Koronare Herzkrankheit –

Wann konservativ - wann interventionell?

Volker Schächinger
Med. Klinik I – Kardiologie, Angiologie, Intensivmedizin

Herz-Thorax Zentrum Fulda

Koronare Herzkrankheit
- Wann konservativ, wann interventionell?

- **Indikation zur Koronarangiographie?**
  - ESC-Leitlinie Stabile KHK
- **Indikation zur PCI bei angiographischen Stenosen**
  - Courage / BARI-2D
  - Druckdrahtmessung (FFR)
- **Aktuelle Entwicklungen bei der PCI**
  - Antiaggregation
  - Bioabsorbierbare Scaffolds

European Heart Journal (2013) 34, 2949–3003
doi:10.1093/eurheartj/eht296

ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

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

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

ESC Committee for Practice Guidelines (CPG): Jose Luis Zamorano (Chairperson) (Spain), Stephan Achenbach (Germany), Helmut Baumgartner (Germany), Jeroen J. Bax (Netherlands), Héctor Bueno (Spain), Veronica Dean (France), Christi Deaton (UK), Çetin Erol (Turkey), Robert Fagard (Belgium), Roberto Ferrari (Italy), David Hasdai (Israel), Arno W. Hoes (Netherlands), Paulus Kirchhof (Germany UK), Juhani Knuuti (Finland), Philippe Kolh, (Belgium), Patrizio Lancellotti (Belgium), Ales Linhart (Czech Republic), Petros Nihoyannopoulos (UK), Massimo F. Piepoli (Italy), Piotr Ponikowski (Poland), Per Anton Sirnes (Norway), Juan Luis Tamargo (Spain), Michal Tendera (Poland), Adam Torbicki (Poland), William Wijns (Belgium), Stephan Windecker (Switzerland).

Document Reviewers: Juhani Knuuti (CPG Review Co-ordinator) (Finland), Marco Valgimigli (Review Co-ordinator) (Italy), Héctor Bueno (Spain), Marc J. Claeys (Belgium), Norbert Donner-Banzhoff (Germany), Cetin Erol (Turkey), Herbert Frank (Austria), Christian Funck-Brentano (France), Oliver Gaemperli (Switzerland), José R. Gonzalez-Juanatey (Spain), Michalis Hamilos (Greece), David Hasdai (Israel), Steen Husted (Denmark), Stefan K. James (Sweden), Kari Kervinen (Finland), Philippe Kolh (Belgium), Steen Dalby Kristensen (Denmark), Patrizio Lancellotti (Belgium), Aldo Pietro Maggioni (Italy), Massimo F. Piepoli (Italy), Axel R. Pries (Germany), Francesco Romeo (Italy), Lars Rydén (Sweden), Maarten L. Simoons (Netherlands), Per Anton Sirnes (Norway), Ph. Gabriel Steg (France), Adam Timmis (UK), William Wijns (Belgium), Stephan Windecker (Switzerland), Aylin Yildirir (Turkey), Jose Luis Zamorano (Spain).

Dilemma der KHK-Diagnostik

KHK = Klinische Diagnose

- *Unsicherheit nicht-invasiver Teste*
- *Koronarstatus nicht zwingend gefordert (bleibt ggf. unklar - trotzdem Medikation)*

Angiographie nur bei definierter Ischämie / Risiko

- *40% keine Stenosen*
- *Stenose ≠ Ischämie*
- *Lumen ≠ Plaque ≠ Risikovorhersage*
- *„Normalbefund“ ≠ keine KHK (Mikrozirkulation, Vasospastik)*

ESC Leitlinie Stabile KHK 2013

European Heart Journal (2013) 34, 2949–3003
doi:10.1093/eurheartj/eht296

ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

1 **Basisdiagnostik**

Prätest-Wahrscheinlichkeit für KHK

↓

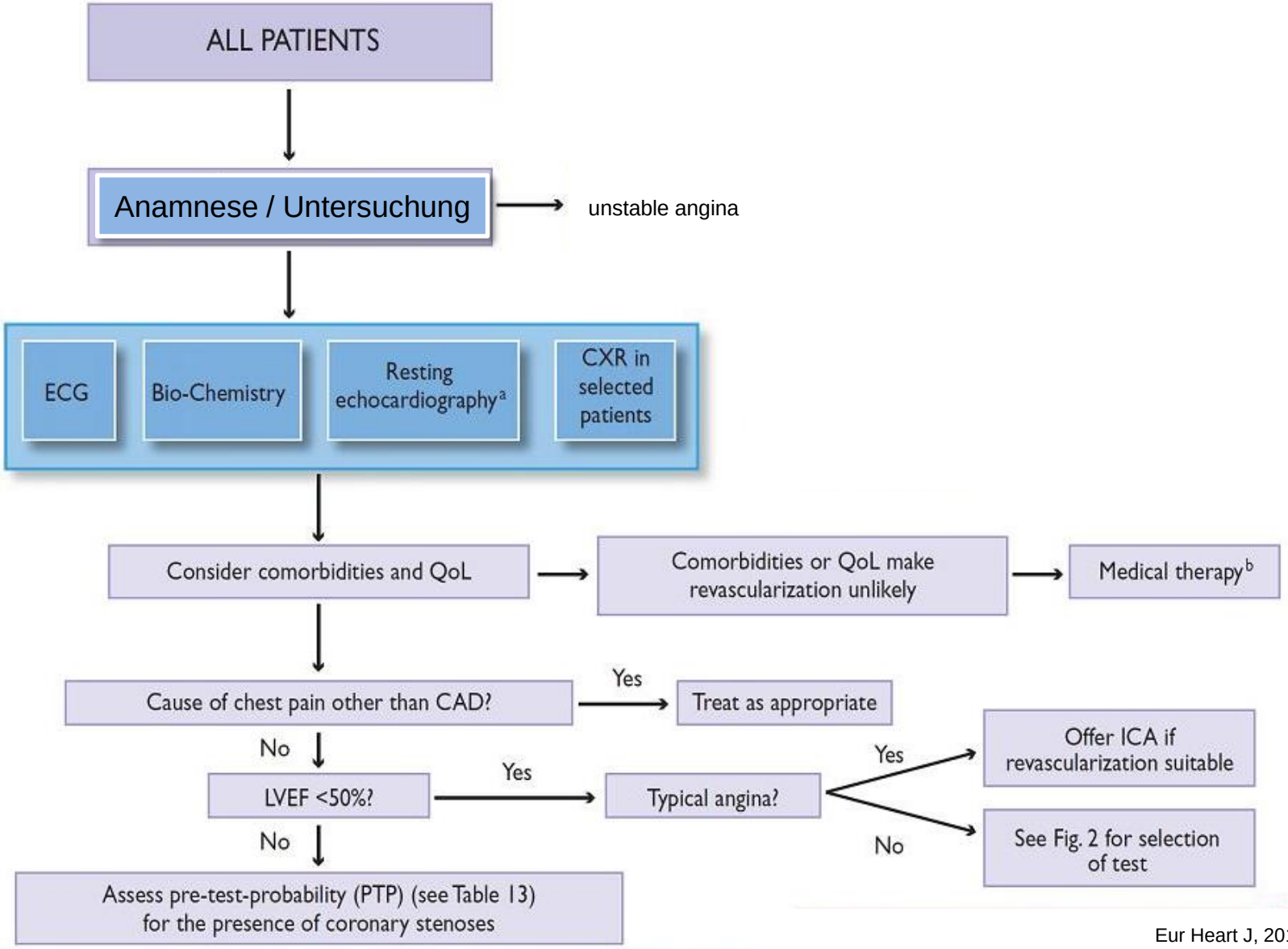
2 **Belastungsteste / erweiterte Bildgebung**

↓

3 **Risiko-Stratifizierung**

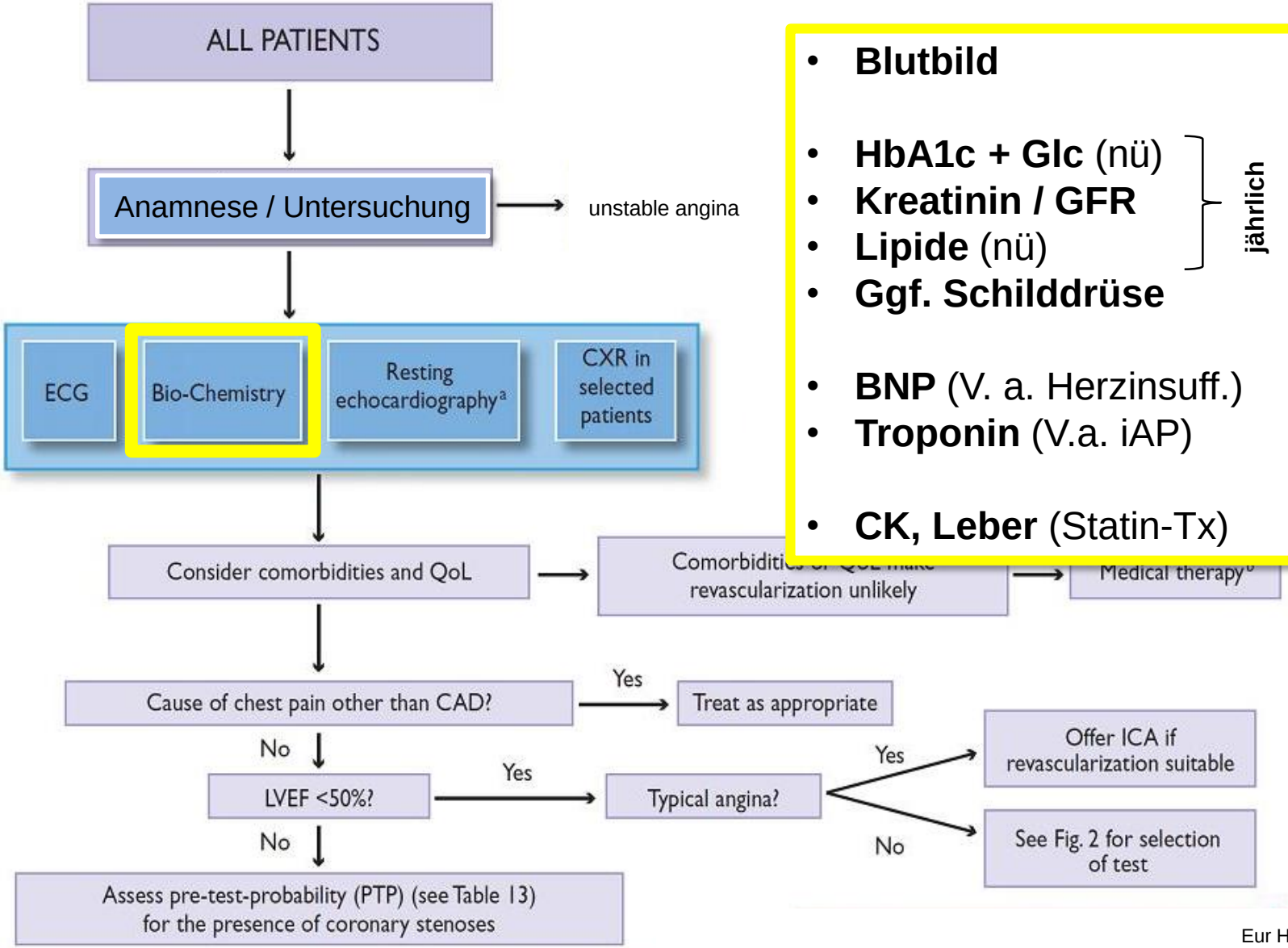
Herzkatheter?

Diagnostik Stabile KHK



Eur Heart J, 2013; 34:2949

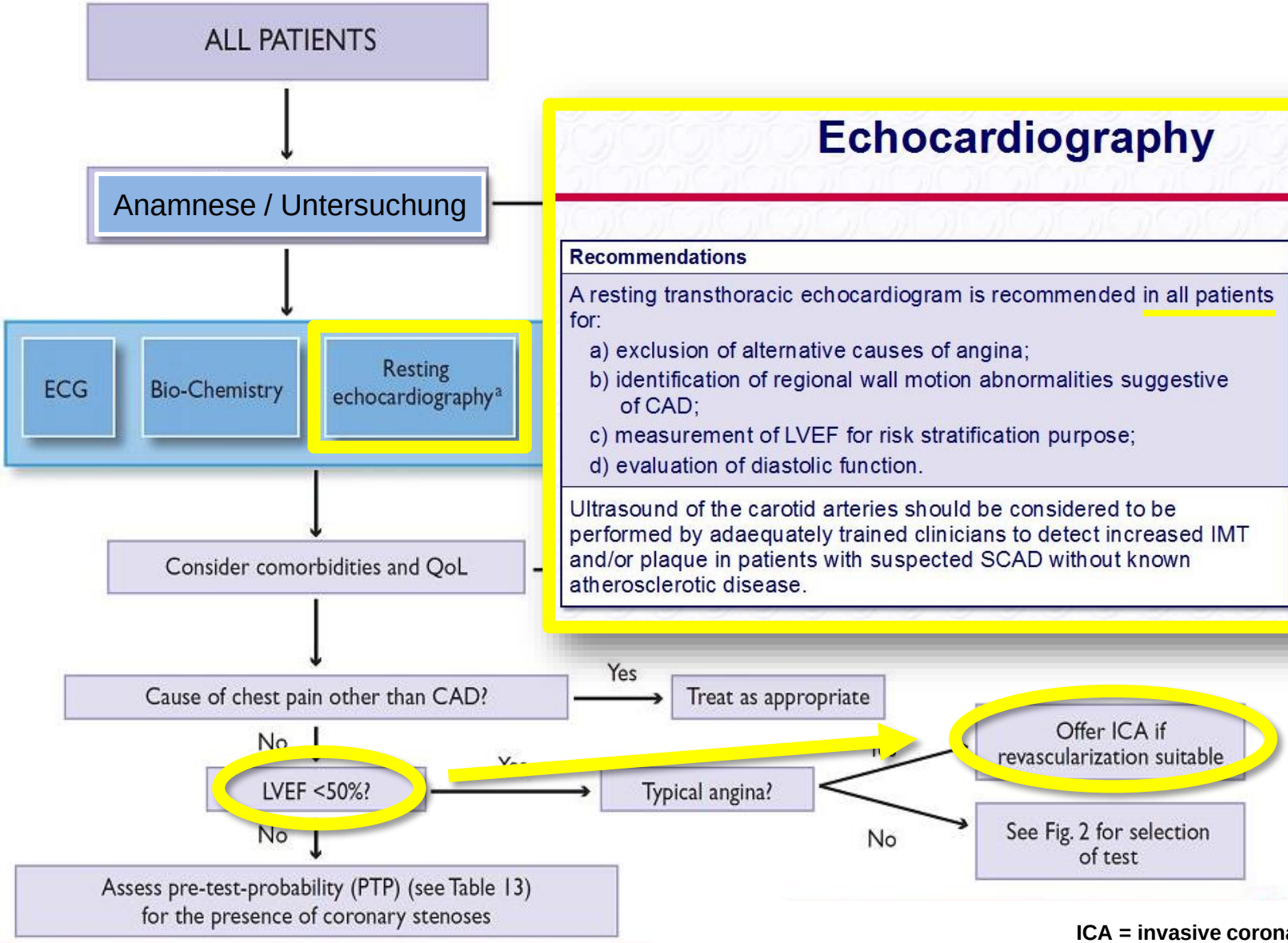
Diagnostik Stabile KHK - Laboruntersuchungen



• **Blutbild**		I B
• **HbA1c + Glc** (nü)	jährlich	I B
• **Kreatinin / GFR**	jährlich	I B
• **Lipide** (nü)	jährlich	I C
• **Ggf. Schilddrüse**		I C
• **BNP** (V. a. Herzinsuff.)		IIa C
• **Troponin** (V.a. iAP)		I A
• **CK, Leber** (Statin-Tx)		I C

Eur Heart J, 2013; 34:2949

Diagnostik Stabile KHK - Echokardiographie

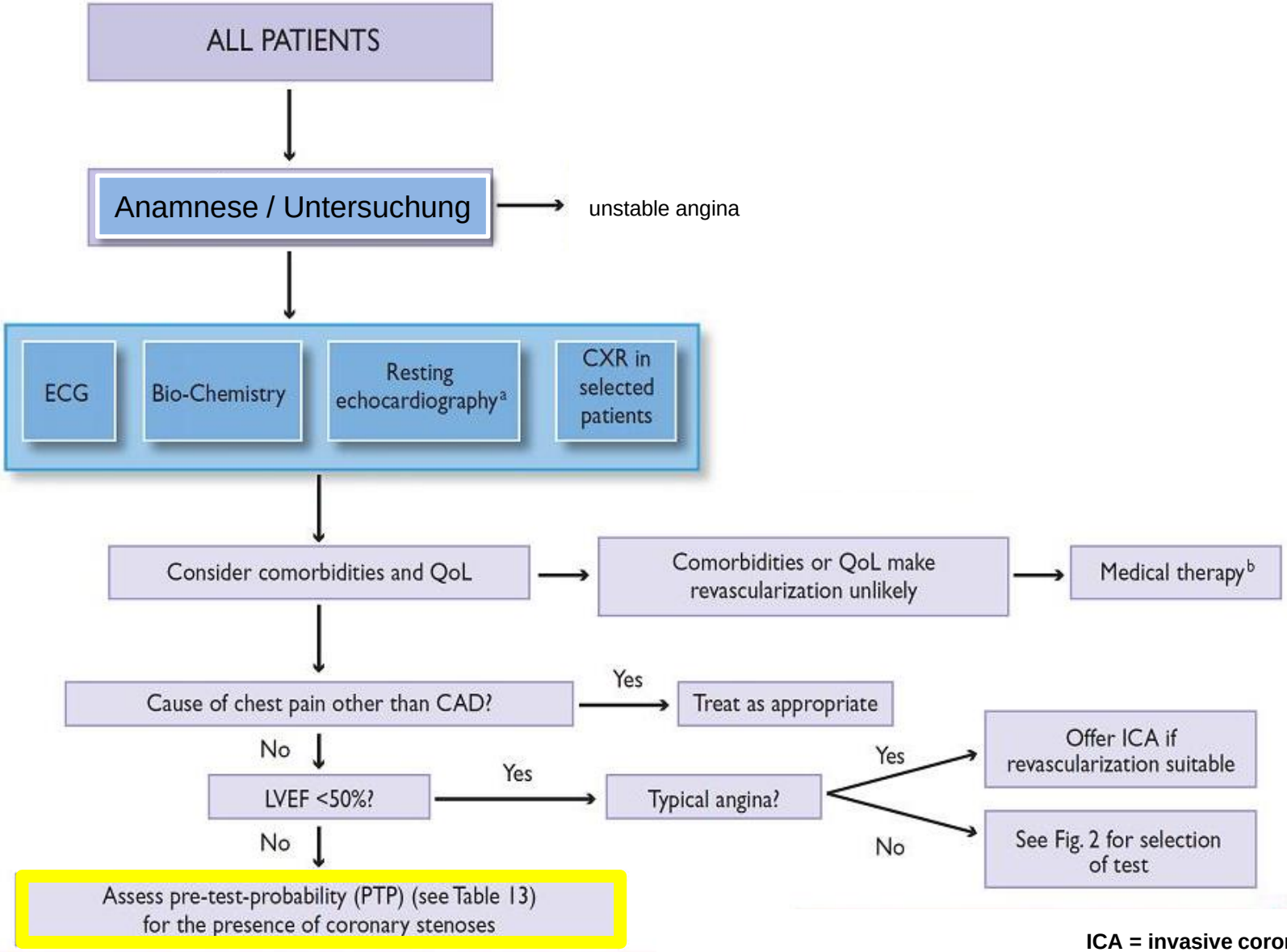


Echocardiography

Recommendations	Class	Level
A resting transthoracic echocardiogram is recommended in all patients for: a) exclusion of alternative causes of angina; b) identification of regional wall motion abnormalities suggestive of CAD; c) measurement of LVEF for risk stratification purpose; d) evaluation of diastolic function.	I	B
Ultrasound of the carotid arteries should be considered to be performed by adaequately trained clinicians to detect increased IMT and/or plaque in patients with suspected SCAD without known atherosclerotic disease.	IIa	C

ICA = invasive coronary angiography

Diagnostik Stabile KHK - Prätestwahrscheinlichkeit (PTP)



ICA = invasive coronary angiography

Diagnostik Stabile KHK - Prätestwahrscheinlichkeit (PTP)

Echo EF > 50%

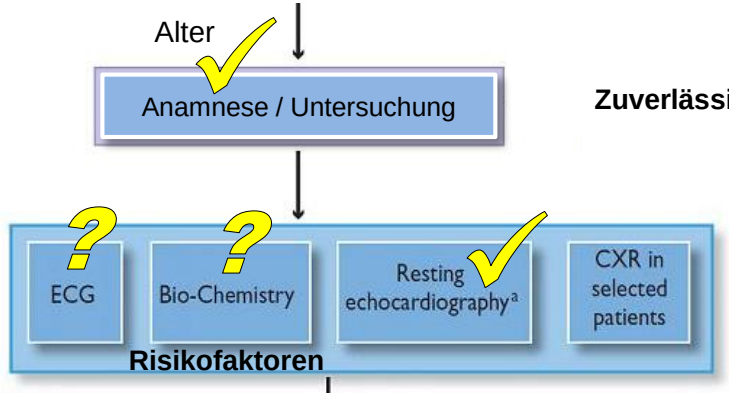
Typical angina (definite)	Meets all three of the following characteristics: • substernal chest discomfort of characteristic quality and duration; • provoked by exertion or emotional stress; • relieved by rest and/or nitrates within minutes.
Atypical angina (probable)	Meets two of these characteristics.
Non-anginal chest pain	Lacks or meets only one or none of the characteristics.

	Typical angina		Atypical angina		Non-anginal pain	
Age	Men	Women	Men	Women	Men	Women
30-39	59	28	29	10	18	5
40-49	69	37	38	14	25	8
50-59	77	47	49	20	34	12
60-69	84	58	59	28	44	17
70-79	89	68	69	37	54	24
>80	93	76	78	47	65	32

[a] Probabilities of obstructive coronary disease shown reflect the estimates for patients aged 35, 45, 55, 65, 75, and 85 years.
This slide corresponds to Table 13 in the full text.

From: Genders TS, et al. Eur Heart J 2011;32:1316–1330.

Diagnostik Stabile KHK - Prätestwahrscheinlichkeit (PTP)



Zuverlässigkeit der Anamnese ?

Echo EF > 50%

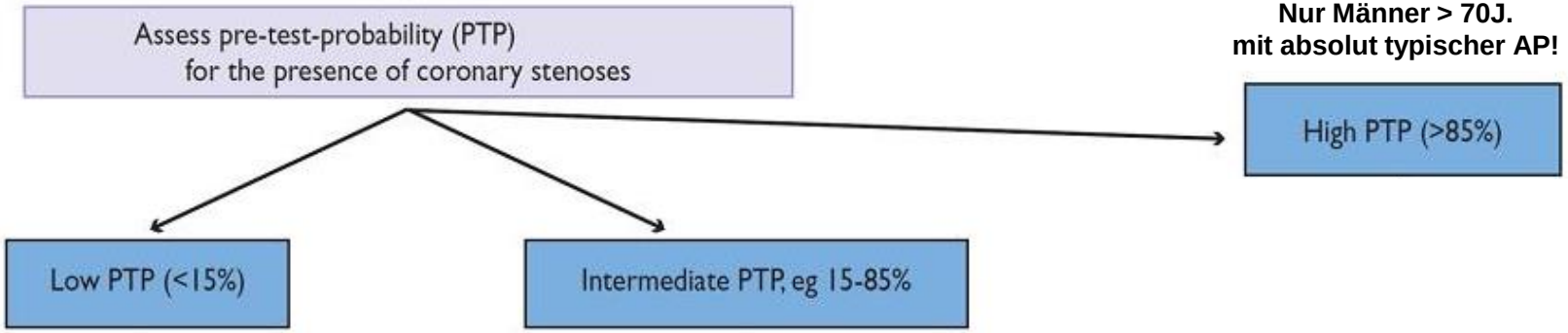
	Typical angina		Atypical angina		Non-anginal pain	
Age	Men	Women	Men	Women	Men	Women
30-39	59	28	29	10	18	5
40-49	69	37	38	14	25	8
50-59	77	47	49	20	34	12
60-69	84	58	59	28	44	17
70-79	89	68	69	37	54	24
>80	93	76	78	47	65	32

[a] Probabilities of obstructive coronary disease shown reflect the estimates for patients aged 35, 45, 55, 65, 75, and 85 years. This slide corresponds to Table 13 in the full text.

Eur Heart J, 2013; 34:2949

From: Genders TS, et al. Eur Heart J 2011;32:1316–1330.

Diagnostik Stabile KHK
- Vorgehen nach Prätestwahrscheinlichkeit (PTP)



Nicht-kardial
oder
Vasomotorik
(incl. Hypertensive HK)

Nicht-invasive Teste
(für Diagnose & Risikostratifikation)

Nicht-invasive Teste
(für Risikostratifikation)
oder
Direkt Herzkatheter
(bei schwerer Angina)

⇩

FFR sollte im Labor verfügbar sein

ICA = invasive coronary angiography

Diagnostik Stabile KHK
- Nicht-invasive Teste für mittlere PTP

	Diagnosis of CAD		
	Sensitivity (%)	Specificity (%)	
Exercise ECG[a]	45-50	85-90	Ungenau, aber einfach => bleibt Basis (I B)
Exercise stress echocardiography	80-85	80-88	Bildgebung mit physiologischer Belastung
Exercise stress SPECT	73-92	63-87	
Dobutamine stress echocardiography	79-83	82-86	Bildgebung mit pharmakologischer Belastung
Dobutamine stress MRI[b]	79-88	81-91	
Vasodilator stress echocardiography	72-79	92-95	
Vasodilator stress SPECT	90-91	75-84	
Vasodilator stress MRI[b]	67-94	61-85	
Coronary CTA[c]	95-99	64-83	CT-Angiographie bei PTP 15 – 50% (IIa-C)
Vasodilator stress PET	81-97	74-91	Aufwändig, wenig verfügbar

Stress imaging is recommended as the initial test option if local expertise and availability permit.	I	B
Exercise stress testing is recommended rather than pharmacologic testing whenever possible.	I	C

Risiko-Stratifizierung
- Definitionen für verschiedene Testmodalitäten

Exercise stress ECG

Angina / ST-Senkung (Duke Risk Score)

High risk	CV mortality >3%/year.
Intermediate risk	CV mortality between 1 and 3%/year.
Low risk	CV mortality <1%/year.

Ischemia imaging

> 10% Ischämieareal

High risk	Area of ischaemia >10% (>10% for SPECT; limited quantitative data for CMR – probably ≥2/16 segments with new perfusion defects or ≥3 dobutamine-induced dysfunctional segments; ≥ 3 segments of LV by stress echo).
Intermediate risk	Area of ischaemia between 1 to 10% or any ischaemia less than high risk by CMR or stress echo.
Low risk	No ischaemia.

Coronary CTA

Risikopathologie

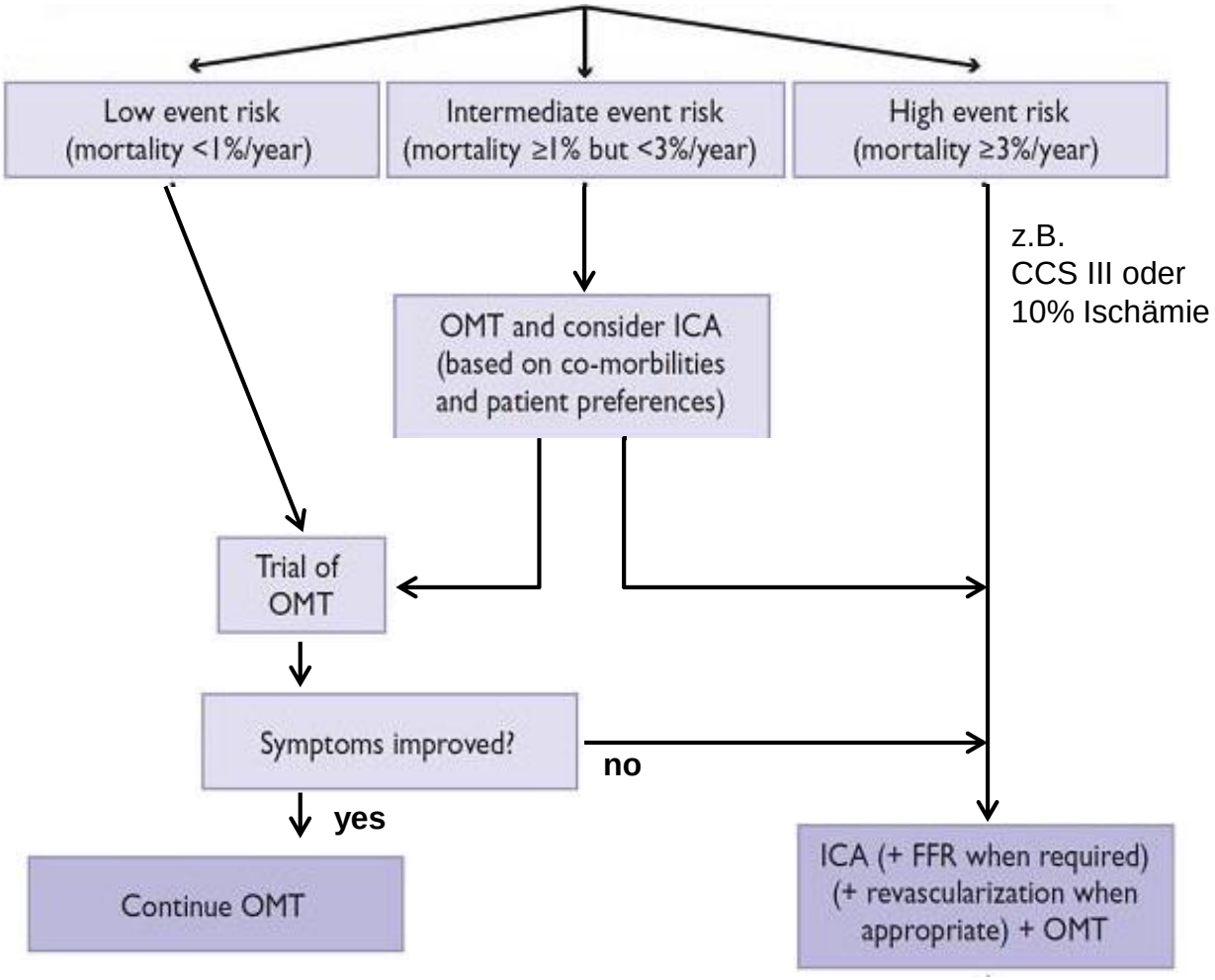
High risk	Significant lesions of high risk category (three-vessel disease with proximal stenoses, LM, and proximal anterior descending CAD).
Intermediate rick	Significant lesion(s) in large and proximal coronary artery(ies) but not high risk category.
Low risk	Normal coronary artery or plaques only.

Eur Heart J, 2013; 34:2949

Management der stabilen KHK - basierend auf Risiko-Stratifizierung

Diagnosis of CAD

pretest probability and results of imaging and stress testing



Modified from : Eur Heart J, 2013; 34:2949

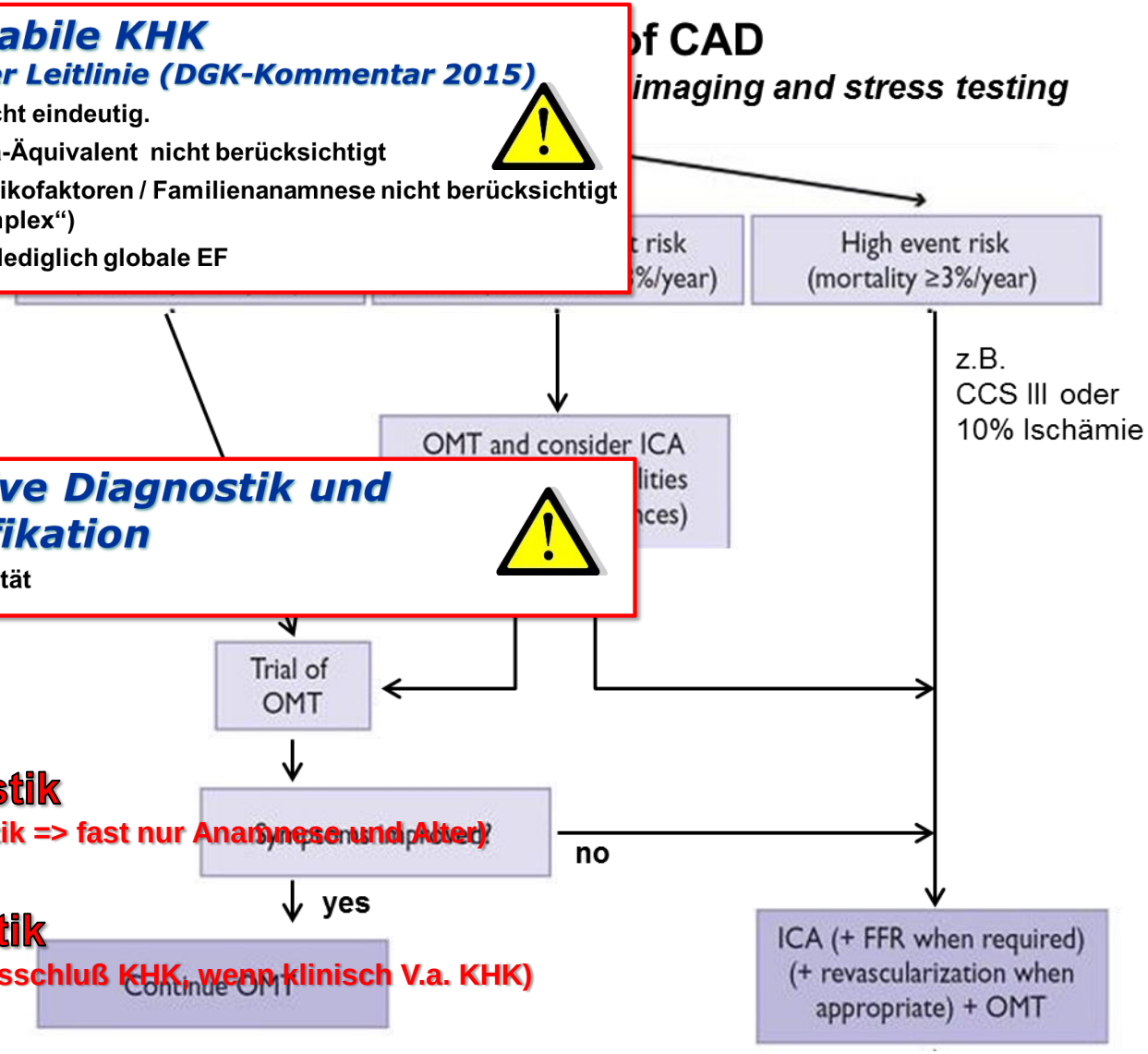
Management der stabilen KHK - basierend auf Risiko-Stratifizierung

Diagnose Stabile KHK
- Limitationen der Leitlinie (DGK-Kommentar 2015)

- Symptomatik oft nicht eindeutig.
- Dyspnoe als Angina-Äquivalent nicht berücksichtigt
- kardiovaskuläre Risikofaktoren / Familienanamnese nicht berücksichtigt (Argument: „zu komplex“)
- Echokardiographie lediglich globale EF

Nicht-invasive Diagnostik und Risikostratifikation

- Sensitivität / Spezifität

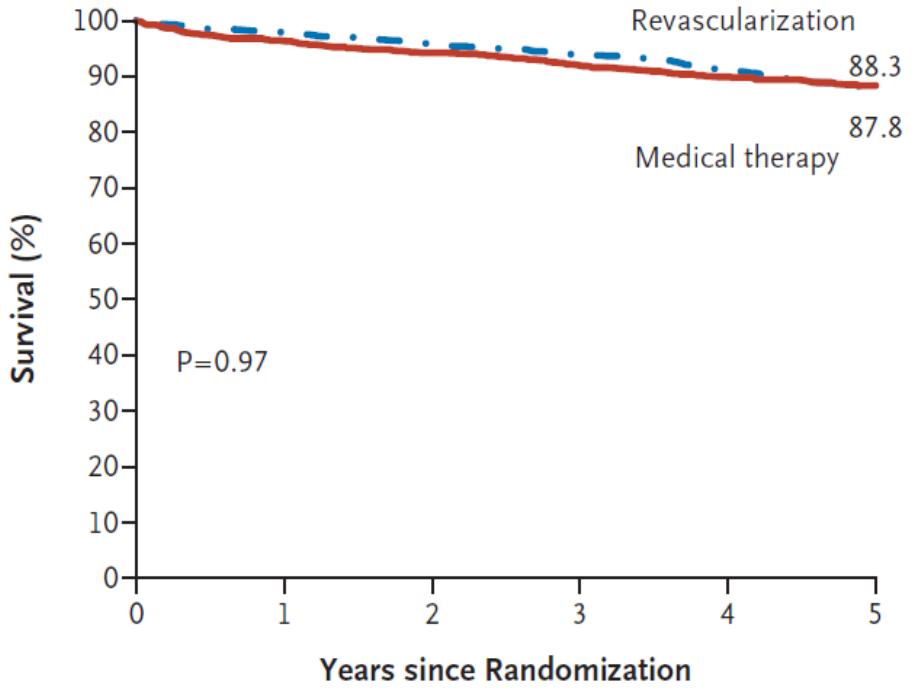


Unterdiagnostik
(Hürde für Diagnostik => fast nur Anamnese und Alter)
&
Überdiagnostik
(bis 40% invasiv Ausschluß KHK, wenn klinisch V.a. KHK)

Modified from : Eur Heart J, 2013; 34:2949

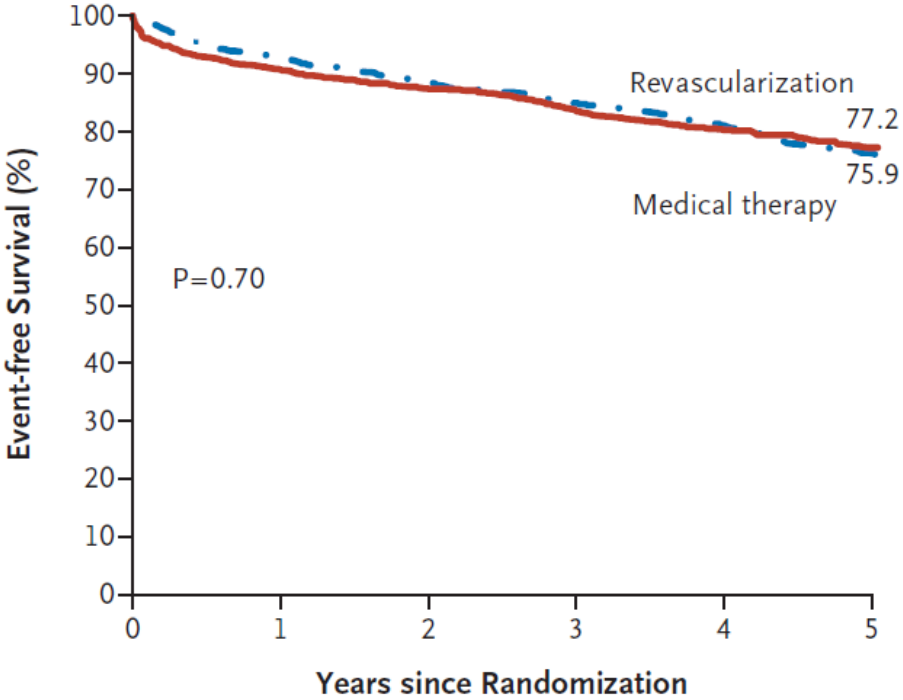
BARI 2D – Therapie bei Diabetes & KHK
⌦ Revaskularisation oder Konservativ?

1° EP
Survival



2368 2296 2247 2197 1892 1196

2° EP
Freedom from MACE
(death, MI, stroke)



2368 2094 1984 1807 1459 823

Revascularization
Medical therapy

N Engl J Med 2009; 360:2503

BARI 2D

➢ Welche Patienten wurden untersucht?

❖ Ausschlußkriterien

and classic angina). All patients had to be candidates for elective percutaneous coronary intervention (PCI) or coronary-artery bypass grafting (CABG). Patients were excluded if they required immediate revascularization or had left main coronary disease, a creatinine level of more than 2.0 mg per deciliter (177 μmol per liter), a glycated hemoglobin level of more than 13.0%, class III or IV heart failure, or hepatic dysfunction or if they had undergone PCI or CABG within the previous 12 months.

- **Revascularization is required for prompt control of severe or unstable angina.**
- **Determination of suitability was made by a physician-investigator at each participating institution.**

Brooks et al., Am J Cardiol 2006;97[suppl]:9G

= 0,94 Patienten / pro Monat / pro Zentrum eingeschlossen

❖ Patientencharakteristika

Normale EF
Ischämieareal unbekannt

} ***Niedriges Risiko!***

N Engl J Med 2009; 360:2503

Nutzen einer Revaskularisation:
- Hämodynamische Relevanz/Ischämie in BARI 2D?

	Alle	PCI
Häufigkeit der Stenosegrade	(n = 8.286)	(n= 4.534)
< 50%	**45 %**	**50 %**
50 – 69%	**32 %**	**31 %**
70 – 89%	**9 %**	**8 %**
90 – 100 %	**15 %**	**11 %**
- davon 99 & 100%	*10 %*	*7 %*
Anzahl Stenosen pro Patient	(n = 1.773)	(n = 1.118)
≥ 20%	**4,6 ±2,3**	**4,1 ±2,0**
≥ 50%	**2,6 ±1,7**	**2,1 ±1,5**
≥ 70%	**1,1 ±1,2**	**0,8 ±1,0**

< 20% aller Läsionen sind hochgradig

Weniger als 1 hochgradige Stenose pro Patient!

Visuelle Einschätzung im Core Lab
Schwartz et al., Am J Cardiol 2009;103:632

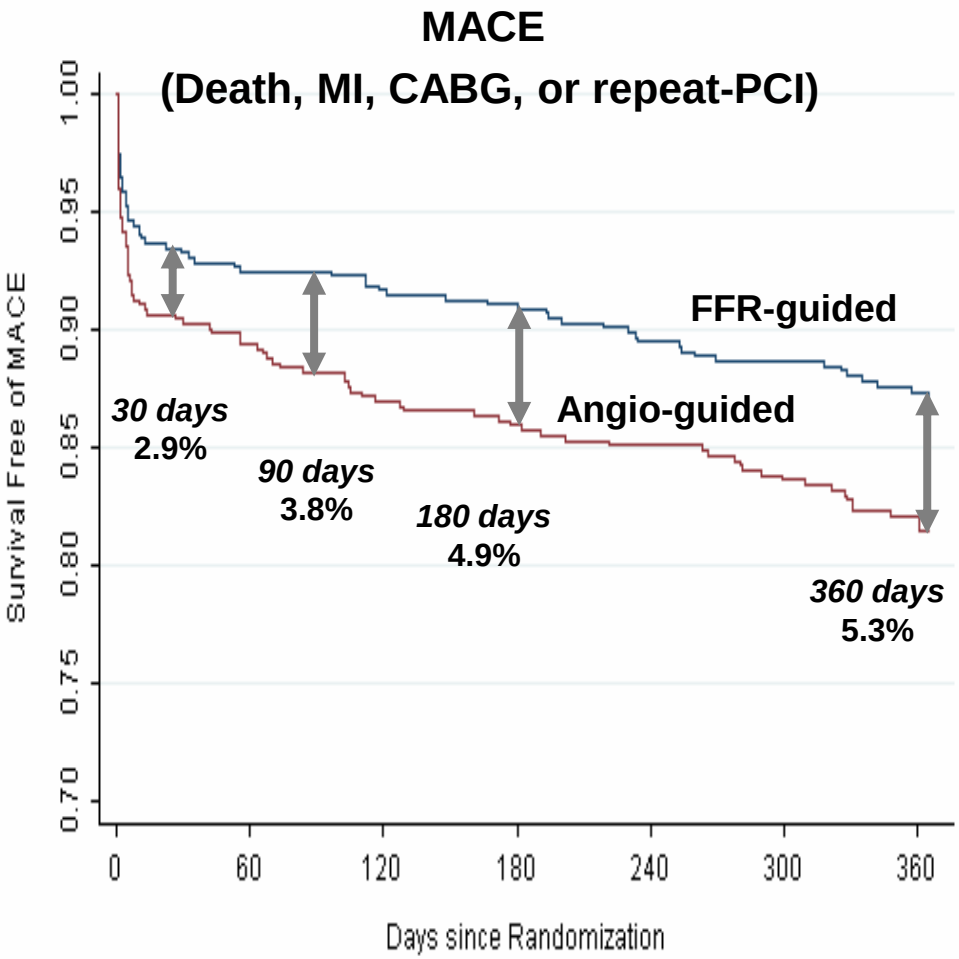
Nutzen einer Revaskularisation:
- Vorteil, wenn PCI Ischämie- (FFR-) gesteuert

	Alle	PCI
Häufigkeit der Stenosegrade	(n = 8.286)	(n= 4.534)
≥ 70%	24 %	19 %
Anzahl Stenosen pro Patient	(n = 1.773)	(n = 1.118)
≥ 70%	1,1 ±1,2	0,8 ±1,0
Anzahl behandelter Stenosen pro Patient		
		1,5 ±0,8

Jede zweite dilatierte Stenose
= nur 20 – 70% Diameterstenose

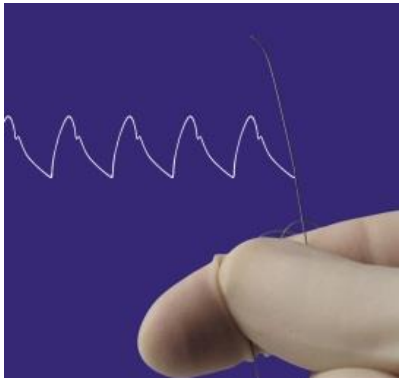
Schwartz et al., Am J Cardiol 2009;103:632
BARI 2D study group, NEJM 2009; 360:2503

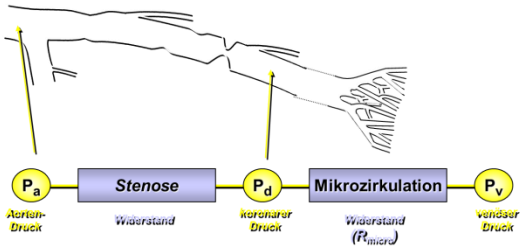
FAME-Studie

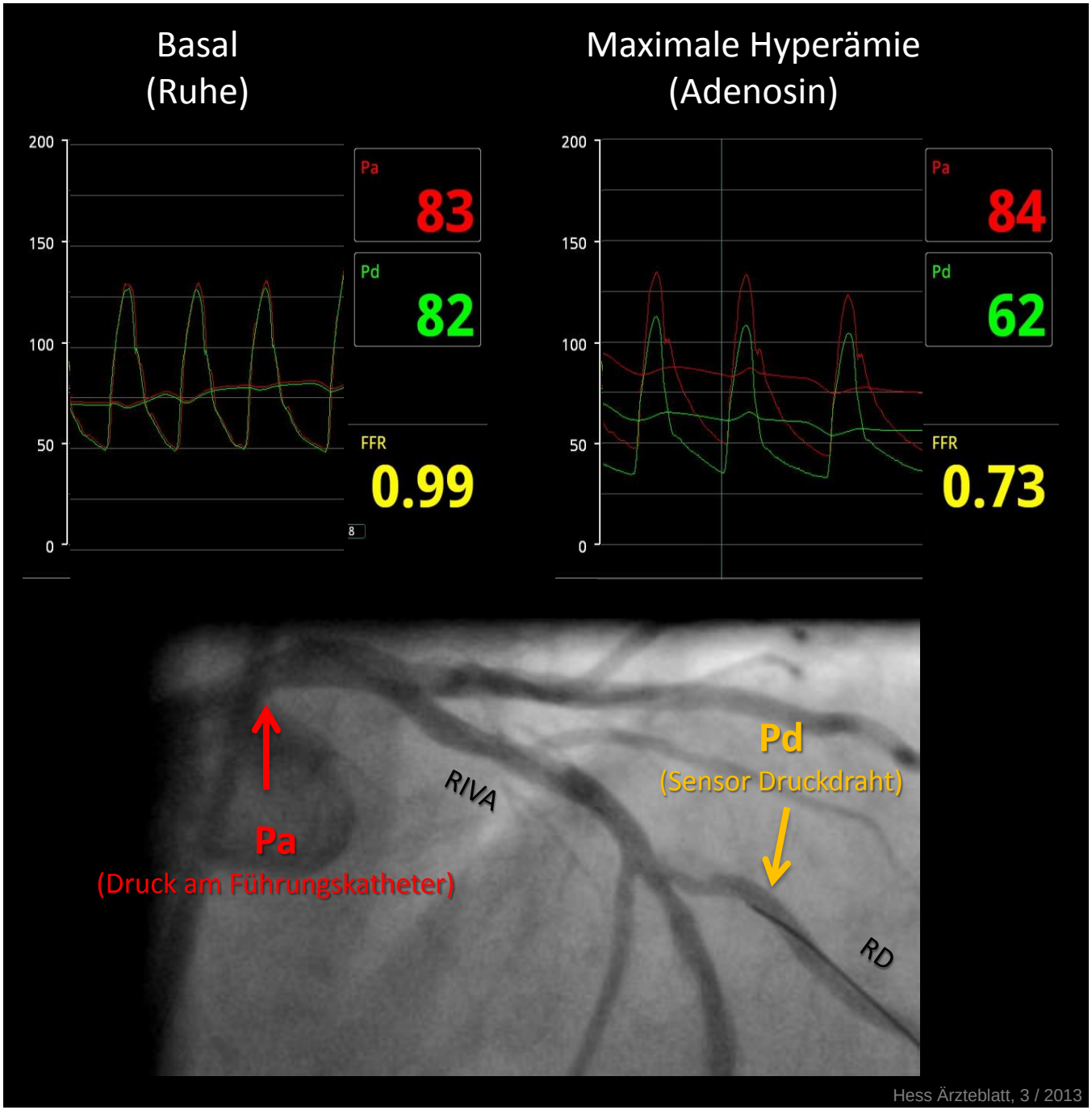


Tonino et al., N Engl J Med 2009;360

Druckdraht
(„Pressure wire“)



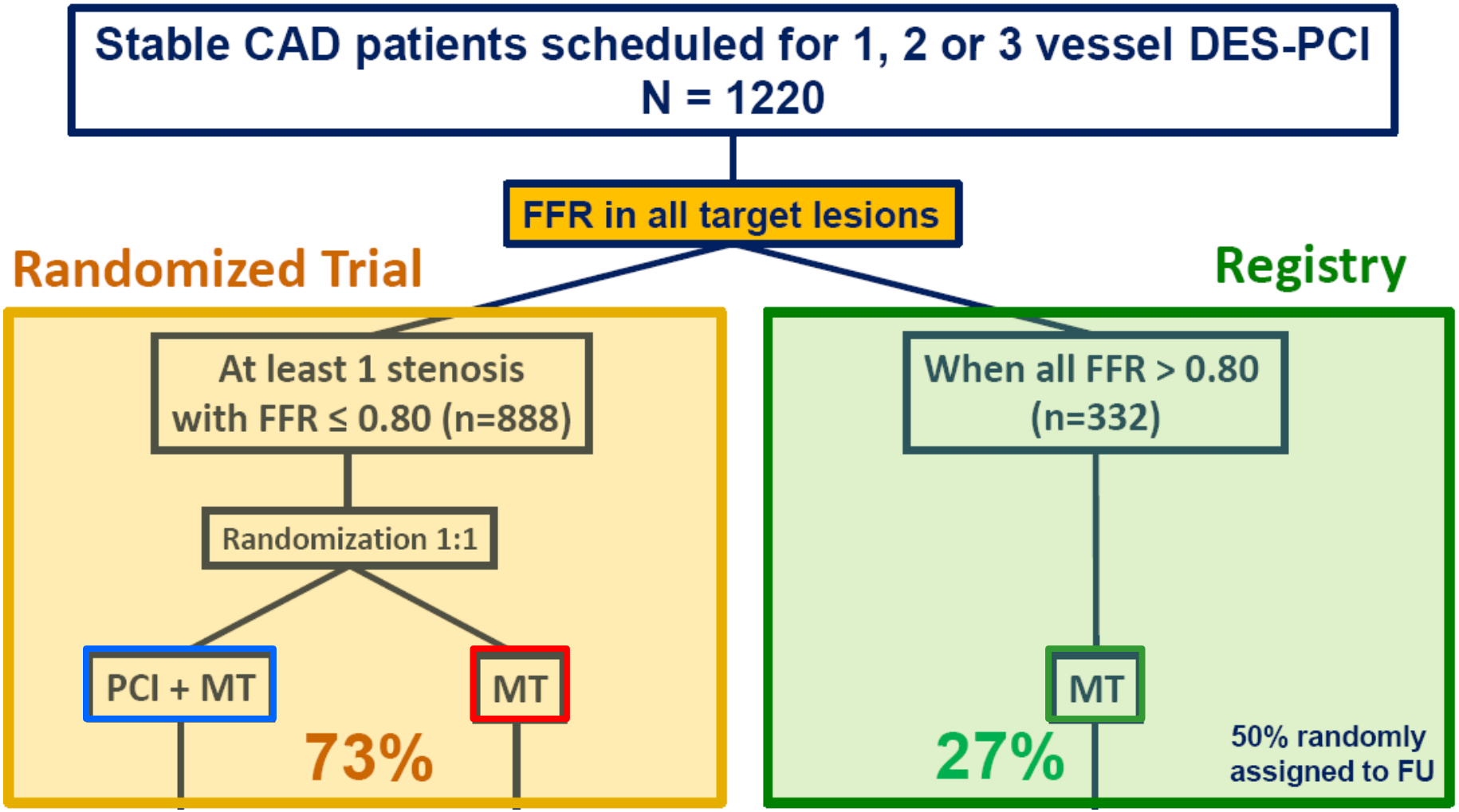




FFR = Fraktionelle Flußreserve

Hess Ärzteblatt, 3 / 2013

FAME II
Druckdrahtmessung zur Entscheidung für PCI

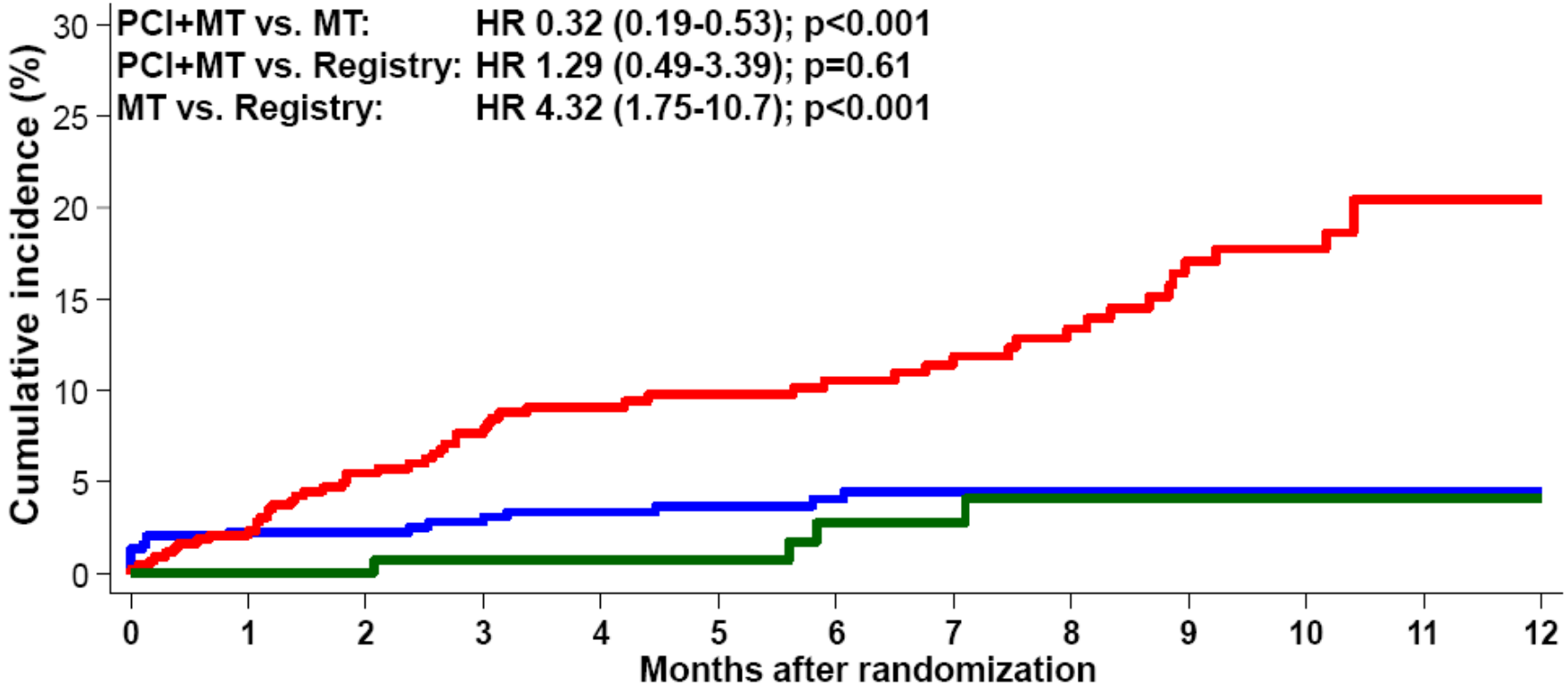


Klinikum Fulda

ESC Kongress 2012 & N Engl J Med 2012

FAME II

Druckdrahtmessung zur Entscheidung für PCI



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

Klinikum Fulda

ESC Kongress 2012 & N Engl J Med 2012

BARI 2D
- Limitationen!

Strategie

- **BARI 2D = Sofortige versus optional spätere Revaskularisation (42%)**
  (Nicht schwarz-weiss: konservativ versus invasiv)

Screening

- **Hoch selektierte Population: Niedriges Risiko, fragliche hämodynamische Stenoserelevanz** ***(unwahrscheinlich Ereignisse zu reduzieren)***

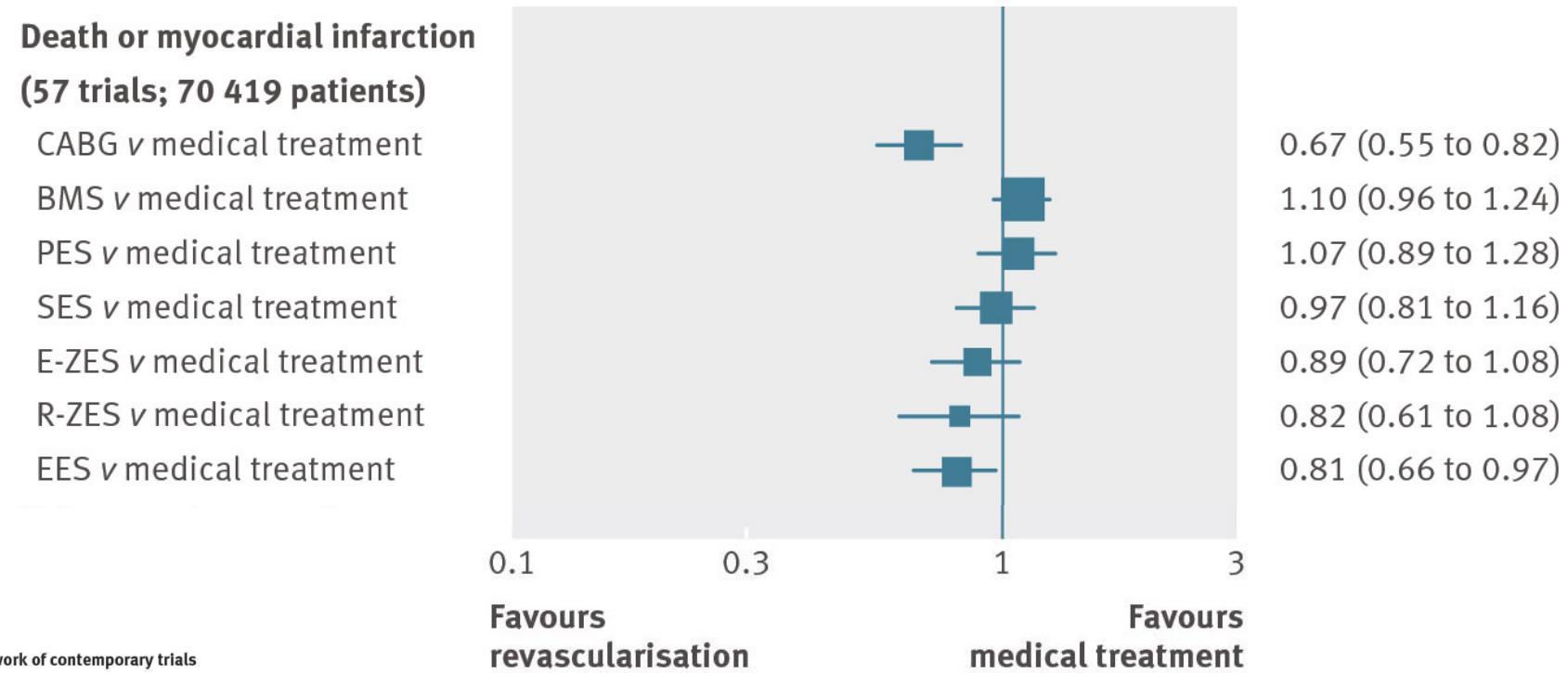
Symptome

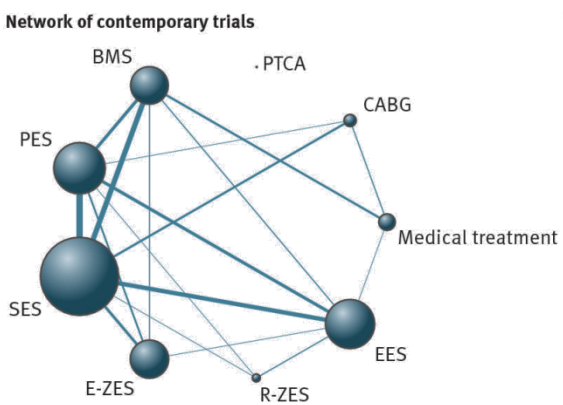
- **Möglicherweise dennoch symptomatischer Nutzen der Revaskularisation**
  (kein Unterschied in harten Endpunkten)

Indikationen

- **BARI 2D spricht nicht gegen etablierte PCI-Indikationen bei Diabetes**
  (schwere Angina, große Ischämie, ACS, STEMI)

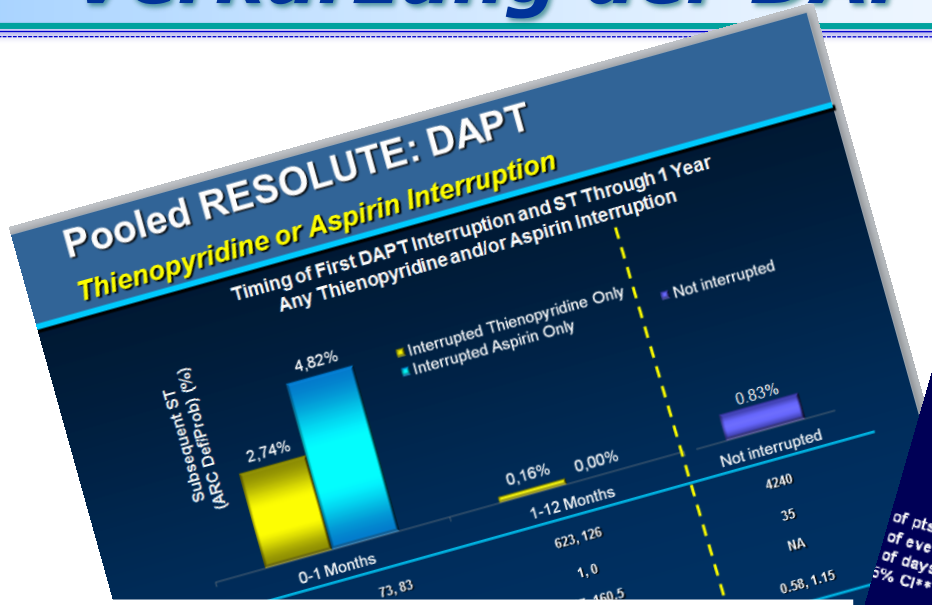
Sind moderne DES besser?
- Network Metaanalyse 2014

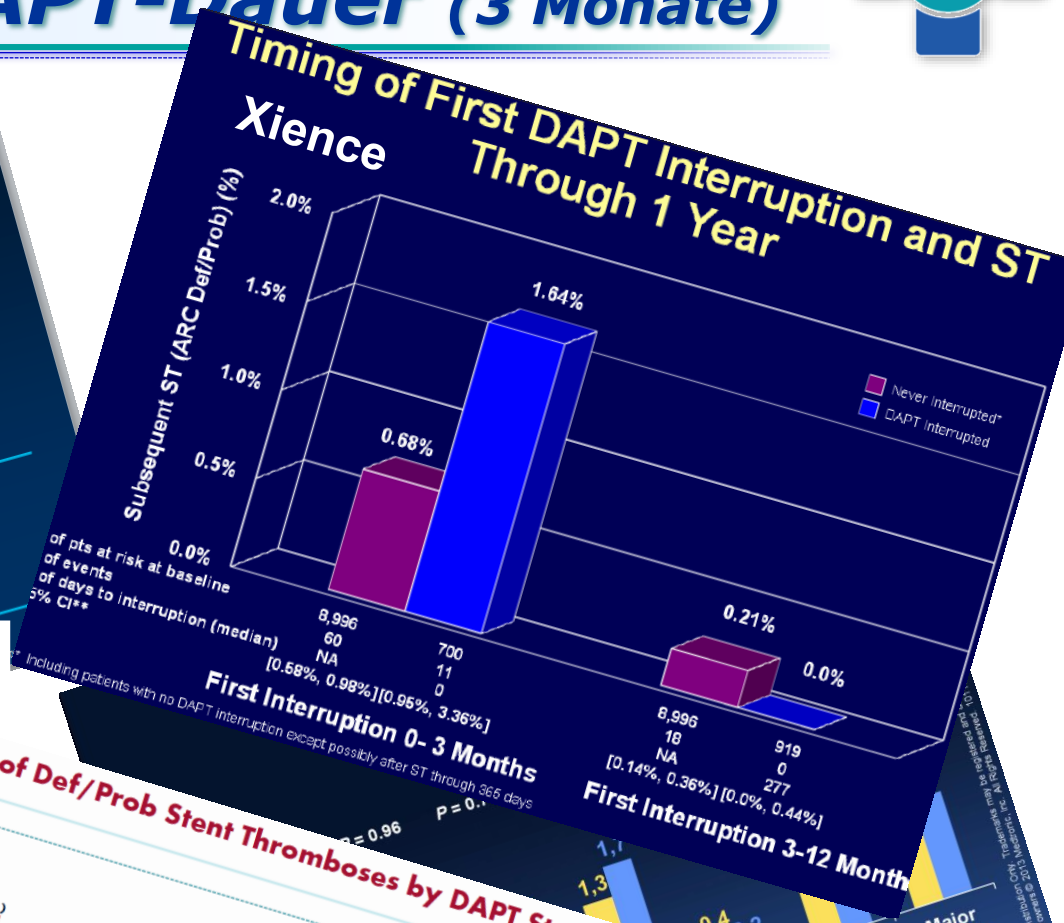




Windecker et al., *BMJ 2014;348:g3859*

2° Generation DES
- Verkürzung der DAPT-Dauer (3 Monate)





PHARMA & HEALTHCARE | 5/15/2012 @ 10:53AM | 834 views

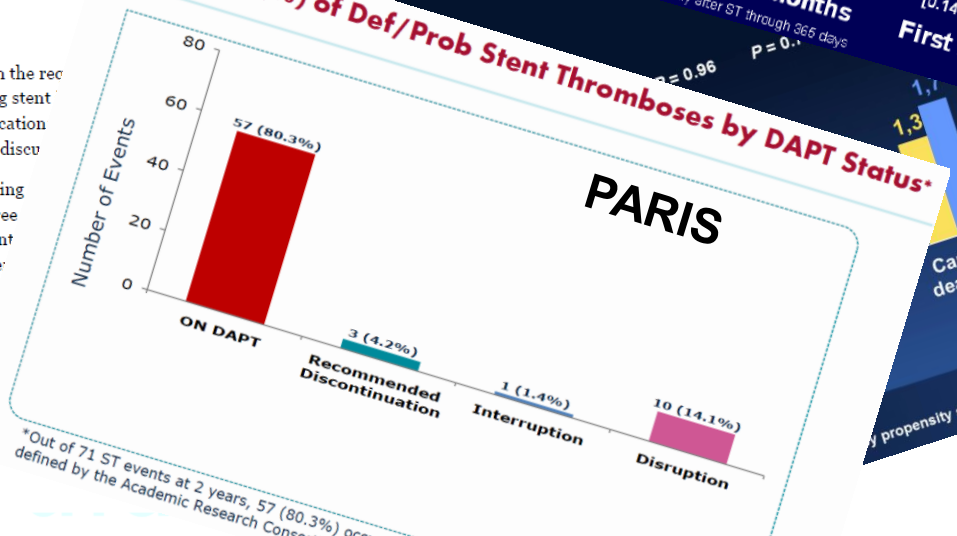
Xience Stents Gain European Nod For Three-Month Dual Antiplatelet Therapy

The biggest drawback to drug-eluting stents has been the rec
prolonged dual antiplatelet (DAPT) therapy following stent
prevent stent thrombosis and other potential complication
length of DAPT has been the subject of considerable discu

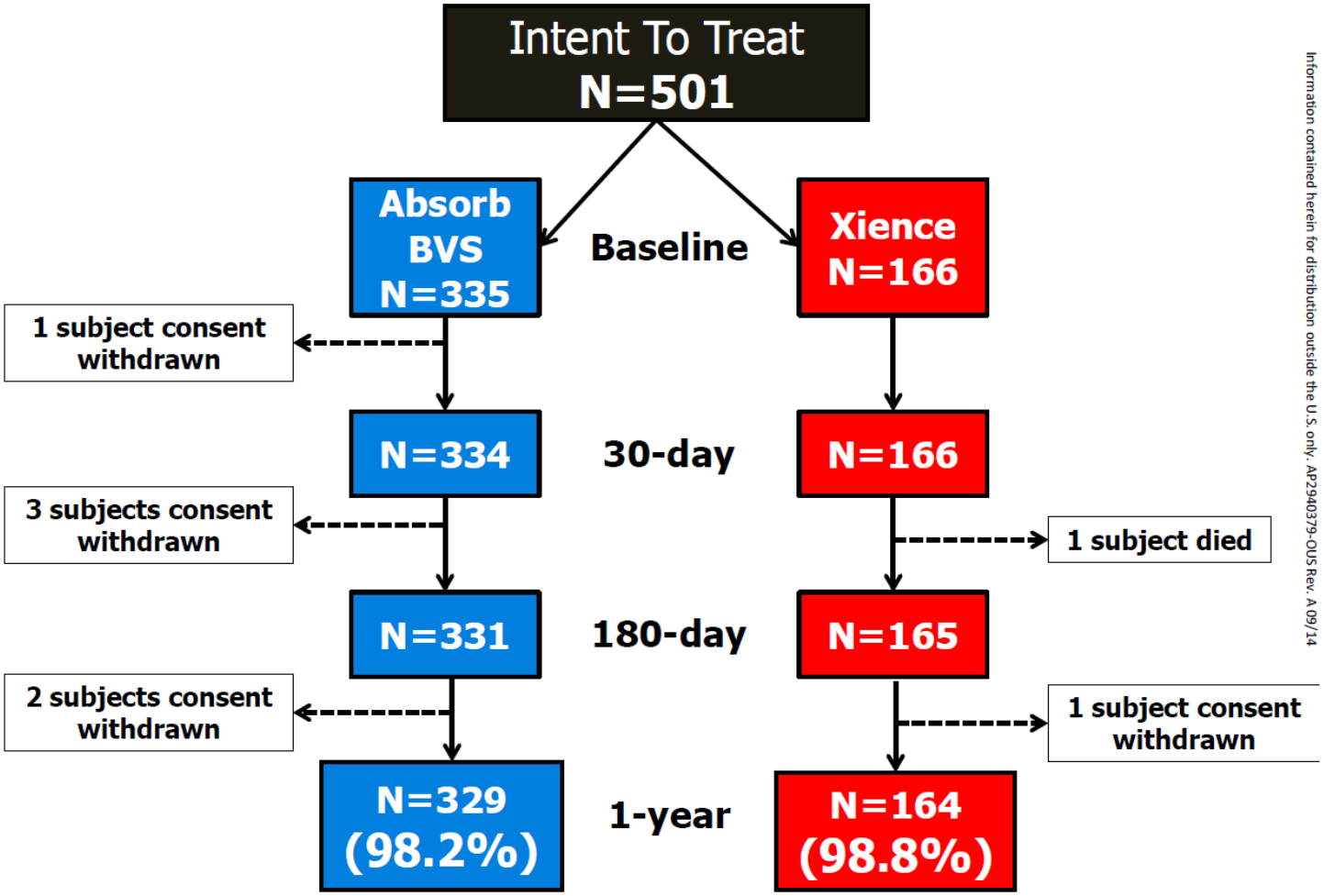
Now the Xience Prime and Xience V everolimus-eluting
the CE Mark in Europe for a DAPT length of only three
an Abbott press release. The manufacturer of the stent
the "shortest duration for any major drug eluting ste

Abbott said that data presented this week at the Eur
cases of stent thrombosis in more than 10,000 pati
stent and who discontinued DAPT after three mor

An Abbott spokesperson told CardioBrief that th
exploring our filing strategies with the FDA for
indication."



ABSORB II – 1. Randomisierte Studie



Information contained herein for distribution outside the U.S. only. AP2940379-OUS Rev. A 09/14

Serruys et al., TCT 2014 / Lancet 2014, Sept. 14th

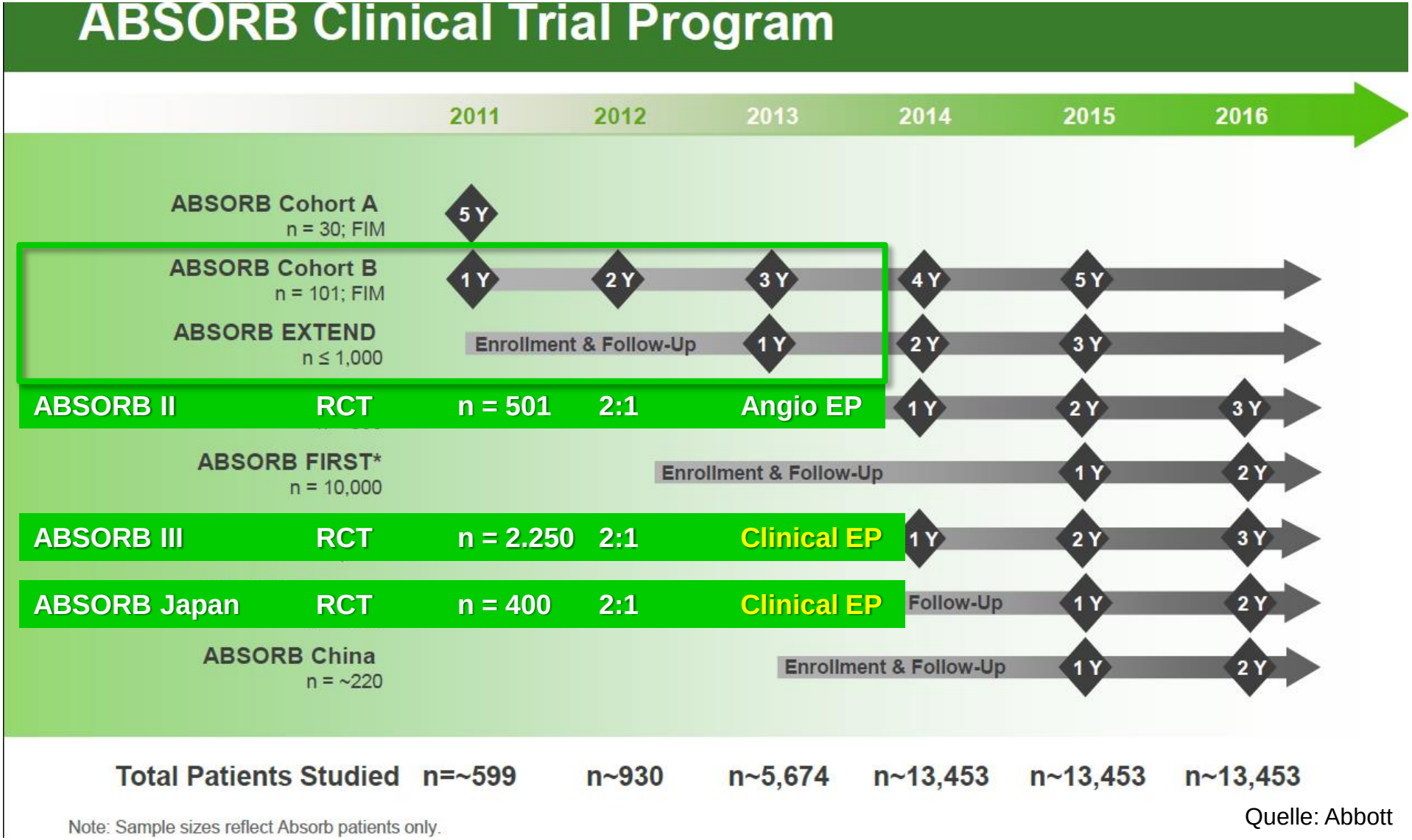
ABSORB II – 1. Randomisierte Studie

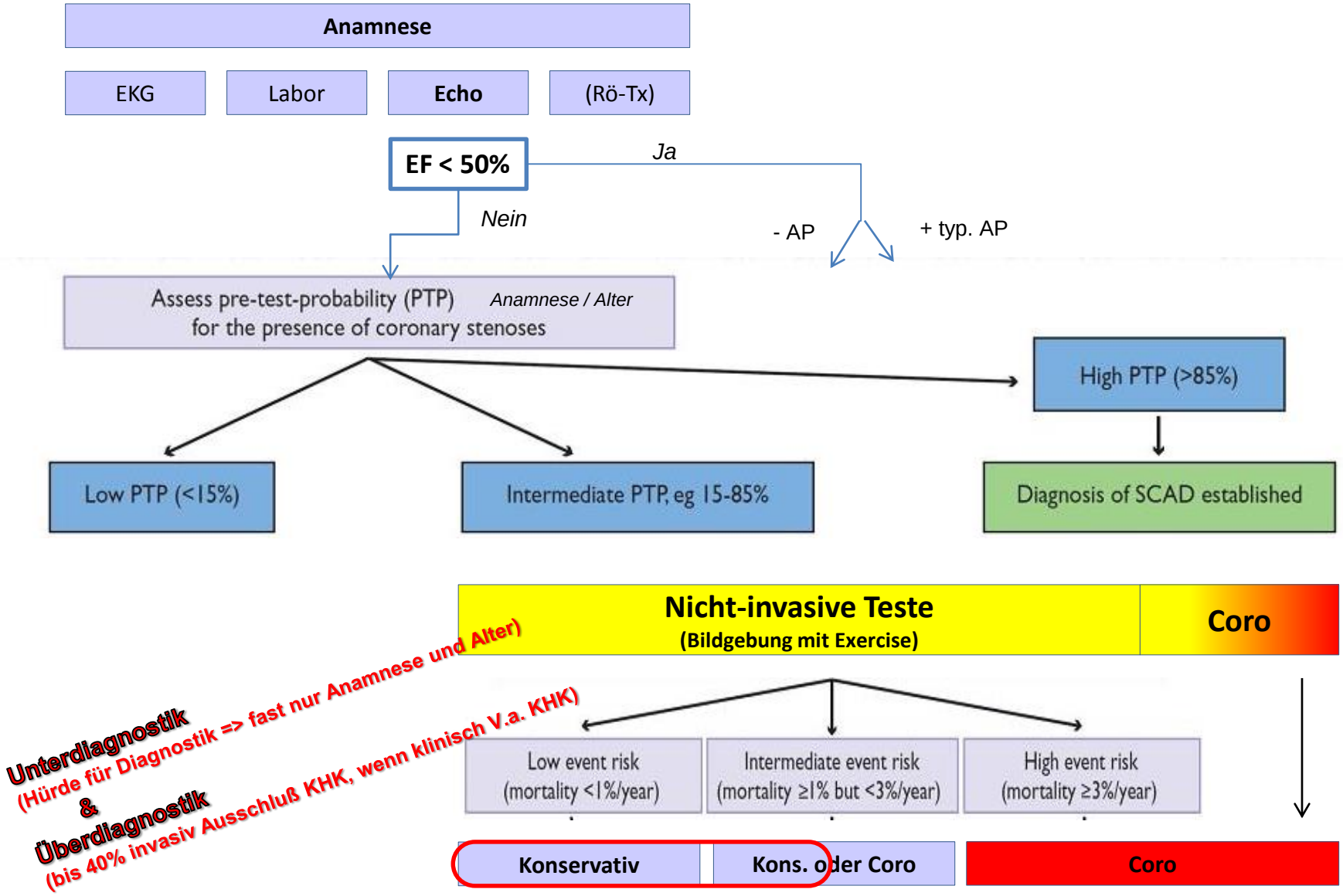
Clinical Outcomes

Cumulative incidence in percentage	Absorb 335 pts	Xience 166 pts	*p* value
Composite of cardiac death, target vessel MI and clinically indicated target lesion revascularization (TLF, DoCE)	**4.8 %**	**3.0 %**	**0.35**
Cardiac death	0 %	0 %	1.00
Target vessel MI	4.2 %	1.2 %	0.07
Clinically indicated TLR	1.2 %	1.8 %	0.69
All TLR	1.2 %	1.8 %	0.69
Composite of all death, all MI and all revascularization (PoCE)	**7.3 %**	**9.1 %**	**0.47**
All death	0 %	0.6 %	0.33
All MI	4.5 %	1.2 %	0.06
All revascularization	3.6 %	7.3 %	0.08

Serruys et al., TCT 2014 / Lancet 2014, Sept. 14th

Wissenschaftliches Programm: ABSORB



Quelle: Abbott

Diagnostik und Risikostratifizierung stabile KHK nach ESC-Leitlinie 2013