1er SEMINAIRE DU LABORATOIRE DE RECHERCHE SUR LE DIABETE
Université Aboubekr Belkaid - Tlemcen
7ème journée du Service de Médecine interne du CHU de Tlemcen et de l'Association de Médecine Interne Universitaire de la Wilaya de Tlemcen (AMIWIT)

Mémoire Métabolique dans le diabète sucré

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Service de Médecine Interne – CHU Tlemcen
Laboratoire de recherche sur le diabète – Université de Tlemcen

Tlemcen, le 29 novembre 2019

Conflits d’intérêts

Aucun

Introduction

Le diabète est un facteur de risque indépendant pour les maladies cardiovasculaires qui restent la 1ère cause de décès des patients.

Son rôle délétère est majoré par la présence concomitante d'autres facteurs de risque CV comme le tabagisme, l'HTA et les dyslipidémies.

Notion de mémoire métabolique

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Antonio Ceriello, Michael A. Ihnat and Jessica E. Thorpe

The "Metabolic Memory": Is More Than Just Tight Glucose Control Necessary to Prevent Diabetic Complications?

« Les études épidémiologiques et prospectives suggèrent l'influence à long terme du contrôle métabolique précoce sur les complications micro et/ou macrovasculaires »

« le concept de mémoire métabolique est celui de stress vasculaire diabétique persistant après la normalisation du glucose »

J Clin. Endocrinol. Metab. 2009 94:410-415

Problématique

Un control intensif du diabète sucré au début du diagnostic améliore t'il le pronostic à long terme ?

« Peut on rattraper le temps perdu ???? »

Grandes études d'interventions

Impact d'une thérapie antidiabétique intensive

Etudes	Microvasc	CVD	Mortalité
UKPDS	↓	↔	↔
DCCT / EDIC*	↓	↔	↔
ACCORD	↓	↔	↑
ADVANCE	↓	↔	↔
VADT	↓	↔	↔

Résultat Initial

Suivi à long terme

* DT1

Post UKPDS

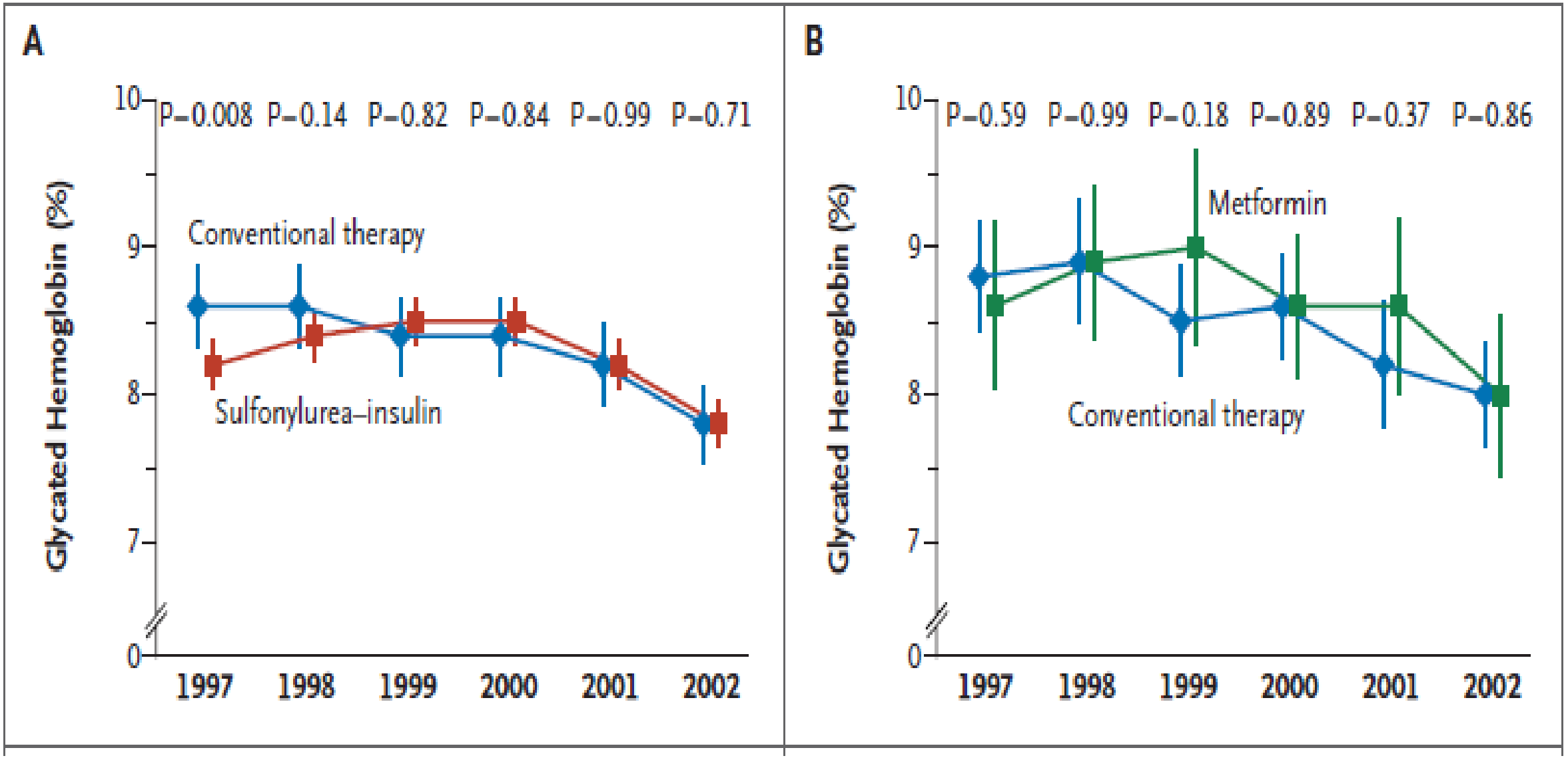
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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.

October 9, 2008
N Engl J Med 2008; 359:1577-1589
DOI: 10.1056/NEJMoa0806470


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

UKPDS: Legacy Effect of Earlier Glucose Control

After median 8.5 years post-trial follow-up

Aggregate Endpoint		1997	2007
Any diabetes related endpoint	*RRR:*	12%	**9%**
	P:	0.029	**0.040**
Microvascular disease	*RRR:*	25%	**24%**
	P:	0.0099	**0.001**
Myocardial infarction	*RRR:*	16%	**15%**
	P:	0.052	**0.014**
All-cause mortality	*RRR:*	6%	**13%**
	P:	0.44	**0.007**

RRR = Relative Risk Reduction, P = Log Rank

N Eng J Med 2008

Post DCCT / EDIC

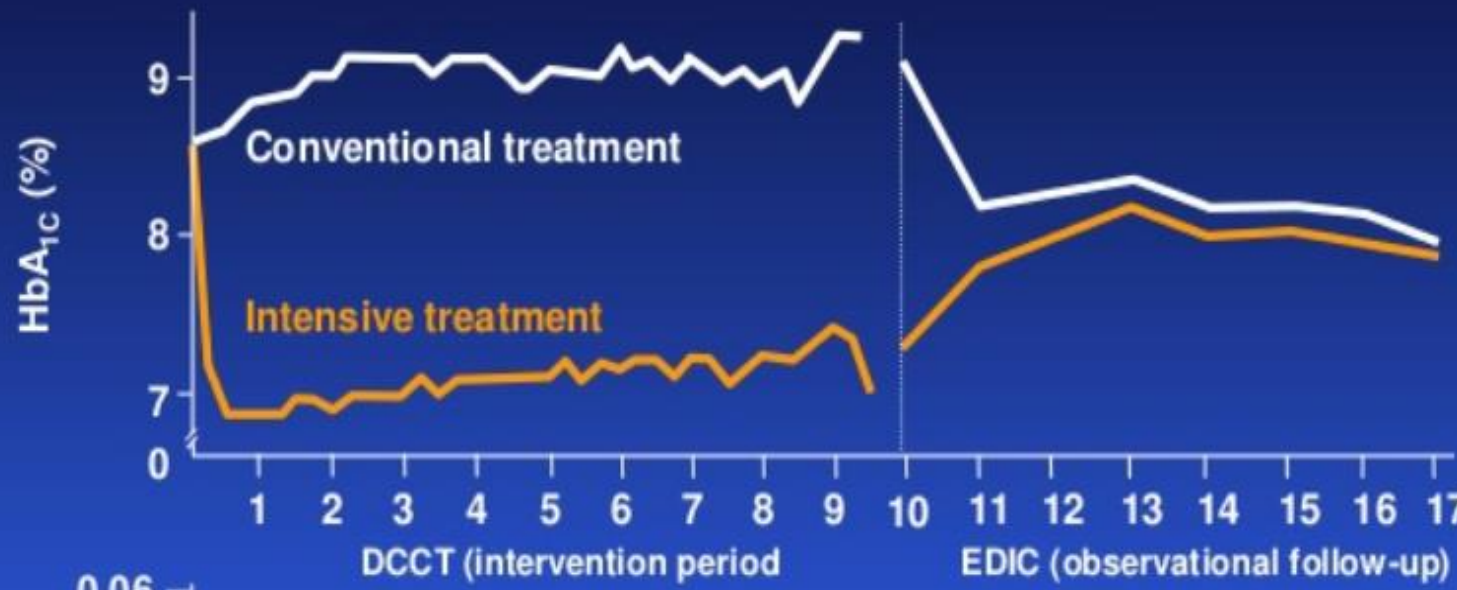
The NEW ENGLAND JOURNAL of MEDICINE

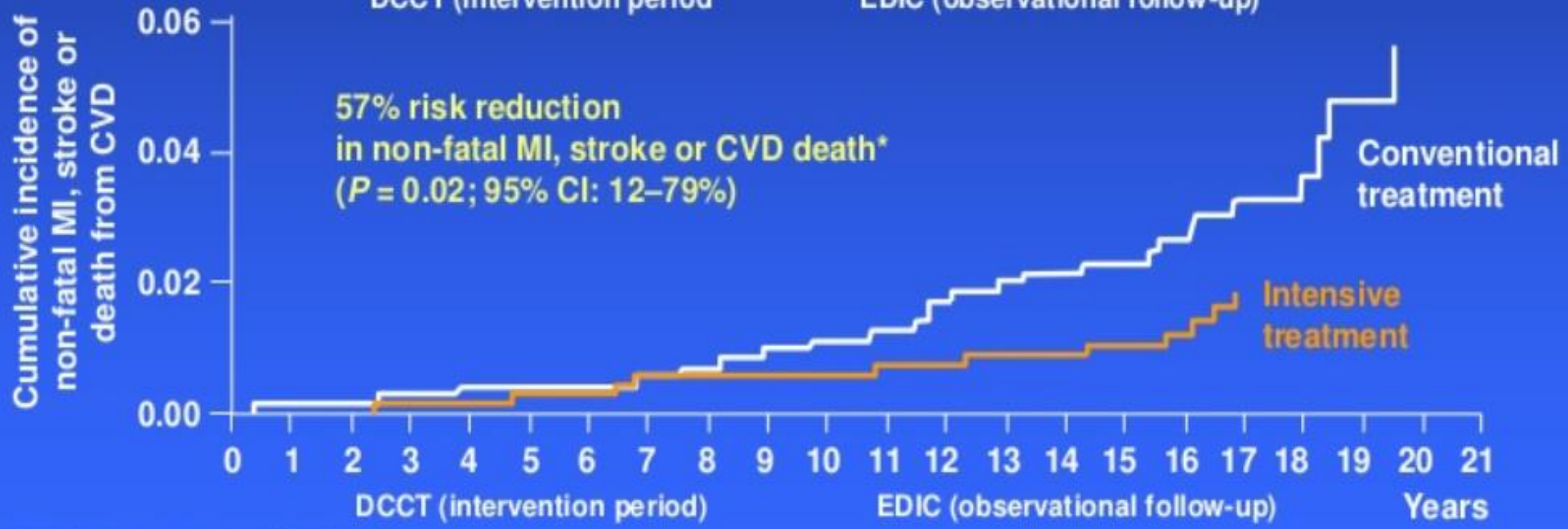
ESTABLISHED IN 1812 DECEMBER 22, 2005 VOL. 353 NO. 25

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: glycaemic control reduces the risk of non-fatal MI, stroke or death from CVD in type 1 diabetes





*Intensive vs conventional treatment

Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes: The DCCT/EDIC Study 30-Year Follow-up

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

Diabetes Care 2016;39:686–693 | DOI: 10.2337/dc15-1990

Après 30 ans de suivi

Résultats maintenues

↓ 30 % des EVC (IDM, AVC ou mort cardiovasculaire) (*P* = 0,016)

↓ 32 % des MACE (*P* = 0,07)

Diabetes Care 2016 Jan; dc152283.
https://doi.org/10.2337/dc15-2283

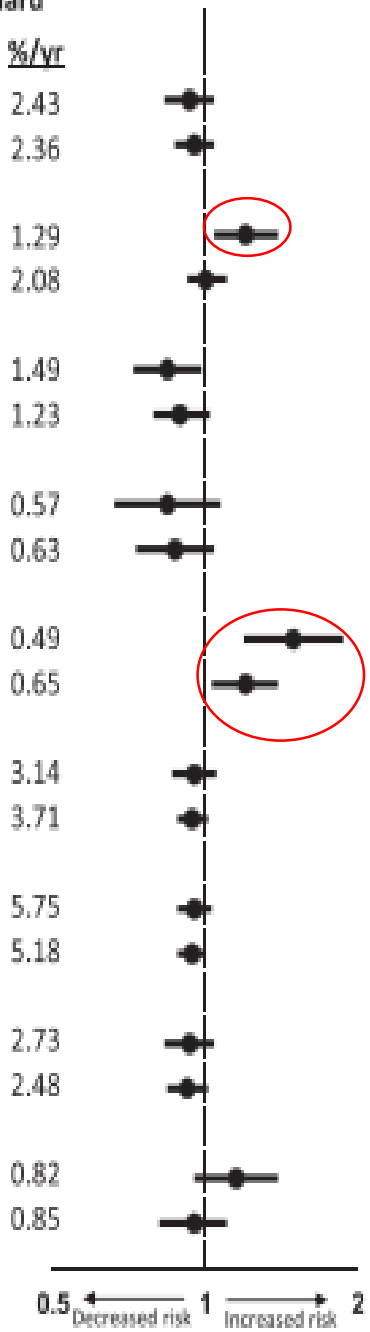
ACCORDION

9-Year Effects of 3.7 Years of Intensive Glycemic Control on Cardiovascular Outcomes

*The ACCORD Study Group Writing Committee**

DOI: 10.2337/dc15-2283

		Intensive		Standard		HR (95%CI)		P
		N	%/yr	N	%/yr			
Primary Outcome	During ACCORD	546	2.26	582	2.43	0.93	(0.83, 1.04)	0.22
	During Full Follow-up	896	2.25	930	2.36	0.95	(0.87, 1.04)	0.27
Death	During ACCORD	391	1.55	327	1.29	1.20	(1.04, 1.39)	0.01
	During Full Follow-up	980	2.09	978	2.08	1.01	(0.92, 1.10)	0.91
Nonfatal MI	During ACCORD	303	1.24	360	1.49	0.84	(0.72, 0.98)	0.02
	During Full Follow-up	444	1.10	492	1.23	0.89	(0.79, 1.02)	0.09
Nonfatal stroke	During ACCORD	119	0.48	142	0.57	0.84	(0.66, 1.07)	0.16
	During Full Follow-up	227	0.55	261	0.63	0.87	(0.73, 1.04)	0.11
Cardiovascular Death	During ACCORD	185	0.73	125	0.49	1.49	(1.19, 1.87)	<0.01
	During Full Follow-up	364	0.78	305	0.65	1.20	(1.03, 1.40)	0.02
Primary or any Death	During ACCORD	722	2.99	753	3.14	0.95	(0.86, 1.05)	0.34
	During Full Follow-up	1407	3.50	1472	3.71	0.94	(0.88, 1.02)	0.12
Primary or Revascularization or Congestive Heart Failure	During ACCORD	1210	5.47	1269	5.75	0.95	(0.88, 1.03)	0.21
	During Full Follow-up	1700	4.84	1792	5.18	0.94	(0.88, 1.00)	0.05
Cardiovascular Death or MI or Unstable Angina	During ACCORD	606	2.54	647	2.73	0.93	(0.83, 1.04)	0.21
	During Full Follow-up	898	2.27	961	2.48	0.92	(0.84, 1.01)	0.08
Congestive Heart Failure Hospitalization	During ACCORD	233	0.83	203	0.82	1.15	(0.95, 1.39)	0.14
	During Full Follow-up	340	0.81	356	0.85	0.95	(0.81, 1.10)	0.45



Advance-On

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes

S. Zoungas, J. Chalmers, B. Neal, L. Billot, Q. Li, Y. Hirakawa, H. Arima, H. Monaghan, R. Joshi, S. Colagiuri, M.E. Cooper, P. Glasziou, D. Grobbee, P. Hamet, S. Harrap, S. Heller, L. Lisheng, G. Mancia, M. Marre, D.R. Matthews, C.E. Mogensen, V. Perkovic, N. Poulter, A. Rodgers, B. Williams, S. MacMahon, A. Patel, and M. Woodward, for the ADVANCE-ON Collaborative Group*

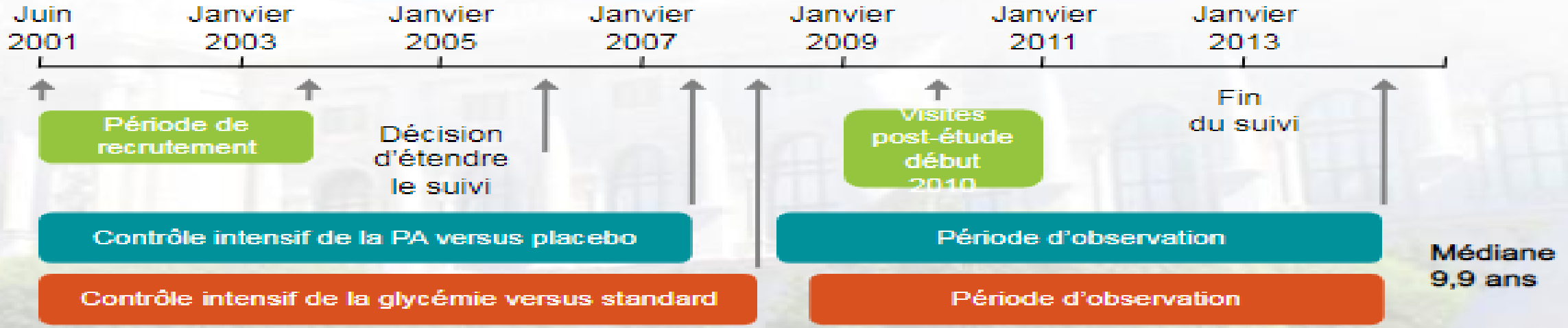
October 9, 2014

N Engl J Med 2014; 371:1392-1406

DOI: 10.1056/NEJMoa1407963

Étude ADVANCE-ON : suivi post essai *(1)*

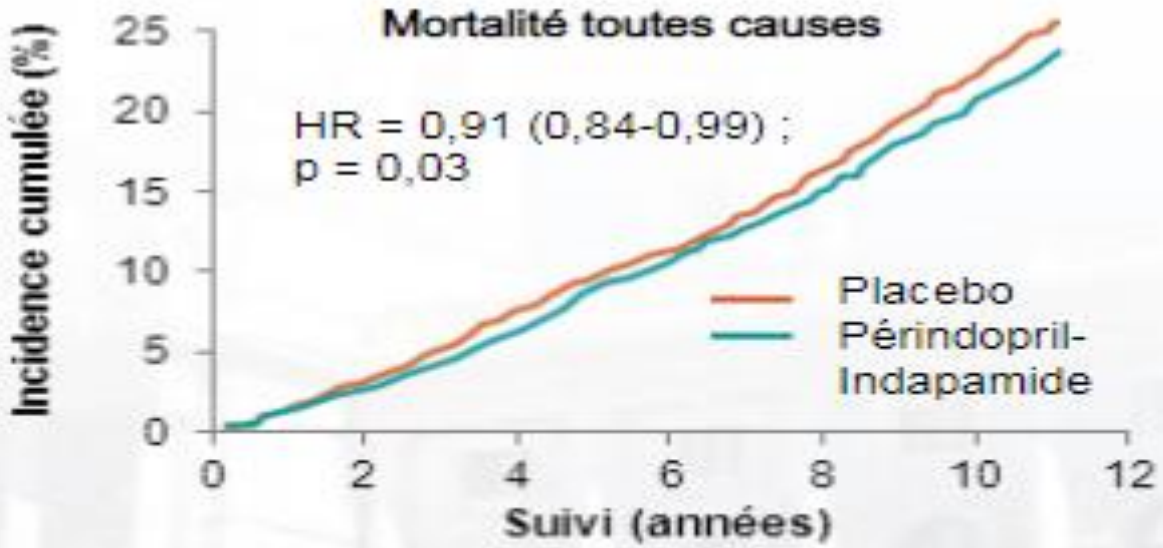
- **L'étude ADVANCE a randomisé 11 140 patients diabétiques de type 2 pour :**
  - Bénéficier d'un traitement intensif sur le contrôle glycémique (objectif d'HbA1c ≤ 6,5 %)
  - Recevoir une association IEC/diurétique périndopril 2 mg/indapamide 0,625 mg pendant 3 mois, puis 4 mg/1,25 mg versus placebo sur une durée supplémentaire de 3 mois (schéma factoriel 2 x 2)
- **Objectif principal :** évaluer le bénéfice de cette stratégie sur les complications
  - Macrovasculaires majeures (IDM, AVC, décès CV)
  - Microvasculaires (néphropathie, rétinopathie diabétique)
- Lancée en janvier 2010, ADVANCE-ON est l'étude observationnelle post-interventionnelle de l'étude ADVANCE. Elle a pour objectif de déterminer les effets à long terme des interventions réalisées lors de l'étude ADVANCE

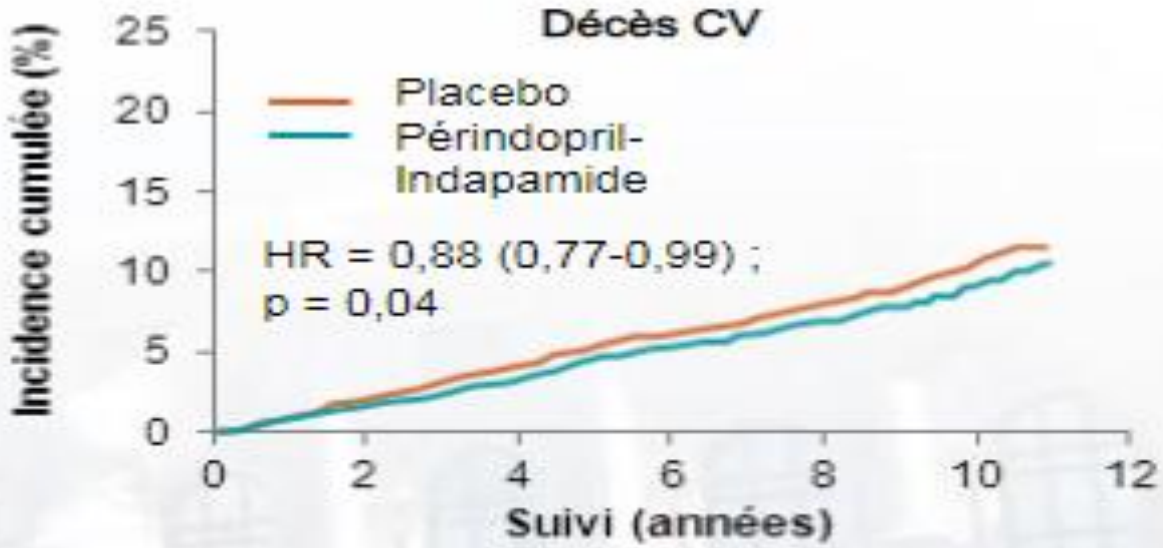


EASD 2014 – D'après Zoungas S, Chalmers J., Hot Topics, actualisé

Étude ADVANCE-ON : suivi post essai *(3)*

- **Effets à long terme de la baisse de la PA**
  - **Persistance des bénéfices à long terme malgré l'arrêt du traitement et l'absence de différence significative en termes de chiffres tensionnels** (PAS/PAD à 137/74 versus 138/75 mm Hg) :
  - mortalité toutes causes - mortalité cardiovasculaire

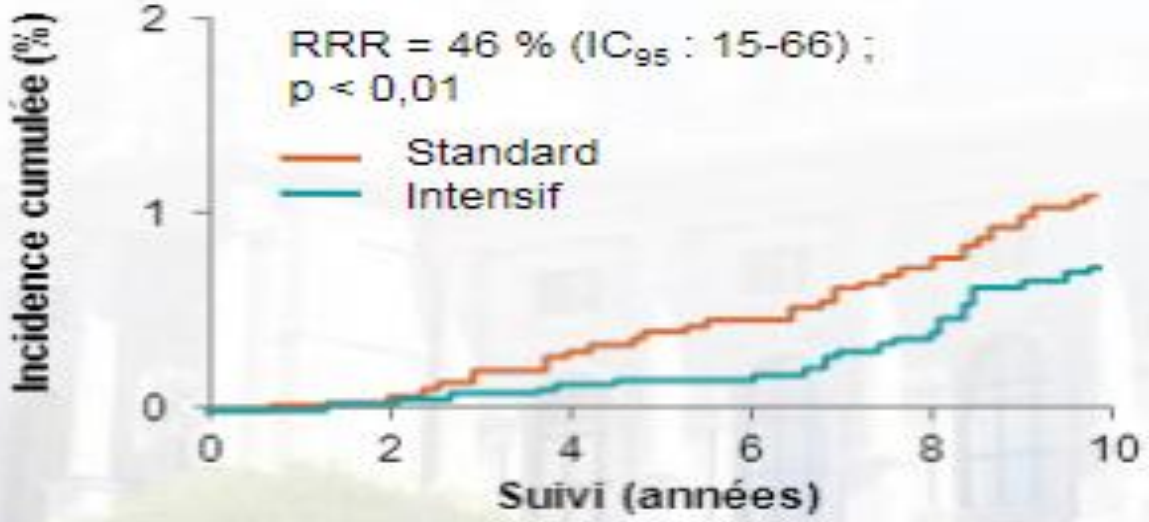




  - non significatif pour les complications cardiovasculaires majeures (HR = 0,92 ; IC 95 % = 0,85-1,00 ; p = 0,06), la survenue d'IDM (HR=0,92; IC 95 % = 0,79-1,06 p=0,24) ou d'AVC (HR=0,94; IC 95 % = 0,83-1,07; p=0,35)

Étude ADVANCE-ON : suivi post essai *(5)*

- **Effets à long terme du contrôle intensif initial de la glycémie**
  - la différence observée en fin d'étude sur l'HbA1c en faveur du bras intensif (- 0,7 %) disparaît dès le début de la période de suivi (7,3 % dans les deux bras)
  - Absence de bénéfice sur :
    - La mortalité toutes causes (HR à 1), CV (HR à 0,97)
    - Les événements macrovasculaires majeurs
    - Les événements microvasculaires cliniques majeurs (HR à 0,97 pour la photocoagulation rétinienne ou la cécité)
  - Réduction significative de la survenue d'insuffisance rénale terminale (IRT)



	ADVANCE (5,0 ans)	ADVANCE -ON (5,4 ans)	Total (9,9 ans)
IRT			
HR (IC_{95})	0,35 (0,15-0,83)	0,65 (0,38-1,11)	0,54 (0,34-0,85)
Nb évts (intensif vs standard	(7 vs 20) -13	(22 vs 33) -11	(29 vs 53) -24

Post VADT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Glucose Control in Patients with Type 2 Diabetes — 15-Year Follow-up

Peter D. Reaven, M.D., Nicholas V. Emanuele, M.D., Wyndy L. Wiitala, Ph.D., Gideon D. Bahn, Ph.D., Domenic J. Reda, Ph.D., Madeline McCarren, Ph.D., William C. Duckworth, M.D., and Rodney A. Hayward, M.D., for the VADT Investigators*

ABSTRACT

n engl j med 380;23 nejm.org June 6, 2019

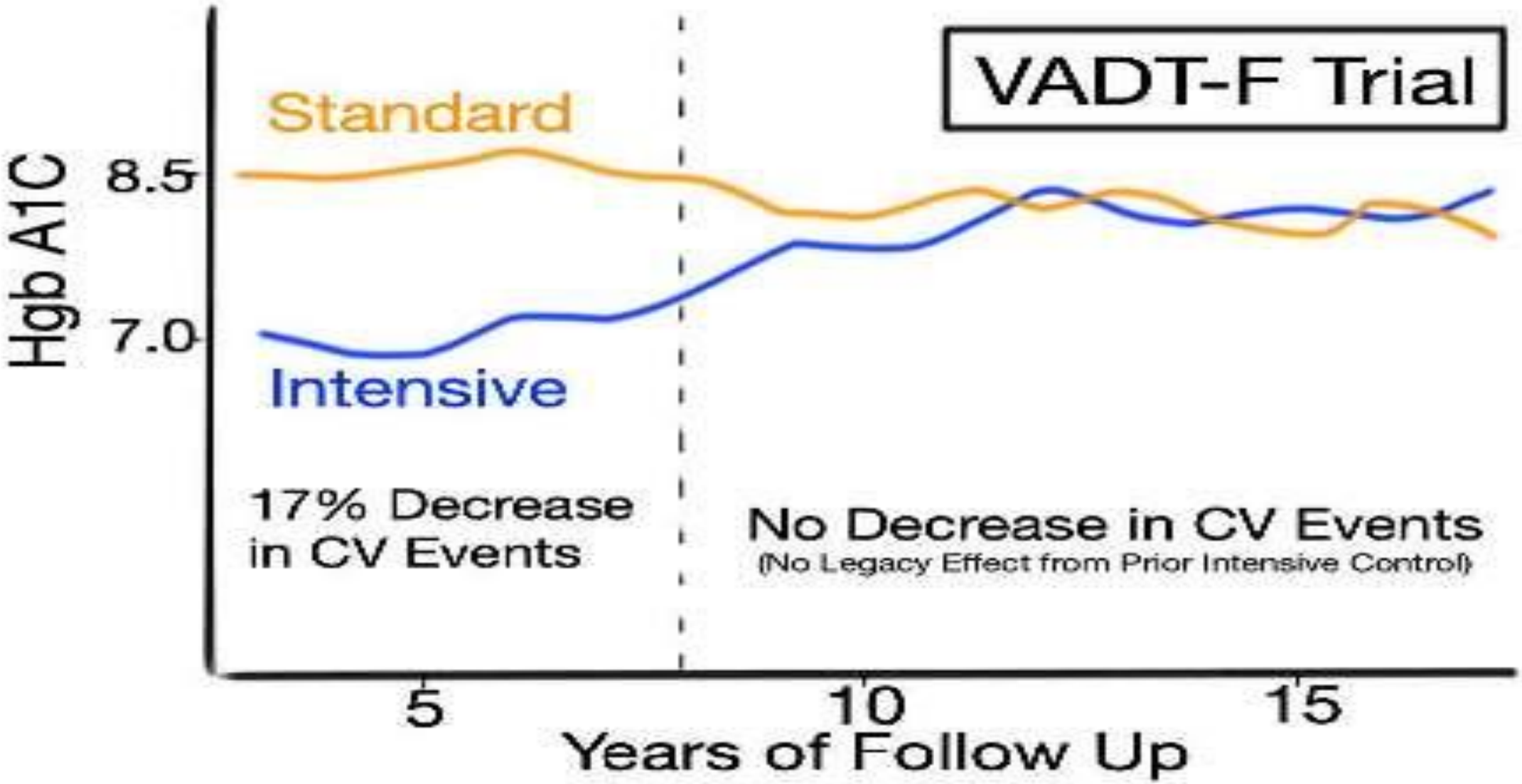

VADT-F Trial
Standard
Intensive
Hgb A1C
8.5
7.0
17% Decrease
in CV Events
No Decrease in CV Events
(No Legacy Effect from Prior Intensive Control)
5
10
15
Years of Follow Up

Table 2. Effect of Intensive Glucose Treatment on Major Cardiovascular Events, Mortality, and Health-Related Quality of Life.*

Outcome	Intensive Therapy	Standard Therapy	Hazard Ratio or Difference (95% CI)	P Value
Primary outcome: major cardiovascular event — no./total no. (rate per 1000 person-yr)	325/703 (47.3)	336/688 (51.8)	0.91 (0.78 to 1.06)	0.23
Secondary outcomes				
Any major diabetes outcome — no./total no. (rate per 1000 person-yr)	342/703 (50.4)	355/688 (55.7)	0.90 (0.78 to 1.04)	
Death from cardiovascular causes — no./total no. (rate per 1000 person-yr)	118/837 (12.3)	125/818 (13.1)	0.94 (0.73 to 1.20)	
Death from any cause — no./total no. (rate per 1000 person-yr)	376/837 (36.6)	366/818 (35.9)	1.02 (0.88 to 1.18)	
Health-related quality-of-life score†	63.8±17.2	62.2±17.6	1.6 (–0.7 to 3.9)	

* The primary outcome was a composite of myocardial infarction, stroke, new or worsening congestive heart failure, amputation for ischemic gangrene, or death from cardiovascular disease causes and was analyzed in the survey cohort. Any major diabetes outcome included the primary composite outcome plus nontraumatic amputations and end-stage renal disease (defined as an estimated GFR of <15 during the original trial period or as an estimated GFR of <15 or dialysis or kidney transplantation during the follow-up study) and, along with health-related quality of life, was analyzed in the survey cohort. Mortality outcomes were analyzed in the complete cohort. All outcomes were pre-specified. The confidence intervals were not adjusted for multiple testing, and inferences drawn from the intervals may not be reproducible.

† Health-related quality of life was assessed on a scale from 0 to 100, with higher scores indicating better quality of life. The difference between the mean values is presented. A difference in the health-related quality-of-life score of 5 points was considered to be clinically meaningful.

Grandes études d'interventions

Impact d'une thérapie antidiabétique intensive

Etudes	Microvasc		CVD		Mortalité	
UKPDS	↓	↓	↔	↓	↔	↓
DCCT / EDIC*	↓	↓	↔	↓	↔	↓
ACCORD	↓		↔	↔	↑	↑
ADVANCE	↓		↔	↔	↔	↔
VADT	↓		↔	↔	↔	↔

Résultat Initial

Suivi à long terme

* DT1

Diabetes care 2012:34;202-34

Meta-analyses of the main trials

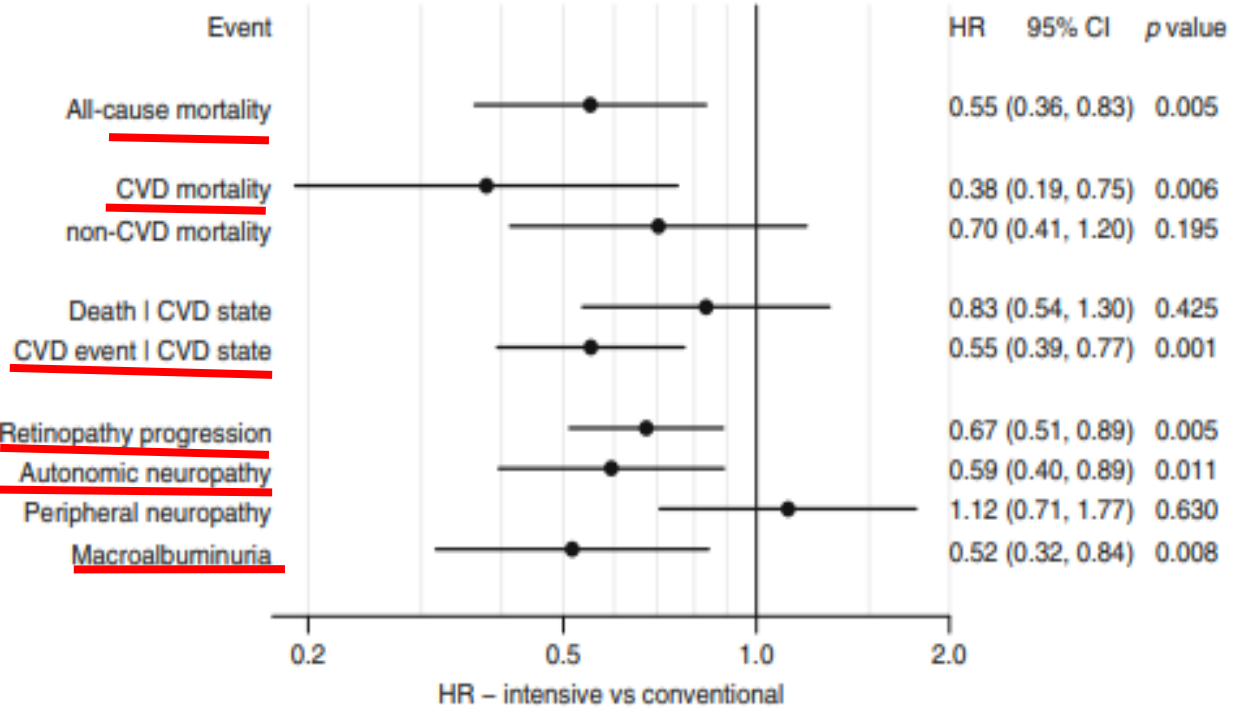
Meta-analysis	Trial	No.	Absolute decreased in HbA1c	Effects of intensive glycemic control		
				MI	Mortality	Hypoglycemia
Ray et al.	UKPDS(33+34 combined) PROactive ACCORD ADVANCE VADT	33,040	0.9%	OR 0.85 (0.77–0.93)	OR 1.02 (0.87–1.19)	NR
Kelly et al.	UKPDS33 UKPDS34 ACCORD ADVANCE VADT	27,802	0.8%	OR 0.89 (0.81–0.96)	OR 0.98 (0.84–1.15)	OR 2.3 (1.46–2.81)
Mannucci et al.	UKPDS(33+34 combined) PROactive ACCORD ADVANCE VADT	32,632	0.9%	OR 0.86 (0.78–0.93)	OR 0.98 (0.77–1.23)	OR 3.01 (1.47–4.60)
Turnbull et al.	UKPDS 33 ACCORD ADVANCE VADT	27,049	0.9%	HR 0.85 (0.76–0.94)	HR 1.04 (0.90–1.20)	HR 2.48 (1.91–3.21)

Diabetologia (2016) 59:2298–2307
DOI 10.1007/s00125-016-4065-6

ARTICLE

Years of life gained by multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial

Peter Gæde[1,2] · Jens Oellgaard[1,2,3] · Bendix Carstensen[3] · Peter Rossing[3,4,5] · Henrik Lund-Andersen[3,5,6] · Hans-Henrik Parving[5,7] · Oluf Pedersen[8]



Traitement des plusieurs facteurs de risque

160 diabétiques type 2 avec microalbuminurie
Age moyen 55 ans

Prise en charge intensive multifactorielle vs conventionelle

The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study)

Neda Laiteerapong,[1] Sandra A. Ham,[2] Yue Gao,[1] Howard H. Moffet,[3] Jennifer Y. Liu,[3] Elbert S. Huang,[1] and Andrew J. Karter[3]

Diabetes Care 2019;42:416–426 | https://doi.org/10.2337/dc17-1144

OBJECTIF : Evaluer l'effet de la **mémoire métabolique** d'un **contrôle glycémique précoce** sur les complications du diabète et le décès.

Matériels et méthodes :

- **Etude de cohorte** portant sur **34 737** de diabétiques type 2 **nouvellement diagnostiqués** entre 1997-2013 avec suivi moyen de **13 ans** et survie minimale **de 10 ans**
- **Age moyen** 56 ans
- **A des niveaux d'HbA1c différents :**
  - ✓ <6,5 %
  - ✓ 6,5 % à <7 %
  - ✓ 7% à <8%
  - ✓ 8% à <9%
  - ✓ ≥ 9,0%
- **Pendant périodes d'exposition** (0–1, 0–2, 0–3, 0–4, 0–5, 0–6 et 0–7 ans)
- **Critères d'évaluation :**
  - ✓ **Complications microvasculaires (IRC terminale, Rétinopathie diabétique avancée, amputation)**
  - ✓ **et macrovasculaires (AVC, cardiopathie / insuffisance vasculaire) et décès**

Limites :

- Durée de diabète plus ancienne
- Les diabétiques à haut risque cardiovasculaire
- Place de l’aspirine

Table 2—Associations among various early HbA_{1c} exposure periods and subsequent outcomes

Early period and mean glycemic control	Microvascular events			Macrovascular events			Death		
	n/total *n*	Adjusted HR (95% CI)	*P* value	*n*/total *n*	Adjusted HR (95% CI)	*P* value	*n*/total *n*	Adjusted HR (95% CI)	*P* value
0–1 year									
HbA_{1c}									
<6.5% (<48 mmol/mol)	864/14,080	Reference		3,668/13,455	Reference		744/14,286	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	372/5,774	1.204 (1.063–1.365)	0.004	1,497/5,552	1.188 (1.116–1.264)	<0.0001	268/5,877	1.137 (0.985–1.313)	0.079
7.0% to <8.0% (53 to <64 mmol/mol)	385/4,656	1.391 (1.226–1.578)	<0.0001	1,244/4,501	1.287 (1.203–1.377)	<0.0001	224/4,730	1.290 (1.104–1.507)	0.001
8.0% to <9.0% (64 to <75 mmol/mol)	154/1,390	1.603 (1.340–1.917)	<0.0001	383/1,351	1.369 (1.227–1.527)	<0.0001	68/1,418	1.262 (0.978–1.628)	0.073
≥9.0% (≥75 mmol/mol)	232/1,259	2.213 (1.892–2.590)	<0.0001	382/1,220	1.485 (1.329–1.659)	<0.0001	66/1,290	1.320 (1.017–1.713)	0.037
Missing	647/7,047	1.354 (1.218–1.505)	<0.0001	1,899/6,867	1.112 (1.050–1.177)	0.0003	437/7,136	1.235 (1.094–1.394)	0.001
0–2 years									
HbA_{1c}									
<6.5% (<48 mmol/mol)	809/14,673	Reference		3,612/13,860	Reference		817/14,940	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	451/7,517	1.259 (1.117–1.419)	0.0002	1,866/7,143	1.158 (1.093–1.228)	<0.0001	368/7,675	1.093 (0.962–1.241)	0.172
7.0% to <8.0% (53 to <64 mmol/mol)	544/7,144	1.497 (1.331–1.684)	<0.0001	1,788/6,842	1.264 (1.189–1.344)	<0.0001	368/7,295	1.240 (1.088–1.414)	0.001
8.0% to <9.0% (64 to <75 mmol/mol)	258/2,529	1.700 (1.460–1.980)	<0.0001	620/2,426	1.279 (1.168–1.401)	<0.0001	128/2,592	1.274 (1.047–1.551)	0.016
≥9.0% (≥75 mmol/mol)	408/2,159	2.756 (2.396–3.170)	<0.0001	624/2,112	1.539 (1.400–1.692)	<0.0001	126/2,235	1.528 (1.245–1.876)	<0.0001
0–3 years									
HbA_{1c}									
<6.5% (<48 mmol/mol)	619/12,475	Reference		2,931/11,635	Reference		717/12,769	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	412/7,883	1.194 (1.049–1.359)	0.007	1,818/7,347	1.126 (1.059–1.197)	0.0001	375/8,057	0.975 (0.856–1.109)	0.696
7.0% to <8.0% (53 to <64 mmol/mol)	551/8,310	1.453 (1.281–1.648)	<0.0001	1,931/7,873	1.208 (1.134–1.286)	<0.0001	433/8,541	1.189 (1.044–1.353)	0.009
8.0% to <9.0% (64 to <75 mmol/mol)	293/3,081	1.835 (1.571–2.145)	<0.0001	732/2,952	1.329 (1.216–1.453)	<0.0001	162/3,188	1.376 (1.145–1.654)	0.001
≥9.0% (≥75 mmol/mol)	406/2,084	3.193 (2.738–3.723)	<0.0001	563/2,041	1.471 (1.327–1.631)	<0.0001	120/2,182	1.503 (1.211–1.865)	0.0002
0–4 years									
HbA_{1c}									
<6.5% (<48 mmol/mol)	493/10,627	Reference		2,322/9,692	Reference		621/10,898	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	401/8,097	1.252 (1.091–1.436)	0.001	1,719/7,410	1.100 (1.031–1.174)	0.004	399/8,302	1.013 (0.889–1.155)	0.842
7.0% to <8.0% (53 to <64 mmol/mol)	542/9,306	1.461 (1.277–1.673)	<0.0001	2,019/8,710	1.224 (1.145–1.308)	<0.0001	482/9,608	1.224 (1.074–1.395)	0.002
8.0% to <9.0% (64 to <75 mmol/mol)	312/3,567	1.894 (1.608–2.231)	<0.0001	770/3,352	1.299 (1.185–1.425)	<0.0001	187/3,697	1.453 (1.211–1.742)	<0.0001
≥9.0% (≥75 mmol/mol)	412/2,115	3.687 (3.123–4.352)	<0.0001	534/2,073	1.535 (1.374–1.714)	<0.0001	118/2,232	1.676 (1.337–2.100)	<0.0001
0–5 years									
HbA_{1c}									
<6.5% (<48 mmol/mol)	399/9,209	Reference		1,862/8,226	Reference		552/9,475	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	377/8,244	1.263 (1.091–1.462)	0.002	1,596/7,389	1.102 (1.027–1.182)	0.007	423/8,465	1.070 (0.937–1.221)	0.318
7.0% to <8.0% (53 to <64 mmol/mol)	519/10,118	1.441 (1.246–1.666)	<0.0001	2,038/9,315	1.259 (1.173–1.352)	<0.0001	518/10,500	1.238 (1.083–1.415)	0.002
8.0% to <9.0% (64 to <75 mmol/mol)	331/3,841	2.111 (1.779–2.506)	<0.0001	727/3,556	1.269 (1.150–1.400)	<0.0001	200/3,984	1.554 (1.294–1.867)	<0.0001
≥9.0% (≥75 mmol/mol)	418/2,184	4.094 (3.427–4.893)	<0.0001	524/2,134	1.596 (1.420–1.794)	<0.0001	114/2,313	1.747 (1.382–2.208)	<0.0001
0–6 years									
HbA_{1c}									
<6.5% (<48 mmol/mol)	343/8,192	Reference		1,524/7,122	Reference		505/8,463	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	319/8,328	1.137 (0.970–1.333)	0.112	1,433/7,362	1.074 (0.996–1.159)	0.064	432/8,580	1.097 (0.959–1.255)	0.177
7.0% to <8.0% (53 to <64 mmol/mol)	523/10,696	1.543 (1.324–1.797)	<0.0001	1,967/9,671	1.299 (1.204–1.402)	<0.0001	547/11,120	1.278 (1.116–1.464)	0.0004
8.0% to <9.0% (64 to <75 mmol/mol)	322/4,034	2.252 (1.879–2.700)	<0.0001	713/3,683	1.368 (1.233–1.517)	<0.0001	207/4,199	1.561 (1.296–1.880)	<0.0001
≥9.0% (≥75 mmol/mol)	424/2,233	4.869 (4.030–5.882)	<0.0001	486/2,158	1.734 (1.530–1.964)	<0.0001	116/2,375	1.932 (1.523–2.451)	<0.0001
0–7 years									
HbA_{1c}									
<6.5% (<48 mmol/mol)	272/7,372	Reference		1,222/6,245	Reference		476/7,660	Reference	
6.5% to <7.0% (48 to <53 mmol/mol)	295/8,371	1.194 (1.006–1.418)	0.043	1,320/7,226	1.135 (1.046–1.232)	0.002	441/8,654	1.076 (0.938–1.233)	0.295
7.0% to <8.0% (53 to <64 mmol/mol)	481/11,178	1.606 (1.359–1.899)	<0.0001	1,783/9,959	1.327 (1.221–1.442)	<0.0001	562/11,672	1.269 (1.106–1.457)	0.001
8.0% to <9.0% (64 to <75 mmol/mol)	310/4,202	2.580 (2.123–3.135)	<0.0001	689/3,797	1.577 (1.412–1.760)	<0.0001	213/4,389	1.661 (1.378–2.003)	<0.0001
≥9.0% (≥75 mmol/mol)	414/2,201	6.437 (5.246–7.899)	<0.0001	447/2,107	2.113 (1.847–2.417)	<0.0001	115/2,362	2.181 (1.713–2.778)	<0.0001

All models adjusted for year of diagnosis, age at diagnosis, sex, race/ethnicity, BMI, systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, smoking status, HbA_{1c} after each early period, and comorbidity

≥6,5%

≥6,5%

>7%

Conclusion de l'étude :

Parmi les diabétiques type 2 nouvellement diagnostiqué et ayant au moins 10 ans de survie, et **après une année du diagnostic**

- Une **HbA1c ≥ 6,5%** est associée à une **augmentation des complications microvasculaires** et **macrovasculaires**
- Une **HbA1c > 7%** est associée à une augmentation de la **mortalité**

Un traitement intensif immédiat pour les patients nouvellement diagnostiqués peut être nécessaire pour éviter les complications ultérieures.

Mécanismes

Lésions tissulaires sont liées aux **produits de glycation avancée :**

- Issues de la fixation d'un sucre sur une protéine, un acide aminé ou un lipide.
- La production est accélérée par l'hyperglycémie chronique
- Persistent à long terme
- Favorisent l'athérosclérose

L'hyperglycémie favorise le **stress oxydant** et **l'inflammation** entrainant des dysfonctions endothéliales vasculaires

Conclusion

L’effet bénéfique de l’équilibre glycémique sur les complications macroangiopathiques ne se manifeste qu’à long terme, contrairement à ce qui se passe pour les microangiopathies.

Un **control intensif** du **diabète sucré au diagnostic** particulièrement **les 1$^{\text{ères}}$ années** réduit à long terme **les évènements et la mortalité cardiovasculaires.**

Merci de votre attention