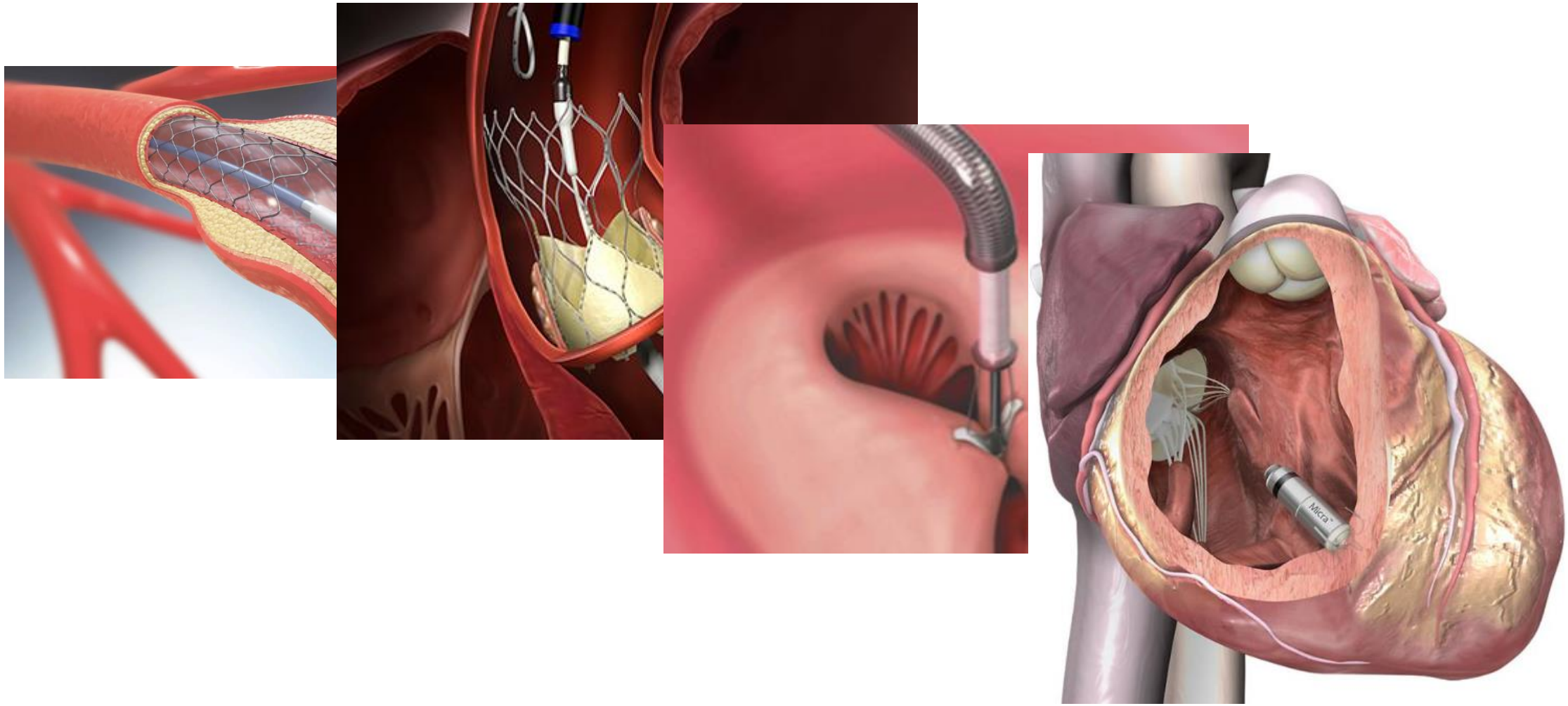
Die 2. Chance des Herzpatienten- Sekundärprevention der Arteriosklerose

Sebastian Globits/ Herz Kreislauf Zentrum Groß Gerungs

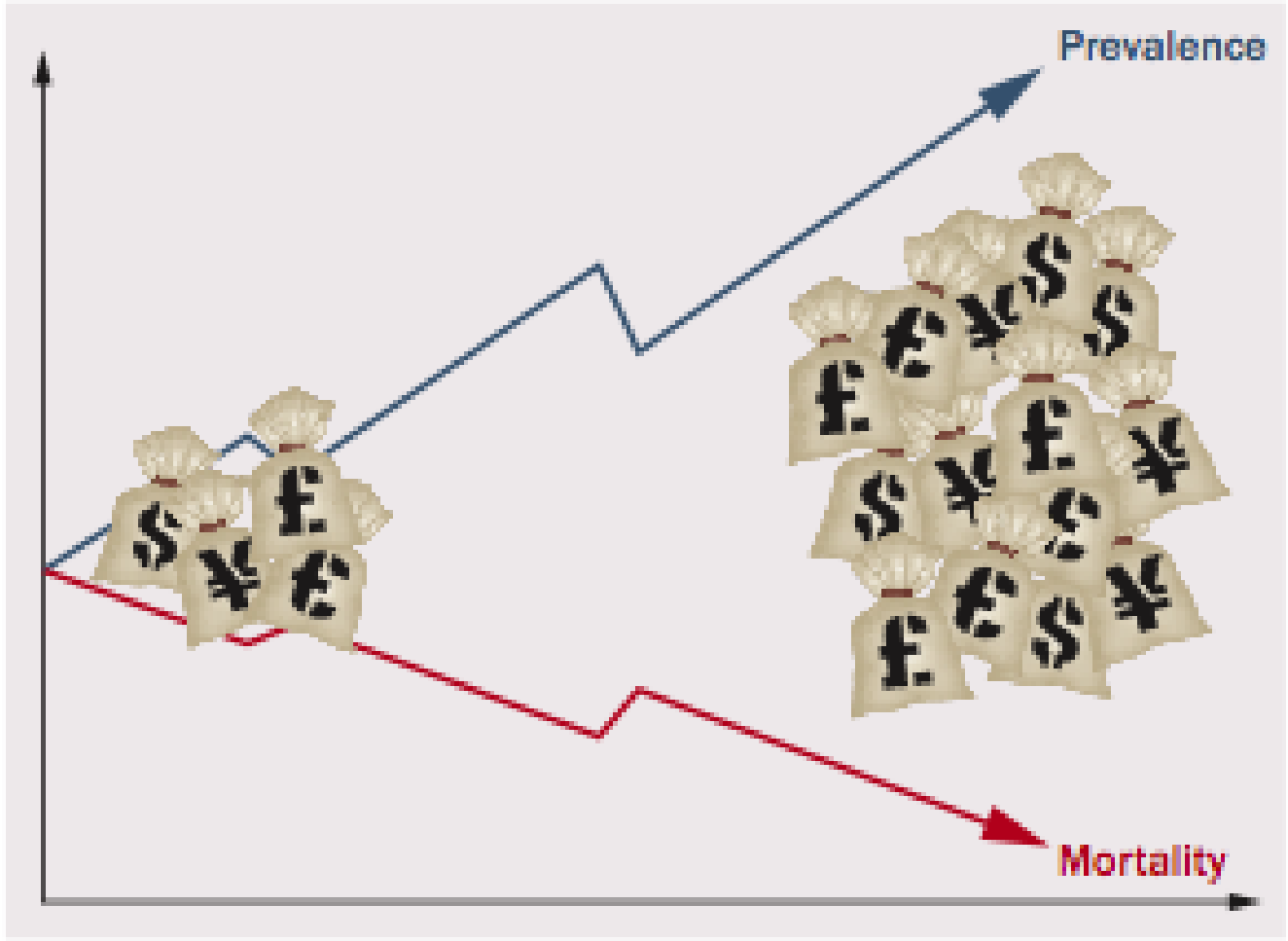
Die Erfolgsgeschichte

Fortschritte in der Kardiologie seit den 1960er Jahren



Fortschritte der Herzchirurgie

Die ökonomische Belastung

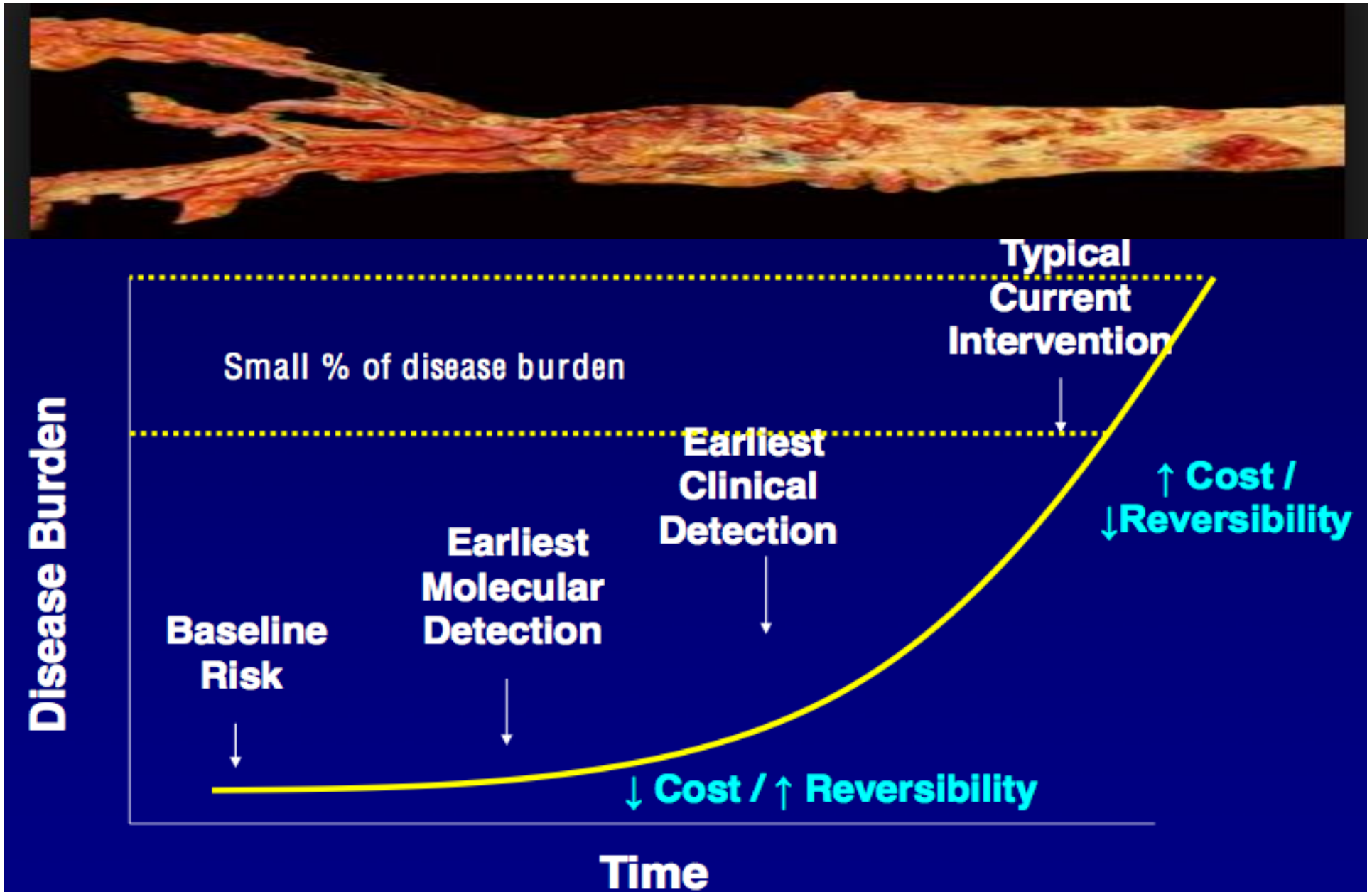


V. Fuster. Nature Reviews. Cardiology 2009

Der Zauberlehrling von Johann Wolfgang von Göthe

Die Geschichte der Arteriosklerose

Arteriosklerose



Kardiovaskuläre Erkrankungen sind häufigste Todesursache in Industrieländern

Arteriosklerose gab es bereits vor 1000en Jahren, vor der Definition der klassischen Risikofaktoren.
z.B. beim 5300 Jahre alten “Ötzi” oder ägyptischen Mumien and (HORUS Studie an 137 Mumien mittels CT)

Reflections on Atherosclerosis: Lesson from the Past and Future Research Directions
S. Minelli, Lecce, Italy
Journal of Multidisciplinary Healthcare 2020:13

Das Wort “Arteriosklerose” wurde 1904 vom deutschen Pathologen Felix Marchand (1846–1928) eingeführt (fettige Läsionen, die zu Einengung und Steifigkeit von Arterien führen)

Reflections on Atherosclerosis: Lesson from the Past and Future Research Directions
S. Minelli, Lecce, Italy
Journal of Multidisciplinary Healthcare 2020:13

2 unterschiedliche Theorien der Entstehung:

Deutsche Pathologe Rudolf Virchow (1821–1902) unterstützte die primäre Entzündungstheorie (“endoarteritis chronica deformans”)

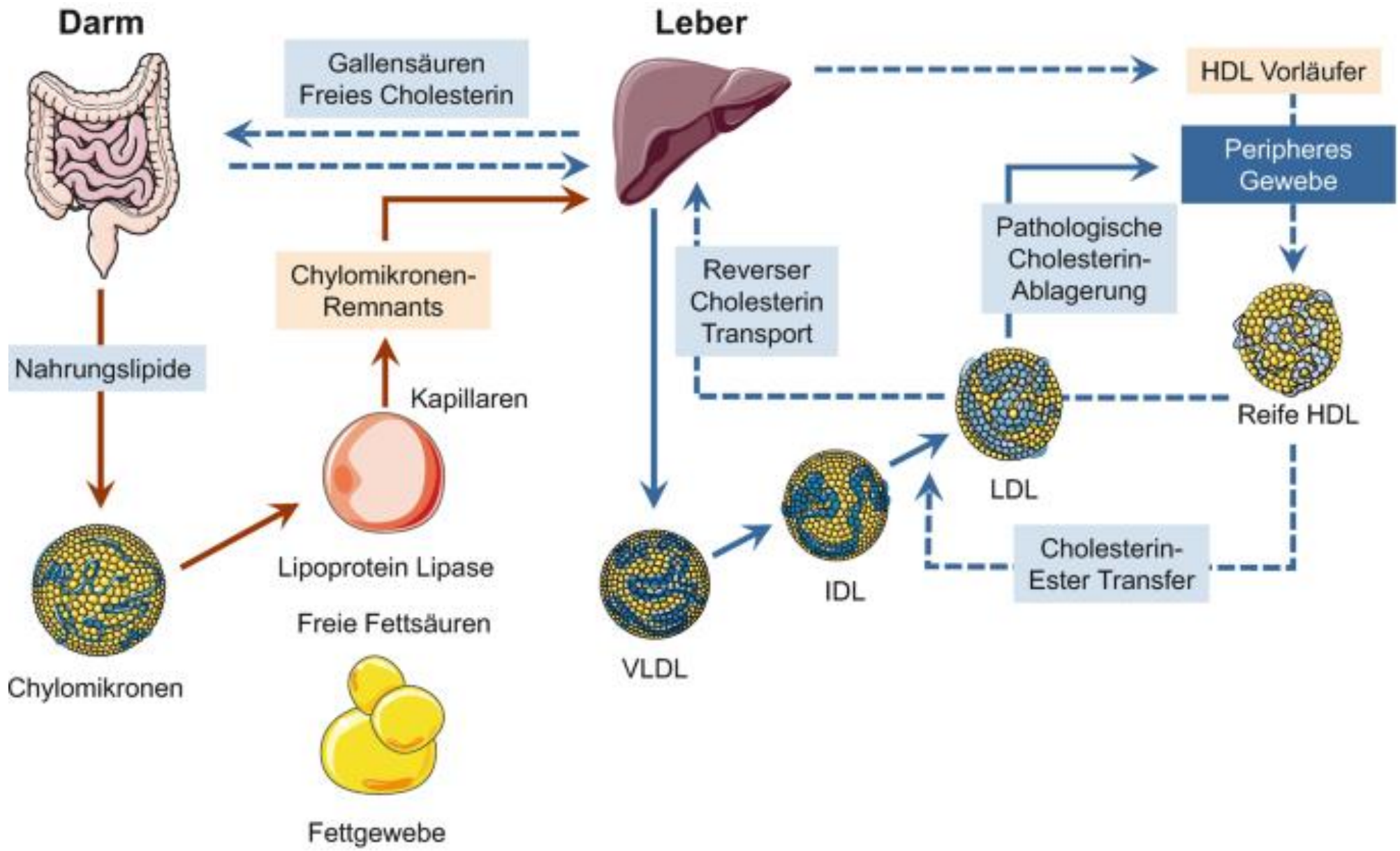
Österreichische Baron Carl von Rokitansky (1804–1878) glaubte die zelluläre Entzündung ist Folge der Ablagerungen in der Arterienwand

Bedeutung des ”cholesterols” in der Atherogenese:

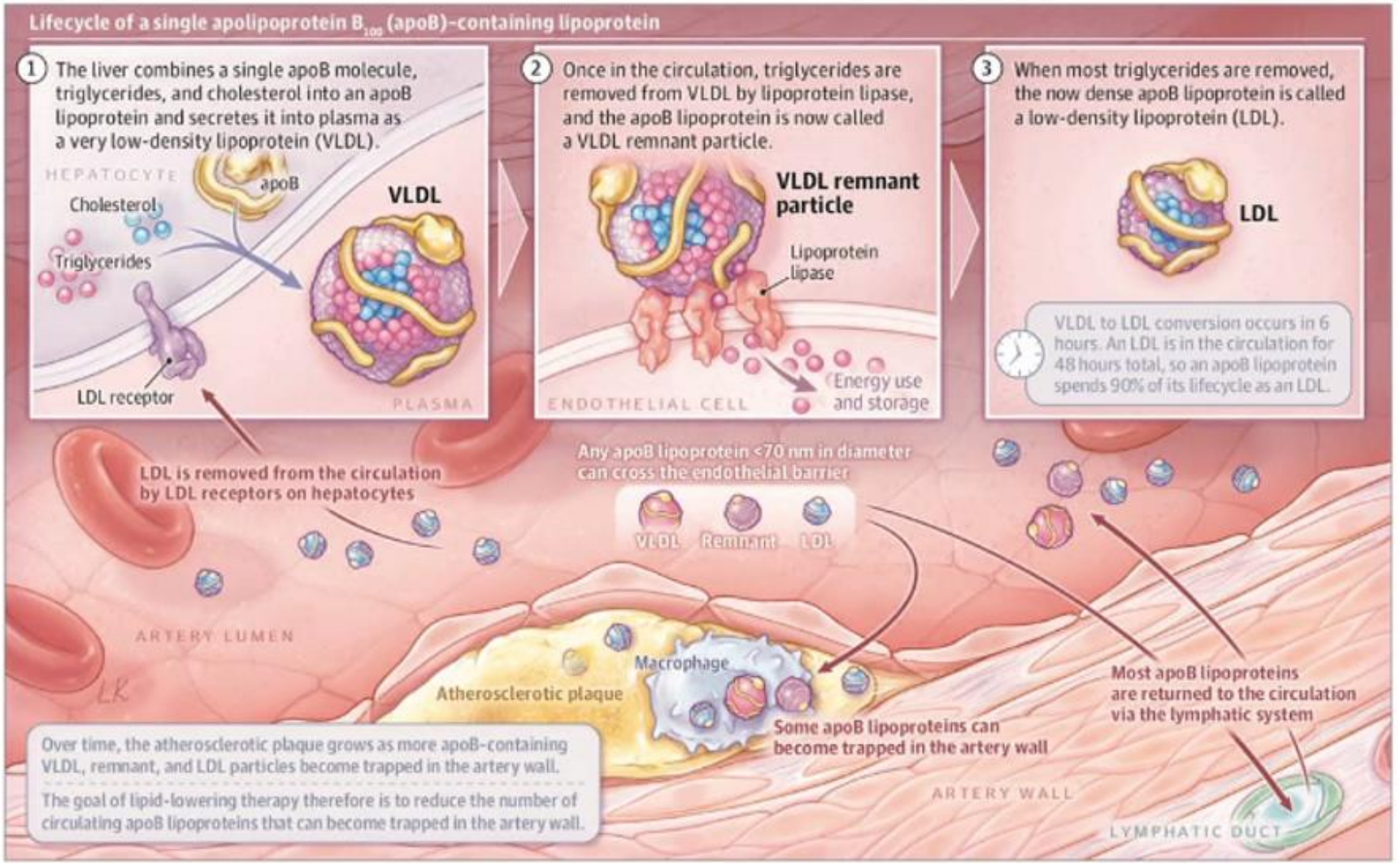
1910, Adol – zeigte, dass in Pla alen Wand

1913 zeigte , die mit reinem Ch n wie humane ar

1973 Micha is in Medizin 19 lten den ersten HMG


Darm
Leber
Gallensäuren
Freies Cholesterin
HDL Vorläufer
Peripheres Gewebe
Chylomikronen-Remnants
Reverser Cholesterin Transport
Pathologische Cholesterin-Ablagerung
Nahrungslipide
Kapillaren
Reife HDL
LDL
IDL
Cholesterin-Ester Transfer
Lipoprotein Lipase
Freie Fettsäuren
VLDL
Chylomikronen
Fettgewebe

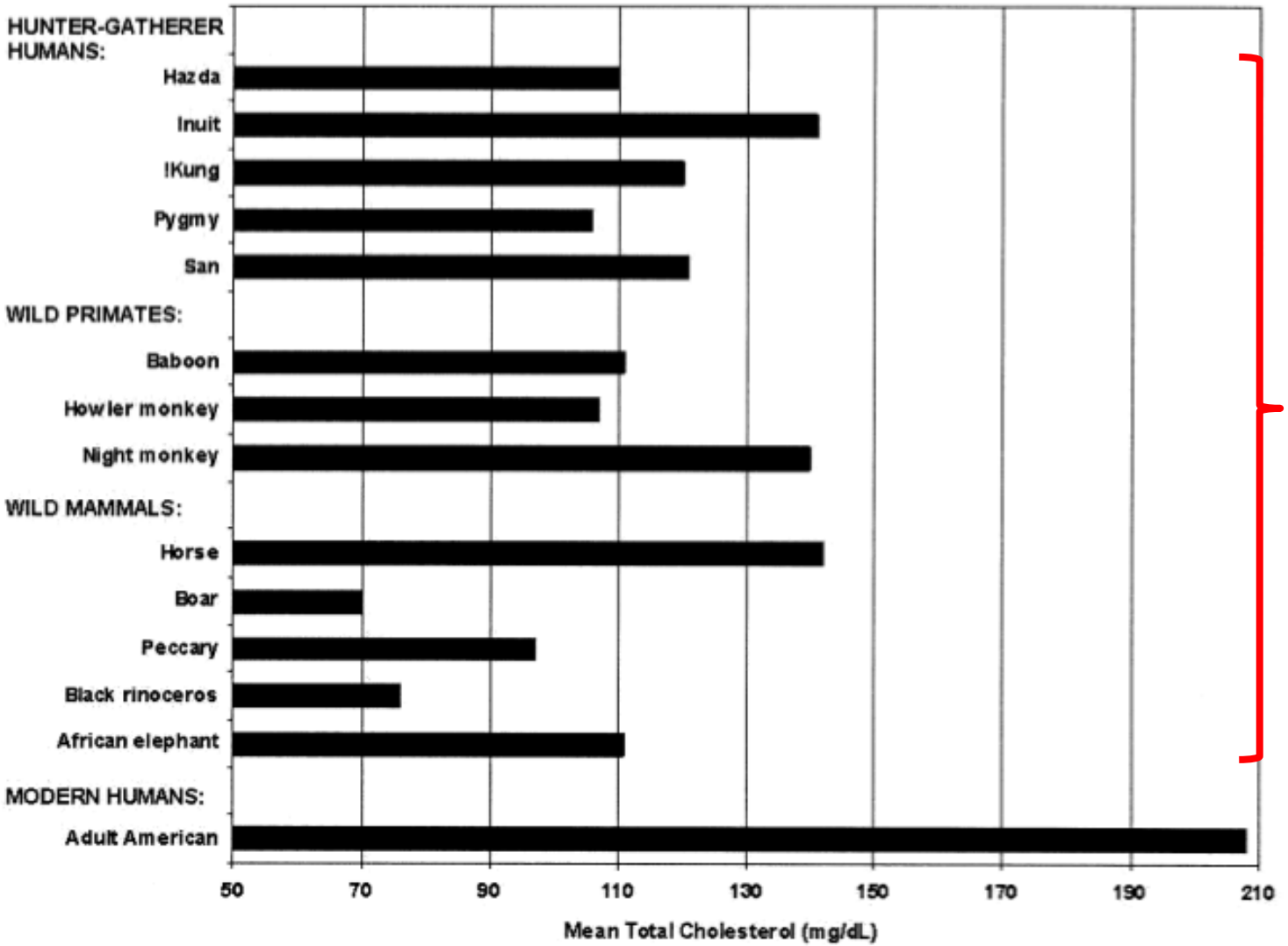
Arteriosklerose ist ein lebenslanger Prozess



Brauchen wir LDL-C?

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	
Atherosklerose	Ja	LDL kausal	GENETIK!

Vergleich der Cholesterinspiegel

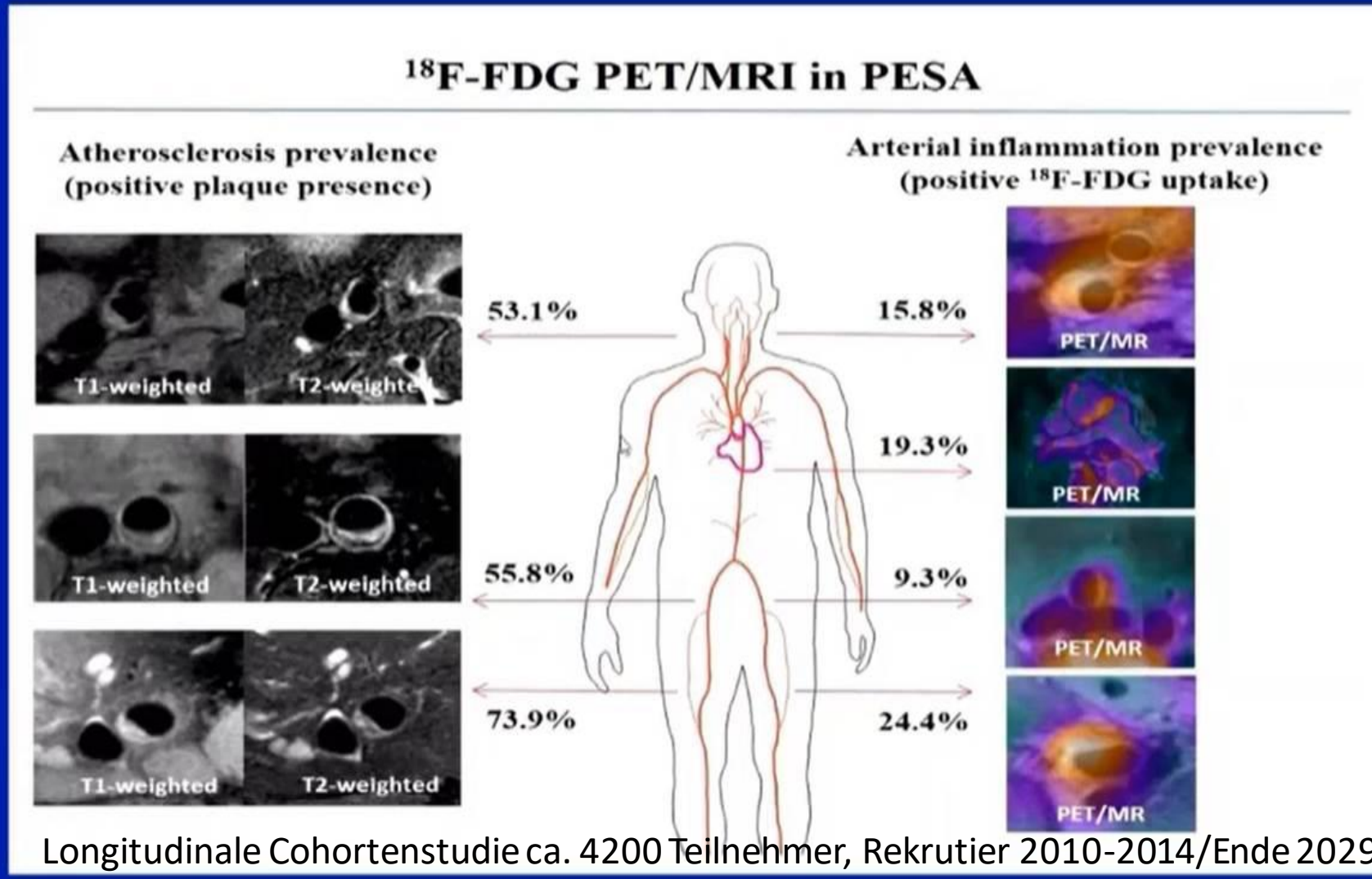


equals
LDL-C 50 – 70 mg/dl

equals
LDL-C 150 mg/dl

Primärprevention

3. Quality of Subclinical Atherosclerosis
Fibrotic - MRI & Inflammation - PET

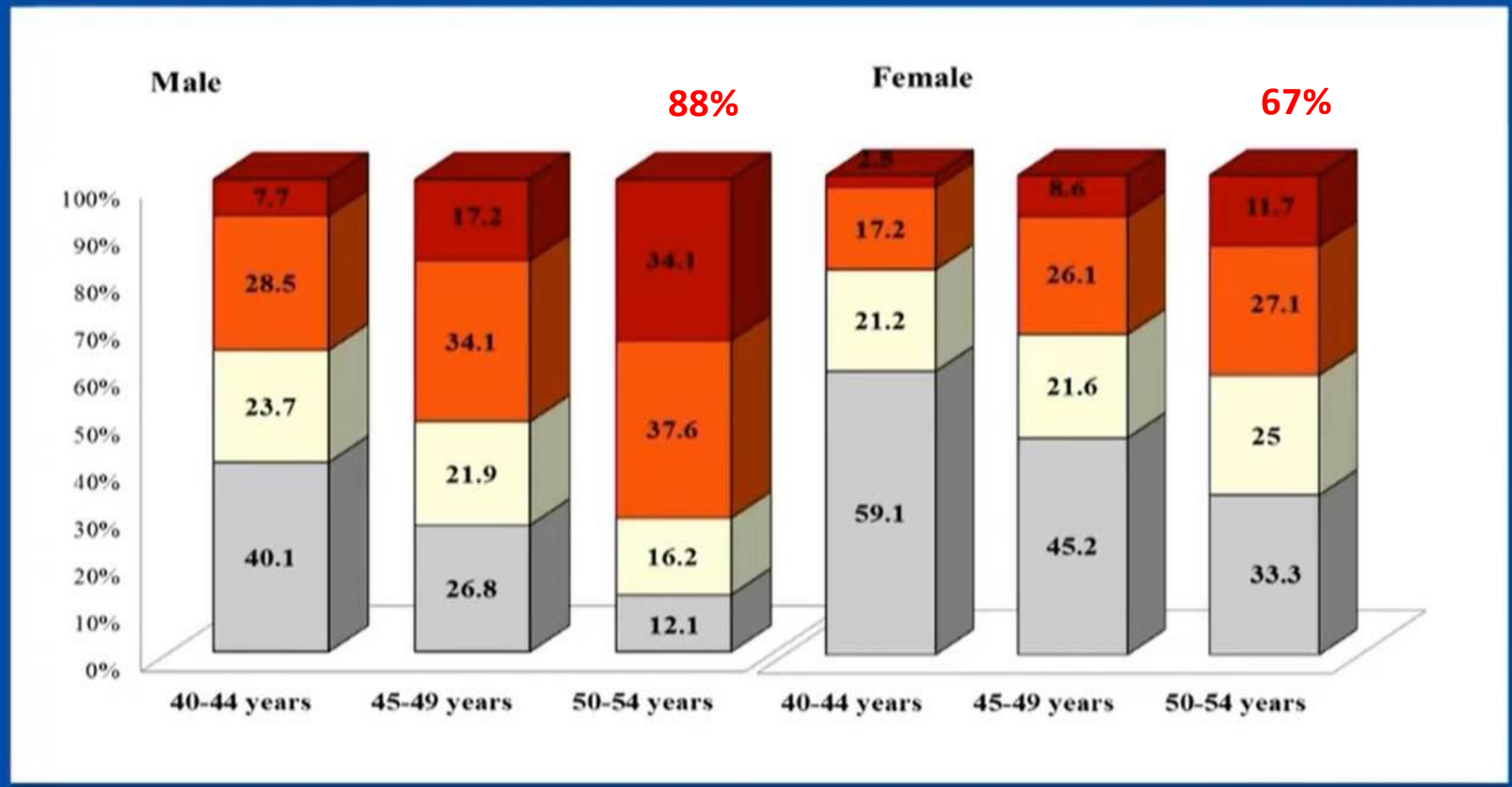


Longitudinale Cohortenstudie ca. 4200 Teilnehmer, Rekrutier 2010-2014/Ende 2029

L Fernández-Friera, V Fuster, J Sanz et. al. J Am Coll Cardiol. 2019; 73: 1371

1. Burden of Subclinical Atherosclerosis

The PESA (N=4184) – Age 40-55 yrs



PESA (L Fernandez-Friera, A Fernandez-Ortiz, V Fuster et.al)

Circulation 2015;131:2104

Primärprevention

Risikofaktor	Odds Ratio korrigiert Geschl, Alter, Rauchen
Rauchen	2,95
Diabetes	3,08
Hypertonie	2,48
Viscerales Fett	2,22
Psychosocialer Status	2,51
Gemüse und Obst	0,70
Körperl. Training	0.72
Alkohol	0,79

Interheart Studie 14.000 MCI Pat. vs 14.000 Kontrollen:
Risiko für akuten MCI in Abhängigkeit vom Risikoprofil

Yusuf S et al, Lancet 2004

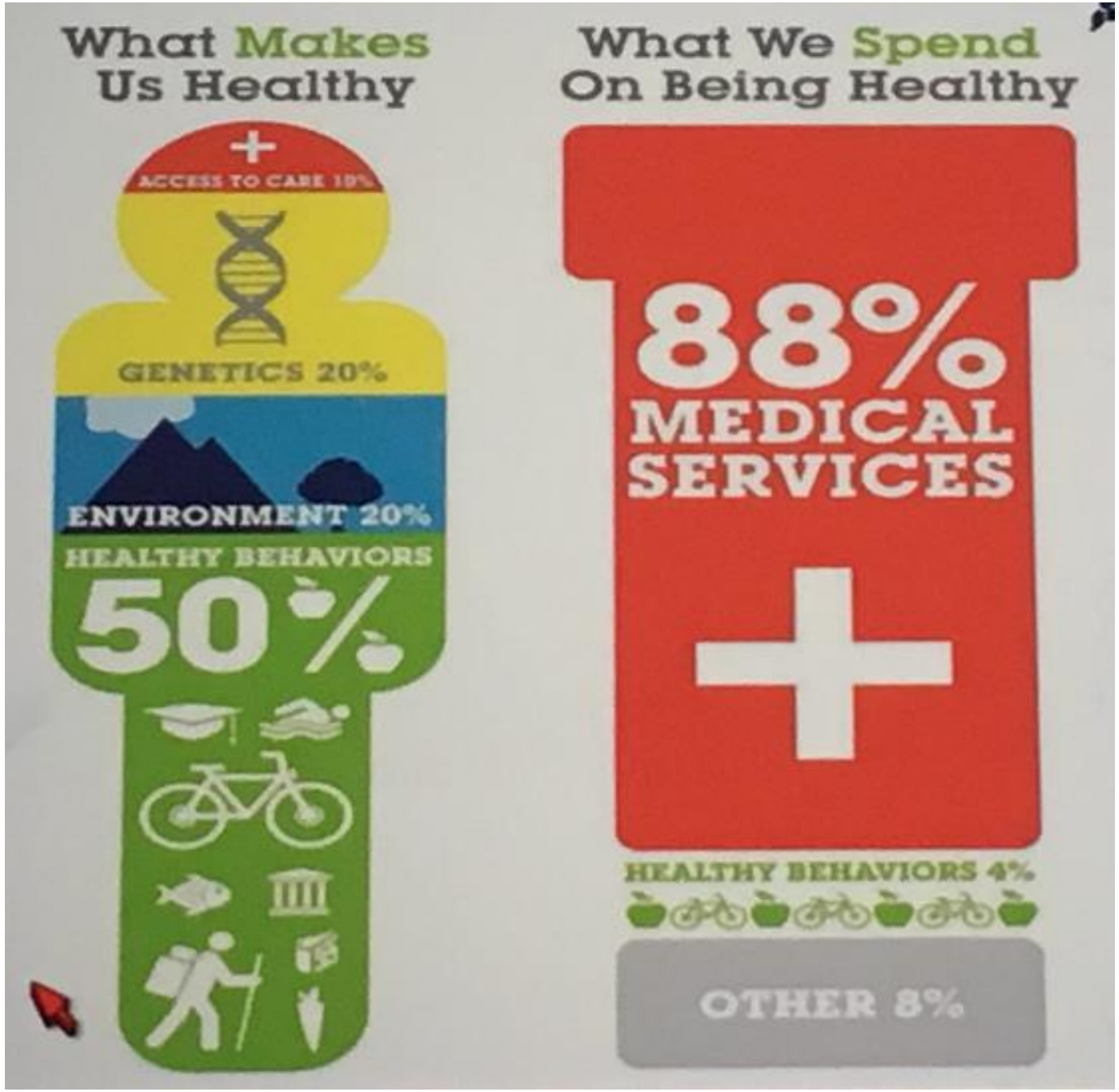
Effektive Lebensstilumstellung

Mediterrane Diät, regelmäßige Bewegung, Gewichtskontrolle und Nikotinstopp sollten so früh wie möglich VERSCHRIEBEN werden, um die Arteriosklerose zu verhindern bzw hinauszuzögern

(Tsimane – eine bolivianische Naturbevölkerung hat weltweit die niedrigste Prävalenz für arteriosklerotische Ereignisse
Lancet. 2017;389(10080):1730–1739)

Preventionsempfehlung der ESC 2019

The elimination of health risk behaviours would make it possible to prevent at least 80% of CVD and even 40% of cancers.


What Makes Us Healthy
ACCESS TO CARE 10%
GENETICS 20%
ENVIRONMENT 20%
HEALTHY BEHAVIORS
50%
What We Spend On Being Healthy
88%
MEDICAL SERVICES
HEALTHY BEHAVIORS 4%
OTHER 8%

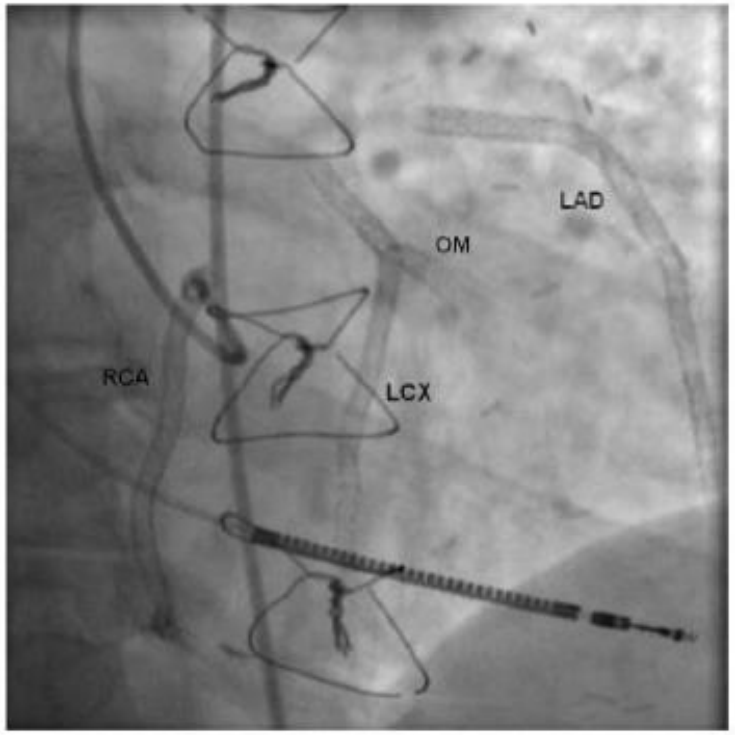
Sekundärprevention

Ist DAS die Lösung (1)?

IMAGES IN CARDIOLOGY

A Heart With 67 Stents

Rami N. Khouzam, MD, Rajvir Dahiya, MD, Richard Schwartz, MD
Mineola, New York



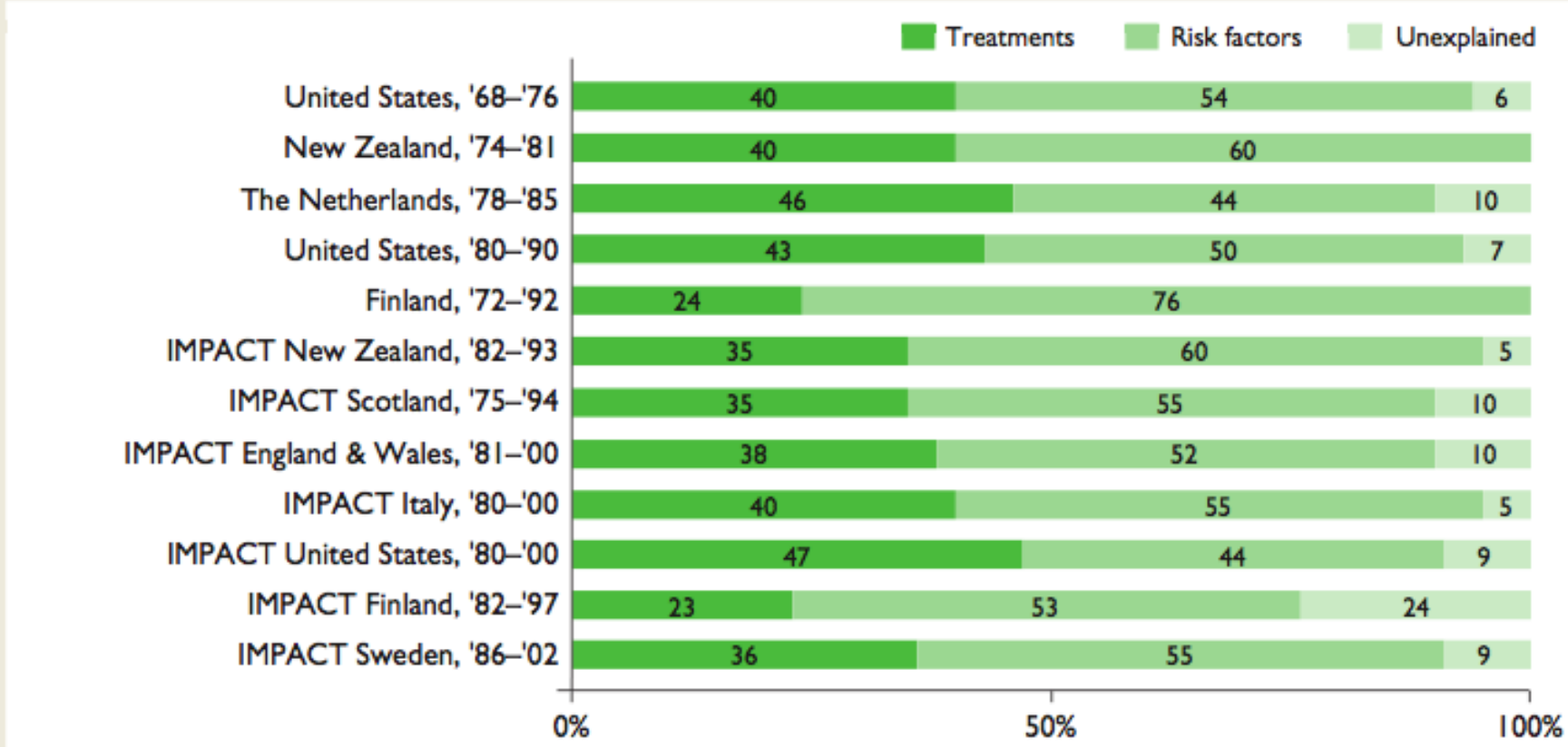
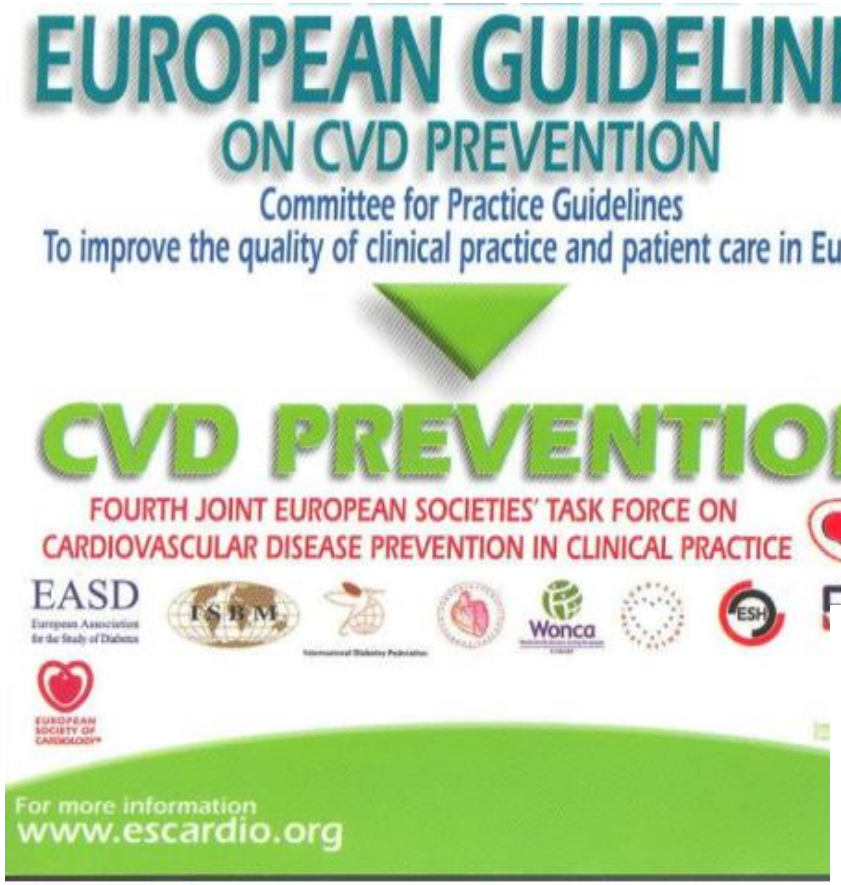
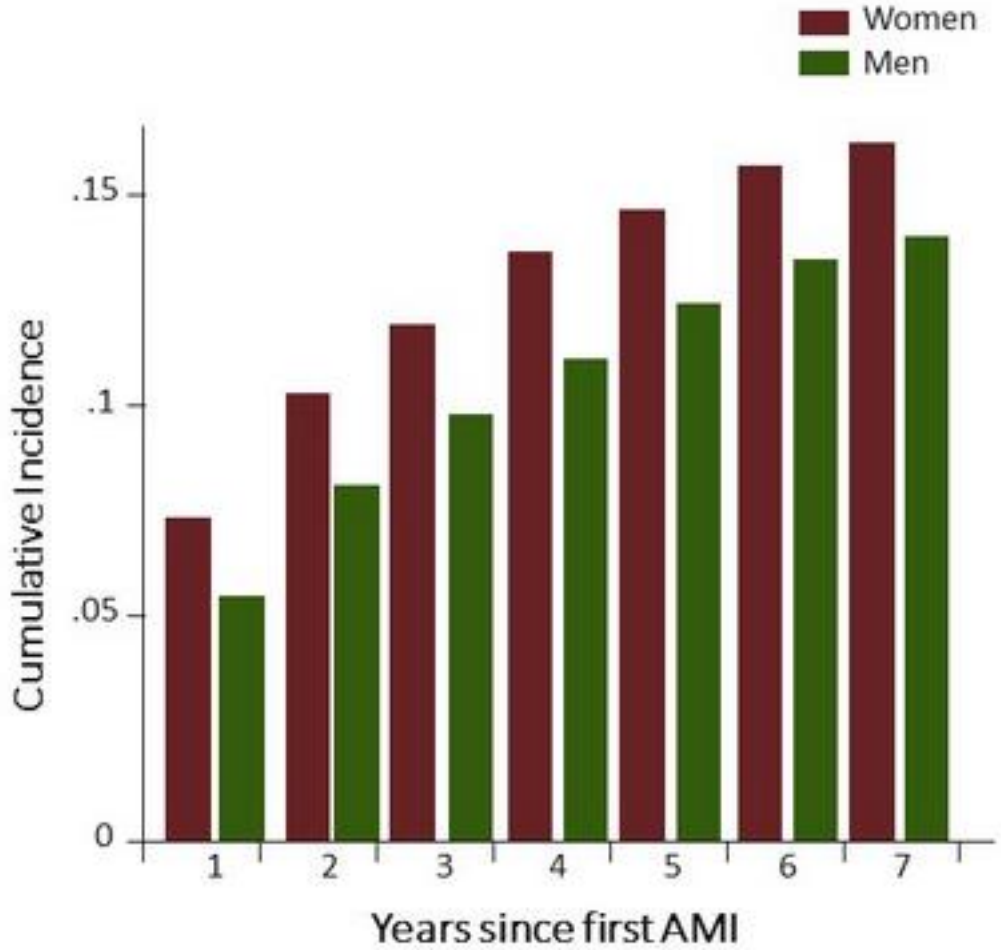


Figure 1 Percentage of the decrease in deaths from coronary heart disease attributed to treatments and risk factor changes in different populations (adapted from Di Chiara *et al.*[31])



- CVD affects both men and women; of all deaths that occur before the age of 75 years in Europe, 42% are due to CVD in women and 38% in men.
- CVD mortality is changing, with declining age-standardized rates in most European countries, which remain high in Eastern Europe.
- Prevention works: >50% of the reductions seen in CHD mortality relate to changes in risk factors, and 40% to improved treatments.
- Preventive efforts should be lifelong, from birth (if not before) to old age.
- Population and high-risk preventive strategies should be complementary; an approach limited to high-risk persons will be less effective; population education programmes are still needed.

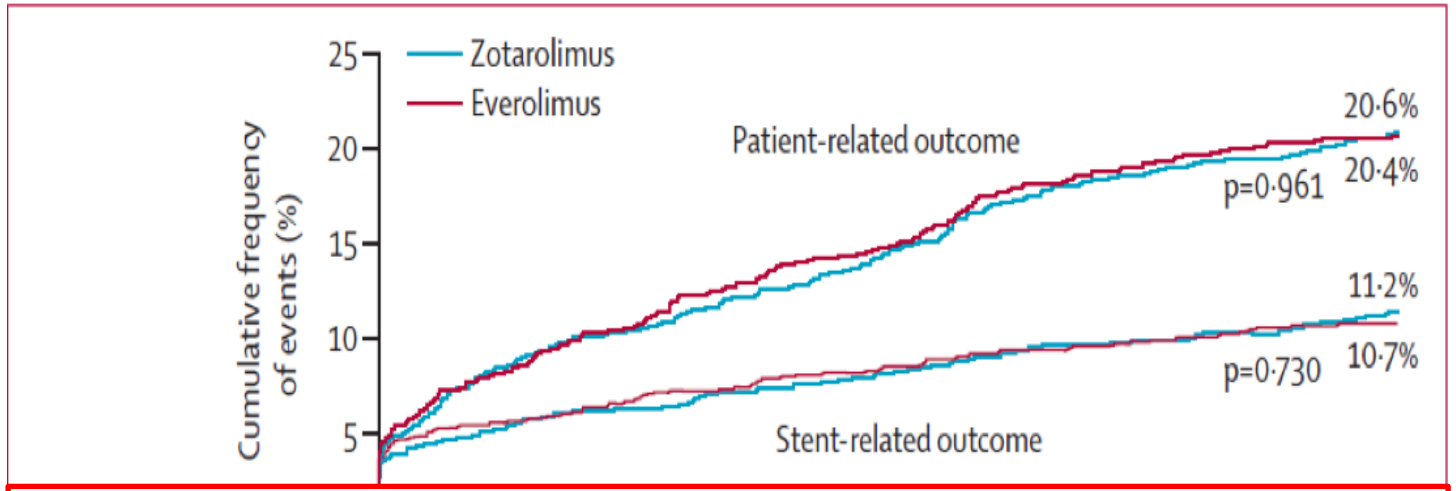
7-Year Risk of a Second MI Among 30-Day Survivors of First MI



- In this study, risk of a second AMI was highest during the first year and increased more gradually thereafter
- For men, 1- and 7-year cumulative risks were 5.6% and 13.9%; for women,7.2% and 16.2%
- Likelihood of recurrence increased with older age

Smolina K, et al. *Circ Cardiovasc Qual Outomces*. 2012;5:532-540.

Patient-related vs. stent-related outcomes



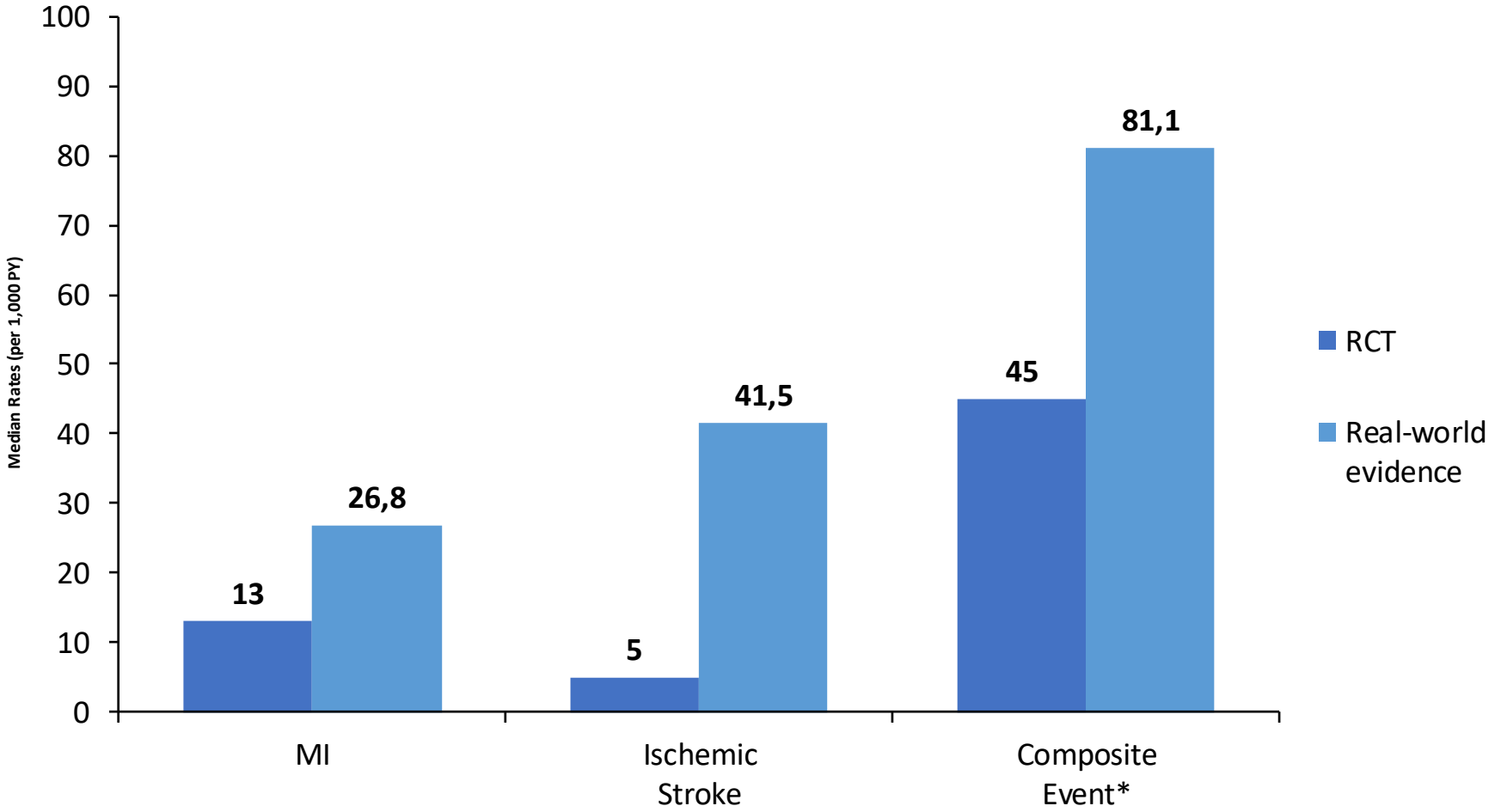
2a follow-up:
Pat. bezogene Komplikationen > # Stent bezogene Komplikationen:
Sekundärprevention ist mindestens so wichtig wie der neueste oder „beste“ Stent

Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial

Sigmund Silber, Stephan Windecker, Pascal Vranckx, Patrick W Serruys, on behalf of the RESOLUTE All Comers investigators

Lancet 2011; 377: 1241–47

2. Ereignis: reale Welt vs. randomisierte Studien



MACE, major adverse cardiovascular event; PY, patient-years; RCTs, randomized controlled trials.

*Definitions of composite of MACE events rates varied between studies.

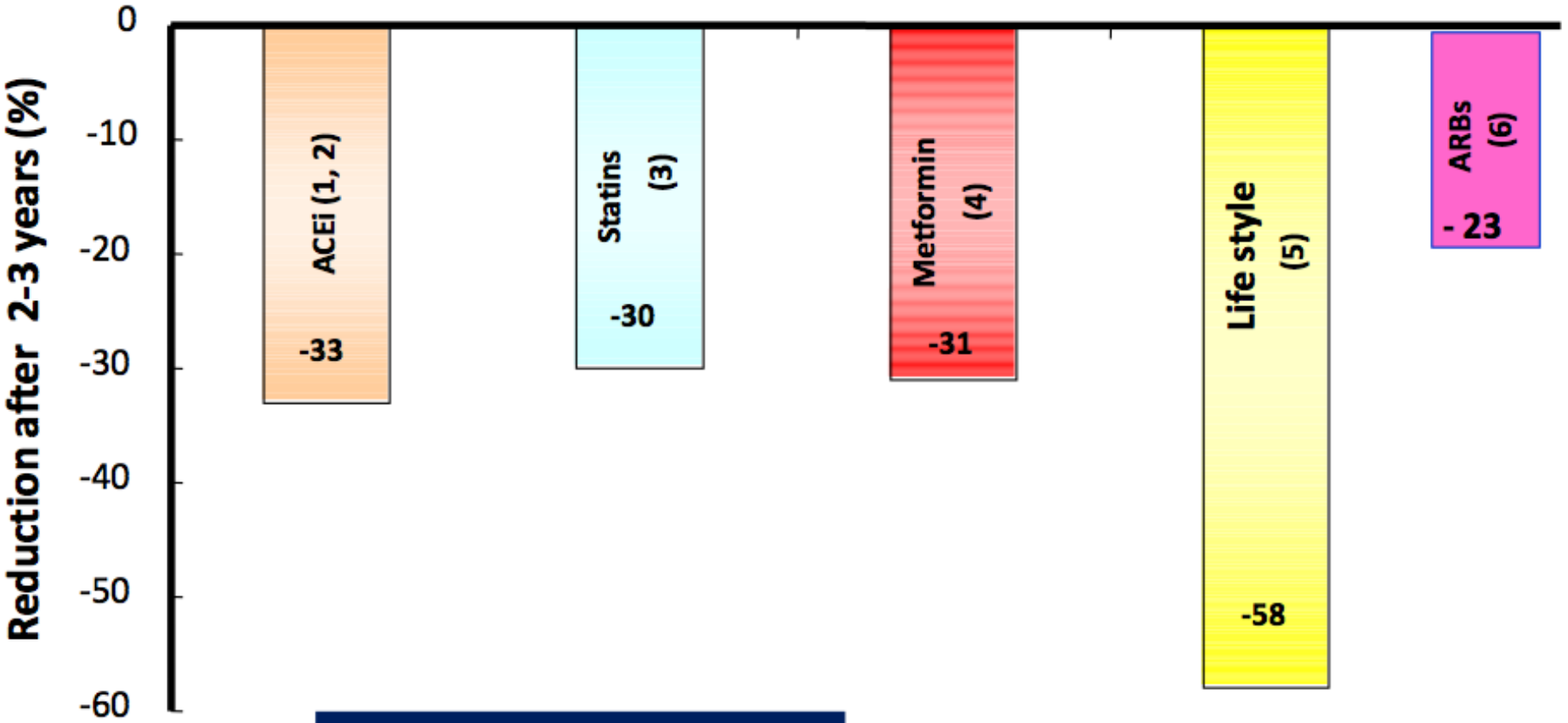
Fourteen studies that reported MACE incidence rates per 1,000 PY were included in the review. Acceptable study designs included retrospective or prospective observational studies.

The population and interventions of interest included patients with a history of ASCVD, elevated LDL-C, hypercholesterolemia, hyperlipidemia, or receiving lipid-lowering treatment (eg, statins).

Cherepanov D, et al. *Curr Med Res Opin*. 2018;34:459-473.

Ist DAS die Lösung (2)?

Reduktion der Entstehung von Typ 2 Diabetes



HOPE Study. NEJM 2000; 342: 145-53
CAPPP, Lancet 1999
WOSCOPS, Circulation 2001
Freeman DJ et al. Circ 2001; 103: 357-62
DPP NIH Study. NEJM 2002; 346: 393-403
Value study

DAS ist die Lösung!

Lebensstilmodifikation

Effect Size Estimates of Lifestyle and Dietary Changes on All-Cause Mortality in Coronary Artery Disease Patients

A Systematic Review

J.A. Iestra, RD; D. Kromhout, MPH, PhD; Y.T. van der Schouw, PhD; D.E. Grobbee, MD, PhD;
H.C. Boshuizen, PhD; W.A. van Staveren, PhD

3 Meta-Analysen, 10 RCT´s, 9 Cohortenstudien

Back ...nainly
su... ...ion in
ag... ...efit of
lif...
Meth ...lity in
CAD patients. Prospective cohort studies and randomized controlled trials of patients with established CAD were included if they reported all-causes mortality and had at least 6 months of follow-up. The effect estimates of smoking cessation (relative risk [RR], 0.64; 95% CI, 0.58 to 0.71), increased physical activity (RR, 0.76; 95% CI, 0.59 to 0.98), and moderate alcohol use (RR, 0.80; 95% CI, 0.78 to 0.83) were studied most extensively. For the 6 dietary goals, data were too limited to provide reliable effect size estimates. Combinations of dietary changes were associated with reduced mortality (RR, 0.56; 95% CI, 0.42 to 0.74).

Conclusions—Available studies show convincingly the health benefits of lifestyle changes in CAD patients. Effect estimates of combined dietary changes look promising. Future studies should confirm these findings and assess the contribution of the individual dietary factors. (***Circulation*****. 2005;112:924-934.**)

TABLE 4. Approximate Mortality Reduction Potential of Lifestyle and Dietary Changes Estimated From Studies in CAD Patients and the General Population

Recommendation	Mortality Risk Reduction Estimated From Studies in CAD Patients	Mortality Risk Reduction Estimated From Cohort Studies in General Population
Smoking cessation	35%	50%
Physical activity	25%	20%–30%
Moderate alcohol	20%	15%
Combined dietary changes	45%	15%–40%

TABLE 5. Approximate Mortality Reduction Potential of Preventive Drug Interventions After MI

Intervention	Mortality Risk Reduction, Mean (95% CI)
Low-dose aspirin[111]	18% (1%–30%)
Statins[112]	21% (14%–28%)
β-Blockers[113]	23% (15%–31%)
ACE inhibitors[114]	26% (16%–35%)

***Circulation*. 2005;112:924-934.**

Association of Diet, Exercise, and Smoking Modification With Risk of Early Cardiovascular Events After Acute Coronary Syndromes

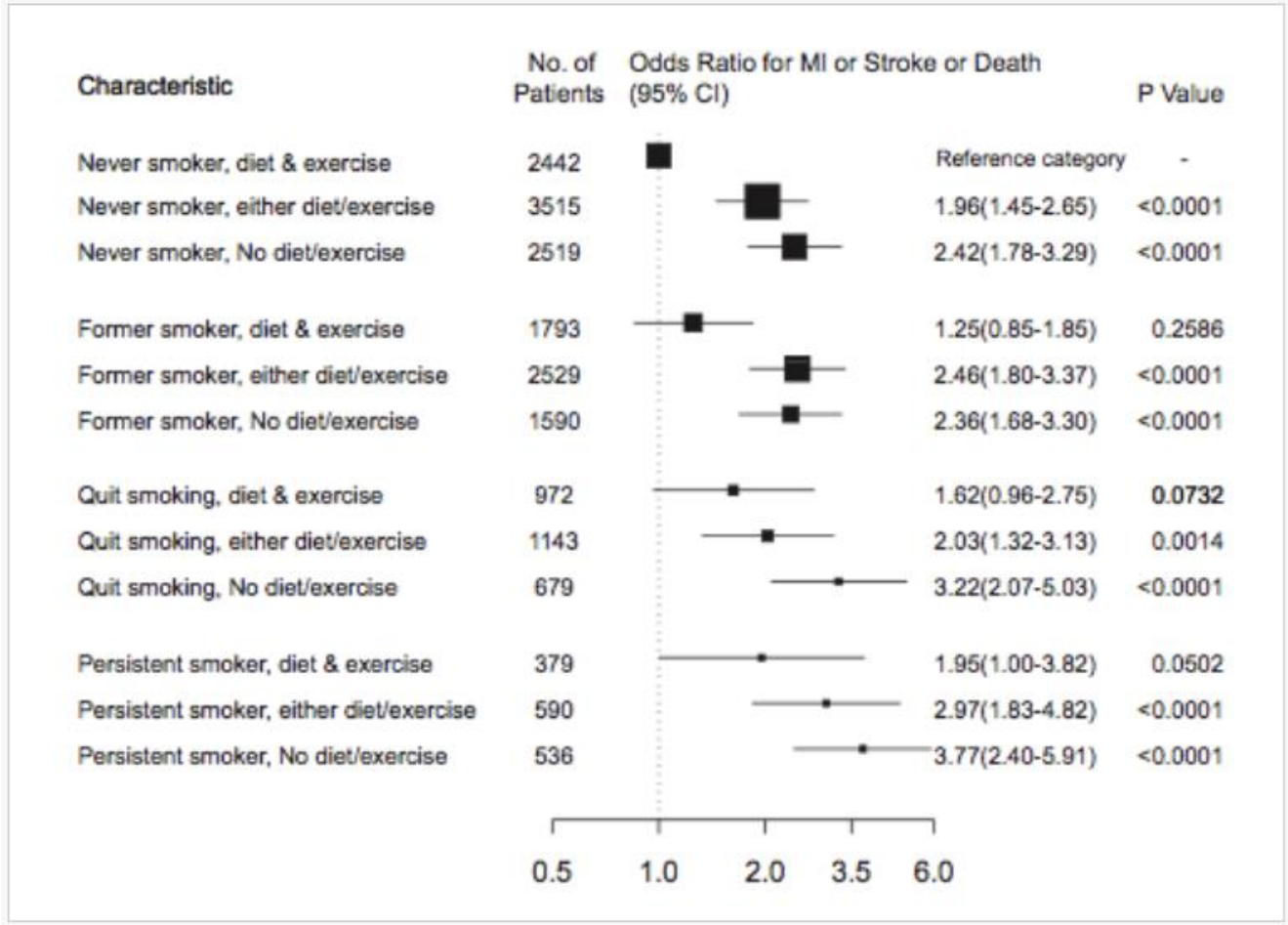
Clara K. Chow, MBBS, FRACP, PhD; Sanjit Jolly, MD, MSc, FRCPC;
Purnima Rao-Melacini, MSc; Keith A.A. Fox, BSc (Hons), MB, ChB, FRCP, FESC, FMedSci;
Sonia S. Anand, MD, PhD, FRCPc; Salim Yusuf, DPhil, FRCPC, FRSC

Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS) 5

Circulation. 2010;121:750-758

18.809 Pat. mit ACS/NSTEMI in 41 Ländern wurden Fondaparinux vs. Enoxaparin verglichen
Tag 30/90/180 Risikostatus evaluiert: Rauchen, Bewegung (> 30 Min. 3x/w) + Diät
Nach 6 Monaten MACE Rate (MCI, Insult, CV-Tod, Gesamtmortalität)

Medication	At Discharge, n (%)	At 30 Days, n (%)	At 6 Months, n (%)
Antiplatelet	18 145 (96.5)	18 069 (96.1)	17 106 (94.7)
Statin	14 820 (78.8)	14 792 (78.0)	13 389 (90.5)
ACE/ARB	13 705 (72.9)	13 643 (72.5)	12 251 (89.8)
β-blocker	15 506 (82.4)	9100 (48.4)	7110 (78.1)



MACE Rate korrigiert Alter, Geschlecht, Region, Hypertonie, Diabetes, MCI, BMI, Kreatinin
Referenz: Niemalsraucher, regelm. Bewegung und gesunde Ernährung

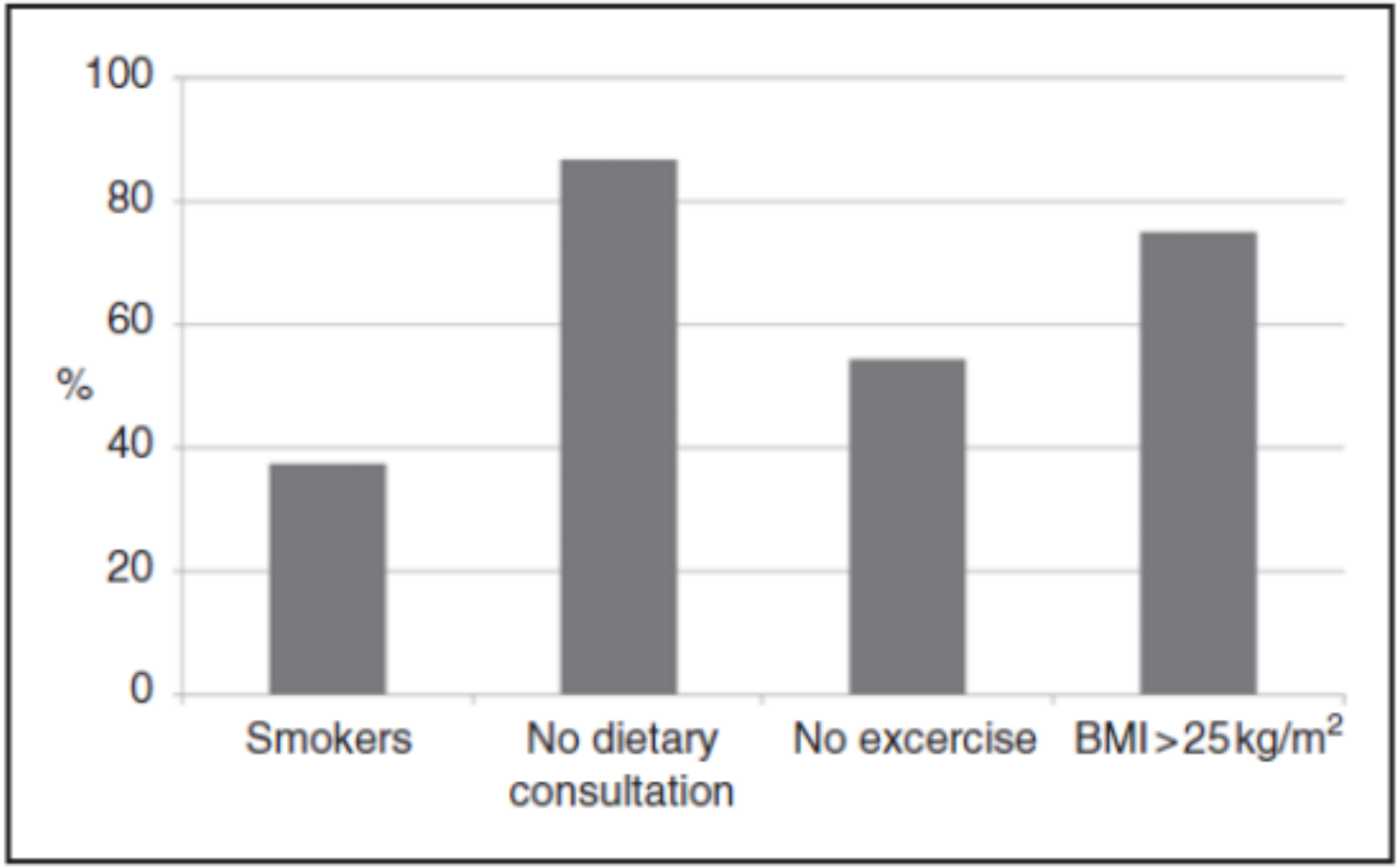
Diaät + Bewegung
- 48%

Rauchstopp
- 43%

Nicht tun
+ 380%

„der innere Schweinehund“

Risikofaktoren 1 Jahr nach PCI



Khattab AA et al. Eur J Prev Cardiol 2012

Positive Rehabilitation effects get lost over 12 months: prospective PIN Studie

2.441 consecutive pat., 78% male
MCI 56%, ACBP 38%, PCI 6%

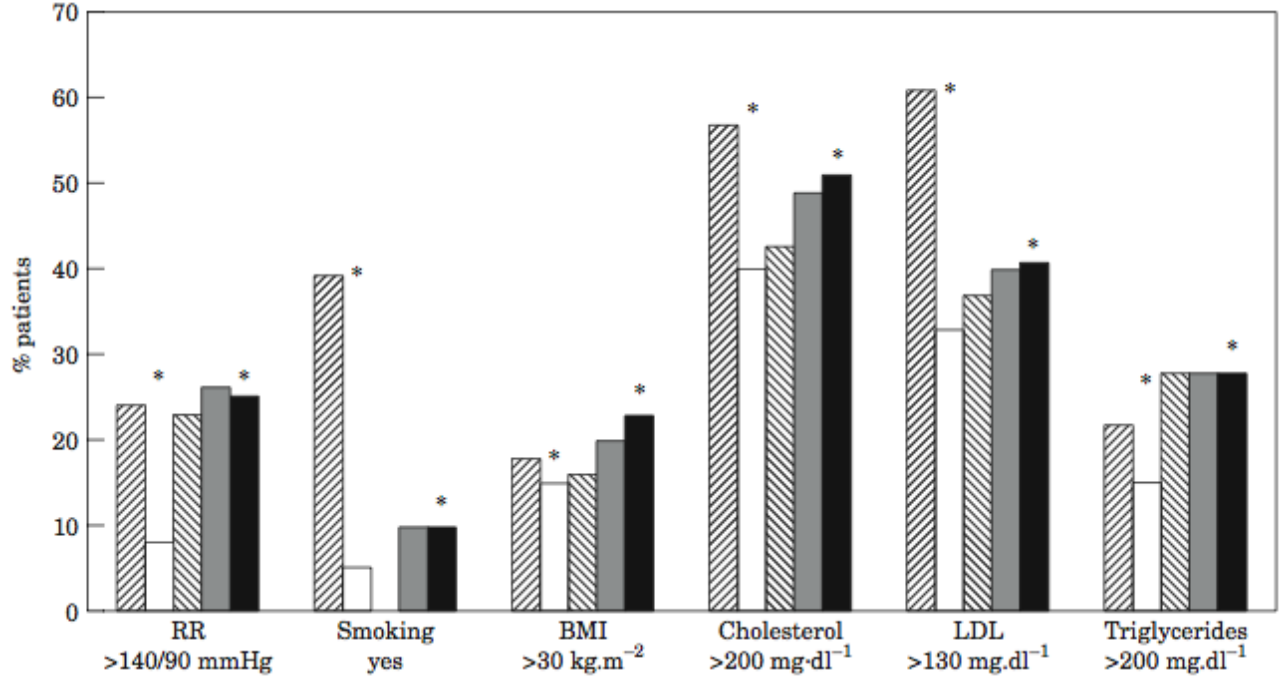
European Heart Journal (2001) **22,** 307–313
doi:10.1053/euhj.2000.2294, available online at http://www.idealibrary.com on IDEAL®

Cardiac risk factors, medication, and recurrent clinical events after acute coronary disease

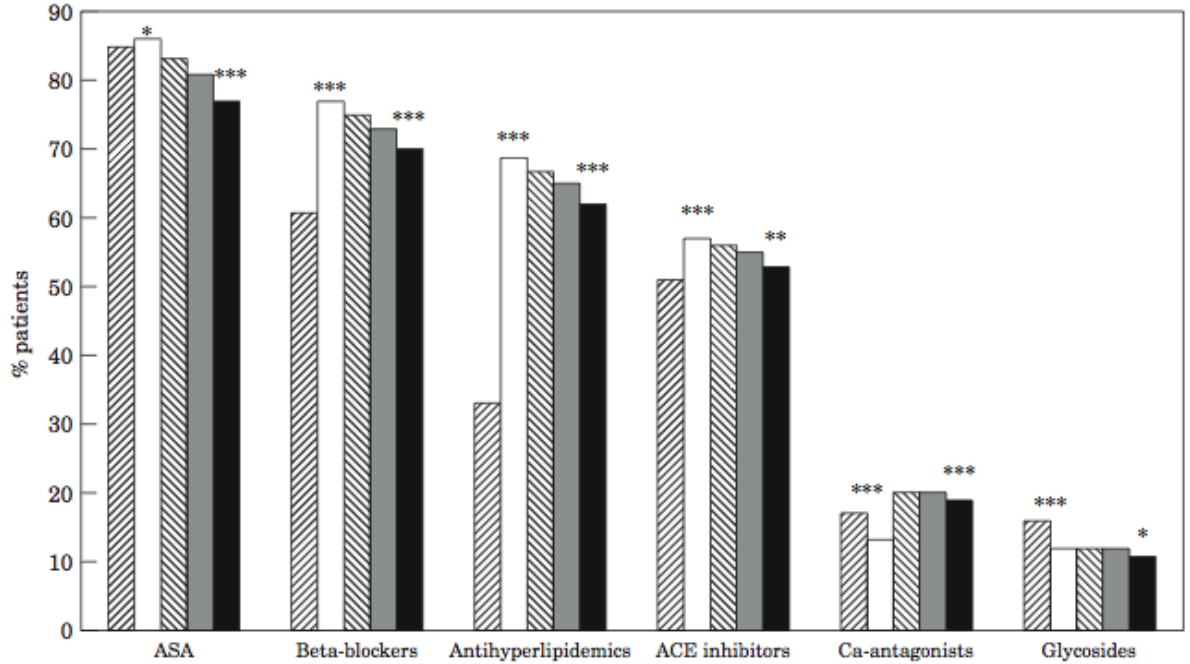
A prospective cohort study

S. N. Willich[1], J. Müller-Nordhorn[1], M. Kulig[1], S. Binting[1], H. Gohlke[2], H. Hahmann[3], K. Bestehorn[4], K. Krobot[4], H. Völler[5] for the PIN Study Group*

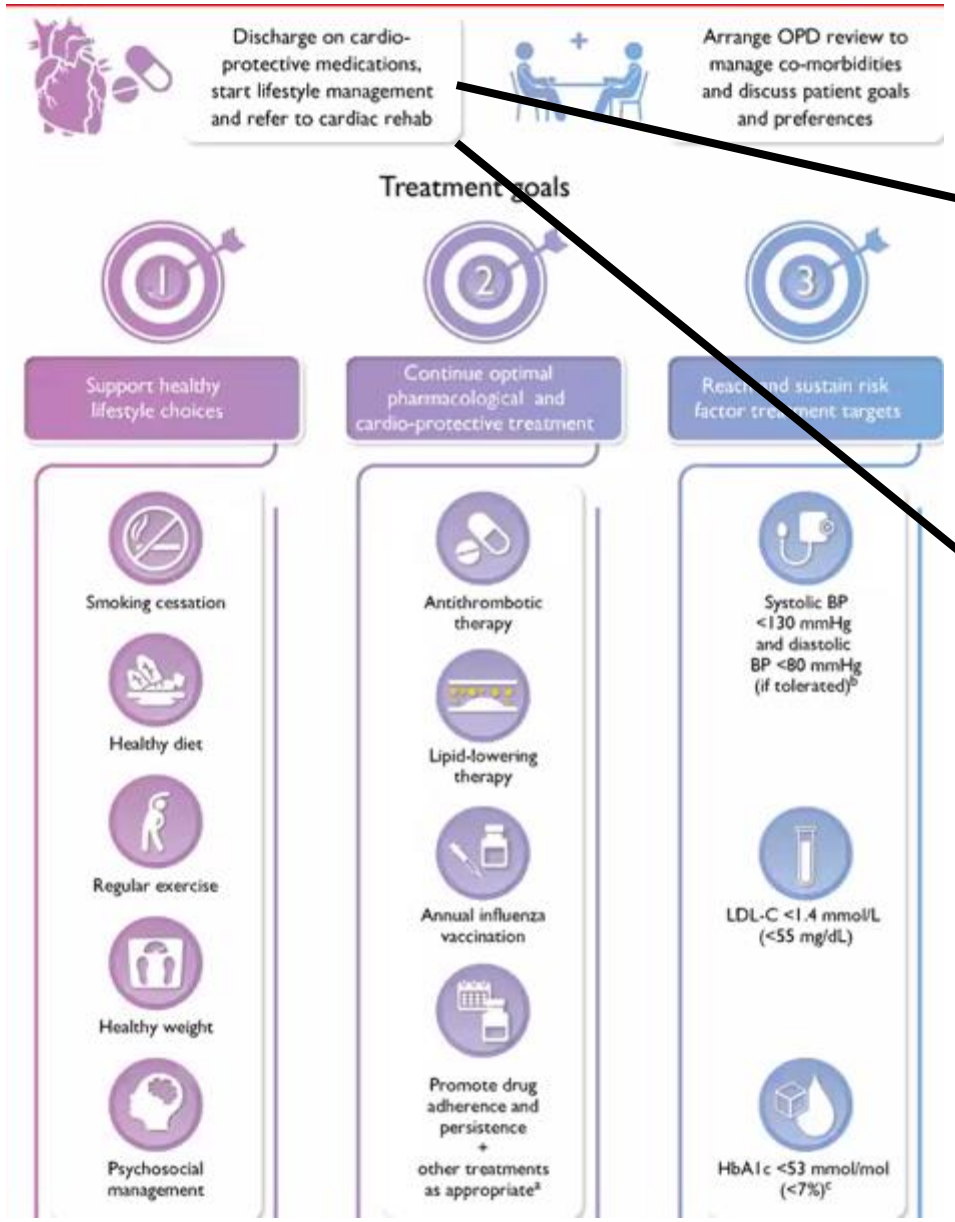
[1]Institute for Social Medicine and Epidemiology, Charité Hospital, Humboldt University of Berlin, Berlin, Germany; [2]Herzzentrum, Bad Krozingen, Germany; [3]Waldburg-Zeil Kliniken, Isny, Germany; [4]MSD Sharp and Dohme GmbH, Haar, Germany; [5]Klinik am See, Rüdersdorf, Germany



▨=admission; □=discharge; ▧=3 months; ▩=6 months; ■=12 months.



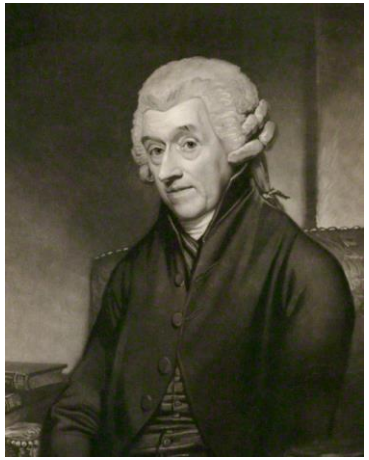
Wir brauchen strukturierte Programme (Rehabilitation+lebenslange Begleitung)



Discharge on cardio-protective medications, start lifestyle management and refer to cardiac rehab

Beginn der Rehabilitation bei MCI

1772: Heberden
6-monatiges Bewegungsprogramm
bei einem Pat. mit Brustschmerzen
tgl. 30 Minuten Sägen



1930er Jahre: zumindest 3-wöchige Bettruhe
und 1 Jahr kein Stiegensteigen nach MCI

Mallory und Weiss: Umwandlung Nekrose in
Narbe dauert ca. 6 Wochen

1970er Jahre Immobilisation ist schlecht, red. Überlebensrate

2000er: modernes Rehabilitationsprogramm mit definierten Inhalten:

- Training: Ausdauer, Kraft, Koordination
- Schulung: Risikofaktoren
- Psychologie
- Med. Optimierung

„Bio-psycho-soziale“ Modell mit GANZHEITLICHER Betrachtung des Menschen

European Cardiac Rehabilitation Inventory Survey (ECRIS)

Birna Bjarnason-Wehrens
AnnDorthe Zwisler

- Israel

- Austria
- Belgium
- Belarus
- Croatia
- Cyprus
- Czech Republic
- Denmark
- France
- Finland
- Germany
- Iceland
- Ireland
- Italy
- Lithuania
- Luxembourg
- Netherlands
- Norway
- Poland
- Portugal
- Romania
- Russian Fed.
- Serbia
- Slovak Rep.
- Spain
- Sweden
- Switzerland
- United Kingdom

Estimated percentage of eligible patients admitted for phase II and III cardiac rehabilitation in 2006

Phase II	
unknown 5 (26%)	≤ 3% - 90% ≤ 30% = 8 > 30-50% = 3 > 70% = 3

Phase III	
unknown 13 (68%)	≤ 5% - 30% 20-30% = 4

	Phase II
Spain	<3%
Romania	10%
France	10-30%
Belgium	15-20%
Italy	25-30%
Netherlands	30%
Austria	30%
Switzerland	30%
Luxembourg	40-50%
Sweden	40-50%
UK	40-50%
Germany	≥ 50%
Iceland	≥ 50%
Lithuania	90%

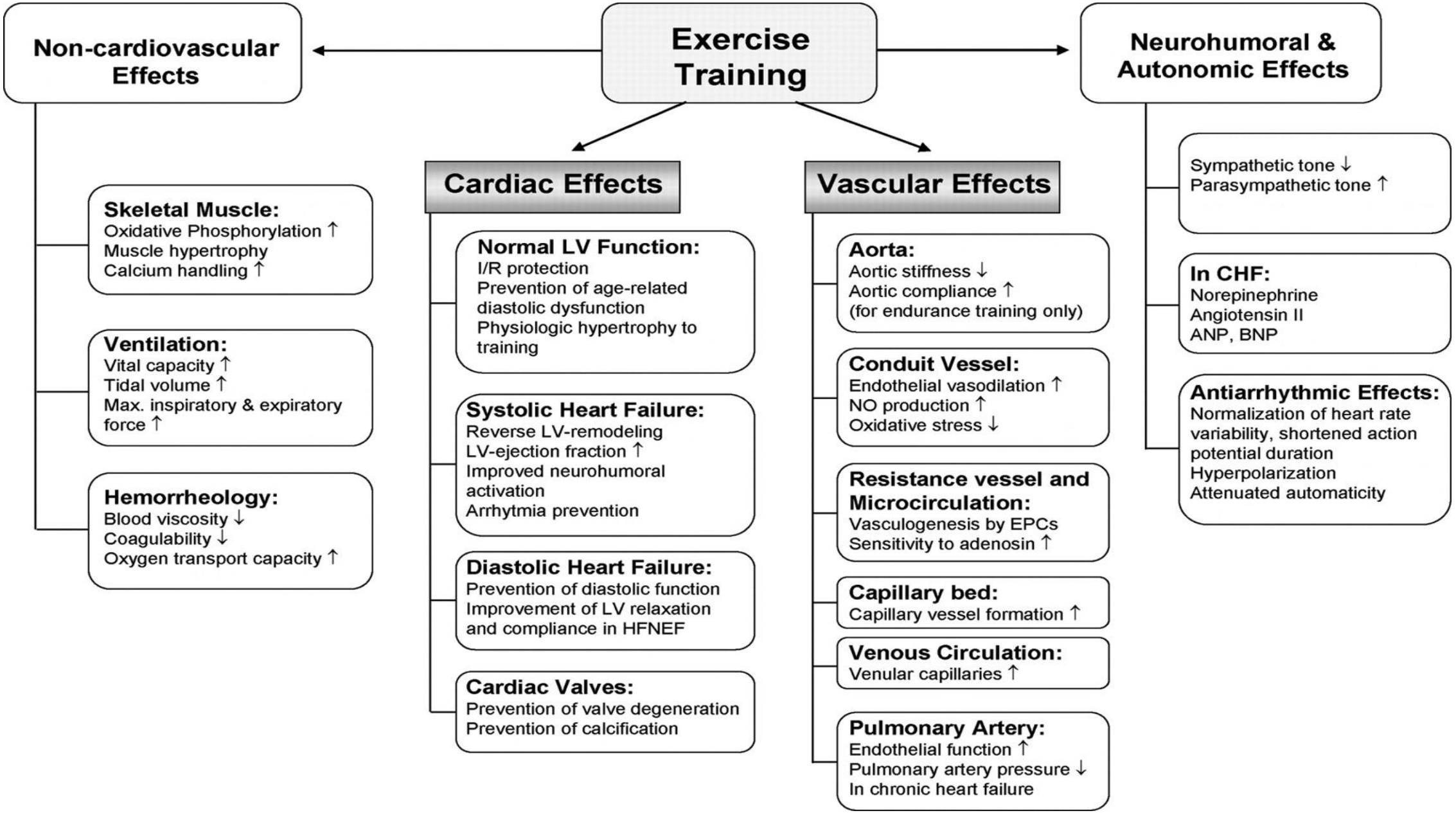
	Phase III
Belgium	5%
Romania	10%
Netherlands	20%
Austria	20%
Germany	25-30%
Lithuania	30%

Rehabilitationsquote

Herz Kreislauferkrankungen		
	2012 %	**2009 %**
Akuter MCI (I21)	40,0	48,0
Sonst. akut. ischäm. Herz-KH (I24)	23,0	30,2
Chron. ischäm. Herz-KH (I25)	24,9	26,0
Mitralklappen-KH (I34)	42,6	51,4
Aortenklappen-KH (I35)	53,4	54,7
CMP (I42)	16,9	16,0

2009
MCI n = 16.000
Rehab n = 6.000 im selben Jahr

Quelle: Chefarzt Prof. Dr. Müller, PVA



Cardiovascular Effects of Exercise Training
Molecular Mechanisms Gielen S,
Circulation. 2010;122:1221–1238

Positive Effect of Exercise

Total mortality correlates with physical fitness

18.102 males, mean age 58 y, symptom- limited exercise test between 1986 und 2011, mean follow-up 10,8 y.
The peak metabolic equivalents (METs) level associated with no increase in all-cause mortality risk (hazard ratio, 1.0) for different age categories was defined as threshold (TH).

- **least fit** 2 METs < TH: OR **1,52**
- low fit 0-2 METs < TH: OR 1,21
- moderate fit 0-2 METs > TH: OR 0,71
- fit 2-4 METs > TH: OR 0,62
- **high fit** > 4 METs > TH: OR **0,46**

VA-Studie. Circulation 2014; 130:653

Positive Effect of Exercise

Every increase of fitness by 1 MET resulted in 12% RRR of mortality!

Recommendations for physical fitness:

< 50 y 8-9 METs
50-59 y 7-8 METs
60-69 y 6-7 METs
> 70 Jahre 5-6 METs

Circulation 2014; 130:653

Effekte von Bewegung (Klasse I Indikation)

Blutdrucksenkung (-7/-5 mmHg)

KARDIA-1 (phase 2 dose-ranging study)

A single subcutaneous injection of

antihypertensive agent **zilebesiran** (RNA interference therapeutic that binds with high affinity to the hepatic asialoglycoprotein receptor, bringing about a reduction in the synthesis of angiotensinogen (Alnylam Pharmaceuticals))

377 patients (average baseline systolic blood pressure 142 mm Hg) randomly assigned to receive one of four different zilebesiran doses (150 mg, 300 mg, or 600 mg once every 6 months or 300 mg once every 2 months) or a placebo.

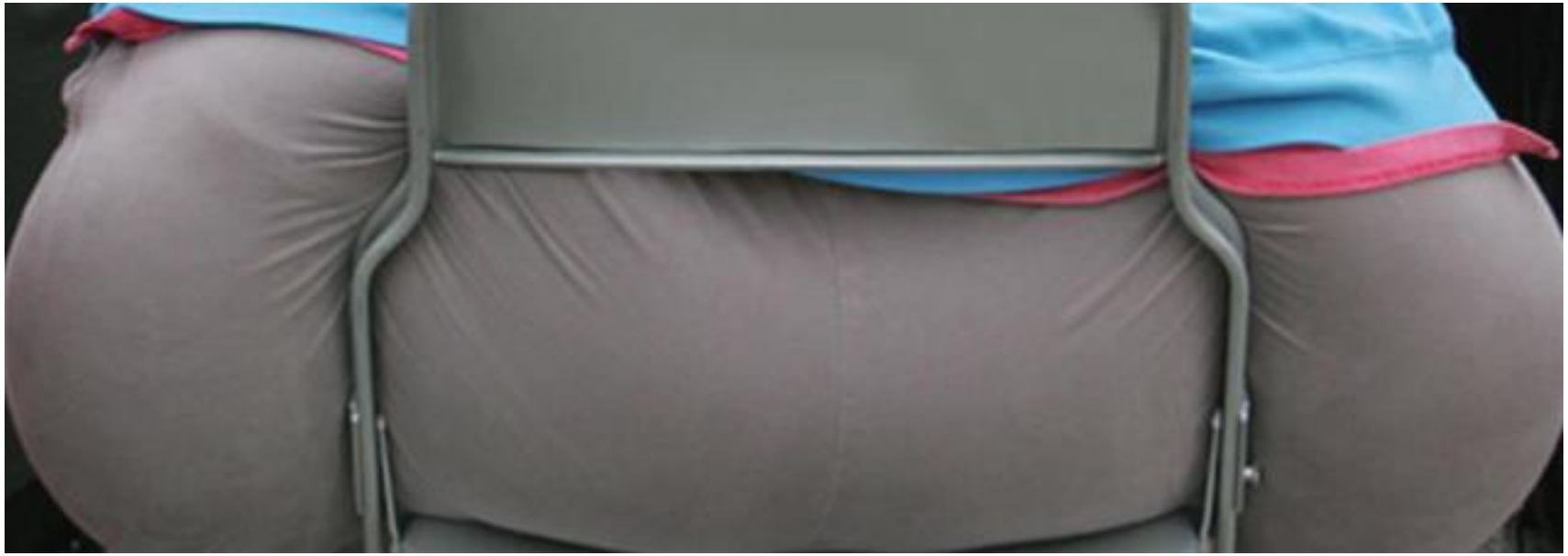
Ambulatory systolic blood pressure measured over 24 hours showed was significantly decreased with all zilebesiran regimens, with a mean reduction from baseline to month 6 of around 10 mm Hg.

Effects of exercise on RF (class IA)

Blutdrucksenkung (-7/-5 mmHg)

Gewichtsreduktion/-stabilisation

Sitzen ist das „neue Rauchen“



Herzgesund Essen im HKZ Groß Gerungs

- Saisonal und Regional
- Hoher Bioanteil (ca. 60%)
- Fettbewusste Zubereitung, Omega 3 Fettsäuren
- Salzreduziert: tägliche Kochsalzzufuhr max. 5-6 g/Tag
- Bewusster Einsatz von Zucker und Süßungsmitteln
- Ballaststoffreich und pflanzenbasiert
- 3 Mahlzeiten/Tag, keine Zwischenmahlzeiten

2023

SELECT TRIAL

M

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

multicenter, double-blind, randomized, placebo-controlled

Objective: to determine the association of subcutaneous semaglutide with cardiovascular (CV) events in a secondary prevention cohort of patients with overweight or obesity and prior CV disease (CVD) without diabetes mellitus (DM)

17,604 patients

Inclusion criteria: Age ≥45 years; BMI ≥27 kg/m2
Prior MI, stroke, or peripheral arterial disease (PAD) with claudication and ankle-brachial index <0.85, prior revascularization, or amputation

Semaglutide (n=8803)

VS.

Placebo (n=8801)

PRIMARY OUTCOME

Semaglutide		Placebo
6.5	composite of CV death, nonfatal MI, and nonfatal stroke % HR 0.80, 95% CI 0.72-0.90, p < 0.001	8.0

SECONDARY OUTCOME

Semaglutide		Placebo
2.5	CV death % HR 0.85, 95% CI 0.71-1.01, p = 0.07	3.0
3.4	CV death or HF hospitalization % HR 0.82, 95% CI 0.71-0.96	4.1

Conclusion: In patients with preexisting cardiovascular disease and overweight or obesity but without diabetes, weekly subcutaneous semaglutide at a dose of 2.4 mg was superior to placebo in reducing the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke at a mean follow-up of 39.8 months.

Effects of exercise on RF (class IA)

Blutdrucksenkung (-7/-5 mmHg)

Gewichtsreduktion/-stabilisation

Prävention von Typ 2 Diabetes

Verbesserte Insulinsensitivität/ Blutzuckersenkung

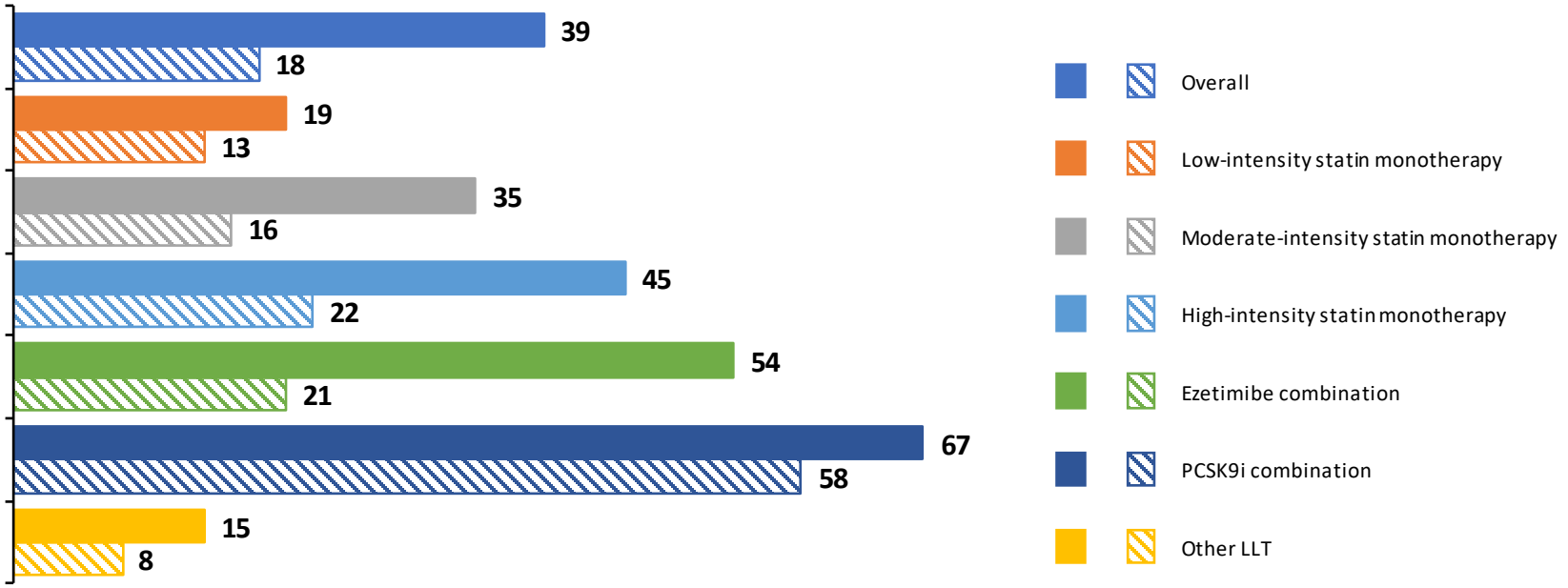
HDL-C Steigerung, Senkung von Triglyceriden und LDL-C

Single products (full dosed)	Expected % LDL-C reduction
Monacolin K	~ −15–25%
Berberine	~−15–20%
Soluble fibers/Glucomannan/Plant sterols	~−8–12%
Soy and lupin proteins/Allicin from garlic	~−6–10%
Policosanols/Chlorogenic acid/gamma-oryzanol/Sylimarin	~−5%

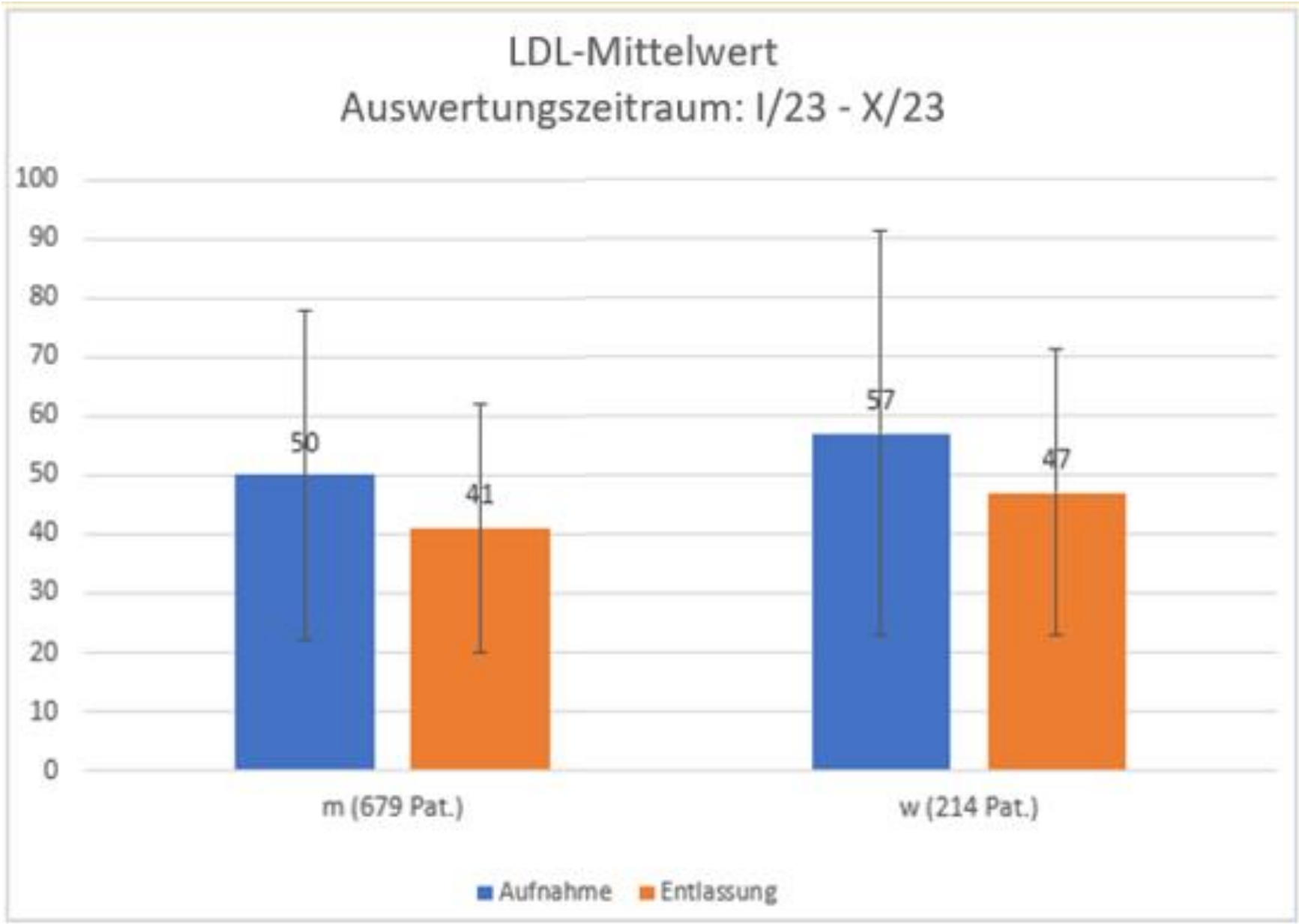
DA VINCI (EU-Wide, Cross-Sectional, Observational Study)
N = 2.039 in 18 European Countries

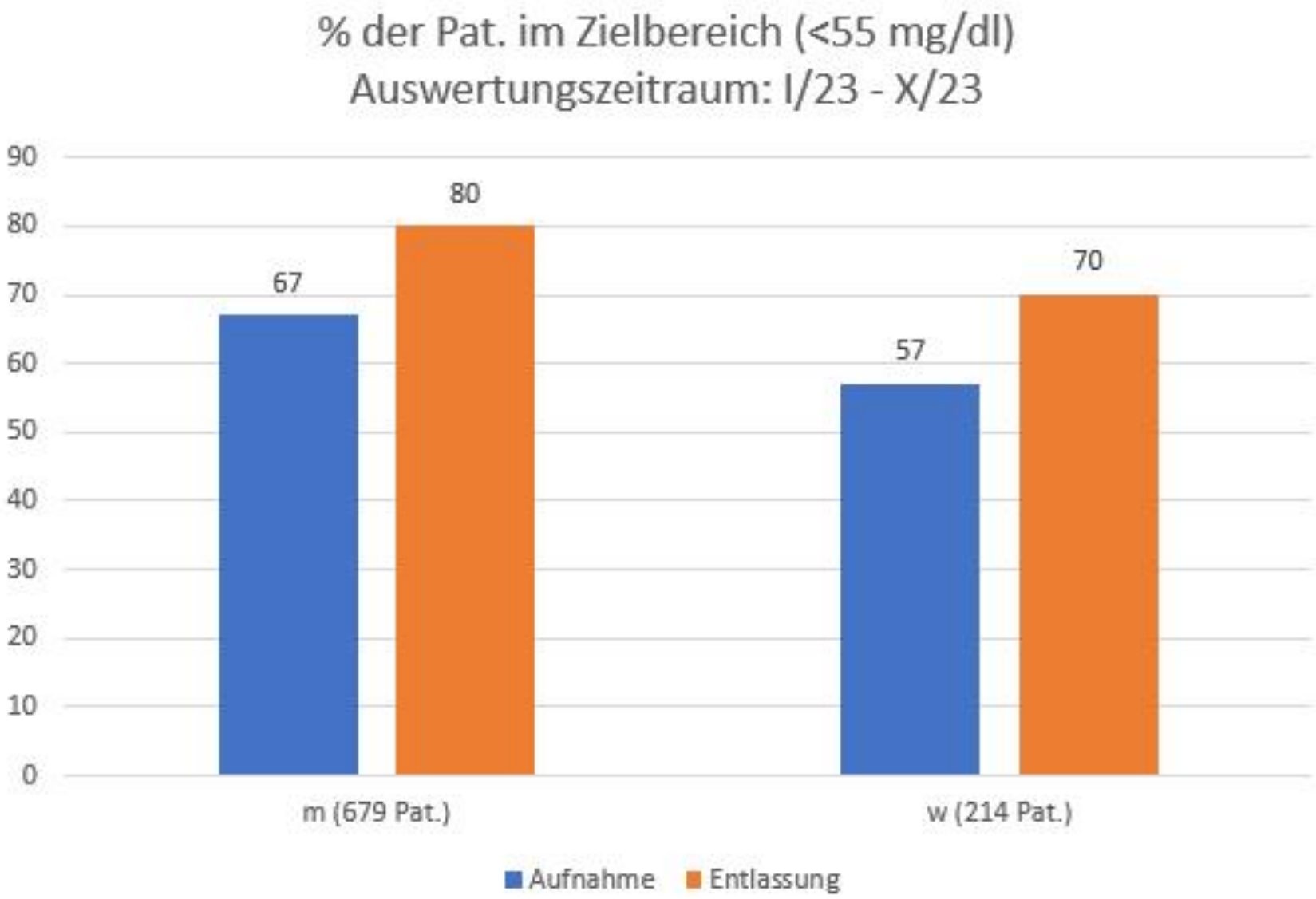
< 40% Reached the 2016 ESC/EAS Guidelines
< 20% Met the 2019 ESC/EAS Guidelines

Solid: 2016 ESC/EAS: LDL-C ≤ 70 mg/dL
Striped: 2019 ESC/EAS: LDL-C ≤ 55 mg/dL



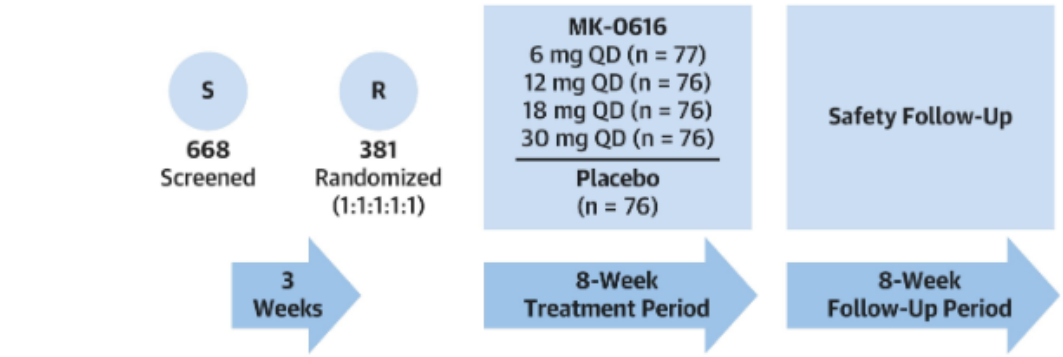
ASCVD: coronary disease, peripheral disease, cerebral disease
Countries participating in DA VINCI were: Austria, Belgium, the Czech Republic, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Poland, Romania, Slovakia, Spain, Sweden, the UK, and Ukraine.
LLT, lipid-lowering therapy.
Ray KK, et al. *Eur J Prev Cardiol*. 2020. doi:10.1093/eurjpc/zwaa047.


LDL-Mittelwert
Auswertungszeitraum: I/23 - X/23
100
90
80
70
60
50
40
30
20
10
0
50
41
57
47
m (679 Pat.)
w (214 Pat.)
Aufnahme
Entlassung


% der Pat. im Zielbereich (<55 mg/dl)
Auswertungszeitraum: I/23 - X/23
90
80
70
60
50
40
30
20
10
0
67
80
57
70
m (679 Pat.)
w (214 Pat.)
Aufnahme
Entlassung

CENTRAL ILLUSTRATION: A Phase 2b Study of MK-0616, an Oral PCSK9 Inhibitor

Study Design



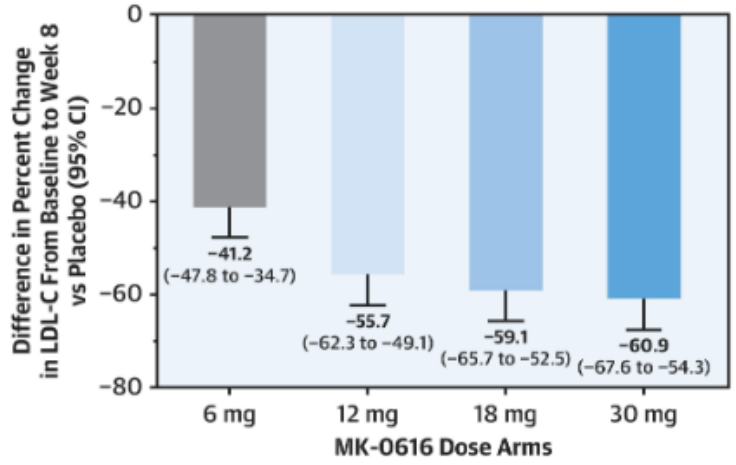
Baseline Participant Characteristics (*n = 381 Randomized Participants*)

Female: 49.3%
Mean LDL-C: 119.5 mg/dL

ASCVD Risk Category:
Clinical ASCVD: 38.6%
Intermediate/High ASCVD Risk: 56.4%
Borderline ASCVD Risk: 4.7%

Statin Intensity:
No Statin: 39.4%
Low-to-Moderate Intensity: 34.6%
High Intensity: 26.0%

Efficacy (*n = 380 Treated Participants*)



Key Points

- All doses of MK-0616 demonstrated statistically superior reductions in LDL-C vs placebo with up to 60.9% placebo-adjusted reduction from baseline values
- MK-0616 was well tolerated with no overall trends in AEs across treatment groups

Ballantyne CM, et al. J Am Coll Cardiol. 2023;81(16):1553-1564.

Table 3
Change From Baseline in Lp(a) (FAS Population)

	MK-0616 6 mg QD	MK-0616 12 mg QD	MK-0616 18 mg QD	MK-0616 30 mg QD	Placebo
Participants evaluated	77	75	76	76	75
Week 8, mg/dL	41.0 ± 54.0	36.7 ± 46.0	27.3 ± 35.8	33.8 ± 41.9	41.4 ± 51.1
Percentage change from baseline at Week 8	−11.8 ± 17.8	−20.8 ± 22.4	−21.3 ± 22.9	−23.2 ± 25.2	0.5 ± 21.8

Values are n or mean ± SD, unless otherwise indicated.

VERVE-101: CRISPR-Based Gene Editing Therapy Shows Promise in Reducing LDL-C and PCSK9 Levels in Patients With HeFH

Nov 12, 2023

ACC News Story

A single infusion of a CRISPR-based gene editing therapy significantly reduced LDL-C and PCSK9 levels in patients with heterozygous familial hypercholesterolemia (HeFH), based on findings from the VERVE-101 trial presented Nov. 12 at AHA 2023. In presenting the findings, **Andrew Bellinger, MD, PhD**, said they provide the first proof-of-concept for in vivo DNA base editing in humans.

The ongoing, first-in-human study enrolled 10 patients (8 men/2 women, mean age 54 years) from the UK or New Zealand, all of whom had HeFH and an average LDL-C of 201 mg/dL. Most study participants had pre-existing severe coronary artery disease and had undergone prior coronary revascularization. Roughly half of participants had experienced at least one myocardial infarction. Nearly all were on statin therapy, and none were taking PCSK9 inhibitors while enrolled in the study.

All patients received a single intravenous infusion of VERVE-101, with the first cohort (n=3) receiving a low dose of 0.1 mg/kg and other cohorts receiving escalating doses, after consultation with an independent safety monitoring board. The highest dose received was 0.6 mg/kg.

Overall findings showed that three patients receiving the highest two VERVE-101 doses (0.45 mg/kg and 0.6 mg) saw the greatest reductions in LDL-C and PCSK9 protein levels. The two patients in the 0.45 mg/kg group saw reductions in LDL-C by 39% and 48%, respectively, and in PCSK9 by 47% and 59%. The one patient in the 0.6 group experienced a reduction in LDL-C of 55% and in PCSK9 of 84%. Bellinger noted that the LDL change has been durable up to six months so far, with follow-up ongoing.

“Instead of daily pills or intermittent injections over decades to lower bad cholesterol, this study reveals the potential for a new treatment option – a single-course therapy that may lead to deep LDL-C lowering for decades,” Bellinger said.

Effects of exercise on RF (class IA)

Blutdrucksenkung (-7/-5 mmHg)

Gewichtsreduktion/-stabilisation

Prävention von Typ 2 Diabetes

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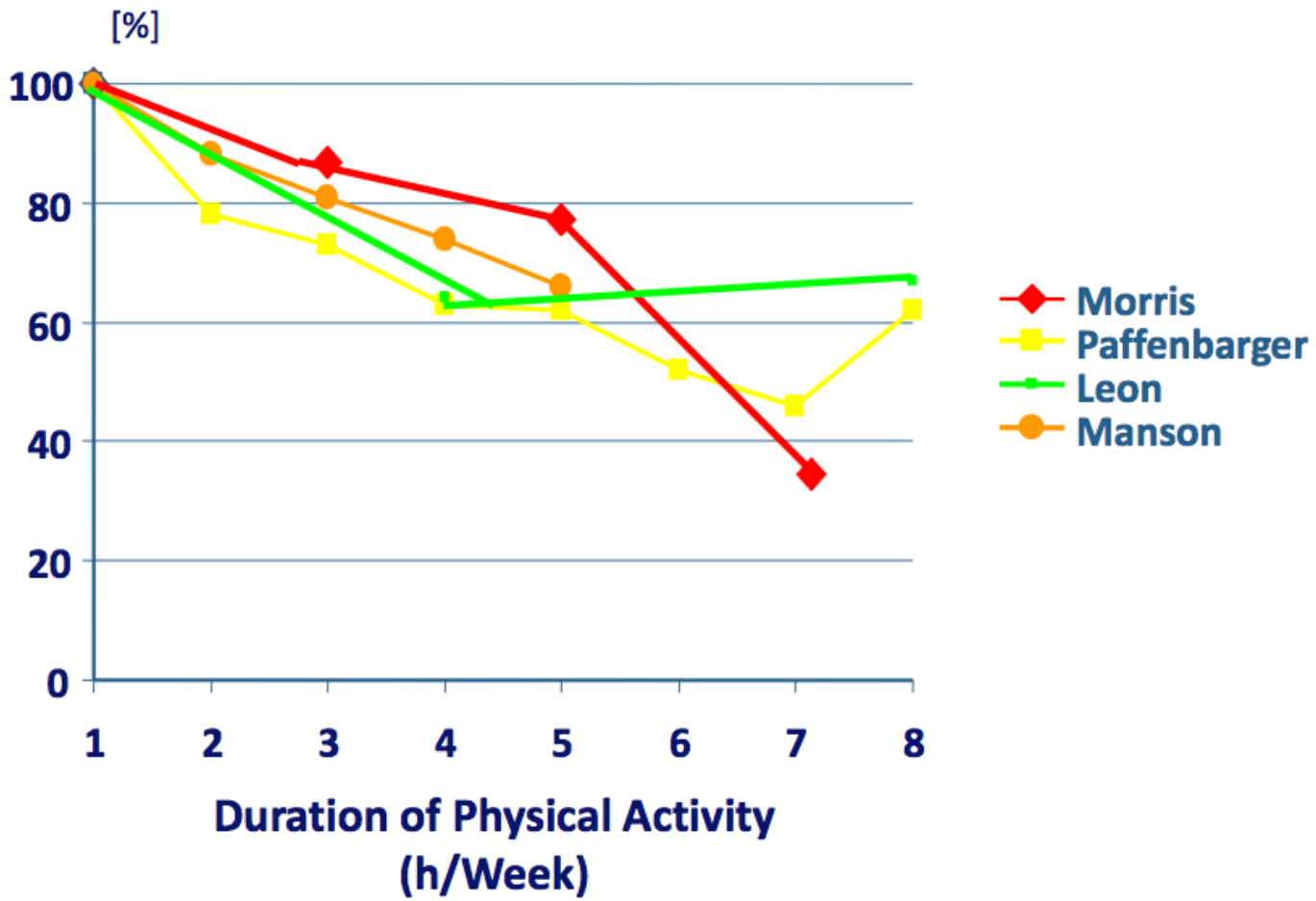
HDL-C Steigerung, Senkung von Triglyceriden und LDL-C

Reduktion der Thrombozytenaktivität

Klare Dosis-Wirkungsbeziehung!

Reduction of Mortality by Physical Activity



Vielen Dank für die Aufmerksamkeit