Type 2 Diabetes
Optimising Multifactorial Care

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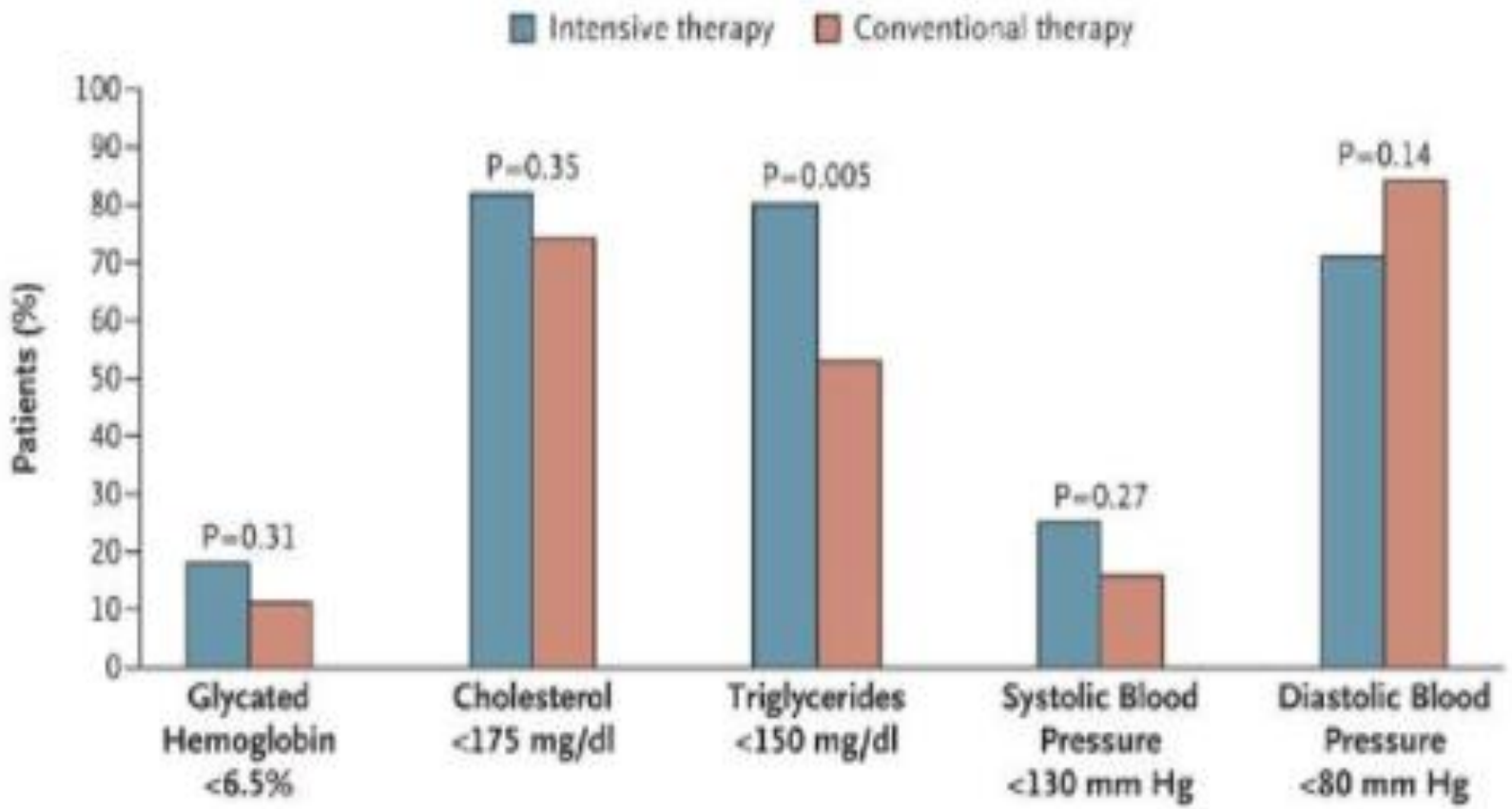
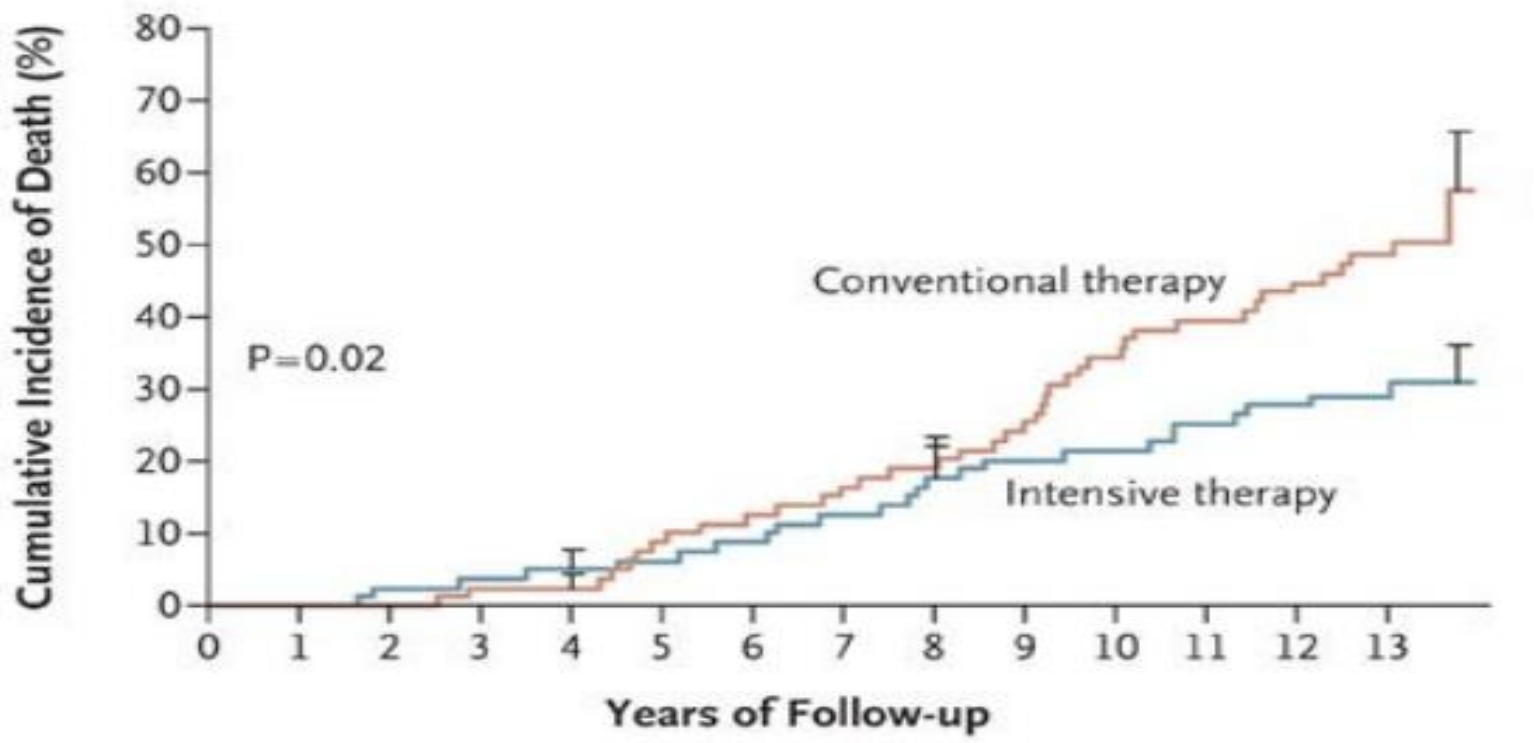
Evidence for multifactorial care

Steno-2 Study- Treatment goals for the intensive-therapy group



Gaede P et al. N Engl J Med 2008; 358:580-591

Steno -2. Cumulative incidence of the risk of death from any cause (Primary end point)

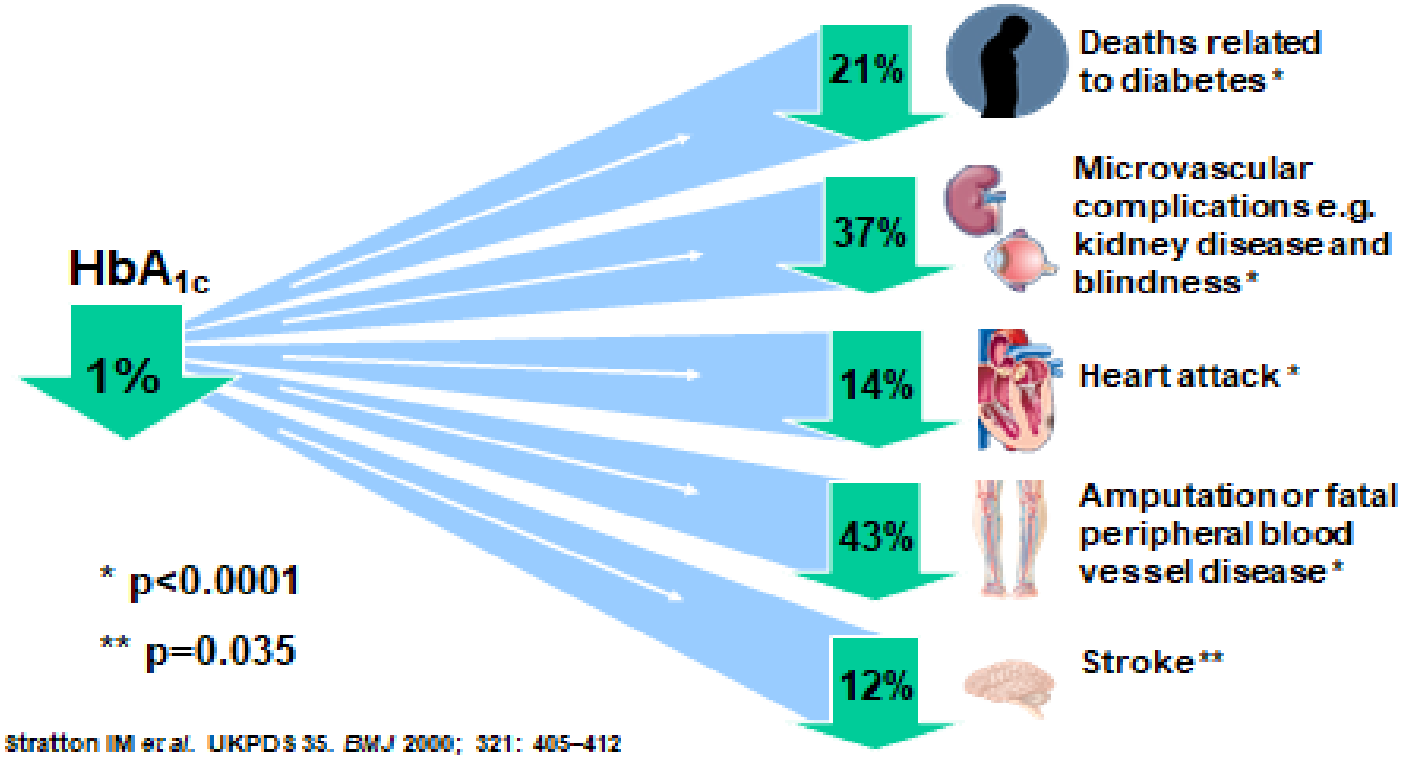


Glucose control

Does HbA1c still matter?

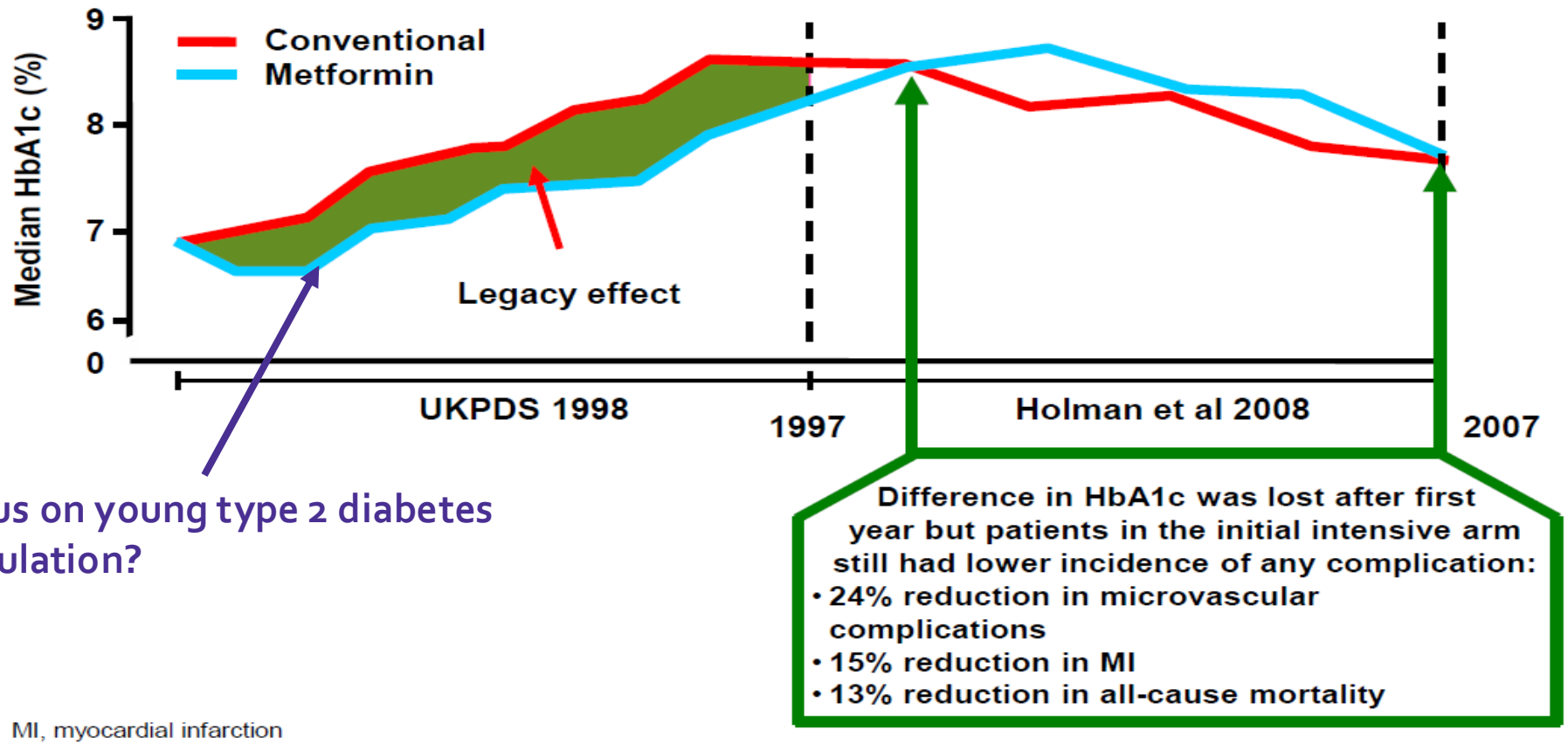
UKPDS: Tight glycaemic control reduces complications

Epidemiological extrapolation showing benefit of a 1% reduction in mean HbA_{1c}



Stratton IM et al. UKPDS 35. BMJ 2000; 321: 405–412

Targeting: Achieving early glycaemic control which may generate a good legacy effect

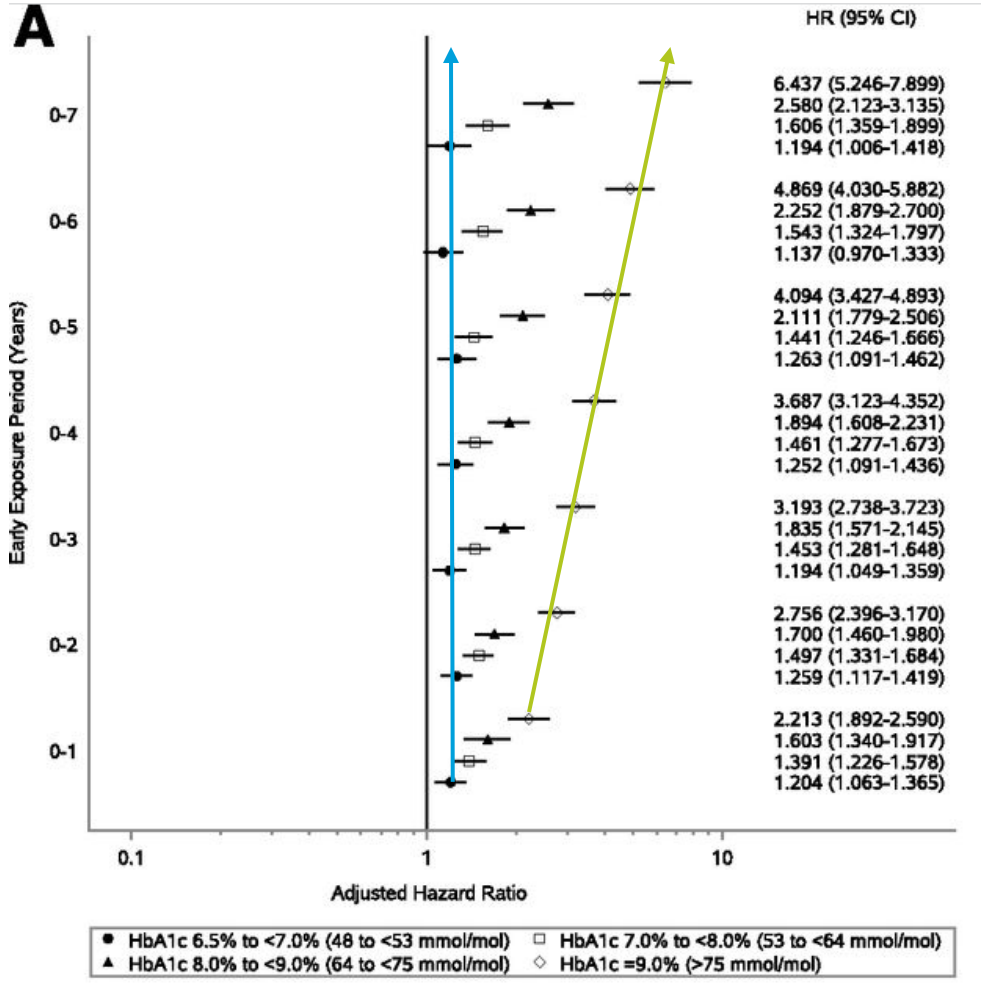


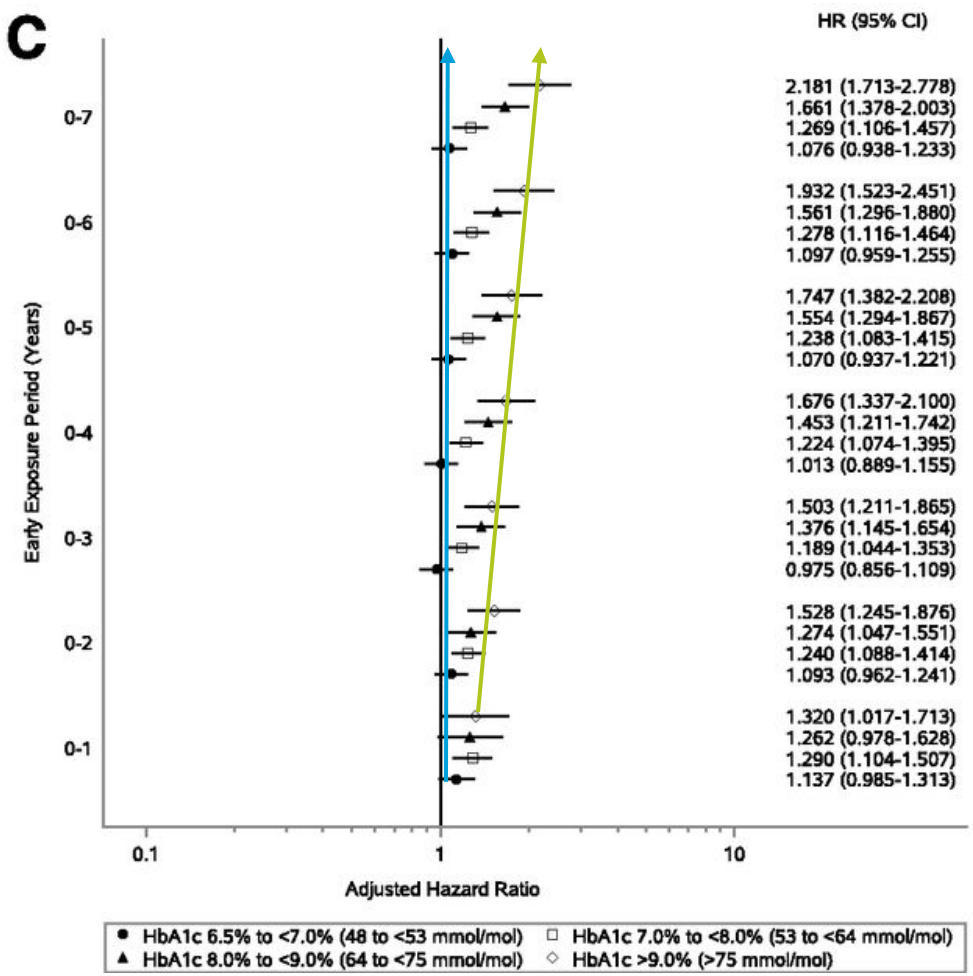
Focus on young type 2 diabetes population?

MI, myocardial infarction

Diabetes Trials Unit. UKPDS Post Trial Monitoring. UKPDS 80 Slide Set. Available at: http://www.dtu.ox.ac.uk/index.php?maindoc=/ukpds/. Accessed 12 September, 2008;
Adapted from Holman RR, et al. N Engl J Med. 2008; 359: 1577–1589; UKPDS 33. Lancet. 1998; 352: 837–853.

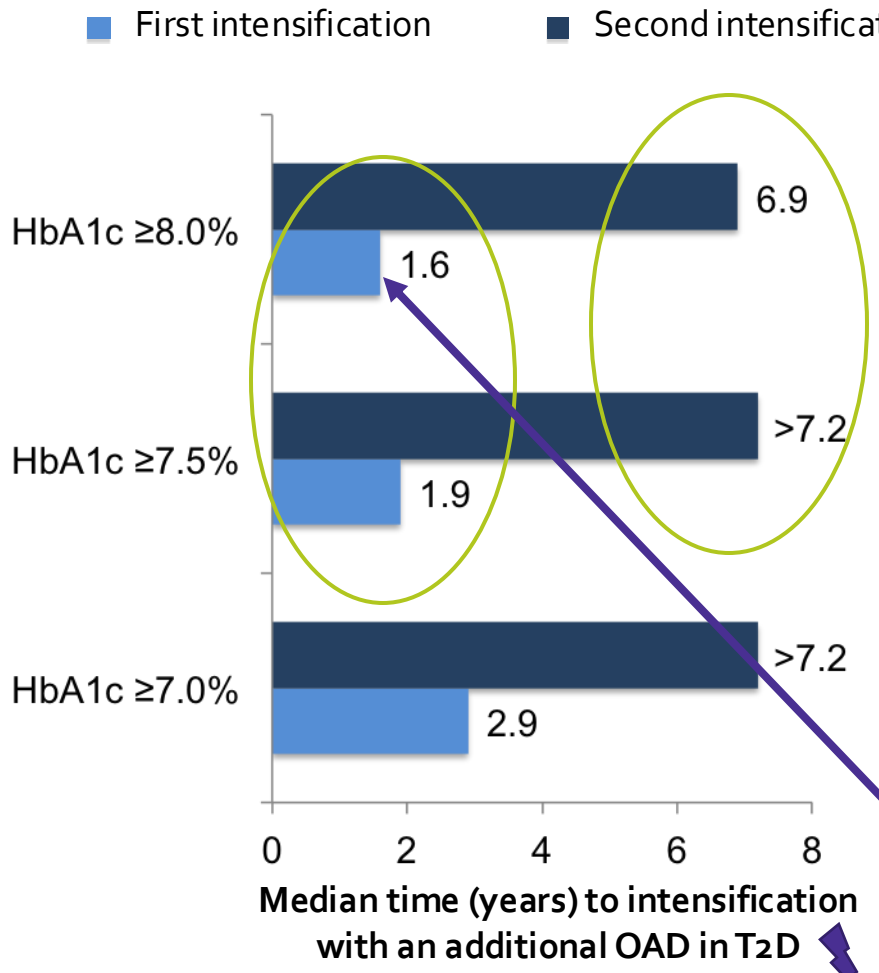
Impact of early glycaemic control on future complications

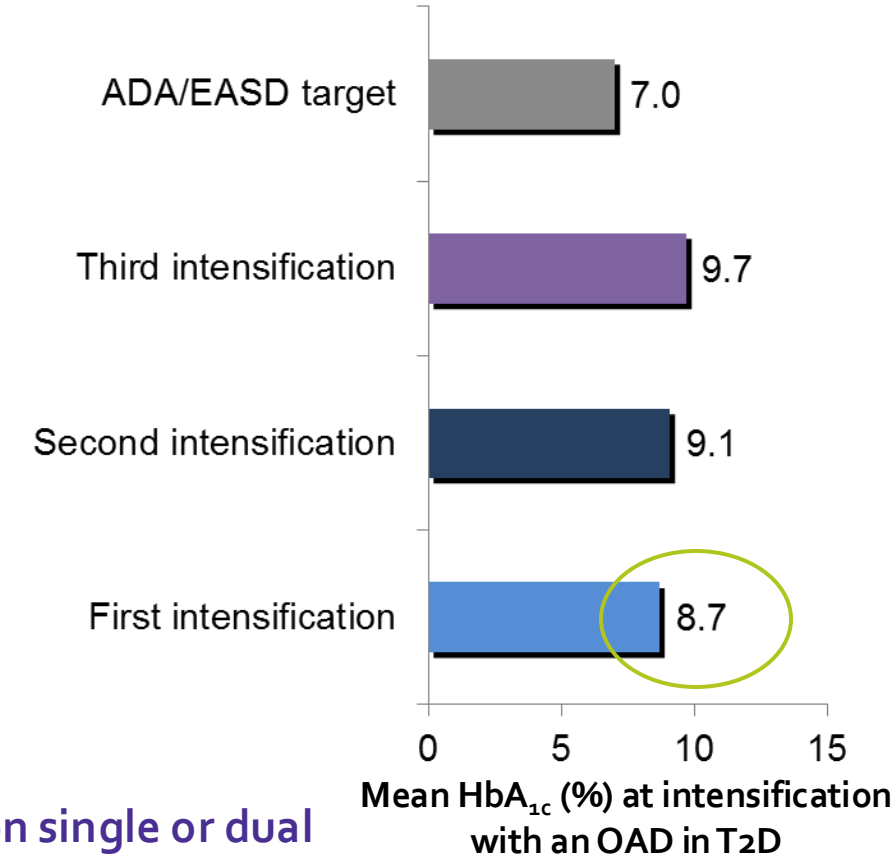




Laiteerapong et al. Diabetes Care 2019; 42(3): 416-426

Therapeutic inertia contributes to poor glycaemic control



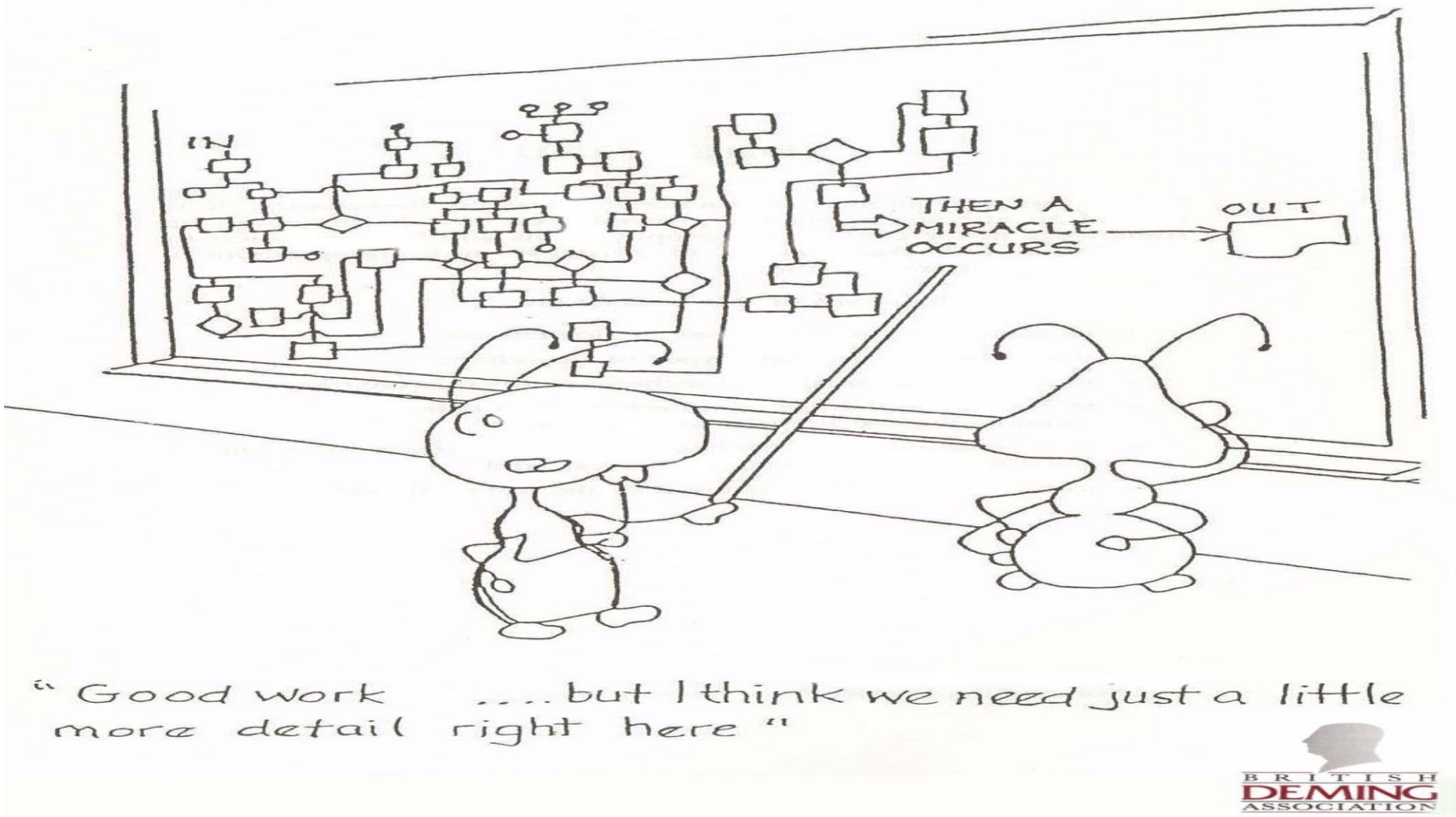


Focus on single or dual therapy?
Medication optimisation?

OAD=Oral anti-diabetic drug; T2D=Type 2 diabetes.

Khunti K et al. *Diabetes Care* 2013;36:3411–3417.

Guidelines


IN
THEN A MIRACLE OCCURS
OUT
" Good work .... but I think we need just a little more detail right here "

NICE NG28 and Type 2 diabetes

Offer SR metformin…aim for an HbA1c level of 48mM/M. For adults on a drug associated with hypoglycaemia…aim for an HbA1c level of 53mM/M. Consider insulin or SU if symptomatic. If they have HF/ASCVD, offer SGLT2i in addition to metformin…introduce drugs sequentially.

- What do I start with and aim for?

3–6-monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy. 6-monthly intervals once the HbA1c level and blood glucose lowering therapy are stable

- When should I review things?

Adopt an individualised approach to diabetes …taking into account their personal preferences, comorbidities, risks from polypharmacy, and…life expectancy. Use decision aid.

- What are we trying to achieve?

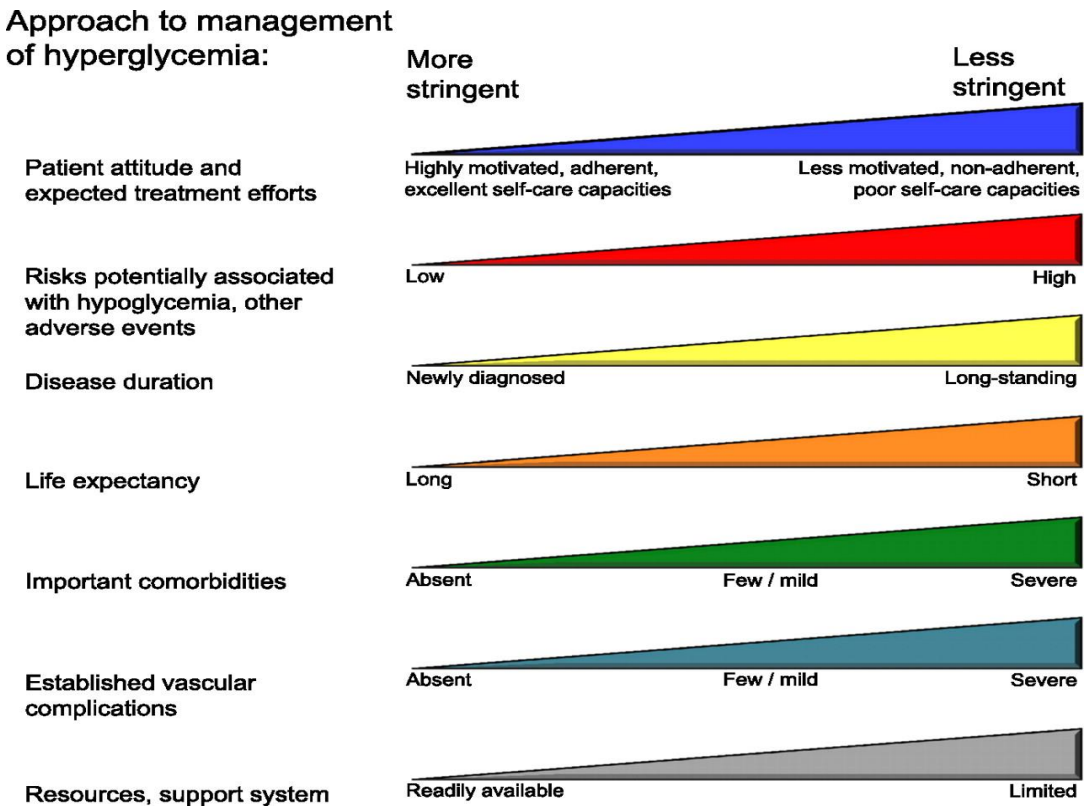
- When do I increase treatment and with what?

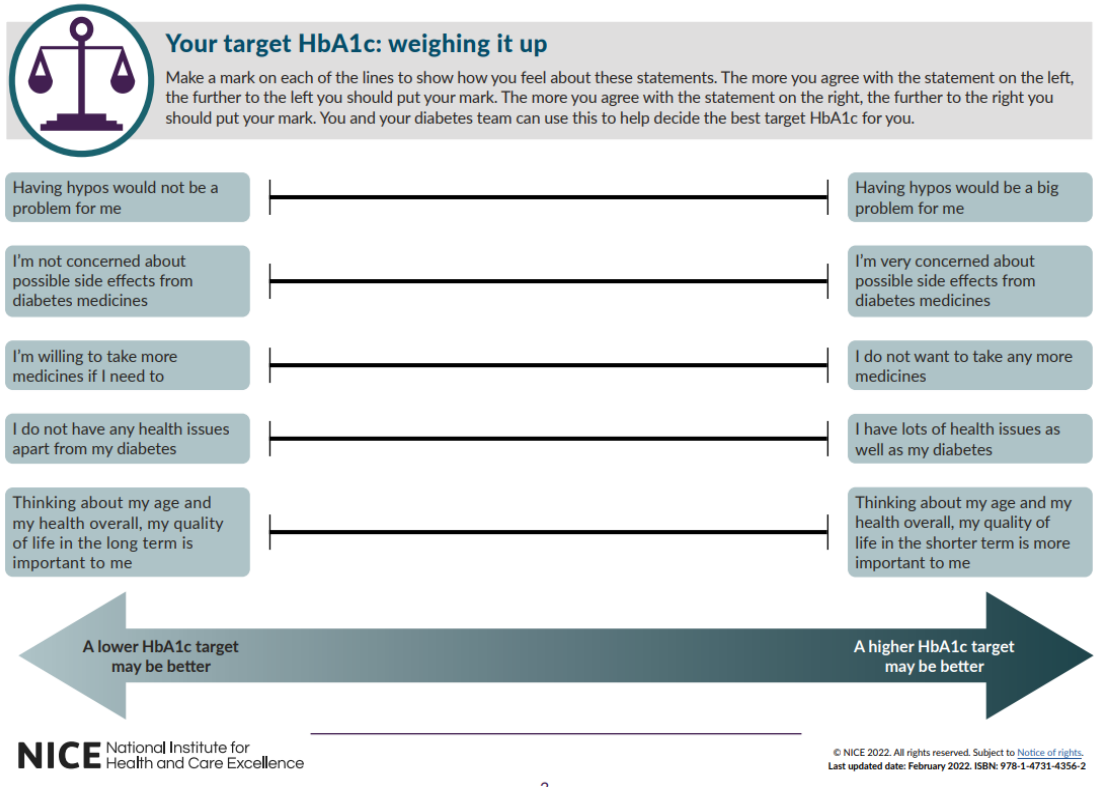
If HbA1c levels are not adequately controlled by a single drug and rise to 58mM/M or higher:
reinforce advice about diet, lifestyle and adherence to drug treatment and support the person to aim for an HbA1c level of 53mM/M and
intensify drug treatment.
Offer SGLT2i for established ASCVD or HF, consider for QRISK>10% or 1+ CVD risk factors in under 40s (BP, lipids, smoking, obesity…)

- Anything else relevant to know?

For CKD (along with ACEi/ARB), offer SGLT2i if ACR>30, consider if ACR 3-30

Individualised treatment





Inzucchi SE, et al. *Diabetes Care.* 2012;35(6)1364-1379

Case study

She is young

- 51 year old female. Caribbean
- BMI 32.4 and renal function ok. Central obesity
- On maximum dose metformin
- Works as cleaner. One large meal a day
- No complications. Diabetes since 2019
- Does not monitor blood glucose
- Only used oral medications. Keen to avoid insulin
- HbA1c was 91mM/M on referral last month
- Current HbA1c 79mM/M

Weight loss would be beneficial

Dietary changes can be made. Regular meals

She is young with no complications…we need to be fairly aggressive still

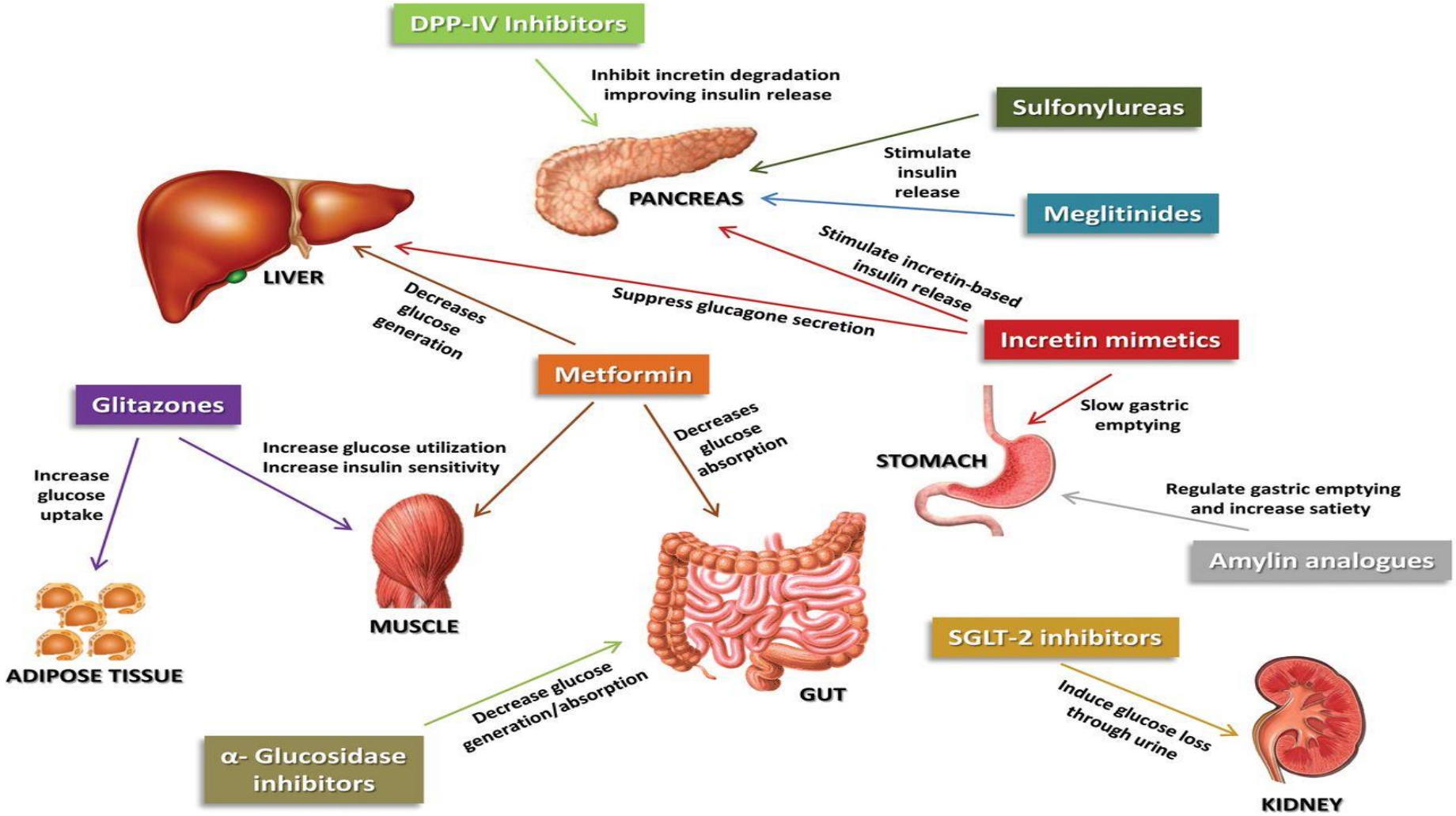
Could be a problem if we use insulin. Will she start doing?

What changed? The power of referral…

Why? Health beliefs?

What is her individualised target?

What do I pick to optimise glycaemic control?



Paul Arnouts et al. Nephrol. Dial. Transplant. 2014;29:1284-1300

What would you do next?

- **3 month follow up, no changes made**
  - HbA1c already improved by 11mmol/mol. Good enough?
- **Add in an SGLT-2 inhibitor**
  - Renal function ok, HbA1c and perhaps weight benefit. Make target?
- **Add in a GLP-1 analogue**
  - HbA1c and weight benefit. Guidelines followed? Make target?
- **Start insulin**
  - Young, reach optimal HbA1c, weight gain. 30 years of injections

Optimisation does not mean Intensification

Declining renal function

- Metformin 30mL/min
- Dose adjustment other medications

New complications develop

- Heart failure and haematuria with Pioglitazone
- Pancreatitis with Incretins
- New CVD diagnosis - review individualised HbA1c target

Side effects

- Hypoglycaemia with gliclazide
- Nausea with metformin
- Genital infections with SGLT-2 inhibitors

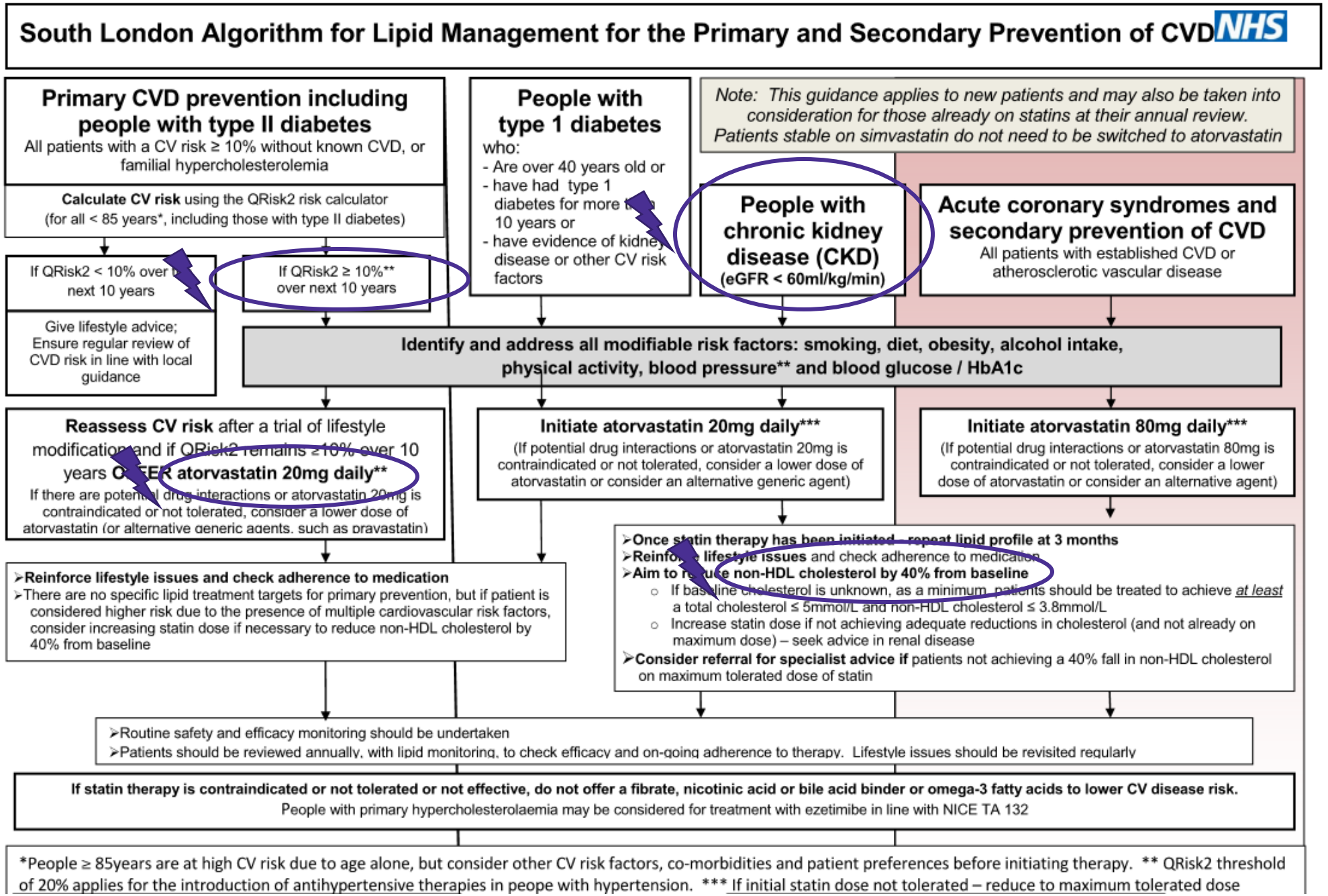
Loss of effect

- GLP-1 analogues HbA1c 1% & weight 3%
- Think adherence

Futility

- Not achieving target
- Avoid collusion. Plan B effect

Lipids


South London Algorithm for Lipid Management for the Primary and Secondary Prevention of CVD
NHS
Primary CVD prevention including people with type II diabetes
All patients with a CV risk ≥ 10% without known CVD, or familial hypercholesterolemia
Calculate CV risk using the QRisk2 risk calculator (for all < 85 years*, including those with type II diabetes)
If QRisk2 < 10% over next 10 years
If QRisk2 ≥ 10%** over next 10 years
Give lifestyle advice; Ensure regular review of CVD risk in line with local guidance
People with type 1 diabetes
who:
- Are over 40 years old or
- have had type 1 diabetes for more than 10 years or
- have evidence of kidney disease or other CV risk factors
People with chronic kidney disease (CKD)
(eGFR < 60ml/kg/min)
Note: This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. Patients stable on simvastatin do not need to be switched to atorvastatin
Acute coronary syndromes and secondary prevention of CVD
All patients with established CVD or atherosclerotic vascular disease
Identify and address all modifiable risk factors: smoking, diet, obesity, alcohol intake, physical activity, blood pressure** and blood glucose / HbA1c
Reassess CV risk after a trial of lifestyle modification and if QRisk2 remains ≥10% over 10 years OFFER atorvastatin 20mg daily**
If there are potential drug interactions or atorvastatin 20mg is contraindicated or not tolerated, consider a lower dose of atorvastatin (or alternative generic agents, such as pravastatin)
Initiate atorvastatin 20mg daily***
(If potential drug interactions or atorvastatin 20mg is contraindicated or not tolerated, consider a lower dose of atorvastatin or consider an alternative generic agent)
Initiate atorvastatin 80mg daily***
(If potential drug interactions or atorvastatin 80mg is contraindicated or not tolerated, consider a lower dose of atorvastatin or consider an alternative agent)
➢Reinforce lifestyle issues and check adherence to medication
➢There are no specific lipid treatment targets for primary prevention, but if patient is considered higher risk due to the presence of multiple cardiovascular risk factors, consider increasing statin dose if necessary to reduce non-HDL cholesterol by 40% from baseline
➢Once statin therapy has been initiated – repeat lipid profile at 3 months
➢Reinforce lifestyle issues and check adherence to medication
➢Aim to reduce non-HDL cholesterol by 40% from baseline
○ If baseline cholesterol is unknown, as a minimum, patients should be treated to achieve at least a total cholesterol ≤ 5mmol/L and non-HDL cholesterol ≤ 3.8mmol/L
○ Increase statin dose if not achieving adequate reductions in cholesterol (and not already on maximum dose) – seek advice in renal disease
➢Consider referral for specialist advice if patients not achieving a 40% fall in non-HDL cholesterol on maximum tolerated dose of statin
➢Routine safety and efficacy monitoring should be undertaken
➢Patients should be reviewed annually, with lipid monitoring, to check efficacy and on-going adherence to therapy. Lifestyle issues should be revisited regularly
If statin therapy is contraindicated or not tolerated or not effective, do not offer a fibrate, nicotinic acid or bile acid binder or omega-3 fatty acids to lower CV disease risk.
People with primary hypercholesterolaemia may be considered for treatment with ezetimibe in line with NICE TA 132
*People ≥ 85years are at high CV risk due to age alone, but consider other CV risk factors, co-morbidities and patient preferences before initiating therapy. ** QRisk2 threshold of 20% applies for the introduction of antihypertensive therapies in peope with hypertension. *** If initial statin dose not tolerated – reduce to maximum tolerated dose

Lipid management

- Every 1 mmol/L reduction in LDL-cholesterol results in an annual cardiovascular risk reduction of up to 28%, regardless of the intervention used.

- • Growing evidence has driven down LDL-C targets over time; the 2019 ESC guideline recommends <1.4 mmol/L and a >50% decrease from baseline for those at very high cardiovascular risk.

- Adding ezetimibe to statins achieves >20% additional reduction in LDL-C (doubling effective statin dose reduces LDL-C by around 6%).

- PCSK9 inhibitors (alirocumab, evolocumab):
  - Primary prevention: only if familial hyperlipidaemia and LDL-C >5.0 mmol/L.
  - Secondary prevention:
  - – In high risk (single CVD event), if LDL-C >4.0 mmol/L.
  - – In very high risk (multiple CVD events or events in different vascular beds), if LDL-C >3.5 mmol/L.
  - – In familial hyperlipidaemia, if LDL-C >3.5 mmol/L.

Box 2. Simon Broome criteria for familial hypercholesterolaemia (FH) diagnosis (adapted from Northern England Lipids Network, 2023).

Definite FH:

Total cholesterol >7.5 mmol/L or LDL >4.9 mmol/L in adults, **or**
Total cholesterol >6.7 mmol/L or LDL >4.0 mmol/L in children (< 16 years).
(Levels either pre-treatment or highest on treatment)

plus

- Tendon xanthomas in patient, first-degree relative (parent, sibling or child) or second-degree relative (grandparent, uncle or aunt).

or

- DNA-based evidence of a variant causing FH.

Possible FH:

Total cholesterol >7.5 mmol/L or LDL >4.9 mmol/L in adults, **or**
Total cholesterol >6.7 mmol/L or LDL >4.0 mmol/L in children (< 16 years).
(Levels either pre-treatment or highest on treatment)

plus

- Family history of premature myocardial infarction in:
  - First-degree relative aged <60 years, or
  - Second-degree relative aged <50 years.

or

- Family history of raised total cholesterol:
  - >7.5 mmol/L in adult first- or second-degree relative, or
  - >6.7 mmol/L in child or sibling <16 years.

- **Do not** use Simon Broome LDL criteria for relatives of index individuals with clinical diagnosis of FH as this will result in underdiagnosis.
- **Do not** use CVD risk estimation tools (e.g. QRISK), as people with FH are already at a high risk of premature coronary heart disease.

Homozygous FH:

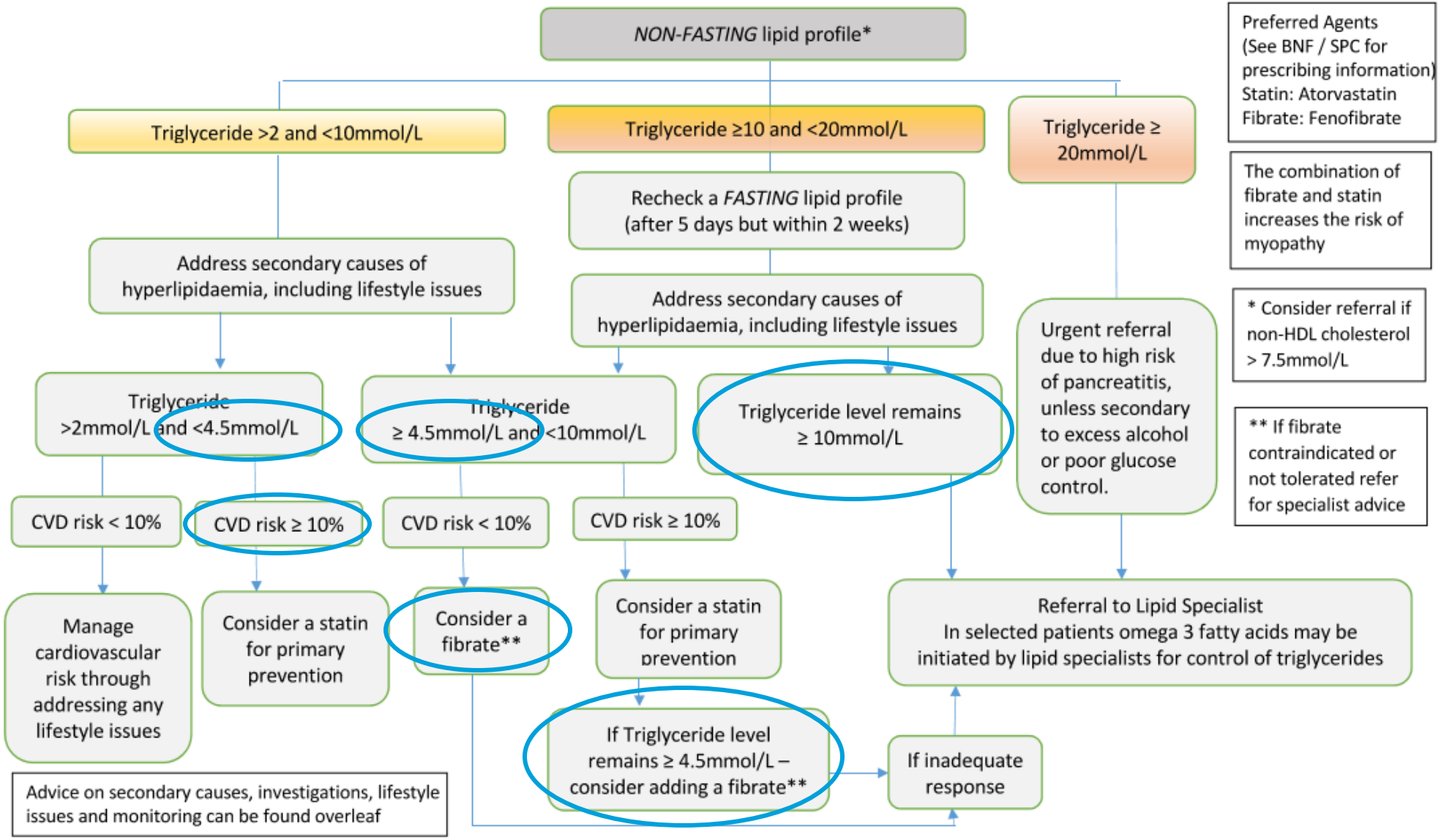
Consider a clinical diagnosis of homozygous FH in:

- Adults with an LDL cholesterol >13 mmol/L.
- Children/young people with an LDL cholesterol >11 mmol/L.

In addition to a clinical diagnosis of FH, the following scenarios warrant referral of the individual to a specialist lipid clinic for further assessment, irrespective of family history:

- Total cholesterol >9 mmol/L.
- LDL cholesterol >6.5 mmol/L.
- Non-HDL cholesterol >7.5 mmol/L.
- Fasting triglycerides >10 mmol/L.

Guidance for the Management of Hypertriglyceridaemia



Statin monitoring

Table 1. NHS England (2023a) and NICE (2023a) recommendations on conducting lipid profiles and liver function tests when initiating a statin.

	Primary prevention		Secondary prevention	
	Lipid profile	ALT or AST	Lipid profile	ALT or AST
Baseline	✓	✓	✓	✓
3 months	✓	✓	✓	✓
6–9 months	If <40% non-HDL cholesterol reduction, uptitration required. Repeat full lipid profile and ALT or AST within 3 months of each uptitration of statin dose or addition of ezetimibe as required			
12 months	✓	✓	✓	✓
Yearly	✓*			✓*

*Offer a full lipid profile for those on treatment for secondary prevention, and consider an annual full lipid profile for those on treatment for primary prevention, to inform the discussion around effectiveness of treatment, medication adherence and titration.

ALT=alanine transaminase; AST=aspartate aminotransferase.

LFTs checked at baseline, 3months and 12months?

Statin potency and comparison

Table 1. Intensity and predicted LDL-lowering effects of various statin regimens (NHS England, 2024).

	Approximate reduction in LDL cholesterol				
Statin dose (mg/day)	5 mg	10 mg	20 mg	40 mg	80 mg
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	

- **Low-intensity statins** will produce an LDL cholesterol reduction of 20–30%.
- **Medium-intensity statins** will produce an LDL cholesterol reduction of 31–40%.
- **High-intensity** statins will produce an LDL cholesterol reduction above 40%.
- **Simvastatin 80 mg** is deemed high-intensity but is not recommended due to risk of muscle toxicity.

Understanding Qrisk

If your QRISK score is 10% over the next 10 years

On average, for every 100 people with this risk score who do not take a statin, over 10 years 10 people will get heart disease or have a stroke and 90 will not.

If 100 people take a statin, over 10 years on average:

- about 90 people will not get heart disease or have a stroke, but would not even if they had not taken a statin
- about 4 people will not get heart disease or have a stroke because they take a statin
- about 6 people will get heart disease or have a stroke even though they take a statin

We cannot say for sure what will happen to any specific person

Blood Pressure

Diagnosis, targets and treatment

- Diagnose hypertension if clinic BP>140/90 and ABPM >135/85

Increase hypertension prevalence and coding?

- Aim for a target of <140/90 (ABPM/home 135/85)
  - If age over 80, aim for <150/90 (ABPM/home 145/85)

- Treatment based on Stage
  - Stage 1 is 140/90 to 159/99 (ABPM 135/85 to 149/94) and CVD risk of 10%+ or established CVD, or DKD
  - Stage 2 is 160/100 to 180/120 (ABPM > 150/95)

Is Qrisk being regularly checked and acted on?

- ACEi/ARB is first line
- CCB and/or thiazide like diuretic
- Spironolactone
- Dietary changes especially salt (<6g/day = 1 teaspoon)

Hypertension Management

- One third of people on hypertension registers remain uncontrolled: 6–8 million people living with undiagnosed or uncontrolled high BP in England (NHS Digital, 2020).

- Reducing systolic blood BP by 10 mmHg reduces stroke risk by 41% and CHD events by 22% (Law et al, 2009). Diabetes increases absolute stroke and CHD risk, so amplifies risks of hypertension and benefits of treatment.

- Delays in follow-up and treatment intensification beyond 6 weeks increases cardiovascular events (Xu et al, 2015).

Hypertension targets

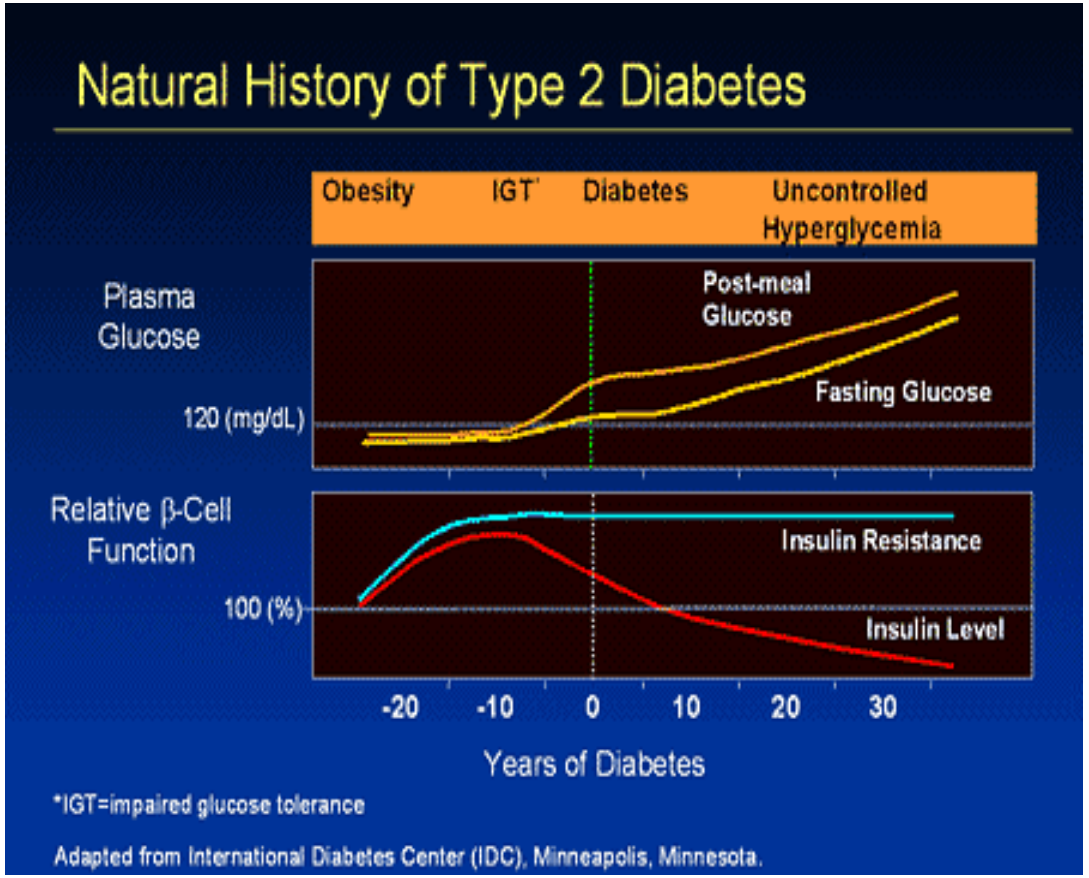
Which BP target? Aim for and maintain at NICE BP targets (or below)[5, 9, 10, 11]

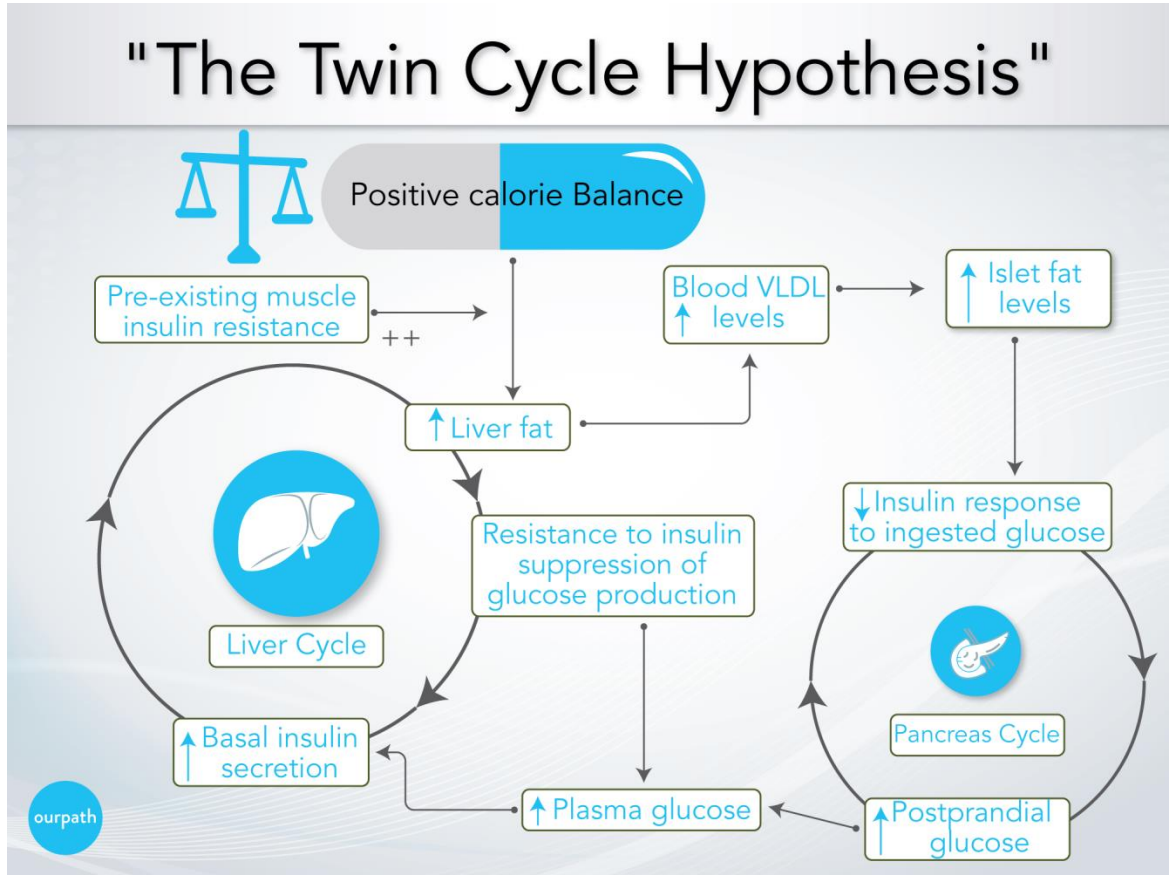
Which condition?	Which cohort within the condition?	NICE Clinic BP Target	QOF BP Targets[16] 2021/2022	
		• Use clinical judgment in frailty/multi-morbidity • Corresponding targets for ABPM/HBPM are 5mmHg lower than for clinic BPs		
Hypertension, including Type 2 Diabetes (but with no CKD)	Age <80yrs	≤140/90mmHg	≤140/90mmHg	*Note QOF Target for **Hypertension in T2DM is ≤140/80mmHg**
	Age ≥80yrs	≤150/90mmHg	≤150/90mmHg	
Diabetes	Type 2 Diabetes	**Same as hypertension if no CKD**	≤140/80mmHg	
	Type 1 Diabetes + no albuminuria	≤135/85mmHg		
	Type 1 Diabetes + albuminuria or ≥ 2 features of metabolic syndrome	≤130/80mmHg		
CKD	ACR <70mg/mmol	<140/90mmHg (systolic range = 120-139mmHg)	No QOF target	
	ACR ≥70mg/mmol or co-existent Diabetes	<130/80mmHg (systolic range = 120-129mmHg)		
IHD/PAD or TIA/Stroke	History of IHD/PAD	**Same as hypertension, if no CKD**	No QOF target for PAD, but for rest based on age i.e. <80yrs ≤140/90mmHg ≥80yrs ≤150/90mmHg	
	History of TIA/Stroke (if with severe bilateral carotid stenosis: systolic BP 140-150mmHg)	**Same as hypertension, if no CKD**		

Clinical Effectiveness South East London
https://selondonccg.nhs.uk/wp-content/uploads/dlm_uploads/2022/08/CESEL-Hypertension-Lambeth-FINAL-VERSION-updated-1.8.22.pdf

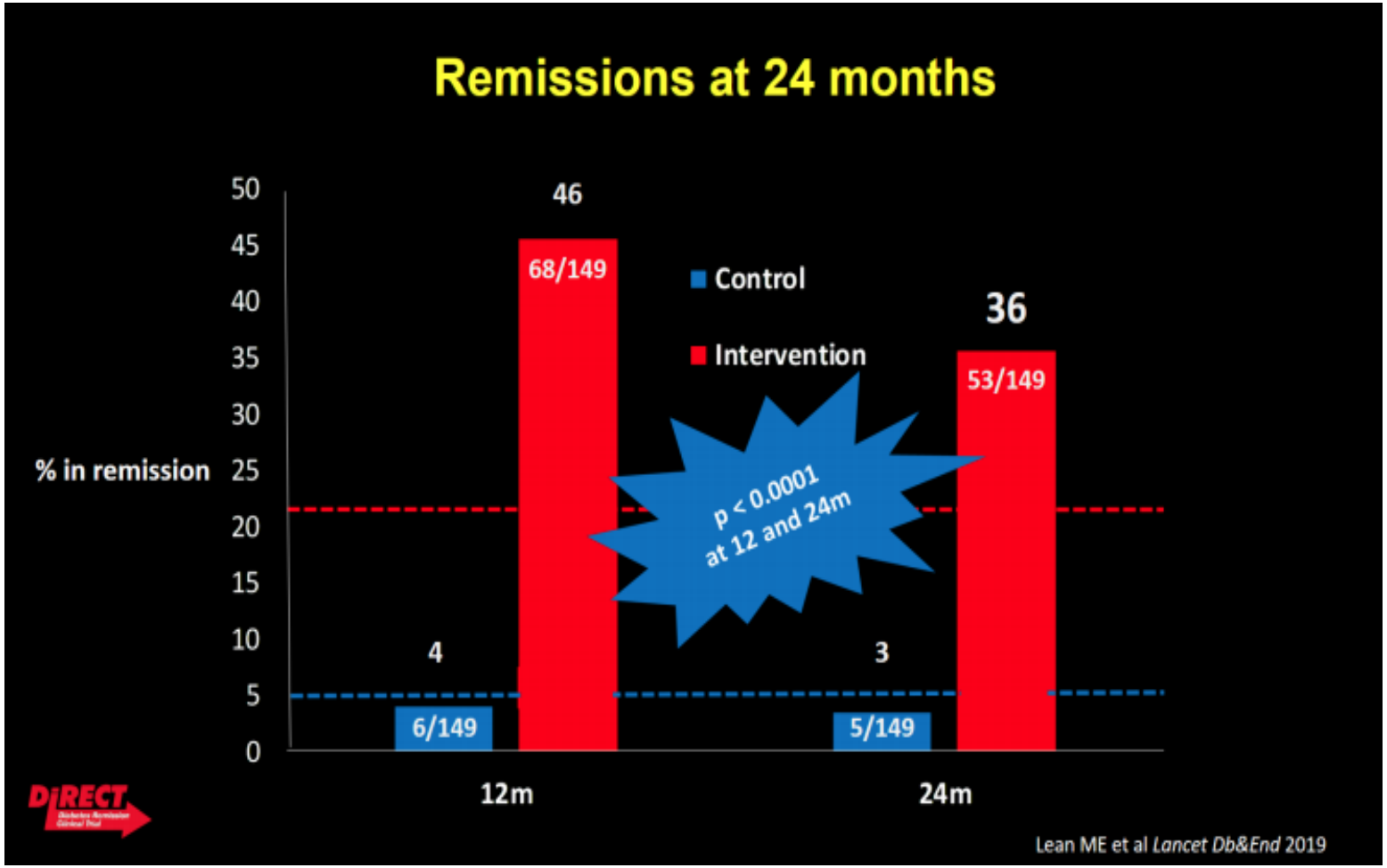
Weight Management and Mental Health support

Pathophysiology





DiRECT Study



Lean MEJ et al. Lancet 2019; 7(5):344-355

Weight management

- Opportunistic support. Make Every Contact Count (MECC)
  - 5-10% weight loss
  - Exercise 30 minutes a day for 5 days a week
- Digital weight management via NHS
- Structured education
- Type 2 diabetes remission
- Tier 3 and 4
  - BMI>30 = Tier 3
  - BMI >35 = Tier 3 expedited

Check knowledge and use of different resources available?

Too often missing (Askew C. Solomons L. Too often missing: making emotional and psychological support routine in diabetes care. Diabetes UK, 2019)

- 70 % of people with diabetes feel overwhelmed
  - ¾ emotional struggle affected self management
  - ¾ could not access specialist mental health support needed

- Health care professionals lack confidence to raise the issue of mental health in people with diabetes

What is diabetes distress

- Burden of living with a demanding long term condition such as type 2 diabetes
- 36% of people with type 2 diabetes
- The worse the distress, the worse the glycaemic control
- DDS2
  - Feeling overwhelmed by the demands of living with diabetes
  - Feeling that I am often failing with my diabetes routine

Despair

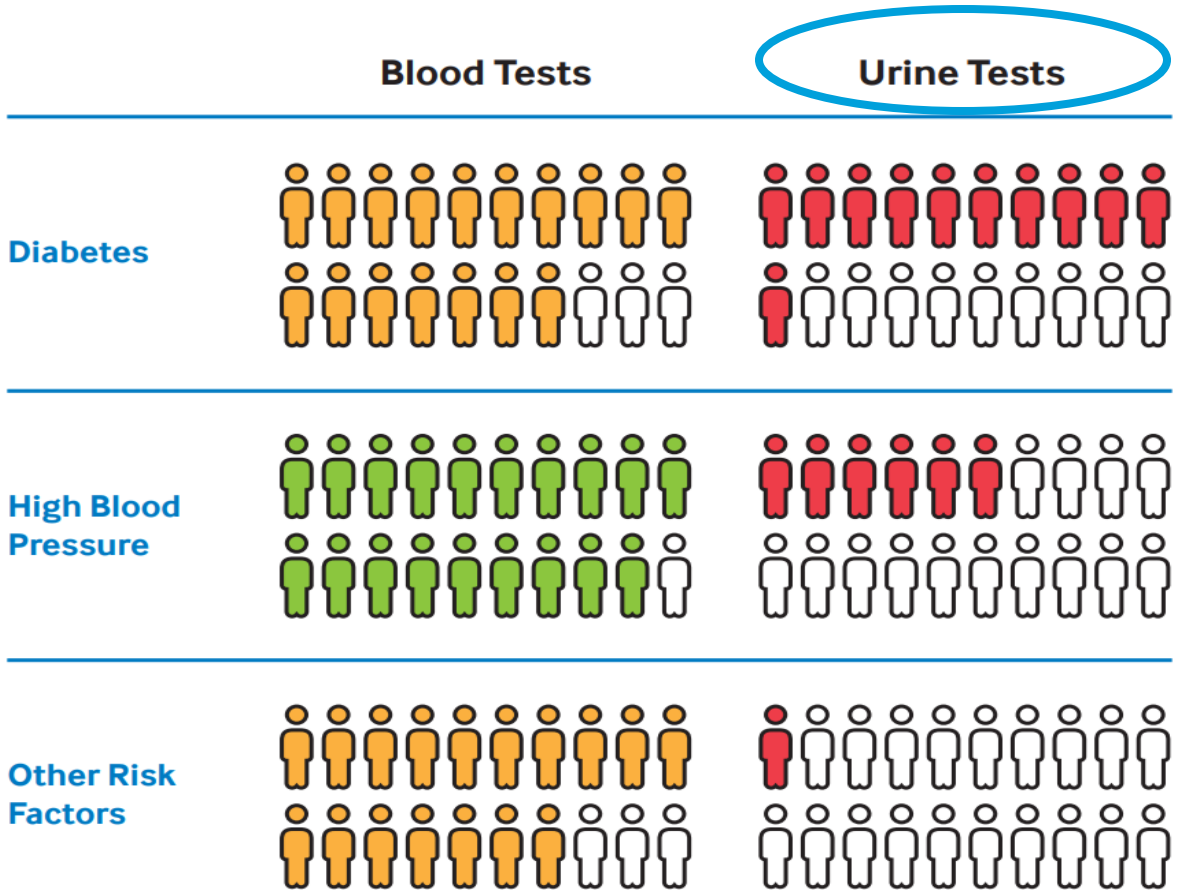
Discouragement

Overwhelmed

Incorporate DDS2 scoring into annual review?

Chronic Kidney Disease

What are the problems?



Key: *There are no formal targets in the guidance, but the audit selected 70% and 90% as quality markers.*
Red < 70% **Amber 71-90%** **Green > 90%**

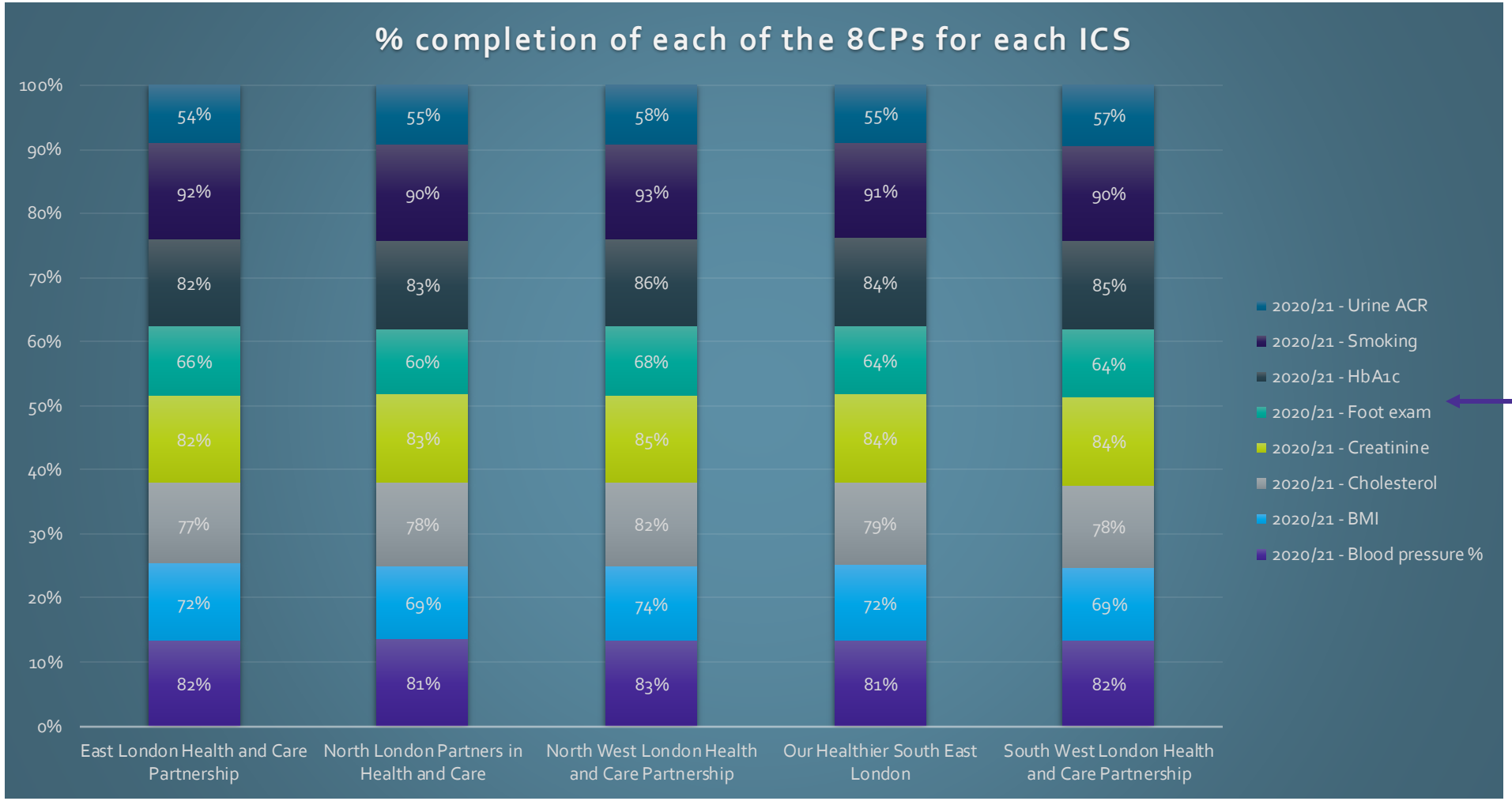
National CKD Audit – National Report (Part 1) January 2017

For people at high risk of CKD, ensure that both blood tests for eGFR and ACR are being included to aid better identification

Improve the coding of patients with CKD

Having identified CKD, regularly review, manage high blood pressure, prescribe cholesterol lowering treatments, and perform vaccinations

8 Care Process (8CP) Completion London 2020/21



Foot checks and ACR being done?

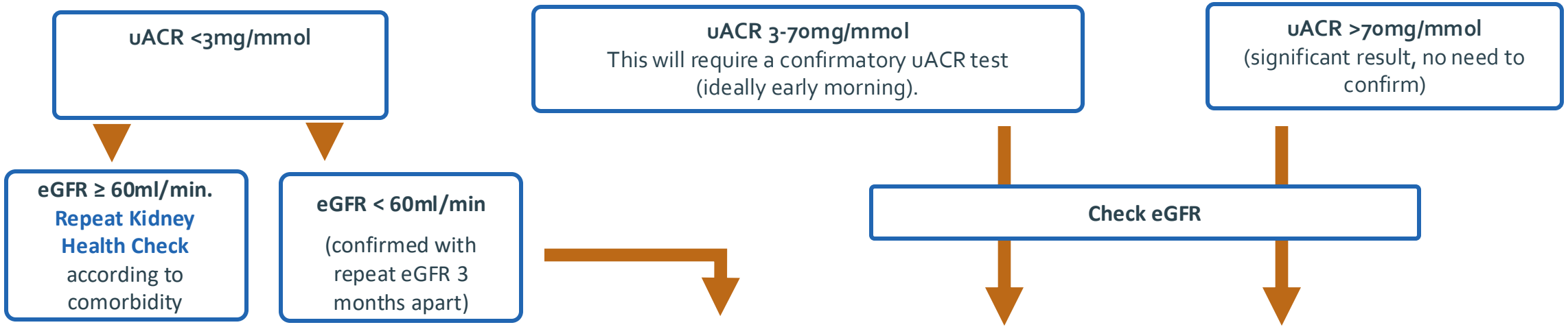
The Kidney Health Check for Adults Living with Diabetes or Hypertension: How to identify Chronic Kidney Disease *early!*

LKN CKD Early Identification Pathway

What is a Kidney Health Check? It is the combination of both an **eGFR** *and* a **uACR** test

Who should have a Kidney Health Check?

1. People living with **diabetes** should have a yearly kidney health check
2. People living with **hypertension** should have a kidney health check every 1-5 years (annually for poorly controlled hypertension)
3. See NICE CKD Assessment and Management for ACR testing in other health conditions



1. INFORM the patient that they have **Chronic Kidney Disease (CKD)**.
2. If eGFR is < 60ml/min, consider discussing Kidney Failure Risk equation see link: KFRE.
3. Add coding for CKD (including CKD G1 and G2) and albuminuria category, into the patient record.
4. Discuss with the person their uACR number, eGFR number, BP and HbA1c if living with diabetes.
5. Explain what each term means *and* the factors that can cause CKD or diabetic kidney disease: raised BP, raised HbA1c, obesity.
6. Give lifestyle advice and connect them with support services where suitable: weight management enhanced services, exercise, and smoking cessation (see online guidance). Offer advice on avoiding NSAIDS/sick day rules.
7. Implement the **LKN CKD Optimisation Pathways** for proteinuric CKD with or without diabetes.

Coding Principles

- Coding should include both the blood (eGFR) and urine (ACR) values relevant to CKD detection

- Higher level coding such as *Chronic Renal Impairment* and *Chronic Kidney Disease* should be avoided, as this does not align to intricacies of CKD staging and management.

- In instances where disease specific nomenclature may be relevant and used such as *Diabetic nephropthy*, the coding should still include both the blood and urine values relevant to that diagnosis

Coding Possibilities

eGFR value (ml/min)	Possible Code Group 1	Possible Code Group 2
Greater than 90	G1	CKD stage 1
60-90	G2	CKD stage 2
45-59	G3a	CKD stage 3
30-44	G3b	CKD stage 3
15-29	G4	CKD stage 4
Less than 15	G5	CKD stage 5

ACR value (mg/mmol)	Possible Code Group 1	Possible Code Group 2
0-3	A1	No code
3-30	A2	Microalbuminuria
Greater than 30	A3	Microalbuminuria/Proteinuria

Coding in Practice

A patient with known type 2 diabetes and hypertension has routine blood and urine tests. The results are shown and highlighted below in yellow. Their eGFR is 74ml/min and the ACR is 5.5mg/mmol.

eGFR value (ml/min)	Possible Code Group 1	Possible Code Group 2
Greater than 90	G1	CKD stage 1
60-90	G2	CKD stage 2
45-59	G3a	CKD stage 3
30-44	G3b	CKD stage 3
15-29	G4	CKD stage 4
Less than 15	G5	CKD stage 5

ACR value (mg/mmol)	Possible Code Group 1	Possible Code Group 2
0-3	A1	No code
3-30	A2	Microalbuminuria
Greater than 30	A3	Albuminuria

Using the coding tables above, possible coding would be:

If using Group 1- **CKD G2A2**

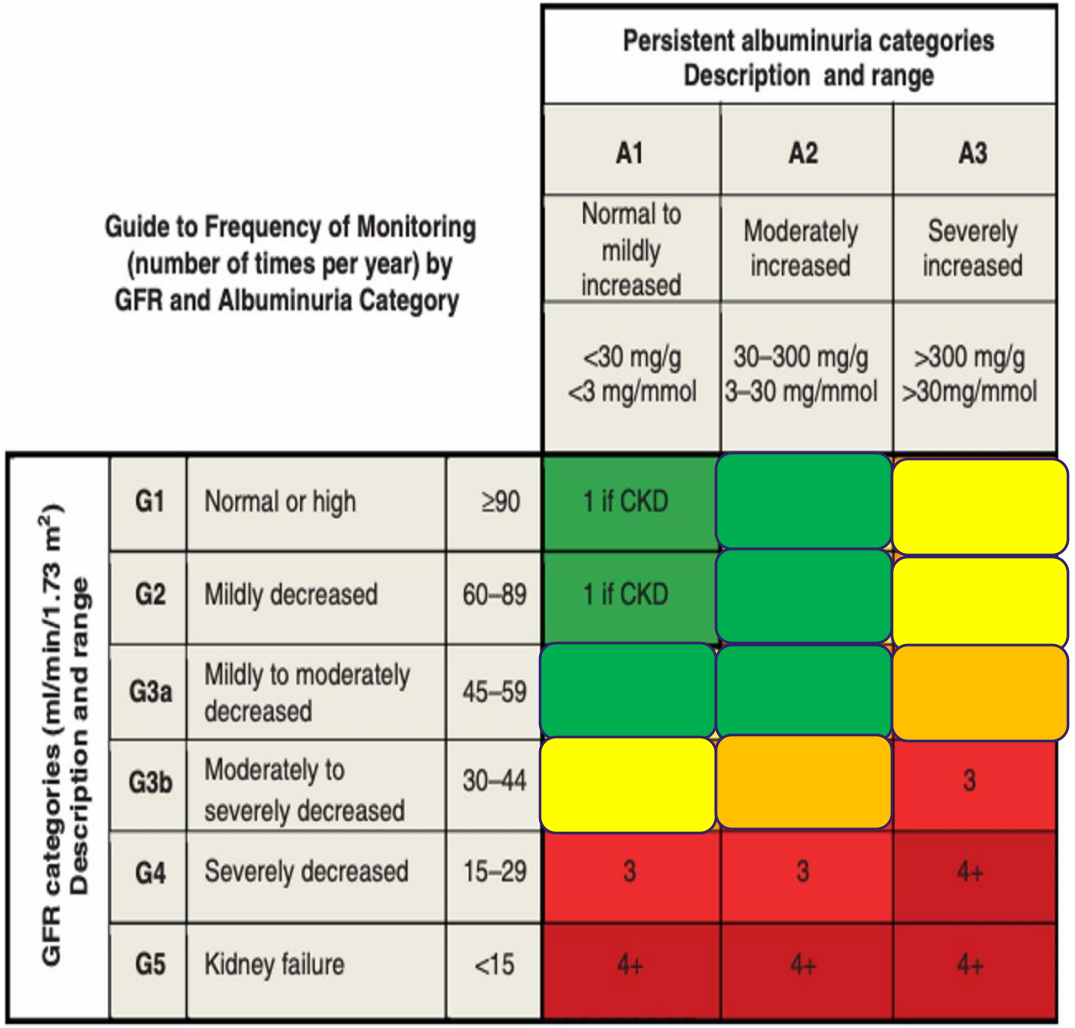
If using Group 2- **CKD2, Microalbuminuria**

Are we coding CKD properly?

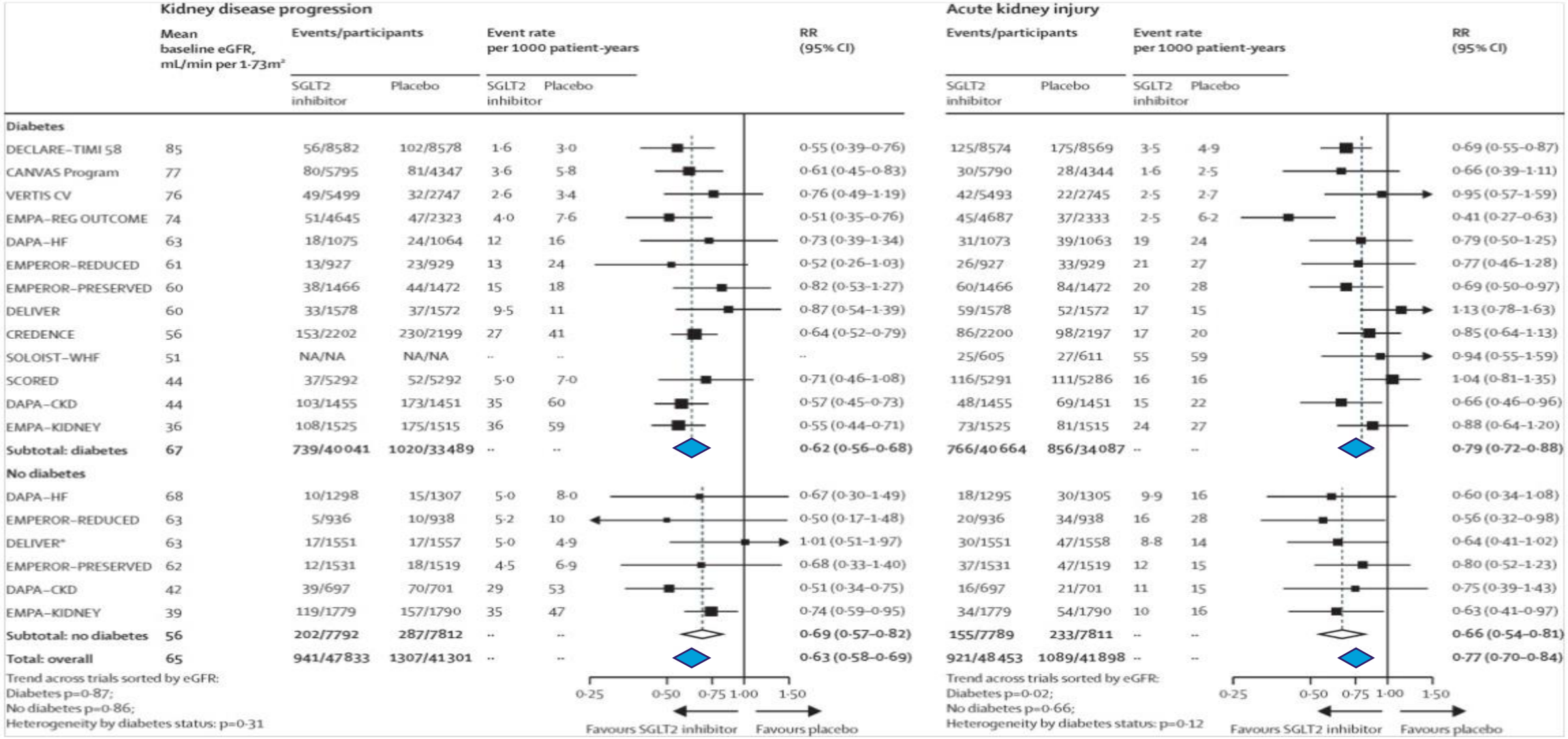
Coding Recommendations

Use Group 1

- Provides the most granularity. Coding is precise and follows the KDIGO guidance and NICE recommendations.
- Requires a single SNOMED code
- Aligns more readily to recommendations around frequency of testing
- Allows for easier tracking of disease progression
- Requires some working knowledge of CKD due to increased granularity
- May require more frequent updates as and when disease progresses
- Some coding is not defined and eligible under QOF business rules e.g. A2



Guide to Frequency of Monitoring (number of times per year) by GFR and Albuminuria Category				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30mg/mmol
GFR categories (ml/min/1.73 m^2) Description and range	G1	Normal or high	≥90	1 if CKD		
	G2	Mildly decreased	60–89	1 if CKD		
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

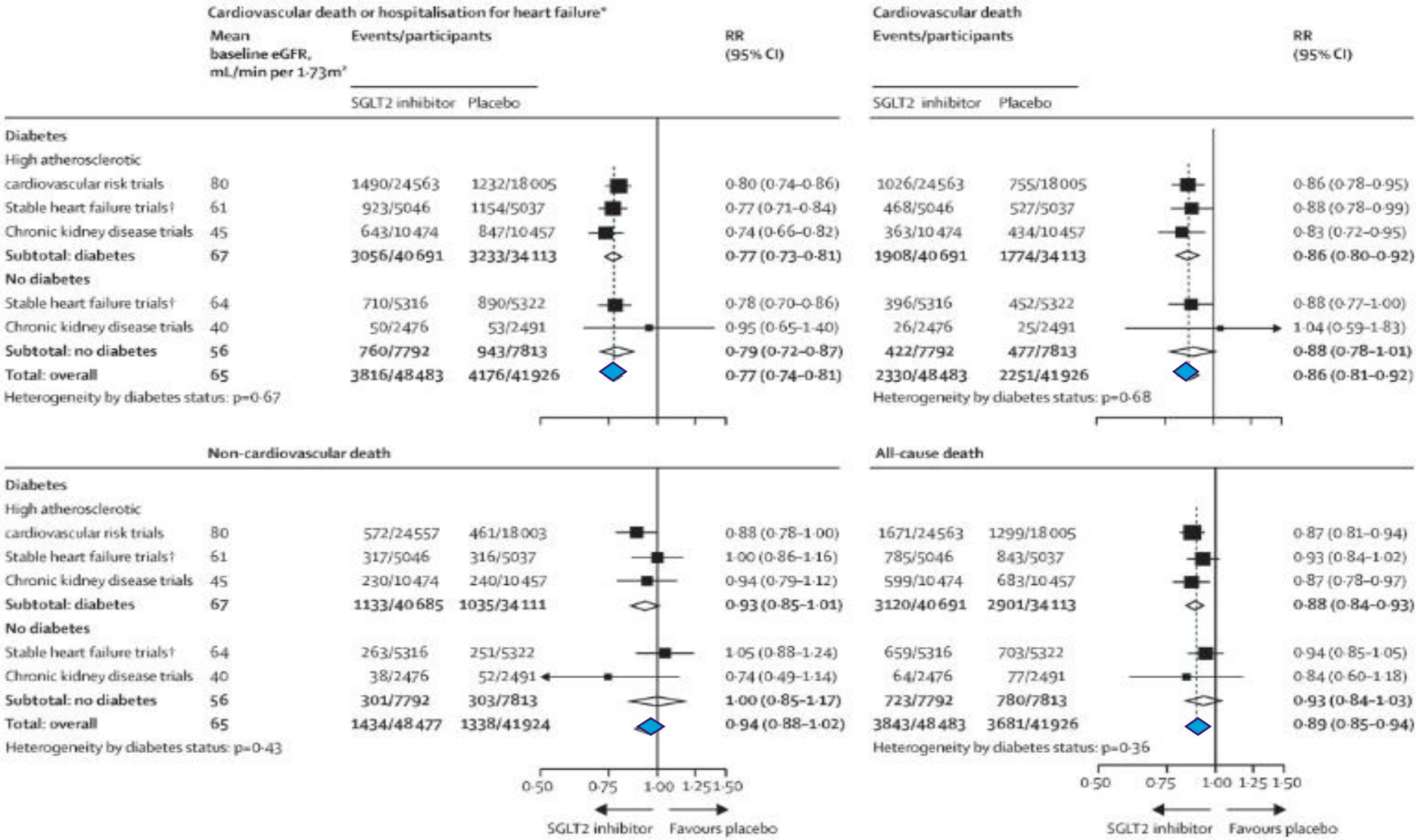


	Mean baseline eGFR, mL/min per 1·73m²	Kidney disease progression: Events/participants SGLT2 inhibitor	Kidney disease progression: Events/participants Placebo	Kidney disease progression: Event rate per 1000 patient-years SGLT2 inhibitor	Kidney disease progression: Event rate per 1000 patient-years Placebo	Kidney disease progression: RR (95% CI)	Acute kidney injury: Events/participants SGLT2 inhibitor	Acute kidney injury: Events/participants Placebo	Acute kidney injury: Event rate per 1000 patient-years SGLT2 inhibitor	Acute kidney injury: Event rate per 1000 patient-years Placebo	Acute kidney injury: RR (95% CI)
Diabetes											
DECLARE–TIMI 58	85	56/8582	102/8578	1·6	3·0	0·55 (0·39–0·76)	125/8574	175/8569	3·5	4·9	0·69 (0·55–0·87)
CANVAS Program	77	80/5795	81/4347	3·6	5·8	0·61 (0·45–0·83)	30/5790	28/4344	1·6	2·5	0·66 (0·39–1·11)
VERTIS CV	76	49/5499	32/2747	2·6	3·4	0·76 (0·49–1·19)	42/5493	22/2745	2·5	2·7	0·95 (0·57–1·59)
EMPA–REG OUTCOME	74	51/4645	47/2323	4·0	7·6	0·51 (0·35–0·76)	45/4687	37/2333	2·5	6·2	0·41 (0·27–0·63)
DAPA–HF	63	18/1075	24/1064	12	16	0·73 (0·39–1·34)	31/1073	39/1063	19	24	0·79 (0·50–1·25)
EMPEROR–REDUCED	61	13/927	23/929	13	24	0·52 (0·26–1·03)	26/927	33/929	21	27	0·77 (0·46–1·28)
EMPEROR–PRESERVED	60	38/1466	44/1472	15	18	0·82 (0·53–1·27)	60/1466	84/1472	20	28	0·69 (0·50–0·97)
DELIVER	60	33/1578	37/1572	9·5	11	0·87 (0·54–1·39)	59/1578	52/1572	17	15	1·13 (0·78–1·63)
CREDENCE	56	153/2202	230/2199	27	41	0·64 (0·52–0·79)	86/2200	98/2197	17	20	0·85 (0·64–1·13)
SOLOIST–WHF	51	NA/NA	NA/NA	..	..	..	25/605	27/611	55	59	0·94 (0·55–1·59)
SCORED	44	37/5292	52/5292	5·0	7·0	0·71 (0·46–1·08)	116/5291	111/5286	16	16	1·04 (0·81–1·35)
DAPA–CKD	44	103/1455	173/1451	35	60	0·57 (0·45–0·73)	48/1455	69/1451	15	22	0·66 (0·46–0·96)
EMPA–KIDNEY	36	108/1525	175/1515	36	59	0·55 (0·44–0·71)	73/1525	81/1515	24	27	0·88 (0·64–1·20)
Subtotal: diabetes	**67**	**739/40041**	**1020/33489**	..	..	**0·62 (0·56–0·68)**	**766/40664**	**856/34087**	..	..	**0·79 (0·72–0·88)**
No diabetes											
DAPA–HF	68	10/1298	15/1307	5·0	8·0	0·67 (0·30–1·49)	18/1295	30/1305	9·9	16	0·60 (0·34–1·08)
EMPEROR–REDUCED	63	5/936	10/938	5·2	10	0·50 (0·17–1·48)	20/936	34/938	16	28	0·56 (0·32–0·98)
DELIVER*	63	17/1551	17/1557	5·0	4·9	1·01 (0·51–1·97)	30/1551	47/1558	8·8	14	0·64 (0·41–1·02)
EMPEROR–PRESERVED	62	12/1531	18/1519	4·5	6·9	0·68 (0·33–1·40)	37/1531	47/1519	12	15	0·80 (0·52–1·23)
DAPA–CKD	42	39/697	70/701	29	53	0·51 (0·34–0·75)	16/697	21/701	11	15	0·75 (0·39–1·43)
EMPA–KIDNEY	39	119/1779	157/1790	35	47	0·74 (0·59–0·95)	34/1779	54/1790	10	16	0·63 (0·41–0·97)
Subtotal: no diabetes	**56**	**202/7792**	**287/7812**	..	..	**0·69 (0·57–0·82)**	**155/7789**	**233/7811**	..	..	**0·66 (0·54–0·81)**
Total: overall	**65**	**941/47833**	**1307/41301**	..	..	**0·63 (0·58–0·69)**	**921/48453**	**1089/41898**	..	..	**0·77 (0·70–0·84)**

Trend across trials sorted by eGFR:
Diabetes p=0·87;
No diabetes p=0·86;
Heterogeneity by diabetes status: p=0·31

Trend across trials sorted by eGFR:
Diabetes p=0·02;
No diabetes p=0·66;
Heterogeneity by diabetes status: p=0·12

Baigent C, Emberson JR, Haynes R et a; Nuffield Department of Population Health Renal Studies Group; SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium (2022) Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: Collaborative meta-analysis of large placebo-controlled trials. *Lancet* **400**: 1788–801



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Prescribing guidance

	Progression of CKD	ASCVD	Heart failure	Glucose-lowering efficacy	Hypoglycemia risk	Weight effects	Cost
Metformin	Neutral	Potential benefit	Potential benefit	High	Low	Neutral	Low
SGLT2 inhibitors	Benefit[a]	Benefit[c]	Benefit	Intermediate	Low	Loss	High
GLP-1 receptor agonists	Benefit[b]	Benefit[c]	Potential benefit	High	Low	Loss	High
DPP-4 inhibitors	Neutral	Neutral	Potential risk[c] (saxagliptin)	Intermediate	Low	Neutral	High
Insulin	Neutral	Neutral	Neutral	Highest	High	Gain	High (analogs) Low (human)
Sulfonylureas	Neutral	Neutral	Neutral	High	High	Gain	Low
Thiazolidinediones	Neutral	Potential benefit (pioglitazone)	Increased risk	High	Low	Gain	Low
α-Glucosidase inhibitors	Neutral	Neutral	Neutral	Intermediate	Low	Neutral	Low

Neutral

Potential benefit or intermediate glucose-lowering efficacy

Benefit (organ protection, high efficacy, low hypoglycemia risk, weight loss, or low cost)

Potential risk or high cost to patient

Increased risk for adverse effects

	Stage 3b (eGFR 30–44 mL/min/1.73 m²)	Stage 4 (eGFR 15–29 mL/min/1.73 m²)	Stage 5 (eGFR <15 mL/min/1.73 m²)
Metformin	Reduce dose to 1000 mg/day	Contraindicated	
Insulin	Initiate and titrate conservatively to avoid hypoglycemia		
SGLT2 inhibitors*			
Canagliflozin	Maximum 100 mg daily	Initiation not recommended; may continue 100 mg daily if tolerated for kidney and CV benefit until dialysis	
Dapagliflozin	10 mg daily†	Initiation not recommended with eGFR <25 mL/min/1.73 m²; may continue if tolerated for kidney and CV benefit until dialysis	
Empagliflozin	10 mg daily‡	Initiation not recommended with eGFR <20 mL/min/1.73 m²; may continue if tolerated for kidney and CV benefit until dialysis	
Ertugliflozin	Use not recommended with eGFR <45 mL/min/1.73 m²		
GLP-1 receptor agonists§			
Exenatide	Caution initiating or increasing dose; avoid once-weekly formulation	Use not recommended	
Dulaglutide	No dose adjustment required		
Liraglutide	No dose adjustment required		
Lixisenatide	No dose adjustment required		Use not recommended
Semaglutide	No dose adjustment required		
DPP-4 inhibitors			
Alogliptin	Maximum 12.5 mg daily	Maximum 6.25 mg daily	
Linagliptin	No dose adjustment required		
Saxagliptin	Maximum 2.5 mg daily		
Sitagliptin	Maximum 50 mg daily	Maximum 25 mg once daily	
Sulfonylureas (2nd generation)			
Glimepiride	Initiate conservatively at 1 mg daily and titrate slowly to avoid hypoglycemia		
Glipizide	Initiate conservatively (e.g., 2.5 mg once daily) and titrate slowly to avoid hypoglycemia		
Glyburide	Use not recommended		
Thiazolidinediones			
Pioglitazone	No dose adjustment required		
α-Glucosidase inhibitors			
Acarbose	No dose adjustment required	Use not recommended	
Miglitol	No dose adjustment required	Use not recommended	

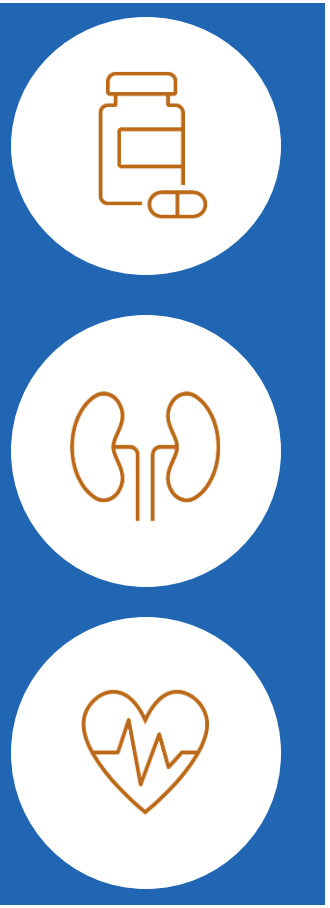
Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO)
Diabetes Care 2022;45(12):3075–3090

“3 within 3”

3 key actions within 3 months to save lives

In adults with Type 2 diabetes and CKD

(uACR > 3mg/mmol)



ACTION 1 (Month 1)
Maximum intensity RAS/ RAAS blockade

First, ensure the patient is on a statin.
Start ACE-inhibitor or ARB and titrate to maximum tolerated (*NICE, NG203*) licensed dose within one month

ACTION 2 (Month 2)
Initiate SGLT-2 inhibitor according to license

Consider/ counsel on risks of diabetic ketoacidosis (which may be euglycaemic), sick day rules, risk of UTI/fungal infections. Consider adjusting sulfonylureas/insulin where eGFR >45ml/min and HbA1c < 58mmol/mol to mitigate risk of hypoglycaemia.

ACTION 3 (Month 3)
Initiate further blood pressure agent to target 140/90mmHg unless uACR >70mg/mmol (then 120-129/80mmHg)

If BP remains above target initiate 2nd line BP agents as per NICE guidance (*NG203/ NG136)*

London Kidney Network, 2021

Thanks for listening

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