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How to Start Insulin in Primary Care Part 1- Pre-Conference Workshop

Thursday, 20 June 2013 Start 8:30am Duration: 120mins Sigma

How to Start Insulin in Primary Care Part 2 - Pre-Conference Workshop

Thursday, 20 June 2013 Start 11:00am Duration: 120mins Sigma



Starting insulin sooner rather than later

June 2013

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Overview

- The global burden
- T2D- a progressive disease
- Early v/s late insulin start
- Hba1c targets

The global burden

- 366 million have diabetes in 2011; by 2030 will have risen to 552 million
- 80% of people with diabetes live in low-and middle-income countries
- The greatest number of people with diabetes are between 40 to 59 years
- 183 million people (50%) with diabetes are undiagnosed
- Diabetes caused 4.6 million deaths in 2011
- Diabetes caused at least USD 465 billion dollars in healthcare expenditures in 2011; 11% of total healthcare expenditures in adults (20-79 years)
- 78,000 children develop type 1 diabetes every year

IDF atlas – 5th Edition

League table (total burden)

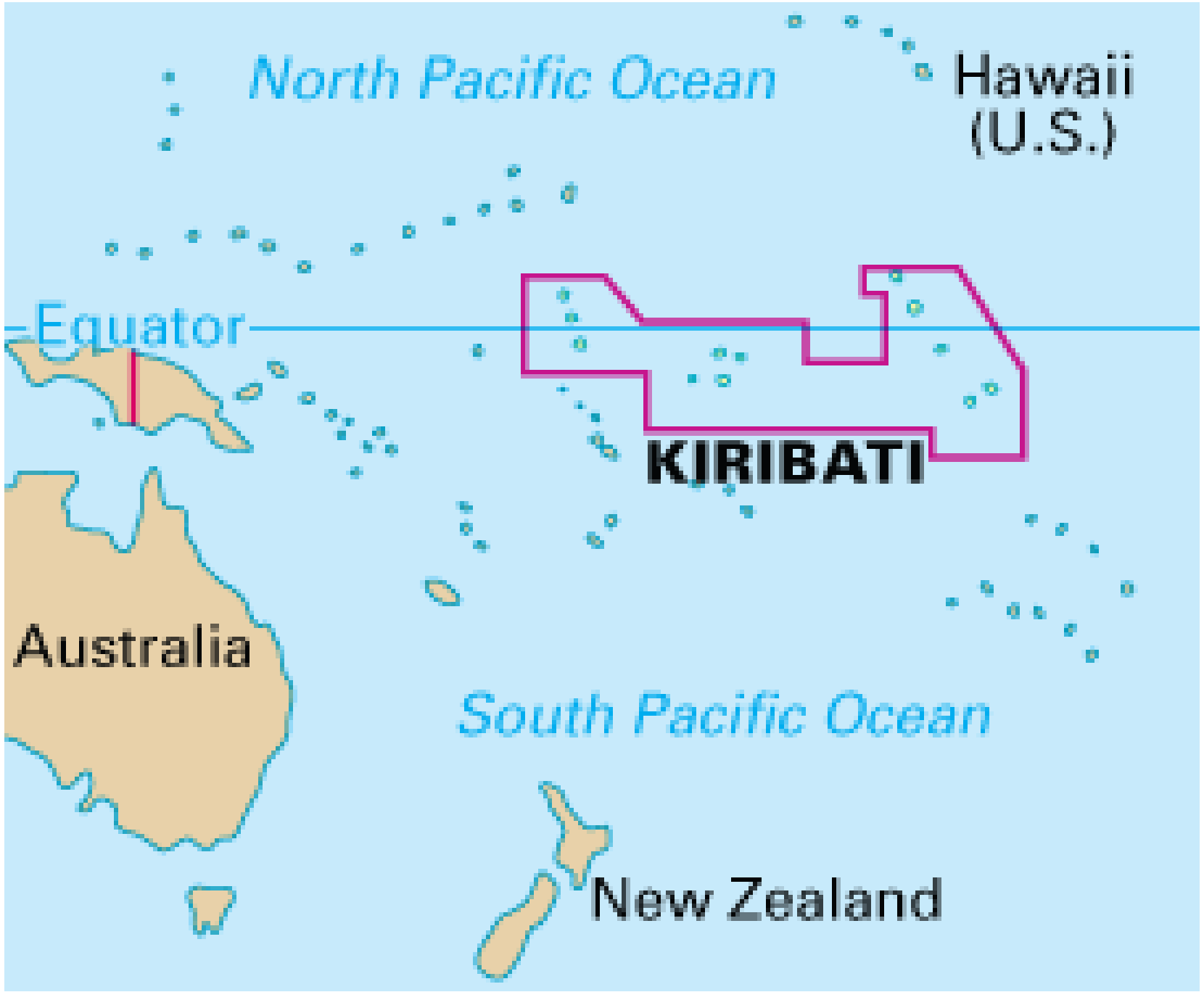
Top 10: Countries/territories of number of people with diabetes (20-79 years), 2011 and 2030

	COUNTRY /TERRITORY	2011 MILLIONS
1	China	90.0
2	India	61.3
3	United States of America	23.7
4	Russian Federation	12.6
5	Brazil	12.4
6	Japan	10.7
7	Mexico	10.3
8	Bangladesh	8.4
9	Egypt	7.3
10	Indonesia	7.3

	COUNTRY /TERRITORY	2030 MILLIONS
1	China	129.7
2	India	101.2
3	United States of America	29.6
4	Brazil	19.6
5	Bangladesh	16.8
6	Mexico	16.4
7	Russian Federation	14.1
8	Egypt	12.4
9	Indonesia	11.8
10	Pakistan	11.4

IDF atlas – 5th Edition

Country with highest prevalence (%)?


North Pacific Ocean
Hawaii
(U.S.)
Equator
KIRIBATI
Australia
South Pacific Ocean
New Zealand

League table (prevalence %)

Table 2.1. Top 10 countries/territories for prevalence* (%) of diabetes (20-79 years), 2011 and 2030

	COUNTRY /TERRITORY	2011 PREVALENCE (%)
1	Kiribati	25.7
2	Marshall Islands	22.2
3	Kuwait	21.1
4	Nauru	20.7
5	Lebanon	20.2
6	Qatar	20.2
7	Saudi Arabia	20.0
8	Bahrain	19.9
9	Tuvalu	19.5
10	United Arab Emirates	19.2

	COUNTRY /TERRITORY	2030 PREVALENCE (%)
1	Kiribati	26.3
2	Marshall Islands	23.0
3	Kuwait	21.2
4	Tuvalu	20.8
5	Nauru	20.7
6	Saudi Arabia	20.6
7	Lebanon	20.4
8	Qatar	20.4
9	Bahrain	20.2
10	United Arab Emirates	19.8

*comparative prevalence

IDF atlas – 5th Edition

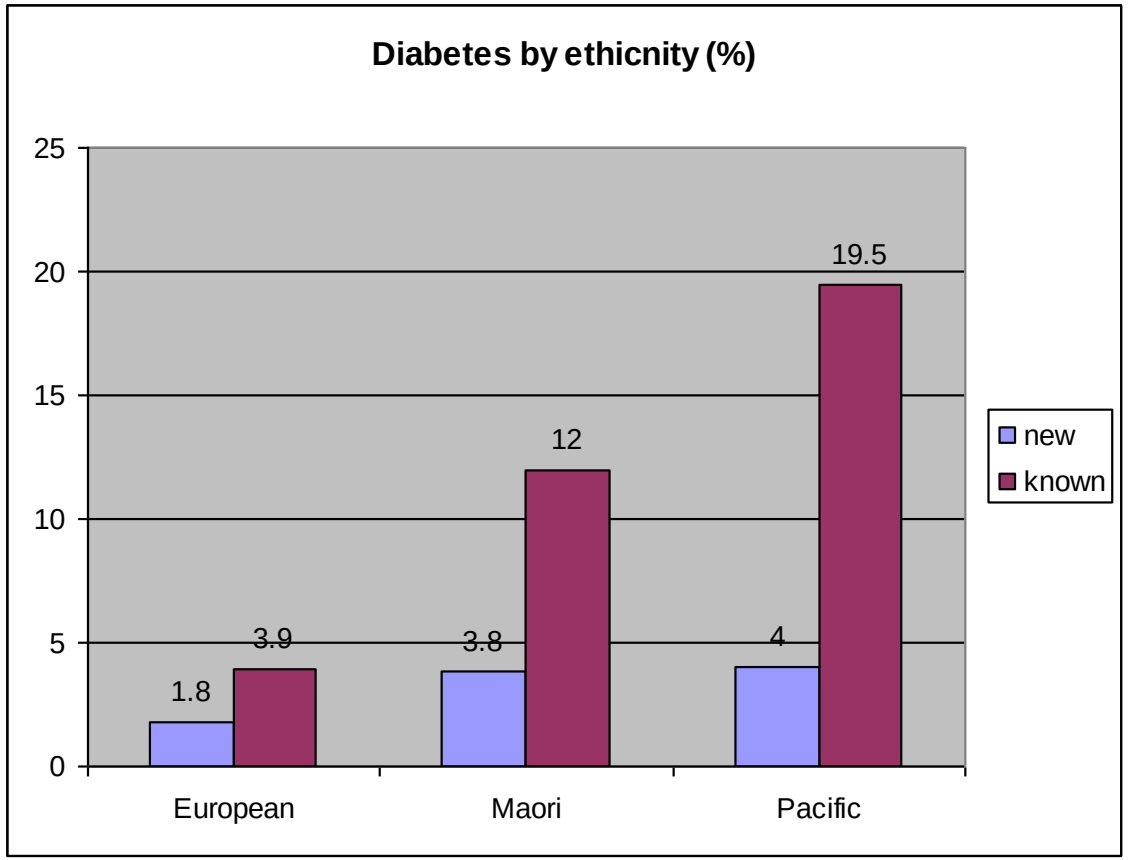
Local NZ prevalence data- NZSSD

	DHBname	European/Other	Indian	Mäori	Pacific people	Grand Total
011	Northland	5941	75	3768	139	9923
021	Waitemata	19278	1945	1898	3414	26535
022	Auckland	13060	3558	1616	5415	23649
023	Counties Manukau	14752	3959	4387	10986	34084
031	Waikato	13526	634	4085	685	18930
042	Lakes	3113	96	1815	178	5202
047	Bay of Plenty	7864	339	2721	206	11130
051	Tairawhiti	1865	22	1590	81	3558
061	Hawkes Bay	5615	105	1931	339	7990
071	Taranaki	6029	65	981	82	7157
081	MidCentral	6446	116	1003	248	7813
082	Whanganui	2539	36	800	62	3437
091	Capital and Coast	7965	757	1054	1789	11565
092	Hutt	4739	339	952	904	6934
093	Wairarapa	1758	10	317	49	2134
101	Nelson Marlborough	5464	41	425	71	6001
111	West Coast	1208	7	117	17	1349
121	Canterbury	18293	299	1230	788	20610
123	South Canterbury	3064	15	148	23	3250
131	Southern	8344	78	363	215	9000
141	Southern	4686	29	407	137	5259
999	Unknown/Unassigned	137	10	32	42	221
Grand Total		155686	12535	31640	25870	225731

Undiagnosed rate ratios

Auckland Heart and health Survey (2007)

1:2 **1:3** **1:5**

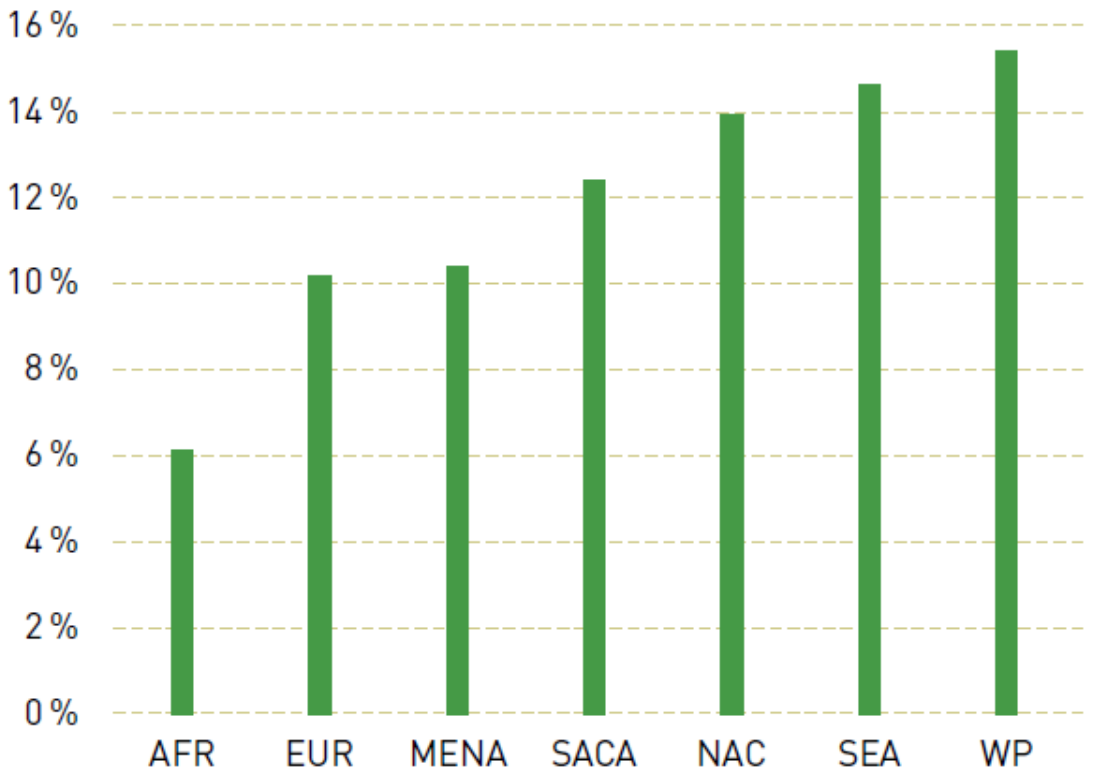


Age 35+

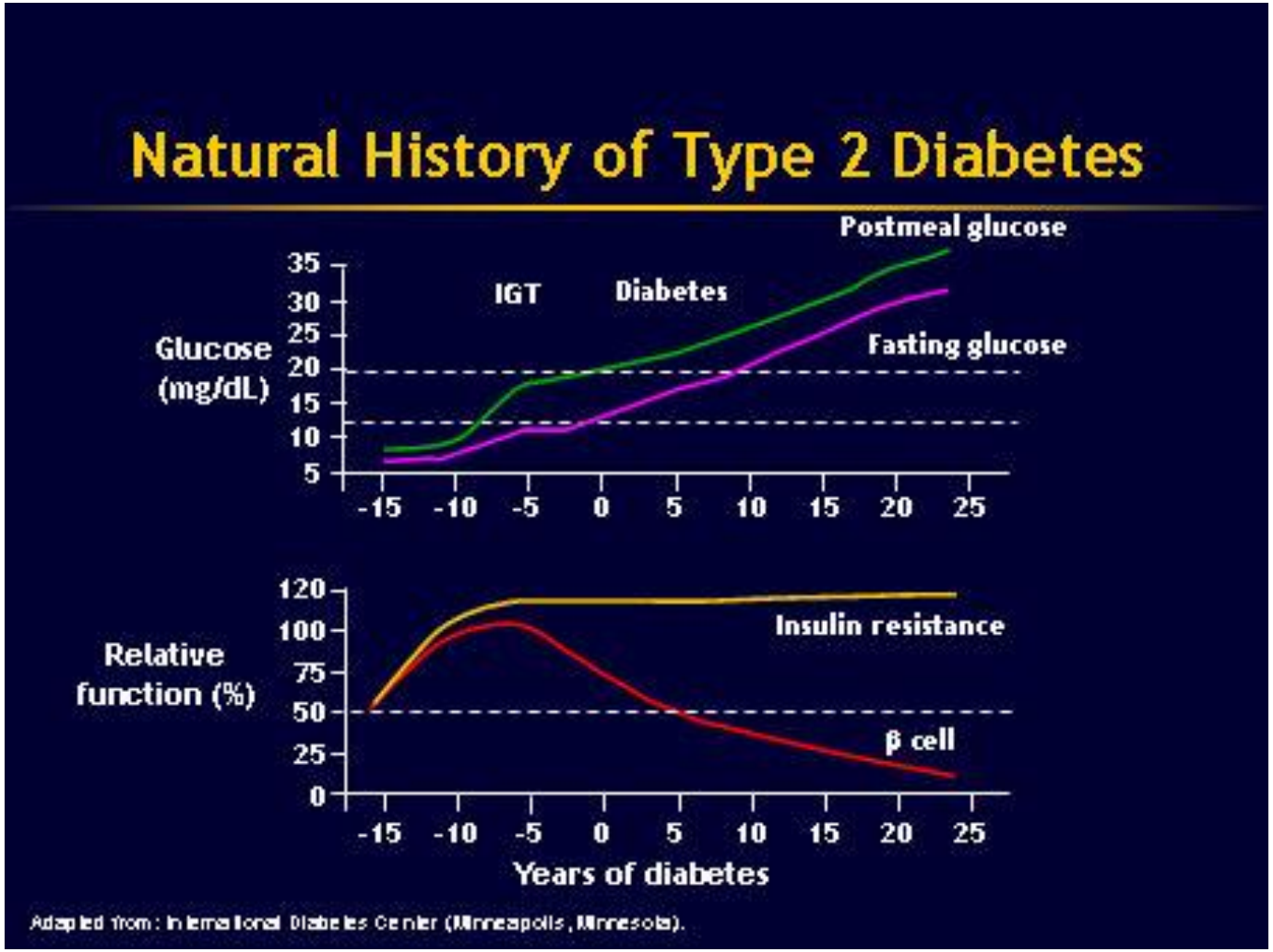
Deaths due to diabetes

- 4.6 million deaths due to diabetes in 2011
- 8.2% of all-cause mortality
- 48% in people under 60

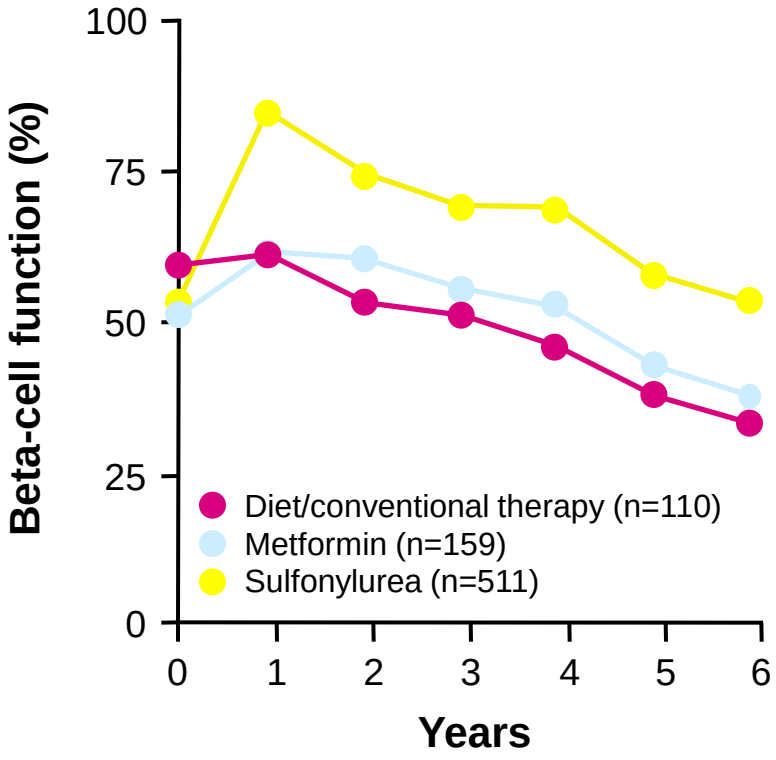
Figure 2.6. Deaths attributable to diabetes as a percentage of all deaths (20-79 years) by IDF region, 2011



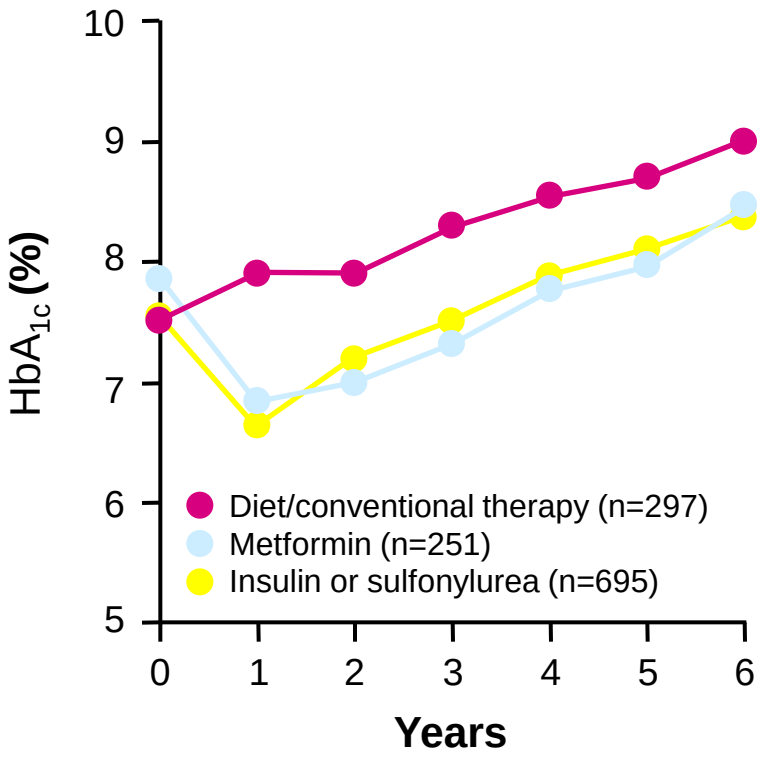
T2D is a progressive condition



Declining Beta-Cell Function Associated with Increasing Hyperglycemia - UKPDS 16



Beta-cell function assessed by HOMA

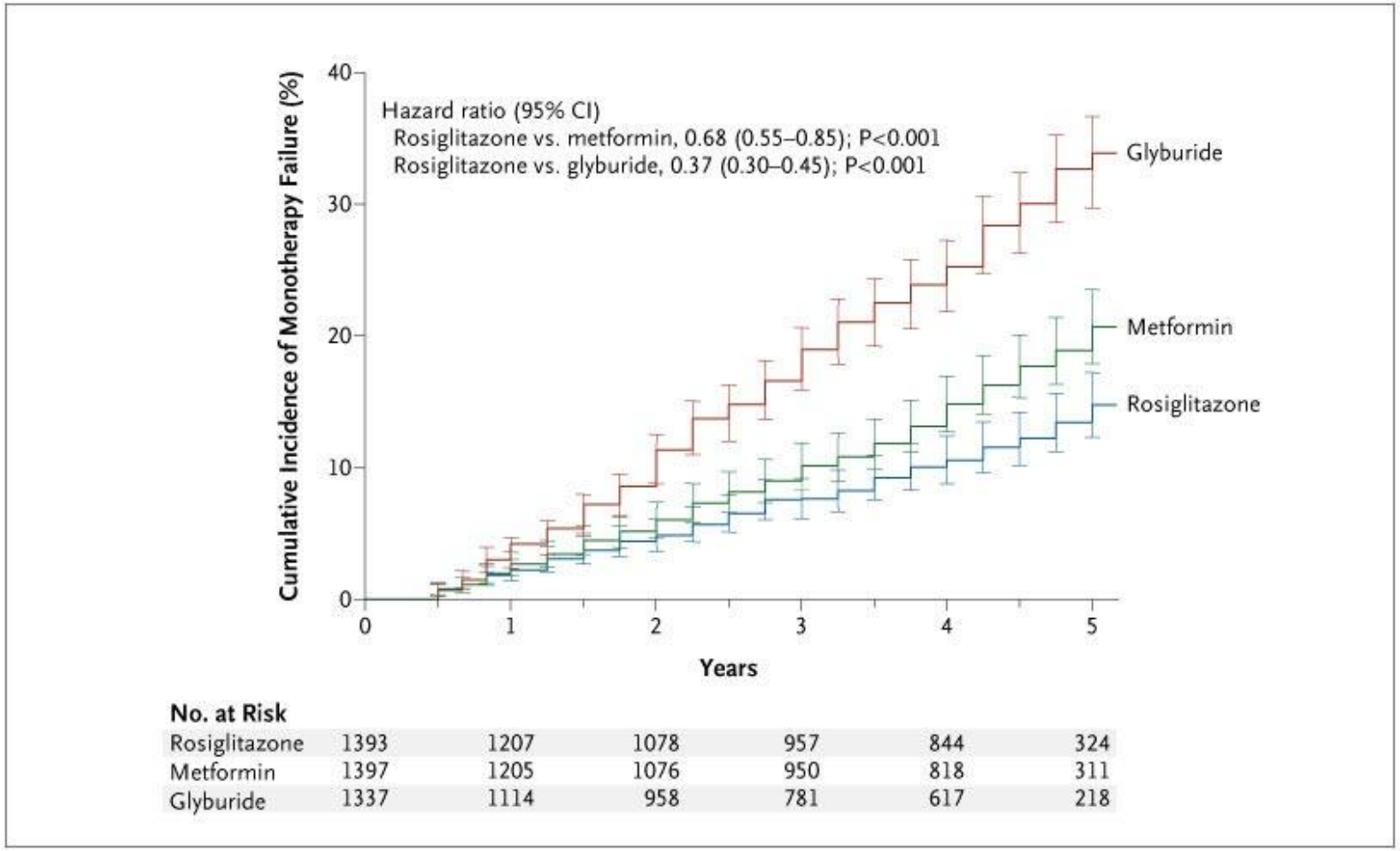


HbA_{1c} results shown from obese patients

UKPDS=United Kingdom Prospective Diabetes Study; HbA_{1c}=glycosylated hemoglobin

Adapted from UKPDS Group *Diabetes* 1995;44:1249–1258.

ADOPT Study: Monotherapy Failure at 5 Years



No. at Risk						
Rosiglitazone	1393	1207	1078	957	844	324
Metformin	1397	1205	1076	950	818	311
Glyburide	1337	1114	958	781	617	218

Kahn SE et al. N Engl J Med 2006;355:2427-2443

The NEW ENGLAND JOURNAL of MEDICINE

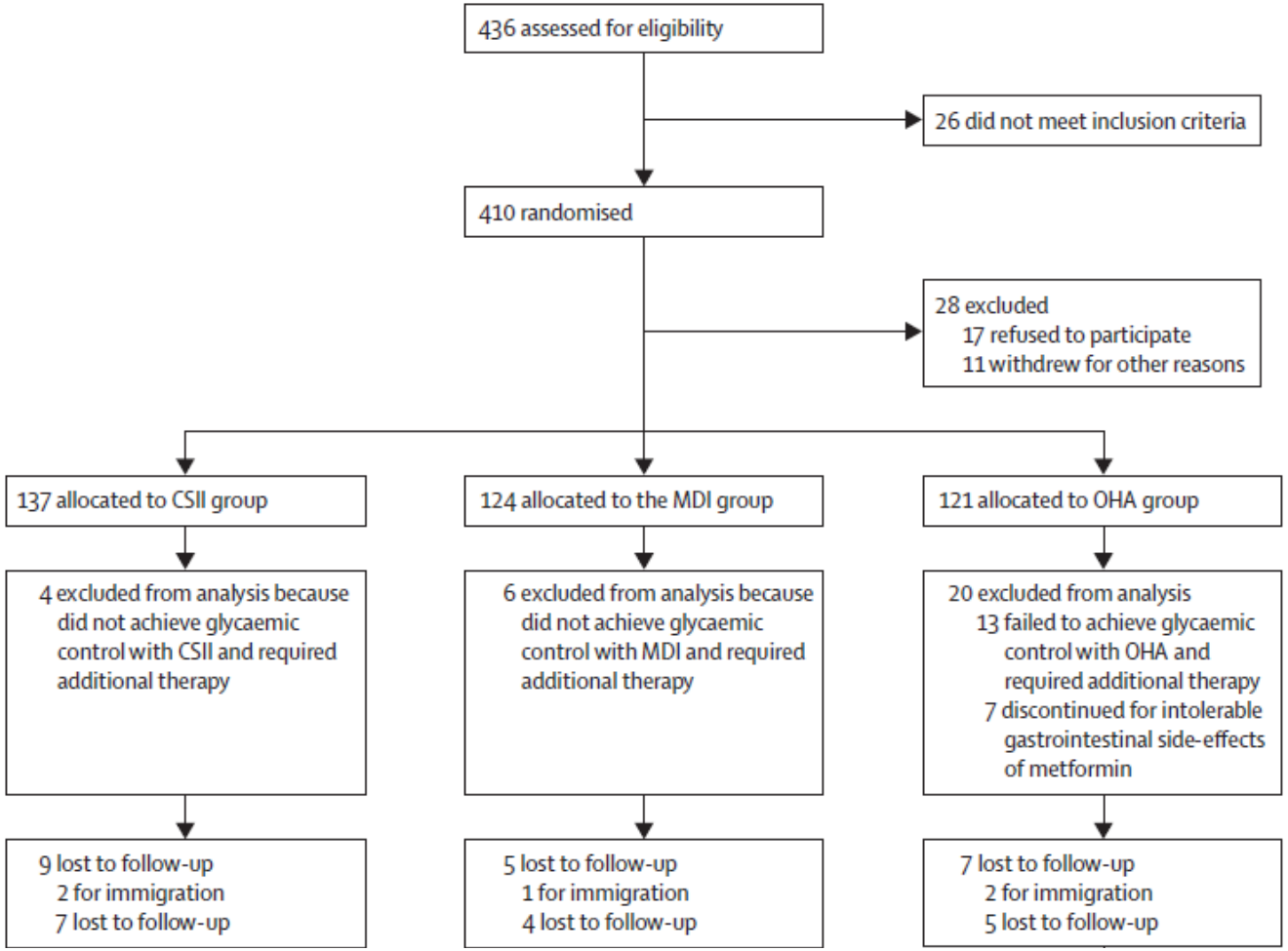
When to think insulin??

- Discuss openly the progressive nature of T2D at start
- Explore myths held about insulin
- Identify barriers

Early insulinisation

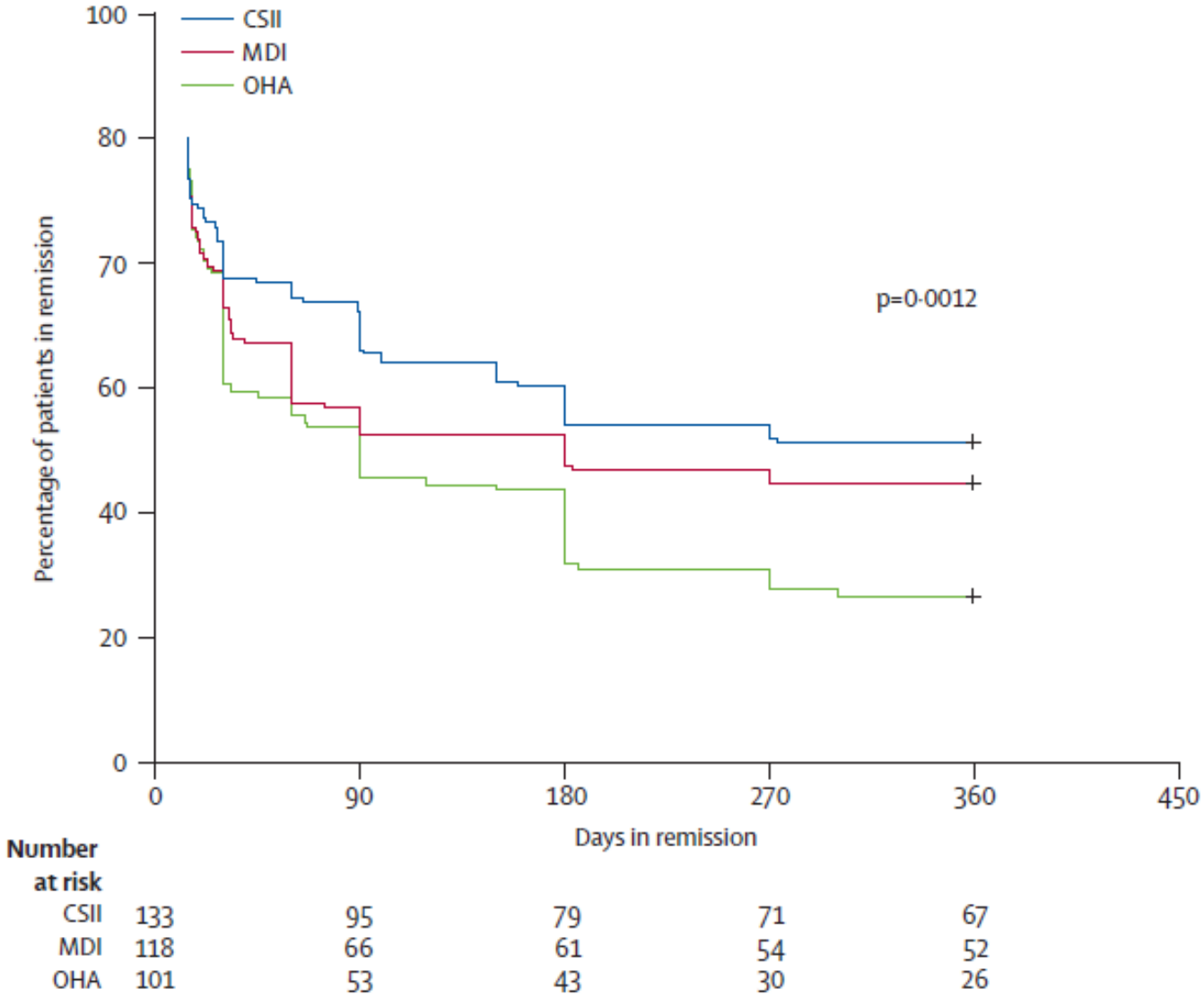
- Glucotoxicity
- Beta cell function
- DM complications
- Never too late to consider- Osmotic sympts/ fatigue/ unintentional wt loss

Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial



Lancet 2008; vol 371; 1753-1760

Results

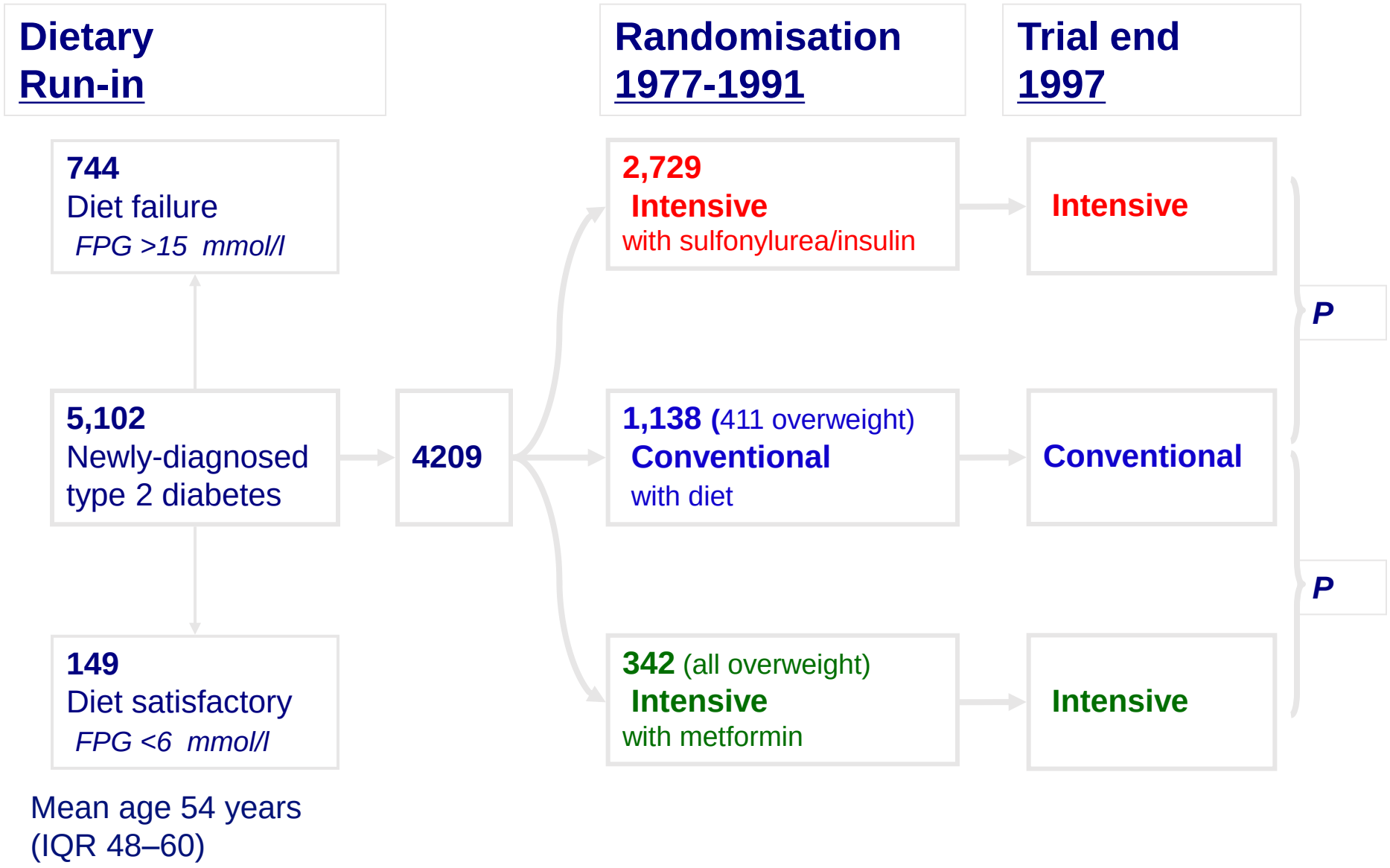


Lancet 2008; vol 371; 1753-1760

The Legacy Effect (Metabolic memory)

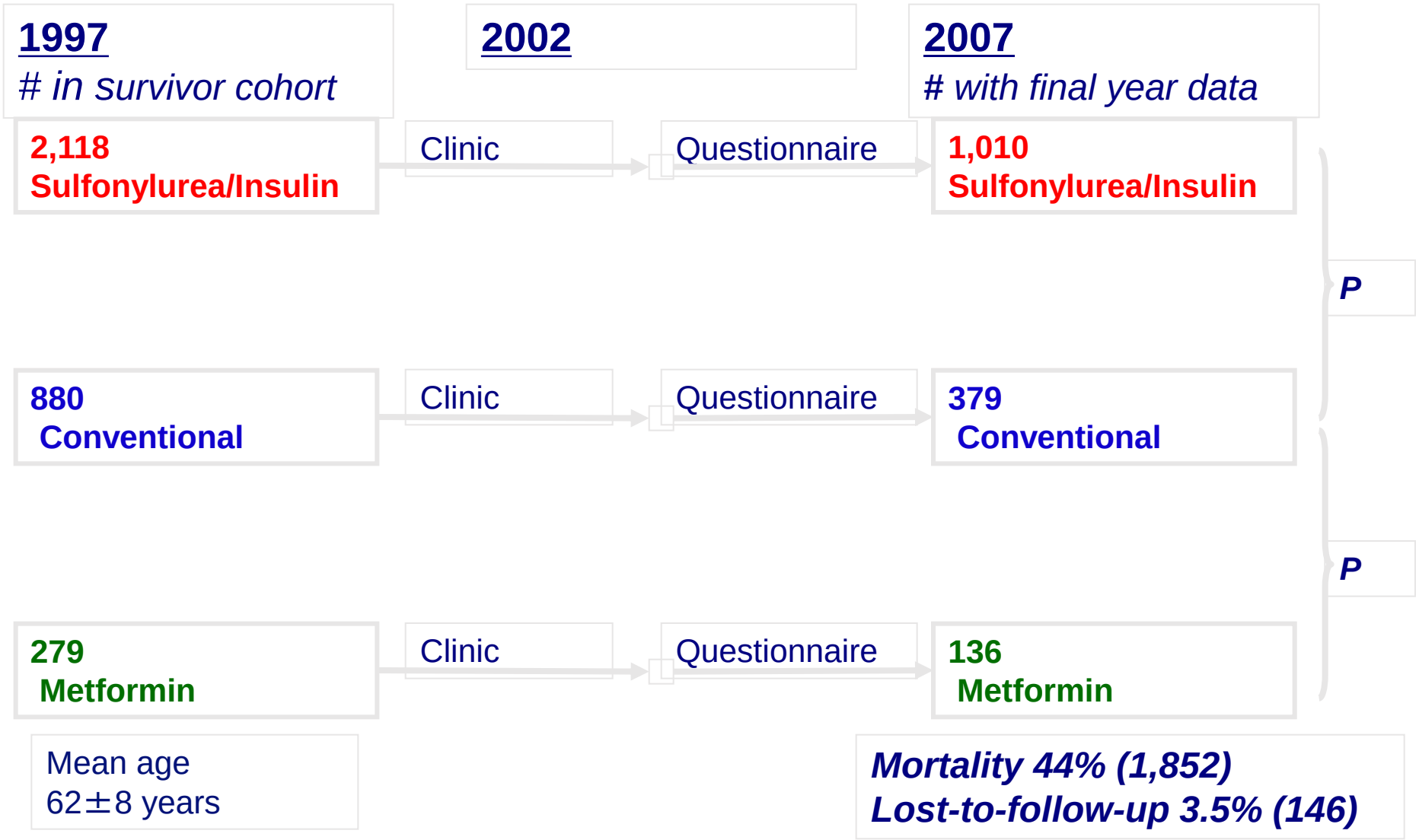
- What is Legacy? Something received from an ancestor or from the past

UKPDS Legacy study; NEJM 2008



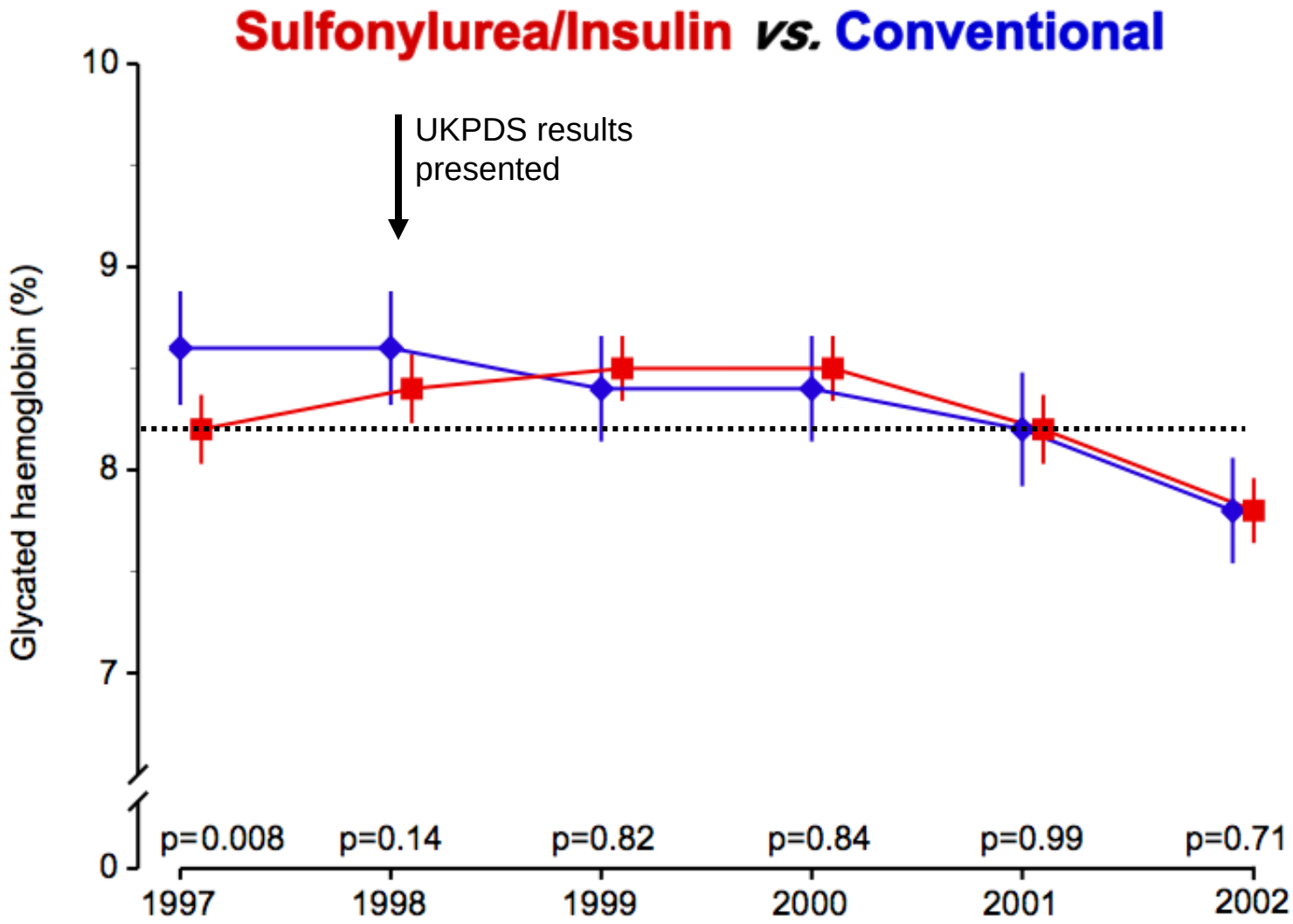
Holman RR et al. NEJM. 2008; 359(15):1577-89

Post-Trial Monitoring: Patients



Holman RR et al. NEJM. 2008; 359(15):1577-89

Post-Trial Changes in HbA_{1c}



Holman RR et al. NEJM. 2008; 359(15):1577-89

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

Holman RR et al. NEJM. 2008; 359(15):1577-89

What about Hba1c targets

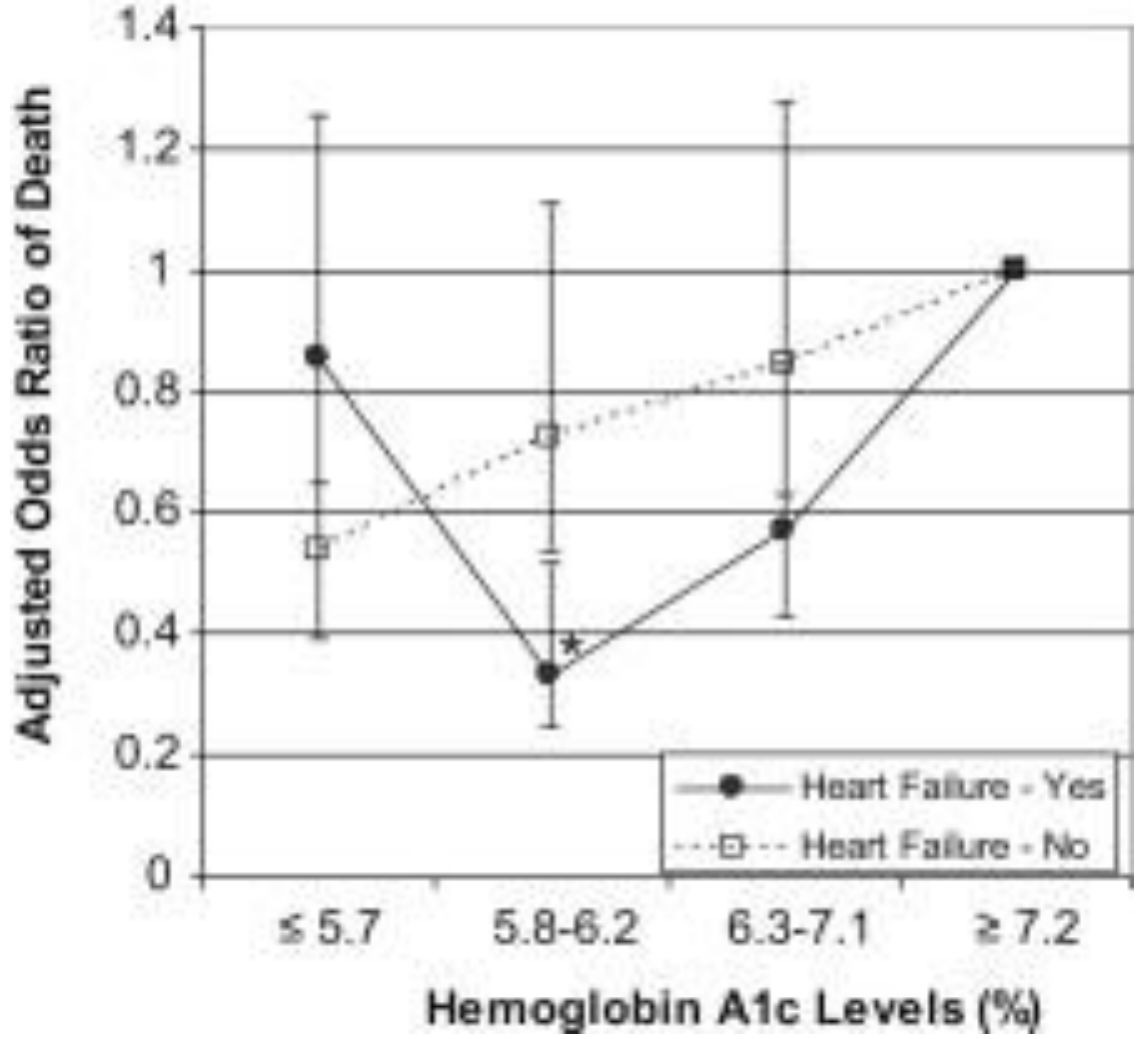
Individualise

Consensus is to aim for 7% (53 mmol/mol)

Elderly, living alone: probably 60-70 mmol/mol

Terminal cancer/advanced dementia: Aim is to reduce osmotic sympts

HbA1c and mortality



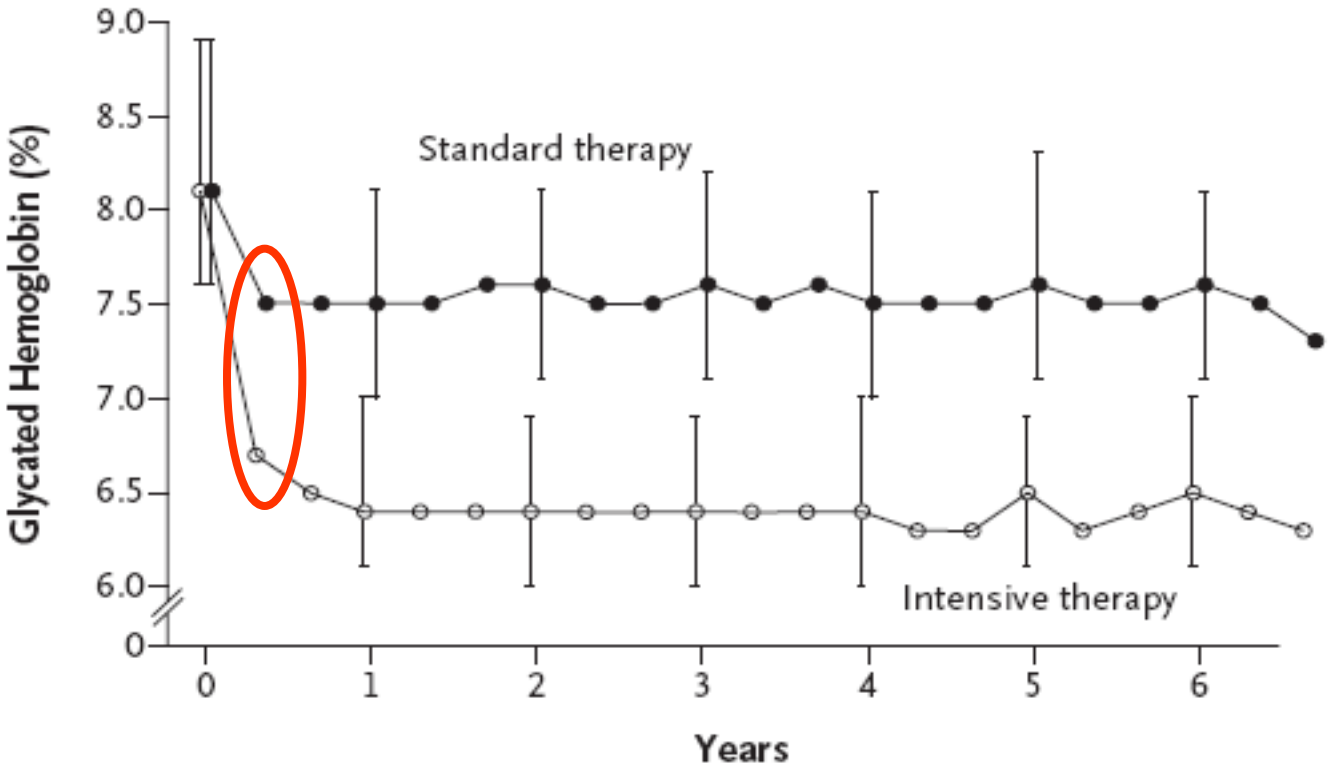
AJC 2013; vol 111; 1209-1213

ACCORD

- 10251 high risk T2DM patients
- Intensive arm target HbA1c < 6%
- Primary: nonfatal MI or stroke or death from CV causes. Secondary: Death from any cause
- **STOPPED 17 months early as increased CV deaths with intensive tx**

The Action to Control Cardiovascular Risk in Diabetes Study Group. NEJM. 2008; 358:2545-2559

Glycaemic control in ACCORD



No. at Risk							
Standard therapy	5109	4774	4588	3186	1744	455	436
Intensive therapy	5119	4768	4585	3165	1706	476	471

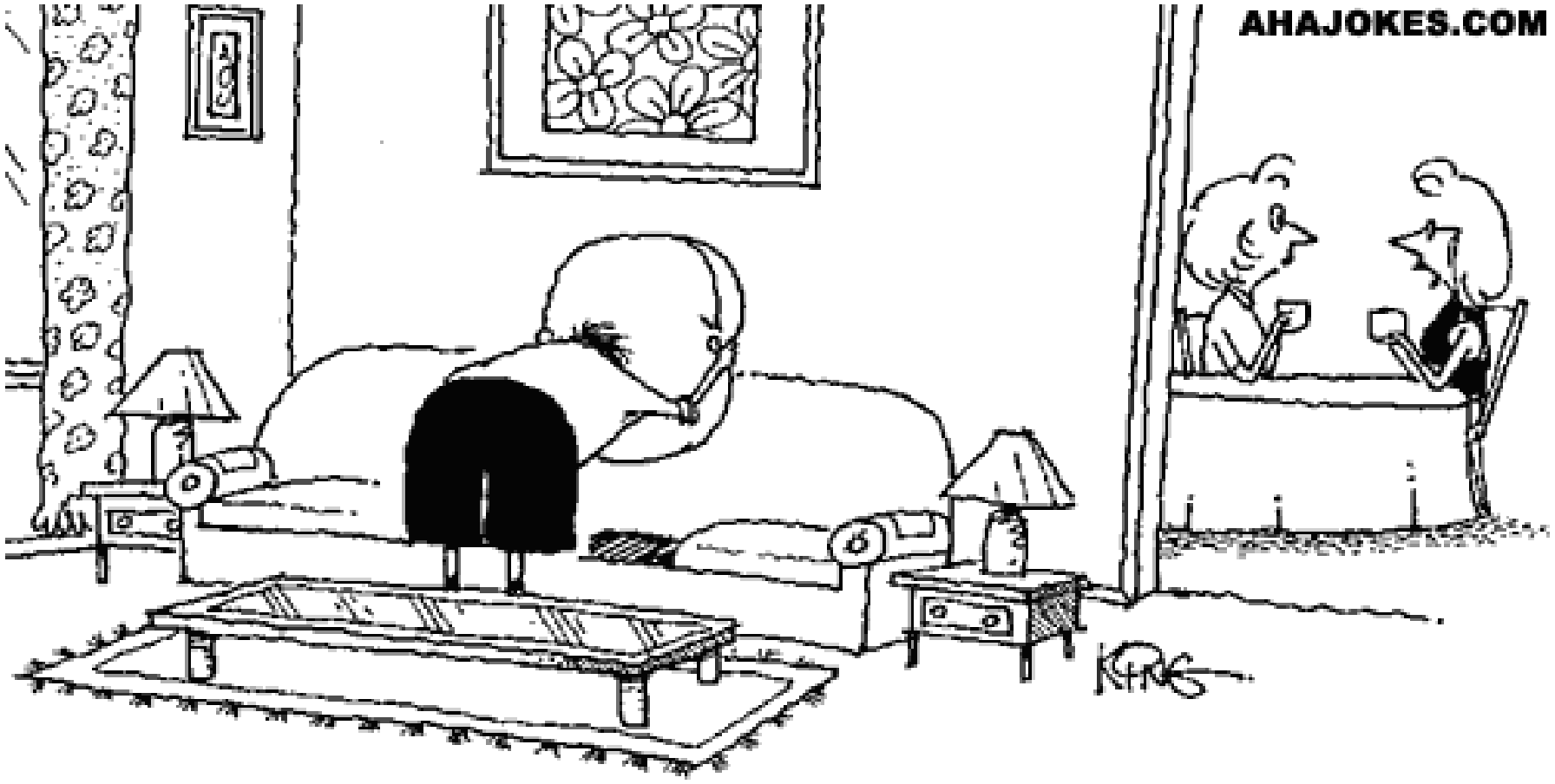
The Action to Control Cardiovascular Risk in Diabetes Study Group. NEJM. 2008; 358:2545-2559

Adverse events

Table 3. Adverse Events, Clinical Measures, Tobacco Use, and Use of Nonglycemic Medication after Randomization.*

Variable	Intensive Therapy (N=5128)	Standard Therapy (N=5123)	P Value†
Adverse events			
Hypoglycemia — no. (%)			
Requiring medical assistance	538 (10.5)	179 (3.5)	<0.001
Requiring any assistance	830 (16.2)	261 (5.1)	<0.001
Fatal or nonfatal heart failure — no. (%)	152 (3.0)	124(2.4)	0.10
Motor vehicle accident in which patient was driver — no./total no. (%)	9/5033 (0.2)	14/5036 (0.3)	0.40
Any nonhypoglycemic serious adverse event — no. (%)	113 (2.2)	82 (1.6)	0.03
Fluid retention — no./total no. (%)‡	3541/5053 (70.1)	3378/5054 (66.8)	<0.001
Clinical measures			
Weight gain >10 kg since baseline — no./total no. (%)	1399/5036 (27.8)	713/5042 (14.1)	<0.001

The Action to Control Cardiovascular Risk in Diabetes Study Group. NEJM. 2008; 358:2545-2559



The doctor said he needed more activity. So I hide his T.V. remote three times a week.

Mr BK, 53 yrs, T2D for 6 years attends for annual rv

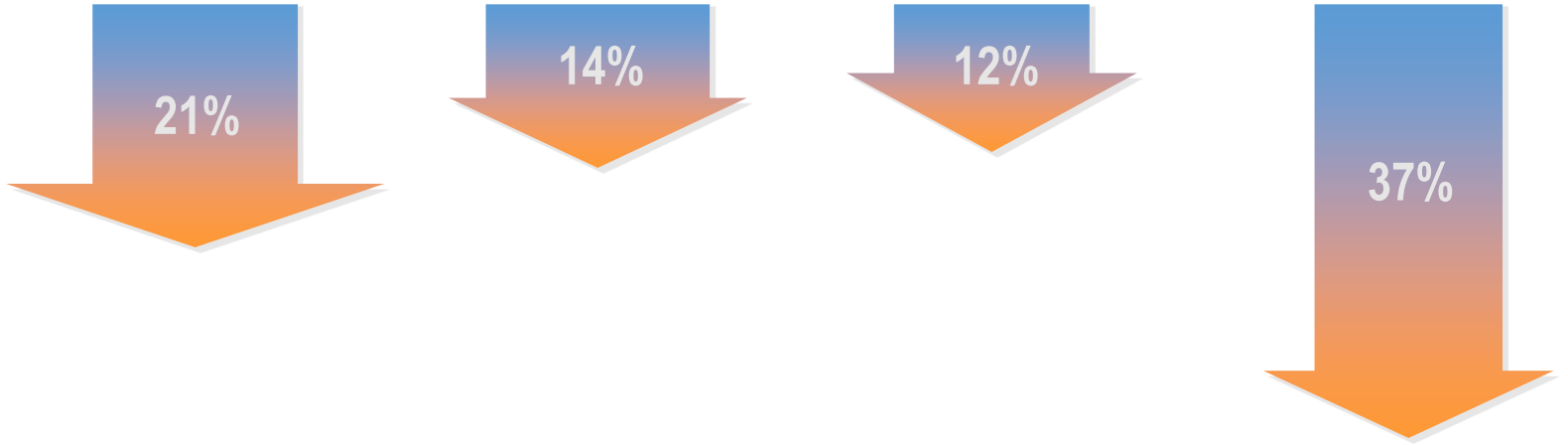
- BMI 33.2 kg/m2
- Known HT, Dyslip
- Retinal screening 6 mths ago: R1M1 Lt eye, R1M2 Rt eye
- Urinary ACR 7.7 g/mmol (<2.5)
- Feet normal

What HbA1c target would you set for this man?

1. <50 mmol/mol
2. 50-60 mmol/mol
3. 60-70 mmol/mol
4. Below 70 mmol/mol

Improved Glycemic Control Has Been Shown to Reduce the Risk of Complications

According to the United Kingdom Prospective Diabetes Study (UKPDS) 35, Every 1% Decrease in A1C Resulted in:



Decrease in risk of any diabetes-related end point (*P*<.0001)

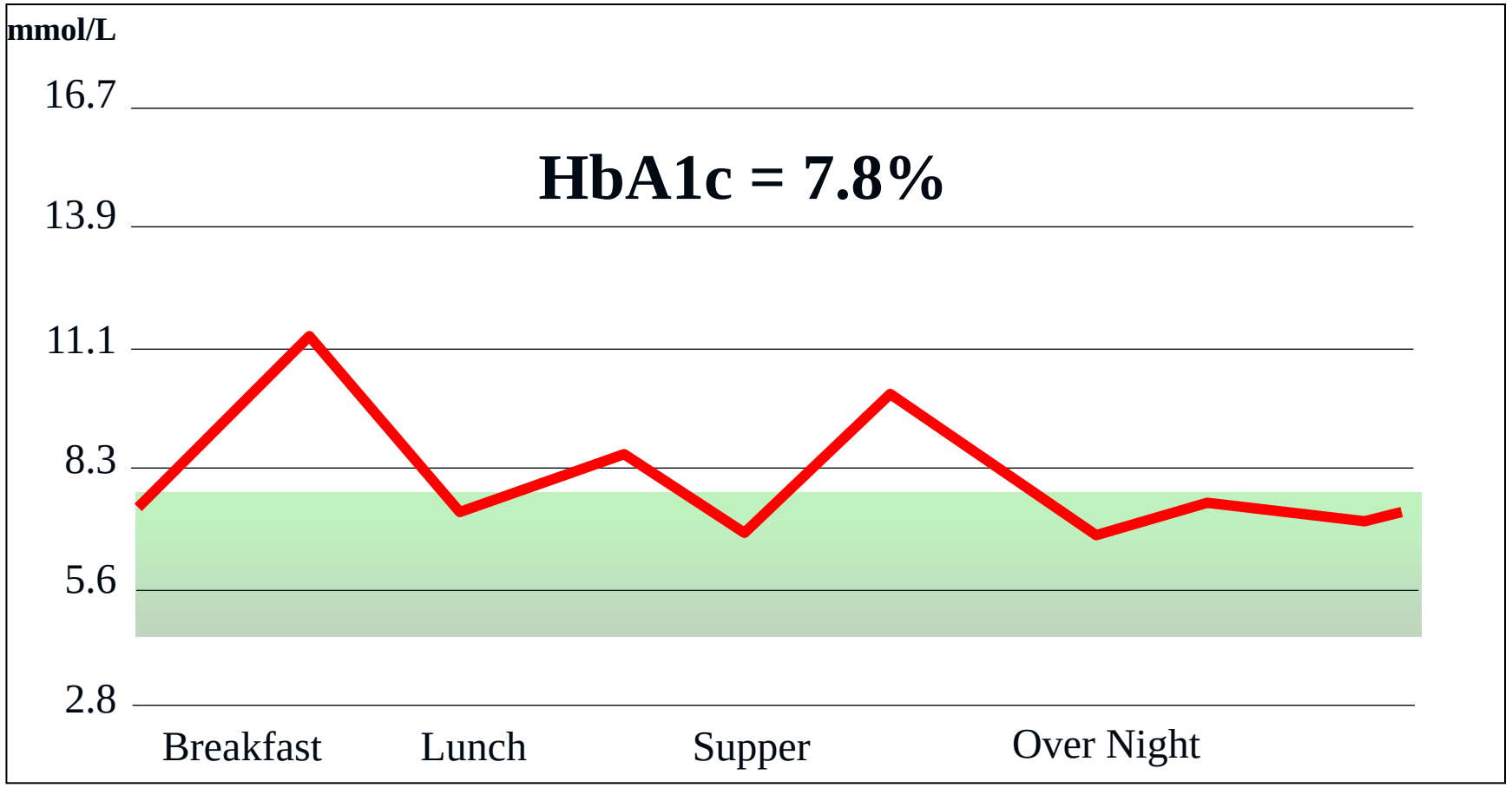
Decrease in risk of MI (*P*<.0001)

Decrease in risk of stroke (*P*=.04)

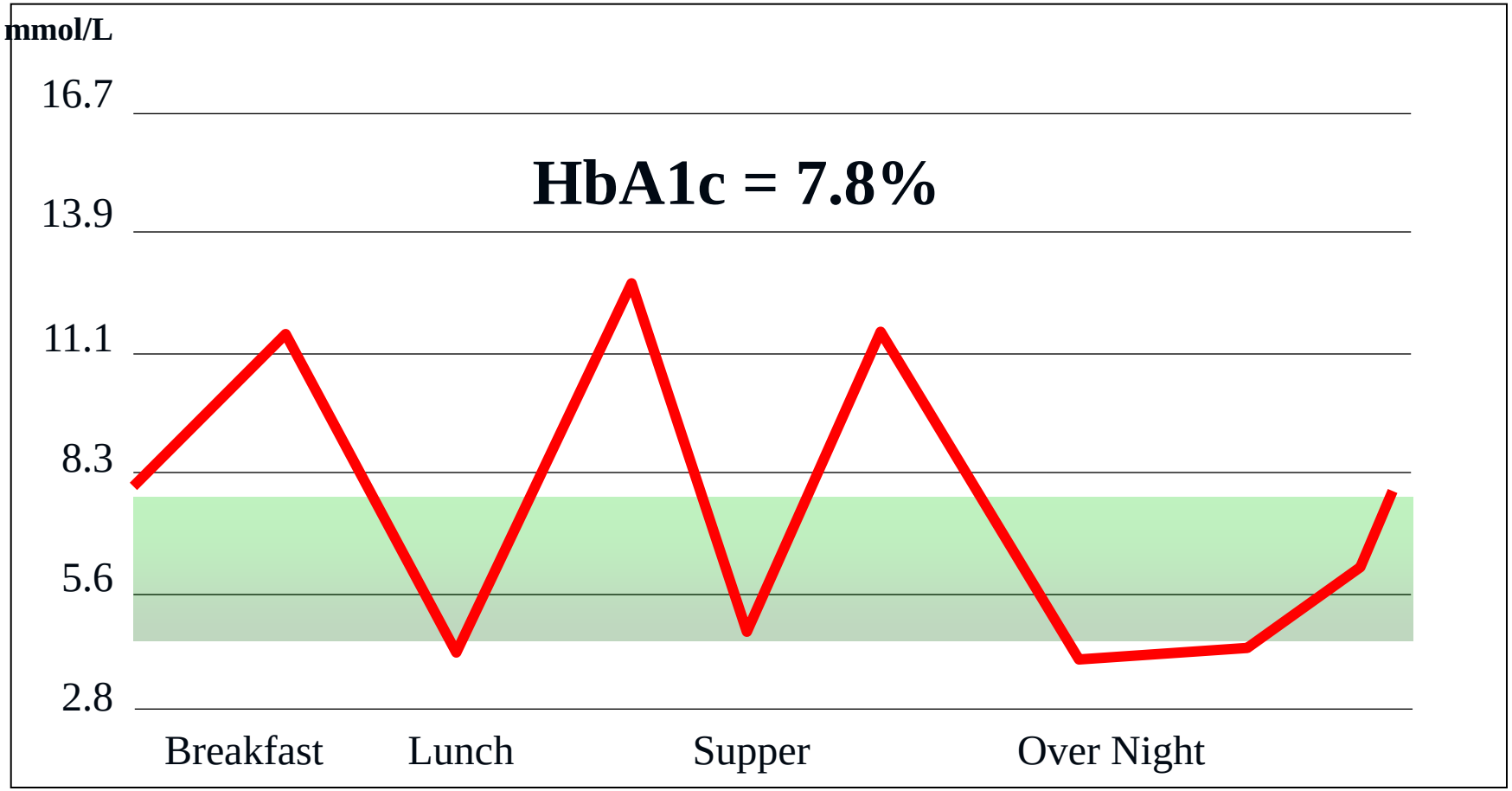
microvascular complications (*P*<.0001)

Stratton IM et al. *BMJ.* 2000;321:405-412.

HbA1c's are not created equal



HbA1c's are not created equal



What will you check before escalating/adding treatments?

1. Lifestyle measures
2. Compliance with medications
3. BG meter use
4. Recent illness/ steroid use
5. All of above

The Therapeutic challenge in managing type 2 diabetes

Ideally need treatments that:

- Can be used in presence of complications (eg kidney failure, heart disease)
- Acceptable to patients
- Minimise rather than worsen complications of diabetes
- (preferably) not increase weight
- (ideally) not cause hypos

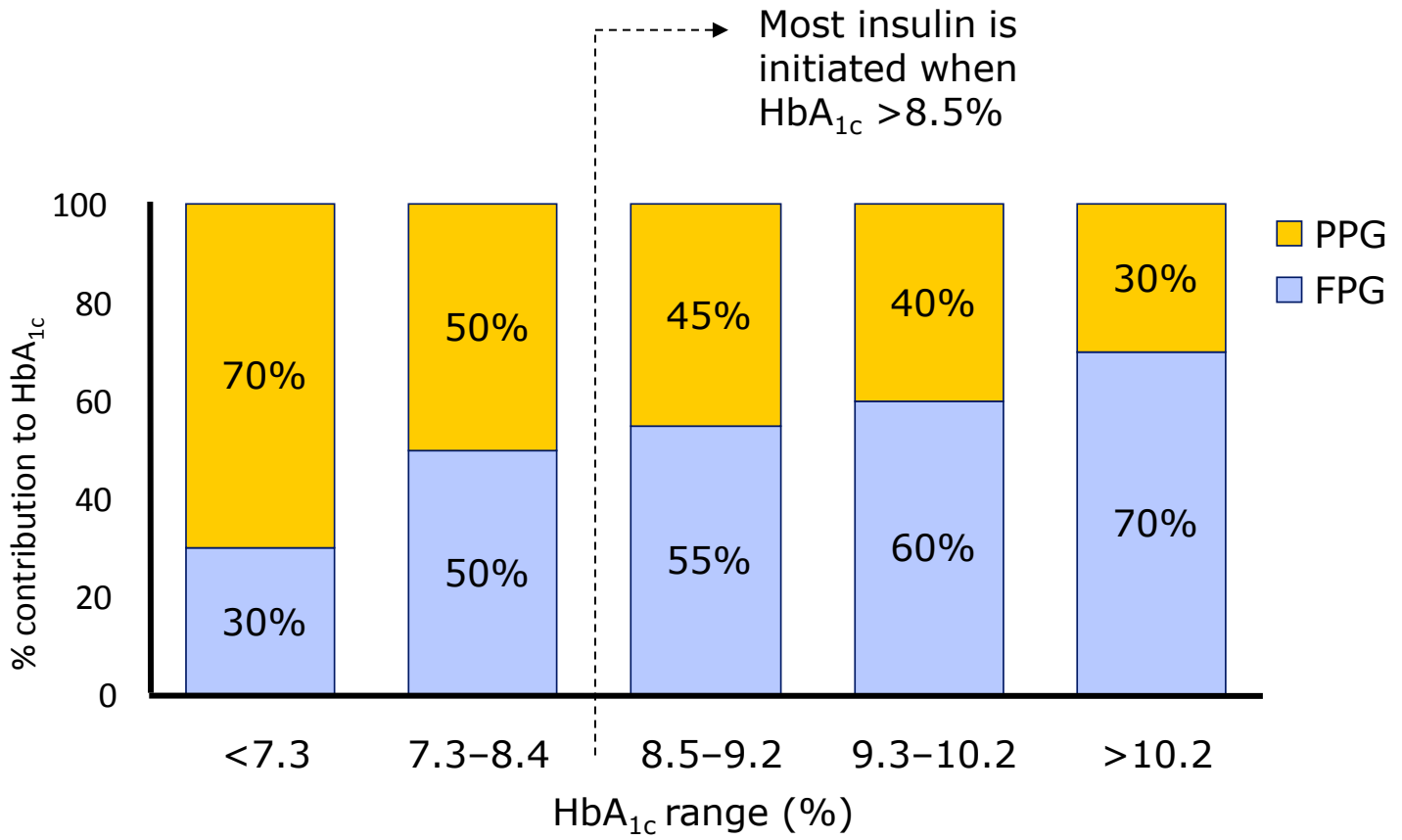
What insulin to initiate?

Limitations of clinical trials on insulin therapy

- ALL ARE OPEN LABELLED
- Protocols differ
- Adherence factors need to be considered

But how do we keep things safe and simple?

Fix the Fasting First



Monnier L *et al. Diabetes Care* 2003;26:881–5

TREATING TO TARGET IN TYPE 2 DIABETES

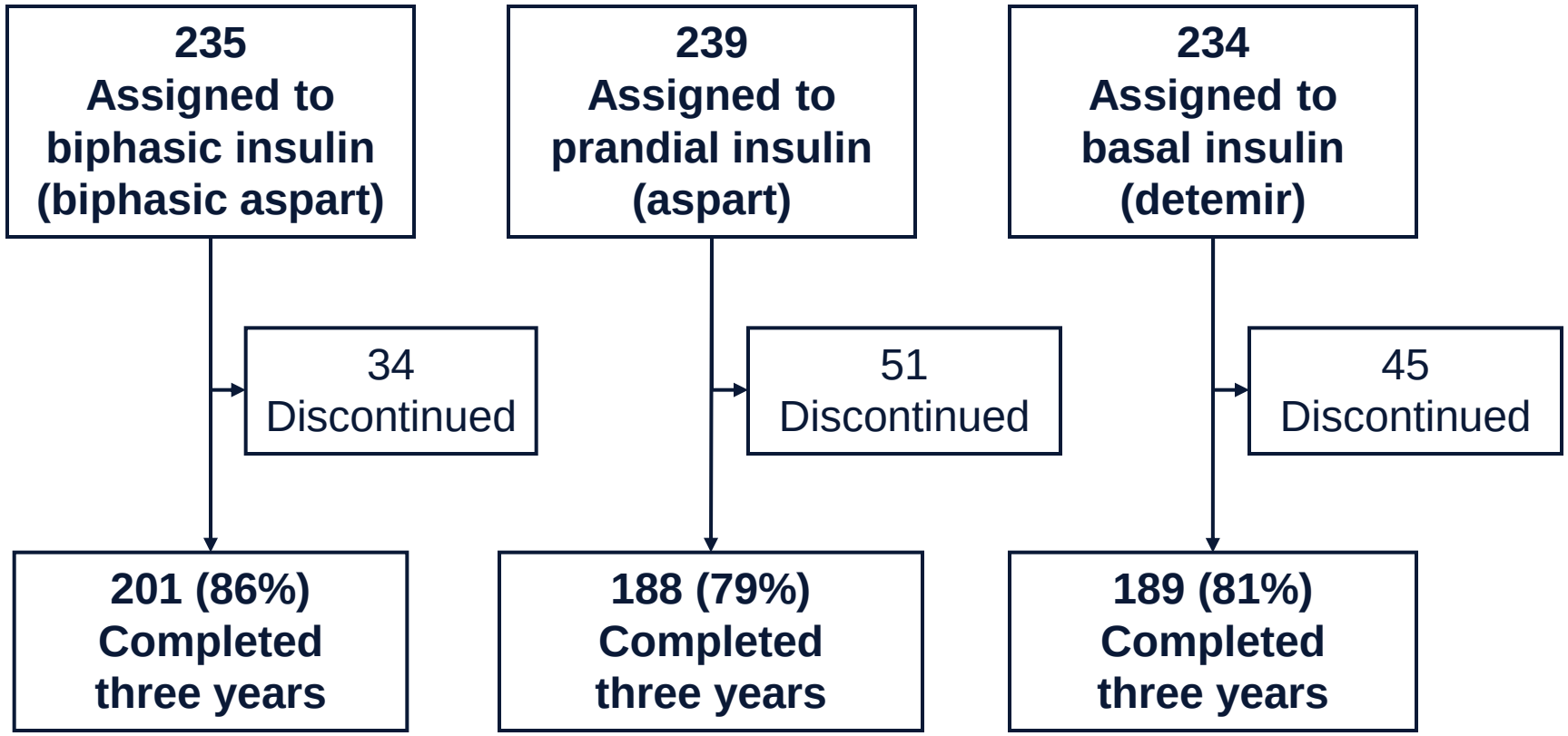
N Engl J Med 2007; 357: 1716-30

Major Inclusion Criteria

- Adults with Type 2 diabetes for one year or more
- On maximal tolerated metformin and sulfonylurea
- HbA_{1c} 7.0% to 10.0% inclusive
- Body mass index not more than 40 kg/m^2

N Engl J Med 2007; 357: 1716-30

Patient Disposition

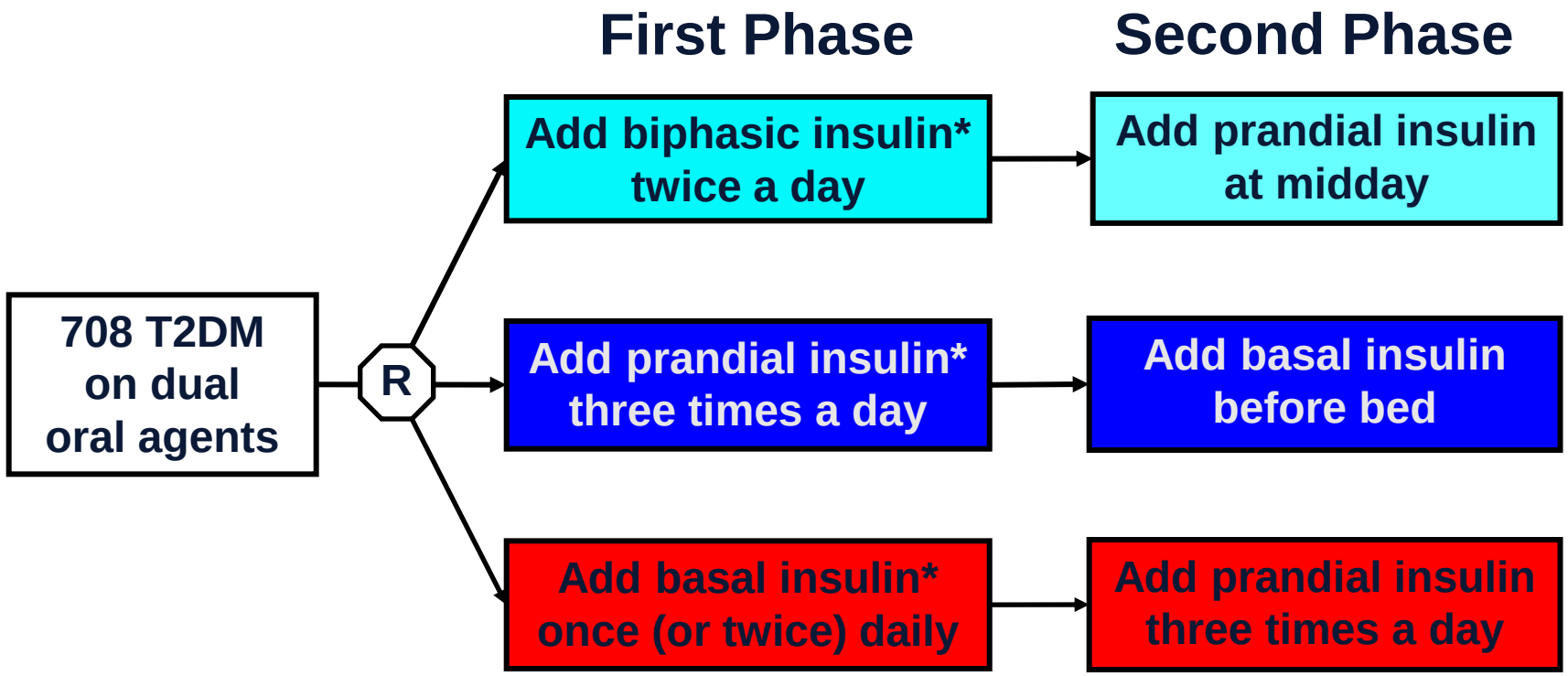


- Overall, 18.4% of patients did not complete three years
- No difference in proportions between groups (p=0.15)
- No difference in baseline characteristics between those who completed or did not complete three years follow up

N Engl J Med 2007; 357: 1716-30

Transition to a Complex Insulin Regimen

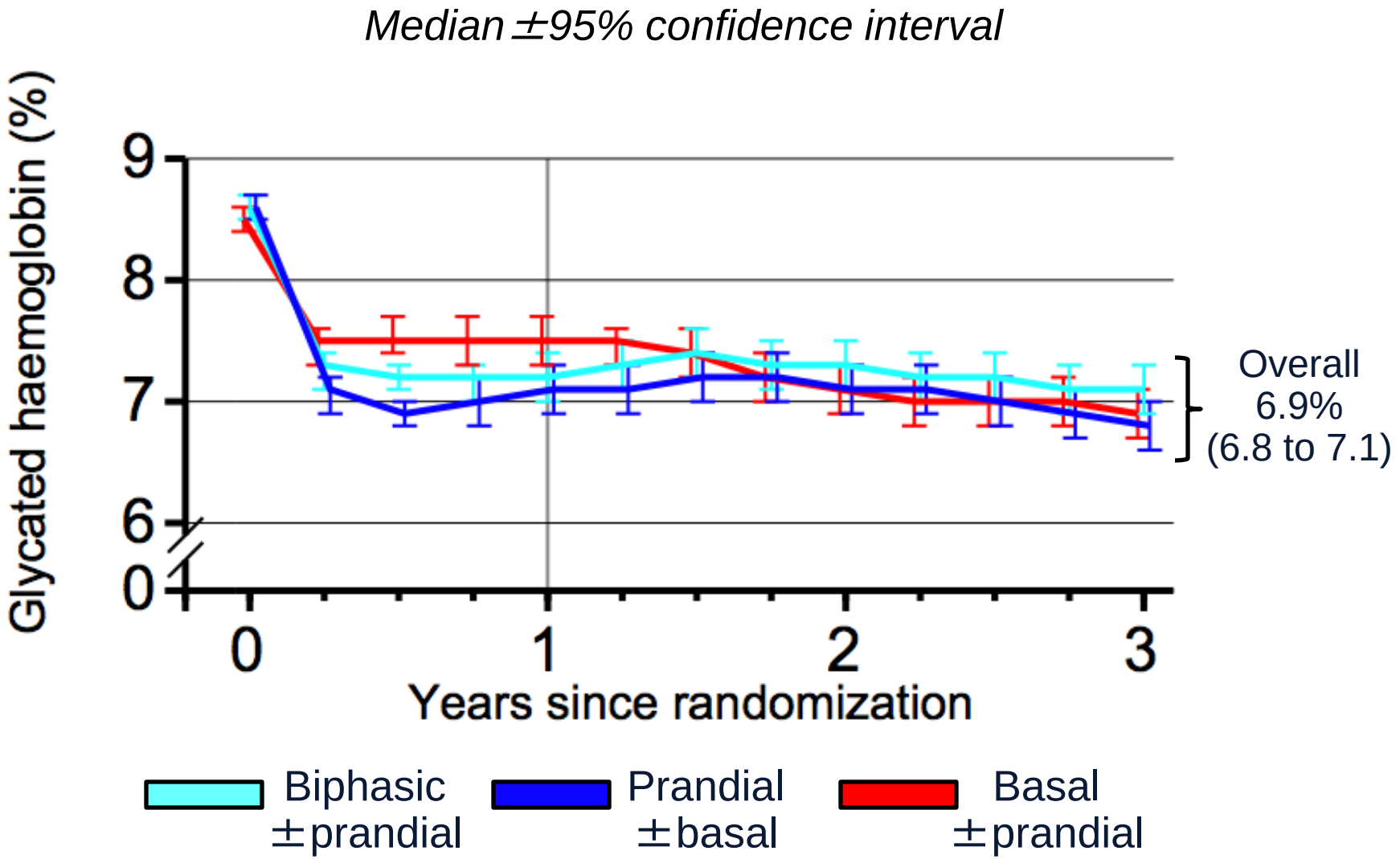
From one year onwards, if HbA_{1c} levels were >6.5%, sulfonylurea therapy was stopped and a second type of insulin was added



* *Intensify to a complex insulin regimen in year one if unacceptable hyperglycaemia*

N Engl J Med 2007; 357: 1716-30

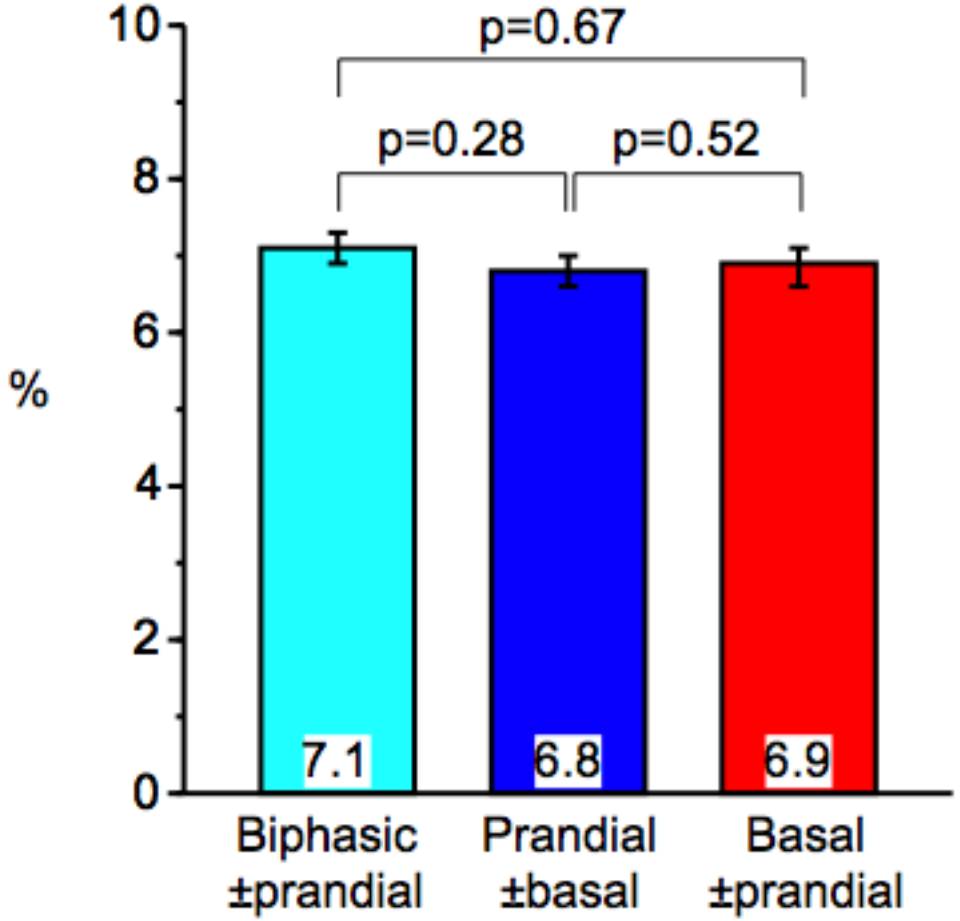
HbA_{1c} Values Over 3 Years



N Engl J Med 2007; 357: 1716-30

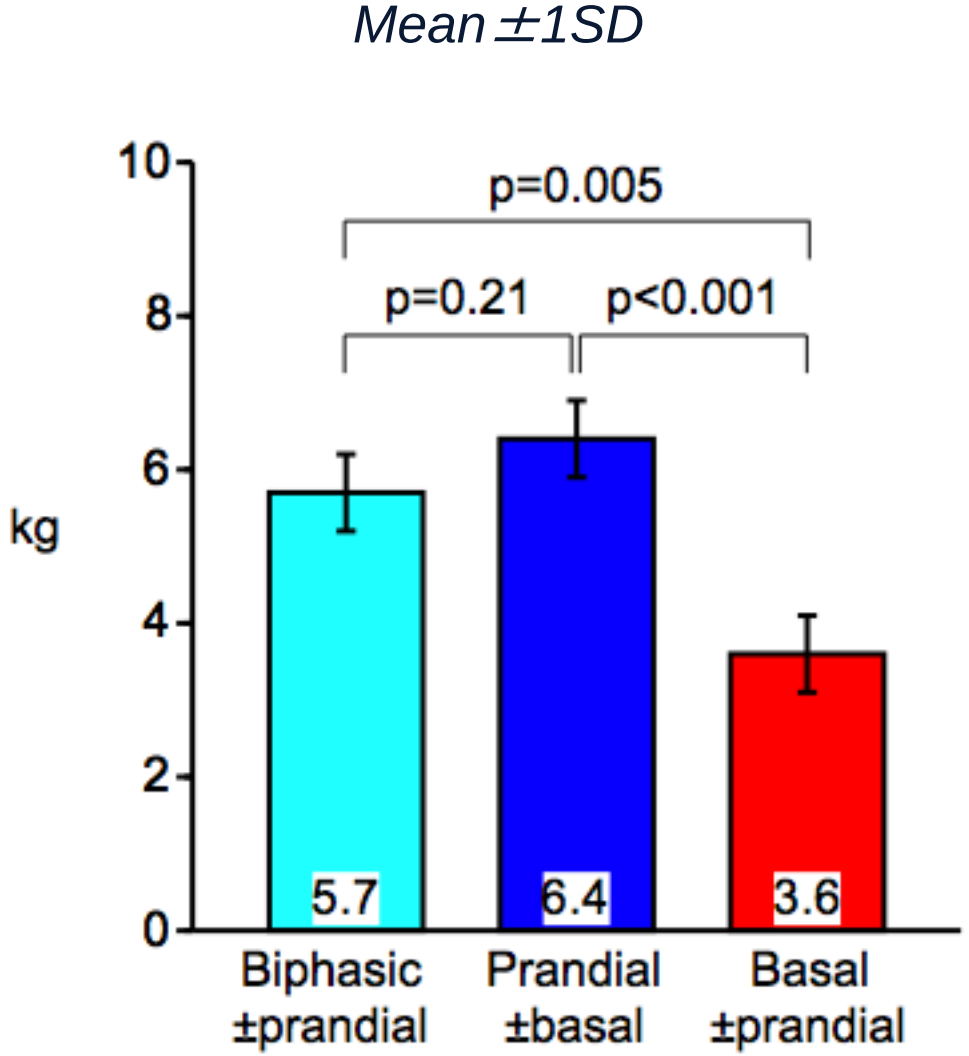
Primary Outcome: HbA_{1c} at 3 Years

Median ±95% confidence interval



N Engl J Med 2007; 357: 1716-30

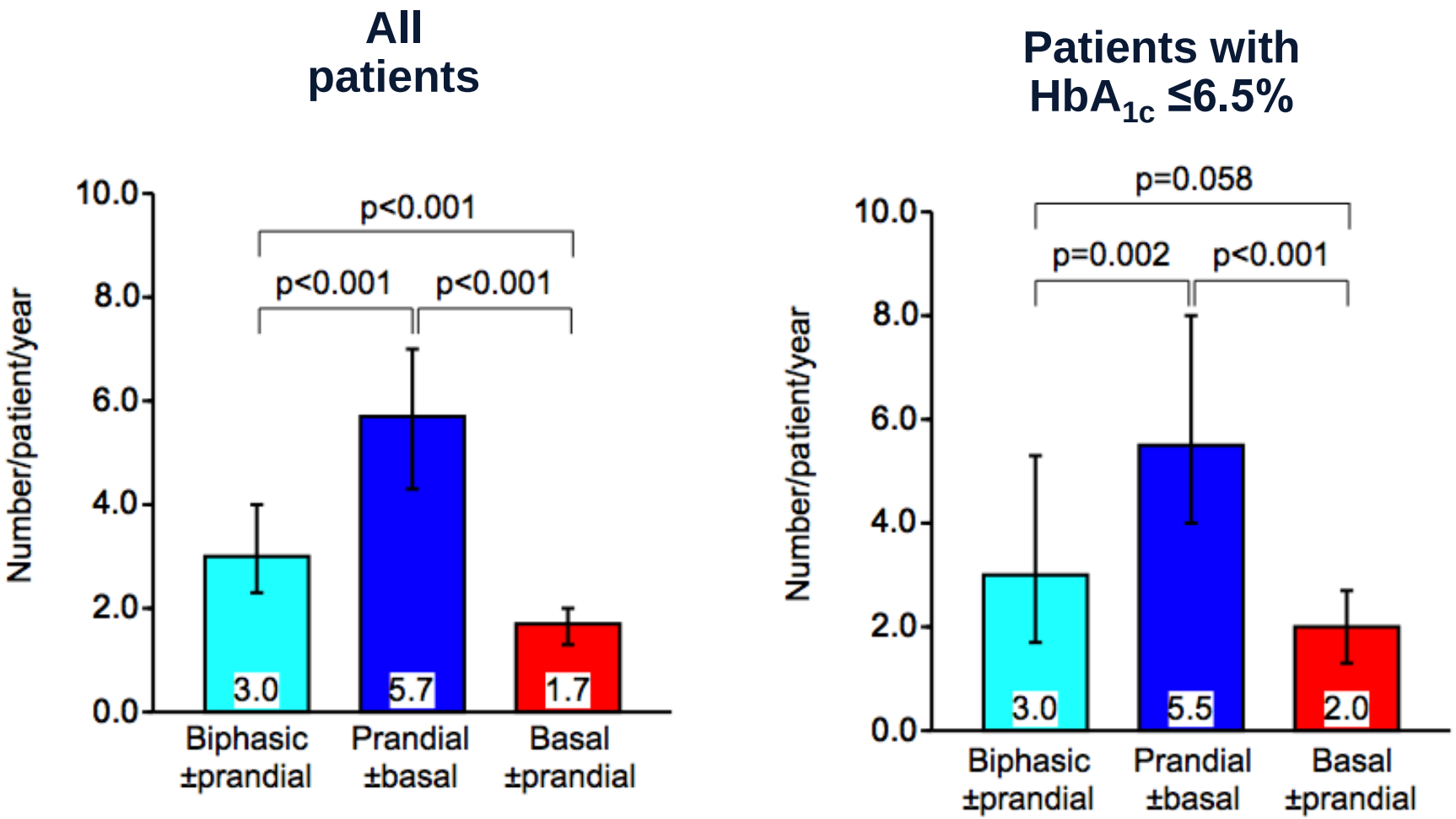
Increase in Body Weight Over 3 Years



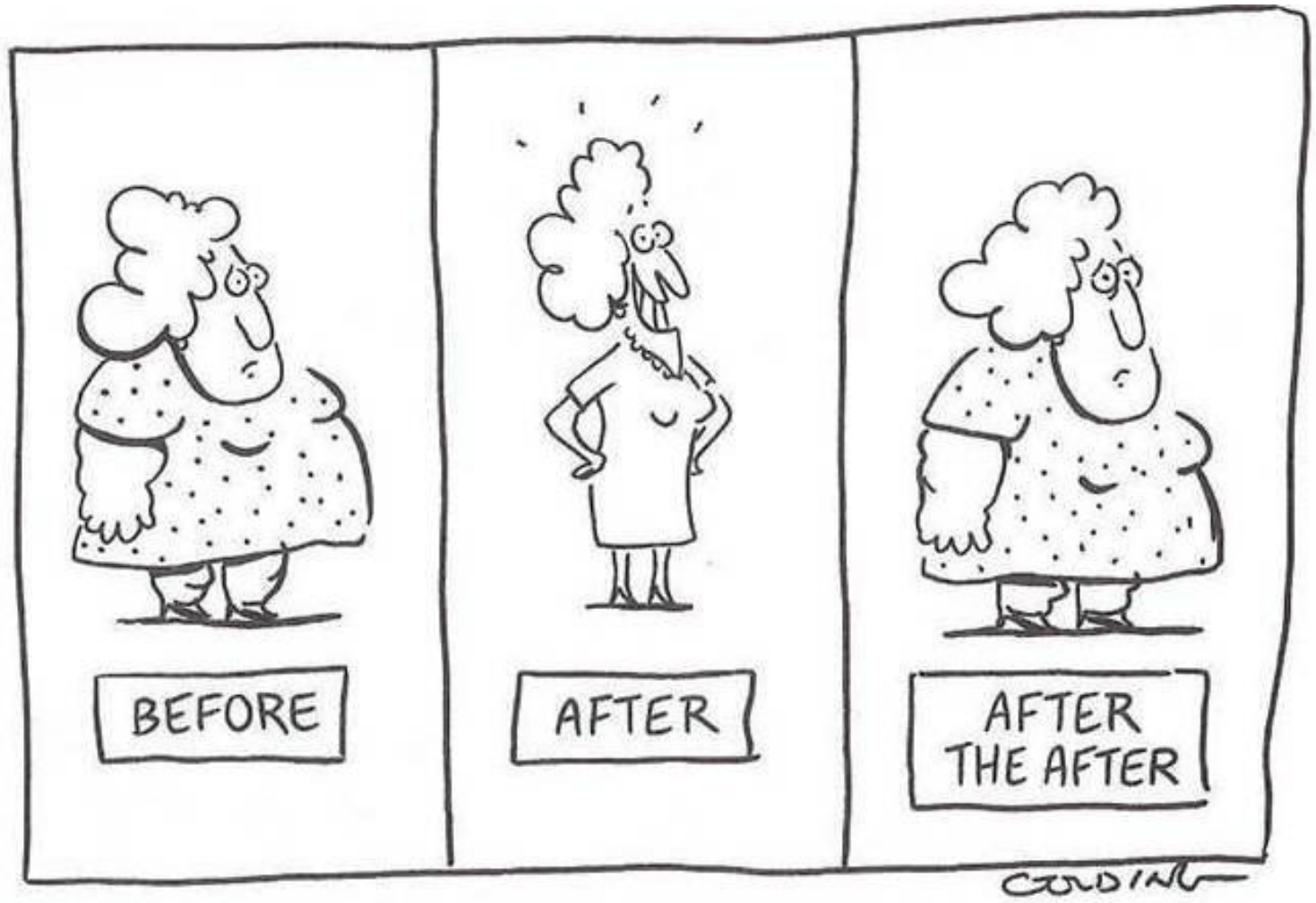
N Engl J Med 2007; 357: 1716-30

Grade 2 or 3 Hypoglycaemia Over 3 Years

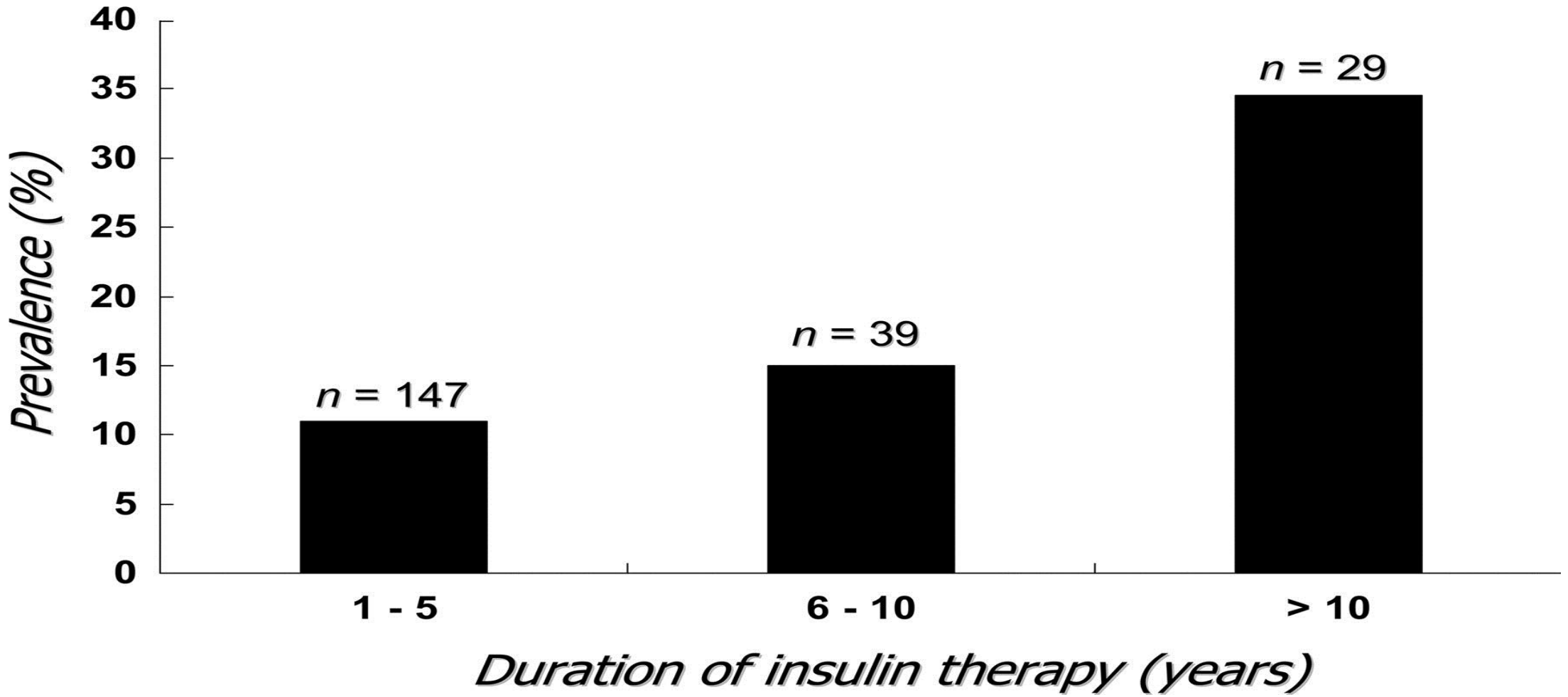
Median ±95% confidence interval



N Engl J Med 2007; 357: 1716-30


BEFORE
AFTER
AFTER
THE AFTER
GOLDING

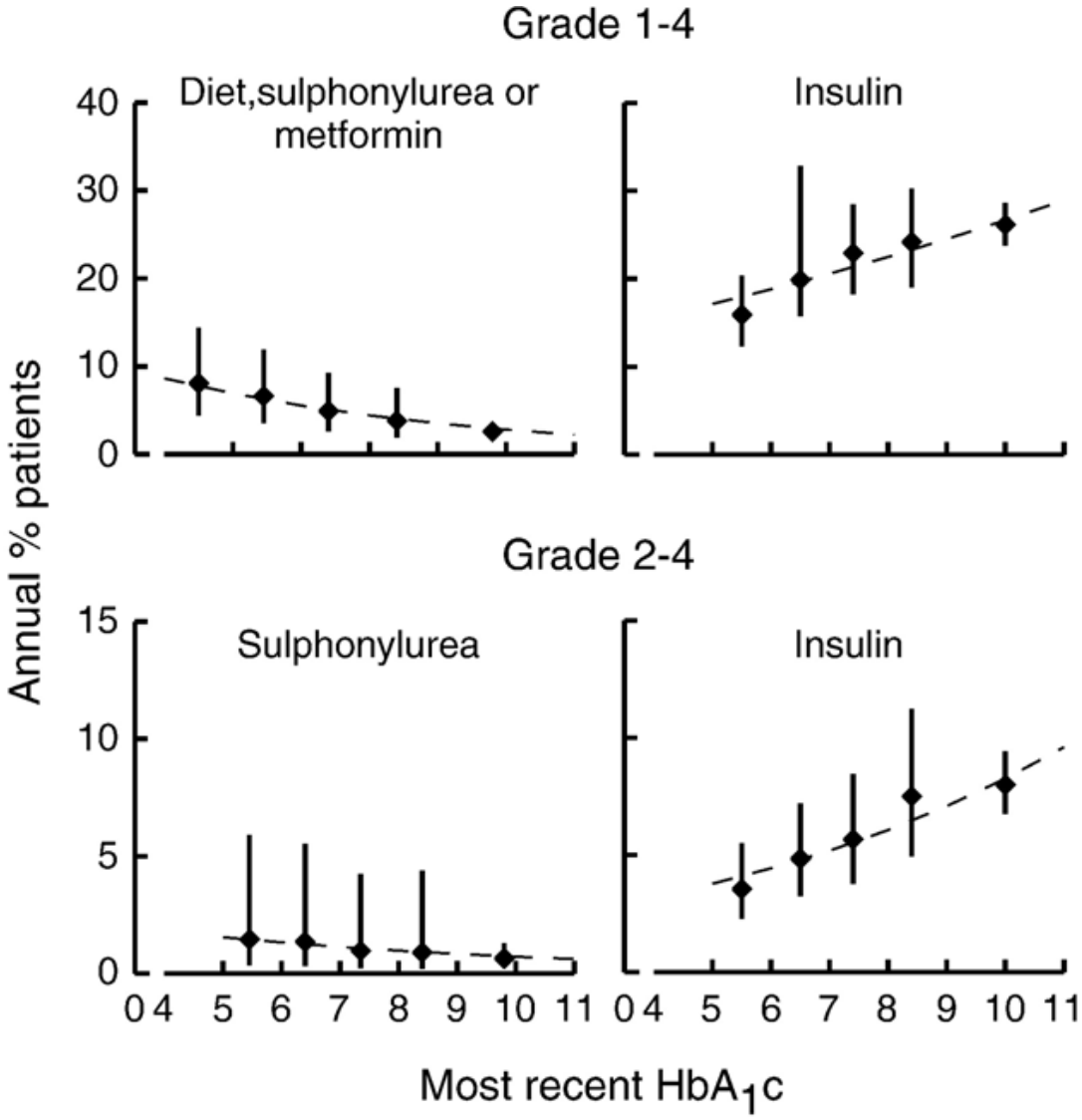
The prevalence of severe hypoglycemia in relation to the duration of type 2 diabetes.



Chiasson J Dia Care 2009;32:S270-S274

American Diabetes Association.

Hypoglycaemia risk in T2D- UKPDS73

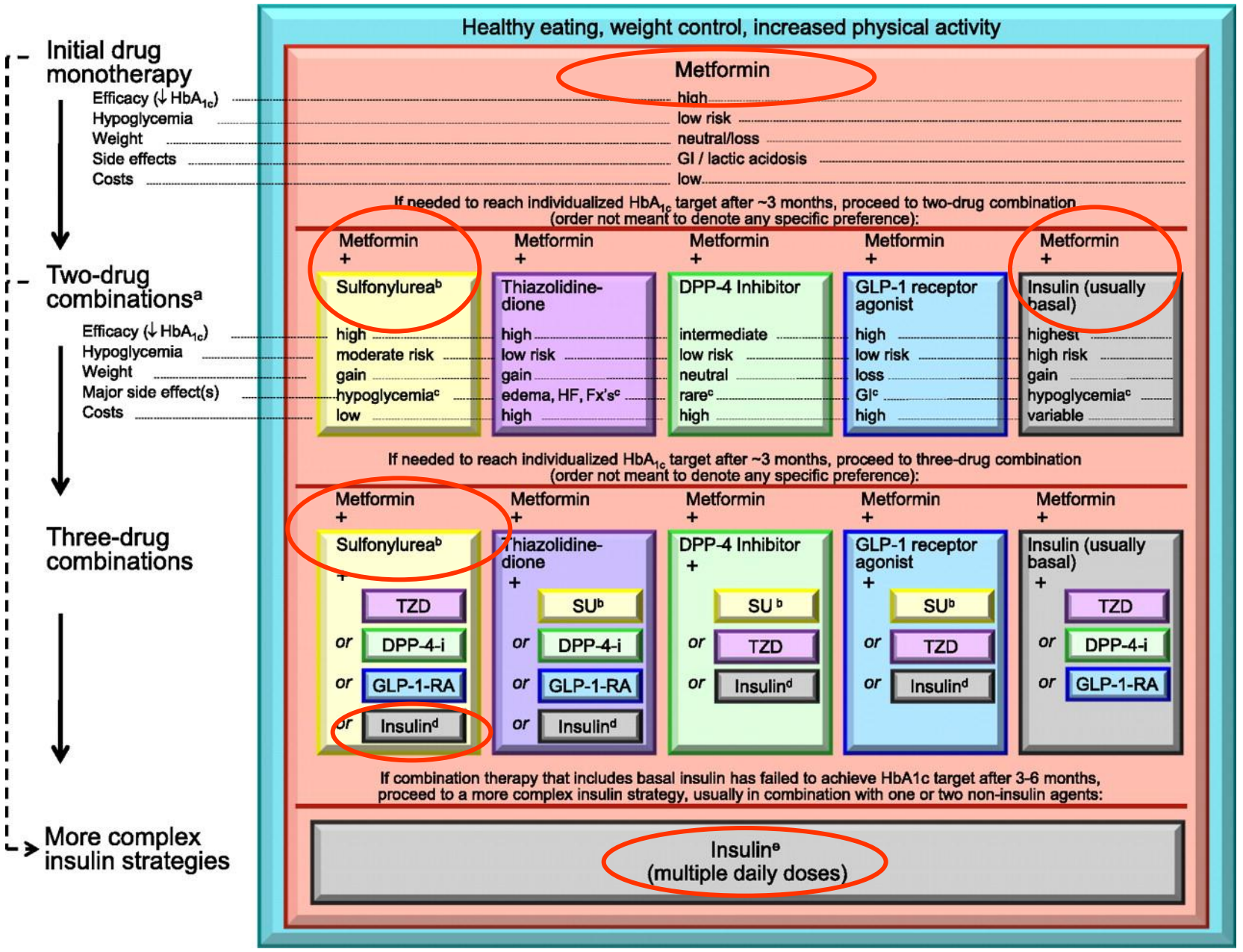


Hypoglycaemia risk increases with time in T2D

Early T2D

Late T2D

Position Statement ADA/EASD 2012



Inzucchi S E et al. Dia Care 2012;35:1364-1379

Summary

- Most patients with type 2 diabetes will eventually need insulin.
- Timely initiation of insulin is important.
- Fix the fasting first to keep things safe and simple.
- Once OHAs fail, good evidence supporting insulin initiation with a basal insulin as less weight gain and hypoglycaemic episodes.