





ESC Pocket Guidelines

Diabetes, pre-diabetes, and cardiovascular diseases*

The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD)

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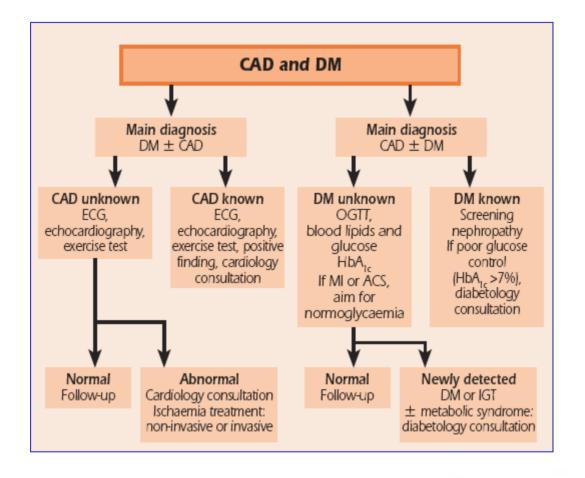
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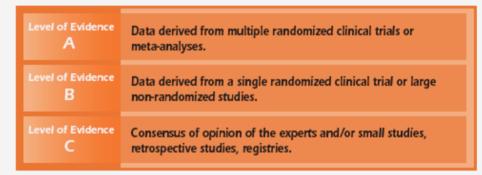




Classes of recommendations

Levels of evidence

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





Recommended treatment targets for patients with diabetes and CAD

	Variable	Treatment target		Variable	Treatment target
Blood pressure	Systolic/diastolic (mm Hg)	< 130/80	Life style counselling	Smoking cessation	Obligatory
	In case of renal impairment or proteinuria			Regular physical activity (min/day)	> 30-45
	> 1 g/24 h	< 125/75		Weight control BMI (kg/m²)	< 25
Glycaemic control	HbA,, (%)*	≤ 6.5		In case of overweight, weight reduction (%)	10
	Glucose (venous plasma; mmol/L) mg/dL			Waist circumference (optimum; ethnic specific; cm) Men (European)	< 94
	Fasting	< 6.0 (108)		Women (European)	< 80
	Post-prandial (peak)			Dietary habits	
	Type 1 diabetes	7.5 -9.0 (135-160)		Salt intake (g/day)	<6
	Type 2 diabetes	< 7.5 (135)		Fibre intake	> 30 g per day
Lipid profile (mmol/L)	Total cholesterol	< 4.5 (175)		Liquid mono- and disaccharides	avoid
(mg/dL)	LDL cholesterol	- 1.0./70l		Fat intake (% of dietary energy)	≤ 30-35
		≤ 1.8 (70)		Saturated	< 10
	HDL cholesterol	- 10 40	Polyunsaturated	Trans-fat	<2
		> 1.0 (40)		Polyunsaturated n-6	4-8
	Women	> 1.2 (46)		Polyunsaturated n-3	2 g/day of linolenic acid
	Triglycerides**	< 1.7 (150)		1 Glydr Isaldrated 175	and 200 mg/day of very
	Total/HDL cholesterol**	< 3			long chain fatty acids



Definition, classification and screening of diabetes and pre-diabetic glucose abnormalities

Recommendation	Class	Level
The definition and diagnostic classification of diabetes and its pre-states should be based on the level of the subsequent risk of cardiovascular complications.	1	В
Early stages of hyperglycaemia and asymptomatic type 2 diabetes are best diagnosed by an oral glucose tolerance test (OGTT) that gives both fasting and 2 h post-load glucose values.	1	В
Primary screening for the potential type 2 diabetes can be done most efficiently by using a non-invasive risk score, combined with a diagnostic OGTT in people with high score values.	1	Α

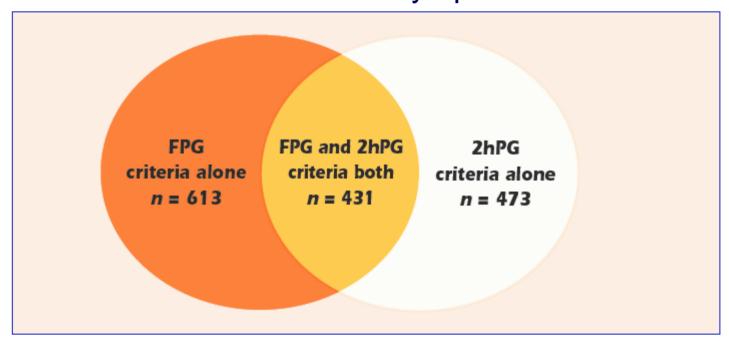


Criteria used for gluco-metabolic classification from WHO (1999) and ADA (1997 and 2003)

Glucometabolic category	Source	Classification criteria Venous plasma glucose mmoUL (mg/dL)
Normal glucose regulation (NGR)	WHO	FPG < 6.1 (110) + 2 h PG < 7.8 (140)
	ADA (1997)	FPG < 6.1 (110)
	ADA (2003)	FPG < 5.6 (100)
Impaired fasting glucose (IFG)	WHO	FPG ≥ 6.1 (110) and < 7.0 (126) + 2 h PG < 7.8 (140)
	ADA (1997)	FPG ≥ 6.1 (110) and < 7.0 (126)
	ADA (2003)	FPG ≥ 5.6 (100) and < 7.0 (126)
Impaired glucose tolerance (IGT)	WHO	FPG < 7.0 (126) + 2 h PG ≥ 7.8 and < 11.1 (200)
Impaired glucose homeostasis (IGH)	WHO	IFG or IGT
Diabetes mellitus (DM)	WHO	FPG ≥ 7.0 (126) or 2 h PG ≥ 11.1 (200)
	ADA (1997)	FPG ≥ 7.0 (126)
	ADA (2003)	FPG > 7.0 (126)



Fasting and post-load glucose levels identify different individuals with asymptomatic diabetes





Appropriate methods for the early detection of people with high risk for diabetes

- measuring blood glucose to determine prevalent impaired glucose homeostasis;
- using demographic, clinical characteristics and previous laboratory tests to determine the likelihood of future incident diabetes;
- collecting questionnaire based information on aetiological factors for type 2 diabetes.



FINnish Diabetes
Risk Score (FINDRISC)
to address 10 year risk
of type 2 diabetes in
adults.

Available www.diabetes.fi/english

Type 2 diabetes risk assessment form Circle the right alternative and add up your points. 1. Age 6. Have you ever taken anti-hypertensive medication regularly? Under 45 years 45-54 years 0 p. No 55-64 years 2 p. Over 64 years 7. Have you ever been found to have high blood glucose (e.g. in a health examination. 2. Body mass Index during an illness, during pregnancy)? Lower than 25 kg/m² 0 p. No 25-30 kg/m² 5 p. Higher than 30 kg/m² 8. Have any of the members of your 3. Waist circumference measured below immediate family or other relatives been the ribs (usually at the level of the navel) diagnosed with diabetes (type 1 or WOMEN type 2)? Less than 94 cm Less than 80 cm 0 p. No 80-88 cm 94-102 cm Yes: grandparent, aunt, uncle, or More than 102 cm More than 88 cm first cousin (but no own parent, brother, sister or child) Yes: parent, brother, sister, or own Total risk score The risk of developing type 2 diabetes within 10 years is Low: estimated one in 100 will develop disease 4. Do you usually have daily at least 30 7-11 Slightly elevated: min of physical activity at work and/or estimated one in 25 will during leisure time (including normal develop disease daily activity)? 12-14 Moderate: estimated one 0 p. Yes in 6 will develop disease 15-20 High: estimated one in three will develop disease 5. How often do you eat vegetables, fruit, Very High: or berries? Higher than 20 estimated one in two Every day will develop disease 1 p. Not every day

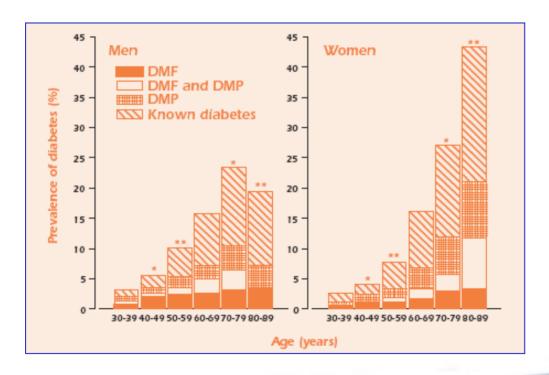


Epidemiology of diabetes, IGH and cardiovascular risk

Recommendation	Class	Level
The relationship between hyperglycaemia and CVD should be seen as a continuum. For each 1% increase of HbA _{1c} , there is a defined increased risk for CVD.	1	Α
The risk of CVD for people with overt diabetes is increased by two to three times for men and three to five times for women compared with people without diabetes.	1	Α
Information on post-prandial (post-load) glucose provides better information about the future risk for CVD than fasting glucose, and elevated post-prandial (post-load) glucose also predicts increased cardiovascular risk in subjects with normal fasting glucose levels.	ı	Α
Glucometabolic perturbations carry a particularly high risk for cardiovascular morbidity and mortality in women, who in this respect need special attention.	lla	В



Age and gender-specific prevalence of diabetes in 13 European population-based cohorts





Identification of subjects at high risk for cardiovascular disease or diabetes

Recommendation	Class	Level
The metabolic syndrome identifies people at a higher risk of CVD than the general population, although it may not provide a better or even equally good prediction of cardiovascular risk than scores based on the major cardiovascular risk factors (blood pressure, smoking, and serum cholesterol).	ii	В
Several cardiovascular risk assessment tools exist and they can be applied to both non-diabetic and diabetic subjects.	E.	Α
An assessment of predicted type 2 diabetes risk should be part of the routine health care using the risk assessment tools available.	II	A
Patients without known diabetes but with established CVD should be investigated with an OGTT.	ř	В
People at high risk for type 2 diabetes should receive appropriate lifestyle counselling and, if needed, pharmacological therapy to reduce or delay their risk of developing diabetes. This may also decrease their risk to develop CVD.	f	Α
Diabetic patients should be advised to be physically active in order to decrease their cardiovascular risk.	Į.	Α



Definition the metabolic syndrome according to International Diabetes Federation

Central Obesity (defined as waist circumference \geq 94 cm for Europid men and \geq 80 cm for Europid women, with ethnicity specific values for other groups)

plus any two of the following four factors:

- Raised TG level: ≥ 1.7 mmol/L (150 mg/dL), or specific treatment for this lipid abnormality.
- Reduced HDL cholesterol: < 1.03 mmol/L (40 mg/dL) in males and < 1.29 mmol/L (50 mg/dL) in females, or specific treatment for this lipid abnormality.
- Raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mmHg, or treatment of previously diagnosed hypertension.
- Raised fasting plasma glucose (FPG) ≥ 5.6 mmol/L (100 mg/dL), or previously diagnosed type 2 diabetes.

If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.



Findings in lifestyle intervention studies aiming at prevention of type 2 diabetes in people with impaired glucose tolerance

Study	Cohort size	Mean BMI (kg/m²)	Duration (years)	RRR (%)	ARR (%)	NNT
Malmö	217	26.6	5	63	18	28
DPS	523	31.0	3	58	12	22
DPP	2161*	34.0	3	58	15	21
Da Qing	500	25.8	6	46	27	25



Treatment to reduce cardiovascular risk

Recommendation	Class	Level
Structured patient education improves metabolic and blood pressure control.	1	Α
Non-pharmacological life style therapy improves metabolic control.	1	Α
Self-monitoring improves glycaemic control.	1	Α
Near normoglycaemic control (HbA _{1c} ≤ 6.5 %*). reduces microvascular complications. reduces macrovascular complications.	1	A A
Intensified insulin therapy in type 1 diabetes reduces morbidity and mortality.	1	Α
Early escalation of therapy towards predefined treatment targets improves a composite of morbidity and mortality in type 2 diabetes.	lla	В
Early initiation of insulin should be considered in patients with type 2 diabetes failing glucose target.	llb	С
Metformin is recommended as first line drug in overweight type 2 diabetes.	lla	В



Suggested policy for the selection of glucose lowering therapy according to the glucometabolic situation

Glucometabolic situation	Policy
Post-prandial hyperglycaemia	Alpha-glucosidase inhibitors, short-acting sulphonylureas, glinides, short-acting regular insulin, or insulin analogs
Fasting hyperglycaemia	Biguanides, long acting sulphonylureas, glitazones, long-acting insulin or insulin analogs
Insulin resistance	Biguanides, glitazones, alpha-glucosidase inhibitors
Insulin deficiency	Sulphonylureas, glinides, insulin



Mean efficacy of pharmacological treatment options in patients with type 2 diabetes

Pharmacological agent	Mean lowering of initial HbA _{1c} (%)		
Alpha-glucosidase inhibitors	0.5–1.0		
Biguanides	1.0–1.5		
Glinides	0.5–1.5		
Glitazones	1.0–1.5		
Insulin	1.0–2.0		
Sulphonylurea derivatives	1.0–1.5		



Potential downsides of pharmacological treatment modalities in patients with type 2 diabetes

Potential problems*	Avoid or reconsider	
Unwanted weight gain	Sulphonylureas, glinides, glitazones, insulin	
Gastrointestinal symptoms	Biguanides, alpha-glucosidase inhibitors	
Hypoglycaemia	Sulphonylureas, glinides, insulin	
Impaired kidney function	Biguanides, sulphonylureas	
Impaired liver function	Glinides, glitazones, biguanides, alpha-glucosidase inhibitors	
Impaired cardio-pulmonary function	Biguanides, glitazones	



Dyslipidemia

Recommendation	Class	Level
Elevated LDL and low HDL cholesterol are important risk factors for CVD in people with diabetes.	1	Α
Statins are first-line agents for lowering LDL cholesterol in diabetic patients.	1	Α
In diabetic patients with CVD, statin therapy should be initiated regardless of baseline LDL cholesterol, with a treatment target of < 1.8–2.0 mmol/L (< 70–77 mg/dL).	1	В
Statin therapy should be considered in adult patients with type 2 diabetes, without CVD, if total cholesterol > 3.5 mmol/L (> 135 mg/dL), with a treatment targeting an LDL cholesterol reduction of 30–40%.	IIb	В
Given the high lifetime risk of CVD, it is suggested that all type 1 patients over the age of 40 years should be considered for statin therapy. In patients 18–39 years (either type 1 or type 2), statin therapy should be considered when other risk factors are present, e.g. nephropathy, poor glycaemic control, retinopathy, hypertension, hypercholesterolaemia, features of the metabolic syndrome, or family history of premature vascular disease.	lib	С
In diabetic patients with hypertriglyceridaemia > 2 mmol/L (177 mg/dL) remaining after having reached the LDL cholesterol target with statins, statin therapy should be increased to reduce the secondary target of non-HDL cholesterol. In some cases, combination therapy with the addition of ezetimibe, nicotinic acid, or fibrates may be considered.	llb	В



Diabetic patients in major secondary prevention trials with statins and risk reduction in patients with and without diabetes

Variables			ortion nts (%)		ntive risk ction (%)	
Trial	Type of event			Diabetes present		pe of perits
			No	Yes	All	Diabetes
4S Diabetes <i>n</i> = 202	CHD death or non-fatal MI	Simvastatin Placebo	19 27	23 45	32	55
4S Reanalysis Diabetes n = 483	CHD death or non-fatal MI	Simvastatin Placebo	19 26	24 38	32	42
HPS Diabetes n = 3050	Major coronary event, stroke, or revascularization	Simvastatin Placebo	20 25	31 36	24	18
CARE Diabetes n = 586	CHD death or non-fatal MI	Pravastatin Placebo	12 15	19 23	23	25
LIPID Diabetes n = 782	CHD death, non-fatal MI, revascularization	Pravastatin Placebo	19 25	29 37	24	19
LIPS Diabetes n = 202	CHD death, non-fatal MI, revascularization	Fluvastatin Placebo	21 25	22 38	22	47
GREACE Diabetes n = 313	CHD death, non-fatal MI, UAP, CHF, revascularization, stroke	Atorvastatin Standard care	12 25	13 30	51 -	58 -



ESC/EASD Pocket Guidelines Diabetes, pre-diabetes and cardiovascular disease Blood pressure and diabetes

Recommendation	Class	Level
In patients with diabetes and hypertension, the recommended target for blood pressure control is <130/80 mm Hg.	1	В
The cardiovascular risk in patients with diabetes and hypertension is substantially enhanced. The risk can be effectively reduced by blood pressure-lowering treatment.	1	Α
The diabetic patient usually requires a combination of several anti-hypertensive drugs for satisfactory blood pressure control.	1	Α
The diabetic patient should be prescribed a renin-angiotensin-system inhibitor as part of the blood pressure-lowering treatment.	1	Α
Screening for microalbuminuria and adequate blood pressure-lowering therapy including the use of ACE-inhibitors and angiotensin receptor II blockers improves micro-and macrovascular morbidity in type 1 and type 2 diabetes.	1	А



ESC/EASD Pocket Guidelines Diabetes, pre-diabetes and cardiovascular disease Management of cardiovascular risk Coronary artery disease

Recommendation	Class	Level
Early risk stratification should be part of the evaluation of the diabetic patient after ACS.	lla	С
Treatment targets, as listed in Table 1, should be outlined and applied in each diabetic patient following an ACS.	lla	С
Patients with acute MI and diabetes should be considered for thrombolytic therapy on the same grounds as their non-diabetic counterparts.	lla	Α
Whenever possible, patients with diabetes and ACS should be offered early angiography and mechanical revascularization.	lla	В
Beta-blockers reduce morbidity and mortality in patients with diabetes and ACS.	lla	В
Aspirin should be given for the same indications and in similar dosages to diabetic and non-diabetic patients.	lla	В
Adenosine diphosphate (ADP) receptor dependent platelet aggregation inhibitor (clopidogrel) may be considered in diabetic patients with ACS in addition to aspirin.	lla	С
The addition of an ACE-inhibitor to other therapies reduces the risk for cardiovascular events in patients with diabetes and established CVD.	T.	Α
Diabetic patients with acute MI benefit from tight glucometabolic control. This may be accomplished by different treatment strategies.	lla	В



Treatment options based on accumulated evidence

Revascularization

Anti-ischaemic medication

Anti-platelet agents

Anti-thrombin agents

Secondary prevention by means of

Lifestyle habits including food and physical activity

Smoking cessation

Blocking the renin-angiotensin system

Blood pressure control

Lipid-lowering medication

Blood glucose control

Acute if needed by means of insulin infusion

Long term as demanded



Risk assessment of patients with diabetes and acute coronary syndromes

Variable	Examination tools
Peripheral, renal and cerebrovascular disease	Case history, clinical examination
Traditional risk factors	
Eating and exercise habits	Case history
Smoking	Case history
Blood lipids	Blood chemistry
Blood pressure	Record (including ankle)
Previous or ongoing diseases	Case history and clinical examination
Autonomic dysfunction	supplemented by special examinations
Hypotension	as indicated (exercise testing, holter monitoring, echo-doppler examination,
Heart failure	magnetic resonance imaging,
Arrhythmias	myocardial scintigraphy, ST-segment
Ischaemic heart disease	monitoring, stress echo)



Management of cardiovascular risk acute coronary syndromes

Recommendation	Class	Level
Treatment decisions regarding revascularization in patients with diabetes should favour coronary artery bypass surgery over percutaneous intervention.	lla	Α
Glycoprotein Ilb/Illa inhibitors are indicated in elective PCI in a diabetic patient.	1	В
When PCI with stent implantation is performed in a diabetic patient, drug-eluting stents (DES) should be used.	lla	В
Mechanical reperfusion by means of primary PCI is the revascularization mode of choice in a diabetic patient with acute MI.	1	Α



Trials addressing diabetes and revascularisation for multivessel disease

Trial	Patients (n)	Follow-up(years)	Mortali CABG	ity (%) PCI	p -value
BARI	353	7	23.6	44.3	< 0.001
CABRI	124	4	12.5	22.6	ns
EAST	59	8	24.5	39.9	ns
BARI registry	339	5	14.9	14.4	ns



Revascularisation of diabetic patients with multivessel disease in the stent area

Trial	Patients (n)	Follow-up (years)	Mortali	ty (%)	Repeat revascularization (%)		Mortality D-value
		, , , , , , , , , , , , , , , , , , ,	CABG	PCI	CABG	PCI	•
ARTS	208	3	4.2	7.1	8.4	41.1	0.39
SoS	150	1	0.8	2.5			ns
AWESOME	144	5	34	26			0.27



Heart failure and diabetes

Recommendation	Class	Level
ACE-inhibitors are recommended as first-line therapy in diabetic patients with reduced left ventricular dysfunction with or without symptoms of heart failure.	1	С
Angiotensin-II receptor blockers have similar effects in heart failure as ACE-inhibitors and can be used as an alternative or even as added treatment to ACE-inhibitors.	1	С
BBs in the form of metoprolol, bisoprolol, and carvedilol are recommended as first-line therapy in diabetic patients with heart failure.	1	С
Diuretics, in particular loop diuretics, are important for symptomatic treatment of diabetic patients with fluid overload owing to heart failure.	lla	С
Aldosterone antagonists may be added to ACE-inhibitors, BBs, and diuretics in diabetic patients with severe heart failure.	IIb	С



Arrhythmias, atrial fibrillation and sudden death

Recommendation	Class	Level
Aspirin and anticoagulant use as recommended for patients with atrial fibrillation should be rigorously applied in diabetic patients with atrial fibrillation to prevent stroke.	1	С
Chronic oral anticoagulant therapy in a dose adjusted to achieve a target international normalized ratio (INR) of 2–3 should be considered in all patients with atrial fibrillation and diabetes, unless contra-indicated.	lla	С
Control of glycaemia even in the pre-diabetic stage is important to prevent the development of the alterations that predispose to sudden cardiac death.	1	С
Microvascular disease and nephropathy are indicators of increased risk of sudden cardiac death in diabetic patients	s. Ila	В



Peripheral and cerebrovascular disease

Recommendation	Class	Level
All patients with type 2 diabetes and CVD are recommended treatment with low-dose aspirin.	lla	В
In diabetic patients with peripheral vascular disease, treatment with clopidogrel or low molecular weight heparin may be considered in certain cases.	IIb	В
Patients with critical limb ischaemia should, if possible, undergo revascularization procedures.	1	В
An alternative treatment for patients with critical limb ischaemia, not suited for revascularization, is prostacyclin infusion.	1	А

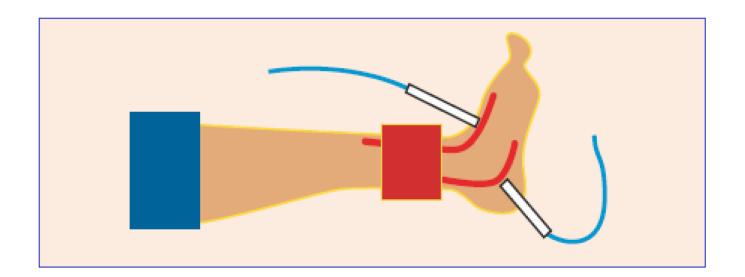


Investigation of the peripheral circulation in diabetic patients

At the physician's office (regularly)				
Inspection	Dependent rubor Pallor with elevation Absence of hair growth Dystrophic toenails Ulcers or gangrenes			
Palpation	Decreased pulses Dry and cool skin Impaired sensibility			
Pressure measurement	Ankle and arm blood pressure			
At the vascular laboratory (if appro	priate)			
Distal and/or segmental pressure measurements Oscillography Treadmill testing (with or without distal pressure after exercise) Duplex sonography For evaluation of the microcirculation Transcutaneous oxygen pressure Vital capillaroscopy				
At the radiology department (if appropriate)				
Magnetic resonance imaging Angiography				



Measurement of ankle blood pressure





Stroke

Recommendation	Class	Level
For stroke prevention, blood pressure lowering is more important than the choice of drug. Inhibition of the renin-angiotensin-aldosterone system may have additional benefits beyond blood pressure lowering per se.	lla	В
Patients with acute stroke and diabetes should be treated according to the same principles as stroke patients without diabetes.	lla	С



Intensive care

Recommendation	Class	Level
Strict blood glucose control with intensive insulin therapy improves mortality and morbidity of adult cardiac surgery patients.	1	В
Strict blood glucose control with intensive insulin therapy improves mortality and morbidity of adult critically ill patients.	1	А



Published trials on intensive insulin therapy

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Patient population ^a	Surgical	Medical	Surgical and medical	Surgical	Heart surgery in diabetes
Number of patients	1548	1200/76 7 ^b	1600	61	4864
Randomized study	Yes	Yes	No	Yes	No
Target glucose (mmol/L)	< 6.1	< 6.1	< 7.8	< 6.7	< 8.3
Mortality-	1	1	1		1
Critical illness polyneuropathy	1				
Bacteraemia/ severe infections	1	-		1	
Acute renal failure	1	1	1		
Red blood cell transfusions	1		1		
Duration of mechanical ventilation	1	1			
Length of stay	1	1	1		1
Deep sternal wound infections					1



Health economy and diabetes

Recommendation	Class	Level
Lipid-lowering provides a cost-effective way of preventing complications.	1	Α
Tight control of hypertension is cost-effective.	1	Α



Direct medical costs and percentage of health care costs for patients with type 2 diabetes in eight European countries

Country	Total costs (million €)	Cost per patient (€)	Cost of healthcare expenditure (%)
Belgium	1 094	3295	6.7
France	3 983	3064	3.2
Germany	12 438	3576	6.3
Italy	5 783	3346	7.4
The Netherlands	444	1889	1.6
Spain	1 958	1305	4.4
Sweden	736	2630	4.5
UK	2 608	2214	3.4
All countries	29 000	2895	5.0







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