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INVOKANA® (canagliflozin) ▼ is subject to additional monitoring and it is therefore important to report any suspected adverse reactions related to this medicinal product. This will allow quick identification of new safety information

What's next after Metformin

Evolving management of Type 2

Diabetes



Gareth Thomas
Diabetes Specialist Nurse
Northern Health and Social Care Trust
Northern Ireland

Areas to be covered in presentation

- Quick overview of Type 2 Diabetes Mellitus and associated complications
- Burden of diabetes in the UK
- What are the options?
- Individualized patient care
- Achieving multiple therapy targets with SGLT2i's.
- Management overview – old vs. newer agents
- Case Studies
- Conclusion

The burden of diabetes: Figures from Diabetes UK

- Every 3 minutes someone in the UK learns that they have diabetes
- There are more than 3 million people in England living with the condition
- >2,700,000 diagnosed (90% with type 2 diabetes)
- Approximately 500,000 people have undiagnosed type 2 diabetes
- A 38% increase in diagnosed diabetes was seen between 2001 and 2013
- Another 7 million people could be at high risk of developing type 2 diabetes
- If current trends continue:
 - By 2025: 5 million people in the UK will have diabetes
 - By 2030: diabetes prevalence could be 14% in some areas

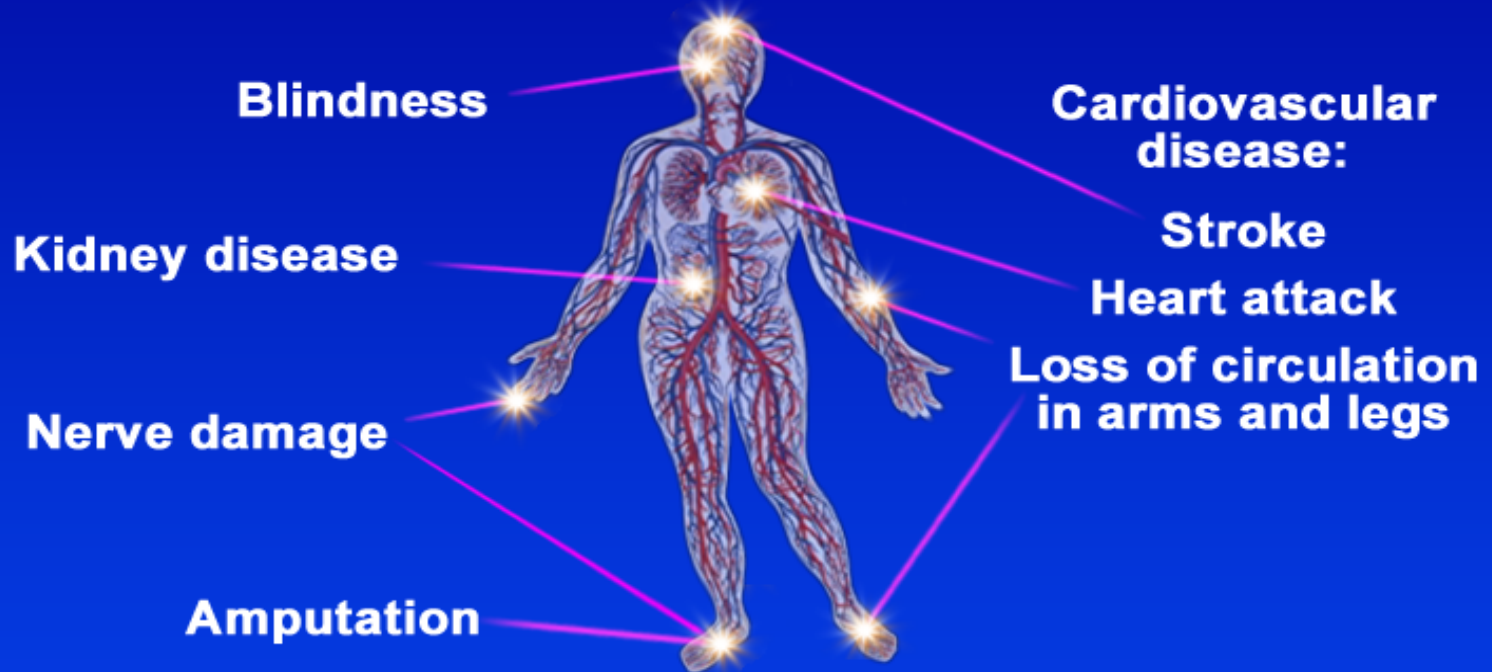


Diabetes UK (2013) State of the Nation 2013. Available at: <http://bit.ly/1gAiJXA> (accessed 01.08.2014)

Associated long-term complications of Type 2 Diabetes

Hyperglycemia Can Cause Serious Long-Term Problems

Chronic complications of diabetes



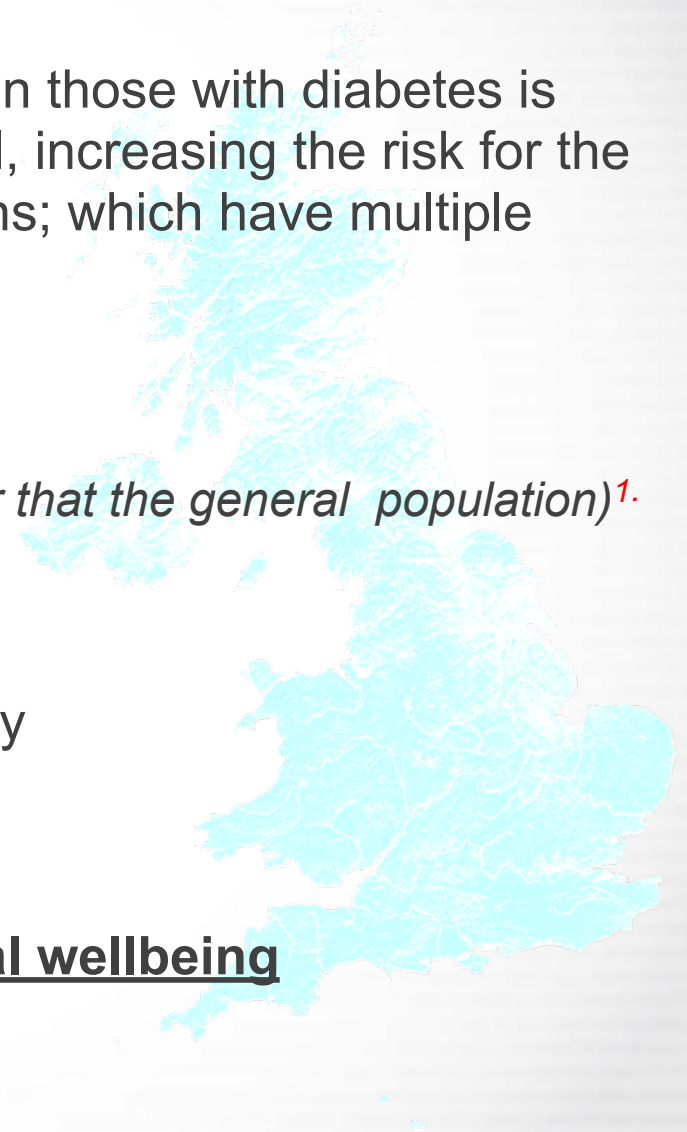
The 'Psychological' burden of diabetes

Poor emotional and psychological wellbeing in those with diabetes is associated with suboptimal glycaemic control, increasing the risk for the development of diabetes related complications; which have multiple impacts on:

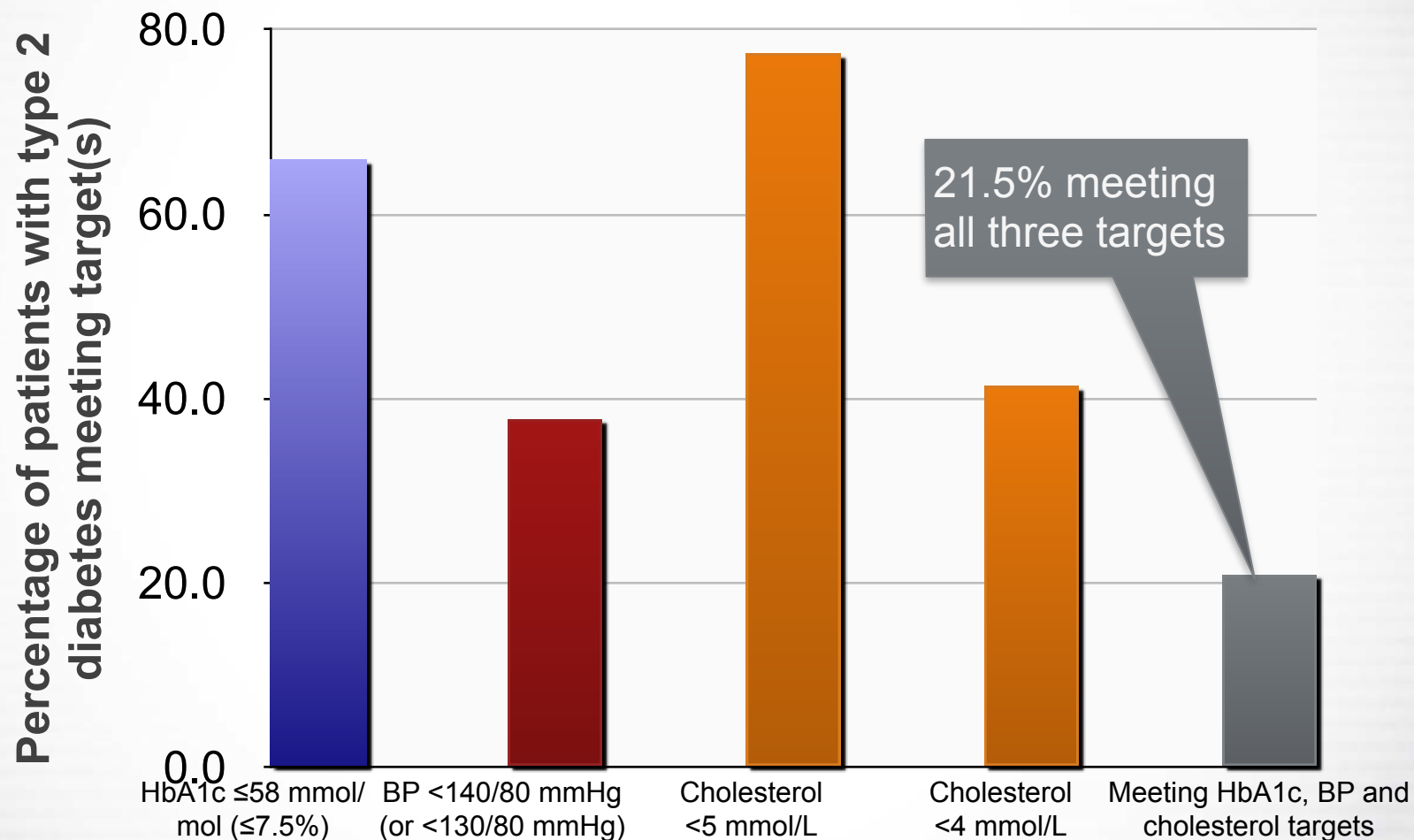
- Reduced quality of life
- Prevalence of depression (*2 to 3 times greater than the general population*)¹.
- Non compliance
- Increased mortality
- Increased healthcare costs & lost productivity

1. (Prescribing for Diabetes England 2005-06 to 2013-14 - Health and Social Care Information Centre, 2014)

Mental wellbeing = physical wellbeing



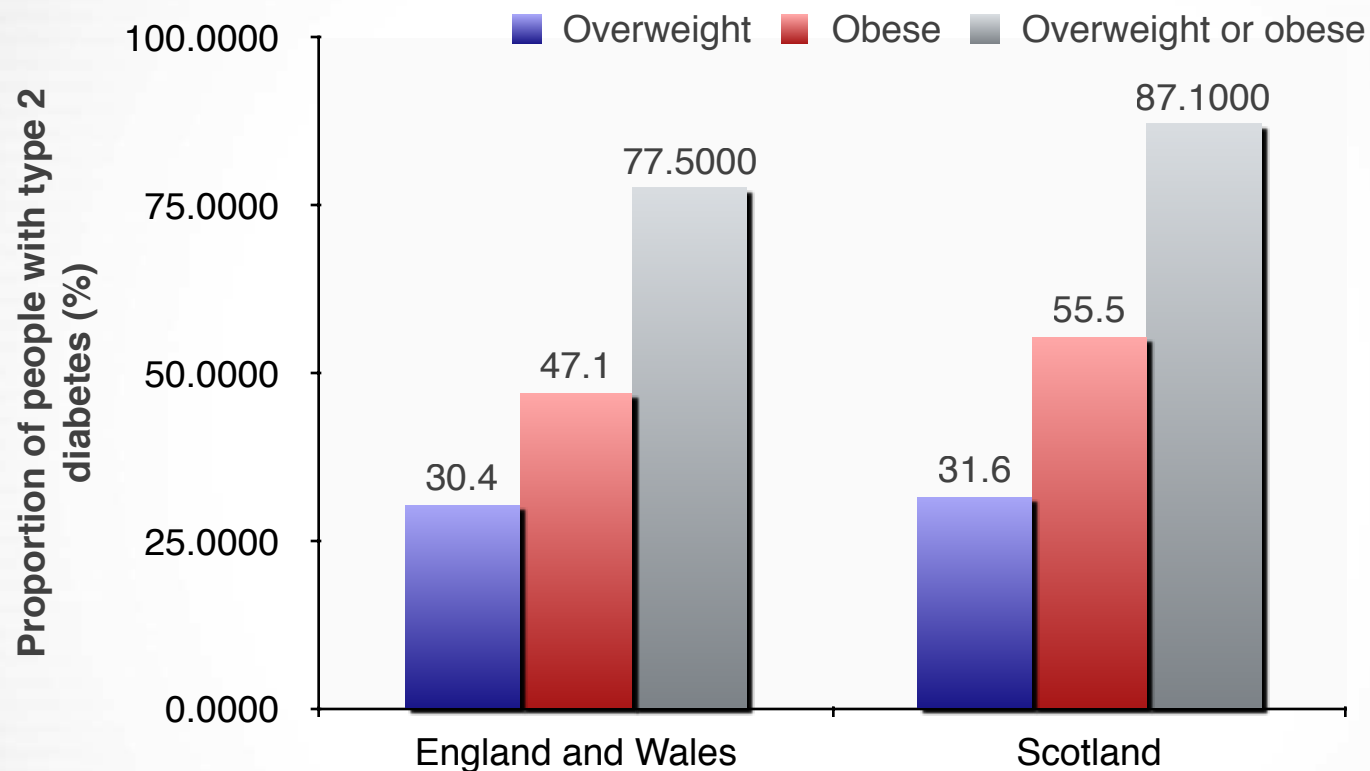
Few people with type 2 diabetes are achieving multiple treatment targets



Data for 2011–2012 for England and Wales, from the National Diabetes Audit. BP=blood pressure

Health and Social Care Information Centre (2013) *National Diabetes Audit 2011–2012. Report 1: Care Processes and Treatment Targets*. Available at: <http://bit.ly/1bk2GIh> (accessed 10.02.2014)

Prevalence of overweight and obesity in people with type 2 diabetes



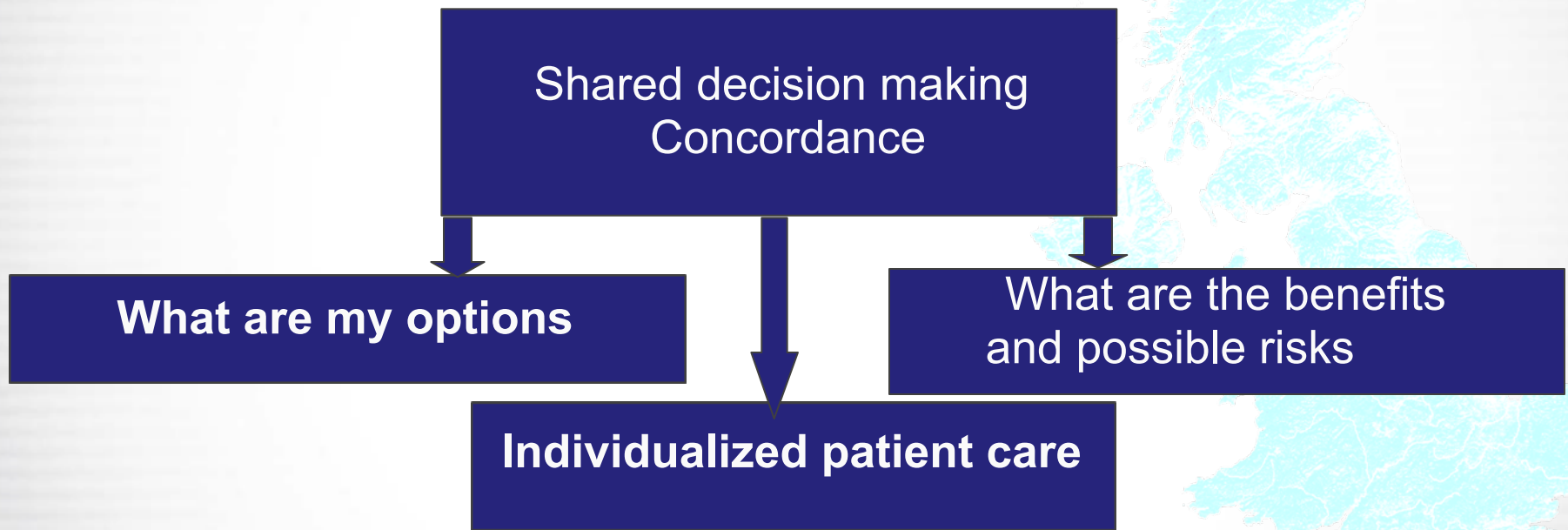
Overweight refers to BMI 25–29.9 kg/m²; obese refers to BMI ≥30 kg/m²

Health and Social Care Information Centre (2013) *National Diabetes Audit 2011–2012. Report 1: Care Processes and Treatment Targets*. Available at: <http://bit.ly/1bk2Glh> (accessed 10.02.2014)

Scottish Diabetes Survey Monitoring Group (2012) *Scottish Diabetes Survey 2012*. Available at: <http://bit.ly/1gdzGGV> (accessed 12.03.2014)

Diabetes; involving the patient

Patients with diabetes will have to make choices with regards their healthcare; but if we are to achieve better outcomes patients must be educated and involved in decisions about their short and long-term care



WHAT NEEDS TO BE DONE?

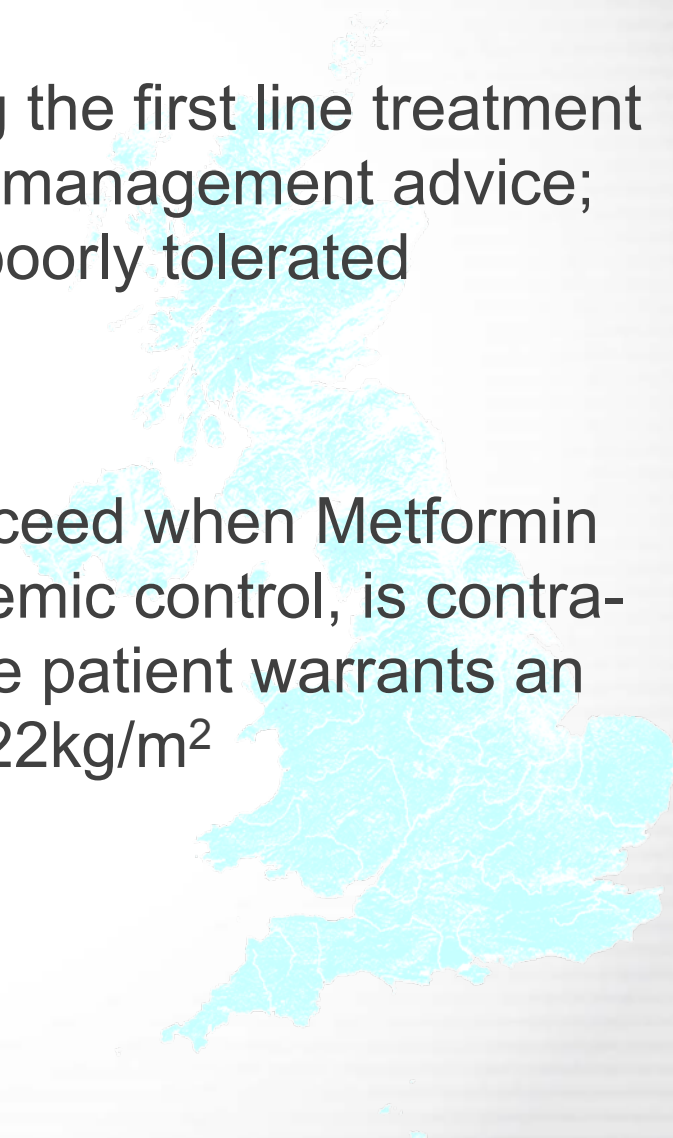
Personalised care planning should be undertaken on a regular basis to identify a patients personal healthcare need (*Guide-15 Healthcare essentials*)¹.

1. <http://www.diabetes.org.uk/Documents/15-healthcare-essentials/15-healthcare-essentials-checklist-0714.pdf>

Metformin - First line treatment

Metformin is widely accepted as being the first line treatment for Type 2 Diabetes as per medicines management advice; unless otherwise contra-indicated or poorly tolerated

BUT – In what direction are we to proceed when Metformin alone does not achieve desired glycaemic control, is contra-indicated or tailored assessment of the patient warrants an alternative to Metformin? e.g. BMI < 22kg/m²



...What next after Metformin



Ideal anti-glycaemic agents

...asking the question

- Controls glucose
- Does not cause weight gain
- Does not impact on quality of life or productivity
- Easy administration
- No/Few side effects

Treatment options for controlling hyperglycaemia in type 2 diabetes¹

Lifestyle intervention

Insulin sensitisation

Metformin, pioglitazone

Glucose excretion (*insulin-independent*¹)

SGLT2 inhibitors²

Insulin replacement

Injected insulin

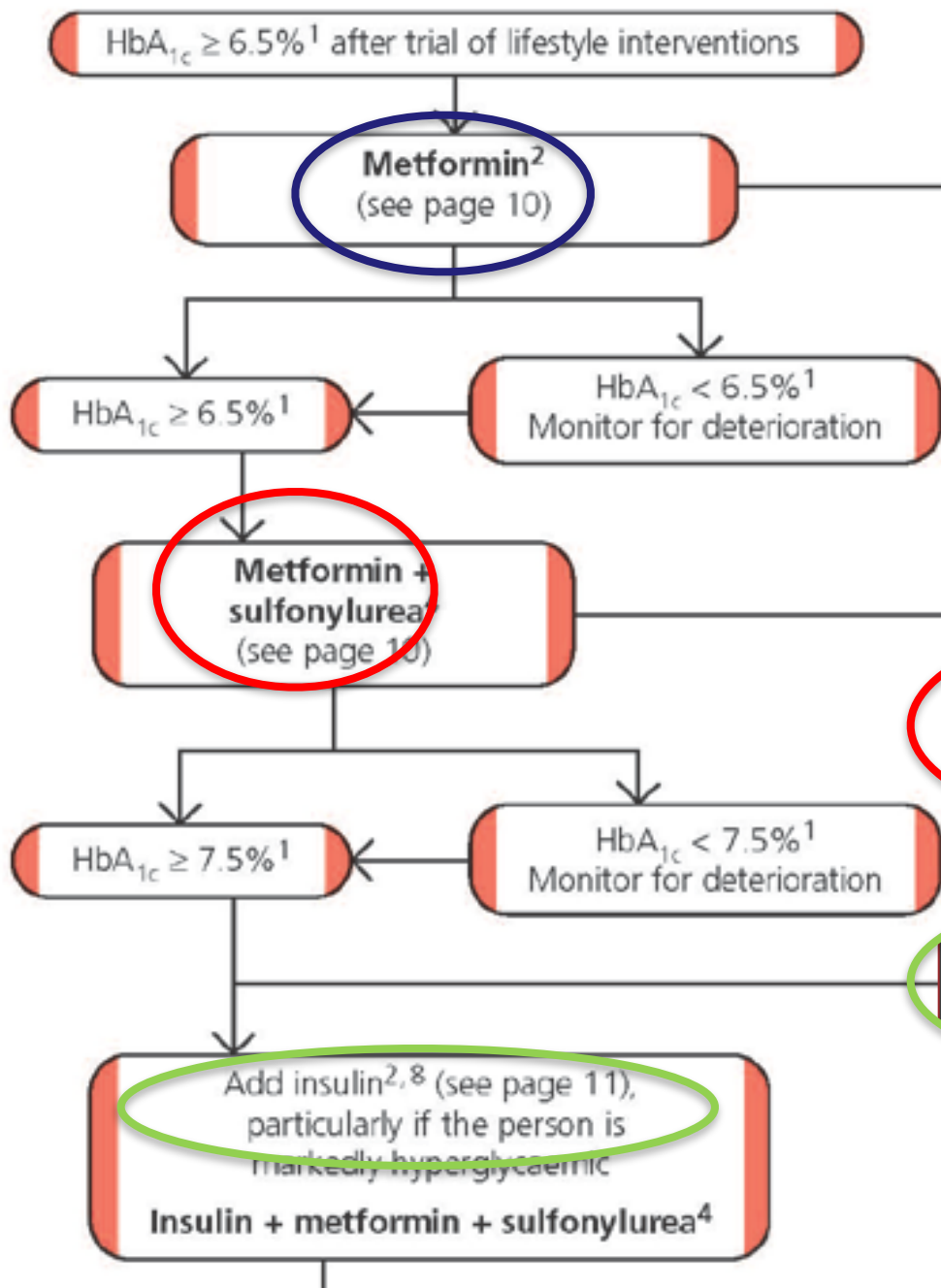
Insulin secretion

DPP-4 inhibitors, GLP-1 receptor agonists, meglitinides, SUs

Acarbose reduces the rate of carbohydrate digestion in the small intestine.¹ Acarbose should be considered if a person is unable to use other glucose-lowering medications.³ DPP-4=dipeptidyl peptidase-4; GLP-1 =glucagon-like peptide-1; SGLT2=sodium–glucose co-transporter 2; SU=sulphonylurea

1. Bailey CJ (2011) *Trends Pharmacol Sci* **32**: 63–71; 2. *Canagliflozin summary of product characteristics*; 3. NICE (2009) *Type 2 Diabetes. The Management of Type 2 Diabetes. NICE Clinical Guideline 87*. Available at: <http://bit.ly/1cTYLVX> (accessed 01.08.2014)

Blood-glucose-lowering therapy



Consider sulfonylurea⁴ here if:

- not overweight (tailor the assessment of body-weight-associated risk according to ethnic group³), or
- metformin is not tolerated or is contraindicated, or
- a rapid therapeutic response is required because of hyperglycaemic symptoms.

Consider a rapid-acting insulin secretagogue for people with erratic lifestyles.

Consider substituting a DPP-4 inhibitor (with a risk of hypoglycaemia consequences) or a sulfonylurea if contraindicated or not tolerated.

MET & TZD or SU & TZD
Add TZD if intolerance to SU or MET/ risk of Hypo

MET + SU + TZD
(If Insulin unacceptable e.g. driving)

Consider adding exenatide⁶ to metformin and a sulfonylurea if:

- BMI ≥ 35 kg/m² in people of European descent⁷ and there are problems



How do SGLT2 inhibitors work?

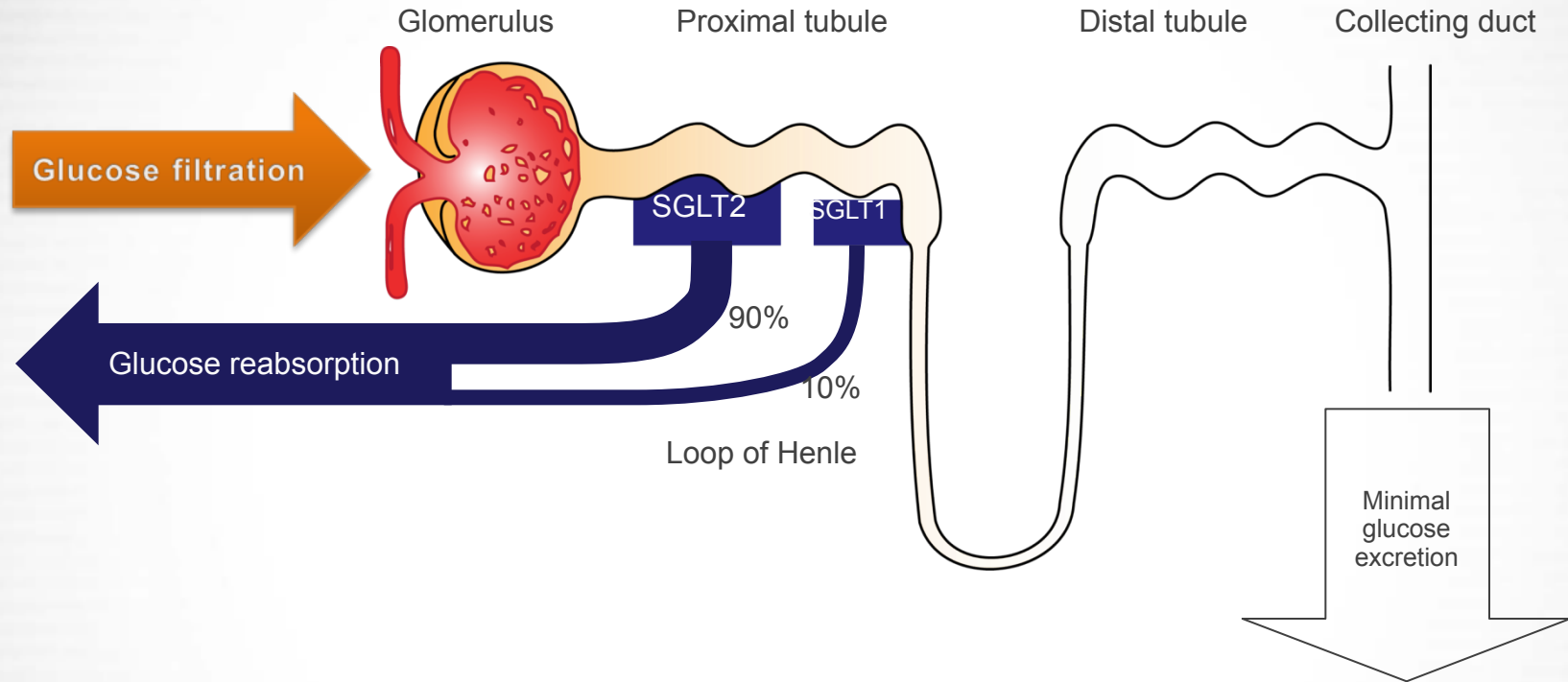
How much clinical experience have you had with SGLT2 inhibitors?

1. None at all
2. A little
3. A moderate amount
4. Quite a lot
5. Lots

For those with experience, at what point in the treatment pathway are you using SGLT2 inhibitors?

1. As a monotherapy
2. As a dual therapy (e.g. add-on to metformin)
3. As a triple therapy (e.g. add-on to metformin and sulphonylurea)
4. As an add-on to insulin
5. More than one of the above

Renal glucose handling in the nephron of the healthy individual

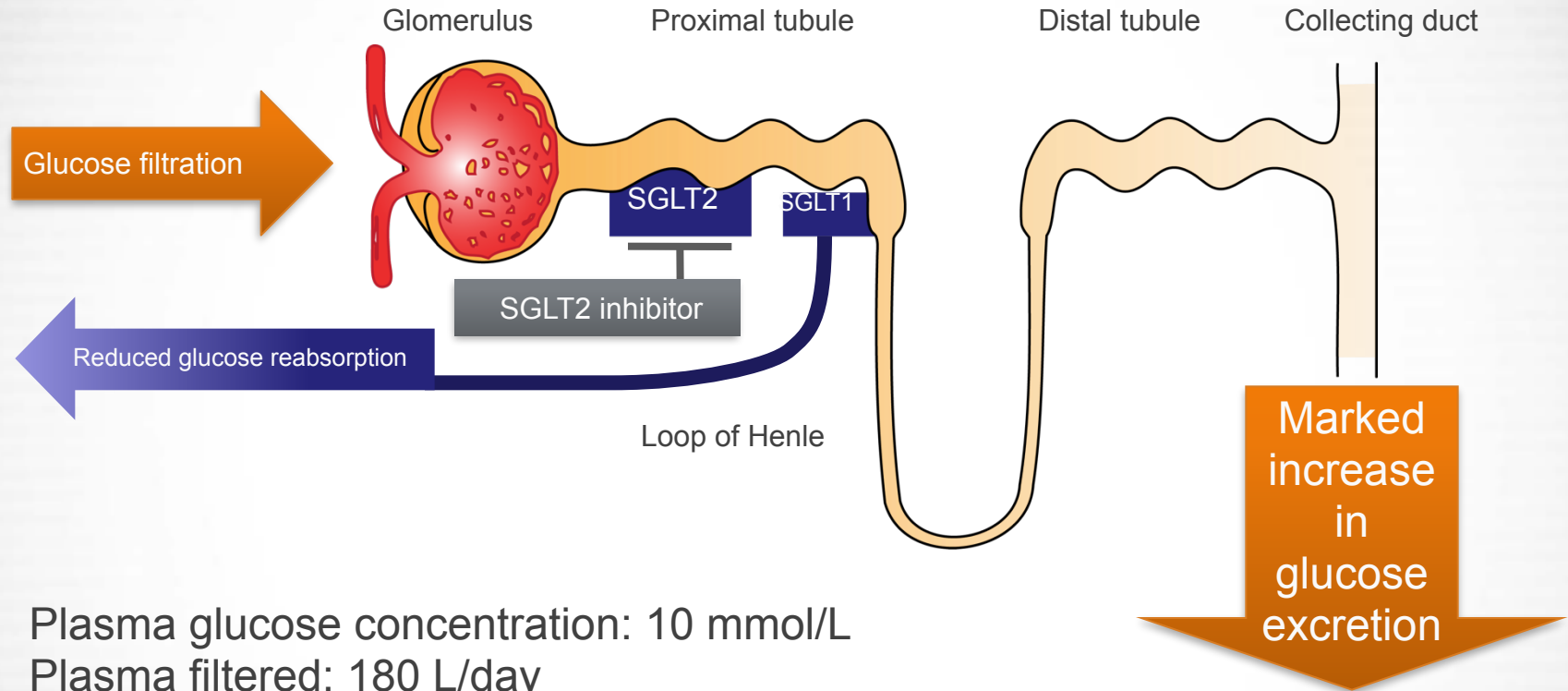


- Plasma glucose concentration: 5–5.5 mmol/L
- Plasma filtered: 180 L/day
- Glucose filtered: 160–180 g/day
- Glucose reabsorbed: 160–180 g/day
- Glucose excreted: Minimal

SGLT=sodium–glucose co-transporter

Figure adapted from Bailey CJ (2011) *Trends Pharmacol Sci* **32**: 63–71

SGLT2 inhibition lowers the inappropriately elevated renal threshold for glucose in type 2 diabetes¹



- Plasma glucose concentration: 10 mmol/L
- Plasma filtered: 180 L/day
- Glucose filtered: ~320 g/day
- Glucose reabsorbed (assuming 20–25% inhibition of reabsorption): ~240–255 g/day
- Glucose excreted: ~65–80 g/day (equivalent to ~260–320 kcal/day)

SGLT=sodium–glucose co-transporter

Figure adapted from Bailey CJ (2011) *Trends Pharmacol Sci* **32**: 63–71

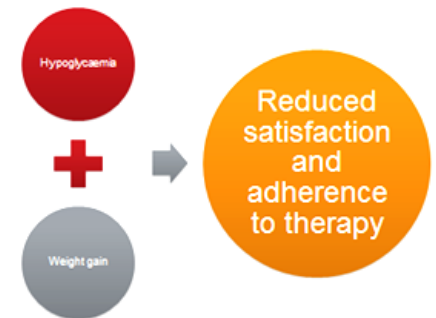
1. DeFronzo RA et al (2012) *Diabetes Obes Metab* **14**: 5–14

The ideal anti-glycaemic agent

...answering the question

- Controls glucose – **Yes, preferably preserves β -cell +/- insulin sparing**
- Does not cause weight gain- **preferably weight loss**
- Are there increased incidence of hypos?- **preferably reduced risk of hypoglycaemia...**
- Easy administration – **once daily; once weekly**
- No/Few side effects

Weight gain and hypoglycaemia influence adherence to therapy



Case Study One

- For confidential reasons this patient shall be called

- **Mr Smith**

Mr Smith

- 58 year old gentleman.
- Type 2 diabetes for 11 years.
- Bus driver.

- Current medication includes
 - 2 grams of Metformin.
 - 100mg Sitagliptin.

- HbA1c currently 67 mmol/mol.
- Previously 60 mmol/mol.

- Cholesterol 4.8 mmol/l.
- Blood pressure 136/88 mmHg.
- BMI 32 kg/m.
- EGFR >60.

What would you do next?

- Refer to dietitian?
- Add Pioglitazone
- Add Sulphonylurea
- Add SGLT2i
- Add GLP-1a
- Commence onto basal insulin.

Discussion points

- **Physical Activity**
- Bus driver so this is reduced.
- Diet - Some changes could be made.
- **What considerations regarding any further medication management?**
- Employment.
- Weight gain.
- Blood pressure control.
- Side effects.
- Adherence.

More discussion points

- **GLP-1 receptor agonist**
 - What reduction in HbA_{1c} might we expect?
- **SGLT2 inhibitor**
 - What outcome might we expect?
- **Insulin**
 - Risk of hypos?
 - Blood glucose monitoring requirements?

Decision and outcome

- **After discussion with the care team, the following was agreed:**
 - Continue metformin 1 g twice daily
 - Stop sitagliptin (beneficial metabolic response as defined by SIGN¹ not demonstrated)
 - Commence SGLT2 inhibitor (canagliflozin 100 mg)
 - Mr Smith was counselled on the possibility of genital mycotic infections and how to manage them.
 - Commence statin therapy

6 months later

- HbA_{1c} has reduced to 57 mmol/mol (7.4%)
- Weight is reducing – has lost 8lbs in weight.
- Total cholesterol 4.6 mmol/L
- Blood pressure 125/85 mmHg

SGLT2=sodium–glucose co-transporter 2

1.SIGN (2010) 116. *Management of Diabetes. A National Clinical Guideline*. Available at: <http://bit.ly/1mJYmuX> (accessed 01.08.2014)

For the purpose of this case study patient identifiers have been removed / changed to maintain patient confidentiality.

Case study two

Mr Lafferty

...Mr Lafferty

Diabetes Status: Type 2 Diabetes

Age at Diagnosis: 49yrs 4mths

Duration of Diabetes: 9yrs 2mths

Levemir Insulin 38 units bd

Novorapid Insulin 18/16/18 units with main meals

Metformin SR 1g bd

HbA1c 106mmol/mol

BMI 34.1kg/m²

Chol 4.3

eGFR >60ml/min



Discussion Points

- **Adherence to medication.**
- How much could non compliance be an issue?
- What would be the risks of greatly increasing insulin doses?
- Adverse effects of insulin.

- **Patients perspective**
- Who's goals are we aiming to reach?
- What would concordance mean for increasing motivation?

- **What effect if any is diabetes distress having on Mr Lafferty?**

What would you do next?

- Increase insulin.
- Commence GLP-1.
- Commence DPP4 Inhibitor.
- Commence SGLT-2i.
- Change insulin.
- Refer to Dietitian.
- Refer to Clinical Psychologist.

...4 months on with Canagliflozin

HbA1c 78mmol/mol.

BMI 32.9kg/m² (34.1kg/m²)

Chol 3.9 (4.3)

eGFR >60ml/min

Treatment:

Canagliflozin 100mgs od (Licensed recommended starting dose is 100mg od)

Metformin SR 1g bd

Levemir insulin 30 units.

Novorapid insulin 14/10/14 units with meals.

Where do you go from here?



Conclusions

There is no right or wrong way to care for those with Type 2 diabetes providing the decisions are patient centred, well informed and reviewed at regular intervals

The Glycaemic approach should be...

- As low as the situation and patient allows
- As early as possible
- For as long as possible
- As safely as possible
- And as rationally as possible

Disease progression:

DECODE – it has been suggested that approx 4% of beta cell function is lost on a yearly basis; with it estimated that approx 40-50% has been lost on diagnosis¹.

1.) [Diabetes Metab.](#) 2000 Sep;26(4):282-6.

•The DECODE study. Diabetes epidemiology: collaborative analysis of diagnostic criteria in Europe.

A red speech bubble with a white outline, containing the text "Discussion question".

Discussion
question

**What will you do differently as a result
of what you've heard?**



for listening...