



EVENTO TERRITORIALE **SID/AMD LAZIO**

Protezione cardio-renale nel Diabete di Tipo 2:

L'integrazione tra **Medici di Medicina generale**
e **Specialisti nella cura del Diabete**

RIETI 17 GIUGNO 2023

«La gestione integrata del paziente a rischio alto/molto alto: le raccomandazioni dei Cardiologi»

Dr.ssa Marzia Schiavoni -U.O.C. Cardiologia -Ospedale San Camillo De Lellis - Rieti

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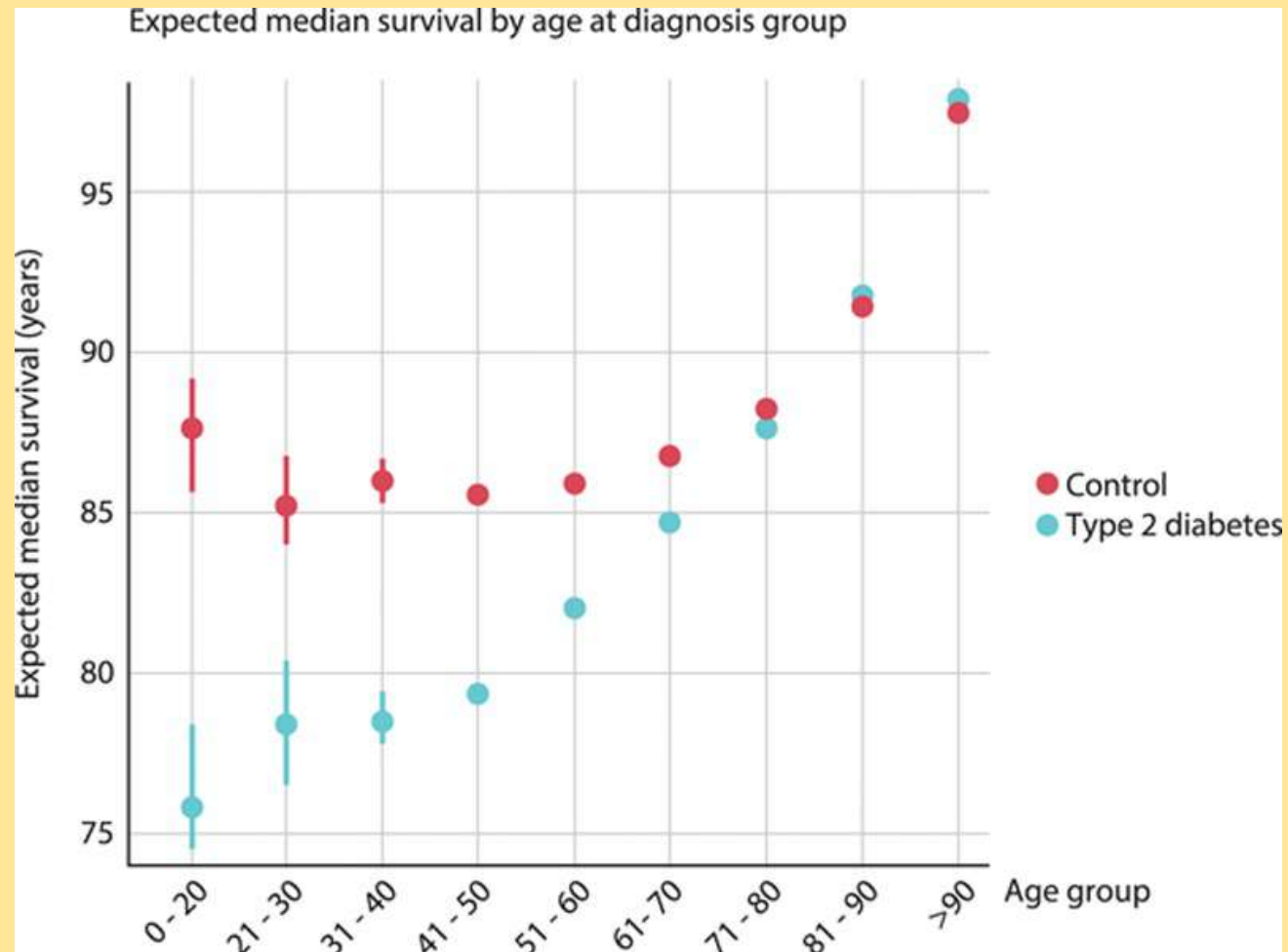
Circulation

ORIGINAL RESEARCH ARTICLE

Age at Diagnosis of Type 2 Diabetes

Mellitus and Associations With Cardiovascular and Mortality Risks

Naveed Sattar, FMedSci* Araz Rawshani, PhD* Stefan Franzén, PhD Aidin Rawshani, MD Ann-Marie Svensson, PhD Annika Rosengren, PhD Darren K. McGuire, MD, MHSc Björn Eliasson, PhD Soffia Gudbjörnsdóttir, PhD, *Circulation*. 2019;139:2228–2237.

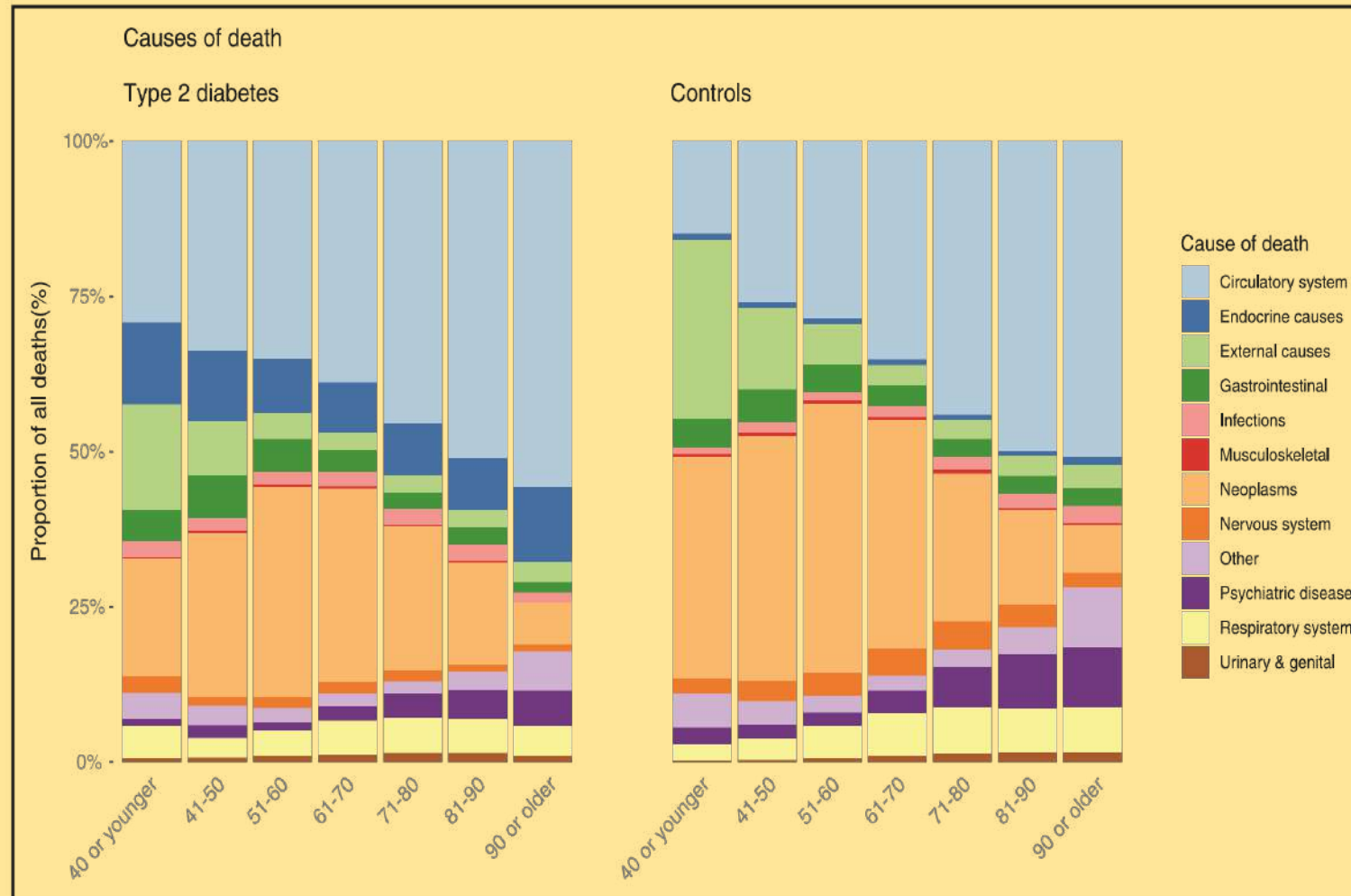


Age at diagnosis of type 2 diabetes mellitus and loss of life-years in persons without previous cardiovascular disease and without any restriction on the duration of type 2 diabetes mellitus.

Age at Diagnosis of Type 2 Diabetes

Mellitus and Associations With Cardiovascular and Mortality Risks

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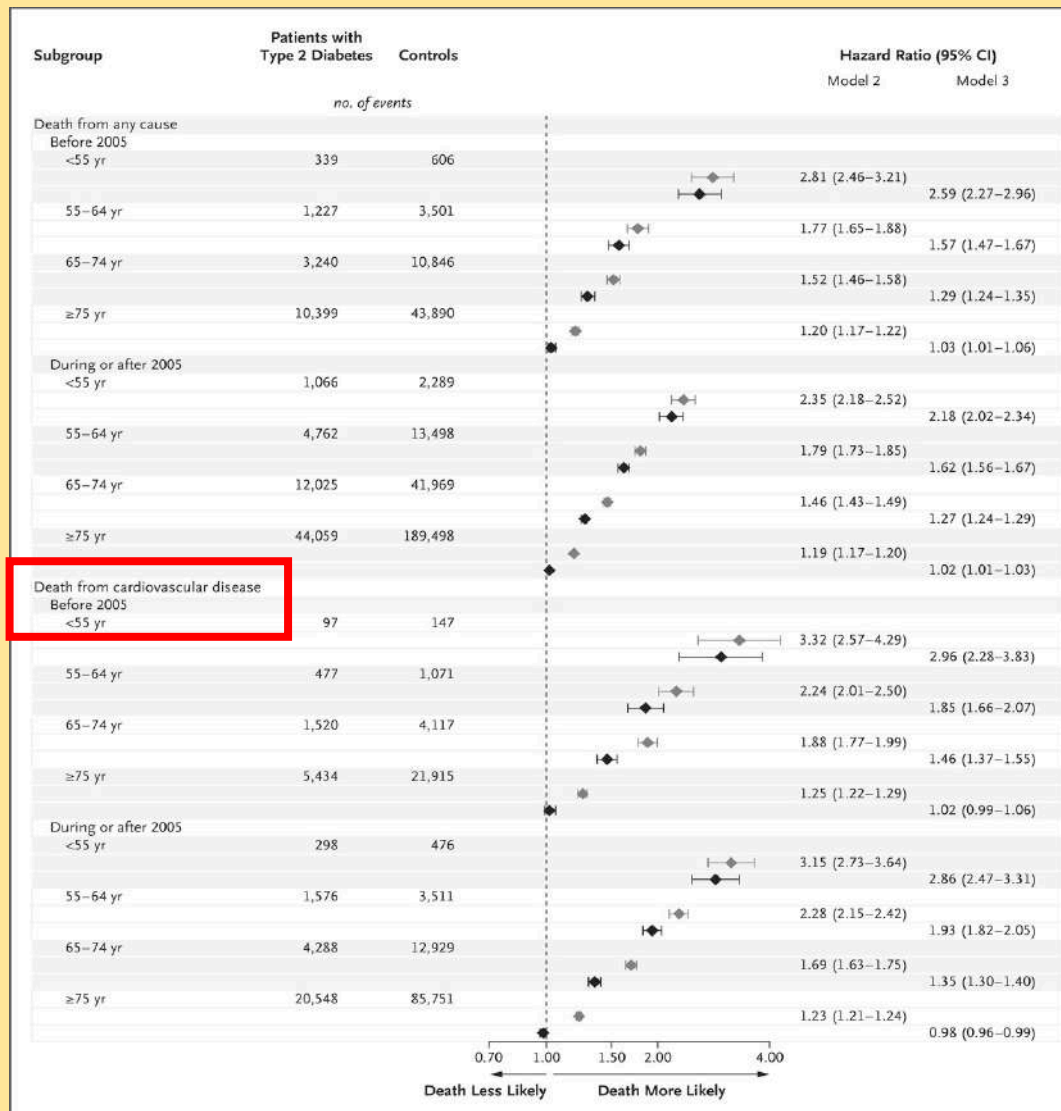
ORIGINAL RESEARCH ARTICLE

Figure 3. Causes of death in relation to age at onset of type 2 diabetes mellitus diagnosis and corresponding matched controls.



Excess Mortality among Persons with Type 2 Diabetes

Mauro Tancredi, M.D., Annika Rosengren, M.D., Ann-Marie Svensson, Ph.D., Mikhail Kosiborod, M.D., Aldina Pivodic, M.Sc., Soffia Gudbjörnsdottir, M.D., Ph.D., Hans Wedel, Ph.D., Mark Clements, M.D., Ph.D., Sofia Dahlqvist, and Marcus Lind, M.D., Ph.D. N Engl J Med 2015;373:1720-1732.



Adjusted Hazard Ratios for Death from Any Cause and Death from Cardiovascular Causes, According to Year Range and Age Category

Clinical burden of diabetes in Italy in 2018: a look at a systemic disease from the ARNO Diabetes Observatory

Enzo Bonora¹, Salvatore Cataudella², Giulio Marchesini³, Roberto Miccoli⁴, Olga Vaccaro⁵, Gian Paolo Fadini⁶, Nello Martini⁷, Elisa Rossi², under the mandate of the Italian Diabetes Society, *BMJ Open Diab Res Care* 2020;8:e001191

	Diabetes (n=697 208)	No diabetes (n=697 208)
Expense items		
Overall	€2833	€1268
All medications	€1116 (39.4%)	€498 (39.3%)
Antihyperglycemic drugs	€249 (8.8%)	€0
Other drugs	€867 (30.6%)	€498 (39.3%)
Devices (strips, lancets, needle, syringes)	€98 (3.4%)	€0
Outpatient care (exams, visits)	€467 (16.5%)	€273 (21.5%)
Hospital care	€1152 (40.7%)	€497 (39.2%)

Overall and specific costs in diabetic and non-diabetic subjects (in euros per subject in year 2018)

CV risk categories in patients with DM

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 plus any other additional risk factor
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors

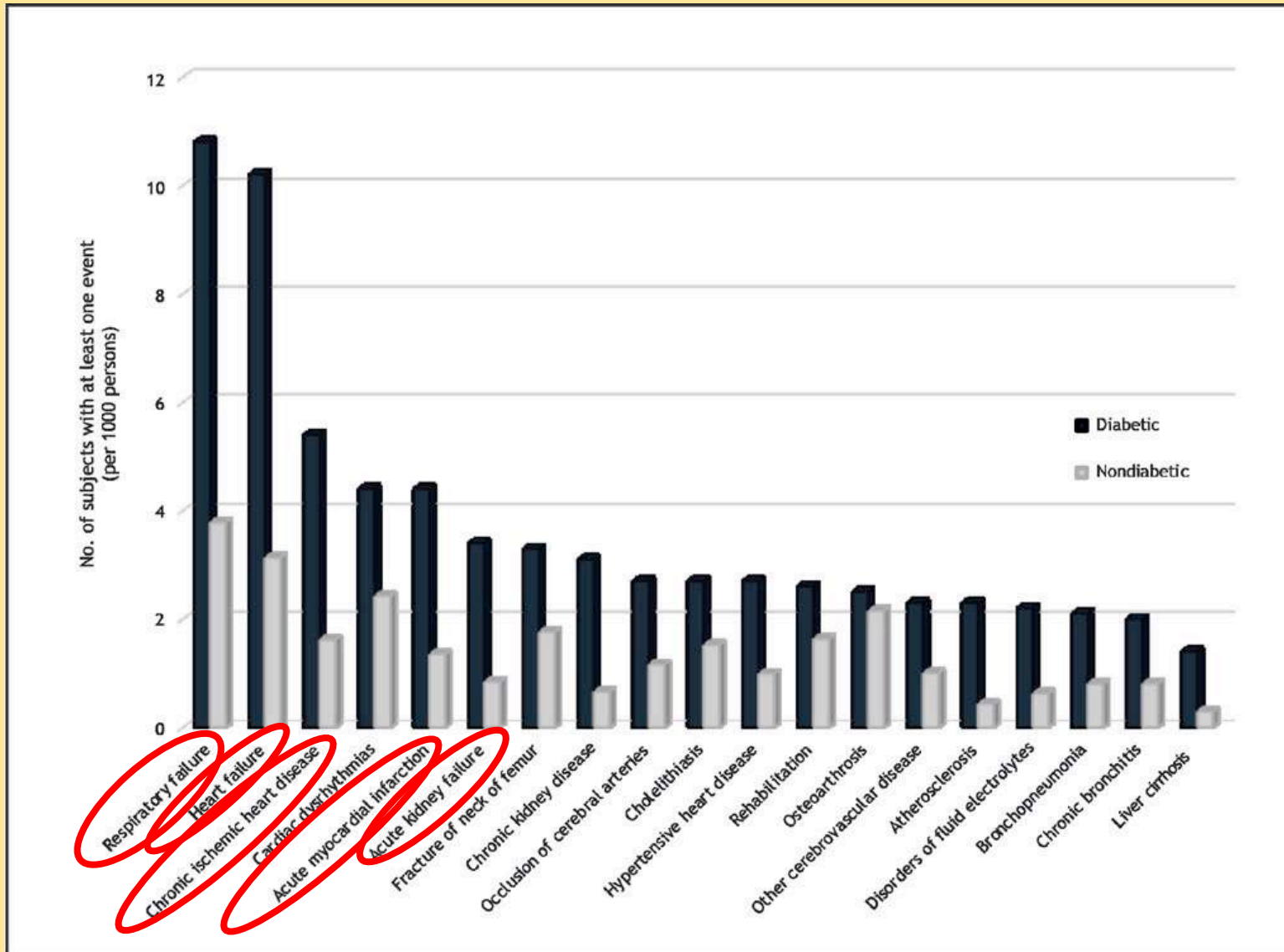
^aProteinuria, renal impairment defined as eGFR < 30mL/min/1.73m², left ventricular hypertrophy, or retinopathy.

^bAge, hypertension, dyslipidaemia, smoking, obesity

Clinical burden of diabetes in Italy in 2018: a look at a systemic disease from the ARNO Diabetes Observatory

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5 Gian Paolo Fadini ⁶, Nello Martini⁷, Elisa Rossi², under the mandate of the Italian Diabetes Society, *BMJ Open Diab Res Care* 2020;8:e001191



Number of subjects with at least one primary diagnosis of selected diseases in discharge medical reports

Recommendations for the management of BP in patients with DM and pre-DM (1)

Recommendations	Class	Level
Treatment targets		
Antihypertensive drug treatment is recommended for people with DM when office BP is >140/90 mmHg.	I	A
It is recommended that patients with hypertension and DM are treated in an individualized manner. The BP goal is to target SBP to 130 mmHg and <130 mmHg if tolerated, but not <120 mmHg. In older people (aged >65 years), the SBP goal is to a range of 130 - 139 mmHg.	I	A
It is recommended to target DBP <80 mmHg, but not <70 mmHg.	I	C
An on-treatment SBP of <130 mmHg may be considered in patients at particularly high risk of a cerebrovascular event, such as those with a history of stroke.	IIb	C

©ESC

Recommendations for the management of BP in patients with DM and pre-DM (3)

Recommendations	Class	Level
Treatment and evaluation		
It is recommended that treatment is initiated with a combination of a RAAS blocker with a calcium channel blocker or thiazide/thiazide-like diuretic.	I	A
In patients with IFG or IGT, RAAS blockers should be preferred to beta-blockers or diuretics to reduce the risk of new-onset DM.	IIa	A
The effects of GLP1-RAs and SGLT2 inhibitor on BP should be considered.	IIa	C

Recommendations for the management of dyslipidaemia with lipid-lowering drugs (1)

Recommendations	Class	Level
Targets		
In patients with T2DM at moderate CV risk, an LDL-C target of <2.6 mmol/L (<100 mg/dL) is recommended.	I	A
In patients with T2DM at high CV risk, an LDL-C target of <1.8 mmol/L (<70 mg/dL) and LDL-C reduction of at least 50% is recommended.	I	A
In patients with T2DM at very high CV risk, an LDL-C target of <1.4 mmol/L (<55 mg/dL) and LDL-C reduction of at least 50% is	I	B
In patients with T2DM, a secondary goal of a non-HDL-C target of <2.2 mmol/L (<85 mg/dL) in very high CV risk patients, and <2.6 mmol/L (<100 mg/dL) in high CV risk patients, is recommended.	I	B

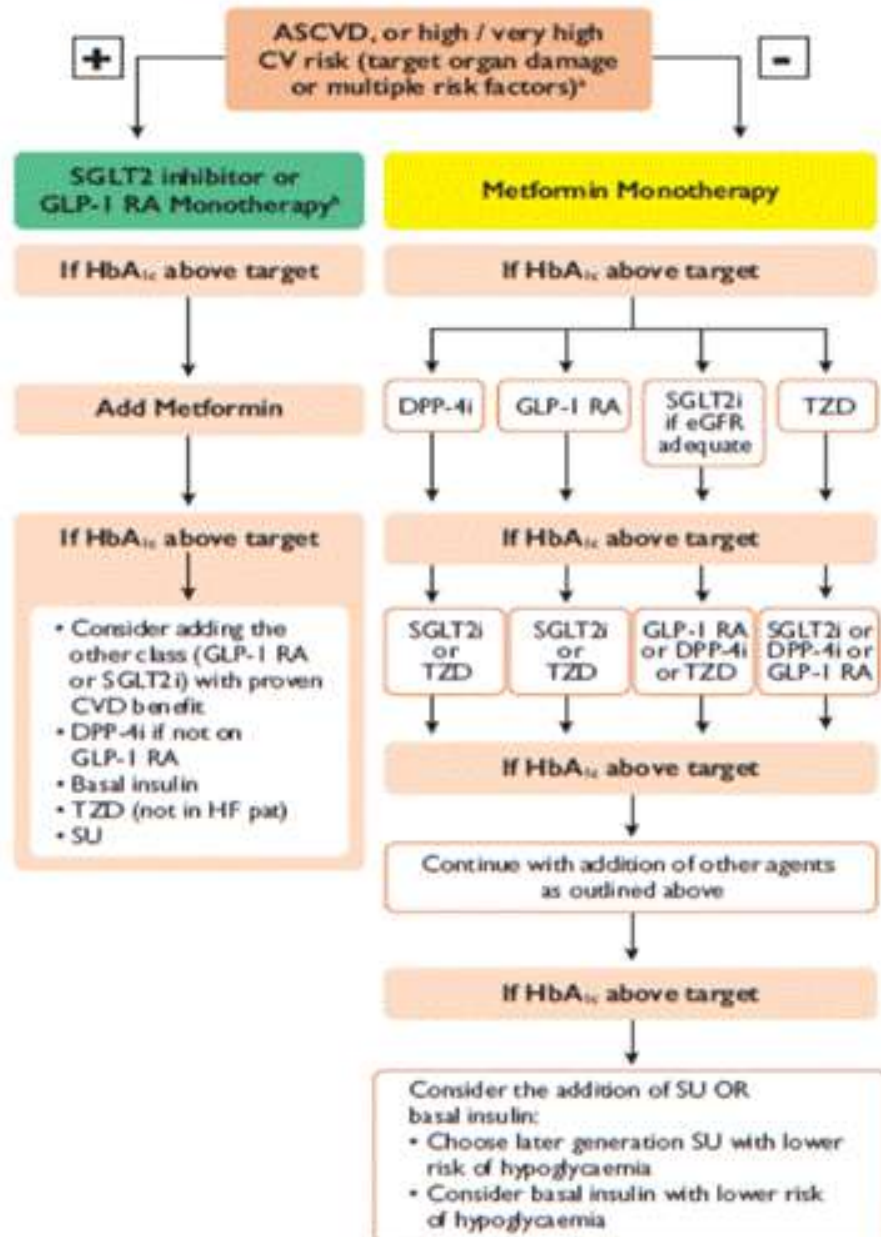
Recommendations for the management of dyslipidaemia with lipid-lowering drugs (2)

Recommendations	Class	Level
Treatment		
Statins are recommended as the first-choice lipid-lowering treatment in patients with DM and high LDL-C levels: administration of statins is defined based on the CV risk profile of the patient and the recommended LDL-C (or non-HDL-C) target levels.	I	A
If the target LDL-C is not reached, combination therapy with ezetimibe is recommended.	I	B
In patients at very high CV risk, with persistent high LDL-C despite treatment with maximum tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor is recommended.	I	A

Recommendations for glycaemic control in individuals with DM

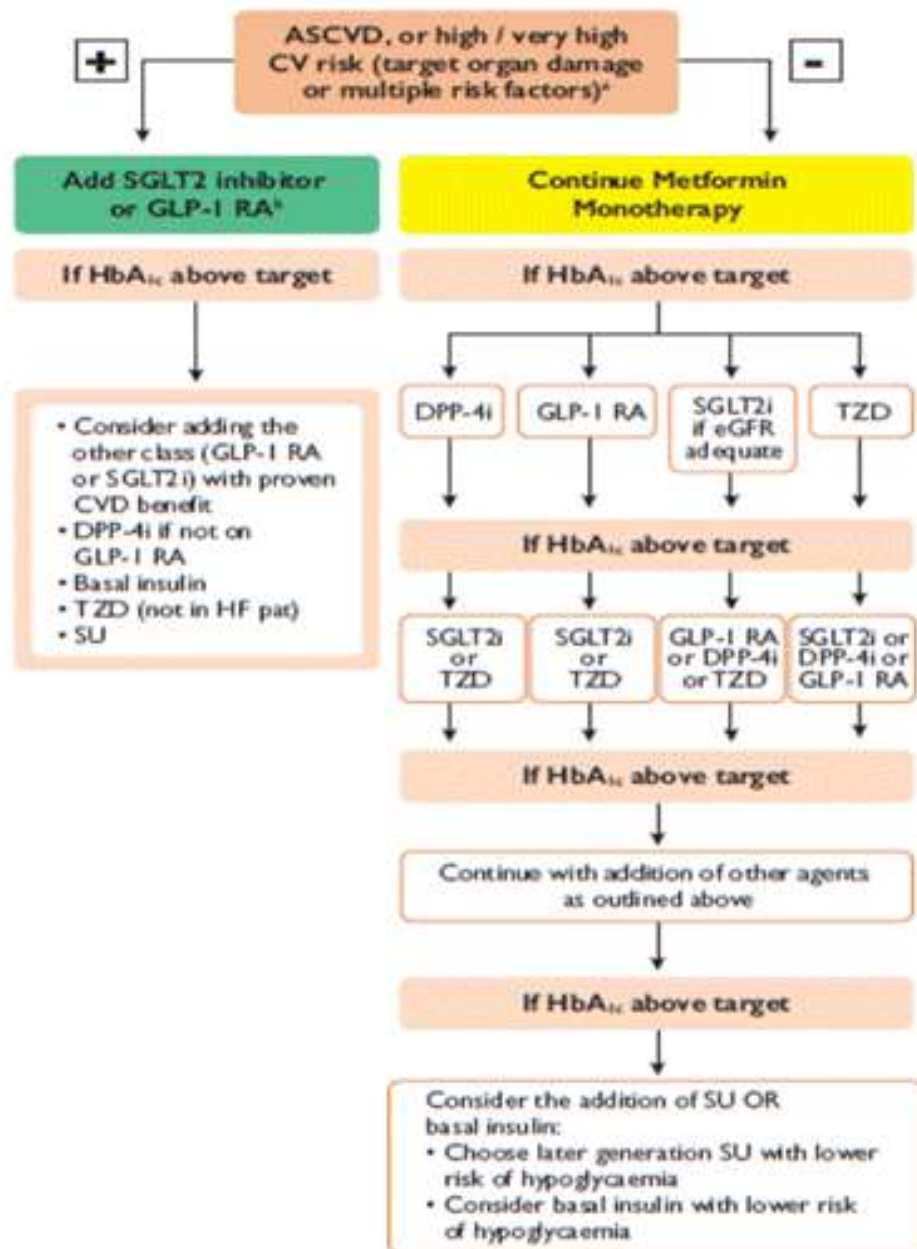
Recommendations	Class	Level
It is recommended to apply tight glucose control, targeting a near-normal HbA1c (<7.0% or <53 mmol/mol), to decrease microvascular complications in DM.	I	A
It is recommended that HbA1c targets are individualized according to duration of DM, comorbidities, and age.	I	C
Avoidance 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

A Type 2 DM - Drug naïve patients



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

B Type 2 DM - On metformin



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

2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD)

Recommendations for glucose-lowering treatment for patients with diabetes

Recommendations	Class ^a	Level ^b
SGLT2 inhibitors		
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD, or at very high/high CV risk, ^c to reduce CV events. ^{306,308,309,311}	I	A
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death. ³⁰⁶	I	B
GLP1-RAs		
Liraglutide, semaglutide, or dulaglutide are recommended in patients with T2DM and CVD, or at very high/high CV risk, ^c to reduce CV events. ^{176,299–300,302–303}	I	A
Liraglutide is recommended in patients with T2DM and CVD, or at very high/high CV risk, ^c to reduce the risk of death. ¹⁷⁶	I	B
Biguanides		
Metformin should be considered in overweight patients with T2DM without CVD and at moderate CV risk. ^{146,149}	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. ^{260–262}	IIa	C
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. ²⁹¹	III	B

ACS = acute coronary syndromes; CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; DPP4 = dipeptidyl peptidase-4; GLP1-RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; SGLT2 = sodium-glucose co-transporter 2; T2DM = type 2 diabetes mellitus.

CORRESPONDENCE



Incidence of Chronic Kidney Disease among Adults with Diabetes, 2015–2020

TO THE EDITOR: The prevalence of kidney failure warranting dialysis or transplantation more than doubled between 2000 and 2019 to nearly 800,000 persons in the United States, with diabetes as the leading cause in 47% of those affected.^{1,2} The incidence of chronic kidney disease (CKD) among patients with diabetes is unknown, yet such data are vital for identifying high-risk populations, determining the effectiveness of interventions, and assessing the effects on health care delivery and public health responses.

a positive result was a glomerular filtration rate lower than 60 ml per minute per 1.73 m² of body-surface area (estimated according to the 2021 Chronic Kidney Disease Epidemiology Collaboration creatinine equation), a urinary albumin-to-creatinine ratio (with albumin measured in milligrams and creatinine measured in grams) of 30 or higher, or a urinary protein-to-creatinine ratio (with protein measured in milligrams and creatinine measured in grams) of 150 or higher (Table S2). The overall incidence of CKD was standard-

CKD classification by eGFR and albuminuria

eGFR (mL/min/1.73 m ²)	Albuminuria categories (albumin:creatinine ratio spot urine)			
	A1 (<3 mg/mmol)	A2 (3–30 mg/mmol)	A3 (>30 mg/mmol)	
G1 (≥90)	No CKD	G1 A2	G1 A3	Increasing risk ↓
G2 (60–89)	No CKD	G2 A2	G2 A3	
G3a (45–59)	G3a A1	G3a A2	G3a A3	
G3b (30–44)	G3b A1	G3b A2	G3b A3	
G4 (15–29)	G4 A1	G4 A2	G4 A3	
G5 (<15)	G5 A1	G5 A2	G5 A3	
	Increasing risk →			

Recommendations for the prevention and management of CKD in patients with DM (1)



Recommendations	Class	Level
It is recommended that patients with DM are screened annually for kidney disease by assessment of eGFR and urinary albumin:creatinine ratio.	I	A
Tight glucose control, targeting HbA1c (<7.0% or <53 mmol/mol) is recommended to decrease microvascular complications in DM.	I	A
It is recommended that patients with hypertension and DM are treated in an individualized manner, SBP to 130 mmHg and <130 mmHg if tolerated, but not <120 mmHg. In older people (aged >65 years) the SBP goal is to a range of 130–139 mmHg.	I	A

Recommendations for the prevention and management of CKD in patients with DM (2)

Recommendations	Class	Level
A RAAS blocker (ACEI or ARB) is recommended for the treatment of hypertension in DM, particularly in the presence of proteinuria, microalbuminuria, or LVH.	I	A
Treatment with a SGLT2 inhibitor (empagliflozin, canagliflozin, dapagliflozin) is associated with a lower risk of renal endpoints and is recommended if eGFR is 30 to <90 mL/min/1.73 m ²).	I	B
Treatment with the GLP1-RAs liraglutide and semaglutide is associated with a lower risk of renal endpoints and should be considered for DM treatment if eGFR is >30 mL/min/1.73m ² .	IIa	B

Recommendations for antiplatelet therapy in primary prevention in DM

Recommendations	Class	Level
In patients with DM at high/very high risk, aspirin (75–100 mg/day) may be considered in primary prevention in the absence of clear contraindications.	IIb	A
In patients with DM at moderate CV risk, aspirin for primary prevention is not recommended.	III	B
Gastric protection		
When low-dose aspirin is used, proton pump inhibitors should be considered to prevent gastrointestinal bleeding.	IIa	A

CABG	PCI
	
1-vessel or 2-vessel CAD, no proximal LAD	
1-vessel or 2-vessel CAD, proximal LAD	
3-vessel CAD	
Low complexity	
Intermediate or high complexity	
Left main CAD	
Low complexity	
Intermediate complexity	
High complexity	
Class I	Class IIa
Class IIb	Class III

Recommendations for coronary revascularization

Phenotypes of left ventricular dysfunction

	HFpEF	HFmrEF	HFrEF
Criterion 1	Symptoms and/or signs	Symptoms and/or signs	Symptoms and/or signs
Criterion 2	LVEF $\geq 50\%$	LVEF 40–49%	LVEF $< 40\%$
Criterion 3	1. Elevated natriuretic peptides 2. At least one additional criterion: a) structural heart disease (i.e. LVH and/ or LAE) b) Diastolic dysfunction	1. Elevated natriuretic peptides 2. At least one additional criterion: a) structural heart disease (i.e. LVH and/ or LAE) b) Diastolic dysfunction	None

Recommendations for T2DM treatment to reduce heart failure risk (1)

Recommendations	Class	Level
SGLT2 inhibitors (empagliflozin, canagliflozin, dapagliflozin) are recommended to lower risk of HF hospitalization in patients with DM.	I	A
Metformin should be considered for DM treatment in patients with HF, if the eGFR is stable and $>30 \text{ mL/min/1.73 m}^2$.	IIa	C
GLP1-RAs (lixisenatide, liraglutide, semaglutide, exenatide, dulaglutide) have a neutral effect on the risk of HF hospitalization, and may be considered for DM treatment in patients with HF.	IIb	A

Recommendations for the use of laboratory, ECG, and imaging testing for CV risk assessment in asymptomatic patients with DM (1)

Recommendations	Class	Level
Routine assessment of microalbuminuria is indicated to identify patients at risk of developing renal dysfunction or at high risk of future CVD.	I	B
A resting ECG is indicated in patients with DM diagnosed with hypertension or with suspected CVD.	I	C
Assessment of carotid and/or femoral plaque burden with arterial ultrasonography should be considered as a risk modifier in asymptomatic patients with DM.	IIa	B

Recommendations for the use of laboratory, ECG, and imaging testing for CV risk assessment in asymptomatic patients with DM (2)

Recommendations	Class	Level
CAC score with CT may be considered as a risk modifier in the CV risk assessment of asymptomatic patients with DM at moderate risk.	IIb	B
CTCA or functional imaging (radionuclide myocardial perfusion imaging, stress cardiac magnetic resonance imaging, or exercise or pharmacological stress echocardiography) may be considered in asymptomatic patients with DM for screening of CAD.	IIb	B

Recommendations for lifestyle modifications in DM and pre-DM (1)

Recommendations	Class	Level
Smoking cessation guided by structured advice is recommended in all individuals with DM and pre-DM.	I	A
Lifestyle intervention is recommended to delay or prevent the conversion of pre-DM states, such as IGT, to T2DM.	I	A
Reduced calorie intake is recommended for lowering excessive body weight in individuals with pre-DM and DM.	I	A

Recommendations for lifestyle modifications in DM and pre-DM (2)

Recommendations	Class	Level
Moderate-to-vigorous physical activity, notably a combination of aerobic and resistance exercise, for ≥ 150 min/week is recommended for the prevention and control of DM, unless contraindicated, such as when there are severe comorbidities or a limited life expectancy.	I	A
A Mediterranean diet, rich in polyunsaturated and monounsaturated fats, should be considered to reduce CV events.	IIa	B
Vitamin or micronutrient supplementation to reduce the risk of DM or CVD in DM is not recommended.	III	B

Quali direzioni future???

Diabetes and cardiovascular disease: it's time to apply the evidence

European Heart Journal: Acute Cardiovascular Care
 2020, Vol. 9(6) 586–588

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Peter J Grant¹ and Nikolaus Marx²

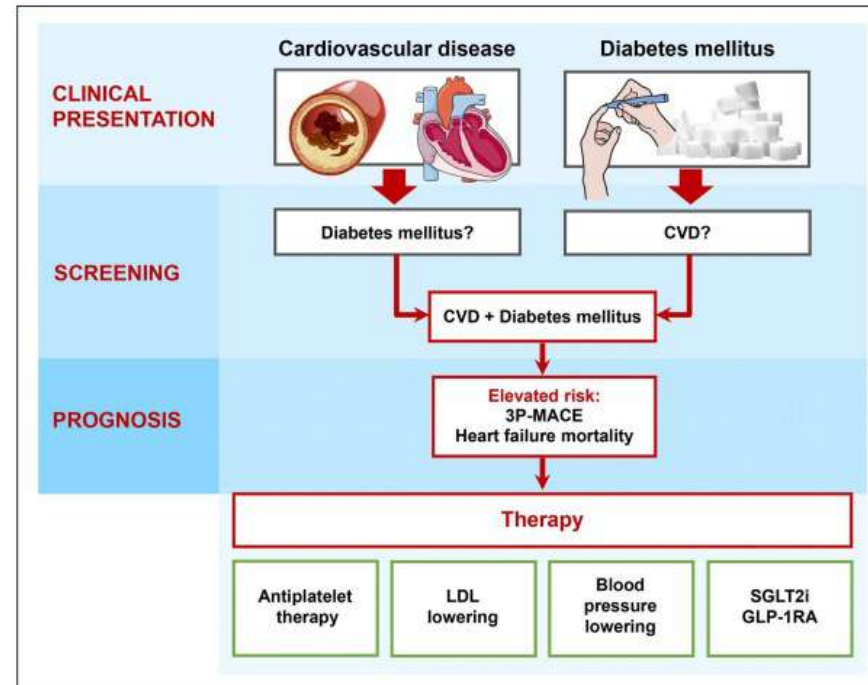


Figure 1. Proposal for screening for cardiovascular disease in patients with diabetes and for the presence of diabetes in patients identified with cardiovascular disease (e.g. coronary artery disease, heart failure). As these two conditions and their complications frequently co-exist, it is critical for the individual patient's wellbeing that the identification of one condition leads to a search for the other, and that both are treated using the most up-to-date evidence-based approaches.

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

3.2.3.8 Risk estimation and risk factor treatment in persons with type 2 diabetes mellitus

Most adults with type 2 DM are at high or very high risk for future CVD, particularly from middle age onwards. On average, type 2 DM doubles CVD risk and reduces life expectancy by 4-6 years, with absolute risks highest in those with any target organ damage (TOD). Type 2 DM also increases the risk for cardiorenal outcomes, in particular HF and CKD. Relative risks (RRs) for CVD in type 2 DM are higher at younger ages of onset and are modestly higher in women compared with men.⁸⁷ Smoking cessation and adoption of a healthy lifestyle are recommended for all people with type 2 DM, and risk factor treatment should be considered in all people with DM, at least those above the age of 40 years (see [sections 4.6](#) and [4.7](#)). Still, there is a wide range in individual risk for CVD events, especially after initial risk factor management.⁸⁸

11193

Does pre-diabetes predict the extent of coronary artery disease?

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Funding Acknowledgements: Type of funding sources: None.

Background: Extensive coronary artery disease (CAD) is common in diabetes mellitus. This relation between the extent of CAD and prediabetes (pDM) is less well established.

Purpose: To explore whether non-diabetic hyperglycaemia, assessed by HbA1c, is associated with extent of angiographic CAD, independent of traditional cardiovascular risk factors.

Methods: Retrospective cohort analysis of consecutive patients, without known DM undergoing coronary angiography for stable angina, who were screened for hyperglycaemia over 18 months. HbA1c was measured; pre-diabetes was defined as HbA1c 5.7-6.4%. Extent of CAD was assessed using the SYNTAX score. Presence of CAD was defined as visually estimated $\geq 50\%$ luminal obstruction in arteries ≥ 1.5 mm diameter. Age, BMI, risk factors for CAD, HbA1c, total and LDL-cholesterol were recorded. The pre-diabetes and normal groups were compared using Mann-Whitney test for continuous variables and chi-squared test for categorical variables. Multiple logistic and linear regressions were used to assess the effect variables on SYNTAX score. Spearman rank correlation was used to assess the relation between HbA1c and SYNTAX score.

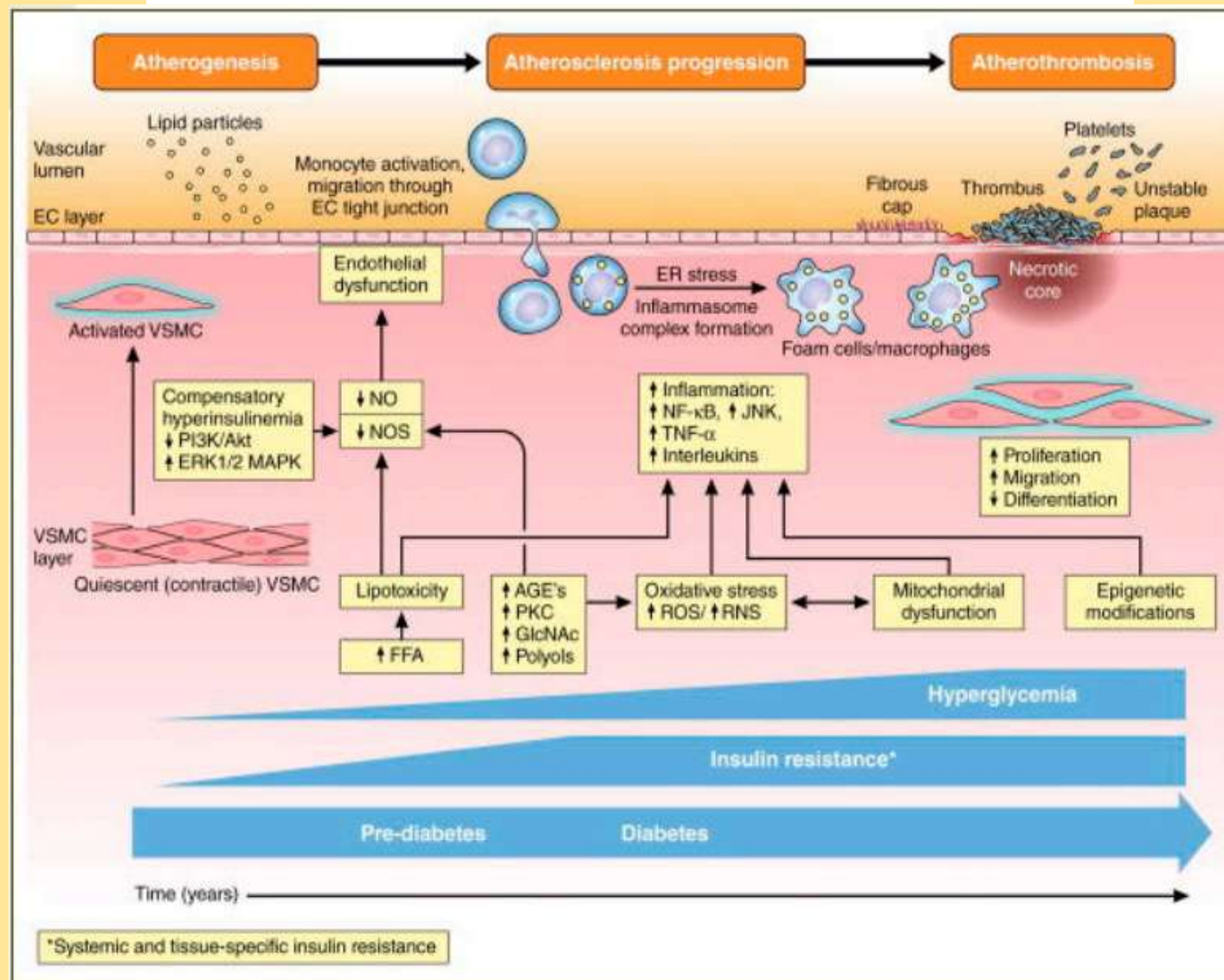
Results: 1071 patients had angiograms done. 207 had DM, 19 had new diagnosis of DM and 181 missed the screening leaving 664 who had HbA1c measured. 51 poor quality angiograms were excluded from SYNTAX calculation. Data was analysed for 613 (306 normal, 307 pDM) patients. The patients with prediabetes were older, had higher prevalence of risk factors, BMI, fasting glucose and SYNTAX score. HbA1c (OR 2.07, 95% CI 1.32 to 3.25, $p=0.002$) and the presence of pDM (OR 1.89, 95% CI 1.32 to 2.69, $p<0.001$) independently predicted the presence of CAD. HbA1c (Coefficient 2.42, SE 1.09, $p=0.027$) and the presence of pDM (Coefficient 2.25, SE 0.92, $p=0.015$) independently predicted the SYNTAX score. The correlation between HbA1c and SYNTAX score was weak but significant (Spearman's coefficient 0.206, 95% CI 0.129 to 0.281, $p<0.0001$).

Conclusion: HbA1c predicts the extent of CAD as measured by SYNTAX score in patients without known diabetes. Presence of pre-diabetes is an independent predictor of extent of CAD.

FATTORI E INDICATORI DI RISCHIO

DIABETE

LUIGI GENTILE



Recommendations for patient-centred care in DM

Recommendations	Class	Level
Group-based structured education programmes are recommended in patients with DM, to improve DM knowledge, glycaemic control, disease management, and patient empowerment.	I	A
Patient-centred care is recommended to facilitate shared control and decision-making within the context of patient priorities and goals.	I	C
Provision of individual empowerment strategies should be considered to enhance self-efficacy, self-care, and motivation in patients with DM.	Ila	B

Grazie per l'attenzione!!!