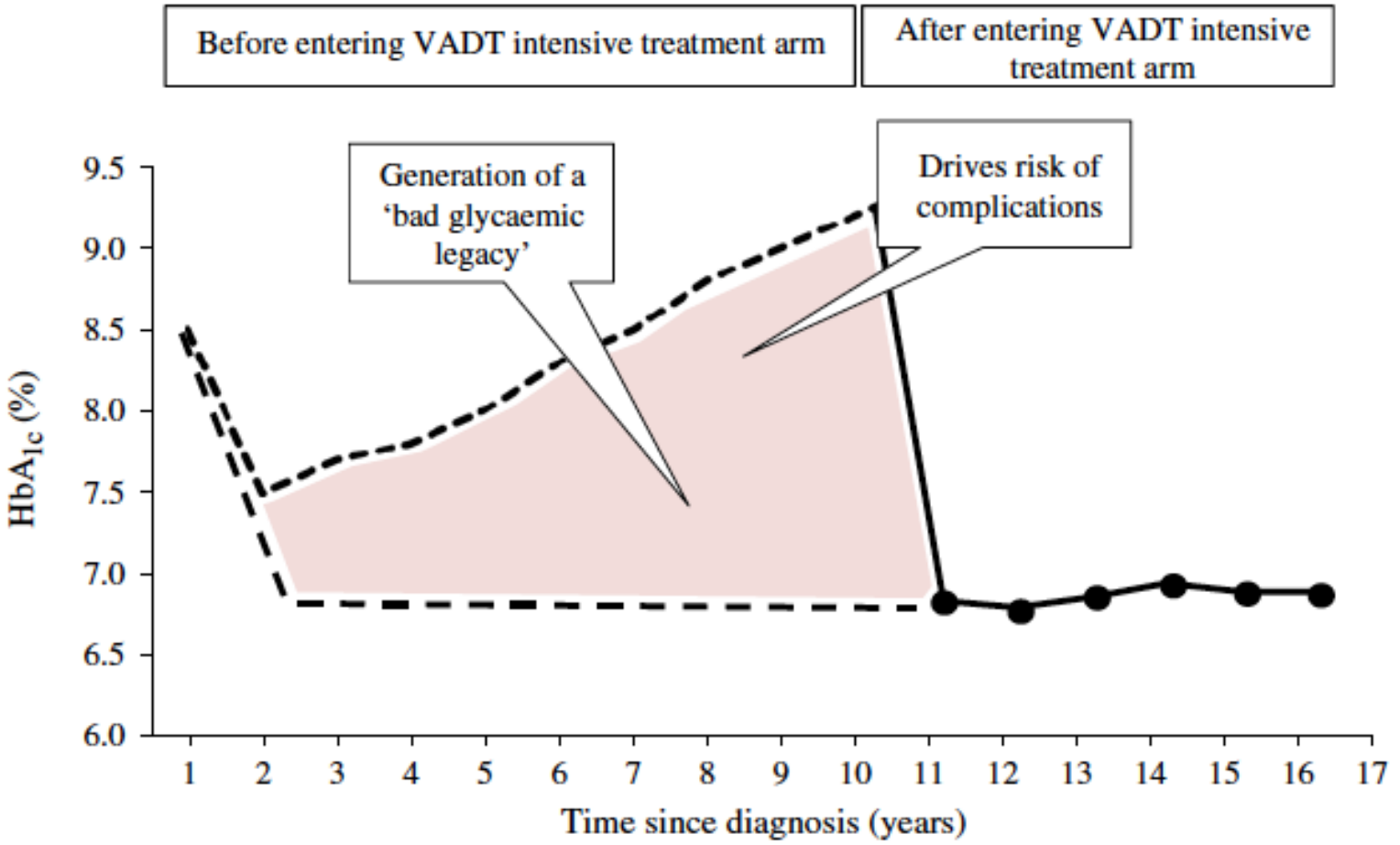
- ACCORD, ADVANCE Y VADT DURACION DE DIABETES DE 8 a 11 AÑOS. ECV O MULTIPLES FACTORES DE RIESGO Y MAS VIEJOS.
- PACIENTES CON ATEROSCLEROSIS ESTABLECIDA
- BENEFICIO MAYOR EN MENOR DURACION DE DIABETES, MENOR HBA1C Y AUSENCIA DE ENF CV PREVIA.
- DCCT/EDIC PX SIN ENF CV 57% REDUCCION DE EV CV.
- UKPDS MEJOR CONTROL DESDE EL DX MENOR IM Y MORTALIDAD

Legado Glucémico

- Control metabólico estricto prolongado en diabetes de recién diagnóstico durante los primeros años de la enfermedad y no en estadios avanzados conduce a efectos benéficos sostenidos respecto a las complicaciones micro y macrovasculares.

N ENGL J MED 359;15 WWW.NEJM.ORG OCTOBER 9, 2008

Legado Glucémico



Diabetologia (2009) 52:1219–1226

Escenarios

1. Paciente 95 años DM2 de nuevo inicio con fragilidad y Demencia.
2. Paciente 80 años DM2 de nuevo inicio funcional y por lo demás sana.
3. Paciente 65 años sin comorbilidades y nuevo inicio de diabetes.
4. Paciente 65 años con 4 comorbilidades y diabetes de 10 años de evolución con complicaciones (nefropatía, amputación de pie derecho y retinopatía) y discapacidad.

Qué tipo de legado induciremos

1. No es recomendable dejarle un buen legado glucémico.
2. Podría valer la pena dejarle un buen legado glucémico.
3. Altamente recomendable dejarle un buen legado glucémico.
4. Ya tiene un mal legado glucémico. Candidata a cuidados paliativos.