Ongoing Diabetes Management Where Next?

Workshop A

Tara Kadis

Workshop Over View

- Considerations/barriers in decision making about insulin verses GLP-1 use in people with type 2 diabetes
- Which Insulin regimes should we consider?

Key Challenges of Type 2 Diabetes

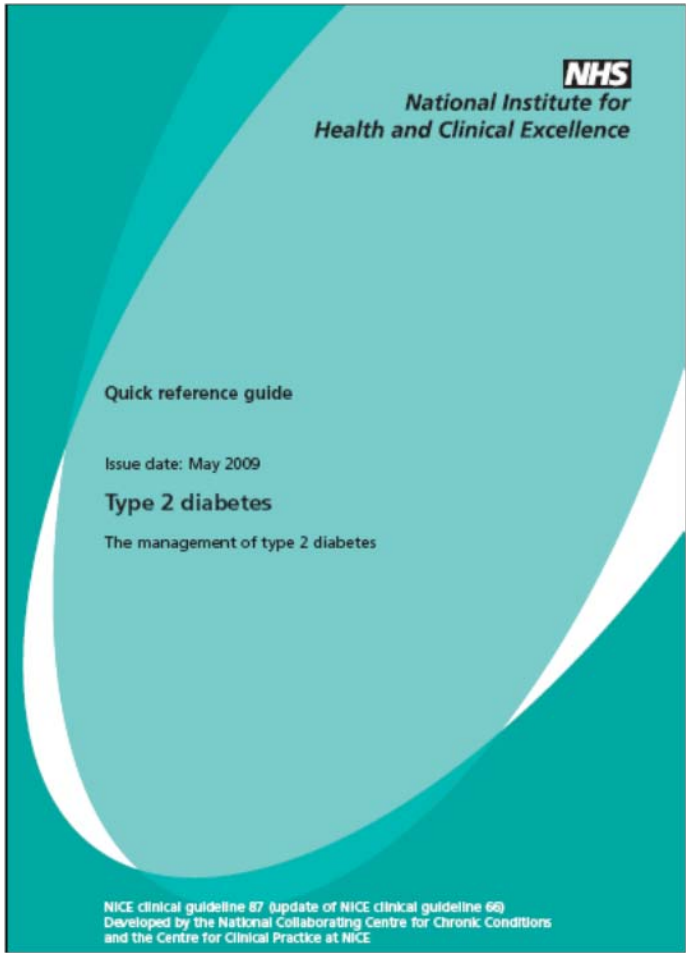
- Diabetes is a progressive multi-system disease characterized by:
  - Declining beta-cell function
  - Increasing insulin resistance
  - Increased risk of cardiovascular disease

The trade off !

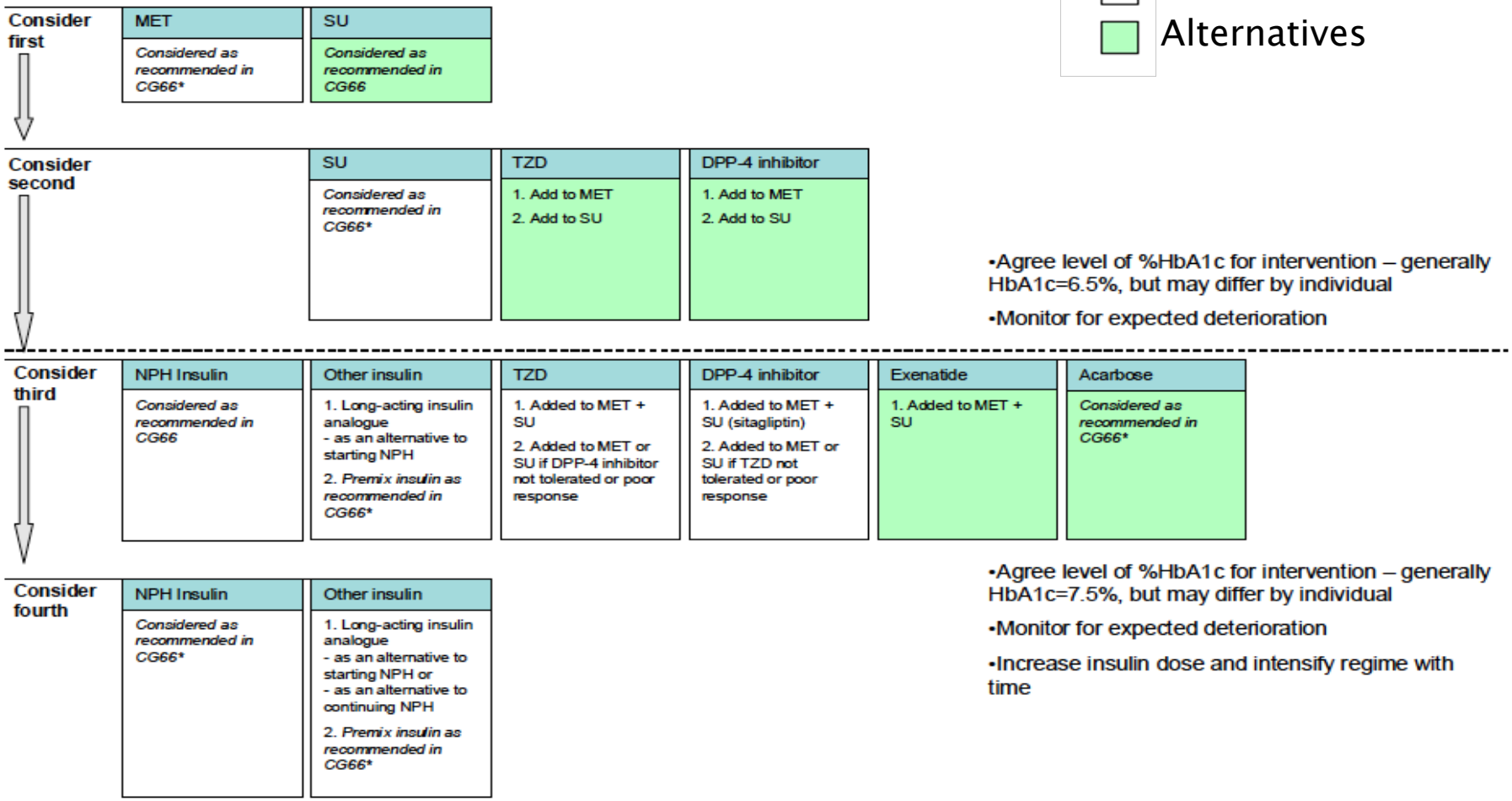
- As diabetes treatments are added to improve glucose control, clinicians & patients face trade-offs such as:
  - Hypoglycaemia
  - Weight gain
  - Complex treatment regimens

Updated NICE clinical guideline 87 (May 2009)

- Update on guideline CG 66 (May 2008)
- First guideline May 2008
- Final publication May 2009



NICE guidelines



NHS National Institute for Clinical Excellence. Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes May 2009:87

Insulin V GLP-1

Nice Recommendation GLP-1

- Consider adding GLP-1 3rd line if patient

  $HbA_{1c} \geq 58mmol/mol$ (7.5%)

  BMI $>35.0kg/m^2$

  BMI$< 35.0kg/m^2$ where insulin is unacceptable because of occupational implications or weight loss would benefit other significant obesity – related co mobidities

- Liraglutide 2nd line

  If person intolerant/contraindicated of either Metformin or Sulfonylurea and

  The person is intolerant/contraindicated of Glitazone and/or DPP-4

GLP-1

- **Appropriate 2nd or 3rd line treatment option in obese patient with Type 2 Diabetes**

  <u>Considerations / barriers</u>

  - Weight loss
  - Minimal titration
  - Less considerations re driving/employment
  - Side effects
  - Contra Indications
  - NICE recommendations for continuation.

Nice Recommendation Insulin therapy

Appropriate 2nd or 3rd line treatment option in patient with Type 2 Diabetes

- If other measures do not keep HbA1c to < 58mmol/mol (7.5%) or agreed target
- Consider for a person on duel therapy who is markedly hyperglycaemic
- Should be initiated with a structured education programme

National Institute for Health and Clinical Excellence. Type 2 diabetes: Newer agents for blood glucose control in type 2 diabetes. *Short Clinical Guideline 87*. London: NICE; 2009 (www.nice.org.uk)

Insulin initiation

Considerations / barriers

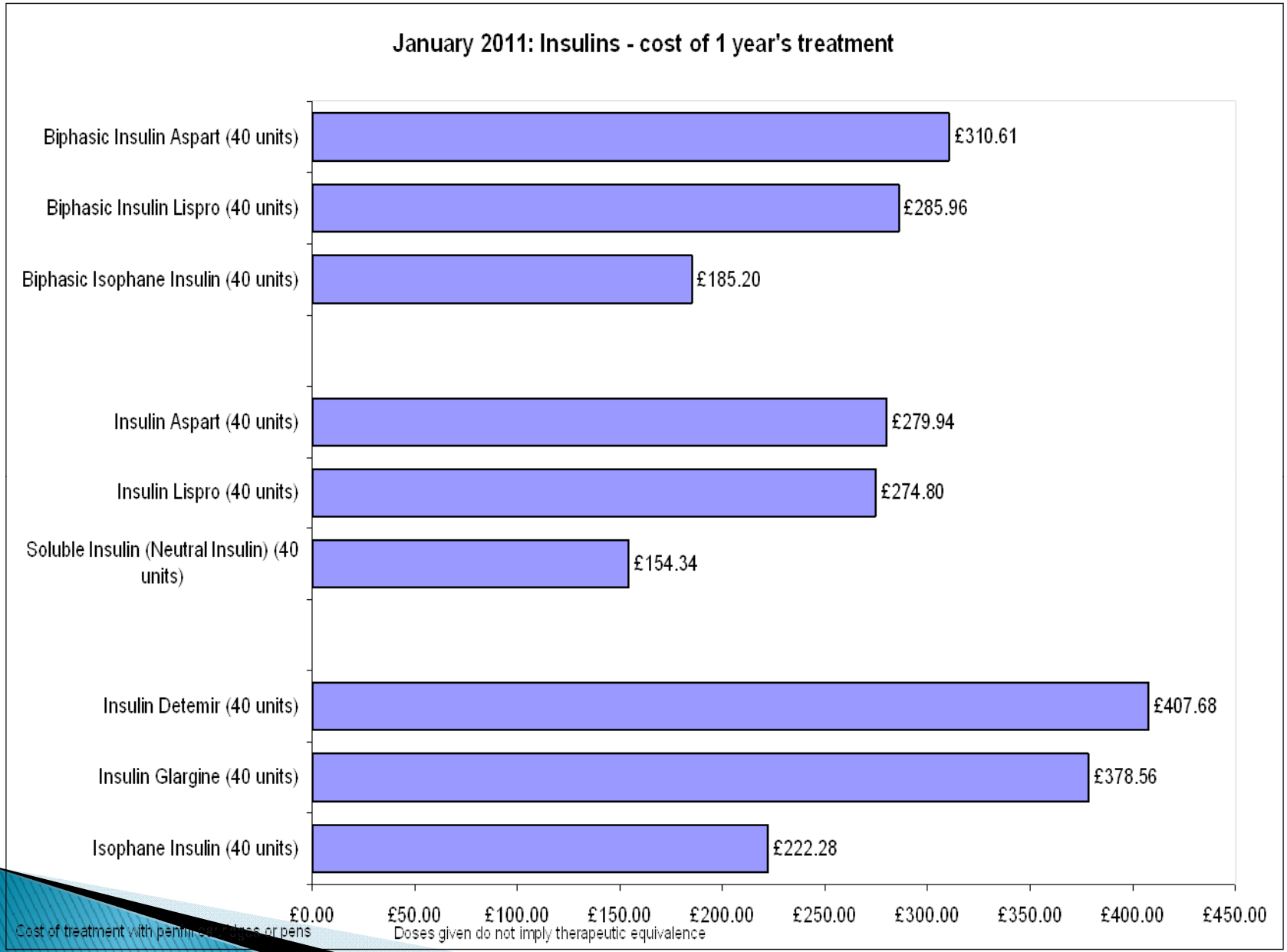
- Weight increase
- Increased risk of hypoglycaemia
- Titration of dose
- Driving/employment considerations

Choice of insulin regime!

- Begin with human NPH insulin at bedtime – twice daily if needed
- Consider as an alternative, using a long acting insulin analogue (Lantus, Levemir) if:
  - The person needs assistance from a carer or healthcare professional to inject insulin and therefore reduce the frequency of injections
  - Persons lifestyle is restricted by recurrent symptomatic hypoglycaemia
  - The person would otherwise need twice daily NPH injections
  - Monitor patient to determine if short acting insulin before meals may be required.

Choice of insulin regime!

- Consider twice daily pre mixed (Biphasic) Human insulin particularly if HbA1c ≥ 75mmol/mol (9%)
- Consider pre mixed preparations that include short acting analogue if
  - Person prefers injecting immediately before a meal
  - Hypoglycaemia is a problem
  - Blood glucose levels rise markedly after a meal.
  - Monitor patient for need for further injection of short acting insulin before meals or change to mealtime plus basal regime (basal bolus)


January 2011: Insulins - cost of 1 year's treatment
Biphasic Insulin Aspart (40 units)
£310.61
Biphasic Insulin Lispro (40 units)
£285.96
Biphasic Isophane Insulin (40 units)
£185.20
Insulin Aspart (40 units)
£279.94
Insulin Lispro (40 units)
£274.80
Soluble Insulin (Neutral Insulin) (40 units)
£154.34
Insulin Detemir (40 units)
£407.68
Insulin Glargine (40 units)
£378.56
Isophane Insulin (40 units)
£222.28
£0.00
£50.00
£100.00
£150.00
£200.00
£250.00
£300.00
£350.00
£400.00
£450.00
Cost of treatment with penfill cartridges or pens
Doses given do not imply therapeutic equivalence

The 4T™ Study

TREATING
TO
TARGET IN
TYPE 2 DIABETES

Outcomes

Primary outcome

- HbA1c level after 1 year

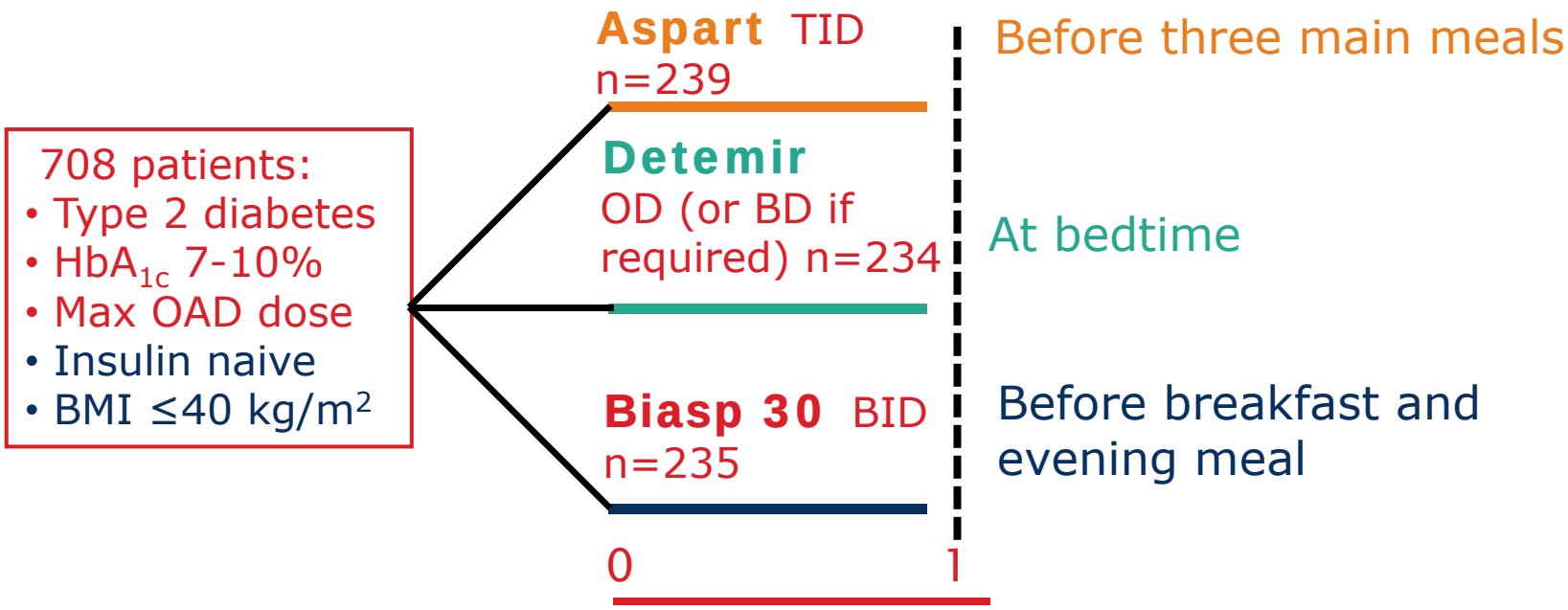
Main secondary outcomes include:

- Proportion of with HbA1c ≤6.5% (≤48 mmol/mol)
- Hypoglycaemia event rate
- Change in body weight

Holman RR et al., New England Journal of Medicine, 2007; 357:1716-30

Randomisation

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

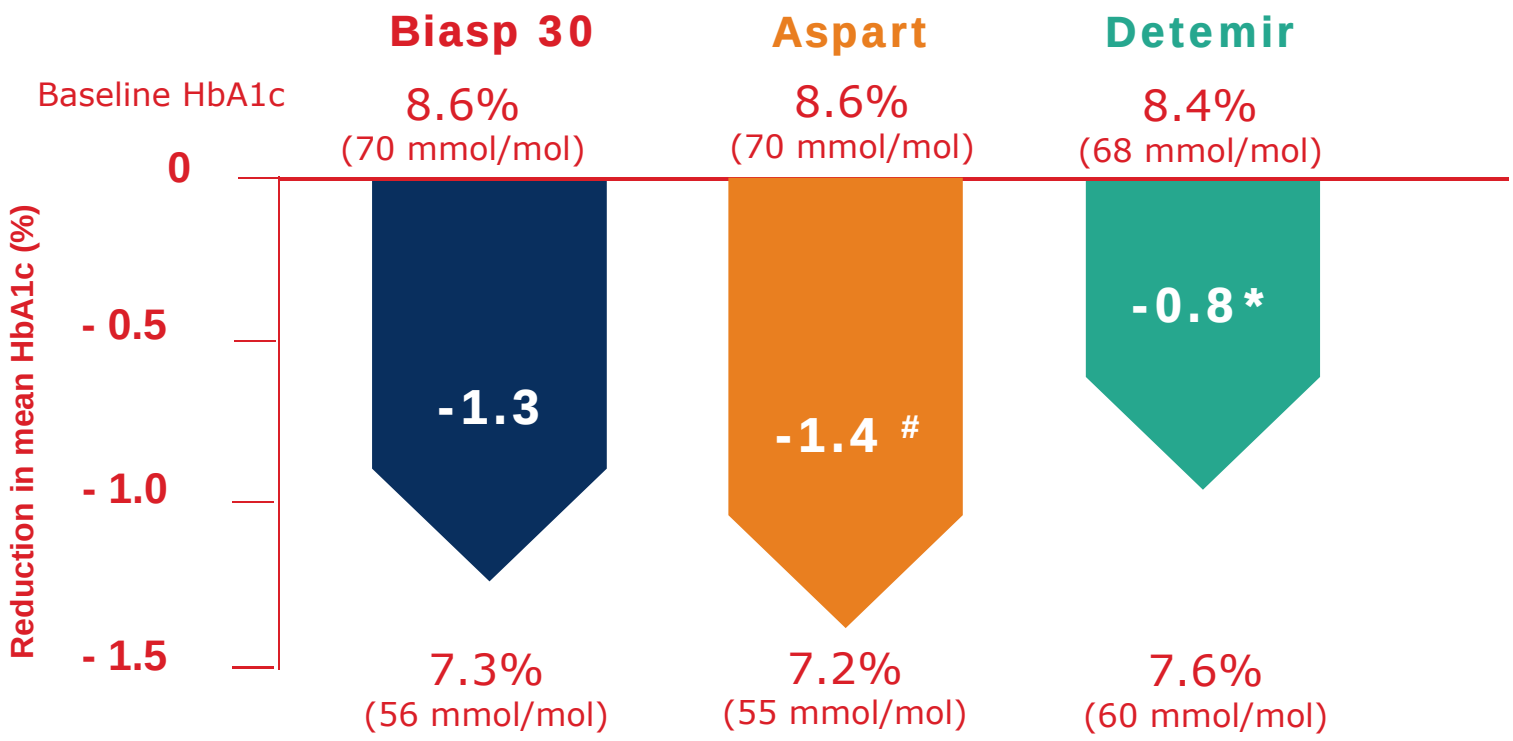


SU therapy replaced by second insulin in the first year if:
- HbA_{1c} ≥10% (≥86 mmol/mol) or
- HbA_{1c} ≥8% (≥64 mmol/mol) on two consecutive occasions

*Maximally tolerated doses of metformin and sulphonylurea for at least 4 months (or one agent if the other was not tolerated).

Holman RR et al., New England Journal of Medicine, 2007; 357:1716-30

Primary outcome – HbA_{1c} reduction



p=ns vs biasp 30

* P<0.001 vs biasp 30 or aspart

Holman RR et al., New [illegible]nal of Medicine, 2007; 357:1716-30

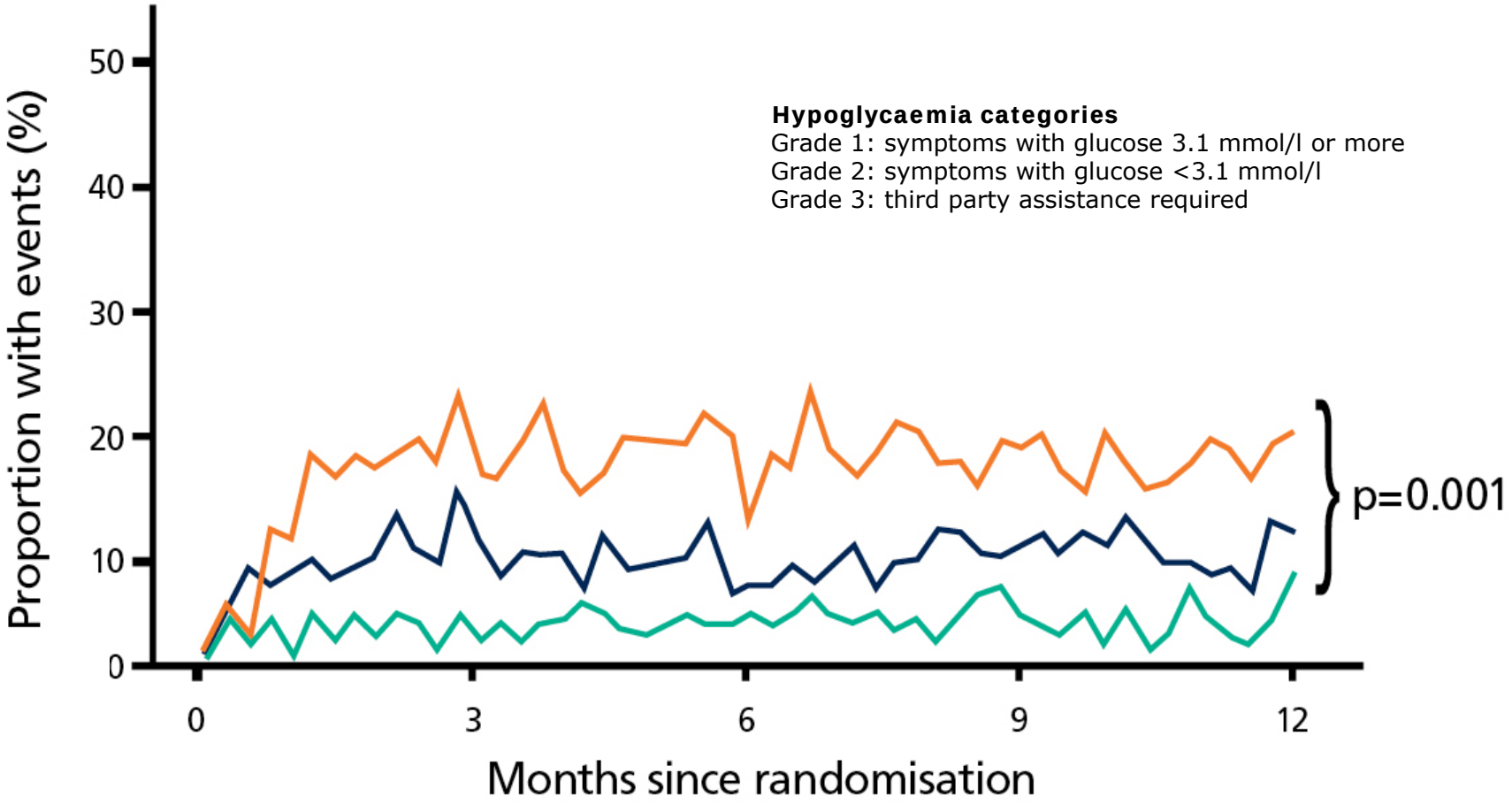
Hypoglycaemia (grade 2 or 3) over one year

Mean at 1 year (events/patient/year)

— Biasp 30 5.7

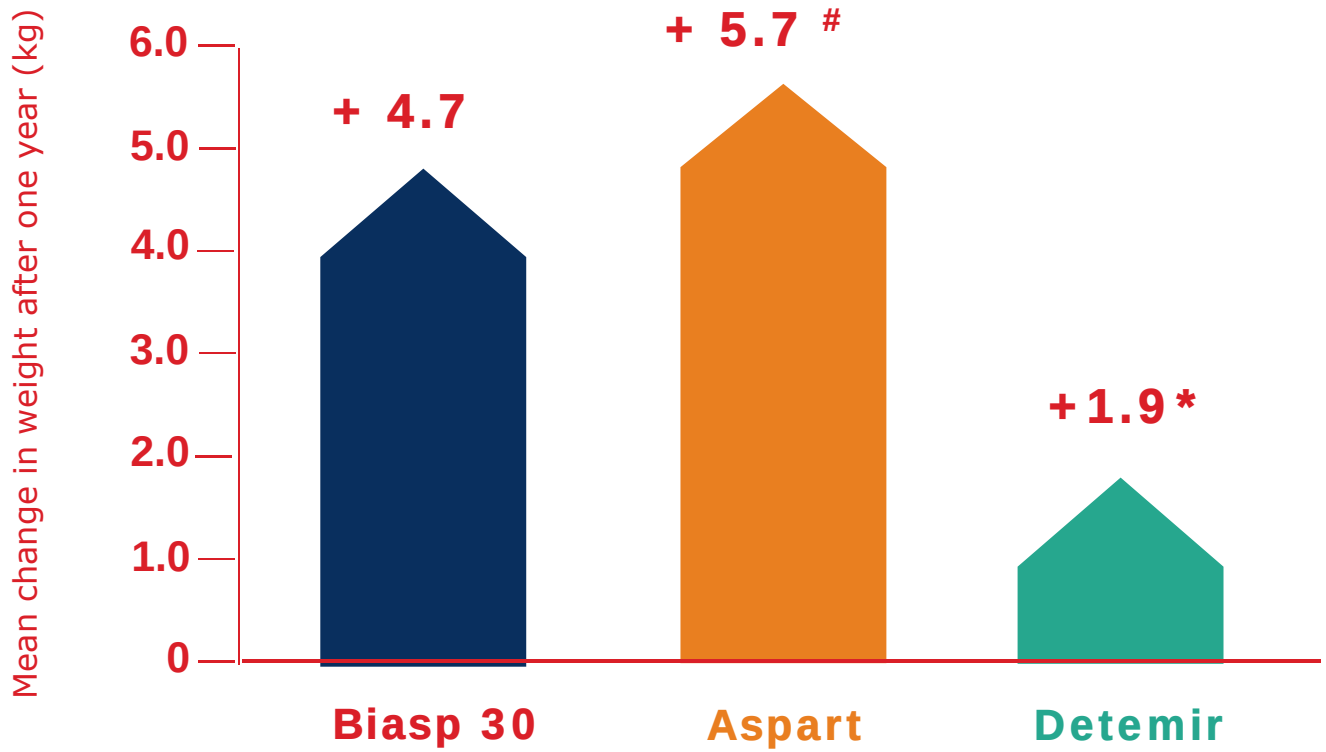
— Aspart 12.0, *p<0.002 vs. biasp 30*

— Detemir 2.3, *p=0.01 vs. biasp 30, p<0.001 vs.aspart*



Holman RR et al., New [illegible] nal of Medicine, 2007; 357:1716-30

Body weight change over one year



Mean baseline weight (kg)

Biasp 30 – 86.9; Aspart – 84.9; Detemir – 85.5

p=0.005 vs biasp 30

* P<0.001 vs biasp 30 or aspart

Holman RR et al., New [illegible]nal of Medicine, 2007; 357:1716-30

1 year conclusions

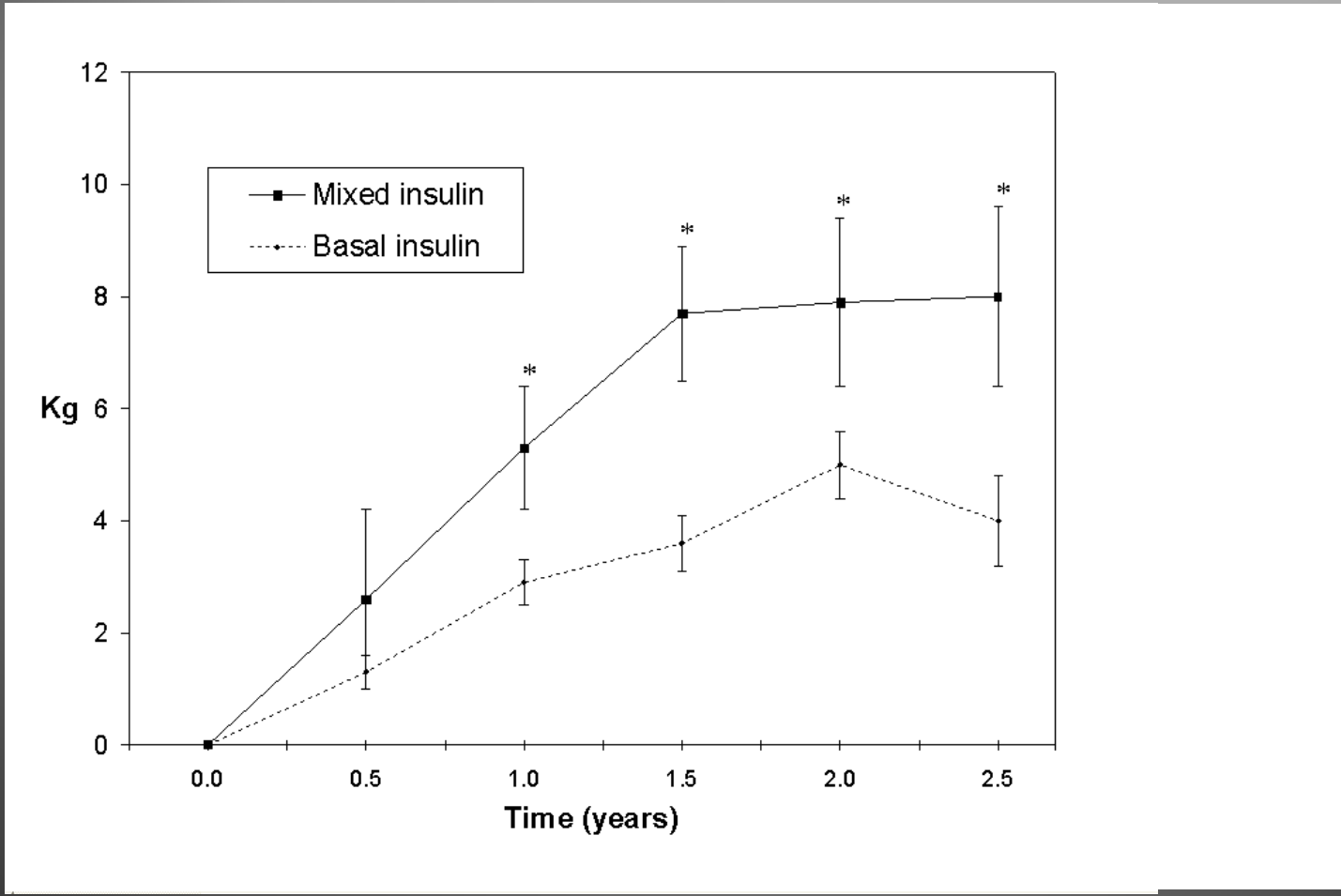
- Addition of an analogue insulin formulation to metformin and sulphonylurea can lower HbA_{1c} by between 0.8 and 1.4%, and sustain these values over one year

- Regimens using biasp 30 or insulin aspart reduced HbA_{1c} to a greater extent than insulin detemir, but were associated with significantly more hypoglycaemic events and weight gain

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

Holman RR et al., New [illegible]nal of Medicine, 2007; 357:1716-30

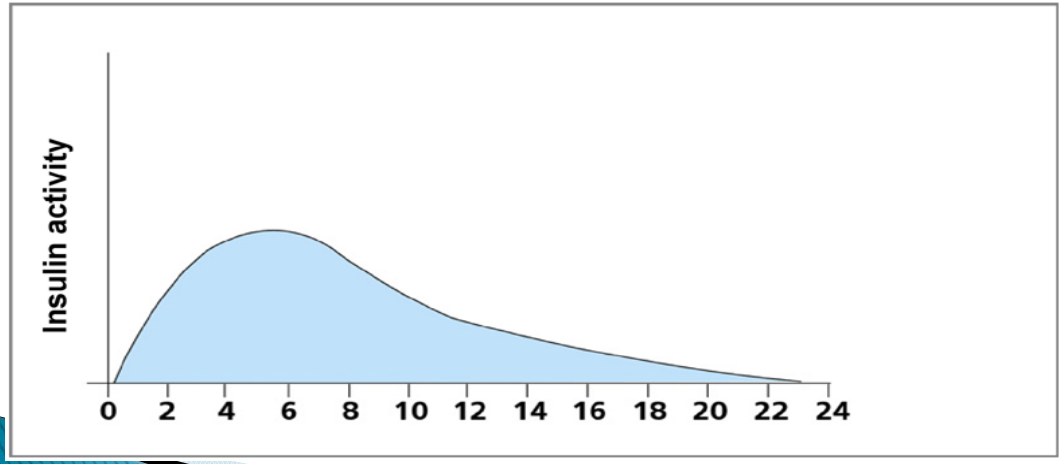
Pinderfield's Experience – 200 patients with T2DM



Pract Diab Int 2007;24:212-216

Starting Insulin therapy

- Isophane insulin (intermediate acting) at bedtime – add in to oral hypoglycaemias
- Usually injected at bedtime.
- Reluctance to starting insulin
- Least weight gain and lower risk of hypoglycaemia
- Will need to progress onto further insulin regimes
- Titration



Humulin I
Insulatard
Insuman basal

Insulin intensification

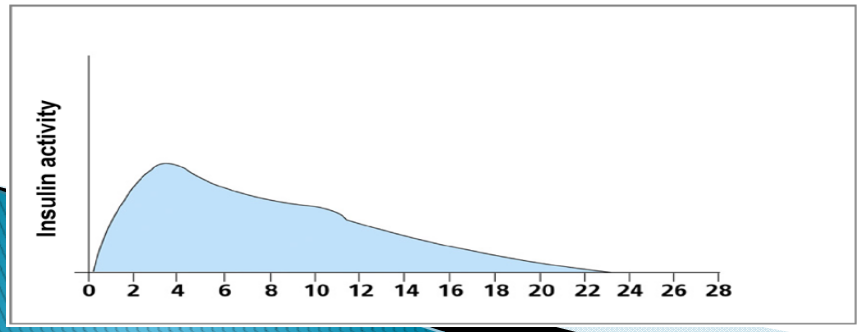
BD – TDS mixed insulin

or

Basal Plus – Addition of fasting acting insulin with main meal (± other meals – leading to basal bolus insulin regime)

Human insulin mixtures *(soluble/isophane)*

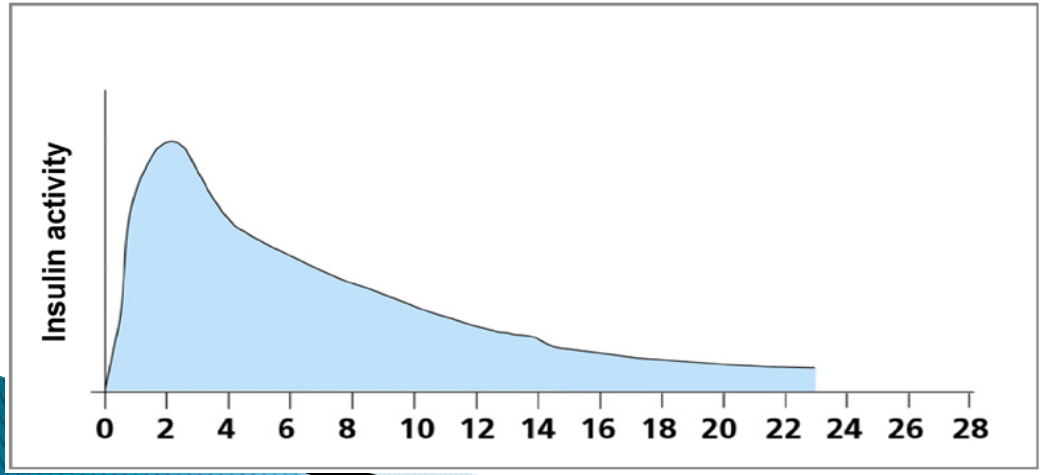
- Injected twice-daily 20-30 minutes before meals.
- Regular lifestyle
- Symptomatic
- Failure of basal insulin
- Increased risk of weight gain / hypoglycaemia than with basal insulin
- In insulin naive patients usually start with 10 units BD
- If switching from once daily basal insulin
  - Consider reducing dose by 10 -20%
  - Either 50 /50 spilt of dose or 2/3rds am 1/3 evening
  - Stop Sulfonylurea's
  - Continue Metformin / Pioglitazone if tolerated



Humulin M3
Insuman Comb
15/25/50

Insulin analogue mixtures

- Inject twice daily, within 0 to 15 minutes before or after meals.
- Useful in rapid post prandial rise
- Increase risks of hypoglycaemia
- Titration



Humalog Mix25, Mix50

Novomix 30

Titration guidelines

- Increase insulin every three – five days and review until individual targets are achieved
  - Morning dose titrated against pre lunch, pre evening meal blood glucose
  - Evening dose titrated against pre bed and pre breakfast blood glucose

Titration guidelines

Fasting blood Glucose mmol/l	Action
>10	Increase by 4 units
8 – 10	Increase by 2 units
5 - 7	No change
3 - 5	Reduce by 2 units
<3	Reduce by 4 units

Basal plus

- Addition of prandial rapid acting insulin to basal insulin
  - Monitor 2hr –post meal blood glucose,
  - Give rapid dose with main meal or highest post meal blood glucose level
  - Stepwise approach leading to injection with each meal
  - Usual starting dose 6 units
    - Novorapid / Humalog / Apidra
- Continue on basal insulin

Summary

- Stepwise approach
- Newer therapies should be considered first especially if weight / hypoglycaemia risk is an issue
- No one insulin regime fits all
- Intensification necessary in majority of patients
- Individual assessment on most appropriate regime

Case Study 1
Frank

- 63 yrs Type 2 DM 5yrs Retired

- HbA1c 109mmol/mol (12.1%) Wt 87.8kgs BMI 29.7
- Non symptomatic
- Complications: Background Retinopathy
- Diabetes Medication:
  - Gliclazide 160mgs BD
  - Pioglitazone/Metformin 15/850 1 BD

Frank

Commenced Insulin

Isophane insulin 10units at bedtime

Continued on Pioglitazone/Metformin and Gliclazide

3.9% drop in HbA1c

5.6kgs increase in weight

	Weight Kg	BMI	HbA1c
Start	87.8	29.7	12.1
3 mts	89.9	30.4	9.1
6 mts	91.2	30.8	8.7
12mts	93.4	31.6	8.2

Case Study 2
Peter

- 68 yrs Type 2 DM 2 yrs Retired
- HbA1c 84mmol/mol (9.8%) Wt 72kgs BMI 24.9
- Symptomatic: thirst, weight loss
- Complications : NAD
- Diabetes Medication:
  - Gliclazide 160mgs BD
  - Pioglitazone 45mgs OD
  - Metformin SR 1G daily

Peter

Commenced BD Pre Mixed Insulin
10 units BD
Gliclazide & Pioglitazone stopped

1.2% drop in HbA1c at 1yr
4.2kg increase in weight

	Wt Kg	BMI	HbA1c%
Start	72	24.9	9.8
3mts	73.6	25.5	9.2
6mts	76.2	26.4	8.6

Case study 3
Christine

- 73 yrs Type 2 DM -11 yrs duration
- HbA1c 73mmol/mol (8.8%) Wt 104.8 BMI 35.8
- Symptomatic – lethargy
- Lives alone
- Complications: CKD stage 4 (eGFR 27, Creatinine 219mmol/l)
- Diabetes Medications:
  - Gliclazide 160mgs BD
  - Pioglitazone 30mgs OD

Christine

Commenced Basal insulin
10 units Basal Analogue

0.9% drop in HbA1c

1.8Kg weight increase

	Wt Kg	BMI	HbA1c%
Start	104.8	35.8	8.8
3mts	106.8	36.5	8.5
6mts	106.6	36.5	7.9

Case Study 4
Shirley

Female 54 yrs old Admin support worker

- **Type 2 Diabetes 4 yrs duration**

- HbA1c 72mmol/mol (8.7%) WT 148.6kgs
  BMI 52.9

- Non Symptomatic

- Medication:
  - Gliclazide 80mgs BD
  - Metformin SR 2G daily
  - Orlistat 120mgs TDS
  - Simvastatin 40mgs daily

Shirley

Commenced on GLP-1
Gliclazide stopped

Wt reduction 13.3Kgs
HbA1c reduction 1.6%

	Weight Kg	BMI	HbA1c
Start	148.6	52.9	8.7
3 mts	139.7	49.7	7.1
6 mts	137	48.8	7
1 year	135.3	48.2	7.4

References

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