What did we cover last time?

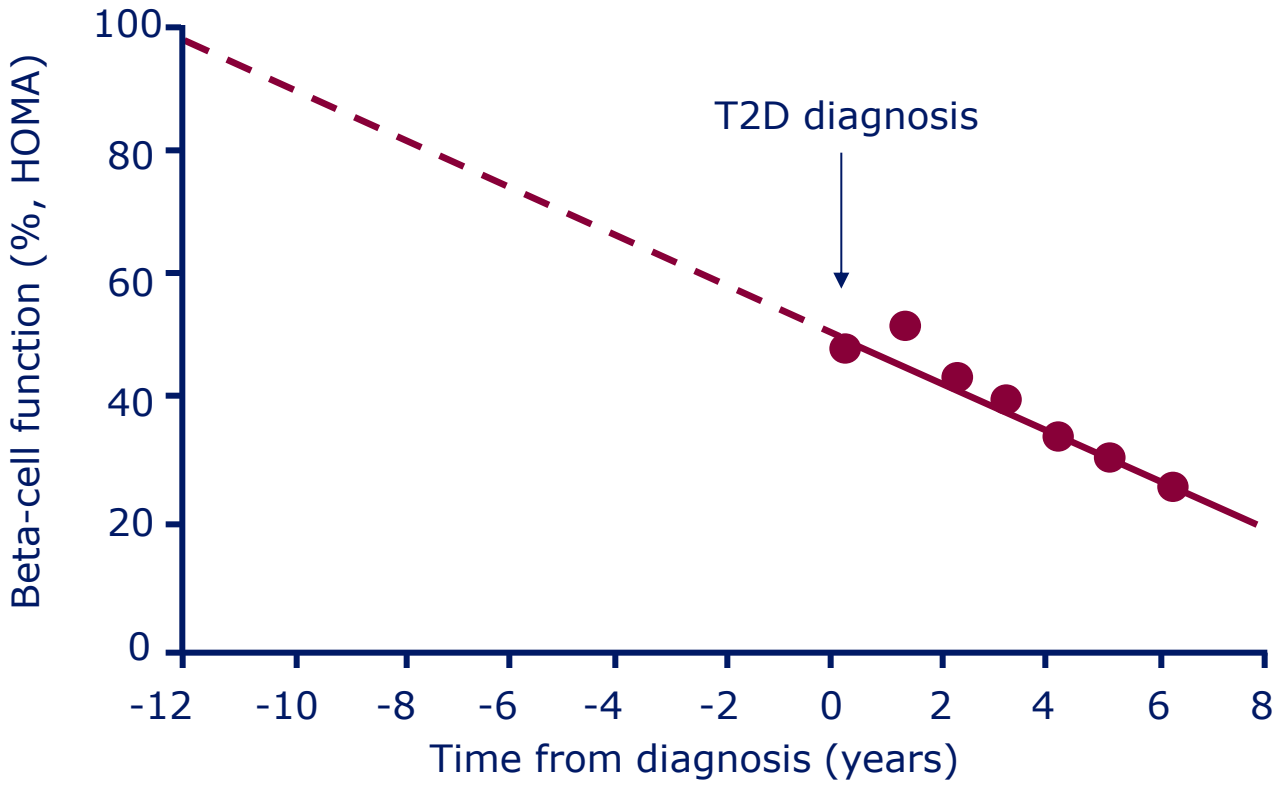
- The annual review, care planning and evidence based interviews
- Multi-risk factor approach
- Diagnosis and categorisation
- What insulins are available and how to use them

What are we going to cover today?

- Choosing oral agents
- When to consider GLP1 agonists
- Trial of treatment – judging success/failure
- When to start insulin and which regime to use

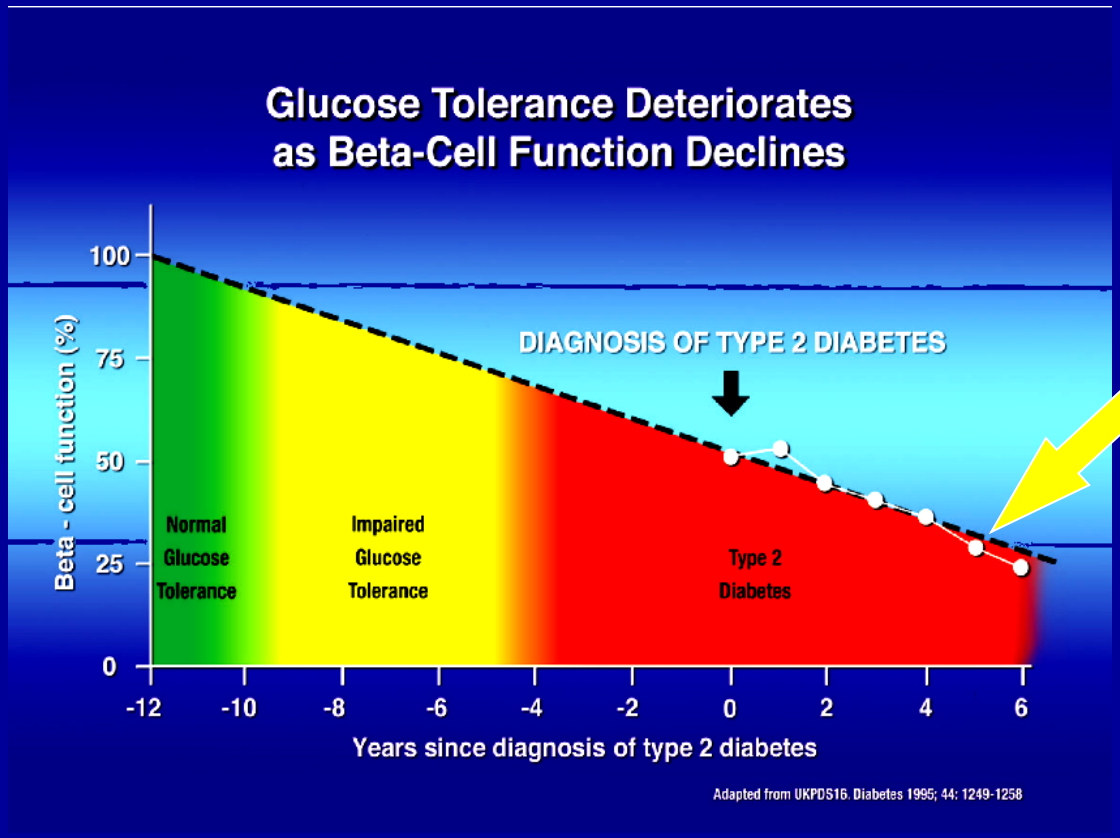
- (We have not covered insulin dose adjustment or insulin management in type 1 diabetes)

Decline in beta-cell function is already advanced at time of diagnosis[1]



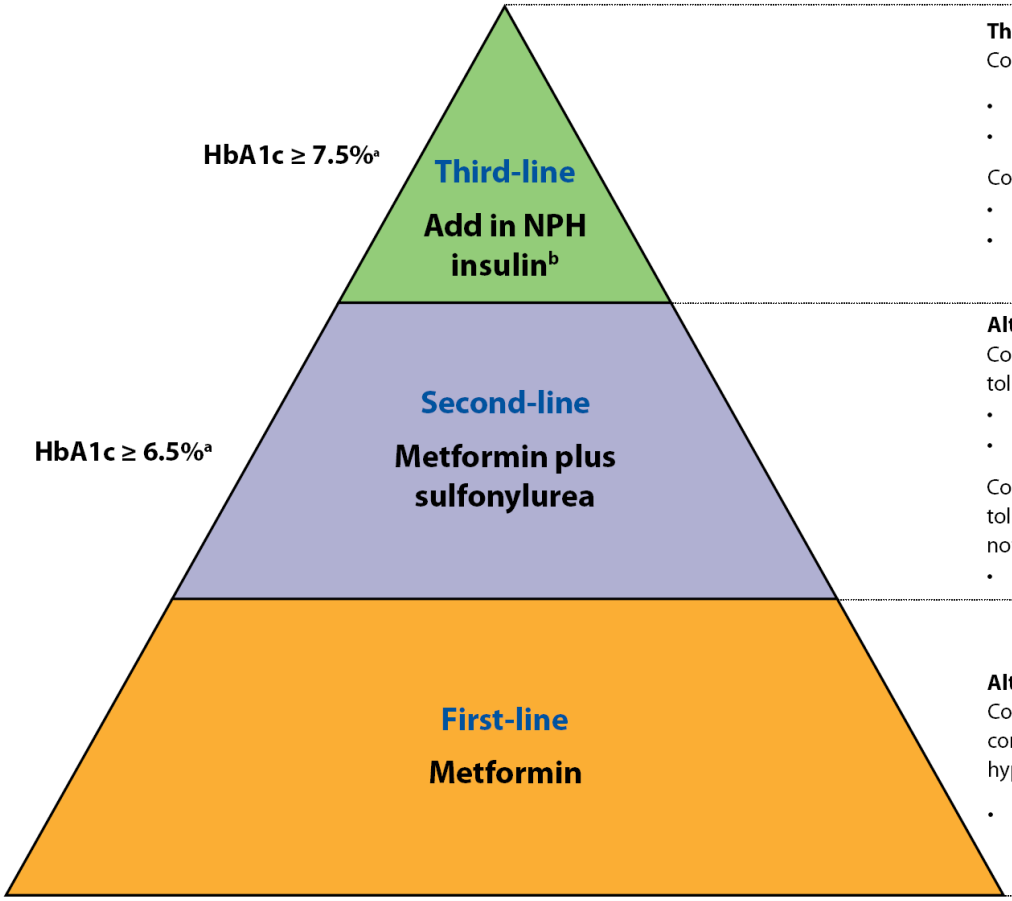
1. Adapted from Lebovitz H. Diabetes Reviews 1999;7:139–153

The Starling Curve of the Pancreas



Oral hypoglycaemic agents will eventually fail to control glycaemia as B cell function declines

Summary of NICE Guidance



Alternative options in specific circumstances

Third-line alternatives (see Appendix 1 for details)
Consider only if insulin[b] is unacceptable or inappropriate:

- Metformin + sulfonylurea + pioglitazone▼
- Metformin + sulfonylurea + sitagliptin▼

Consider only if specific BMI criteria are met:

- Metformin + sulfonylurea + exenatide▼
- Metformin + sulfonylurea or pioglitazone▼ + liraglutide▼ 1.2mg

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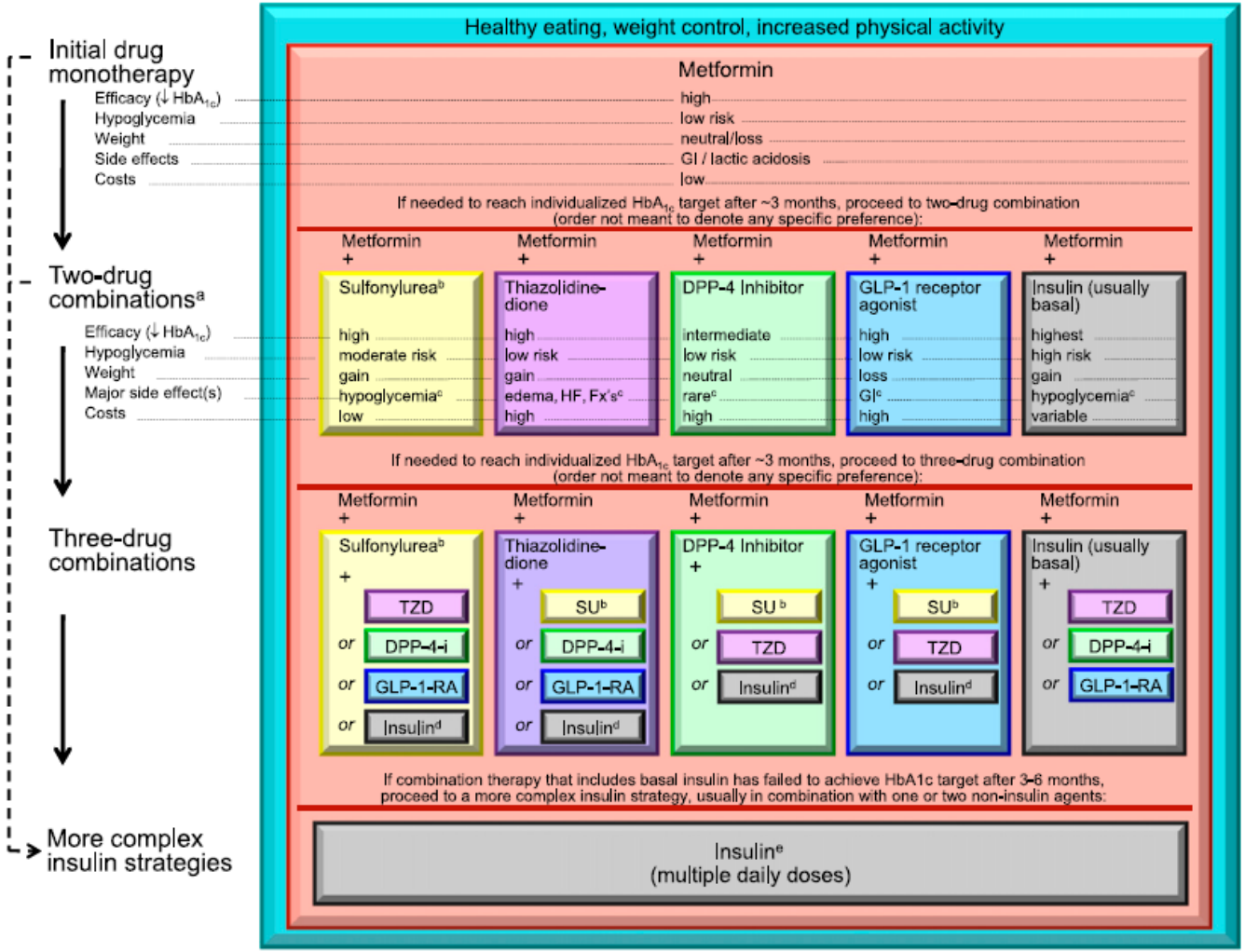
Newer hypoglycaemic drugs are effective at reducing HbA1c levels, but they all lack robust clinical outcome data

New guidance due for publication in August 2015

ADA/EASD Position Statement



Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach

Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Composite endpoint HbA_{1c} and weight loss

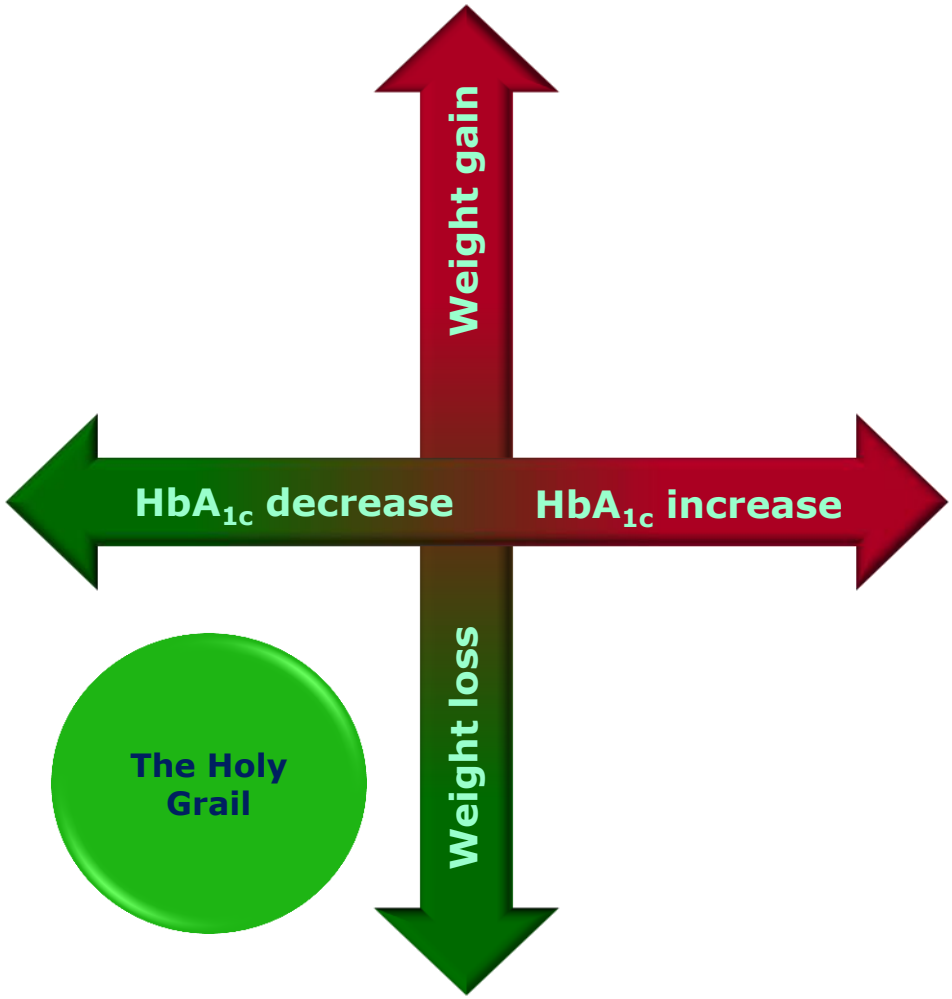
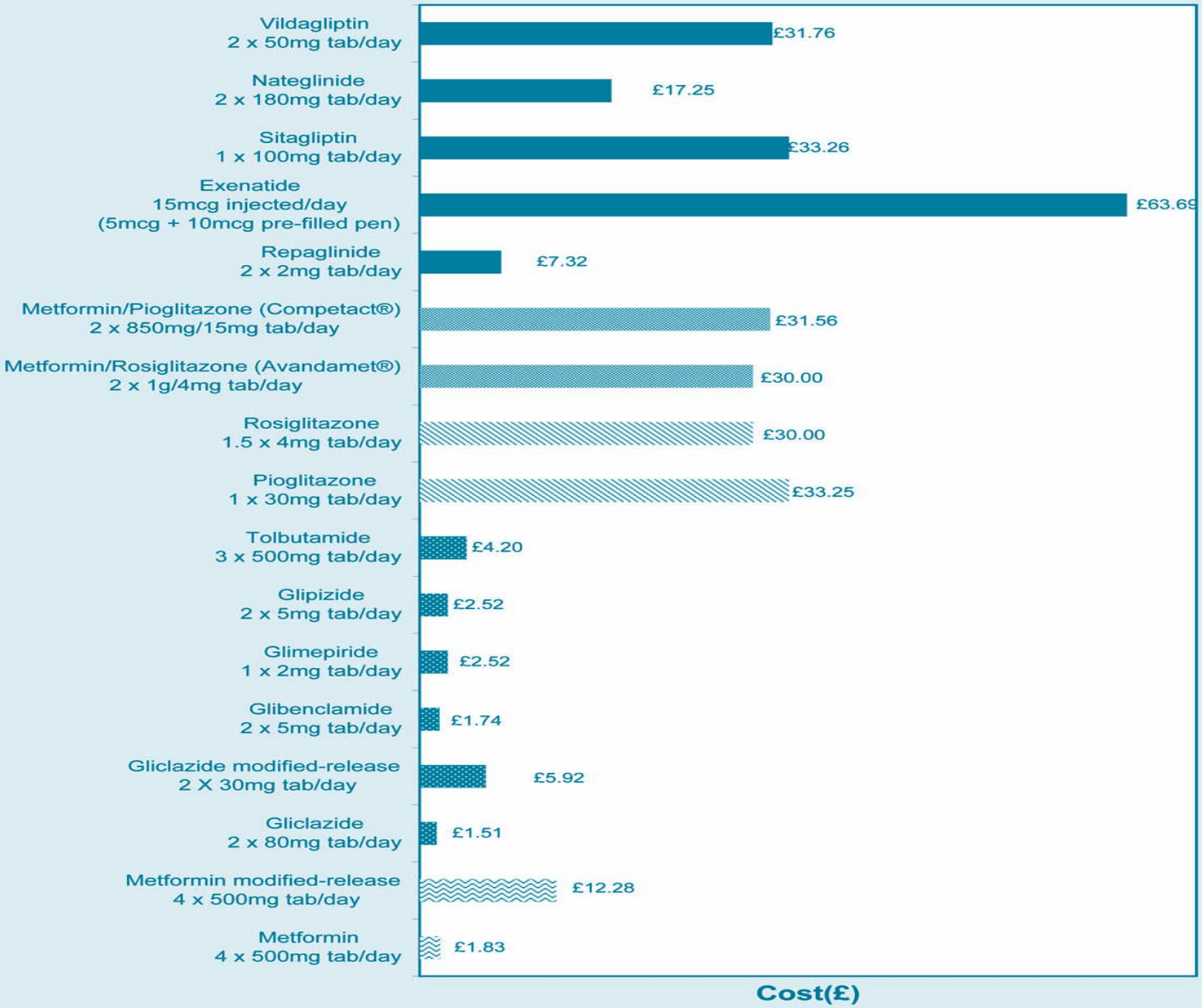


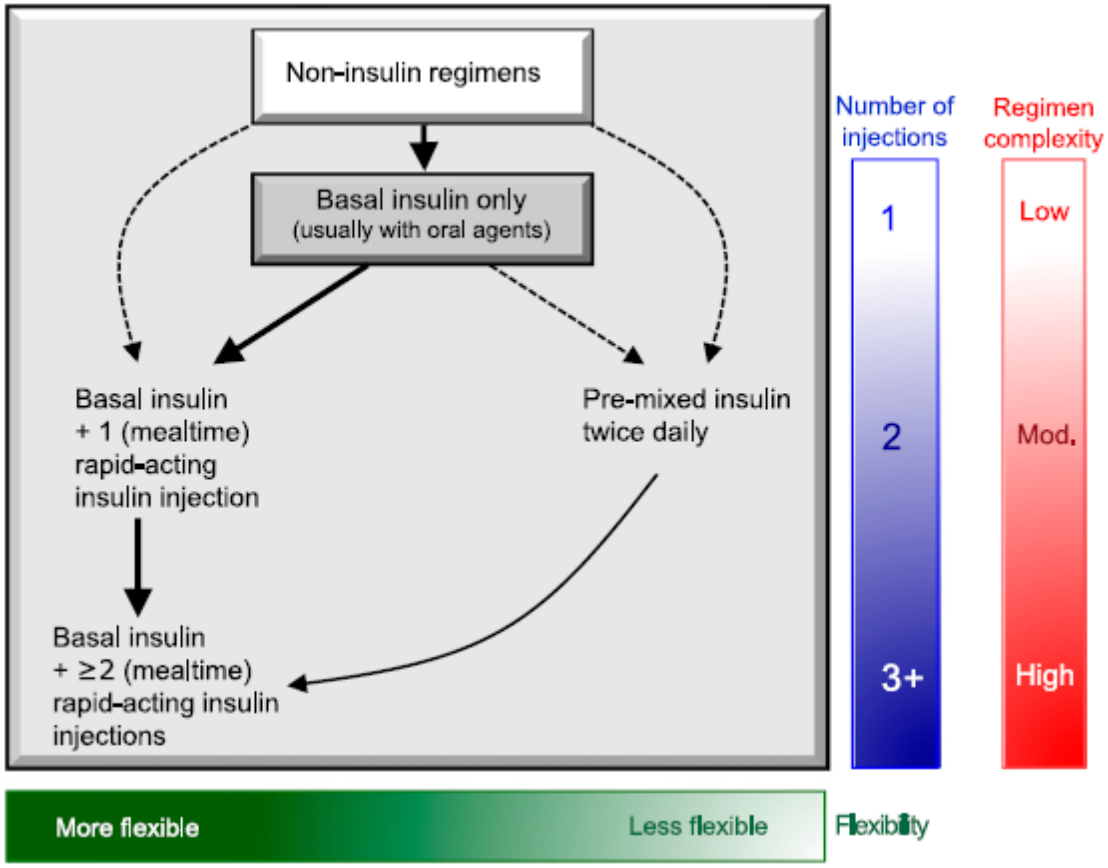
Figure 17: Cost for 28 Days Treatment

Insulin not included



Prices based on Drug Tariff May 2009 or Chemist and Druggist May 2009. Dose based on WHO DDDs where possible, otherwise BNF stated dose. The WHO DDD is a unit of measurement based on the assumed average maintenance dose in adults. It may not necessarily reflect the actual dose used.

Approach to Insulin Regimes



Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach

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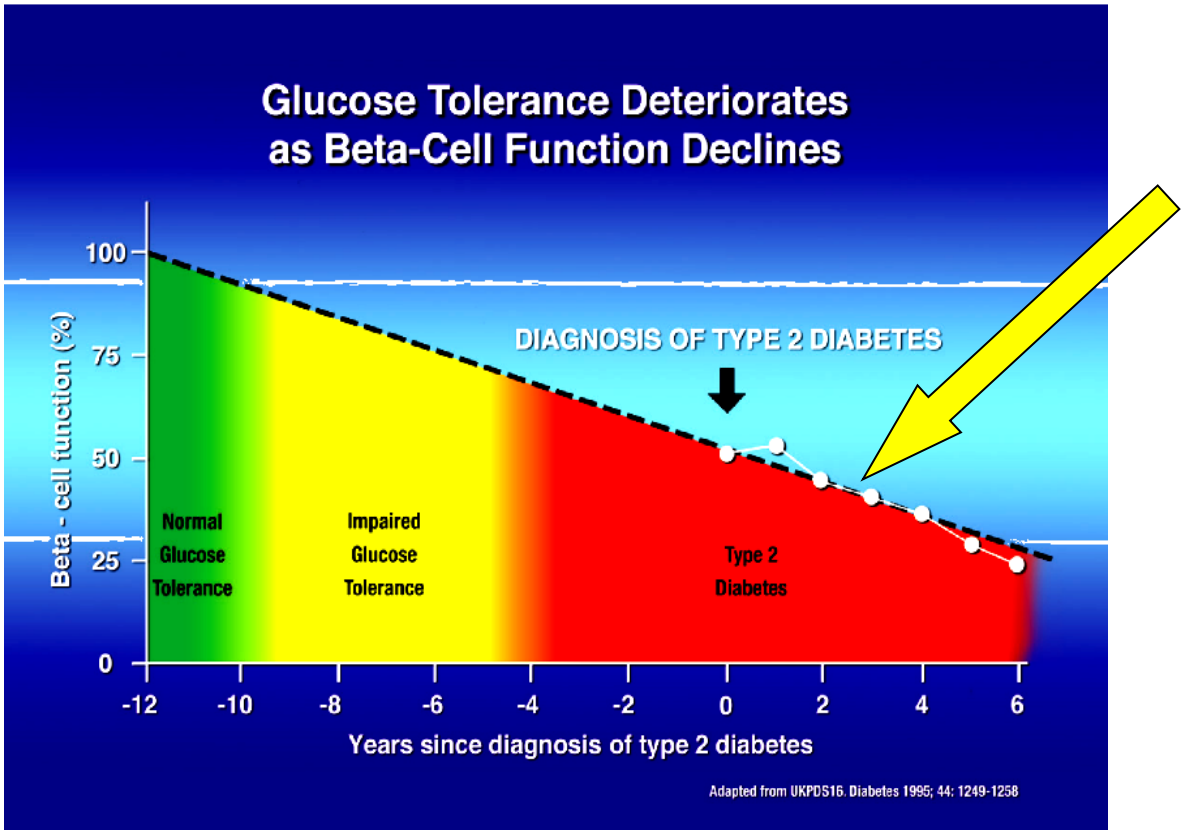
Case 1

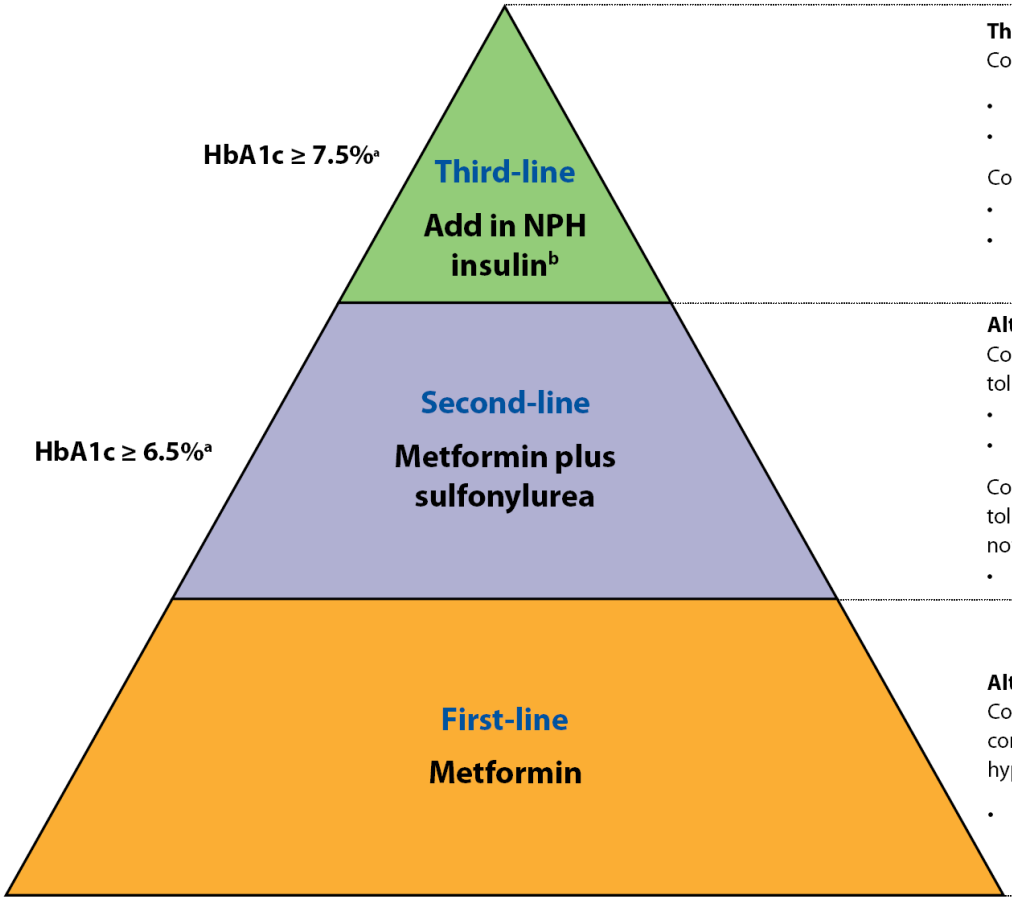
- 48 year old man who drives a delivery van. He has type 2 diabetes (detected 4 years ago) and takes metformin and gliclazide in maximum doses. BMI is 37 (36, 37 in recent past) and HbA1c is 70.

- What are his options and what will you recommend?

Where is this person on the curve?



Summary of NICE Guidance



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- Sulfonylurea

Newer hypoglycaemic drugs are effective at reducing HbA1c levels, but they all lack robust clinical outcome data

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

NICE Recommendation

Only continue GLP-1 mimetic (Exenatide) therapy if the person has had a beneficial metabolic response

"a reduction of at least 1.0% (11mmol/mol) in HbA1c & weight loss of at least 3% of initial body weight at 6 months."

GLP-1 agonists (NICE with local adaptation)

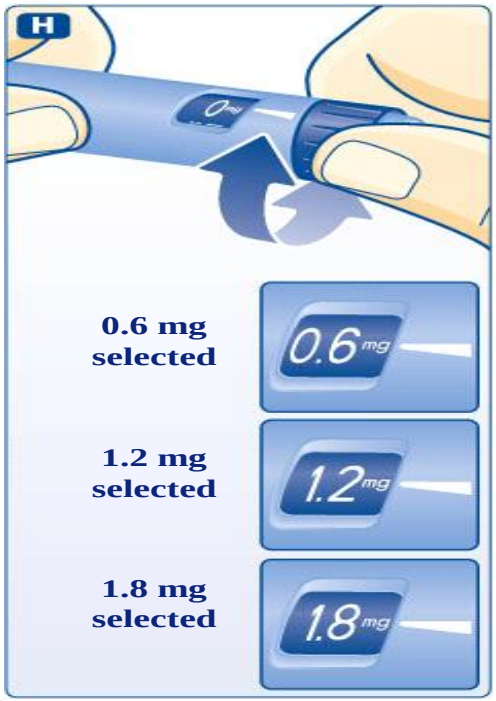
Consider adding as third-line therapy to metformin and a sulphonylurea if a person has:

- a body mass index (BMI) ≥35 kg/m^2
- a BMI <35 kg/m^2 and for whom initiation of insulin therapy would have significant occupational implications (or starting insulin would increase BMI to >35)
- Continue therapy only if a beneficial metabolic response (minimum 6 mmol/mol (0.5%) reduction in HbA1c and/or 3% weight reduction in 3 months)

1. NICE CG87 Short Guideline – Type 2 diabetes newer agents

Liraglutide(Victoza)

- Prefilled, disposable pen for s.c. injection
- Contains 18 mg liraglutide in 3 ml

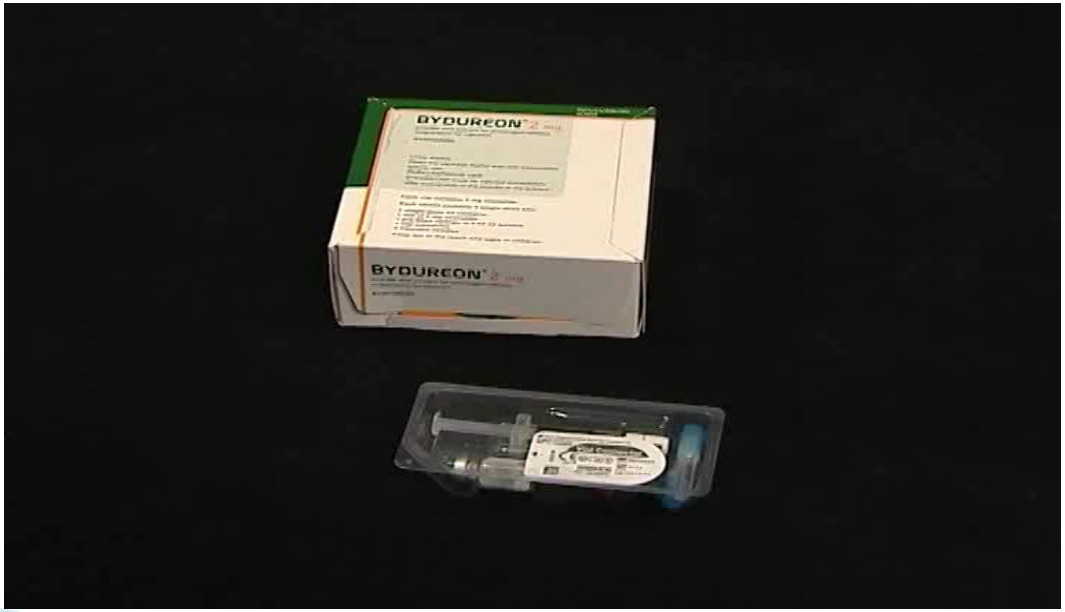


- Once-daily s.c. injection
- Select dose (0.6, 1.2 or 1.8 mg)
- Inject at any time, independent of mealtimes (preferably same time each day)
- Start with 0.6mgs for 1 week increasing to 1.2 mgs there after

Victoza® Summary of Product Characteristics

Bydureon

- Once weekly Byetta
- 2mgs dry powder for prolonged release



Contraindications of GLP-1

- Not recommended in moderate/severe renal impairment
- Pregnancy/breast feeding
- Type 1 Diabetes
- Pancreatitis
- Risk of Hypoglycaemia in combination with sulphonylurea

Patient Education for GLP-1

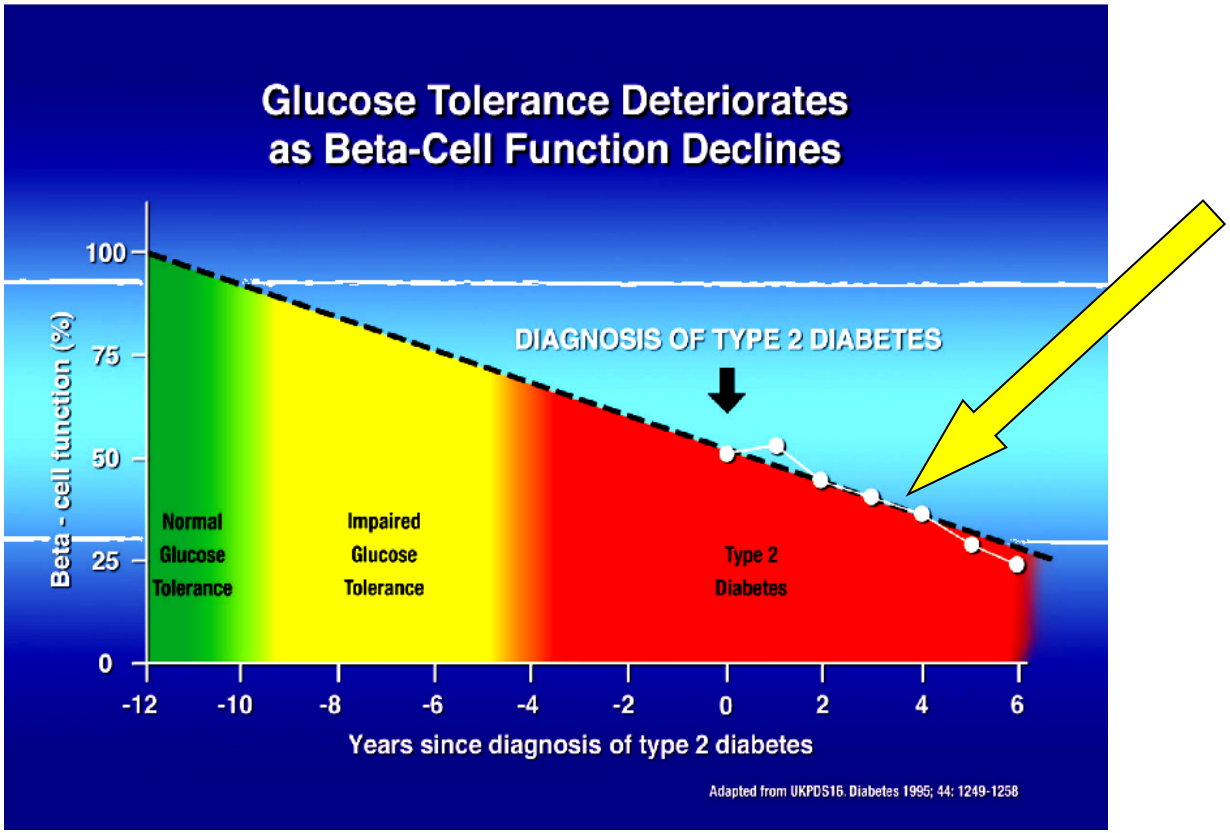
- Management of potential side effects
- Hypoglycaemia management
- Blood glucose monitoring
- Check prescribing information for warnings regarding potential drug interactions (oral contrapetives/antibitotics
- Injection technique/ safe use of sharps
- Expectations of therapy

Case 2

- 68 year old retired man with T2DM detected 10 years ago. BMI stable at 40 and HbA1c 74 (and rising) on metformin and sitagliptin.

- What are his options and what will you recommend?

Where is this person on the curve?



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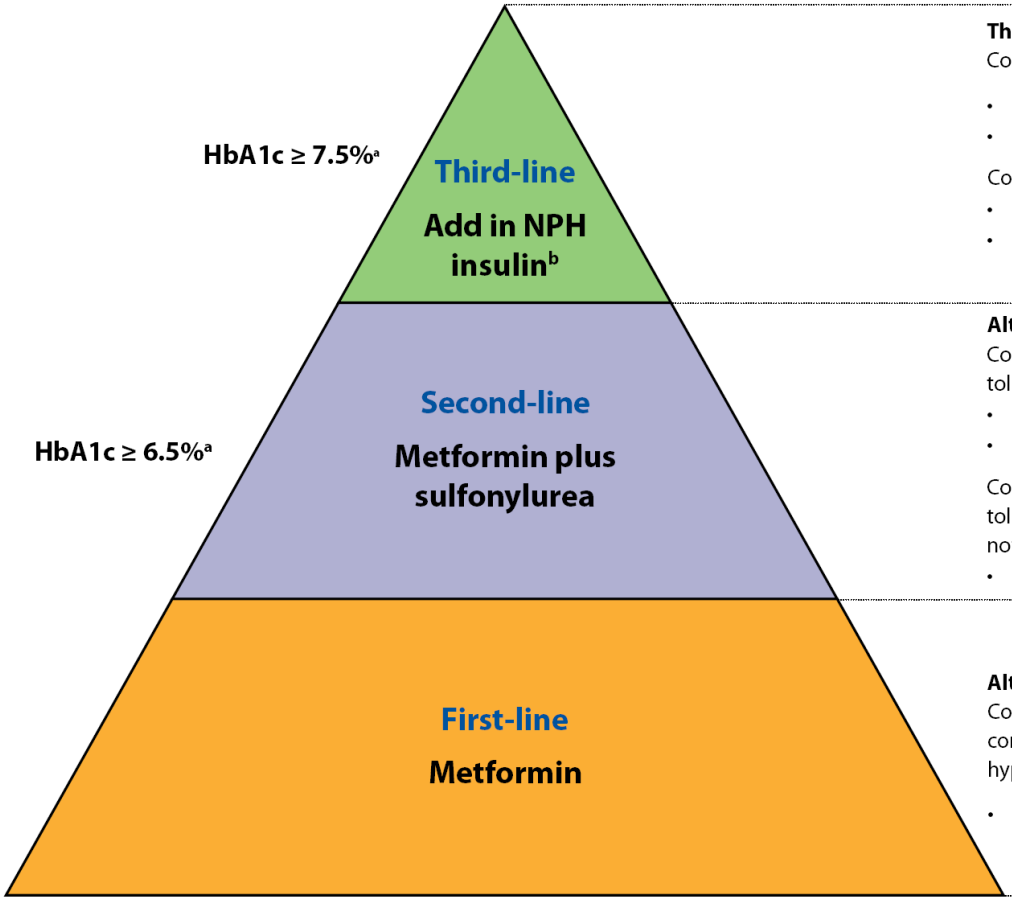

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- Sulfonylurea

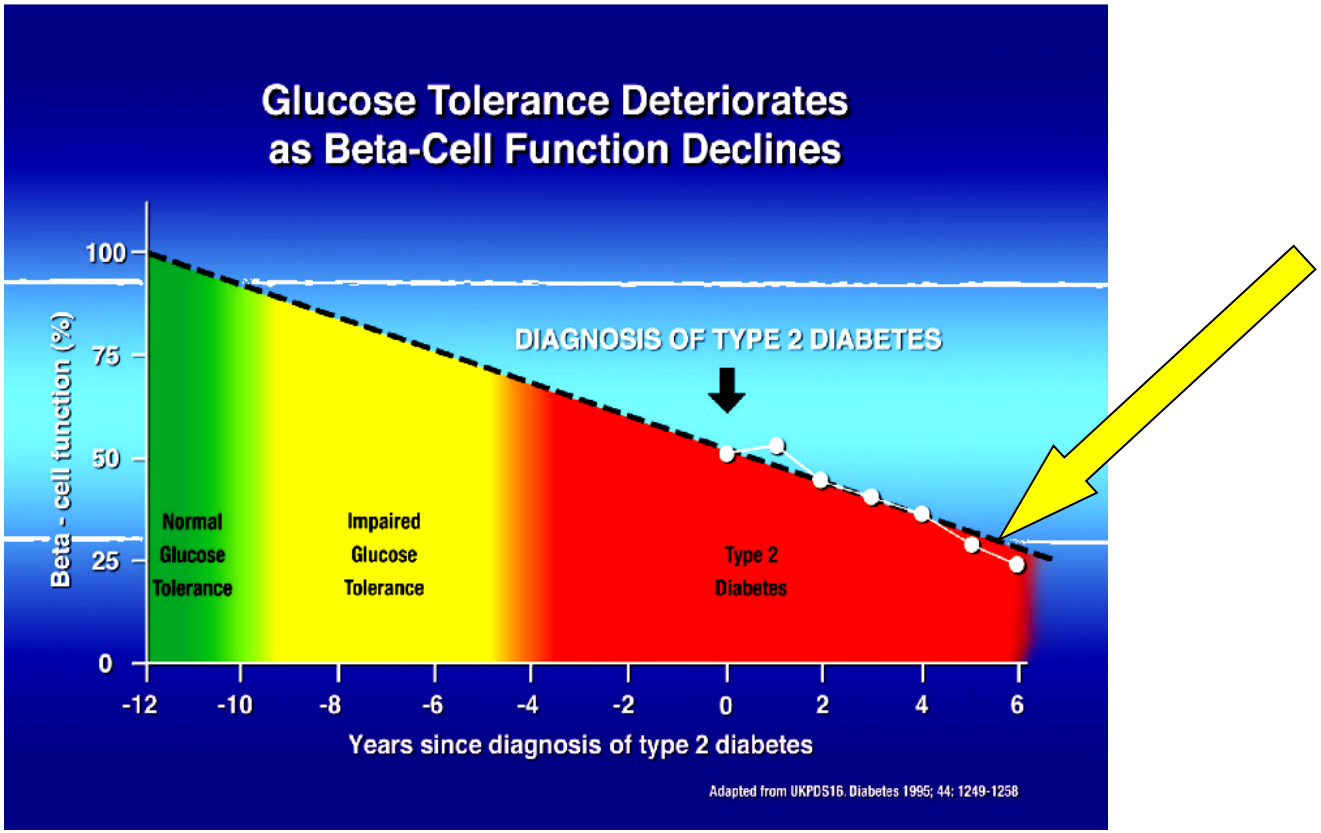
Newer hypoglycaemic drugs are effective at reducing HbA1c levels, but they all lack robust clinical outcome data

Case 3

- 74 year old woman with type 2 diabetes detected 4 years ago (HbA1c at diagnosis was 90). Current HbA1c is 90 on metformin, gliclazide 80mg bd, and sitagliptin. BMI is 32. She feels tired and thirsty at times. She also has hypertension treated with bendro and amlodipine. She has developed diarrhoea which is severe at times

- What are his options and what will you recommend?

Where is this person on the curve?



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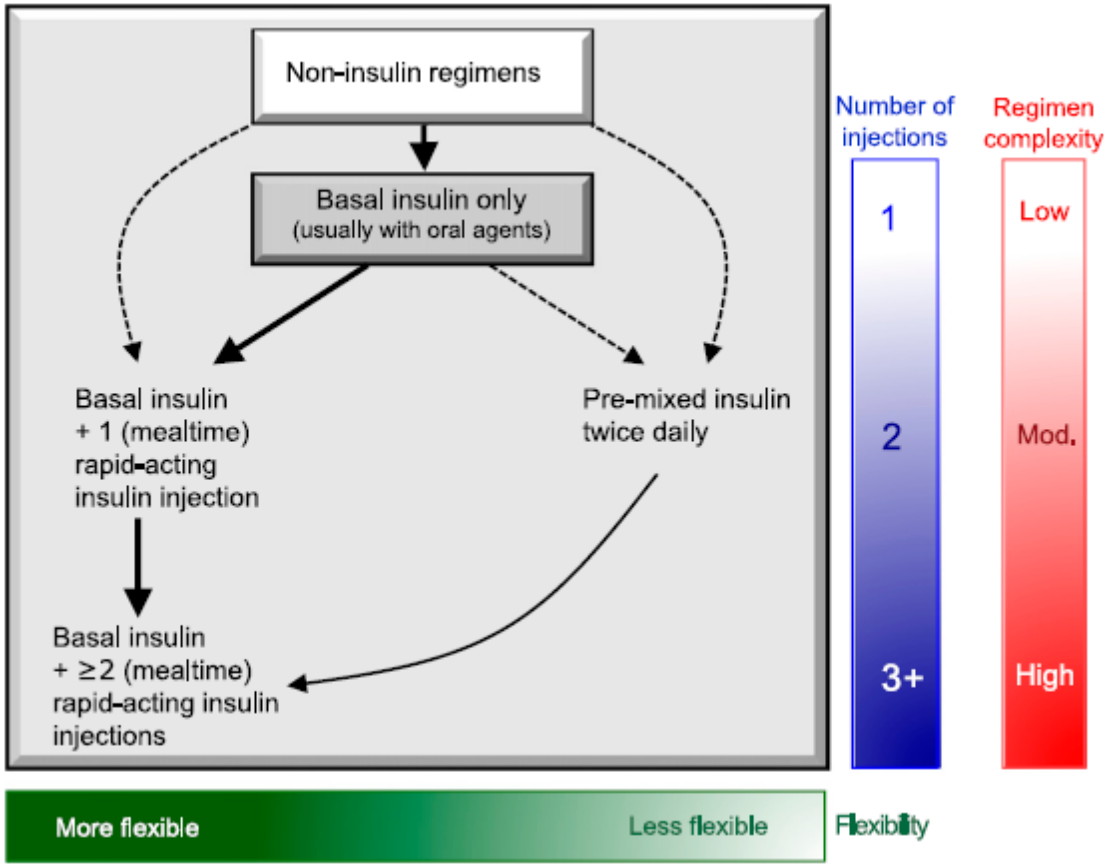

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Case 4

- 52 year old woman with long history of obesity (BMI currently 54) and mobility has been declining as a result. Her type 2 diabetes is poorly controlled on metformin, gliclazide and exenetide. She has been taking the latter for a year and having initially lost some weight is now back to where she started. She is thirsty and has significant polyuria

- What advice would you give?

Case 5

- A 54 year old man drives a lorry for a living. He eats a poor diet because that's all that's available and has little time for exercise. His HbA1c is 80 and rising and he likes his glucose to be about 10 whilst he's at work. He has no symptoms. His BMI is stable at 33. He takes metformin, gliclazide and sitagliptin.

- What advice would you give him?

Case 6

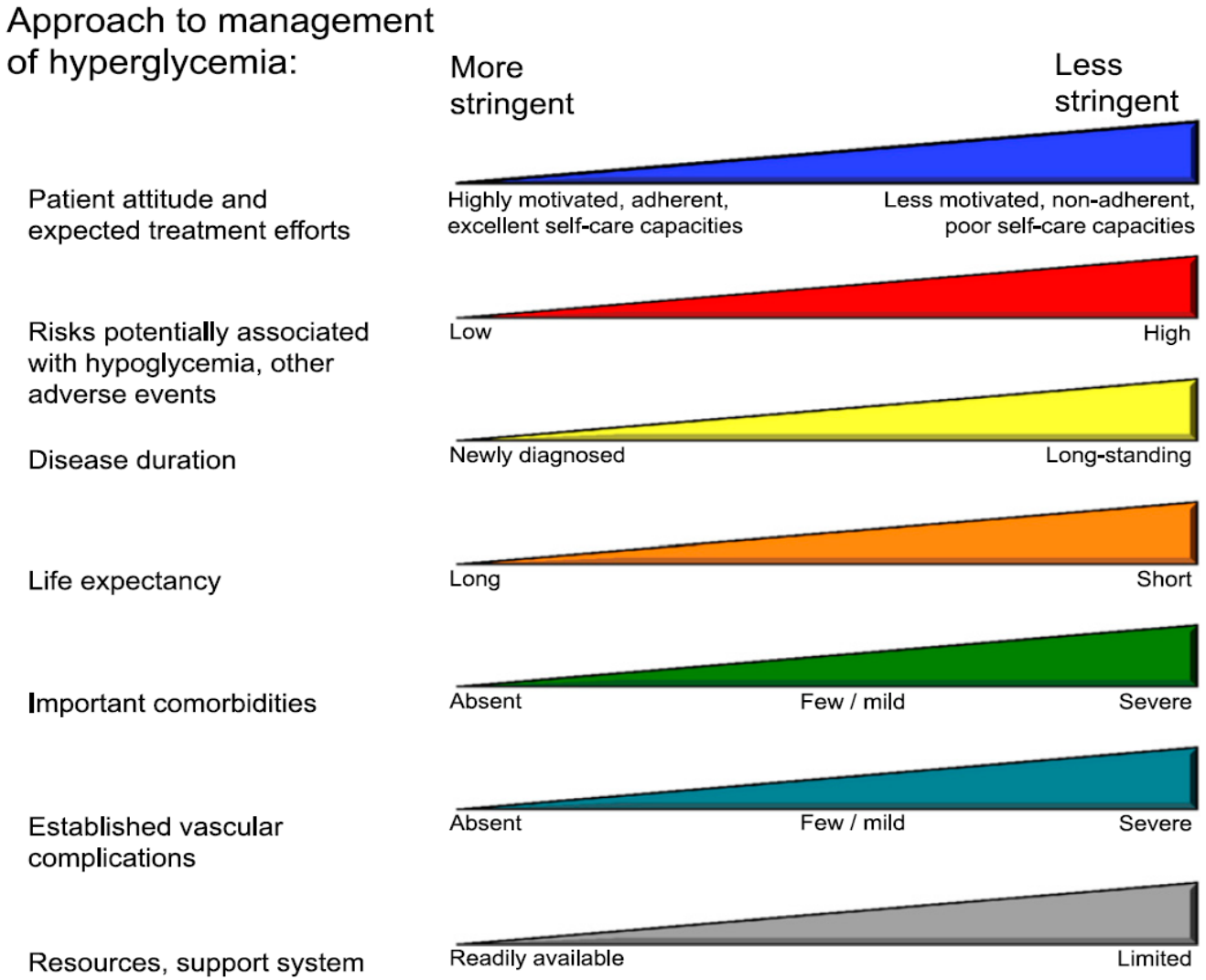
- A 55 year old man drives a lorry for a living. He eats a poor diet because that's all that's available and has little time for exercise. His HbA1c is 90 and rising and he likes his glucose to be about 10 whilst he's at work. He has no symptoms. His BMI is stable at 34. He takes metformin, gliclazide and liraglutide.

- What advice would you give him?

Case 7

- An 84 year old woman who has had diabetes for 5 years. She remains active and apart from some tiredness at times she is well. Her HbA1c is 86 and her BMI is 28. She takes gliclazide and sitagliptin (metformin stopped because of change in bowel habit). She has had one fall where she tripped in town one afternoon whilst shopping.
- What advice would you give?

An Aid to Decision Making in Type 2 Diabetes



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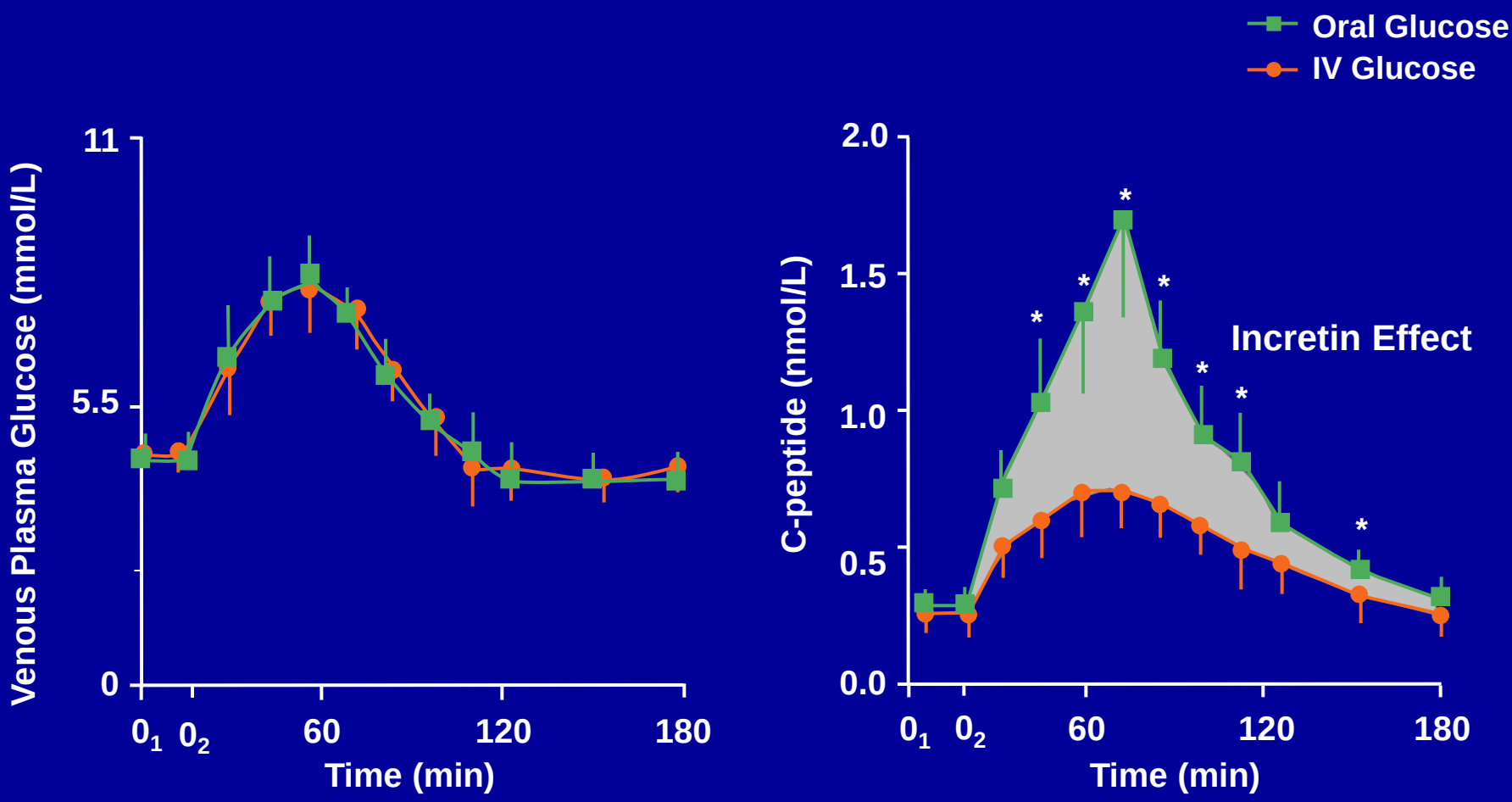
Treatment Trials

- Metformin – should be continued regardless of glucose response
- Sulphonylurea – lack of response rare until late in beta-cell decline
- DPP4 inhibitors, GLP1 agonsists and glitazones – 3-6 month trial with variable criteria for success or failure
- Insulin – trial may be justified in some

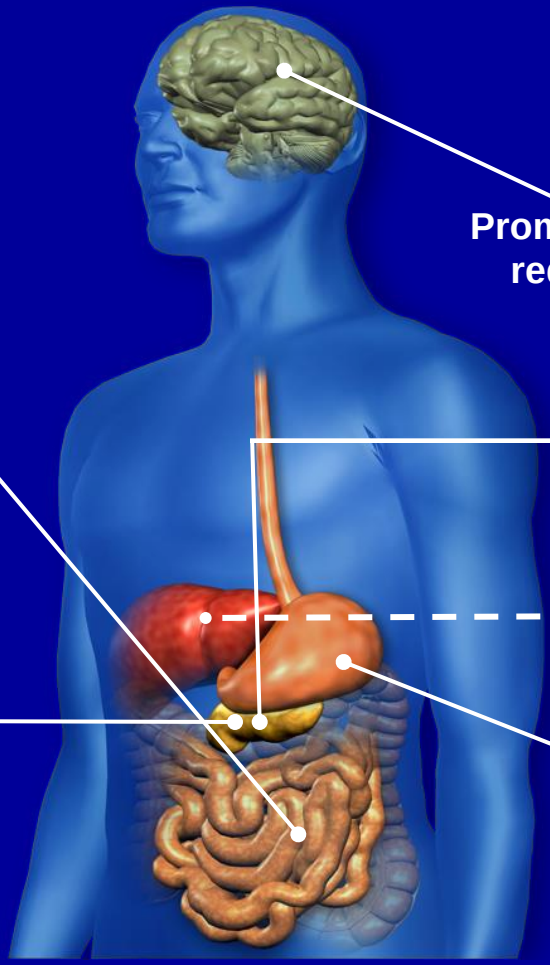
The Incretin Effect Demonstrates the Response to Oral vs IV Glucose



Mean ± SE; N = 6; *$P \leq .05$; 0_1-0_2 = glucose infusion time.

Nauck MA, et al. Incretin effects of increasing glucose loads in man calculated from venous insulin and C-peptide responses. *J Clin Endocrinol Metab.* 1986;63:492-498.

GLP-1 Effects in Humans: Understanding the Glucoregulatory Role of Incretins



GLP-1 secreted upon the ingestion of food

↑ Beta-cell response

↓ Beta-cell workload

Promotes satiety and reduces appetite

Alpha cells:
↓ Postprandial glucagon secretion

Liver:
↓ Glucagon reduces hepatic glucose output

Beta cells:
Enhances glucose-dependent insulin secretion

Stomach:
Helps regulate gastric emptying

Adapted from Flint A, et al. *J Clin Invest*. 1998;101:515-520.; Adapted from Larsson H, et al. *Acta Physiol Scand*. 1997;160:413-422.; Adapted from Nauck MA, et al. *Diabetologia*. 1996;39:1546-1553.; Adapted from Drucker DJ. *Diabetes*. 1998;47:159-169.

GLP1 agonists - a sea change?.....

……or just more of the same?