

Acknowledgements

The guidance is designed to enable Health Care Professionals (HCPs) to gain information on elements of insulin and non-insulin therapies and management of Type 2 diabetes.

This work is based on the previous excellent guidelines developed by **Heather Daly, Nurse Consultant** and **Professor Melanie Davies**.

Many thanks to **Shehnaz Jamal** for developing the new format of the guidance and also to Professor Melanie Davies and Dr Rob Gregory and Dr James Medcalf, Dr Hina Trivedi for their expert clinical and practical advice.

June James - Nurse Consultant in Diabetes

Background

There are 4.0 million people with diabetes in the United Kingdom

- 8% of these people will have Type 1 diabetes and these people will require insulin within 24 hours after diagnosis and continue it life long
- 50% of the remaining 92% with Type 2 diabetes will require additional insulin therapy within 6 years of diagnosis
- There are many different insulin and non-insulin therapies available to treat Type 2 diabetes, this guidance aims to inform you about these medications, clinical targets and recommendations for use.

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Referral Criteria to Specialist Services

Those requiring urgent admission to A&E Department 🏥

- Unconscious hypoglycaemia
- Suspected diabetic ketoacidosis/hyposmolar/hyperglycaemic state
- Newly diagnosed Type 1 with ketones when diabetes specialist services unavailable

Same day referral 📅

- Newly diagnosed children with diabetes refer to Paediatric Service ☎ 0116 258 6222 or 0116 258 6923
- Newly diagnosed Type 1 Diabetes especially urgent in those who present with ketonuria and/or vomiting ☎ 0116 258 4919 ✉ diabetes.helpline@uhl-tr.nhs.uk (Mon - Fri) (Ref: NICE NG17 (2015))
- Patients with infected, necrotic or gangrenous foot ulceration or suspected Charcot Foot
- Sudden loss of vision Eye Casualty ☎ 0116 258 6273
- Outside normal working hours contact the on-call SpR via switchboard ☎ 0300 303 1573


Referral within 48 hours

- All women with pre-existing Type 1 or Type 2 diabetes who become pregnant (Ref: NICE Diabetes and Pregnancy NG3 (2015))
- Women who develop Gestational Diabetes (Ref: NICE Diabetes and Pregnancy NG3 (2015))

Priority/early referral

- Women with Type 1 or Type 2 Diabetes contemplating pregnancy (Ref: NICE Diabetes and Pregnancy NG3 (2015))
- Retinopathy/reduced visual acuity, those with sight threatening retinopathy refer to Ophthalmology Department. Eye Casualty ☎ 0116 258 6273
- Patients presenting with persistent proteinuria Currently, this is not a locally agreed super 7 criteria for referral unless accompanied with CKD 3 (if GFR deteriorating despite optimisation) or CKD 4 and above.
- Patients with active foot problems should be referred to the specialist Multidisciplinary Diabetic Foot Clinic within 24 hours of assessment ☎ 0116 258 8304

Others where specialist advice may be considered

Referral to Diabetes Specialist Nurse (DSN), community DSN Integrated Community Diabetes Service (Refer to Community DSN) or specialist diabetes doctor for core practices. 

- Recurrent hypoglycaemia (Refer to Community DSN)
- Poor glycaemic control despite intensive management (Refer to Community DSN)
- Persistent hypertension and/or hyperlipidaemia despite intensive management as per guidelines (refer to Specialist Care)
- Painful neuropathy not responding to treatment (refer to Specialist Care)
- Erectile dysfunction requiring additional intervention (refer to Specialist Care)
- People with Type 1 Diabetes with previous failure to attend but now receptive to specialist referral (Always refer to Specialist Care - DSN, core and enhanced practices)
- Dialysis patient (Always refer to Specialist Care, core and enhanced practices)
- Need for psychosocial/counselling support to overcome barriers to self-care (Refer to Community DSN)
- Patients CKD 3 for optimisation of glucose, BP and lipids if control suboptimal (Refer to Community DSN)
- Patients for DAFNE programme (Always refer to Specialist Care - DSN, core and enhanced practices)
- Patients on insulin Pump Therapy (Always refer to Specialist Care - DSN, core and enhanced practices)

Be aware the following groups of patients should be under the care of the specialist team:

- Children and young people
- Pump patients
- Pregnancy
- Transplant patients
- Inpatients
- People with complex diabetes



Community Diabetes Specialist Nurses



University Hospitals of Leicester Diabetes Specialist Nurse (DSN's)
Leicester General Hospital: 0116 258 4919 (9.00am - 5.00pm Mon-Fri)
Glenfield Hospital: 0116 250 2390

Diabetes Clinic Information




Complex Diabetic Clinics (New patients, follow-up and annual review appointments)					
			Regularity		
Professor Melanie Davies melanie.davies@uhl-tr.nhs.uk	Tuesday	am	Weekly	LGH	0116 258 6481 (sec) 0116 258 2876 (appts)
Dr Alison Gallagher alison.gallagher@uhl-tr.nhs.uk	Tuesday	pm	Weekly	LGH	0116 258 7545 (sec) 0116 258 5964 (appts)
Dr Rob Gregory rob.gregory@uhl-tr.nhs.uk	Thursday	pm	Weekly	LGH	0116 258 8017 (sec) 0116 258 4973 (appts)
Dr Steve Jackson steve.jackson@uhl-tr.nhs.uk	Wednesday	pm	Weekly	LGH	0116 258 8017 (sec) 0116 258 4973 (appts)
Dr Ram Kela ram.kela@uhl-tr.nhs.uk	Tuesday Fridays	pm am	Weekly	LGH GGH	0116 258 5402 (sec) 0116 258 5964 (appts) 0116 256 3495 (appts)
Dr Marie-France Kong marie-france.kong@uhl-tr.nhs.uk	Friday	pm	2nd & 4th	LGH	0116 258 8304 (sec)
Dr Ian Lawrence ian.lawrence@uhl-tr.nhs.uk	Monday Tuesday Friday	am pm am	Weekly Weekly Weekly	LGH LGH GGH	0116 258 5402 (sec) 0116 258 5964 (appts) 0116 256 3495 (appts)
Dr Paul McNally paul.mcnally@uhl-tr.nhs.uk	Alternates monthly Wednesday	am/pm	Weekly	LGH	0116 258 6182 (sec) 0116 258 2876 (appts)
Specialist Diabetes Clinics					
Ante-Natal Diabetes	Tuesday Wed & Thur	am & pm pm	Weekly	LGH LRI	0116 258 4885 0116 258 6471
Diabetes Eye Laser clinics & FU Diabetes Laser & FU & Retinal Screening Retinal Screening	Monday Tuesday Wed & Friday	am am am	Weekly Weekly Weekly	LRI LRI LRI	0116 258 5928
Diabetes Foot Clinic	Mon Wed Thurs & Fri	pm am	Weekly	LGH LGH	0116 258 8304
Medical Andrology - Dr Jackson Medical Andrology - Dr McNally	1st Friday 2nd Friday	pm pm	Monthly Monthly	LGH LGH	0116 258 8017 0116 258 6182
Nephrology - Dr Gregory Nephrology - Dr Kong	2nd & 4th Tuesday 1st & 3rd Friday	pm am	Monthly Monthly	LGH LGH	0116 258 8017 0116 258 8304
Insulin Pump	Monday, Tuesday & Fridays	pm am	Monthly	LGH GGH	0116 258 8249
Transition/ Diabetes Young Adults Clinic Endocrine Young Adult Clinic (ages 16-19)	3rd & 4th Thursday 3rd Thursday	pm pm	Monthly Monthly	LGH LRI	0116 258 6481 / 5402 / 6222 0116 258 6140

Community Based Diabetes Clinic Information

Community Based Diabetes Clinics - Leicestershire County Melton and Rutland

		
Dr Rob Gregory	Coalville	01530 467431 (appts)
Dr Paul McNally	Hinckley	01455 441817 (appts)
Dr Steve Jackson	Loughborough	01509 564355 (appts)
Dr Rob Gregory	Melton	01664 854915 (appts)
Dr Alison Gallagher	Market Harborough	01858 438135 (appts)
Dr Paul McNally / Dr Kath Higgins	Oakham	01572 722025 (appts)

Community Based Diabetes Clinics - Leicester City

		Regularity	
Diabetes Care, Leicester General Hospital	Monday, Tuesday, Wednesday, Thursday and Friday	Weekly	0116 258 8249
Manor Medical Centre			
Rusheymead Health Centre			
Springfield Road Health Centre			
The Hedges Medical Centre			
The Merlyn Vaz Health and Social Centre			
Westcotes Health Centre			

GP Mentors for Enhanced Practices

NORTH EAST LEICESTER	PRIMARY	CENTRAL
Dr Tun Than Email: Tun.Than@leics.nhs.uk	Dr Sam Seidu Email: Samuel.Seidu@uhl-tr.nhs.uk	Dr Hina Trivedi Email: Hina.Trivedi@GP-C82018.nhs.uk

Screening and Diagnosis: Who To Test?

It is very important to identify diabetes as early as possible: 50% of newly presenting people with Type 2 diabetes already have 1 or more complications at diagnosis ⁽¹⁾

Remember to test for diabetes if patients present with the following symptoms:

- Excess thirst
- Polyuria (especially if nocturia)
- Weight loss
- Urinary incontinence
- Tiredness
- Pruritis vulvae / recurrent candidiasis
- Recurrent infections / abscesses
- Balanitis
- Blurred vision / changes in visual acuity
- Erectile dysfunction (ED)
- Pain / numbness / foot ulcers
- Non specific or unexplained symptoms

High Risk for Diabetes

- White European people aged over 40 and people from Black, Asian and minority ethnic groups aged over 25 with:
 - First degree relative with diabetes
 - BMI >30
 - or BMI of 25-30 (i.e. are overweight) and who have a sedentary lifestyle
 - > or BMI 23 in South Asian people
- Women with Polycystic Ovary Syndrome (PCOS)
- Cerebrovascular disease, peripheral vascular disease or hypertension/hyperlipidaemia.
- Patients on prolonged steroid therapy
- Patients on anti-psychotic drugs

Diabetes is often missed in the elderly and vulnerable people

At least half of people with Type 2 diabetes are asymptomatic

Pre-determined risk of Diabetes

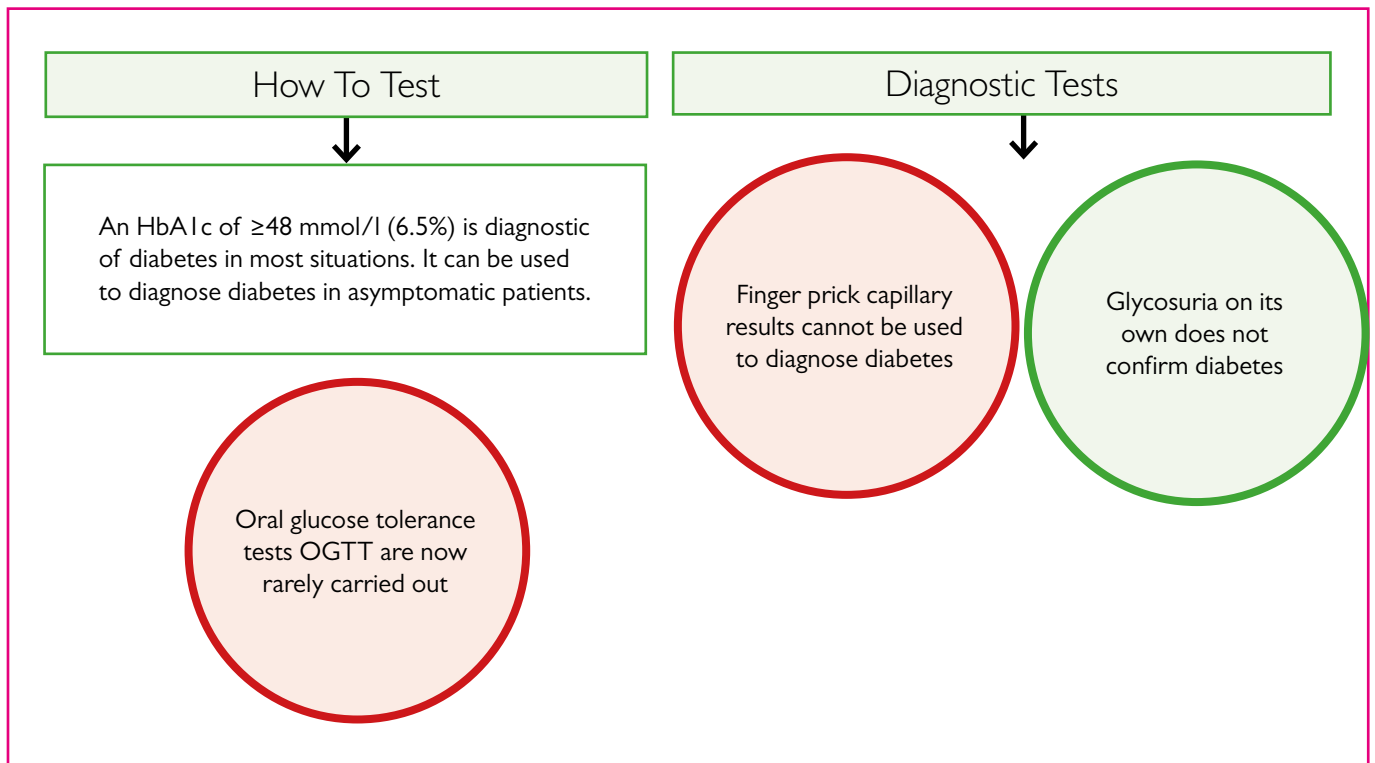
- Coronary Heart Disease (CHD)
- Women who have had Gestational Diabetes (screen at 6 weeks and one year post-partum, and then yearly)
- Those known to have impaired glucose tolerance HbA1c 42 mmol/mol - 46 mmol/mol (6.0 - 6.4%) or oral glucose tolerance test 2-hour value between 7.8 mmol/l and 11.1 mmol/l

Diagnosis of Type 2 diabetes can be made using HbA1c in those who are asymptomatic.

It should not be used for diagnosis in children, pregnancy and those who are acutely ill or who have abnormal haemoglobins, anaemia and altered red blood cell lifespan.

1. UKPDS Group. UK Prospective Diabetes Study 6. Complications in newly diagnosed Type 2 diabetic patients and their association with different clinical and biochemical risk factors. Diabetes Research. 1990;13:1-11



How to Test?



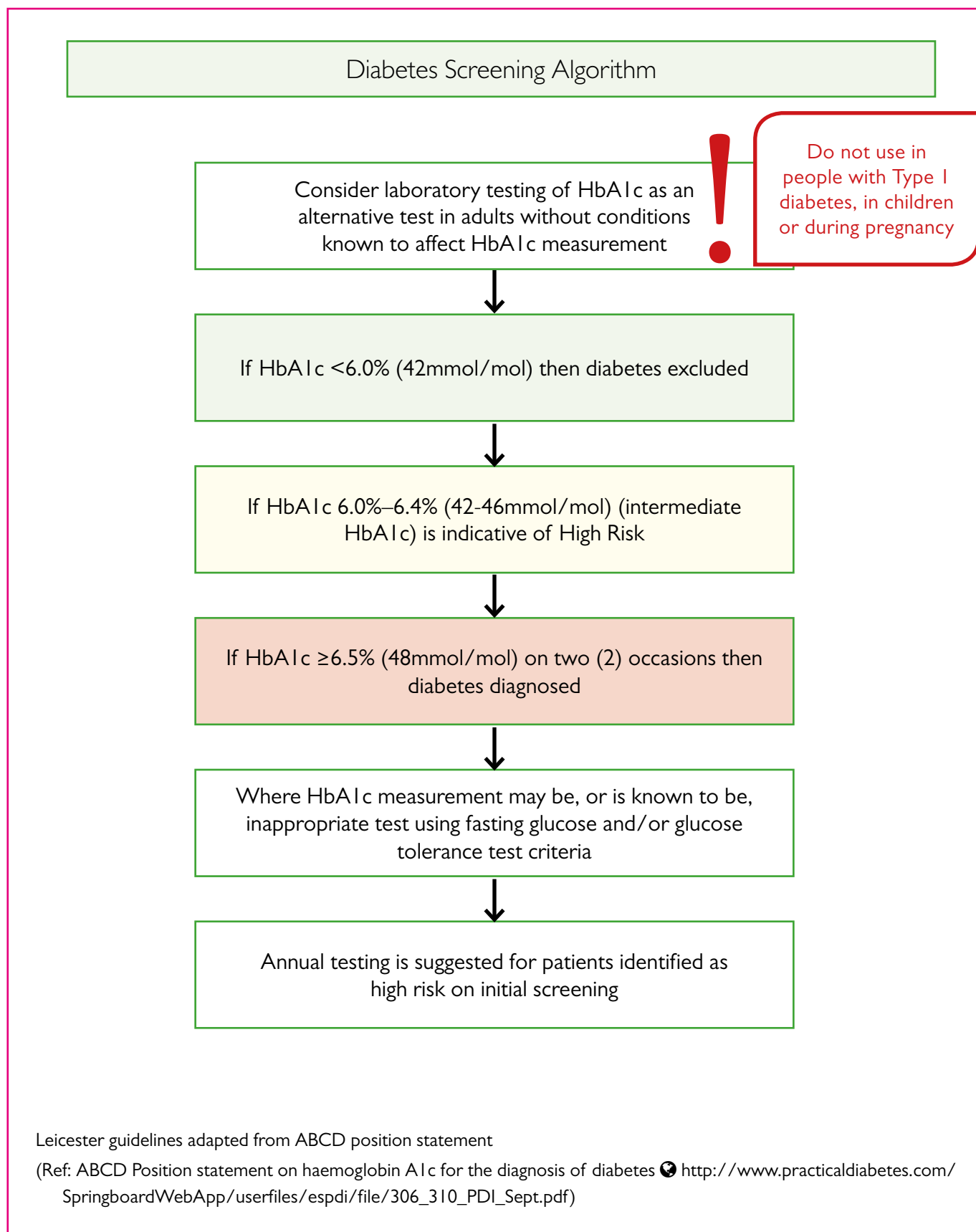
Diagnosis and Screening Using HbA1c

Advantages and disadvantages to using plasma glucose and HbA1c thresholds for the diagnosis of diabetes

Advantages	Disadvantages
<ul style="list-style-type: none"> • Directly measures the molecule thought to cause diabetes complications • Not subject to misleading results due to non-glycaemic factors • Smaller differences in results between laboratories compared to HbA1c • Less expensive to measure than HbA1c 	<p>Requires patient to be tested in the fasting state and for the sample to be analysed promptly:</p> <ul style="list-style-type: none"> • May require a glucose tolerance test for diagnosis • A measurement of glucose at a single time-point • Higher within-individual variability than that of HbA1c • Oral glucose tolerance testing laborious and time consuming

Suggested Diabetes Screening Algorithm



Glycaemic Management: Principles of Treatment

Offer structured education (i.e. DESMOND equivalent programme which fulfils The National Recommended Criteria from the Department of Health (DH) on Structured Education 2004) to include diet/lifestyle advice to everyone. Usually wait 6-12 weeks before glucose lowering agents are introduced.

Offer structured education to adults with Type 2 diabetes and/or their family members or carers (as appropriate) at and around the time of diagnosis, with annual reinforcement and review.

Explain to people and their carers that structured education is an integral part of diabetes care.

Ensure that any structured education programme for adults with type 2 diabetes includes the following components:

- It is evidence-based, and suits the needs of the person
- It has specific aims and learning objectives, and supports the person and their family members and carers in developing attitudes, beliefs, knowledge and skills to self manage diabetes
- It has a structured curriculum that is theory driven, evidence based and resource effective, has supporting materials, and is written down
- It is delivered by trained educators who have an understanding of educational theory appropriate to the age and needs of the person, and who are trained and competent to deliver the principles and content of the programme.
- It is quality assured, and reviewed by trained, competent, independent assessors who measure it against criteria that ensure consistency
- The outcomes are audited regularly

Ensure the patient-education programme provides the necessary resources to support the educators, and that educators are properly trained and given time to develop and maintain their skills.

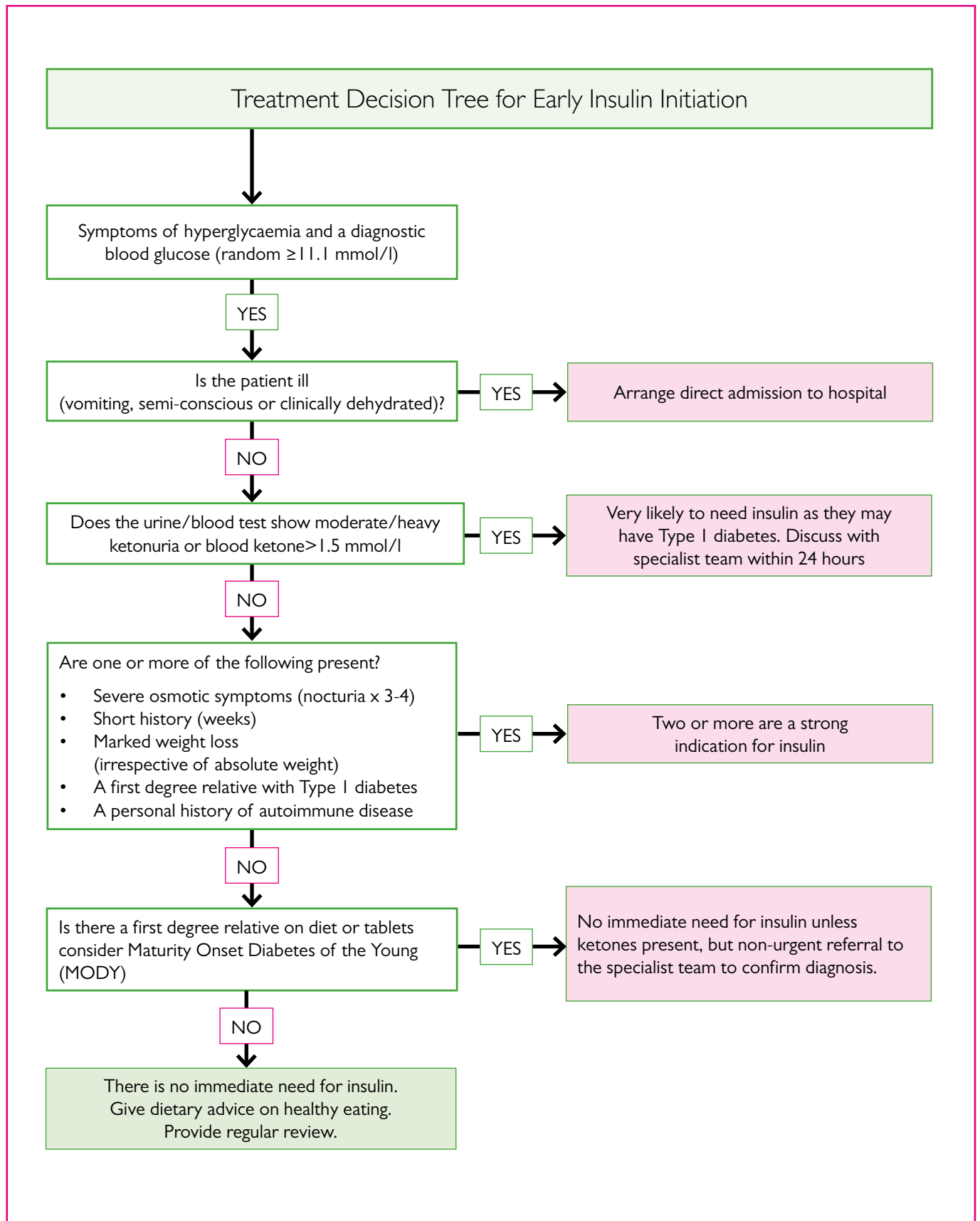
However:

- Individualise treatment plans and targets
- Introduce oral hypoglycaemic agents early if fasting plasma glucose >15 mmol/l and symptomatic
- Test for ketones if very symptomatic
- Ensure patients are shown how to monitor their own diabetes, and know what to do if results do not fall in the target range
- Regular monitoring will identify the need to actively titrate treatment
- Measure HbA1c every 3-6 months
- Target HbA1c 48 mmol/mol (6.5%) in newly diagnosed Type 2 diabetes. Aim for HbA1c of 53 mmol/mol for ongoing care. Implement additional medication if HbA1c is ≥ 58 mmol/mol. Involve the person in discussions about individual HbA1c target
- In South Asian people BMI underestimates adiposity. Weight measurements need to be considered

Type 2 diabetes is becoming more common in the under 40s.

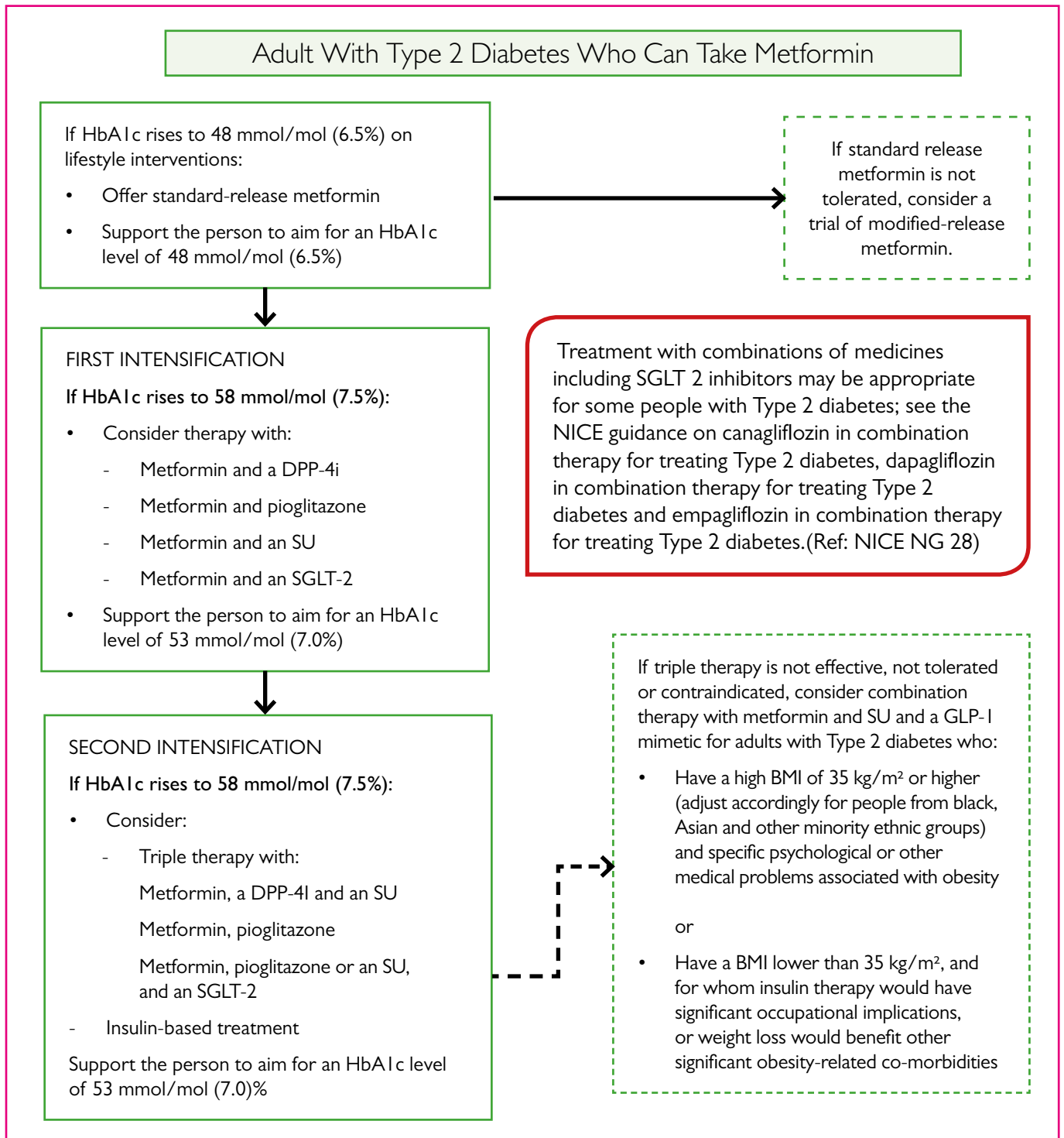
These patients need proactive management as they are at increased risk of developing early cardiovascular complications

Treatment Decision Tree for Early Insulin Initiation



NICE NG28 separates the management of glycaemia in Type 2 patients depending on whether they can safely tolerate Metformin. It then offers much more flexibility in the use of other oral and non-Insulin therapies and promotes treatments aligned to the individual patient. Insulin can be commenced at any stage of the pathway.

If the person is symptomatically hyperglycaemic, consider insulin or Sulphonylurea (SU). Review treatment when blood glucose (BG) control has been achieved.



Glucose Lowering Therapies - Algorithm for T2DM

Metformin Contraindicated Or Not Tolerated

If HbA1c rises to 48 mmol/mol (6.5%) on life cycle interventions:

- Consider one of the following:
 - a DPP-4i, pioglitazone or an SU
- Support the person to aim for an HbA1c level of 48 mmol/mol (6.5%) for people on a DPP-4i or pioglitazone or 53 mmol/mol (7.0%) for people on an SU



FIRST INTENSIFICATION

If HbA1c rises to 58 mmol/mol (7.5%):

- Consider a dual therapy with:
 - a DPP-4i and pioglitazone
 - a DPP-4i and an SU
 - pioglitazone™ and an SU
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)



SECOND INTENSIFICATION

If HbA1c rises to 58 mmol/mol (7.5%)

- Consider insulin-based treatment
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

Treatment with combinations of medicines including SGLT 2 inhibitors may be appropriate for some people with Type 2 diabetes; see the NICE guidance on canagliflozin in combination therapy for treating Type 2 diabetes, dapagliflozin in combination therapy for treating Type 2 diabetes and empagliflozin in combination therapy for treating Type 2 diabetes. (Ref: NICE NG 28)

Glycaemic Management

Key Principles of Practice

- 95% of the care people with diabetes receive is self-care and all patients should have access to high quality structured education programmes e.g. DESMOND equivalent
- The ability to monitor their own glucose level gives people with diabetes the feedback they need in order to learn how to manage their condition optimally
- Monitoring should be based on the individual's clinical needs and in the context of diabetes education and self-management
- People should receive appropriate training in the technique and the actioning of the results
- The frequency of testing will be different for different people and will change with their circumstances. Any guidelines can only be used as a framework and then adapted to meet individual needs
- People may move between different methods of monitoring dependent on their needs at that time
- Equipment used for monitoring should be based on choice and agreed with patient

Diabetes and Driving

No matter how diabetes is treated insurance companies must be informed when someone has diabetes. People with diabetes **MUST** inform the DVLA if they are on Insulin treatment.

Group 1 Entitlement

- Must have awareness of hypoglycaemia. If there is a total loss of 'hypo' warning signs their licence will be withdrawn
- Must not have had more than one episode of hypoglycaemia requiring third party assistance within the preceding 12 months. If they have had more than one episode they must inform the DVLA and their licence will be withdrawn for one year following the first episode
- Patients with blood glucose levels < 5 mmol/l should not drive until they have eaten and retested
- If blood glucose less than 4 mmol/l treat as a hypo and do not drive for 45 minutes following successful treatment
- Insulin users and those using non-insulin therapies with a risk of hypoglycaemia, e.g. SU's must inform the DVLA and test before driving
- People on SU may need to BG test before driving

It is the responsibility for the principle clinician caring for these patients to advise whether testing is required.

Group 2 Entitlement

People with diabetes on insulin and has:

- Must be under the care of a Consultant Diabetologist
- Had no episodes of hypoglycaemia requiring third party assistance within the previous 12 months
- Total awareness of hypoglycaemia and can demonstrate understanding of its risks
- Meter recorded evidence of regular monitoring (at least twice a day and at times relevant to driving)
- Been reviewed annually by an independent Consultant Diabetologist

 www.dft.gov.uk/dvla/medical

HbA1c Targets (Haemoglobin A1c)

Recommended Targets for the General Population

- HbA1c level of 48 mmol/mol (6.5%) or lower, to minimise the risk of long-term vascular complications at diagnosis
- If the HbA1c increases to 58 mmol/mol - add in additional therapy and aim for 53 mmol/mol (see algorithm pg 12)

HbA1c values should be expressed in mmol/mol	HbA1c as %
42 mmol/mol	6.0 %
48 mmol/mol	6.5%
53 mmol/mol	7.0 %
58 mmol/mol	7.5%
64 mmol/mol	8.0%
75 mmol/mol	9.0%
Newly diagnosed Type 2 and short duration diabetes <48 mmol/mol	

HbA1c Targets

Although we need to strive for these levels, targets should be set with the individual patient.

- Should not be measured more frequently than 2 monthly, except in pregnancy, and should be measured at least 6-12 monthly
- Avoid pursuing highly intensive management to levels of < 48 mmol/mol



Remember people who are frail and/or elderly or with multiple co-morbidities will require different glycaemic targets to ensure safety

Caution: the renal threshold will reduce with age

Self-Blood Glucose Monitoring (SBGM)

Discuss its purpose and how it should be interpreted and acted upon:

- Use in people with Type 1 Diabetes
- Use in people with Gestational Diabetes
- Use in Type 2 Diabetes on oral hypoglycaemic agents such as sulphonylureas (SU), where there is significant risk of hypoglycaemia. Patient new to SU are advised to test for 3 months (ABCD guidance)
- Use for those using insulin or insulin in combination with oral hypoglycaemic agents
- Use in those patients able to adjust their own oral medication between HbA1c measurements
- May be useful for a limited period to address needs at that time, i.e. Adjustment or change in oral medication or intercurrent illness
- Use where there is erratic lifestyles or those who undertake high levels of physical activity
- Only use in newly diagnosed Type 2 Diabetes as an integral part of self-management education

Targets for Self-Blood Glucose Monitoring

These should be set with the individual patient taking into account age, infirmity, and clinical factors.

Recommended Targets Pregnancy

- < 5.3 mmol/L before meals
- < 7.8 mmol/L one hour after meals
- < 6.4 mmol/L two hours post meals

Urine Testing

- May be appropriate for people with Type 2 Diabetes not on insulin or sulphonylureas when HbA1c is above target and there are no hypoglycaemic events
- Where self blood glucose monitoring is considered inappropriate, or of no benefit, or causes increased anxiety to the individual

Using HbA1c in the diagnosis of type 2 diabetes: Clinical Considerations

Advantages and disadvantages to using plasma glucose and HbA1c thresholds for the diagnosis of diabetes

Advantages

Established as a means of monitoring patients already known to have diabetes:

- Does not require a fasting sample and is more stable after sample collection than glucose
- A marker of glucose control over the previous weeks/months
- Lower within-individual variability than that of glucose
- Initially more costly than glucose, but when used as part of a screening/diagnostic tool may be less costly overall



Disadvantages

Measurement can be misleading in patients with haemoglobinopathies, anaemia or renal failure:

- May differ between patients of different ages and ethnicity
- A surrogate marker of hyperglycaemia with between-individual discrepancies between glucose and HbA1c
- Not to be used in the diagnosis of children - diabetes in pregnancy or to diagnose Type 1 diabetes



Diabetes Blood Glucose Monitoring

Typical Self-Monitoring Regimens	
A	Periodic testing to meet needs at that time
B	1-2 tests daily, varying times of testing
C	4 tests per day x 2 week
D	4 tests per day each day
E	7 tests per day pre & post meals and before bed

Type 2 Diabetes - Diet & lifestyle management only

Self blood glucose monitoring is not recommended as part of routine care if HbA1c is within target but may be useful as an educational tool to understand lifestyle interventions.

If self-monitoring of blood glucose is considered appropriate.

HbA1c Monitoring

Measure HbA1c 3 monthly until target is reached, then monitor 6 monthly

Possible regime is: A

Type 2 Diabetes - Oral therapy

Re-assess patient needs if urine testing and HbA1c monitoring inadequate, or if there is risk of hypoglycaemia which cannot be addressed by using an alternative oral hypoglycaemic agent. Consider self blood glucose monitoring. Frequency of testing should be agreed with patient and adequate training provided.

Some patients benefit from blood testing for short periods of time and then stop or return to urine testing, e.g. when oral medication is changed or adjusted.

Continue to measure HbA1c 3-6 monthly

Possible regimen:
A B C

Type 2 Diabetes – Insulin with/without oral agents

Self blood glucose monitoring is recommended. Regular testing is required at initiation and during adjustment of doses. Frequency may be reduced when glycaemic target reached. Increased testing may be required during intercurrent illness and when there is risk of hypoglycaemia. Adequate training must be provided.

Those unable to self-monitor blood glucose may find urine testing helpful or may require more frequent HbA1c measurement.

HbA1c should be measured 3-6 monthly

Possible regimes:
B C D

Type 1 Diabetes

It is recommended that all people with Type 1 Diabetes monitor their blood glucose levels. Self-monitoring may be used to adjust insulin doses prior to meals (e.g. basal bolus therapy and carbohydrate counting, pump therapy, DAFNE patients) and so frequent daily testing will be required. In more stable Type 1 Diabetes less frequent monitoring may be acceptable depending on patients daily routine.

HbA1c should be measured 3-6 monthly in all Type 1 Diabetes Patients.

Children with Diabetes or their parents may need to do frequent testing and this will be decided between themselves and the specialist paediatric team but could range from 1-7 tests per day

Possible regimes:
B C D E

Pregnant Women

Type 1 and Type 2 Diabetes

- Required to test at least 2-4 times daily pre and one hour post-prandial (Up to 7 times a day)

Possible regimes:
D E

Gestational Diabetes

- Not requiring insulin - will need to test 4 times per day pre meals and one hour post meals
- Treated with insulin - will need to test as Type 1 Diabetes

Targets for SBGM During Pregnancy	
Pre meals	<5.3 mmol/L
One hour post prandial	< 7.8 mmol/L
Two hours post prandial	<6.4 mmol/L

BEFORE DRIVING

If on insulin therapy or at risk of hypoglycaemia, blood glucose (BG) must be ≥ 5 mmol/L

Non-Insulin Therapies: Medication Profiles

Oral Hypoglycaemic Agents

Metformin			
Dosage	Usage	How it works / Side effects	Precautions/Avoid
<p>Start with 500mg O.D. for 1-2 weeks</p> <p>Titrate every 2-4 weeks to achieve glycaemic target</p> <p>Maximum dose is 1 gram B.D. or 850mg T.D.S</p>	<p>As first line therapy in overweight or obese patients</p> <p>Metformin MR as an option in patients poorly tolerant of generic Metformin</p> <p>Metformin dissolvable powder in preference to Metformin syrup</p> <p>Tablets should be taken with or immediately after a meal</p> <p>Not associated with weight gain, and associated with reduced cardiovascular disease in overweight or obese patients - hence first line therapy in these patients</p>	<p>Reduces hepatic glucose production and appetite</p> <p>Reduces cardiovascular events in overweight and obese patients to a greater extent than predicted by its glucose lowering effects and stimulates insulin release from the pancreas</p> <p>Diarrhoea occurs in up to 10%, but is dose dependent and may resolve with dose reduction</p>	<p>Do not initiate in patients with:</p> <p>Severe heart failure</p> <p>Severe liver disease (because of the increased risk of lactic acidosis) or alcohol dependency</p> <p>Do not start if eGFR <45 ml/mins</p> <p>If already on Metformin stop if eGFR <30 ml/min</p>

Sulphonylureas, Gliclazide, Glipizide, Glimepiride, Tolbutamide, Chlorpropamide			
Dosage	Usage	How it works / Side effects	Precautions/Avoid
<p>Gliclazide start with 40-80 mg O.D. with titration every 4-6 weeks to achieve glycaemic target or until maximum dose of 160mg B.D. is reached</p> <p>Glimepiride 1mg O.D. titrate up to 4mg O.D.</p> <p>Gliclazide MR start at 30mg O.D. at breakfast and titrate up to 120 mg O.D.</p>	<p>Tablets should be taken before or with meals</p> <p>Always re-assess the patient and emphasise lifestyle issues before prescribing</p> <p>People on sulphonylureas should BG test during the first 3 months following initiation and may need to continue testing if they are at risk of hypoglycaemia (ABCD guidance)</p>	<p>Sulphonylureas work by stimulating the pancreas to release more insulin</p> <p>They are only effective when there is some pancreatic beta cell activity still present</p> <p>Weight gain averaging 2-4 kg is a recognised consequence of sulphonylurea therapy; in some patients it may exceed 10kg</p> <p>Gliclazide MR is associated with less hypoglycaemia than generic gliclazide</p>	<p>Sulphonylurea in people at increased risk of hypoglycaemia, e.g. the frail and/or the elderly, those with dementia or poor cognitive function</p> <p>End of life care patients</p> <p>Those with poor eating patterns</p> <p>People with deteriorating renal function</p> <p>Long acting sulphonylureas, (Glibenclamide and Chlorpropamide) in patients over 70 years old and in those with eGFR of <60mls/min</p>

ALL patients should be told about recognition and management of hypoglycaemia when prescribed a sulphonylurea and be issued with a hypo information leaflet and if the patient is considered to be at high risk of hypoglycaemia issue blood glucose monitoring equipment and provide training

USING SULPHONYLUREA IN DOSSET BOXES

Patients and carers using these should be aware that if the patient is unable or unwilling to eat the SU should not be taken.

Oral Hypoglycaemic Agents

Thiazolidinediones (pioglitazone)			
Dosage	Usage	How it works / Side effects	Precautions/Avoid
<p>Pioglitazone is the only thiazolidinedione currently available.</p> <p>Start with 30mg O.D. increasing to 45mg O.D. after 3 months</p>	<p>Pioglitazone is licensed for use with insulin</p> <p>Monitoring of liver function tests prior to commencing therapy, and periodically thereafter is recommended</p> <p>Continue pioglitazone only if there is a reduction in HbA1c of $\geq 0.5\%$ in 6 months unless substituting pioglitazone for another hypoglycaemic agent</p>	<p>Reduces insulin resistance and increases glucose uptake into peripheral tissues</p> <ul style="list-style-type: none"> • Oedema and fluid retention • Weight gain • Increased risk of fractures • Small falls in haemoglobin concentration <p>Hypoglycaemia may occur in patients already taking a sulphonylurea or insulin and in such circumstances the sulphonylurea or insulin dose needs to be reduced</p>	<p>Do not initiate or continue in individuals who have:</p> <ul style="list-style-type: none"> • A history of heart failure • A history of bladder cancer • Is at risk of or has sustained a bone fracture • Contra-indicated in patients with: <ul style="list-style-type: none"> - Heart failure - Active liver disease - Women of child-bearing age considering pregnancy - Post-menopausal women - Discontinue/ do not commence Glitazone therapy if the ALT is 2.5 times the upper limit of normal

SGLT-2 Inhibitors: (Sodium Glucose Co-Transporter 2 Agents)

How they work

SGLT-2 inhibitors prevent the re-absorption of glucose from the kidneys back into the blood, leading to increased glucose in the urine and reduced glucose levels in the blood.

These newer agents are showing clinical benefits such as weight loss as well as HbA1c reduction in some patients. Be aware that there have been a small number of reports relating to the development of DKA in patients. The blood glucose may not be higher than 15 mmol/l when this occurs. These cases seem to be related to the use of SGLT2s in people who either have Type 1 diabetes late onset Type 1 Diabetes, LADA or who are insulin and or nutrition depleted people (Type 2 diabetes).

SGLT2 Advice for healthcare professionals

When treating patients who are taking a sodium-glucose co-transporter 2 (SGLT2) inhibitor (canagliflozin, dapagliflozin, or empagliflozin

- Inform them of the signs and symptoms of diabetic ketoacidosis (DKA) and advise them to seek immediate medical advice if they develop any of these
- Discuss the risk factors for DKA with patients (see pg 26)
- Discontinue treatment with the SGLT2 inhibitor immediately if DKA is suspected or diagnosed
- Do not restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use, unless another cause for DKA was identified and resolved
- Interrupt treatment with the SGLT2 inhibitor in patients who are hospitalised for major surgery or acute serious illnesses; treatment may be restarted once the patient's condition has stabilised
- Report suspected side effects to SGLT2 inhibitors or any other medicines on a Yellow Card

If they become acutely unwell and particularly if they develop breathlessness or are admitted to hospital for any reason they should discontinue these drugs and seek urgent medical advice.

Always test for blood ketones as ketones will not always be shown in the urine.

The effect on cardiovascular risk look promising - in the results of the EMPA-REG OUTCOME trial (Zinman et al)

The EMPA Reg study randomized 4687 patients with type 2 diabetes and established cardiovascular disease to treatment with empagliflozin versus placebo (n=2333)

In the treatment arm there was:

- A reduced in hospitalisation for heart failure by 35%
- A reduction in CV death by 38%
- Improved survival by reducing all-cause mortality by 32%

It is not yet known whether these results are generalisable to people with Type 2 Diabetes without cardiovascular disease or to other drugs in this class.

Side effects

- Vulvovaginal candidiasis
- Balanitis or balanoposthitis

SGLT-2 Inhibitors: (Sodium Glucose Co-Transporter 2 Agents)

For preferred first line choice see list at [Leicestershire Health Community Formulary](#).

Dapagliflozin (Forxiga)	
Dosage	Usage
<p>Start at 10mg O.D. unless there is severe liver failure when a 5mg dose should be used and tolerance reviewed before dose titration</p> <p>If used in combination with insulin then the insulin dose /doses may need to be reduced to reduce the risk of hypoglycaemia</p>	<p>Monotherapy only if Metformin is not tolerated or in combination with insulin or Metformin (dual therapy)</p> <p>If patient cannot take an SU</p> <p>If at significant risk of hypo</p>
Empagliflozin Jardiance (R)	
Dosage	Usage
<p>Start at 10mg O.D.</p> <p>If eGFR ≥ 60 ml/min/1.73m² the dose can be increased to 25mg O.D.</p> <p>Maximum daily dose 25mg</p> <p>No dose adjustment is required for patients with an eGFR ≥ 60ml/min/1.73m² or CR/CL ≥ 60 ml/min</p> <p>If eGFR falls persistently below 60ml/min/1.73m² or CrCl below 60ml/min, the dose of empagliflozin should be adjusted to or maintained at 10mg O.D.</p> <p>No dose adjustment is required for patients with hepatic impairment</p> <p>No dose adjustment is recommended based on age</p> <p>In patients 75 years and older, an increased risk for volume depletion should be taken into account</p>	<p>Use as mono-therapy in adults >18yr to improve glycaemic control when diet and exercise alone do not provide adequate glycaemic control in patients where metformin cannot be used</p> <p>Add-on combination therapy (can be used as triple therapy)</p> <p>If used in combination with an SU or insulin consider reducing the dose of the SU or insulin to reduce the risk of hypoglycaemia</p>
Canagliflozin (Invokana)	
Dosage	Usage
<p>Recommended starting dose 100 mg O.D.</p> <p>In patients who have an eGFR ≥ 60 mL/min/1.73 m² or CR/CL ≥ 60 mL/min and need tighter glycaemic control, the dose can be increased to 300mg O.D.</p> <p>If eGFR falls persistently below 60 mL/min/1.73 m² or CR/CL 60 mL/min, the dose of should be adjusted to or maintained at 100 mg once daily</p> <p>If eGFR 60 mL/min/1.73 m² to < 90 mL/min/1.73 m² or CR/CL 60 mL/min to < 90 mL/min, no dose adjustment is needed</p> <p>For patients with mild or moderate hepatic impairment, no dose adjustment is required</p>	<p>Use as mono-therapy in adults >18yr to improve glycaemic control when diet and exercise alone do not provide adequate glycaemic control in patients where Metformin can not be used</p> <p>Use as add-on therapy with other glucose-lowering medications including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control</p> <p>If used in combination with an SU or insulin consider reducing the dose of the SU or insulin to reduce the risk of hypoglycaemia</p> <p>The tablets can be taken with or without food, swallowed whole with water.</p> <p>If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day.</p>

SGLT-2 Inhibitors: Risk Factors

DKA risk factors

The mechanism by which SGLT2 inhibitors might lead to DKA has not been established. However, the following factors may predispose patients taking an SGLT2 inhibitor to DKA:

- a low beta cell function reserve (eg, patients with type 2 diabetes who have low C-peptide levels, latent autoimmune diabetes in adults [LADA], or a history of pancreatitis)
- Conditions leading to restricted food intake or severe dehydration
- Sudden reduction in insulin
- Increased insulin requirements due to acute illness
- Surgery
- Alcohol abuse

Discuss these risk factors with patients and use SGLT2 inhibitors with caution in patients who have them.

SGLT2	Precautions	Avoid in patients with renal impairment
Dapagliflozin	Do not use in combination with a loop diuretic Do not use in combination with Pioglitazone	It should not be used if eGFR is <60mls/min
Empagliflozin	Not recommended for patients >85 years and older	Do not initiate if eGFR <60 ml/min/1.73 m ² or CrCl <60 ml/min Discontinue if eGFR is persistently <45ml/min/1.73 m ² or CR/CL persistently below 45ml/min DO NOT USE in patients with end stage renal disease (ESRD) or in patients on dialysis Empagliflozin exposure is increased in patients with severe hepatic impairment Not recommended for patients with severe hepatic impairment
Canagliflozin	Patients with evidence of volume depletion will need this correcting before initiation Use with care in patients ≥75 years, patients with known cardiovascular disease, or other patients for whom the initial canagliflozin-induced diuresis poses a risk Risk of foot problems (amputation) small increased risk of foot amputation shown in the CANVAS study and linked to peripheral vascular disease. Patients should be advised to check feet regularly.	Do not initiate in patients with an eGFR < 60 mL/min/1.73 m ² or CrCl < 60 mL/min. Discontinue if eGFR is persistently <45 mL/min/1.73m ² or CR/CL persistently < 45 mL/min Stop if eGFR <45 Do not use in patients with end stage renal disease (ESRD) or in patients on dialysis. Not recommended for severe hepatic impairment

DPP-4 Inhibitors

These drugs are incretin enhancers.

These stimulate insulin response to glucose and prevent glucagon release after meals

Alogliptin, Linagliptin, Saxagliptin, Sitagliptin, Vildagliptin

Dosage	Usage	Precautions/Avoid
<p>Starting dose Alogliptin 6.25mg / 12.5mg/25mg (depending on renal function)</p> <p>Usual dose in patient with normal renal function 25mg OD</p> <p>Linagliptin 5mg OD</p> <p>No dose adjustment for use in CKD</p> <p>Saxagliptin 2.5 /5mg OD (depending on renal function)</p> <p>Sitagliptin 25mg/ 50mg/ 100mg OD (depending on renal function)</p> <p>Vildagliptin 50mg BD</p>	<p>All DPP-4s are licensed for use in combination with Metformin</p> <p>They are also licensed for use with Pioglitazone if treatment fails to achieve adequate glycaemic control (triple therapy)</p> <p>Sitagliptin and Saxagliptin are also licensed for use with insulin</p> <p>Neutral effect on body weight</p> <p>Low incidence of hypoglycaemia unless used in combination with sulphonylurea and/or insulin</p> <p>Sitagliptin, Linagliptin and Vildagliptin are licensed for use in CKD5 patients. There is no need to reduce the dose with Linagliptin. In sitagliptin and Vildagliptin there needs to be a dose reduction</p> <p>There is no increase in the rates of admission for heart failure when using Sitagliptin (TECOS Study)</p> <p>Vildagliptin is not recommended for prescribing in Leicestershire (due to need for LFT monitoring and no evidence of superiority over other agents)</p> <p>Monitoring of renal function should be undertaken regularly in patients on DPP-4s</p>	<p>Contra-indicated in women of child-bearing age considering pregnancy</p> <p>Use in CKD</p> <p>Alogliptin - No dose adjustment in > 65s but be conservative due to risk of decreased renal failure in this population.</p> <p>In patients with moderate renal impairment:</p> <ul style="list-style-type: none"> If CR/CL 30-50 ml/min give 12.5mg daily If CR /CL <50 or in end stage renal failure give 6.25mg daily <p>Saxagliptin - In patients with moderate and severe renal insufficiency reduce dose to 2.5mg. It is not recommended in CKD 5</p> <p>Sitagliptin - For moderate renal insufficiency (eGFR >30-<50 ml/min) reduce dose to 50mg OD. For severe renal insufficiency (eGFR <30ml/min) reduce to 25mg OD</p> <p>Vildagliptin - In patients with moderate or severe renal impairment and end stage renal disease the recommended dose is 50mg OD. Use with caution in CKD 5</p>

Non-Insulin Injectable Therapies

Injectable Therapies but not Insulin: GLP-1 Receptor Agonists (GLP-1s)

What are GLP-1s and how do they work?

GLP-1s are injected to stimulate the insulin response to glucose and prevent glucagon release after meals in normal subjects. The incretin effect is described by the fact that an oral load of glucose induces a greater insulin response than when glucose is administered by IV. This is due to the release of gut hormones, particularly glucagon-like peptide-1 (GLP-1s).

Their effect includes stimulating glucose dependent insulin secretions, increasing satiety and slowing gastric emptying. These actions can lead to reduction in HbA1c with a low risk of hypoglycaemia (unless used with sulphonylureas and or insulin). This action is often accompanied by weight loss.

GLP-1 injections can be used to improve glucose control in adults with Type 2 diabetes by reducing fasting and post prandial glucose levels. They can be used with Metformin, a sulphonylurea or both. In very obese patients and those intolerant of Metformin and sulphonylureas, GLP-1s can be used in combination with a single oral agent.

See Glycaemic Management algorithm for recommendations as to where GLP-1s fit with other glycaemic treatments.

Who should use GLP-1s?

Treatment with GLP-1s is associated with the prevention of weight gain and possible promotion of weight loss:

- GLP-1s should be considered in people with a body mass index of 35 kg/m² or higher
- In those with a body mass index of less than 35 kg/m² where:
 - Insulin treatment would be unacceptable for significant occupational reasons
 - Where weight loss would benefit other significant obesity related co-morbidities
 -
 -

Precautions

- These are not licensed for use with Type 1 diabetes. GLP-1s are not substitutes for insulin in insulin-dependent patients
- Persistent and severe abdominal pain with or without vomiting may be a sign of acute pancreatitis. If this is suspected, the GLP-1 should be stopped, and if confirmed, not be resumed
- Not recommended for use in patients with severe renal failure
- Not recommended for patients with severe gastro-intestinal problems. Patients receiving a GLP-1 in combination with sulphonylurea may be at increased risk of hypoglycaemia, therefore consider a reduction in the dose of sulphonylurea
- There are no specific restrictions for drivers with Class 1 licences (cars and motorcycles) when being treated with a GLP-1. Normal precautions to avoid low blood glucose when driving apply. Drivers holding Class 2 (LGV or PCV) licences need to inform the DVLA if they are being treated with a GLP-1 and a sulphonylurea and individual assessments will be made
- Not recommended during pregnancy or where pregnancy is planned, or for nursing mothers

Adjust need for GLP-1 therapy accordingly from people from black, Asian and other ethnic groups or other specific psychological or other medical problems associated with obesity

Advice to Patients

- Provide them with patient information pack
- Discuss the risk of hypoglycaemia and symptoms, treatment and prevention
- Discuss common side effects such as nausea, vomiting, diarrhoea, dizziness, headache and stomach acid
- Advise that nausea is most common when first starting a GLP-I but decreases over time in most patients
- If they experience severe and persistent symptoms they must contact their health care provider as a matter of urgency
- Advise patients that GLP-Is increase satiety
- Medication such as contraceptives and antibiotics should be taken at least 1 hour before a GLP-I injection
- Patients receiving GLP-Is in combination with a sulphonylurea or insulin may be at increased risk of hypoglycaemia, therefore consider reduction in dose of sulphonylurea or insulin if HbA1c <64mmol/mol (8%)
- Stop use if planning to be, or are pregnant, or when lactating

Patient Information

Patients will need to understand the following:

- That GLP-Is are injectable treatments but not insulin
- Storage of GLP-Is – see below
- Injection techniques- Subcutaneous injection arm, thigh, abdomen
- Timing of dose
- Glucose monitoring - regular daily monitoring required to identify any risk of hypoglycaemia
- If used in combination with insulin - Consider BG monitoring people using in combination with an SU
- Pen needles use/supply - a variety of pen needles are available, HCP should discuss which needle is best for them. A new one should be used for each injection

Indications for continued use

NICE recommends that treatment with GLP-Is is continued only if HbA1c has reduced by 1% and a weight loss of 3% is achieved within 6 months of commencing treatment

Storage of GLP-I Pen Devices

- Unopened GLP-I pre-filled pens should be stored in the refrigerator 2-8°C (36-46°F). Do not freeze
- The GLP-I pen in use can be kept at room temperature but away from direct light
- It should be discarded after 30 days from first use even if there is still some liquid in the pen

GLP-1 Receptor Agonists (GLP-1s) Incretin Mimetics

How it works

This type of medication works by increasing the levels of hormones called 'incretins'

These hormones help the body produce more insulin only when needed and reduce the amount of glucose being produced by the liver when it's not needed

They reduce the rate at which the stomach digests food and empties, and can also increase satiety

Side Effects

- Lipodystrophy
- Gastrointestinal

Exenatide (Byetta) - Short-acting: has a greater impact on post prandial blood glucose

Dosage	Usage	Precautions/Avoid
<p>There are 2 strengths, 5 microgram & 10 microgram pre-filled pens with 60 doses in each (30 days supply)</p> <p>The pen gives same dose each time it is used</p> <p>Initiate with the 5microgram dose</p> <p>After one month the dose can be increased to 10 micrograms twice daily</p> <p>No dose adjustment needed in hepatic impairment</p>	<p>Byetta can be used in combination with:</p> <ul style="list-style-type: none"> • Metformin • Metformin and sulphonylurea • Sulphonylurea • Metformin and pioglitazone • Pioglitazone • Basal Insulin* <p>Inject subcutaneously into either the thigh, abdomen or arm</p> <p>Inject within a 60-minute period before the morning and evening meal</p> <p>Injections should be given more than 6 hours apart</p>	<p>Do not use in Type 1 diabetes or for the treatment of diabetic ketoacidosis.</p> <p>Use with caution if eGFR 30–50 mL/minute/1.73m²</p> <p>Avoid if eGFR less than 30 mL/minute/1.73m²</p> <p>Do not use if there is a history of pancreatitis</p> <p>Pregnancy and or women of child bearing age</p>

GLP-1 Receptor Agonists (GLP-1s)

Exenatide Sustained Release (Bydureon) - Long-acting: has a greater effect on fasting blood glucose

Dosage	Usage	Precautions/Avoid
<p>The recommended dose is 2 mg once weekly</p> <p>Comes in a powder and solvent for prolonged-release suspension for injection - 2mgs per dose in packs of 4</p> <p>Bydureon should be administered once a week on the same day each week</p> <p>The day of weekly administration can be changed if necessary as long as the next dose is administered at least one day (24 hours) later</p> <p>Injection site reactions such as nodules or swelling are normally mild and transitory and they normally disappear during continued treatment</p>	<p>Bydureon can be used in combination with:</p> <ul style="list-style-type: none"> • Metformin • Metformin and sulphonylurea • Sulphonylurea • Metformin and pioglitazone • Pioglitazone <p>In adults who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies</p> <p>Patients switching from Exenatide twice daily (Byetta) to Bydureon may experience transient elevations in blood glucose concentrations, which generally improve within the first two weeks after initiation of therapy</p> <p>When Bydureon is added to existing metformin and/or thiazolidinedione therapy</p> <p>The current dose of metformin and/or thiazolidinedione can be continued</p> <p>When bydureon is added to sulphonylurea therapy, a reduction in the dose of sulphonylurea should be considered to reduce the risk of hypoglycaemia</p> <p>Bydureon can be administered at any time of day, with or without meals</p> <p>If a dose is missed, it should be administered as soon as practical. Thereafter, patients can resume their once weekly dosing schedule</p> <p>Two injections should not be given on the same day</p>	<p>Blood glucose self-monitoring may be necessary to adjust the dose of sulphonylurea</p> <p>If a different non-Insulin therapy treatment is started after the discontinuation of Bydureon consideration should be given to the prolonged release of Bydureon</p> <p>No dose adjustment needed in hepatic impairment</p> <p>Do not use if eGFR < 50ml/min</p>

GLP-1 Receptor Agonists (GLP-1s)

Liraglutide (Victoza) - Long-acting: has a greater impact on fasting blood glucose

Dosage	Usage	Precautions/Avoid
<p>Comes in a pre-filled pen - 6mgs/ml</p> <p>The pen can be adjusted to give either 0.6mgs, 1.2mgs or 1.8mg</p> <p>Starting dose is 0.6mg daily to improve gastrointestinal tolerability</p> <p>Increase to 1.2mg after at least 1 week.</p> <p>Some patients may benefit from an increase to 1.8mg daily</p>	<p>Liraglutide can be used in combination with:</p> <ul style="list-style-type: none"> • Metformin • Metformin and pioglitazone • Metformin and sulphonylurea or basal insulin • Insulin detemir (Levemir) is now licensed as an add-on for Liraglutide <p>Self-monitoring of blood glucose is not needed in order to adjust the dose of Liraglutide.</p> <p>Liraglutide is administered once daily, at any time, independent of meals, as a subcutaneous injection into the abdomen, thigh or upper arm</p>	<p>Do not use in people with Type I diabetes</p> <p>When initiating treatment with Liraglutide in combination with a sulphonylurea, blood glucose self-monitoring may become necessary to adjust the dose of the sulphonylurea</p> <p>Dose adjustment is not required based on age</p> <p>No dosage adjustment is required for mild renal impairment.</p> <p>Do not use in CR/CL < 30ml/Min</p>

Once-Daily Injectable GLP- I Receptor Agonists

Lixisenatide (Lyxumia) - Short-acting: has a greater impact on post prandial blood glucose

Dosage	Usage	Precautions
<p>Starting dose: initiate at 10 microgram Lyxumia once daily for 14 day</p> <p>Maintenance dose: a fixed maintenance dose of 20 microgram Lyxumia once daily is started on Day 15</p>	<p>Can be used in combination with: Metformin, a sulphonylurea or insulin</p> <p>When Lyxumia is added to existing Metformin therapy, the current Metformin dose can be continued unchanged</p> <p>When added to existing therapy of a sulphonylurea or a basal insulin, a reduction in the dose of the sulphonylurea or the basal insulin should be considered to reduce the risk of hypoglycaemia</p> <p>Lyxumia should not be given in combination with basal insulin and a sulphonylurea due to increased risk of hypoglycaemia</p> <p>It is administered once daily, within the hour prior to the first meal of the day or the evening meal</p> <p>If a dose of Lyxumia is missed, it should be injected within the hour prior to the next meal</p>	<p>Do not use in people with Type I Diabetes</p> <p>Its use does not require specific blood glucose monitoring.</p> <p>However, when used in combination with a sulphonylurea or a basal insulin, blood glucose monitoring or blood glucose self-monitoring may become necessary to adjust the doses of the sulphonylurea or the basal insulin</p> <p>Use in caution CR/CL 30-50ml/Min</p> <p>Do not use if eGFR <30</p>

Once Weekly Injectable GLP-1 Receptor Agonists

Trulicity (Dulaglutide) Once weekly GLPI - Long-acting so has a greater impact on fasting blood glucose		
Dosage	Usage	Precautions
<p>The recommended dose is 1.5 mg once weekly</p> <p>For potentially vulnerable populations, such as patients ≥ 75 years, 0.75 mg once weekly can be considered as a starting dose</p> <p>Trulicity is to be injected subcutaneously in the abdomen, thigh or upper arm. It should not be administered intravenously or intramuscularly</p>	<p>Can be used as:</p> <ul style="list-style-type: none"> • Monotherapy • In combination with other non oral non-Insulin therapies • or insulin <p>When Trulicity is added to existing Metformin and/or pioglitazone therapy, the current dose of Metformin and/or pioglitazone can be continued</p> <p>When it is added to an sulphonylurea or prandial insulin, a reduction in the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia</p> <p>Trulicity does not require blood glucose self-monitoring</p> <p>Self-monitoring may be necessary to adjust the dose of sulphonylurea or prandial insulin.</p> <p>The dose can be administered at any time of day, with or without meals</p> <p>If a dose is missed, it should be administered as soon as possible if there are at least 3 days (72 hours) until the next scheduled dose</p> <p>If less than 3 days (72 hours) remain before the next scheduled dose, the missed dose should be skipped and the next dose should be administered on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule</p>	<p>No dose adjustment is required based on age</p> <p>However, the therapeutic experience in patients ≥ 75 years is very limited, and in these patients 0.75 mg once weekly can be considered as a starting dose</p> <p>Patients with renal impairment</p> <p>No dosage adjustment is required in patients with mild or moderate renal impairment</p> <p>There is very limited experience in patients with severe renal impairment (eGFR [by CKD-EPI] < 30 ml/min/1.73 m²) or end stage renal disease, therefore Trulicity is not recommended in this population</p> <p>Patients with hepatic impairment</p> <p>No dosage adjustment is required in patients with hepatic impairment</p>

Injectable Therapies - GLP-1 Receptor Agonists and Insulin

Xultophy (GLP-1 and Insulin Combination)

The GLP1 element is long acting and so has a greater impact on the fasting blood glucose

Dosage	Usage	How it works/ side effects	Precautions
<p>Xultophy is administered once daily as dose steps. One dose step contains 1 unit of insulin degludec and 0.036 mg of liraglutide</p> <p>The pre-filled pen provides from 1 up to 50 dose steps in one injection in increments of one dose step</p> <p>The recommended starting dose of Xultophy is 10 dose steps (10 units insulin degludec and 0.36 mg liraglutide)</p> <p>The maximum daily dose of Xultophy is 50 dose steps (50 units insulin degludec and 1.8 mg liraglutide)</p> <p>EACH DOSE CHANGE IS MEASURED AS A DOSE STEP</p>	<p>Aim to optimise glycaemic control via dose adjustment based on fasting plasma glucose</p> <p>Xultophy is given once daily by subcutaneous administration and can be administered at any time of the day, preferably at the same time of the day in accordance with the individual patient's needs</p> <p>Can be added on to other oral glucose lowering therapies</p> <p>If used in combination with an SU or insulin consider reducing the dose of the SU or insulin to reduce the risk of hypoglycaemia</p> <p>Transfer from basal insulin</p> <p>Basal insulin should be discontinued prior to initiation of Xultophy. When transferring from basal insulin therapy, the recommended starting dose of Xultophy is 16 dose steps (16 units insulin degludec and 0.6 mg liraglutide) This starting dose should not be exceeded and close monitoring is required</p> <p>Patients who forget a dose are advised to take it as soon as possible</p> <p>A minimum of 8 hours between injections should always be ensured</p> <p>Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness</p> <p>In combination with sulphonylurea, the risk of hypoglycaemia may be lowered by a reduction in the dose of sulphonylurea</p>	<p>This is a combination of insulin degludec and liraglutide</p> <p>Side effects</p> <p>The side effects will relate to the individual drugs and include:</p> <ul style="list-style-type: none"> Hypoglycaemia Allergic reactions Gastrointestinal adverse reactions may occur more frequently at the beginning of Xultophy therapy and usually diminish within a few days or weeks on continued treatment Injection site reactions such as nodules or swelling are normally mild and transitory and they normally disappear during continued treatment Lipodystrophy Hypoglycaemia may occur if the dose of Xultophy is higher than required 	<p>Xultophy should not be used in Type 1 diabetes or for the treatment of diabetic ketoacidosis</p> <p>Not recommended in patients ≥ 75 years In those aged 65-75 years intensify glucose monitoring and dose adjust on individual basis</p> <p>In mild renal impairment, dose can be adjusted on an individual basis</p> <p>Not recommended for use in patients with moderate or CKD 5</p> <p>Not recommended in patients with hepatic impairment</p> <p>Discontinue if pancreatitis is suspected or confirmed, and do not restart</p> <p>Do not use in pregnancy or breast feeding</p>

Preventing Complications

Cardiovascular Risk: Lifestyle Intervention

There is now no need to estimate cardiovascular risk in those with diabetes before deciding whether to intervene to improve individual cardiovascular risk factors in people with either Type 1 or Type 2 diabetes.



All people with diabetes are considered to be at high cardiovascular risk
All require lifestyle advice and multifactorial risk factor intervention

Smoking

Please assess patients for smoking status and refer to Smoking Cessation Teams for patient support.

- Leicester City Patients: 0116 295 4141
- Leicester County Patients: 0845 0452 828

3 fatty acids (at least 2 portions of fish per week)

Exercise

The benefits of regular exercise should be explained and patients should be advised to perform regular aerobic activity. Clinical studies show that walking for 30 minutes every day has cardiovascular benefits.

Dietary intervention

- Should include weight loss for those with high waist circumferences
 - > 94cm in Northern European White male
 - > 80cm in Northern European White females
 - > 90cm in South Asian males
 - > 80cm in South Asian females
 - And, for all should include advice about a low fat diet high in fruit and vegetables (at least 5 portions per day)
- Should include advice to decrease total dietary fat to <30% of total energy intake
- Should include advice to decrease saturated fats to <10% of total fat intake
- Should include advice about lowering salt intake to be less than 6g of salt (=2.4 g sodium chloride) per day
- Alcohol intake should be discussed, with the advice for males to limit to 21 units per week and females to 14 units perweek
- Regular intake of oily fish and other sources of omega

Blood Pressure

All patients with diabetes (Type 1 or Type 2) should be treated to a blood pressure target of 140/80 with a combination of lifestyle intervention (see previous) and drug therapy.



- If kidney, eye or cerebrovascular damage set a target <130/80
- Up to half the patients with Type 2 diabetes will need three (3) or more anti-hypertensive agents, and it is important for patients to be made aware of this when discussion around hypertension occurs
- ACE inhibitors and ARBs are preferred first line therapy in people with any degree of nephropathy (micro or macro albuminuria)
- In all patients measure renal functions and electrolytes 1-2 weeks after initiation of ACE inhibitors and ARBs and with each increase in dose

The British Hypertension Society's Guidelines should be followed:

- Assess blood pressure at least 3 monthly until targets are achieved, and monitor every 4-6 months once targets are achieved.
- Patients who do not achieve target should be referred for further management. Remember that, if the patient does not achieve target despite greatest efforts by the multidisciplinary team, any improvement towards the target is better than the patient's baseline.

Lifestyle advice is integral to the management of diabetes and should be reinforced at every available opportunity.

Lipids - When to Consider Prescribing a Statin

- All those who are aged 40 or more with either Type 1 or Type 2 diabetes
- Those aged 18-39 with either Type 1 or Type 2 diabetes who have at least one of the following with poor CV risk factor profile:
 - Significant retinopathy (pre-proliferative, proliferative or maculopathy)
 - Any degree of nephropathy (micro or macro albuminuria)
 - HbA1c > 75mmol/mol (9%)
 - Requirement of antihypertensive therapy
 - Total cholesterol >5 mmol/l
 - Family history of premature cardiovascular disease in a first degree relative (<55 years in males, <65 years in females)
 - Features of metabolic syndrome (increased waist circumference, increased triglycerides, decreased HDL and hypertension)

Treatment Targets

- Dietary interventions alone only reduce cholesterol by <10%. To reach targets, often drug therapy will be required
- The initial target is to achieve a total cholesterol of <4.0 mmol/l and an LDL of <2.0 mmol/l
- Statins are first line drugs for this indication. In accordance with NICE guidelines, low cost statins should be first choice e.g. Simvastatin 40mgs once daily and dose titrated - Check adherence
- If Simvastatin not tolerated or if targets consider Atorvastatin 40 mgs OD
- The dose of the statin should be increased until these targets are achieved
- If targets are not achieved a more potent statin such as Atorvastatin should be considered.
- If Atorvastatin is not tolerated consider using Rosuvastatin, and then the addition of a second agent Ezetimibe.

Lipids

- Monitor LFTs 6 weeks post initiation of statin. If normal check annually. If ALT > 3 times the normal discontinue statin and repeat LFTs in a month

Once the total cholesterol and LDL targets have been achieved, it is important to consider both HDL and triglycerides, particularly in those with cardiovascular disease.

- It is important to note that the target triglyceride level is a fasting target, so an individual with a non-fasting result >2.3 mmol/l should be invited back to have a fasting triglyceride estimation.

- HDL and triglyceride interventions include lifestyle (predominantly weight loss and exercise) and drug therapies. The drug of choice is a fibrate, usually Fenofibrate 160mg. If using a combination lipid lowering regimen, monitoring of ALT and CK is appropriate.
- Monitor lipids 6 weekly until targets have been achieved, and annually thereafter

Remember that, if the patient does not achieve target despite greatest efforts by the multidisciplinary team, any improvement towards the target is better than the patient's baseline.

Exception women of child-bearing potential or pregnant

	Optimal HDL levels are:	Fasting Triglyceride target:
Males	>1.0 mmol/l	<1.7 mmol/l
Females	>1.2 mmol/l	<1.7 mmol/l

Fibrates should not be commenced if eGFR is <45. They should be discontinued with deterioration of renal function

In females who are planning a pregnancy or who are pregnant these lipid lowering drugs should be withheld until breast feeding has ceased

Anti-Platelet Agents

Do not prescribe as primary prevention. Aspirin 75 mg daily is indicated for all patients with diabetes who have any form of cardiovascular disease. In those who are hypertensive the blood pressure should be controlled to 145/90 or below before commencement of aspirin. If aspirin is not tolerated or is contraindicated, clopidogrel 75 mg daily should be considered.

Preventing Specific Complications: Obesity

Background

Obesity is a major modifiable risk factor in the development of Type 2 diabetes. Decrease in weight in those who are obese can improve diabetes control enormously without the need for escalation in therapy.

- Weight loss can be effective enough to induce remission Type 2 diabetes.

Guidance

Those people with diabetes whose adipose tissue mass is likely to contribute to the progression of their diabetes control should be offered the opportunity to discuss their weight. The benefits to the patient of weight loss should be made clear. If the individual does not wish to consider making any changes then this should be reviewed at future consultations. Any choice of weight loss intervention should be negotiated between patient and health care professional. Consideration of what has been tried before is important.

Interventions

Interventions include lifestyle advice, specific drug therapy and obesity surgery.

General Points

Realistic targets for weight loss should be discussed. Aim to lose 5-10% of original weight. Realistic targets for exercise will vary greatly depending on the individual. Ideally, individuals should be encouraged to take up to 45 minutes of exercise per day, 5 times per week. Encouragement to join a commercial weight loss organisation can be beneficial.

Lifestyle intervention

This is the mainstay of obesity management. Any advice offered is more likely to be accepted by the patient if we as health care professionals offer the advice in an enthusiastic manner. Ideally, a combination of reduction of calorie intake and an increase in energy expenditure should be considered. The Leicestershire Dietetics and Nutrition website has useful documents about this.

 www.LNDS.nhs.uk

Obesity Surgery

Bariatric surgery is recommended as a treatment option for adults with obesity if all of the following local criteria are fulfilled:

- They have Type 2 diabetes and a BMI of 35 kg/m² or more
- All appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least 6 months
- The person has been receiving or will receive intensive management in a specialist obesity service
- The person is generally fit for anaesthesia and surgery
- The person commits to the need for long-term follow-up

Before deciding to start treatment, and choosing the drug, discuss with the patient the potential benefits and limitations, including the mode of action, adverse effects and monitoring requirements, and their potential impact on the patient's motivation.

- When prescribing, make arrangements for appropriate healthcare professionals to offer information, support and counselling on additional diet, physical activity and behavioural strategies
- Give information on patient support programmes
- Follow the drugs summary of product characteristics

Drug therapy

Pharmacological agents are only to be used once lifestyle interventions have been instigated and the patient has reached a plateau in their weight loss but still wishes to lose more weight. It is important to set achievable targets for weight loss of no more than 10% of body weight.

When considering the use of pharmacological agents to aid weight loss, ensure that the patient:

1. Wishes to lose weight (the benefits of weight loss should be discussed)
2. Is prepared to make changes to their calorie intake following appropriate dietary advice, preferably from a dietitian with an interest in obesity
3. Is prepared to increase the level of physical activity (if able), preferably up to 45 minutes of moderate exercise at least 5 times per week
4. Is prepared to consider joining a commercial weight loss programme
5. Understands that, if the drug is deemed not to be successful then it will be withdrawn

All studies showing the greatest benefit with the weight loss drugs involved lifestyle intervention as part of the management.

Specific advice on Orlistat

(NICE guidance available)

- Use only in those with diabetes or endocrine conditions who have a BMI $>28\text{kg}/\text{m}^2$
- Continue beyond 3 months of therapy only if the patient has lost at least 5% of their body weight.
- Continue beyond 12 months for weight maintenance only after discussion of potential benefits and limitations with the patient.
- The co-prescribing of orlistat with other drugs aimed at weight reduction is not recommended

Continued prescribing and withdrawal

- Review regularly to monitor the effect of drug treatment, and to reinforce lifestyle advice and need for adherence
- Drug treatment may be used to help people to maintain weight loss, as well as to continue to lose weight
- Consider withdrawing drug treatment if the person does not lose enough weight

Agree goals with the person and review regularly

- If concerned about micro-nutrient intake, consider giving a supplement providing the reference nutrient intake for all vitamins and trace elements, including fat soluble vitamins A, D, E and K. This is particularly important for vulnerable groups such as older people, who may be at risk of malnutrition
- If withdrawing a person's drug treatment, offer support to help maintain weight loss because their self-confidence and belief in their ability to make changes may be low

Foot Problems/Ischaemia /Neuropathy

All patients with diabetes should be on a register and minimum data should include annual measures for microvascular disease. Please see Cardiovascular Risk (pg 38) for additional requirements.

Background

People with Diabetes identified as at increased risk of developing lower limb complications can reduce this by participating in a foot care programme that provides education, podiatry and, where required, protective footwear.

Principal Recommendations

Foot care for all people with diabetes

- Arrange recall and annual review of complications and their risk factors, by trained and competent personnel
- Examine feet as part of annual review to identify risk status, this should include:
 - Testing of foot sensation using a 10g mono-filament or 128Hz tuning fork
 - Palpitation of foot pulses
 - Inspection of foot shape and footwear
- Classify foot risk as:
 - Low risk
 - Moderate risk
 - High risk
 - Active foot problem

Foot Care For All Diabetic Patients

- Risk assessment
- Agree a management plan
- Review education/footwear/vascular status
- Ensure special arrangements for those people with disabilities or immobility
- Referral to specialist team as required



FOOT CARE EMERGENCY ADMISSION

- Critical limb ischaemia
- Spreading infection
- Fever or signs and symptoms of systemic sepsis, abscess or collection, admit to secondary care IMMEDIATELY

Identifying Foot Care Risk Status

1. Low risk

- No risk factors present except callus

Moderate risk

- Deformity or
- Neuropathy or
- Non-critical limb ischaemia
- Refer to community podiatry team
- Reinforce foot care education
- Advise on appropriate footwear

2. High risk

- Previous ulceration or
- Previous amputation or
- On renal replacement therapy
- Neuropathy and non-critical limb ischaemia together or
- Neuropathy in combination with callus and/ or deformity or combination with callus and/ or deformity
- Refer for urgent community podiatry assessment
- Reinforce foot care education
- Advise on appropriate footwear

3. Active diabetic foot problem

- Ulceration or
- Spreading infection or
- Critical limb ischaemia or
- Gangrene or
- Suspicion of an acute charcot arthropathy, or an unexplained hot, red, swollen foot with or without pain
- Refer to the specialist MDT within 24 hours of foot assessment

Foot Care for the Active Foot Problems

- Urgently refer active foot problems to specialist Multi-Disciplinary Foot Clinic (NICE NG19).
- Use Leicestershire [Foot Clinic Referral](#) form. Urgent referral LGH ☎ 0116 258 8304 Fax 0116 273 3067
- Referring Patient for Foot Care: www.leicestershirediabetes.org.uk/515.html

In those with diabetes who develop foot ulceration, **prompt** intervention can minimise the risk of subsequent disability and amputation

- Consider referral to the vascular team
- Expect that team to ensure, as a minimum:
 - Local wound management, appropriate dressings,
 - If required commence antibiotic therapy as per [UHL guidelines](#) or antibiotic therapy. (<http://www.leicestershirediabetes.org.uk/uploads/123/documents/UHL%20Antimicrobial%20Guidelines%20Diabetic%20Foot%20Infections.pdf>)
 - Minimum mobilisation until seen by the specialist MDT

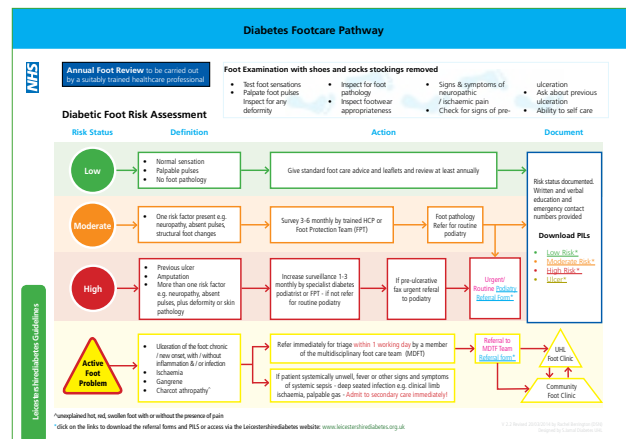
Patient Information Leaflets

A number of useful leaflets are available to patients, and can be downloaded from

www.leicestershirediabetes.org.uk/461.html

- Advice about your footwear
- Diabetes Footcare - Low risk
- Diabetes Footcare - Moderate
- Diabetes Footcare - High risk
- Looking after your diabetic foot ulcer

Leicestershire Diabetes Foot Care Pathway



Neuropathy

Background

Neuropathic pain in people with diabetes is common and often goes undiagnosed or may not be associated with their diabetes. It can be extremely debilitating and can have physical and psychosocial implications (NICE CG 173). All clinicians involved in the care of people with diabetes are responsible for the diagnosis, treatment and monitoring of neuropathic symptoms. Some patients will require referral to specialist diabetes care or pain service at UHL for advice and treatment plan.

Other Neuropathic Complications

Erectile Dysfunction

- Review annually as part of complication screening and care planning
- Discuss causes and contributory factors
- Discuss treatment options available
 - Medical treatment
 - Surgery
 - Psychological support
- Involve partner where appropriate
- Consider referral to erectile dysfunction clinic

Autonomic Neuropathy

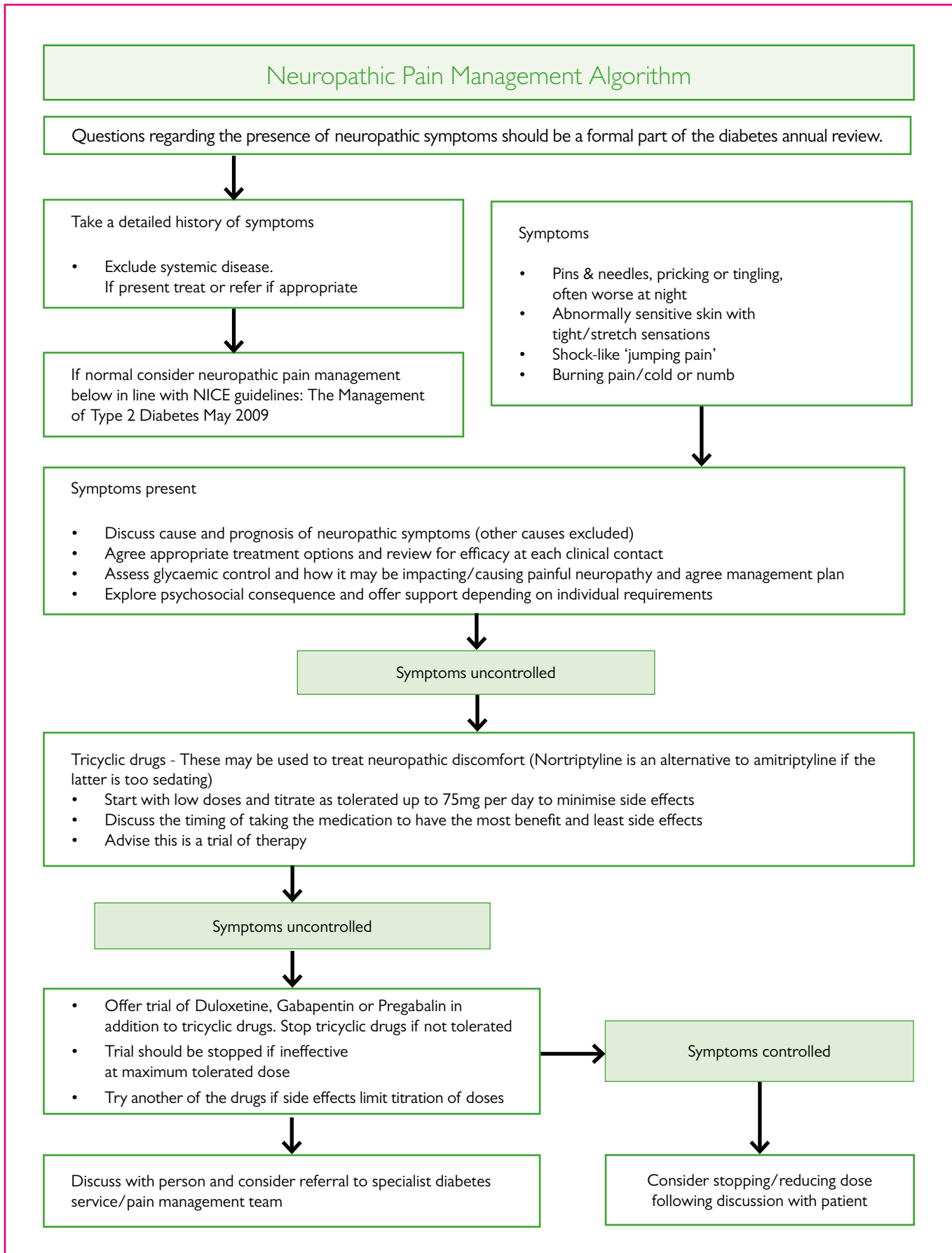
If any of the following symptoms exist consider autonomic neuropathy as a possible cause

- Unexplained gastric bloating or vomiting
- Loss of warning signs for hypoglycaemia
- Unexpected diarrhoea especially at night
- Unexpected bladder emptying problems
- Postural hypotension
- Erratic blood glucose readings

Management

Further investigations are required to exclude other causes and diseases. Requires referral to specialist services if uncertainty about diagnosis and management.

Neuropathic Pain Management Algorithm



Retinopathy

Background

Diabetic Retinopathy is the most common cause of blindness in people of working age⁽¹⁾

- About 38% of Type 2 diabetics have retinopathy at diagnosis.⁽²⁾
- Progresses over the years: after 15 years, at least two thirds of patients may have background retinopathy

NSF key intervention

Regular surveillance for diabetic retinopathy in adults with diabetes and early laser treatment of those identified as having sight threatening retinopathy can reduce the incidence of new visual impairment and blindness in people with Diabetes.

Screening

Examine eyes of people with Type 2 Diabetes at diagnosis and at least annually thereafter, including those blind and partially sighted, and all those with Type 1 Diabetes from 12 months after diagnosis.

Use Quality Assured screening test.
Leicestershire has a community based Retinal Screening Programme. Tel : 0116 2586876

Algorithm for the early management of diabetic retinopathy in Type 2 Diabetes

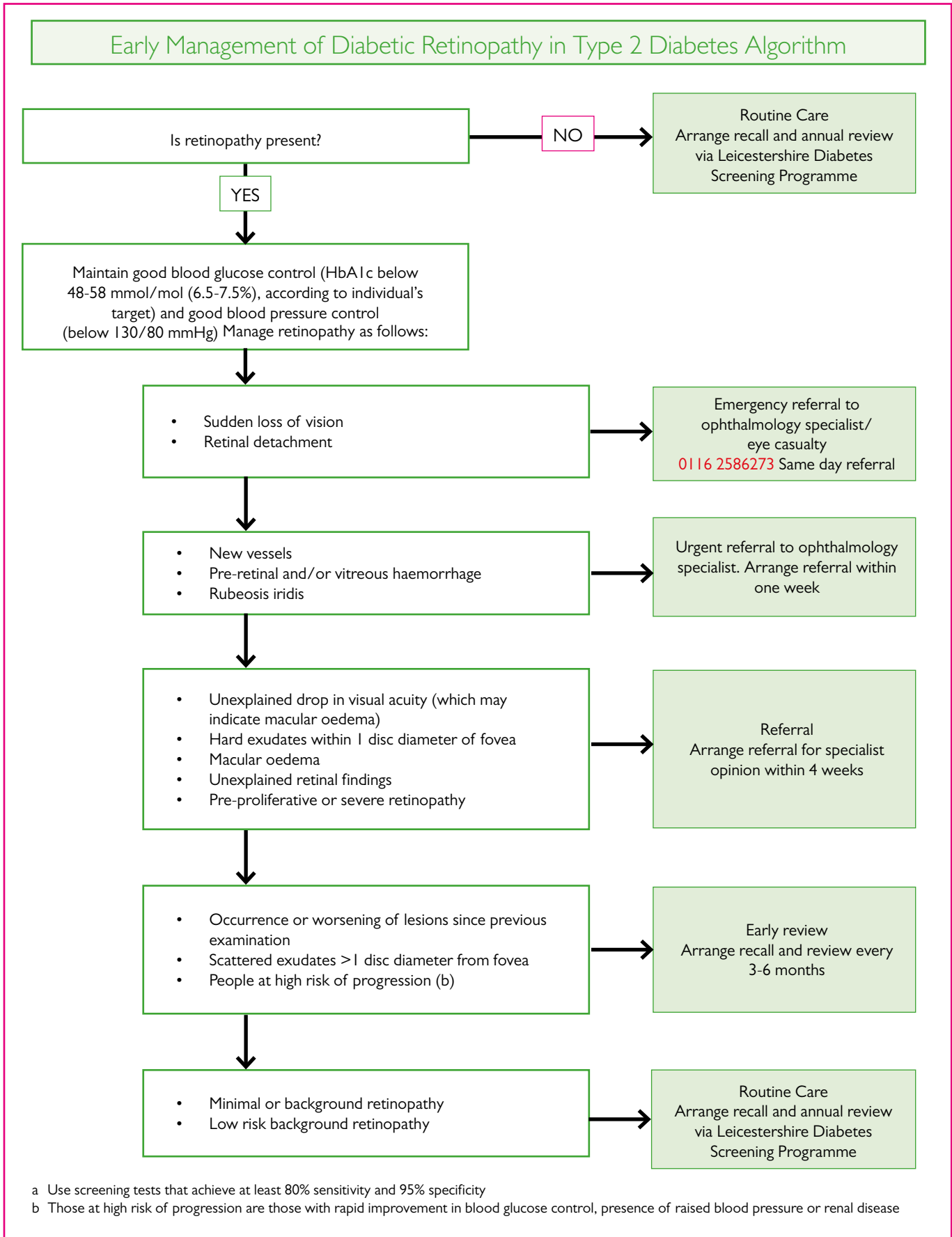
On diagnosis of Type 2 Diabetes, examine eyes:

- Check visual acuity, corrected with spectacles or pinhole - if problem, including cataract, seek ophthalmologic opinion
- Examine for diabetic retinopathy following dilation of pupils with tropicamide or take a photograph with a digital camera of sufficient specification

1. Audit Commission 2000. Testing Times: A Review of Diabetes Services in England and Wales.

2. UKPDS Group. UKPDS 6. Complications in newly diagnosed Type 2 diabetic patients and their association with different clinical and biochemical risk factors. Diabetes Research 1990;13:1-11

Retinopathy Management



Nephropathy and Diabetes

Background

Diabetic nephropathy or diabetic kidney disease affects nearly 20-30% individuals with Type 2 diabetes. The earliest sign of kidney involvement in Type 2 diabetes is abnormal amounts of albumin excretion in the urine which is assessed by laboratory measurement of the albumin creatinine ratio (ACR). Depending on this measure, individuals are categorized into the stages of microalbuminuria or proteinuria.

Glomerular Filtration Rate (GFR) is the best available parameter of kidney function and should be monitored in all individuals with diabetic nephropathy.

Microalbuminuria is an independent CV risk factor. It is also associated with a higher risk of progression to proteinuria. Reduction in albuminuria is a viable target and aggressive targeted control of multiple risk factors is the corner stone of management.

Proteinuria is associated with a high risk of worsening kidney function and progression to end stage kidney disease.

Diabetic Nephropathy is characterised by the excretion of abnormal amounts of albumin in the urine, arterial hypertension and progressive decline in kidney function.

Proteinuria measurements and blood pressure targets

	ACR	PCR (Protein creatinine ratio)	Albumin concentration	Target
Proteinuria (low)	<70	<100	<500mg/24 hrs	140/80
Proteinuria (high)	>70	>100	>500mg/24 hrs	130/80

People with diabetes can develop CKD for reasons other than diabetic nephropathy. According to the pathology there may or may not be any proteinuria

Ref: NICE CG66 Type 2 diabetes

Nephropathy Classification

Chronic Kidney Disease (CKD) is staged according to the estimated Glomerular Filtration Rate (eGFR). eGFR is calculated from the age, sex and serum creatinine level and will be reported alongside any creatinine measurement by the chemical pathology laboratory.

Classification of Chronic Kidney Disease GFR and ACR categories

	GFR and ACR categories and risk of adverse outcomes		ACR categories (mg/mmol), description and range		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73m ² : description and range	≥ 90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60-89 Mild reduction related to normal range for a young adult	G2			
	45-59 Mild–moderate reduction	G3a ¹			
	30-44 Moderate–severe reduction	G3b			
	15-29 Severe reduction	G4			
	<15 Kidney failure	G5			
			Increasing risk		

Consider using eGFR_{cystatinC} for people with CKD G3aA1 (see recommendations 1.1.14 and 1.1.15)
Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–15

Nephropathy Assessment

Who Should Be Tested for CKD?

Monitor renal function at least annually in people with prescribed drugs known to be nephrotoxic (e.g. NSAIDS)

- Offer people testing for CKD if they have any of the following risk factors:
 - Diabetes
 - Hypertension
 - Cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and cerebral vascular disease)
 - Structural renal tract disease, renal calculi or prostatic hypertrophy
 - Multi-system disease with potential kidney involvement, e.g. Systemic Lupus Erythematosus (SLE)
 - Family history of stage G5 CKD or hereditary kidney disease
 - Opportunistic detection of haematuria or proteinuria

Assessment of individual with Diabetic Nephropathy

- Take a full history. List all medications taken
- Physical examination, evaluate for presence of cardiovascular disease
- Urine analysis (ACR), assess kidney function (GFR), Full Blood Count to exclude anaemia, kidney imaging studies and other investigations as appropriate
- Look for presence of retinopathy, peripheral vascular disease, other diabetes complications including erectile dysfunction
- The presence of haematuria, red cell casts on urine microscopy, vasculitis, nephrotic range proteinuria or rapid deterioration in GFR in the absence of long standing diabetes should raise suspicion of non-diabetic kidney disease (refer to nephrology for advice/management)

Testing for Proteinuria

Measure albumin:creatinine ratio on a spot urine sample (preferably early morning)

- If the initial ACR is >30 and <70 mg/mmol, confirm by a subsequent early morning sample. If the initial ACR is >70 mg/mmol a repeat sample need not be tested
- In people without diabetes, clinically significant proteinuria is present when ACR >30 mg/mmol.

Testing for Haematuria

- Use reagent strips rather than urine microscopy
- Evaluate further if there is a result of 1+ or more
- Do not use urine microscopy to confirm a positive result

Protein Positive

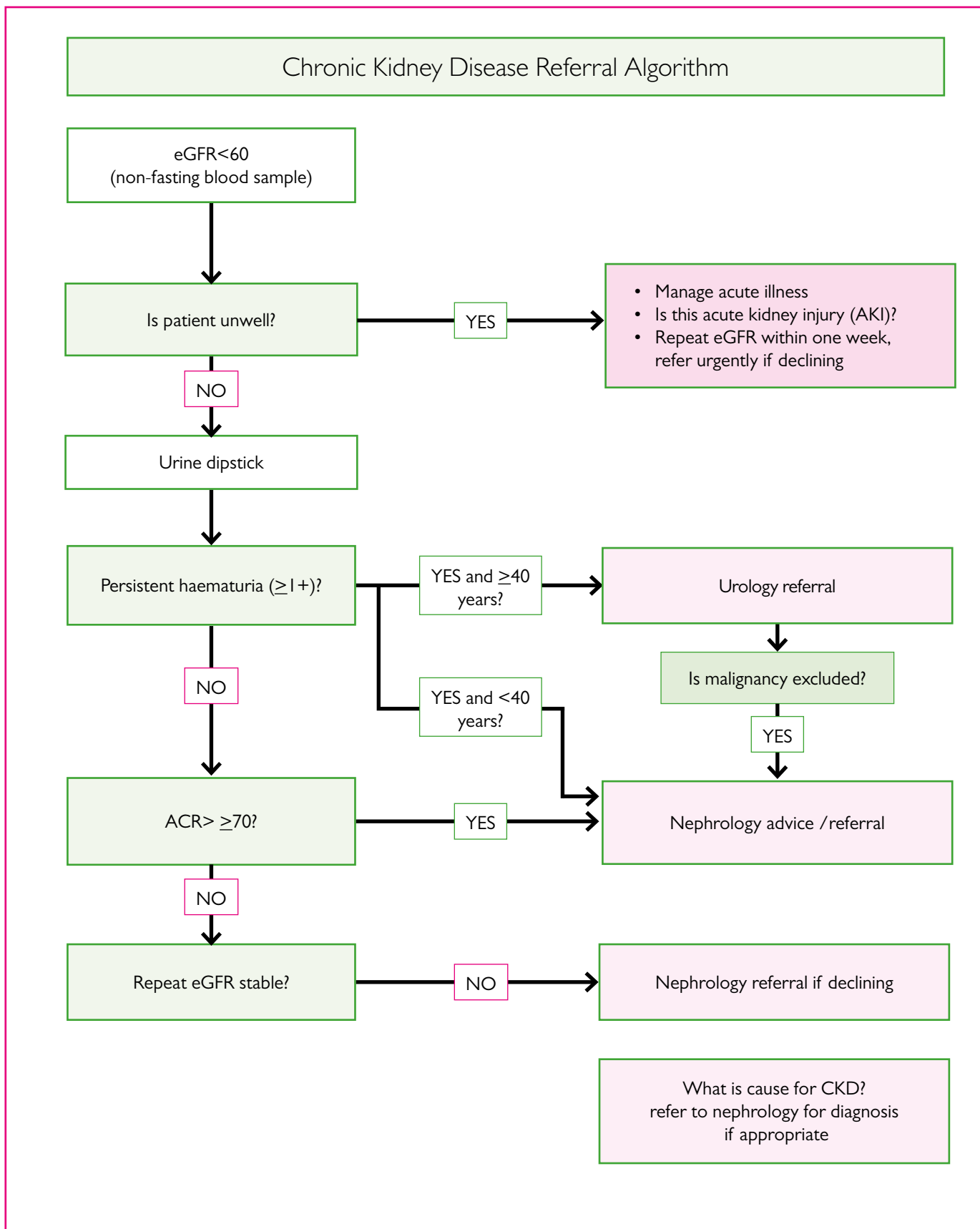
- If protein is detected in the urine on simple dipstick testing (proteinuria) this should be repeated after one or two weeks. If this subsequent test is positive, and the patient has persistent proteinuria the result should then be further quantified by requesting a laboratory measured “protein:creatinine ratio”
- Persons with any degree of proteinuria should be offered treatment with an ACE inhibitor or ARB regardless of the initial blood pressure. See renal guidelines about starting ACE or ARB and subsequent monitoring of eGFR
- If the urine is negative for proteinuria, an early morning urine specimen should be sent to the laboratory for an “albumin:creatinine ratio”
- Offer a low-cost renin–angiotensin system antagonist to people with CKD: and diabetes and an ACR of 3 mg/mmol or more. [See renal guidelines about starting ACE or ARB and subsequent monitoring of eGFR](#)
- Metformin should not be started if eGFR <45 , and should be stopped if eGFR <30

- Patients with G1 and G2 should have annual review of their renal status
- Patients with G3 should have 6 monthly assessment of their renal status and review of their medication to ensure that prescription of potentially nephrotoxic drugs is avoided as much as possible
- Patients with G4 and G5 should be referred to nephrology for an assessment
- Patients with G5 should also be under the care of the Diabetes Specialist Team and have access to diabetes specialist nurse support

When using the nephropathy algorithm it is important to understand that this is not designed to be used in isolation from the other diabetes-related guidelines.

Nephropathy may not necessarily be due to diabetes but could, instead, be secondary to other pathologies such as hypertension.

Nephropathy Management Algorithm



Nephropathy Management Algorithm

When considering initial referral to specialist care send Hb, Ca Pi, K, Bicarbonate, PTH Consider:

- Ultrasound
- Smoking cessation advice
- Weight and exercise advice
- BP – encourage home monitoring
- Aim for target BP:
 - < 140/80 if ACR <70 (PCR <100)
 - <130/80 if ACR>70 (PCR >100)
- Use maximal doses of ACEi or ARB
- For elderly patients or those with diabetes consider targeting to standing BP
- Dyslipidaemia – treat to guidelines
- Aspirin - start if CV disease 10 year risk >20 or secondary prevention

STAGE G1 and G2

Monitor in Primary Care

STAGE G3 and G3b

eGFR every 6 months Annual Hb/K/Ca/Pi/Bicarb PTH if needs nephrology referral

Refer if:

- Sustained decrease in eGFR of $\geq 25\%$, and a change in eGFR category
- Sustained decrease in eGFR of $\geq 15\text{ml/min}$ within 12 months

STAGE G4

Most patients with CKD 4 should be being followed in secondary care

Discuss with nephrology
Repeat eGFR every 3 months
Consider stopping Metformin

Refer if:

- Sustained decrease in eGFR of $\geq 25\%$, and a change in eGFR category
- Sustained decrease in eGFR of $\geq 15\text{ml/min}$ within 12 months
- Diabetic
- eGFR<20
- PTH>11
- Hb<10.5, K>6, Ca<2.1
Pi>1.5

Nephropathy Management

Patients with diabetes and CKD 4 or above should be reviewed after initial assessment to the Consultant Nephrologist in a combined diabetes and renal clinic.

Management of individual with Diabetic nephropathy

- Tight Blood Glucose control aim for target HbA1c 48 - 53mmol/mol (6.5% - 7%) (individualisation of targets is recommended in partnership with the patient)
- Maintain blood pressure below 130/80mmHg
 - ACE inhibitors or Angiotensin II receptor blockers (ARB's) are recommended first line drugs (unless contraindicated)
 - Calcium channel blocker (non-dihydropyridine class) drugs and low dose thiazide diuretics are useful second line agents
 - Loop diuretics are useful in the presence of volume overload (e.g. leg oedema)
 - Additional anti-hypertensive therapy may be required
 - Combination therapy with ACE inhibitor and ARB has superior anti-proteinuric effect, however watch out for hypotensive symptoms (syncope) and hyperkalaemia
- Treat dyslipidaemia (serum cholesterol, LDL cholesterol and serum triglycerides treated to targets)
- Aspirin therapy if indicated (See page 57)
- Lifestyle changes, weight loss and smoking cessation should be advised
- Dietary protein restriction is not routinely advised however in the face of overt nephropathy and or established kidney failure, restriction to 0.6-0.8 gm protein/kg/day has been recommended
- Patient education is an integral part of overall management

Starting ACE inhibitor or ARB therapy

- Caution in individuals with impaired kidney function
- Assess kidney function and electrolytes 1-2 weeks after initiating therapy, watch out for hyperkalaemia
- Assess kidney function after any subsequent increase in dose
- Small rise in creatinine or a mild fall in eGFR values is expected with therapy
- STOP therapy - If serum creatinine rises by >30% or >25% fall in estimated GFR seek specialist advice (to exclude possible renovascular disease)
- Check renal function and electrolytes 1-2 weeks after starting/dose change
- If potassium >6mmol/l and not on Spironolactone. Stop ACEi or ARB. Consider arranging low potassium diet and re-instituting ACEi or ARB once potassium normalised

Information required for referral or letter of advice

As a minimum, the following information is required with any referral:

- List of previous renal function results with dates to assess stability
- Past medical and drug history
- Blood pressure
- ACR results
- FBC, bicarbonate, calcium, phosphate, albumin
- Renal ultrasound (if performed)
- Retinopathy Screening

Leicestershire Diabetes Guidelines
Type 2 Diabetes Management Guidelines
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