A disease state approach to the pharmacological management of T2D in primary care

A position statement by
Primary Care Diabetes Europe

PCDE
primary care diabetes europe

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Today's agenda

- Samuel Seidu: Background, rationale and methodology
- Kamlesh Khunti: Categorization of risk phenotypes in type 2 diabetes from the primary care perspective
- Stefan Jansson: Consensus recommendations
- Francesc Xavier Cos Claramunt: Practical implications of the guidance in various countries across Europe
- **Q & A**
- **Wrap up**

Why a PCDE treatment position statement?

For primary care teams supporting patients with T2D:

- The consensus report aims to aid clinicians to manage the whole patient, not just their glycaemia
- Aims for practicality in the choices of medications
- Defines various cohorts of patients
- Recommends preferred evidence-based options for risk management

Introduction and background

- ✓ Clinical Guidelines are defined as the “new tower of Babel”, one report identified 855 publications of guidelines targeted for the general practitioner alone, as “68 cm high, and weighing 28 kilos”
  - ✓ They are “*systematically developed statements to assist health care providers, consumers, payers, and policy makers in making decisions on how specific health conditions can be most effectively and appropriately prevented, treated, and managed*”
    - ✓ A comprehensive review of all published guidelines would be as impossible and unproductive for PCPs, especially considering most guidelines do not involve primary care in their development
      - ✓ The clinical algorithm (flow chart) is a format that is specially suited for representing a sequence of clinical decisions, for teaching clinical decision making, and for guiding patient care
        - ✓ In contrast to guidelines, algorithms are intended to be practical

PCP, primary care physician.

1. Guidelines in general practice: the new tower of Babel?. BMJ 1998;317:862-863; 2.Uses of Clinical Algorithms JAMA. 1983;249(5):627-632.

Aims

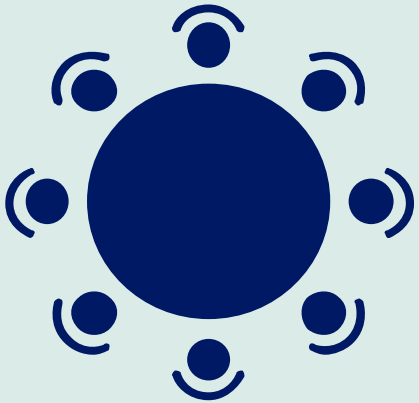
- To provide a simple and pragmatic tool for primary care clinicians and other HCPs for the pharmacological management of people with T2D and other comorbidities
- To offer a novel risk stratification approach and practical recommendations to help link patients with appropriate care and prevent diabetes-associated complications
- Provide additional direction to supplement but not replace well established national and international guidelines

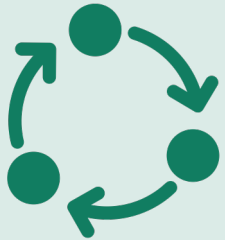
Seidu S et al. [published online ahead of print, 2020 Jun 9]. Prim Care Diabetes. 2020;S1751-9918(20)30189-3.

Composition of the faculty

The faculty reflects the stakeholder group in primary care

8 primary care physicians and 1 nurse





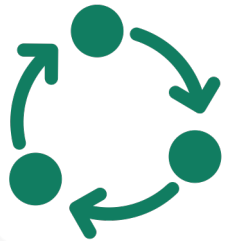
All are experts in diabetes

All participants equally influence the outcome[1]

All participants must be involved in the debate

1. Vella K et al. Br Med J. 2000; 320 (7240): 976-980.

Methodology

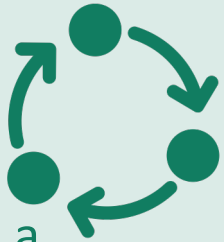


- Definition of consensus
  - For each question, Likert scale of
    - strongly disagree,
    - disagree,
    - agree
    - and strongly agree
  - Consensus is established when the combined **agree and strongly agree** votes exceeded **90%**
- Methods of dealing with outliers
  - Any outlier should be offered to chance to present any information or data and then allow a re-vote
- Applicable research was aggregated
- Evidence was solicited from experts in the field[1]
- Authors considered the key questions and worked to reach consensus
- Dialogue: debate and discussion between participants at author meetings and with each position statement draft

1. Black N et al. J Health Serv Res Policy. 1999; 4(4):236-248; 2. Campbell SM et al. Br Med J.2003; 326(7393):816-819.

Structure of the debates

- The facilitator plays a vital role in providing structure:
  - Moderates the dialogue
  - Maintains the agenda, manages conflict and creates a positive environment[1]

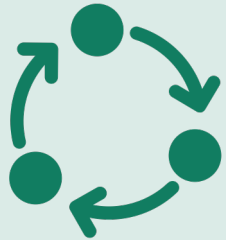


  - All voices to be heard and minimise the potential of group dynamics to generate coercion[2]

1. Duncan EA. Research in occupational therapy: Methods of inquiry for enhancing practice. 2006: 401-410; 2. Rycroft-Malone J. Quality and Safety in Health Care. 2001;10 (4): 238-244.

Presentations

- Consistent themes for all the drug classes
- Presentations reflected real life issues



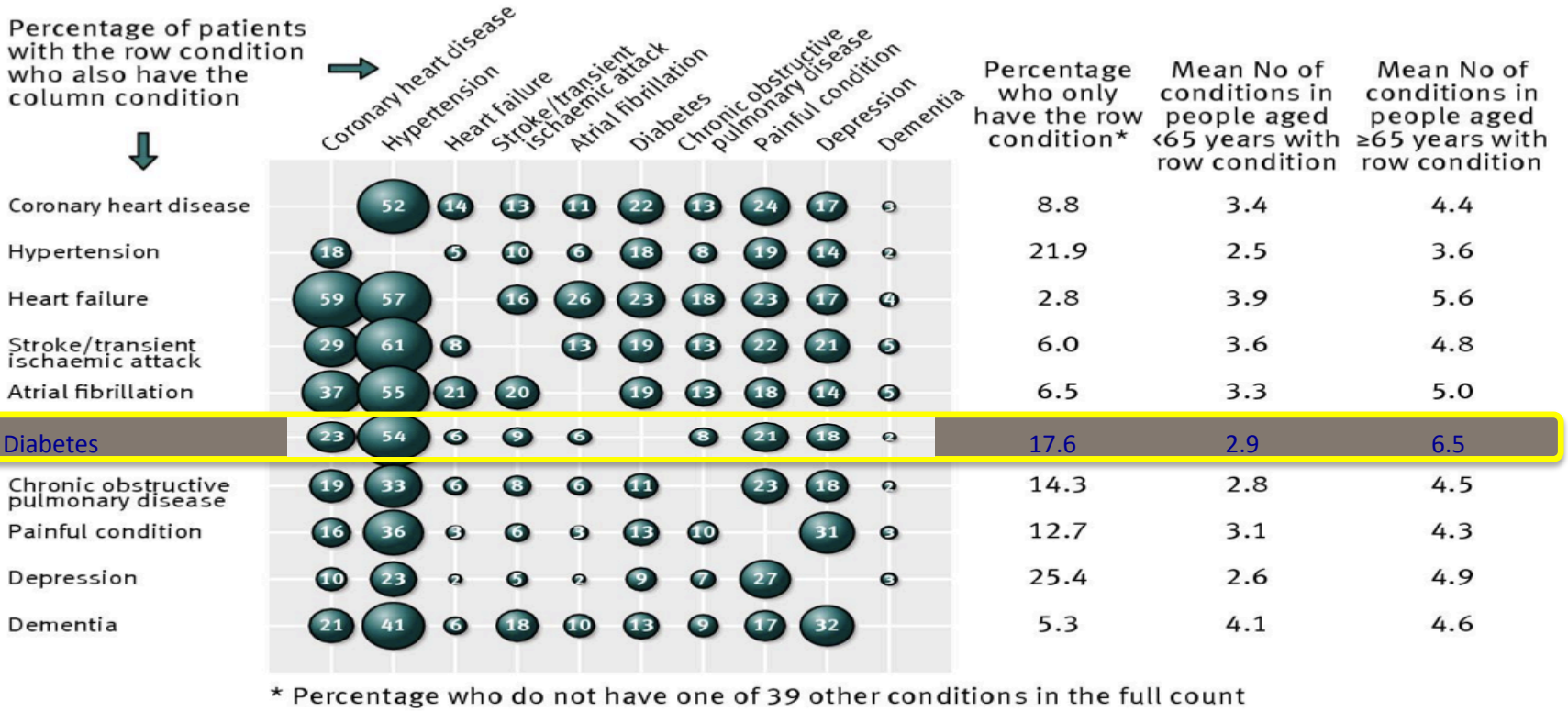
1. What is the drug class and the options available within that class?
2. What is the current evidence to support the use of each drug within the class including for prevention of recurrent CVD in diabetes?
3. Should the various drugs be prioritised within the class?
4. Any additional information to support the use of each drug

CVD, cardiovascular disease.

Main Drivers for decisions in the consensus report

- Simplicity
  - Simpler risk stratification
- Addressing multi-morbidity with drug treatment where the evidence exists.
  - Especially cardio-renal multi-morbidity, where there is now ample evidence with certain drug classes.
- Addressing therapeutic inertia
  - Early combination therapy where appropriate.
- Maintaining patient safety.
  - Prescribing guide.

Comorbidity of top 10 common conditions

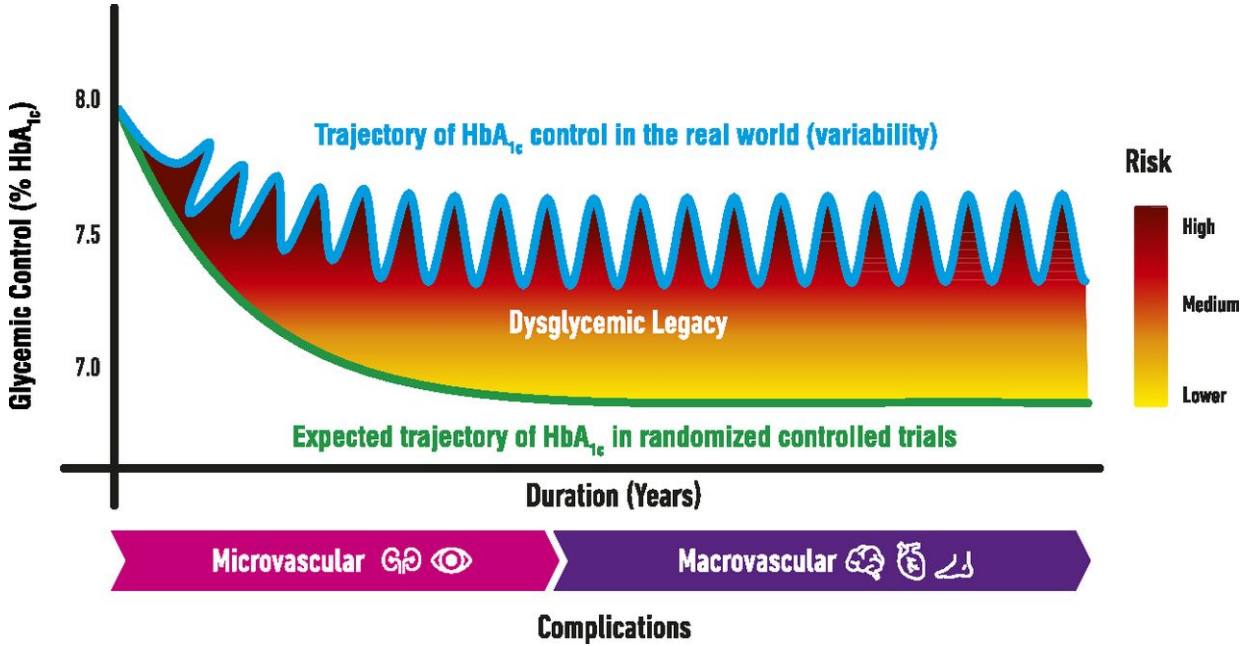


Percentage of patients with the row condition who also have the column condition	Coronary heart disease	Hypertension	Heart failure	Stroke/transient ischaemic attack	Atrial fibrillation	Diabetes	Chronic obstructive pulmonary disease	Painful condition	Depression	Dementia	Percentage who only have the row condition*	Mean No of conditions in people aged <65 years with row condition	Mean No of conditions in people aged ≥65 years with row condition
Coronary heart disease		52	14	13	11	22	13	24	17	5	8.8	3.4	4.4
Hypertension	18		5	10	6	18	8	19	14	2	21.9	2.5	3.6
Heart failure	59	57		16	26	23	18	23	17	4	2.8	3.9	5.6
Stroke/transient ischaemic attack	29	61	8		13	19	13	22	21	5	6.0	3.6	4.8
Atrial fibrillation	37	55	21	20		19	13	18	14	5	6.5	3.3	5.0
Diabetes	23	54	6	9	6		8	21	18	2	17.6	2.9	6.5
Chronic obstructive pulmonary disease	19	33	6	8	6	11		23	18	2	14.3	2.8	4.5
Painful condition	16	36	3	6	3	13	10		31	3	12.7	3.1	4.3
Depression	10	23	2	5	2	9	7	27		3	25.4	2.6	4.9
Dementia	21	41	6	18	10	13	9	17	32		5.3	4.1	4.6

* Percentage who do not have one of 39 other conditions in the full count

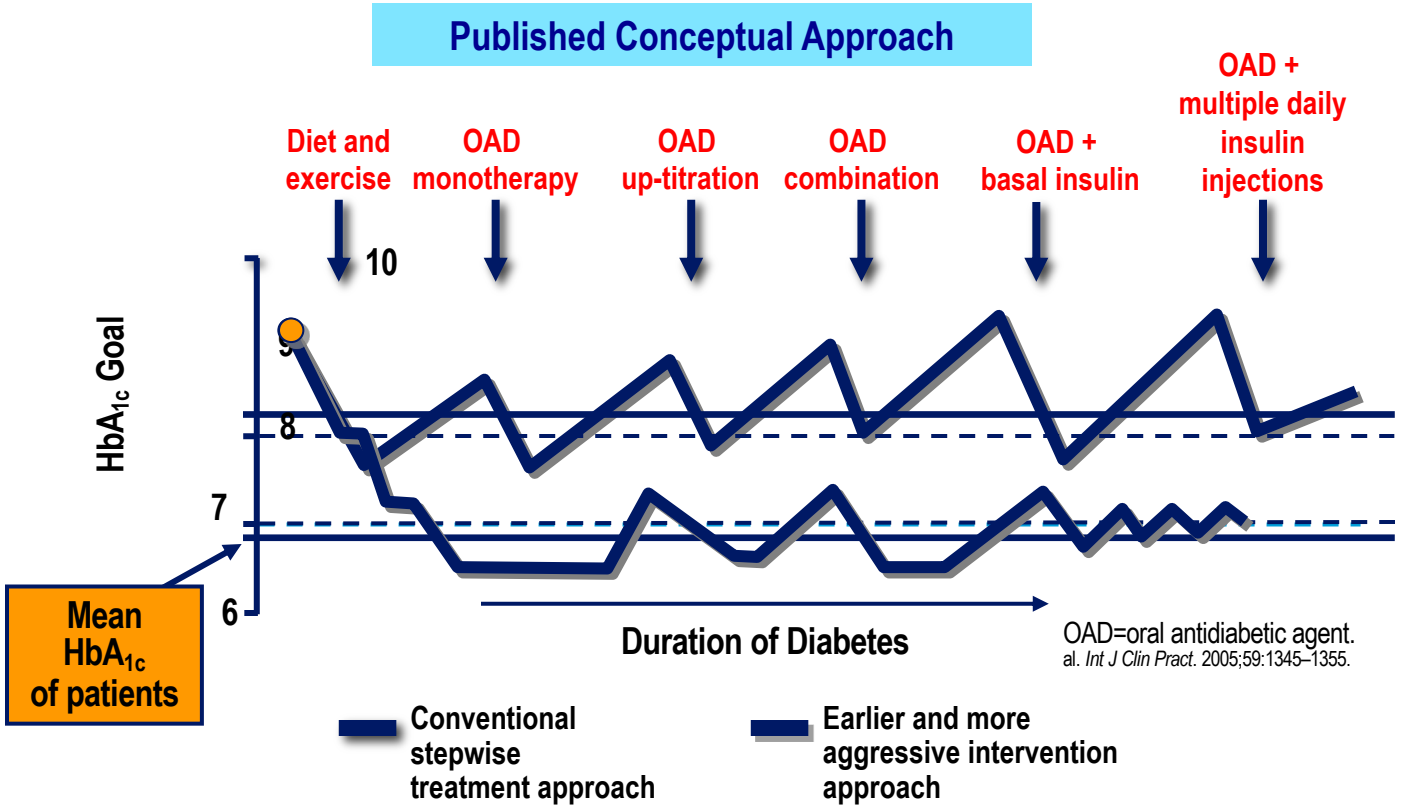
Guthrie B, et al. BMJ 2012;345:e6341.

A schematic representation of the effects of early intensive glycaemic control in preventing initial microvascular complications and then macrovascular complications several years later.

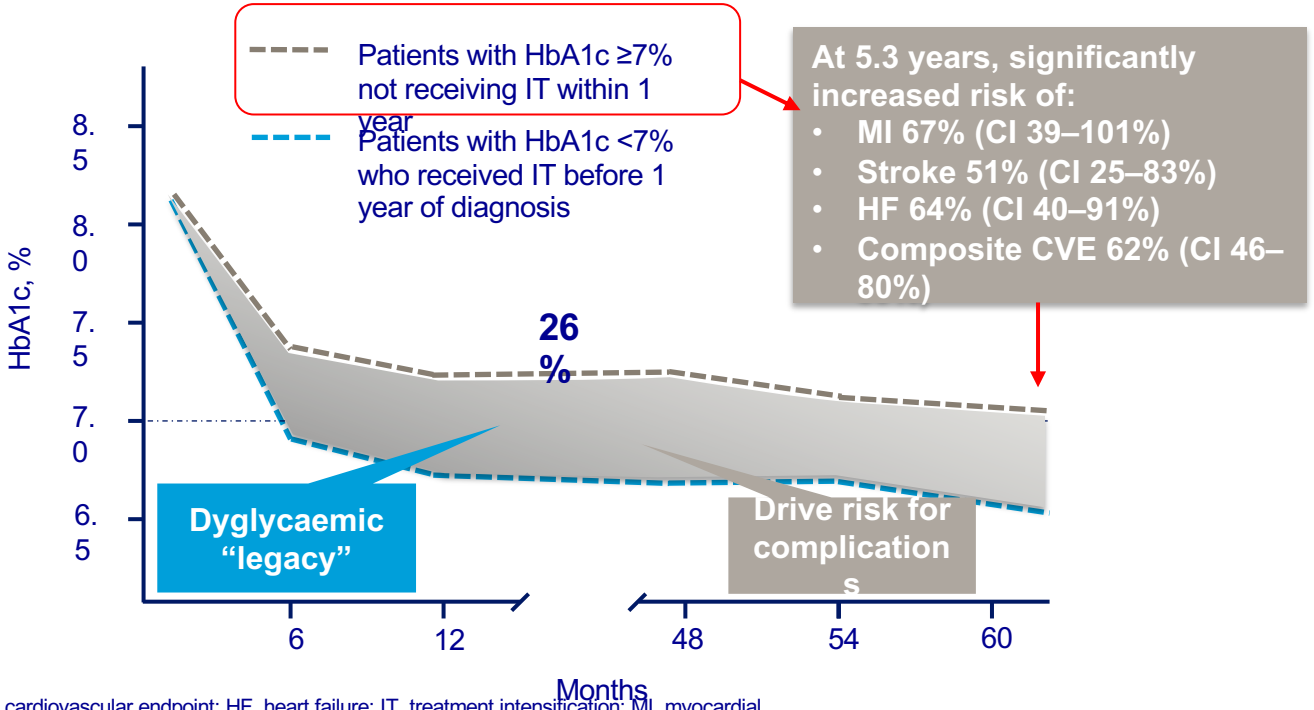


Kamlesh Khunti, and Samuel Seidu Dia Care 2019;42:349-351

Earlier and Appropriate Intervention May Improve Patients' Chances of Reaching Goal



CVD consequences of delayed intervention



CVE, cardiovascular endpoint; HF, heart failure; IT, treatment intensification; MI, myocardial infarction

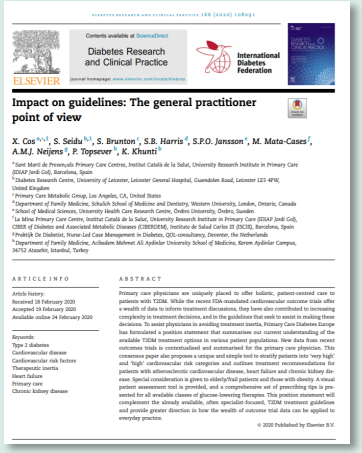
Khunti K et al. *Primary Care Diabetes* 2017;11:3-12
Paul S, et al. *Cardiovasc Diabetol* 2015;14:100 doi:10.1186/s12933-015-0260-x

Early combination therapy

- Systematic review and meta-analysis
  - In 15 RCTs (N = 6693) combination therapy with metformin provided statistically significant reductions in A1c (WMD −0.43%, 95% CI −0.56, −0.30), increases in attainment of A1c goal of less than 7%. Phung et al Diabetes Obes Metab 2013
- VERIFY
  - Early combination therapy delayed treatment escalation in newly-diagnosed young-onset type 2 diabetes . Reduced time to treatment failure. Chan et al . Diabetes Obes Metab 2020
- EDICT
  - Initial combination therapy with metformin, pioglitazone and exenatide is more effective than sequential add-on therapy in subjects with new-onset diabetes. Abdul-Ghani et al Diabetes Obes Metab 2015

Publication output

A disease state approach to the pharmacological management of Type 2 diabetes in primary care: A position statement by Primary Care Diabetes Europe



Impact on guidelines: The general practitioner point of view

Cos X et al. [published online ahead of print, 2020 Feb 24]. *Diabetes Res Clin Pract*. 2020;166:108091;.
Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

CV risk stratification in T2D patients

Patients with T2D are considered to be at **very high CV risk** if they have any of the following:

History of **CVD**

Multiple uncontrolled CVD **risk factors** (hypertension, hyperlipidaemia, obesity, smoking and/or physical inactivity)

eGFR <60mL/min/1.73m^2

Albuminuria (>30 mg/day)

<40 years **age** at diagnosis

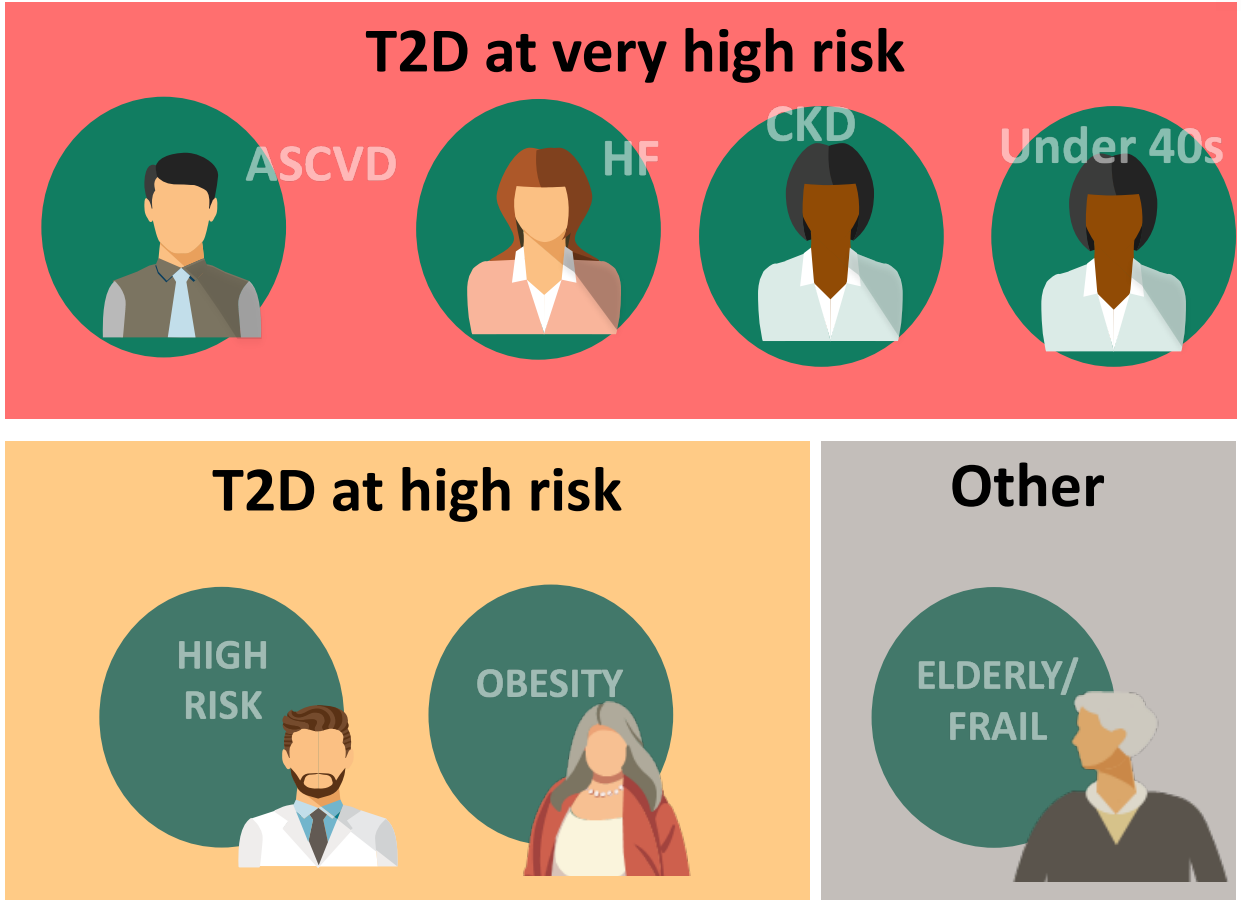
All other patients with T2D are at **high CV risk**

Lifestyle counselling is recommended for all patients with T2D

CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.

Cosentino F et al. *Eur Heart J* 2019;34:3035-87.; Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

CV risk stratification in T2D patients



T2D at very high risk

- Consider initiating metformin + SGLT2i/GLP-1RA rather than stepwise
- Metformin as first-line therapy
- SGLT2i or GLP-1RA with proven CV benefit as second-line therapy
- Use basal insulin with caution when other options have failed and glycaemic targets are not met

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF heart failure; SGLT2i, sodium-glucose co-transporter-2 inhibitor.

Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

T2D at very high risk

- Consider initiating metformin + SGLT2i rather than stepwise
- Metformin as first-line therapy
- SGLT2i as second-line therapy
- Avoid pioglitazone and saxagliptin and use basal insulin with caution

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF heart failure; SGLT2i, sodium-glucose co-transporter-2 inhibitor.

Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

T2D at very high risk

- Consider initiating metformin + SGLT2i rather than stepwise, according to the approved restrictions of dose and indications by eGFR
- Metformin as first-line therapy if eGFR >30mL/min/1.73m^2
- SGLT2i as second-line therapy if eGFR >45mL/min/1.73m^2, even if well controlled on metformin alone
- GLP-1RA as third-line therapy or if previous treatments are not tolerated, followed by DPP-4i
- Reduce dose of glinides and reduce dose or discontinue SUs if eGFR<45mL/min/1.73m^2 to reduce risk of hypoglycaemia
- Consult prescribing information for specific agents for dosing instructions based on eGFR

CKD, chronic kidney disease; DPP-4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SU, sulphonylurea.

Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

T2D at high risk

- Consider initiating metformin + SGLT2i/GLP-1RA/DPP-4i rather than stepwise
- Metformin as first-line therapy
- SGLT2i or GLP-1RA or DPP-4i as second-line therapy where cost is not prohibitive. Of these, SGLT2i or GLP-1RA with proven CV benefit is preferred
- Newer generation SUs or glinides when drug cost must be minimised
- Pioglitazone in patients with NAFLD and where insulin resistance predominates
- Basal insulin when other therapies have been explored and glycaemic targets are not met
- Full basal–bolus insulin therapy only as a last resort

CV, cardiovascular; DPP-4i; dipeptidyl peptidase-4 inhibitor; GLP-1RA, glucagon-like peptide 1 receptor agonist; NAFLD, non-alcoholic fatty liver disease; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SU, sulphonylurea.

Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

T2D at high risk

- Consider initiating metformin + GLP-1RA/SGLT2i rather than stepwise
- Metformin as first-line therapy
- GLP-1RA or SGLT2i as second-line therapy
- Where possible, avoid treatments that cause weight gain, including most SUs, glinides, pioglitazone and insulin
- If basal insulin is required, consider fixed-ratio insulin/GLP-1RA combinations

DPP-4i; dipeptidyl peptidase-4 inhibitor; GLP-1RA, glucagon-like peptide 1 receptor agonist; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SU, sulphonylurea.

Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

Other risk groups

- Avoid stringent glycaemic targets that increase risk of hypoglycaemia
- Metformin as first-line therapy if tolerated and not contraindicated
- DPP-4i is safe and easy to use
- Assess adherence and avoid multiple daily injectable medications when possible

DPP-4i; dipeptidyl peptidase-4 inhibitor; GLP-1RA, glucagon-like peptide 1 receptor agonist; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SU, sulphonylurea.

Seidu S et al. [published online ahead of print, 2020 Jun 9]. *Prim Care Diabetes*. 2020;S1751-9918(20)30189-3.

Take home messages

- The position statement is intended to be a **practical counterpart** to national and international management guidelines
- The position statement has been compiled by a series of presentations and discussions among experts to identify the **key issues** in CVD risk management in patients with T2D
- **Patients** are categorised into different risk groups based on individual factors
- **Pharmacotherapeutic** suggestions are highlighted for individuals in different risk groups, but should be reevaluated on an individual basis

CVD, cardiovascular disease.