KHK unter dem Aspekt der „Gender Medicine“

PD Dr. med. Jean-Paul Schmid

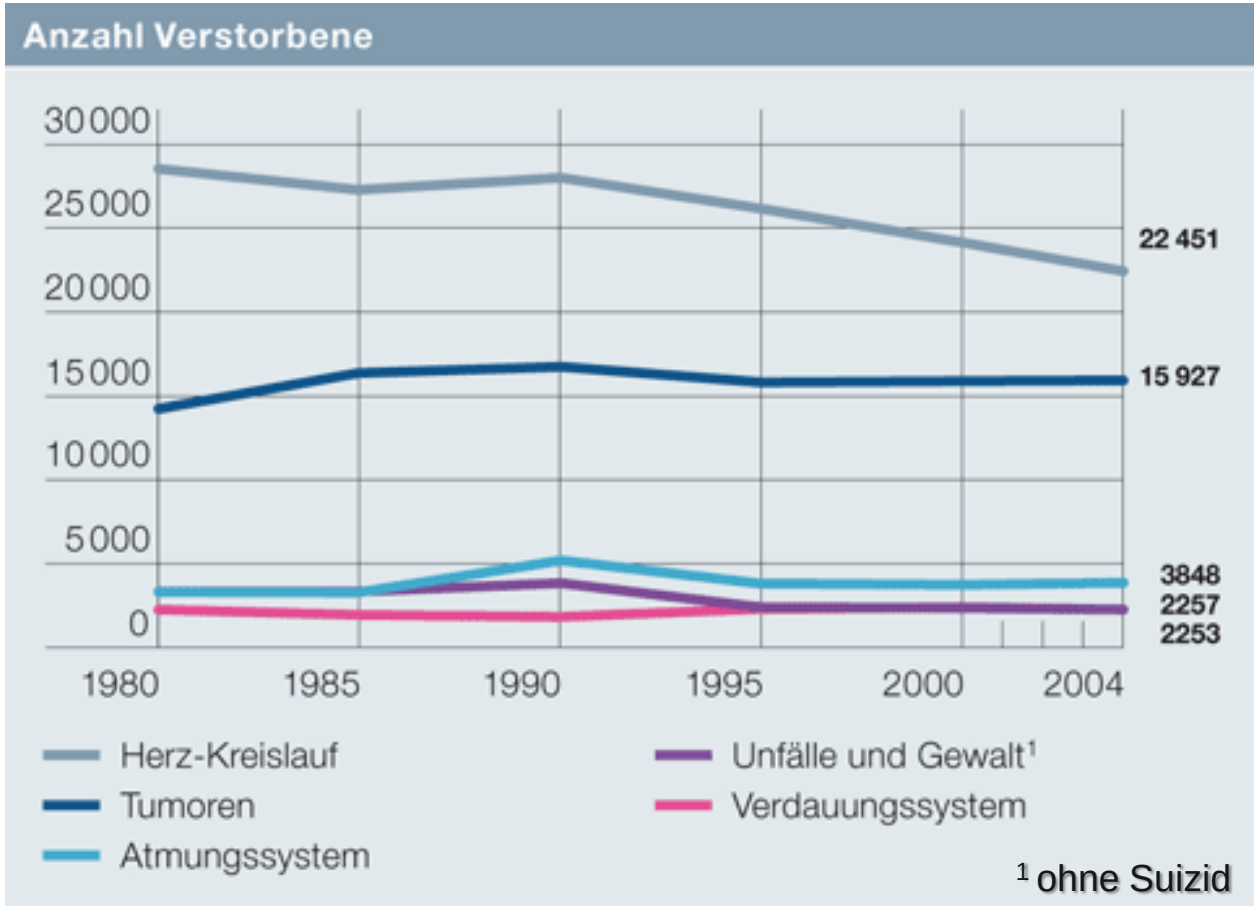
INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

UNIVERSITÄT BERN

Ausgangslage

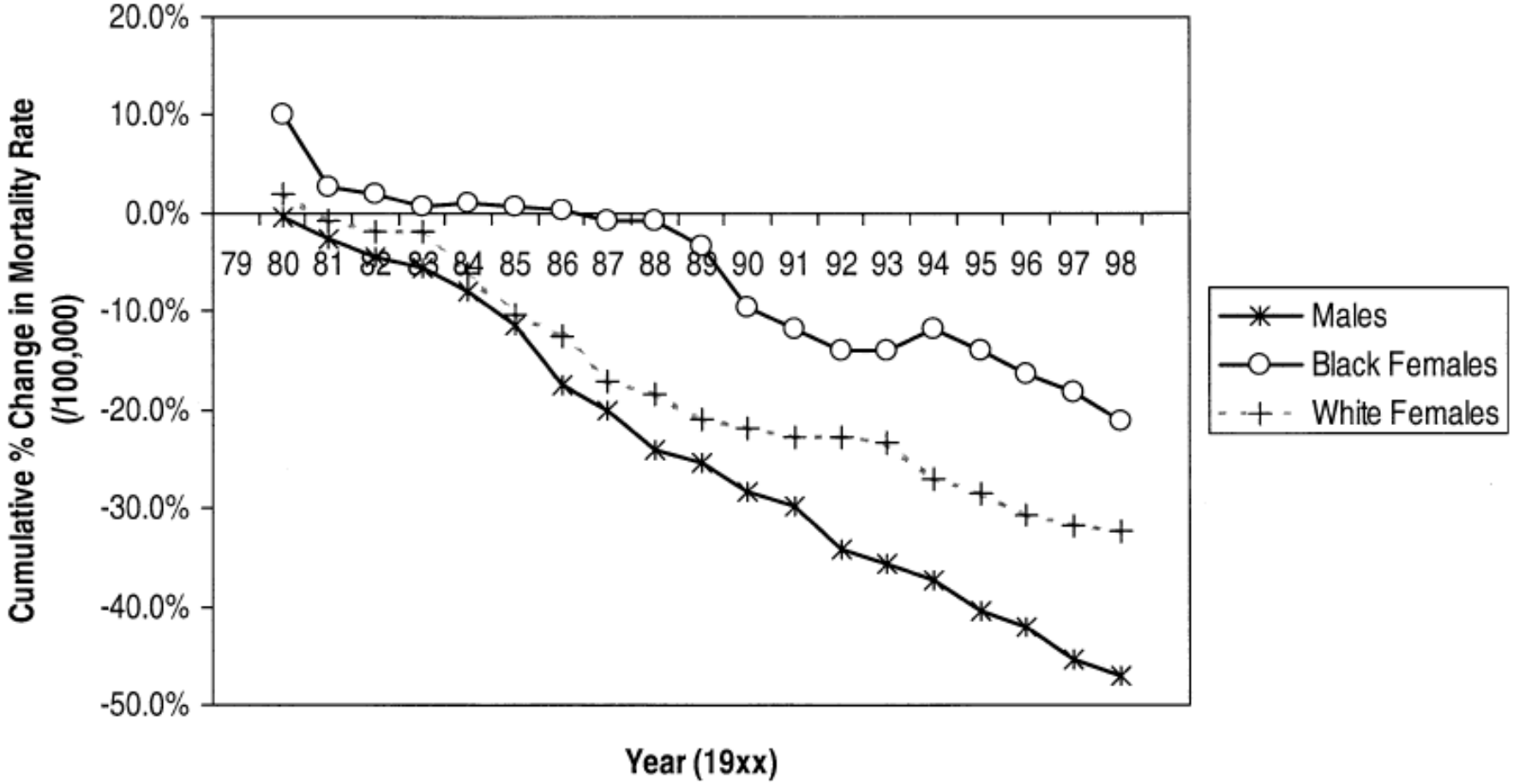
- In der westlichen Welt sterben aktuell jährlich mehr Frauen als Männer an ischämischer Herzkrankheit
- Trendumkehr im Vergleich zu den letzten Jahren, am ausgeprägtesten bei den relativ jungen Frauen

Verlauf der wichtigsten Todesursachen



Todesursachen-Statistik, diverse Jahrgänge, Bundesamt für Statistik, Neuchâtel.

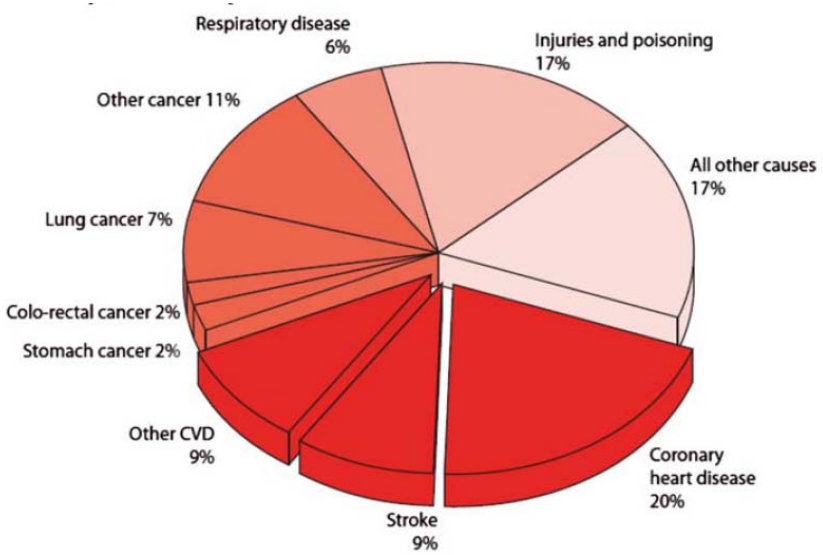
Prozentuale Änderung der Todesraten durch Myokardinfarkt in den USA



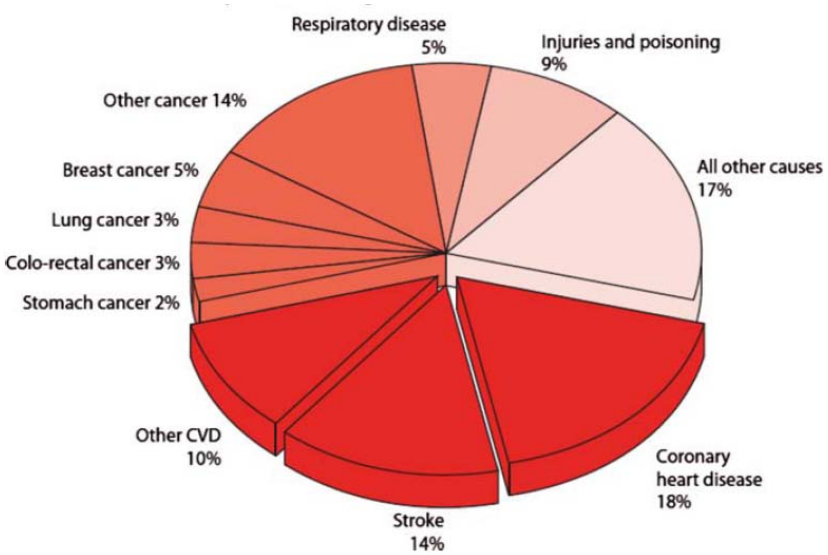
Benjamin EJ et al. J Am Coll Cardiol 2002;40:588–603

Todesrate < 75 Jh. (letztes verfügbares Jahr, Europa)

Männer

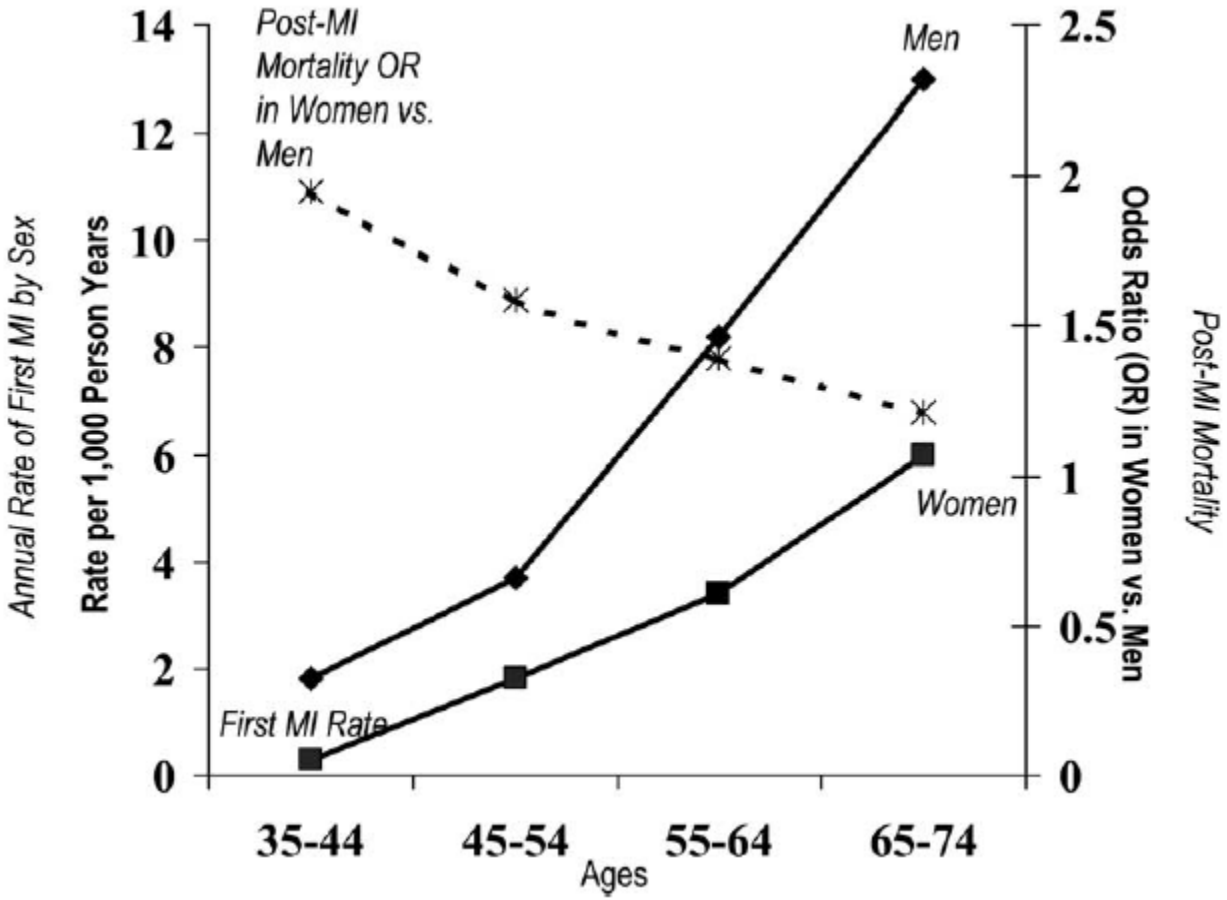


Frauen



Maas A. et al. European Heart Journal (2011) 32, 1362–1368

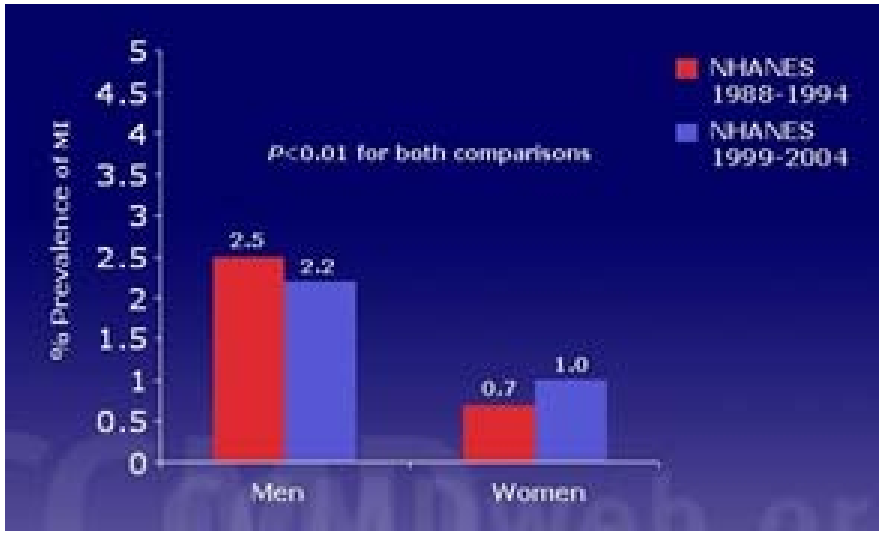
Todesrate nach Myokardinfarkt bei Männern und Frauen

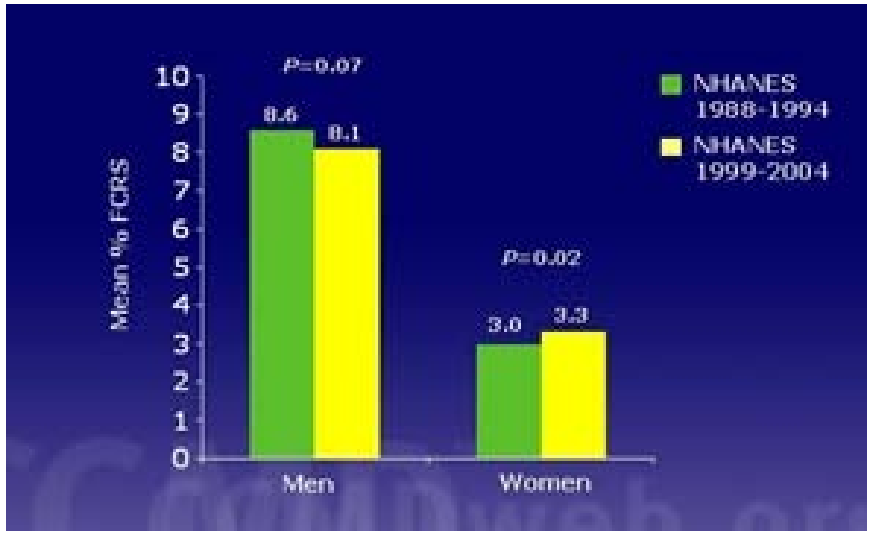


C. Noel Bairey Merz et al. J Am Coll Cardiol 2006;47:21S–9S

Geschlechtsspezifische Prävalenz des Myokard-infarktes und der Risikofaktorenkonstellation

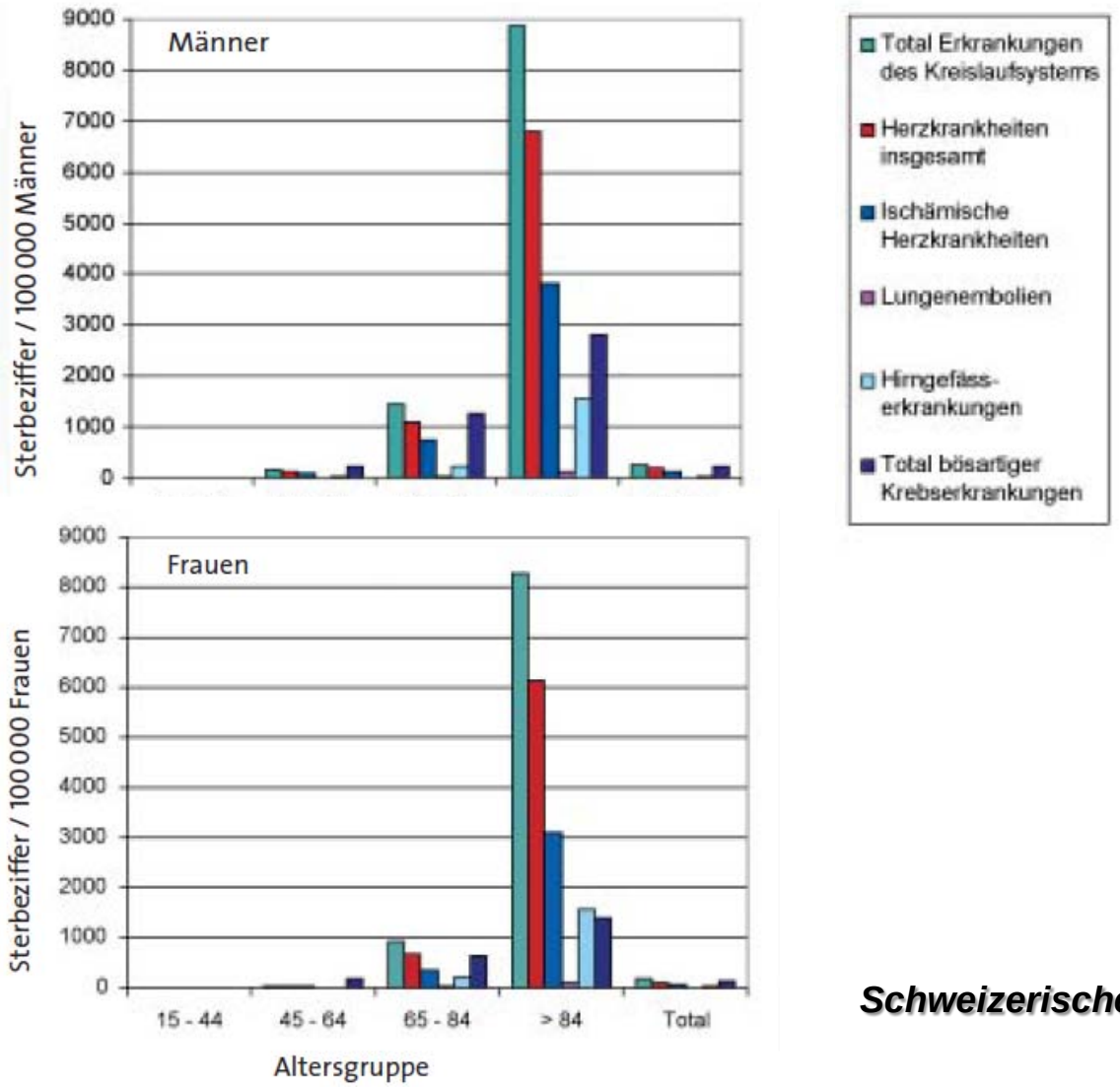
- In den USA ist die ischämische Kardiopathie Haupttodesursache der Frauen in allen Alterskategorien mit höheren jährlichen Todesraten verglichen mit Brustkrebs auch bei Frauen unter 35, 45, und 55 Jahren
- Deutlicher Anstieg der Anzahl plötzlicher Herztode und höherer Anteil an “out of hospital” Todesfällen als bei den Männern.





Towfighi A, Zheng L, Ovbiagele B. Sex-specific trends in midlife coronary heart disease risk and prevalence. Arch Intern Med 2009;169:1762–1766.

Herz-Kreislauf-Krankheiten sind Alterskrankheiten



Schweizerische Gesundheitsbefragung 2002. Bundesamt für Statistik, 2004.

Euro Heart Survey Programme

ESC Quality Assurance Programme to Improve Cardiac Care in Europe

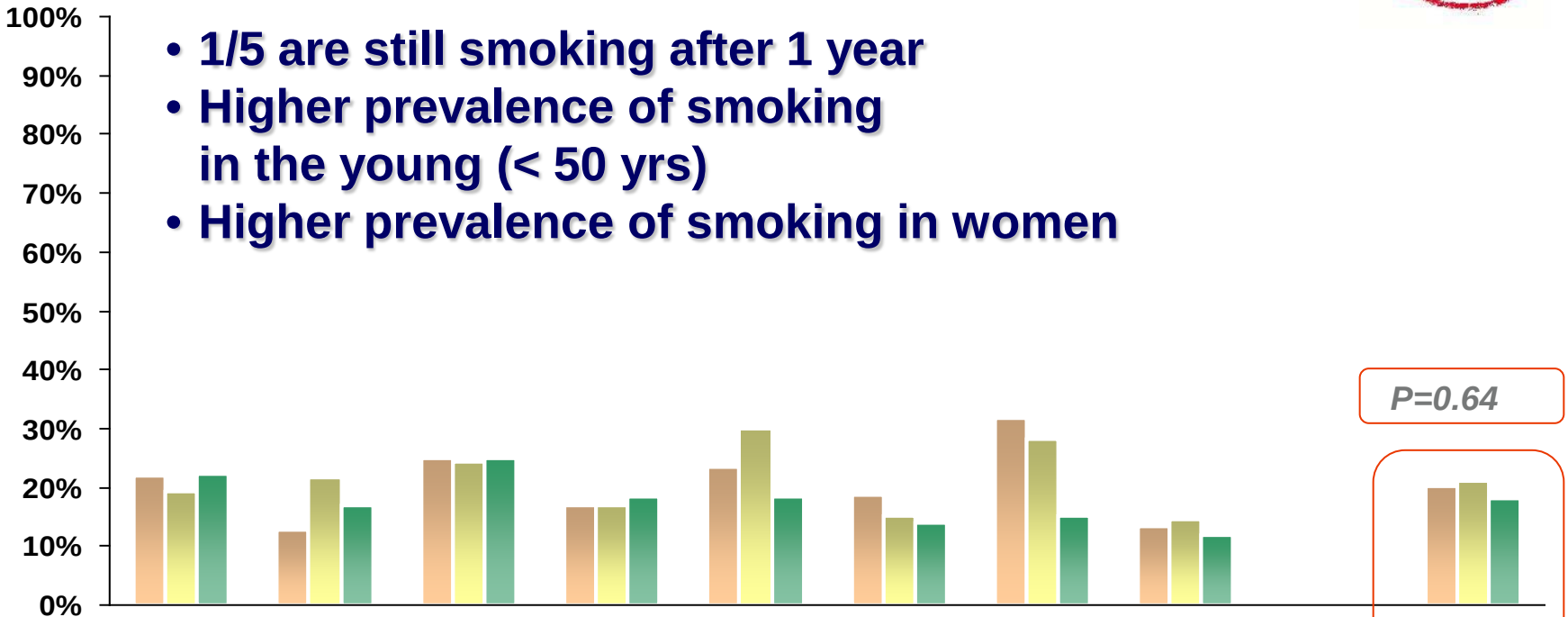
1994	First Joint Task Force Recommendations
1995-96	EUROASPIRE I Coronary patients in 9 countries
1998	Second Joint Task Force Recommendations
1999-2000	EUROASPIRE II Coronary patients in 15 countries Relatives of patients with premature CHD
2003	Third Joint Task Force Guidelines
2006/2007	EUROASPIRE III Coronary patients in 22 countries Relatives of patients with premature CHD Asymptomatic high risk individuals in primary care in 12 countries
2007	Fourth Joint Task Force Guidelines

www.escardio.org

Kotseva K et al., for the EUROASPIRE Study Group. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I,II, and III surveys in eight European countries. Lancet 2009;373:929–940.

Prevalence of Smoking

- **1/5 are still smoking after 1 year**
- **Higher prevalence of smoking in the young (< 50 yrs)**
- **Higher prevalence of smoking in women**



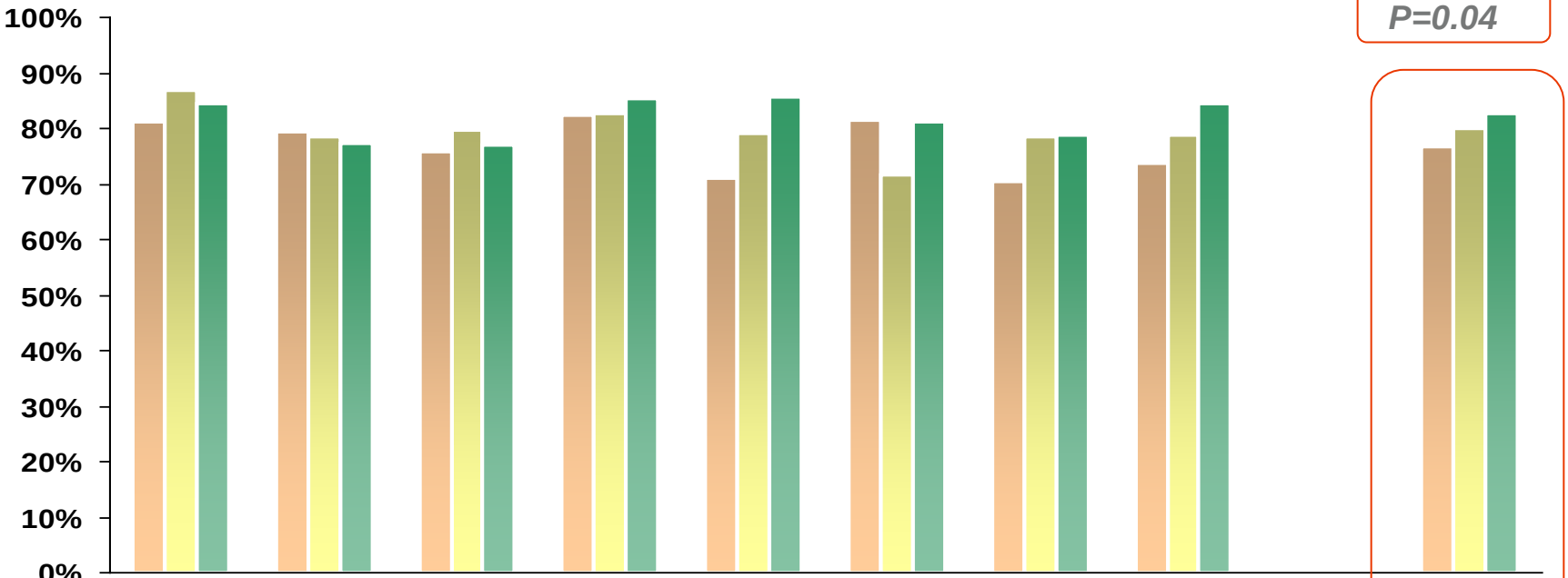
	Czech Rep.	Finland	France	Germany	Hungary	Italy	Nether-lands	Slovenia	ALL
Survey 1	22.0%	12.8%	25.0%	16.8%	23.3%	18.6%	31.8%	13.3%	20.3%
Survey 2	19.3%	21.6%	24.2%	16.8%	30.1%	15.1%	28.3%	14.6%	21.2%
Survey 3	22.2%	16.8%	24.8%	18.4%	18.3%	14.0%	15.1%	12.0%	18.2%

* Self-reported smoking or CO in breath > 10 ppm

S2 vs. S1 : P=0.83
S3 vs. S2 : P=0.37
S3 vs. S1 : P=0.48

Prevalence of Overweight (BMI ≥ 25 kg/m²)

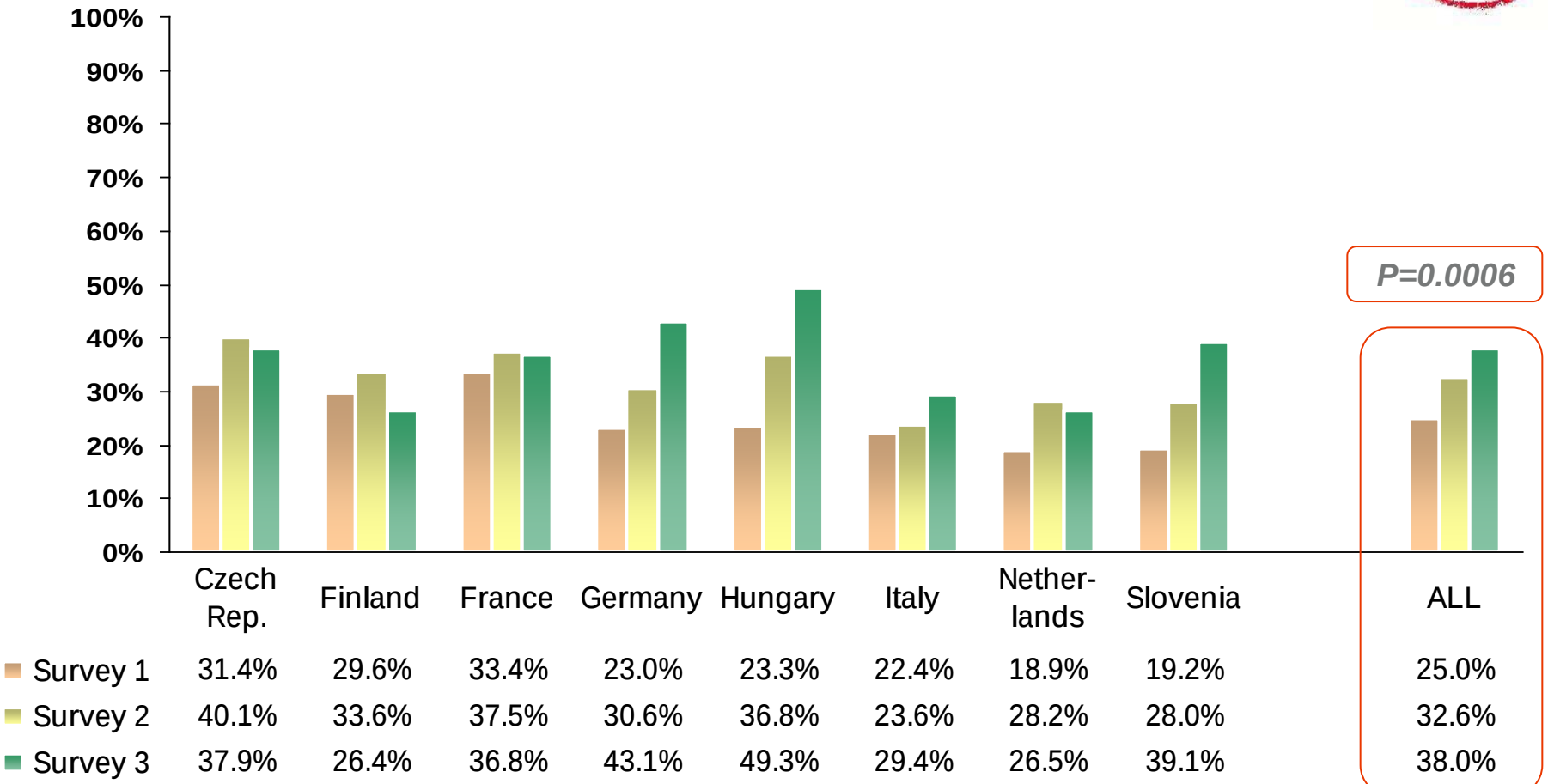
P=0.04



	Czech Rep.	Finland	France	Germany	Hungary	Italy	Nether-lands	Slovenia	ALL
Survey 1	81.3%	79.3%	75.8%	82.4%	71.0%	81.4%	70.5%	73.8%	76.8%
Survey 2	87.0%	78.4%	79.7%	82.7%	79.2%	71.7%	78.5%	78.7%	79.9%
Survey 3	84.6%	77.2%	77.1%	85.3%	85.6%	81.3%	78.9%	84.4%	82.7%

S2 vs. S1 : P=0.15
S3 vs. S2 : P=0.22
S3 vs. S1 : P=0.02

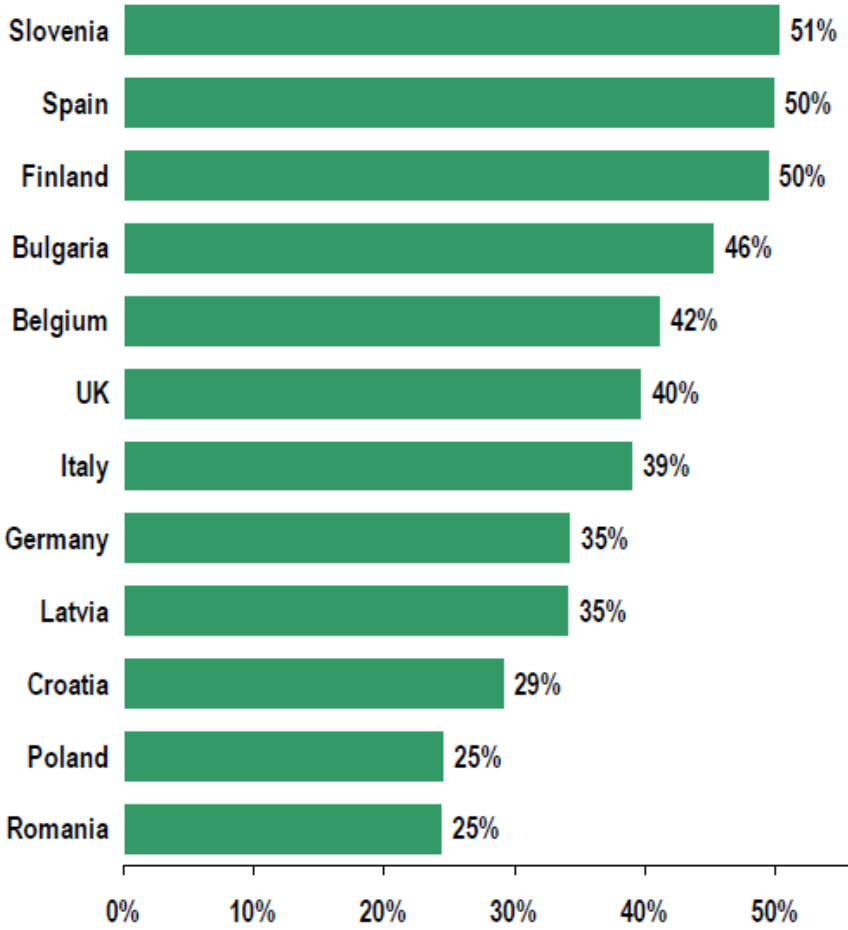
Prevalence of Overweight (BMI ≥ 30 kg/m²)



	Czech Rep.	Finland	France	Germany	Hungary	Italy	Nether-lands	Slovenia	ALL
Survey 1	31.4%	29.6%	33.4%	23.0%	23.3%	22.4%	18.9%	19.2%	25.0%
Survey 2	40.1%	33.6%	37.5%	30.6%	36.8%	23.6%	28.2%	28.0%	32.6%
Survey 3	37.9%	26.4%	36.8%	43.1%	49.3%	29.4%	26.5%	39.1%	38.0%

S2 vs. S1 : P=0.009
S3 vs. S2 : P=0.051
S3 vs. S1 : P=0.0002

Prävalenz von diagnostiziertem oder nicht diagnostiziertem Diabetes mellitus



Diagnosed or undiagnosed
All patients: 39%

Men 43% , Women 35%

Diagnosed (self-report)
All patients: 30%

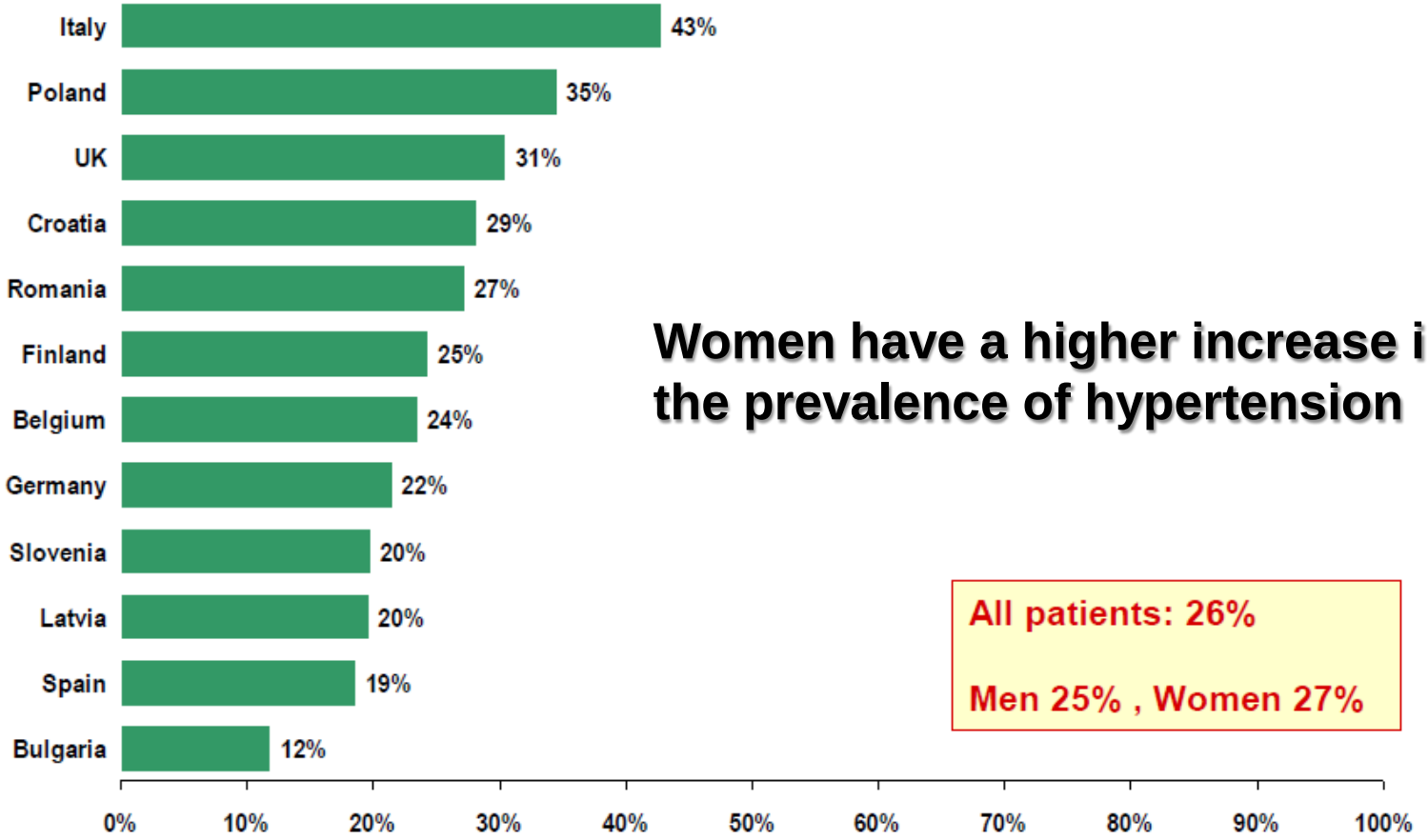
Men 33% , Women 28%

Undiagnosed among non-diabetics
All patients: 13%

Men 16% , Women 11%

* Self-reported diabetes or fasting plasma glucose ≥ 7.0 mmol/L

Therapeutische Kontrolle der arteriellen Hypertonie



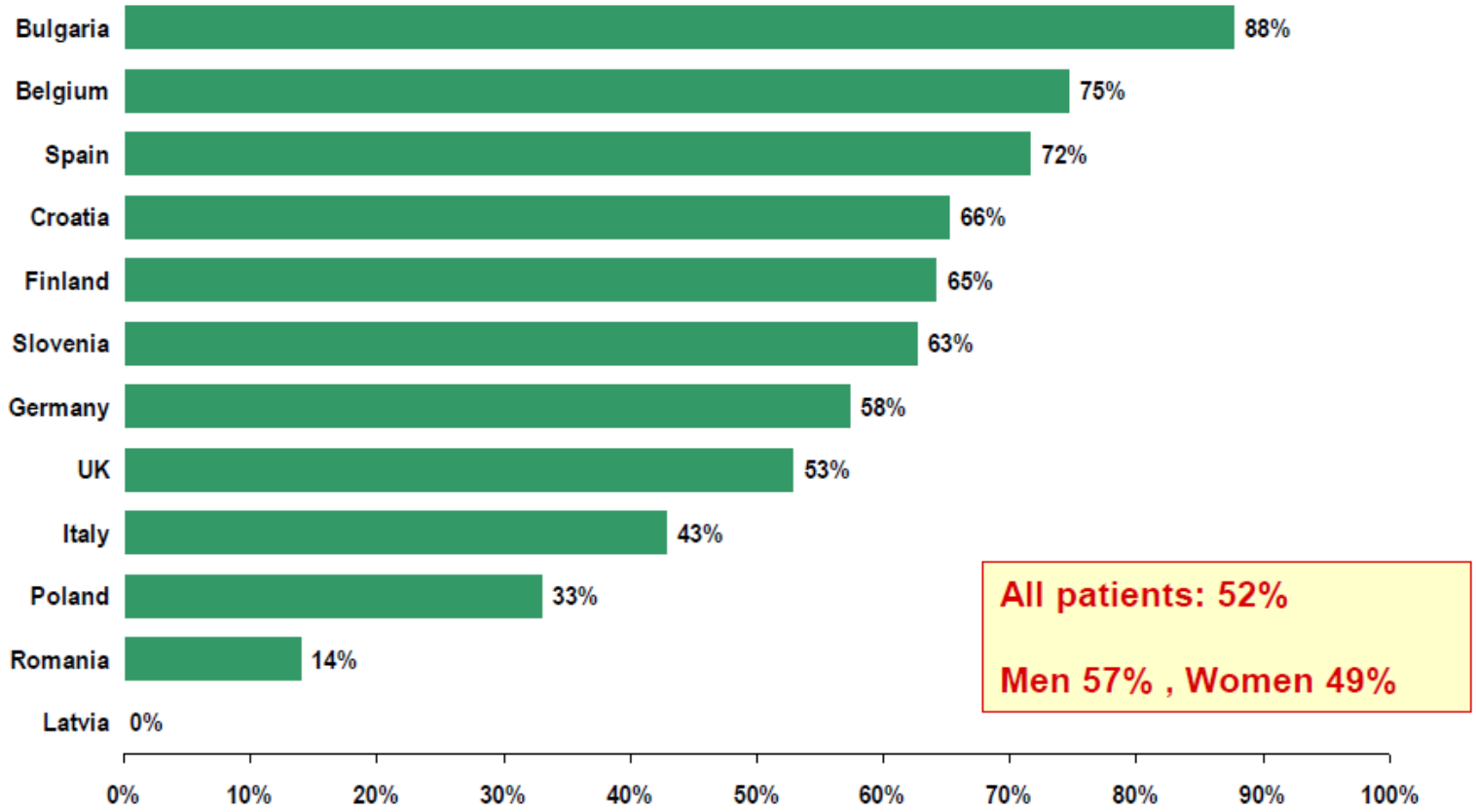
Women have a higher increase in the prevalence of hypertension

All patients: 26%

Men 25% , Women 27%

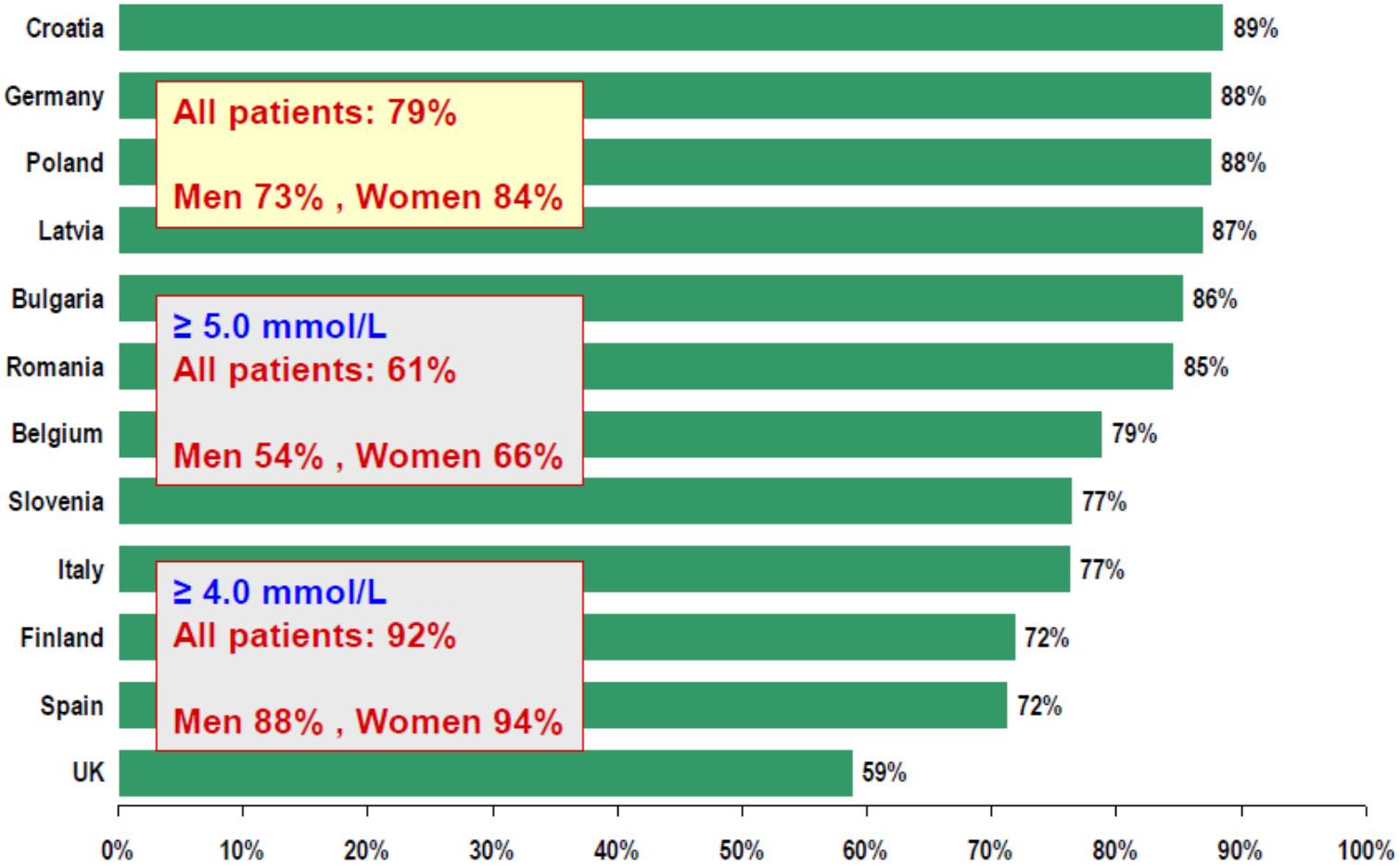
•SBP < 140 mmHg and DBP < 90 mmHg for non-diabetic patients and SBP < 130 mmHg and DBP < 80 mmHg for diabetics among patients using antihypertensive drugs

Unkenntnis über arterielle Hypertonie

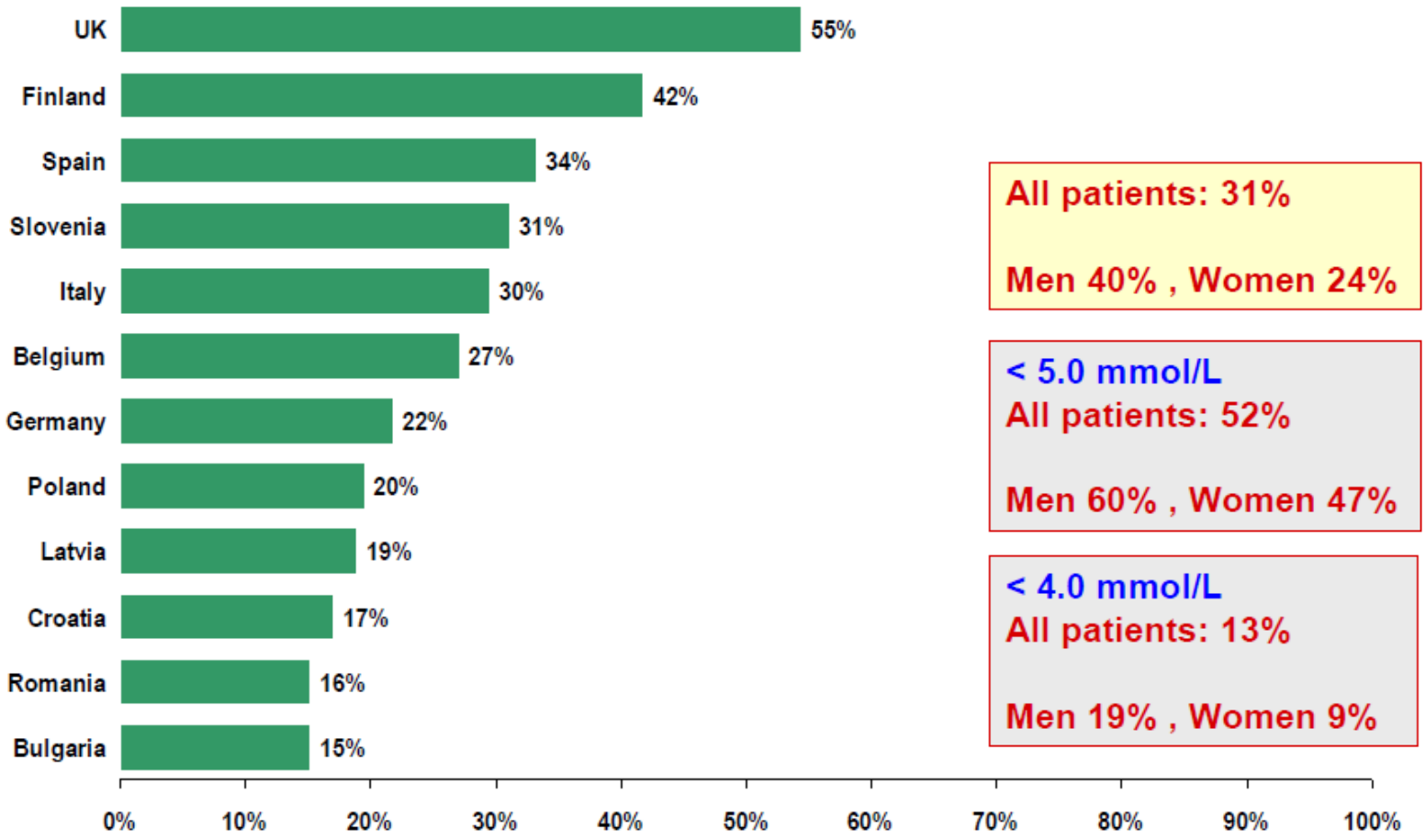


* Proportion of patients answering negatively to the question 'Have you ever been told by a health professional that you have high blood pressure?' among patients with 'measured hypertension' (SBP/DBP ≥ 140/90 mmHg for non-diabetic patients and SBP/DBP ≥ 130/80 mmHg diabetic patients)

Prävalenz der Hypercholesterinämie

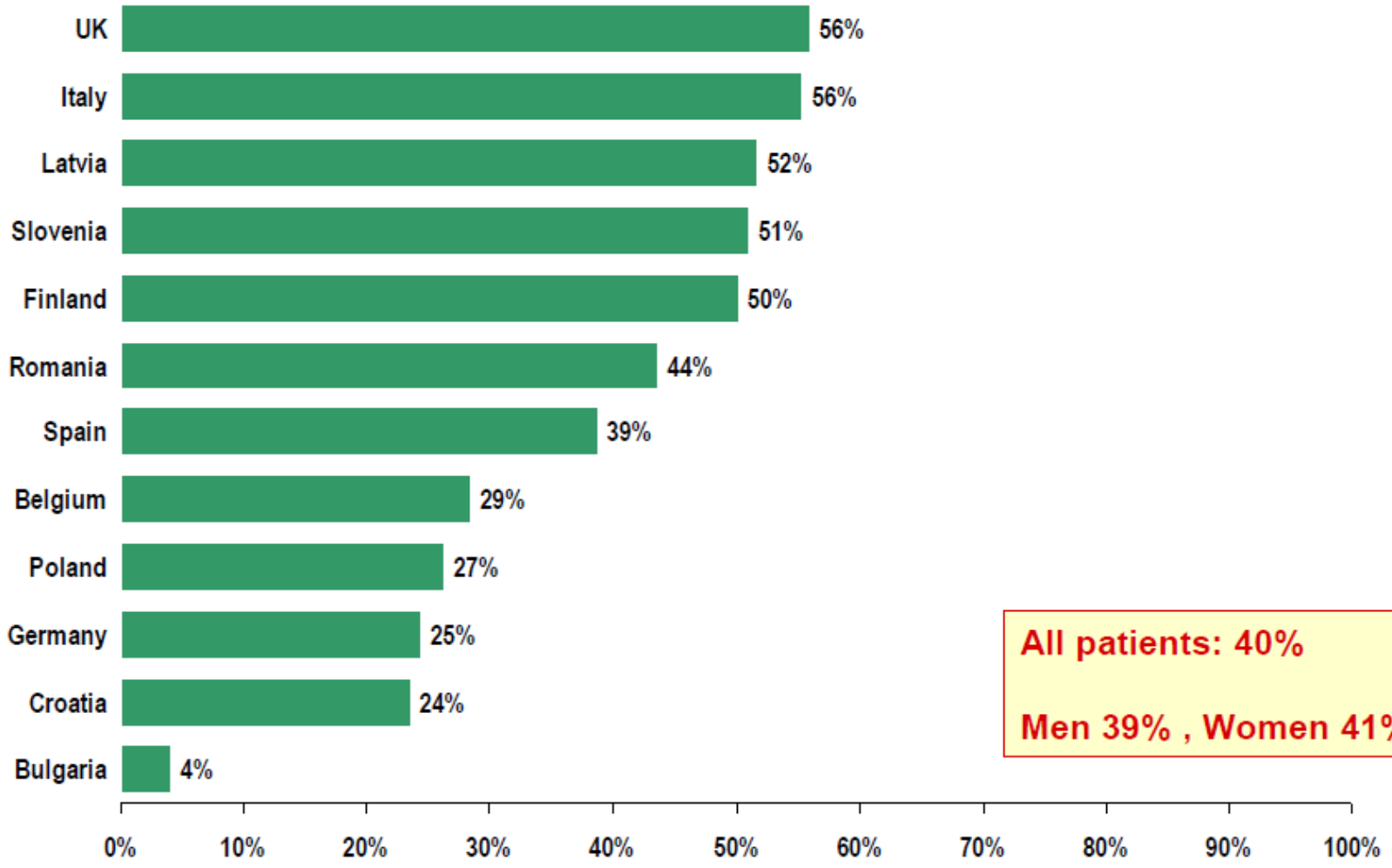


Kontrolle der Hypercholesterinämie



* Total cholesterol < 4.5 mmol/L among patients using lipid-lowering drugs

Verschreibung von Statinen



All patients: 40%

Men 39% , Women 41%

Kardiovaskuläres Risikofaktorenprofil der Frauen

- Traditional risk conditions
  - Higher prevalence in postmenopausal women
  - More frequent clustering
  - When present, higher level (e.g., if hypertensive, higher BP, higher LDL, and so on)
  - Older age
  - More frequent vasculitis (e.g., lupus, temporal arteritis, Takayasu's, and so on)
- Conditions unique to women
  - Peripartum
    - Hypertensive disorders of pregnancy
    - Gestational diabetes
    - Delivering a thin baby
    - Coronary or aortic root dissection
  - Polycystic ovarian syndrome
  - Hypoestrogenemia of hypothalamic origin
  - Hormone replacement therapy
  - Others

Pepine CJ et al. J Am Coll Cardiol 2006;47:30S–5S

Postmenopausale Hormontherapie und das Risiko kardiovaskulärer Erkrankungen (Primärprävention)

TABLE 1 Relative Risk for Major Coronary Artery Disease Among Current Postmenopausal Hormone Users and Nonusers (Nurses' Health Study, 1976–1996)

Hormone Use	Person-Years of Follow-up	Cases (n)	Relative Risk (95% Confidence Interval)
Never	358,125	662	1.0
Past	185,497	337	0.82 (0.72–0.94)
Current (yr*)	265,203	259	0.61 (0.52–0.71)
<1	20,091	9	0.40 (0.21–0.77)
1–1.9	19,155	9	0.41 (0.21–0.80)
2–4.9	78,928	60	0.53 (0.41–0.70)
5–9.9	77,435	74	0.58 (0.45–0.74)
≥10	69,594	107	0.74 (0.59–0.91)

Grodstein F et al. A prospective, observational study of postmenopausal hormone therapy and primary prevention of cardiovascular disease. Ann Intern Med 2000;133:933–941

Effekt der Oestrogen-Ersatz Therapie auf die Progression der koronaren Herzkrankheit

Herrington D et al.
NEJM 2000;343:522-9

Subjects and Variable	Estrogen (N=79)	Estrogen plus MPA (N=85)	Placebo (N=84)	P Value: Estrogen vs. Placebo	P Value: Estrogen plus MPA vs. Placebo
All subjects					
Minimal coronary-artery diameter (mm)					
Base line	1.98±0.03	1.91±0.04	1.98±0.04	0.93	0.17
Follow-up	1.91±0.04	1.80±0.05	1.88±0.04	0.64	0.22
Adjusted follow-up†	1.87±0.02	1.84±0.02	1.87±0.02	0.81	0.23
Adjusted change‡	−0.09±0.02	−0.12±0.02	−0.09±0.02	0.97	0.38
Stenosis (%)					
Base line	28.53±0.84	29.65±0.90	27.80±0.84	0.56	0.13
Follow-up	31.77±0.97	33.86±1.55	31.48±1.23	0.88	0.19
Adjusted follow-up†	32.72±0.93	33.68±0.93	32.44±0.94	0.81	0.27
Adjusted change‡	4.01±0.92	4.75±0.92	4.11±0.93	0.93	0.56
Subjects who complied with treatment§					
Minimal coronary-artery diameter (mm)					
Base line	1.99±0.04	1.87±0.05	1.98±0.04	0.88	0.07
Follow-up	1.91±0.04	1.77±0.06	1.88±0.04	0.72	0.12
Adjusted follow-up†	1.85±0.03	1.84±0.03	1.85±0.03	0.99	0.63
Adjusted change‡	−0.11±0.03	−0.11±0.03	−0.10±0.02	0.95	0.86
Stenosis (%)					
Base line	28.60±0.84	30.49±1.06	27.63±0.92	0.49	0.03
Follow-up†	31.83±1.06	33.96±1.81	31.02±1.23	0.70	0.14
Adjusted follow-up†	33.19±1.03	33.10±0.95	32.63±0.92	0.65	0.68
Adjusted change‡	4.38±1.03	4.02±0.95	4.23±0.92	0.90	0.85

Postmenopausale Hormontherapie: labiles Risiko – Benefit Gleichgewicht

Benefit:

- Kardiovaskuläre Erkrankungen
- Osteoporose
- Peri-, postmenopausale Symptomatik

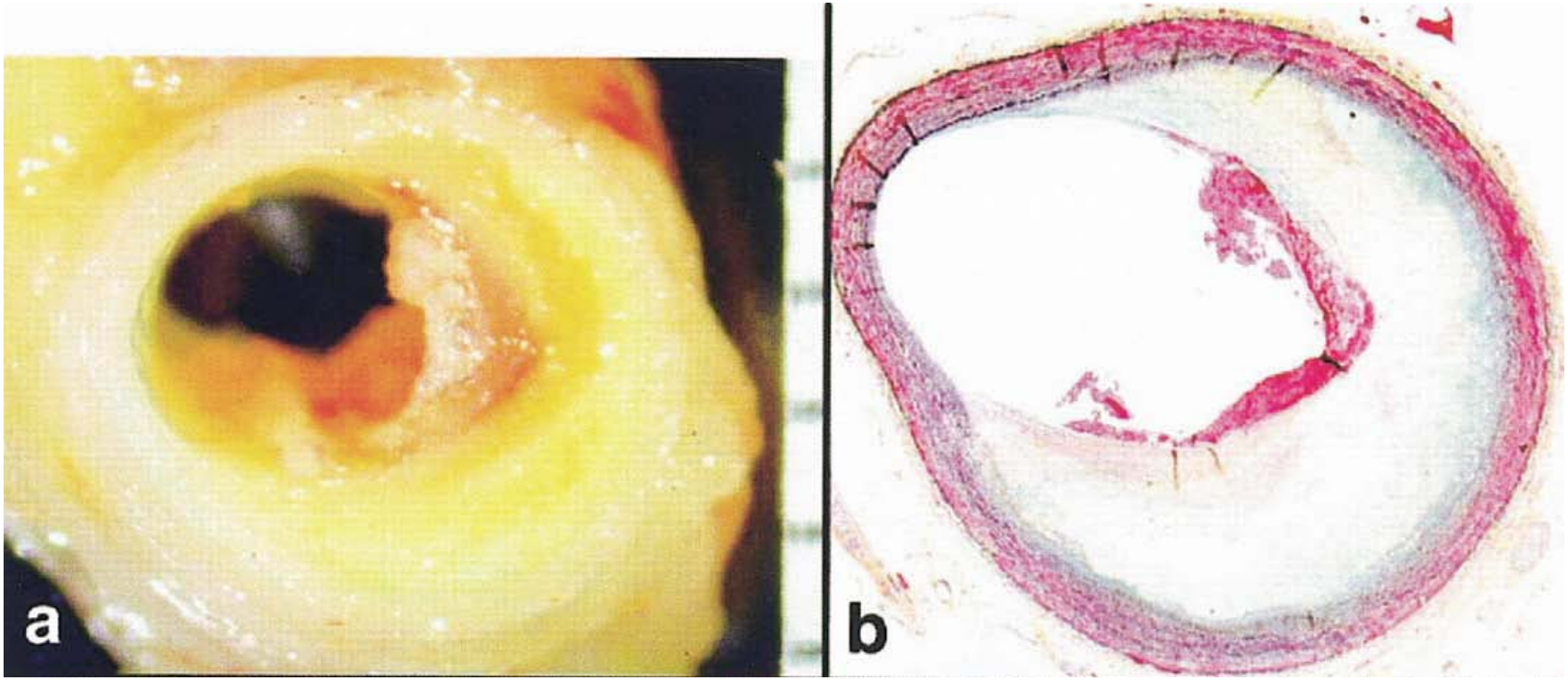
Risiko:

- Brust- , Gebärmutter-, Colo-rektal-Carcinom
- Thrombose (!)

Struktur und Funktion der Koronarien bei den Frauen

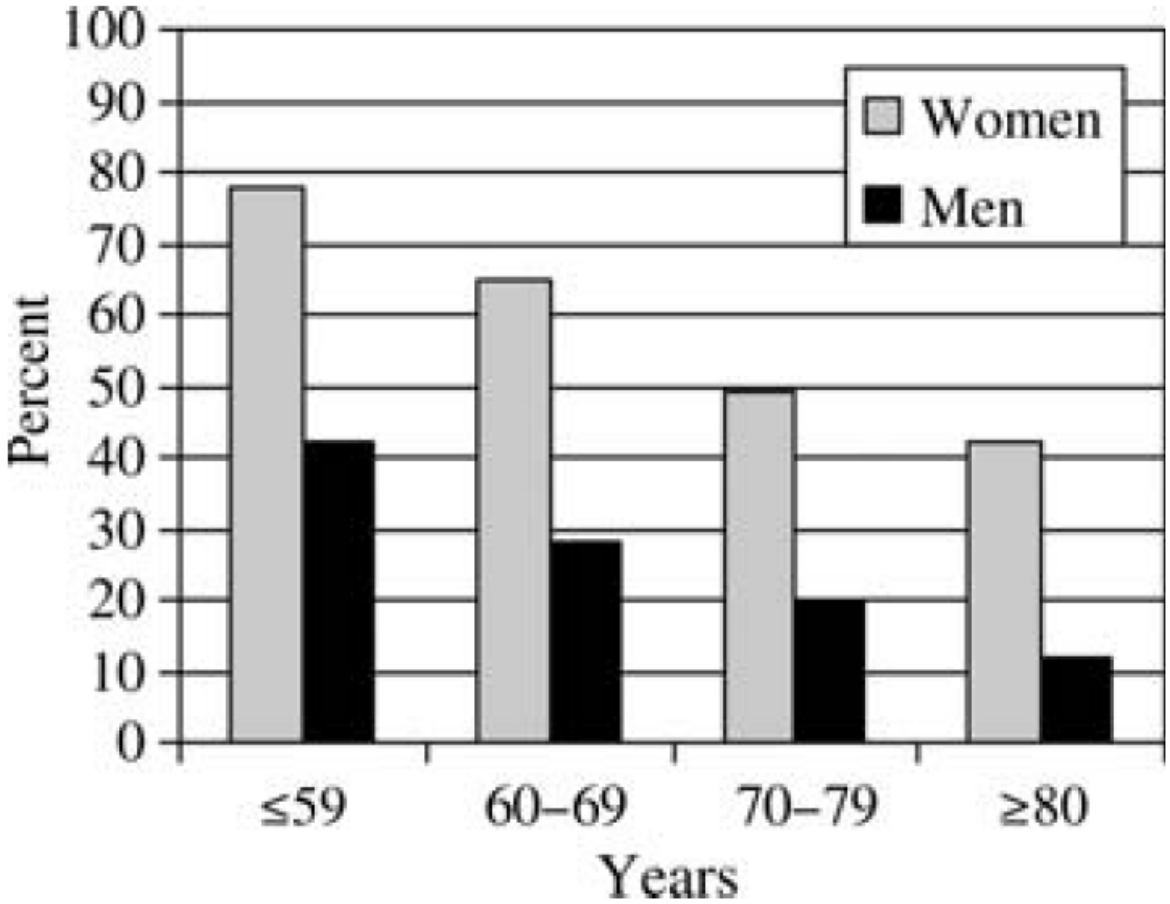
- Structural findings
  - Macrovessels and microvessels
    - Smaller size
    - Increased stiffness (fibrosis, remodeling, and so on)
    - More diffuse disease, erosion >rupture
    - Microemboli, rarefaction (drop out), disarray, and so on
- Functional findings
  - Macro- and microvessels
    - Endothelial dysfunction
    - Smooth muscle dysfunction (Raynaud's, migraine, CAS)
    - Inflammation
      - Plasma markers
      - Vasculitis (Takayasu's, rheumatoid, SLE, CNSV, giant cell, and so on)

Plaque erosion: typische Manifestation der Koronaropathie bei jüngeren Frauen



C. Noel Bairey Merz et al. J Am Coll Cardiol 2006;47:21S–9S

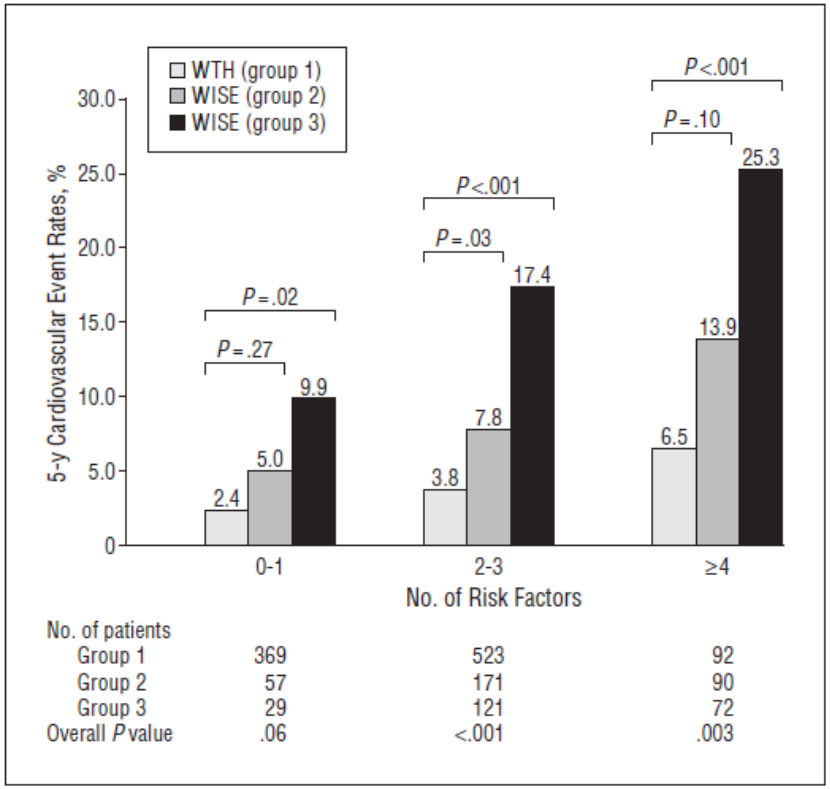
Anteil der Patienten mit „normalem“ Koronarbefund

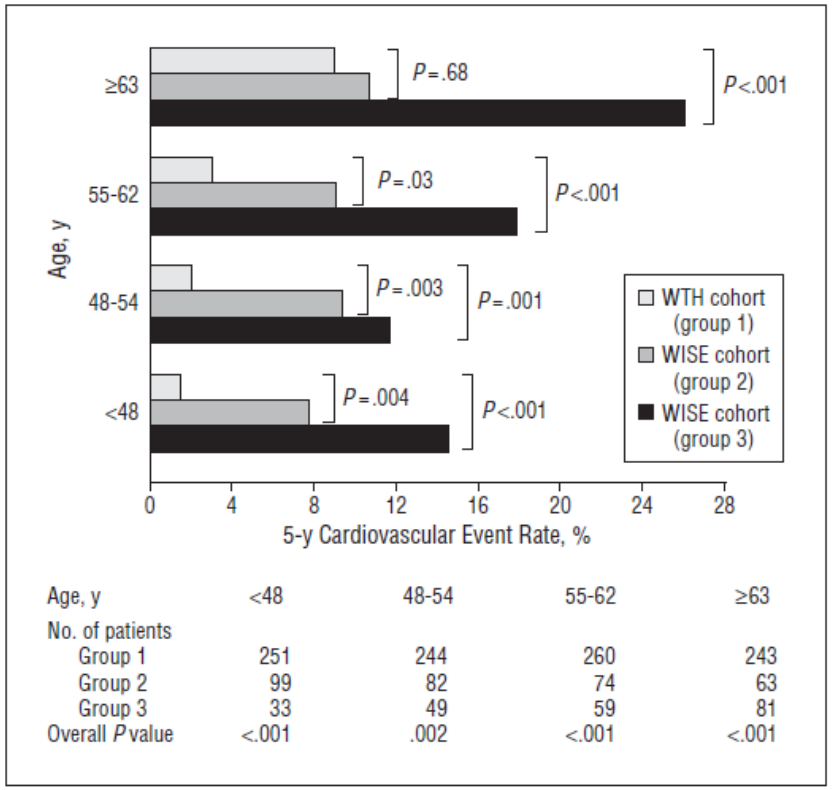


Johnston N et al. European Heart Journal (2011) 32, 1331–1336

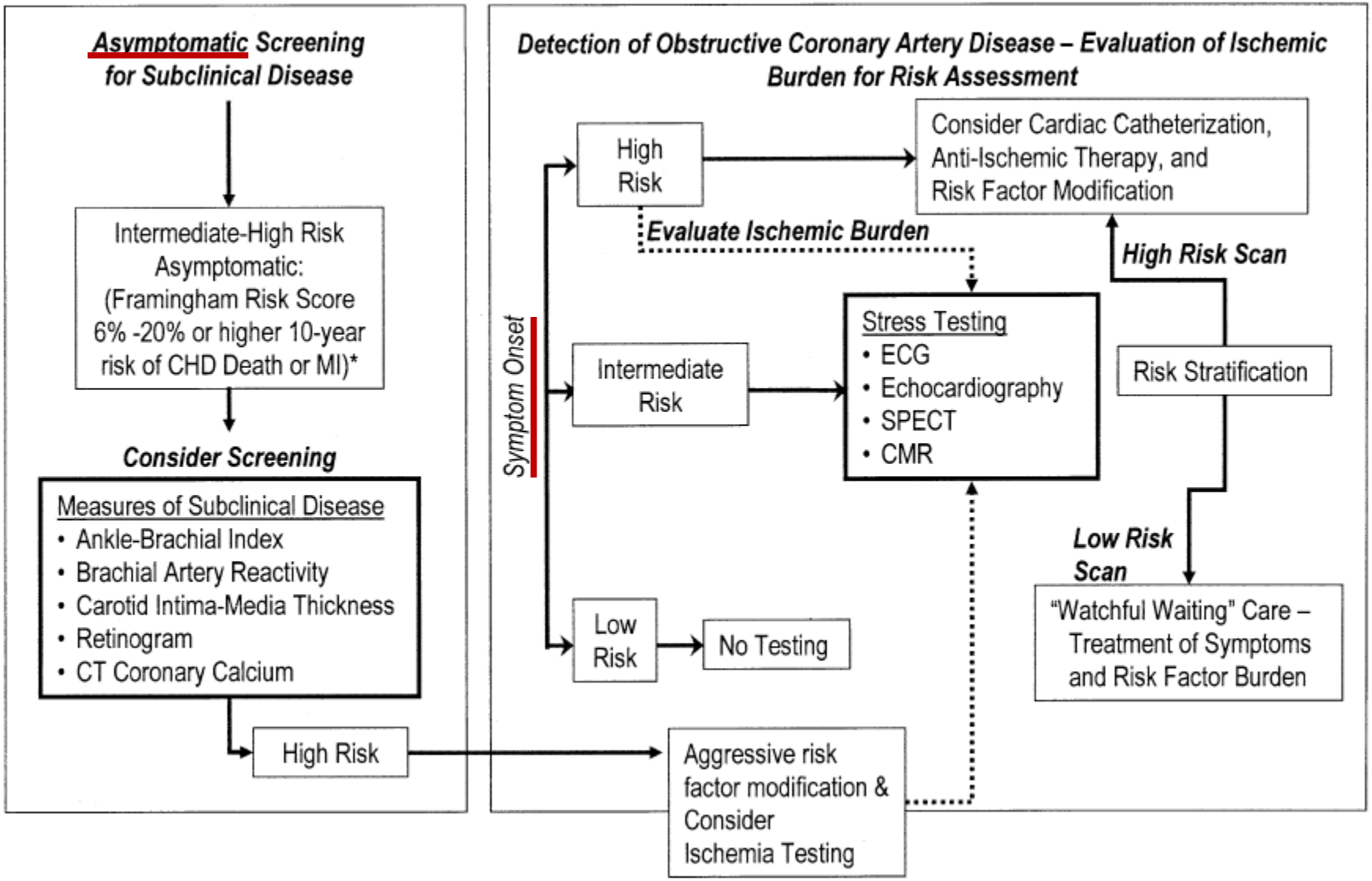
Frauen haben einen höheren Anteil an ‚nicht-obstruktiver' koronarer Herzkrankheit

1. Asymptomatic women vs.
2. symptomatic women with normal coronary arteries (0% stenoses) vs.
3. nonobstructive coronary artery disease (stenosis in any coronary artery of 1%-49%)



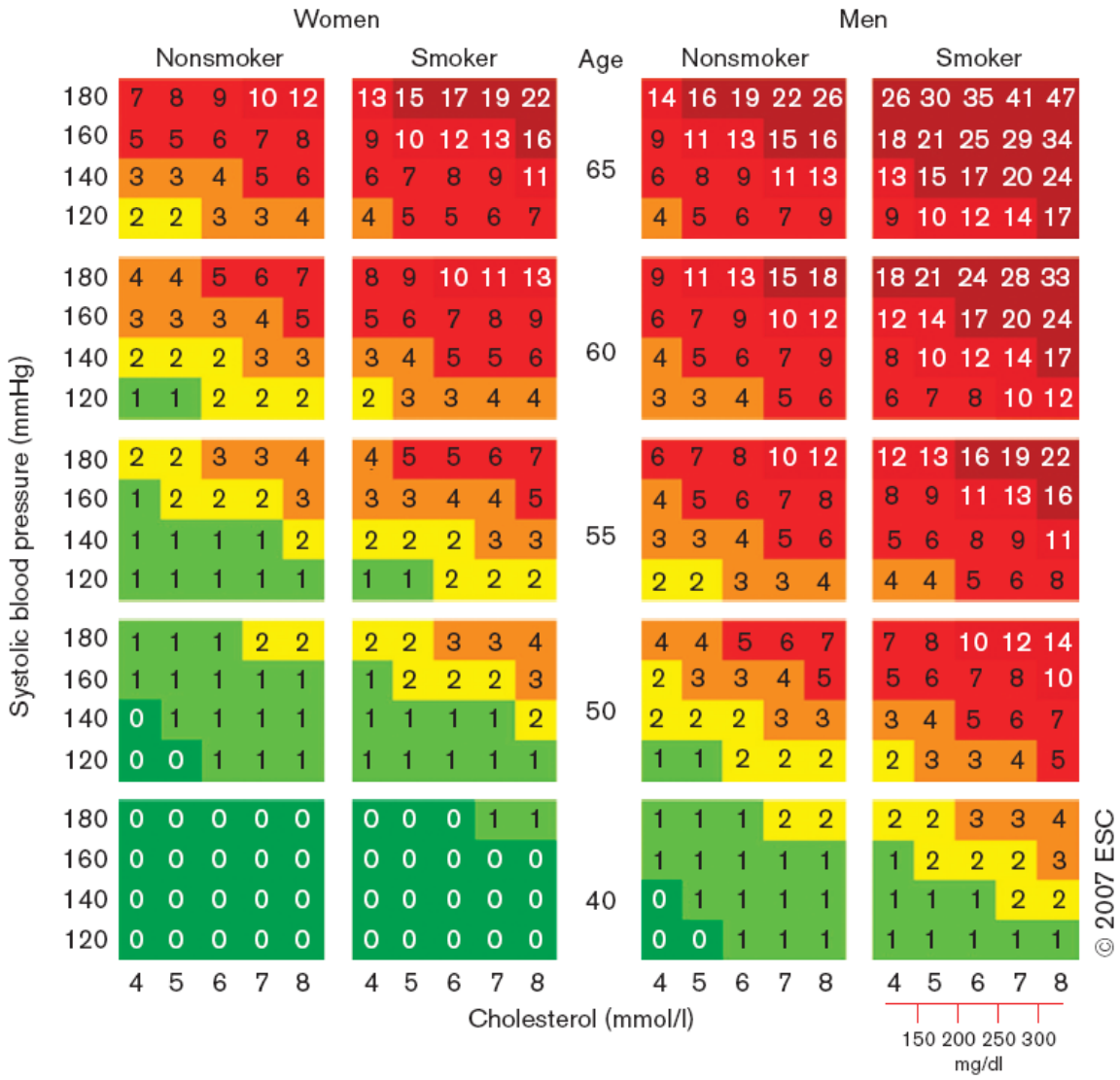


Martha Gulati et al. Arch Intern Med. 2009;169(9):843-850



Shaw L. J Am Coll Cardiol 2006;47:4S–20S

Risikostratifizierung



Nicht berücksichtigt:

- **Diabetes**
- **Zentrale Adipositas**
- **Bewegungsmangel**
- **Familiäre Belastung**
- **Psychosoziales Umfeld**
- **HDL-Cholesterin, TG, Lipoprotein(a), high-sensitivity CRP**

SCORE

- 15% and over
- 10–14%
- 5–9%
- 3–4%
- 2%
- 1%
- <1%

10-year risk of fatal CVD in populations at high CVD risk

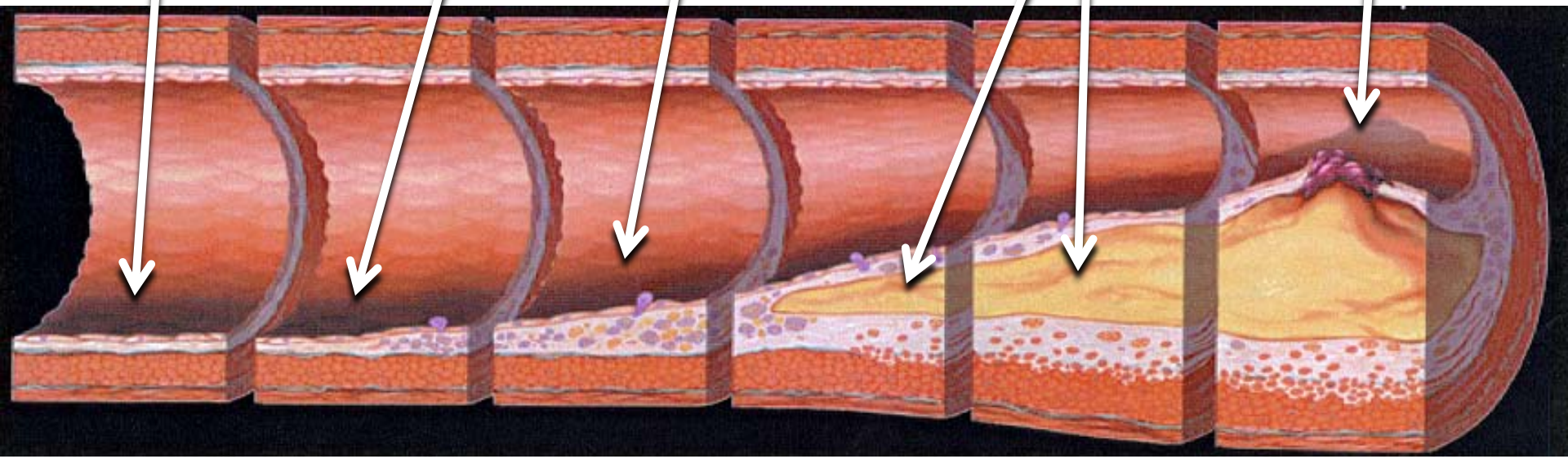
Endotheliale Dysfunction

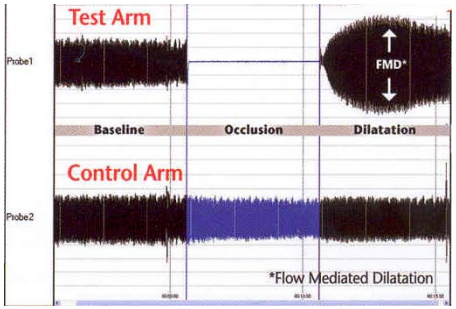
Erhöhte Steifheit der Arterien

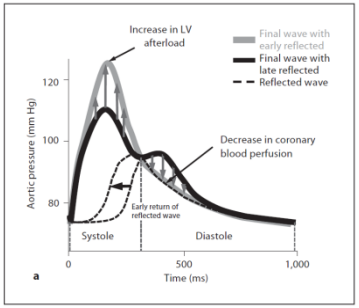
Verdickung der Intima Media

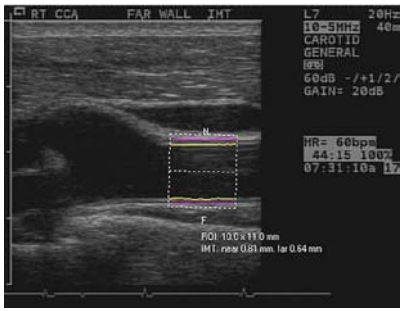
Calcium-Ablagerung

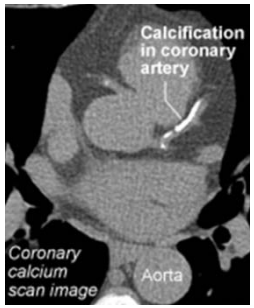
Symptome



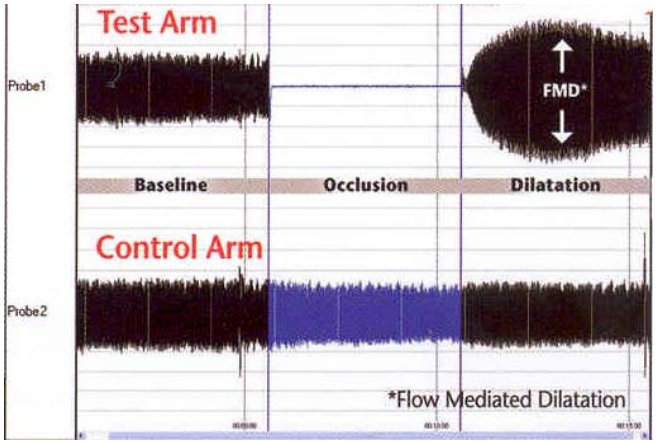






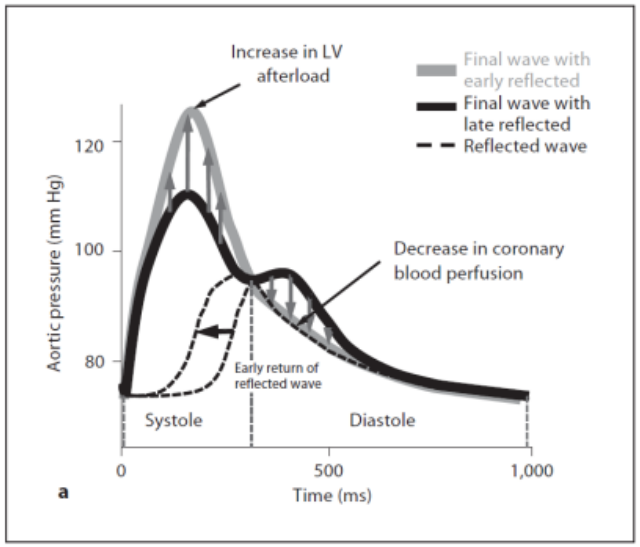


Frühe Veränderungen der Gefässfunktion



Endo-PAT (periperal arterial tone)

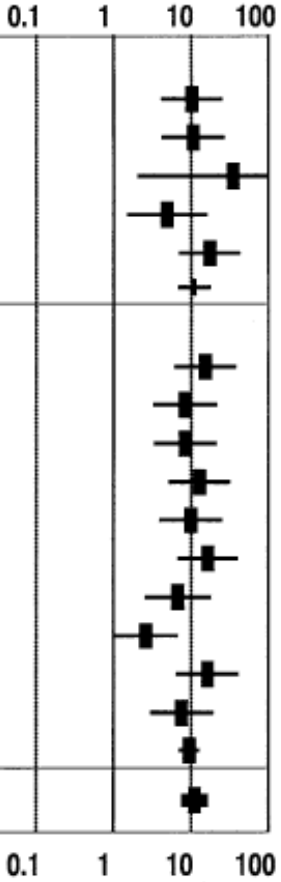
Endotheliale Dysfunktion



Erhöhte Arterien-steifheit

Risiko für kardiovaskuläre Ereignisse bei gestörter endothelialer Funktion

		Relative Risk	95% CI		p Value
Coronary Circulation (5)					
Halcox	2002	10.25	4.16	25.27	<0.0001
Schachinger	2000	10.66	4.19	27.11	<0.0001
Suwaidi	2000	35.07	2.02	>100.00	<0.0001
Targonski	2003	4.92	1.49	16.22	0.003
Von Mering	2004	17.48	7.12	42.89	<0.0001
Summary Relative Risk (5)		**11.07**	**6.89**	**17.79**	**<0.000**
Peripheral Circulation (10)					
Brevetti	2003	15.28	6.14	38.05	<0.0001
Chan	2003	8.42	3.25	21.85	<0.0001
Fichtlscherer	2003	8.43	3.31	21.46	<0.0001
Gokce	2002	12.92	5.21	32.05	<0.0001
Gokce	2003	9.96	3.96	25.05	<0.0001
Heitzer	2001	16.51	6.80	40.13	<0.0001
Hyrniewicz	2003	6.78	2.55	18.06	<0.0001
Murakami	2003	2.60	0.99	6.82	0.043
Neunteufl	2000	16.35	6.45	41.42	<0.0001
Perticone	2001	7.60	2.99	19.37	<0.0001
Summary Relative Risk (10)		**9.55**	**7.113**	**12.82**	**<0.0001**
Combined (15)		**9.95**	**7.75**	**12.78**	**<0.0001**



0.01 0.1 1 10 100

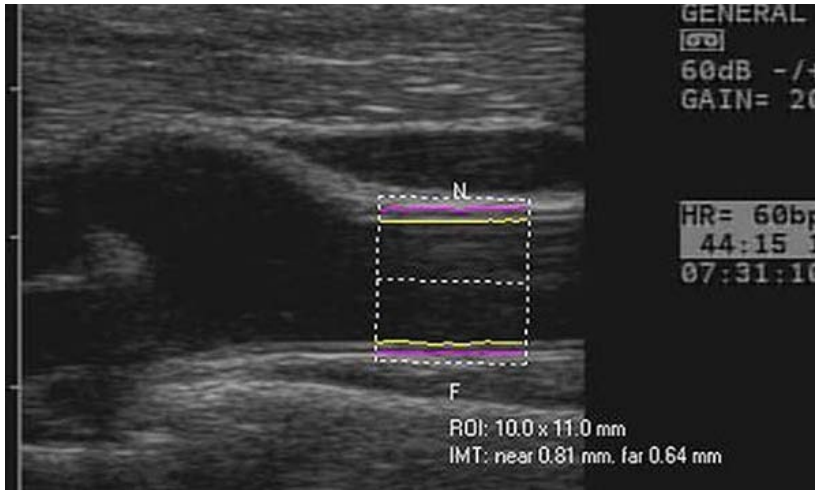
Decreased Risk ← → Increased Risk

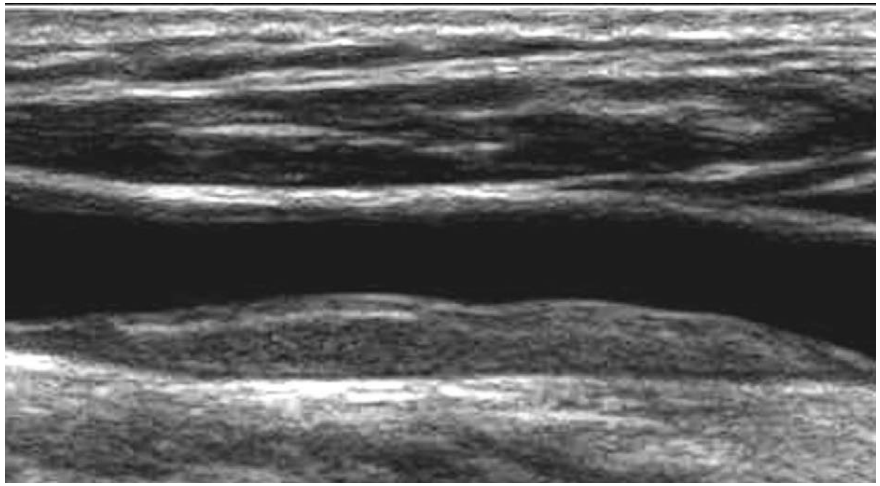
Merz B et al. J Am Coll Cardiol 2006;47:21S–9S

Veränderungen an der Carotis cummunis

Intima Media Dicke (IMT):

Normal: Altersdekade + 0.2
(z.B. 56-jährig: 6. Dekade
0.6 + 0.2 < 0.8 = normal)

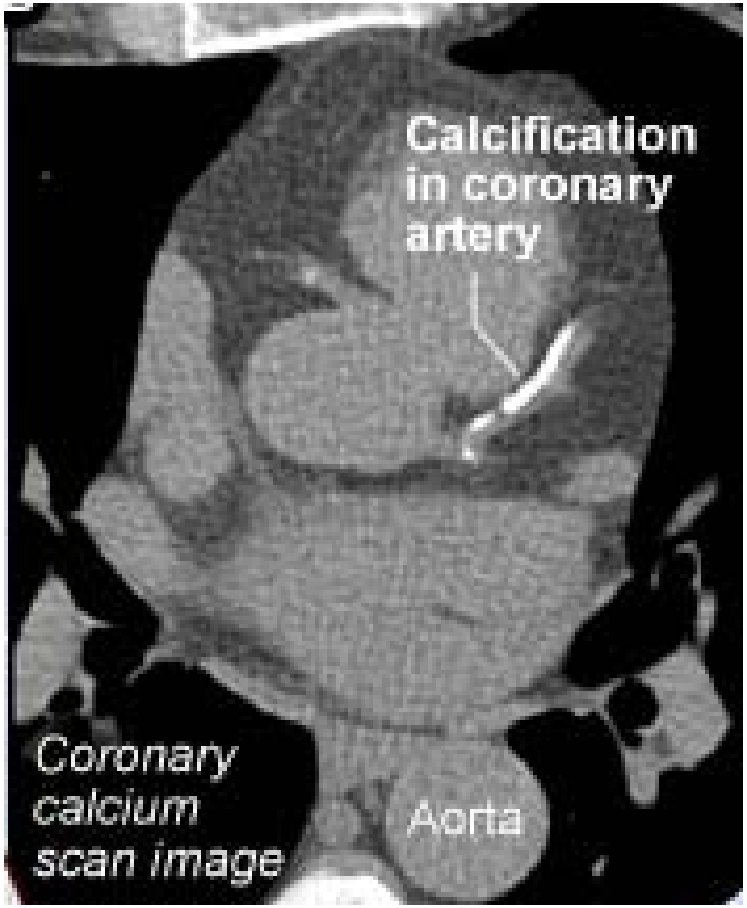




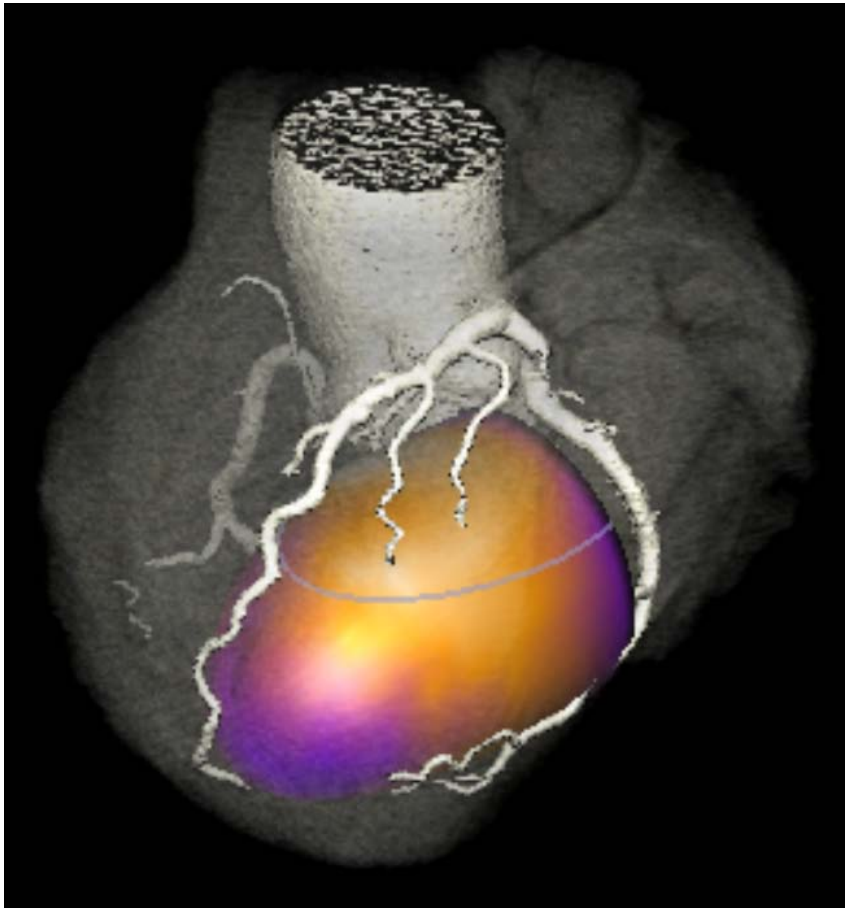
Screening:

Männer: 45 – 75 years
Frauen: 55 – 75 years

Koronar-Kalk Score

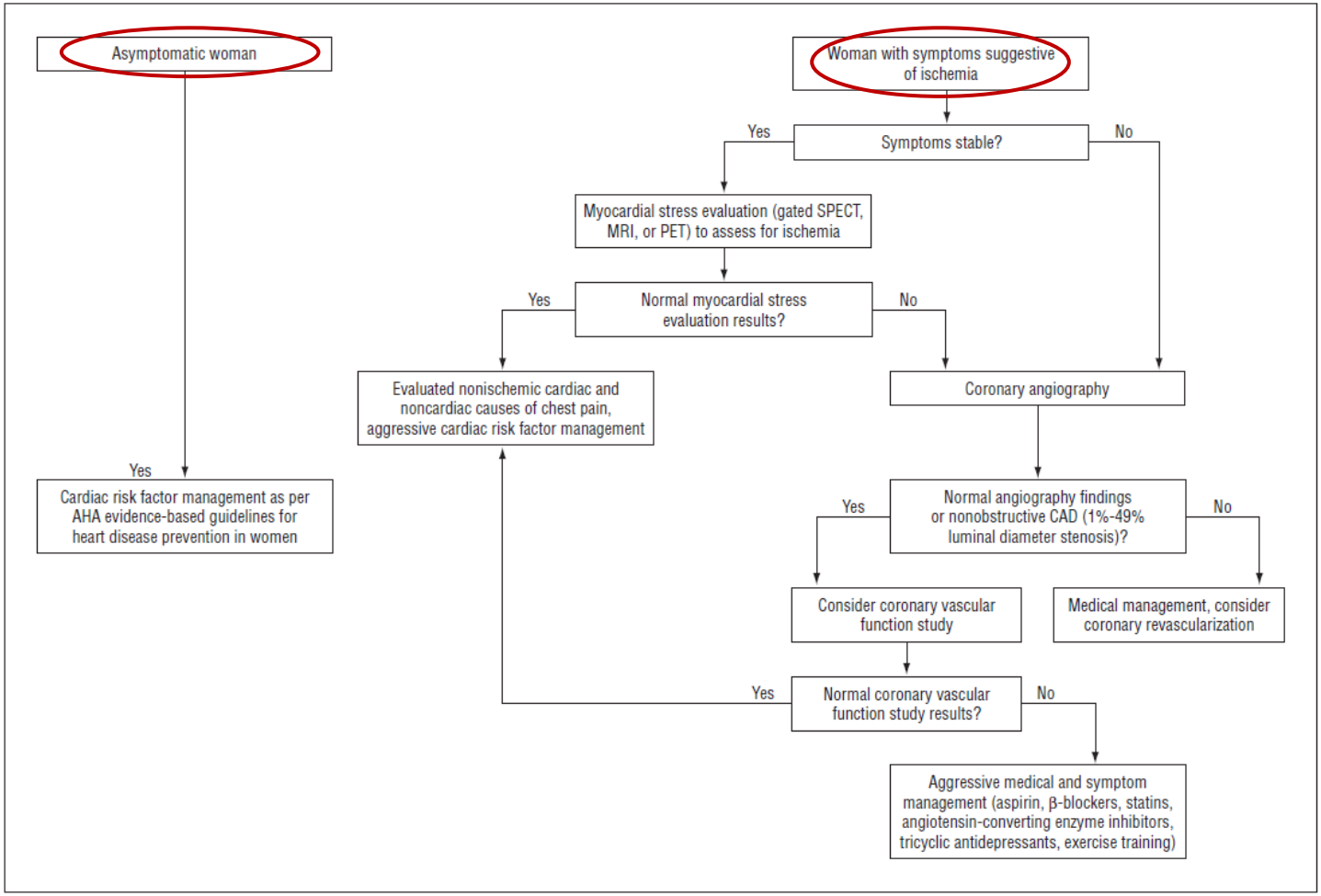


Darstellung von Koronarkalk



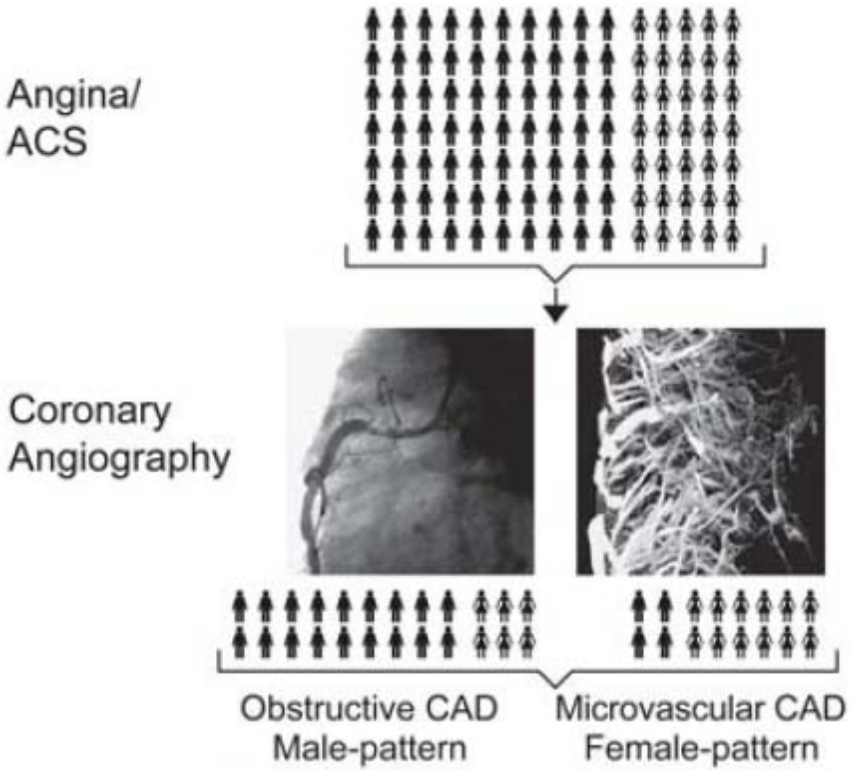
Hybrid-Herz-CT

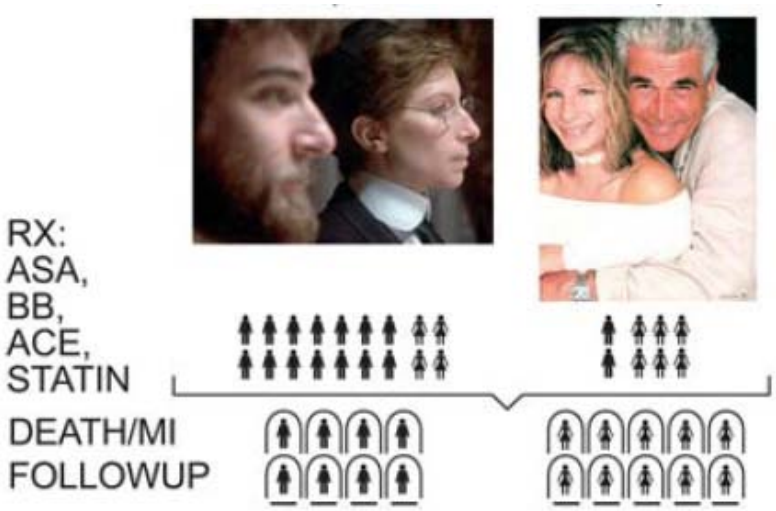
Behandlung der ‚nicht-obstruktiven' koronaren Herzkrankheit



Martha Gulati et al. Arch Intern Med. 2009;169(9):843-850

Das „Yentl-Syndrom“





Take home messages

- Die koronare Herzkrankheit nimmt bei Frauen an Bedeutung zu und der Verlauf ist „maligner“ als bei Männern
  - Optimale Erfassung der Risikofaktoren, insbesondere nach der Menopause ist wichtig
  - frauenspezifische (peripartale) Risikokonstellationen sind zu berücksichtigen
  - „aggressive“ Kontrolle der Risikofaktoren
  - Lebensstilmodifikation und optimale medikamentöse Sekundärprävention unbedingt notwendig bei „Angina pectoris“ und nicht-obstruktiver Koronaropathie
  - Funktionelle und bildgebende Risikostratifizierung bei noch asymptomatischen Patientinnen im „mittleren“ Risikobereich empfohlen

www.kardiorehab.insel.ch

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

Kardiovaskuläre Prävention und Rehabilitation

Über uns | Ambulante Rehabilitation | Spezial-sprechstunden | Sportkardiologie | Forschung / Research | Fort-, Aus- und Weiterbildung

- Risikoabschätzung
- Lipid-Sprechstunde
- Fachstelle Rauchen
- Ernährungsberatung
- Psychologische Beratung
- Psychokardiologie
- Stosswellentherapie

www.insel.ch > Kardiale Rehabilitation > Spezial-sprechstunden > Risikoabschätzung

Sprechstunde für kardiovaskuläre Risikofaktoren

Diese Sprechstunde richtet sich an Personen, welche eine Beratung oder Abklärung ihres Risikos für eine zukünftige Herz- oder Gefässerkrankung wünschen (Check-up) oder an Patienten mit einer bekannten Herz-Kreislauferkrankung, deren kardiovaskuläre Risikofaktoren noch ungenügend eingestellt sind.