Dokter ik ben toch niet te oud: indicaties en contra-indicaties van cardiologische innovaties bij de ouderen?

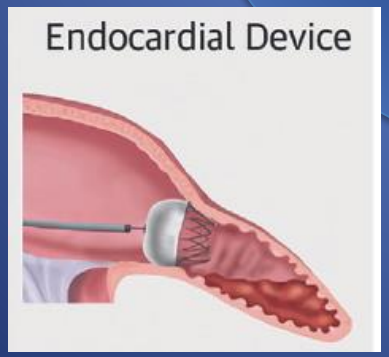
P Van Herck

Antwerp University Hospital

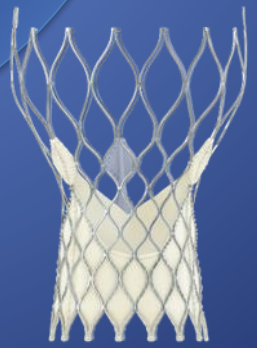
Coronary artery disease

Geriatric patient

Atrial fibrillation

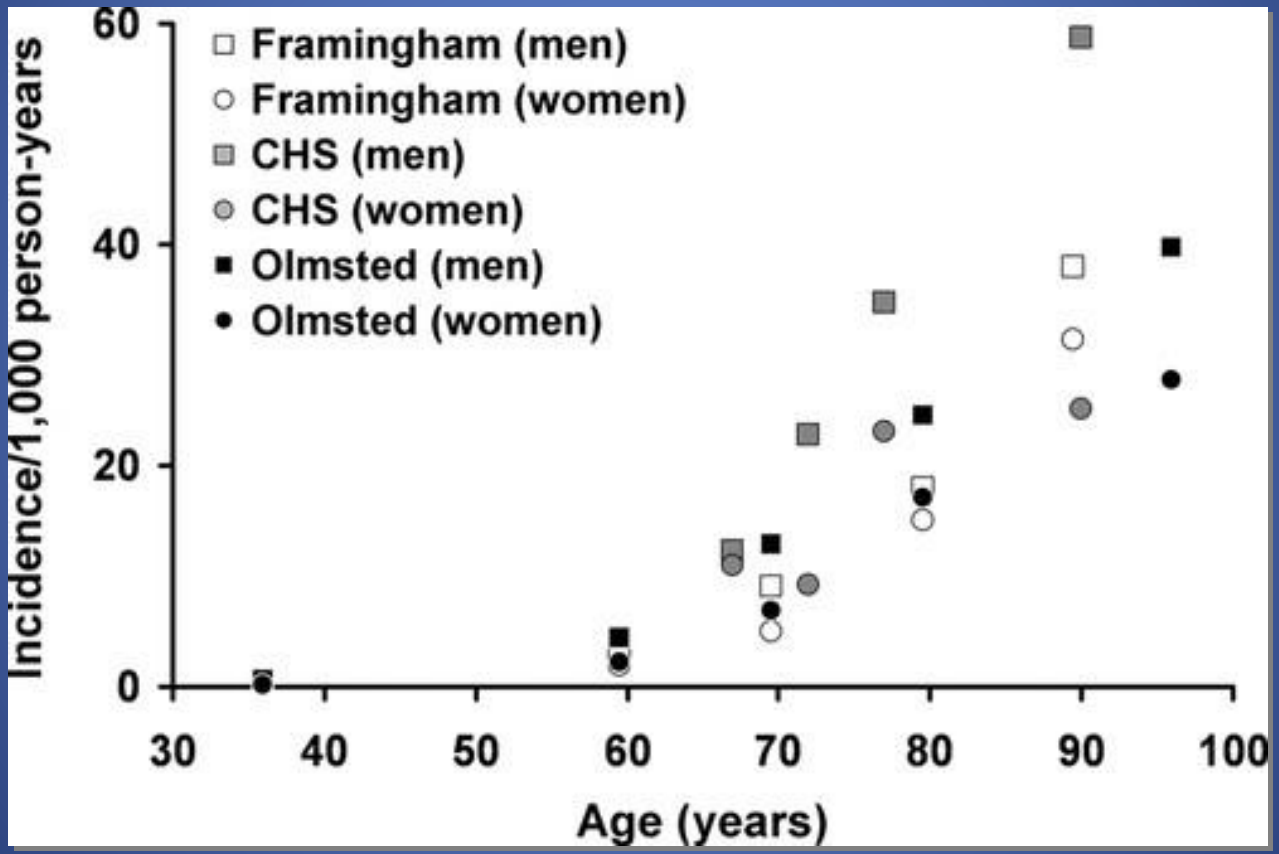


Valvular heart disease



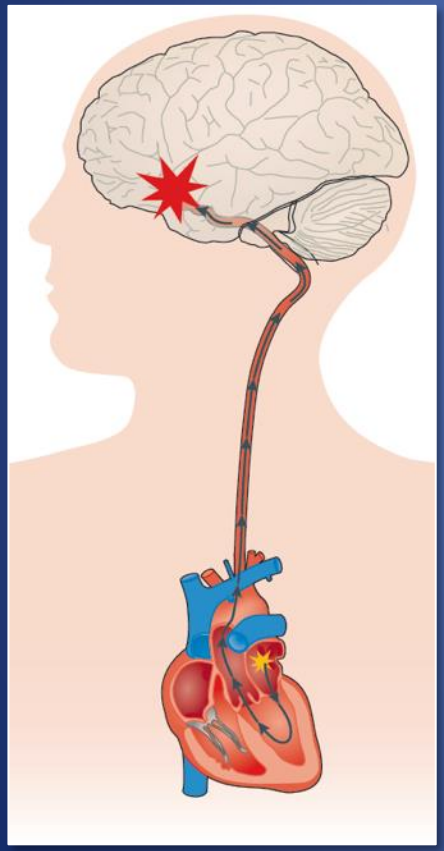
Atrial fibrillation

Atrial fibrillation and age



Miyasaka et al, 2006

Stroke



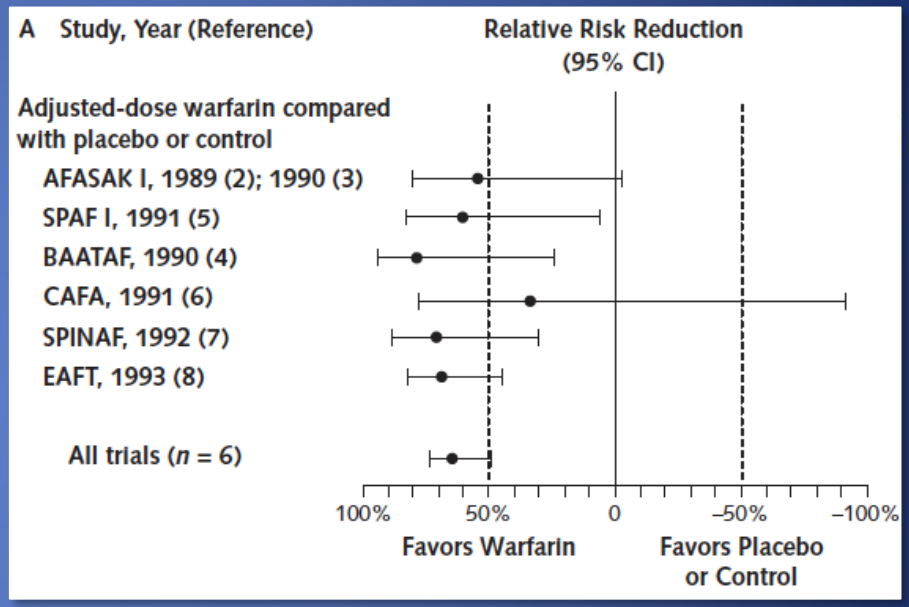
	Estimates	95% CI	*p*
Association of AF compared to no AF with each outcome among all AIS patients			
Mortality,[a] OR	1.93	1.89–1.98	<0.001
Cost, $[b]	2310.20	2226.19 to 2394.22	<0.001
Length of stay, d[b]	1.13	1.10–1.16	<0.001

McGrath et al, 2013

Vit K antagonist

- Inexpensive
- Antidote
- Confirmation of anticoagulation

- Monitoring requirements
- Drug and food interactions
- Compliance
- Time in therapeutic range



Hart et al, 2007

Risk

Table 1. CHA_2DS_2-VASC score.

Stroke risk factors	Score
Congestive heart failure/left ventricular dysfunction	1
Hypertension	1
Age ≥ 75 years	2
Diabetes mellitus	1
Stroke	2
Vascular disease	1
Age 65–74 years	1
Sex (female sex)	1

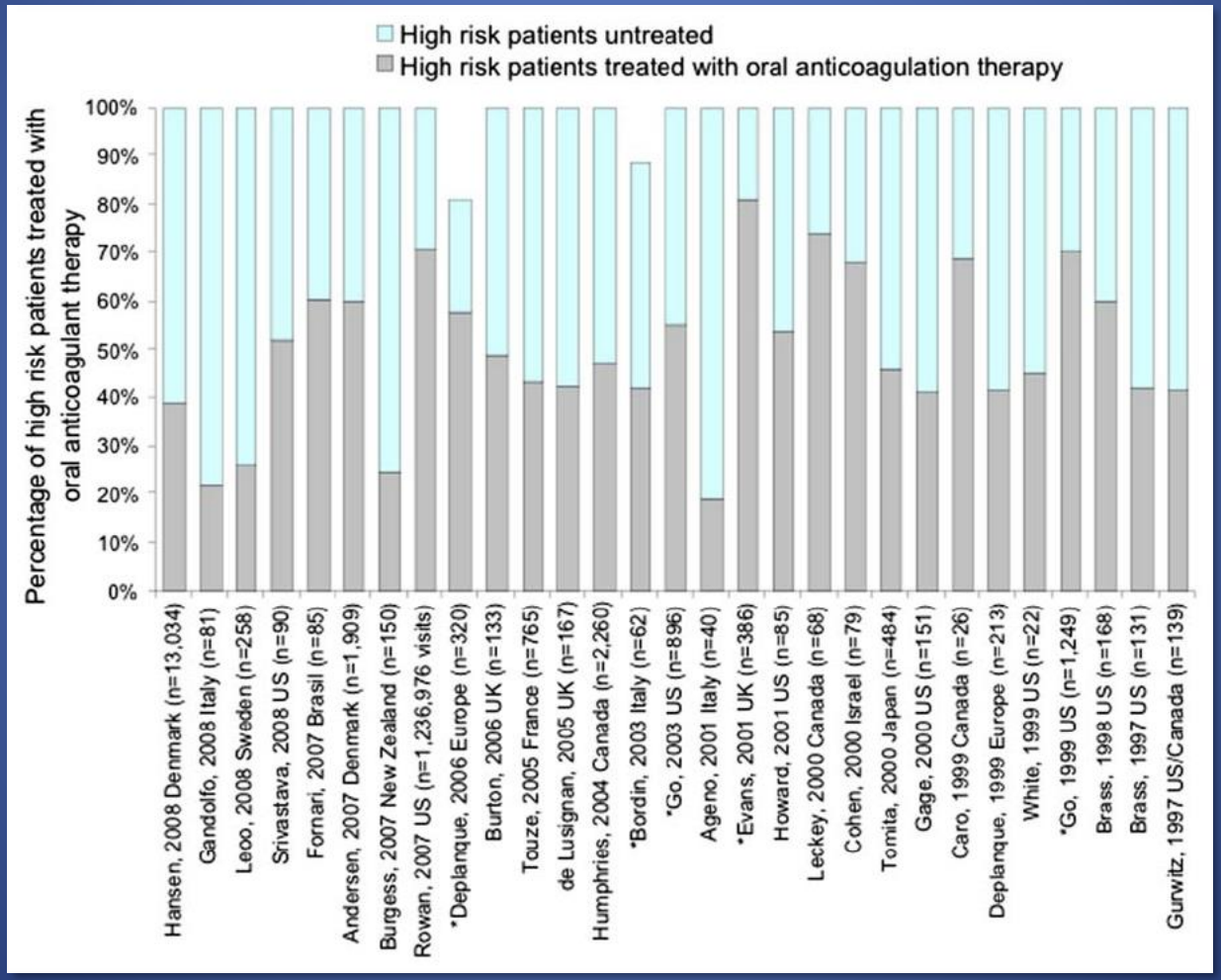
Table 2. HASBLED score.

Letter	Clinical characteristic	Points
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly	1
D	Drugs or alcohol (1 point each)	1 or 2

INR: international normalized ratio.

Modifiable risk factors?

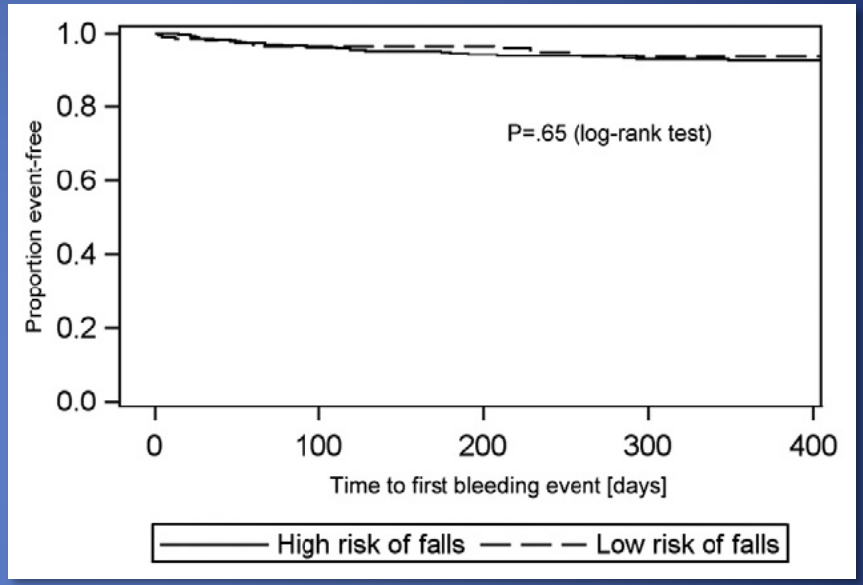
Underuse



Ogilvie et al, 2010

Underuse

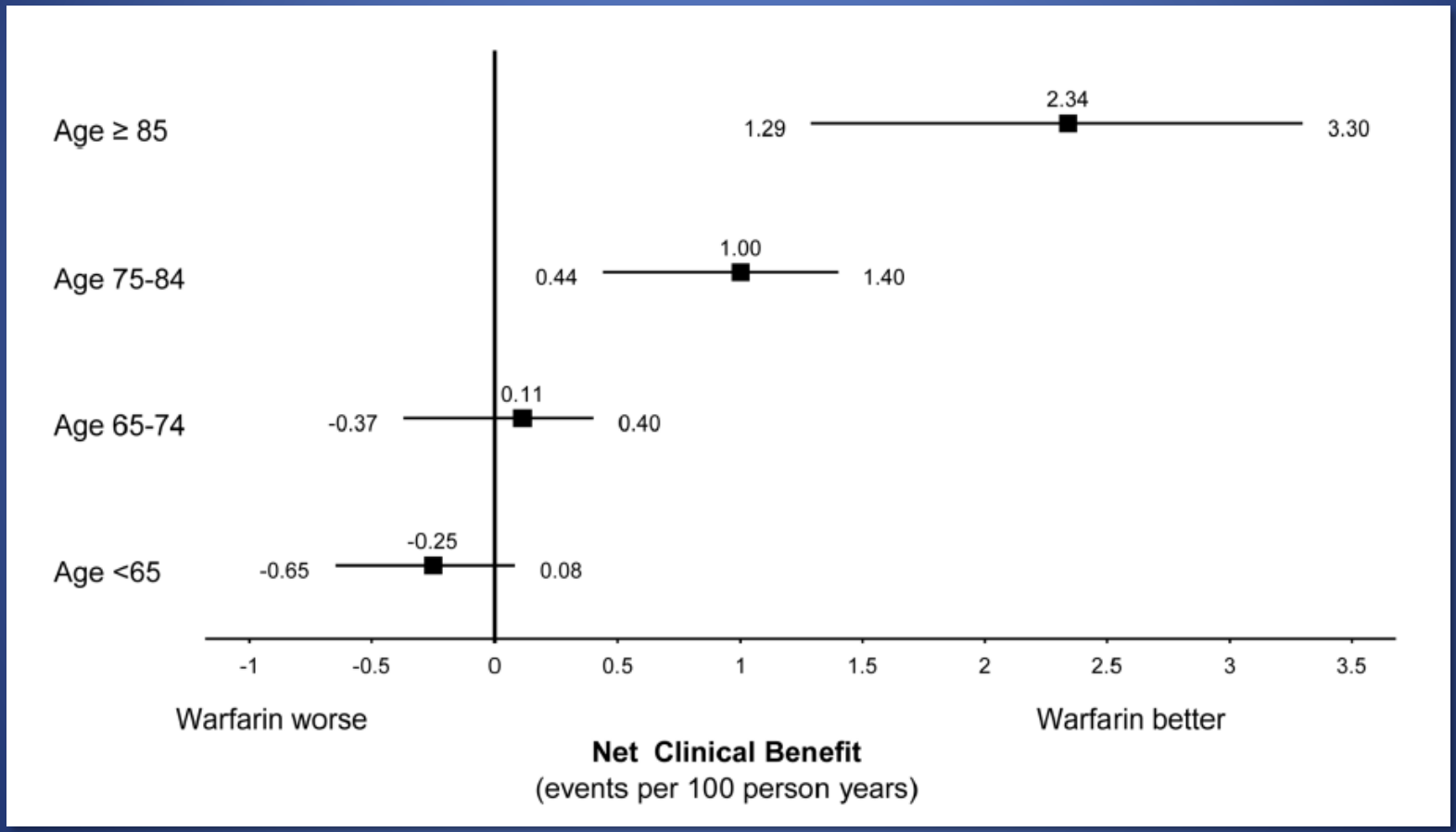
- risk of falls
- patient noncompliance
- bleeding risk
- older age



a patient would need to fall approximately
300 times
in one year for the risk of increased intracranial hemorrhage to outweigh the benefits of anticoagulation

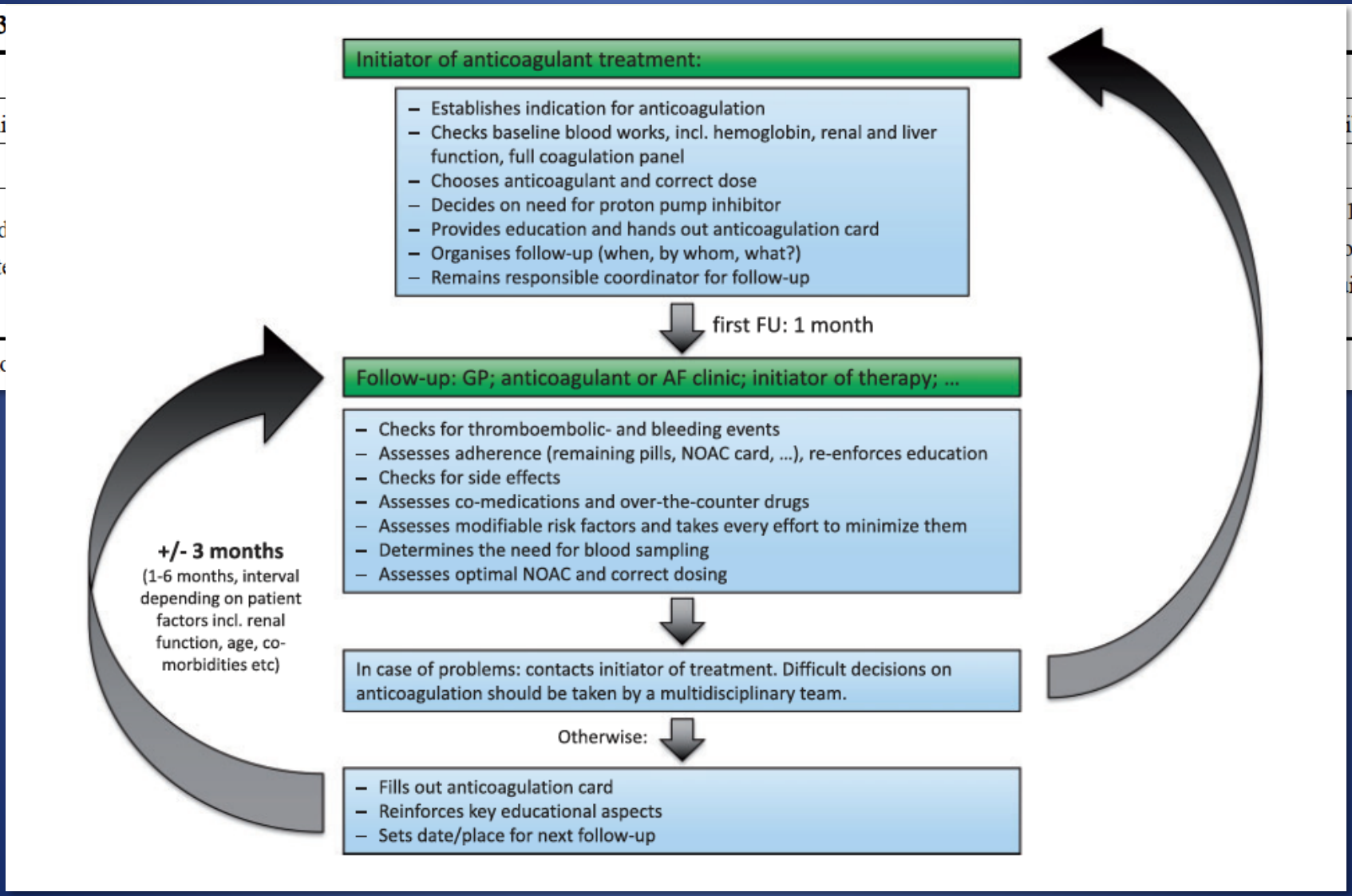
Donzé et al, 2012; Gage et al, 2010

Age



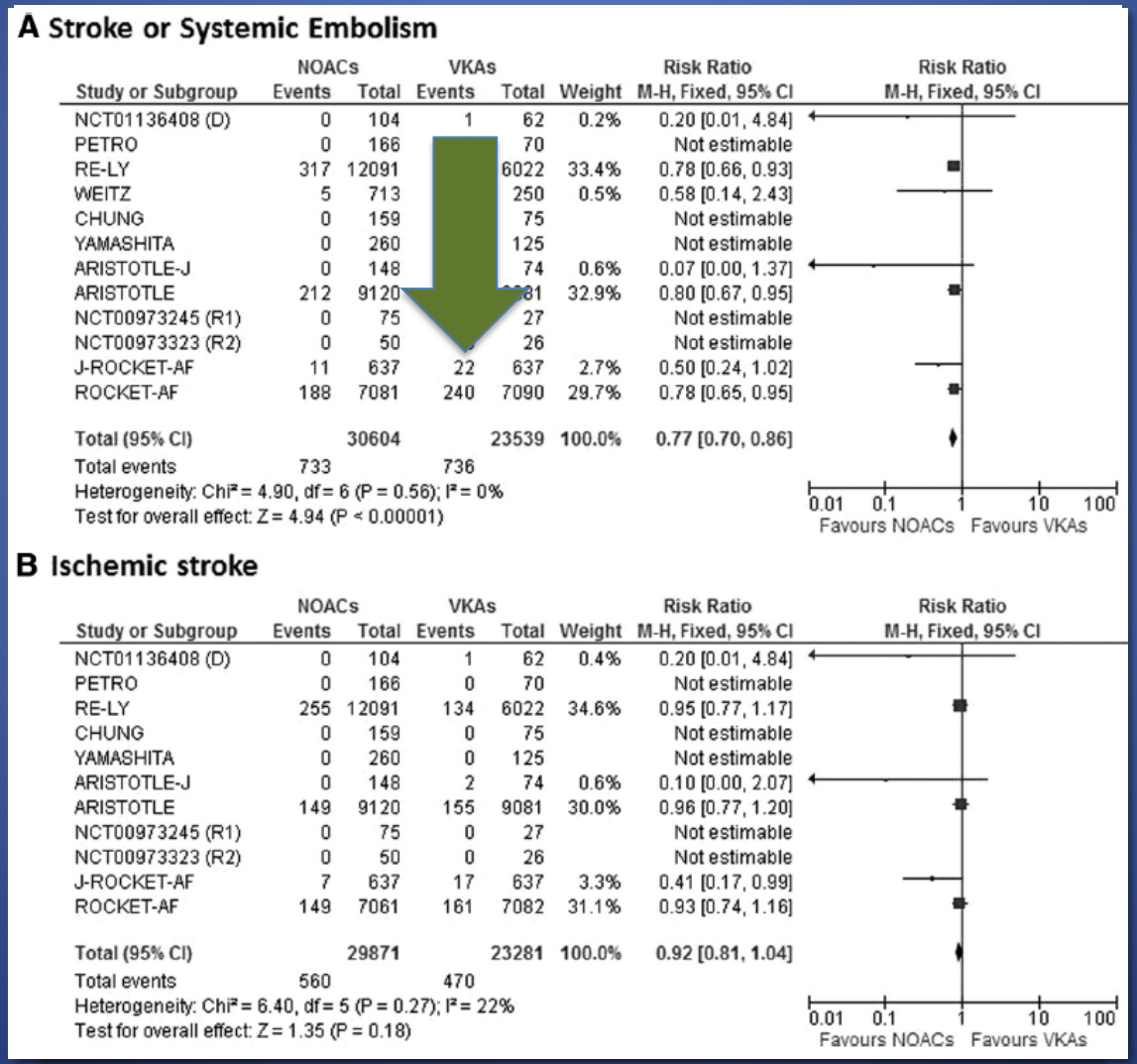
Singer et al, 2009

NOAC



Díez-Villanueva et al, 2019; Steffel et al, 2018

NOAC



Dentali et al, 2012

Era with NOACs (Year 2012 - 2015)

Ischemic stroke	Hazard ratio (95% CI)	*P* value
Warfarin	Reference	-
NOACs		0.900
		0.905
		0.654
ICH		
Warfarin		-
NOACs		0.038
		0.046
		0.044
Major blee		
Warfarin		-
NOACs		0.455
Adjusted model[+]	0.88 (0.58 - 1.32)	0.536
Competing risk[#]	0.95 (0.63 - 1.44)	0.866

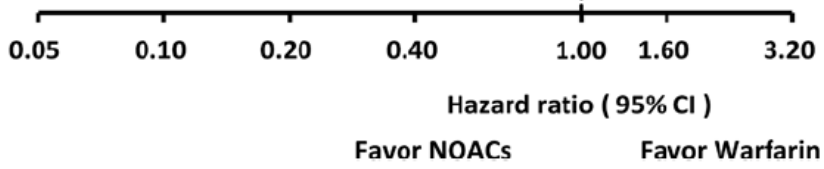
CORRECTED PROOF

Safety and efficacy of non-vitamin K antagonist oral anticoagulants in elderly patients with atrial fibrillation: systematic review and meta-analysis of 22 studies and 440 281 patients

Angelo Silverio, Marco Di Maio, Costantina Prota, Elena De Angelis, Ilaria Radano, Rodolfo Citro, Albino Carrizzo, Michele Ciccarelli, Carmine Vecchione, Davide Capodanno, Gennaro Galasso ✉

European Heart Journal - Cardiovascular Pharmacotherapy, pvz073, https://doi.org/10.1093/ehjcvp/pvz073

Published: 12 December 2019 **Article history** ▾



Chao et al, 2018, Silverio et al, 2019

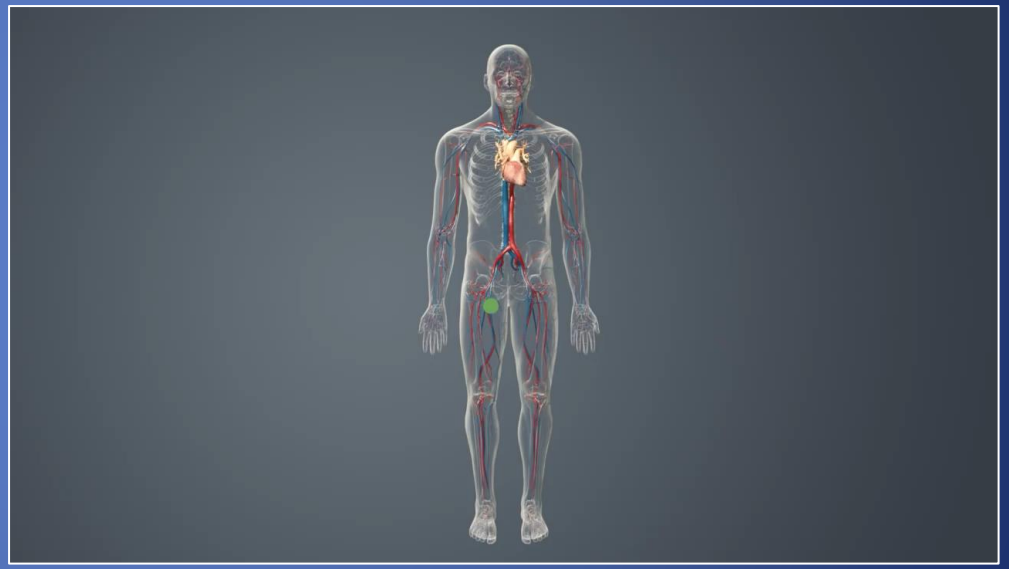
Contraindication to OAC

Table 1
Relative contraindications for anticoagulation (indications for left atrial appendage closure referral)

System	Relative Contraindication to Long-Term OAC or DOAC
Gastrointestinal	• History of gastric antral venous ectasia • History of arteriovenous malformations • Gastrointestinal bleeding requiring transfusion (major when >4 U PRBC required) • Ulcerative disease, ulcerative colitis, Crohn disease • Diverticular disease causing recurrent lower gastrointestinal bleeding
Hepatic	• Cirrhosis • Labile INR due to liver dysfunction in patient on warfarin • Thrombocytopenia related to cirrhosis • Persistent atrial fibrillation in cirrhosis
Chronic renal disease	• CKD III-V due to unfavorable metabolism of novel oral anticoagulants • ESRD on hemodialysis • Patients following renal transplant (drug interactions and frequent renal biopsies)
Hematologic	• Treatment with ibrutinib • Von Willebrand's disorder with frequent bleeding events • Hemorrhagic hereditary telangiectasias (Osler Weber Rendu) • Immune thrombocytopenic purpura • Chronic anemias with transfusion requirements
Neurologic	• History of Parkinson disease • Previous stroke with significant disability, related fall risks • Frequent falls (related to tremor, previous stroke, peripheral neuropathy, autonomic neuropathy) • Seizure disorders
Frailty	• Frequent falls • Unstable gait • Drug metabolism issues (age related) • Unable to maintain reliable NOAC adherence
Lifestyle considerations	• High-risk occupations (law enforcement, paratrooper, roofing, high-voltage electrical line workers, firefighters)

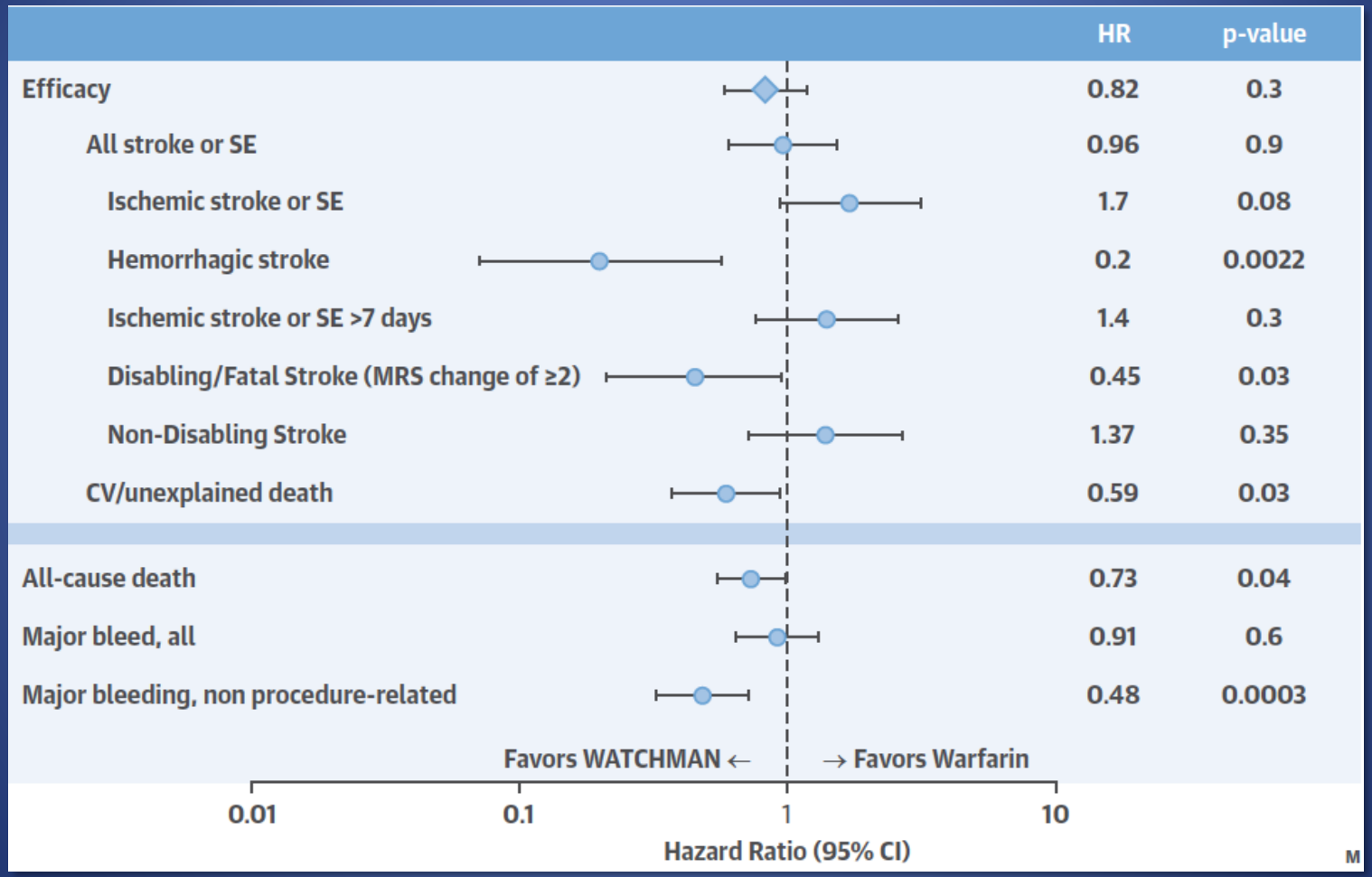
Abbreviations: CKD III–V, chronic kidney disease III–V; DOAC, direct oral anticoagulation; ESRD, end-stage renal disease; INR, international normalized ratio; OAC, oral anticoagulation; NOAC, new oral anticoagulant; PRBC, packed red blood cells.

LAA closure



Ellis et al, 2019

Closure device vs Warfarin



Reddy et al, 2017

Complications

TABLE 4 LAAC Device- or Procedure-Related Complications

	Early (≤7 Days) Occurrence	Late (>7 Days) Occurrence	Total
Pericardial effusion	0	2*	2
Device embolization	1†	0	1
Device-related death	0	1‡	1
Procedure-related death	1‡	0	1
Vascular complications	2§	0	2
Other complications	0	2‖	2
Total	4	5	9

*Late pericardial effusions occurred at 89 and 194 days after implantation with the Amulet device. One was treated with pericardiocentesis and the other conservatively; both patients had good outcomes. †Acute device embolization during the procedure, requiring surgical removal. ‡See details in the Supplemental Appendix. §Includes 1 femoral pseudoaneurysm and 1 large groin hematoma, both treated with vascular surgery. ‖One device malposition at the left inferior pulmonary vein, with successful removal and reimplantation. One large device-related thrombus was diagnosed by TEE imaging 113 days after implantation. The thrombus was considered potentially malignant (although no embolic event had occurred), so surgical removal was successfully performed.

LAAC = left atrial appendage closure.

4,5%

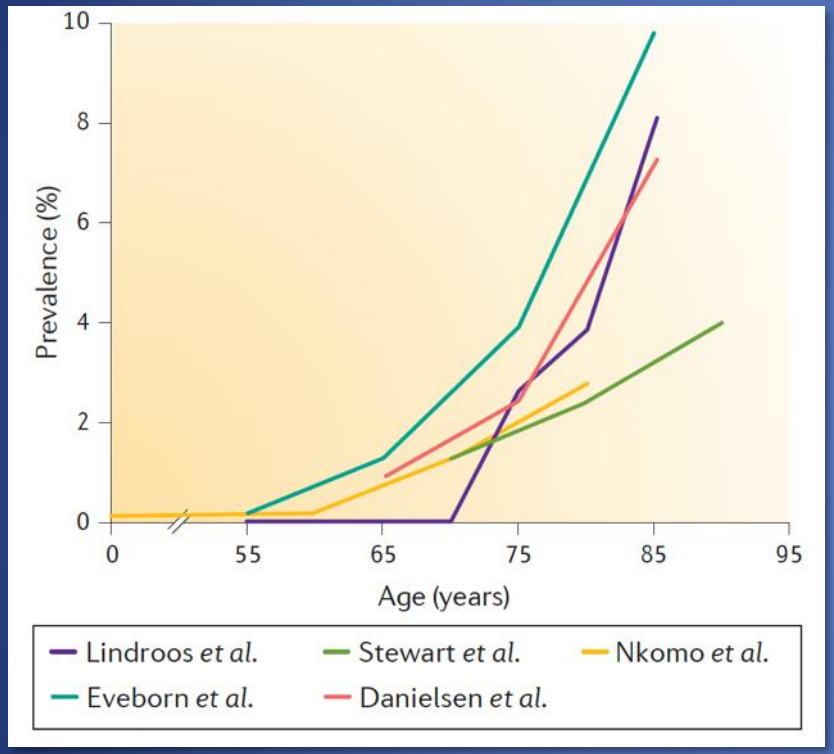
Osmancik et, 2020

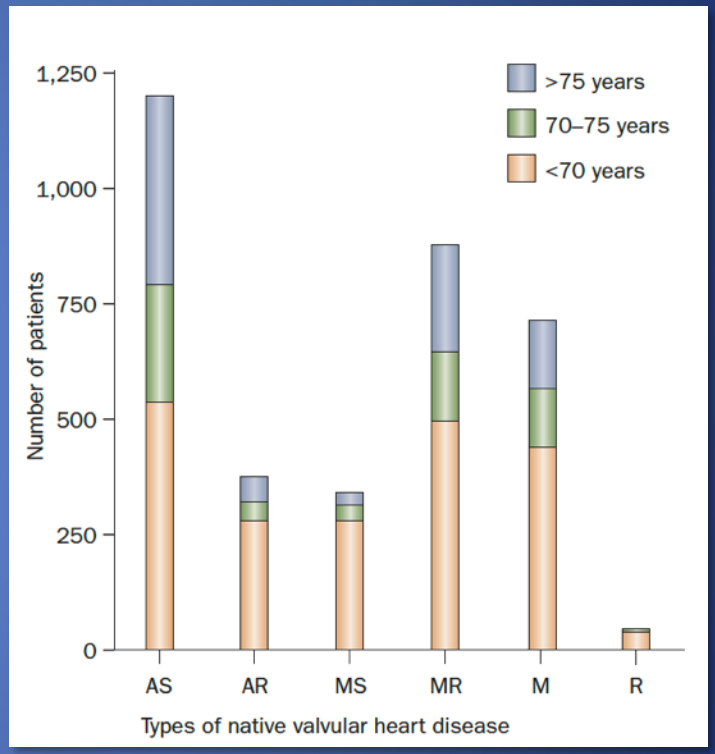
Conclusion

- Except when there is a high risk of bleeding, OACs are associated with a net clinical benefit, which increases with age in patients with AF
- In patients aged 75 years or older, compared with VKAs, the efficacy and safety of NOACs seem consistent with those pertaining to the overall population
- Regular assessment of patients on NOACs is essential
- In patients with a contraindication for OACs a closure device should be considered

Aortic stenosis

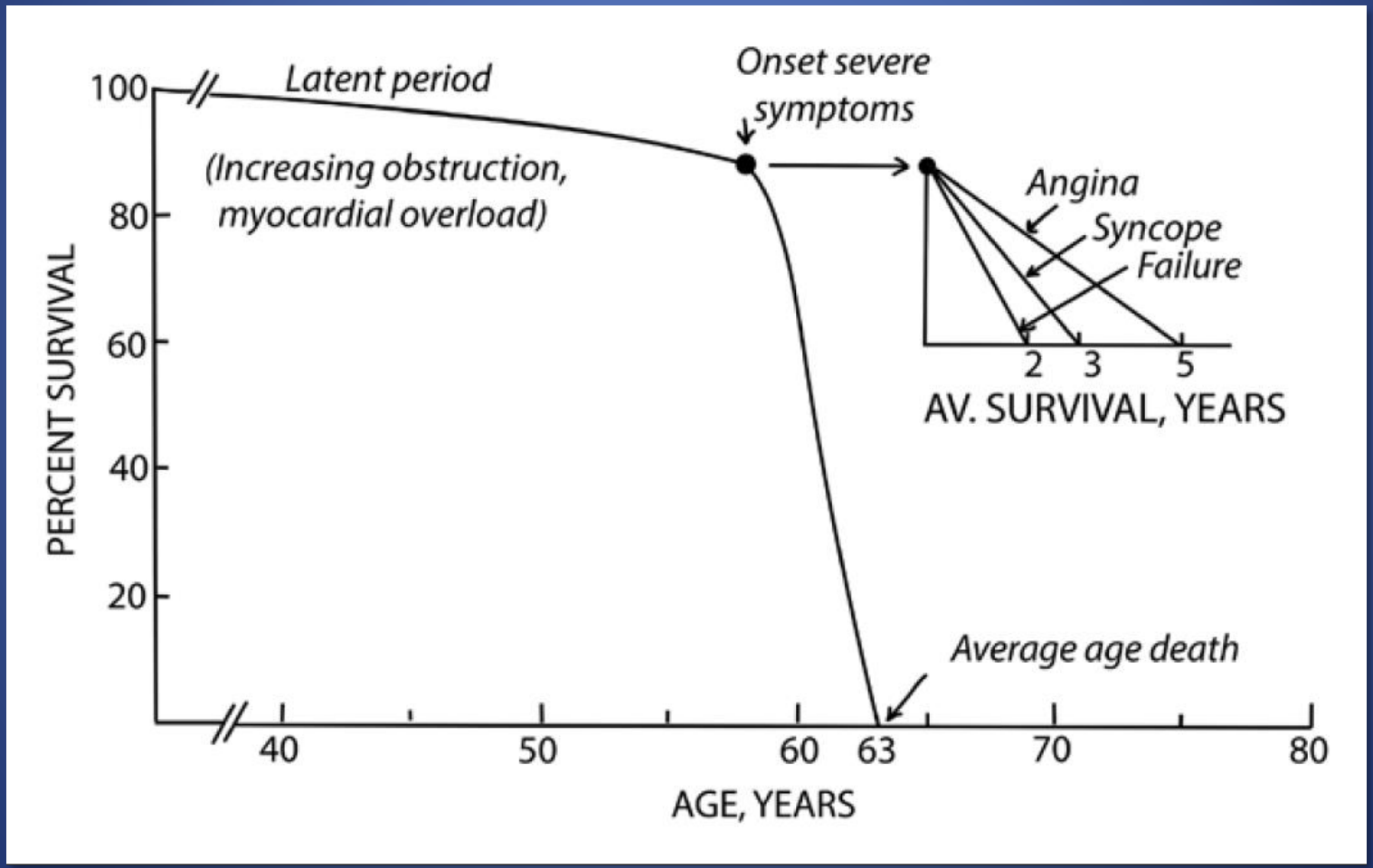
Aortic stenosis and age





Lindman et al, 2016; Lung et al, 2011

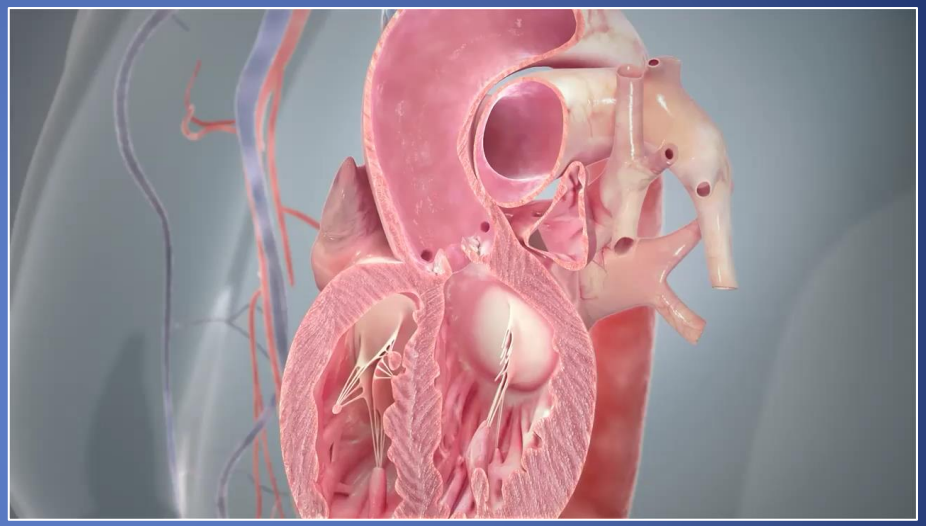
Aortic stenosis and prognosis



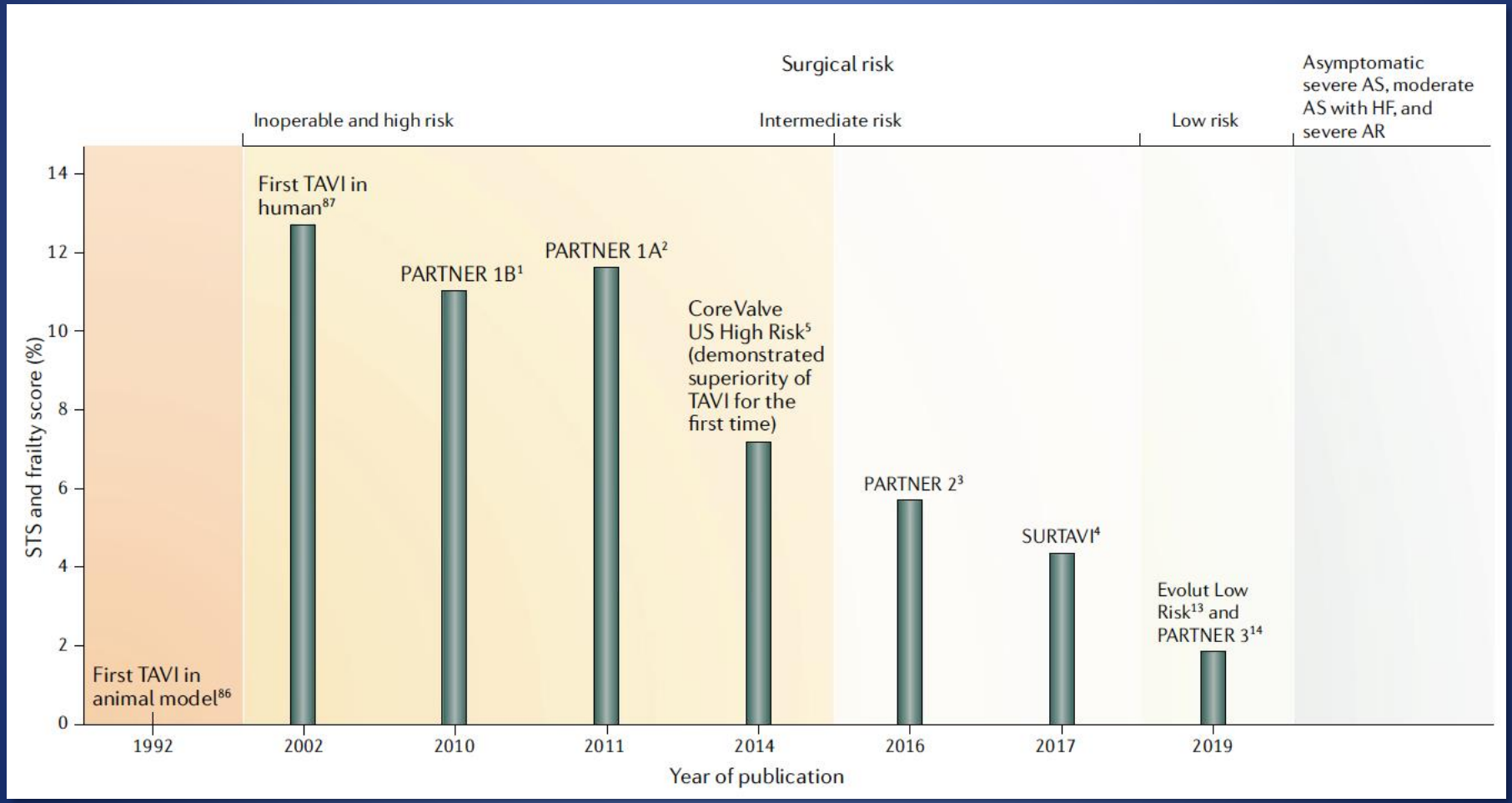
RossJ Jr et al, 1968

Therapy

- Medical therapy
- Balloon valvuloplasty
- Surgical aortic valve replacement (SAVR)
- Transcatheter aortic valve implantion (TAVI)



TAVI



Rahhab et al, 2019

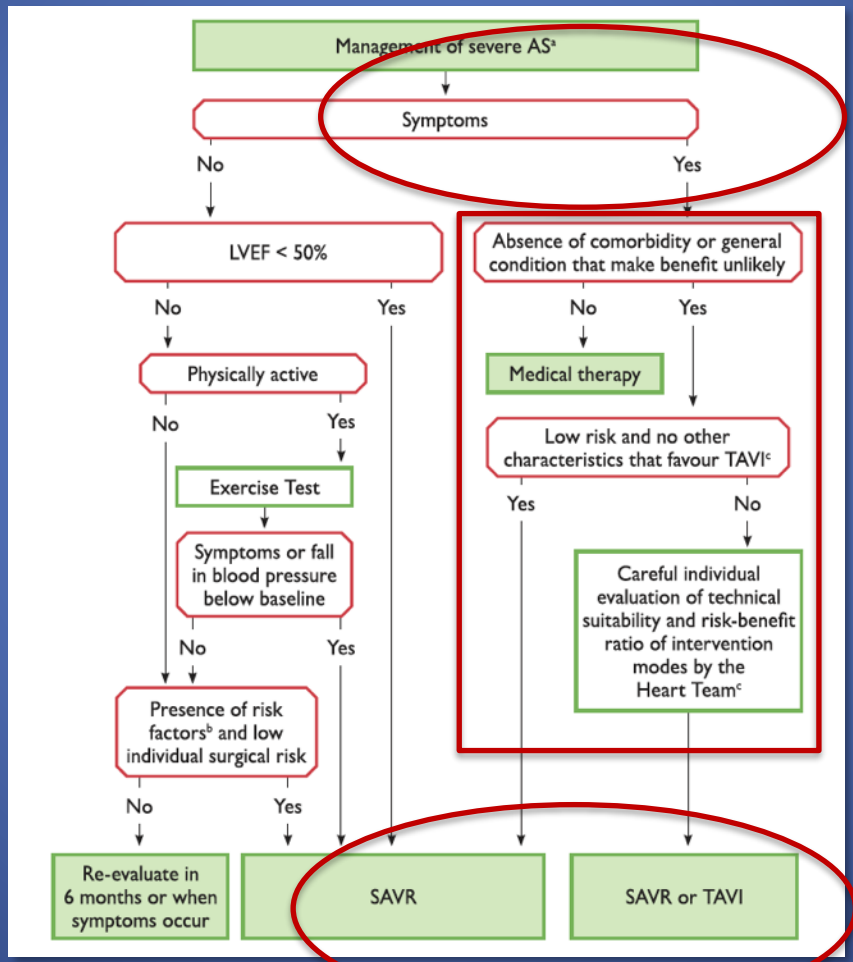
TAVI

Table 1 Major randomized clinical trials for transcatheter aortic valve replacement (TAVR)

Clinical trial	Publication year	Surgical risk	Type of valve	Number of patients	Main result
PARTNER 1B (23)	2010	Inoperable/extreme risk	Balloon-expandable (SAPIEN)	358	TAVR better than medical therapy
CoreValve Extreme Risk Pivotal Trial (24)	2014	Extreme risk	Self-expandable (CoreValve)	506	TAVR better than medical therapy
PARTNER 1A (25)	2011	High risk	Balloon-expandable (SAPIEN)	699	TAVR similar to SAVR
U.S. CoreValve High Risk Pivotal Study (26)	2014	High risk	Self-expandable (CoreValve)	795	TAVR better than SAVR
PARTNER 2A (27)	2016	Intermediate risk	Balloon-expandable (Sapien XT)	2,032	TAVR similar to SAVR
SURTAVI (28)	2017	Intermediate risk	Self-expandable (CoreValve and Evolut R)	1,746	TAVR similar to SAVR
NOTION (29)	2015	All comers (81,8% low risk)	Self-expandable (CoreValve)	280	TAVR similar to SAVR
PARTNER 3 (30)	2019	Low risk	Balloon-expandable (Sapien 3)	1,000	TAVR better than SAVR
Low Risk Evolut (31)	2019	Low risk	Self-expandable (CoreValve, Evolut R, or Evolut PRO)	1,468	TAVR similar to SAVR

Mas-Peiro et al, 2020

Guidelines



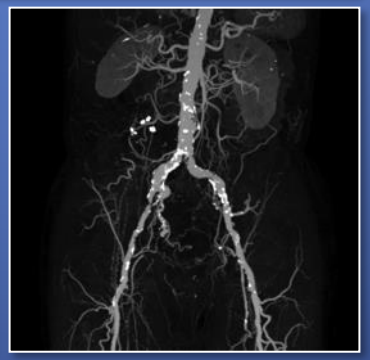
Baumgartner et al, 2017

Guidelines

	Favours TAVI	Favours SAVR
Clinical characteristics		
STS/EuroSCORE II <4% (logistic EuroSCORE I <10%)[a]		+
STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)[a]	+	
Presence of severe comorbidity (not adequately reflected by scores)	+	
Age <75 years		+
Age ≥75 years	+	
Previous cardiac surgery	+	
Frailty[b]	+	
Restricted mobility and conditions that may affect the rehabilitation process after the procedure	+	
Suspicion of endocarditis		+

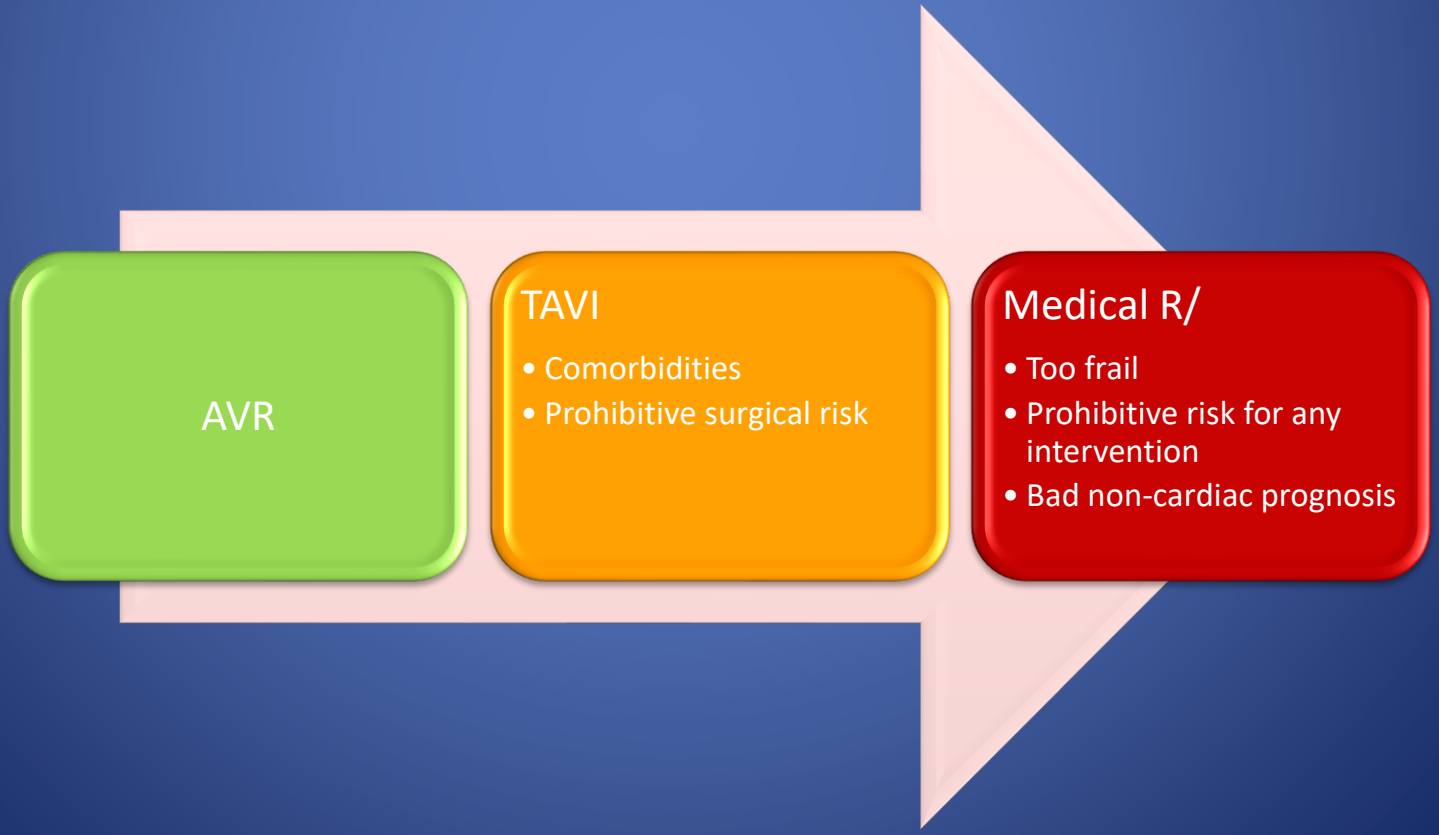
	Favours TAVI	Favours SAVR
Anatomical and technical aspects		
Favourable access for transfemoral TAVI	+	
Unfavourable access (any) for TAVI		+
Sequelae of chest radiation	+	
Porcelain aorta	+	
Presence of intact coronary bypass grafts at risk when sternotomy is performed	+	
Expected patient–prosthesis mismatch	+	
Severe chest deformation or scoliosis	+	
Short distance between coronary ostia and aortic valve annulus		+
Size of aortic valve annulus out of range for TAVI		+
Aortic root morphology unfavourable for TAVI		+
Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI		+
Presence of thrombi in aorta or LV		+

	Favours TAVI	Favours SAVR
Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention		
Severe CAD requiring revascularization by CABG		+
Severe primary mitral valve disease, which could be treated surgically		+
Severe tricuspid valve disease		+
Aneurysm of the ascending aorta		+
Septal hypertrophy requiring myectomy		+



Heart team

surgeon, interventional cardiologist, referral cardiologist, general practicioner, geriatrician, organ specialist, …



Patient refused for AVR and potential candidate for TAVI

- **1: is the aortic valve stenosis indeed severe?**
- **2: does the patient has symptoms?**
- **3: are the symptoms of the patient mainly related to the aortic valve stenosis?**
- **4: what are patient life expectancy and expected quality of life?**
- **5: do the expected benefits of the intervention (versus spontaneous outcome) outweigh its actual risks?**
- **6: what are the patient's wishes?**

Frailty

Fried index

Exhaustion	Self-report of “moderate or most of the time” for either of two questions: - I felt that everything I did was an effort in the last week - I could not get going in the last week	
Weakness	Low grip strength if: Men ≤29 kg for BMI ≤24 ≤30 kg for BMI 24.1–26 ≤30 kg for BMI 26.1–28 ≤32 kg for BMI >28	Women ≤17 kg for BMI ≤23 ≤17.3 kg for BMI 23.1–26 ≤18 kg for BMI 26.1–29 ≤21 kg for BMI >29
Slowness	Slow gait speed to walk 4,57 m if: Men ≥7 s for height ≤173 cm ≥6 s for height >173 cm	Women ≥7 s for height ≤159cm ≥6 s for height >159cm
Low activity level	≤270 kcal of physical expenditure on activity scale per week	
Loss of weight	> 3 kg weight loss during the last three months	

FRAIL scale

Fatigue	How much time during the past 4 weeks you felt tired? Most of the time or all of the time
Resistance	Any difficulty walking up 10 steps alone without help
Ambulation	Any problems with walking (<=5/10 on a scale of 0 (bedridden) to 10 (no problems))
Illness	Presence of 5 to 11 of the following illnesses: hypertension, diabetes, cancer, chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke and kidney disease
Loss of weight	> 3 kg weight loss during the last three months

Mortality

	Total population (n=119)	Non – Frail	Frail	P-value
Male	58 (48,7%)	28 (51,9%)	17 (44,7%)	,501
Age (yrs)	82 (77-87)	82 (75-86)	84 (80-88)	,480
Length (m)	1,65 ± 0,08	1,65 ± 0,08	1,65 ± 0,09	,854
Weight (kg)	73,5 ± 14,6	74,5 ± 15,5	73,6 ± 12,9	,770
BSA (m^2)	1,83 ± 0,20	1,84 ± 0,22	1,83 ± 0,18	,845
BMI (kg/m^2)	27,01 ± 4,70	27,35 ± 4,50	27,11 ± 4,79	,810
Mean gradiënt (mmHg)	39 ± 15	37 (30-52)	36 (28-51)	,670
AVA (cm^2)	0,70 ± 0,20	0,69 (0,53-0,80)	0,66 (0,54-0,78)	,810
Ejection fraction (%)	62,8 (50,5-68,0)	59,5 (45,0-67,8)	63,7 (48,6-70,6)	,870
Logistic EuroScore (%)	14,7 (9,5-24,0)	12,0 (9,0-24,5)	15,1 (12,0-23,5)	,228
EuroScore II (%)	4,7 (2,7-8,8)	4,6 (2,7-7,4)	5,3 (2,8-9,8)	,265
STS-Score (%)	4,2 (3,0-5,8)	3,7 (2,5-4,6)	4,5 (3,1-7,4)	,020
Mortality after TAVI				
30 day	**2 (1,7%)**	**0 (0,0%)**	**3 (7,9%)**	**,067**
6 months	**6 (6,1%)**	**1 (2,1%)**	**5 (15,6%)**	**,035**
1 year	**10 (15,4%)**	**3 (8,3%)**	**7 (33,3%)**	**,028**

Quality of life

	Improvement in QOL	N	No Improvement in QOL	N	P
Age (years)	80 ± 7	40	81 ± 7	26	0.594
Gender (male)	23 (57.5)	40	10 (38.5)	26	0.131
Body Mass Index (kg/m^2)	26.3 ± 4.4	40	26.4 ± 4.7	26	0.929
Aortic Valve area (cm^2)	0.63 ± 0.24	24	0.66 ± 0.11	17	0.634
Logistic EuroSCORE (%)	14.9 (9.8-20.9)	40	15.3 (9.8-23.5)	26	0.803
STS-score (%)	4.2 (3.2-5.4)	40	4.8 (3.2-8.1)	26	0.147

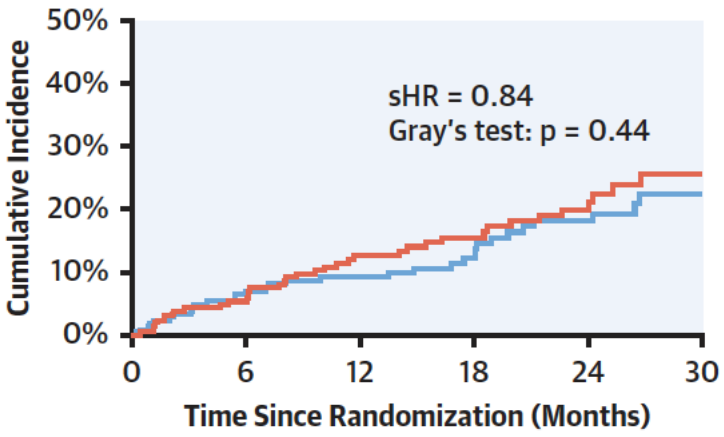
Quality of life

	Improvement in QOL	N	No Improvement in QOL	N	P
Dependence					
Katz independent	31 (77.5)	40	16 (61.5)	26	0.162
Cognition and depression					
Mini-Mental State Exam	28 (27-29)	27	28 (26-29)	18	0.612
Geriatric depression scale ≥5	6 (15.0)	40	6 (23.1)	26	0.571*
Nutrition					
Mini nutritional assessment	24.0 (22.0-25.0)	35	23 (20.3-24.5)	24	0.108
Function					
Six-Minute Walking test (m)	297 (250-360)	29	250 (116-300)	11	0.087
Grip strength (kg)	21.1 (16.7-30.8)	38	16.6 (12.4-18.0)	21	0.002
Frailty					
Fried-criteria	18.4%	38	47.1%	17	0.047

Conclusion

- TAVI is indicated in patients
  - with severe symptomatic AS
  - who are not suitable for surgical AVR
  - who are likely to gain improvement in their quality of life
  - who have life expentancy of at least 1 yr
- A multidisciplinary assessment is crucial for an optimal patient selection.

Closure device vs NOAC



No. at Risk*

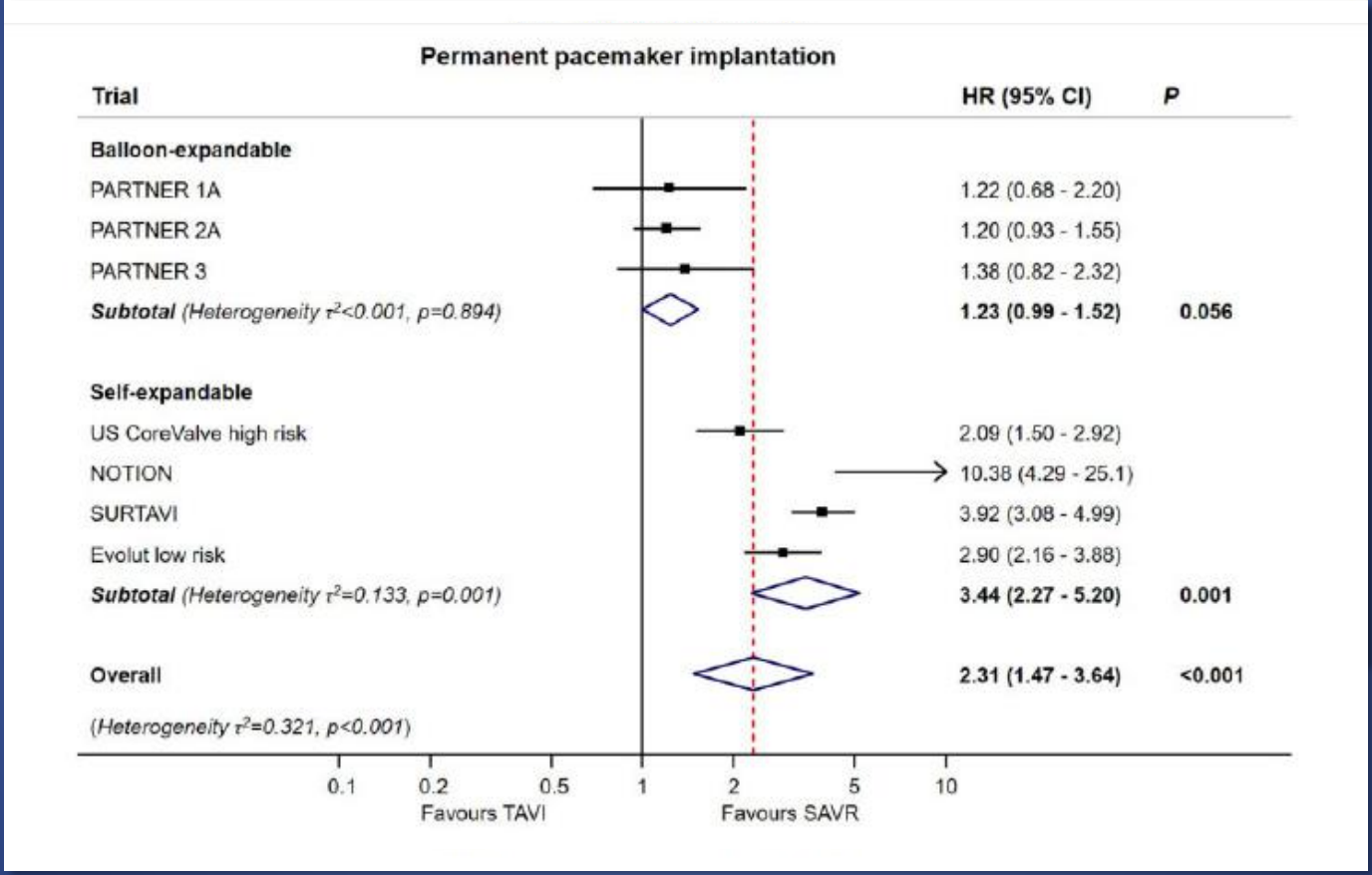
LAAC	201 (0)	178 (1)	144 (3)	107 (6)	74 (6)	41 (7)
DOAC	201 (0)	181 (0)	136 (1)	102 (2)	67 (4)	32 (4)

	Primary Endpoint – CIF (95% CI)				
	6M	12M	18M	24M	30M
LAAC	7.0% (3.5% to 10.6%)	9.4% (5.2% to 13.5%)	12.3% (7.4% to 17.2%)	18.4% (12.0% to 24.7%)	22.5% (14.9% to 30.2%)
DOAC	5.5% (2.3% to 8.6%)	12.7% (7.9% to 17.5%)	15.6% (10.2% to 21.0%)	20.1% (13.7% to 26.5%)	25.6% (17.6% to 33.6%)

	sHR (95% CI)	p value
Primary Endpoint		
mITT	0.84 (0.53-1.31)	0.44
Per Protocol	0.82 (0.52-1.30)	0.40
On-Treatment	0.79 (0.49-1.25)	0.31
All-Stroke/TIA	1.00 (0.40-2.51)	0.99
CV Death	0.75 (0.34-1.62)	0.46
Major + NMCR Bleeding		
All	0.81 (0.44-1.52)	0.51
Nonprocedural	0.53 (0.26-1.06)	0.07

Osmancik et, 2020

TAVI



Siontis et al, 2019