# Satellite Symposium

## Atrial Fibrillation – A Bystander or Cause of Morbidity and Mortality: Insights from the GARFIELD-AF Registry

ESC CONGRESS 2017, BARCELONA, SPAIN

TRI Thrombosis Research Institute

www.garfieldregistry.org

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield
global anticoagulant registry in the field

# GARFIELD-AF landmark: First-year outcomes of 52,000 prospective patients

Rt Hon Professor the Lord Kakkar

Thrombosis Research Institute and University College London, London, UK

TRI Thrombosis Research Institute

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# Disclosures

**Research support: Bayer AG**

**Personal fees: Bayer AG, Boehringer-Ingelheim Pharma, Daiichi Sankyo Europe, Janssen Pharma, Sanofi SA**



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# About GARFIELD-AF

The **largest** prospective AF registry

Newly diagnosed AF patients from **35 countries**

Over **1000 sites** representative of national AF care settings

Recruitment complete; **57,262 patients** enrolled

5 sequential prospective **cohorts**

Follow-up period – **2 to 8 years; 1-year outcomes data** available for all 5 cohorts

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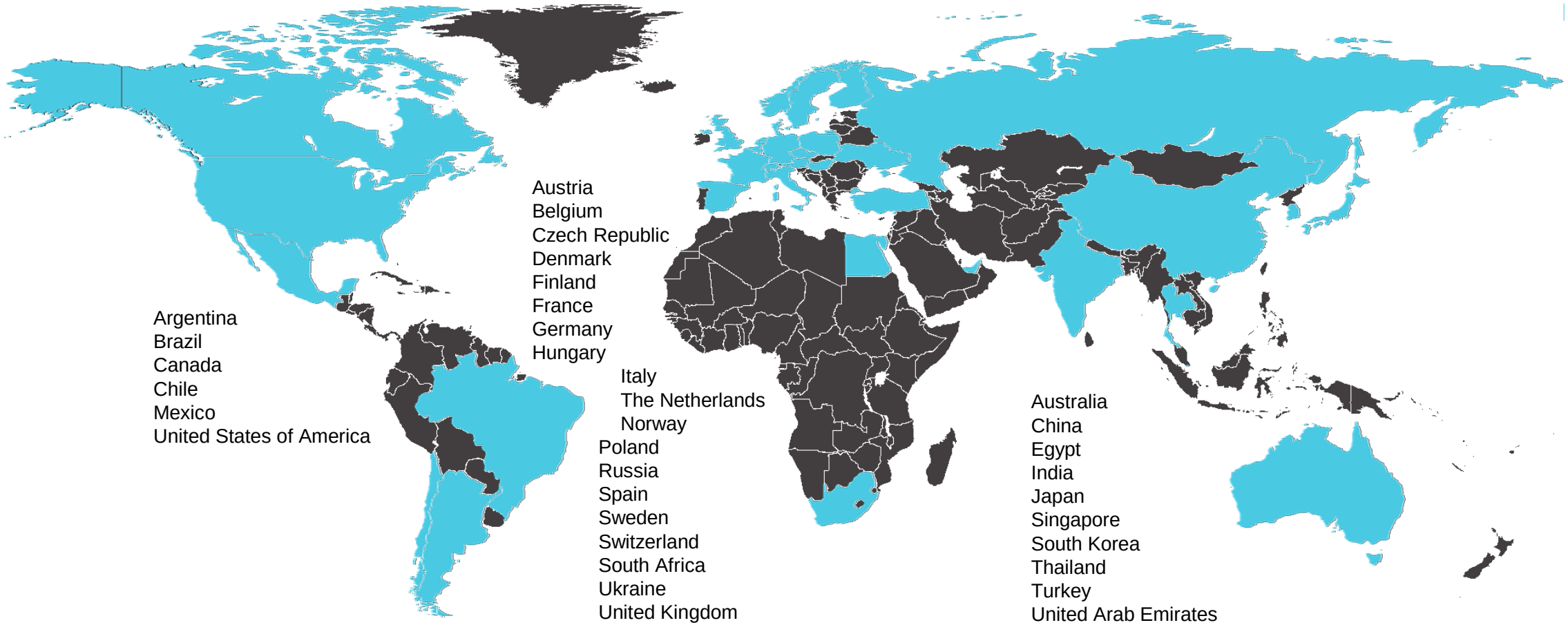
# 57,262 patients in 35 countries

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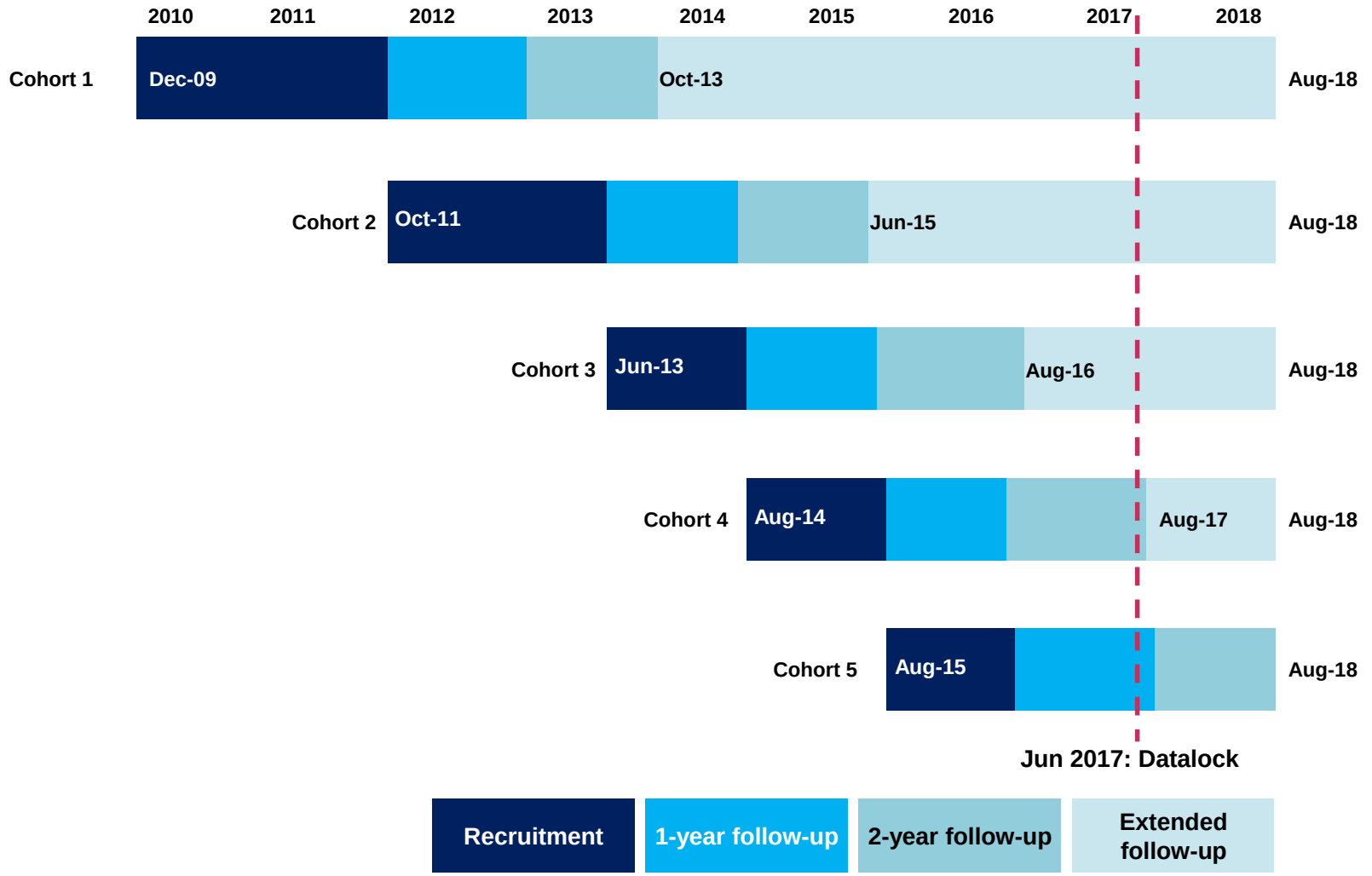
# Design and scope of GARFIELD-AF registry

## Design

- Independent academic research initiative
- Randomised selection of sites representative of national AF care settings
- Unselected prospective patients enrolled consecutively
- Long-term follow-up (minimum of 2 yrs, up to 8 yrs)

## Audit requirements

- 20% of all case report forms monitored against source documentation
- Electronic audit trail for all data modifications
- Critical variables subjected to additional audit
- Compliant with Declaration of Helsinki







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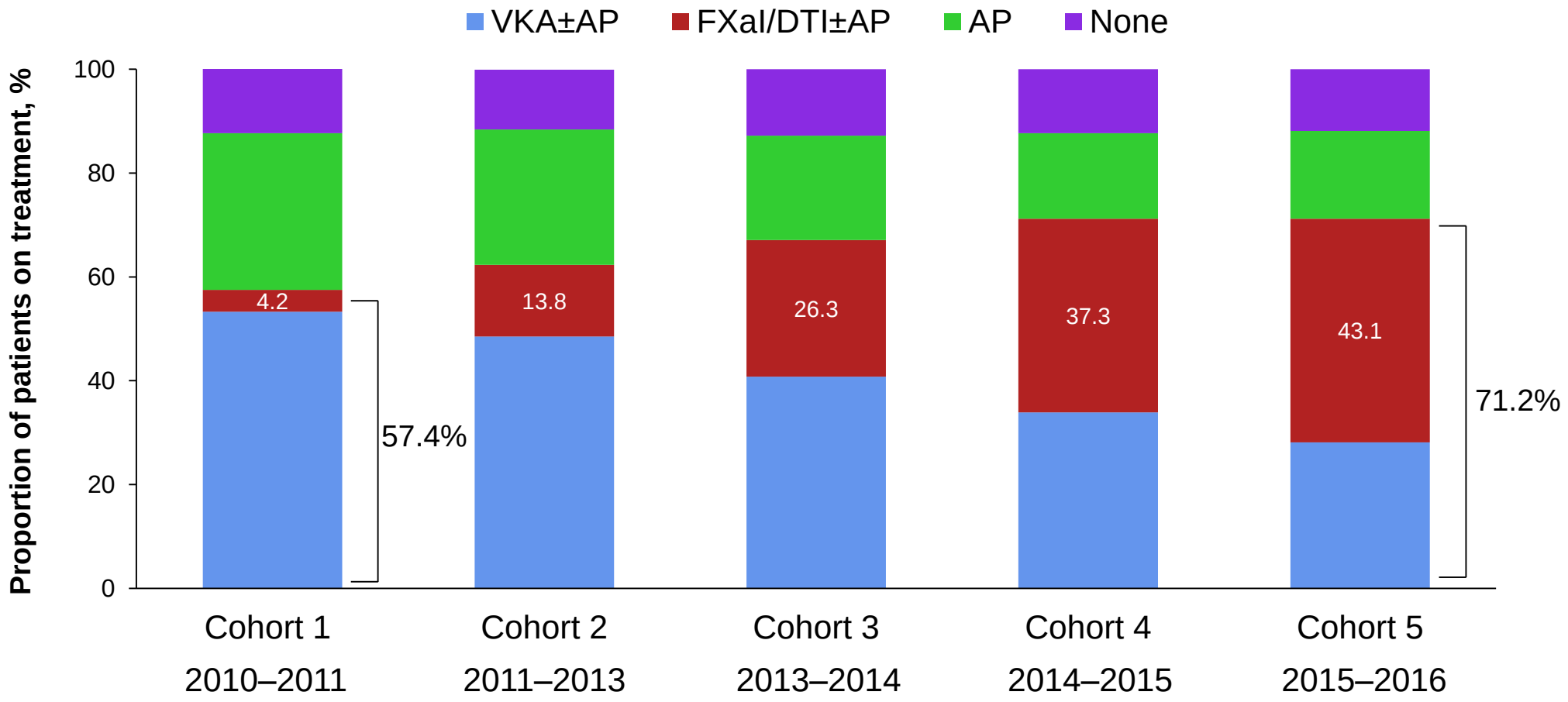
# Evolution in baseline treatment for patients enrolled in sequential cohorts of GARFIELD-AF




Cohorts 1–5, N=52,081; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

Unpublished Data



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# One-year incidence event rates

| Outcome | Events | Event rate (per 100 person-years) | 95% CI |
|---|---|---|---|
| **All-cause mortality** | 2103 | 4.38 | 4.20 to 4.57 |
| Cardiovascular | 789 | 1.64 | 1.53 to 1.76 |
| Non-cardiovascular | 771 | 1.61 | 1.50 to 1.72 |
| Undetermined cause | 543 | 1.13 | 1.04 to 1.23 |
| **Stroke/systemic embolism** | 650 | 1.36 | 1.26 to 1.47 |
| **Major bleeding** | 407 | 0.85 | 0.77 to 0.94 |
| **Acute coronary syndromes** | 378 | 0.79 | 0.71 to 0.87 |
| **Congestive heart failure** | 1052 | 2.22 | 2.09 to 2.35 |

Cohorts 1–5, N=52,081

Unpublished Data



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# Causes of death during first-year follow-up

| | Events | % |
|---|---|---|
| **Cardiovascular deaths (n=789)[1]** | | |
| Congestive heart failure | 262 | 33.2 |
| Sudden or unwitnessed death | 127 | 16.1 |
| Myocardial infarction | 89 | 11.3 |
| Ischaemic stroke | 86 | 10.9 |
| Other | 223 | 28.3 |
| **Non-cardiovascular deaths (n=771)[2]** | | |
| Malignancy | 233 | 30.2 |
| Infection/sepsis | 155 | 20.1 |
| Respiratory failure | 142 | 18.4 |
| Accidental/trauma | 17 | 2.2 |
| Other | 221 | 28.7 |

Cohorts 1–5, N=52,081; [1]missing: 2 deaths; [2]missing: 3 deaths

Unpublished Data

# Types of stroke during first-year follow-up

| | Events | % |
|---|---|---|
| **Stroke (not including systemic embolism)** | 585 | 100 |
| Primary ischaemic stroke | 406 | 69.4 |
| Primary intracerebral haemorrhage | 71 | 12.1 |
| Undetermined | 108 | 18.5 |

Cohorts 1–5, N=52,081

Unpublished Data



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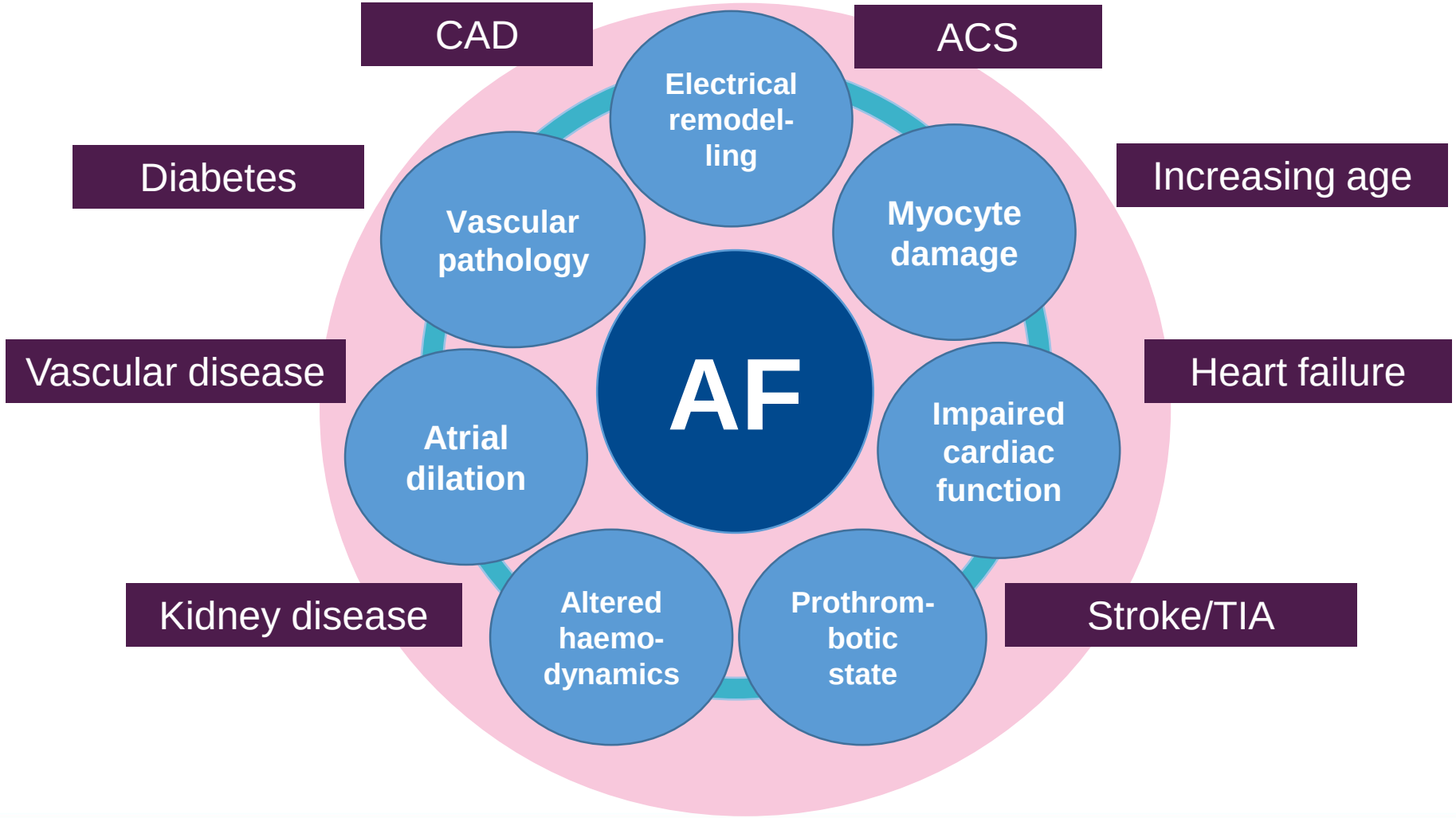
# Integrated care is needed for comorbid conditions with common risk factors and pathologies




ACS, acute coronary syndromes; AF, atrial fibrillation; CAD, coronary artery disease; TIA, transient ischaemic attack

# Our symposium today

**This symposium outlines the real-world outcomes 1 or 2 years after atrial fibrillation diagnosis in patients prospectively recruited into the GARFIELD-AF registry**

**The learning objectives for this symposium are:**

- **To understand how comorbidities impact the prognosis of patients with atrial fibrillation**
- **To appreciate the importance of a comprehensive management strategy for atrial fibrillation**



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# Atrial fibrillation burden: Morbidity and mortality

**Professor Samuel Z. Goldhaber**

**Brigham and Women's Hospital and Harvard Medical School, Boston, USA**

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AF Garfield global anticoagulant registry in the field

# Disclosures

**Research support: $BiO_2$ Medical, Boehringer-Ingelheim, BMS, BTG EKOS, Daiichi, Janssen, NHLBI, Thrombosis Research Institute**

**Consultant: Agile, Bayer, Boehringer-Ingelheim, BMS, Daiichi, Janssen, Portola, Zafgen**



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# GARFIELD-AF: 2-year outcomes

| N=17,162 patients | Incidence event rate per 100 person-yrs (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/systemic embolism** | **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** | **2.41 (2.24; 2.59)** |

Bassand J.P. et al Eur Heart J 2016; 37: 2882-9



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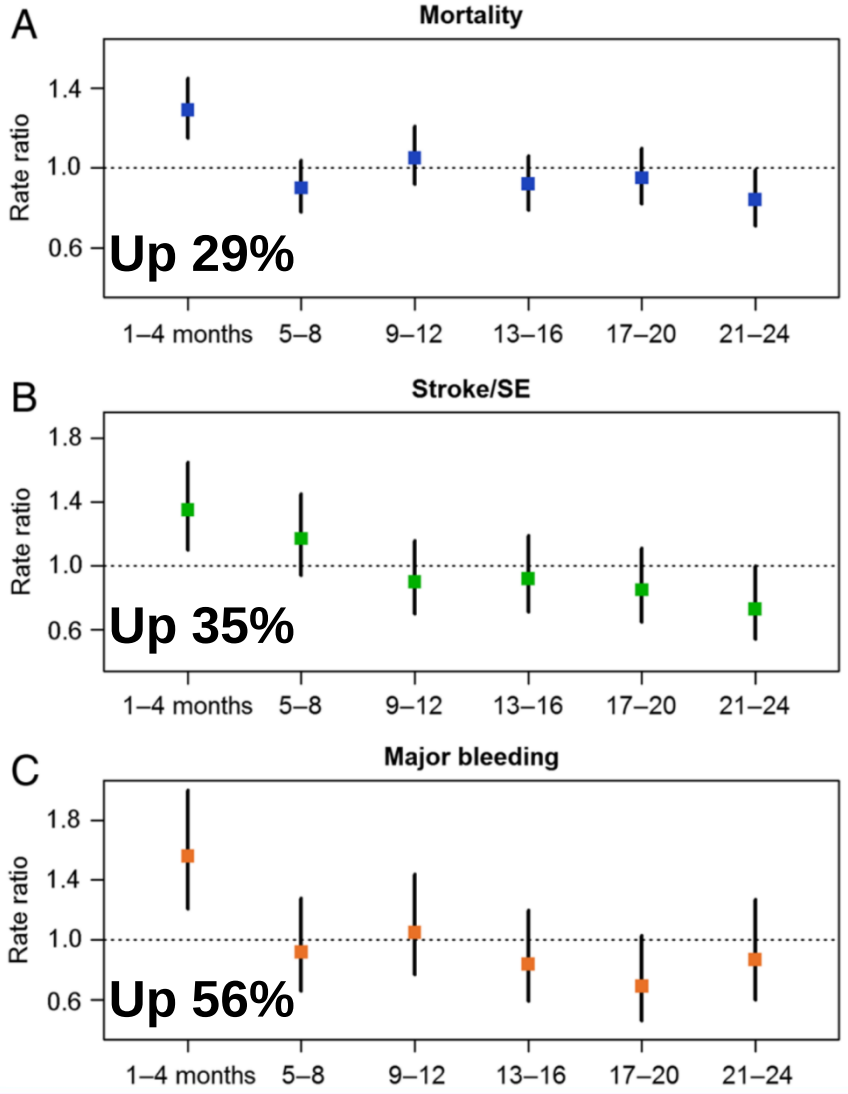
# GARFIELD-AF: 2-year outcomes




Bassand J.P. et al Eur Heart J 2016; 37: 2882-9

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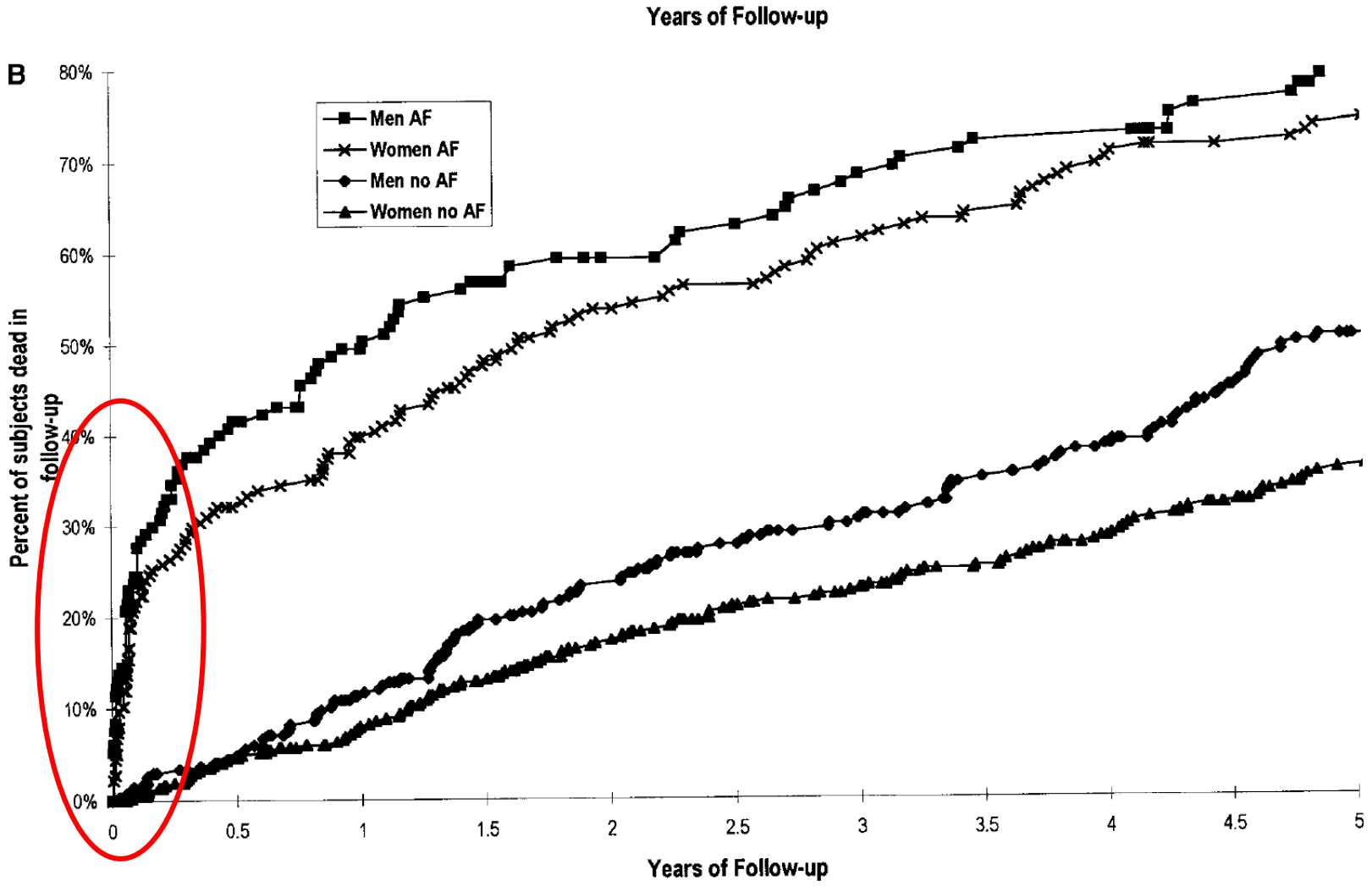
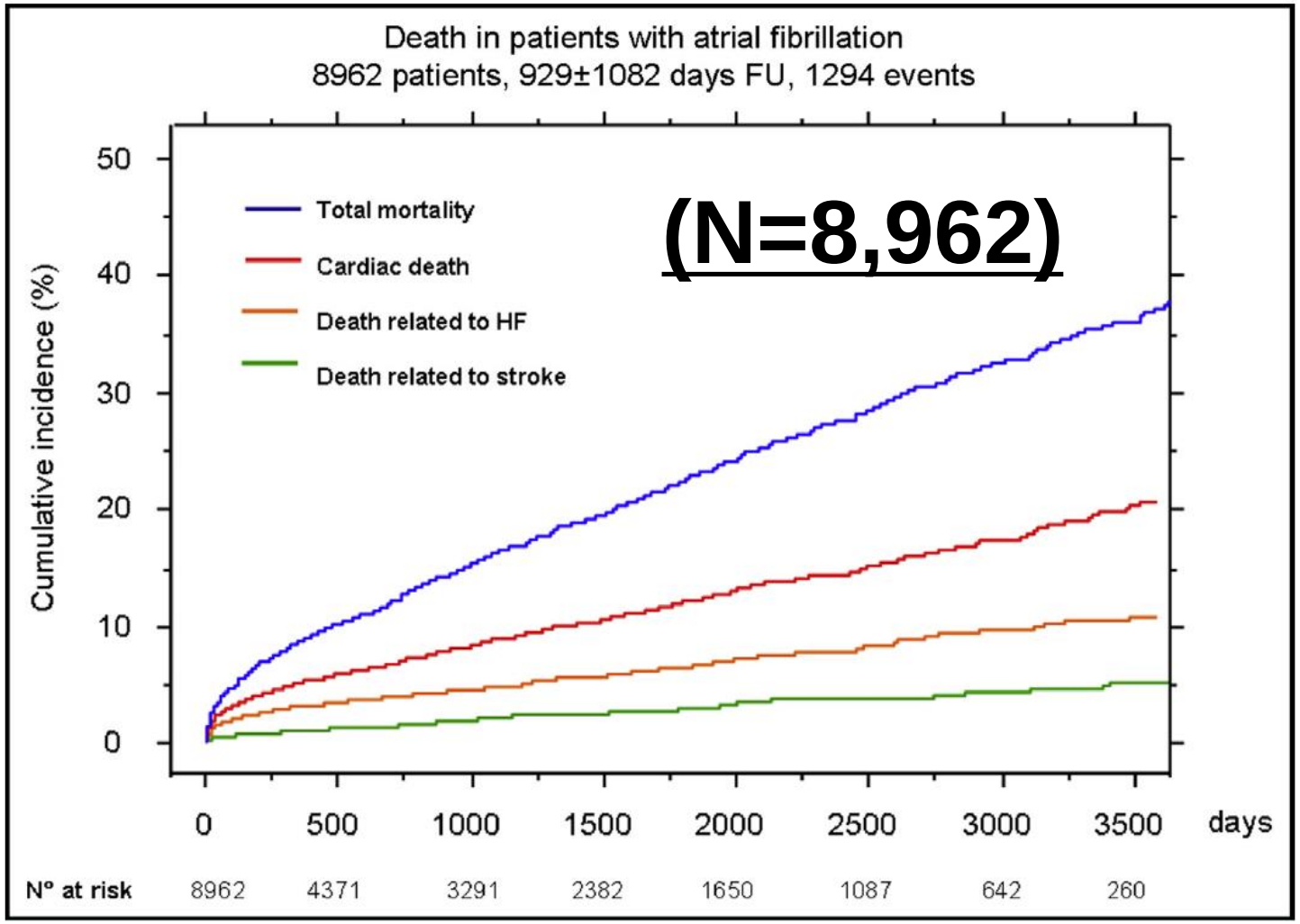
# Framingham Heart Study mortality, ages 75–94




Benjamin E.J. et al. Circulation 1998; 98: 946-52

# AF: Causes of death




HF, heart failure;
Fauchier L. et al Am J Med 2016; 129: 1278-87




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# AF: Death, CHF, MI, stroke, GIB (Fee-for-Service US Medicare; N=230,940)

CHF, congestive heart failure; GIB, gastrointestinal bleeding; MI, myocardial infarction; Piccini J.P. et al Eur Heart J 2014; 35: 250-6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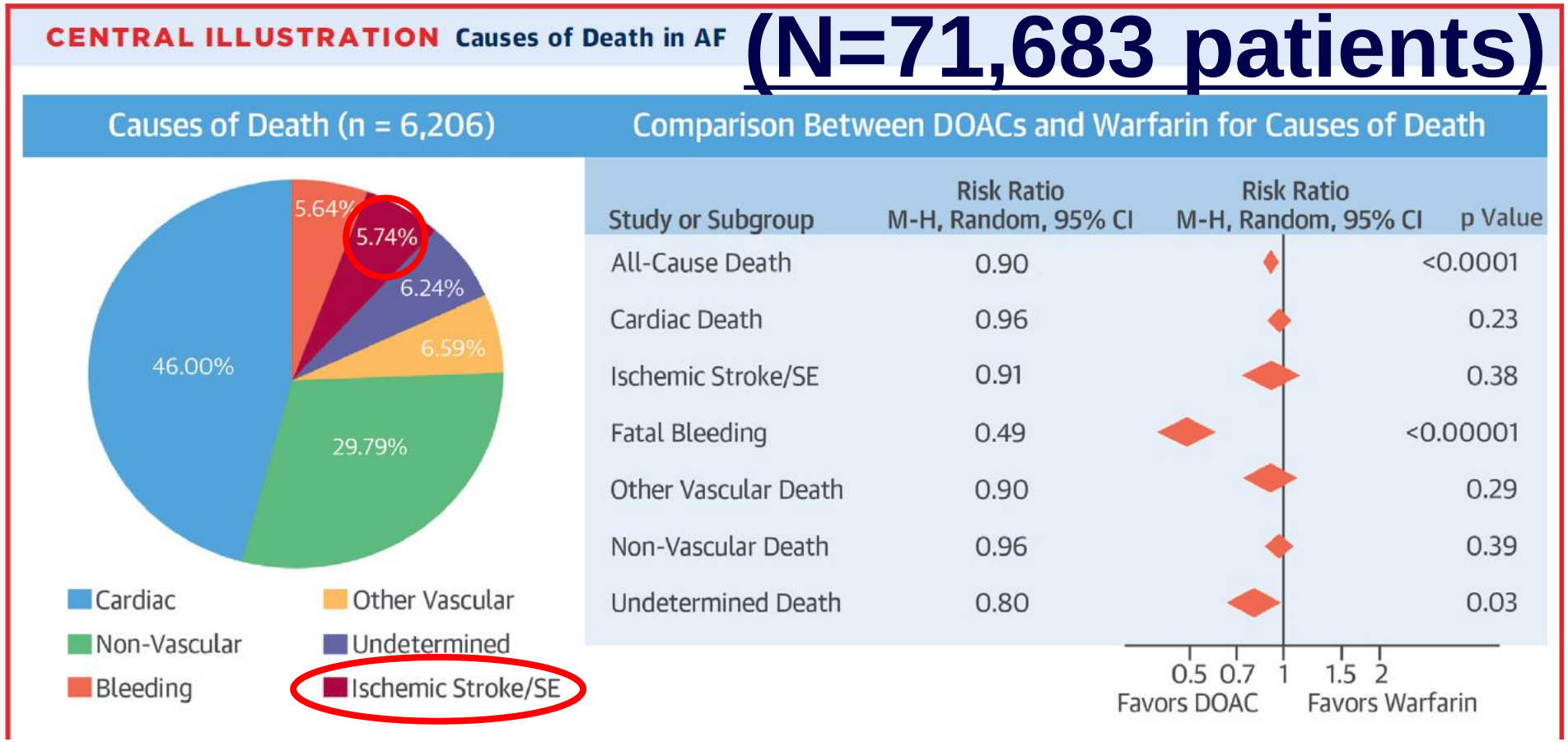
# AF: Causes of death




DOAC, direct oral anticoagulant; SE, systemic embolism; Gómez-Outes A. et al J Am Coll Cardiol. 2016; 68: 2508-21

# Prevention of AF morbidity and mortality



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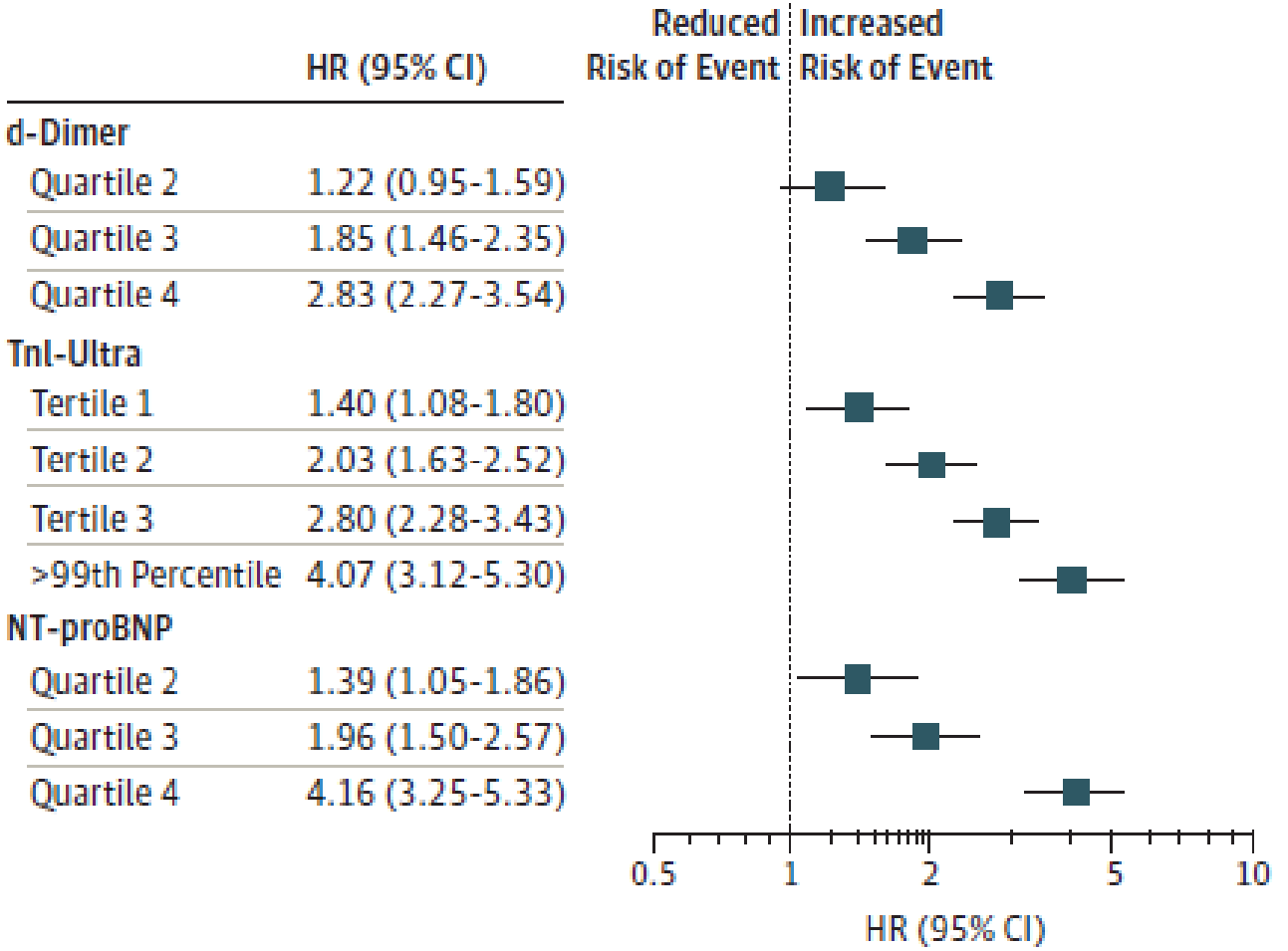
# AF mission statement

The first mission in AF patients is to prevent stroke



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

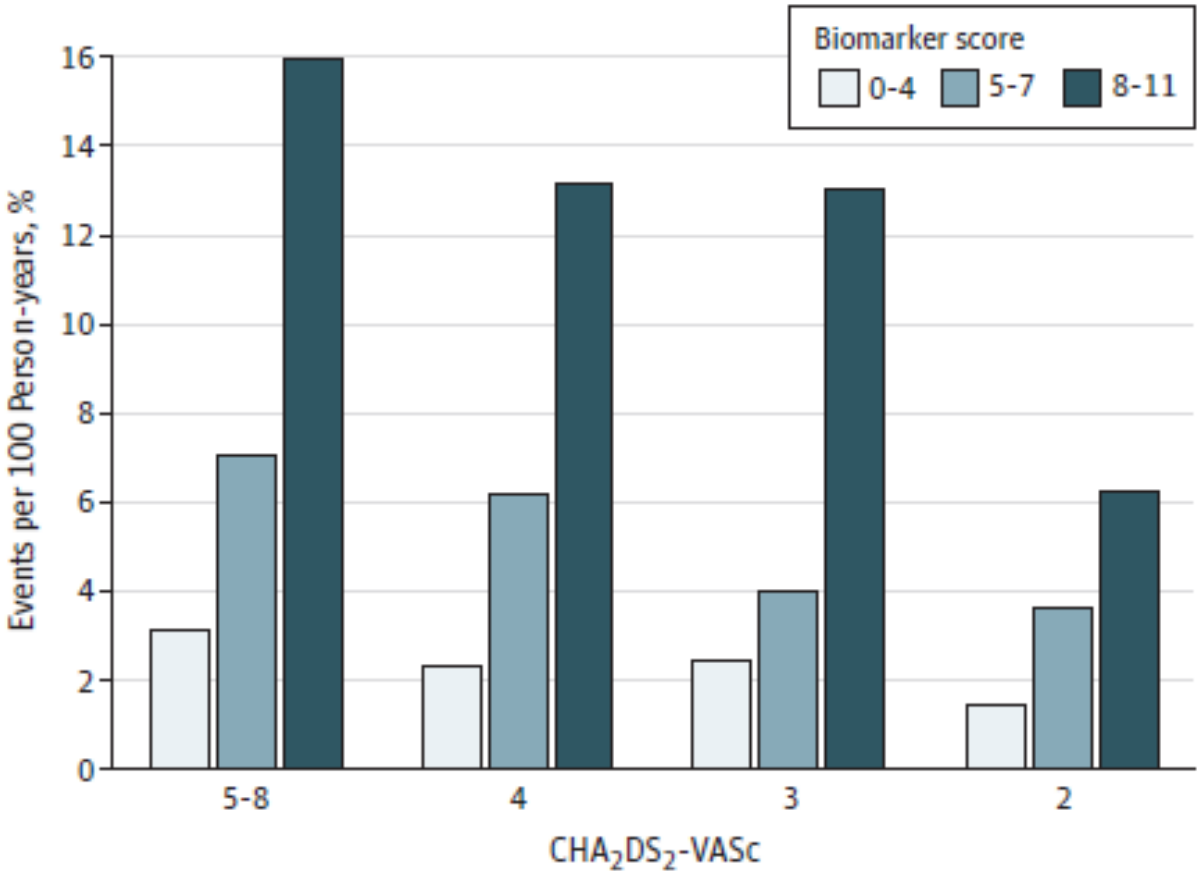
## Figure 1. Risk of Stroke, Systemic Embolic Event (SEE), and Death Associated With Individual Biomarker Levels




NT-proBNP, N-terminal pro-brain natriuretic peptide;

Ruff C.T. et al JAMA Cardiol. 2016; 1: 999-1006

# High biomarker score trumps $CHA_2DS_2$-VASc to predict death/stroke




Ruff C.T. et al JAMA Cardiol. 2016; 1: 999-1006



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# AF morbidity and mortality: Women versus men



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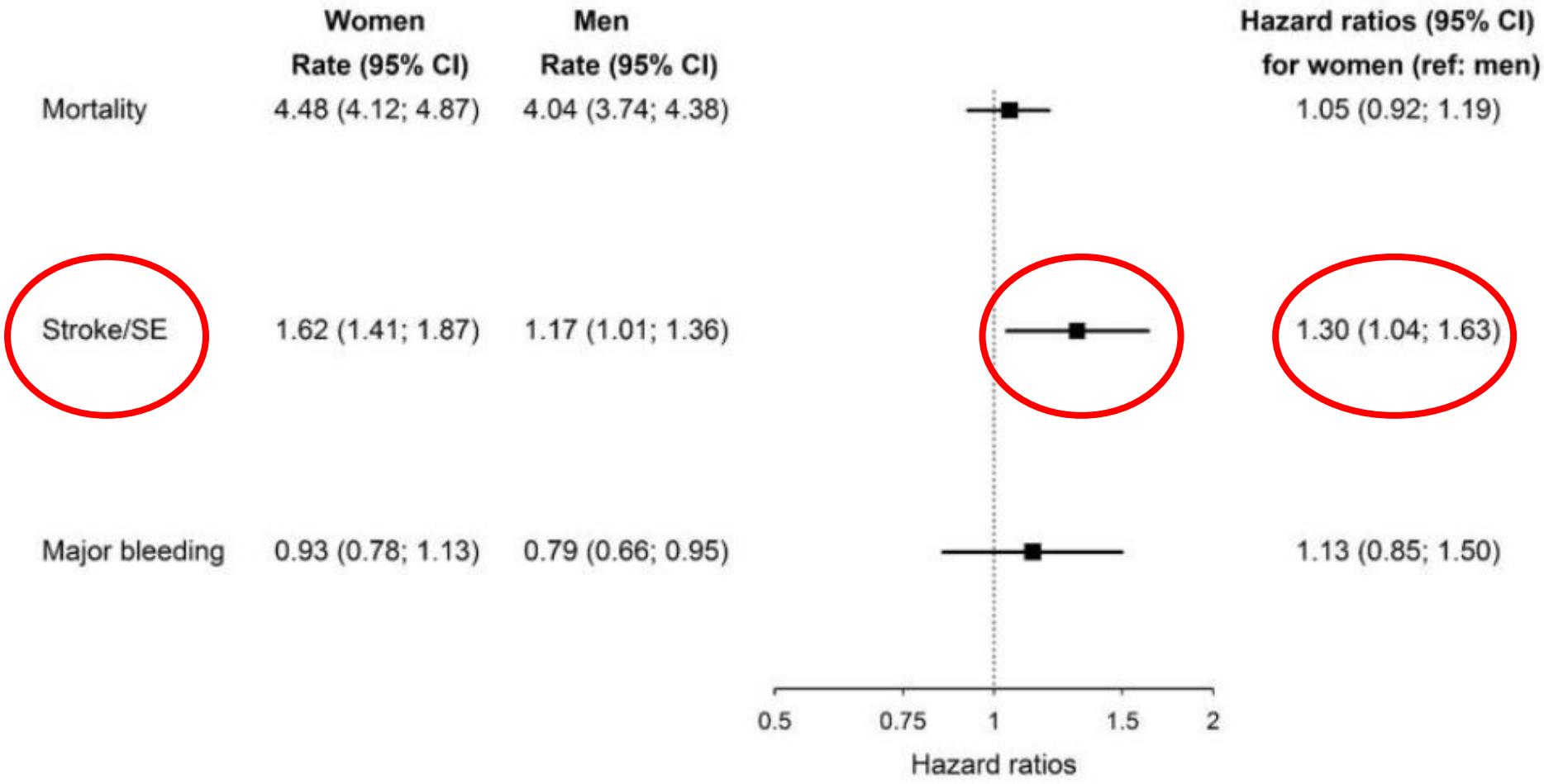
# GARFIELD-AF: Mortality, stroke, major bleeds – Gender

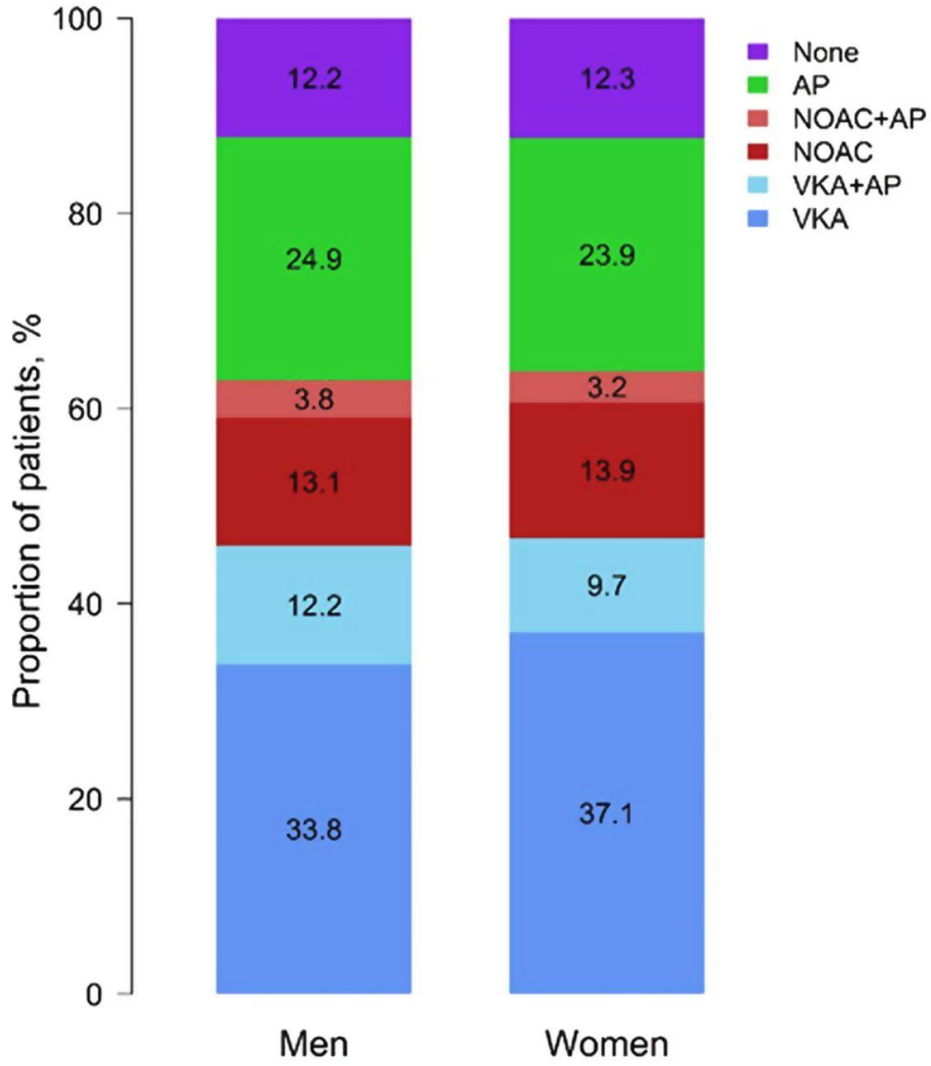



SE, systemic embolism; Camm A.J. et al BMJ Open. 2017; 7: e014579



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# GARFIELD-AF therapy: Gender




AP, antiplatelet; NOAC, non-vitamin K antagonist oral anticoagulant; VKA, vitamin K antagonist;

Camm A.J. et al BMJ Open. 2017; 7: e014579




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# AF morbidity and mortality: Different types of AF



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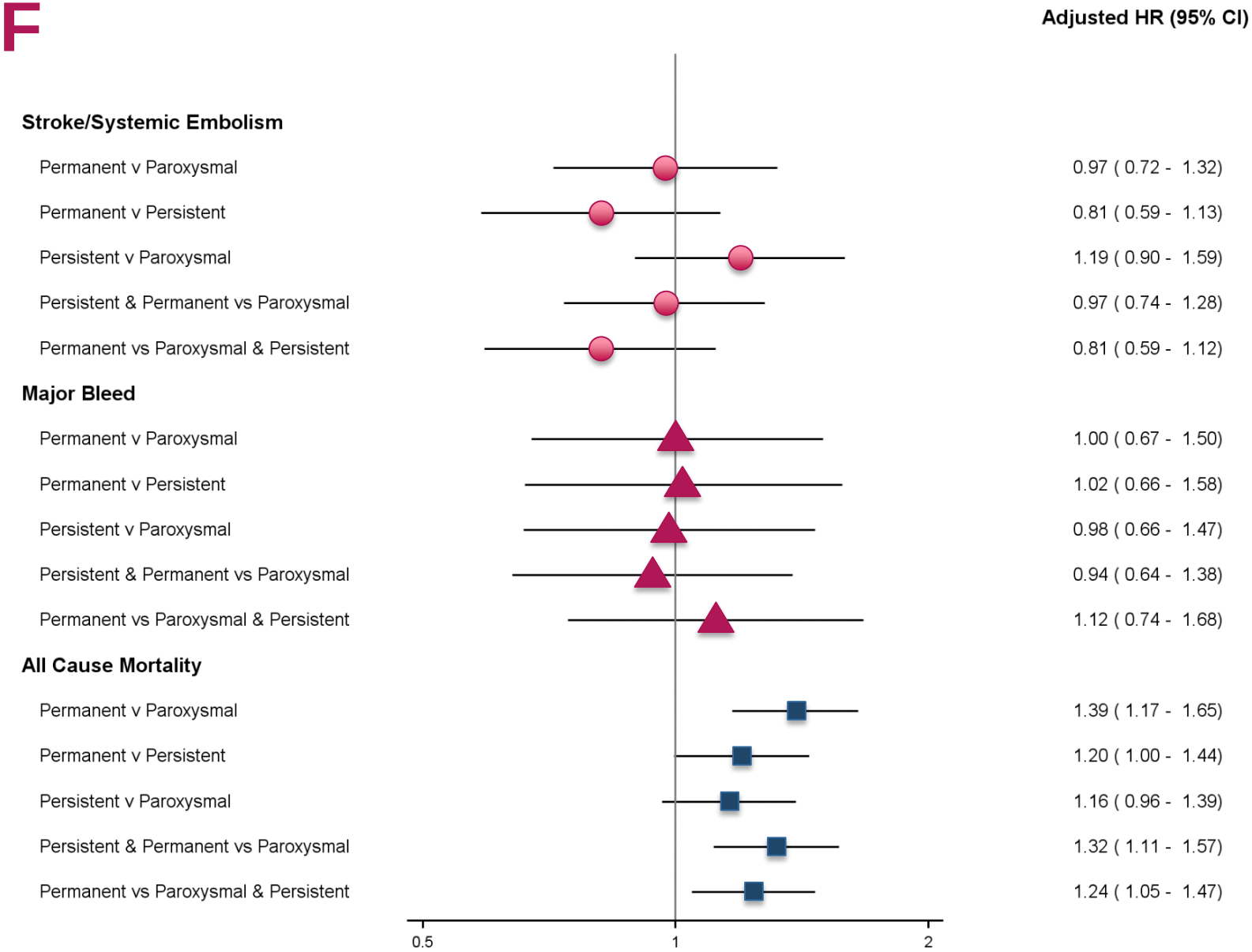
# GARFIELD-AF: Mortality, stroke, major bleeds – Type of AF




Cohorts 1–5, N=52,081

Unpublished Data

# Is AF primarily a risk factor for stroke, or is AF a risk marker for systemic diseases such as heart failure?



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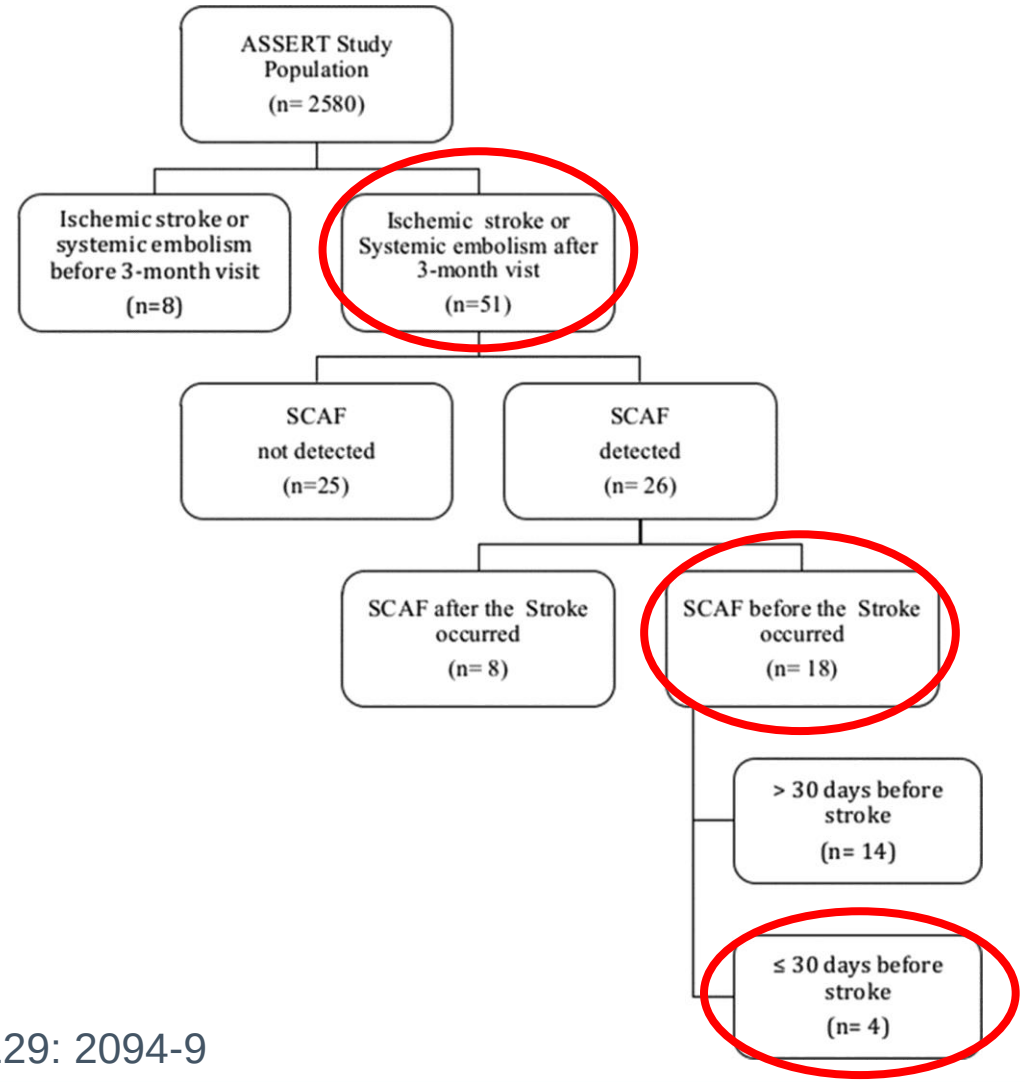
# Temporal relationship of AF to stroke




SCAF, subclinical atrial fibrillation;

Brambatti M. et al Circulation. 2014; 129: 2094-9



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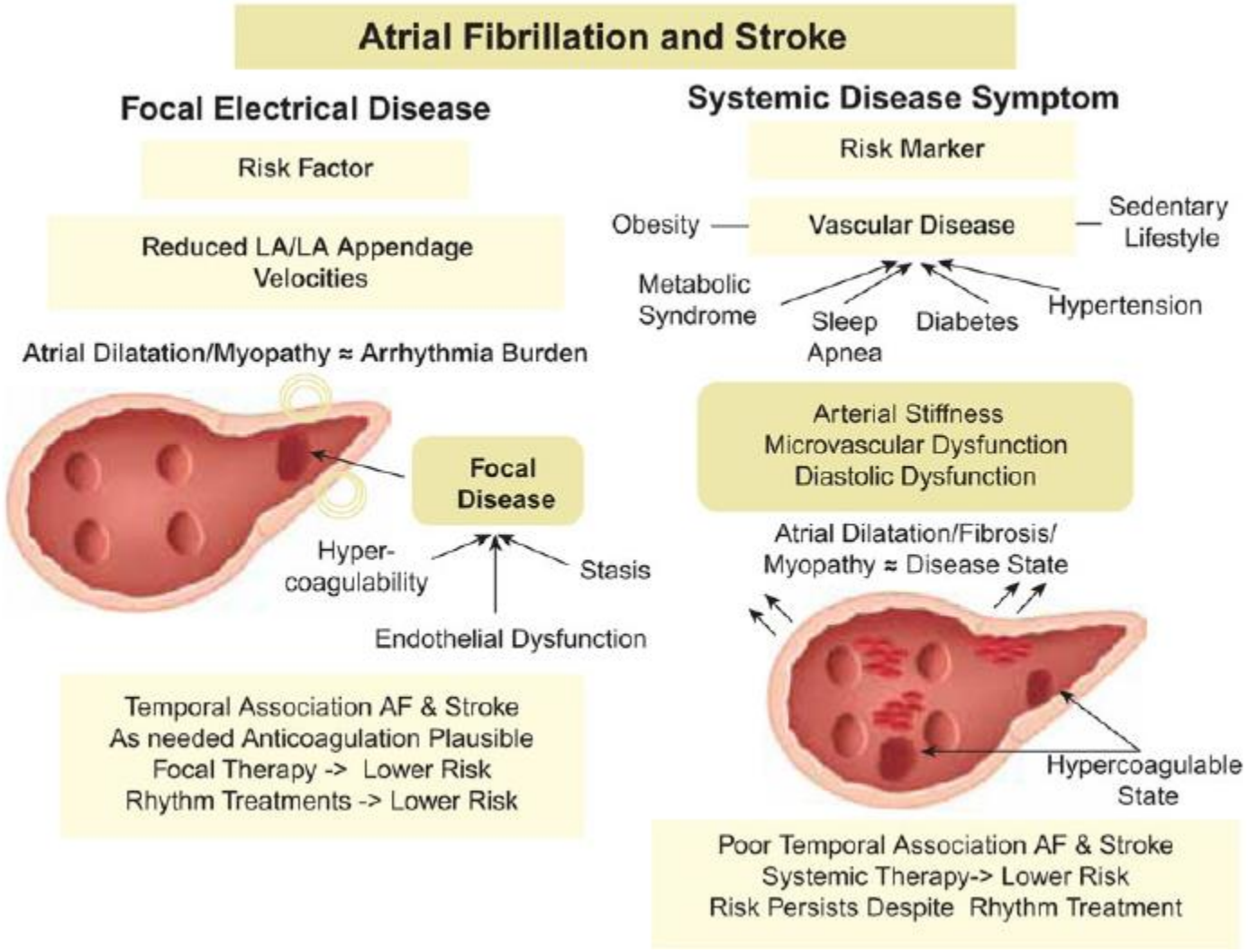
# AF: Risk factor or risk marker




LA, left atrium;

Bunch T.J. & May H.T. Eur Heart J. 2016; 37: 2890-2

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# Take home messages

- AF is a risk marker for systemic disease and a risk factor for stroke. The first mission in AF patients is to prevent stroke
- Heart failure is a more common cause of death than stroke
- Elevations of d-dimer, troponin, and BNP are more predictive of stroke than $CHA_2DS_2$-VASc


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# Take home messages

- Women receive equal rates and quality of anticoagulation as men. Yet, for unknown reasons, their risk of stroke with AF is higher than that of men
- Integrated AF care requires patient involvement and empowerment, educational guidance, and shared decision-making


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# Heart failure and atrial fibrillation: Patient profile and outcomes in the real world

**Professor Alexander G.G. Turpie**
**McMaster University, Hamilton, Canada**

TRI Thrombosis Research Institute

www.garfieldregistry.org

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# Disclosures

**Personal fees: Bayer Healthcare, Janssen Pharmaceutical Research & Development LLC, Astellas, Portola, Takeda**



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# Background

- Atrial fibrillation (AF) and heart failure (CHF) often co-exist and are associated with a worse prognosis than either condition alone[1]
- In patients with AF, biomarkers (e.g. N-terminal pro-B-type natriuretic peptide) are highly predictive of increased risk of stroke/systemic embolism and death[2]
- Heart failure is a leading cause of 30-day readmissions among patients initially hospitalised for AF[3]


1. Lubitz S.A. et al Heart Fail Clin. 2010; 6: 87-200
2. Chatterjee N.A. et al JACC Heart Fail. 2017; 5: 552-60
3. Ruff C.T. et al JAMA Cardiol. 2016; 1: 999-10062





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# Objectives of GARFIELD-AF analysis

- **To evaluate the characteristics of patients with newly diagnosed AF who present with comorbid heart failure**
- **To assess the patterns of antithrombotic and heart failure treatments according to the presence and severity of heart failure**
- **Describe the increased risk of heart failure for**
  - All-cause mortality
  - Stroke or systemic embolism (SE)
  - Major bleeding

  **over the first year after the diagnosis of AF**


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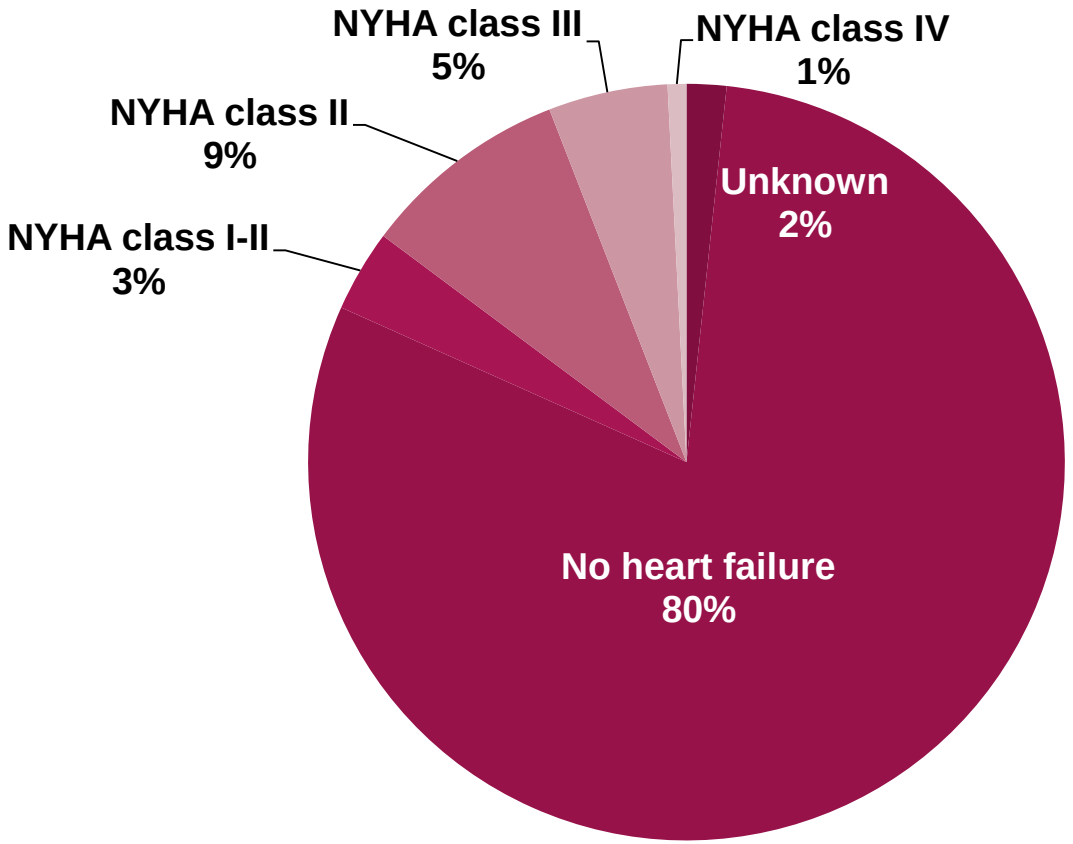
# Methods

**52,081 patients were recruited into GARFIELD-AF between March 2010 and August 2016**

**NYHA classification was available for 51,180 patients**




Cohorts 1–5, N=52,081; NYHA, New York Heart Association

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# Clinical characteristics of patients

| | No CHF (n=41,676) | NYHA Class I–II (n=6441) | NYHA Class III–IV (n=3063) |
|---|---|---|---|
| Female, % | 44.0 | 45.2 | 45.0 |
| ≥75 yrs, % | 36.5 | 38.4 | 42.5 |
| Type 2 diabetes, % | 21.9 | 21.9 | **26.1** |
| History of hypertension, % | 75.6 | 80.7 | 77.4 |
| Vascular disease, % | 13.0 | 19.3 | 26.4 |
| Moderate-to-severe CKD, % | 9.1 | 12.9 | **20.8** |
| Prior stroke/TIA | 11.5 | 10.7 | 11.7 |
| History of bleeding | 2.4 | 2.8 | **3.7** |
| $CHA_2DS_2$-VASc score, mean (SD) | **2.9 (1.5)** | **4.0 (1.5)** | **4.2 (1.6)** |
| HAS-BLED score, mean (SD) | 1.4 (0.9) | 1.5 (0.9) | 1.7 (1.0) |

Cohorts 1–5, N=52,081; CKD, chronic kidney disease; TIA, transient ischaemic attack

Unpublished Data

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# Clinical characteristics of patients

| | No CHF (n=41,676) | NYHA Class I–II (n=6441) | NYHA Class III–IV (n=3063) |
|---|---|---|---|
| **Coronary artery disease, %** | 17.5 | **36.1** | **44.9** |
| **Type of AF characterised shortly after diagnosis, %** | | | |
| Permanent | 11.9 | 14.2 | **20.8** |
| Persistent | 13.8 | 19.7 | 19.6 |
| Paroxysmal | 29.0 | 24.2 | 15.5 |
| Unknown | 45.2 | 41.9 | 44.1 |

LVEF, left ventricular ejection fraction

Unpublished Data



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# Care setting at diagnosis of AF in patients with CHF

| % Patients | No CHF (n=41,676) | NYHA Class I–II (n=6441) | NYHA Class III–IV (n=3063) |
|---|---|---|---|
| Cardiology | 64.5 | 70.0 | 73.8 |
| Internal medicine | 17.9 | 18.2 | 18.3 |
| Primary care | 15.4 | 10.6 | 7.0 |
| Neurology | 1.9 | 0.8 | 0.4 |
| Geriatrics | 0.4 | 0.4 | 0.6 |

ARB, Angiotensin receptor blockade

Unpublished Data



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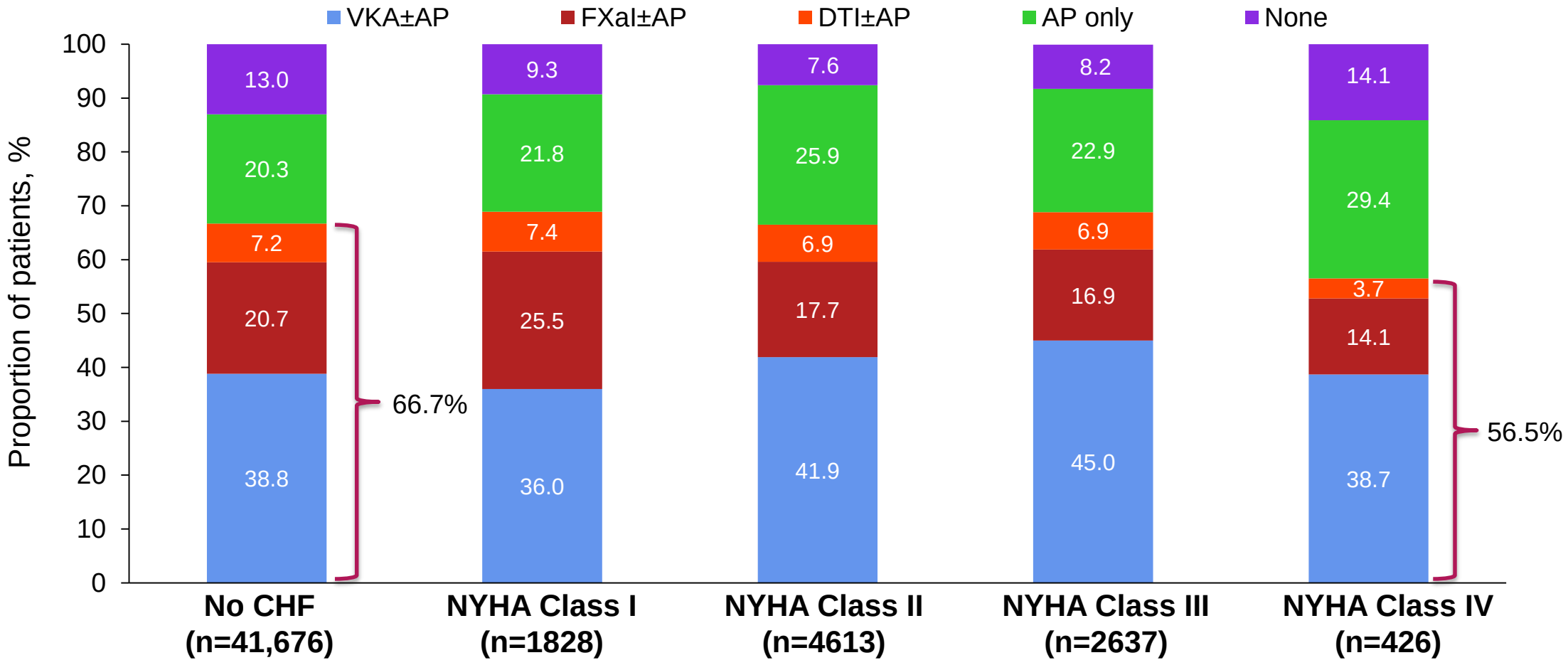
# Antithrombotic treatment patterns




AP, antiplatelet; CHF, congestive heart failure; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonists

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# CHF therapy according to disease severity

| | No CHF (n=41,676) | NYHA class I–II (n=6441) | NYHA class III–IV (n=3063) |
|---|---|---|---|
| ACE inhibitor/ARB | 50.3 | 64.7 | 69.6 |
| Aldosterone blocker | 3.9 | 15.1 | 28.5 |
| Loop or other diuretic | 26.4 | 49.5 | 73.2 |
| Beta-blocker | 47.3 | 56.8 | 57.6 |
| Digoxin/digitalis | 3.5 | 7.8 | 13.0 |

ACE, angiotensin-converting enzyme; ARB, Angiotensin receptor blockade

Unpublished Data



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# CHF therapy according to care setting at diagnosis of AF

| % Patients | ACE inhibitor/ ARB | Beta-blocker | Aldosterone blockade |
|---|---|---|---|
| Cardiology (n=7355) | 66.4 | 57.5 | 20.5 |
| Internal medicine (n=1916) | 65.0 | 57.8 | 16.1 |
| Primary care (n=1009) | 61.0 | 50.2 | 11.0 |

ACE, angiotensin-converting enzyme; ARB, Angiotensin receptor blockade

Unpublished Data



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# Outcomes by presence and severity of CHF

## One-year event rates per 100 person-years

| | No CHF (n=41,676) | NYHA Class I (n=1828) | NYHA Class II (n=4613) | NYHA Class III (n=2637) | NYHA Class IV (n=426) |
|---|---|---|---|---|---|
| Stroke/SE rate (95% CI) | 1.25 (1.14 to 1.37) | 1.36 (0.90 to 2.04) | 1.82 (1.46 to 2.28) | 2.00 (1.49 to 2.66) | 2.57 (1.34 to 4.93) |
| Major bleeding rate (95% CI) | 0.85 (0.76 to 0.95) | 0.71 (0.40 to 1.24) | 0.45 (0.29 to 0.70) | 1.47 (1.05 to 2.06) | 2.00 (0.95 to 4.19) |
| All-cause mortality rate (95% CI) | 3.36 (3.18 to 3.55) | 2.53 (1.87 to 3.40) | 6.23 (5.52 to 7.03) | 14.87 (13.38 to 16.53) | 24.34 (19.71 to 30.07) |



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Outcomes by presence and severity of CHF

## One-year event rates per 100 person-years

| | No CHF (n=41,676) | NYHA Class I (n=1828) | NYHA Class II (n=4613) | NYHA Class III (n=2637) | NYHA Class IV (n=426) |
|---|---|---|---|---|---|
| CV death | 1.07 (0.97 to 1.17) | 1.00 (0.62 to 1.61) | 3.01 (2.53 to 3.58) | 7.24 (6.23 to 8.42) | 11.61 (8.55 to 15.76) |
| Non-CV death | 1.40 (1.28 to 1.52) | 0.88 (0.53 to 1.46) | 1.83 (1.47 to 2.29) | 3.79 (3.08 to 4.68) | 6.51 (4.33 to 9.80) |
| New ACS | 0.68 (0.60 to 0.77) | 0.53 (0.28 to 1.02) | 1.34 (1.04 to 1.74) | 1.55 (1.12 to 2.15) | 1.69 (0.76 to 3.76) |
| New and worsened CHF | 0.98 (0.89 to 1.09) | 4.38 (3.48 to 5.51) | 7.17 (6.40 to 8.04) | 8.29 (7.18 to 9.58) | 12.71 (9.39 to 17.19) |

Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Conclusions

- 18% patients with newly diagnosed AF present with CHF
- These patients are older/sicker (particularly NYHA class IV) than those without CHF
- Anticoagulation was similar between groups, except NYHA class IV patients were more likely to receive AP therapy
- There was better implementation CHF treatments in NYHA class III/IV, particularly aldosterone blockade
- Prescribing of digitalis remains high
- Gradual increase in events rates with NYHA class
- Patients with NYHA class I seem to have similar outcomes to patients without CHF, but still suffer from a high rates of new-onset or worsened CHF

Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Management and outcomes in acute coronary syndromes with atrial fibrillation: Where can we improve?

Professor Keith A.A. Fox

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www.garfieldregistry.org

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield global anticoagulant registry in the field

# Disclosures

**Grants: Bayer, Johnson and Johnson, Astra Zeneca**

**Personal fees: Bayer AG, Johnson and Johnson, Lilly, Astra Zeneca, Sanofi/Regeneron**



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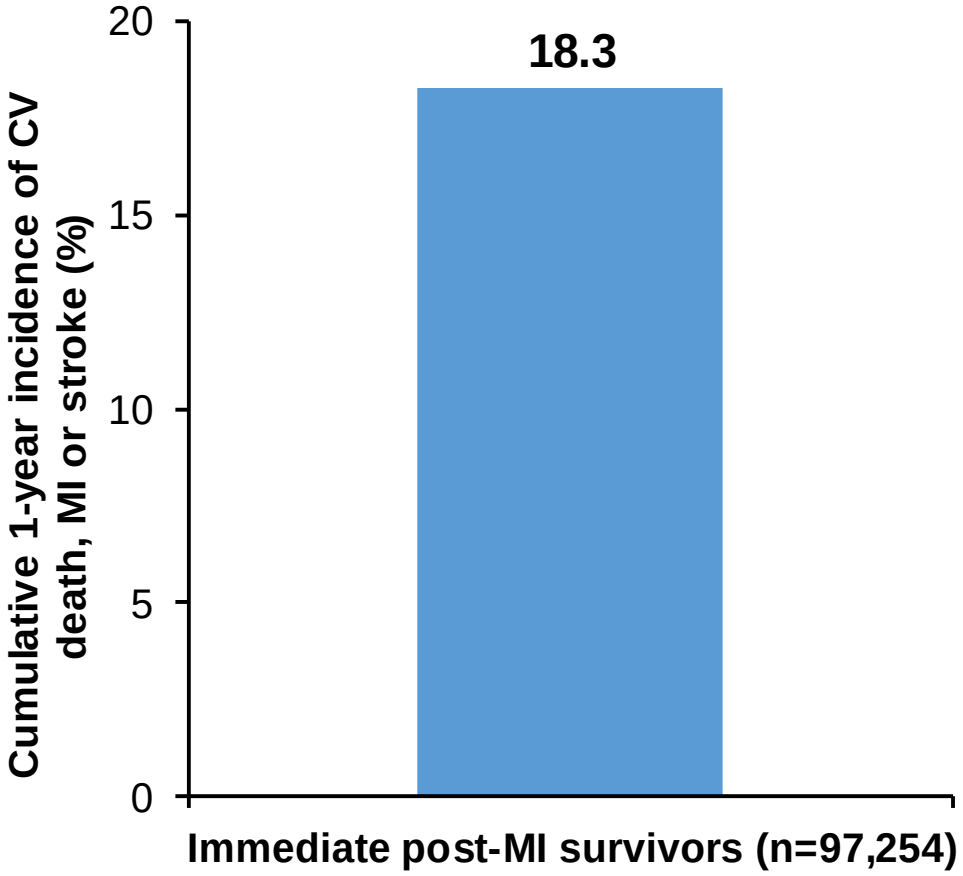
# CV death, MI or stroke within 365 days of index MI

## ~1 in 5 patients suffered a MI, stroke or CV death within the first year after a MI



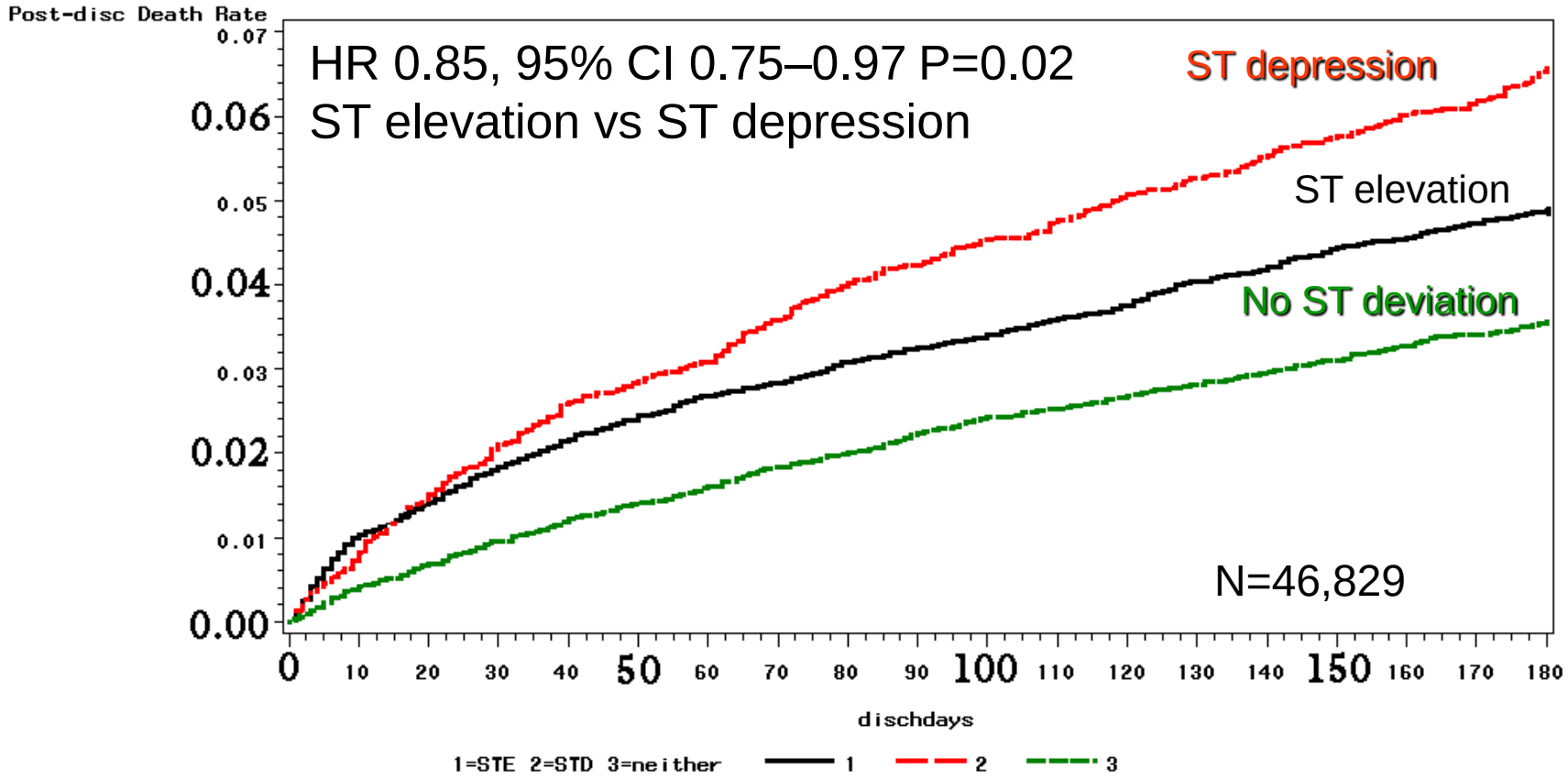

CV, cardiovascular; MI, myocardial infarction; Jernberg T. et al Eur Heart J. 2015; 36: 1163-70



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# All ACS: Time course of events beyond 15 days (landmark analysis) N=46,829

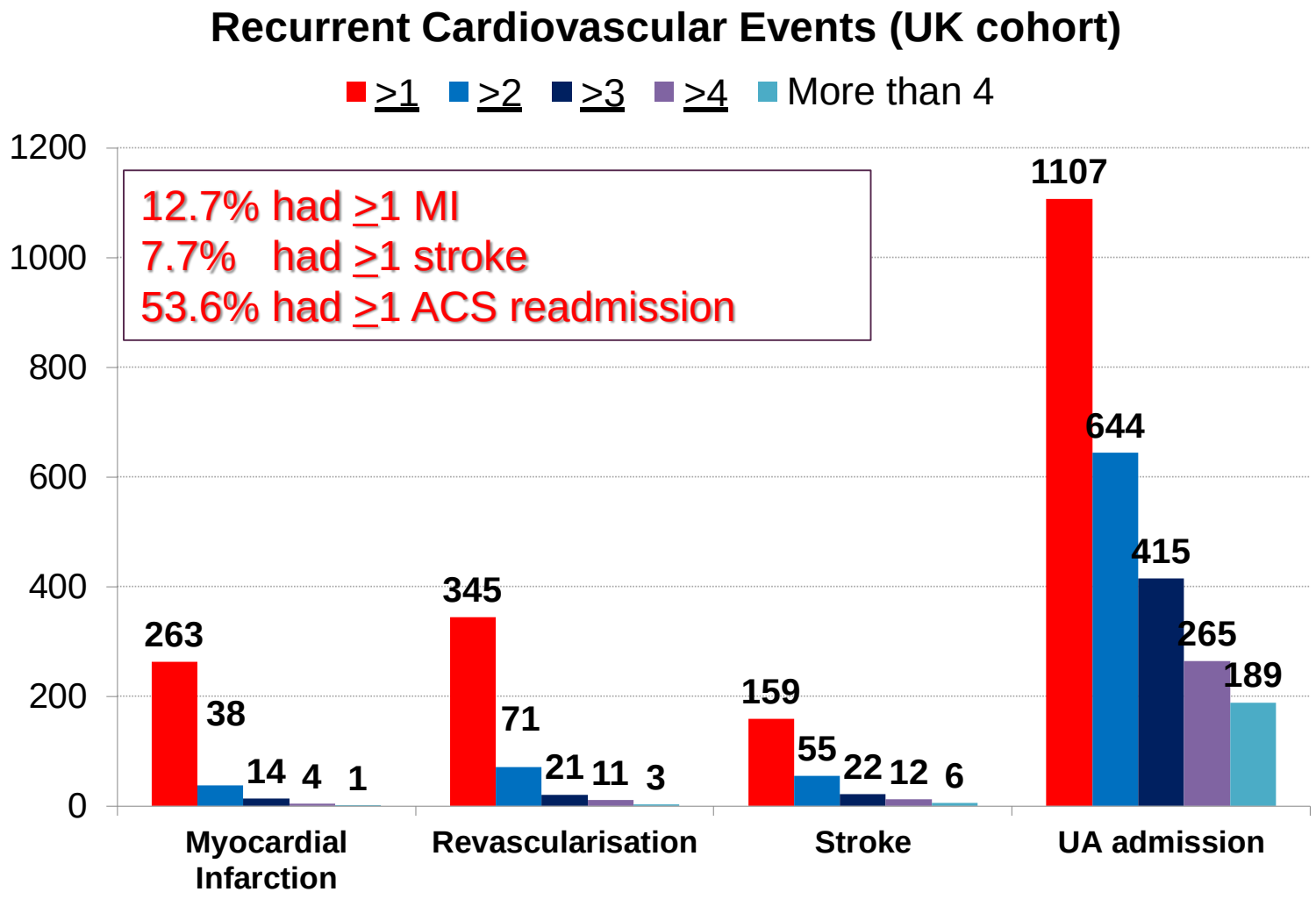
## Kaplan Meier Cumulative Death Rate: by ST Group




ACS, acute coronary syndromes; Fox K.A.A. et al Nat Clin Pract Cardiovasc Med. 2008; 5: 580-9

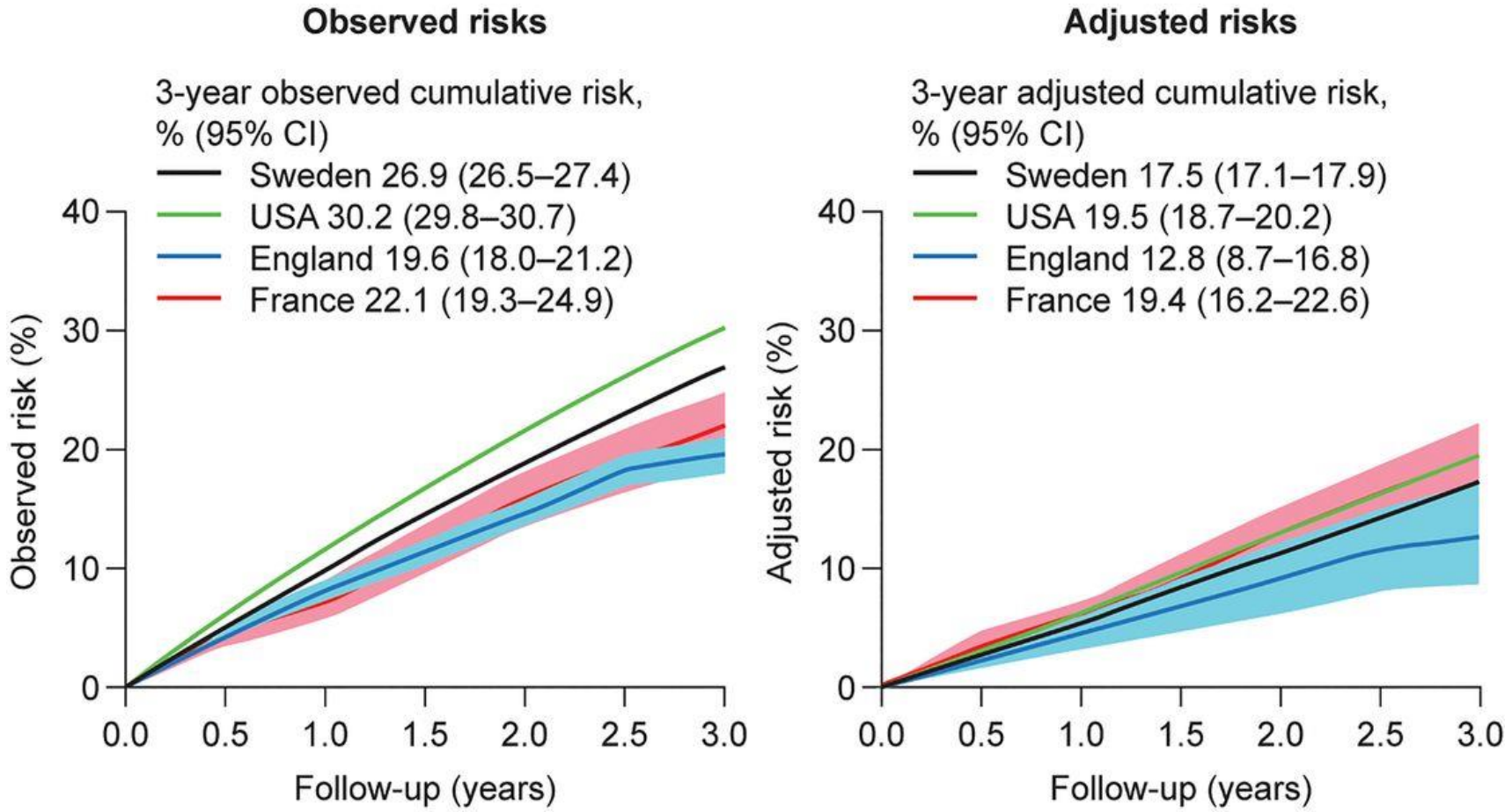
GRACE™ GLOBAL REGISTRY OF ACUTE CORONARY EVENTS

# Under-estimated and under-recognised: The late consequences of ACS




ACS, acute coronary syndromes; MI, myocardial infarction; UA, unstable angina; Fox K.A.A. et al Eur Heart J. 2010; 31: 2755-64

# Beyond the first year: All-cause death in post-myocardial infarction survivors aged 65 years and older from 1 year after the index myocardial infarction




Rapsomaniki E. et al Eur Heart J Qual Care Clin Outcomes. 2016; 2: 172-83

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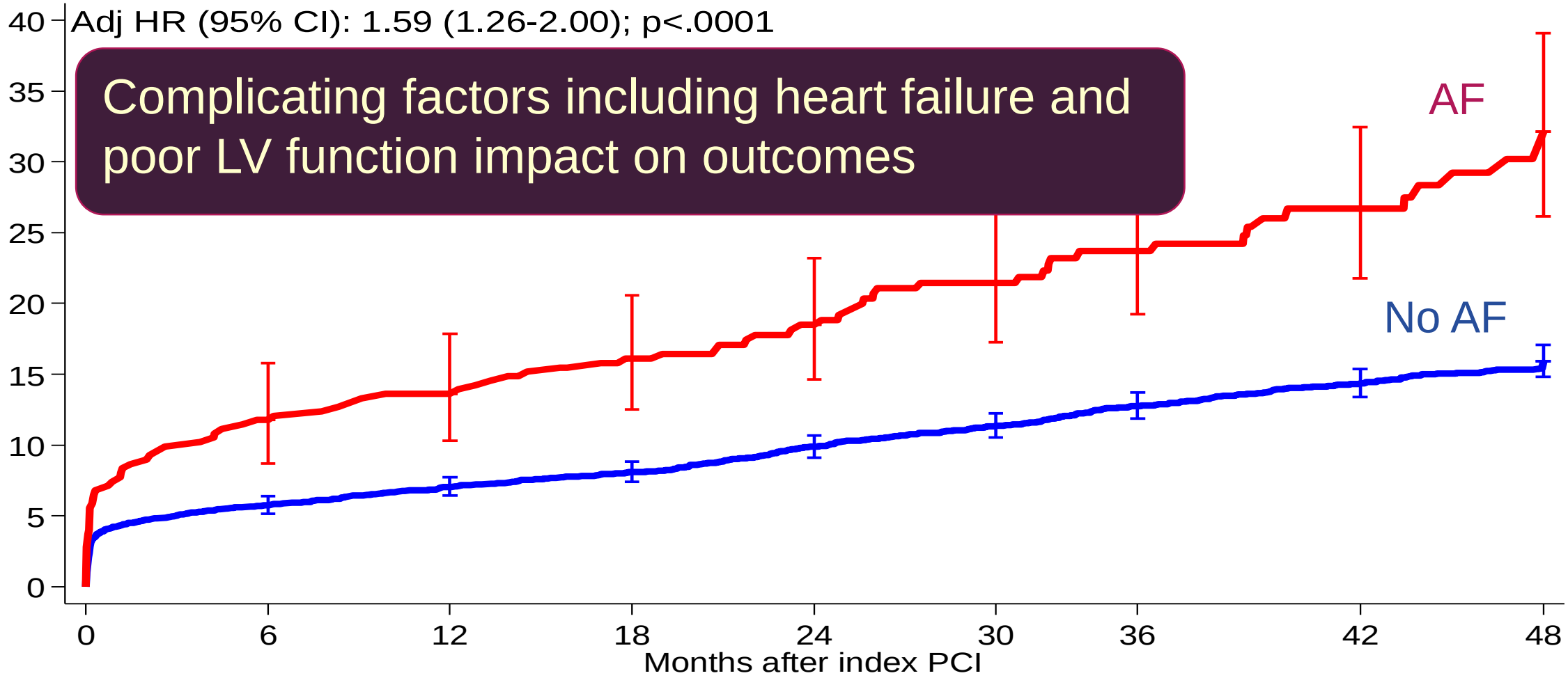
European Heart Journal - Quality of Care & Clinical Outcomes

# Atrial fibrillation and outcome in patients undergoing PCI

## *Death, MI, Ischaemic Stroke, and BARC Bleeding 3b, 3c, 5a, 5b*




AF, atrial fibrillation; BARC, Bleeding Academic Research Consortium; LV, left ventricular; MI, myocardial infarction; PCI, percutaneous coronary intervention; Pilgrim T. et al Eurointervention. 2013; 8: 1061-71

# Rates of bleeding after MI or PCI in patients with AF treated with different antithrombotic combinations

| Danish registry 2000–2009 | Crude incidence rate of non-fatal and fatal bleeding at 1 year, % year (95% CI) |
|---|---|
| **Monotherapy** | |
| ASA | 7.0 (6.0–8.1) |
| Clopidogrel | 6.6 (4.7–9.1) |
| VKA | 7.0 (5.2–9.3) |
| **Dual therapy** | |
| ASA + clopidogrel | 7.0 (6.0–8.2) |
| VKA + ASA | 9.5 (7.9–11.3) |
| VKA + clopidogrel | 10.6 (7.8–14.5) |
| **Triple therapy** | |
| ASA + clopidogrel + VKA | 14.2 (11.8–17.1) |

11,480 subjects, mean age 75.6 years

ASA, acetylsalicylic acid; MI, myocardial infarction; PCI, percutaneous coronary intervention; VKA, vitamin K antagonist;

Lamberts M. et al Circulation. 2012; 126: 1185-93

# Objectives for GARFIELD-AF analysis

- To describe the clinical characteristics of patients with newly diagnosed AF and risk of stroke who have a history of ACS
- To determine differences in antithrombotic treatment patterns
  - **With ACS and without ACS and with increasing $CHA_2DS_2$-VASc**
- To describe antithrombotic therapy patterns over time
  - **Baseline, 4 months, 8 months, and 12 months**
- To describe the impact of prior ACS on clinical outcomes

Cohorts 1–5, N=52,081


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Demographics and clinical characteristics of GARFIELD-AF patients with and without history of ACS

| | No ACS (N=46,916) | ACS (N=4914) |
|---|---|---|
| **Female, %** | 45.5 | 31.7 |
| **Age at AF diagnosis (years), median** | 71.0 | 73.0 |
| Congestive heart failure | 18.8 | 30.3 |
| Coronary artery bypass graft | 1.3 | 21.2 |
| Hypercholesterolaemia | 38.9 | 67.0 |
| Vascular disease | 5.7 | 99.0 |
| Stenting | 3.1 | 42.5 |
| Diabetes mellitus | 20.9 | 33.4 |

Cohorts 1–5, N=52,081

Unpublished Data

# Demographics and clinical characteristics of GARFIELD-AF patients with and without history of ACS cont'd

| | No ACS (N=46,916) | ACS (N=4914) |
|---|---|---|
| **Smoking, %** | | |
| Non-smoker | 66.7 | 53.1 |
| Ex-smoker | 22.3 | 36.1 |
| **$CHA_2DS_2$-VASc score, median** | 3.0 | 4.0 |
| **HAS-BLED score, median** | 1.0 | 2.0 |

Cohorts 1–5, N=52,081

Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

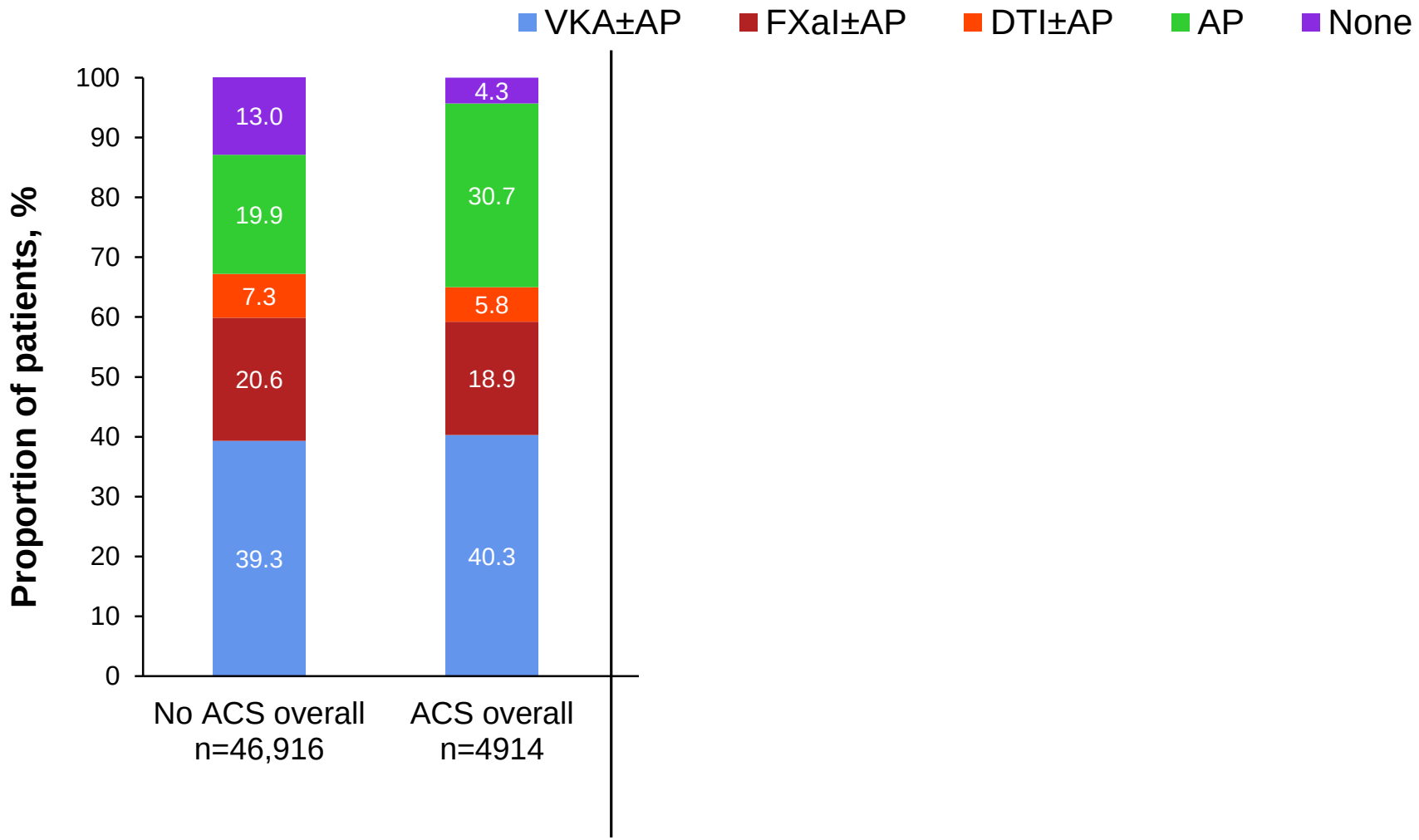
# Main reasons why anticoagulants were not given in $CHA_2DS_2$-VASc ≥2 patients with and without history of ACS

| Reason, % | No ACS (n=9010) | ACS (n=1214) |
|---|---|---|
| **Already taking antiplatelet drugs for other medical condition** | 4.9 | 17.5 |
| **Patient refusal** | 9.5 | 10.5 |
| **Previous bleeding event** | 2.1 | 2.3 |
| **Other/unknown** | **53.8** | **41.8** |
| **Physician's choice** | **29.2** | **25.9** |
| Bleeding risk | **27.6** | **46.3** |
| Concern over patient compliance | 14.2 | 15.6 |
| Guideline recommendation | 10.2 | 7.9 |
| Fall risk | 13.9 | 11.7 |
| Low risk of stroke | 34.1 | 18.4 |

Cohorts 1–5, N=52,081

Unpublished Data

# Antithrombotic therapy at diagnosis in patients with and without history of ACS, according to $CHA_2DS_2$-VASc



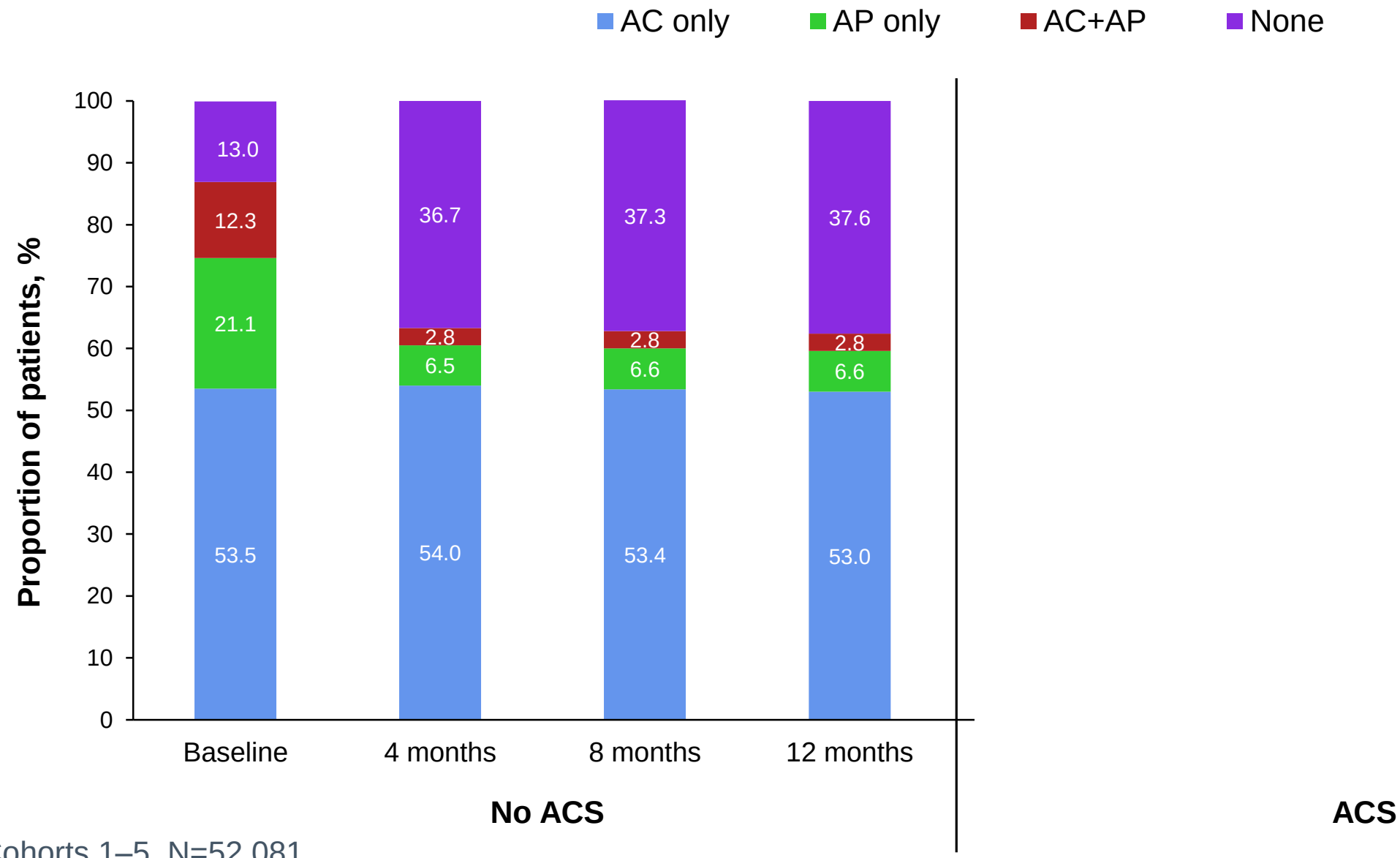

Cohorts 1–5, N=52,081

**$CHA_2DS_2$-VASc**

AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

Unpublished Data

# Antithrombotic therapy over time



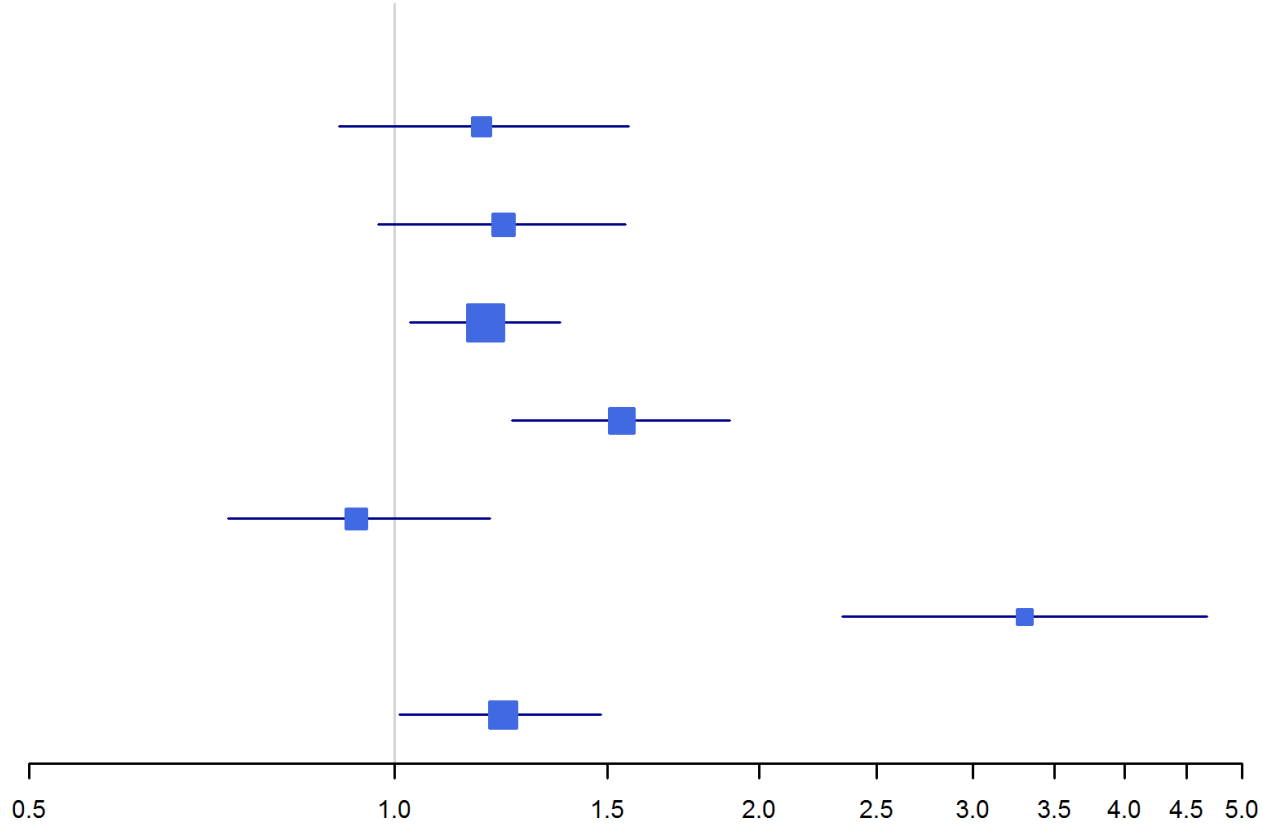

Cohorts 1–5, N=52,081

AC, anticoagulant; AP, antiplatelet

Unpublished Data

# Adjusted HRs for 1-year outcomes for patients with vs without history of ACS

| Outcomes | n (%) | aHR |
|---|---|---|
| Stroke/SE | 650 (1.2) | 1.18 |
| Major bleeding | 407 (0.8) | 1.23 |
| All-cause mortality | 2103 (4.0) | 1.19 |
| Cardiovascular mortality | 789 (1.5) | 1.54 |
| Non-cardiovascular mortality | 771 (1.5) | 0.93 |
| New ACS | 378 (0.7) | 3.31 |
| Congestive heart failure | 1052 (2.0) | 1.23 |




Cohorts 1–5, N=52,081
SE, systemic embolism

Unpublished Data


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Conclusions

1. After ACS, especially with AF, event rates increase over time
2. In patients with AF, with prior ACS, patients are increasingly on combined AP and AC therapy
3. This combined antithrombotic therapy is associated with a modest increase in bleeding
4. The major contributors to adverse outcomes in patients with AF and prior ACS are cardiovascular death and new ACS

Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Chronic kidney disease and atrial fibrillation: Geographic differences in routine care


**Professor Shinya Goto**

**Tokai University School of Medicine, Kanagawa, Japan**



TRI Thrombosis Research Institute

www.garfieldregistry.org

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield global anticoagulant registry in the field

# Disclosures

**Personal fees: Thrombosis Research Institute, Harvard University, American Heart Association, Medscape, Boehringer Ingelheim, Armethrom, Medtronic, Bayer, AstraZeneca**

**Grants: Sanofi, Ono, Pfizer**



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Background

- **Renal dysfunction is an independent predictor of bleeding in patients with atrial fibrillation (AF) treated with oral anticoagulants (ACs)[1] and is part of the HAS-BLED bleeding risk score[2]**
- **A recent meta-analysis of observational studies[3] showed:**
  - Warfarin was beneficial in patients with AF and non-end-stage chronic kidney disease (CKD), reducing stroke risk and mortality without increasing the risk of major bleeding
  - In contrast, in patients with AF and end-stage CKD, warfarin had no effect on stroke and mortality but led to a higher risk of major bleeding
- **Few global data are available for clinical outcomes in newly diagnosed AF accompanied by various stages of CKD**


1. King A. Nat Rev Cardiol. 2011; 8: 64
2. Pisters R. et al Chest. 2010; 138: 1093-100
3. Dahal K. Chest. 2016; 149: 951-9





The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Objectives

- To describe the relationship between CKD stage and baseline characteristics, antithrombotic usage, and clinical outcomes in real-world clinical practice

- To confirm the hypothesis that CKD influences clinical outcomes in AF with a global cohort of newly diagnosed patients with AF

Cohorts 3–5, N=34,929


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Methods

- **Patients recruited into cohorts 3–5 (N=34,929) were classified as having no CKD, mild CKD (National Kidney Foundation's Kidney Disease Outcomes Quality Initiative Stages I–II), or moderate-to-severe CKD (Stages III–V)**

- **Patient characteristics and antithrombotic therapy at baseline and clinical outcomes at 1 year were analysed:**
  - In the three cohorts
  - In patients enrolled in different geographic regions

- **Event rates are displayed as rates per 100 person-years plus 95% confidence intervals. Cox proportional hazards models were used to determine the effects of CKD severity on clinical outcomes**



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

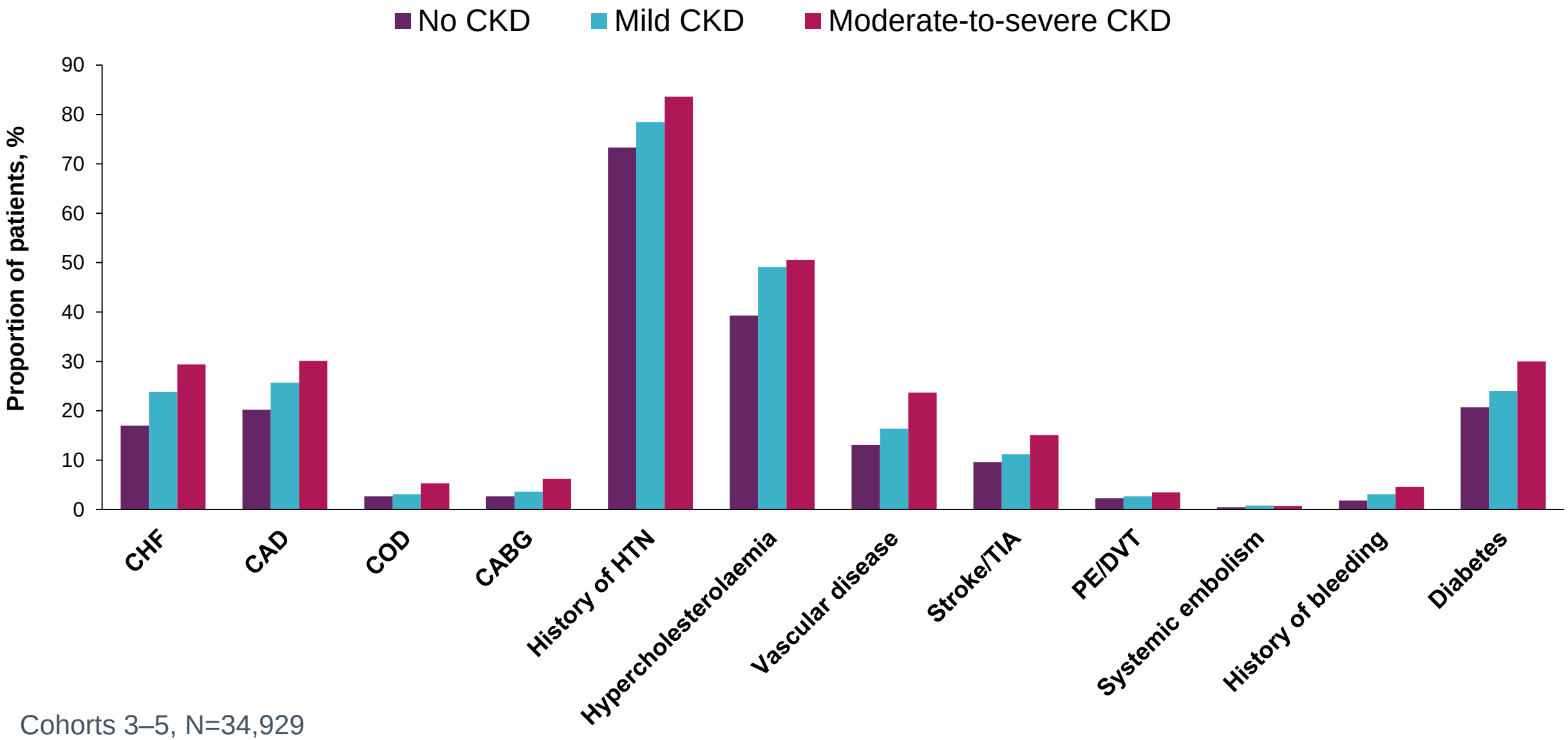
# Demographics, clinical characteristics, and care settings of patients according to CKD group

| | No CKD (n=23,883) | Mild CKD (n=5602) | Moderate-to-severe CKD (n=3619) |
|---|---|---|---|
| **Female, %** | 43.6 | 43.3 | **50.5** |
| **Age at AF diagnosis (years), median (IQR)** | 69.0 (61.0 to 77.0) | 71.0 (63.0 to 78.0) | **78.0 (71.0 to 83.0)** |
| **Care setting specialty at diagnosis, %** | | | |
| Cardiology | **70.8** | 61.4 | 57.7 |
| Internal medicine | 15.8 | 20.2 | 21.0 |
| Primary care/general practice | 11.8 | 16.3 | 18.3 |
| **$CHA_2DS_2$-VASc score, median (IQR)** | 3.0 (2.0 to 4.0) | 3.0 (2.0 to 4.0) | **4.0 (3.0 to 5.0)** |
| **HAS-BLED score, median (IQR)** | 1.0 (1.0 to 2.0) | 1.0 (1.0 to 2.0) | **2.0 (2.0 to 3.0)** |

Cohorts 3–5, N=34,929

Unpublished Data

# Prevalence of comorbidities according to CKD group

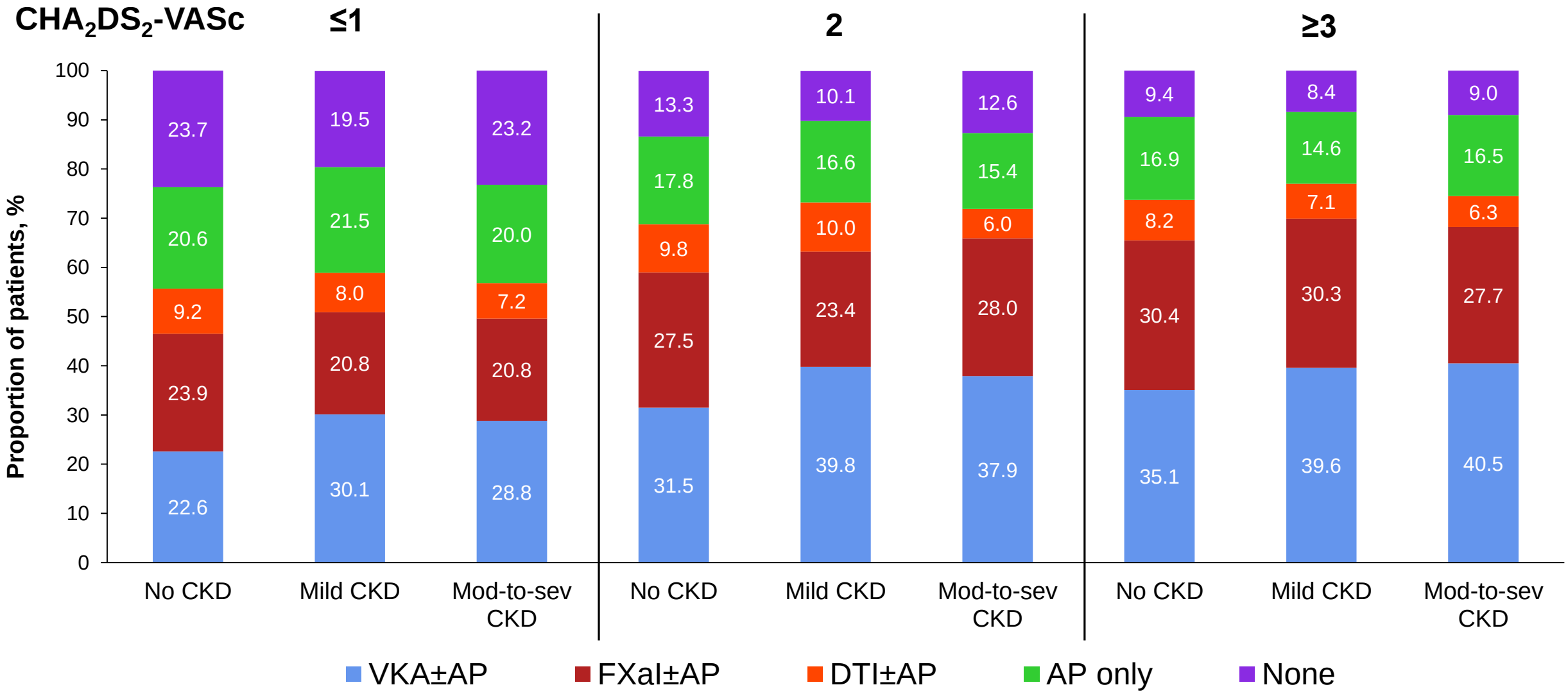



Cohorts 3–5, N=34,929

CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; COD, carotid occlusive disease; DVT, deep vein thrombosis; HTN, hypertension; PE, pulmonary embolism; TIA, transient ischaemic attack

Unpublished Data

# Antithrombotic therapy at diagnosis according to CKD group and $CHA_2DS_2$-VASc score




Cohorts 3–5, N=34,929

AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

Unpublished Data

# Incidence rates (per 100 person-years) and 95% CI of 1-year outcomes according to CKD group

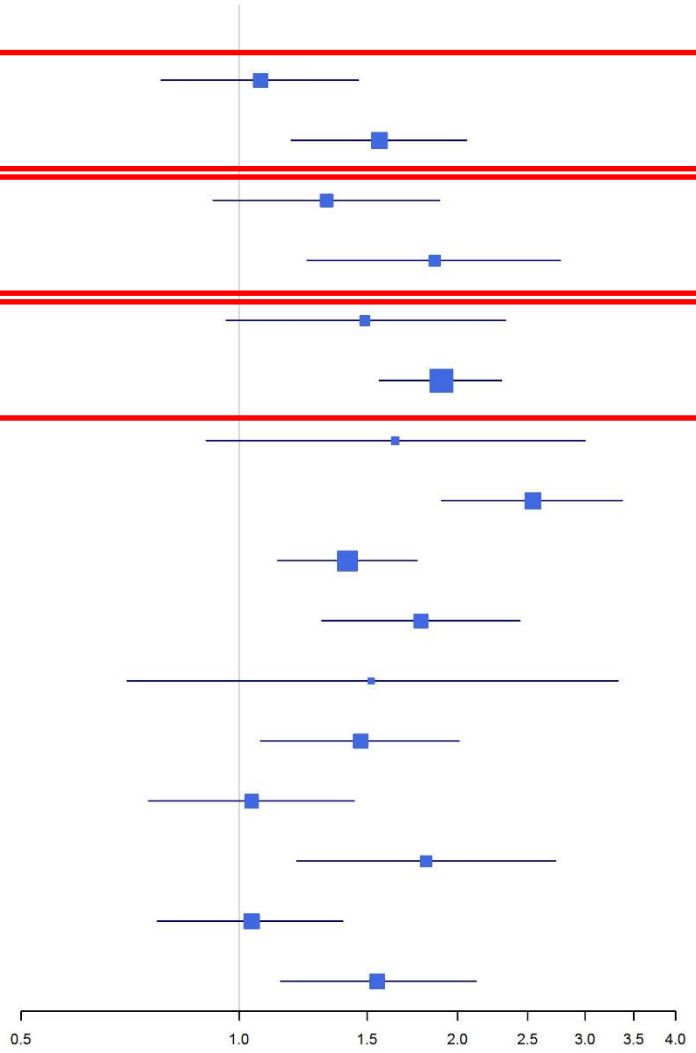
| | No CKD (n=23,883) | Mild CKD (n=5602) | Moderate-to-severe CKD (n=3619) |
|---|---|---|---|
| **Stroke/systemic embolism** | 1.07 (0.94; 1.21) | **1.22 (0.95; 1.56)** | **2.29 (1.82; 2.88)** |
| **Major bleeding** | 0.66 (0.56; 0.78) | **1.02 (0.78; 1.34)** | **1.82 (1.41; 2.35)** |
| **All-cause mortality** | 3.27 (3.04; 3.52) | **5.76 (5.14; 6.46)** | **10.40 (9.34; 11.57)** |
| Cardiovascular mortality | 1.02 (0.89; 1.16) | **1.99 (1.64; 2.42)** | **4.48 (3.81; 5.28)** |
| Non-cardiovascular mortality | 1.29 (1.15; 1.45) | **2.03 (1.68; 2.46)** | **3.67 (3.07; 4.40)** |
| Undetermined cause of mortality | 0.96 (0.84; 1.10) | **1.74 (1.41; 2.14)** | **2.24 (1.78; 2.82)** |
| **New ACS** | 0.63 (0.53; 0.74) | **0.71 (0.51; 0.98)** | **1.60 (1.21; 2.10)** |
| **Congestive heart failure** | 1.33 (1.18; 1.49) | **1.75 (1.43; 2.16)** | **3.33 (2.75; 4.03)** |

Cohorts 3–5, N=34,929; ACS, acute coronary syndromes

Unpublished Data

# Adjusted HRs for 1-year outcomes according to severity of CKD (mild or moderate-to-severe vs no CKD)

| Outcomes | CKD Severity | aHR | 95% CI |
|---|---|---|---|
| Stroke/SE | Mild | 1.07 | (0.78, 1.46) |
| | Moderate to severe | 1.56 | (1.18, 2.06) |
| Major bleeding | Mild | 1.32 | (0.92, 1.89) |
| | Moderate to severe | 1.86 | (1.24, 2.77) |
| All-cause mortality | Mild | 1.49 | (0.96, 2.33) |
| | Moderate to severe | 1.90 | (1.56, 2.30) |
| Cardiovascular mortality | Mild | 1.64 | (0.90, 3.00) |
| | Moderate to severe | 2.54 | (1.90, 3.37) |
| Noncardiovascular mortality | Mild | 1.41 | (1.13, 1.76) |
| | Moderate to severe | 1.78 | (1.30, 2.44) |
| Undetermined cause of mortality | Mild | 1.52 | (0.70, 3.33) |
| | Moderate to severe | 1.47 | (1.07, 2.01) |
| New ACS | Mild | 1.04 | (0.75, 1.44) |
| | Moderate to severe | 1.81 | (1.20, 2.73) |
| Congestive heart failure | Mild | 1.04 | (0.77, 1.39) |
| | Moderate to severe | 1.55 | (1.14, 2.12) |



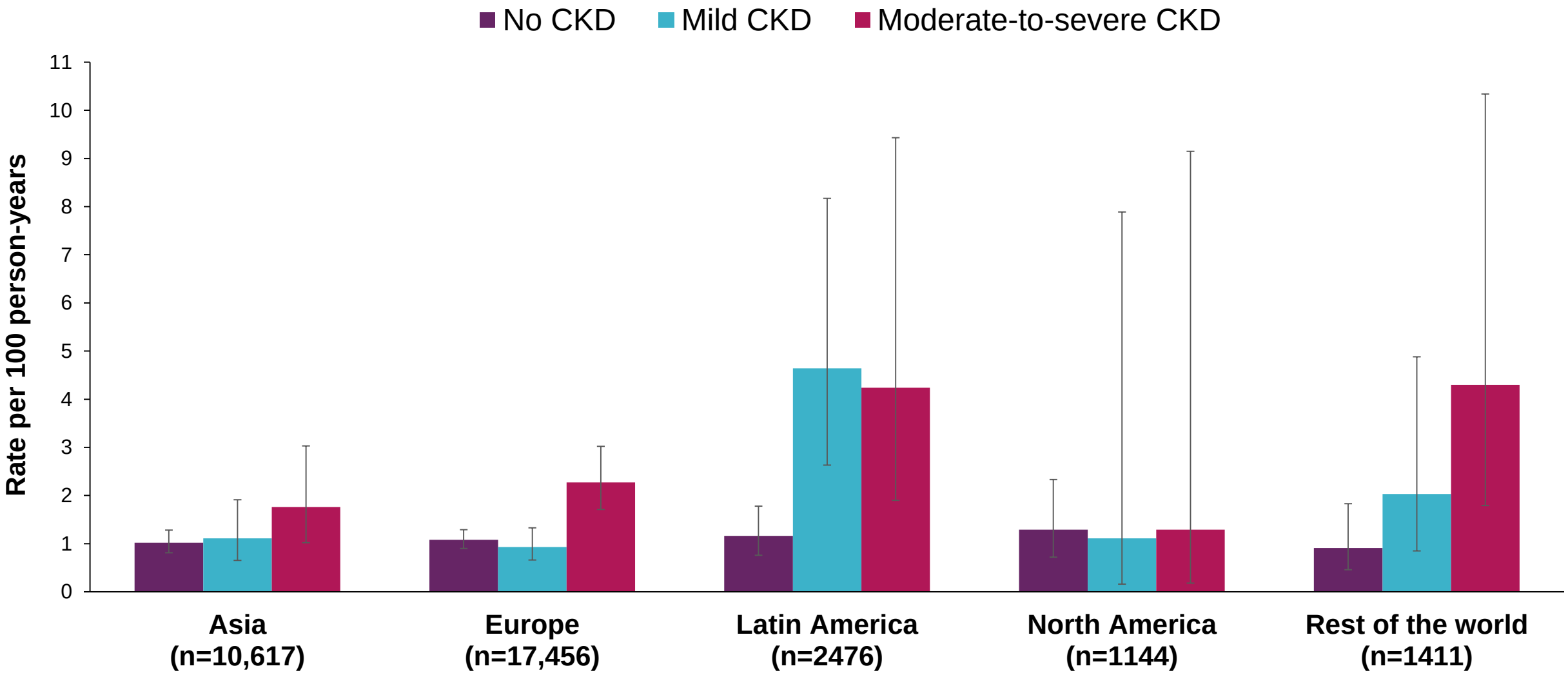

Cohorts 3–5, N=34,929

ACS, acute coronary syndromes; SE, systemic embolism

Hazard ratios were adjusted for age, gender, race, smoking, diabetes, hypertension, previous stroke/transient ischaemic attack/systemic embolism, history of bleeding, congestive cardiac failure, peripheral vascular disease, anticoagulant therapy, type of AF, and alcohol consumption

Unpublished Data

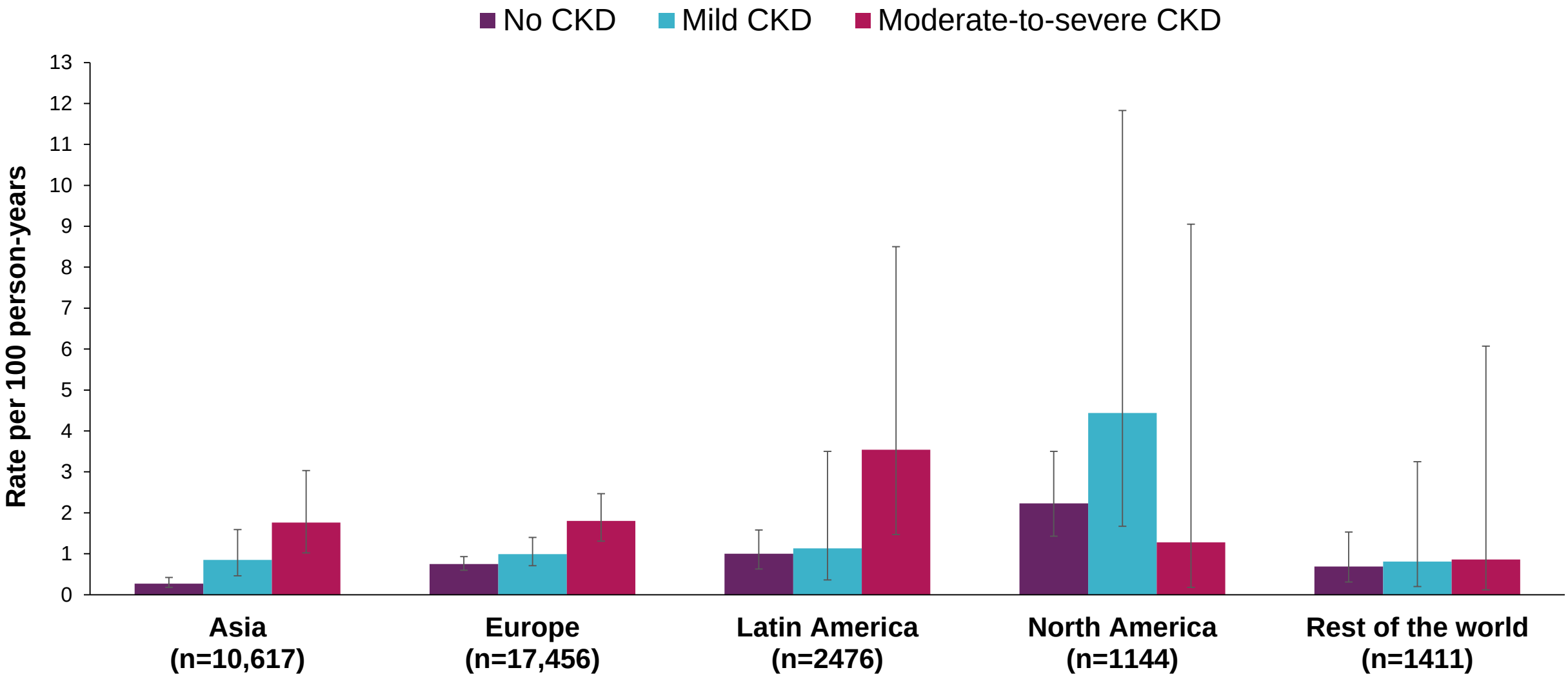
# One-year incidence rate of stroke/SE (95% CI) according to CKD group and region




Cohorts 3–5, N=34,929; SE, systemic embolism

Unpublished Data

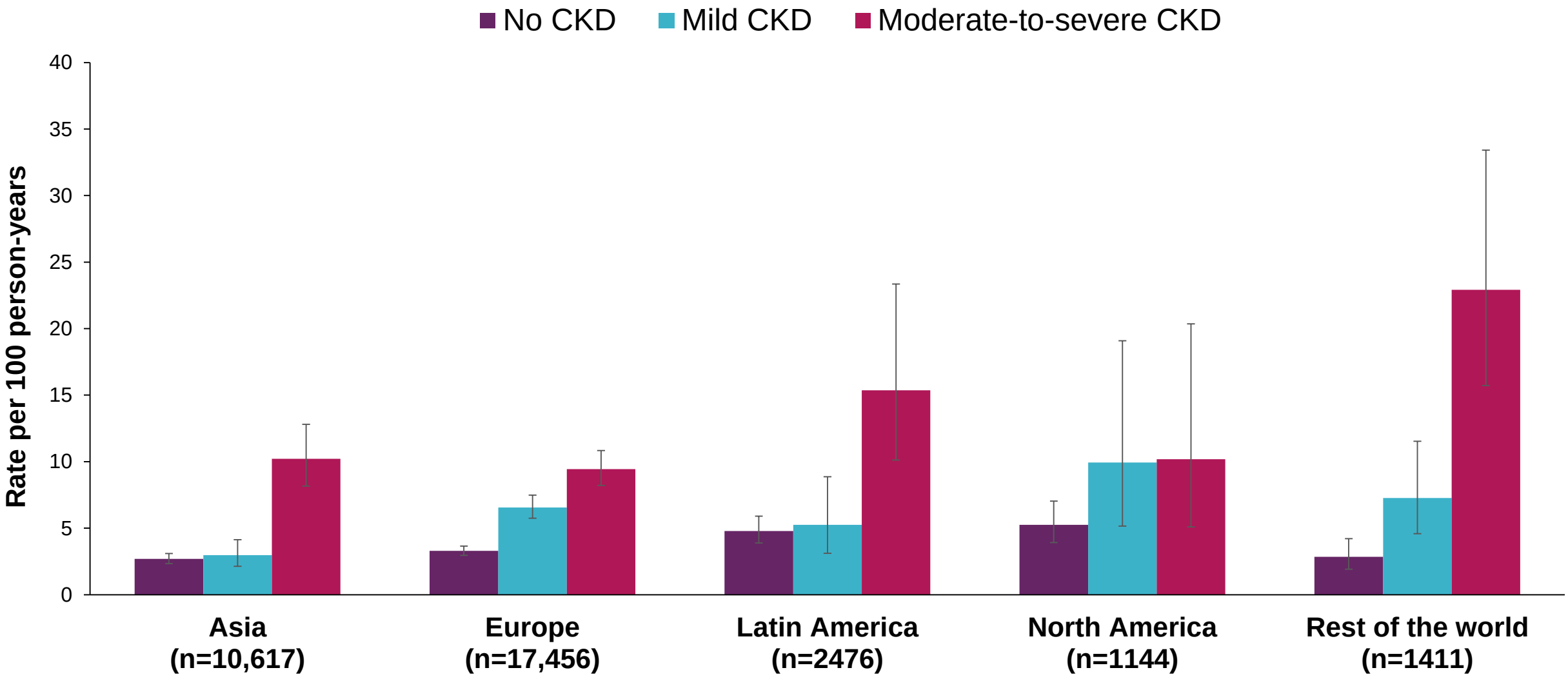
# One-year incidence rate of major bleeding (95% CI) according to CKD group and region




Cohorts 3–5, N=34,929

Unpublished Data

# One-year incidence rate of all-cause mortality (95% CI) according to CKD group and region




Cohorts 3–5, N=34,929

Unpublished Data

# Conclusions

- The international prospective registry GARFIELD-AF shows that globally, 17% and 11% of patients newly diagnosed with AF have mild and moderate-to-severe CKD, respectively
- There was tendency of increased comorbidity in patients with advanced CKD stage
- The use of oral anticoagulants in patients with AF at low or high risk of stroke was similar across the stages of CKD
- Our international registry data demonstrated a higher risk of stroke/SE, serious bleeding, and mortality in moderate-to-severe CKD versus no CKD
- Similar trends were shown in most regions for the three endpoints

Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Impact of body mass index and the metabolic syndrome on outcomes in atrial fibrillation

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St. George's University of London, London, UK

TRI Thrombosis Research Institute

www.garfieldregistry.org

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield global anticoagulant registry in the field

# Disclosures

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**Institutional grant income: Bayer, Boehringer Ingelheim, Pfizer/BMS, Daiichi Sankyo**



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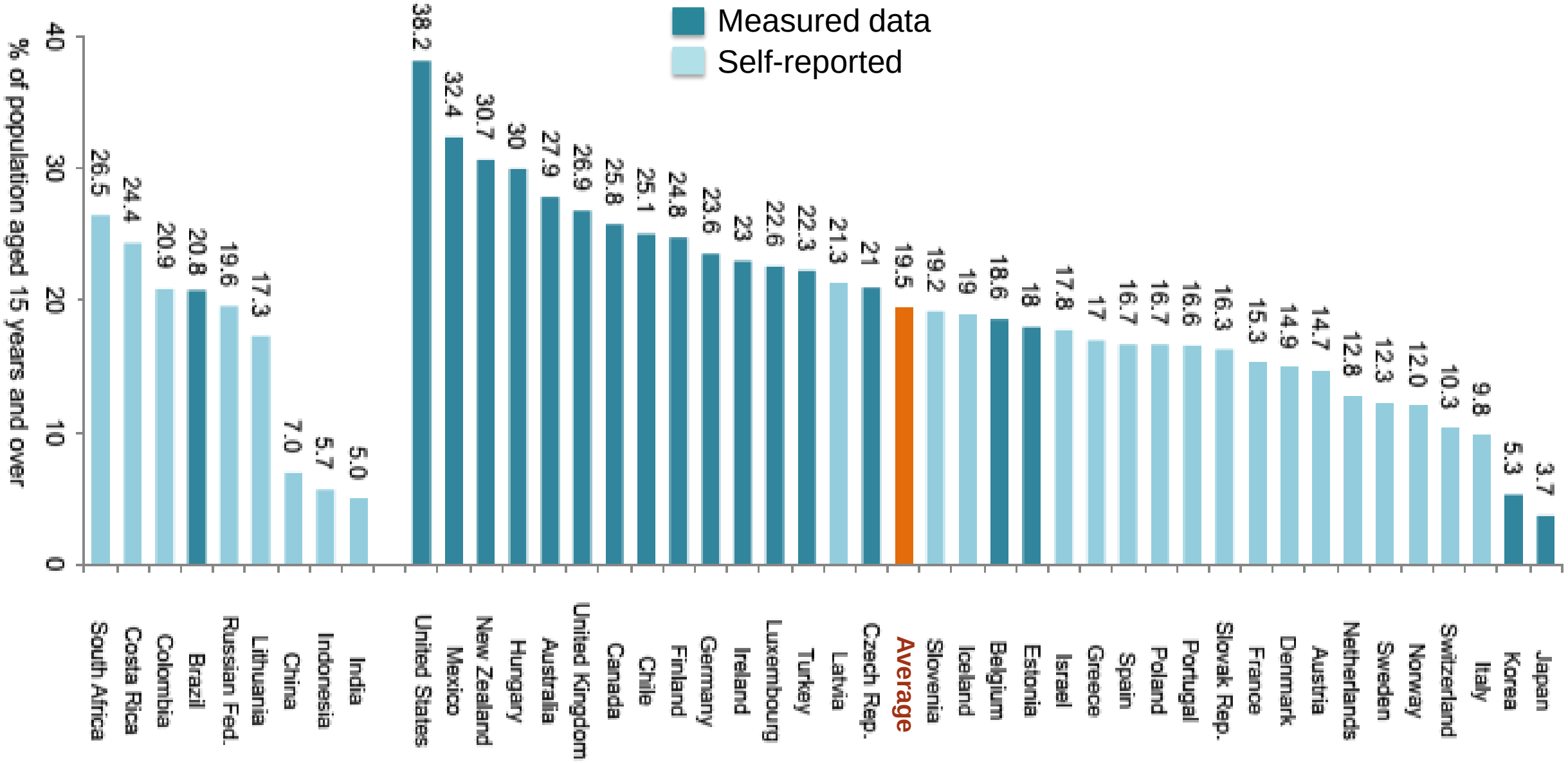
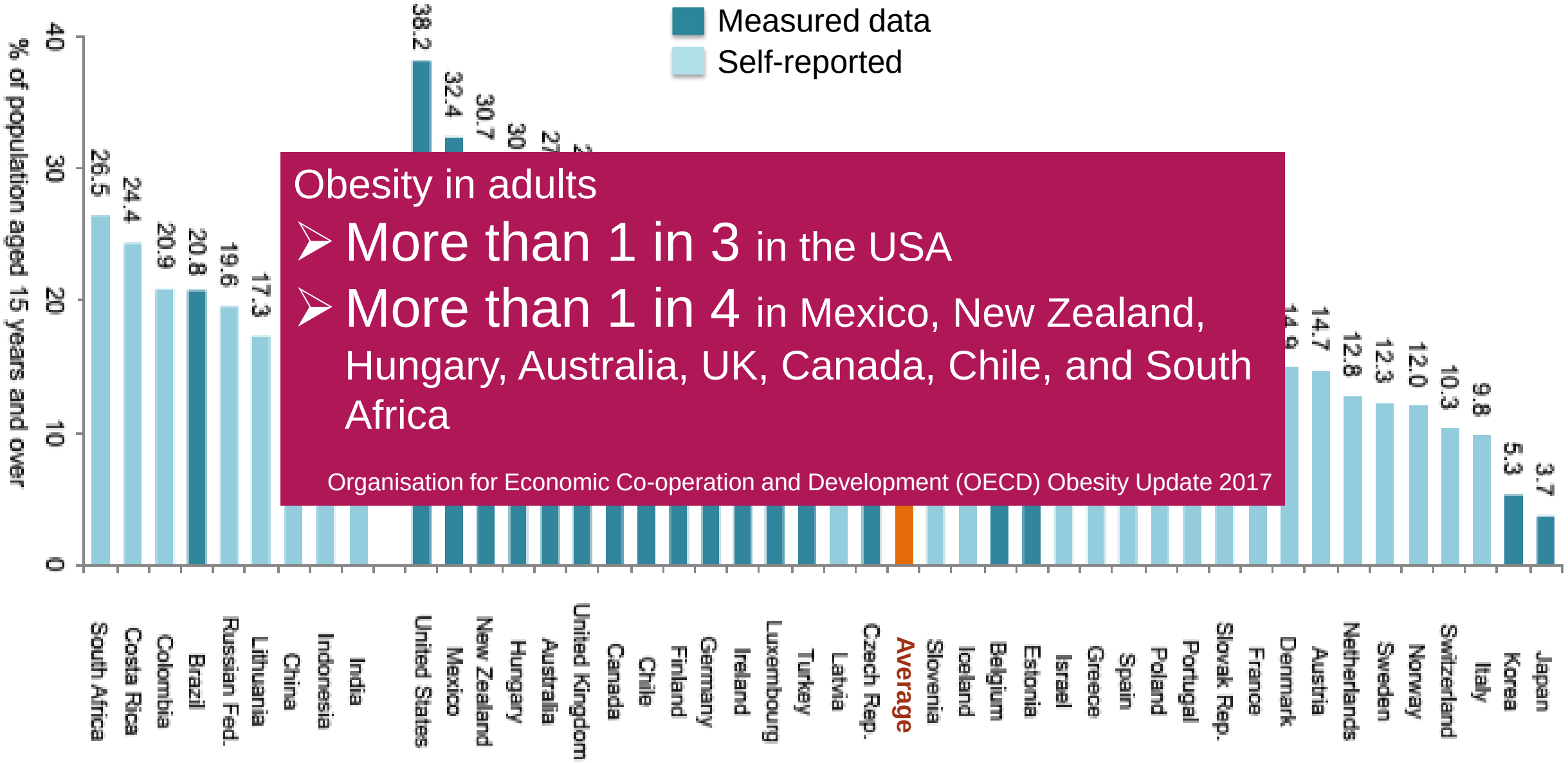
# Prevalence of obesity among adults ≥15 years in 2015




Organisation for Economic Co-operation and Development (OECD) Obesity Update 2017. http://www.oecd.org/

# Prevalence of obesity among adults ≥15 years in 2015



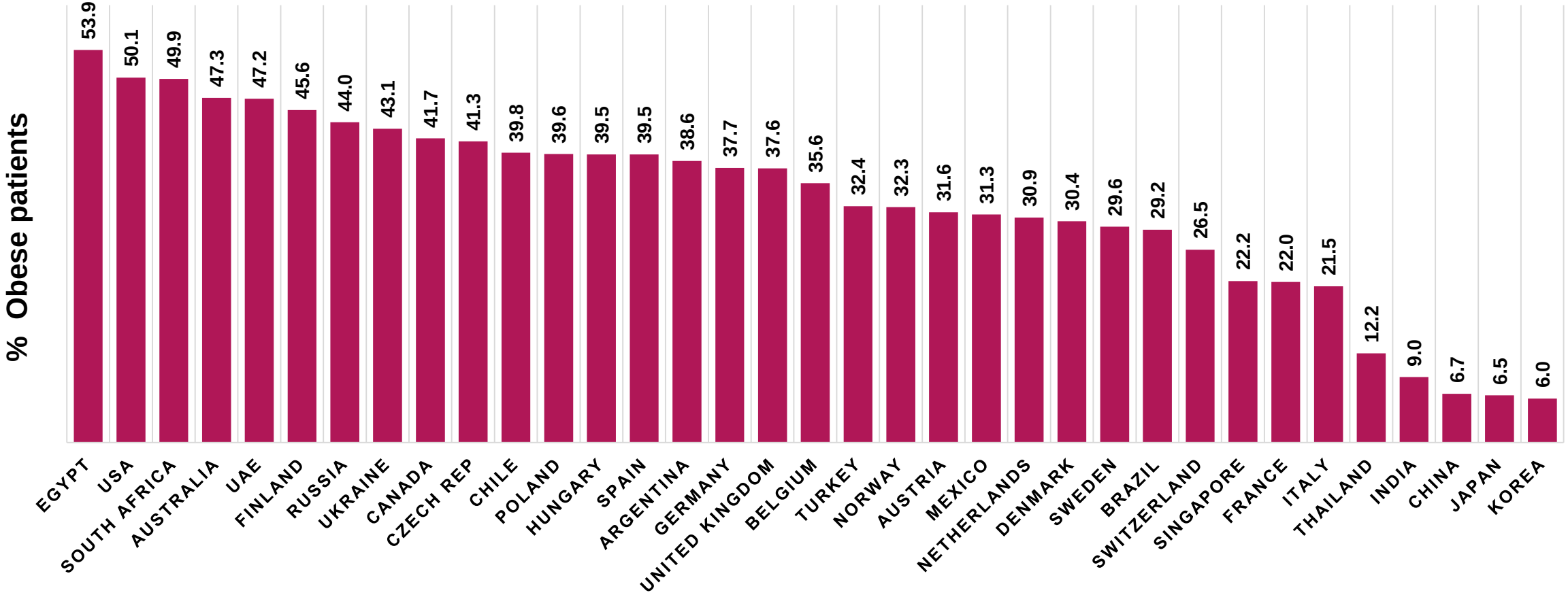

Obesity in adults

- More than 1 in 3 in the USA
- More than 1 in 4 in Mexico, New Zealand, Hungary, Australia, UK, Canada, Chile, and South Africa

Organisation for Economic Co-operation and Development (OECD) Obesity Update 2017

Organisation for Economic Co-operation and Development (OECD) Obesity Update 2017. http://www.oecd.org/

# Prevalence of obesity among patients with newly diagnosed AF from GARFIELD-AF




Obesity, body mass index ≥ 30 kg/m$^2$

Cohorts 1–5, N=52,081

Unpublished Data

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

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AF Garfield global anticoagulant registry in the field

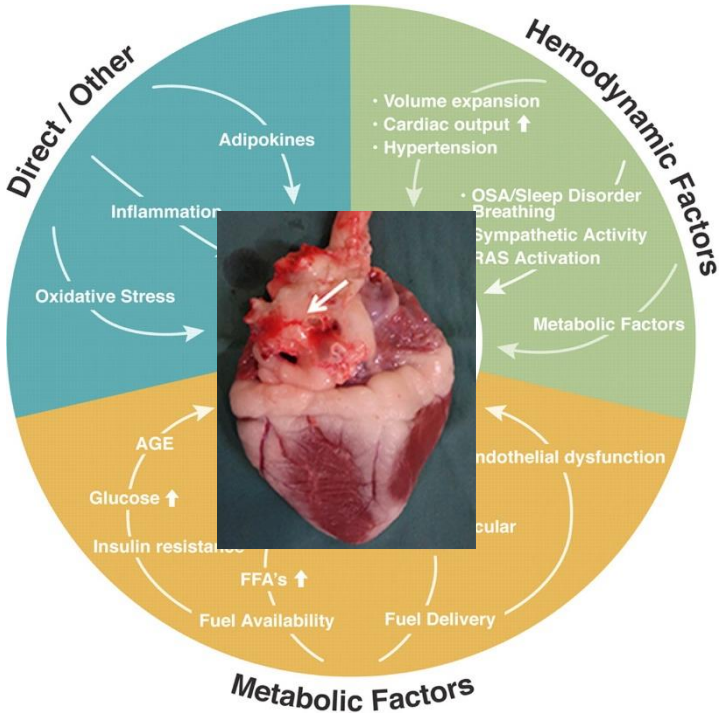
# Every unit increase in BMI raises AF risk by 4% (Framingham Heart study)

## Indirect mechanisms

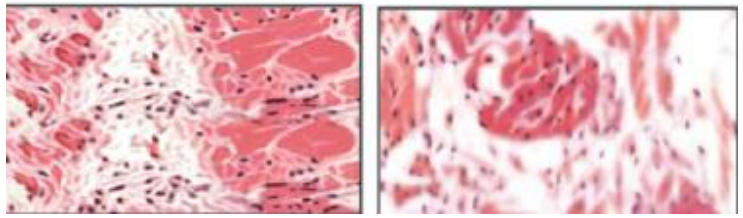
- coexistence of type 2 diabetes, coronary artery disease and obstructive sleep apnoea (OSA)
- associated hypertension, enlarged left atria, ventricular dysfunction

## Direct effect of adipose tissue

- low-grade systemic inflammation, increased renin-angiotensin-aldosterone system and endothelin pathway activities
- direct local inflammatory effects of epicardial adipose – leading to the structural and functional modifications of myocardium




**Transition from fatty to fibrotic infiltrates in the myocardium**



Auer J. Eur Heart J. 2017; 38: 62-6




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

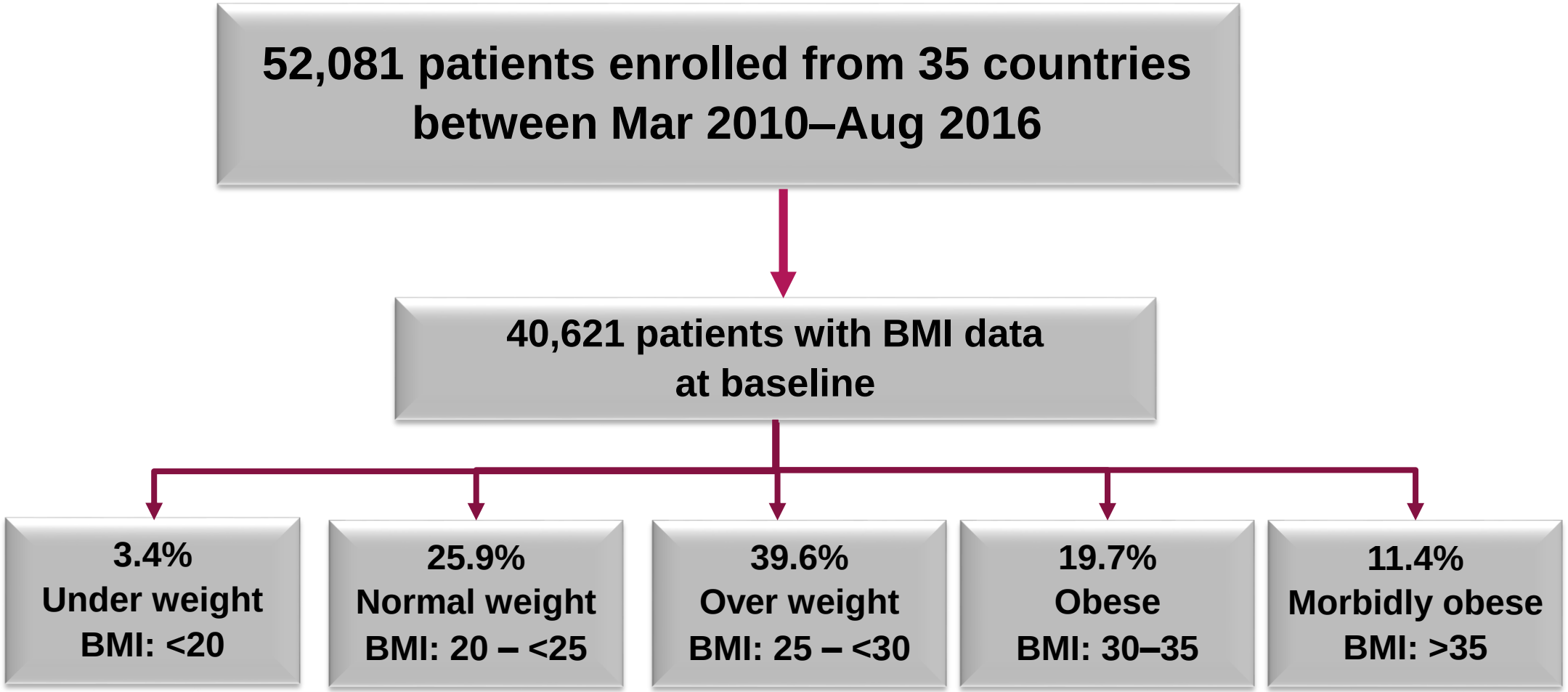
# Objectives of GARFIELD-AF analysis

- **To describe the clinical characteristics of patients with newly diagnosed AF and at least one investigator-defined risk factor for stroke – stratified according to their body mass index (BMI; kg/m$^2$)**
- **To assess the impact of BMI on antithrombotic treatments patterns**
- **To describe the impact of increasing BMI (± type 2 diabetes) on:**
  - all-cause mortality, cardiovascular and non-cardiovascular deaths
  - stroke or systemic embolism (SE)
  - major bleeding

**over the first year after the diagnosis of AF**


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Study population




Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Demographics and clinical characteristics of patients according to BMI category

| Group BMI (kg/m$^2$) | Underweight <20 (n=2365) | Normal 20 to <25 (n=10,534) | Overweight 25 to <30 (n=16,083) | Obese 30 to <35 (n=8014) | Morbidly obese 35 to <40 (n=3150) | Morbidly obese ≥40 (n=1474) |
|---|---|---|---|---|---|---|
| **Female, %** | 60.0 | 45.3 | 38.3 | 43.4 | 51.0 | 57.3 |
| **Median (IQR) age at AF diagnosis, years** | 76 (67.0 to 83.0) | 73.0 (64.0 to 80.0) | 71.0 (62.0 to 78.0) | 69.0 (61.0 to 76.0) | **67.0** (60.0 to 74.0) | **64.0** (57.0 to 71.0) |
| **Hypercholesterolaemia, %** | 23.8 | 32.4 | 43.3 | 51.6 | **53.4** | **51.8** |
| **Current/ex smoker, %** | 29.0 | 33.2 | 33.7 | 35.9 | **36.4** | **36.5** |
| **Type of AF at diagnosis, %** | | | | | | |
| Permanent | 10.2 | 12.2 | 13.4 | 13.8 | **14.0** | **15.3** |
| Persistent | 15.9 | 15.1 | 16.3 | 16.3 | 16.6 | 16.3 |
| Paroxysmal | 38.5 | 33.6 | 28.4 | 25.2 | **22.1** | **17.8** |
| New-onset | 35.4 | 39.1 | 41.9 | 44.7 | 47.3 | 50.6 |

IRI Research Institute

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Garfield global anticoagulant registry in the field

Unpublished Data

# Demographics and clinical characteristics of patients according to BMI category

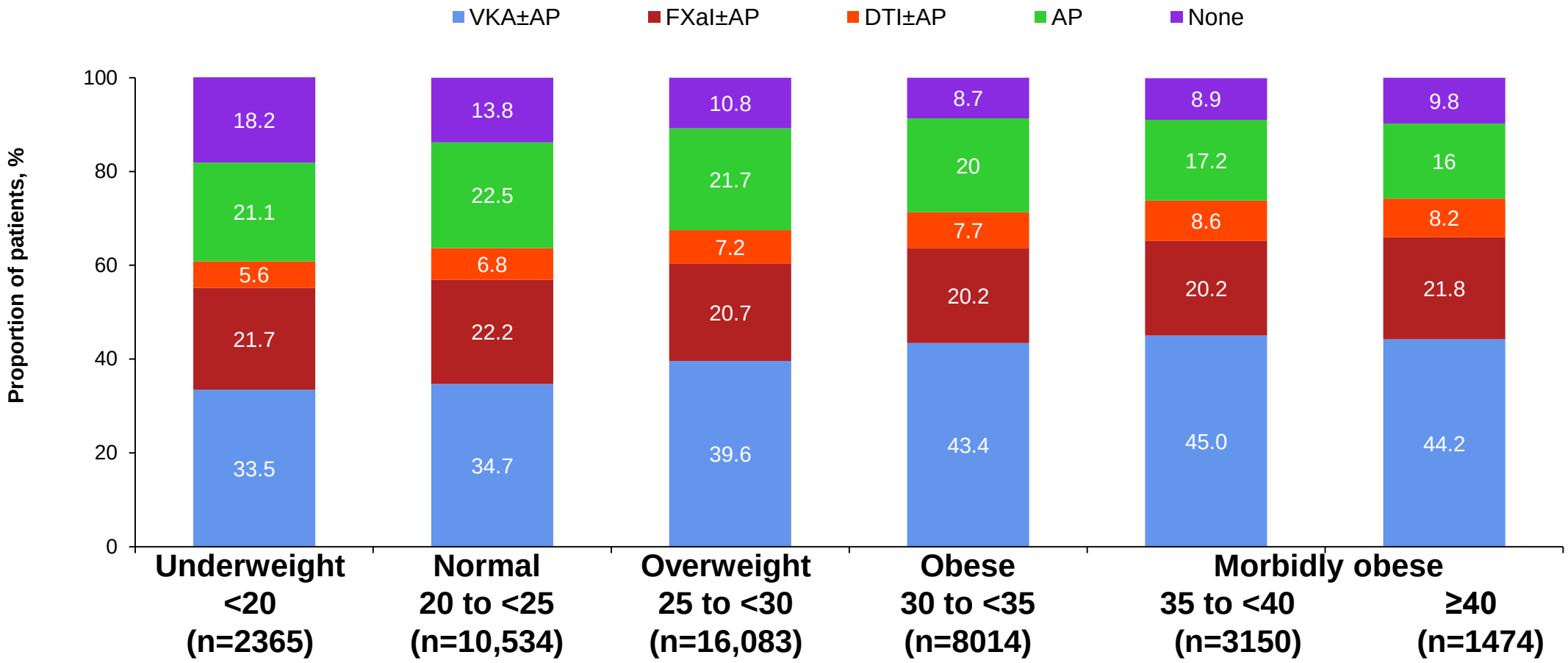
| Group BMI (kg/m$^2$) | Underweight <20 (n=2365) | Normal 20 to <25 (n=10,534) | Overweight 25 to <30 (n=16,083) | Obese 30 to <35 (n=8014) | Morbidly obese 35 to <40 (n=3150) | Morbidly obese ≥40 (n=1474) |
|---|---|---|---|---|---|---|
| Diabetes mellitus, % | **9.7** | **15.7** | **20.7** | **28.9** | **36.1** | **43.1** |
| Heart failure, % | 24.2 | 20.0 | 19.1 | 23.0 | 26.8 | 28.1 |
| History of acute coronary syndrome | 7.0 | 8.2 | 10.3 | 11.2 | 10.7 | 8.2 |
| Vascular disease | 13.2 | 13.8 | 15.2 | 16.7 | 16.4 | 11.8 |
| $CHA_2DS_2$-VASc score, mean (SD) | 3.4 (1.6) | 3.1 (1.6) | 3.1 (1.6) | 3.2 (1.6) | 3.3 (1.6) | 3.2 (1.5) |
| HAS-BLED score, mean (SD) | 1.5 (0.9) | 1.5 (0.9) | 1.4 (0.9) | 1.4 (0.9) | 1.3 (0.9) | 1.2 (0.9) |

Unpublished Data



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Antithrombotic therapy at diagnosis in patients according to BMI




BMI, body mass index; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

TRI Thrombosis Research Institute

Cohorts 1–5, N=52,081

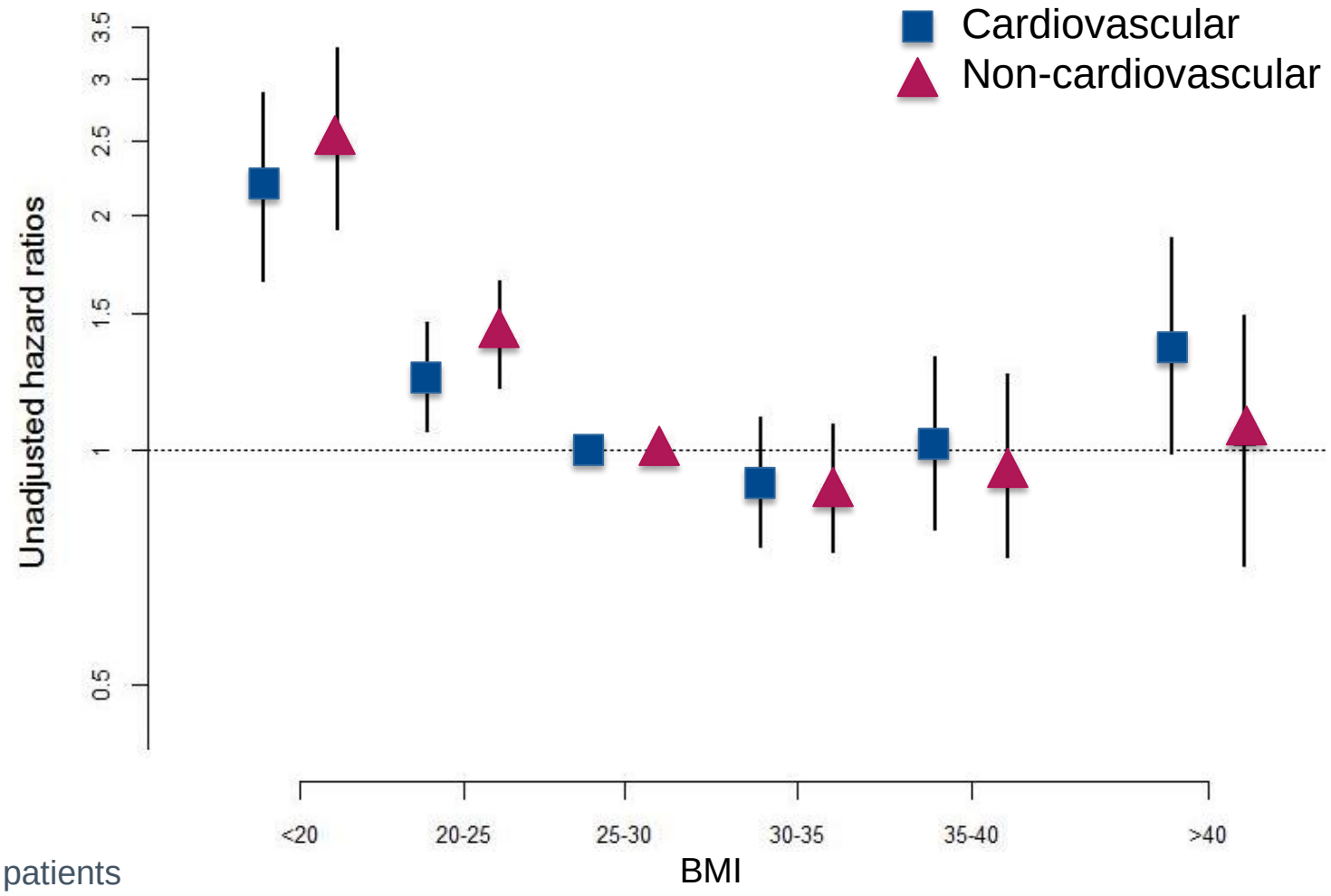
The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Unpublished Data

AF Garfield global anticoagulant registry in the field

# Hazard ratios* for 1-year outcomes by BMI group

## Cardiovascular and non-cardiovascular death




*Reference group: overweight patients

Unpublished Data

TRI Thrombosis Research Institute

Cohorts 1–5, N=52,081

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield global anticoagulant registry in the field

# Causes of death by BMI group

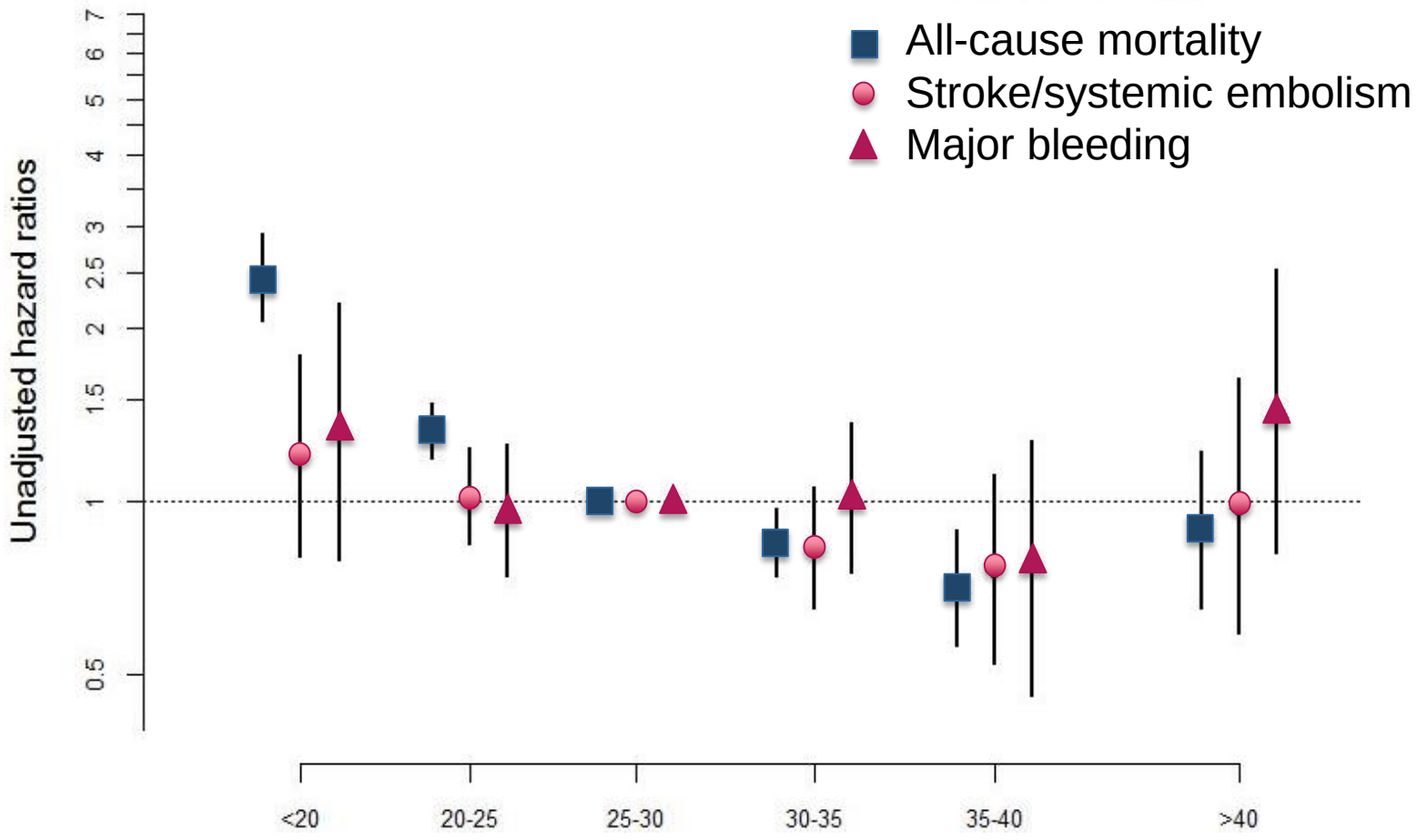
| Group BMI (kg/m$^2$) | Underweight <20 (n=2365) | Normal 20 to <25 (n=10,534) | Overweight 25 to <30 (n=16,083) | Obese 30 to <35 (n=8014) | Morbidly obese 35 to <40 (n=3150) | Morbidly obese ≥40 (n=1474) |
|---|---|---|---|---|---|---|
| **Cardiovascular deaths** | | | | | | |
| **Congestive heart failure** | **43.9** | **28.6** | **32.7** | **34.4** | **20.4** | **37.9** |
| Sudden/unwitnessed | 14.6 | 21.4 | 15.7 | 17.8 | 10.2 | 10.3 |
| ACS | 4.9 | 7.7 | 13.5 | 13.3 | 18.4 | 3.6 |
| Ischaemic stroke | 4.9 | 13.3 | 12.1 | 10.0 | 12.2 | 10.3 |
| Other | 31.7 | 28.6 | 25.6 | 24.4 | 38.8 | 37.9 |
| **Non-cardiovascular deaths** | | | | | | |
| Malignancy | 28.9 | 25.0 | 33.2 | 40.7 | 33.3 | 31.3 |
| Respiratory failure | 24.4 | 22.8 | 17.4 | 12.1 | 11.1 | 31.3 |
| Infection/sepsis | 13.3 | 18.5 | 19.5 | 13.2 | 27.8 | 25.0 |
| Other | 33.3 | 33.2 | 29.0 | 34.1 | 27.8 | 12.5 |



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Hazard ratios* for 1-year outcomes by BMI group

## Without Type 2 diabetes




*Reference group: overweight patients

Unpublished Data

Cohorts 1–5, N=52,081

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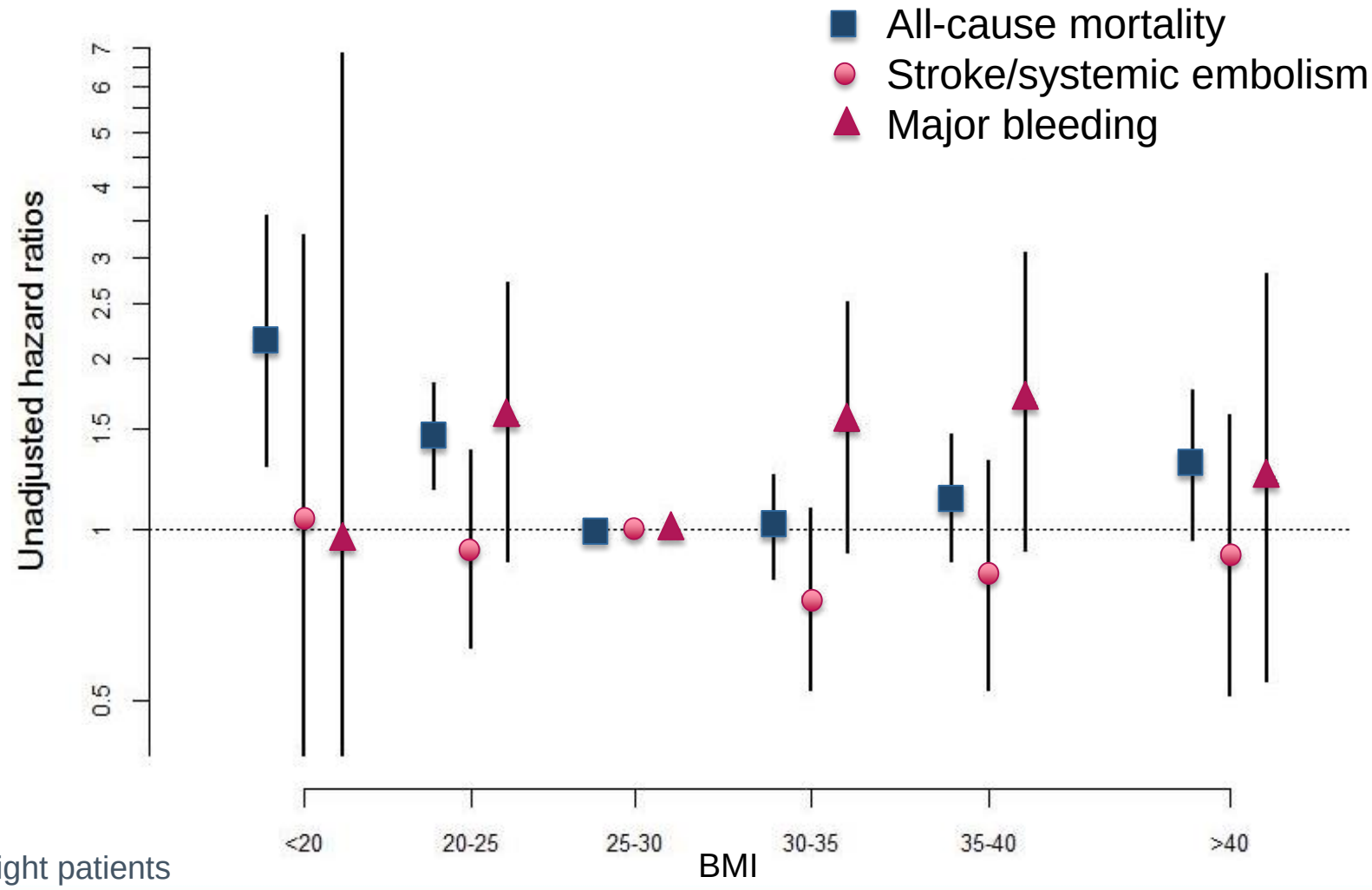
# Hazard ratios* for 1-year outcomes by BMI group

## With Type 2 diabetes




*Reference group: overweight patients

Unpublished Data

Cohorts 1–5, N=52,081

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# Conclusions

- The majority of patients with newly diagnosed AF are overweight or obese
- Patients with morbid obesity (and associated metabolic syndrome) are almost 10 years younger (median) than patients of normal weight when diagnosed with AF
- Higher BMI is associated with greater use of anticoagulants
- Underweight patients are at higher risk of death (vs normal weight patients) 1 year after AF diagnosis, predominantly due to increased heart failure deaths
- As BMI increases, mortality paradoxically decreases in GARFIELD-AF; although this effect may be reduced after adjustment for baseline characteristics such as age
- In patients with type 2 DM this paradox is not apparent



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Panel discussion – Treating the whole patient

**Professor Lorenzo G. Mantovani**
**University of Milan Bicocca, Monza, Italy**

**Professor Freek W.A. Verheugt**
**Onze Lieve Vrouwe Gasthuis (OLVG), Amsterdam, The Netherlands**

TRI Thrombosis Research Institute

www.garfieldregistry.org

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

AF Garfield global anticoagulant registry in the field

# Disclosures

## Professor Lorenzo G. Mantovani

Grants and personal fees: Bayer AG, Boehringer Ingelheim, Daiichi Sankyo, Pfizer, Medtronic

## Professor Freek W.A. Verheugt

Educational and research grants: Bayer AG

Personal fees: Bayer AG, BMS/Pfizer, Daiichi-Sankyo, Boehringer Ingelheim



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# Treating the whole patient

- Competing risks
- Complicated (disease) vs Complex (patient)
- Integrated care


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# Treating the whole patient

- **Competing risks**
- **Complicated (disease) vs Complex (patient)**
- **Integrated care**


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Treating the whole patient

- Men have higher prevalence/incidence of ACS (at a younger age)

- Women have higher incidence of stroke (at an older age)

**Is this because ACS more frequently kills “bad-risks” men before they can develop a stroke at an older age?**


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# Treating the whole patient

- Competing risks
- Complicated (disease) vs Complex (patient)
- Integrated care


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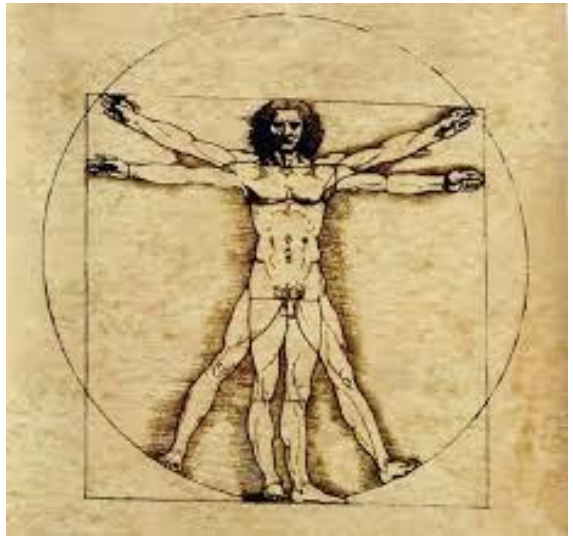
# Complication vs Complexity

*"Complicated systems have many moving parts, but they operate in patterned ways"*

*"Complex systems are imbued with features that may operate in patterned ways but whose interactions are continually changing"*





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# Treating the whole patient

- Competing risks
- Complicated (disease) vs Complex (patient)
- **Integrated care**


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Modifiable Risk Factors for Incident Heart Failure in Atrial Fibrillation

Neal A. Chatterjee, MD, MSc,[a,b] Claudia U. Chae, MD, MPH,[b] Eunjung Kim, MSc,[a] M. Vinayaga Moorthy, PhD,[a] David Conen, MD, MPH,[a,c] Roopinder K. Sandhu, MD, MPH,[d] Nancy R. Cook, ScD,[a] I-Min Lee, MBBS, ScD,[a,e] Christine M. Albert, MD, MPH[a,f]

## Impact of incidence HF on CV mortality, stroke and MI in new onset AF

| | No HF | HF | p Value |
|---|---|---|---|
| All-cause mortality | | | |
| Events, n | 241 | 69 | |
| Incidence rate (95% CI)* | 25.2 (21.1-29.4) | 42.3 (28.9-55.7) | |
| HR (95% CI) | | | |
| Age-adjusted | 1.00 (Reference) | 2.11 (1.60-2.77) | <0.0001 |
| Multivariable-adjusted† | 1.00 (Reference) | 1.83 (1.37-2.45) | <0.0001 |
| CV mortality | | | |
| Events, n | 59 | 26 | |
| Incidence rate (95% CI) | 6.3 (4.3-8.3) | 16.0 (7.6-24.4) | |
| HR (95% CI) | | | |
| Age-adjusted | 1.00 (Reference) | 3.47 (2.15-5.60) | <0.0001 |
| Multivariable-adjusted | 1.00 (Reference) | 2.87 (1.70-4.85) | <0.0001 |

Chatterjee N.A. et al JACC Heart Fail. 2017; 5: 552-60



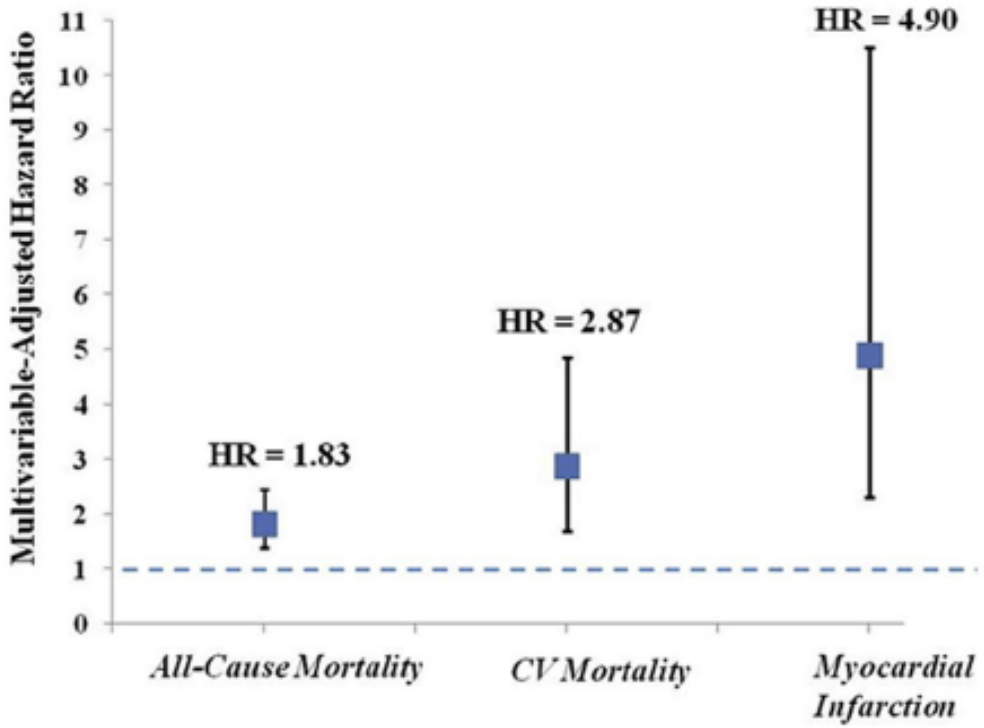
The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

**A**

***HF is associated with ↑ mortality in AF***

*Once HF develops after new-onset AF*

*All-Cause Mortality, CV Mortality, and MI ↑*




Chatterjee N.A. et al JACC Heart Fail. 2017; 5: 552-60



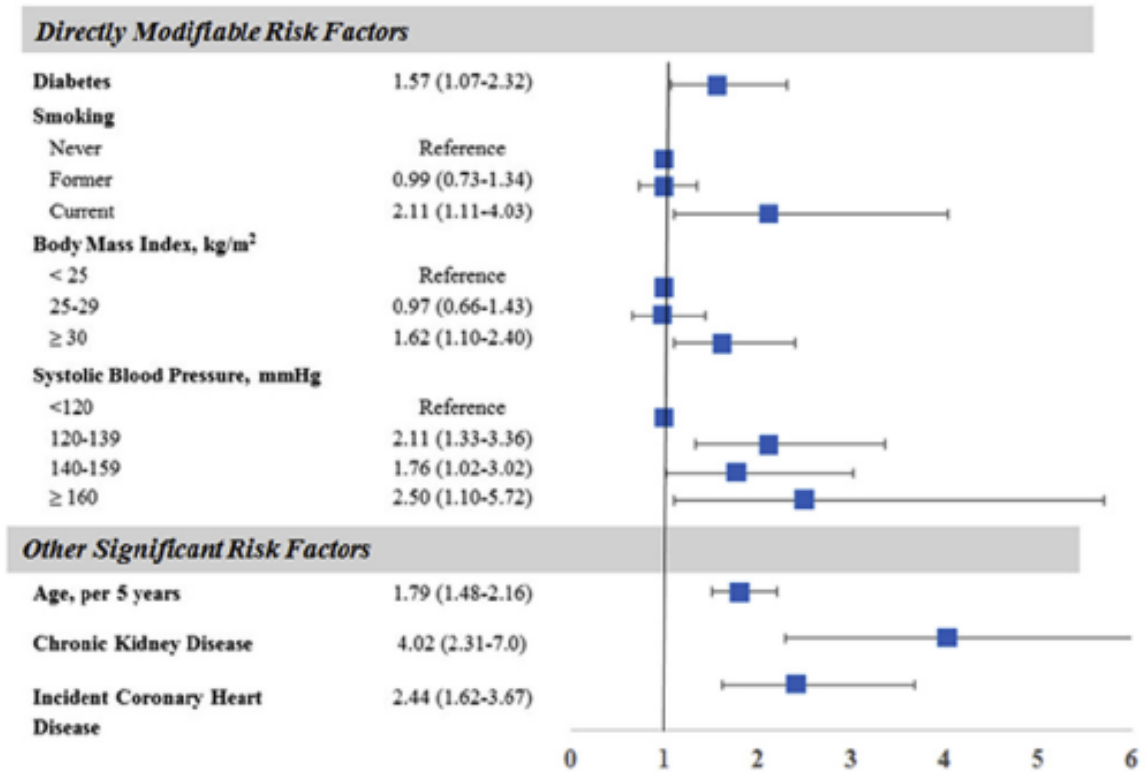

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

**B**

## *HF risk in AF is modifiable*

*Diabetes, Smoking, Obesity, Hypertension*

*accounted for 62% of HF events*



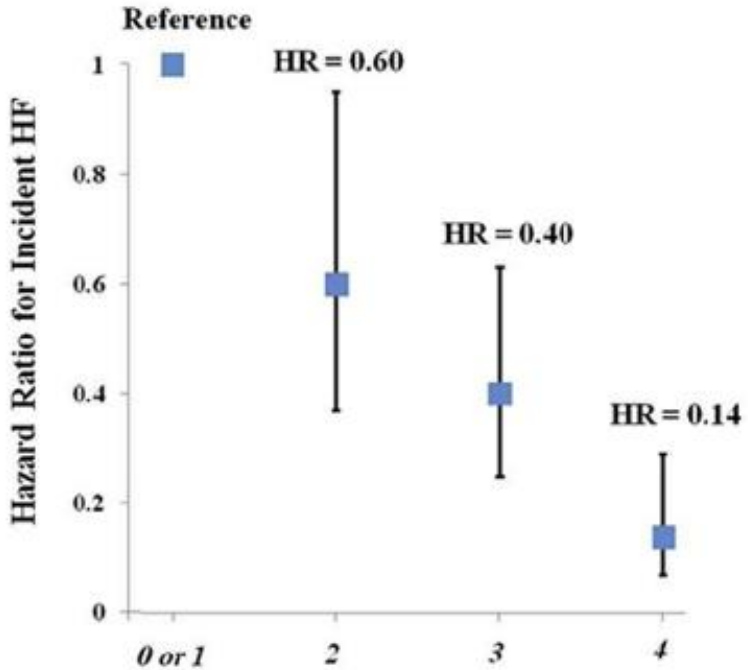

Chatterjee N.A. et al JACC Heart Fail. 2017; 5: 552-60




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

**C** ***Impact of Risk Factor Modification on HF Risk in AF***

*Risk factor modification was associated with progressive ↓ HF risk*




| Subgroup N at AF Diagnosis | 125 | 381 | 758 | 231 |
|---|---|---|---|---|

Chatterjee N.A. et al JACC Heart Fail. 2017; 5: 552-60




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Patient Preference and Adherence

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HYPOTHESIS

# Proposed model of integrated care to improve health outcomes for individuals with multimorbidities

Tara Sampalli
Roy A Fox
Robert Dickson
Jonathan Fox

Integrated Chronic Care Service, Primary Health Care, Capital Health, Nova Scotia, Canada

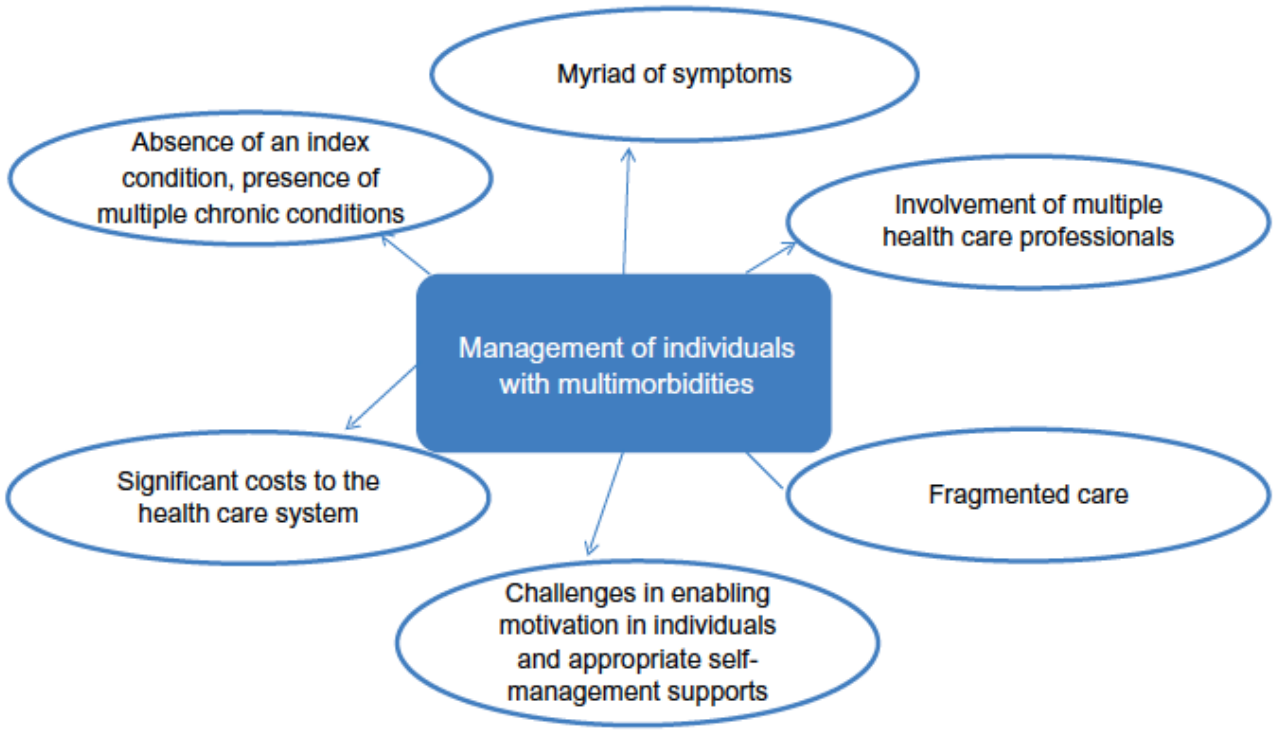
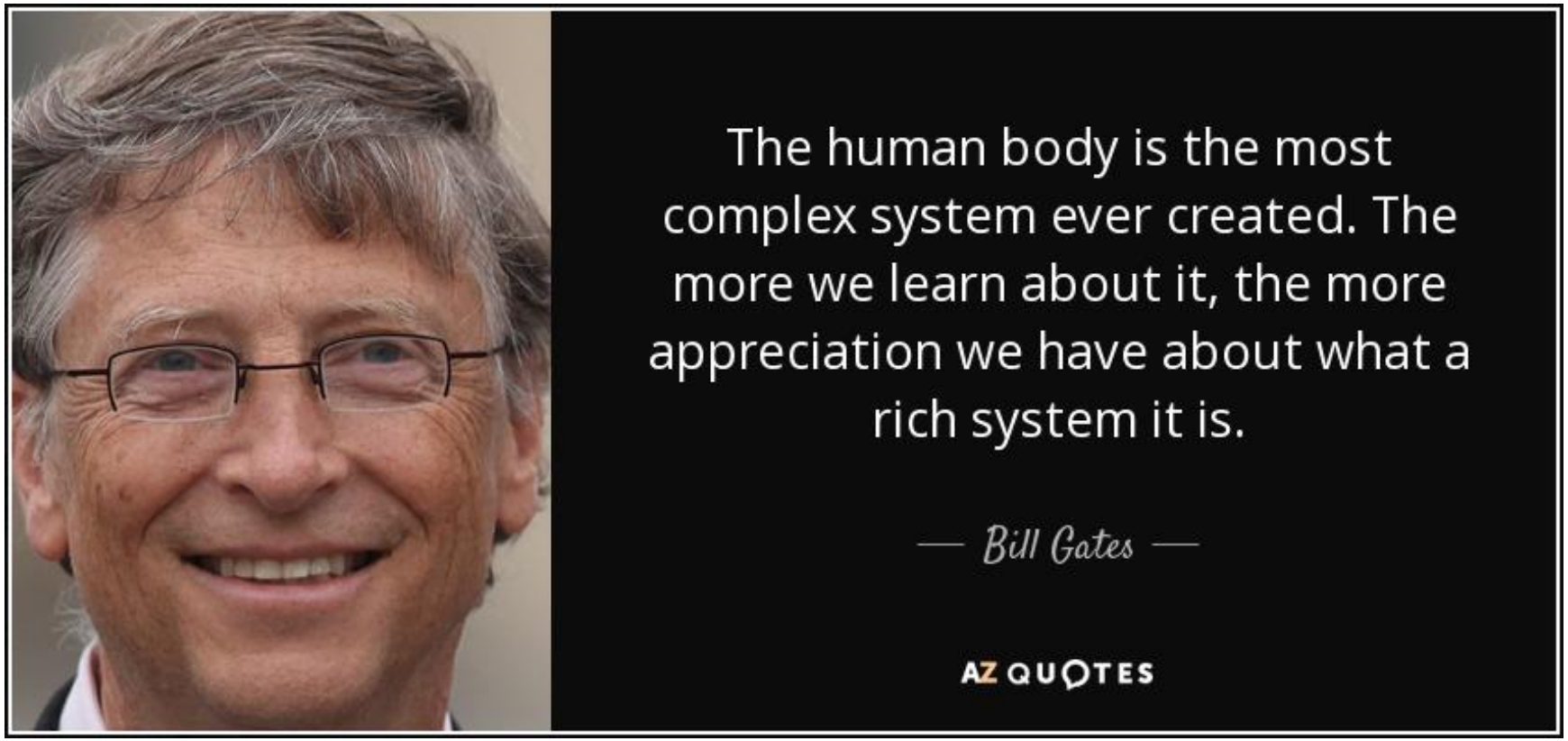



**Figure 1** Challenges of managing multimorbidity.

Patient Preference and Adherence 2012:6 757–764
© 2012 Sampalli et al, publisher and licensee Dove Medical Press Ltd. This is an Open Access article which permits unrestricted noncommercial use, provided the original work is properly cited.






The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

"The decision maker has a choice between optimal decisions for an imaginary simplified world or decisions that are 'good enough, that satisfice', for a world approximating the complex real one more closely."

***Herbert A Simon, Nobel Laureate 1978***

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Treating the whole patient

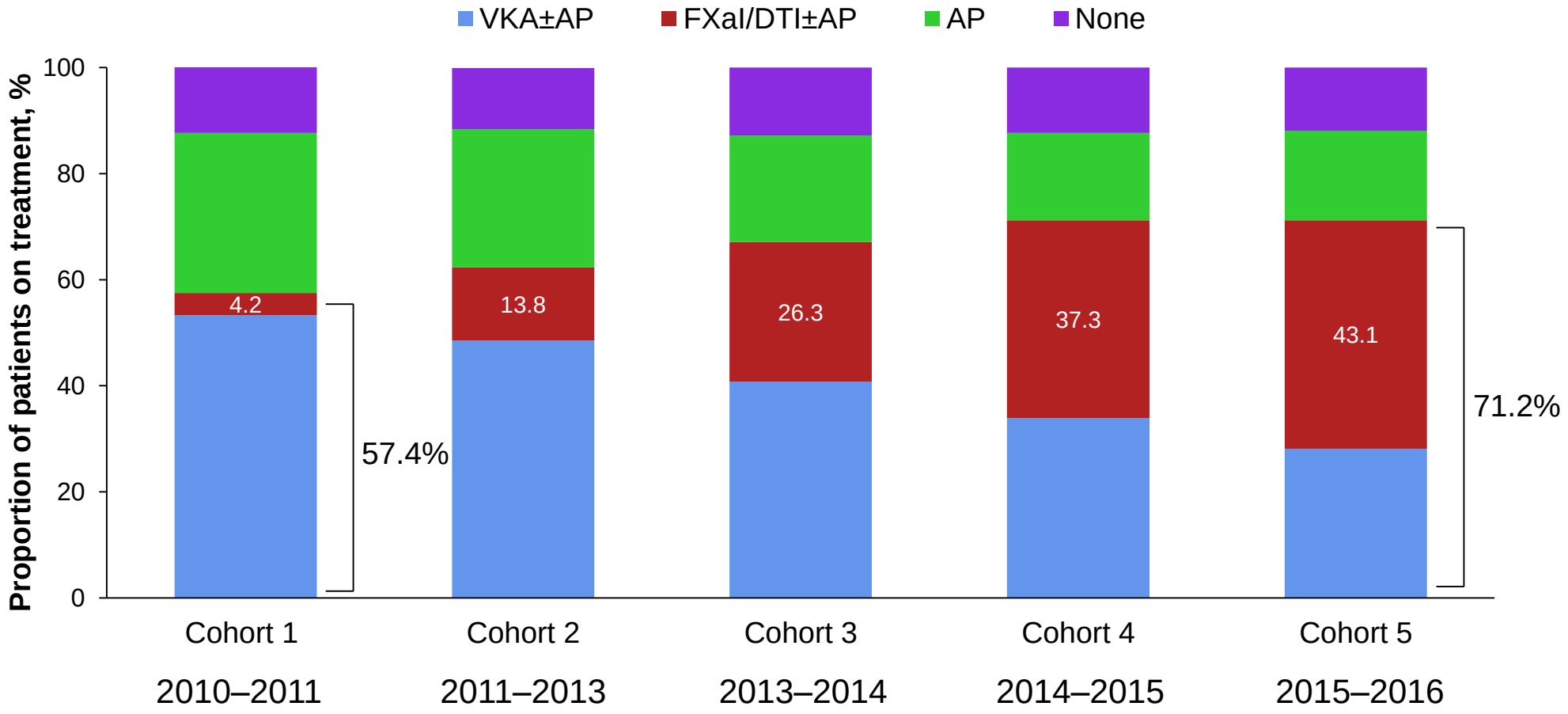
- **Antithrombotic therapy in AF varies largely according to comorbidity**

- **Heart failure**
- **History of ACS**
- **Obesity**
- **Chronic kidney disease**


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Evolution in baseline treatment for patients enrolled in sequential cohorts of GARFIELD-AF

A.K. Kakkar




Cohorts 1–5, N=52,081; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

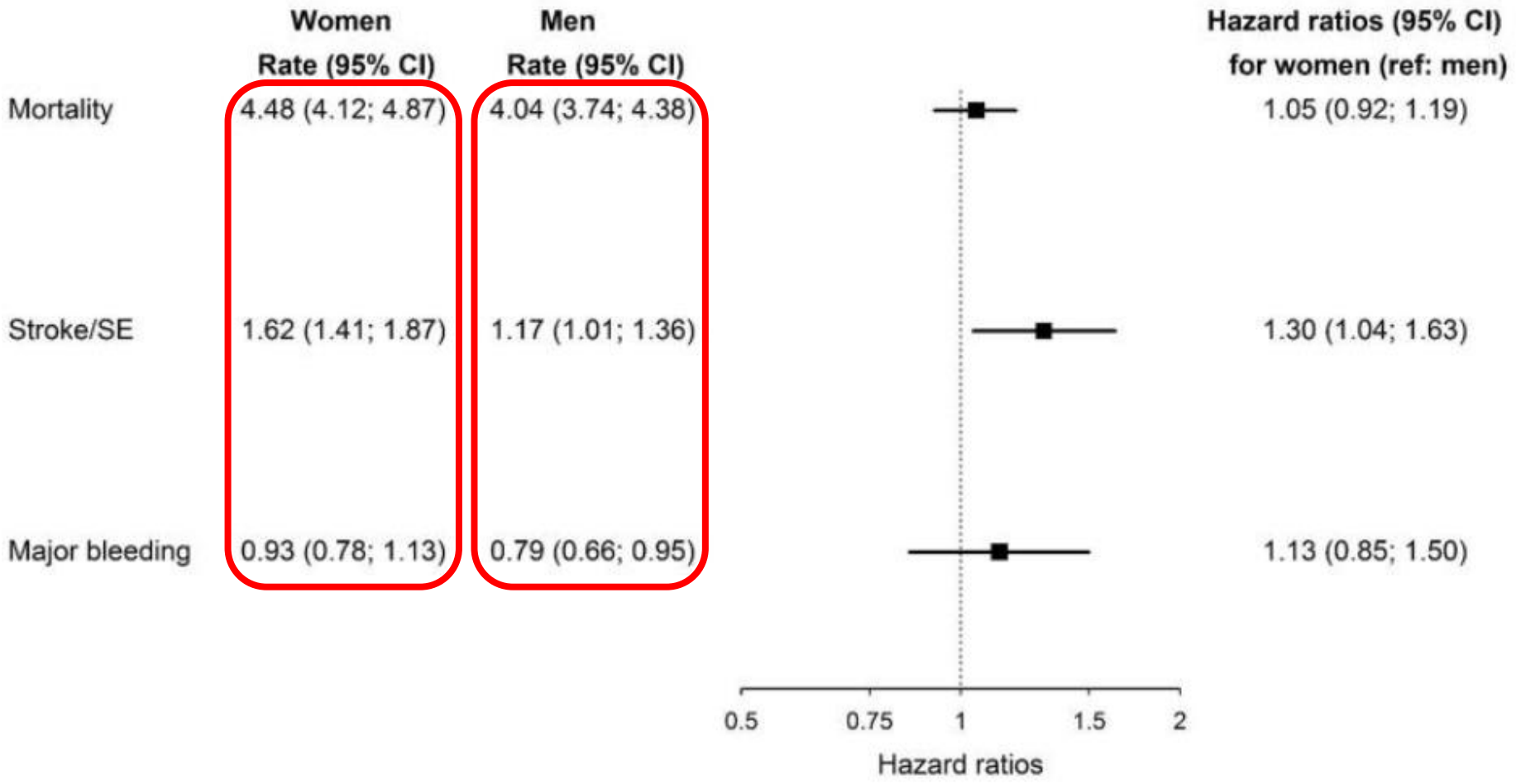
Unpublished Data




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# GARFIELD-AF: Mortality, stroke, major bleeds

S.Z. Goldhaber




Camm A.J. et al BMJ Open. 2017; 7: e014579

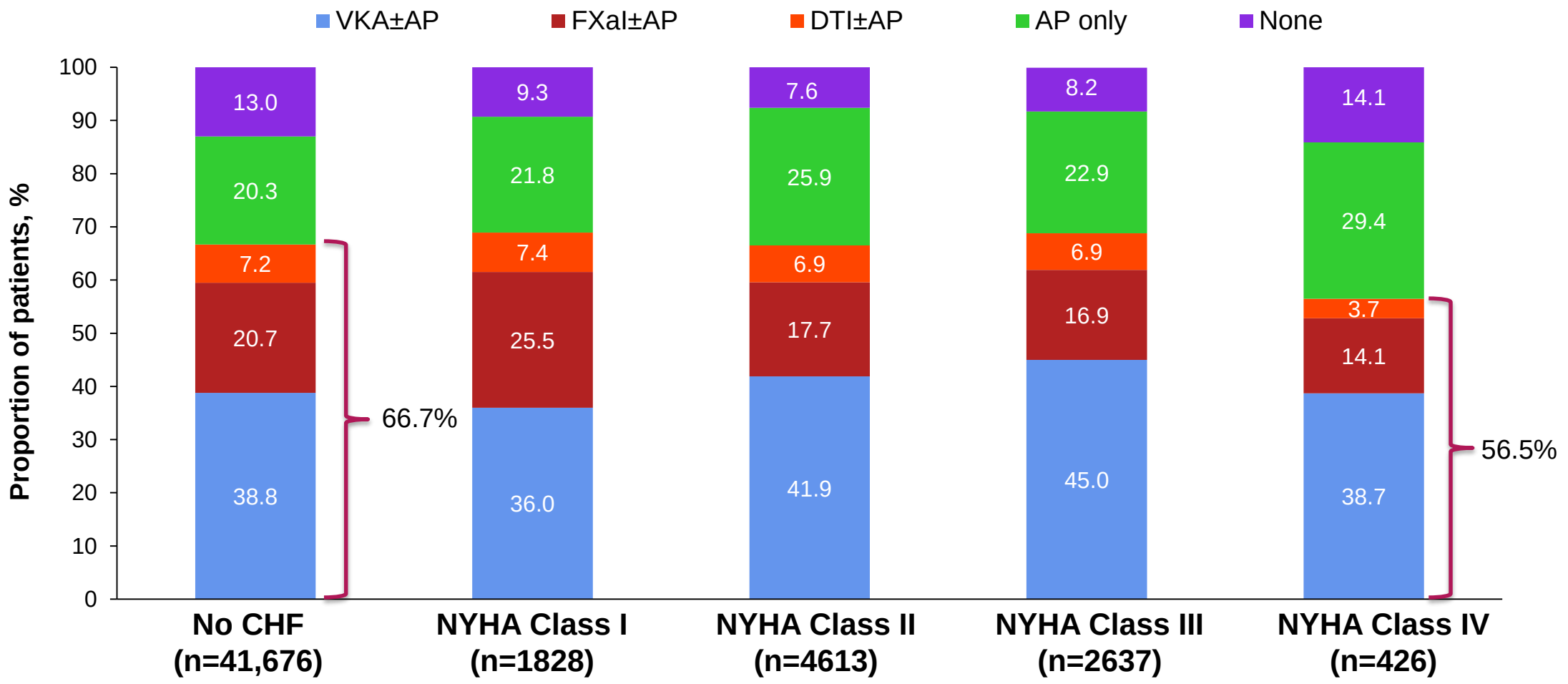
Unpublished Data




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Antithrombotic treatment patterns in heart failure

A.G.G. Turpie




AP, antiplatelet; CHF, congestive heart failure; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

Unpublished Data

TRI Thrombosis Research Institute

Cohorts 1–5, N=52,081

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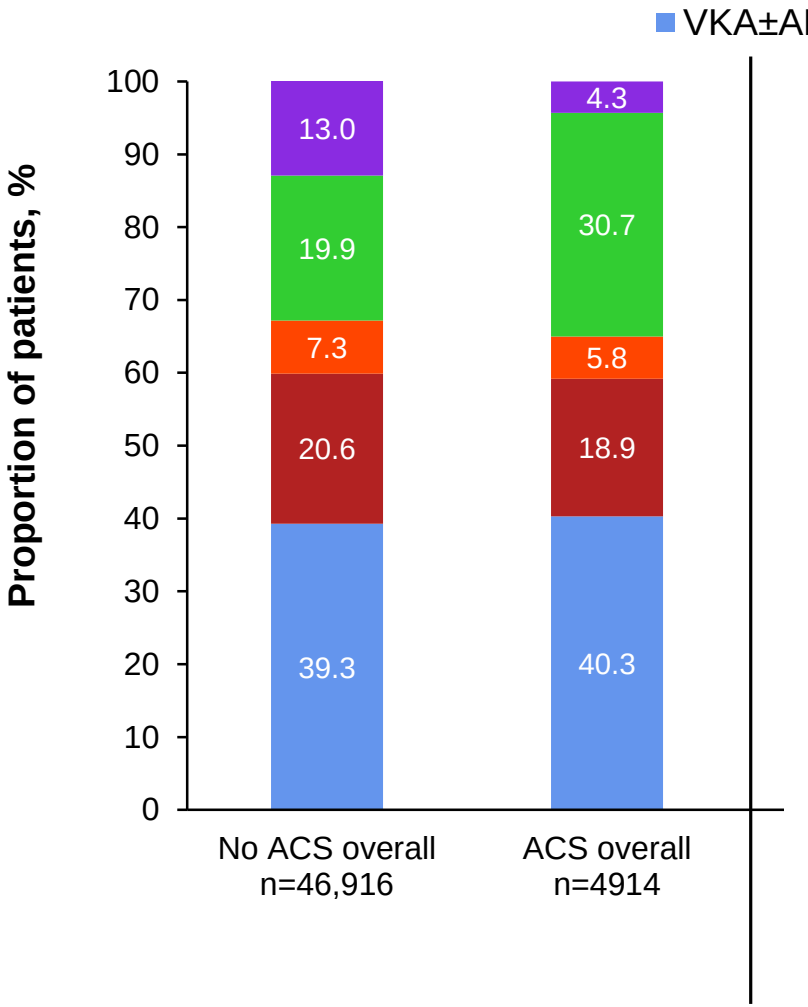
AF Garfield global anticoagulant registry in the field

# Antithrombotic therapy at diagnosis in patients with and without history of ACS, according to $CHA_2DS_2$-VASc

K.A.A. Fox




**$CHA_2DS_2$-VASc**

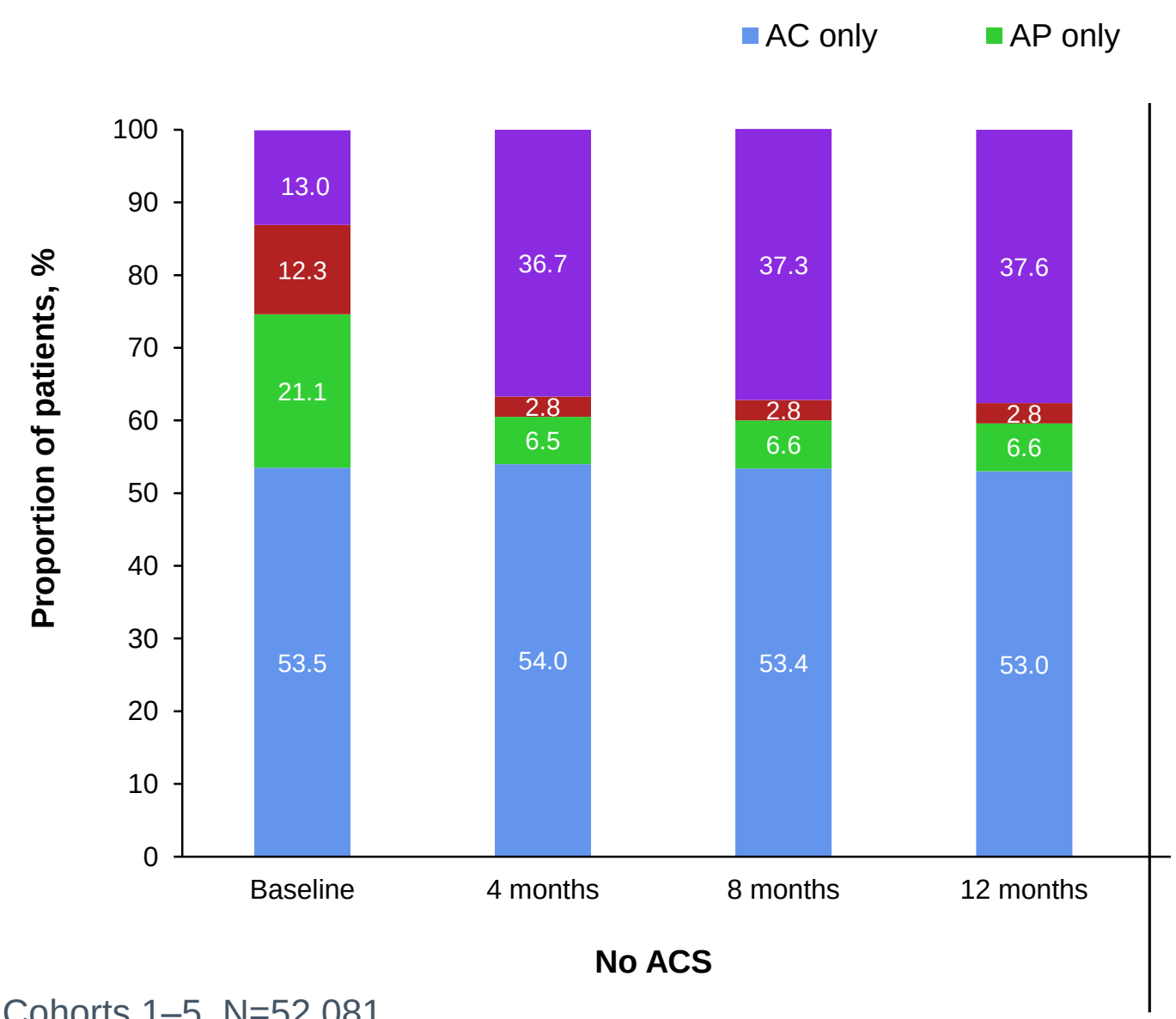
Cohorts 1–5, N=52,081

Unpublished Data

ACS, acute coronary syndromes; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

# Antithrombotic therapy over time with ACS history

K.A.A. Fox




Cohorts 1–5, N=52,081

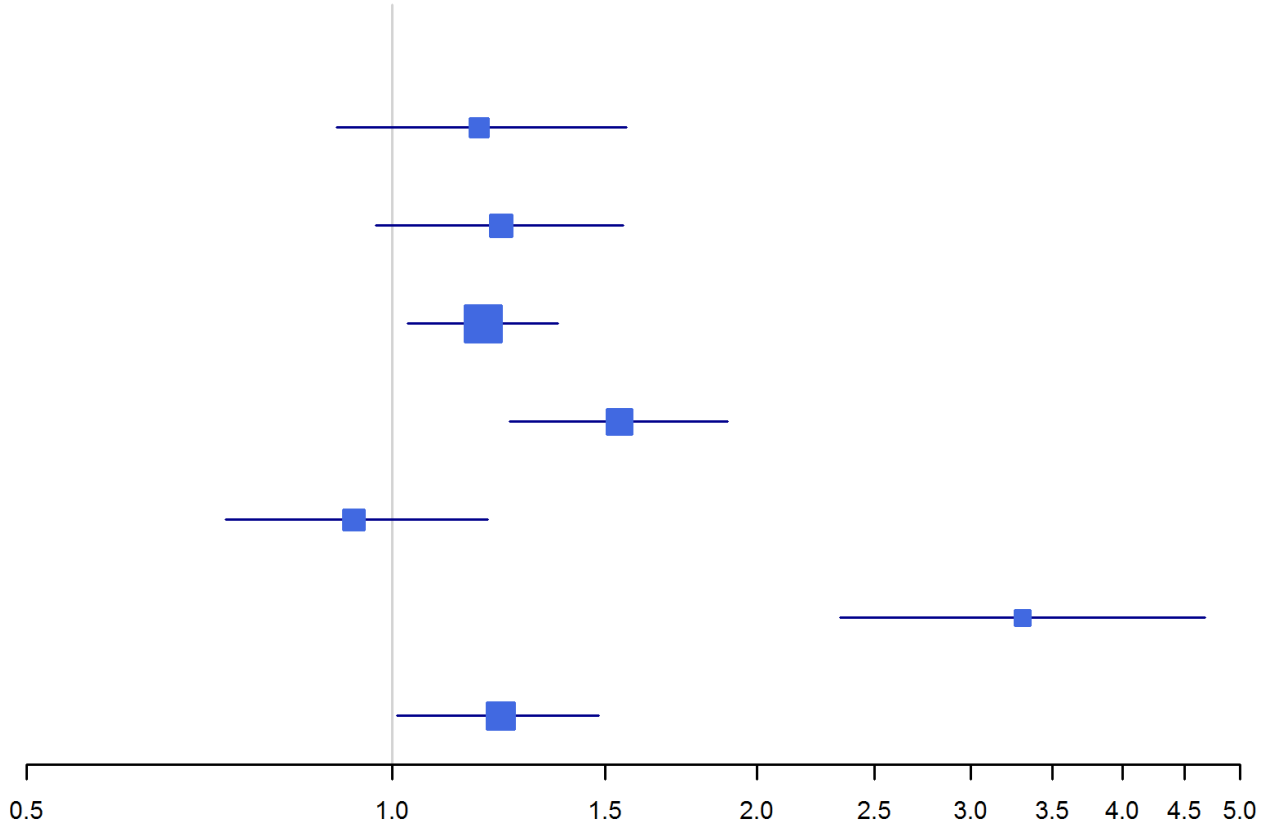
ACS, acute coronary syndromes; AC, anticoagulant; AP, antiplatelet

Unpublished Data

# Adjusted HRs for 1-year outcomes for patients with vs without history of ACS

K.A.A. Fox

| Outcomes | n (%) | aHR |
|---|---|---|
| Stroke/SE | 650 (1.2) | 1.18 |
| Major bleeding | 407 (0.8) | 1.23 |
| All-cause mortality | 2103 (4.0) | 1.19 |
| Cardiovascular mortality | 789 (1.5) | 1.54 |
| Non-cardiovascular mortality | 771 (1.5) | 0.93 |
| New ACS | 378 (0.7) | 3.31 |
| Congestive heart failure | 1052 (2.0) | 1.23 |



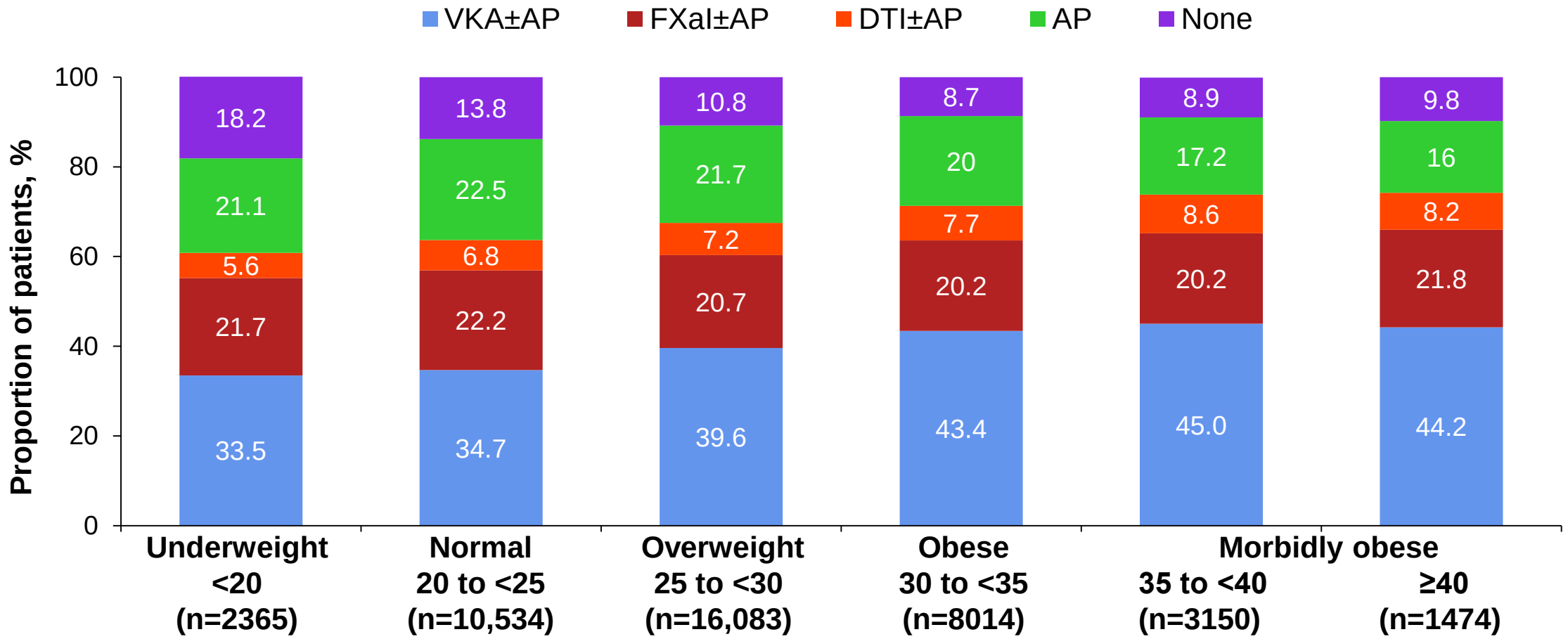

Cohorts 1–5, N=52,081

ACS, acute coronary syndromes; HR, hazard ratio; SE, systemic embolism

Unpublished Data

# Antithrombotic therapy at diagnosis in patients according to BMI

A.J. Camm



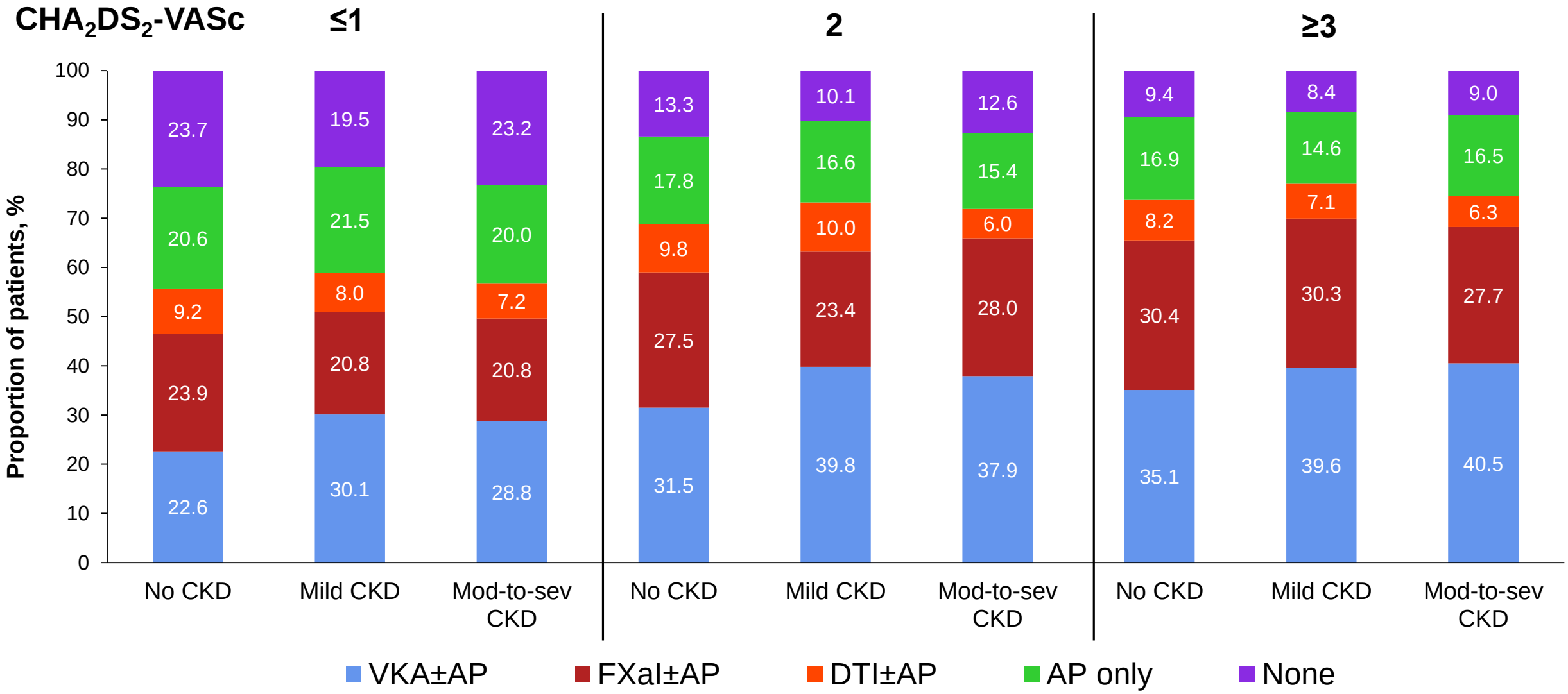

BMI, body mass index; AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist




The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Antithrombotic therapy at diagnosis according to CKD group and $CHA_2DS_2$-VASc score

S. Goto




Cohorts 3–5, N=34,929

Unpublished Data

AP, antiplatelet; CKD, chronic kidney disease; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

# Take home messages

**Professor Jean-Pierre Bassand**
**University of Besançon, France**

# Disclosures

## None



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Take home messages

- 57,262 pts with 1-year follow-up (52,081 prospective)
- Striking changes in the patterns of anticoagulation from cohort 1 to 5
  - AC therapy rate from 57.4% up to 71.2%
  - NOACs uptake from 4.2% to 43.1%


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Take home messages

- Death is the most frequent adverse event in AF, occurring at a 3-fold higher rate than stroke/SE and 5-fold higher rate than major bleeding
- Similar rates of cardiovascular and non-cardiovascular death
- CHF, malignancy, infection/sepsis, respiratory failure, and sudden death are the most frequent known causes of death
- Stroke is accountable for only 5.5% of all known causes of death


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Take home messages

- Is AF primarily a risk factor for stroke, or is AF a risk marker for systemic diseases such as heart failure and/or other CV or non-CV comorbidities?
- AF is definitely a risk marker for systemic disease and a risk factor for stroke
- The first mission in AF patients is to prevent stroke
- However, management of systemic disease is equally important


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Take home messages

## High rate of comorbidities in GARFIELD-AF registry* (not mutually exclusive)

| | |
|---|---|
| **Congestive heart failure** | **20.0%** |
| **History of coronary artery disease** | **21.6%** |
| **History of acute coronary syndrome** | **9.4%** |
| **History of hypertension** | **76.3%** |
| **Overweight/obese** | **67.4%** |
| **Diabetes mellitus** | **22.2%** |
| **Moderate-to-severe CKD** | **11.7%** |

*Cohorts 1–5, 52,081 patients



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Take home messages

- Women have a higher risk of stroke even with a similar rate of anticoagulation as men
- Obesity paradox is confirmed in GARFIELD-AF. See poster #P87116 to know more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# Take home messages

- CHF is associated with a dramatic impact on all three major outcome measures (including major bleeding), particularly in NYHA classes 3 & 4. See poster #P85662 to know more
- The same is true for CKD patients, particularly those with moderate-to-severe renal impairment
- AF patients with a history of ACS suffer from a high rate of recurrent events and death. Perceived bleeding risk may lead to non-anticoagulation


The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Take home messages

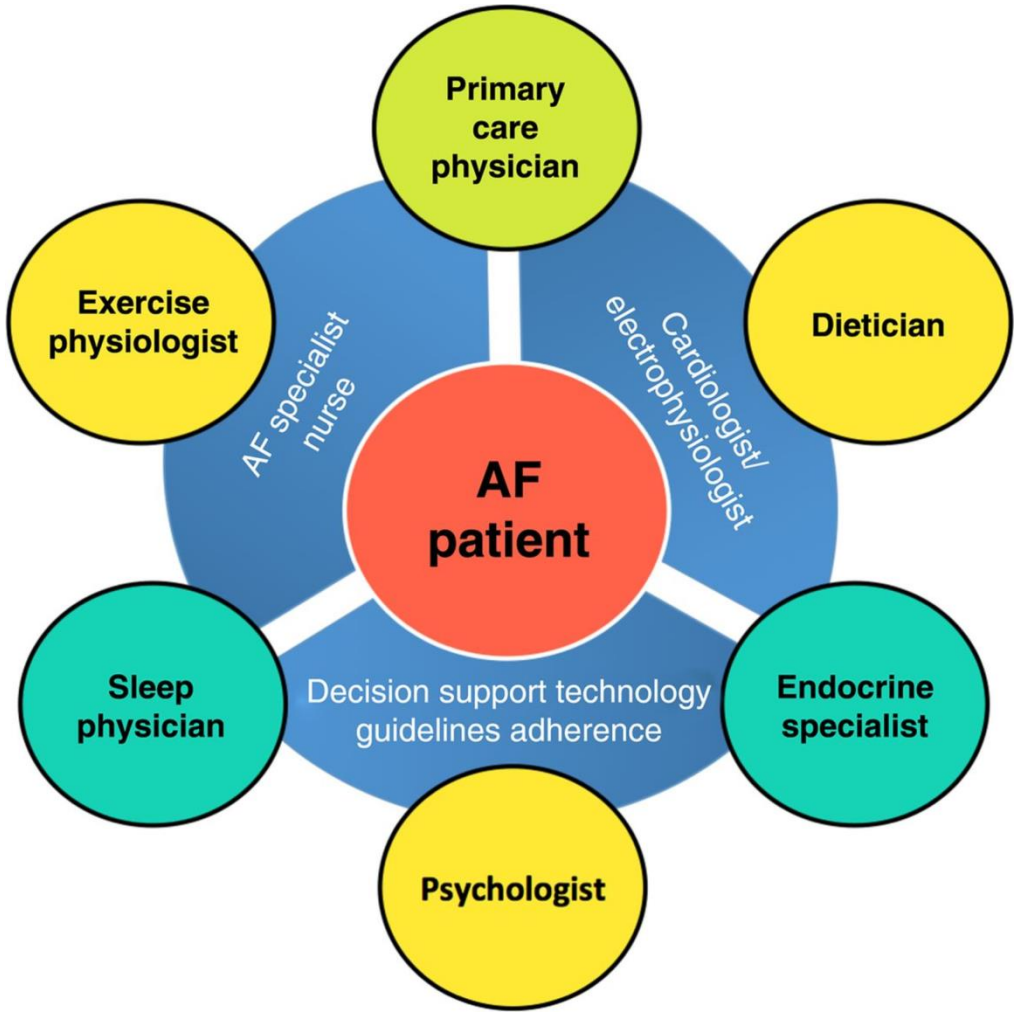
- The rate of anticoagulation is suboptimal in the sickest patients, irrespective of the comorbidity under consideration. In addition, generally speaking, up to two-thirds of patients have no antithrombotic treatment after 4 months, AC rate remaining stable
- Moreover, the comorbidities associated with the worse outcomes in AF patients, namely, CHF, vascular disease, and CKD are suboptimally treated in ~50% of the cases as regards the rate of prescription of guideline-recommended drugs in these three conditions
- Integrated care may result in improved outcomes*

*Chatterjee NA et al. JACC Heart Failure 2017



The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

# Integrated care: AF




Lau D.H. et al Eur Heart J. 2016; 37: 1573-81



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# Acknowlegements

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