Challenges in the management of Type 2 Diabetes: Insulin Therapy

Type 2 DM Insulin Initiation Therapy : Rationale

Type 2 diabetes is a *progressive* condition with the majority of patients requiring insulin therapy in the longer term

The rapidly rising diabetes prevalence means that *insulin initiation* will increasingly be undertaken in primary care

There is currently no evidence-based consensus about how best to initiate insulin therapy, and in particular *which insulin preparation should be advocated.*

Type 2 DM : Insulin Initiation Therapy Strategies

Initiating Insulin Therapy - OPTIONS

Basal insulin

Prandial insulin

Premixtures of insulins

Basal plus bolus (prandial) insulin

+/- Oral hypoglycaemic agents

TARGETS*: HbA1c<7% (<6.5%), FBG<5.6mM, PPBG<7.8mM * individualise

Type 2 DM : Insulin Initiation Therapy Strategies

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes

Holman et al for the 4-T Study Group
N Engl J Med 2007;357:1716-30

Once-daily basal insulin glargine versus thrice-daily prandial insulin lispro in people with type 2 diabetes on oral hypoglycaemic agents (APOLLO) : an open randomised controlled trial

Bretzel et al Lancet 2008;371:1073-84

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study group)

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Trial Design :

Three-arm trial in 708 patients with type 2 diabetes from 58 centres in UK and Ireland

Evaluating addition of three different analogue insulin regimens to dual oral hypoglycaemic therapy (sulphonylurea and metformin)

Open-label randomisation to:

1. Twice a day biphasic insulin (NovoMix 30) n=222 or
2. Three times a day prandial insulin (NovoRapid) n=222 or
3. Once a day basal insulin (detemir) before bed, with a morning injection added if necessary n=224

sc injections using 3 ml disposable-pen devices (FlexPen)

TREATING TO TARGET IN TYPE 2 DIABETES

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Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Year 1
Comparison of three single insulin regimens, added to OHAs*

Years 2 and 3
If HbA_{1c} >6.5%, stop sulfonylurea and add a second insulin formulation

708 T2DM on dual OAD

R

- Add biphasic insulin twice a day → Add prandial insulin at midday
- Add prandial insulin three times a day → Add basal insulin before bed
- Add basal insulin once (or twice) daily → Add prandial insulin three times a day

Male = [(FPG [mM]–5)x2] x weight [kg] ÷ (14.3*x height [m]-height [m]); F*13.2

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

TREATING TO TARGET IN TYPE 2 DIABETES

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Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Sample Size

700 patients required to detect a 0.4% difference in achieved HbA_{1c}, allowing for 15% loss to follow up

Statistical Methods

Missing data handled by multiple imputation

Analyses by intention to treat (ITT)

Mixed-effect regression or logistic models used to compare treatment groups overall

Closed-test procedure allows pair wise comparisons when overall treatment effect was significant

TREATING TO TARGET IN TYPE 2 DIABETES

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Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Primary at 1 year

To compare HbA_{1c} levels achieved by the three regimens

Secondary outcomes at 1 year include:

Proportion achieving HbA_{1c} ≤6.5% with or without 'hypos'*

Proportion with unacceptable hyperglycaemia

i.e. HbA_{1c} >10% or 2 successive values >8.5% at ≥ 24 wks

Rates of hypoglycaemic events

Eight-point self-measured capillary blood glucose (SMBG)

Proportion requiring twice daily basal insulin (detemir)

Impact on body weight

Quality of Life (EQ-5D) – EuroQol self-reported Q**nnaire**

* weeks 48-52

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Major Inclusion Criteria

Aged 18 years or more,
Type 2 diabetes ≥ 1 years
On maximal tolerated doses of metformin + sulfonylurea for ≥ 4 months
HbA_{1c} 7.0% to 10.0% inclusive
Body mass index ≤ 40 kg/m^2
Written informed consent

Major Exclusion Criteria

Taking insulin therapy
Taking TZD or triple oral antidiabetic agents within the previous 6 months
Plasma creatinine >130 µmol/l
ALT ≥2x upper limit of normal
Life threatening CV Disease
Lactating or potentially pregnant females, severe retinopathy

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

- Hypoglycaemia :
  - Grade 1: symptoms only (glucose 3.1 mmol/l or more)
  - Grade 2: symptoms with glucose <3.1 mmol/l
  - Grade 3: third party assistance required
- Safety Measures :
  - Unexpected and/or serious adverse events
  - Plasma ALT, creatinine and lipid levels
  - Blood pressure
  - Metformin discontinued if plasma creatinine
  - ≥150 µmol/l on two successive occasions
  - Data Safety Monitoring Board

TREATING TO TARGET IN TYPE 2 DIABETES

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Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Insulin Initiation and Titration

Starting dose : men [(fasting plasma glucose (mmol/l) – 5) X 2]
X weight (kg)] ÷ (14.3 X height (m) – height (m)]
women [fasting plasma glucose (mmol/l) – 5) X2]
X weight (kg) ÷ (13.2 X height (m) – height (m)]

Clinic visits : scheduled at 2, 6, 12, 24, 38 and 52 weeks preceded by 3 capillary glucose profiles
(i) biphasic and basal insulin groups
pre-breakfast and pre-evening meal
(ii) prandial insulin group
pre-meals, 2 hr postprandial & bedtime

Targets : pre-meal 72-99 mg/dl (4.0-5.5 mmol/l)
2 hour postprandial 90-126 mg/dl (5.0-7.0 mmol/l)

TREATING TO TARGET IN TYPE 2 DIABETES

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Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Insulin Dose Titration :

The online Trial Management System suggested dose adjustments using a common algorithm for all groups

Doses increased if 1/3 or more of glucose values were above target, and in proportion to the gap from target

Doses reduced in the presence of hypoglycaemia

Investigators encouraged to amend suggested doses, as necessary, on clinical grounds in consultation with patients

Patients also educated how to modify doses between visits

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Insulin Initiation and Titration

Insulin : Morning basal-insulin introduce when FPG at target but not pre-evening meal PG and when nocturnal hypoglycaemia limited increases at bed time

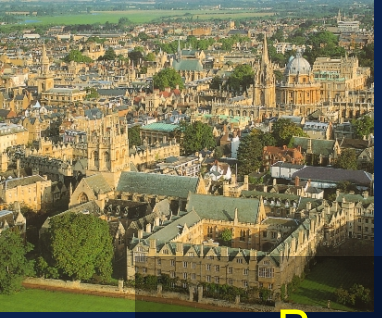
Hypoglycaemia :

Grade 1: symptoms with SMBG of 56 mg/dl (mmol/l)
Grade 2: *minor* – symptoms plus SMBG < 56 mg/dl
Grade 3; *major* – if third party assistance required

Hyperglycaemia : *Unacceptable* – HbA1c > 10% or 2 consecutive values ≥ 8% after 24 weeks, then second type of insulin added and sulfonylurea discontinued,
(i) prandial insulin added mid-day to biphasic insulin or thrice pre-prandially to basal insulin
(ii) add basal insulin to prandial insulin at bedtime

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30



Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Baseline Demography	Biphasic n=235	Prandial n=239	Basal n=234
Male	68%	64%	61%
White Caucasian	94%	90%	93%
Asian	5%	6%	4%
Black	1%	2%	1%
Other or mixed	<1%	2%	2%
Retinopathy	15%	19%	18%
Neuropathy	17%	23%	17%
Nephropathy	9%	10%	10%
Macroangiopathy	22%	18%	19%
On sulfonylurea	98%	100%	99%
On metformin	96%	95%	97%

No significant differences between groups

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Baseline Demography	Biphasic n=235	Prandial n=239	Basal n=234
Age (years)	61.7 ±8.9	61.6 ±10.5	61.9±10.0
Diabetes duration (years)*	9 (6-2)	9 (6-4)	9 (6-12)
Body weight (kg)	86.9 ±16.8	84.9 ±14.4	85.5 ±16.3
Body mass index (kg/m^2)	30.2 ±4.8	29.6 ±4.5	29.7 ±4.6
HbA_{1c} (%)	8.6 ±0.8	8.6 ±0.8	8.4 ±0.8
Fasting plasma glucose (mmol/l)	9.7 ±2.8	9.6 ±2.7	9.5 ±2.6
LDL cholesterol (mmol/l)	2.5 ±0.7	2.4 ±0.7	2.3 ±0.7
HDL cholesterol (mmol/l)	1.0 ±0.3	1.0 ±0.2	1.0 ±0.3
Triglycerides (mmol/l)*	1.6 (1.2-2.1)	1.5 (1.2-2.3)	1.5 (1.1-2.2)

*median interquartile range

No significant differences between groups

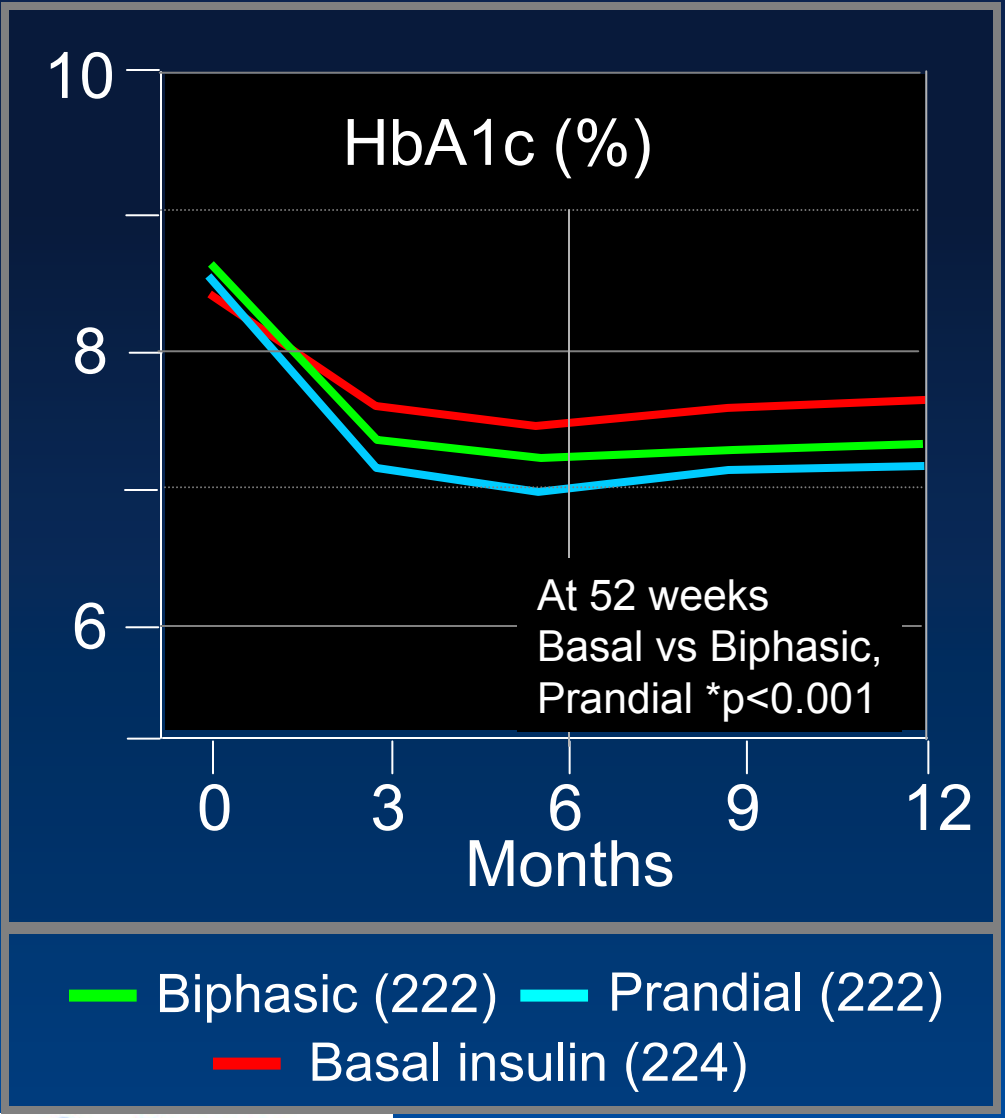
TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

TREATING
TO
TARGET IN
TYPE 2 DIABETES

ONE YEAR RESULTS

T2DM : Biphasic, Prandial or Basal Insulin (4-T)



	HbA1c (%)		
	0	1yr	delta
Biphasic	8.6	7.3	-1.3
Prandial	8.6	7.2	-1.4
Basal	8.4	7.6	-0.8*

HbA1c %	<7.0	<6.5
Prandial	49	24
Biphasic	42	17
Basal	28*	8*

Insulin dose U/d (kg)		
Prandial	56	0.61
Biphasic	48	0.53
Basal	42	0.48

TREATING TO TARGET IN TYPE 2 DIABETES

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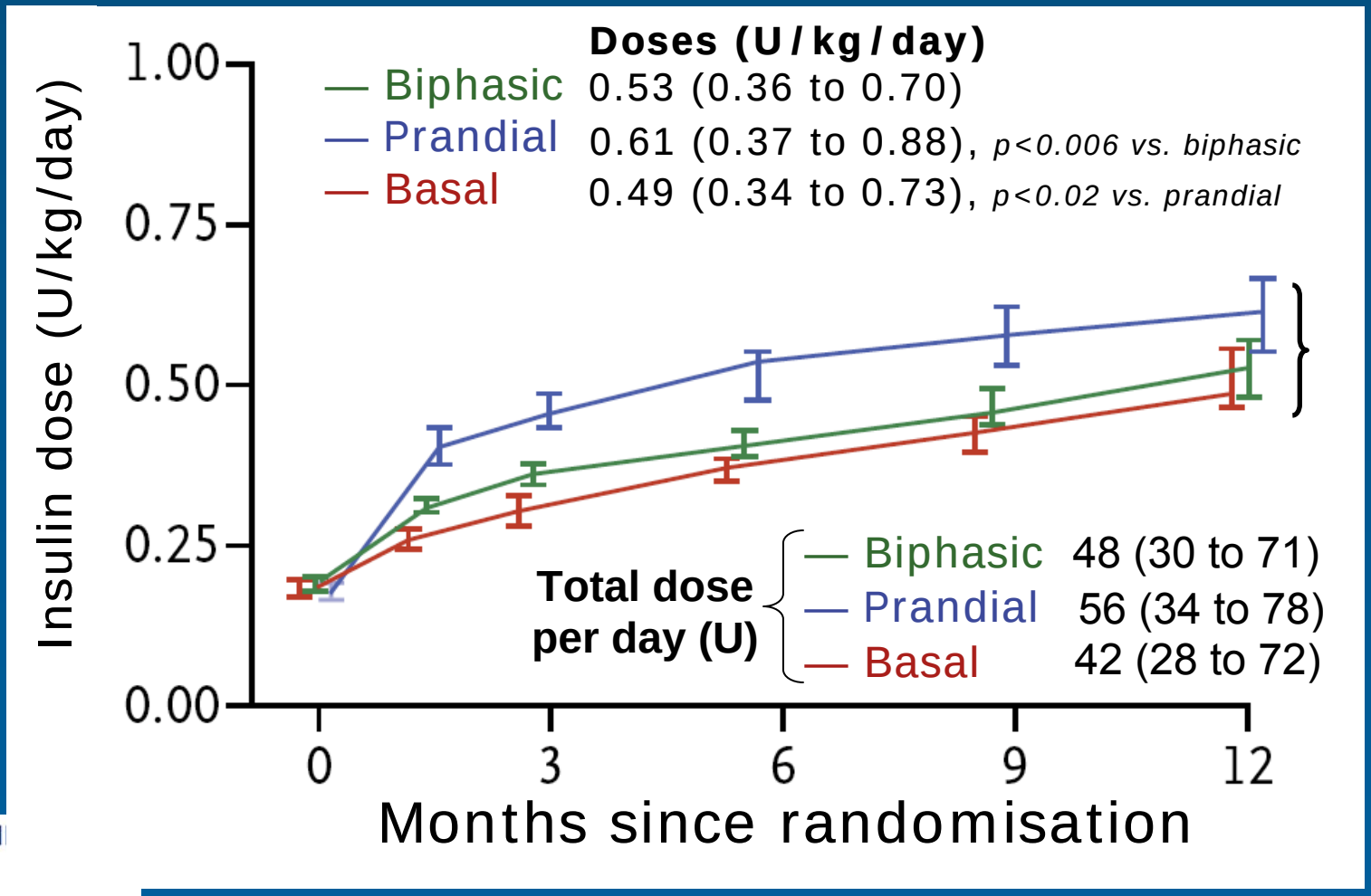
T2DM : Biphasic, Prandial or Basal Insulin (4-T)

Results : Insulin doses (median) at 1 year



TREATI TO TARGET IN TYPE 2 DIABETES

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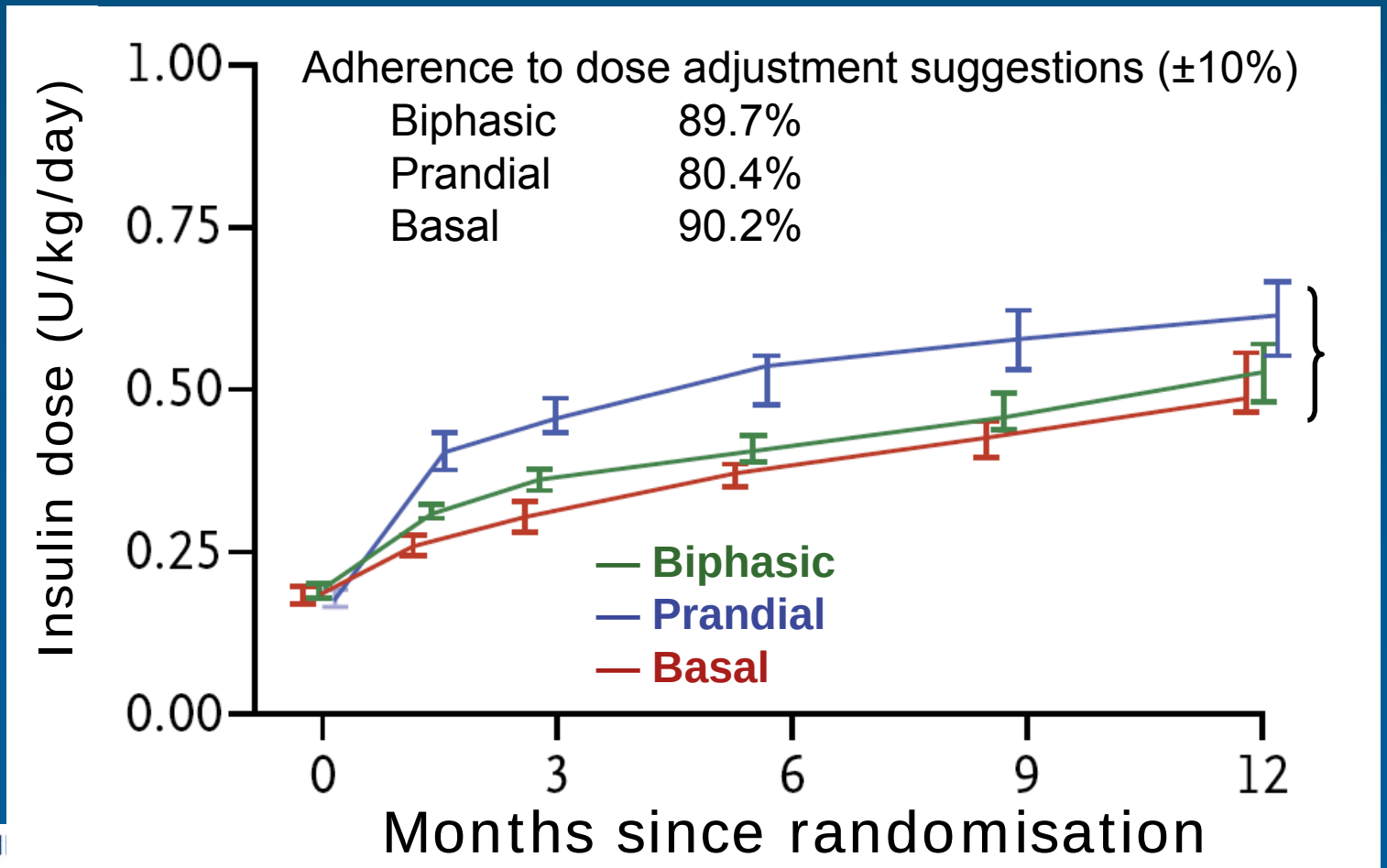
T2DM : Biphasic, Prandial or Basal Insulin (4-T)

Results : Insulin doses (median) at 1 year



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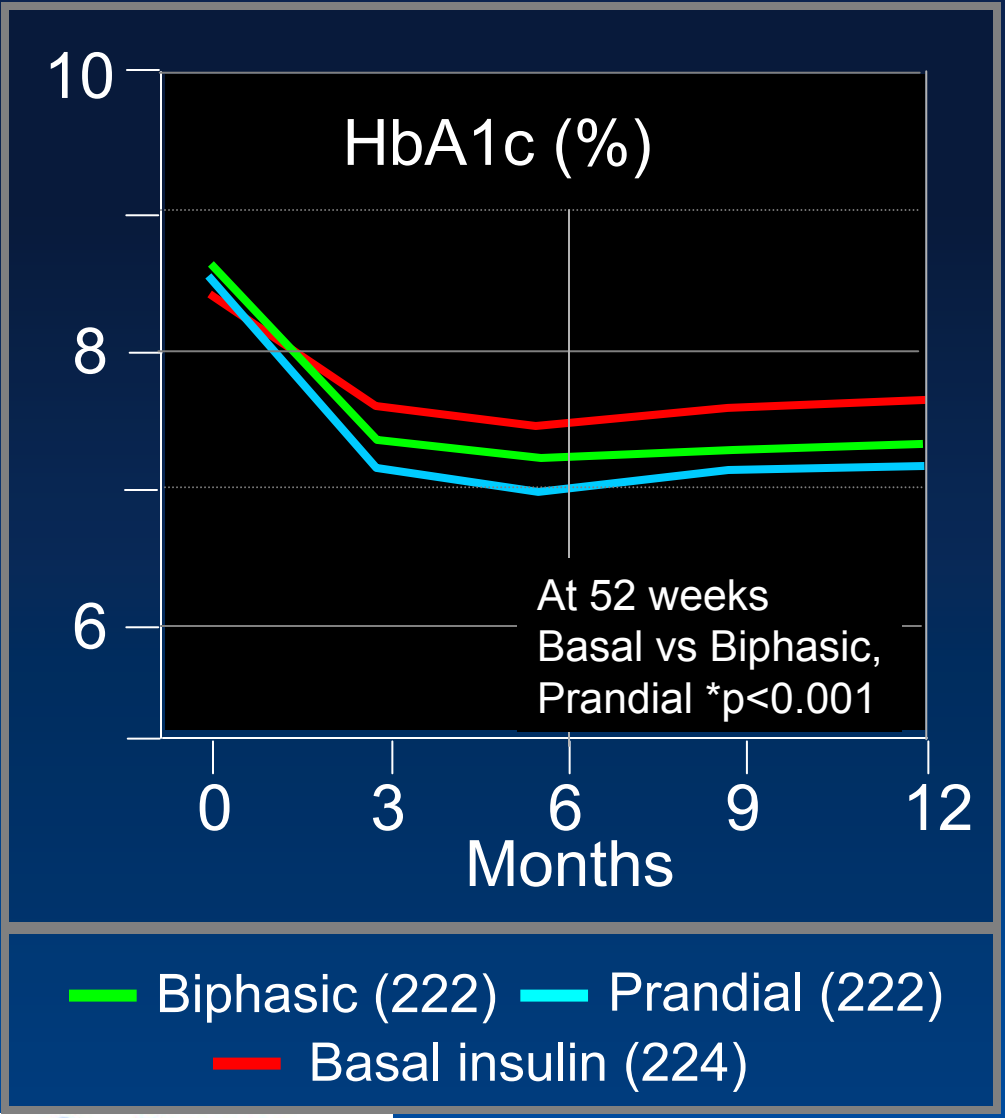
T2DM : Biphasic, Prandial or Basal Insulin (4-T)



	HbA1c (%)		
	0	1yr	delta
Biphasic	8.6	7.3	-1.3
Prandial	8.6	7.2	-1.4
Basal	8.4	7.6	-0.8*

Need for 2nd Insulin dose of 'basal' insulin 33.8%

Need for 2nd type of Insulin at or after 24 weeks;

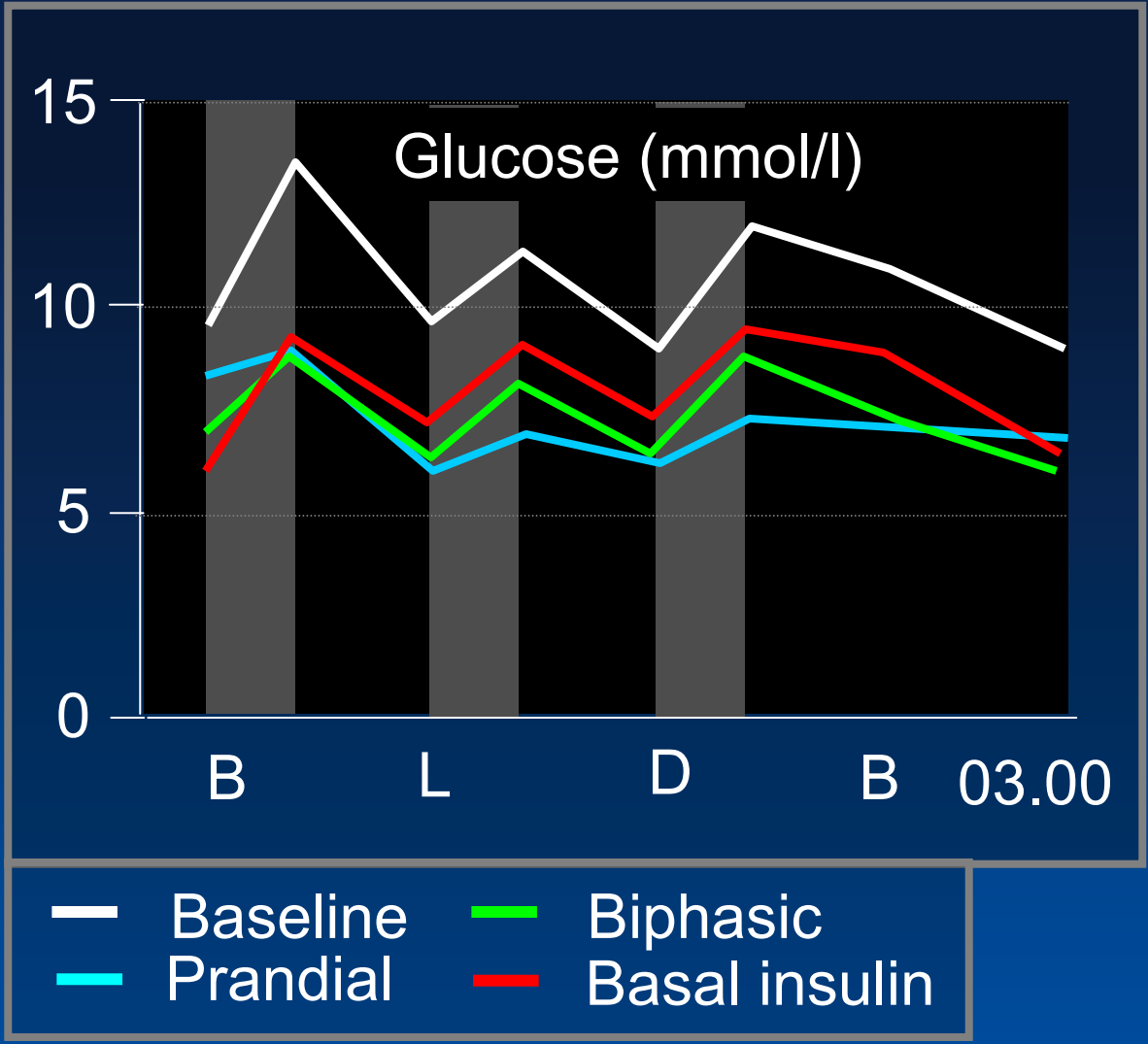
biphasic 8.9%
prandial 4.2%
basal 17.9%

p<0.001 for all comparisons

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

T2DM : Biphasic, Prandial or Basal Insulin (4-T)



delta FPG (mmol/l)	
Basal	-3.3±2.9
Biphasic	-2.5±3.1
Prandial	-1.3±2.7

delta PPG (mmol/l)	
Prandial	-4.6±3.0
Biphasic	-3.8±3.5
Basal	-2.6±3.0

Self-monitoring BG:

1. Fasting BG:

Basal < Biphasic < Prandial

2. Postprandial BG:

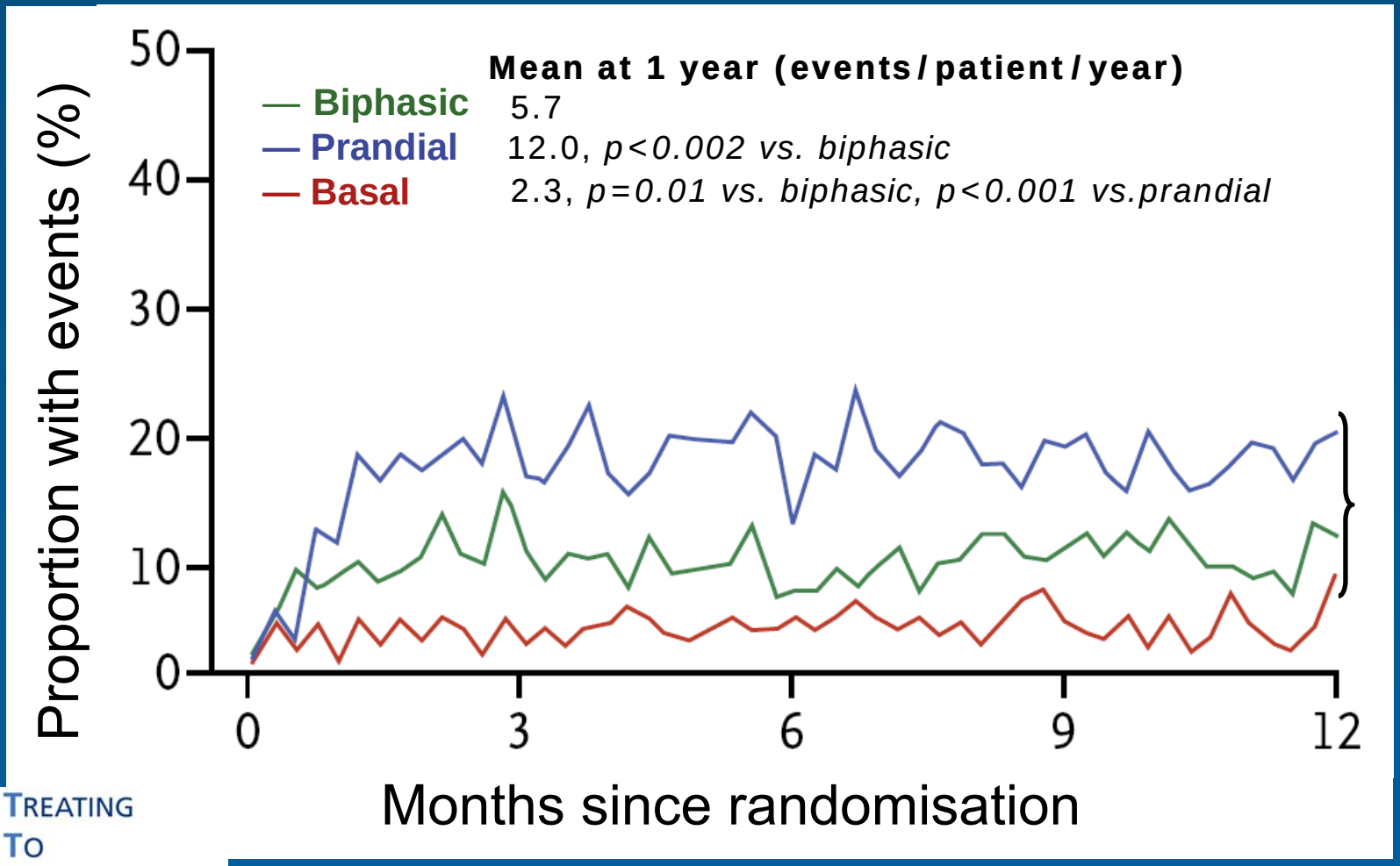
Prandial < Biphasic < Basal

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

T2DM : Biphasic, Prandial or Basal Insulin (4-T)

Results : Hypoglycaemic Events Grade 2 or 3



TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

T2DM : Biphasic, Prandial or Basal Insulin (4-T)

Results : Haemoglobin A1c %

	Biphasic aspart insulin		Prandial aspart		Basal insulin detemir	
	Pre- and post-		Pre- and post-		Pre- and post-	
HbA1c %	8.6	7.3	8.6	7.2	8.4	7.6
<7.0%	41.7		48.7		27.8*	
<6.5%	17.0		23.9		8.1*	
+ no 'hypos'	52.5		43.9		78.9	

*p<0.001

HbA1c > 8.5%: biphasic, prandial more effective than basal

HbA1c < 8.5%: no diff. between insulins to achieve <6.5%

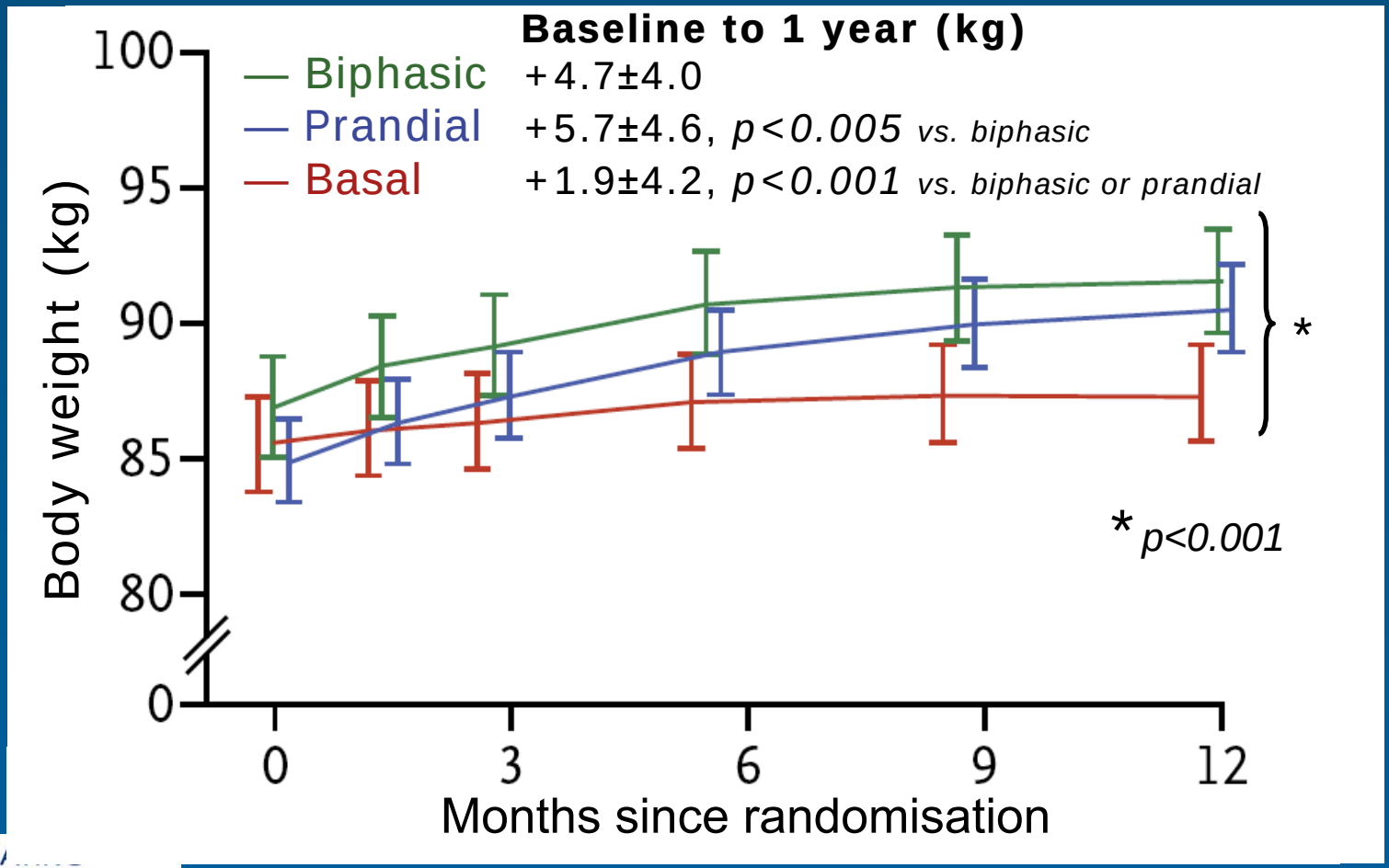
40% of basal insulin group required second dose

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

T2DM : Biphasic, Prandial or Basal Insulin (4-T)

Results : Body Weight



TREATING TO TARGET IN TYPE 2 DIABETES

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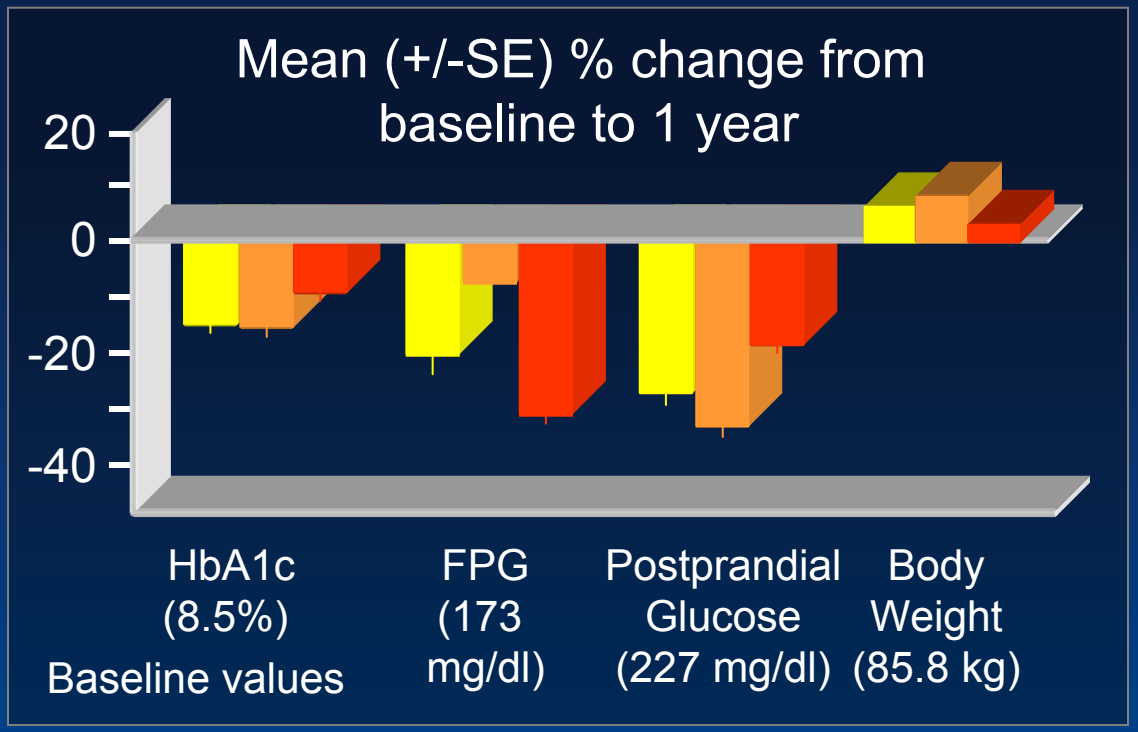
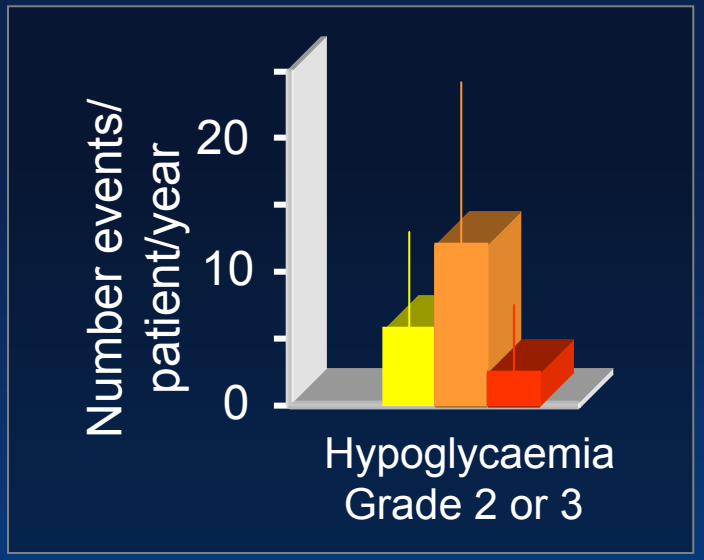
T2DM : Biphasic, Prandial or Basal Insulin (4-T)





Endpoint	Biphasic	Prandial	Basal
HbA1c %	7.3	7.2	7.6
≤6.5%	17	23.9	8.1
Weight kg	+4.7	+5.7	+1.9
'Hypos'	5.7	12	2.3

HbA1c >8.5% basal less likely to achieve HbA1c ≤6.5%
HbA1c <8.5% no difference between insulins in achieving HbA1c ≤6.5%

Holman et al NEJM 2007;357:1716-30

Addition of Biphasic, Prandial or Basal Insulin to Oral Therapy in Type 2 Diabetes (4-T Study)

Conclusions from study

Addition of a single analogue insulin formulation to metformin and sulfonylurea can lower HbA_{1c} by between 0.8 and 1.4%, and sustain these values over one year

Regimens using biphasic or prandial insulin reduced HbA_{1c} to a greater extent than basal, but were associated with greater risks of hypoglycemia and more weight gain

The one-year results of the 4-T study suggest that similar patients are likely to need more than one type of insulin to achieve target glucose levels in the longer term

The final two years of the trial will examine specifically the use of complex insulin regimens in these patients

TREATING TO TARGET IN TYPE 2 DIABETES

Holman et al NEJM 2007;357:1716-30

THE APOLLO CHALLENGE

APOLLO : Open Randomised Control Trial

P arallel design trial comparing an

O ral antidiabetic drug combination Rx with either

L antus once daily or

L ispro at mealtimes in T2DM persons failing

O ral treatment

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Study objective and design :

Primary objective: to show non-inferiority of insulin glargine once-daily plus oral antidiabetic drugs (OADs) vs insulin lispro three-times daily plus OADs in terms of change in HbA_{1c} (baseline to endpoint)

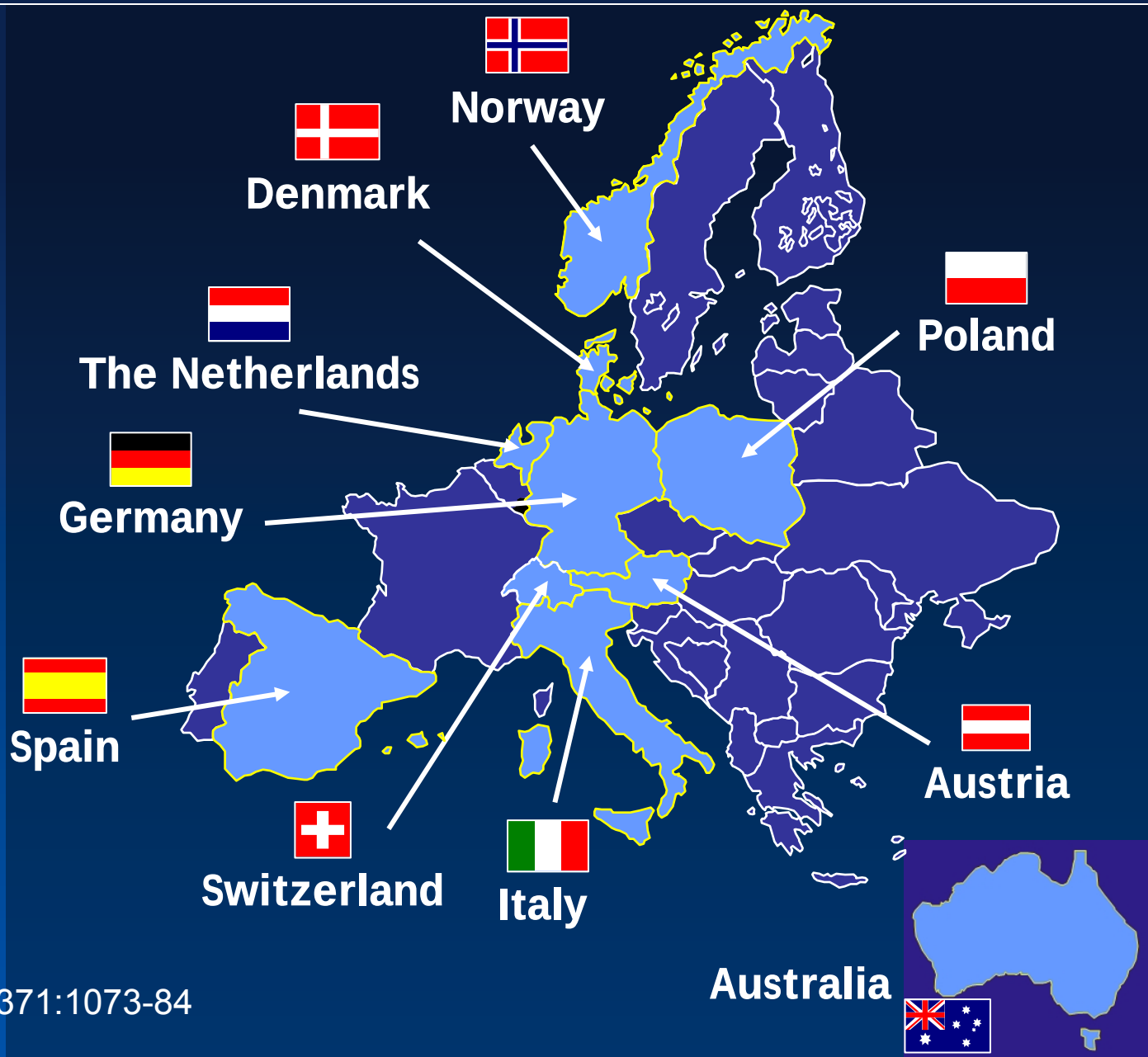
Study design: 44 week, randomised, open-label, parallel, multinational, multi-centre (69) clinical trial in subjects with T2DM inadequately controlled on OADs

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Participating countries :
69 centres

A
Parallel design comparing an **O**AD combination therapy with either **L**antus once-daily or **L**ispro at mealtimes in type 2 diabetic patients failing **O**ral treatment



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The APOLLO Trial

Objectives

Primary

Change in HbA1c levels

Secondary

Proportion of subjects achieving target HbA1c (≤ 7%)

Change in fasting blood glucose (FBG) levels

Proportion of subjects achieving target FBG (≤ 100 mg/dl)

Change in 8-point self-monitored blood glucose (SMBG)

Incidence of hypoglycemic events

Safety

Adverse events

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Study Location : Multicentre (69) Europe and Australia (1)
Duration : 44 weeks
Inclusion criteria : Aged 18-75 yrs; T2DM ≥ 1 yr; HbA1c 7.5-10.5% and on antidiabetic agents for 6m with stable doses for 3 m; FPG ≥ 6.7mM; BMI ≤ 35 kg.m² ,SMBG users
Exclusion criteria : insulin Rx in the past 4 weeks, GAD +ve, severe retinopathy, significant CVD, renal & hepatic disease, significant other co-morbidities and pregnancy
Procedure : Ethical approval and informed consent
Open labelled RCT, randomisation centrally, Stratified by centre and co-Rx with metformin on a 1:1 basis
Medications : insulin glargine (205), insulin lispro (210)
SMBG : 8-point day profile monthly after 12 week forced titration phase up to 44 weeks

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Study Design

weeks	Pre-screening	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	10	12	16 *	20	24 *	28	32 *	36	40	44
						Forced titration															Titration fine-tuning			

Screening Phase (4 weeks)
Entry criteria
Patient training
Start SMBG

Treatment Phase (44 weeks)

OAD + insulin glargine (10 IU, once daily)
OAD + insulin lispro (4 IU, 3x daily at mealtimes)

Enrolment (n=477)
Patients with T2DM
HbA_{1c} ≥7.5% ≤ 10.5%
FBG ≥ 6.7 mmol/L

Treatment randomisation 1:1 (N=418)

Insulin titration regimen	Target Blood Glucose (mmol/l)
	FBG ≤5.5
	preprandial BG ≤5.5
	postprandial BG 2h ≤7.5

* Additional weekly calls to adjust insulin dose if HbA1c >7.0%
T2DM=type 2 diabetes mellitus; BG=blood glucose; SMBG=self-monitored BG; FBG=fasting BG

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Demographics and baseline characteristics*

		Insulin glargine (186)	Insulin lispro (191)
Sex M(%)		55.0	59.0
Age (yrs)		59.7 (9.0)	59.7 (9.0)
BMI (kg.m^2)		29.2 (3.6)	29.3 (3.5)
DM duration (yrs)		9.1 (6.8)	8.6 (6.3)
HbA1c (%)		8.73 (0.97)	8.67 (0.97)
FBG (mmol/l)		10.40 (2.0)	9.80 (2.20)
Previous Rx (%)	SUs	92.0	91.0
	metformin	78.0	77.0
	alpha GI	2.0	3.0
	TZDs	2.0	3.0
Current Rx (%)	metformin	76.0	75.0
	glimepiride	94.0	93.0

* Per-protocol population

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Demographics and baseline characteristics*

Full analysis set (n=412)	Insulin glargine (n=204)	Insulin lispro (n=208)
Age (years)	60.0 ± 9.0	59.68 ± 9.01
BMI (kg/m^2)	29.2 ± 3.7	29.37 ± 3.51
male (n [%])	107 (52.5)	122 (58.7)
Duration of diabetes (years)	9.0 ± 6.8	8.5 ± 6.1
Duration of OAD treatment (years)	7.0 ± 5.8	7.0 ± 5.5
Taking metformin (n [%])	155 (76.0)	153 (73.6)
HbA_{1c} (%)	8.7 ± 1.0	8.7 ± 1.0
FBG (mg/dL)	186 ± 36	178 ± 41
(mmol/L)	10.3 ± 2.0	9.9 ± 2.3
Nocturnal BG (mg/dL)	177 ± 44	177 ± 53
(mmol/L)	9.8 ± 2.5	9.8 ± 2.9

* Intension-to-treat population

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Insulin Dose Titration algorithm and SMBG*

Insulin glargine		Insulin lispro
10 units	**Stating dose**	4 units
FBG mmol/l — dose	**Insulin dose titration algorithm (weekly) in units/day**	PrePBG mmol/l — dose**
>8.9 — +8U		>11.1 — +3U
>7.8 - ≤8.9 — +6U		>8.3 - ≤11.1 — +2U
>6.7 - ≤7.8 — +4U		> 5.5 - ≤ 8.3 — +1U
>5.5 - ≤6.7 — +2U		≤ 5.5 — NIL
≤5.5 — NIL		
Forced titration regimen – European Diabetes Policy Group		PostPBG mmol/l — dose**
		>10.3 — +2U
		>7.5 - ≤10.3 — +1U
		≤ 7.5 — NIL

*Self-Monitoring of BG : AccuCheck, Roche Diagnostics

** Before main meal

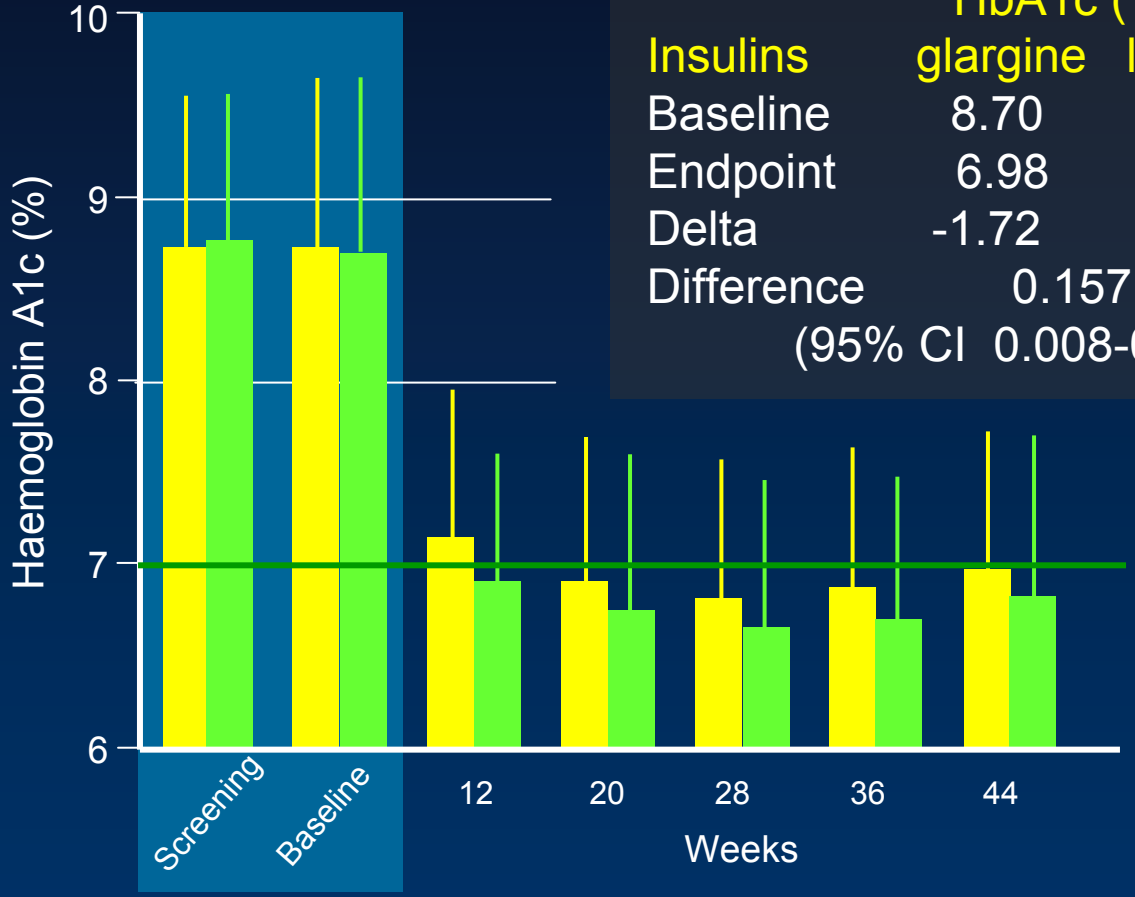
TARGETS : FBG & preprandial BG < 5.5 mmol/l; Postprandial < 7.5 mmol/l

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Results : Improvement in Haemoglobin A1c

	HbA1c (%)	
Insulins	glargine	lispro
Baseline	8.70	8.67
Endpoint	6.98	6.80
Delta	-1.72	-1.87
Difference	0.157	
	(95% CI 0.008-0.322)	



Insulin glargine + OHAs
Insulin lispro + OHAs

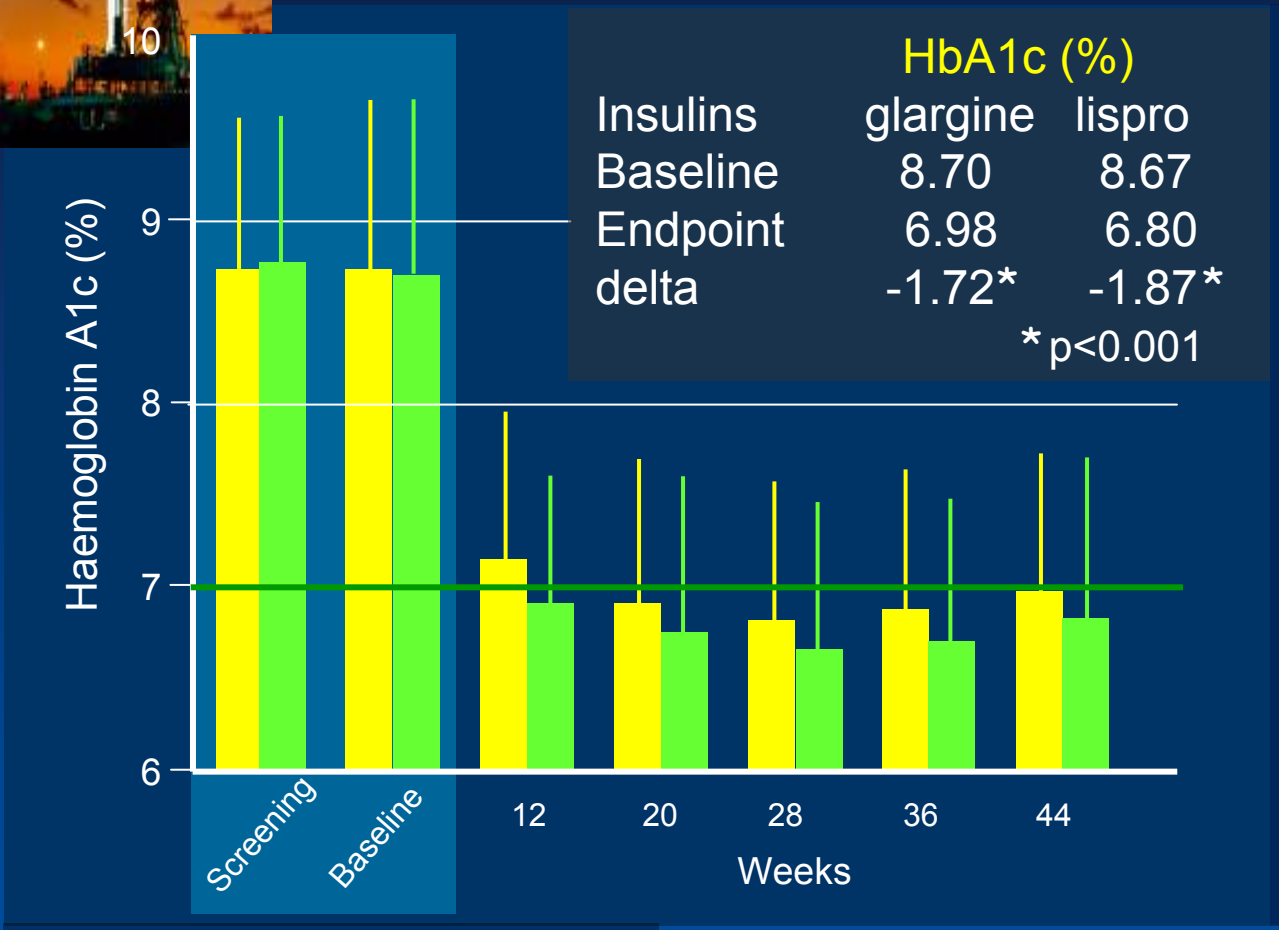
Bretzel et al Lancet 2008;371:1073-84

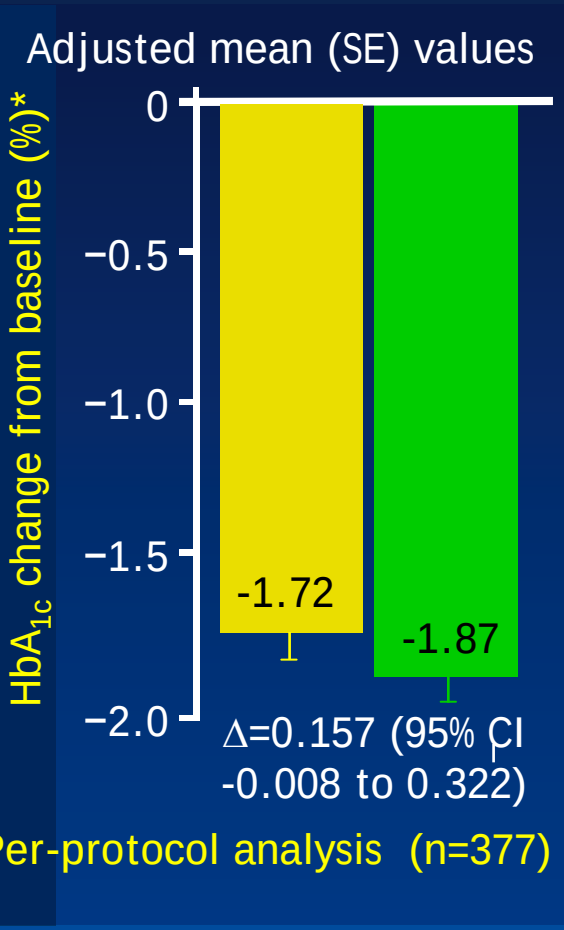
The APOLLO Trial

Results : Improvement in Haemoglobin A1c

Insulins	HbA1c (%) glargine	lispro
Baseline	8.70	8.67
Endpoint	6.98	6.80
delta	-1.72*	-1.87*

* p<0.001



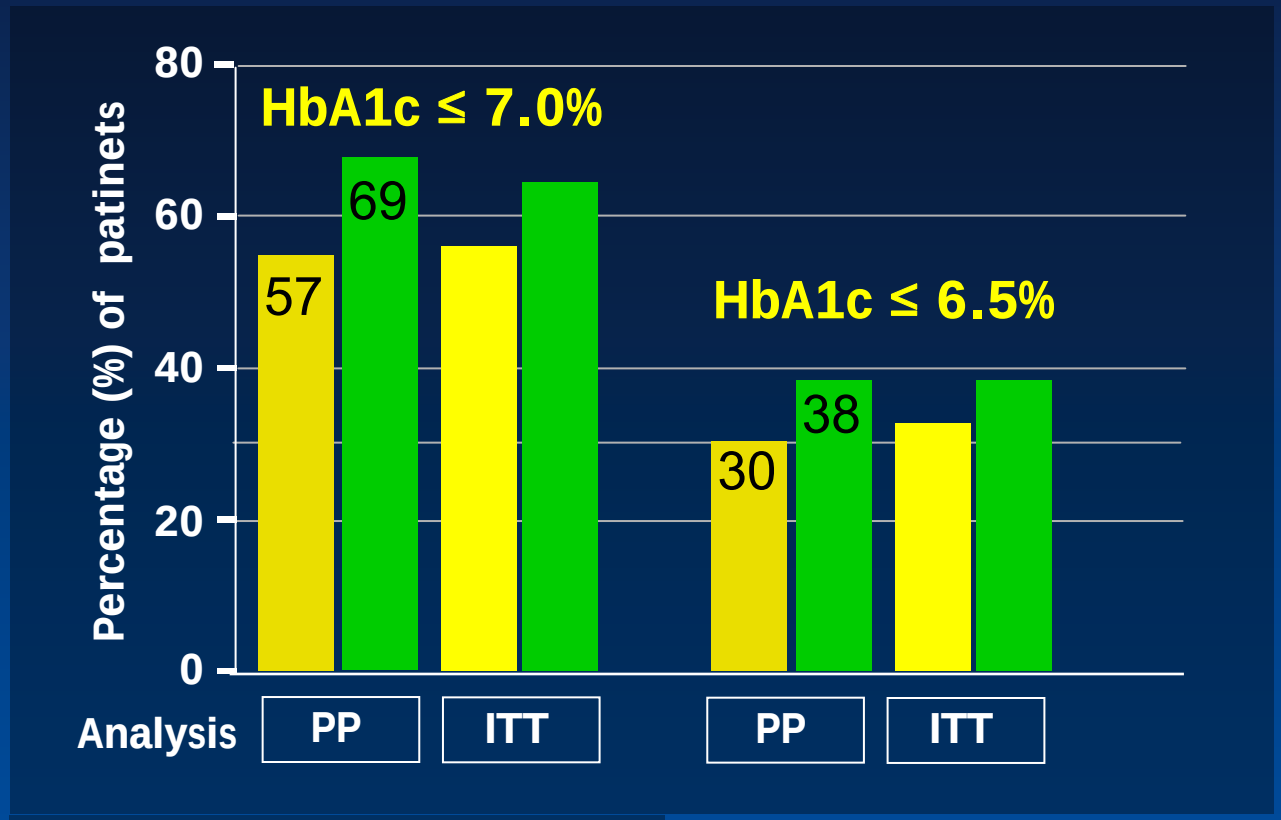


Insulin glargine + OHAs
Insulin lispro + OHAs

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

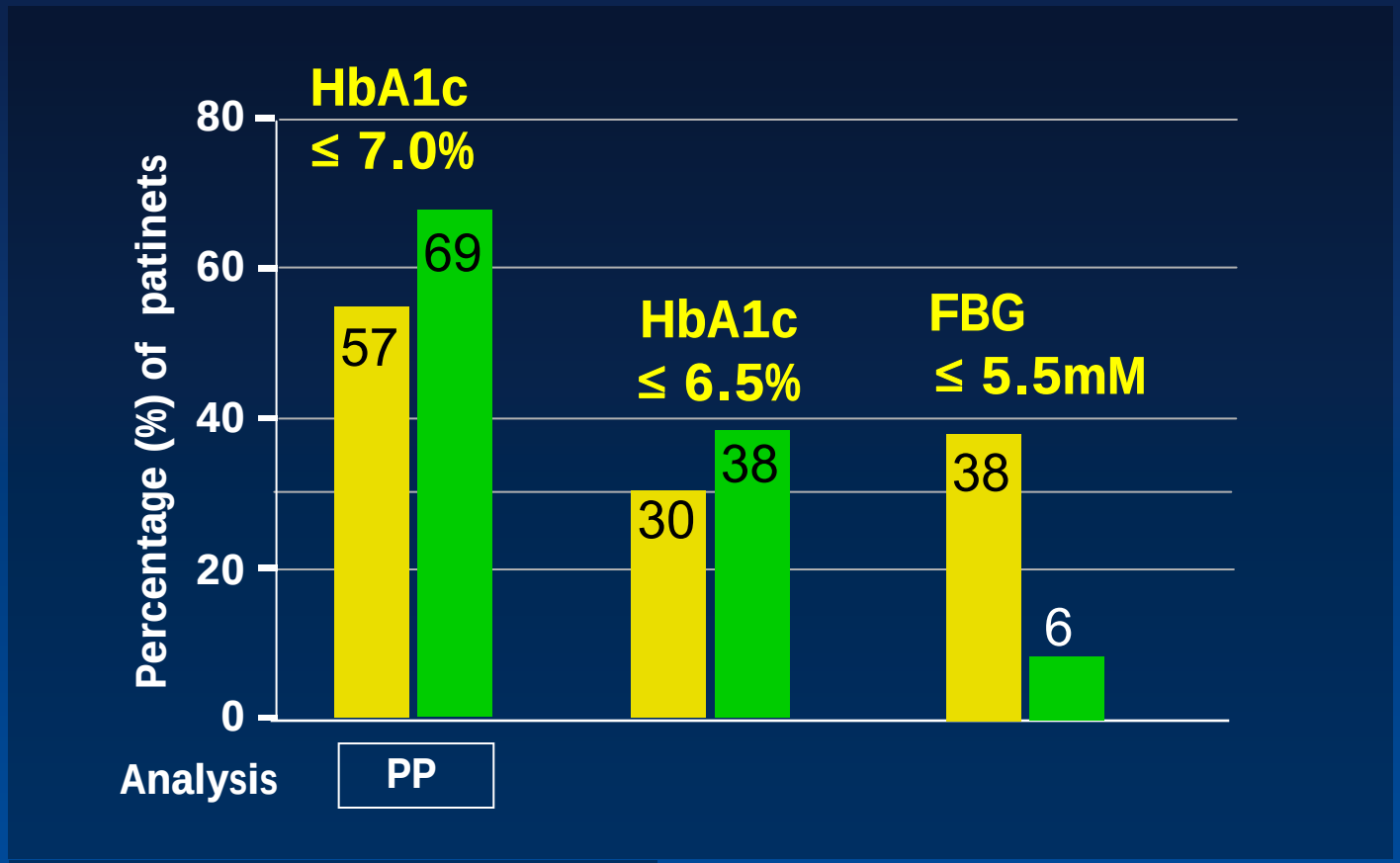
Results : Patients reaching Haemoglobin A1c Targets



Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

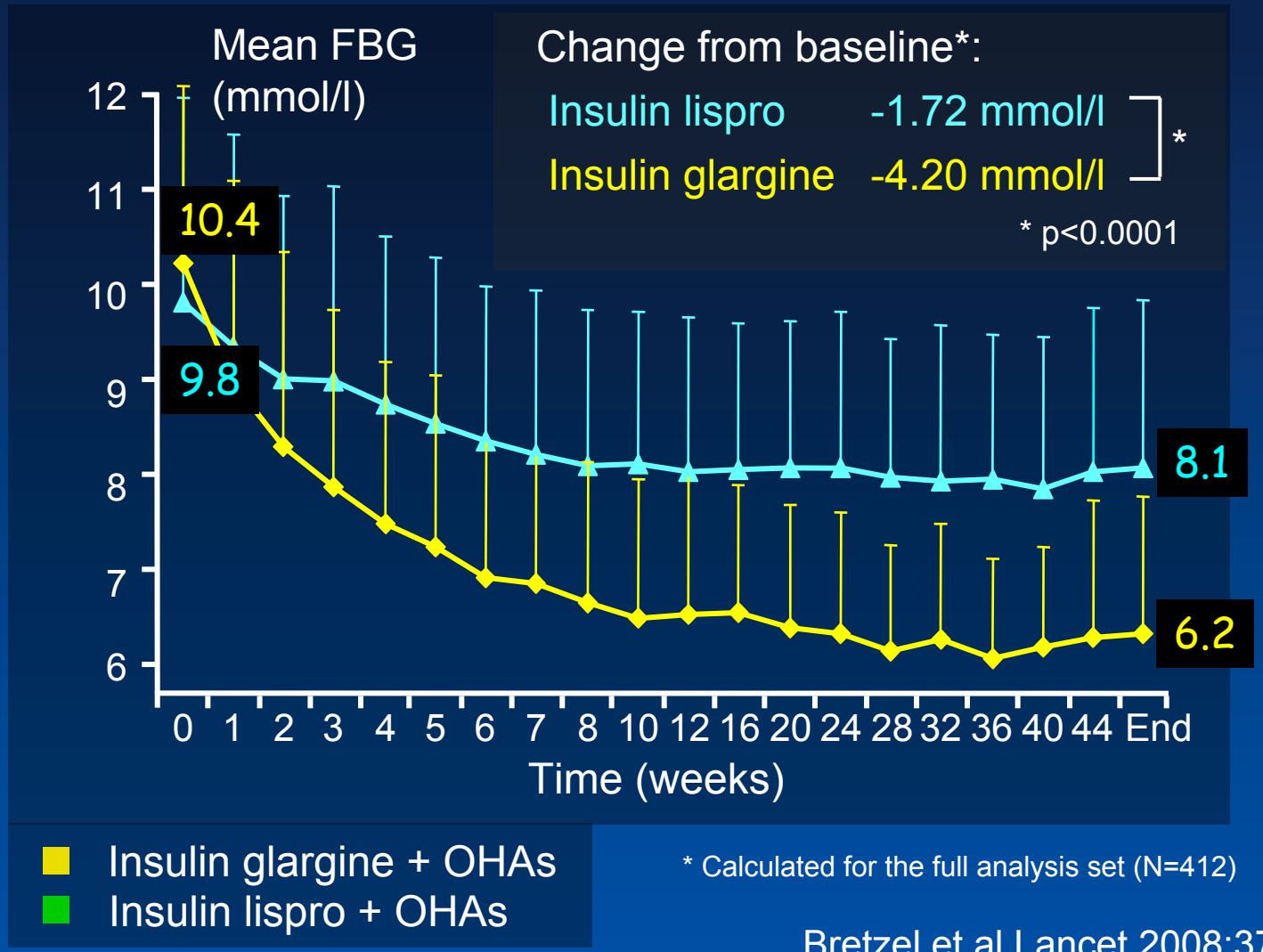
Results : Patients reaching Haemoglobin A1c Targets



Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

Results : Improvement in Fasting Blood Glucose

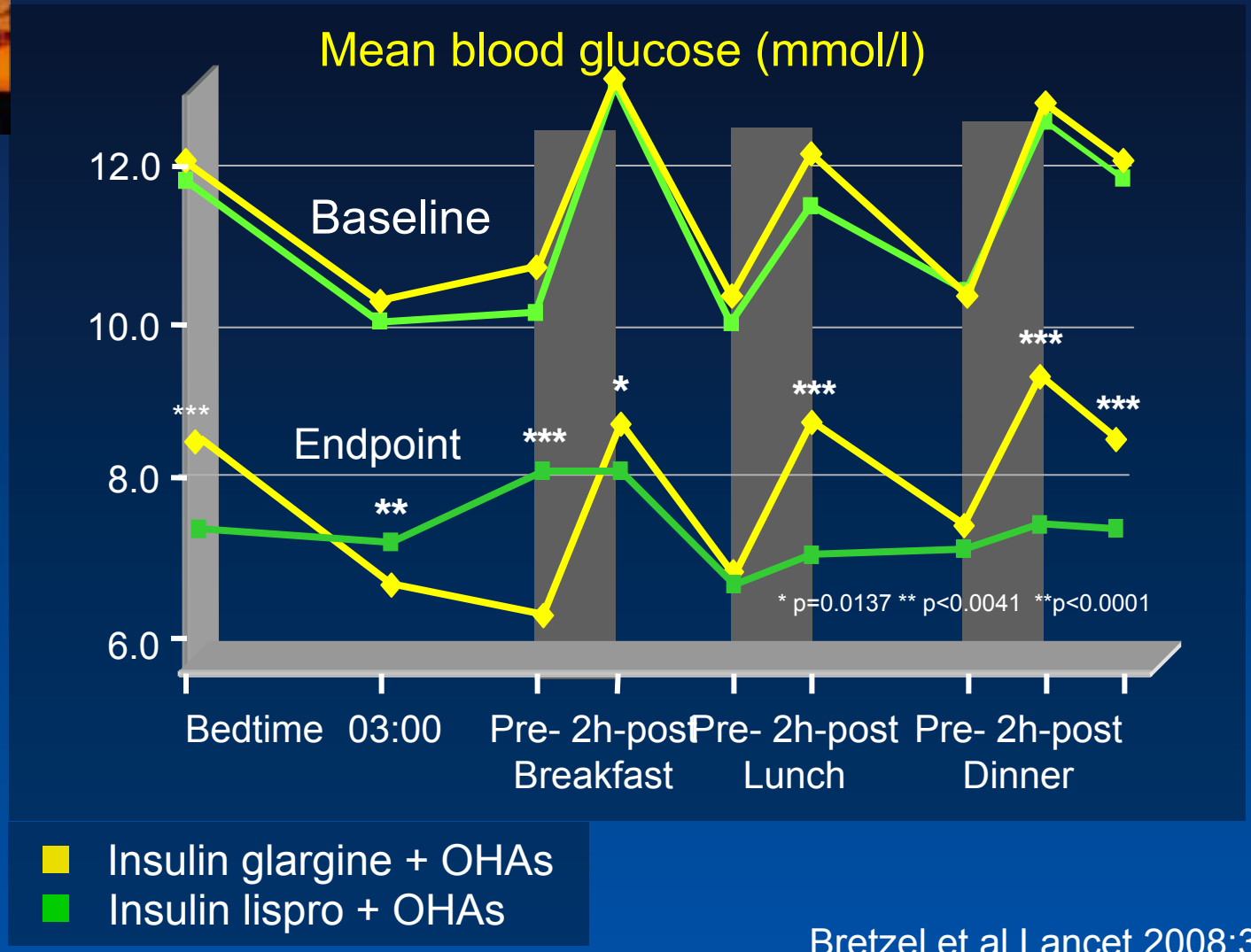


* Calculated for the full analysis set (N=412)

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

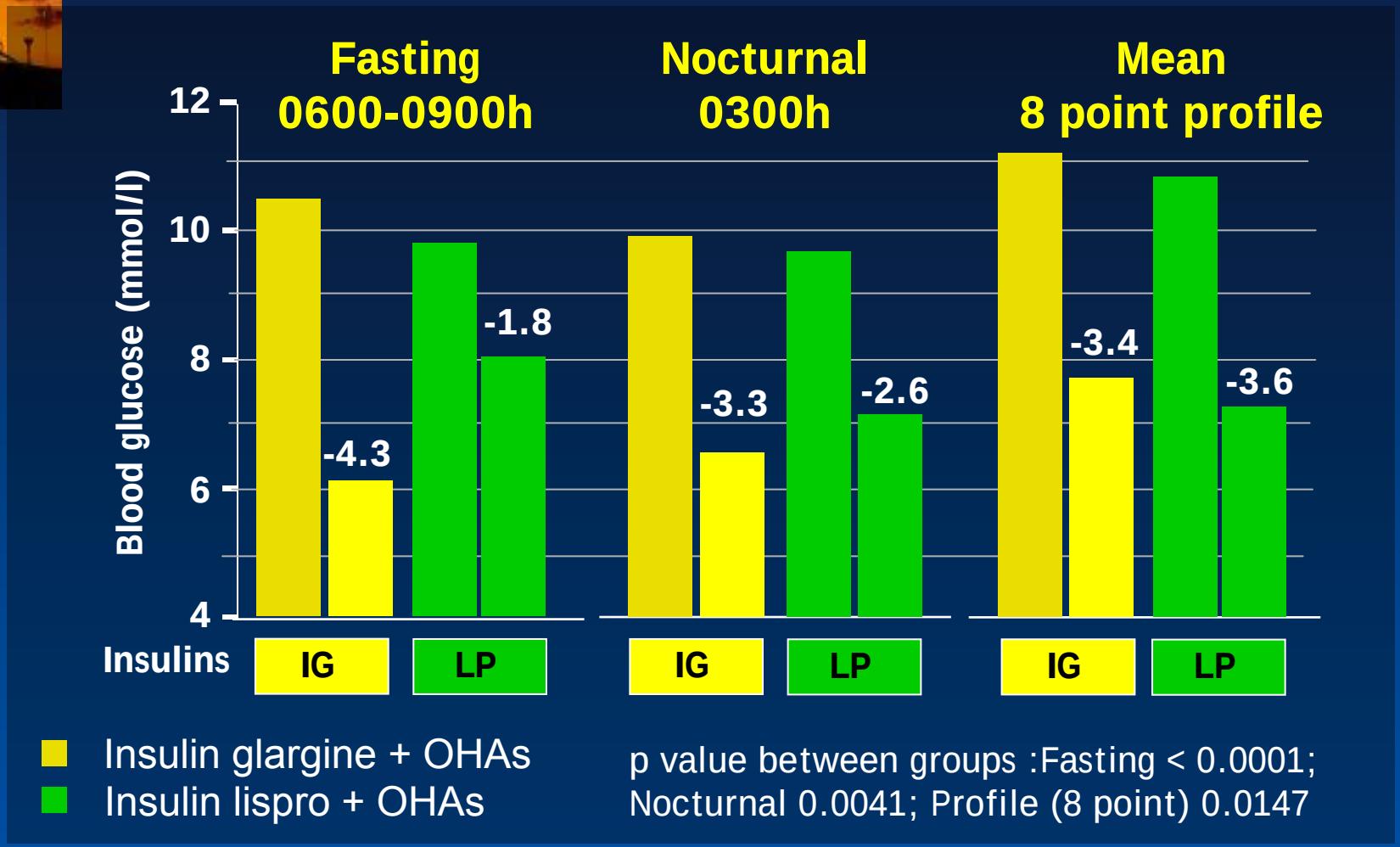
Results : SMBG day profiles at baseline and endpoint



Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

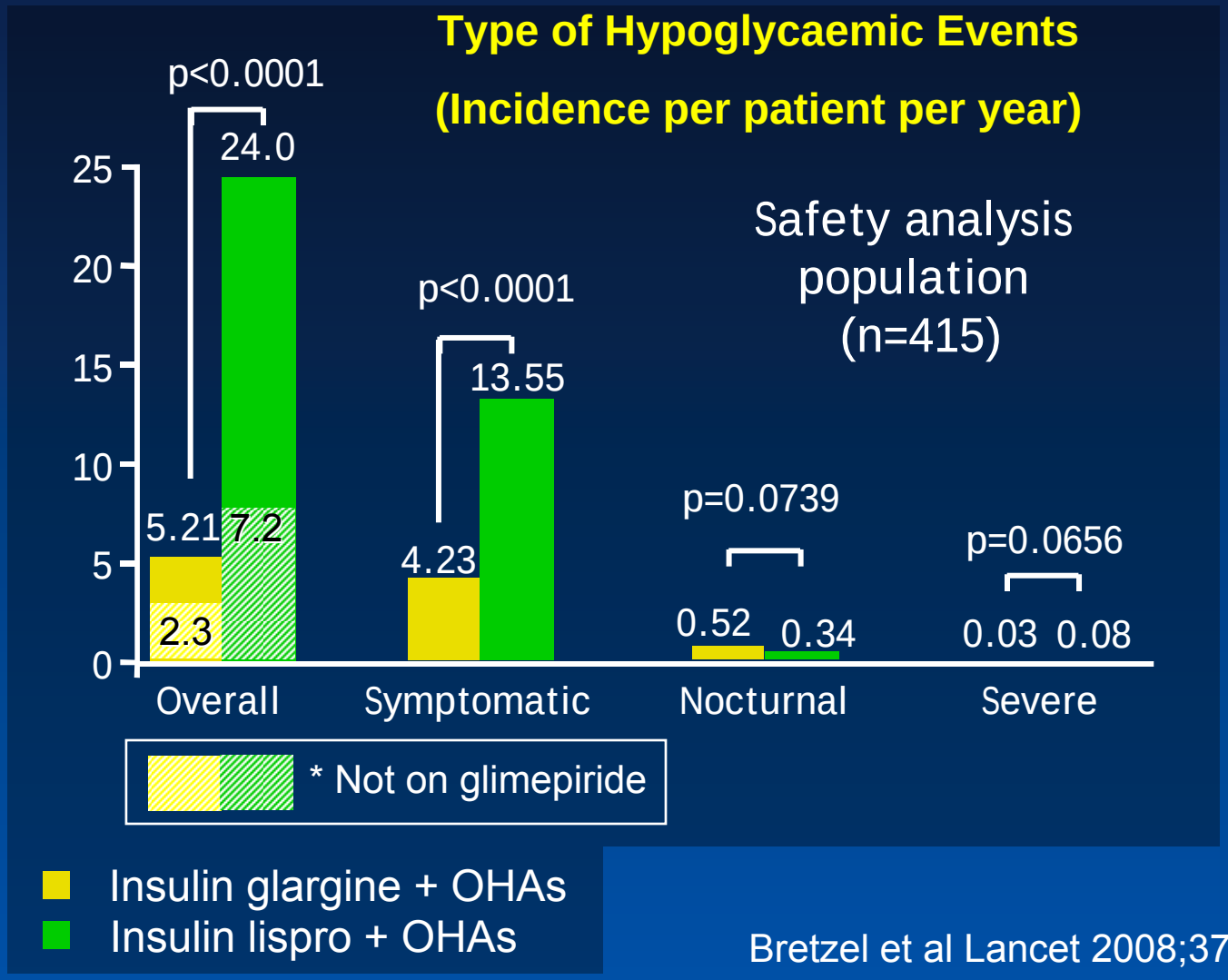
Results : Blood Glucose at Baseline and Endpoint



Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

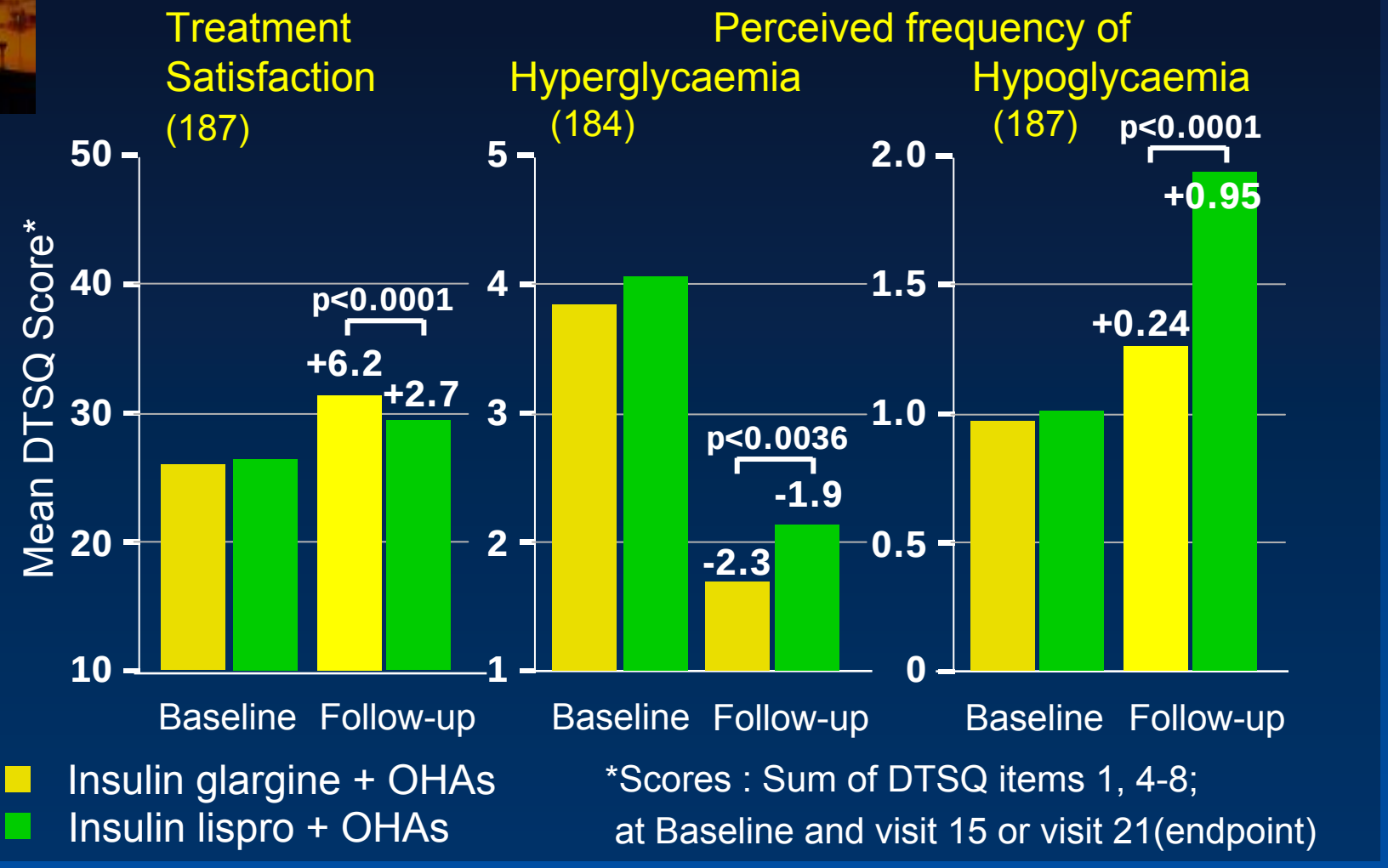
Results : Incidence of hypoglycaemic events



Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

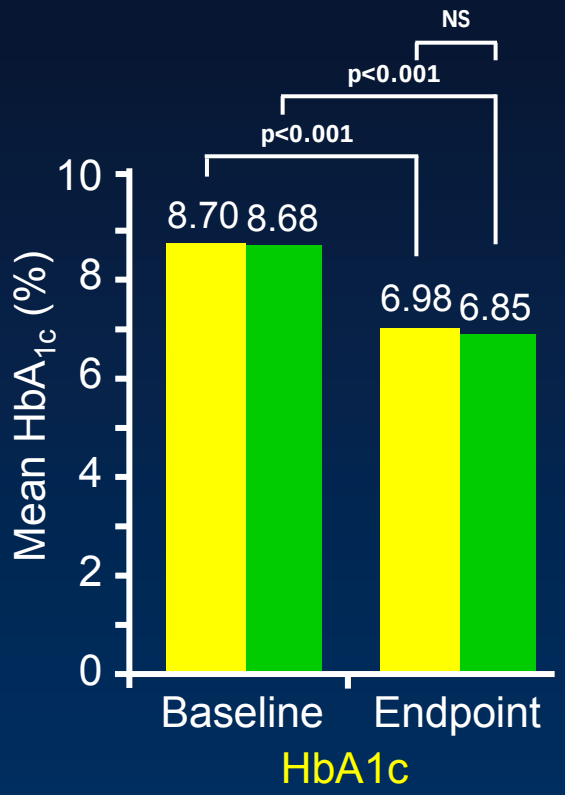
Results : Assessment of Treatment Satisfaction

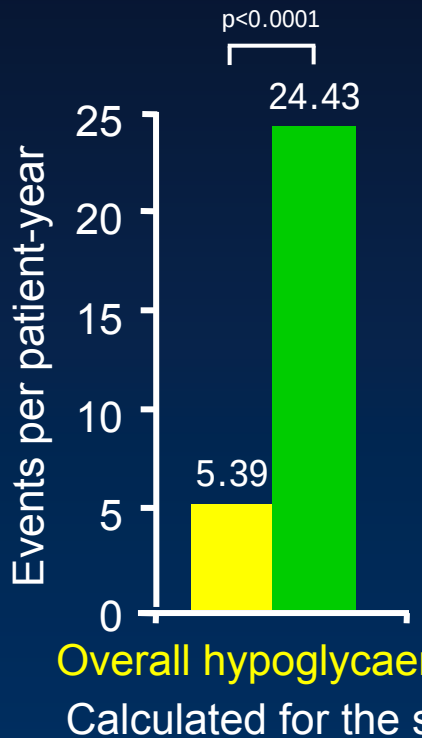


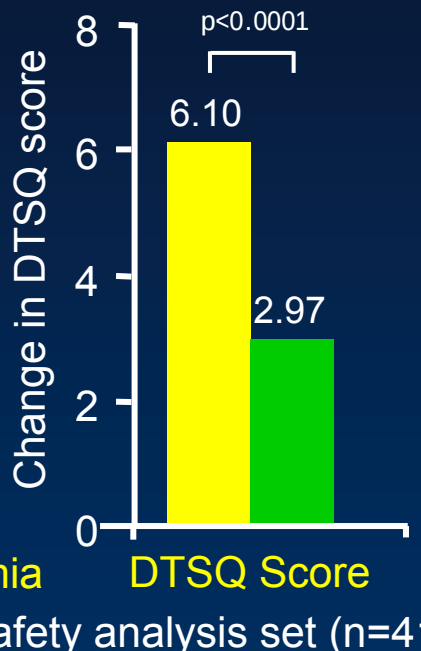
Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

SUMMARY of RESULTS







Calculated for the safety analysis set (n=415)

‘Basal’ insulin glargine like ‘prandial’ insulin lispro lower HbA1c equally to target HbA1c ≤7.0%, but with fewer hypoglycaemic events and greater treatment satisfaction

Bretzel et al Lancet 2008;371:1073-84

The APOLLO Trial

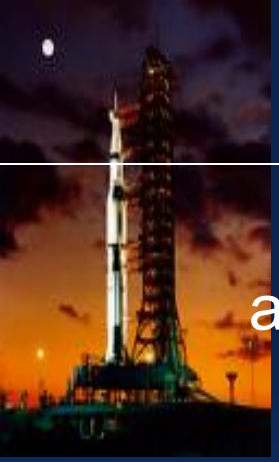
THE LANCET

Volume 371 · Number 9618 · Pages 1045–1136 · March 29–April 4, 2008 www.thelancet.com

"Addition of insulin glargine to therapies with oral hypoglycaemic agents can be regarded as a first-line insulin initiation approach in type 2 diabetes mellitus."

See Articles page 1073

Bretzel et al Lancet 2008;371:1073-84



The APOLLO Trial

Annual Treatment Costs in T2DM on OHAs and either Basal Insulin Glargine or Prandial Insulin Lispro

Cost Analysis

	GLARGINE (€ per Yr)	LISPRO (€ per Yr)	Δ Costs (€ per Yr)
Insulin	693.09	655.74	+37.35
Needles	98.22	294.66	-196.44
BG test strips	240.17	720.51	-480.34
Lancets	41.15	123.46	-82.31
Total costs (€ per Yr)	1,072.63,	1,794.37	-721.74

A basal strategy with Insulin Glargine is 40% cost saving !

Bretzel et al Personal communication

Initial Insulin Therapy in Type 2 Diabetes

Main outcomes	APOLLO Study		4T Study	
	basal	prandial	basal	prandial
HbA1c (%)				
at baseline	8.73	8.67	8.40	8.60
at endpoint	6.98	6.80	7.60	7.20
Δ (change)	-1.75	-1.87	-0.80	-1.40
Responder Rate (% pts. achieving HbA1c target)				
≤ 7.0 %	57	69	28	49
≤ 6.5 %	30	38	8	24
Responder Rate (% pat. achieving FBG target)	38	6		
Insulin-Dose (IU/d) (at endpoint)	42	45	42	56
Treatment Satisfaction Score (DTSQ-APOLLO; EuroQol5-D-4T)	+6.23	+2.74	±0	-0.02
No. of overall hypoglycemic events per patient-year	5.2	24.0 (x4.6)	2.3	12.0 (x5.2)
Change in body weight (kg)	+3.0	+3.5	+1.9	+5.7

Mod. from Bretzel RG et al., Diabetes Care 2009 (in press)

Challenges in the management of T2DM

Summary

T2 Diabetes is a progressive disease

Oral Hypoglycaemic agents (OHA) are ‘temporarily’ effective

Fasting hyperglycaemia is a key component in OHA failures

Basal insulin is FIRST LINE THERAPY (ADA/EASD Consensus)

- Ensure adequate dose titration
- Treat-To-Target safely
- Not all basal insulins are the same

Basal insulins when HbA1c ≤ 8.5% offers benefits of

- SIMPLICITY – one injection with flexible timing, one SMBG,
- PATIENT FRIENDLY – convenient with less ‘hypos’ and suitable for Primary Care