Atrial fibrillation: not just an arrhythmia

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René Laënnec lecture
ESC Paris 2019

Disclosures

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- Travel support BMS

Vraag 1

Waar bent u het MINST in geinteresseerd bij patienten met hypertensie ?

1. Bloeddruk
2. Hartkloppingen
3. Gewicht
4. Verandering in inspanningsniveau

AF is not just an arrhythmia

- AF is a wake up call
- AF almost never comes alone
- AF is a progressive disease
- AF is a complex disease, treatment thus not simple

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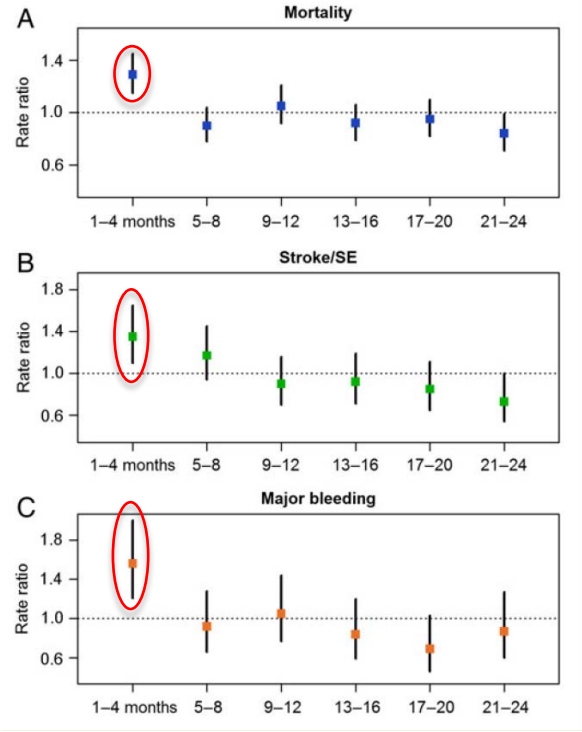
AF is a wake up call !

- It often starts with symptoms of palpitations, impaired exercise tolerance and fatigue
- It is your wake up call ! Not an alarm, AF is not immediately life-threatening
- Just a sign that something is going on: AF is not benign

- 17.162 outpatient dept AF pts 2010-2013
- Prospective registry
- 858 sites; 30 countries
- 2 year FU in 97%
- Age 70 yrs, 44% female
- CHA_2DS_2-VASc 3.3
- New onset AF in 46%

Events early after start AF



Bassand for the GARFIELD Investigators Eur Heart J 2016

AF is a wake up call !

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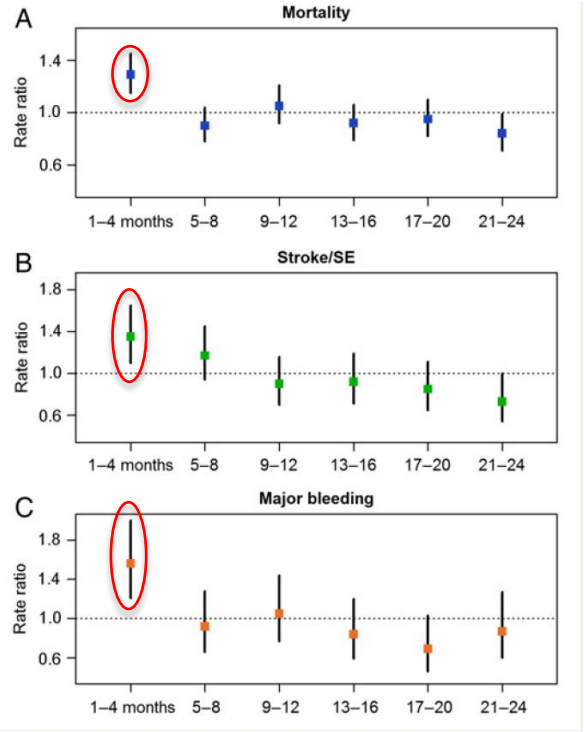
Table 2 **Event rates (per 100 person-years) for selected clinical outcomes at 2 years of follow-up[a]**

	Rate (95% CI)
Death	3.83 (3.62; 4.05)
Cardiovascular death	1.55 (1.42; 1.70)
Non-cardiovascular death	1.37 (1.25; 1.51)
Undetermined cause	0.91 (0.81; 1.02)
Stroke/SE	1.25 (1.13; 1.38)
Major bleeding	0.70 (0.62; 0.81)
Acute coronary syndromes	0.63 (0.55; 0.73)
Congestive heart failure[b]	2.41 (2.24; 2.59)



Bassand for the GARFIELD Investigators Eur Heart J 2016

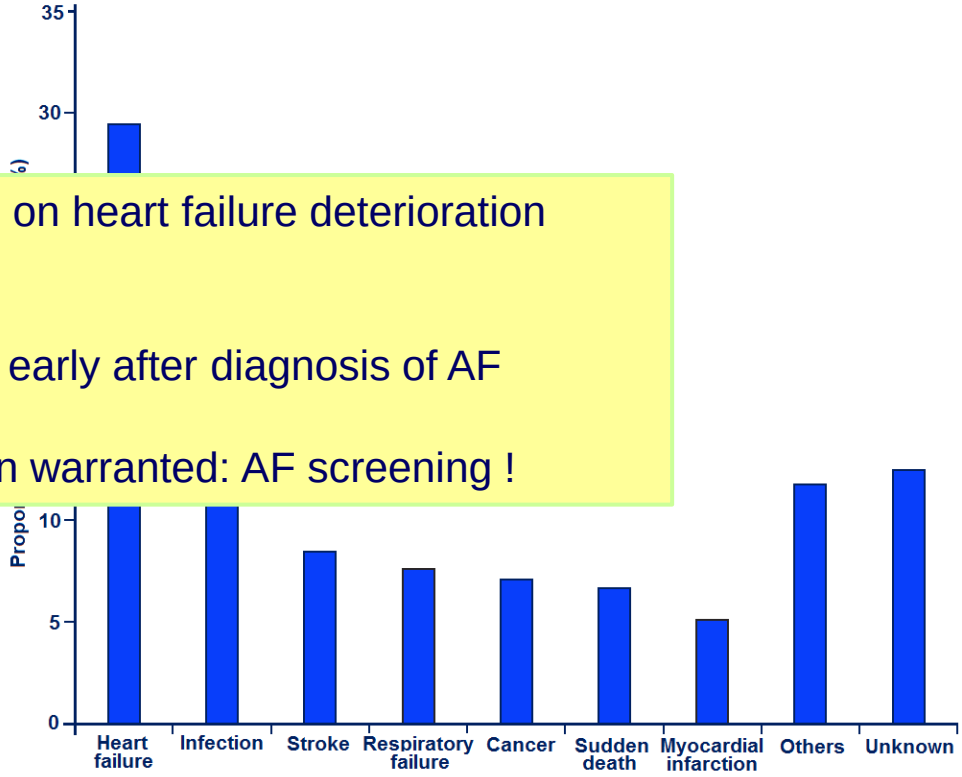
Causes of death in RE-LY AF registry

- RE-LY AF registry
- 15.400 patients
- AF at emergency department
- 47 countries
- Follow-up 1
- Age 65.9 yr
- 1758 (11%)
- Due to heart failure in 519: 30%

Focus now also on heart failure deterioration

Events occur early after diagnosis of AF

Early detection warranted: AF screening !



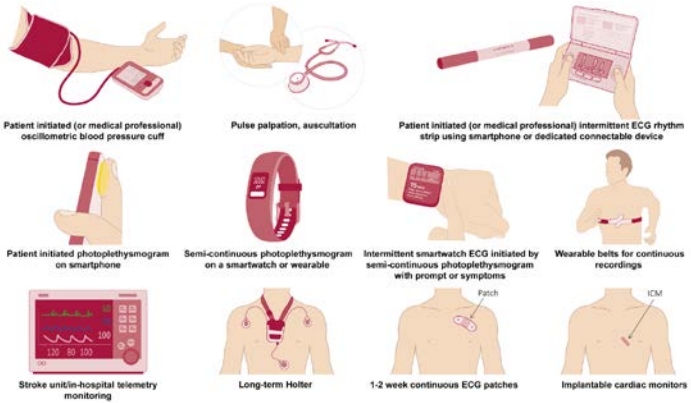
Healey et al. RELY-AF registry Lancet 2016

Relevance of AF screening

- AF may just start, without notifying you
- Or symptoms are ignored, neglected or not recognized
- All of the sudden:
  - Severe dyspnea due to heart failure
  - Neurological symptoms, stroke !

- Screening is recommended in high risk patients

Opportunistic screening for AF is recommended by pulse taking or ECG rhythm strip in patients >65 years of age.	I	B
In patients with TIA or ischaemic stroke, screening for AF is recommended by short-term ECG recording followed by continuous ECG monitoring for at least 72 hours.	I	B
It is recommended to interrogate pacemakers and ICDs on a regular basis for atrial high rate episodes (AHRE). Patients with AHRE should undergo further ECG monitoring to document AF before initiating AF therapy.	I	B



Selection of devices currently available for AF screening

Kirchhof et al. ESC guidelines Eur Heart J 2016; Schnabel, Freedman for AF screen consortium Circulation 2019 in press

Vraag 2

Wat is niet een bewezen risicofactor voor boezemfibrilleren ?

1. Hypertensie
2. M.Crohn
3. Glaucoom
4. Fysieke inactiviteit

AF is not just an arrhythmia

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- AF is a progressive disease
- AF is a complex disease, treatment thus not simple

Increasing list with risk factors for AF

Non-modifiable	Modifiable

- Advancing age
- Male gender
- Ethnicity
- Genetic background
- Height

Increasing list with risk factors for AF

Non-modifiable demographic factors

- Advancing age
- Male gender
- Ethnicity
- Genetic background
- Height

Modifiable

Others
- Air pollution
- Non CV surgery

Endothelial dysfunction
- Coronary artery disease
- Hypertension
- [illegible]h-normal blood pressure
- ([illegible]e-) diabetes mellitus
- High BMI, Obesity
- Physical inactivity
- Renal dysfunction/ CKD
- Smoking

Lone AF does hardly exist anymore in daily practice

Vagal and adrenergic stimuli
- Psychosocial stress
- Alcohol
- Caffeine
- Drugs

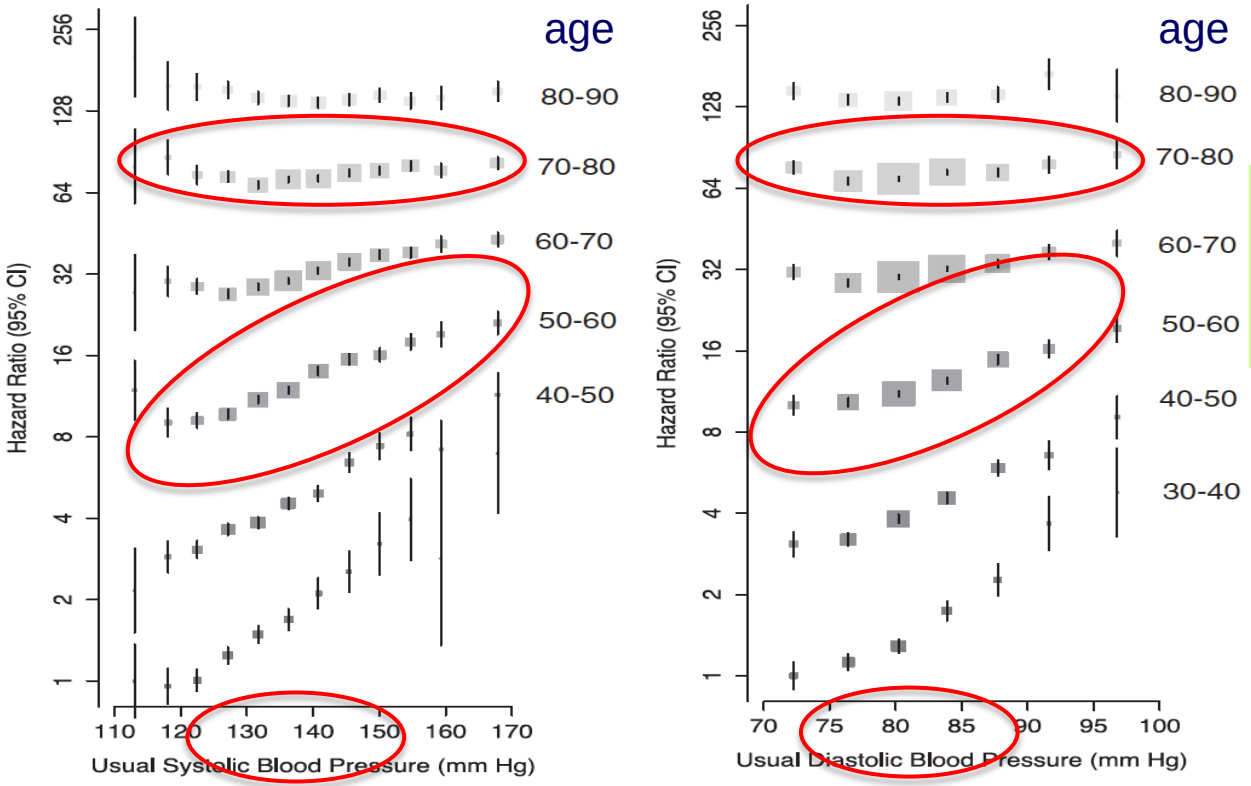
Inflammation
- CRP, IL-6, WBC
- Sepsis
- Inflammatory diseases

Atrial stretch
- HFpEF and HFrEF
- Valvular disease
- Excessive exercise
- Chronic obstructive pulmonary disease
- Obstructive sleep apnea syndrome
- (Subclinical) hyperthyroidism

Wyse JACC 2015

Role of hypertension for risk on AF

Primary care research database, UK population (87% white)
Linked with secondary care data and cause-specific mortality data
4.3 million adults, included at standard GP with 1 RR 1990-2013 FU 7 yrs



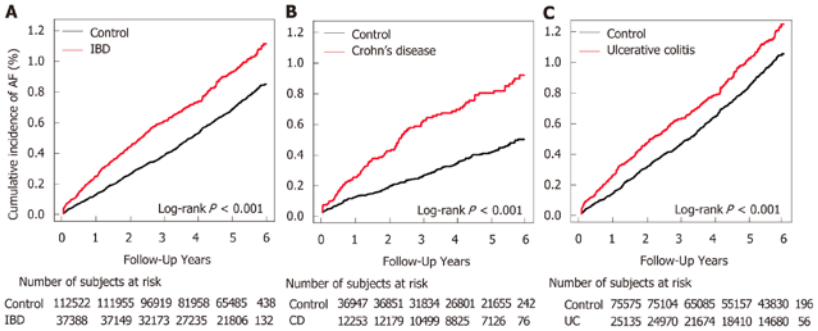
Even borderline elevated blood pressure of importance, also at younger age

HR relative to reference group:
30-40 yr
RR < 115 mmHg

Emdin Int J Epidemiol 2016

Role of inflammation

- Korean Population Cohort
- NHI database 2010-2014
- 37.696 pts with inflammatory bowel disease:
  - 12.349 M Crohn
  - 25.397 Ulcerative Colitis
- Compared with age- and sex matched cohort
- FU 4.9 years
- 36% increased risk new AF (95% CI 20-54%)



Choi et al from South Korea World J Gasteroenterology 2019

Vraag 3

Welke bewering is niet waar ?

1. Paroxysmaal boezemfibrilleren gaat bij < 10% van de patienten < 1 jaar over in permanent AF
2. Permanent boezemfibrilleren is geassocieerd met meer complicaties
3. Alleen door het boezemfilleren zelf is de ritmestoornis progressief en leidt BF to meer complicaties

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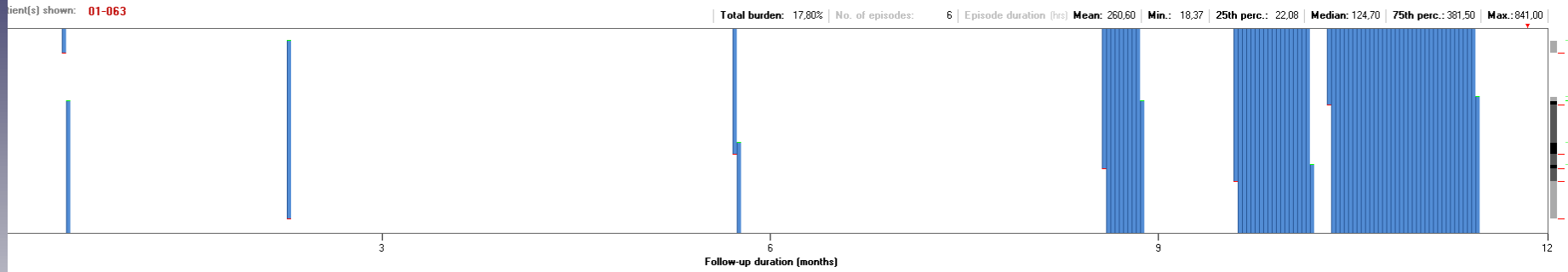
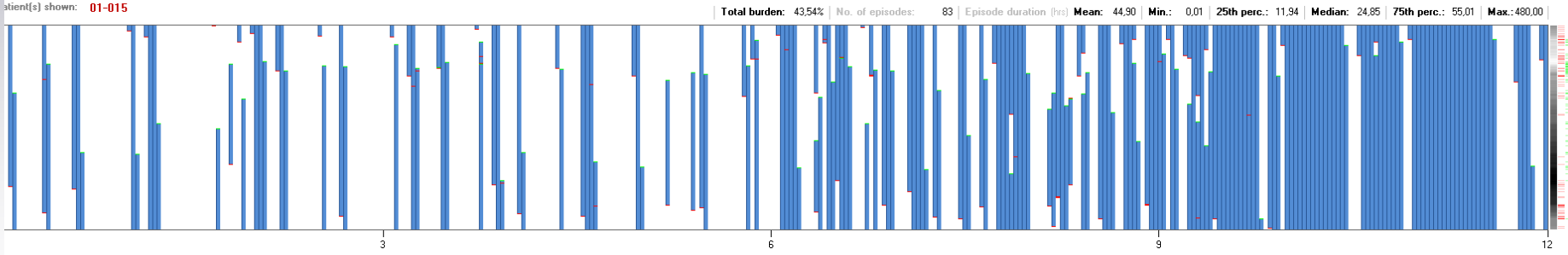
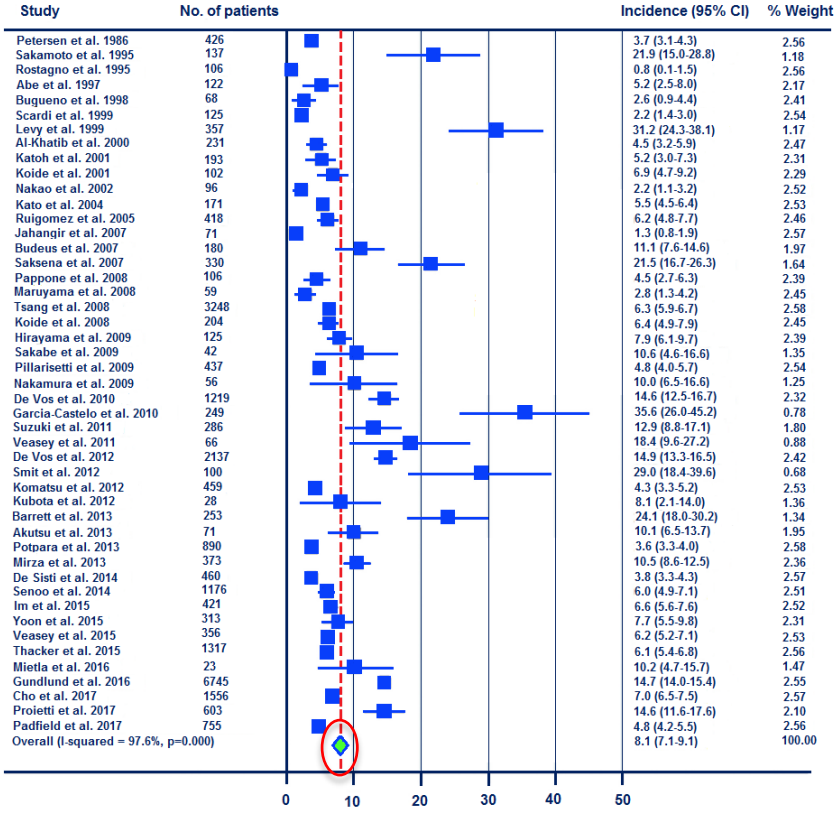
AF progression documented 12 months ILR





AF progression meta-analysis predictors



AF progression: 8.1% per 100 patient years FU

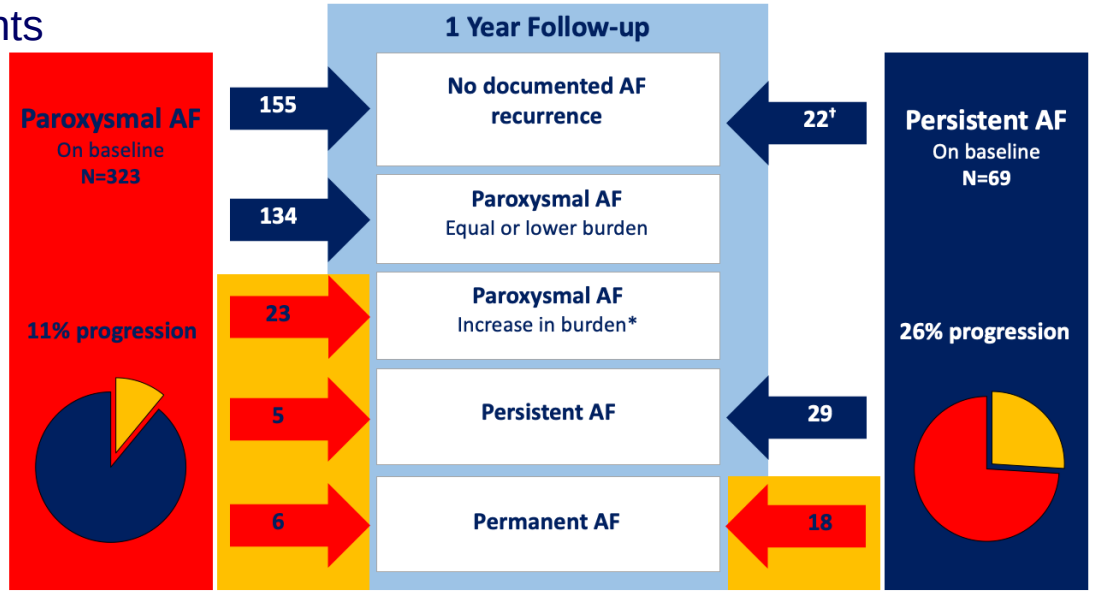
Predictors

	Beta	95% CI	P
History hypertension	5.2	1.0 - 9.4	0.02
History of heart failure	7.9	1.4 – 14.5	0.02
Age	5.4	1.4 – 9.4	0.01

Blum et al HR 2019

AF progression in early low risk AF patients

- 393 parox and pers AF patients
- Mean age 60 years
- 62% male
- FU 1.9 years
- CHA_2DS_2-VASc 1.7
- Nr RFs and comorbidites 1.9



De With et al for the AF Risk Investigators Europace 2019

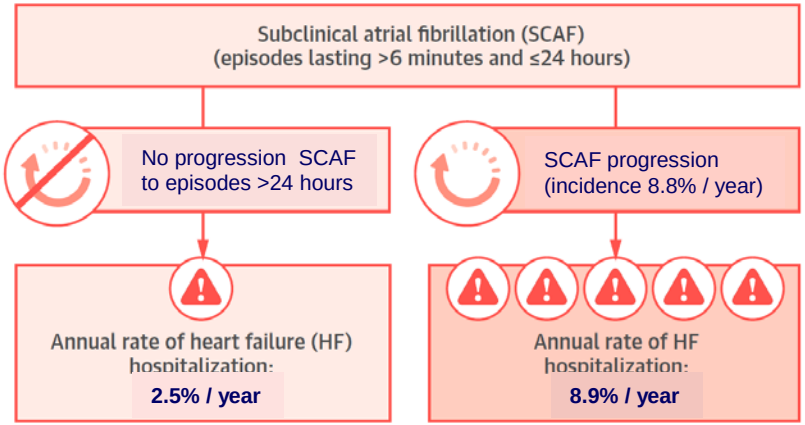
Progression of SCAF associated with events

- 2580 patients with hypertension, > 65 yrs
- no AF
- Atrial lead because of pacemaker or ICD
- Follow-up: 2.5 years
- Subclinical AF: > 6 min > 190 bpm
- SCAF progression:

  development SCAF > 24 h or clinical AF

  in patients with SCAF 6min – 24hrs

  during 1st year of FU



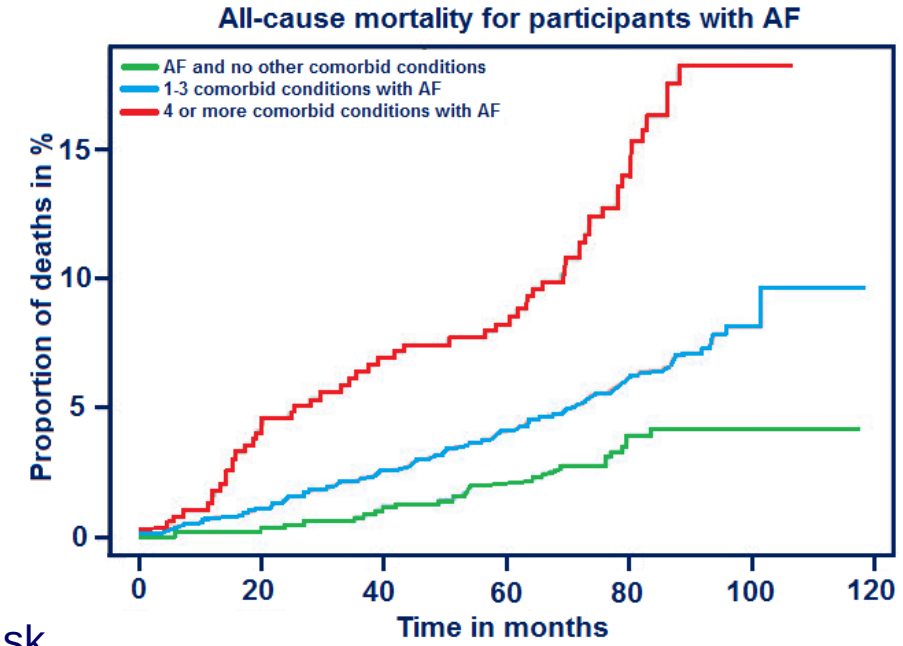
SCAF progression associated with increased risk of HF hospitalizations
HR: 4.6; 95% CI: 1.6 – 12.8; p = 0.004

But is not only AF !
It is the number of risk factors next to AF that matters

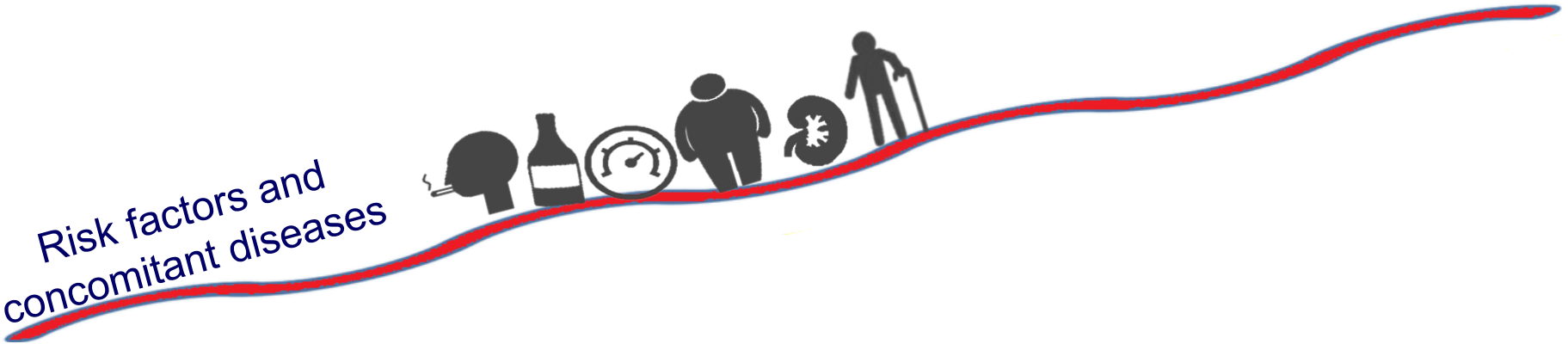
- Community cohort UK Biobank
- 502.637 participants (2006-2010)
- Age 37-73 years, 32% female
- FU 7 years
- 3651 (0.7%) developed AF
- All cause mortality 6.7%

- Presence of AF and > 4 risk factors:

  6-fold increased all cause mortality risk



Risk factors and AF both involved in AF progression



Cosio Europace 2007; De Groot, Allessie Circ 2010; Kottkamp JACC 2015; Siebermair JACC CE 2017; Kloosterman thesis

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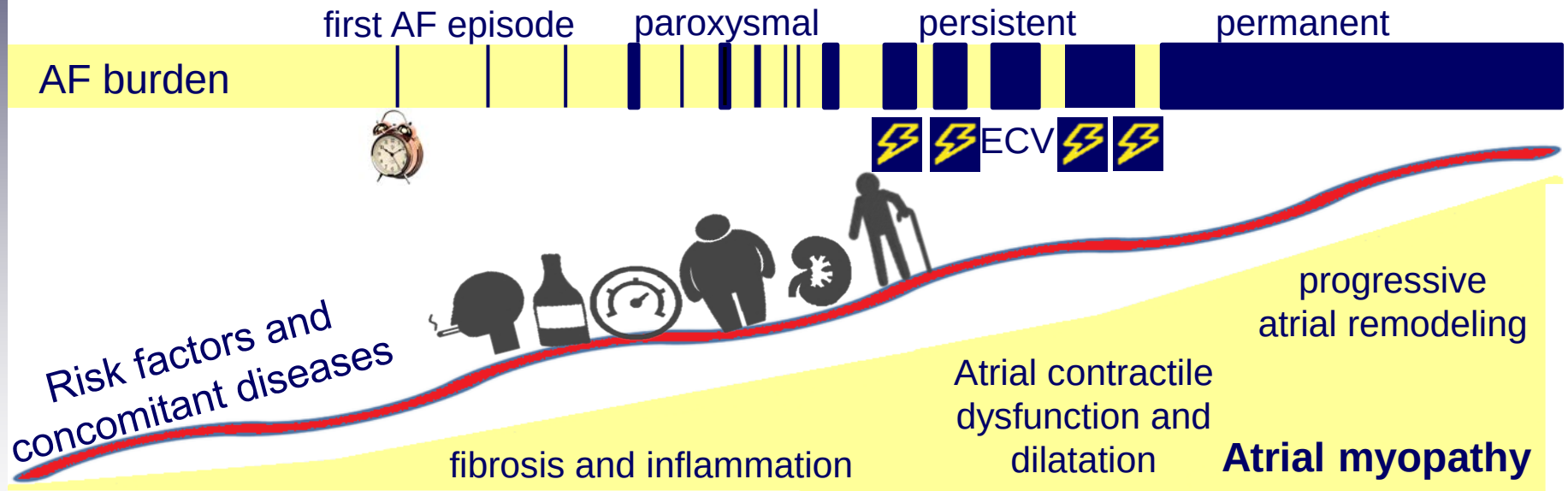

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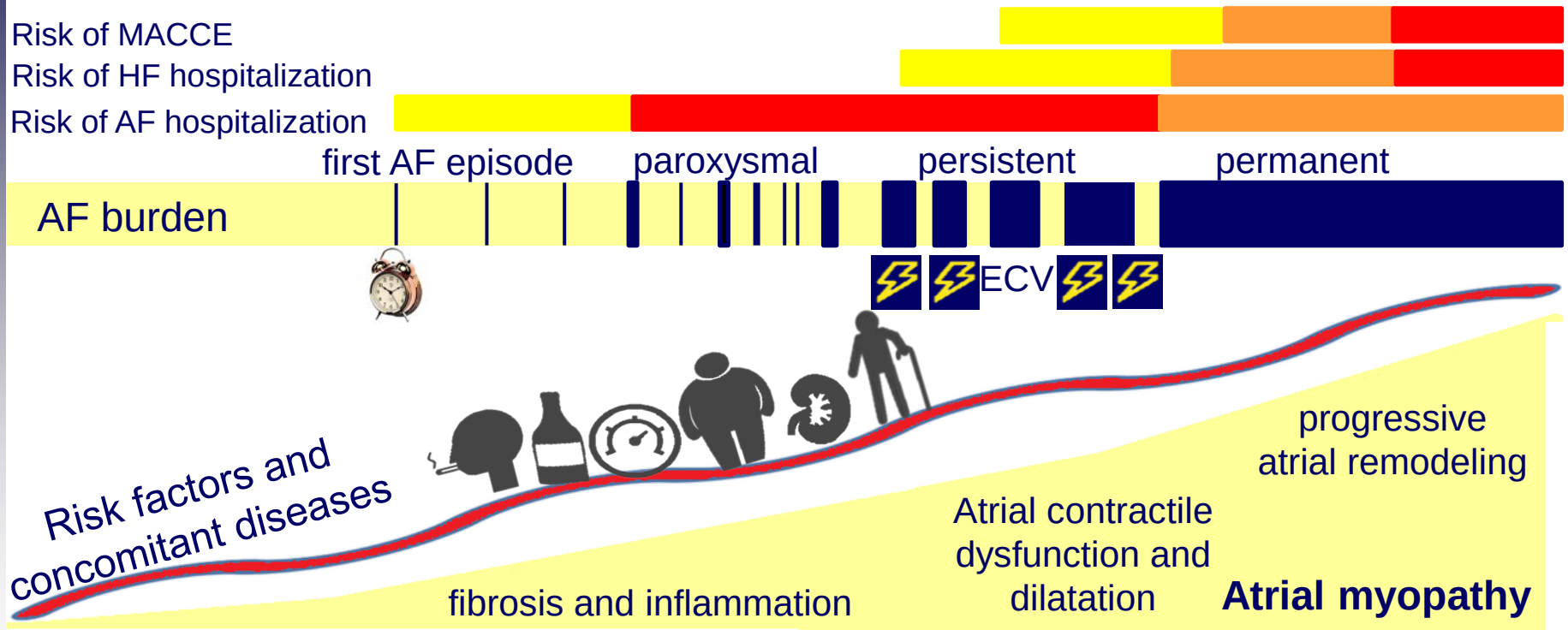

Cosio Europace 2007; De Groot, Allessie Circ 2010; Kottkamp JACC 2015; Siebermair JACC CE 2017; Kloosterman thesis

Vraag 4

Welke bewering is niet waar ?

1. Boezemfibrilleren is de meest voorkomende ritmestoornis
2. Antistolling is een het eerste waar ik aan denk als ik boezemfibrilleren constateer
3. De CHA_2DS_2-VASc gebruik ik alleen voor het inschatten van risico op een herseninfarct

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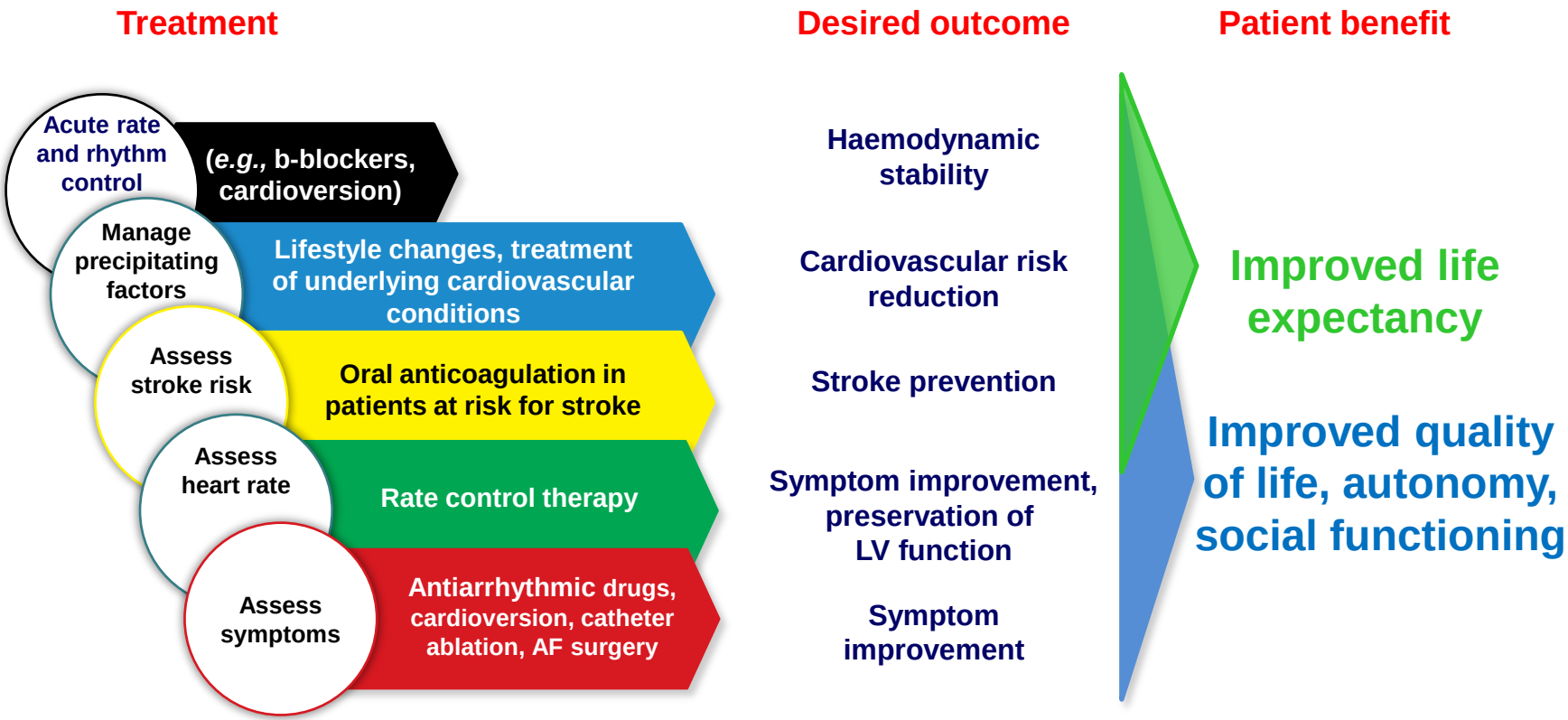
Treatment of AF is complex

Disease burden determined by:

- Atrial fibrillation
- Risk factors
- Comorbidities
- Number of risk factors
- Lifestyle
- Stress
- Anxiety

Comprehensive integrated care is clearly needed in AF patients including cardiovascular risk management

It is already in our guidelines !

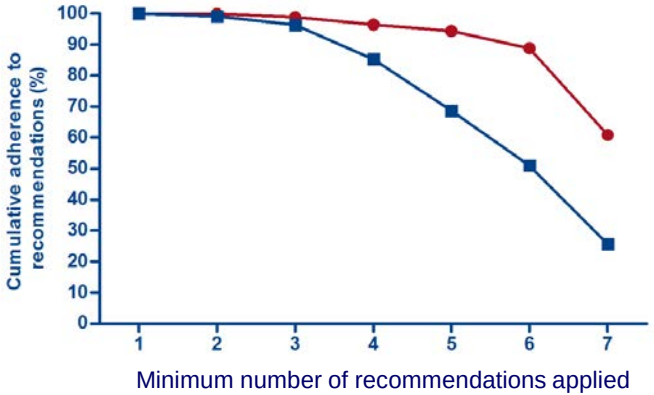


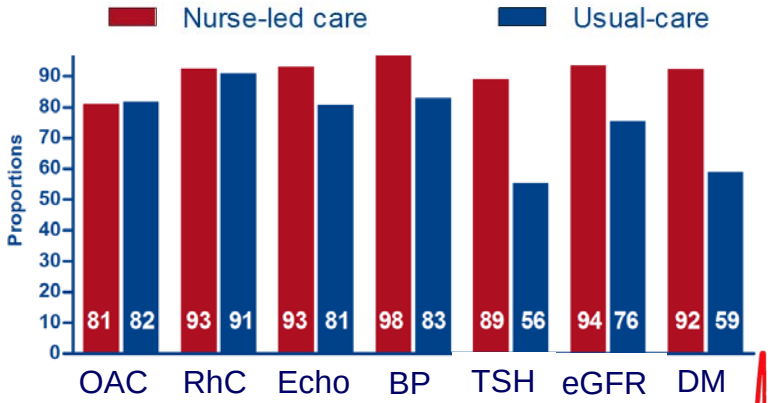
Kirchhof et al for the TF ESC AF guidelines 2016 Eur Heart J 2016

But what is the adherence now ?

- Nurse-led care versus routine
- 1354 new-detected AF patients
- Age 64 years
- 34% Female
- CHA_2DS_2-VASc > 1 in 57%
- FU 3.1 years

recommendations for cardiovascular risk management were better implemented under nurse-led care





Wijtvliet, .. Crijns Eur Heart J 2019

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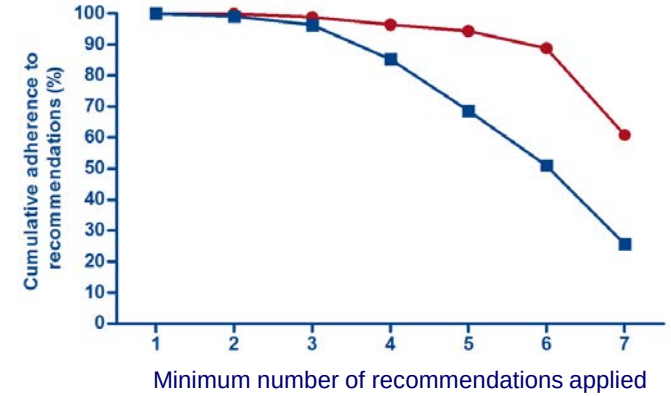
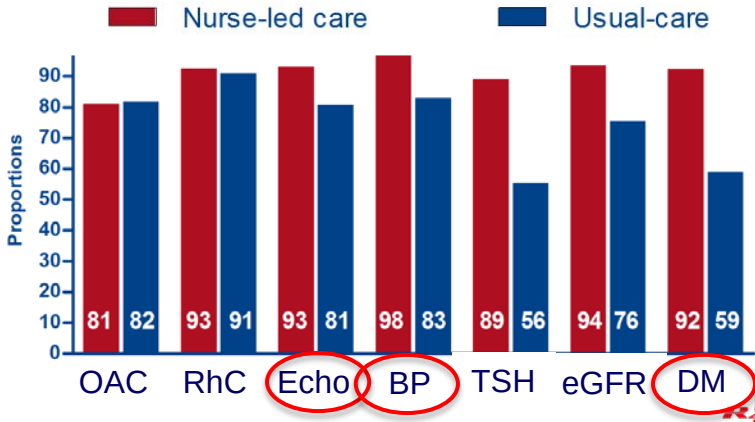
CHA_2DS_2-VASc
may also help to assess
some comorbidities





Wijtvliet, .. Crijns Eur Heart J 2019

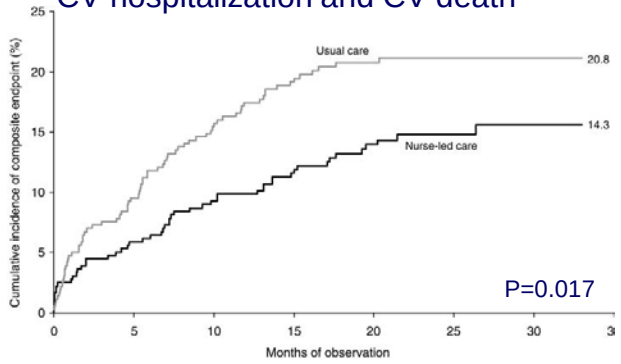
Morbidity and mortality

- The role of comprehensive care in reducing morbidity and mortality

Comprehensive nurse-led care in experienced center

- Nurse-led comprehensive care vs usual
- 712 outpatient department patients
- One experienced center
- No focus on lifestyle
- Age 67 years; 41% Female
- CHA_2DS_2-VASc > 1 in 66%
- FU 1.9 years
- Composite endpoint: CV hospitalization and CV death
- Secondary outcome: all cause mortality

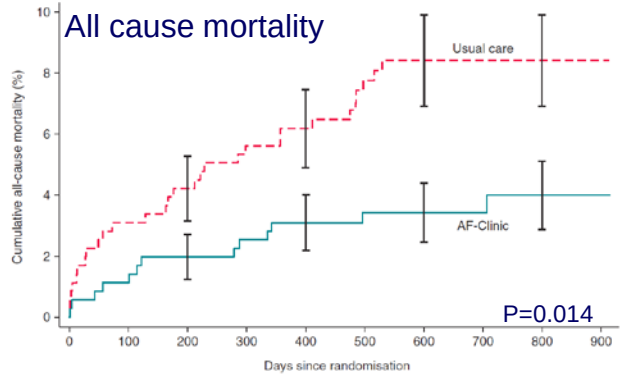
CV hospitalization and CV death



No. at risk

NLC	356	355	323	285	229	126	55
UC	356	321	300	265	206	107	37

All cause mortality



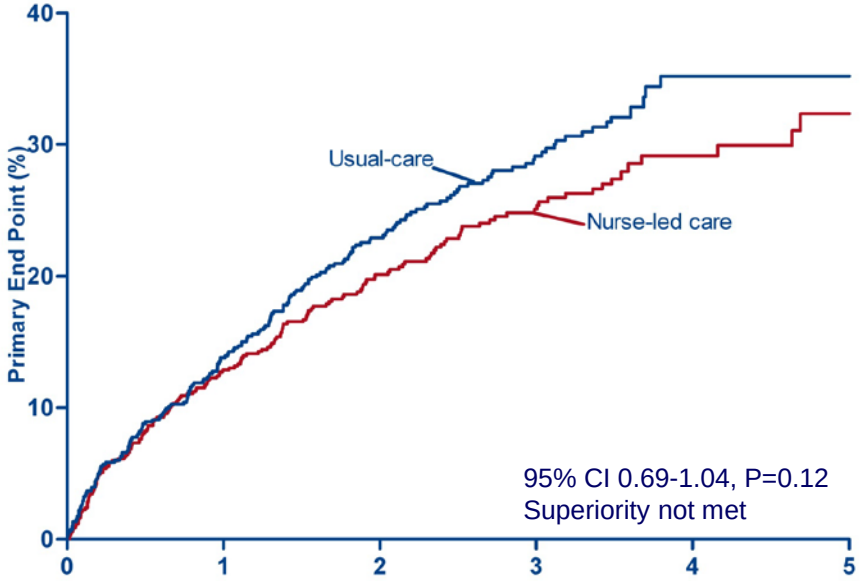
No. at risk

AF-Clinic	356	352	349	347	334	295	256	181	119	62
Usual care	356	345	341	336	323	289	241	168	79	46

Hendriks Eur Heart J 2012 and Hendriks Europace 2019

Comprehensive multicenter nurse-led care

- Nurse-led comprehensive care vs usual
- 1354 new-detected AF patients
- Multicenter
- No focus on lifestyle
- Age 64 years; 34% Female
- CHA_2DS_2-VASc > 1 in 57%
- FU 3.1 years
- Composite endpoint unplanned CV hospitalisation or CV death



Wijtvliet, .. Crijns Eur Heart J 2019

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- 1354 new-detected AF patients
- Multicenter
- No focus on lifestyle
- Age 64 years; 34% l
- CHA_2DS_2-VASc > 1
- FU 3.1 years
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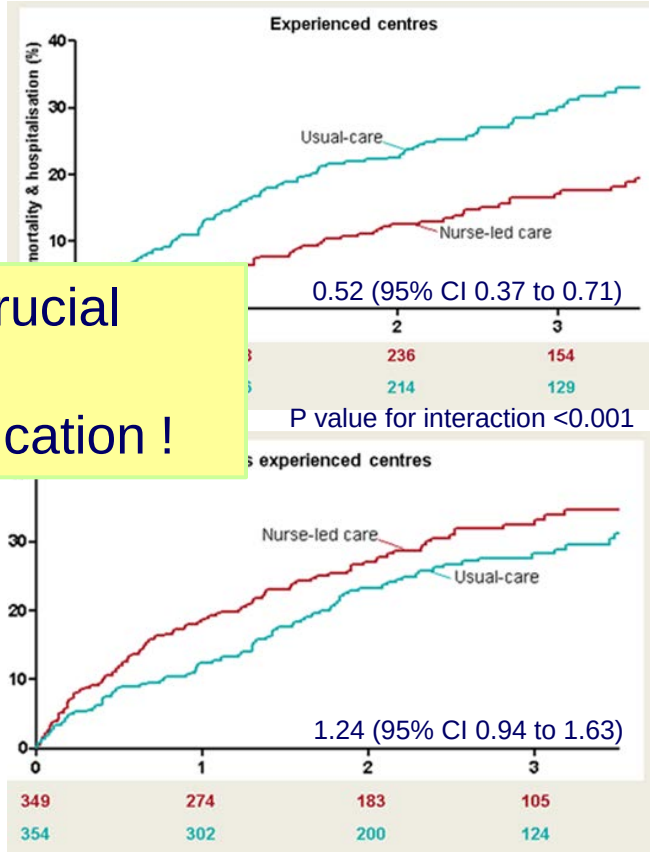
Experience crucial

Continuous education !



Wijtvliet, .. Crijns Eur Heart J 2019

Take home message

- AF is not just an arrhythmia, it is a complex disease
- It comes in combination with and due to risk factors and comorbidities
- Together they determine the arrhythmia and the clinical prognosis

Take home message

- For optimal outcome early and comprehensive diagnosis making is needed
- Followed by comprehensive therapy by dedicated health care professionals
- Focusing not only on the ECG but also on underlying risk factors
- Continuous education for both HCPs and patients seems essential

Thank you for your attention

University Medical Center Groningen

ESC European Society of Cardiology

EHRA European Heart Rhythm Association

ESC Council Stroke

funded by the dutch heart foundation Hartstichting

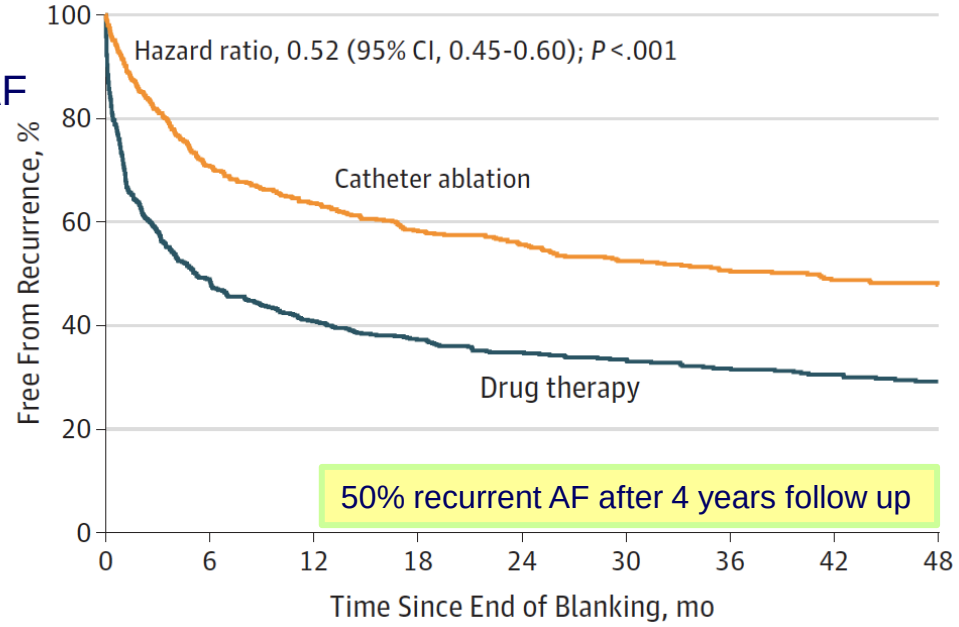
René Laënnec lecture
ESC Paris 2019

Success of rhythm control

- The role of comprehensive care in restoring sinus rhythm

Ablation without comprehensive care

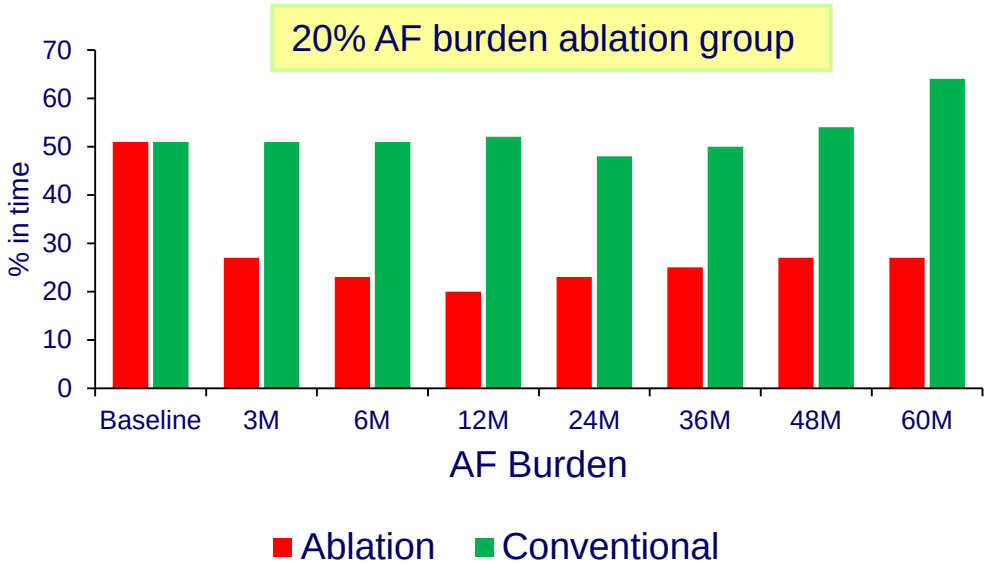
- CABANA
- 2204 paroxysmal and persistent AF
- Mean age 68 years
- 27% female
- FU 4 years
- CHA_2DS_2-VASc 3
- Hypertension 85%
- NYHA II and III 35%
- Heart failure 15%



Packer et al CABANA JAMA 2019

Ablation plus HF therapy; no comprehensive care

- CASTLE-AF
- 363 patients
  - 30% PAF
  - 70% persistent AF
- Mean age 64 years
- 87 % male (!)
- FU 4 years
- LVEF 32.5%; 60% NICM

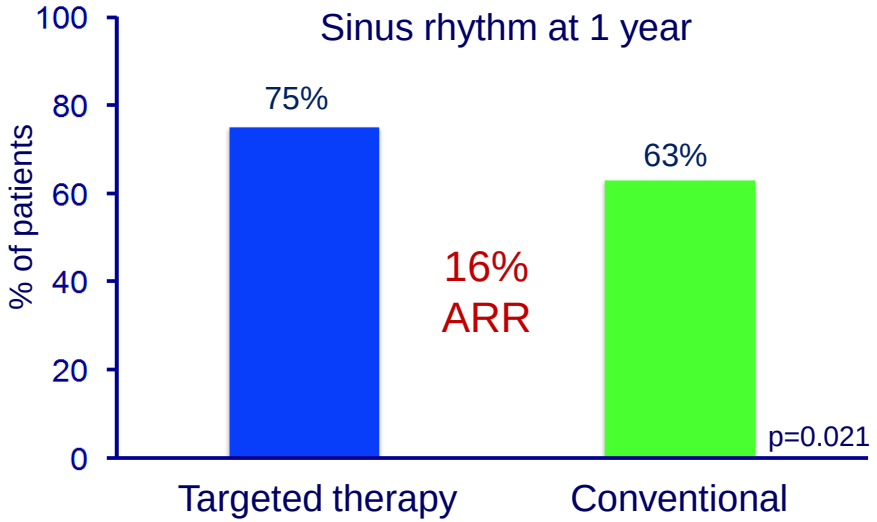


Marrouche et al. CASTLE-AF New Engl J Med 2018

All-in-one comprehensive care plus lifestyle

- RACE 3
- Targeted versus conventional therapy
- Symptomatic early persistent AF + modest HF

- 4 Targeted therapies in intervention group:
  1. Mineralocorticoid receptor antagonists
  2. Statins
  3. ACE-inhibitors and/or ARBs
  4. Cardiac rehabilitation:
     - physical activity
     - dietary restrictions
     - counselling every 6 weeks

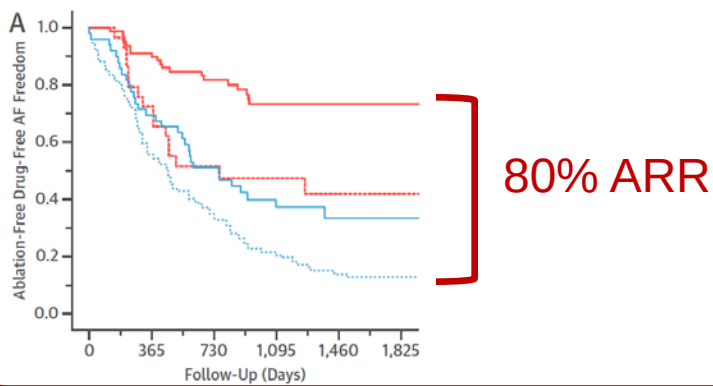


Rienstra for the RACE 3 investigators Eur Heart J 2018

Aggressive comprehensive care plus lifestyle

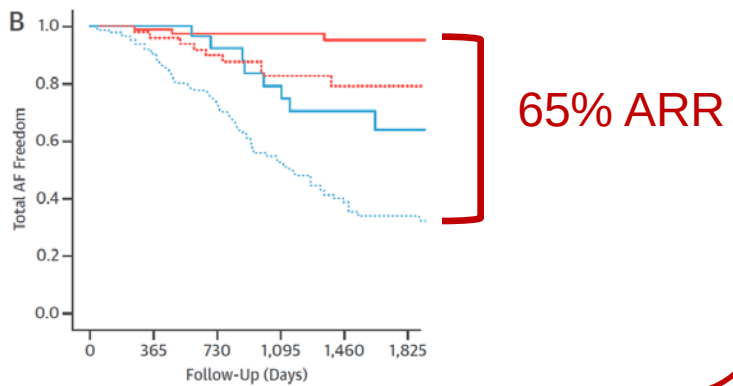
- Observational CARDIO-FIT registry
- 308 obese patients, BMI > 27 kg/m^2, symptomatic paroxysmal or persistent AF
- Treated with a risk factor management and exercise program
- 24/7 e-mail and telephonic support available and face-to-face visits every 3 months
  - Group 1: fit and weight loss
  - Group 2: unfit and weight loss
  - Group 3: fit and no weight loss
  - Group 4: unfit and no weight loss

No AF recurrences
(with multiple ablations and AADs)



80% ARR

No AF recurrences



65% ARR

Pathak, Sanders, CARDIO-FIT trial JACC 2015