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Personalised Care for people with Type 2 Diabetes

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Collaborative Quality Improvement in General Practice Clusters

This paper is in a series that relates to areas of quality and safety on which general practice clusters could usefully focus improvement activity. Each paper summarises research, guidelines and other evidence about areas of care which can be improved, and improvement methods and interventions.

Personalised Care for people with Type 2 Diabetes

Type 2 diabetes (T2D) is a common long-term condition and is characterised by hyperglycaemia, insulin resistance and a relative insulin deficiency. There are many risk factors for T2D including obesity, sedentary lifestyle, certain ethnicities (e.g. South Asian), a history of gestational diabetes, a family history of T2D, polycystic ovarian syndrome and metabolic syndrome. T2D can lead to both microvascular disease (e.g. diabetic retinopathy) and macrovascular disease (e.g. ischaemic heart disease) if not managed effectively.

In Scotland, the management of T2D is guided by the Scottish Intercollegiate Guideline Network (SIGN) diabetes guidelines^{1,2} (SIGN 116 & 154) which both give key clinical recommendations on lifestyle interventions, optimal targets for glycaemic control, management of diabetes complications and the pharmacological management of T2D.

As with most long-term health problems, much of the responsibility for good care depends on patients and their family. Scotland's MyDiabetesMyWay and Diabetes UK provide useful resources to help them. Primary care teams are now the main clinical custodians of uncomplicated T2D care. Effective diabetes management can substantially improve both the quality and quantity of life of those living with diabetes in Scotland. The burden on healthcare systems (particularly from the complications of diabetes) could also be significantly reduced by practices and clusters who organise care effectively.

The Problem

The Scottish Diabetes Survey 2017³ revealed that 4.8% of the Scottish population (263,271 people) have type 2 diabetes (T2D).

87.3% of those with T2D were overweight or obese. 16.6% of those with T2D were current smokers. 91.8% of those with T2D had an HbA1c recorded in the previous 15 months and 58.7% of these individuals had a result of less than 58mmol/mol. Importantly, and relevant to new key clinical recommendations in SIGN 154, 9.7% of those with T2D had previously had a myocardial infarction (MI).

https://www.mydiabetesmyway.scot.nhs.uk/ https://www.diabetes.org.uk/

"State of the Nation 2015: The Age of Diabetes" published by Diabetes Scotland tragically informs us that around 2000 people with diabetes die early every year, predominantly from vascular complications. Since 2008, there has been a 20% increase in those individuals recorded as having a MI, and a 39% increase in those undergoing coronary revascularisation. Furthermore, there has been a 19% increase in those individuals recorded as suffering a stroke, and an 82% increase in those with established end-stage renal disease (ESRD).

Overall, cardiovascular disease (CVD) remains the leading cause of death in those with T2D; the risk of CVD is around double in those with T2D compared to those without CVD⁵.

Moreover, even when the optimal treatment of risk factors has been achieved, there is still significant residual CV risk in those with diabetes.

Individualisation of Care

Hyperglycaemia is an independent risk factor for both microvascular and microvascular CVD. However, for many years, the management of T2D has been very glucose-centric focusing on the attainment of stringent HbA1c targets when in fact one size does not fit all. HbA1c targets should be individualised to ensure that the benefits of treatment continue to outweigh any harms such as hypoglycaemia and weight gain.

Hyperglycaemia is important, but it is a much weaker risk factor for CVD than smoking, physical inactivity, cholesterol or blood pressure. Lowering glucose is important but the added benefit of an HbA1c of 53mmol/ mol versus 64 mmol/mol reduces with age and life expectancy.__ Good glucose control does offer protection against microvascular disease, but smoking cessation, appropriate exercise, blood pressure and lipid management can be more effective clinical interventions especially in older frail individuals (see Figure 1).



Interventional relationships between cholesterol, blood pressure and $\mathsf{HbA}_{\mathsf{lc}}$ with CVD events



For each variable, data shown are for a change corresponding to the mean change of the variable in intervention studies.

BP=blood pressure; CVD=cardiovascular disease; NNT=number needed to treat. Adapted from Yudkin JS et al (2010) Diabetologia 53: 2079–85

Figure 1

A joint position statement from the European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA)⁷ concluded that comprehensive CV risk reduction should remain the major focus of diabetes management rather than this glucose -centric approach that has been followed for many years.

What Evidence Supports the Management of Type 2 Diabetes in Primary Care Guidelines?

The Scottish Intercollegiate Guidelines Network (SIGN) Diabetes Guidelines 116 & 154^{1,2}

SIGN 116: Management of Diabetes was originally published during 2010; since then important new clinical trial data has been published focusing on CV outcomes of diabetes drugs, rather than simply their glucose-lowering effects.

SIGN 154 specifically addresses the pharmacological treatment of glucose-lowering in those with T2D and discusses the risks and benefits of the main classes of oral and injectable glucose-lowering agents including insulins.

SIGN 154 also offers an updated algorithm (see Figure 2) to guide the choice of therapies after metformin. Intensification of therapy is recommended after 3-6 months and should be guided by the patient profile. Drugs should be continued at each stage if *either* <u>individualised</u> HbA1c target is achieved *or* HbA1c falls >5.5mmol/mol. Note the algorithm does not apply to severe renal or liver impairment and smarter decision support tools are being developed.

SIGN 154 offers two key new clinical recommendations which encompass seminal new outcome trial data showing significant reductions in CV events:

- In individuals with T2D and established cardiovascular disease, SGLT2 inhibitors with proven cardiovascular benefit (currently empagliflozin and canagliflozin) should be considered
- For individuals with T2D and established cardiovascular disease, GLP-1 receptor agonist therapies with proven cardiovascular benefit (currently liraglutide) should be considered

Individualised HbA1c Targets

SIGN 154 reiterates that an HbA1c target of 53mmol/mol (7.0%) in those with T2D is reasonable to reduce the risk of microvascular and macrovascular complications. A target of 48mmol/mol (6.5%) may be appropriate at diagnosis, however HbA1c targets should be <u>individualised</u> to ensure that the benefits of treatment outweigh any harms, particularly the risk of hypoglycaemia.



Figure 2

1st LINE	SET GLYCAEMIC TARGET: HbA1c <7% (53 mmol/mol) OR INDIVIDUALISED AS AGREED								
IN ADDITION to lifestyle measures	USUAL APPROACH		ALTERNATIVE APPROACH: if osmotic symptoms or intolerant of metformin						
	METFORMIN*	_		SULPHON	IYLUREA*	The following are also accepted by the SMC for first-line use where metformin and subhanylureas are not talerated:			
EFFICACY	MODERATE				GH - canagliflozin, dapagliflozin or empagliflozin (SGLT2 inhibitors); - linaglifptin, sitagliptin or vildagliptin (DPP-4 inhibitors); - indifference (blazalificadino)				
CV BENEFIT	YES			N					
HYPOGLYCAEMIA RISK	LOW			HI	GH				
WEIGHT	REDUCTION		RESOLVED, ADD GAIN		AIN	WEIGHT LOSS OR POSSIBILITY OF			
MAIN ADVERSE EVENTS	GASTROINTESTINAL			HYPOGLYCAEMIA CAREFUL MONITORING ¹		TYPE 1 DIABETES (URGENT - PHONE	_		
IN CKD STAGE 3A	MAXIMUM 2 g DAILY					DRING 1 SECONDARY CARE IMMEDIATELY)			
2nd LINE	IF NOT REACHING TARGET AFTER 3-6 MONTHS ² , REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE								
n ADDITION to lifestyle measures	ADD ONE OF:								
	SULPHONYLUREA* OR	SGLT2 INHIBITOR* OR	DPP-4	INHIBITOR* OR		PIOGLITAZONE*			
EFFICACY	HIGH	MODERATE	LOW/MODERATE		MODERATE				
CV BENEFIT	NO	YES (SPECIFIC AGENTS) ³	NO		PROBABLE (BUT FLUID RETENTION)				
HYPOGLYCAEMIA RISK	HIGH	LOW	LOW		LOW				
WEIGHT	GAIN	LOSS	NEUTRAL		GAIN				
MAIN ADVERSE EVENTS	HYPOGLYCAEMIA	GENITAL MYCOTIC	FEW		OEDEMA/FRACTURES 6				
IN CKD STAGE 3A	CAREFUL MONITORING 1	DO NOT INITIATE 4	DO NOT INITIATE 4 REDUCE DOSE 5			DOSE UNCHANGED			
3rd LINE	IF NOT REACHING TARGET AFTER 3–6 MONTH5, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE ⁷								
n ADDITION to lifestyle measures	ADD EITHER AN ADDITIONAL ORAL AGENT FROM A DIFFERENT CLASS								
	SULPHONYLUREA* OR	SGLT2 INHIBITOR* OR DPP-		4 INHIBITOR* OR PIOGLITAZONE*		PIOGLITAZONE*			
	If BMI > 30 kg/m ²			JECTABLE AGENT	IGENT If BMI < 30 kg/m ²				
	GLP-1 AGONIST*		BASAL INSULIN*						
EFFICACY	HIGH			HIGH	inject before bed use NPH (isophane) insulin - or longer-acting analogues according to risk of hypoglycaemia ¹⁰				
CV BENEFIT	YES (SPECIFIC AGENTS) 3	 stop DPP-4 inhibitor 	Γ	NO					
HYPOGLYCAEMIA RISK	LOW	consider reducing sulphonylu	urea	HIGHEST					
WEIGHT	LOSS	continue metformin		GAIN	• can continue metformin, pioglitazone, DPP-4 inhibitor or SGLT2 inhibitor • can reduce or stop sulphonylurea		IF INSULIN INTENSIFICAT		
MAIN ADVERSE EVENTS	GASTROINTESTINAL	can continue pioglitazone		HYPOGLYCAEMIA			INPUT)		
IN CKD STAGE 3A	DOSE UNCHANGED 8	can continue SGLT2 inhibitor		DOSE UNCHANGED 9					
4th LINE	IF NOT REACHING TARGET AFTER 3-6 MONTHS, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE ADD ADDITIONAL AGENT(S) FROM 3rd LINE OPTIONS (NEED SPECIALIST INPUT)								

Prescribers should refer to the British National Formulary (www.medicinescomplete.com), the Scottish Medicines Consortium (www.scottishmedicines.org.uk) and Medicines and Healthcare products Regulatory Agency (MHRA) warnings for updated guidance on licensed indications, full contraindications and monitoring requirements.

*Continue medication at each stage if EITHER individualised target achieved OR HbA1c falls more than 0.5% (5.5 mmol/mol) in 3–6 months. Discontinue if evidence that ineffective. NOTES: 1 Consider dose reduction, 2. Do not delay if first line options not tolerated / inappropriate, 3. See guideline pages 23 & 26-27, 4. See BNF: specific agents can be continued at reduced dose, 5. See BNF: no dose reduction required for linagliptin 6. Plogitizations is contraindicated in people with or with a history of) heart failure or bladder cancer, 7. Do not combine dapagifidizin with piogitazone, 8. Caution with exenatide when eGFR<50 m/min/1.73 m⁵, 9. Adjust according to response, 10. Driving, occupational hazards, risk of falls, previous history.

ABBREVIATIONS: CKD 3A = chronic kidney disease stage 3A (estimated glomerular filtration rate 45-59 ml/min/1.73 m²) CV = cardiovascular

International Diabetes Federation Managing Older People With Type 2 Diabetes Global Guideline 2013⁸

Individualising HbA1c targets in older frail individuals is particularly challenging and important as priorities for glycaemic control should shift to favour safety and avoidance of hypoglycaemia rather than achieving HbA1c targets.

The International Diabetes Federation published a global guideline during 2013 on managing older people with T2D, which suggested functional categories of older people with diabetes and recommended HbA1c, blood pressure, and lipid targets according to each functional category (see Table 1). The authors refer to this guideline as a "guiding philosophy", respecting the fact that older people are very individual and that their needs can differ considerably.

Similarly, a framework⁹ has been suggested for the management of older frail individuals with T2D according to their frailty status with the intention of reducing complications and improving quality of life for these older people (see Table 2).

Importantly, this framework suggests treatment targets and therapies to consider according to frailty status, but also de-escalation HbA1c thresholds, where consideration should be given to the de-prescribing of diabetes therapies that may cause harm.



Table 1 (Adapted from IDF Global Guideline)

Functional Category	Category Def- inition	Suggested HbA1c Target (mmol/mol)	Suggested BP Target (mmHg)	Suggested Li- pid Control Strategy
Functionally Independent	Living inde- pendently with no important impairments of ADLs	53-59	<140/90	Actively manage to reduce CV risk. Statins 1 st line therapy
Functionally Dependent	Impairments of ADLs with risk of admission to a care home	53-64	<140/90	Actively manage to reduce CV risk. Statins 1 st line therapy
	Subcategory: Frail. Severe restriction in mobility & strength and high falls risk	Up to 70 may be appropriate	<150/90	Statin use as clinically indicat- ed
	Subcategory: Dementia. Cognitive im- pairment, diso- rientation, per- sonality change and unable to self- care	Up to 70 may be appropriate	<140/90 in cognitive im- pairment. In advanced de- mentia strict BP control may not offer any advantage	Consider appro- priateness of statin in non- atherosclerotic dementia
End of Life Care	Significant medical illness or malignancy with life expec- tancy of <1 year	Target is to avoid sympto- matic hyper- glycaemia	BP control not necessary un- less readings are immediate- ly life- threatening; consider stop- ping therapy	Lipid control not necessary; con- sider stopping therapy



Table 2(adapted from Type 2 Diabetes Mellitus in Older People: A Brief Statement of Key Principles of Modern Day Management including the Assessment of Frailty. A National Collaborative Stakeholder Initiative 2018⁹)

	De-escalation threshold (mmol/mol)	Suggested interventions
The fit older adult with diabe- tes	53	Review long-acting SU & insulin ther- apy that may cause hypoglycaemia. Consider appropriate dosage in con- text of renal impairment
Moderate-severe frailty	58	Discontinue any SU if HbA1c below threshold. Avoid TZDs because of risk of heart failure. Cautious use of insulin and metformin in renal impair- ment.
Very severe frailty	64	Withdraw SUs & short-acting insulins due to risk of hypoglycaemia. Re- view timings & suitability of NPH in- sulin again due to risk of hypoglycae- mia. Therapies that promote weight loss may worse sarcopenia

Core Elements for Quality Improvement

HbA1c targets should be tailored to the patient's needs and circumstances. This is particularly important for those with significant comorbidities, older frail individuals, those who have a reduced life expectancy, or those whose job involves driving or operating machinery, where a less stringent HbA1c target may be considered on a case-by-case basis. The person's needs and circumstances should be reassessed at each reivew, and treatment targets re-assessed. This is consistent with 'Practising Realistic Medicine' published during 2018 which strives for a more personalised approach to care and highlingts the importance of shared decision-making.

The use of cardioprotective diabetes medications should be considered in those with T2D and established CVD consistent with key new clinical recommendations in SIGN 154. Specifically, the use of the SGLT2 inhibitors empagliflozin and canagliflozin, and the GLP-1 receptor agonist liraglutide, have resulted in significant reductions in major CV events.

Implementation in Real-Life NHS Practice & Implications for Collaborative Quality Improvement in General Practice Clusters

<u>Audit:</u> Consider stopping sulphonylurea therapy in those over the age of 75 years with an HbA1c equal or less than 58mmol/mol to avoid harm particularly hypoglycaemia. Hypoglycaemia is twice as common in those older than 75 years of age. The UK Hypoglycaemia Study Group¹¹ demonstrated that the frequency of hypoglycaemia in those treated with SUs was similar to the hypoglycaemia rate during early insulin use in T2D. Furthermore, 1:10 of those with T2D taking SUs suffered a major hypoglycaemic event each year.

Older people have different responses to hypoglycaemia:

- More likely to have neuroglycopenic symptoms (confusion, drowsiness, lack of coordination, slurring of speech, atypical behaviour & aggression)
- Less adrenaline-mediated symptoms (hunger, palpitations, sweating, shaking, dizziness & tachycardia)
- More likely to go undetected
- May present as chronic confusion / dementia; severe or recurrent hypos may also make dementia worse
- Reduced appetite, weight loss, muscle loss or deteriorating renal function can also contribute to a higher risk of hypoglycaemia



- May present as chronic confusion / dementia; severe or recurrent hypos may also make dementia worse
- Reduced appetite, weight loss, muscle loss or deteriorating renal function can also contribute to a higher risk of hypoglycaemia
- Hypoglycaemia in the elderly can lead to cardiac & stroke events, confusion, convulsions and falls leading to fracture or other injuries

The person's needs and circumstances should be reassessed at each review, and treatment choices and targets should be considered as part of the review.

<u>Audit:</u> The proportion of those with T2D and coexisting CVD who are on a cardioprotective diabetes medication

Notably, even if individuals with T2D have <u>achieved</u> a mutually agreed HbA1c target, introduction of cardioprotective diabetes medication should still be considered given the significant reduction in adverse CV outcomes.

Further Reading

Being Mortal: Illness, Medicine and What Matters in the End (Wellcome Collection). Atul Gawande. Profile Books Ltd. 1 July 2015

Resources

SIGN 154 usefully provides a checklist of information for all classes of diabetes drugs (including insulin) that healthcare professionals (HCPs) can use when discussing glucose-lowering in those with T2D and their carers. This information can also be used to guide the development of locally produced information materials.

SIGN 154 also provides a list of useful sources of further information for HCPs and those with diabetes and their carers:

- Diabetes in Scotland
 <u>www.diabetesinscotland.org.uk</u>
- Diabetes UK (Scottish Office)
 <u>www.diabetes.org.uk</u>
- Driver & vehicle Licensing Agency <u>www.gov.uk/</u> <u>diabetes-driving</u>
- Healthtalk <u>www.healthtalk.org</u>
- My Diabetes My Way
 <u>www.mydiabetesmyway.scot.nhs.uk</u>

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