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# Akzelerierte Arteriosklerose bei CKD

## *Leitlinien zu Screening, Therapie und Nachbetreuung*

Klaus Bonaventura
Klinik für Kardiologie und Angiologie
Zentrum für Innere Medizin, Klinikum Ernst von Bergmann, Potsdam

# ESC Guidelines 2012

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European Heart Journal (2012) **33**, 1635–1701
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JOINT ESC GUIDELINES

## European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

**The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts)**

**Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)†**

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2012) 33, 1635–1701

# ESC Guidelines 2012
# Recommendations regarding risk estimation

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| Recommendations | Class[a] | Level[b] | GRADE | Ref[c] |
|---|---|---|---|---|
| Total risk estimation using multiple risk factors (such as SCORE) is recommended for asymptomatic adults without evidence of CVD. | I | C | Strong | 36 |
| High-risk individuals can be detected on the basis of established CVD, diabetes mellitus, moderate to severe renal disease, very high levels of individual risk factors, or a high SCORE risk, and are a high priority for intensive advice about all risk factors. | I | C | Strong | 36,37 |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# SCORE Charts: 10-year risk of fatal CVD

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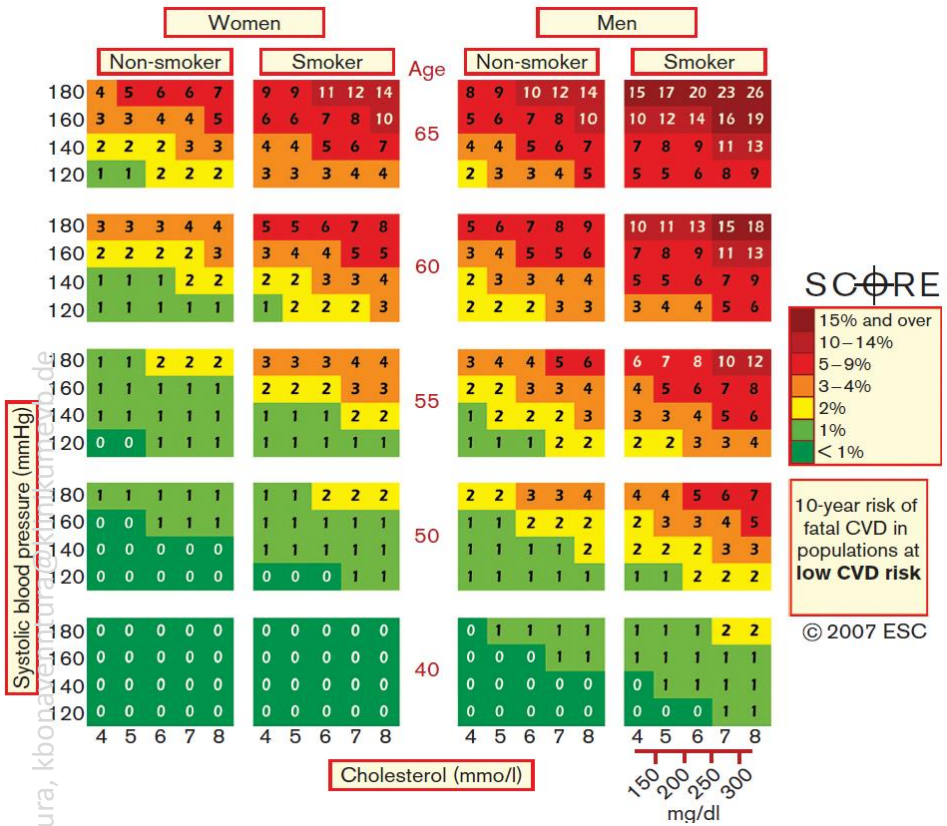


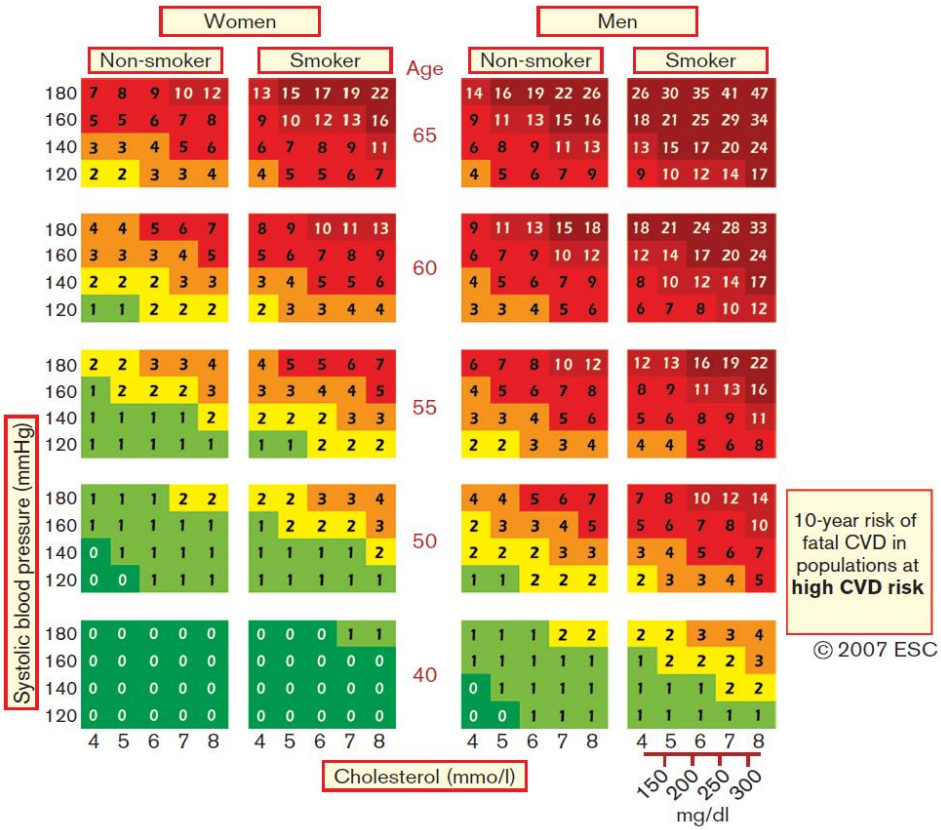


**Low CVD countries** are Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, **Germany**, Greece, Iceland, reland, Israel, Italy, Luxembourg, Malta, Monaco, The Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom.

**High CVD risk countries** are Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Macedonia FYR, Moldova, Russia, Ukraine, and Uzbekistan.

Eur J Cardiovasc Prev Rehabil 2007;14 (suppl 2:S1-S113)

Prof. Klaus Bonaventura, kbonaventura@ernst-von-bergmann.de

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*Risk may also be higher than indicated in the charts in:*

- Sedentary subjects and those with central obesity; these characteristics determine many of the other aspects of risk listed below. The increased risk associated with overweight is greater in younger subjects than in older subjects.
- Socially deprived individuals and those from ethnic minorities.
- Individuals with diabetes: SCORE charts should be used only in those with type 1 diabetes without target organ damage. Risk rises with increasing blood sugar concentration before overt diabetes occurs.
- Individuals with low HDL cholesterol, increased triglycerides, fibrinogen, apolipoprotein B (apoB), and lipoprotein(a) [Lp(a)] levels, especially in combination with familial hypercholesterolaemia, and perhaps increased high-sensitivity CRP (hsCRP). In particular, a low HDL level will indicate a higher level of risk in both sexes, all age groups, and at all levels of risk.[51]
- Asymptomatic individuals with preclinical evidence of atherosclerosis, for example plaque on carotid ultrasonography.
- Those with moderate to severe chronic kidney disease [glomerular filtration rate (GFR) $<60$ mL/min/1.73 $m^2$].
- Positive family history of premature CVD.

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Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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*Priorities*

The higher the risk the greater the benefit from preventive efforts, which guides the following priorities:

1. Very high risk

Subjects with any of the following:

- Documented CVD by invasive or non-invasive testing (such as coronary angiography, nuclear imaging, stress echocardiography, carotid plaque on ultrasound), previous myocardial infarction, ACS, coronary revascularization (PCI, CABG), and other arterial revascularization procedures, ischaemic stroke, peripheral artery disease (PAD).
- Diabetes mellitus (type 1 or type 2) with one or more CV risk factors and/or target organ damage (such as microalbuminuria: 30–300 mg/24 h).
- Severe chronic kidney disease (CKD) (GFR $<30$ mL/min/1.73 $m^2$).
- A calculated SCORE $\geq 10\%$.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# Recommendations regarding imaging methods

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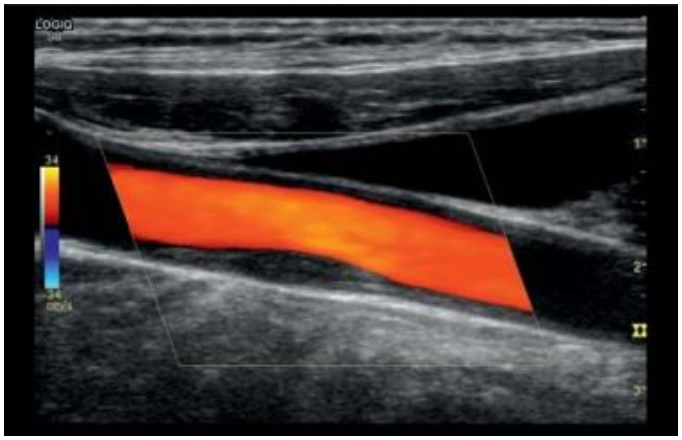

| Recommendations | Class[a] | Level[b] | GRADE | Ref[c] |
|---|---|---|---|---|
| Measurement of carotid intima-media thickness and/or screening for atherosclerotic plaques by carotid artery scanning should be considered for cardiovascular risk assessment in asymptomatic adults at moderate risk. | IIa | B | Strong | 130–132 |
| Measurement of ankle–brachial index should be considered for cardiovascular risk assessment in asymptomatic adults at moderate risk. | IIa | B | Strong | 133–135 |
| Computed tomography for coronary calcium should be considered for cardiovascular risk assessment in asymptomatic adults at moderate risk. | IIa | B | Weak | 136–138 |
| Exercise electrocardiography may be considered for cardiovascular risk assessment in moderate-risk asymptomatic adults (including sedentary adults considering starting a vigorous exercise programme), particularly when attention is paid to non-electrocardiogram markers such as exercise capacity. | IIb | B | Strong | 46, 139, 140 |

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Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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## Blood tests in assessment of patients with known or suspected SCAD in order to optimize medical therapy

| Recommendations | Class [a] | Level [b] | Ref. [c] |
|---|---|---|---|
| If evaluation suggests clinical instability or ACS, repeated measurements of troponin preferably using high sensitivity or ultrasensitive assays are recommended to rule out myocardial necrosis associated with ACS. | I | A | 73, 74 |
| Full blood count including haemoglobin and white cell count is recommended in all patients. | I | B | 75 |
| It is recommended that screening for potential T2DM in patients with suspected and established SCAD is initiated with HbA1c and fasting plasma glucose and that an OGTT is added if $HbA_{1c}$ and fasting plasma glucose are inconclusive | I | B | 57, 58, 76 |
| Creatinine measurement and estimation of renal function (creatinine clearance) are recommended in all patients | I | B | 77 |
| A fasting lipid profile (including LDL) is recommended in all patients[d] | I | C | - |
| If indicated by clinical suspicion of thyroid disorder assessment of thyroid function is recommended | I | C | - |
| Liver function tests are recommended in patients early after beginning statin therapy | I | C | - |
| Creatine kinase measurement are recommended in patients taking statins and complaining of symptoms suggestive of myopathy | I | C | - |
| BNP/NT-proBNP measurements should be considered in patients with suspected heart failure | IIa | C | - |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# Chronic kidney disease

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⇨ **- Hypertension**,
- **dyslipidaemia**,
- **diabetes mellitus**
are common among patients with CKD.

⇨ They are **major risk factors** for the development and progression of endothelial dysfunction and atherosclerosis, and contribute to the progression of renal failure.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# ESC Guidelines 2012
# Chronic kidney disease

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Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

**Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease: A Report From the National Cardiovascular Data Acute Coronary Treatment and Intervention Outcomes Network Registry**

Caroline S. Fox, Paul Muntner, Anita Y. Chen, Karen P. Alexander, Matthew T. Roe, Christopher P. Cannon, Jorge F. Saucedo, Michael C. Kontos and Stephen D. Wiviott

*Circulation.* 2010;121:357-365; originally published online January 11, 2010;
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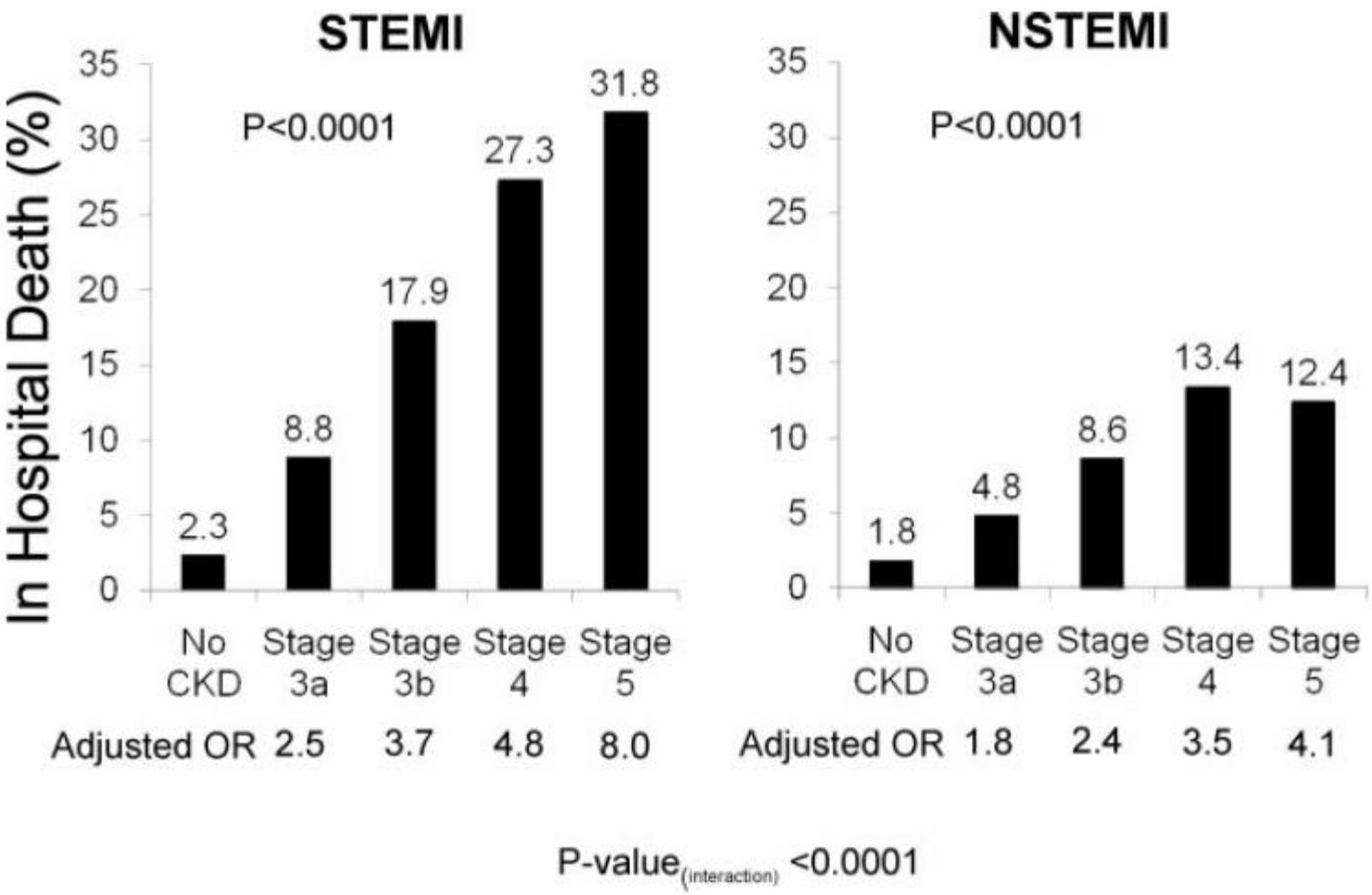
Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

Circulation. 2010;121:357-365.

# Patients with CKD have substantially higher mortality rates




Circulation. 2010;121:357-365.

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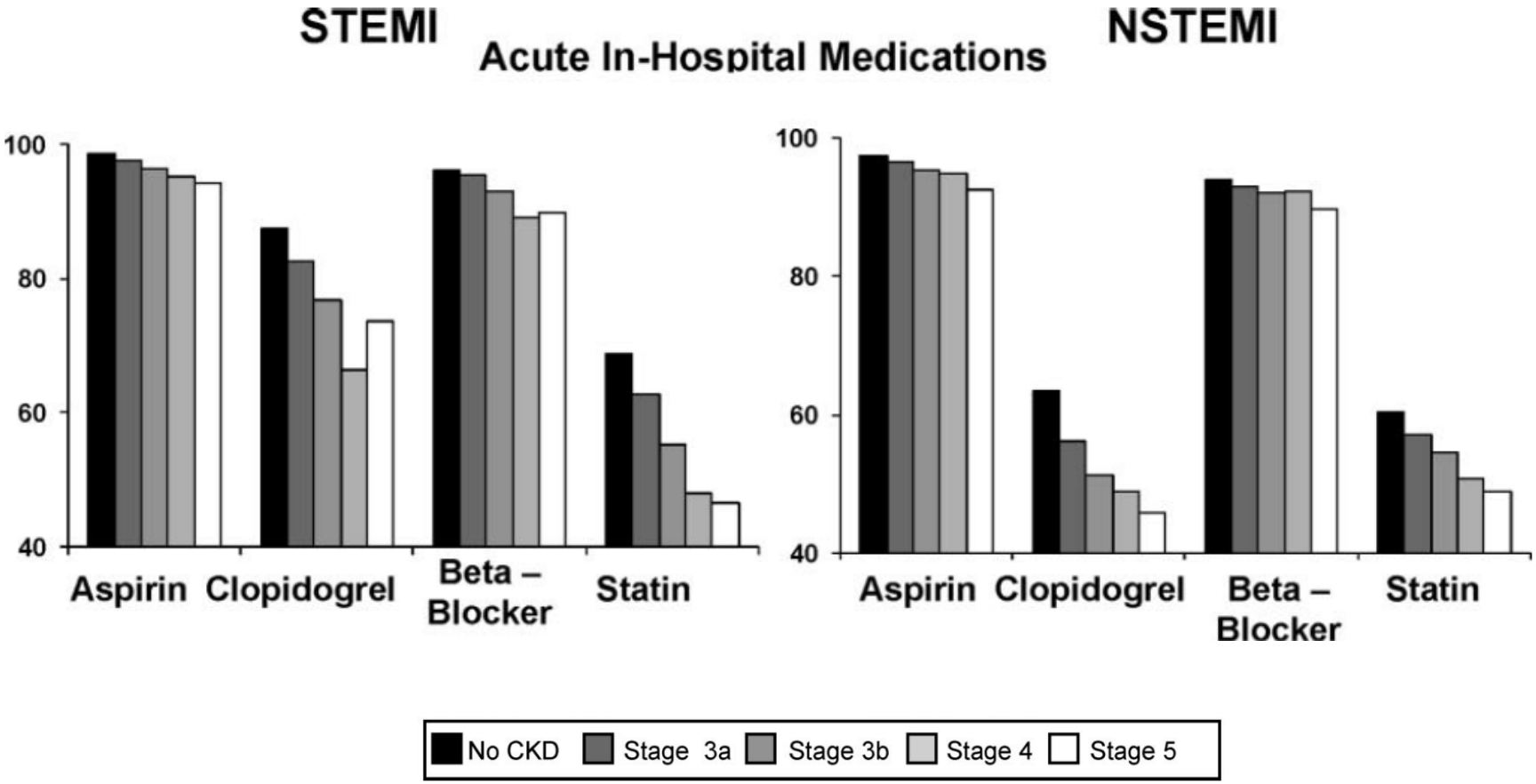
# Patients with CKD still receive fewer evidence-based therapies.

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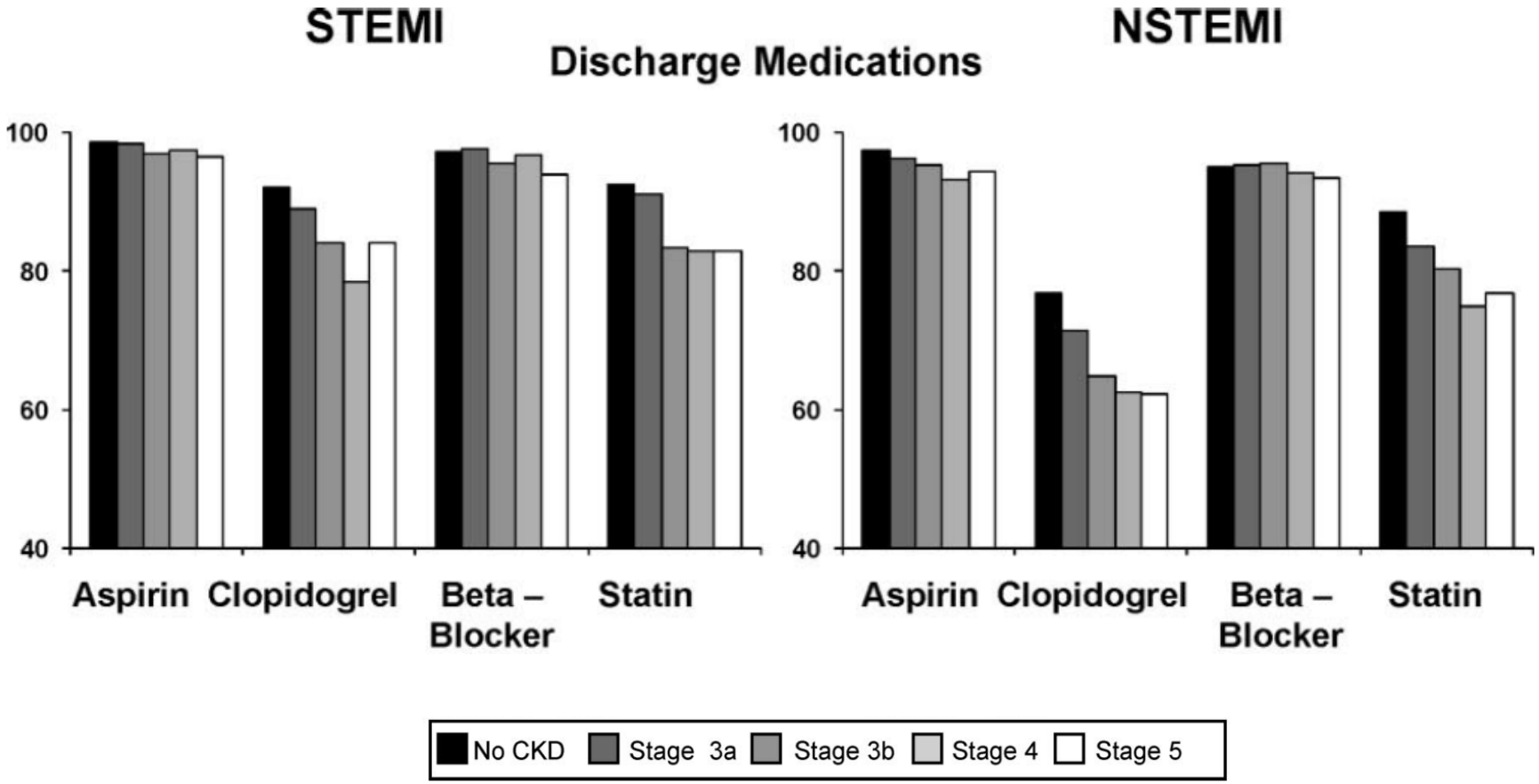


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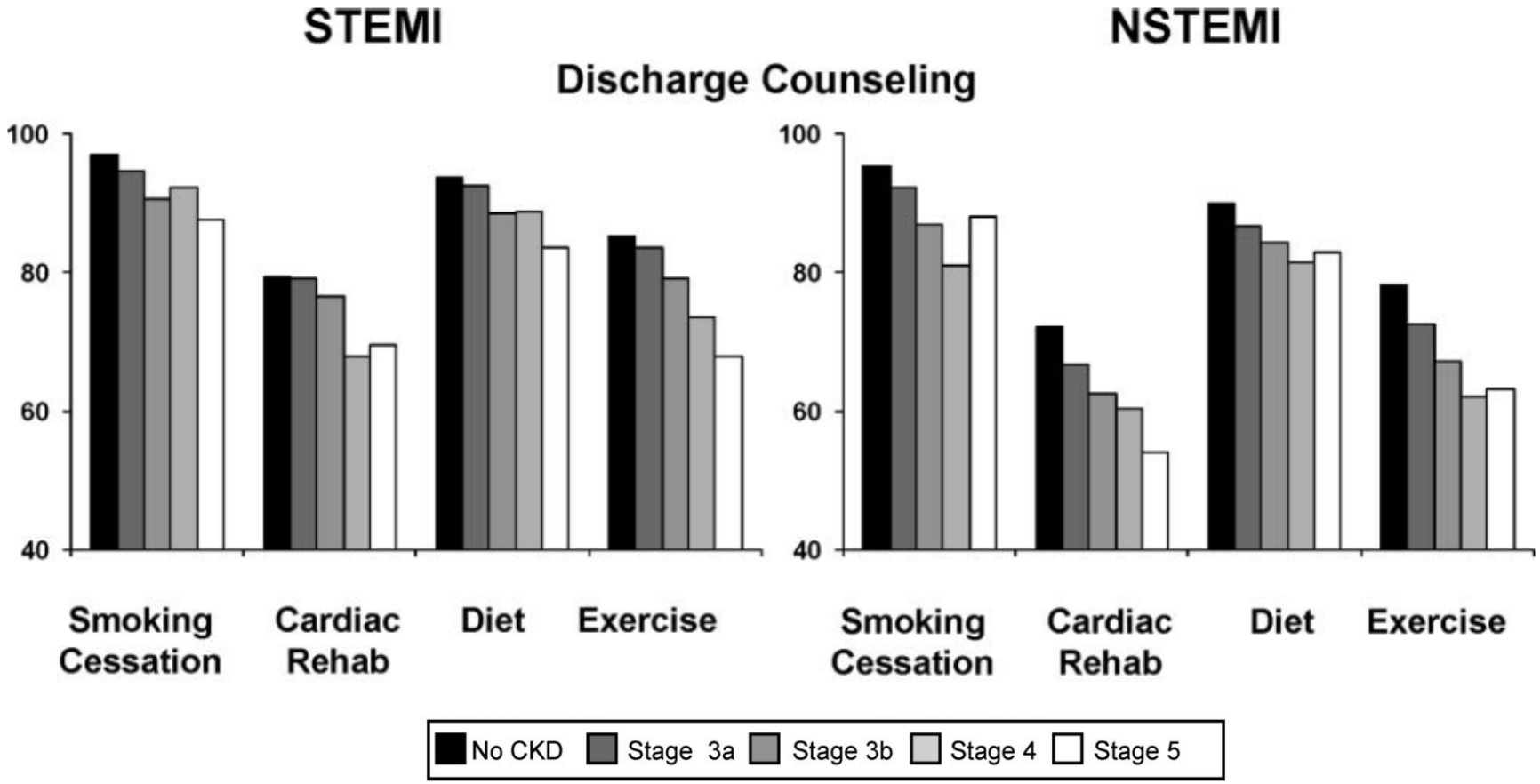


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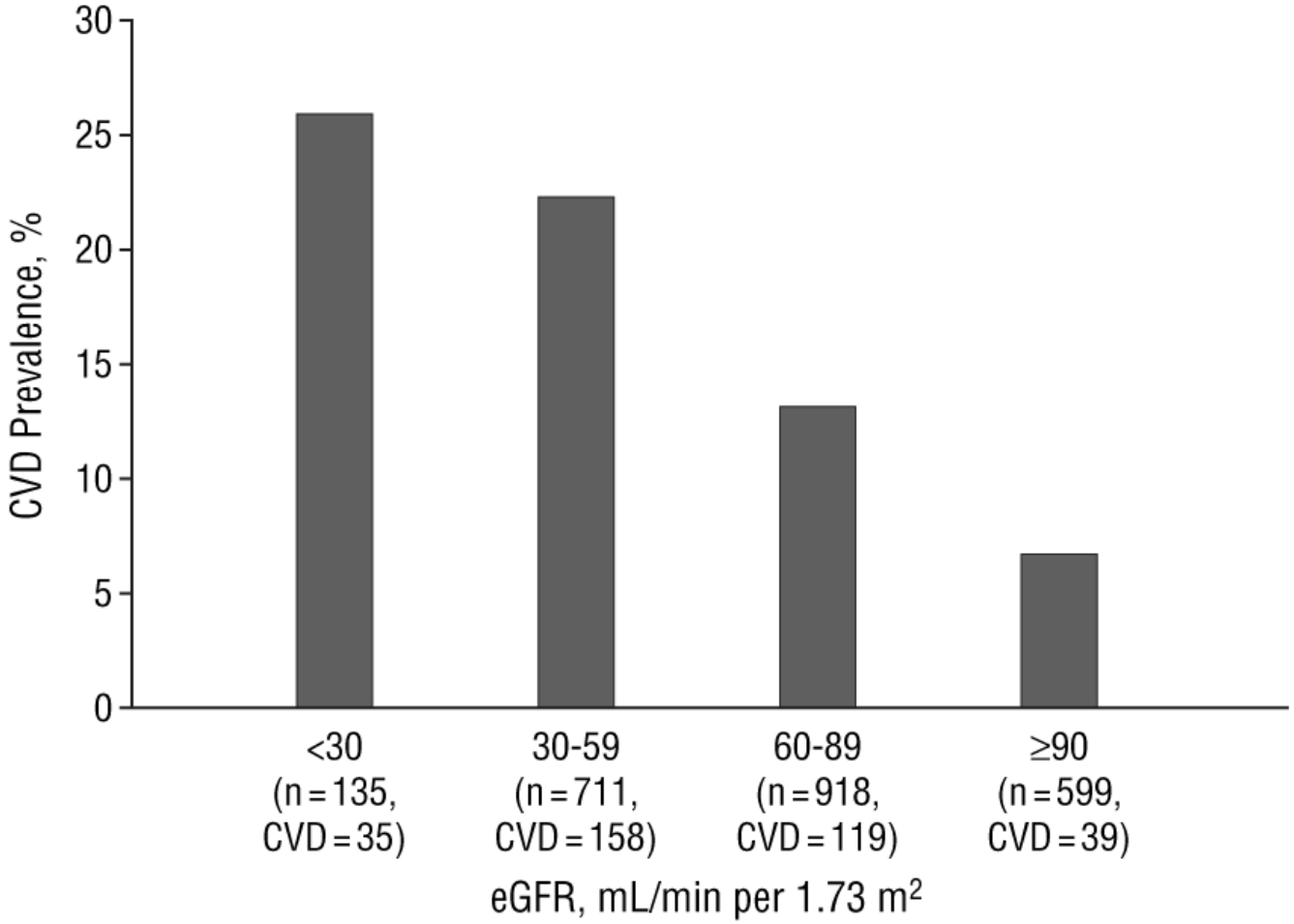
Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Results From the Kidney Early Evaluation Program (KEEP)




Arch Intern Med. 2007;167(11):1122-1129.

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

# Results From the Kidney Early Evaluation Program (KEEP)

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**Table 3. Age-Adjusted Independent Risk Factors for Prevalent Cardiovascular Disease**

| Variable | Odds Ratio (95% Confidence Interval) | *P* Value |
|---|---|---|
| Male sex | 1.64 (1.47-1.83) | <.001 |
| Race/ethnicity | | |
| White | 1 [Reference] | |
| African American | 0.79 (0.71-0.89) | <.001 |
| Other | 0.97 (0.85-1.10) | .63 |
| Current smoker | 1.73 (1.50-1.99) | <.001 |
| Health insurance coverage | 1.02 (0.88-1.18) | .81 |
| High school education or higher | 0.74 (0.66-0.83) | <.001 |
| Family history of hypertension, diabetes mellitus, or kidney disease | 1.22 (1.04-1.43) | .01 |
| Body mass index | 1.01 (1.00-1.02) | .03 |
| Diabetes mellitus | 1.66 (1.50-1.83) | <.001 |
| Hypertension | 1.77 (1.56-2.01) | <.001 |
| Microalbuminuria category, mg/L | | |
| ≤10 | 1 [Reference] | |
| 11 to 20 | 0.77 (0.51-1.16) | .21 |
| 21 to 30 | 1.09 (0.90-1.31) | .40 |
| >30 | 1.28 (1.06-1.55) | .01 |
| Estimated glomerular filtration rate category, mL/min per 1.73 $m^2$ | | |
| <30 | 1.29 (0.88-1.92 | .21 |
| 30-59 | 1.37 (1.13-1.67) | .001 |
| 60-89 | 1.07 (0.95-1.21) | .29 |
| ≥90 | 1 [Reference] | |
| Anemia | 0.92 (0.77-1.11) | .40 |
| Hemoglobin quartile, g/dL | | |
| ≤12.8 | 1.45 (1.20-1.75) | <.001 |
| 12.9-13.6 | 1.17 (1.00-1.35) | .04 |
| 13.7-14.6 | 1.10 (0.96-1.26) | .17 |
| >14.6 | 1 [Reference] | |
| Prevalent chronic kidney disease | 1.00 (0.81-1.24) | .97 |

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Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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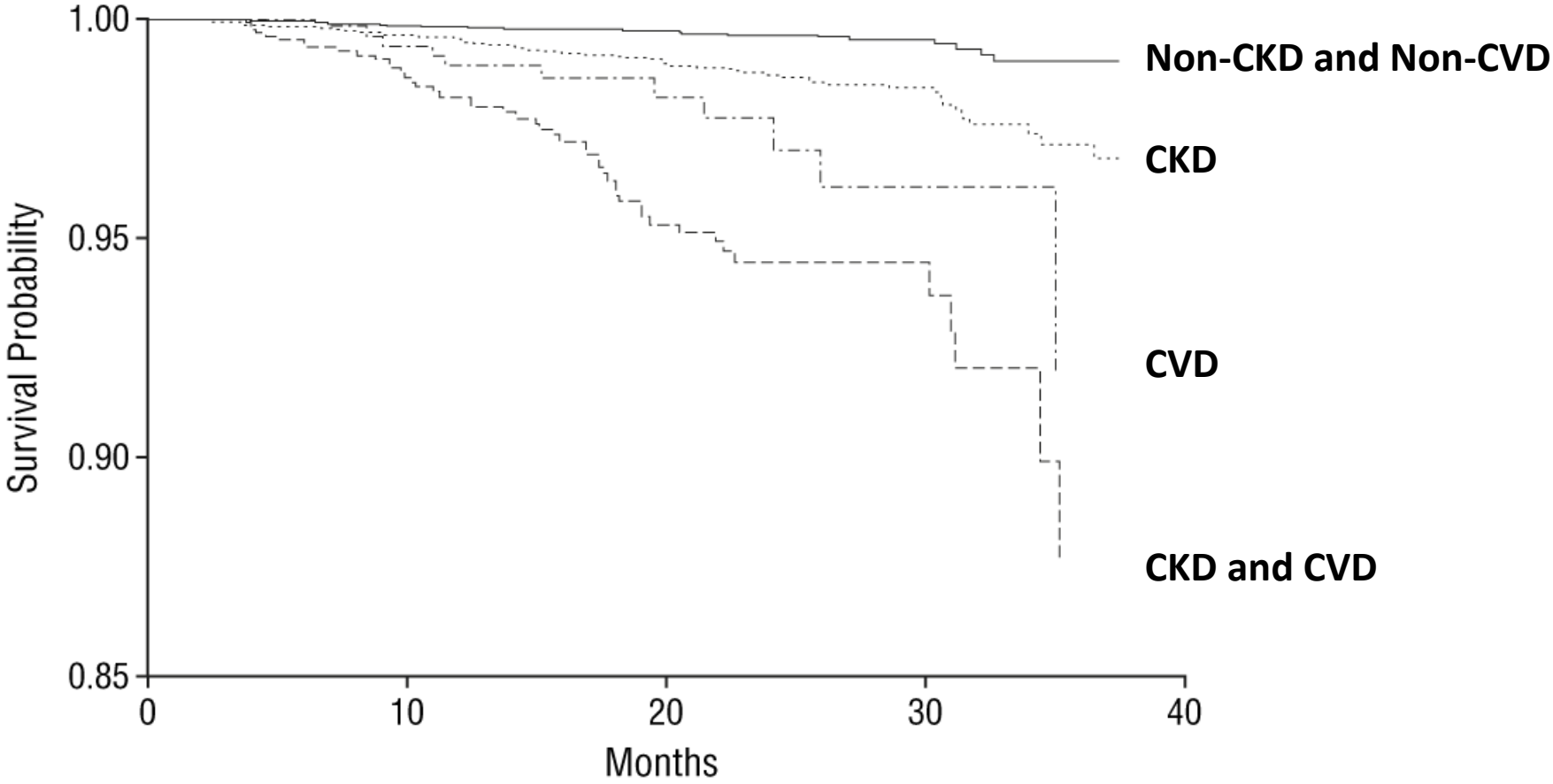


Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

Arch Intern Med. 2007;167(11):1122-1129.

# Inflammatory mediators and promoters of calcification ↑ + inhibitors of calcification ↓ in CDK

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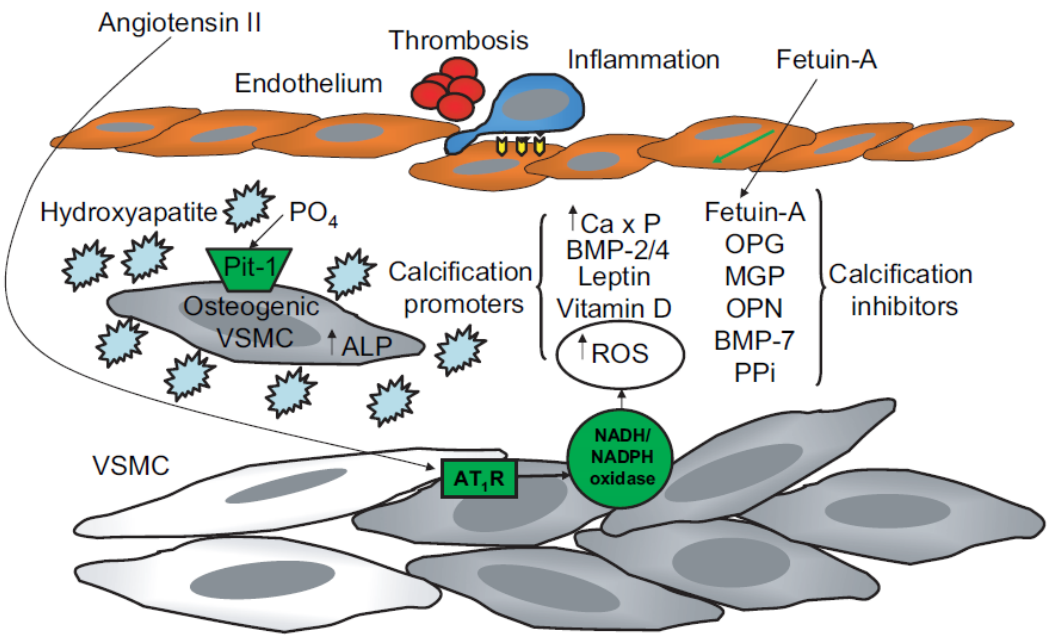
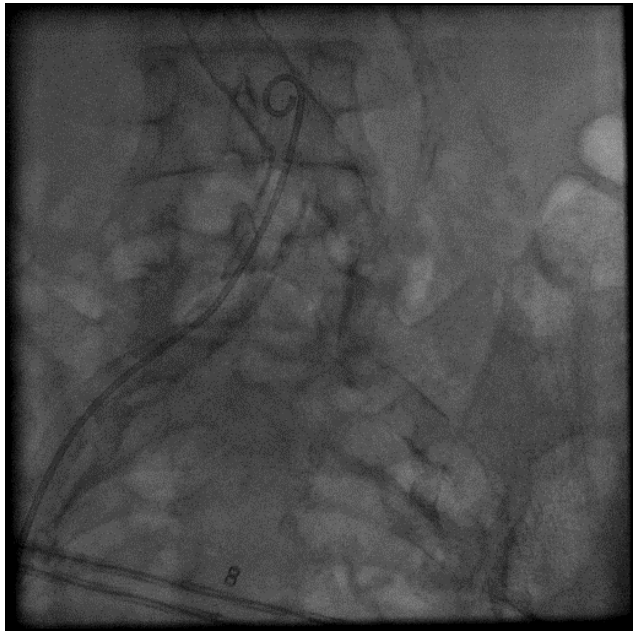
## = vascular calcification and vascular injury ↑



Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

Circulation. 2007;116:85-97

# Stages of Chronic kidney disease

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| Stage | Description | GFR, mL/min per 1.73 $m^2$ |
|---|---|---|
| 1* | Kidney damage with normal or increased GFR | ≥90 |
| 2 | Kidney damage with mildly decreased GFR | 60 to 89 |
| 3 | Moderately decreased GFR | 30 to 59 |
| 4 | Severely decreased GFR | 15 to 29 |
| 5 | Kidney failure | <15 or dialysis |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

Circulation. 2007;116:85-97

# CV Risk According to Stages of CKD

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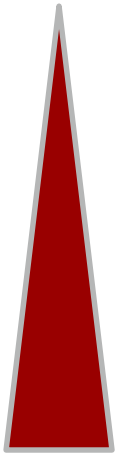
| Stage | CV Risk (Odds Ratio, Univariate) |
|---|---|
| 1 | Depending on degree of proteinuria |
| 2 | 1.5 |
| 3 | 2 to 4 |
| 4 | 4 to 10 |
| 5 | 10 to 50 |
| ESRD | 20 to 1000 |



Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

Circulation. 2007;116:85-97

# Reduction of LDL cholesterol with simvastatin plus ezetimibe reduces the incidence of major atherosclerotic events in CKD

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- ⇨ **Study of Heart and Renal Protection**
- ⇨ 9,270 patients with
  - **chronic kidney disea**se (3023 on dialysis and 6247 not)
  - **with no known history of myocardial infarction or coronary revascularisation**
- ⇨ Patients were randomly assigned to
  - **simvastatin 20 mg plus ezetimibe 10 mg daily**
  - **versus matching placebo**

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

Lancet 2011; 377: 2181–92

# Reduction of LDL cholesterol with simvastatin plus ezetimibe reduces the incidence of major atherosclerotic events in CKD

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| | LDL-cholesterol-lowering drug use | | | LDL cholesterol difference (mmol/L)* | | |
|---|---|---|---|---|---|---|
| | Simvastatin plus ezetimibe | Placebo | Absolute difference | Simvastatin plus ezetimibe | Placebo | Absolute difference (SE) |
| 8–13 months | 77% | 3% | 74% | –1·08 | 0·02 | –1·09 (0·06) |
| 26–31 months | 71% | 9% | 61% | –1·00 | –0·15 | –0·85 (0·02) |
| 44–49 months | 68% | 14% | 55% | –0·84 | –0·08 | –0·77 (0·06) |

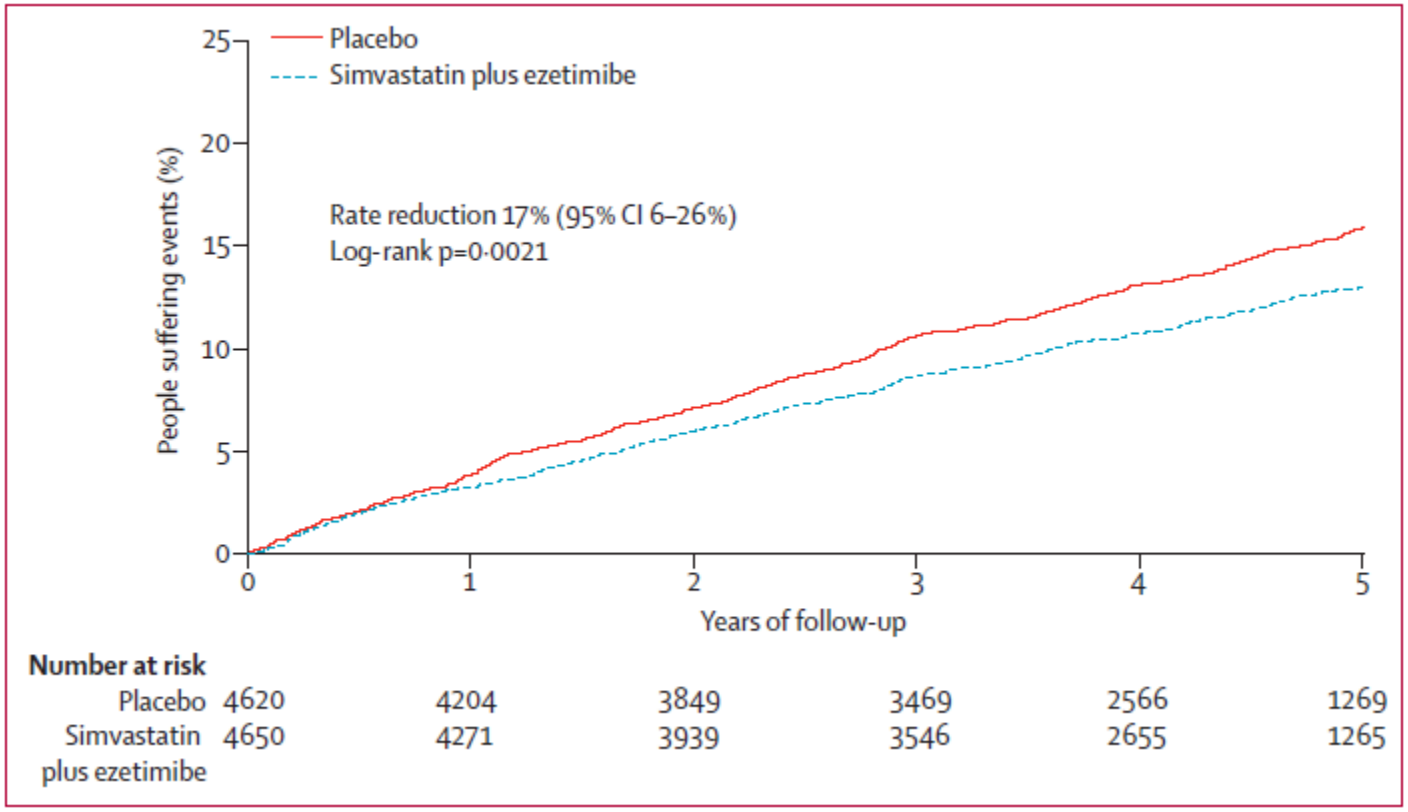
*In patients initially allocated to simvastatin, no 1-year sample was collected, while samples scheduled for collection at 2·5 and 4 years were collected at 1·5 and 3 years after rerandomisation.

*Table 2:* Average use of study simvastatin plus ezetimibe or non-study statin and average change in plasma LDL cholesterol from baseline, by period of follow-up

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

Lancet 2011; 377: 2181–92

# Reduction of LDL cholesterol with simvastatin plus ezetimibe reduces the incidence of major atherosclerotic events in CKD

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# Reduction of LDL cholesterol with simvastatin plus ezetimibe reduces the incidence of major atherosclerotic events in CKD

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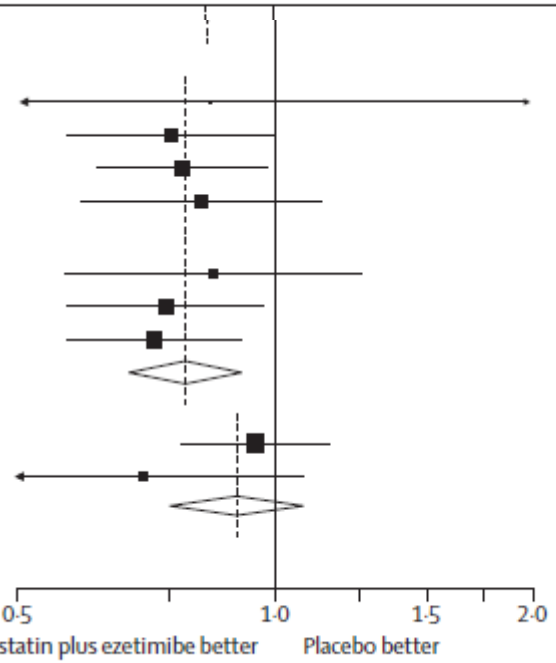
| | Simvastatin plus ezetimibe (n=4650) | Placebo (n=4620) | Risk ratio (95% CI) |
|---|---|---|---|
| **Not on dialysis** | | | |
| **MDRD estimated GFR (mL/min per 1·73 m²) ($\chi^2_1$=0·12; p=0·73)** | | | |
| ≥60 | 3/44 (6·8%) | 3/44 (6·8%) | 0·84 (0·17–4·18) |
| ≥30 <60 | 87/1100 (7·9%) | 110/1055 (10·4%) | 0·75 (0·57–1·00) |
| ≥15 <30 | 127/1246 (10·2%) | 168/1319 (12·7%) | 0·78 (0·62–0·98) |
| <15 | 67/614 (10·9%) | 81/607 (13·3%) | 0·82 (0·59–1·13) |
| **Urinary albumin:creatinine ratio (mg/g) ($\chi^2_1$=0·38; p=0·54)** | | | |
| <30 | 44/545 (8·1%) | 53/562 (9·4%) | 0·85 (0·57–1·26) |
| ≥30 ≤300 | 93/1032 (9·0%) | 128/1076 (11·9%) | 0·75 (0·57–0·97) |
| >300 | 123/1203 (10·2%) | 160/1156 (13·8%) | 0·72 (0·57–0·91) |
| **Subtotal: not on dialysis** | **296/3117 (9·5%)** | **373/3130 (11·9%)** | **0·78 (0·67–0·91)** |
| **Dialysis ($\chi^2_1$=1·54; p=0·21)** | | | |
| Haemodialysis | 194/1275 (15·2%) | 199/1252 (15·9%) | 0·95 (0·78–1·15) |
| Peritoneal dialysis | 36/258 (14·0%) | 47/238 (19·7%) | 0·70 (0·46–1·08) |
| **Subtotal: on dialysis** | **230/1533 (15·0%)** | **246/1490 (16·5%)** | **0·90 (0·75–1·08)** |

Heterogeneity between patients on dialysis and not on dialysis ($\chi^2_1$=1·34; p=0·25)




Lancet 2011; 377: 2181–92

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# ESC Guidelines 2012
# Recommendations on management of hyperlipidaemia

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| Recommendations | Class[a] | Level[b] | GRADE | Ref[c] |
|---|---|---|---|---|
| The recommended target levels are <5 mmol/L (less than ~190 mg/dL) for total plasma cholesterol and <3 mmol/L (less than ~115 mg/dL) for LDL cholesterol for subjects at low or moderate risk. | I | A | Strong | 457,458 |
| In patients at high CVD risk, an LDL cholesterol goal <2.5 mmol/L (less than ~100 mg/dL) is recommended. | I | A | Strong | 459–461 |
| In patients at very high CVD risk, the recommended LDL cholesterol target is <1.8 mmol/L (less than ~70 mg/dL) or a ≥50% LDL cholesterol reduction when the target level cannot be reached. | I | A | Strong | 459, 462, 463 |
| All patients with familial hypercholesterolaemia must be recognized as high-risk patients and be treated with lipid-lowering therapy. | I | A | Strong | 464, 465 |
| In patients with an ACS, statin treatment in high doses has to be initiated while the patients are in hospital. | I | A | Strong | 466–468 |
| Prevention of non-haemorrhagic stroke: treatment with statins must be started in all patients with established atherosclerotic disease and in patients at high risk for developing CVD. Treatment with statins must be started in patients with a history of non-cardioembolic ischaemic stroke. | I | A | Strong | 469, 470 |
| Occlusive arterial disease of the lower limbs and carotid artery disease are CHD risk-equivalent conditions and lipid-lowering therapy is recommended. | I | A | Strong | 471, 472 |
| Statins should be considered as the first-line drugs in transplant patients with dyslipidaemia. | IIa | B | Strong | 473 |
| Chronic kidney disease (stages 2–5, i.e. GFR <90 mL/min/1.73 $m^2$) is acknowledged as a CHD risk-equivalent and the LDL cholesterol target in these patients should be adapted to the degree of renal failure. | IIa | C | Strong | 474 |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2012) 33, 1635–1701

# ESC Guidelines 2012
# Recommendations on diabetes mellitus

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| Recommendations | Class[a] | Level[b] | GRADE | Ref[c] |
|---|---|---|---|---|
| The target $HbA_{1c}$ for the prevention of CVD in diabetes of <7.0% (<53 mmol/mol) is recommended. | I | A | Strong | 434, 435 |
| Statins are recommended to reduce cardiovascular risk in diabetes. | I | A | Strong | 166, 436 |
| Hypoglycaemia and excessive weight gain must be avoided and individual approaches (both targets and drug choices) may be necessary in patients with complex disease. | I | B | Strong | 435, 437, 438 |
| Metformin should be used as first-line therapy if tolerated and not contraindicated | IIa | B | Strong | 439 |
| Further reductions in $HbA_{1c}$ to a target of <6.5% (<48 mmol/mol) (the lowest possible safely reached $HbA_{1c}$) may be useful at diagnosis. For patients with a long duration of diabetes this target may reduce risk of microvascular outcomes. | IIb | B | Weak | 435 |
| BP targets in diabetes are recommend to be <140/80 mmHg. | I | A | Strong | 440, 441 |
| Target LDL cholesterol is <2.5 mmol/L, for patients without atherosclerotic disease total cholesterol may be <4.5 mmol/L, with a lower LDL cholesterol target of <1.8 mmol/L (using higher doses of statins) for diabetic patients at very high CVD risk. | IIb | B | Weak | 442 |
| Antiplatelet therapy with aspirin is not recommended for people with diabetes who do not have clinical evidence of atherosclerotic disease. | III | A | Strong | 443 |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# ESC Guidelines 2012
# Dyslipidaemia in Diabetes mellitus

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- ⇨ **Heart Protection Study (HPS)**
- ⇨ **Simvastatin 40 mg reduces the risk of CHD and stroke**
  **-** in diabetic and non-diabetic individuals
  - without prior myocardial infarction or angina pectoris.
- ⇨ The reactive treatment **effect was independent of baseline cholesterol**, although the absolute risk and treatment effect increased with rising cholesterol concentration.

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

European Heart Journal (2012) 33, 1635–1701

# ESC Guidelines 2012
# Antithrombotic therapy in Diabetes mellitus

ERNST VON BERGMANN KLINIKUM

- ⇨ Patients with type 1 or type 2 diabetes have an increased tendency to develop thrombotic phenomena.
- ⇨ **The Antiplatelet Trialists' Collaboration meta-analysis:** antithrombotic therapy in diabetic patients <u>with clinically established CHD, cerebrovascular disease, or other forms of atherothrombotic disease</u>:

  **↓ 25% reduction in risk of cardiovascular events**.

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

European Heart Journal (2012) 33, 1635–1701

# ESC Guidelines 2012
# Antithrombotic therapy in Hypertension & Diabetes mellitus

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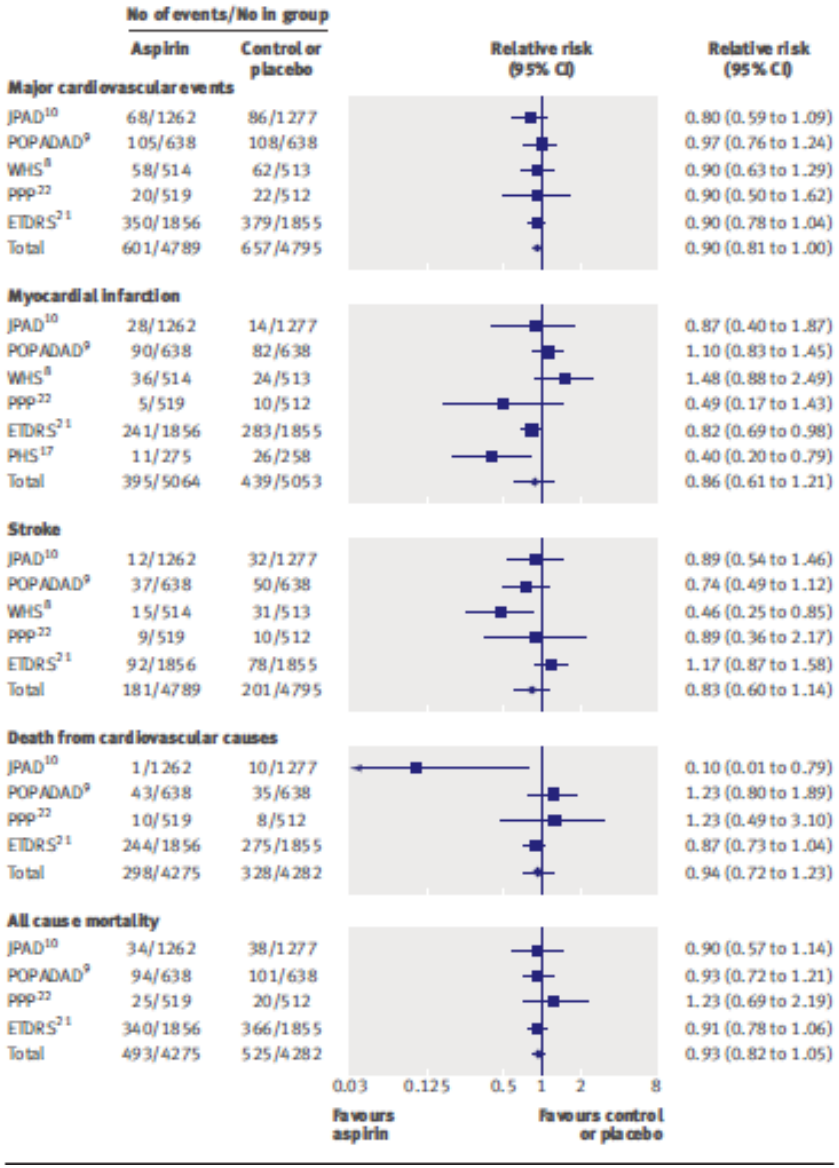
- ⇨ **HOT study:**
  **75 mg of aspirin reduced the risk of major cardiovascular events** in well-controlled **hypertensive patients** with diabetes, but non-fatal major bleeds.

- ⇨ **Antithrombotic Trialists' Collaboration:**
  **non-significant 7% reduction** in risk of vascular events in patients with diabetes.

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

European Heart Journal (2012) 33, 1635–1701

# Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials



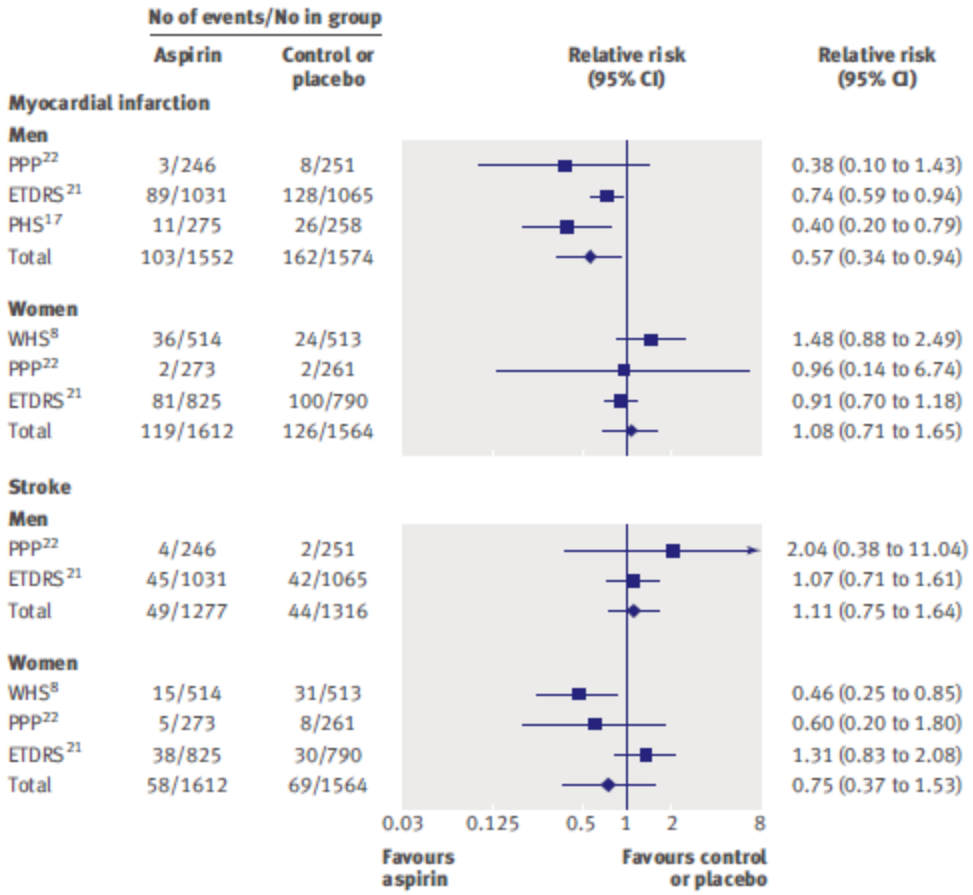

⇨ Aspirin was compared with placebo or no aspirin in people with **<u>diabetes and no pre-existing CVD</u>**.

⇨ **No statistically significant reduction** in the risk of major cardiovascular events or all-cause mortality

BMJ 2009;339:b4531

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials




⇨ **Aspirin significantly reduced the risk of myocardial infarction in men,** but not in women. Evidence relating to harm was inconsistent.

BMJ 2009;339:b4531

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# ESC Guidelines 2012
# Antithrombotic therapy in Diabetes mellitus

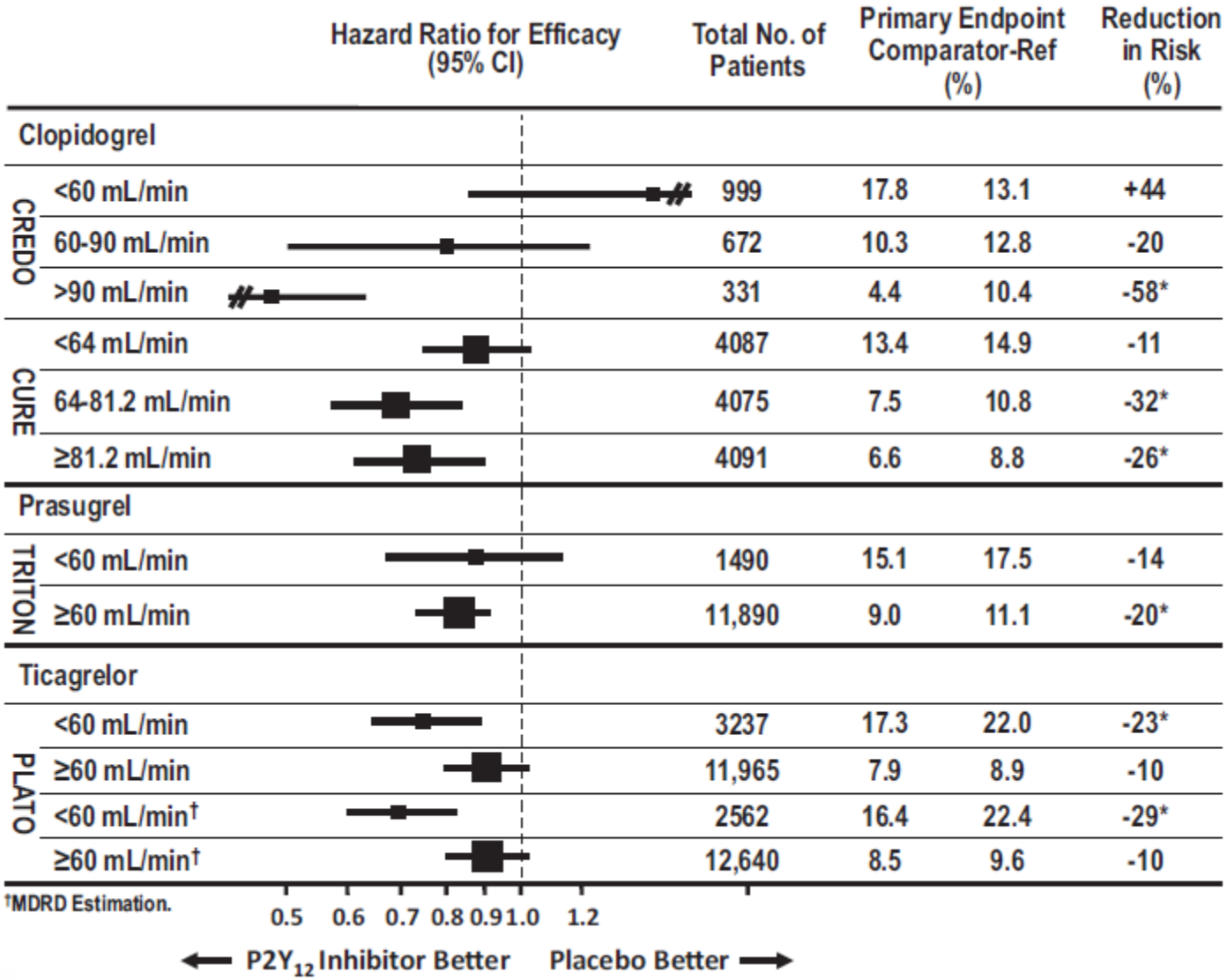
ERNST VON BERGMANN KLINIKUM

⇨ The role of aspirin in primary prevention remains unproven.

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

European Heart Journal (2012) 33, 1635–1701

# Antithrombotic therapy in CKD




Circulation. 2012;125:2649-2661

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# ESC Guidelines 2013

ERNST VON BERGMANN KLINIKUM

European Heart Journal (2013) **34**, 2159–2219
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

## 2013 ESH/ESC Guidelines for the management of arterial hypertension

### The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

**Authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland), Josep Redon (Section co-ordinator) (Spain), Alberto Zanchetti (Section co-ordinator) (Italy), Michael Böhm (Germany), Thierry Christiaens (Belgium), Renata Cifkova (Czech Republic), Guy De Backer (Belgium), Anna Dominiczak (UK), Maurizio Galderisi (Italy), Diederick E. Grobbee (Netherlands), Tiny Jaarsma (Sweden), Paulus Kirchhof (Germany/UK), Sverre E. Kjeldsen (Norway), Stéphane Laurent (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Luis Miguel Ruilope (Spain), Roland E. Schmieder (Germany), Per Anton Sirnes (Norway), Peter Sleight (UK), Margus Viigimaa (Estonia), Bernard Waeber (Switzerland), Faiez Zannad (France)**

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Definition and classification of hypertension

ERNST VON BERGMANN KLINIKUM

- ⇨ The recommended classification is **unchanged** from the 2003 and 2007 ESH/ESC guidelines.
- ⇨ Hypertension is defined as values **≥140 mmHg SBP** and/or **≥90 mmHg DBP**, based on the evidence from RCTs that in patients with these BP values treatment-induced BP reductions are beneficial.

Prof. Klaus Bonaventura, kbonavenntura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Definition and classification of hypertension

ERNST VON BERGMANN KLINIKUM

⇨ The recommended classification is **unchanged** from the 2003 and 2007 ESH/ESC guidelines.

**Table 3 Definitions and classification of office blood pressure levels (mmHg)[a]**

| Category | Systolic | | Diastolic |
|---|---|---|---|
| Optimal | <120 | and | <80 |
| Normal | 120–129 | and/or | 80–84 |
| High normal | 130–139 | and/or | 85–89 |
| Grade 1 hypertension | 140–159 | and/or | 90–99 |
| Grade 2 hypertension | 160–179 | and/or | 100–109 |
| Grade 3 hypertension | ≥180 | and/or | ≥110 |
| Isolated systolic hypertension | ≥140 | and | <90 |

[a]The blood pressure (BP) category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.

European Heart Journal (2013) 34, 2159–2219

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Hypertension and total cardiovascular risk

ERNST VON BERGMANN KLINIKUM

| Other risk factors, asymptomatic organ damage or disease | Blood Pressure (mmHg) | | | |
|---|---|---|---|---|
| | High normal SBP 130–139 or DBP 85–89 | Grade 1 HT SBP 140–159 or DBP 90–99 | Grade 2 HT SBP 160–179 or DBP 100–109 | Grade 3 HT SBP ≥180 or DBP ≥110 |
| No other RF | | Low risk | Moderate risk | High risk |
| 1–2 RF | Low risk | Moderate risk | Moderate to high risk | High risk |
| ≥3 RF | Low to Moderate risk | Moderate to high risk | High Risk | High risk |
| OD, CKD stage 3 or diabetes | Moderate to high risk | High risk | High risk | High to very high risk |
| Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs | Very high risk | Very high risk | Very high risk | Very high risk |

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

**Figure 1** Stratification of total CV risk in categories of low, moderate, high and very high risk according to SBP and DBP and prevalence of RFs, asymptomatic OD, diabetes, CKD stage or symptomatic CVD. Subjects with a high normal office but a raised out-of-office BP (masked hypertension) have a CV risk in the hypertension range. Subjects with a high office BP but normal out-of-office BP (white-coat hypertension), particularly if there is no diabetes, OD, CVD or CKD, have lower risk than sustained hypertension for the same office BP.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Diagnostic evaluation

ERNST VON BERGMANN KLINIKUM

- ~~Office or clinic blood pressure~~
- **Out-of-office blood pressure:**
  The major advantage of out-of-office BP monitoring is that it provides a large number of BP measurements away from the medical environment, which represents **a more reliable assessment of actual BP than office BP**.
- Office BP is usually higher than ambulatory and home BP and the difference increases as office BP increases.
- Out-of-office BP is commonly assessed by
  - **ABPM** (Ambulatory blood pressure monitoring) or
  - **HBPM** (Home blood pressure monitoring),
  usually by self-measurement.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Diagnostic evaluation

ERNST VON BERGMANN KLINIKUM

- ⇨ **Office or clinic blood pressure**
- ⇨ **Out-of-office blood pressure**

**Table 6** Definitions of hypertension by office and out-of-office blood pressure levels

| Category | Systolic BP (mmHg) | | Diastolic BP (mmHg) |
|---|---|---|---|
| Office BP | ≥140 | and/or | ≥90 |
| Ambulatory BP | | | |
| Daytime (or awake) | ≥135 | and/or | ≥85 |
| Nighttime (or asleep) | ≥120 | and/or | ≥70 |
| 24-h | ≥130 | and/or | ≥80 |
| Home BP | ≥135 | and/or | ≥85 |

BP = blood pressure.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# Hypertension and total cardiovascular risk

ERNST VON BERGMANN KLINIKUM

| Other risk factors, asymptomatic organ damage or disease | Blood Pressure (mmHg) | | | |
|---|---|---|---|---|
| | High normal SBP 130–139 or DBP 85–89 | Grade 1 HT SBP 140–159 or DBP 90–99 | Grade 2 HT SBP 160–179 or DBP 100–109 | Grade 3 HT SBP ≥180 or DBP ≥110 |
| No other RF | • No BP intervention | • Lifestyle changes for several months<br>• Then add BP drugs targeting <140/90 | • Lifestyle changes for several weeks<br>• Then add BP drugs targeting <140/90 | • Lifestyle changes<br>• Immediate BP drugs targeting <140/90 |
| 1–2 RF | • Lifestyle changes<br>• No BP intervention | • Lifestyle changes for several weeks<br>• Then add BP drugs targeting <140/90 | • Lifestyle changes for several weeks<br>• Then add BP drugs targeting <140/90 | • Lifestyle changes<br>• Immediate BP drugs targeting <140/90 |
| ≥3 RF | • Lifestyle changes<br>• No BP intervention | • Lifestyle changes for several weeks<br>• Then add BP drugs targeting <140/90 | • Lifestyle changes<br>• BP drugs targeting <140/90 | • Lifestyle changes<br>• Immediate BP drugs targeting <140/90 |
| OD, CKD stage 3 or diabetes | • Lifestyle changes<br>• No BP intervention | • Lifestyle changes<br>• BP drugs targeting <140/90 | • Lifestyle changes<br>• BP drugs targeting <140/90 | • Lifestyle changes<br>• Immediate BP drugs targeting <140/90 |
| Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs | • Lifestyle changes<br>• No BP intervention | • Lifestyle changes<br>• BP drugs targeting <140/90 | • Lifestyle changes<br>• BP drugs targeting <140/90 | • Lifestyle changes<br>• Immediate BP drugs targeting <140/90 |

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Initiation of antihypertensive drug treatment

ERNST VON BERGMANN KLINIKUM

## Initiation of antihypertensive drug treatment

| Recommendations | Class [a] | Level [b] | Ref. [c] |
|---|---|---|---|
| Prompt initiation of drug treatment is recommended in individuals with grade 2 and 3 hypertension with any level of CV risk, a few weeks after or simultaneously with initiation of lifestyle changes. | I | A | 260, 265, 284 |
| Lowering BP with drugs is also recommended when total CV risk is high because of OD, diabetes, CVD or CKD, even when hypertension is in the grade 1 range. | I | B | 260, 284 |
| Initiation of antihypertensive drug treatment should also be considered in grade 1 hypertensive patients at low to moderate risk, when BP is within this range at several repeated visits or elevated by ambulatory BP criteria, and remains within this range despite a reasonable period of time with lifestyle measures. | IIa | B | 266, 267 |
| In elderly hypertensive patients drug treatment is recommended when SBP is ≥160 mmHg. | I | A | 141, 265 |
| Antihypertensive drug treatment may also be considered in the elderly (at least when younger than 80 years) when SBP is in the 140–159 mmHg range, provided that antihypertensive treatment is well tolerated. | IIb | C | - |
| Unless the necessary evidence is obtained it is not recommended to initiate antihypertensive drug therapy at high normal BP. | III | A | 265 |
| Lack of evidence does also not allow recommending to initiate antihypertensive drug therapy in young individuals with isolated elevation of brachial SBP, but these individuals should be followed closely with lifestyle recommendations. | III | A | 142 |

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; OD = organ damage; SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendation(s).

Prof. Klaus Bonaventura, kbonaventura@klinikumemden.de

European Heart Journal (2013) 34, 2159–2219

# Antihypertensive drug treatment

ERNST VON BERGMANN KLINIKUM

⇨ **Antihypertensive Pharmakotherapie**

⇨ - Diuretika (inkl. Thiazide, Chlorthalidon und Indapamid),
- Betablocker
- Kalziumantatgonisten
- ACE-Hemmer und AT1-Antagonisten

sind als **Monotherapie** oder in bestimmten **Kombinationen** für den Beginn und Fortführung der Behandlung geeignet. (Klasse-1-Empfehlung und Evidenzgrad A)

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

ERNST VON BERGMANN KLINIKUM

**TABELLE**

**Arzneimittelempfehlungen für bestimmte Situationen**

| | |
|---|---|
| **Asymptomatischer Organschaden** | |
| Linksventrikuläre Hypertrophie | ACE-Hemmer, Calciumantagonist, ARB |
| Atherosklerose | Calciumantagonist, ACE-Hemmer |
| Mikroalbuminurie | ACE-Hemmer, ARB |
| Niereninsuffizienz | ACE-Hemmer, ARB |
| **Kardiovaskuläre Komplikation** | |
| Z.n. Schlaganfall | Jedes effektive Antihypertensivum |
| Z.n. Myokardinfarkt | Betablocker, ACE-Hemmer, ARB |
| Angina pectoris | Betablocker, Calciumantagonist |
| Herzinsuffizienz | Diuretika, Betablocker, ACE-Hemmer, ARB, Mineralokortikoidrezeptorantagonist |
| Aortenaneurysma | Betablocker |
| Vorhofflimmern (Prävention) | Erwägen: ARB, ACE-Hemmer, Betablocker oder Mineralokortikoidrezeptorantagonist |
| Vorhofflimmern (ventrikuläre HF-Kontrolle) | Betablocker, Calciumantagonist (außer: Dihydropyridine!) |
| Terminale Niereninsuffizienz/ Proteinurie | ACE-Hemmer, ARB |
| Periphere art. Verschlusskrankheit | ACE-Hemmer, Calciumantagonist |
| **Andere** | |
| Isolierte syst. Hypertonie (Ältere) | Diuretikum, Calciumantagonist |
| Metabolisches Syndrom | ACE-Hemmer, ARB, Calciumantagonist |
| Diabetes mellitus | ACE-Hemmer, ARB |
| Schwangerschaft | Methyldopa, Betablocker, Calciumantagonist |
| Afrikanische Abstammung | Diuretikum, Calciumantagonist |

ACE = Angiotensin-converting-Enzym; ARB =Angiotensinrezeptorblocker;
Quelle: ESH/ESC-Leitlinie 2013, Seite 32, Tabelle 5

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Monotherapy vs. drug combination strategies

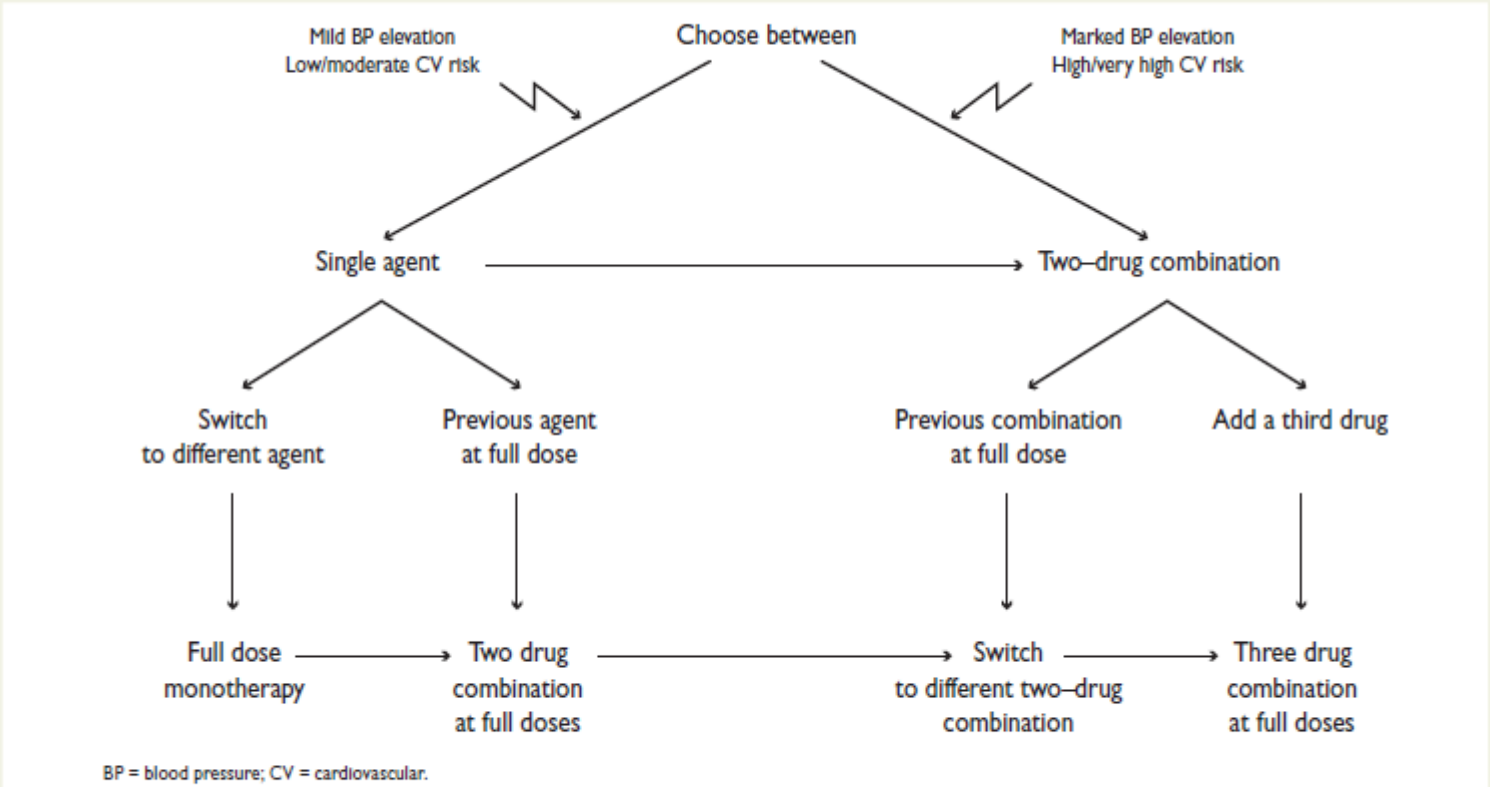


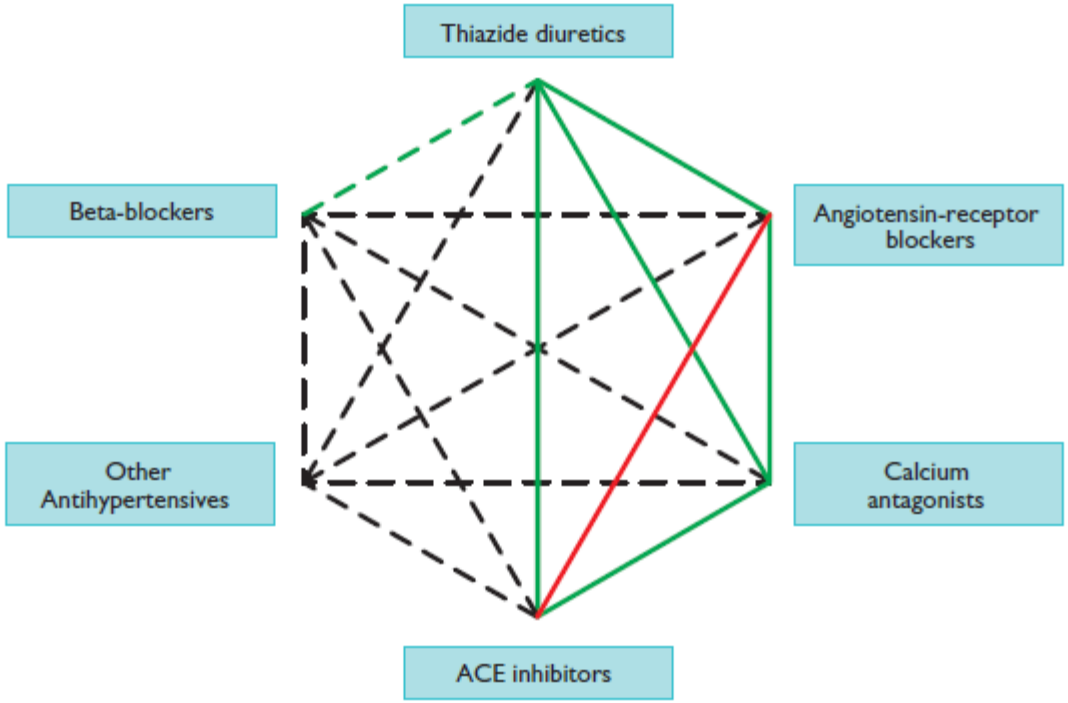

**Figure 3** Monotherapy vs. drug combination strategies to achieve target BP. Moving from a less intensive to a more intensive therapeutic strategy should be done whenever BP target is not achieved.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Possible combinations of classes of antihypertensive drugs






ACE = angiotensin-converting enzyme.

**Figure 4** Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed line: useful combination (with some limitations); black dashed lines: possible but less well-tested combinations; red continuous line: not recommended combination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

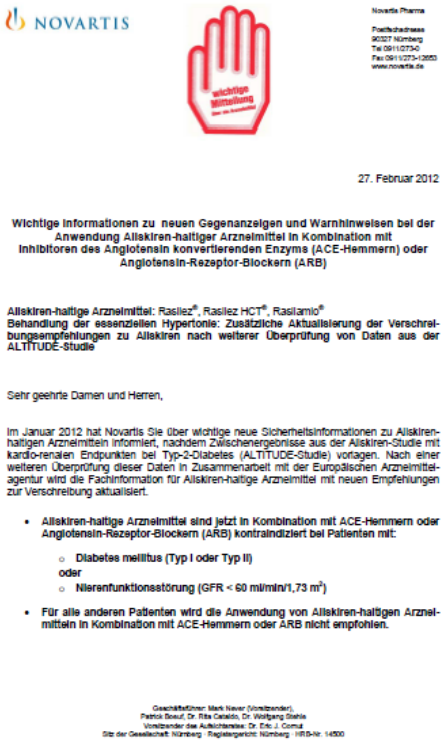
Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Antihypertensive drug treatment

ERNST VON BERGMANN KLINIKUM

⇨ **Aliskiren:**
Kontraindiziert in Kombination mit ACEH/AT2-RA bei Diabetes oder NI; für die übrigen Patienten wird davon abgeraten



NOVARTIS

Novartis Pharma

Postfachadresse
90327 Nürnberg
Tel 0911/273-0
Fax 0911/273-12653
www.novartis.de

27. Februar 2012

**Wichtige Informationen zu neuen Gegenanzeigen und Warnhinweisen bei der Anwendung Aliskiren-haltiger Arzneimittel in Kombination mit Inhibitoren des Angiotensin konvertierenden Enzyms (ACE-Hemmern) oder Angiotensin-Rezeptor-Blockern (ARB)**

**Aliskiren-haltige Arzneimittel:** Rasilez®, Rasilez HCT®, Rasilamlo®
**Behandlung der essenziellen Hypertonie: Zusätzliche Aktualisierung der Verschreibungsempfehlungen zu Aliskiren nach weiterer Überprüfung von Daten aus der ALTITUDE-Studie**

Sehr geehrte Damen und Herren,

Im Januar 2012 hat Novartis Sie über wichtige neue Sicherheitsinformationen zu Aliskiren-haltigen Arzneimitteln informiert, nachdem Zwischenergebnisse aus der Aliskiren-Studie mit kardio-renalen Endpunkten bei Typ-2-Diabetes (ALTITUDE-Studie) vorlagen. Nach einer weiteren Überprüfung dieser Daten in Zusammenarbeit mit der Europäischen Arzneimittelagentur wird die Fachinformation für Aliskiren-haltige Arzneimittel mit neuen Empfehlungen zur Verschreibung aktualisiert.

- **Aliskiren-haltige Arzneimittel sind jetzt in Kombination mit ACE-Hemmern oder Angiotensin-Rezeptor-Blockern (ARB) kontraindiziert bei Patienten mit:**
  - **Diabetes mellitus (Typ I oder Typ II)**
    **oder**
  - **Nierenfunktionsstörung (GFR < 60 ml/min/1,73 m²)**
- **Für alle anderen Patienten wird die Anwendung von Aliskiren-haltigen Arzneimitteln in Kombination mit ACE-Hemmern oder ARB nicht empfohlen.**

Geschäftsführer: Mark Never (Vorsitzender),
Patrick Boeuf, Dr. Rita Calabro, Dr. Wolfgang Stehle
Vorsitzender des Aufsichtsrates: Dr. Ernst J. Cornuz
Sitz der Gesellschaft: Nürnberg · Registergericht: Nürnberg · HRB-Nr. 14500

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Therapeutic strategies in the elderly

ERNST VON BERGMANN KLINIKUM

**Antihypertensive treatment strategies in the elderly**

| Recommendations | Class[a] | Level[b] | Ref.[c] |
|---|---|---|---|
| In elderly hypertensives with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg. | I | A | 141, 265 |
| In fit elderly patients <80 years old antihypertensive treatment may be considered at SBP values ≥140 mmHg with a target SBP <140 mmHg if treatment is well tolerated. | IIb | C | - |
| In individuals older than 80 years with an initial SBP ≥160 mmHg it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions. | I | B | 287 |
| In frail elderly patients, it is recommended to leave decisions on antihypertensive therapy to the treating physician, and based on monitoring of the clinical effects of treatment. | I | C | - |
| Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual becomes octogenarian. | IIa | C | - |
| All hypertensive agents are recommended and can be used in the elderly, although diuretics and calcium antagonists may be preferred in isolated systolic hypertension. | I | A | 444, 449, 451, 452 |

SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendation(s).

## Ältere Patienten

Beginn der Therapie bei RR > 160 mmHg

Pat. > 80 Jahre
RR 140-150 mmHg

Bei gebrechlichen Patienten entscheidet der behandelnde Arzt

Alle Antihypertensiva möglich, Diuretika und Calciumantagonisten bevorzugt bei syst. Hypertonie

European Heart Journal (2013) 34, 2159–2219

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# Therapeutic strategies in patients with diabetes

ERNST VON BERGMANN KLINIKUM

**Treatment strategies in patients with diabetes**

| Recommendations | Class [a] | Level [b] | Ref. [c] |
|---|---|---|---|
| While initiation of antihypertensive drug treatment in diabetic patients whose SBP is ≥160 mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is ≥140 mmHg. | I | A | 275, 276 290–293 |
| A SBP goal <140 mmHg is recommended in patients with diabetes. | I | A | 270,275, 276,295 |
| The DBP target in patients with diabetes is recommended to be <85 mmHg. | I | A | 290, 293 |
| All classes of antihypertensive agents are recommended and can be used in patients with diabetes; RAS blockers may be preferred, especially in the presence of proteinuria or microalbuminuria. | I | A | 394,513 |
| It is recommended that individual drug choice takes comorbidities into account. | I | C | - |
| Simultaneous administration of two blockers of the RAS is not recommended and should be avoided in patients with diabetes. | III | B | 433 |

DBP = diastolic blood pressure; RAS = renin–angiotensin system; SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendation(s).

**Patienten mit Diabetes mellitus**

Einen Einfluss auf diese **Neubewertung** hatten die enttäuschenden Ergebnisse der **ACCORD-Studie** gehabt (NEJM 2010; 362: 1575– 85).

Danach war die aggressive antihypertensive Therapie nicht in der Lage, Typ-2-Diabetiker deutlicher vor Herz-Kreislauf-Erkrankungen zu bewahren.

Stattdessen verdoppelte sich die Zahl der Patienten mit einem Abfall der glomerulären Filtrationsrate auf unter 30 ml/min/1,73 $m^2$, was auf eine Nierenschädigung hinweist.

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Therapeutic strategies in patients with diabetes

ERNST VON BERGMANN KLINIKUM

**Treatment strategies in patients with diabetes**

| Recommendations | Class [a] | Level [b] | Ref. [c] |
|---|---|---|---|
| While initiation of antihypertensive drug treatment in diabetic patients whose SBP is ≥160 mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is ≥140 mmHg. | I | A | 275, 276 290–293 |
| A SBP goal <140 mmHg is recommended in patients with diabetes. | I | A | 270,275, 276,295 |
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| It is recommended that individual drug choice takes comorbidities into account. | I | C | - |
| Simultaneous administration of two blockers of the RAS is not recommended and should be avoided in patients with diabetes. | III | B | 433 |

DBP = diastolic blood pressure; RAS = renin–angiotensin system; SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendation(s).

**Patienten mit Diabetes mellitus**

Beginn Antihypertensiva bei RR >140 mmHg

Zielblutdruck < 140/85 mmHg

RAS-Blockade bevorzugt, besonders bei Proteinurie oder Mikroalbuminurie

Kombination von 2 RAS Blockern vermeiden

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

European Heart Journal (2013) 34, 2159–2219

# Therapeutic strategies in hypertensive patients with nephropathy

ERNST VON BERGMANN KLINIKUM

**Therapeutic strategies in hypertensive patients with nephropathy**

| Recommendations | Class[a] | Level[b] | Ref.[c] |
|---|---|---|---|
| Lowering SBP to <140 mmHg should be considered. | IIa | B | 303, 313 |
| When overt proteinuria is present, SBP values <130 mmHg may be considered, provided that changes in eGFR are monitored. | IIb | B | 307, 308, 313 |
| RAS blockers are more effective in reducing albuminuria than other antihypertensive agents, and are indicated in hypertensive patients in the presence of microalbuminuria or overt proteinuria. | I | A | 513, 537 |
| Reaching BP goals usually requires combination therapy, and it is recommended to combine RAS blockers with other antihypertensive agents. | I | A | 446 |
| Combination of two RAS blockers, though potentially more effective in reducing proteinuria, is not recommended. | III | A | 331, 433, 463 |
| Aldosterone antagonists cannot be recommended in CKD, especially in combination with a RAS blocker, because of the risk of excessive reduction in renal function and of hyperkalaemia. | III | C | - |

BP = blood pressure; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; RAS = renin–angiotensin system; SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendation(s).

**Patienten mit Nierenerkrankung**

Bei Proteinurie RR < 130 mmHg

RAS-Blockade bei Albuminurie

Kombinationstherapie meistens erforderlich (RAS-Blocker plus anderes Antihypertensivum)

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# Zusammenfassung ESH/ESC 2013

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| | ESH/ESC 2013 |
|---|---|
| Alle Patienten | < 140/90 mmHg |
| Hohes CV-Risiko | < 140/90 mmHg |
| Diabetes mellitus | < 140/85 mmHg |
| Niereninsuffizienz | < 140/90 mmHg |
| Proteinurie > 1g/Tag | < 130 syst. mmHg |
| > 80 Jahre | 140-150 syst. mmHg |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# ESC Guidelines 2013

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ESC GUIDELINES

## 2013 ESC guidelines on the management of stable coronary artery disease

### The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

**Task Force Members: Gilles Montalescot* (Chairperson) (France), Udo Sechtem* (Chairperson) (Germany), Stephan Achenbach (Germany), Felicita Andreotti (Italy), Chris Arden (UK), Andrzej Budaj (Poland), Raffaele Bugiardini (Italy), Filippo Crea (Italy), Thomas Cuisset (France), Carlo Di Mario (UK), J. Rafael Ferreira (Portugal), Bernard J. Gersh (USA), Anselm K. Gitt (Germany), Jean-Sebastien Hulot (France), Nikolaus Marx (Germany), Lionel H. Opie (South Africa), Matthias Pfisterer (Switzerland), Eva Prescott (Denmark), Frank Ruschitzka (Switzerland), Manel Sabaté (Spain), Roxy Senior (UK), David Paul Taggart (UK), Ernst E. van der Wall (Netherlands), Christiaan J.M. Vrints (Belgium).**

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

# ESC Guidelines 2013
# Testing in asymptomatic patients at risk for stable coronary artery disease

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| Recommendations | Class [a] | Level [b] | Ref. [c] |
|---|---|---|---|
| In asymptomatic adults with hypertension or diabetes a resting ECG should be considered for CV risk assessment. | IIa | C | - |
| In asymptomatic adults at intermediate risk (see SCORE for definition of intermediate risk - www.heartscore.org) measurement of carotid intima-media thickness with screening for atherosclerotic plaques by carotid ultrasound, measurement of ankle-brachial index or measurement of coronary calcium using CT should be considered for CV risk assessment. | IIa | B | 221-225 |
| In asymptomatic adults with diabetes, 40 years of age and older, measurement of coronary calcium using CT may be considered for CV risk assessment. | IIb | B | 226, 227 |
| In asymptomatic adults without hypertension or diabetes a resting ECG may be considered. | IIb | C | - |
| In intermediate-risk asymptomatic adults (see SCORE for definition of intermediate risk - www.heartscore.org), (including sedentary adults considering starting a vigorous exercise programme), an exercise ECG may be considered for CV risk assessment particularly when attention is paid to non-ECG markers such as exercise capacity. | IIb | B | 228, 229 |
| In asymptomatic adults with diabetes or asymptomatic adults with a strong family history of CAD or when previous risk assessment testing suggests high risk of CAD, such as a coronary artery calcium score of 400 or greater stress imaging tests (MPI, stress echocardiography, perfusion CMR) may be considered for advanced CV risk assessment. | IIb | C | - |
| In low- or intermediate-risk (based on SCORE) asymptomatic adults stress imaging tests are not indicated for further CV risk assessment. | III | C | - |

Prof. Klaus Bonaventura, bonaventura@klinikum-ev.de

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# ESC Guidelines 2013
# Indications to perform CABG or PCI in stable CAD

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| Clinical conditions | Type of preferred revascularization[a] |
|---|---|
| Single-vessel disease, non-proximal LAD, with or without diabetes mellitus. | PCI |
| Multi-vessel disease with SYNTAX score <22 and high surgical risk (e.g. EuroSCORE >6). | PCI |
| Revascularization in patient with contra-indication to surgery (severely impaired lung function, prior mediastinal irradiation, prior CABG or non-coronary cardiac surgery, bilateral carotid artery stenoses). | PCI |
| Elderly patient (>80 years) and co-morbidities or frailty [b] | PCI |
| Left main disease with SYNTAX score ≥33. | CABG |
| Multi-vessel disease (with or without diabetes) with LAD involvement and SYNTAX score >22. | CABG |
| Recurrent in-stent re-stenosis after DES implantation in proximal-mid LAD. | CABG |
| Revascularization in patients with concomitant significant structural heart disease also requiring surgery. | CABG |
| Multi-vessel disease or left main disease with SYNTAX score <22 and low surgical risk (e.g. EuroSCORE <6) | CABG or PCI |
| Left main disease with SYNTAX score <33. | CABG or PCI |
| Impaired LV function. | CABG or PCI |
| Renal insufficiency or dialysis. | CABG or PCI |

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de

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# Akzelerierte Arteriosklerose bei CKD und Diabetes

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- ⇨ Fokus SCORE
- ⇨ Interdisziplinäres Problem
- ⇨ Strategie: frühzeitige Therapie weitere Risikofaktoren
- ⇨ HbA1c 6.5-7%
- ⇨ Hyperlipidämie: Statin
- ⇨ Hypertonie: RAS-Blockade
- ⇨ DAPT: Keine Änderung
- ⇨ Interventionell: PCI vs. OP im Herzteam

Prof. Klaus Bonaventura, kbonaventura@klinikumevb.de