Rheumatologie und Kardiologie – entzündliche Erkrankungen, kardiovaskuläres Risiko, Lipidmanagement

Dr. med. Michael Stiefel
Oberarzt Kardiologie USZ
Email: michael.stiefel@usz.ch

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Übersicht

- Koronare Herzkrankheit – weltweit führende Todesursache
- Kardiovaskuläre Risikofaktoren
- Erhebung kardiovaskuläres Risiko / SCORE2
- Therapieempfehlungen
  - Bewegung
  - Ernährung
  - Lipidkontrolle (Statine, Ezetimib, PCSK-9-Hemmer, Bempedoinsäure)
- Fall-Beispiel
- Zusammenfassung

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ESC European Society of Cardiology European Heart Journal (2019) 00, 1–78 doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

ESC European Society of Cardiology European Heart Journal (2021) 00, 1–111 doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

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

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

2022 Prävention der Atherosklerose

Fokus auf Dyslipidämie

Übersicht zu den Empfehlungen der Arbeitsgruppe Lipide und Atherosklerose (AGLA) der Schweizerischen Gesellschaft für Kardiologie (SGK) sowie der European Society of Cardiology (ESC), der European Atherosclerosis Society (EAS) und weiterer medizinischer Gesellschaften

www.agla.ch

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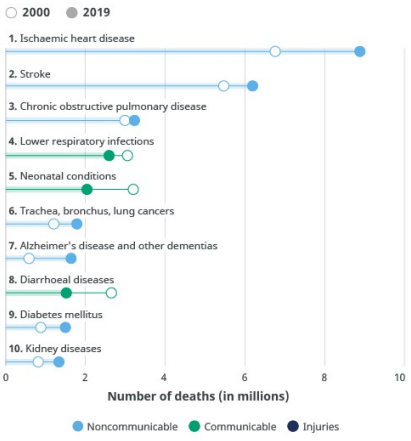
Koronare Herzerkrankung – weltweit führende Todesursache

- Kardiovaskuläre Erkrankungen verursachen ungefähr 31% (17,9 Millionen) aller Todesfälle weltweit[2]
  - 45% (3,9 Millionen) aller Todesfälle in Europa[4]
  - 23% (0,65 Millionen) aller Todesfälle in den USA[5]
- CVD sind auch eine führende Ursache vorzeitiger Todesfälle und sind verantwortlich für jährlich ungefähr 6,2 Millionen vorzeitige Todesfälle weltweit von Menschen im Alter von 30 bis 70 Jahren[6]



Source: WHO Global Health Estimates.

1 Roth GA et al. J Am Coll Cardiol. 2017;70(1):1-25; 2 WHO Fact cardiovascular-diseases_May 2017 Zugriff im Juli 2020; 3 Foreman KJ et al. Lancet 2018; 392: 2052–90; 4 European Cardiovascular Disease Statistics 2017 European heart network; 5 Kochanek KD, et al. National Vital Stat Rep. 2019; 68(9); 6 Cao B et al., Lancet Glob Health 2018; 6: e1288–96; 7 WHO Fact sheet_non-communicable diseases_Jun 2018: Zugriff im Juli 2020.

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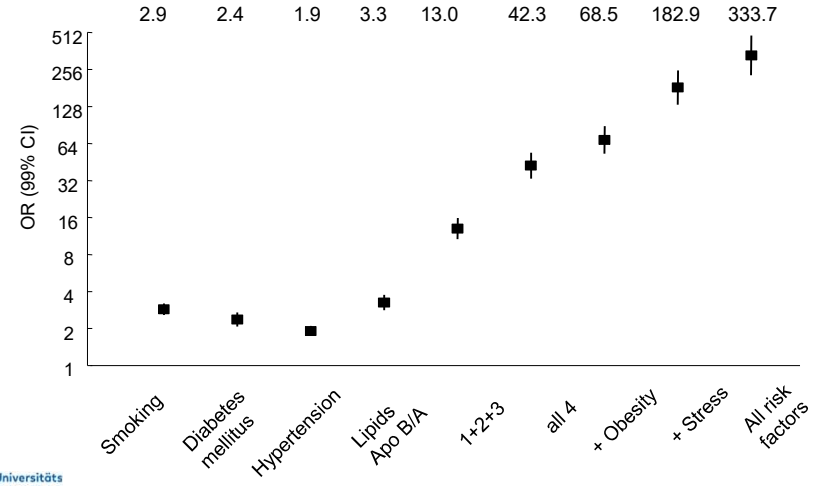
Auswirkungen potenziell veränderbarer Risikofaktoren im Zusammenhang mit Herzinfarkt in 52 Ländern (INTERHEART-Studie 2004): Fall-Kontroll-Studie (15'152 Fälle & 14'820 Kontrollen, weltweit)



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Yusuf S et al. Lancet 2004; 364: 937–52

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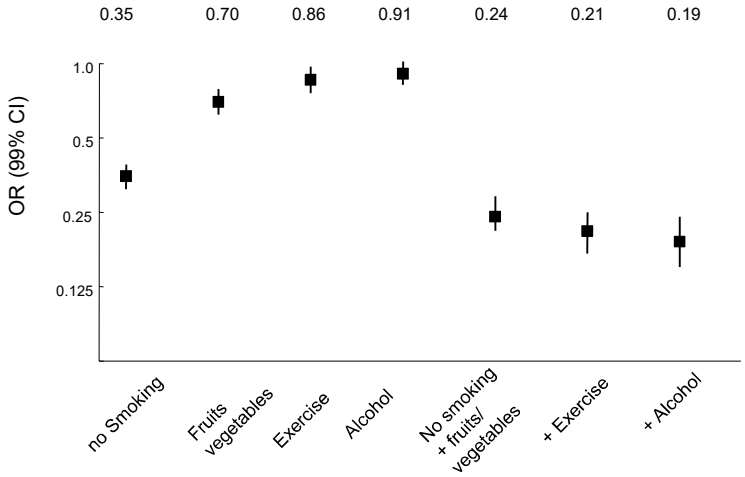
INTERHEART: Protektive Faktoren für Herzinfarkt



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Yusuf S et al. Lancet 2004; 364: 937–52

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Entzündliche Erkrankungen (akut und chronisch) erhöhen CV-Risiko

- Beste Evidenz: **Rheumatoide Arthritis: +50% Risiko**
- **Aktiv entzündliche Darmerkrankung: +20% Risiko**
- **Psoriasis, ankylosierende Spondylitis: erhöhtes Risiko** (weniger Evidenz)
- Krankheitslast und Entzündungsgrad entscheidend
- Ziel: Optimale antiinflammatorische Therapie und traditionelle Risikoreduktion

Inflammatory conditions	Assessment of total CVD risk may be considered in adults with chronic inflammatory conditions.[176]	IIb	B
	Multiplication of calculated total CVD risk by a factor of 1.5 should be considered in adults with rheumatoid arthritis.[177,178]	IIa	B

recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update.|

Körperliche Inaktivität ist wie Rauchen…

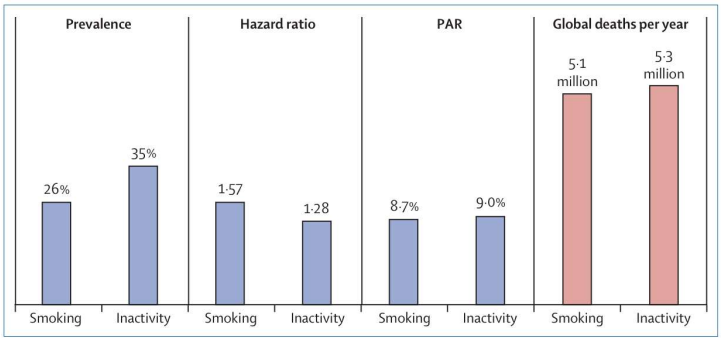


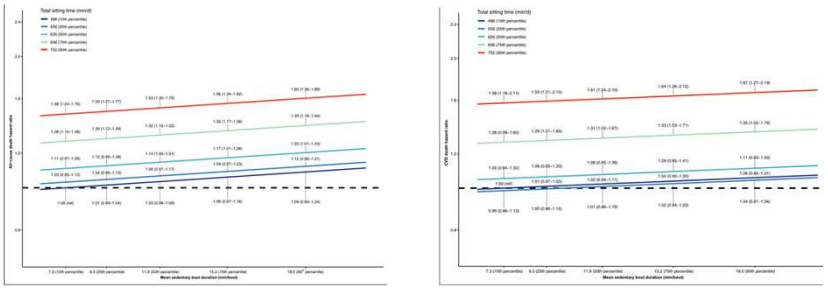
Figure: **Comparison of global burden between smoking and physical inactivity**
Prevalence of smoking, population attributable risk (PAR), and global deaths for smoking were obtained from WHO.[7] Hazard ratio for all-cause mortality of smoking was obtained from meta-analysis studies.[8,9] All inactivity data were obtained from Lee and colleagues.[5]

Stressing harms of physical inactivity to promote exercise, Lancet 2012, http://dx.doi.org/10.1016/ S0140-6736(12)60954-4

Höhere Gesamtzeit im Sitzen und längere durchschnittliche Sitzdauer sind mit einem höheren Sterberisiko verbunden

- Women's Health Initiative **O**bjective **P**hysical **A**ctivity and **C**ardiovascular **H**ealth (OPACH) Study 2024
- 5'856 woman, mean age 79; Hip accelerometer for ~7 days
- Mean follow up 8.4 years; 1733 / 30% deaths (632 CVD / 36%)

- **> 11.6 h/d** vs. **< 9.3 h/d** → **57%** higher risk of all-cause death and **78%** higher risk of CVD death
- **> 15 minutes** vs. **< 9.3 minutes** → **43%** higher risk of all-cause death and **52%** higher risk of CVD death



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Journal of the American Heart Assoc. 2024;13:e031156. DOI: 10.1161/JAHA.123.031156

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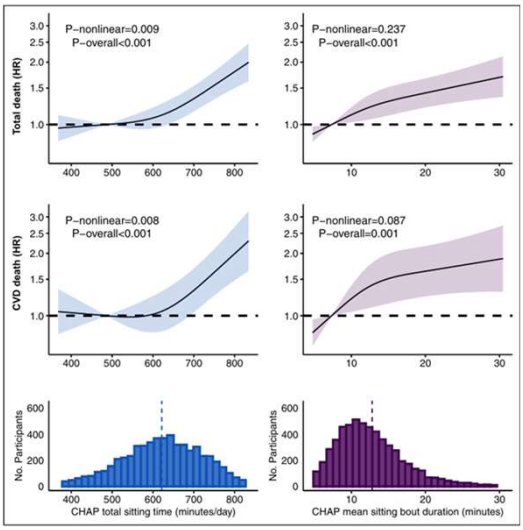
Exponentieller Anstieg der Mortalität bei einer Gesamtsitz-Zeit von > 660 – 700 Minuten (11 – 11.7 Stunden)



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Journal of the American Heart Assoc. 2024;13:e031156. DOI: 10.1161/JAHA.123.031156

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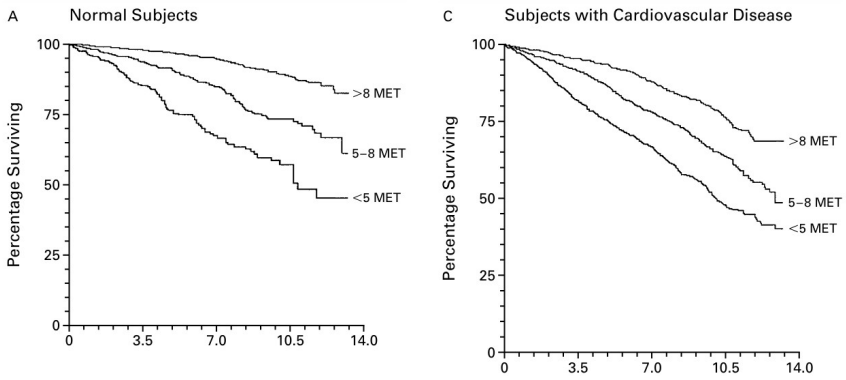
Körperliche Leistungsfähigkeit: der stärkste Prädiktor für das Sterberisiko (NEJM, 2002)

- 6213 Männer 59±11 Jahre; Maximale Ergometrie
- Follow-up: 6.2±3.7 Jahre; 1256 Todesfälle (20%)



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Myers et al. N Engl J Med 2002;346:793-801

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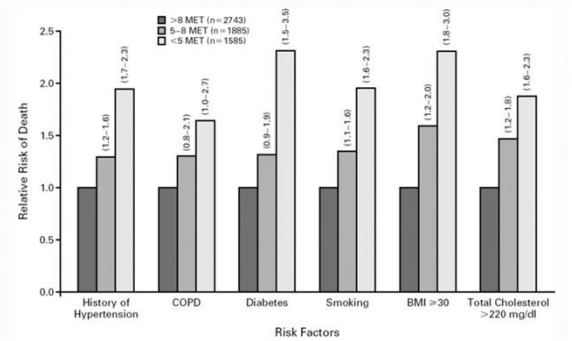
Körperliche Leistungsfähigkeit: der stärkste Prädiktor für das Sterberisiko (NEJM, 2002)



→ **the peak exercise capacity measured in metabolic equivalents (MET) was the strongest predictor of the risk of death among both normal subjects and those with cardiovascular disease.**

→ stronger predictor than clinical variables / established risk factors such as hypertension, smoking, and diabetes, as well as other exercise-test variables, including ST-segment depression, the peak heart rate, or the development of arrhythmias during exercise.

→ protective role of a higher exercise capacity even in the presence of other risk factors.

→ **Each 1-MET increase in exercise capacity conferred a 12 percent improvement in survival.**

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Myers et al. N Engl J Med 2002;346:793-801

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Bestimmung des kardiovaskulären Risikos

Patients with CKD				
CKD without diabetes or ASCVD	Moderate CKD (eGFR 30–44 mL/min/1.73 m² and ACR <30 **or** eGFR 45–59 mL/min/1.73 m² and ACR 30–300 **or** eGFR ≥60 mL/min/1.73 m² and ACR >300)	**High-risk**	N/A	
	Severe CKD (eGFR<30 mL/min/1.73 m² **or** eGFR 30–44 mL/min/1.73 m² and ACR >30)	**Very high-risk**	N/A	
Familial Hypercholesterolemia				
Associated with markedly elevated cholesterol levels	N/A	**High-risk**	N/A	
Patients with type 2 diabetes mellitus				
Patients with type 1 DM above 40 years of age may also be classified according to these criteria	Patients with well controlled short-standing DM (e.g. <10 years), no evidence of TOD and no additional ASCVD risk factors	**Moderate-risk**	N/A	**LDL<2.6 mmol/L**
	Patients with DM without ASCVD and/or severe TOD, and not fulfilling the moderate risk criteria.	**High-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the ADVANCE risk score or DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).	**LDL<1.8 mmol/L**
	Patients with DM with established ASCVD and/or severe TOD:[87, 93-95] • eGFR <45 mL/min/1.73 m² irrespective of albuminuria • eGFR 45-59 mL/min/1.73 m² and microalbuminuria (ACR 30 -300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 3 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	**Very high-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the SMART risk score for established CVD or with the ADVANCE risk score or with the DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).	**50% Senkung und LDL<1.4 mmol/L**

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Patienten mit bekannter atherosklerotischer kardiovaskulärer Erkrankung

Patients with established ASCVD				
Documented ASCVD, clinical or unequivocal on imaging. Documented clinical ASCVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented ASCVD on imaging includes plaque on coronary angiography or carotid ultrasound or on CTA. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery.	N/A	**Very high-risk**	Residual CVD risk estimation after general prevention goals (e.g. 10-year risk with the SMART risk score for patients with established CVD or 1- or 2-year risk with EUROASPIRE risk score for patients with CHD). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. SMART-REACH model; or DIAL model if diabetes).	**50% Senkung und LDL<1.4 mmol/L**

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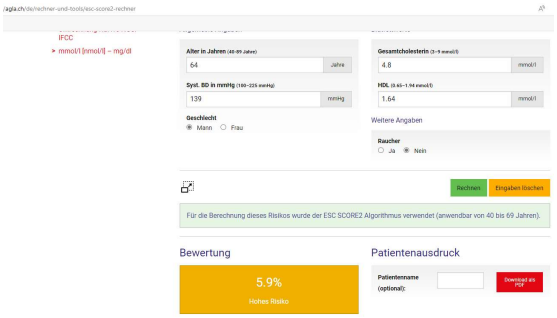
ESC SCORE2 Risikorechner - für scheinbar gesunde Personen



Sex	Male	Female
Smoking status	Non-Smoking	Smoking
Age	64	years
Systolic blood pressure	139	mmHg
Non-HDL cholesterol	3.2	mmol/l ⇄

SCORE2: 6 %

10-year risk of fatal and non-fatal cardiovascular disease

Interpretation

Age	10-year risk of fatal and non-fatal cardiovascular disease		
< 50 years	<2.5%	2.5 to <7.5%	≥7.5%
50 - 69 years	<5%	5 to <10%	≥10%
≥ 70 years	<7.5%	7.5 to <15%	≥15%

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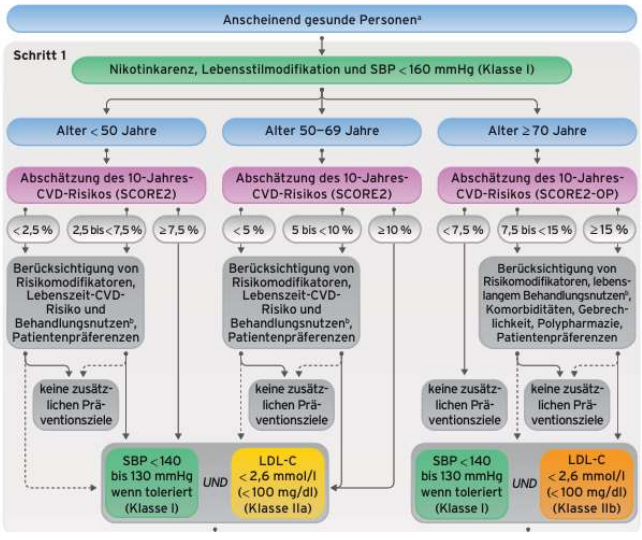
Behandlung nach kardiovaskulärem Risiko bei scheinbar Gesunden

Abbildung 6: Flussdiagramm des kardiovaskulären Risikos und der Behandlung von Risikofaktoren bei anscheinend gesunden Personen



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Lebensstil: Bewegungs-Empfehlungen für gesunde Personen

Empfehlungen	Empf.-grad	Evidenz-grad
Allen gesunden Erwachsenen wird pro Woche mindestens 150 Minuten moderaten Trainings oder 75 Minuten intensiven aeroben Trainings oder eine gleichwertige Kombination davon empfohlen.	I	A
Für einen zusätzlichen Nutzen wird allen gesunden Erwachsenen eine allmähliche Erhöhung des aeroben Trainings auf 300 Minuten pro Woche bei moderater Intensität oder auf 150 Minuten pro Woche bei intensivem aerobem Training oder eine gleichwertige Kombination empfohlen.	I	A
Eine regelmäßige Beurteilung und Beratung zur Förderung der Einhaltung des Programms und ggf. zur Unterstützung einer Erhöhung des Trainingsvolumens wird empfohlen.	I	B
Es werden mehrere Trainingseinheiten über die Woche verteilt, d.h. an 4–5 Tagen in der Woche und vorzugsweise an jedem Tag der Woche, empfohlen.	I	B
Bei älteren sturzgefährdeten Erwachsenen wird an mindestens 2 Tagen pro Woche Krafttraining zur Verbesserung des Gleichgewichts und der Koordination empfohlen.	I	B

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2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *European Heart Journal*; 42. DOI: 10.1093/eurheartj/ehaa605.

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Lebensstil: Mediterrane Diät und Rauchstopp

It is recommended to adopt a Mediterranean or similar diet to lower risk of CVD.[403,404]	I	A
It is recommended to replace saturated with unsaturated fats to lower the risk of CVD.[405–409]	I	A
It is recommended to reduce salt intake to lower BP and risk of CVD.[410]	I	A
It is recommended to choose a more plant-based food pattern, rich in fibre, that includes whole grains, fruits, vegetables, pulses, and nuts.[411,412]	I	B
It is recommended to restrict alcohol consumption to a maximum of 100 g per week.[413–415]	I	B
It is recommended to eat fish, preferably fatty, at least once a week and restrict (processed) meat.[406,416–418]	I	B
It is recommended to restrict free sugar consumption, in particular sugar-sweetened beverages, to a maximum of 10% of energy intake.[419,420]	I	B

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Recommendations	Class[a]	Level[b]
All smoking of tobacco should be stopped, as tobacco use is strongly and independently causal of ASCVD.[487,488]	I	A
In smokers, offering follow-up support, nicotine replacement therapy, varenicline, and bupropion individually or in combination should be considered.[489–494]	IIa	A
Smoking cessation is recommended regardless of weight gain, as weight gain does not lessen the ASCVD benefits of cessation.[495]	I	B

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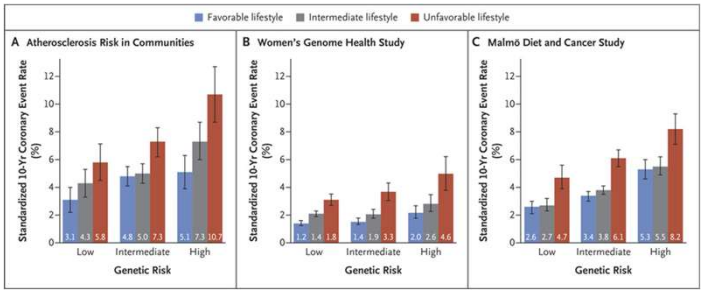
10-Year Coronary Event Rates, According to Lifestyle and Genetic Risk in Prospective Cohorts (NEJM, 2016)

- 55'685 Teilnehmer (4 Studien)
- Genetic risk and lifestyle (no current smoking, no obesity, regular physical activity, healthy diet)



- ➔ **Ein gesunder Lebensstil halbiert das Risiko für das erste kardiovaskuläre Ereignis unabhängig vom genetischen Risiko**

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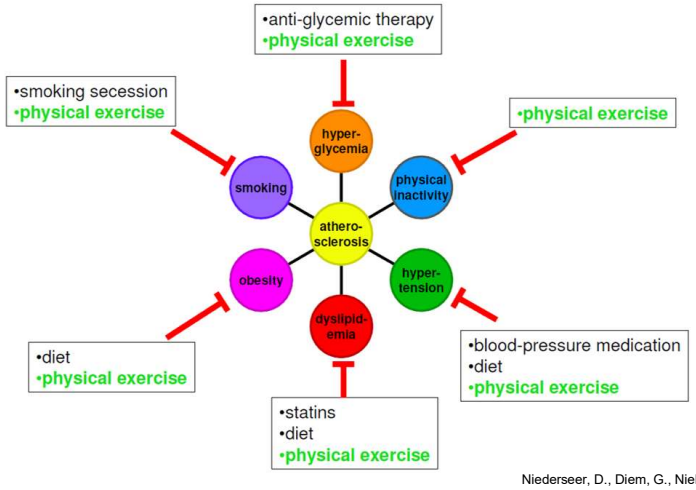
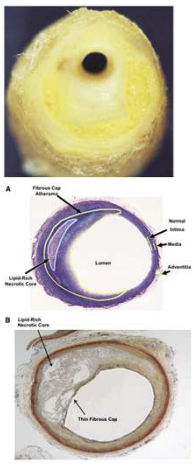
Khera AV et al. N Engl J Med 2016;375:2349-2358.

Effekte von Bewegung auf die kardiovaskulären Risikofaktoren und Arteriosklerose





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Niederseer, D., Diem, G., Niebauer, J. (2017). Diabetes Mellitus Type 2 and Cardiovascular Disease. In: Niebauer, J. (eds) Cardiac Rehabilitation Manual. Springer, Cham. https://doi.org/10.1007/978-3-319-47738-1_6

www.medpertise.de/arteriosklerose-atherosklerose/verlauf

The Pathology of Atherosclerosis: Plaque Development and Plaque Responses to Medical Treatment. William Insull, The American Journal of Medicine (2009) 122, S3–S14

Statine

ESC European Society of Cardiology
European Heart Journal (2022) 43, 249–250
https://doi.org/10.1093/eurheartj/ehab532

Braunwald's Corner

How to live to 100 before developing clinical coronary artery disease: a suggestion

Eugene Braunwald [1,2]*

[1]TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Hale Building for Transformative Medicine, Suite 7022, 60 Fenwood Road, Boston, MA 02115, USA; and [2]Department of Medicine, Harvard Medical School, Boston, MA, USA

Despite extensive basic and clinical research, **arteriosclerotic cardiovascular disease (ASCVD) remains the most frequent cause of death worldwide.** There is general agreement that **low-density lipoprotein cholesterol (LDL-C) is the most important risk factor** for atherosclerosis and plays a causal role in the development of ASCVD. Despite **the widespread availability** of **effective**, **safe cholesterol-lowering drugs**, levels of circulating **LDL-C still exceed optimum levels in a majority of the population**.

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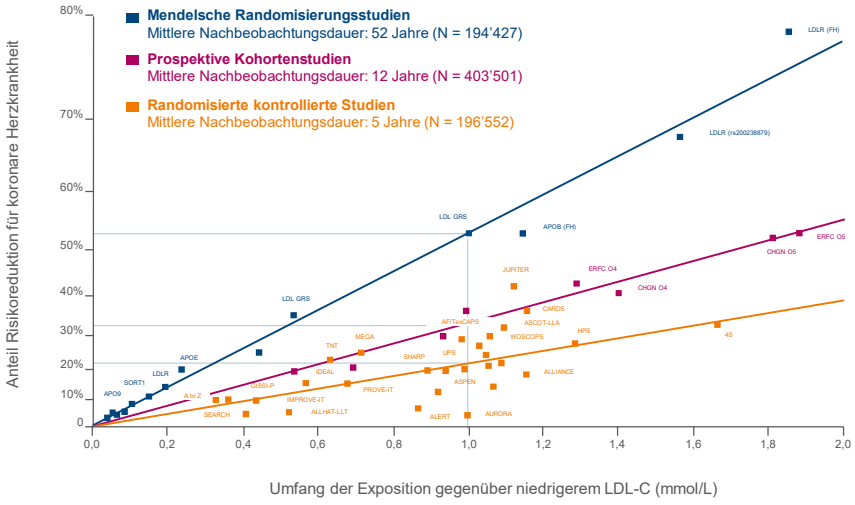
Solide genetische und pharmakologische Daten für einen linearen Kausalzusammenhang zwischen LDL-C und Risiko für koronare Herzkrankheit



Ference BA, Ginsberg HN, Graham I, et al. Eur Heart J 2017;38:2459-72.

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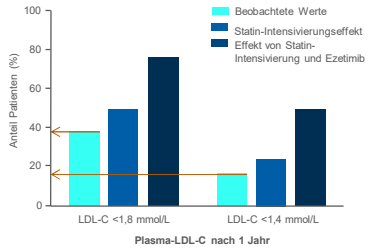
Erreichen des LDL-C-Ziels in der Schweiz
<20% für Patienten mit sehr hohem Risiko

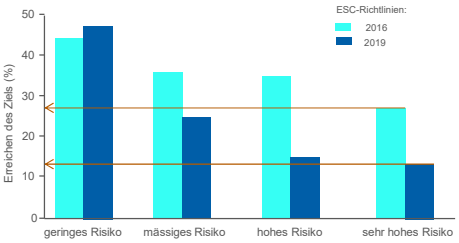
Daten aus der **ELIPS**-Studie: Eine prospektive, multizentrische Kohorten-Beobachtungsstudie aufeinanderfolgender Patienten mit ACS (akutem koronarem Syndrom) mit dem Ziel der Beurteilung von Betreuungsqualität und Adhärenz bezüglich der empfohlenen vorbeugenden Behandlungen in vier akademischen Zentren (n = 2521)



Anteil Patienten mit LDL-Cholesterin im Plasma unter 1,8 mmol/L (<70 mg/dL) und unter 1,4 mmol/L (<55 mg/dL) 1 Jahr nach einem ACS-Indexereignis

Koskinas et al. European J Preventive Cardiology 2020;

Daten aus der internationalen Klassifikation der hausärztlichen Versorgung (ICPC) unter Verwendung elektronischer Patientenakten **(FIRE):** Eine retrospektive Querschnittsanalyse (n = 24'356)



Anteil Patienten mit LDL-Cholesterin im Plasma gemäss ESC-Richtlinien von 2016 (unter 1,8 mmol/L [<70 mg/dL]) und 2019 (unter 1,4 mmol/L [<55 mg/dL]), stratifiziert nach Risikokategorie[2]

Meier et al. 2020 Journal of Clinical Medicine 2020

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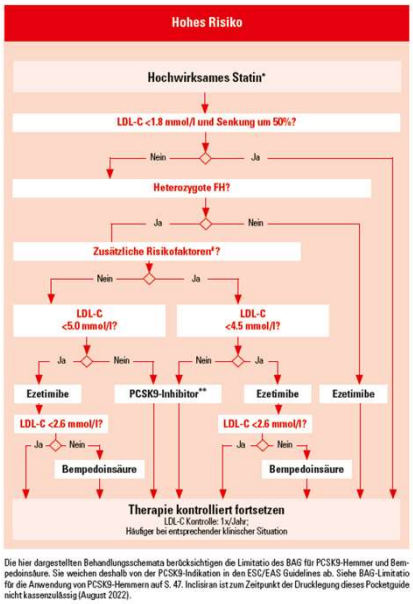
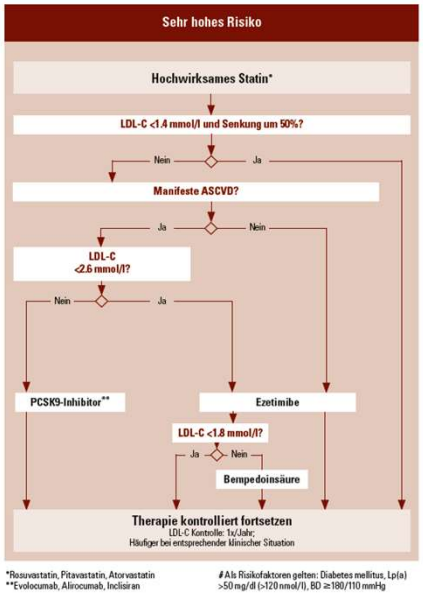


Die hier dargestellten Behandlungsschemata berücksichtigen die Limitatio des BAG für PCSK9-Hemmer und Bempedoinsäure. Sie weichen deshalb von der PCSK9-Indikation in den ESC/EAS Guidelines ab. Siehe BAG-Limitatio für die Anwendung von PCSK9-Hemmern auf S. 47. Inclisiran ist zum Zeitpunkt der Drucklegung dieses Pocketguide nicht kassenzulässig (August 2022).



*Rosuvastatin, Pitavastatin, Atorvastatin
**Evolocumab, Alirocumab, Inclisiran

Als Risikofaktoren gelten: Diabetes mellitus, Lp(a) >50 mg/dl (>120 nmol/l), BD ≥180/110 mmHg

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AGLA Prävention der Atherosklerose 2022

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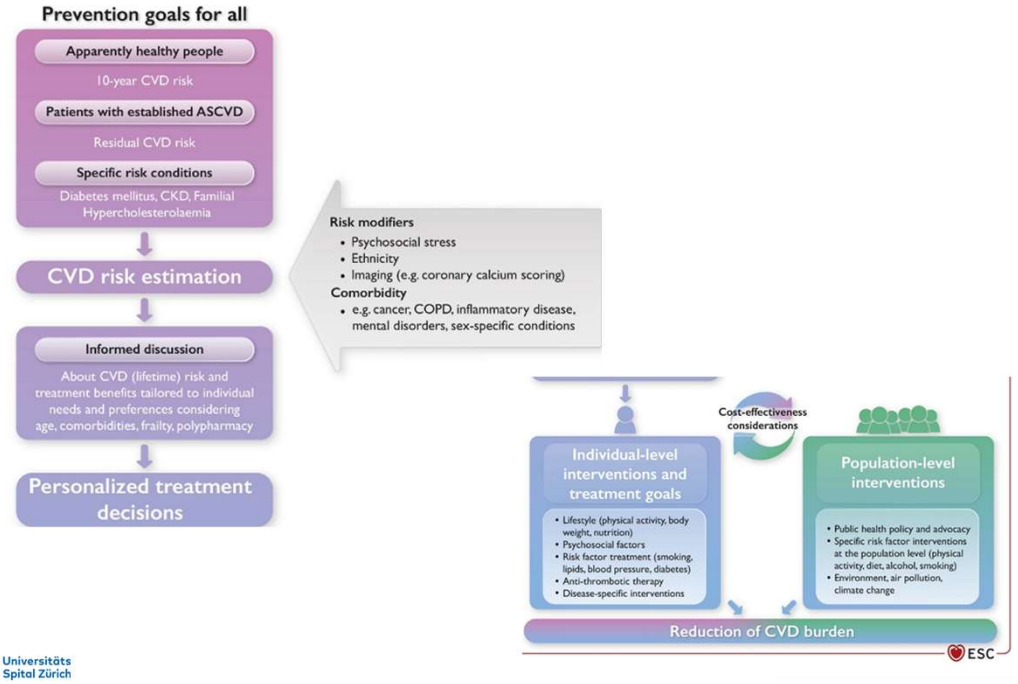

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ESC Guidelines for cardiovascular prevention Eur. Heart J 2021

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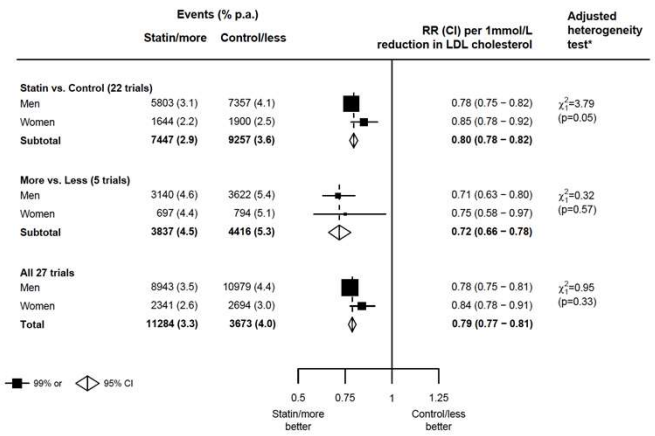
Ca. 20%-ige Risiko-Reduktion / 1 mmol/l LDL-Senkung



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Cholesterol Treatment Trialists' (CTT) Collaboration. Lancet 2015

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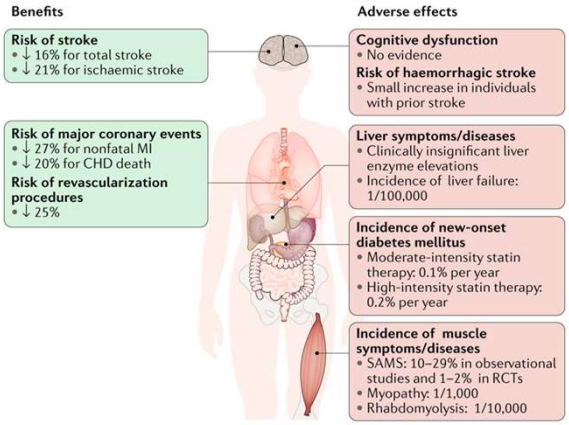
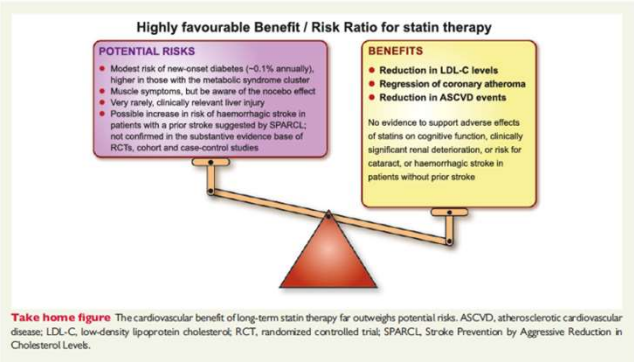
Statine – Nutzen / Risiko





Take home figure The cardiovascular benefit of long-term statin therapy far outweighs potential risks. ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; RCT, randomized controlled trial; SPARCL, Stroke Prevention by Aggressive Reduction in Cholesterol Levels.

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Nat Rev Cardiol. 2018 Dec;15(12):757-769

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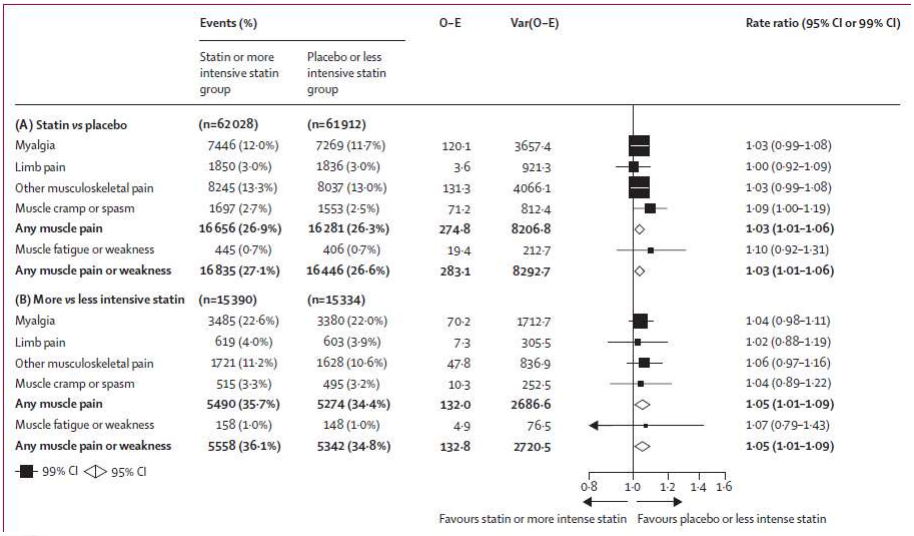
Statin-assoziierte Muskelschmerzen in randomisiert-kontrollierten Studien um 1%



	Events (%)		O–E	Var(O–E)	Rate ratio (95% CI or 99% CI)
	Statin or more intensive statin group	Placebo or less intensive statin group			
(A) Statin vs placebo	**(n=62 028)**	**(n=61 912)**			
Myalgia	7446 (12·0%)	7269 (11·7%)	120·1	3657·4	1·03 (0·99–1·08)
Limb pain	1850 (3·0%)	1836 (3·0%)	3·6	921·3	1·00 (0·92–1·09)
Other musculoskeletal pain	8245 (13·3%)	8037 (13·0%)	131·3	4066·1	1·03 (0·99–1·08)
Muscle cramp or spasm	1697 (2·7%)	1553 (2·5%)	71·2	812·4	1·09 (1·00–1·19)
Any muscle pain	**16 656 (26·9%)**	**16 281 (26·3%)**	**274·8**	**8206·8**	**1·03 (1·01–1·06)**
Muscle fatigue or weakness	445 (0·7%)	406 (0·7%)	19·4	212·7	1·10 (0·92–1·31)
Any muscle pain or weakness	**16 835 (27·1%)**	**16 446 (26·6%)**	**283·1**	**8292·7**	**1·03 (1·01–1·06)**
(B) More vs less intensive statin	**(n=15 390)**	**(n=15 334)**			
Myalgia	3485 (22·6%)	3380 (22·0%)	70·2	1712·7	1·04 (0·98–1·11)
Limb pain	619 (4·0%)	603 (3·9%)	7·3	305·5	1·02 (0·88–1·19)
Other musculoskeletal pain	1721 (11·2%)	1628 (10·6%)	47·8	836·9	1·06 (0·97–1·16)
Muscle cramp or spasm	515 (3·3%)	495 (3·2%)	10·3	252·5	1·04 (0·89–1·22)
Any muscle pain	**5490 (35·7%)**	**5274 (34·4%)**	**132·0**	**2686·6**	**1·05 (1·01–1·09)**
Muscle fatigue or weakness	158 (1·0%)	148 (1·0%)	4·9	76·5	1·07 (0·79–1·43)
Any muscle pain or weakness	**5558 (36·1%)**	**5342 (34·8%)**	**132·8**	**2720·5**	**1·05 (1·01–1·09)**

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The Lancet, published **Online** August 29, 2022

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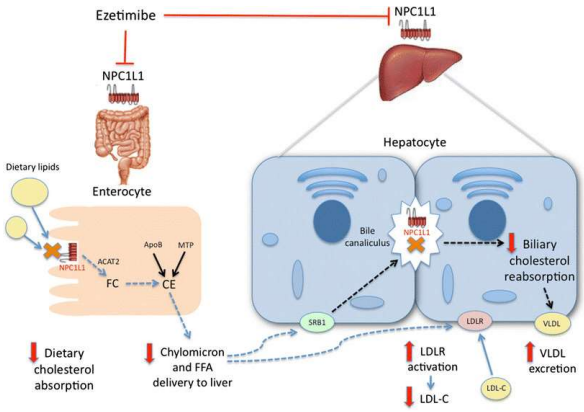
Ezetimib Wirkmechanismus



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Simon TG, Digestive Diseases and Sciences

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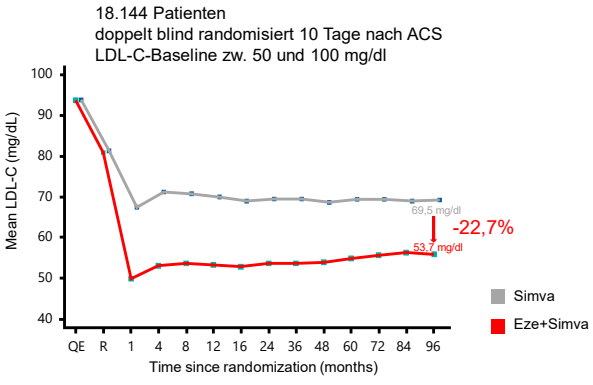
IMPROVE-IT 2015
Ezetimib+Simvastatin vs Simvastatin



modifiziert nach Cannon CP, NEJM 2015;372:2387-97 and supplementary appendix

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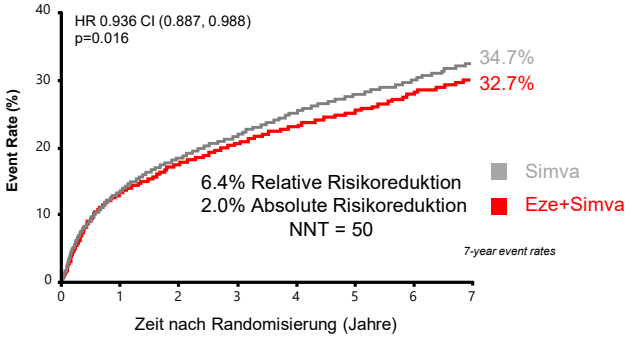
Primärer Endpunkt der IMPROVE-IT-Studie 2015 niedriges LDL-C = weniger CV-Ereignisse

Primärer Endpunkt: kardiovaskulärer Tod, nicht-fataler Myokardinfarkt, unstabile Angina pectoris mit Rehospitalisierung, koronare Revaskularisierung (≥ 30d nach Randomisierung), oder nicht-fataler Schlaganfall



modifiziert nach Cannon CP, NEJM 2015;372:2387-97 and supplementary appendix
NNT = number needed to treat

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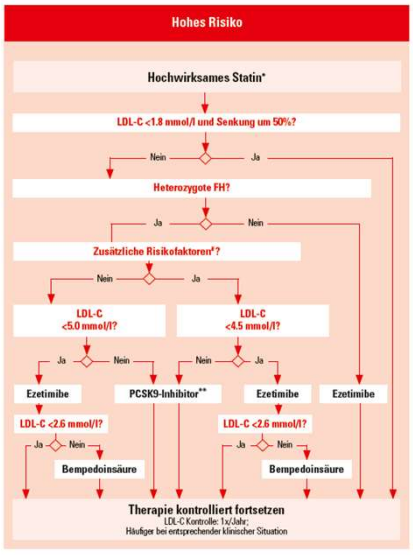
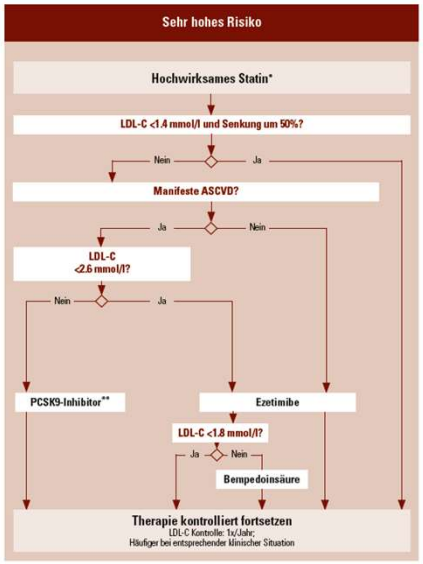


Die hier dargestellten Behandlungsschemata berücksichtigen die Limitatio des BAG für PCSK9-Hemmer und Bempedoinsäure. Sie weichen deshalb von der PCSK9-Indikation in den ESC/EAS Guidelines ab. Siehe BAG-Limitatio für die Anwendung von PCSK9-Hemmern auf S. 47. Inclisiran ist zum Zeitpunkt der Drucklegung dieses Pocketguide nicht kassenzulässig (August 2022).



*Rosuvastatin, Pitavastatin, Atorvastatin
**Evolocumab, Alirocumab, Inclisiran

Als Risikofaktoren gelten: Diabetes mellitus, Lp(a) >50 mg/dl (>120 nmol/l), BD ≥180/110 mmHg

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AGLA Prävention der Atherosklerose 2022

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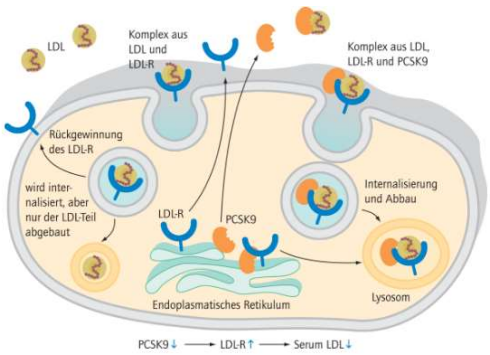
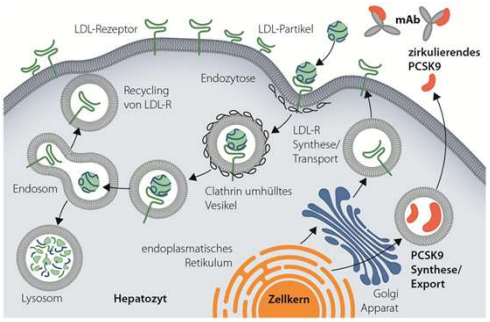
Regulation des LDL-Rezeptors – ProproteinConvertase Subtilisin Kexin Typ 9





- **LDL-Rezeptor persistiert auf Leberzelloberfläche**
- **Antikörper:**
  Evolocumab (Repatha)
  Alirocumab (Praluent)
- **siRNA:**
  Inclisiran (Leqvio)

Lambert G. et al. J. Lipid Res. 2012 53, 2515.

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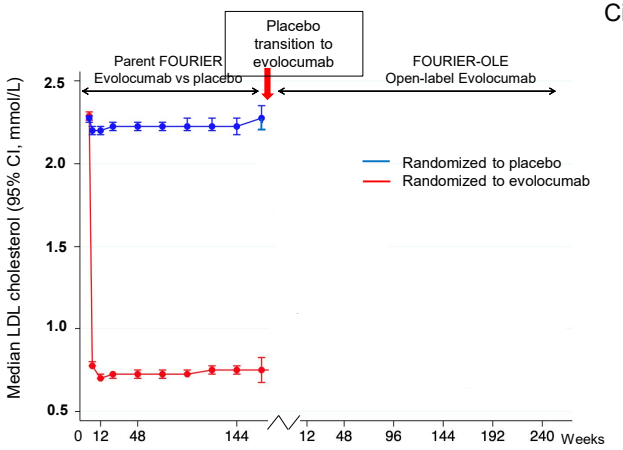
Effect on LDL-C

fourier - OLE

Circulation 2022



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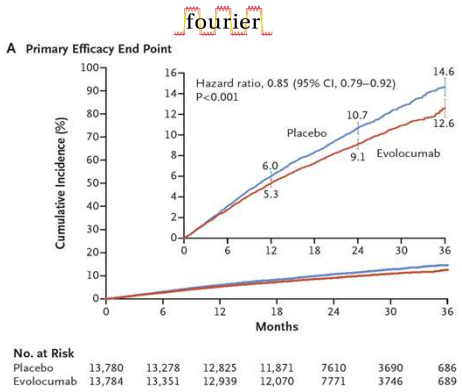
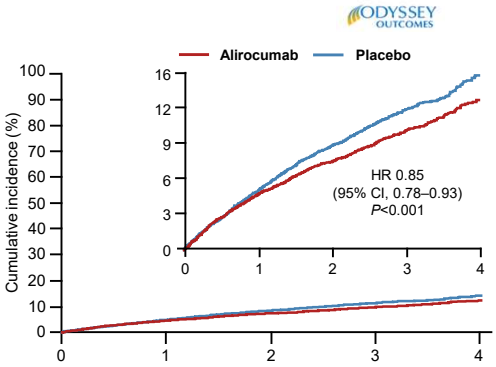
Primary Endpoint



- primary efficacy end point was the composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization
- There was **no significant difference between the study groups with regard to adverse events** (including new-onset diabetes and neurocognitive events), with the exception of injection-site reactions

Sabatine MS et al, NEJM 2017



Schwartz GG et al. *N Engl J Med* 2018

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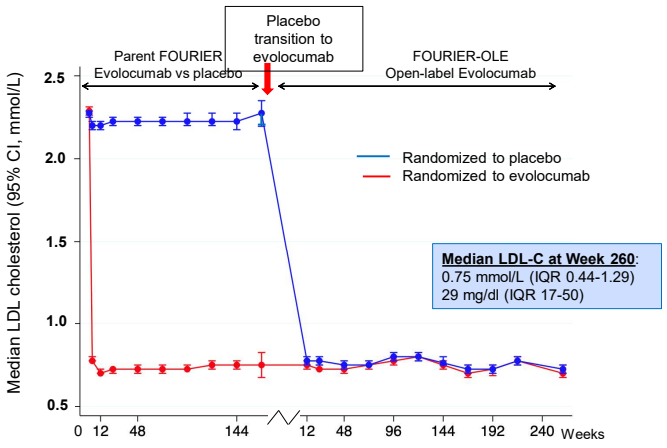
Anhaltende LDL-Senkung über mind. 5 Jahre



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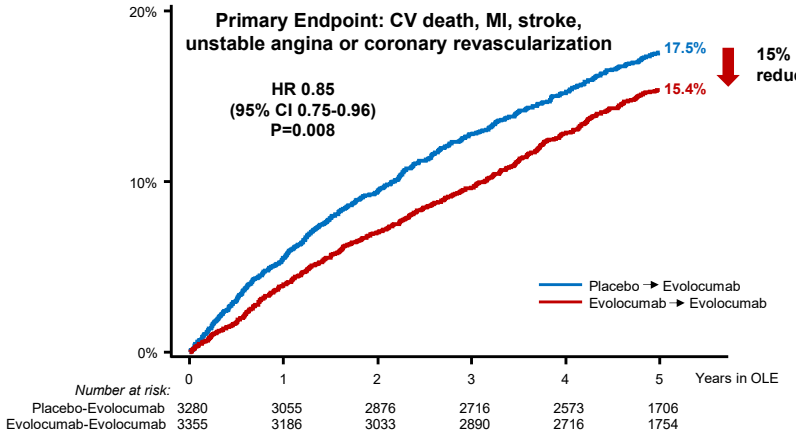
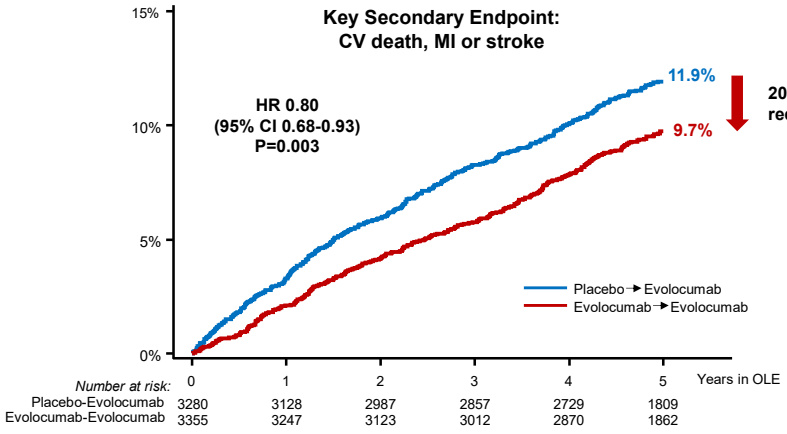
Efficacy during FOURIER-OLE



37

Efficacy during FOURIER-OLE



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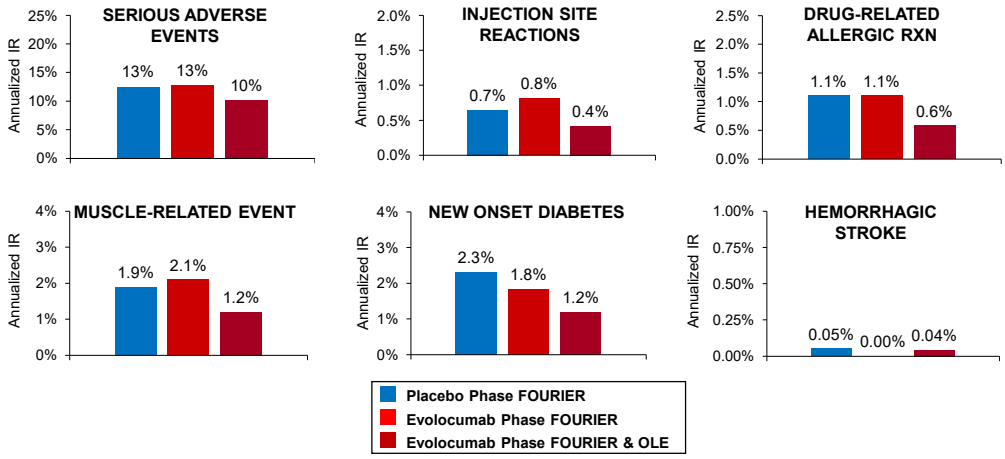
Long-Term Safety

Conclusions: Long-term LDL-C lowering with evolocumab was associated with persistently low rates of adverse events for >8 years that did not exceed those observed in the original placebo arm during the parent study and led to further reductions in cardiovascular events compared with delayed treatment initiation.

fourier - OLE



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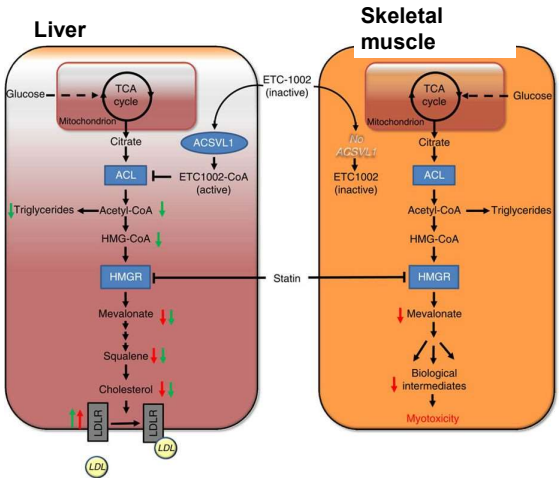
Bempedoinsäure- einzigartiger Wirkmechanismus – ACL-Inhibition

- Activated primarily in the liver, bempedoic acid inhibits the **A**TP-**C**itrate-**L**yase in the well-known cholesterol synthesis pathway, upstream of the statin target
- Upregulation of the LDL receptor results in an increased uptake and removal of LDL particles by the liver
- Due to its novel mechanism of action, bempedoic acid is not activated in skeletal muscle



Pinkosky S et al. *Nat Commun*. 2016;7:13457.

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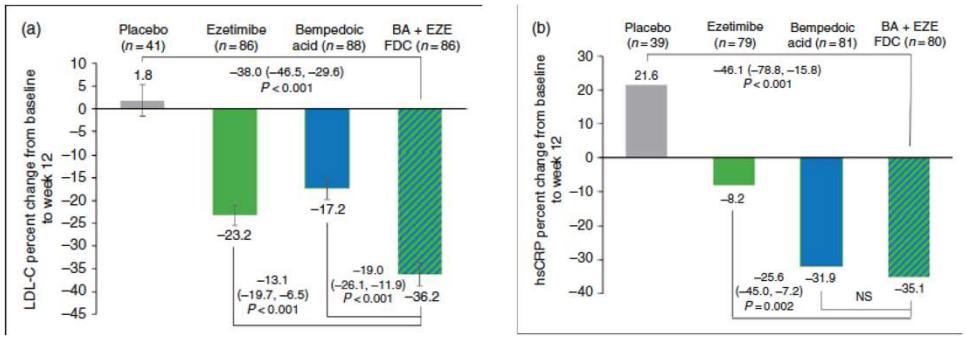
Efficacy of Bempedoic Acid on LDL and hsCRP



Ballantyne CM et al, EJCP 2019

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Safety of Bempedoic Acid

Table 2. Adverse Events and Key Safety Laboratory Findings.*

Variable	Bempedoic Acid (N=1487)	Placebo (N=742)	P Value†
Adverse events			
Any adverse event — no. (%)	1167 (78.5)	584 (78.7)	0.91
Serious adverse event — no. (%)	216 (14.5)	104 (14.0)	0.80
Leading to discontinuation of trial agent — no. (%)	162 (10.9)	53 (7.1)	0.005
Death — no. (%)	13 (0.9)	2 (0.3)	0.17
Adjudicated major adverse cardiac event — no. (%)	68 (4.6)	42 (5.7)	0.30
Death from cardiovascular causes	6 (0.4)	1 (0.1)	0.44
Nonfatal myocardial infarction	19 (1.3)	13 (1.8)	0.45
Nonfatal stroke	5 (0.3)	2 (0.3)	1.00
Coronary revascularization	38 (2.6)	24 (3.2)	0.41
Hospitalization for unstable angina	14 (0.9)	11 (1.5)	0.29
Other major adverse cardiac event–related event — no. (%)			
Death from noncardiovascular causes	2 (0.1)	1 (0.1)	1.00
Noncoronary arterial revascularization	4 (0.3)	6 (0.8)	0.09
Hospitalization for heart failure	9 (0.6)	1 (0.1)	0.18
Event of special interest — no. (%)			
Muscular disorder	195 (13.1)	75 (10.1)	0.05
Muscular disorder leading to discontinuation of trial agent	31 (2.1)	14 (1.9)	0.87
Myalgia	89 (6.0)	45 (6.1)	0.92
Muscle spasms	62 (4.2)	20 (2.7)	0.09
Pain in extremity	50 (3.4)	16 (2.2)	0.14
Muscular weakness	9 (0.6)	4 (0.5)	1.00
New-onset or worsening diabetes	49 (3.3)	40 (5.4)	0.02
Gout	18 (1.2)	2 (0.3)	0.03
Increase in blood creatinine level	12 (0.8)	3 (0.4)	0.41
Decrease in glomerular filtration rate	8 (0.5)	0	0.06
Neurocognitive disorder	11 (0.7)	7 (0.9)	0.62

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Ray K et al, NEJM 2019

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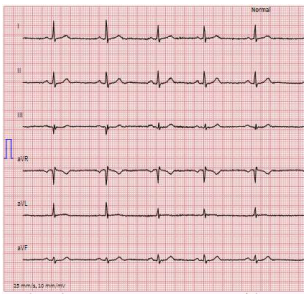
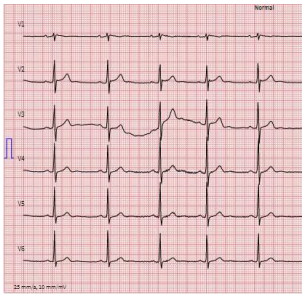
64 jähriger Hobbysportler - Selbstzuweisung zur kardiologischen Standortbestimmung vor Skimarathon

- Anamnese:
  - Beschwerdefrei, regelmässig sportlich aktiv
  - Blutdruck in Selbstmessungen um 120/80 mmHg
  - Nichtraucher
  - Blande Familienanamnese





- Status:
  - Blutdruck: **139/93 und 145/92 mmHg**, Puls: 61 bpm
  - 173 cm, 84 kg, **BMI 28.1 kg/m2**
  - Reine, rhythmische Herztöne, keine Stauungszeichen, vesikuläres Atemgeräusch über allen Lungenfeldern

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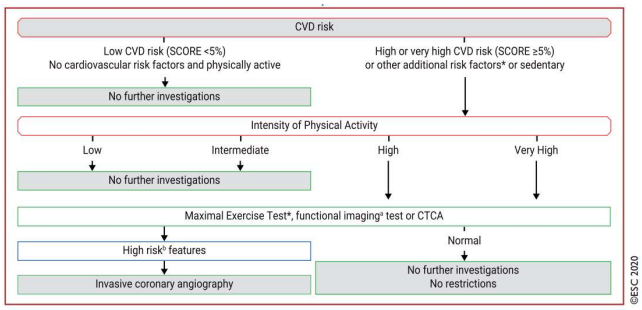
Brauchen wir weitere Diagnostik?



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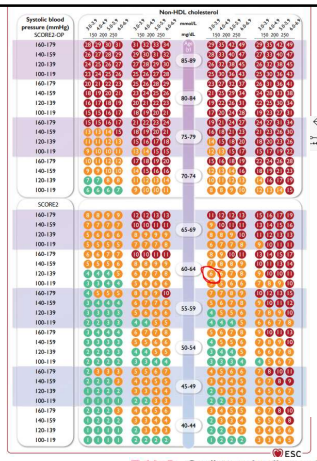
Labor

Lipidstoffwechsel und Arter...			
Cholesterin, total	< 5.0 $	mmol/l	4.8
HDL-Cholesterin	> 1.0 $	mmol/l	1.64
non-HDL-Cholesterin	< 3.9 $	mmol/l	3.2 (3)
LDL-Cholesterin Sampson	< 3.0 $	mmol/l	2.9
Triglyceride	< 2.0 $	mmol/l	0.71
Elektrolyt- und Wasserhaus...			
Natrium	136 - 145	mmol/l	138
Kalium	3.4 - 4.5	mmol/l	4.2
Niere			
Harnstoff	2.86 - 8.21	mmol/l	6.4
Kreatinin	62 - 106	µmol/l	78
eGFR(Krea) CKD-EPI 2009		ml/min	91 (1)
Enzyme			
ALT(GPT)Alanin-Aminotransf.	< 50	U/l	32
Entzündung			
CRP (C-reakt.Prot.)	< 5	mg/l	2.3
Herz und Muskel			
NT-proBNP (Roche)	< 210	ng/l	8
Diabetes und Energiestoffw...			
HbA1c n.NGSP	4.4 - 5.6	%	6.6 * (2)
HbA1c nach IFCC	25 - 38	mmol/mol	49 *



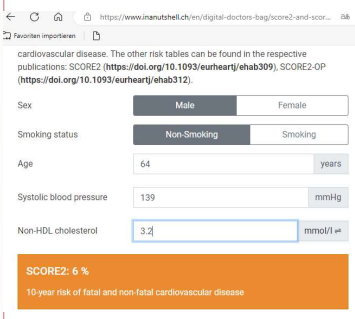


Table 5 Cardiovascular disease risk categories based on SCORE2 and SCORE2-OP in apparently healthy people according to age

	<50 years	50–69 years	≥70 years*
Low-to-moderate CVD risk: risk factor treatment generally not recommended	<2.5%	<5%	<7.5%
High CVD risk: risk factor treatment should be considered	2.5 to <7.5%	5 to <10%	7.5 to <15%
Very high CVD risk: risk factor treatment generally recommended*	≥7.5%	≥10%	≥15%

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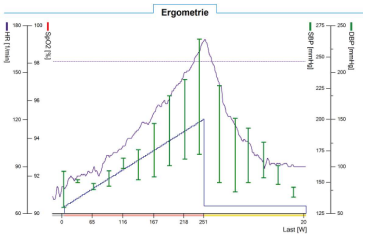
Ergometrie

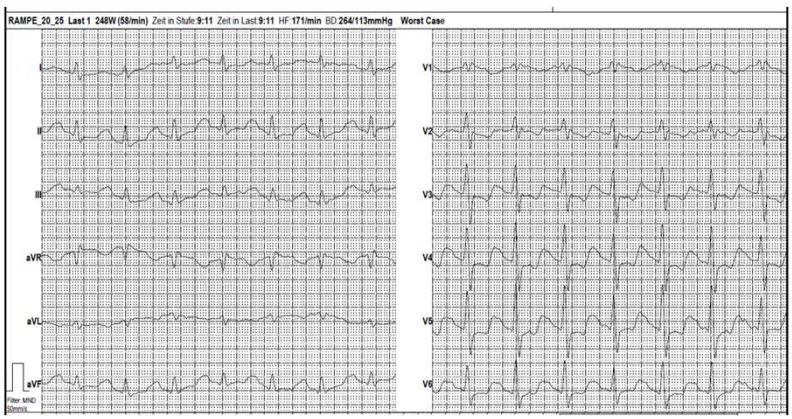
Stufe	Zeit in Stufe	Zeit in Last	Last (W)	Drehzahl (/min)	HF (/min)	BD (mmHg)	HFxBD /100	ST (V3) (mm)	VES	
Ruhe	0:49	0:00	0	24	81	130/95	105	0,6		
Last 1	2:00	2:00	68	66	87	144/82	125	0,4		
	4:00	4:00	119	68	108	169/98	183	0,2		
	6:00	6:00	170	71	128	197/89	252	-0,5	2	
	8:00	8:00	218	66	151	219/101	331	-1,2	5	
	9:18	9:18	251	24	168	264/113	444	-1,8	4	
Erholung	6:03	9:18	20	0	90	138/78	124	0,5	5	

Zusammenfassung

Typ: Fahrrad
Protokoll: RAMPE_20_25
Belastungszeit: 9:18
Erholungszeit: 6:03
Abbruchgrund: Allgemeine Erschöpfung

Max. Last: 251W / 11,4 METs => 160% von 157W
(Zielleistberechnung nach Standard)

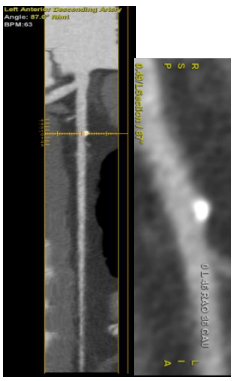


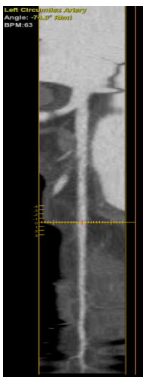


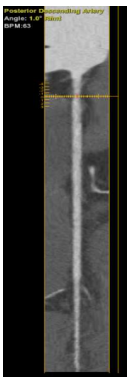
CCT: Leichte, nicht-stenosierende Koronarsklerose

RIVA: Kalzifizierte Plaque mit <20% Lumeneinengung proximal.

Kalzium-Score (0.57mSv): LMA: 0, RIVA: 19, RCX: 0, RCA: 0, insgesamt: 19 (25. bis 50. Perzentile).







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Take home messages

- **Kardiovaskuläre Erkrankungen – weltweit führende Todesursache**
- **Risikofaktoren erkennen und behandeln: Genetisches Risiko – Lebensstil – Risikofaktoren**
- **Körperliche Inaktivität als globales Problem**
- **Mangelnde Fitness ist der beste Prädiktor für Mortalität**
- **LDL-Senkung: the lower and earlier the better (→ py bei Zigaretten)**
- **Statine, Ezetimib, Bempedoinsäure und PCSK9-Hemmer**
  - **Mechanismus der LDL-Senkung von untergeordneter Bedeutung**

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Herzlichen Dank für Ihre Aufmerksamkeit.

michael.stiefel@usz.ch

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