대한당뇨병학회 진료지침위원회
KDA 2015 guidelines: a preview

대한당뇨병학회 2015 가이드라인:
혈당조절목표와 방법

김 대 중

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대한당뇨병학회 진료지침위원회 위원

대한당뇨병학회
Korean Diabetes Association

성인에서 혈당조절의 목표(1)

- 미세혈관합병증 및 대혈관합병증의 발생 위험을 감소시키기 위해 적극적인 혈당조절이 필요하다. [A]
- 혈당조절의 목표는 **당화혈색소 6.5% 미만**으로 한다. [B]
- **초기 당뇨병**이면서 동반된 합병증이 없고 저혈당 발생이 적은 경우는 당화혈색소 목표를 **더 낮출 수** 있다. [E]

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성인에서 혈당조절의 목표(2)

- 중증 저혈당의 병력, 짧은 기대여명, 진행된 미세혈관 및 대혈관합병증, **75세 이상 노인**에서는 **저혈당의 발생 위험**을 고려하여 혈당조절 목표를 개별화 할 수 있다. [B]
- 자가혈당 측정시 목표는 **공복혈당 80-130, 식후 180mg/dL 미만**으로 한다.[E]
- **제1형당뇨병** 환자의 경우 혈당조절 목표를 **7.0% 미만**으로 한다. [A]

혈당조절의 모니터링 및 평가(1)

- **당화혈색소 측정**

1. 당화혈색소는 **3개월 마다** 측정하나 환자의 상태에 따라 시행 주기를 결정할 수 있다. 적어도 **매년 2회 이상** 시행하는 것이 필요하다.[E]

2. 혈당 변화가 심할 때, 약제를 변경했을 때, 그리고 좀더 철저한 조절이 필요할 때 (예로 임신시) 더 자주 당화혈색소를 측정할 수 있다.[E]

혈당조절의 모니터링 및 평가(2)

- **자가혈당 측정**

1. 자가혈당 측정기 사용에 앞서 **환자교육**이 선행되어야 하며, 매년 기기의 사용방법이나 정확도에 대한 점검이 필요하다. [E]
2. **제1형 당뇨병이나 인슐린을 사용중인 제2형 당뇨병환자**에서 자가혈당 측정을 권고한다. [A]
3. **비인슐린 치료**를 하는 제2형 당뇨병환자에서 자가혈당 측정은 혈당조절에 도움이 될 수 있다. [E]
4. 자가혈당 측정은 매 식사 전후, 취침전, 새벽, 운동 전후, 저혈당 유발시 등 다양하게 할 수 있으며, 환자의 상태에 따라 측정 시기나 횟수는 다르게 할 수 있다. [E]

혈당조절의 모니터링 및 평가(3)

- **지속적 혈당 측정 (CGMS)**

1. 다회인슐린요법이나 인슐린펌프 치료를 하는 제1형당뇨병 환자에서 지속적 혈당측정기기 사용은 혈당조절에 도움이 된다. [A]
2. **혈당의 변동폭이 크거나 저혈당이 빈번한 경우에** 혈당조절을 감시하는 방법으로 지속적 혈당 측정기기를 사용할 수 있다. [E]

당화혈색소의 목표

6.5%

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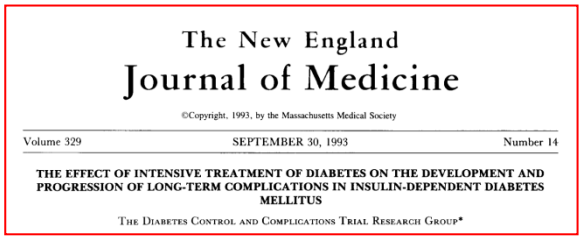
국제적인 가이드라인 비교

기관	당화혈색소 목표치
미국당뇨병학회 (ADA) 2015	<7.0%
미국임상내분비협회 (AACE) 2015	≤6.5%
세계당뇨병연맹 (IDF) 2014	<7.0%
일본당뇨병학회 (JDS)	<7.0%
캐나다당뇨병학회 (CDA) 2013	≤7.0%
영국당뇨병학회 (NICE, UK)	<6.5%

IDF 2014; Recent studies have failed to provide conclusive results in favour of tight versus standard glycaemic control and adding additional glucose-lowering therapy **below 7.0% is of limited efficacy and consequently cost-ineffective**.

제1형당뇨병: DCCT


The New England
Journal of Medicine

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Volume 329 SEPTEMBER 30, 1993 Number 14

THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

The Diabetes Control and Complications Trial Research Group*

- Type 1 diabetes
- N=1441
- F/U: 6.5yrs
- ΔHbA1C=1.9%
- Exponential relationship with HbA1C
- No threshold

- Compared to conventional therapy, **intensive therapy** reduced the incidence of
- Retinopathy: 63%
- Nephropathy: 39%
- Neuropathy: 60%

New Engl J Med. 1993;219:977-986

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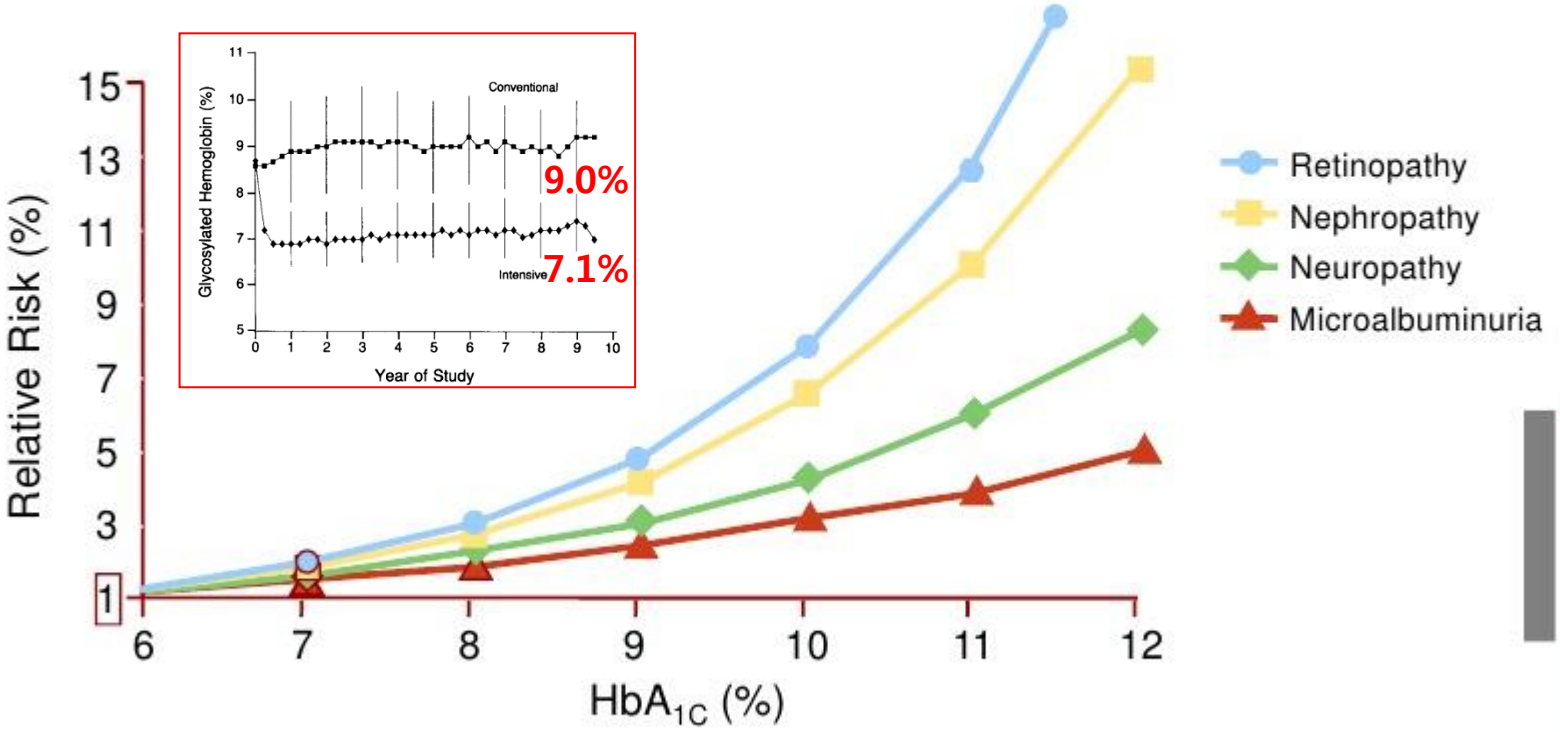
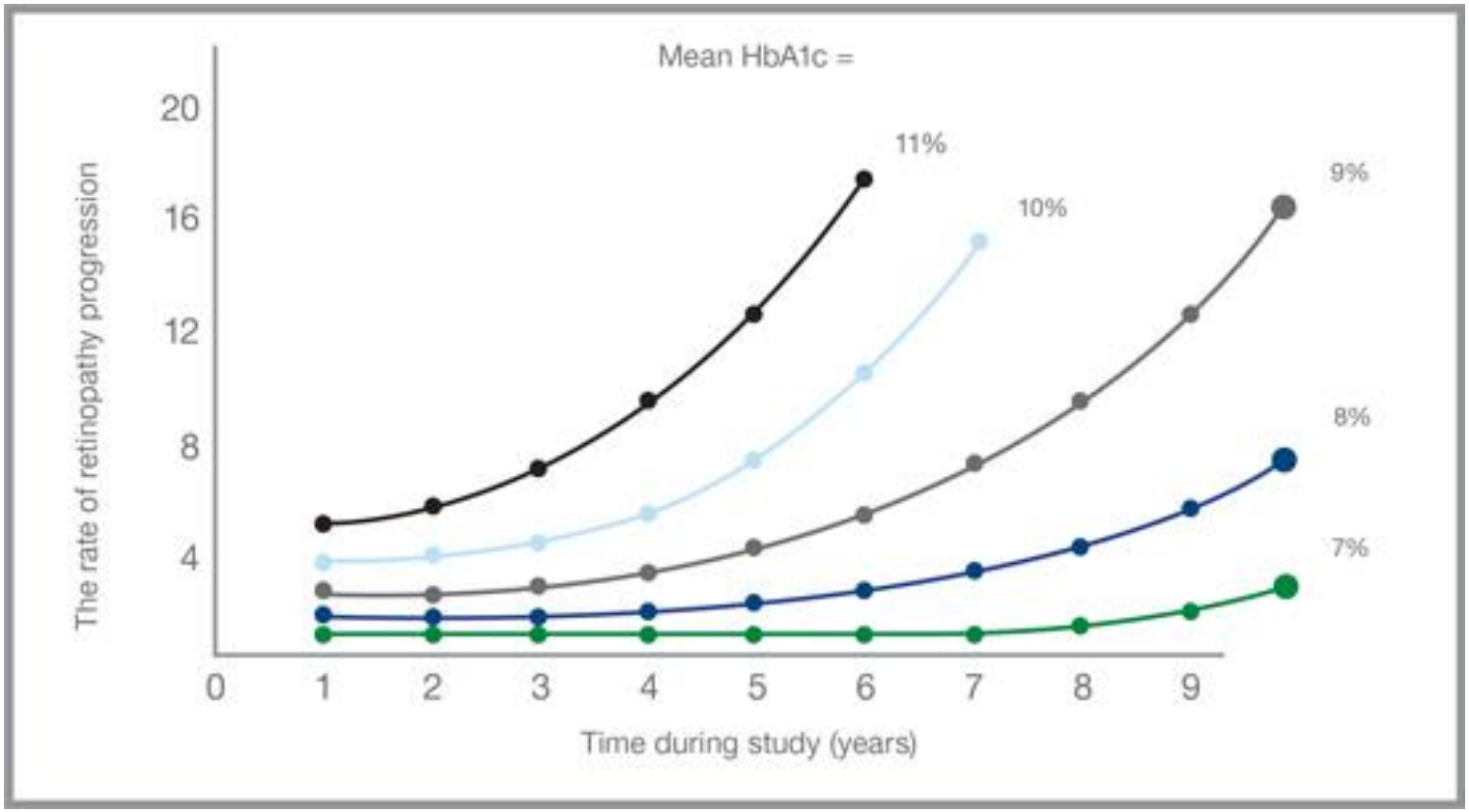
Relationship of HbA_{1C} to Risk of Microvascular Complications

Diabetes Control and Complications Trial (DCCT)



Skyler JS. Endocrinol Metab Clin North Am. 1996;25:243-254.

제1형당뇨병의 혈당조절 목표



Diabetes, 44: 968-983, 1995

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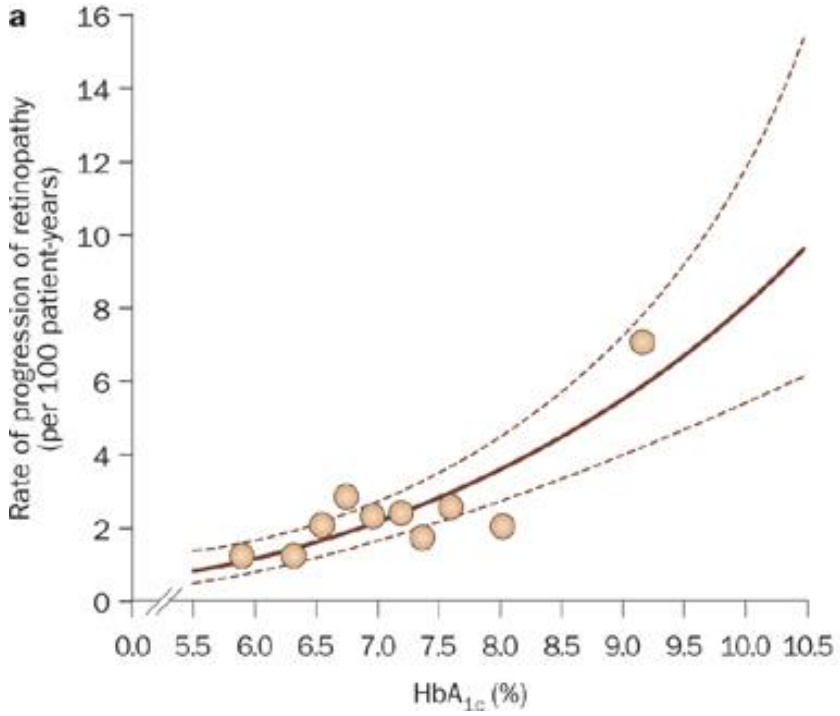
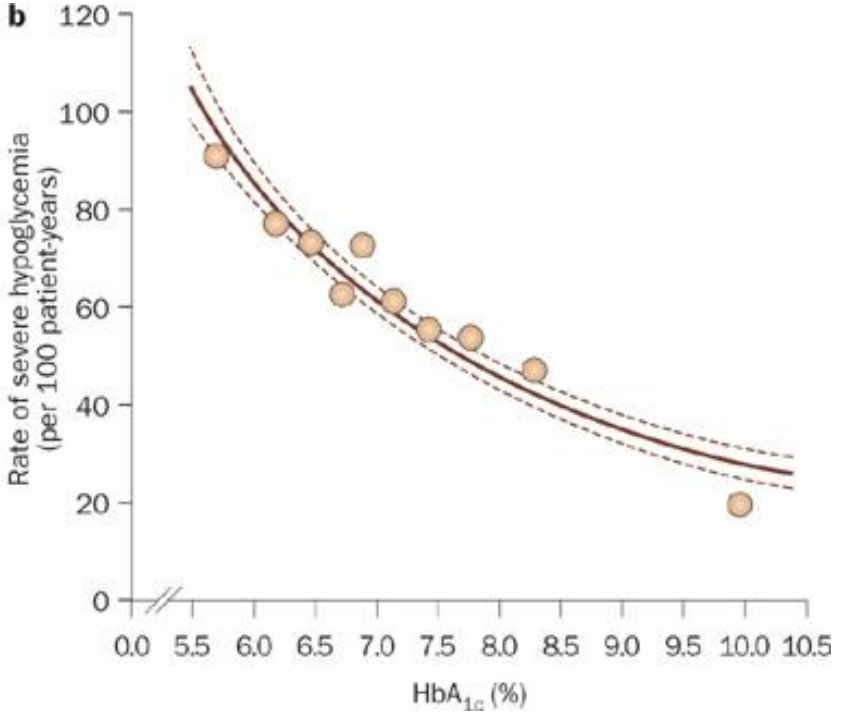
HbA_{1c} level and risk of retinopathy or hypoglycemia





New Engl J Med. 1993;219:977-986

제1형당뇨병: 당화혈색소의 목표

7.0%

제2형당뇨병의 혈당조절연구

연구	대조군	치료군	미세혈관 합병증	대혈관 합병증
UKPDS	7.9%	**7.0%**	Yes (37%↓)	Yes (14%↓)
Kumamoto	9.4%	**7.1%**	Yes	NA
ACCORD	7.5%	**6.4%**	NA (EYE?)	CV death↑ MI ↓
ADVANCE	7.3%	**6.5%**	Yes (nephro 21%↓)	No benefit
VADT	8.4%	**6.9%**	No	No benefit

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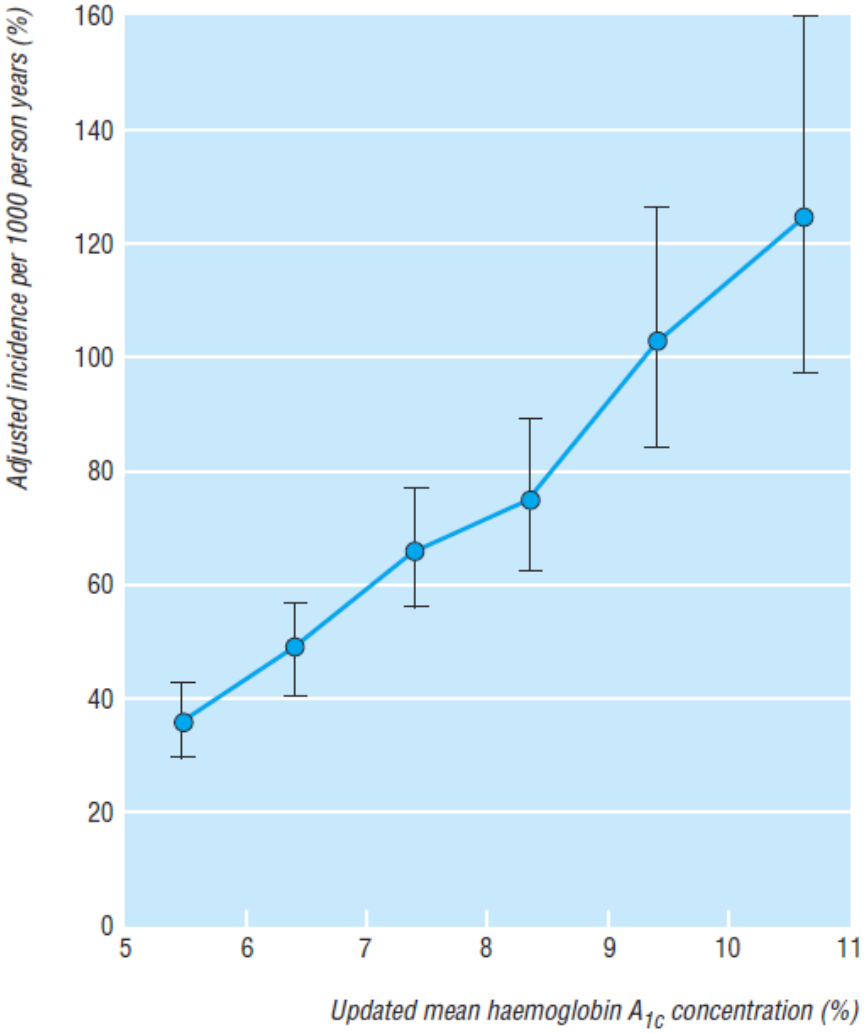
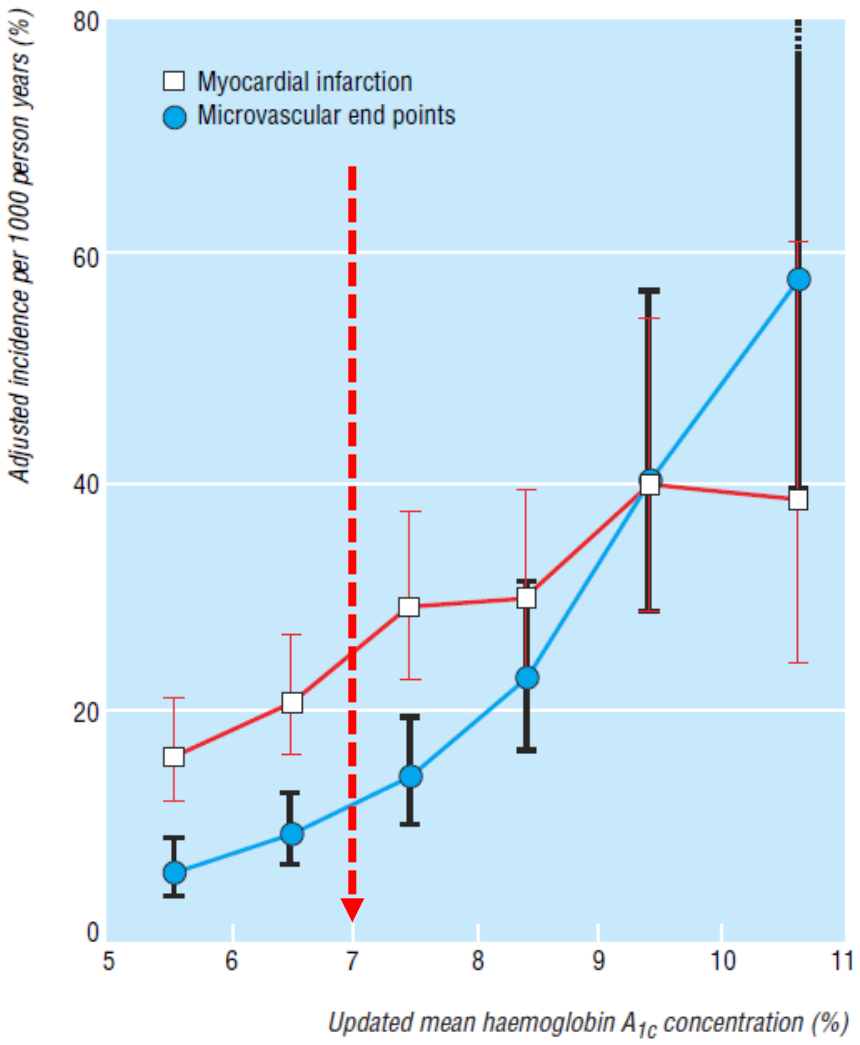
UKPDS 35:
평균 당화혈색소와 합병증





BMJ 2000;321:405-412

UKPDS 35:
평균 당화혈색소와 합병증

		Observational analysis				Clinical trial of intensive *v* conventional policy[1]		
		Baseline HbA_{1c}		Updated mean HbA_{1c}				
	No of events	Decrease in risk (%)/1% reduction (95% CI)	P value	Decrease in risk (%)/1% reduction (95% CI)	P value	No of events	Decrease in risk (%) seen for 0.9% difference in HbA_{1c} (95% CI)	P value
Aggregate end points								
Any end point related to diabetes	1255	11 (8 to 13)	<0.0001	21 (17 to 24)	<0.0001	1401	12 (1 to 21)	0.029
Deaths related to diabetes	346	9 (3 to 14)	0.0018	21 (15 to 27)	<0.0001	414	10 (–11 to 27)	0.34
All cause mortality	597	6 (2 to 10)	0.0081	14 (9 to 19)	<0.0001	702	6 (–10 to 20)	0.44
Myocardial infarction	496	5 (0 to 9)	0.067	14 (8 to 21)	<0.0001	573	16 (0 to 29)	0.052
Stroke	162	–4 (–14 to 6)	0.44	12 (1 to 21)	0.035	203	–11 (–49 to 19)	0.52
Peripheral vascular disease*	41	28 (18 to 37)	<0.0001	43 (31 to 53)	<0.0001	47	35 (–18 to 64)	0.15
Microvascular disease	323	23 (20 to 27)	<0.0001	37 (33 to 41)	<0.0001	346	25 (7 to 40)	0.0099
Single end points								
Heart failure	104	0 (–12 to 11)	0.99	16 (3 to 26)	0.016	116	9 (–35 to 39)	0.63
Cataract extraction	195	9 (2 to 16)	0.013	19 (11 to 26)	<0.0001	229	24 (0 to 42)	0.046

*Lower extremity amputation or fatal peripheral vascular disease.

BMJ 2000;321:405-412

UKPDS 35:
평균 당화혈색소와 합병증

What this study adds

There is a direct relation between the risk of complications of diabetes and glycaemia over time

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No threshold of glycaemia was observed for a substantive change in risk for any of the clinical outcomes examined

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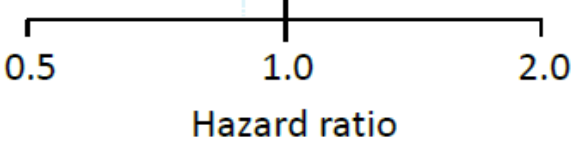
The lower the glycaemia the lower the risk of complications

The rate of increase of risk for microvascular disease with hyperglycaemia is greater than that for macrovascular disease

BMJ 2000;321:405-412

ADVANCE : Renal events

	% of patients with event				
	Intensive (n=5,571)	Standard (n=5,569)	Favours Intensive	Favours Standard	Relative risk reduction (95% CI)
Total renal events	**26.9%**	**30.0%**			**11% (5 to 17)** †
New microalbuminuria	23.7%	25.7%			9% (2 to 15)‡
New macroalbuminuria	2.9%	4.1%			30% (15 to 43) †
New or worsening nephropathy	4.1%	5.2%			21% (7 to 34) ***



† P=<0.001

‡ P=0.02

***** P=0.006**

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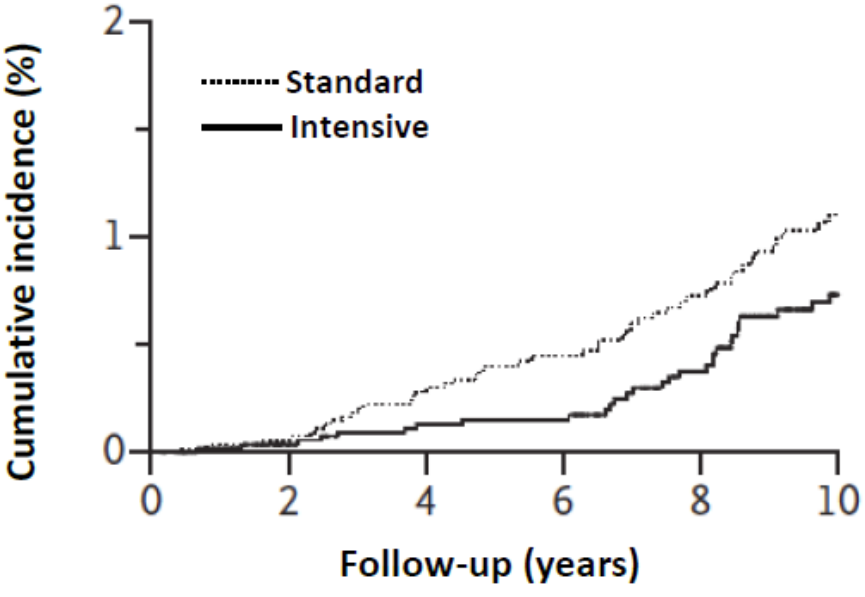
ADVANCE

NEJM 2008;358:2560-2572

End-stage kidney disease (overall in-trial and post-trial follow-up)



	In-trial (5.0 yrs)	Post-trial (5.4 yrs)	Overall (9.9 years)
End-stage kidney disease			
HR (95%CI)	0.35 (0.15-0.83)	0.65 (0.38-1.11)	0.54 (0.34-0.85)
Event no. (intensive vs standard)	(7 vs 20) **-13**	(22 vs 33) **-11**	(29 vs 53) **-24**

Relative risk reduction 46%
95% CI: 15 to 66%
p<0.01

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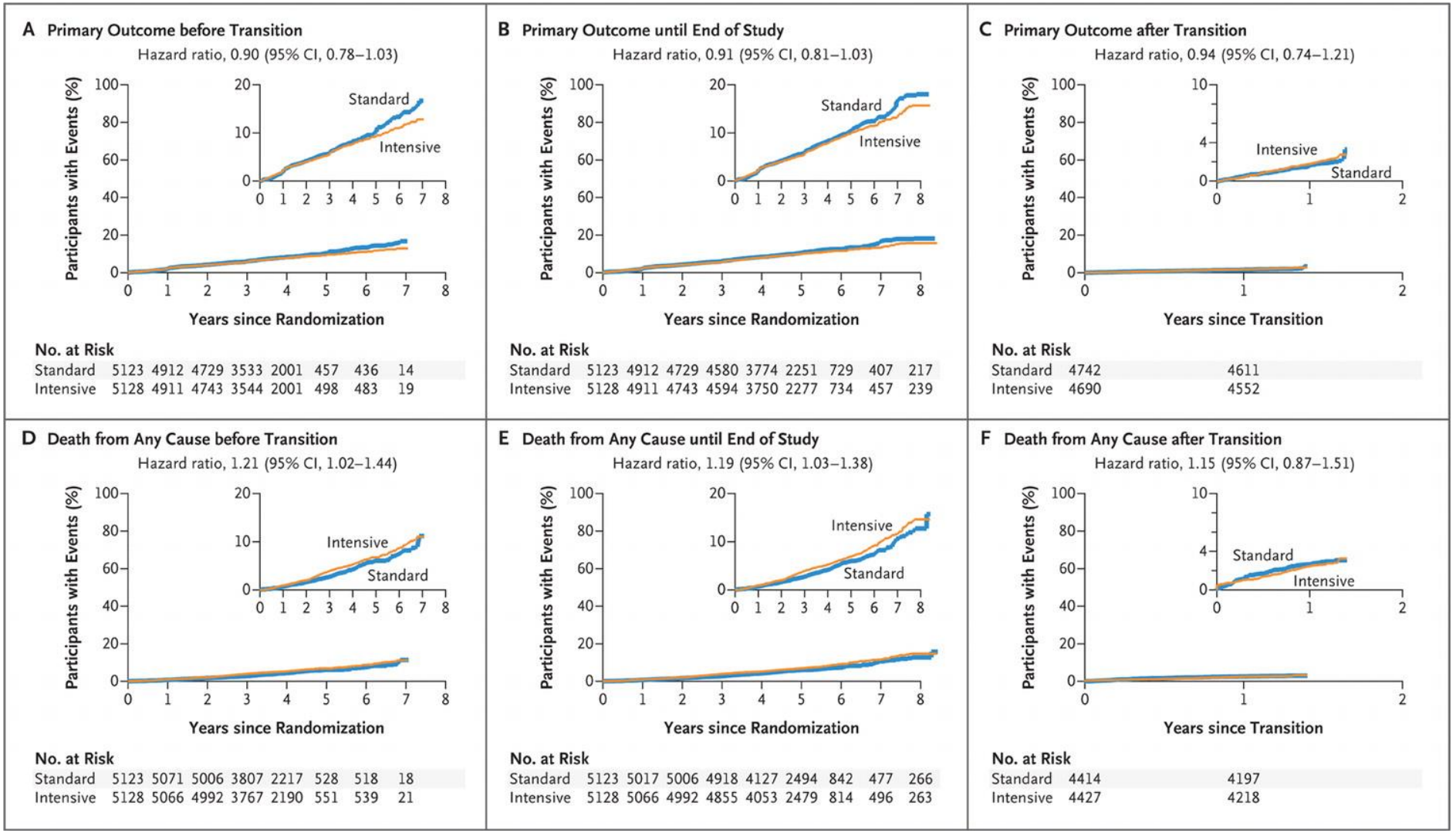
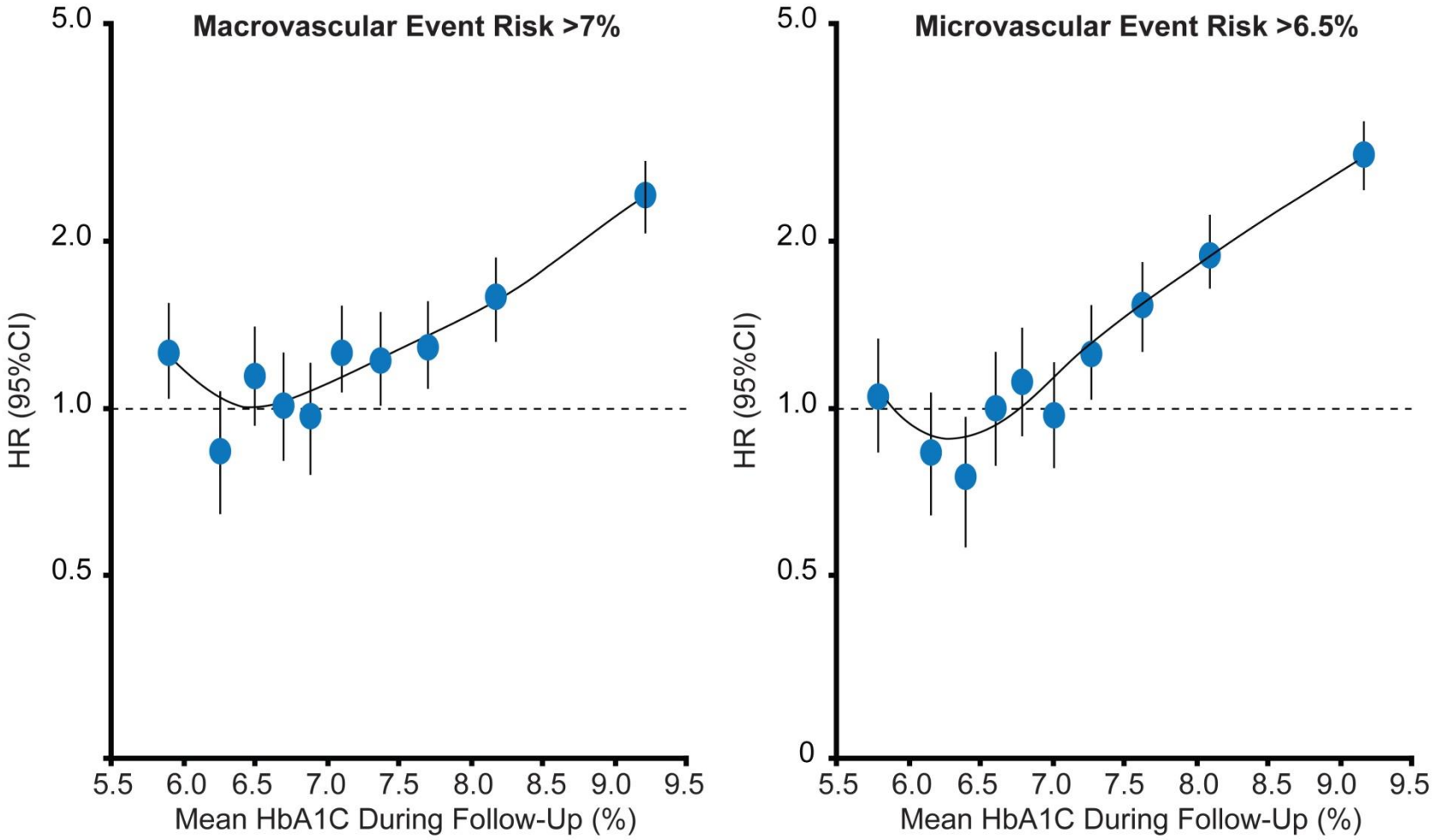
ADVANCE-ON
ACTION IN DIABETES AND VASCULAR DISEASE: PRETERAX AND DIAMICRON MR CONTROLLED EVALUATION POST-TRIAL OBSERVATIONAL STUDY

ACCORD 연구: 혈당조절과 사망



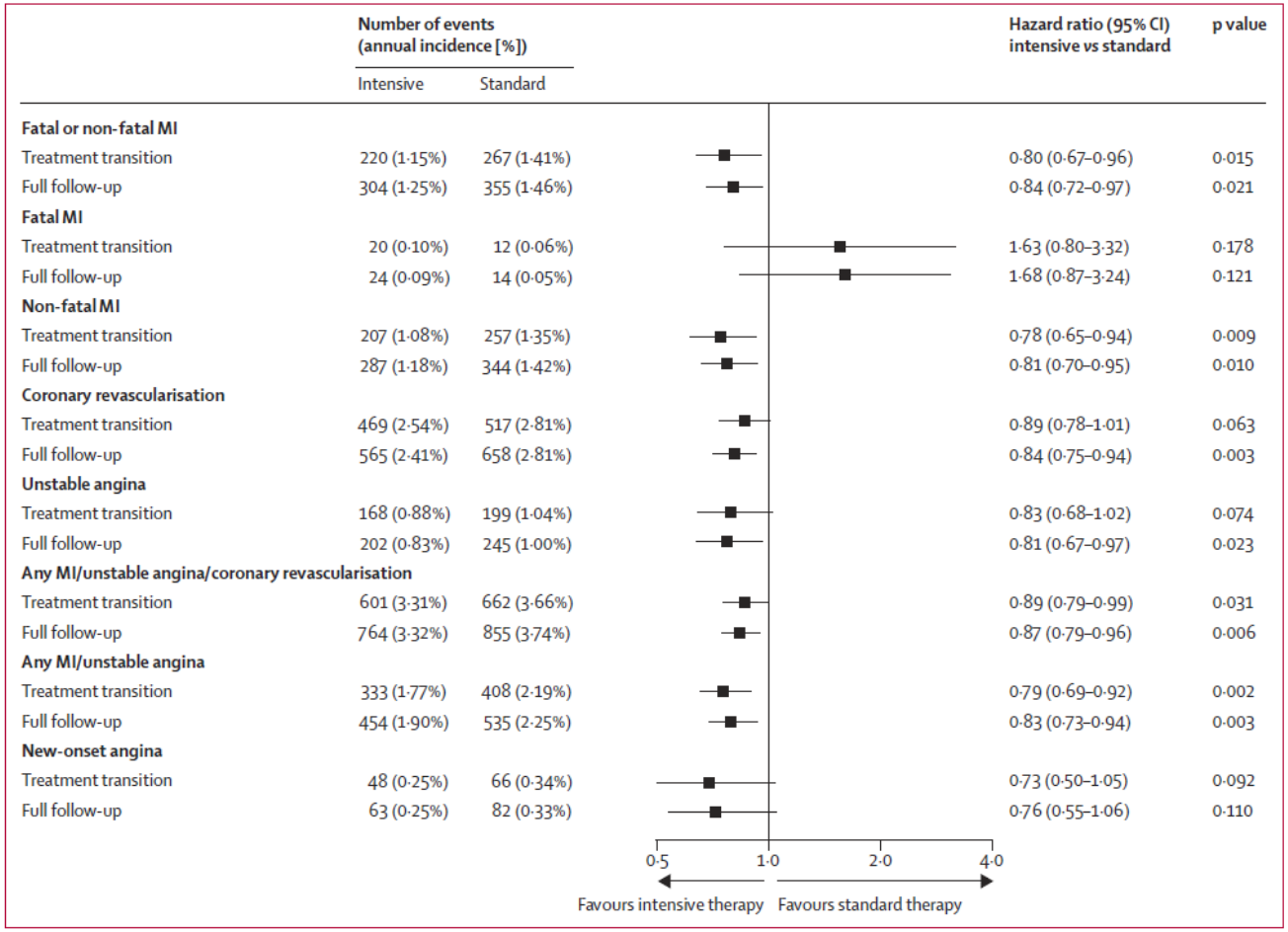
The ACCORD Study Group. N Engl J Med 2011;364:818-828.

ADVANCE 연구: 당화혈색소



Diabetologia (2012) 55:636–643

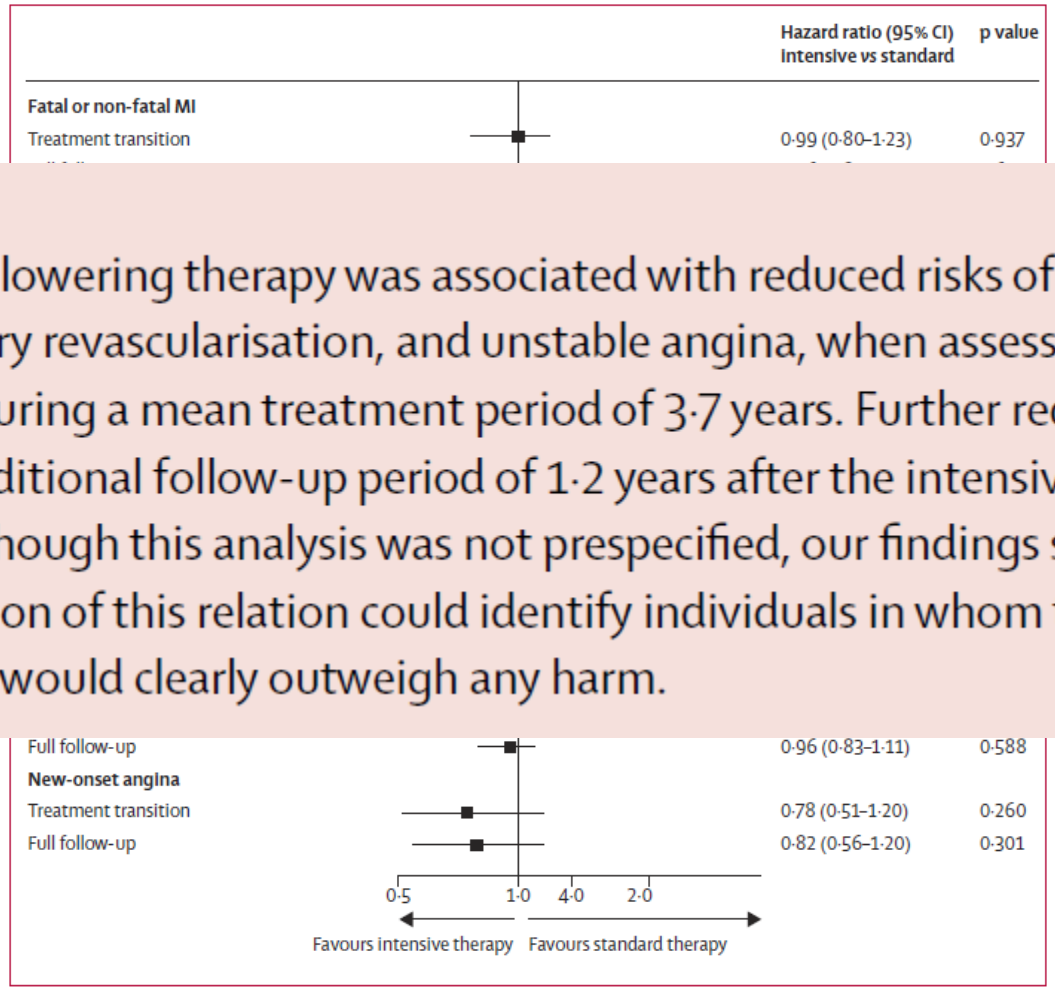
ACCORD 연구: 혈당조절과 **심장**



	Number of events (annual incidence [%])		Hazard ratio (95% CI) intensive *vs* standard	p value
	Intensive	Standard		
Fatal or non-fatal MI				
Treatment transition	220 (1·15%)	267 (1·41%)	0·80 (0·67–0·96)	0·015
Full follow-up	304 (1·25%)	355 (1·46%)	0·84 (0·72–0·97)	0·021
Fatal MI				
Treatment transition	20 (0·10%)	12 (0·06%)	1·63 (0·80–3·32)	0·178
Full follow-up	24 (0·09%)	14 (0·05%)	1·68 (0·87–3·24)	0·121
Non-fatal MI				
Treatment transition	207 (1·08%)	257 (1·35%)	0·78 (0·65–0·94)	0·009
Full follow-up	287 (1·18%)	344 (1·42%)	0·81 (0·70–0·95)	0·010
Coronary revascularisation				
Treatment transition	469 (2·54%)	517 (2·81%)	0·89 (0·78–1·01)	0·063
Full follow-up	565 (2·41%)	658 (2·81%)	0·84 (0·75–0·94)	0·003
Unstable angina				
Treatment transition	168 (0·88%)	199 (1·04%)	0·83 (0·68–1·02)	0·074
Full follow-up	202 (0·83%)	245 (1·00%)	0·81 (0·67–0·97)	0·023
Any MI/unstable angina/coronary revascularisation				
Treatment transition	601 (3·31%)	662 (3·66%)	0·89 (0·79–0·99)	0·031
Full follow-up	764 (3·32%)	855 (3·74%)	0·87 (0·79–0·96)	0·006
Any MI/unstable angina				
Treatment transition	333 (1·77%)	408 (2·19%)	0·79 (0·69–0·92)	0·002
Full follow-up	454 (1·90%)	535 (2·25%)	0·83 (0·73–0·94)	0·003
New-onset angina				
Treatment transition	48 (0·25%)	66 (0·34%)	0·73 (0·50–1·05)	0·092
Full follow-up	63 (0·25%)	82 (0·33%)	0·76 (0·55–1·06)	0·110

***Lancet* 2014; 384: 1936–41**

ACCORD 연구: 혈당조절과 **심장**



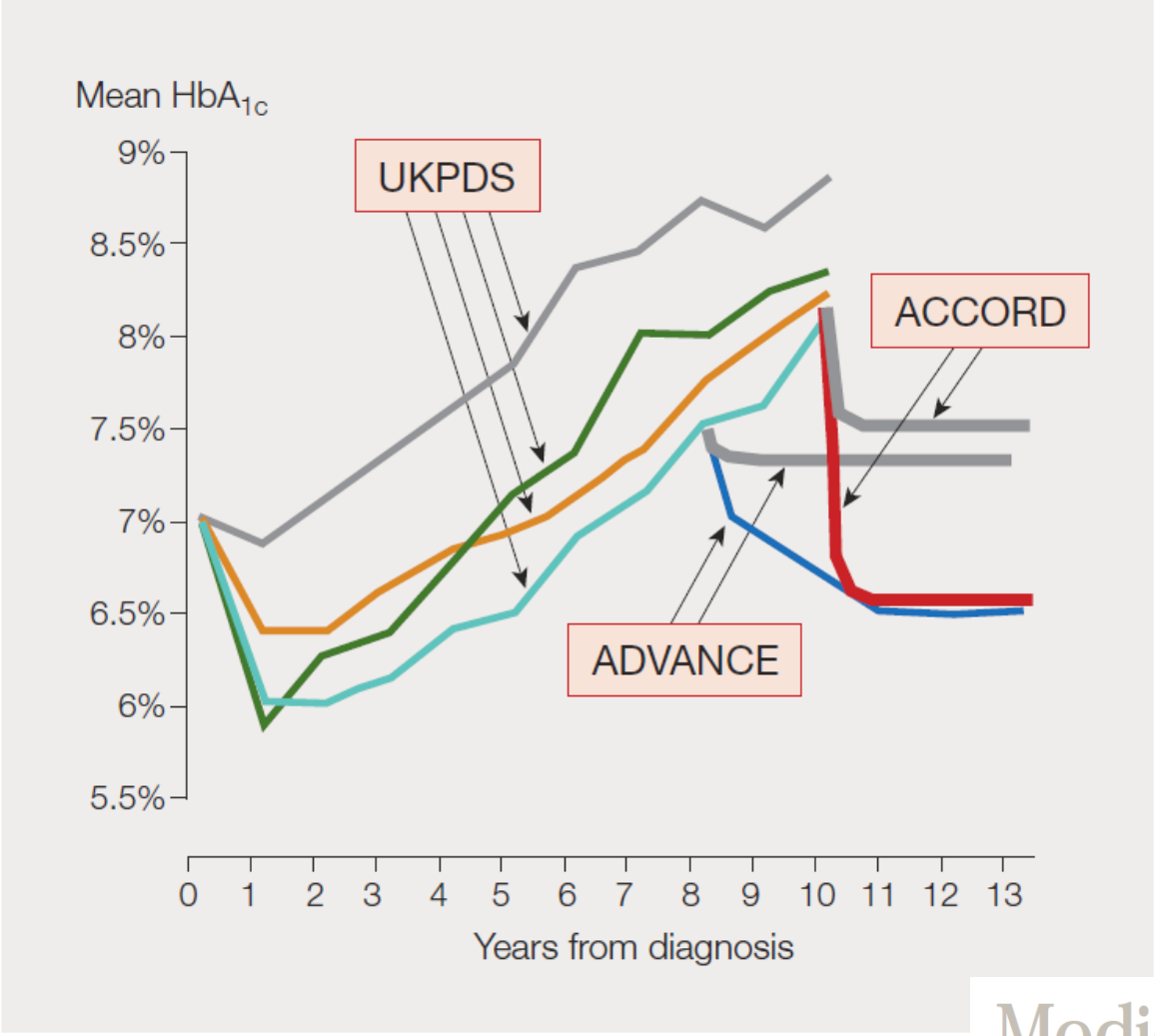
Interpretation

Intensive glucose-lowering therapy was associated with reduced risks of any myocardial infarction, coronary revascularisation, and unstable angina, when assessed separately and in combination, during a mean treatment period of 3·7 years. Further reductions were seen during an additional follow-up period of 1·2 years after the intensive treatment had been stopped. Although this analysis was not prespecified, our findings suggest that further investigation of this relation could identify individuals in whom the benefit of glycaemic control would clearly outweigh any harm.

Figure 3: **Risk of ischaemic heart disease events after adjustment for glycated haemoglobin A_{1c} concentrations achieved during active treatment, by follow-up period**
Glycated haemoglobin A_{1c} concentrations were included as a time-dependent covariate and take account of competing risk due to death. MI=myocardial infarction.

***Lancet* 2014; 38**

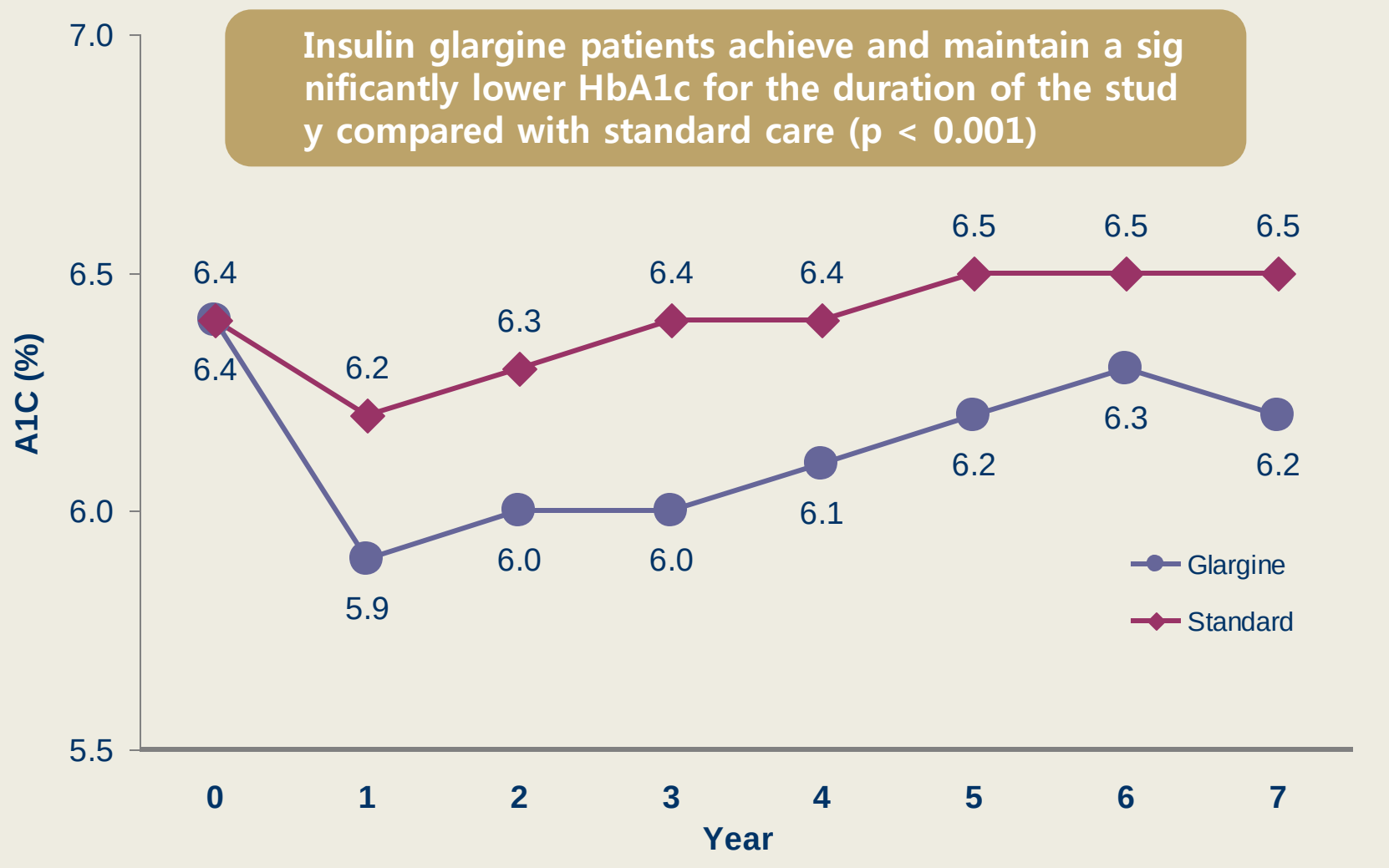
UKPDS vs. Recent 3 Trials



David R. MATTHEWS,MA, DPhil, BM, BCh, FRCP

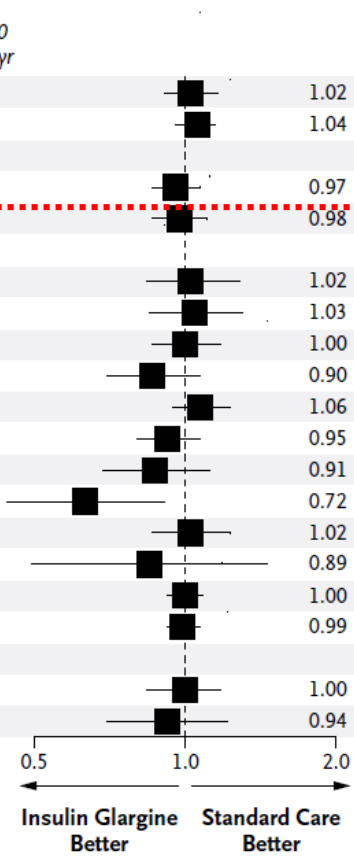
Medicographia
A Servier publication

ORIGIN 연구: 미세혈관합병증



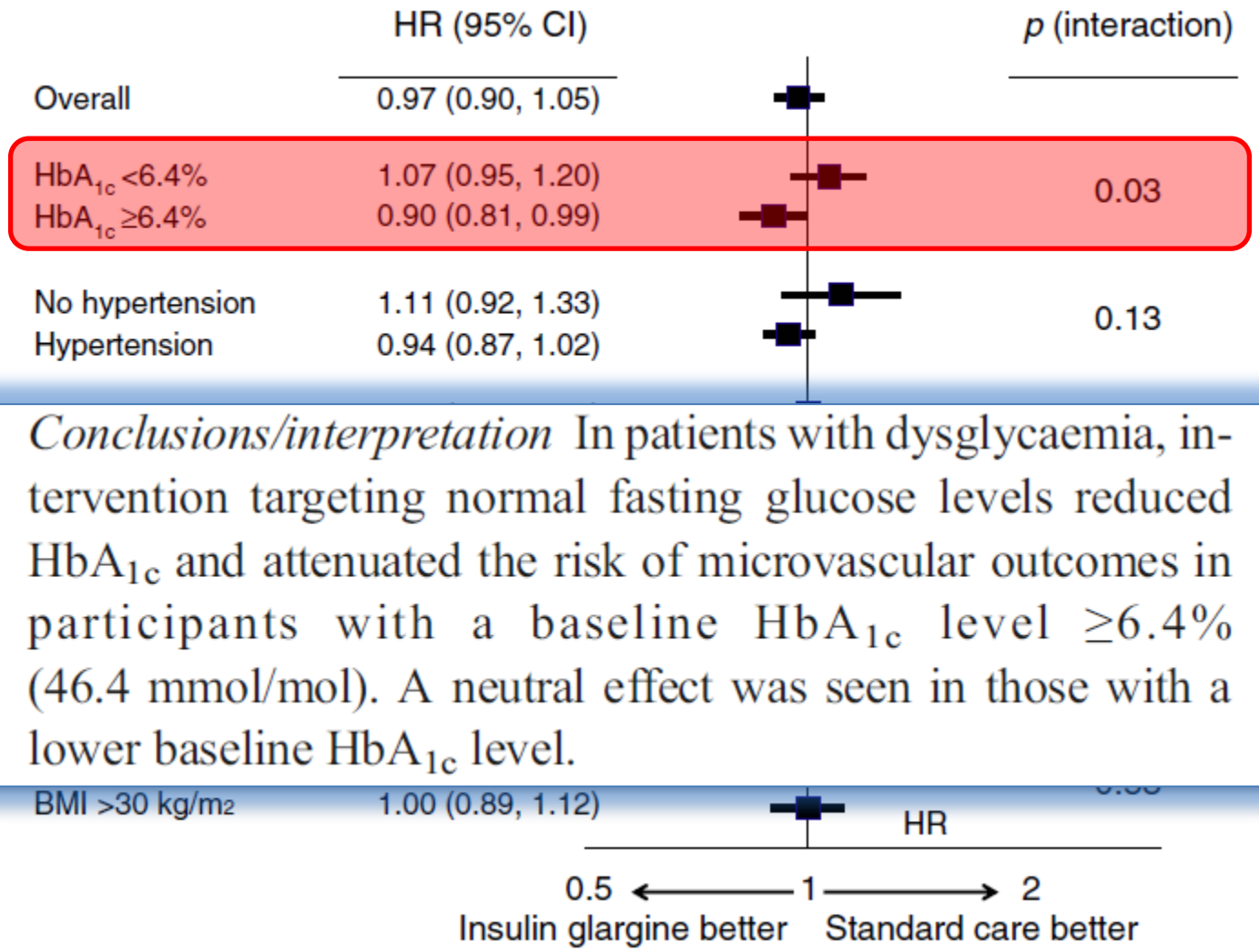
ORIGIN 연구: 미세혈관합병증

Outcome	Insulin Glargine (N=6264)		Standard Care (N=6273)		Hazard Ratio (95% CI)	P Value
	no. (%)	*no./100 patient-yr*	*no. (%)*	*no./100 patient-yr*		
First coprimary outcome	1041 (16.6)	2.94	1013 (16.1)	2.85	1.02 (0.94–1.11)	0.63
Second coprimary outcome	1792 (28.6)	5.52	1727 (27.5)	5.28	1.04 (0.97–1.11)	0.27
Microvascular outcomes	1323 (21.1)	3.87	1363 (21.7)	3.99	0.97 (0.90–1.05)	0.43
Total mortality	951 (15.2)	2.57	965 (15.4)	2.60	0.98 (0.90–1.08)	0.70
Total myocardial infarctions	336 (5.4)	0.93	326 (5.2)	0.90	1.02 (0.88–1.19)	0.75
Total strokes	331 (5.3)	0.91	319 (5.1)	0.88	1.03 (0.89–1.21)	0.69
Death from cardiovascular causes	580 (9.3)	1.57	576 (9.2)	1.55	1.00 (0.89–1.13)	0.98
Hospitalization for congestive heart failure	310 (4.9)	0.85	343 (5.5)	0.95	0.90 (0.77–1.05)	0.16
Revascularization	908 (14.5)	2.69	860 (13.7)	2.52	1.06 (0.96–1.16)	0.24
Angina	709 (11.3)	2.07	743 (11.8)	2.17	0.95 (0.85–1.05)	0.29
Unstable	238 (3.8)	0.66	261 (4.2)	0.72	0.91 (0.76–1.08)	0.28
New	100 (1.6)	0.27	138 (2.2)	0.38	0.72 (0.56–0.93)	0.01
Worsening	455 (7.3)	1.29	446 (7.1)	1.26	1.02 (0.89–1.16)	0.80
Limb or digit amputation	47 (0.8)	0.13	53 (0.8)	0.14	0.89 (0.60–1.31)	0.55
Cardiovascular hospitalization	2081 (33.2)	6.98	2071 (33.0)	6.91	1.00 (0.94–1.07)	0.90
Noncardiovascular hospitalization	2339 (37.3)	7.90	2349 (37.4)	7.93	0.99 (0.94–1.05)	0.85
Any cancer	476 (7.6)	1.32	477 (7.6)	1.32	1.00 (0.88–1.13)	0.97
Death from cancer	189 (3.0)	0.51	201 (3.2)	0.54	0.94 (0.77–1.15)	0.52



N Engl J Med 2012; 367:319-328
Diabetologia (2014) 57:1325–1331

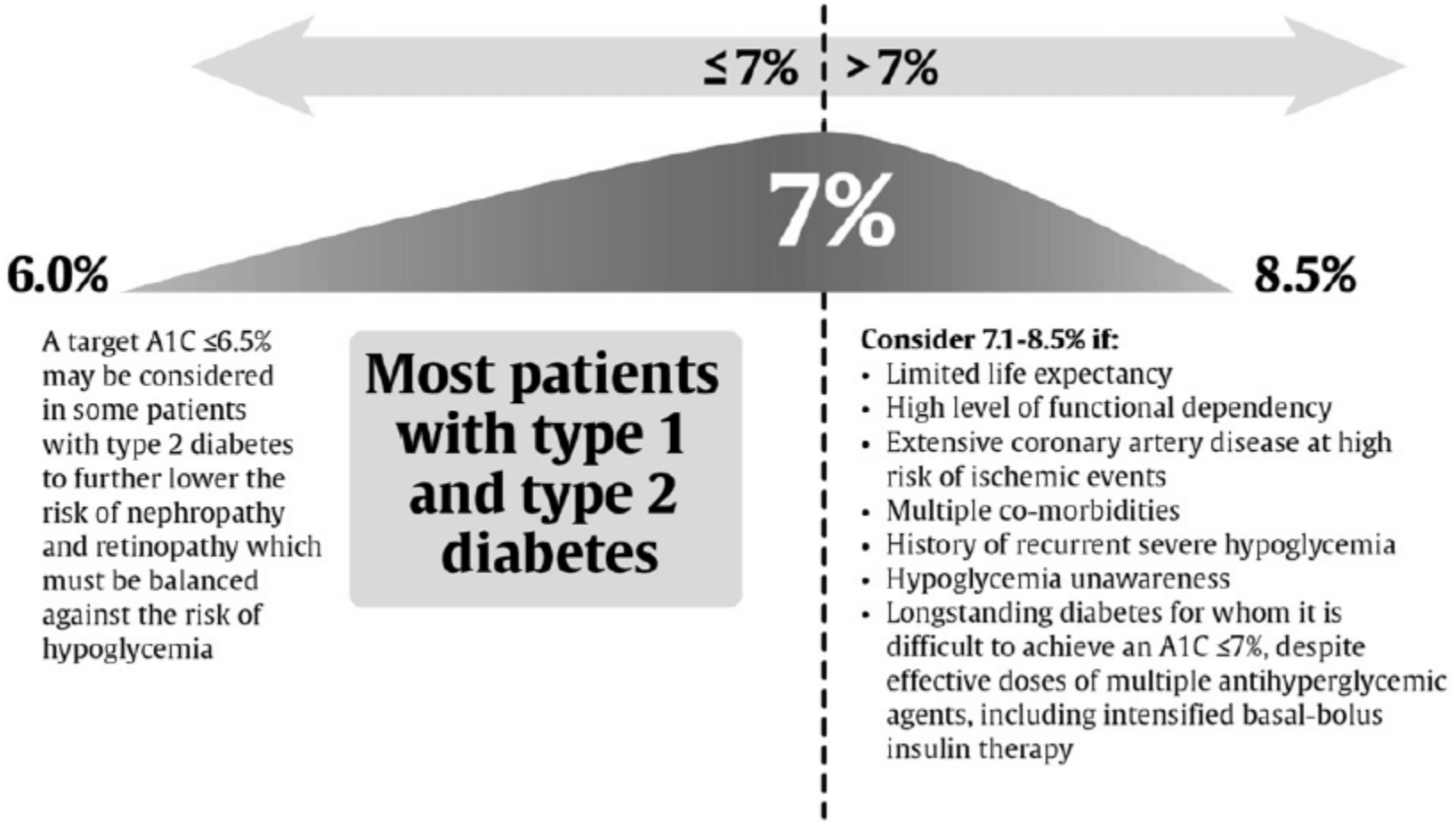
ORIGIN 연구: 미세혈관합병증



Conclusions/interpretation In patients with dysglycaemia, intervention targeting normal fasting glucose levels reduced HbA_{1c} and attenuated the risk of microvascular outcomes in participants with a baseline HbA_{1c} level ≥6.4% (46.4 mmol/mol). A neutral effect was seen in those with a lower baseline HbA_{1c} level.

Diabetologia (2014) 57:1325–1331

캐나다당뇨병학회 2013



Can J Diabetes 37 (2013) S31-S34

제2형당뇨병: 당화혈색소의 목표

6.5%

대한당뇨병학회
Korean Diabetes Association