

XXIV. Diagnostiksymposium Schaan, 08.03.2018

## **Globales Assessment des kardiovaskulären Risikos und dessen Reduktion: ein Update**

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## **Conflict of Interest**

Kein Interessenskonflikt

Akademisches Referat

## **Disclosure**

Honorare für Vorträge,  
Forschungsunterstützung und  
Beratungsaktivitäten:

NovoNordisk, Merck, MSD, Pfizer, Sanofi-  
Aventis, AstraZeneca, Bayer, Takeda,  
Daiichi-Sankyo, Novartis, Amgen,  
Boehringer Ingelheim, BMS, Abbott,  
Janssen-Cilag, Genericon

## **Outline**

1. Zusammenfassung
2. Patientenbeispiel
  - a. Lipide
  - b. Diabetes
  - c. Blutdruck
3. Die Quintessenz

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## **Zusammenfassung**

## Risikoforschung am Beispiel des Verkehrsunfalls

- Kausalität: Geschwindigkeit
- Ko-Kausalität
  - Zustand der Straße
  - Zustand der Bremsen
  - Zustand der Reifen
  - Aufmerksamkeit des Fahrers
  - Alkohol
  - Handy.....



## Definition von absolutem und relativem Risiko

**Absolutes Risiko ist**

a) definiert durch die Population



b) Reduktion von Studiendauer abhängig

**Relatives Risiko ist**

a) definiert durch die Intervention



b) Reduktion nicht von Studiendauer abhängig



**Risiko = Gefahr ≠ Unfall**



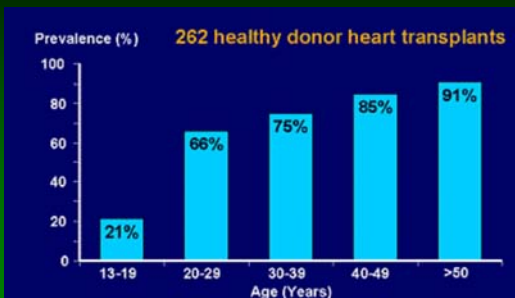
**Risiko = Gefahr ≠ Unfall**

**Population vs. Individuum**

z.B. 20%

0% oder 100%

## Prävalenz asymptomatischer KHK



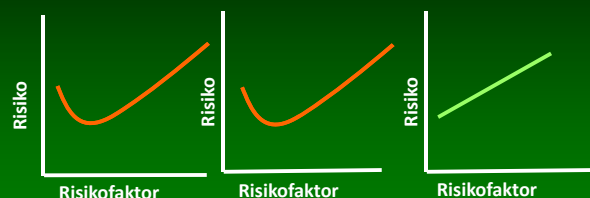
Tuzcu EM et al. Circulation 2001;103:2705-2710

## Physiologischer Level = Optimales Risiko?

Blutdruck

HbA1c

LDL-C




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## Patientenbeispiel

Parameter	Patientenbeispiel: Mann
Alter	65
	Akutes Koronarsyndrom mit LAD-PCI Diabetes mellitus
Raucher	30 PY
Blutdruck	170/100

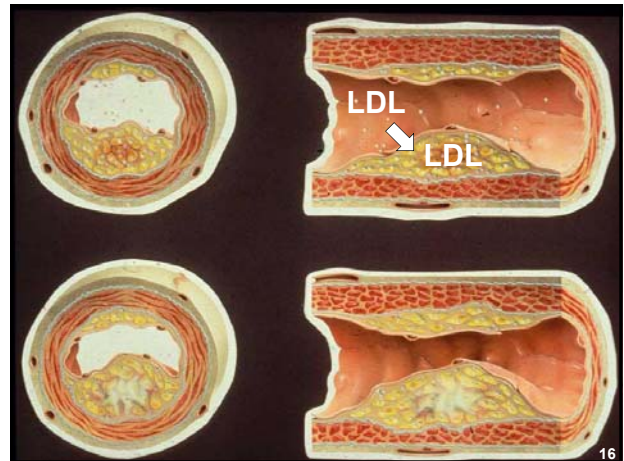
 European Heart Journal (2017) 38, 1–14  
doi:10.1093/eurheartj/ehw144

**CURRENT OPINION**

### Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel

Brian A. Ference<sup>1</sup>, Henry N. Ginsberg<sup>2</sup>, Ian Graham<sup>3</sup>, Kausik K. Ray<sup>4</sup>, Chris J. Packard<sup>5</sup>, Eric Bruckert<sup>6</sup>, Robert A. Hegele<sup>7</sup>, Ronald M. Krauss<sup>8</sup>, Frederick J. Raal<sup>9</sup>, Heribert Schunkert<sup>10,11</sup>, Gerald F. Watts<sup>12</sup>, Jan Borén<sup>13</sup>, Sergio Fazio<sup>14</sup>, Jay D. Horton<sup>15,16</sup>, Luis Masana<sup>17</sup>, Stephen J. Nicholls<sup>18</sup>, Børge G. Nordestgaard<sup>19,20,21</sup>, Bart van de Sluis<sup>22</sup>, Marja-Riitta Taskinen<sup>23</sup>, Lale Tokgözoğlu<sup>24</sup>, Ulf Landmesser<sup>25,26</sup>, Ulrich Laufs<sup>27</sup>, Olov Wiklund<sup>28,29</sup>, Jane K. Stock<sup>30</sup>, M. John Chapman<sup>31</sup>, and Alberico L. Catapano<sup>32</sup>

Ference BA et al. Eur Heart J 2017; 38: 2459–2472. 15



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## Charakteristika eines Risikofaktors

1. Plausibel
2. Starke Assoziation
3. Unabhängig
4. Dosisabhängig
5. Prädiktiv
6. Konsistent
7. Kohärent
8. Reversibel

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## Risiko für kardiovaskuläre Erkrankungen: Pooled Cohort Equations

**Risk Factors for ASCVD**

Gender:  Male  Female    Systolic BP: 118 mmHg

Age: 40 years    Receiving treatment for high blood pressure (if SBP > 120 mmHg):  No  Yes

Race: White or other    Diabetes:  No  Yes

Total Cholesterol: 210 mg/dL    Smoker:  No  Yes

HDL Cholesterol: 60 mg/dL

Goff DC et al. *Circulation* 2014;129:S49-73.  
<http://clincalc.com/cardiology/ascvd/pooledcohort.aspx>

## Risiko für kardiovaskuläre Erkrankungen: Pooled Cohort Equations



Goff DC et al. *Circulation* 2014;129:S49-73.  
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## Guidelines Dyslipidämie

European Heart Journal  
doi:10.1093/eurheartj/ehw272

ESC/EAS GUIDELINES

### 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias

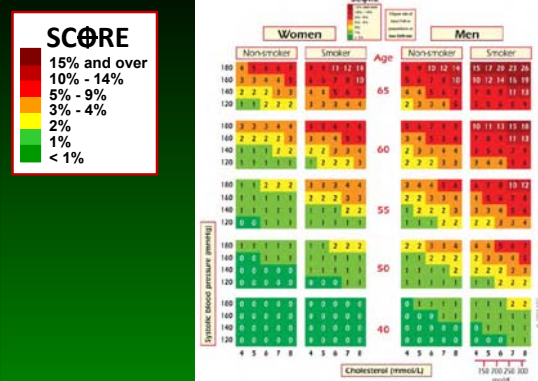
The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

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

Authors/Task Force Members: Alberico L. Catapano\* (Chairperson) (Italy), Ian Graham\* (Chairperson) (Ireland), Guy De Backer (Belgium), Olov Wiklund (Sweden), M. John Chapman (France), **Heinz Drexel (Austria)**, Arno W. Hoes (The Netherlands), Catriona S. Jennings (UK), Ulf Landmesser (Germany), Terje R. Pedersen (Norway), Zeljko Reiner (Croatia), Gabriele Riccardi (Italy), Marja-Riita Taskiran (Finland), Lale Tokgozoglu (Turkey), W. M. Monique Verschuren (The Netherlands), Charalambos Vlachopoulos (Greece), David A. Wood (UK), Jose Luis Zamorano (Spain)

Additional Contributor: Marie-Therese Cooney (Ireland)

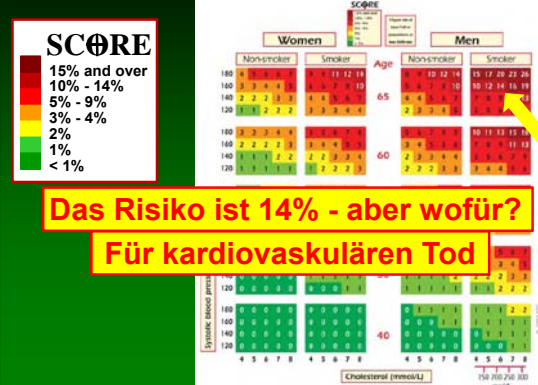
## Länder mit niedrigem CV Risiko



## Patientenbeispiel: Ausgangswerte

Parameter	Patientenbeispiel
Alter	65
Raucher	Akutes Koronarsyndrom mit PCI und 2x DES in LAD Diabetes mellitus
Blutdruck	170/100
Lipidstatus	Total cholesterol: 250 mg/dl $\pm$ 6.5 mmol/L LDL cholesterol: 170 mg/dl $\pm$ 4.4 mmol/L HDL cholesterol: 50 mg/dl $\pm$ 1.3 mmol/L Triglyceride: 150 mg/dl $\pm$ 1.7 mmol/L
HbA1c	8,1%
Therapie	Metformin 1000 mg 1-0-1 ASS 100 mg 0-1-0 Amlodipin 5 mg 1-0-0

## Länder mit niedrigem CV Risiko



## ESC/EAS Guidelines 2016

### VERY HIGH RISK

**LDL-C < 70 mg/dl bzw.  
≥ 50% Reduktion wenn Baseline  
LDL-C zw. 70 und 135 mg/dl**

bei KHK, PAVK, Insult  
Typ 2 Diabetes  
Niereninsuffizienz (GFR < 30 ml/min)

**>10% SCORE 10a Risiko  
für CV Tod**

Catapano AL et al. EHJ 2016; 37: 2999-3058.

## ESC/EAS Guidelines 2016

**Wenn dieser Patient keinen Diabetes  
und keine KHK hätte: 9% SCORE  
So aber  
HÖCHSTRISIKO**

## ESC/EAS Guidelines 2016

### HIGH RISK

**LDL-C < 100 mg/dl  
≥ 50% Reduktion wenn Baseline  
LDL-C zw. 100 und 200 mg/dl**

**5-10% SCORE 10a Risiko  
für CV Tod**

Catapano AL et al. EHJ 2016; 37: 2999-3058.

## ESC/EAS Guidelines 2016

### MODERATE RISK

**LDL-C <115 mg/dl**

**≥ 1 und < 5 % SCORE 10a Risiko  
für CV Tod**

Catapano AL et al. EHJ 2016; 37: 2999-3058.

## ESC/EAS Guidelines 2016

### LOW RISK

**LDL-C <115 mg/dl**

**< 1% SCORE 10a Risiko  
für CV Tod**

Catapano AL et al. EHJ 2016; 37: 2999-3058.

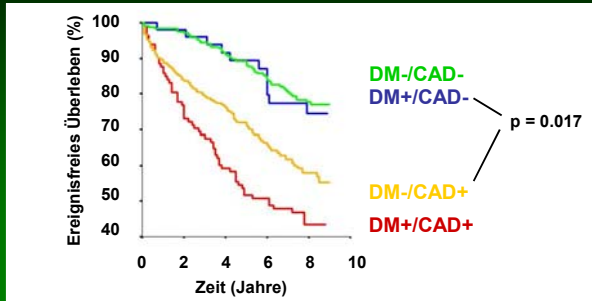
International Journal of Cardiology 167 (2013) 770–780  
Contents lists available at SciVerse ScienceDirect  
ELSEVIER International Journal of Cardiology journal homepage: www.elsevier.com/locate/ijcard

**Type 2 diabetes and the progression of visualized atherosclerosis to clinical cardiovascular events<sup>☆</sup>**

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## Diabetes + KHK: Höchstisiko



Saely CH et al. Int J Cardiol 2013;167:776-80.

## LDLC Zielwerte in Verschiedenen Risikokategorien

Risikokategorie	LDL-C Ziel (mg/dl)	LDL-C Ziel (mmol/l)
Sehr hohes Risiko	< 70	<1.8
Hohes Risiko	<100	<2.6
Niederes oder moderates Risiko	<115	<3.0

Risikokategorie	Non-HDL Ziel (mg/dl)	Non-HDL Ziel (mmol/l)
Sehr hohes Risiko	<100	<2.6
Hohes Risiko	<130	<3.4
Niederes oder moderates Risiko	<145	<3.8

Catapano AL et al. EHJ 2016; 37: 2999-3058.

## ESC/EAS Guidelines 2016

### Zielwerte für LDL-C

Recommendations	Class*	Level <sup>†</sup>
In patients at VERY HIGH CV risk <sup>1</sup> , an LDL-C goal of <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C <sup>2</sup> is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.	I	B
In patients at HIGH CV risk <sup>1</sup> , an LDL-C goal of <2.6 mmol/L (100 mg/dL), or a reduction of at least 50% if the baseline LDL-C <sup>2</sup> is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B
In subjects at LOW or MODERATE risk <sup>2</sup> an LDL-C goal of <3.0 mmol/L (<115 mg/dL) should be considered.	IIa	C

Catapano AL et al. EHJ 2016; 37: 2999-3058.

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## Leitlinien der ÖDG: Individuelles HbA1c Ziel

6.5-8.0

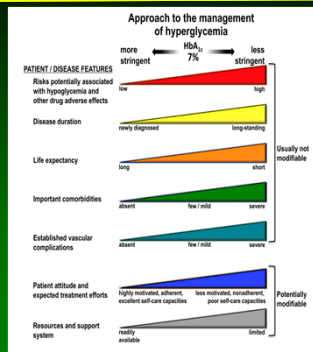
Clodi M et al. Wien Klin Wochenschr 2012; 124: 10-16.

## HbA1c Ziel zur Verhinderung mikrovaskulärer Komplikationen

<7.0

Diabetes Care 2015; Suppl 1: S01-93.

## HbA1c Ziele ADA / EASD Konsensus



Inzucchi SE et al. Diabetes Care 2015;38:140-149.

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## LDL-C Ziel (ESC/EAS)



Diabetes Care 2017; 40:Suppl 1:S01-142.

## Bei <60a Behandlungsziel <140/90 mmHg

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
Lifestyle measures (weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fruits, vegetables, and low-fat dairy products) are recommended in all patients with hypertension and in individuals with high normal BP.	I	A	337, 428-430
All major BP-lowering drug classes (i.e., thiazide, ACE inhibitor, angiotensin II receptor blocker, and calcium channel blocker) do not differ significantly in their BP-lowering efficacy and thus are recommended as BP-lowering treatment.	I	A	431-432
In asymptomatic subjects with hypertension but free of CVD, CKD, and DM, total CV risk stratification using the SCORE model is recommended.	I	B	30

**SBP <140 mmHg and DBP <90 mmHg are recommended in all treated hypertensive patients <60 years old. IB**

In patients >60 years old with SBP <160 mmHg, it is recommended to reduce SBP to between 130 and 140 mmHg.	I	B	434
In patients >60 years old, a target SBP <140 mmHg may be considered if treatment is well tolerated. In some of these patients a target SBP <130 mmHg may be considered if at (very) high-risk and tolerate multiple BP-lowering drugs.	IIa	B	424, 425
In individuals >60 years old with initial SBP <160 mmHg, it is recommended to reduce SBP to between 130 and 140 mmHg, provided they are in good physical and mental conditions.	I	B	434
In frail elderly patients, a careful treatment intensity (i.e., number of BP-lowering drugs) and BP targets should be considered, and clinical effects of treatment should be carefully monitored.	IIa	B	436
Initiation of BP-lowering therapy with a two-drug combination may be considered in patients with markedly elevated baseline BP or at high CV risk. Combination of two drugs as fixed doses in a single pill may be considered because of improved adherence.	IIa	C	437
Diuretics with metabolic effects are not recommended in hypertensive patients with multiple metabolic risk factors. Due to the increased risk of DM.	III	B	438

Piepoli MF et al. Eur Heart J 2016 (in press)

## Bei >60a Behandlungsziel generell 140-150 mmHg

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
Lifestyle measures (weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fruits, vegetables, and low-fat dairy products) are recommended in all patients with hypertension and in individuals with high normal BP.	I	A	337, 428-430
All major BP-lowering drug classes (i.e., thiazide, ACE inhibitor, angiotensin II receptor blocker, and calcium channel blocker) do not differ significantly in their BP-lowering efficacy and thus are recommended as BP-lowering treatment.	I	A	431-432
In asymptomatic subjects with hypertension but free of CVD, CKD, and DM, total CV risk stratification using the SCORE model is recommended.	I	B	30
Drug treatment is recommended in patients with grade 3 hypertension irrespective of CV risk, as well as in patients with grade 2 hypertension.	I	B	433

**In patients >60 years old with SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg. IB**

In patients >60 years old, a target SBP <140 mmHg may be considered if treatment is well tolerated. In some of these patients a target SBP <130 mmHg may be considered if at (very) high-risk and tolerate multiple BP-lowering drugs.	IIa	B	434, 435
In individuals >60 years old with initial SBP <160 mmHg, it is recommended to reduce SBP to between 130 and 140 mmHg, provided they are in good physical and mental conditions.	I	B	434
In frail elderly patients, a careful treatment intensity (i.e., number of BP-lowering drugs) and BP targets should be considered, and clinical effects of treatment should be carefully monitored.	IIa	B	436
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Diuretics with metabolic effects are not recommended in hypertensive patients with multiple metabolic risk factors. Due to the increased risk of DM.	III	B	438

Piepoli MF et al. Eur Heart J 2016

## Patientenbeispiel: Strategie

Parameter	Patientenbeispiel
Alter	65
Raucher	Akutes Koronarsyndrom, Diabetes mellitus, Dyslipidämie, Nierentests
Blutdruck	170/100 mmHg
Lipidstatus	LDL-Cholesteroll: 250 mg/dl ± 6.5 mmol/L HDL-Cholesteroll: 170 mg/dl ± 4.4 mmol/L Triglyceride: 150 mg/dl ± 1.7 mmol/L
HbA1c	8,1%
Therapie	Empagliflozin 10 mg, Rosuvastatin 40 mg, Metformin 1000 mg 1-0-1, ASS 100 mg, Amlodipin 10mg 1-0-0, Candesartan 16 mg

**Patient mit sehr hohem Risiko!  
Behandlungsziel: LDL-C <70 mg/dl,  
Oder < 1.8 mmol/L**

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## Wozu benötigt der Organismus Glucose?

Funktion	Glucose notwendig	Grund	Kommentar
Zellenergie	ja	Zufuhr	alle
Gehirn, Nerv	Ja	obligat	Kein Fett
Leber	(Ja)	Speicher	Eigenprodukt
(Herz)Muskel	Ja	Ökonomie	2. Fettsäuren
Blutzellen	Ja	Energie	Permeabel
Niere	Ja	Energie	2. Fettsäuren

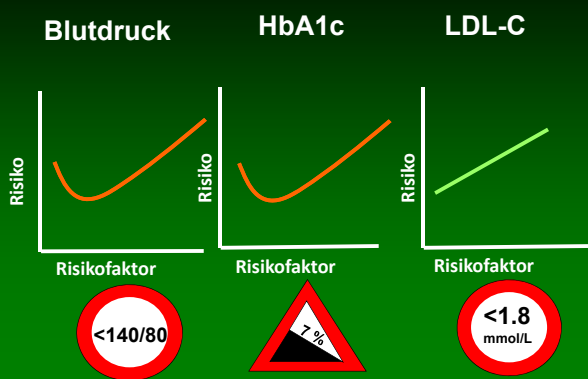
## Wozu benötigt der Organismus LDL Cholesterin?

Funktion	LDL-C notwendig	Grund	Kommentar
Zellwand	Nein	Zelle selbst	Synthese
Zellernährung	Nein	kein Chol.	Trigl., Gluc.
Steriodsynthese	Nein	Andere Lp.	z.B. HDL
Kognition	Nein	unabhängig	LDL nicht im Gehirn
Blutzellen	Nein	Andere Lp	

## Wozu benötigt der Organismus LDL Cholesterin?

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Zellwand	Nein	Zelle selbst	Synthese
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Steriodsynthese	Nein	Andere Lp.	z.B. HDL
Kognition	Nein	unabhängig	LDL nicht im Gehirn
Blutzellen	Nein	Andere Lp	
<b>Atherosklerose</b>	<b>Ja</b>	<b>LDL kausal!</b>	<b>GENETIK!</b>

## Physiologischer Level = Optimales Risiko?



## Fallbeispiel



XXIV. Diagnostiksymposium Schaan, 08.03.2018

**Globales Assessment des  
kardiovaskulären Risikos  
und dessen Reduktion – Update**

**Vielen Dank für Ihre Aufmerksamkeit!**

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