## **Optimising Multifactorial Care**

Type 2 Diabetes and Chronic Kidney Disease

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### **Disclosures**

Speaker honoraria from the following:

• NAPP, Sanofi, Novo Nordisk, Eli Lily, Merck, Astra Zeneca, Takeda

Educational support from the following:

• Novo Nordisk, Sanofi, Boehringer-ingelheim



## Evidence for multifactorial care



## What do multifactorial and optimisation mean?

#### **Multifactorial**

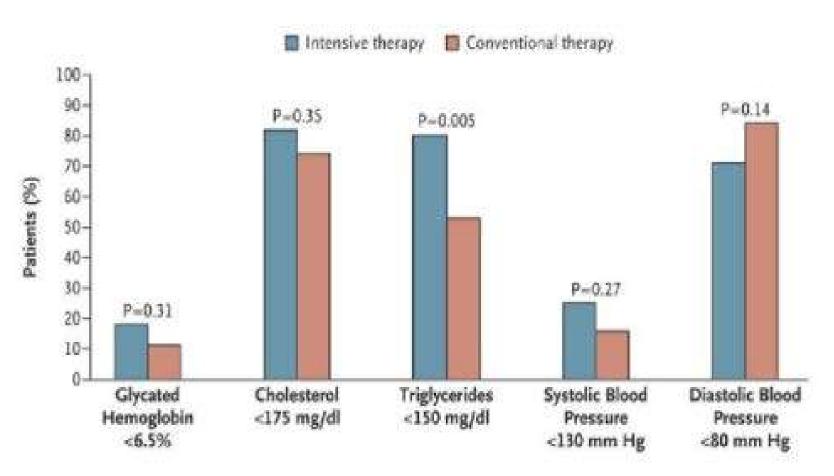
- An individualised multifactorial intervention is an intervention with multiple components that aims to address the risk factors that are identified based on an assessment of risk.
- Interventions can either be individualised or where the same component interventions are provided to all people

### **Optimisation**

Medicines optimisation is defined as 'a person-centred approach to safe and
effective medicines use, to ensure people obtain the best possible
outcomes from their medicines. Medicines optimisation applies to people
who may or may not take their medicines effectively. Shared
decision-making is an essential part of evidence-based medicine, seeking to
use the best available evidence to guide decisions about the care of the
individual patient, taking into account their needs, preferences and values

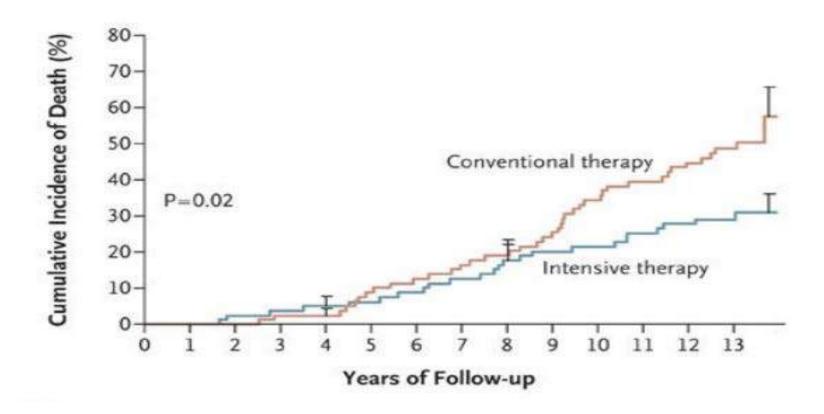


## Steno-2 Study-Treatment goals for the intensive-therapy group





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

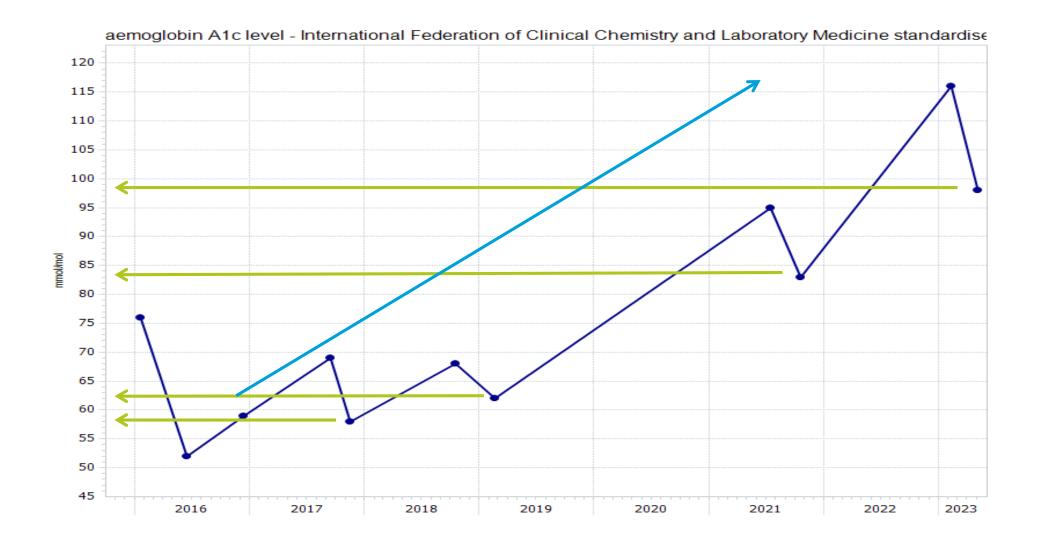




## Glucose control



## A (fairly) typical glycaemic pattern

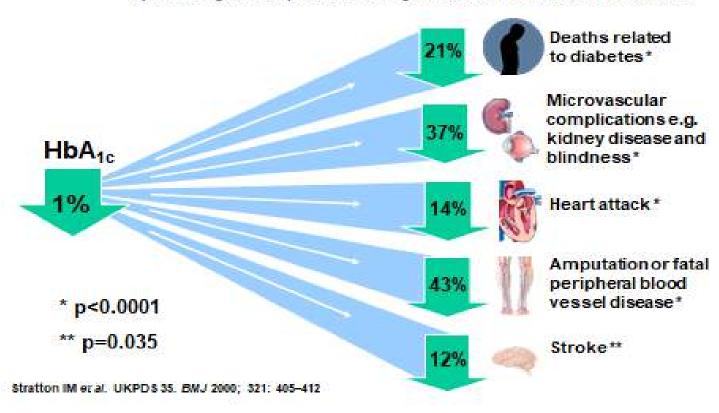




## Why bother with HbA1c?

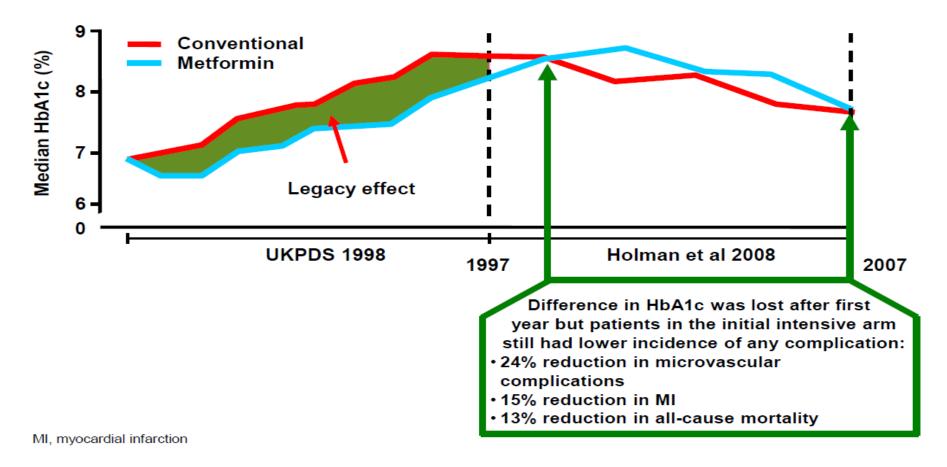
## UKPDS: Tight glycaemic control reduces complications

Epidemiological extrapolation showing benefit of a 1% reduction in mean HbA<sub>1c</sub>





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

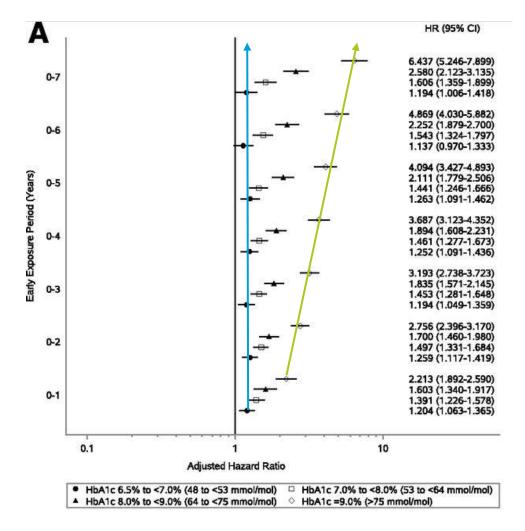


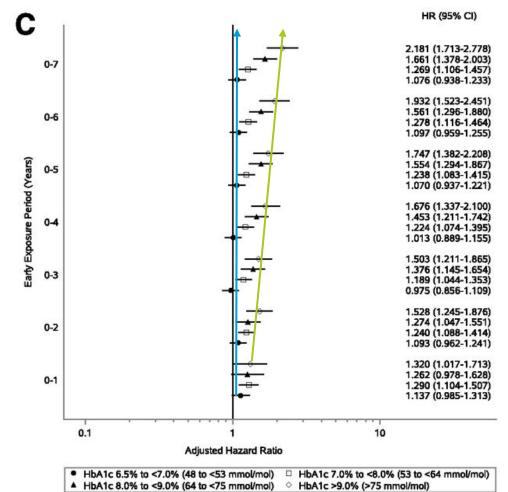
Diabetes Trials Unit. UKPDS Post Trial Monitoring. UKPDS 80 Slide Set. Available at: http://www.dtu.ox.ac.uk/index.php?maindoc=/ukpds/. Accessed 12 September, 2008;

Adapted from Holman RR, et al. N Engl J Med. 2008; 359: 1577–1589; UKPDS 33. Lancet. 1998; 352: 837–853.



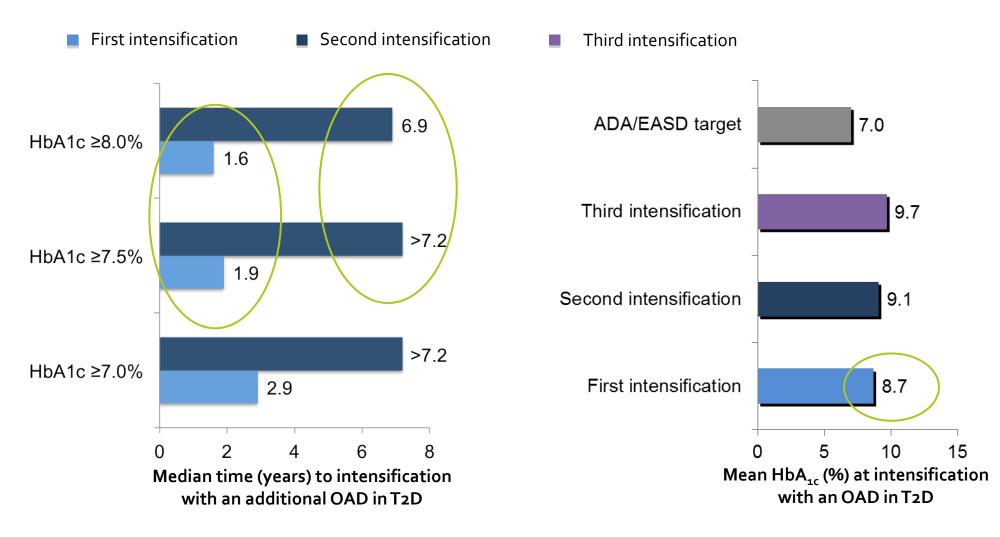
## Impact of early glycaemic control on future complications







## Therapeutic inertia contributes to poor glycaemic control



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

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

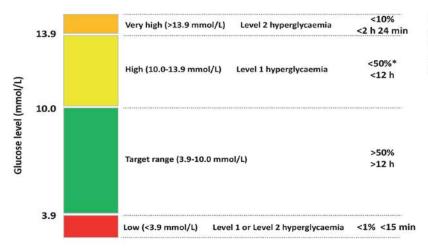


## Different ways to measure blood glucose

- Intermittently scanned (isCGM)
- Real time (rtCGM)
- Measures glucose in interstitial fluid
- Addresses glycaemic variability
- Improvements in Time in Range (TIR) reduce risks of microalbuminuria and retinopathy
- On average a TIR of 70% is associated with a HbA1c of 57mM/M
- NICE NG28. Offer isCGM to adults with type 2 diabetes on multiple daily insulin injections (>1 injection)
  - Recurrent or severe hypoglycaemia (Frequent hypos affecting QoL or requiring 3<sup>rd</sup> party assistance)
  - Impaired hypo awareness
  - Can't self monitor for whatever reason
  - SMBG > 8x/day



## Time in Range: targets for older people and those at high-risk of hypoglycaemia



<sup>\*</sup> Readings >13.9 mmol/L are also included in the <50% target

#### Thinking about individualised targets

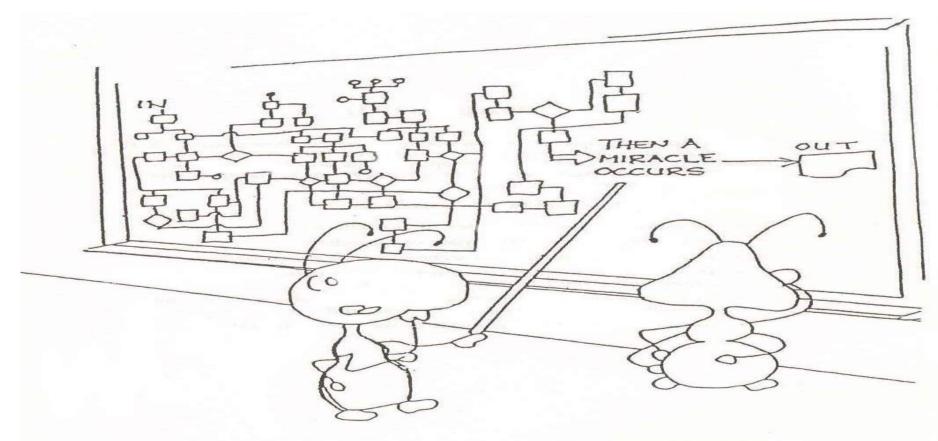
Emphasise the need to prioritise hypoglycaemia avoidance, reducing the 5TBR <3.9 mmol/L

Remommendation is to keep %TBR <3.9 mmol/L to <1% or 15 min per day





## **Guidelines**



"Good work ... but I think we need just a little more detail right here"



### NICE NG28 and Type 2 diabetes

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

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

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...)

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?

• When should I review things?

• What are we trying to achieve?

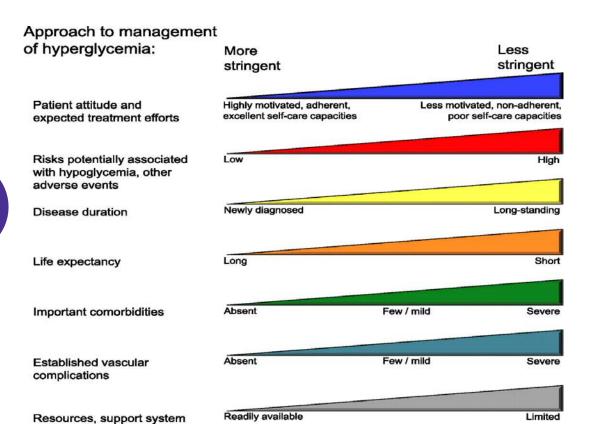
• When do I increase treatment and with what?

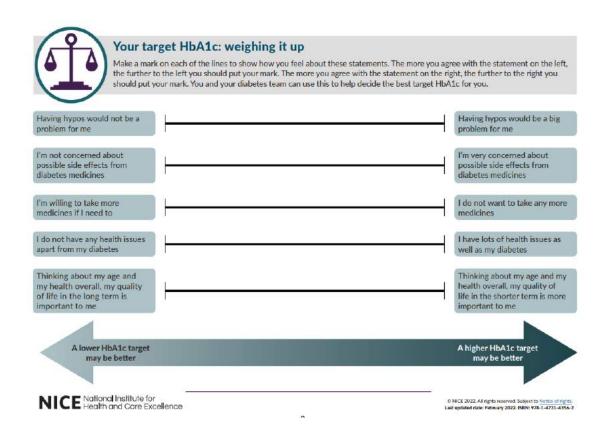
Anything else relevant to know?

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



## Individualised treatment







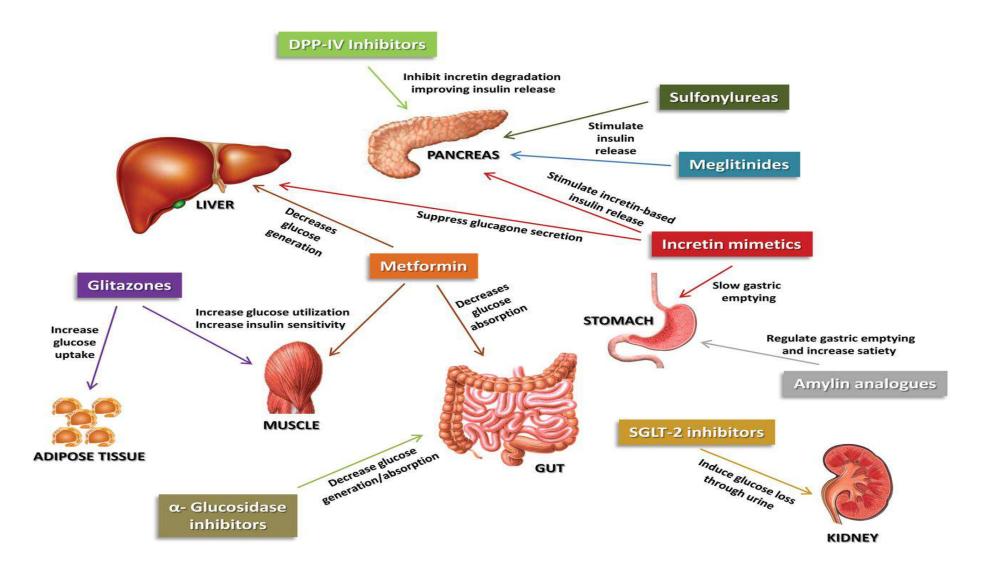
## Case study

• 51 year old female. Caribbean Weight loss would be BMI 32.4 and renal function ok. Central beneficial obesity On maximum dose metformin Dietary changes can be Works as cleaner. One large meal a day made. Regular meals No complications. Diabetes since 2019 She is young with no Does not monitor blood glucose complications...we need to be fairly aggressive still Only used oral medications. Keen to avoid Why? insulin Health Could be a problem if we use insulin. Will she start doing? beliefs? HbA1c was 91mM/M on referral last month → Current HbA1c 79mM/M What changed? The power of referral...

She is young



## What do I pick to optimise glycaemic control?





## 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 3omL/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**

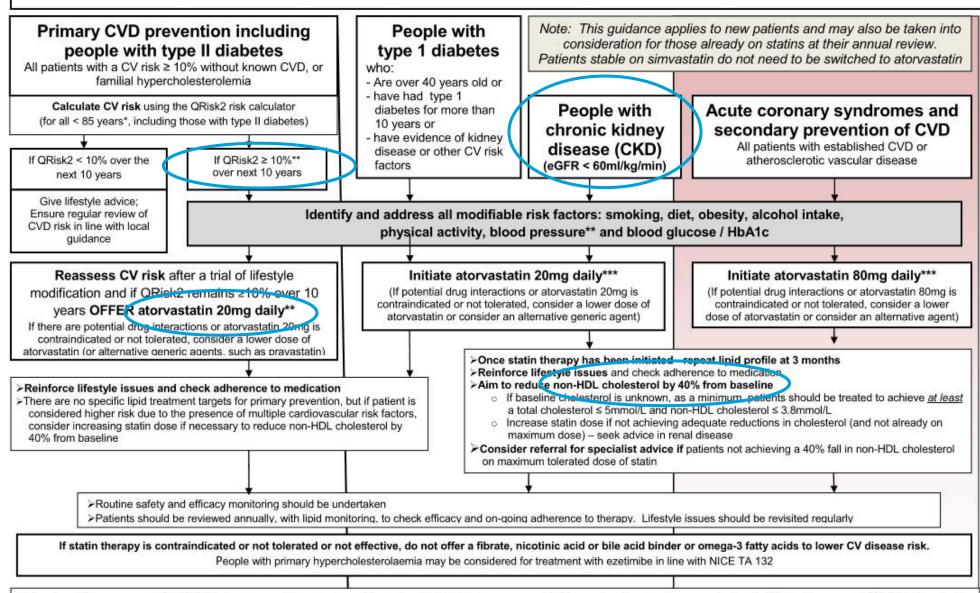
- Not achieving target
- Avoid collusion. Plan B effect

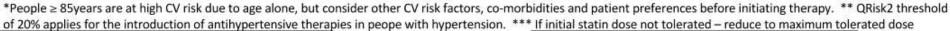


# Lipids



### South London Algorithm for Lipid Management for the Primary and Secondary Prevention of CVD WHS





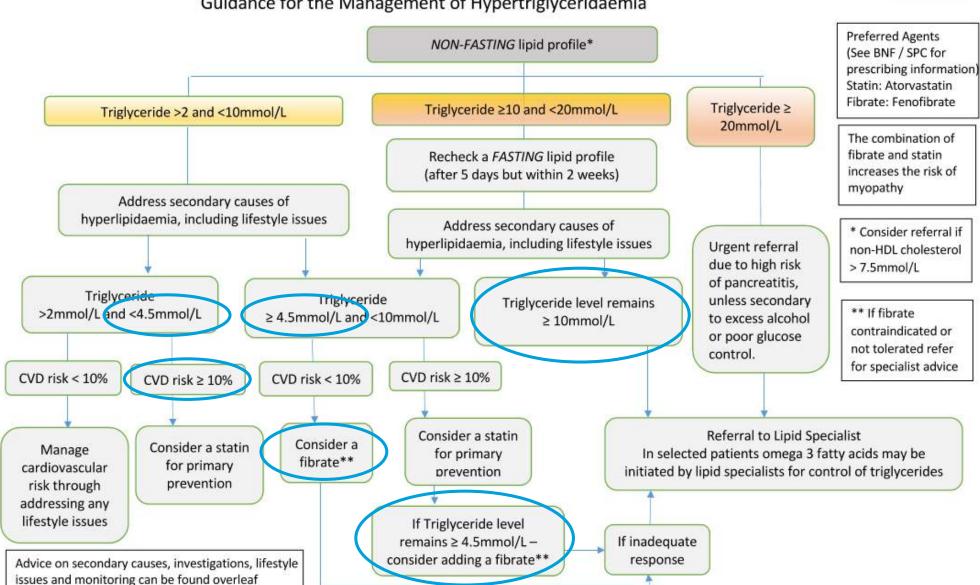


## Lipid management

- 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
   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.



#### Guidance for the Management of Hypertriglyceridaemia





## **Blood Pressure**



## Diagnosis, targets and treatment

- Diagnose hypertension if clinic BP>140/90 and ABPM >135/85
- Aim for a target of <140/90 (ABPM/home 135/85)
  - If age over 80, aim for <150/90 (ABPM/home 145/85)</li>
- 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)
- ACEi/ARB is first line
- CCB and/or thiazide like diuretic
- Spironolactone
- Dietary changes especially salt (<6g/day = 1 teaspoon)</li>



## **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

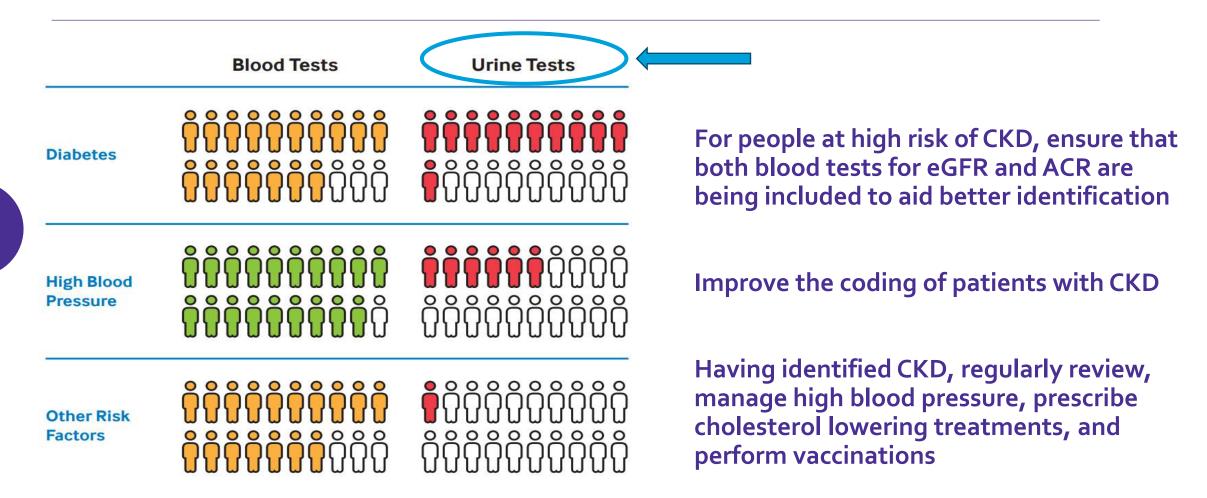
Which condition?	Which cohort within the condition?	NICE Clinic BP Target	QOF BP Targets <sup>1</sup>	2021/2022
		Use clinical judgment in frailty/multi-morbidity     Corresponding targets for ABPM/HBPM are 5mmHg lower than for clinic BPs		
Hypertension, including Type 2 Diabetes (but with no CKD)	Age <80yrs	≤140/90mmHg	≤140/90mmHg  *Note QOF Target for Hypertension in T2DM is ≤140/80mmHg	*Note QOF Target for
	Age ≥80yrs	≤150/90mmHg		T2DM is
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		



# Chronic Kidney Disease



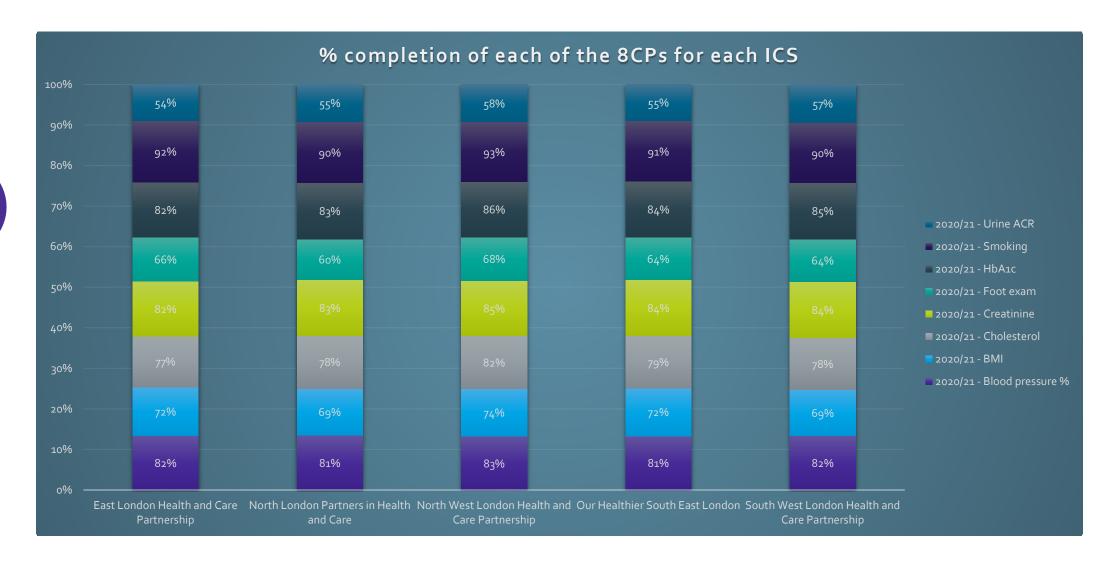
## What are the problems?



**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%** 



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



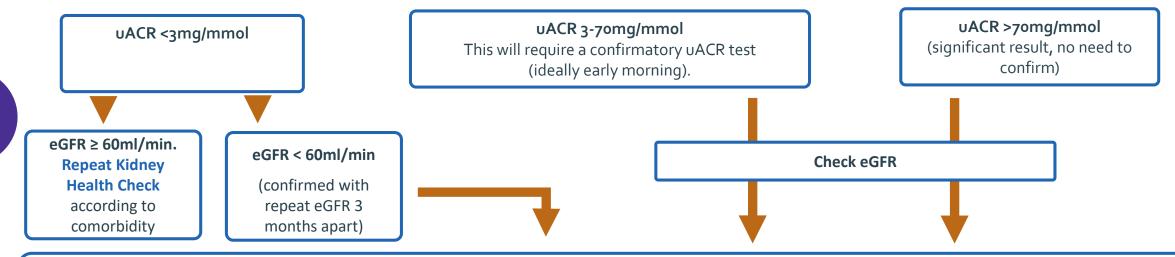


# The Kidney Health Check for Adults Living with Diabetes or Hypertension: How to identify Chronic Kidney Disease early! LKN CKD Early Identification Pathway

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**

ACR value (mg/mmol)	Possible Code Group 1	Possible Code Group 2
0-3	A1	No code
3-30	A <sub>2</sub>	Microalbuminuria
Greater than 30	A <sub>3</sub>	Microalbuminuria/Proteinuria

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	G <sub>3</sub> a	CKD stage 3
30-44	G <sub>3</sub> b	CKD stage 3
15-29	G <sub>4</sub>	CKD stage 4
Less than 15	G5	CKD stage 5



## **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
<mark>60-90</mark>	<mark>G2</mark>	CKD stage 2
45-59	G <sub>3</sub> a	CKD stage 3
30-44	G <sub>3</sub> b	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
<mark>3-30</mark>	A2	Microalbuminuria
Greater than 30	A <sub>3</sub>	Albuminuria

Using the coding tables above, possible coding would be:

If using Group 1- CKD G2A2

If using Group 2- CKD2, Microalbuminuria



## **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** 

Normal or high

Mildly decreased

decreased

Moderately to

Kidney failure

Mildly to moderately

severely decreased

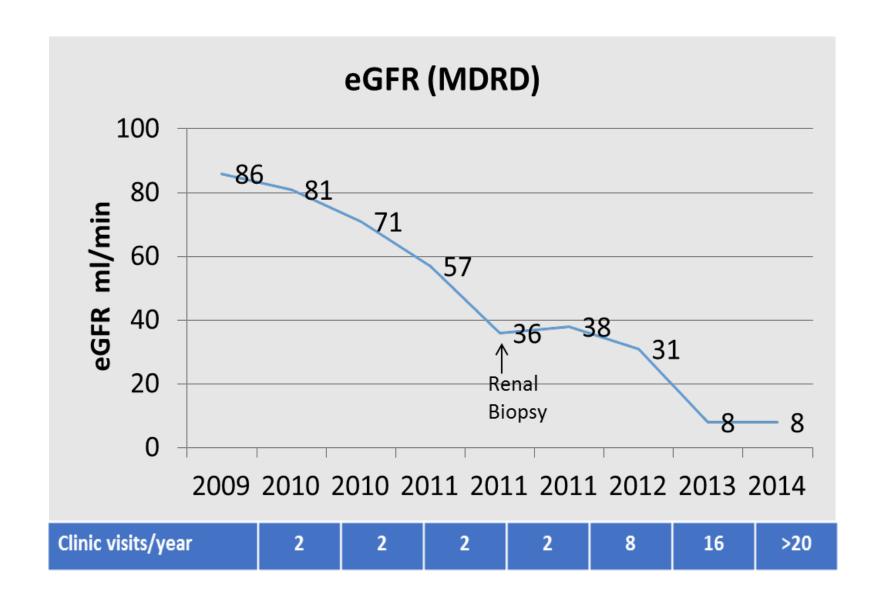
Severely decreased

<15

categories (ml/min/1.73 Description and range

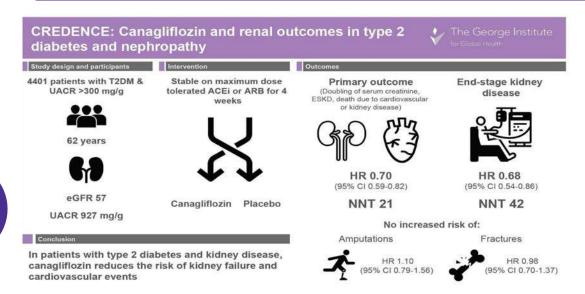
	Persistent albuminuria categories Description and range			
	A1	A2	A3	
ng /	Normal to mildly increased	Moderately increased	Severely increased	
	<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30mg/mmol	
≥90	1 if CKD			
60–89	1 if CKD			
45–59				
30–44			3	
15–29	3	3	4+	
<15	4+	4+	4+	

## **Avoid Preventable CKD Progression**





## **Changing guidelines**



## Could dapagliflozin improve kidney and cardiovascular outcomes in patients with CKD?





**Conclusion:** Among patients with chronic kidney disease, the risk of any composite kidney or cardiovascular outcomes or death was significantly lower with dapagliflozin than with placebo.

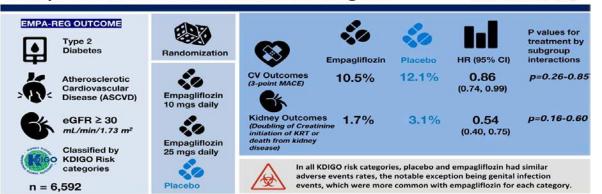
Reference:Heerspink HJL et al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020 Sep 24. DOI: 10.1056/NEJMoa2024816.





### Effects of empagliflozin versus placebo on cardiovascular and kidney outcomes were across the KDIGO risk categories

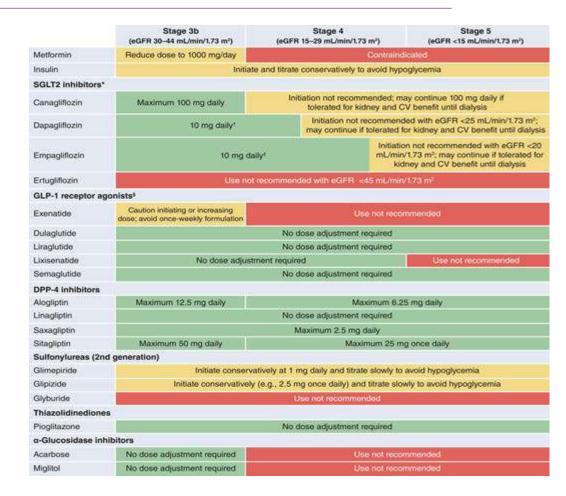






## Prescribing guidance

	Progression of CKD	ASCVD	Heart failure	lowering efficacy	Hypoglycemia risk	Weight effects	Cost
Metformin	Neutral	Potential benefit	Potential benefit	High	Low	Neutral	Low
GLT2 inhibitors	Benefitt	Benefit*	Benefit	Intermediate	Low	Loss	High
GLP-1 receptor igonists	Benefit <sup>b</sup>	Benefit*	Potential benefit	High	Low	Loss	High
OPP-4 inhibitors	Neutral	Neutral	Potential risk* (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
x-Glucosidase nhibitors	Neutral	Neutral	Neutral	Intermediate	Low	Neutral	Low
Neutral					Potentia	al risk or high co	ost to patient
Potentia	al benefit or interme	ediate glucose-lowe	ring efficacy		Increas	ed risk for adve	rse effects



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 2<sup>nd</sup> line BP agents as per NICE guidance (NG203/NG136)

### "3 within 3"

### 3 key actions within 3 months to save lives

## In adults with albuminuria, without Type 2 diabetes

 $(uACR \ge 22.6mg/mmol and eGFR 25 - 75ml/minute/1.73m^2)$ 



### 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 licensed dose (*NICE, NG203*) within one month



### ACTION 2 (Month 2)

Initiate SGLT-2 inhibitor according to license

Counsel patient on sick day rules, and the risk of UTI/fungal infection.



### **ACTION 3 (Month 3)**

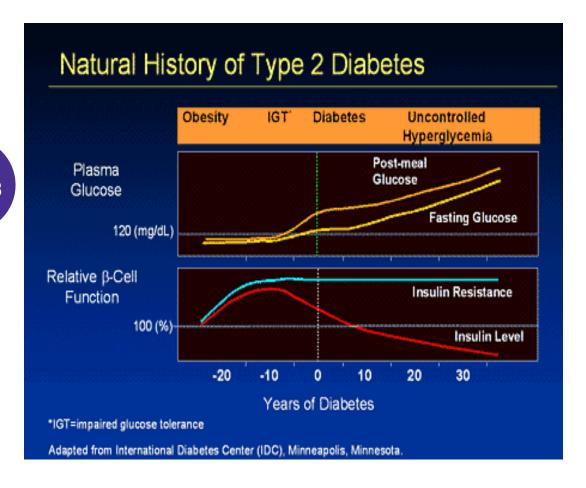
Initiate further blood pressure agent to target <140/90mmHg unless uACR >70mg/mmol (then <130/80mmHg)

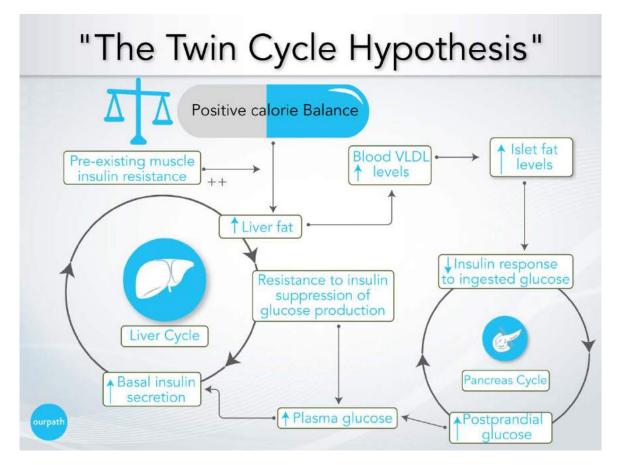
If BP remains above target initiate 2<sup>nd</sup> line BP agents as per NICE guidance (*NG203/NG136*)

# Weight Management and Mental Health support



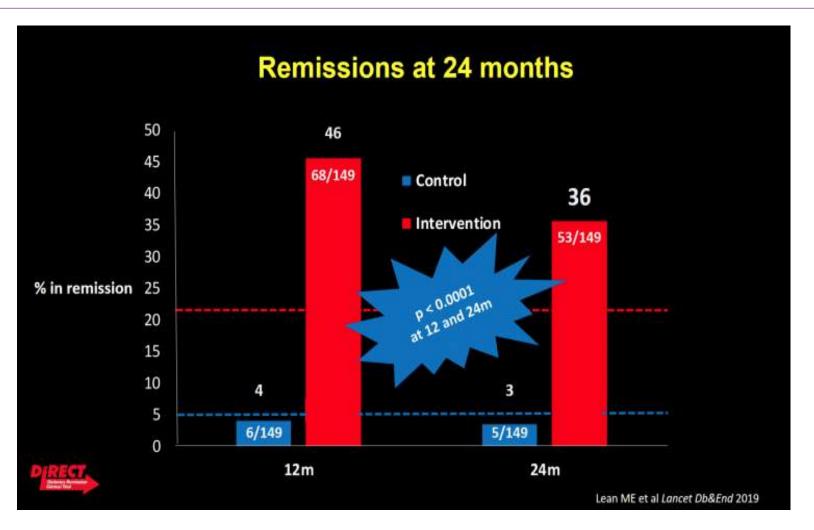
## Pathophysiology







## **DiRECT Study**





## 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



## It's not just about tablets...



- 14 tablets a day
- 98 tablets a week
- 392 tablets a month
- 5110 tablets a year
- For what?????



## **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
  - 3/4 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** 



## Three question approach to diabetes distress

Ask

Acknowledge

Normalise

Transment toront	England (per cent)						
Treatment target	2015-16	2016-17	2017-18	2018-19	2019-20		
HbA1c ≤ 58 mmol/mol	65.9	67.0	65.8	66.5	65.6		
Blood pressure ≤ 140/80	73.7	74.4	73.8	74.5	73.6		
Statins for Primary Prevention of CVD	-	-	72.2	70.9	72.3		
Statins for Secondary Prevention of CVD	_	-	86.7	85.8	86.4		
Statins for Combined Prevention of CVD	-	-	76.1	74.9	76.1		
Meeting all three treatment targets NEW*	-	-	40.2	40.5	40.1		



# Communication Attendance at structured education

"To improve uptake at structured education we need to consider how health professionals in primary care communicate with their patients on the subject of structured diabetes education.... Health-care professional attitude to courses is key...."

## **DAFNE**

### **Non-attenders**

- Male
- BME
- Older age
- Social deprivation

### **Attenders**

- Positive HCP message
- Female
- Educational attainment
- HbA1c

## **DESMOND**

### **Non-attenders**

- Lack of information/perceived benefit of the programme
- Unmet personal preferences
- Shame and stigma of diabetes



# Thanks for listening

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healthinnovationnetwork.com



