2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases

Developed in collaboration with EASD

ESC European Society of Cardiology

Task Force

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ESC Classes of recommendations

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	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

ESC Levels of evidence

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Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

What is new in the 2019 Guidelines?

- ✓ Reclassification of CV risk in diabetes
- ✓ New treatment algorithms with glucose-lowering agents for management/prevention of CVD
- ✓ New recommendations regarding the role of aspirin and NOACs / Duration of DAPT post-ACS in diabetes
- ✓ Choice of revascularization techniques
- ✓ New lipid targets relating to severity of CV risk / new recommendations for the use of PCSK9 inhibitors
- ✓ Individualised blood pressure targets

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Diabetes and CVD - key points

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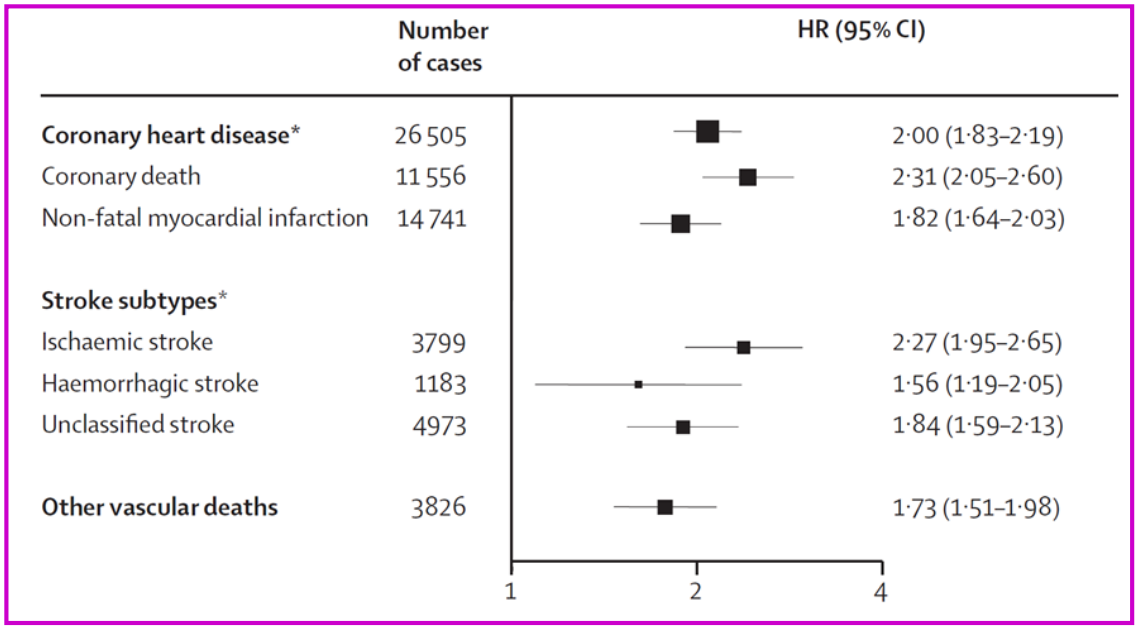
DM: double CVD risk <u>on average</u>

Hazard ratios for vascular outcomes DM vs. no DM



ERFC, *Lancet* 2010

Diabetes and CVD - key points

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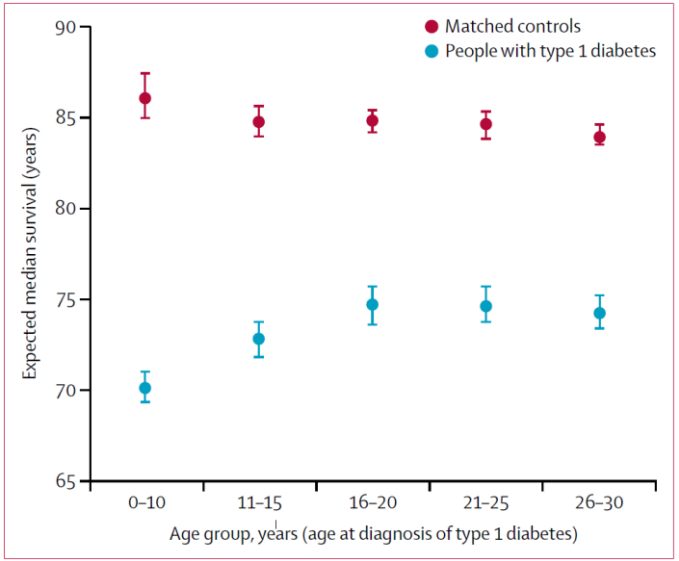
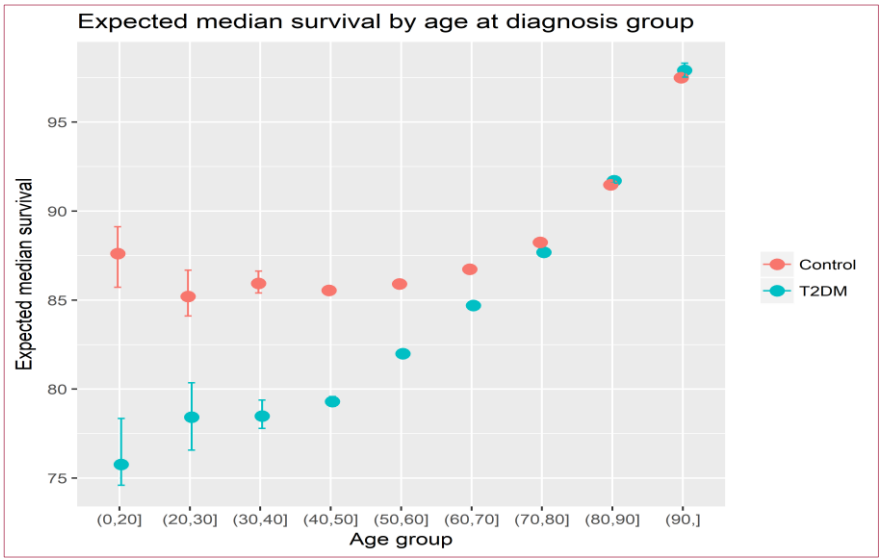
Younger age of diagnosis associated with greater loss of life years

T1DM



Rawshani et al. *Lancet 2018*

T2DM



Sattar et al. *Circulation* 2019

Diagnostic criteria for DM and pre-DM according to the 2006/2011 WHO and 2019 ADA

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Table 3 Diagnostic criteria for DM and pre-DM according to the 2006/2011 WHO and 2019 ADA

Diagnosis/ measurement	WHO 2006/2011	ADA 2019
DM		
HbA1c	**Can be used** If measured, ≥6.5% (48 mmol/mol)	**Recommended** ≥6.5% (48 mmol/mol)
FPG	**Recommended** ≥7.0 mmol/L (126 mg/dL)	≥7.0 mmol/L (126 mg/dL)
	or	**or**
2hPG	≥11.1 mmol/L (≥200 mg/dL)	≥11.1 mmol/L (≥200 mg/dL)
RPG	Symptoms plus ≥11.1 mmol/L (≥200 mg/dL)	Symptoms plus ≥11.1 mmol/L (≥200 mg/dL)
IGT		
FPG	<7.0 mmol/L (<126 mg/dL)	<7.0 mmol/L (<126 mg/dL)
2hPG	≥7.8 to <11.1 mmol/L (≥140 to 200 mg/dL)	≥7.8 to <11.0 mmol/L (≥140 to 199 mg/dL)
IFG		
FPG	6.1 to 6.9 mmol/L (110 to 125 mg/dL)	5.6 to 6.9 mmol/L (100 to 125 mg/dL)
2hPG	<7.8 mmol/L (<140 mg/dL)	<7.8 mmol/L(<140 mg/dL)

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Cardiovascular risk categories in patients with DM

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Very high-risk	Patients with DM **and** established CVD **or** other target organ damage[a] **or** three or more major risk factors[b] **or** early onset T1DM of long duration (>20 years)
High-risk	Patients with DM duration ≥10 years without target organ damage[a] plus any other additional risk factor[b]
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors

[a] proteinuria, renal impairment defined as eGFR≤30mL/min/1.73m^2.
[b] age, hypertension, dyslipidemia, smoking, obesity.

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

2019 new recommendations (1)

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CV risk assessment
Resting ECG in patients with DM with hypertension or suspected CVD
Carotid or femoral ultrasound for plaque detection as CV risk modifier
Screening for CAD with coronary CT angiography and functional imaging
CAC scoring as risk modifier
ABI as risk modifier
Carotid ultrasound intima-media thickness for CV risk is not recommended

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Recommendations for glycaemic control in individuals with DM

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Recommendations	Class	Level
It is recommended to apply tight glucose control, targeting a **near-normal HbA1c (<7.0% or <53 mmol/mol)** to decrease **microvascular complications** in DM.	I	A
It is recommended that **HbA1c targets are individualized** according to duration of DM, comorbidities, and age.	I	C
Avoidance of hypoglycaemia is recommended.	I	C
The use of **structured self-monitoring of blood glucose and/or continuous glucose monitoring** should be considered to facilitate optimal glycaemic control.	IIa	A
An **HbA1c target of <7.0%** (or <53 mmol/mol) should be considered for the **prevention of macrovascular complications in individuals with DM.**	IIa	C

www.escardio.org/guidelines

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Cardiovascular outcome trials with newer glucose-lowering agents

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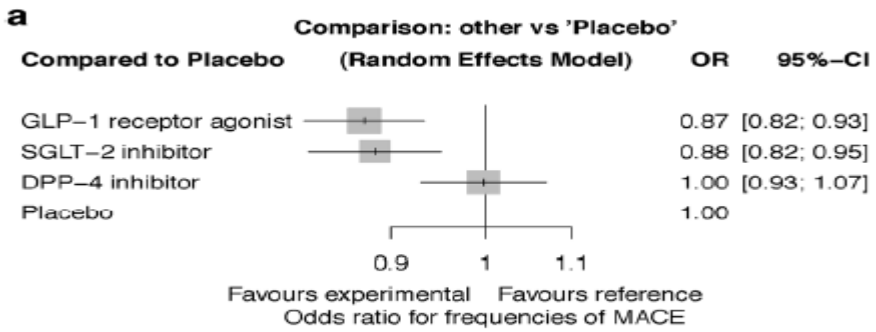
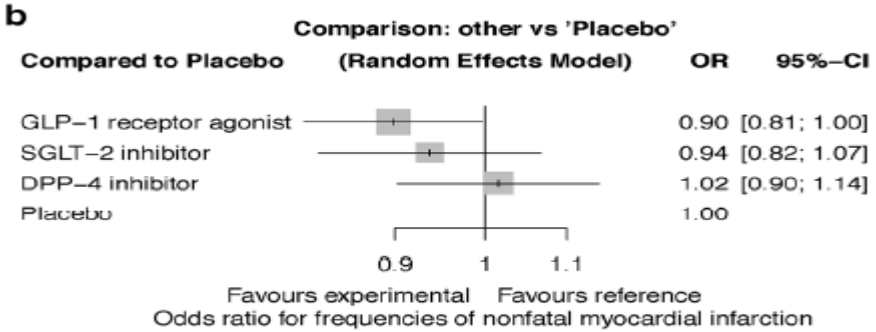
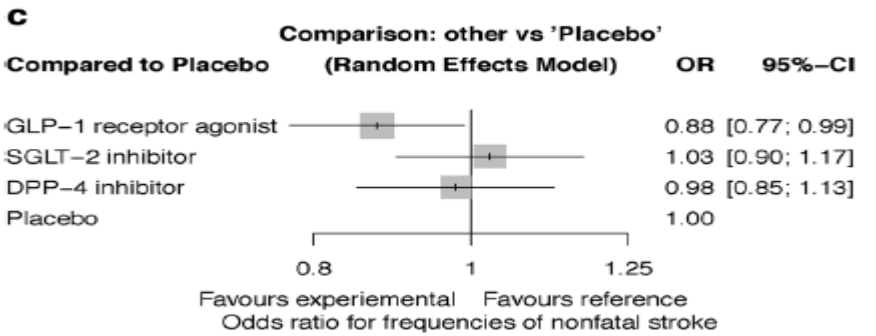
	SGLT2 inhibitors				GLP-1 RAs							DPP-IV inhibitors				
Trial	**EMPA-REG OUTCOME**[306]	**CANVAS**[309]	**DECLARE–TIMI 58**[311]	**CREDENCE**[313]	**ELIXA**[297]	**LEADER**[176]	**SUSTAIN-6**[299]	**EXSCEL**[158]	**Harmony Outcomes**[301]	**REWIND**[303]	**PIONEER 6**[300]	**SAVOR–TIMI 53**[291]	**EXAMINE**[292]	**TECOS**[293]	**CARMELINA**[294]	**CAROLINA**[277]
Baseline	**Empagliflozin vs. placebo**	**Canagliflozin vs. placebo**	**Dapagliflozin vs. placebo**	**Canagliflozin vs. placebo**	**Lixisenatide vs. placebo**	**Liraglutide vs. placebo**	**Semaglutide vs. placebo**	**Exenatide vs. placebo**	**Albiglutide vs. placebo**	**Dulaglutide vs. placebo**	**Oral Semaglutide vs. placebo**	**Saxagliptin vs. placebo**	**Alogliptin vs. placebo**	**Sitagliptin vs. placebo**	**Linagliptin vs. placebo**	**Linagliptin vs. glimiperide**
n	7020	10 142	17160	4401	6068	9340	3297	14 752	9463	9901	3182	16 492	5400	14 671	6979	6033
Age (years)	63	63	63	63	60	64	64	62	64	66	66	65	61	66	65	64
DM (years)	57% >10	13.5	11.8	15.8	9.3	12.8	13.9	12.0	14.1	10.5	14.9	10	7.2	9.4	14.7	6.2
Body mass index (kg/m^2)	30.6	32.0	32.1	31.3	30.1	32.5	32.8	31.8	32	32.3	32.3	31	29	30	31.3	30.1
Insulin (%)	48	50	~40	65	39	44	58	46	60	24	61	41	30	23	58	0
HbA1c (%)	8.1	8.2	8.3	8.3	7.7	8.7	8.7	8.0	8.7	7.2	8.2	8.0	8.0	7.3	7.9	7.2
Previous CVD (%)	99	65	40	50.4	100	~81	~83	73	100	31	35	78	100	100	57	42
CV risk inclusion criteria	**MI, CHD, CVD, or PVD**	**MI, CHD, CVD, or PVD**	**CVD or at least one CVRF**	**CKD**	**ACS <180 days**	**Age ≥50 years and CVD,[b] or CKD, or age ≥60 years and at least one CVRF**		**CHD, CVD, or PVD27% no previous CV event**	**MI, CHD, CVD, or PVD**	**Age ≥50 years and CVD or CVRFs**	**Age ≥50 years and CVD, or CKD, or age ≥60 years and CVRFs**	**Age ≥40 years and CVD (CHD, CVD, or PVD), or age ≥55 years and at least one CVRF**	**ACS<90 days**	**CHD, CVD, or PVD**	**CVD and/or CKD**	**CVD or evidence of vascular-related end-organ damage, or age ≥70 years, or at least two CVRFs**
Hypertension (%)	94	89	89	96.8	76	92	92	90	86	93	94	81	83	86	95	90
Follow-up (years)	3.1	2.4	4.5	2.6	2.1	3.8	2.1	3.2	1.6	5.4	1.3	2.1	1.5	2.8	2.2	6.3

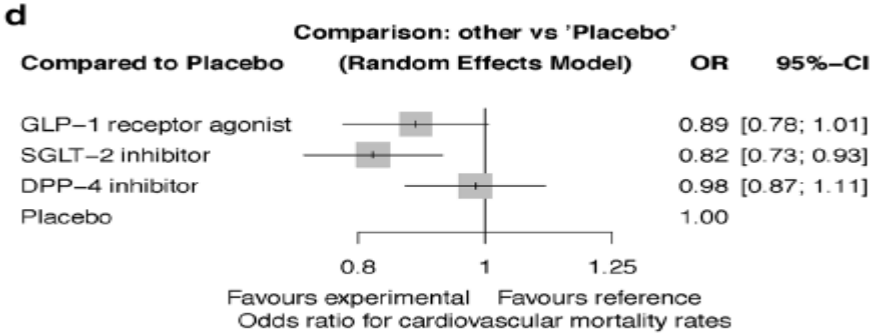
ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Network metaanalysis





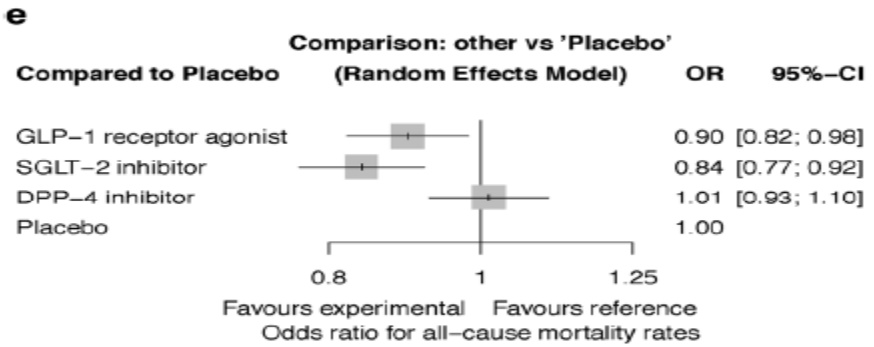


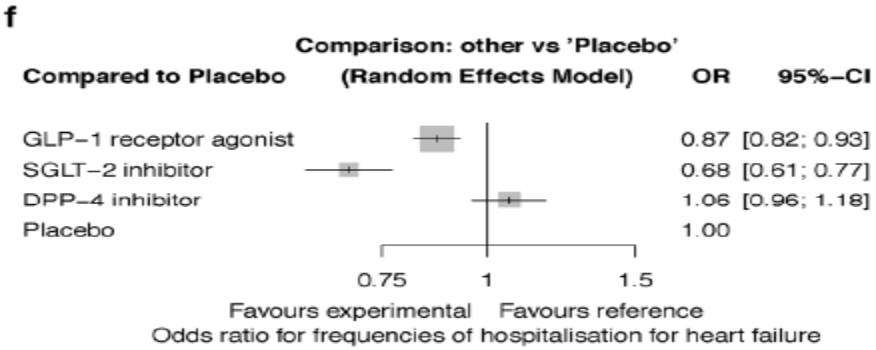


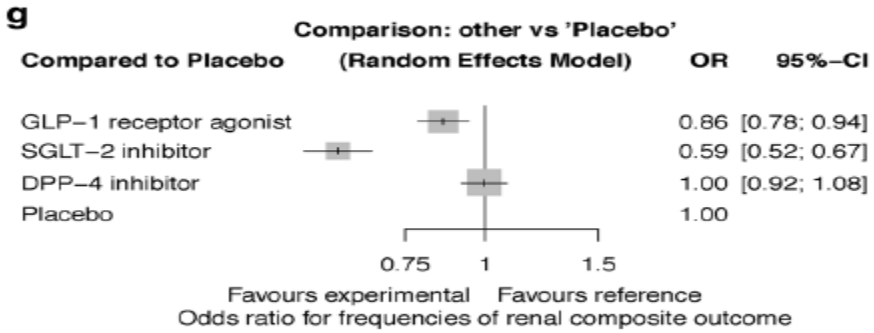
Risk of outcomes with different antidiabetic drug classes compared to placebo. a MACE (major adverse cardiovascular events). b Nonfatal myocardial infarction. c Nonfatal stroke. d Cardiovascular mortality. e All-cause mortality. f Hospitalisation for heart failure. g Renal composite outcome

Fei et al. Cardiovasc Diabetol (2019) 18:112

Network meta analysis







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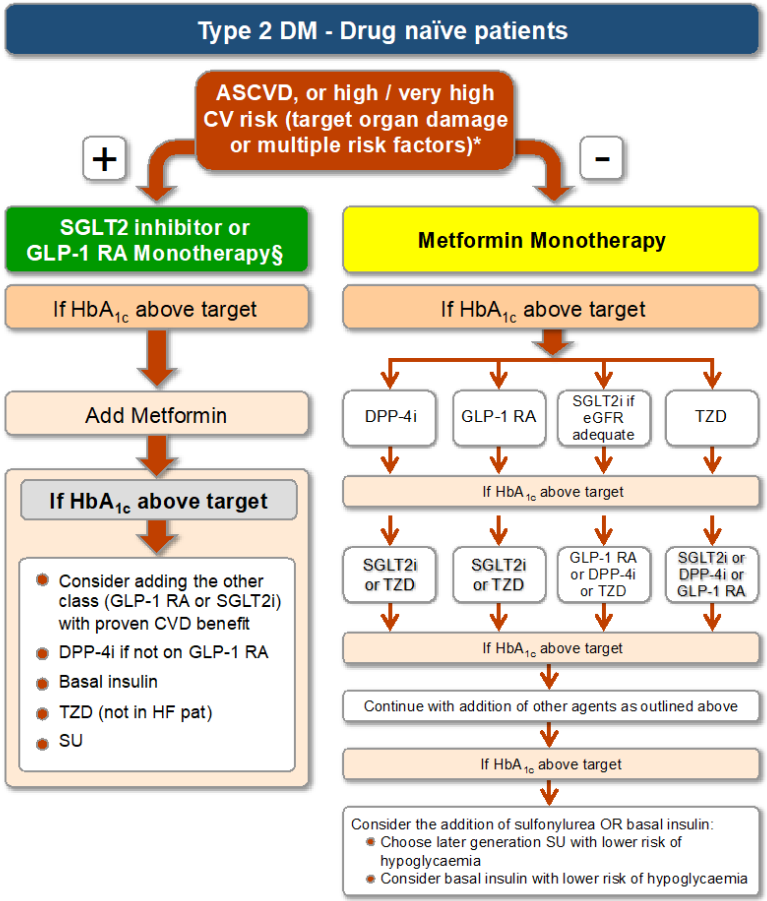
New treatment algorithms



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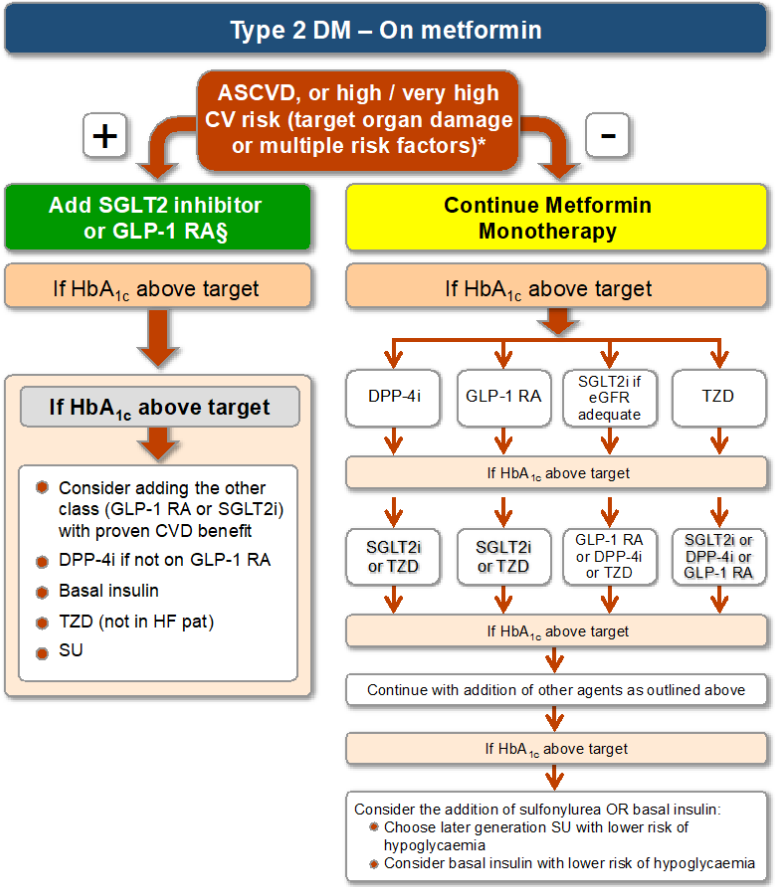

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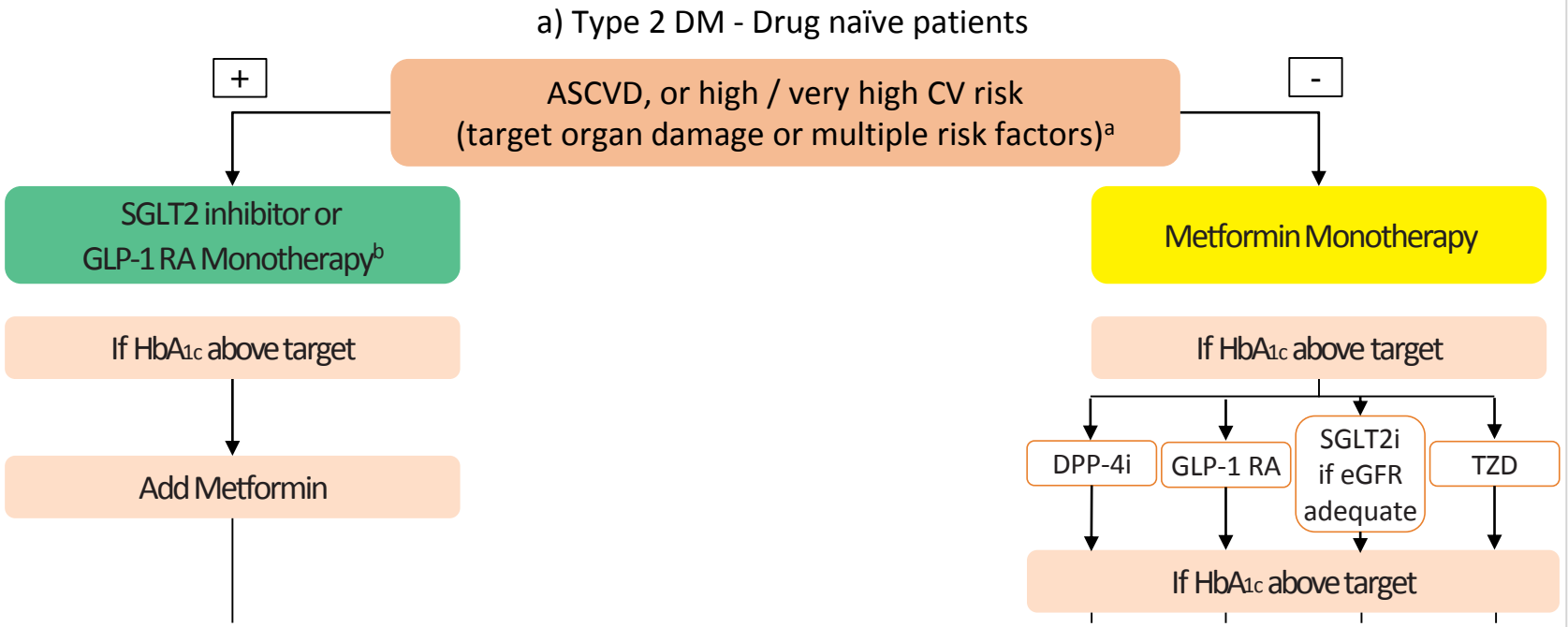
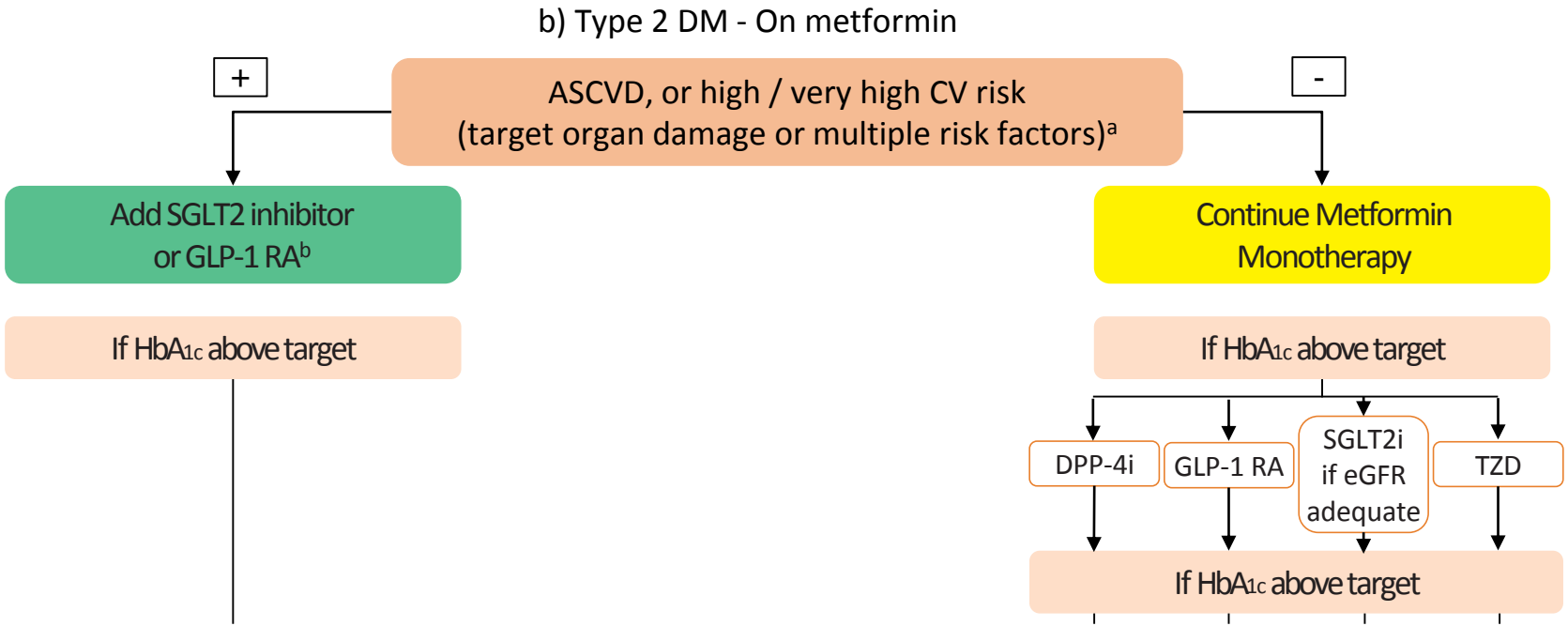
Treatment algorithm in patients with T2DM and ASCVD or high/very high CV risk - drug naïve (1)



ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Treatment algorithm in patients with T2DM and ASCVD or high/very high CV risk - metformin treated (1)



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Recommendations for glucose-lowering treatment in DM (1)

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Recommendations	Class	Level
SGLT2 inhibitors		
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD or at very high/high CV risk to reduce CV events.	I	A
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death.	I	B

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Recommendations for glucose-lowering treatment in DM (2)

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Recommendations	Class	Level
GLP1-RAs		
Liraglutide, semaglutide or dulaglutide are recommended in patients with T2DM and CVD or at very high/high CV risk to reduce CV events.	I	A
Liraglutide is recommended in patients with T2DM and CVD or at very high/high CV risk to reduce the risk of death.	I	B

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Recommendations for glucose-lowering treatment in DM (3)

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Recommendations	Class	Level
Biguanides		
Metformin should be considered in overweight patients with T2DM without CVD and at moderate CV risk.	IIa	C
Insulin		
Insulin-based glycaemic control should be considered in patients with ACS with significant hyperglycaemia (>10 mmol/L or >180 mg/dL), with the target adapted according to comorbidities.	IIa	C

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Recommendations for glucose-lowering treatment in DM (4)

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Recommendations	Class	Level
Thiazolidinediones		
Thiazolidinediones are not recommended in patients with HF.	III	A
DPP4 inhibitors		
Saxagliptin is not recommended in patients with T2DM and a high-risk of HF.	III	B

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Invidualized blood pressure targets

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Change in recommendations

2013	2019
BP targets	
BP target <140/85 mmHg for all	SBP to 130 mmHg and, if well tolerated, <130 mmHg, but not <120 mmHg In older people (>65 years) target SBP to a range of 130–139 mmHg DBP to <80 mmHg but not <70 mmHg
	On-treatment SBP to <130 mmHg for patients at high risk of cerebrovascular events or diabetic kidney disease

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2019 new recommendations (3)

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BP management
Lifestyle changes encouraged in hypertension
RAAS blockers rather than beta-blockers/diuretics for BP control in pre-DM
Initiate pharmacological treatment with the combination of a RAAS blocker with a calcium-channel blocker or thiazide/thiazide-like diuretic
Home BP self-monitoring encouraged in patients with DM
24-h ABPM for BP assessment, and adjustment of antihypertensive treatment

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New lipid targets

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Change in recommendations

2013	2019
Lipid targets	
In patients with T2DM at • high CV risk, an LDL-C target of <2.5 mmol/L (<100 mg/dL) • very high CV risk, an LDL-C target of <1.8 mmol/L (<70 mg/dL)	In patients with T2DM at • moderate CV risk, an LDL-C target of <2.6 mmol/L (<100 mg/dL) • high CV risk, an LDL-C target of <1.8 mmol/L (<70 mg/dL) and LDL-C reduction of at least 50% • very high CV risk, an LDL-C target of <1.4 mmol/L (<55 mg/dL) and LDL-C reduction of at least 50%

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ODYSSEY OUTCOMES

Alirocumab in patients with/without diabetes after ACS

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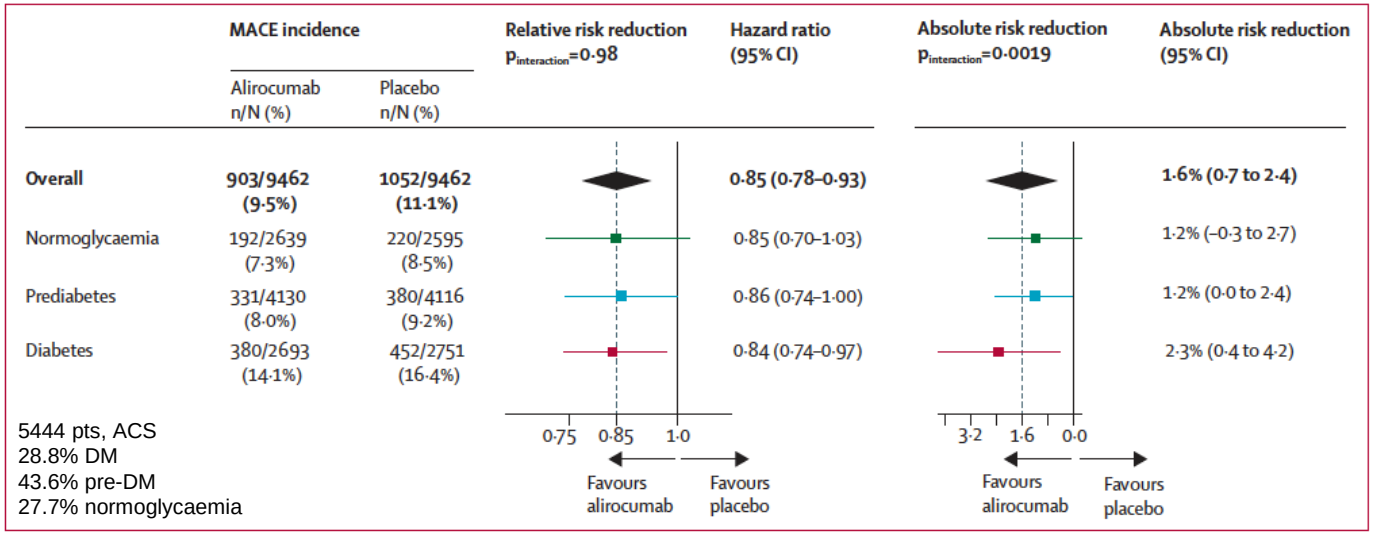
prespecified analysis: *effect by glycaemic status*



Ray KK et al. Lancet Diabetes Endocrinol 2019

2019 new recommendations (7)

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Revascularization
Same revascularization techniques in patients with and without DM
Treatment of HF in DM
Device therapy with an ICD, CRT, or CRT-D
Sacubitril/valsartan instead of ACEIs in HFrEF and DM remaining symptomatic despite treatment with ACEIs, beta-blockers, and mineralocorticoid receptor antagonists
CABG in HFrEF and DM and two- or three-vessel CAD
Ivabradine in patients with HF and DM in sinus rhythm and with a resting heart rate ≥70 beats per minute if symptomatic despite full HF treatment
Aliskiren (direct renin inhibitor) in HFrEF and DM is not recommended

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2019 new recommendations (9)

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DM treatment to reduce HF risk
SGLT2 inhibitor (empagliflozin, canagliflozin, and dapagliflozin) to lower risk of HF hospitalization if eGFR >30 mL/min/1.73 m^2
Metformin in patients with DM and HF if eGFR >30 mL/min/1.73 m^2
GLP1-RAs and DPP4 inhibitors sitagliptin and linagliptin have a neutral effect on risk of HF
Insulin treatment in HF
DPP4 inhibitor saxagliptin in HF is not recommended
Thiazolidinediones (pioglitazone, rosiglitazone) in HF is not recommended

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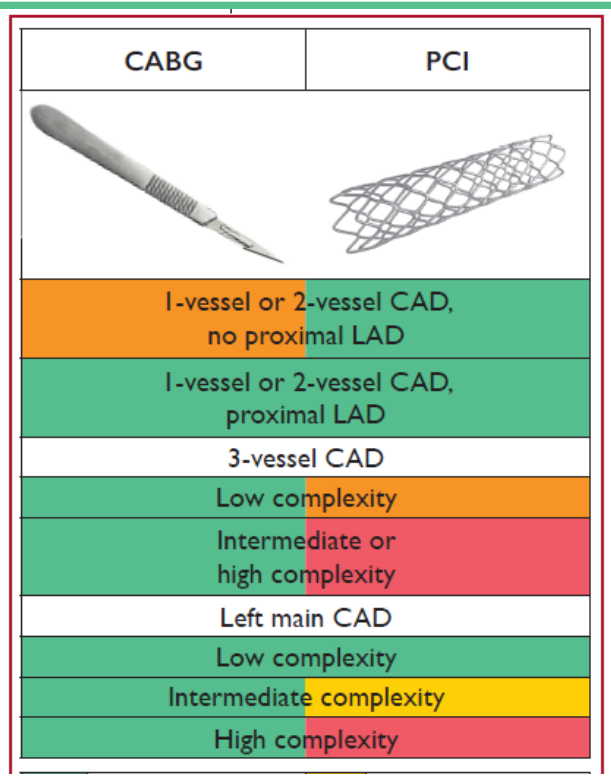
Coronary revascularization

2013	2019
DES rather than BMS in DM	Same tech … (2018 ESC … s)
… as an alternative to CABG in patients with DM and less complex CAD (SYNTAX score …	
CABG recommended in complex CAD (SYNTAX score >22)	

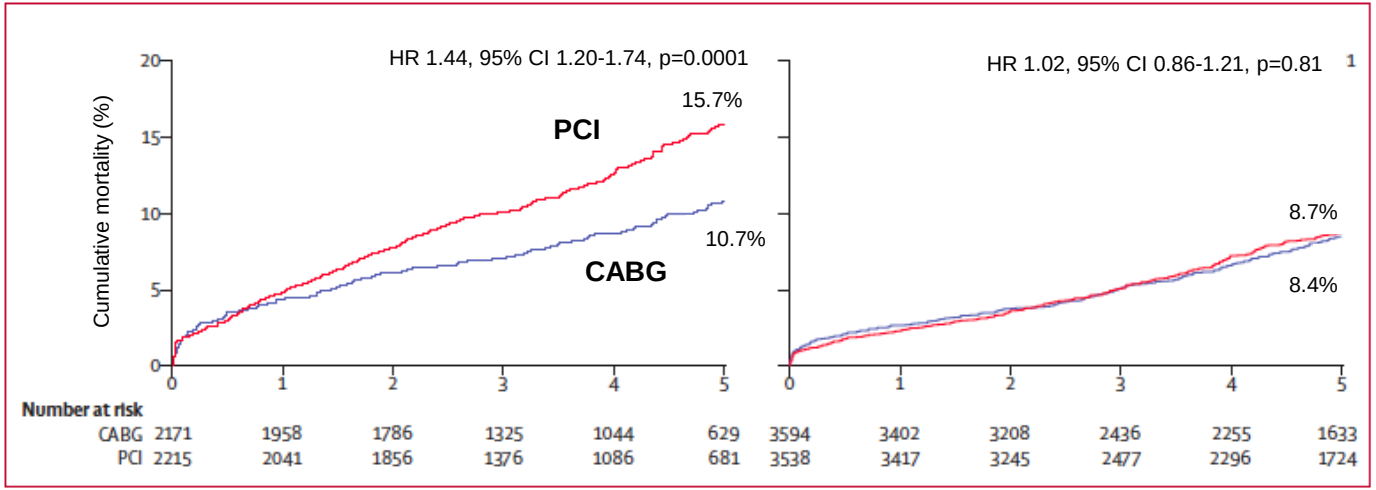


NEW

Impact of diabetes on mortality after CABG vs PCI

Pooled analysis of individual patient data from 11 trials

Diabetes **No Diabetes**



Head SJ et al. Lancet 2018

Antiplatelet therapy in primary prevention in DM

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Change in recommendations

2013	2019
Antiplatelet therapy	
Aspirin for primary prevention is not recommended in DM at low CVD risk	**Aspirin (75–100 mg/day) for primary prevention may be considered in patients with DM at very high/high risk in the absence of clear contraindications**
	Aspirin for primary prevention is not recommended in patients with DM at moderate CV risk

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

2019 new recommendations (5)

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Antiplatelet and antithrombotic drugs

Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, or oral anticoagulant monotherapy who are at high risk of gastrointestinal bleeding

Prolongation of DAPT beyond 12 months should be considered for up to 3 years in patients with DM at very high risk who have tolerated DAPT without major bleeding complications

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Change in recommendations (7)

Management of arrhythmias	
Oral anticoagulation in AF (paroxysmal or persistent)	
VKAs or NOACs (e.g. dabigatran, rivaroxaban, or apixaban)	Prefer NOACs (e.g. dabigatran, rivaroxaban, apixaban, or edoxaban)

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2019 new recommendations (10)

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Management of arrhythmias
Attempts to diagnose structural heart disease in patients with DM with frequent premature ventricular contractions
Hypoglycaemia should be avoided as it can trigger arrhythmias
Diagnosis and management of PAD
Low-dose rivaroxaban 2.5 mg twice daily plus aspirin 100 mg once daily in patients with DM and symptomatic LEAD
Management of CKD
SGLT2 inhibitors to reduce progression of diabetic kidney disease

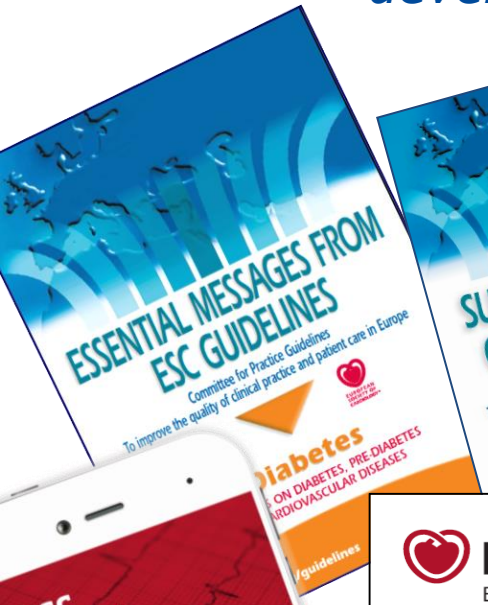
ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

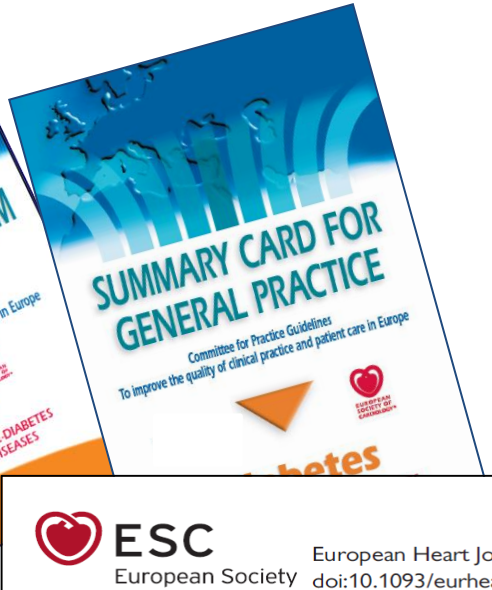
2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases

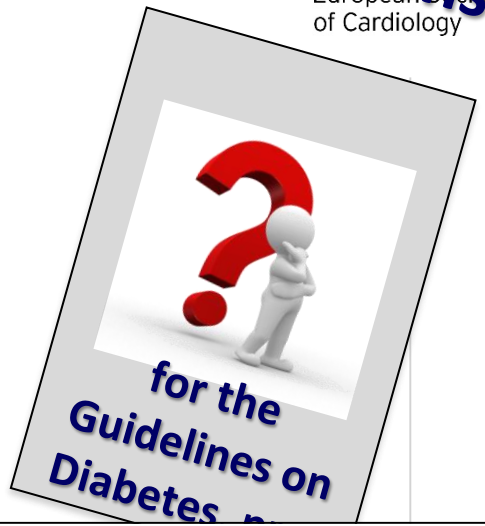
developed in collaboration with EASD

CME-Questions

ESC European Society of Cardiology







DIABETES
Guidelines on Diabetes,
Pre-diabetes and Cardiovascular

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ESC GUIDELINES

ESC Guidelines YEARS

19 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD