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Predictors of intracranial haemorrhage in patients with atrial fibrillation treated with oral anticoagulants: results from the GARFIELD-AF and ORBIT-AF registries

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Declaration of interest

- Research contracts (Research support from Bayer, Boehringer-Ingelheim, and Pfizer.)

Conflicts of interest

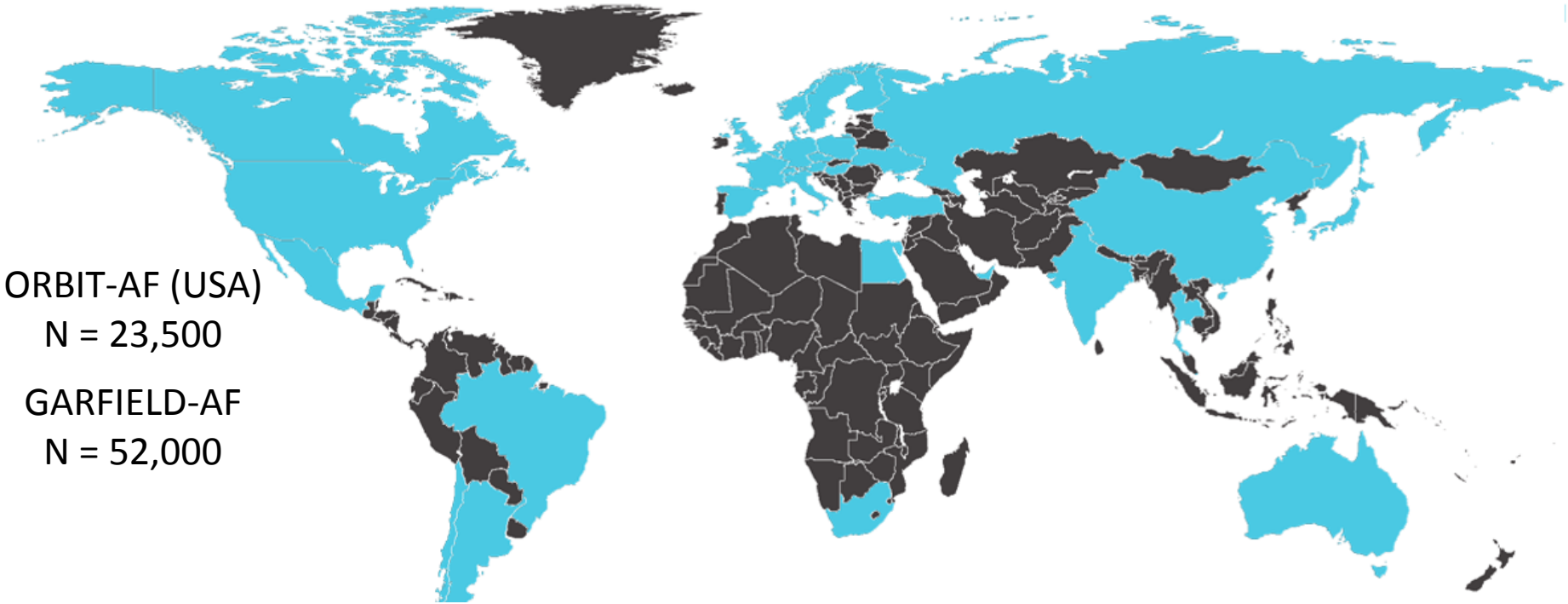
T.W.L.has received research support from Bayer, Boehringer-Ingelheim, and Pfizer. A.J.C. has received institutional grants and personal fees from Bayer, Boehringer-Ingelheim, Daiichi Sankyo, Pfizer, Medtronic, Abbott, and Boston Scientific. D.E.S. has performed consultancy/advisory board functions for Boehringer-Ingelheim, Johnson & Johnson, Merck, Pfizer (all modest), and Bristol-Myers Squibb (significant) and contracted research for Boehringer-Ingelheim and Bristol-Myers Squibb (both significant). J.-P.B.reports personal fees from Thrombosis Research Institute. G.C.F. has consulted for Abbott, Bayer, Janssen, Medtronic, and Novartis. K.A.A.F. has received grants and personal fees from Bayer/Janssen and AstraZeneca and personal fees from Sanofi/Regeneron and Verseon outside the present work. M.E. has consulted for Boehringer-Ingelheim, Daiichi Sankyo, Bristol-Myers Squibb, and Janssen Scientific Affairs. B.J.G. is on a Data Safety Monitoring Board at Janssen. E.H. has consulted for Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Janssen, Medtronic, and Pfizer. A.K.K. discloses research grants from Bayer Healthcare and personal fees from Bayer Healthcare, Boehringer-Ingelheim Pharma, Daiichi-Sankyo Europe, Sanofi SA, Janssen Pharma, Verseon Inc., and Pfizer. K.W.M.'s financial disclosures can be viewed at: http://med.Stanford.edu/profiles/kenneth-mahaffey. E.D.P. has received research grants from Janssen and Eli Lilly has consulted for Janssen and Boehringer-Ingelheim. J.P.P.receives grants for clinical research from Abbott, Bayer, Boston Scientific, and JNJ and serves as consultant to Abbott, Boston Scientific, and Medtronic. S.V. and K.S.P. declare no conflicts of interest.

Background

- Intracranial haemorrhage (ICH) is a devastating complication of anticoagulant-associated bleeding in patients with atrial fibrillation (AF).[1]
- ICH is associated with increased risk of death, myocardial infarction, and ischaemic stroke.[2]
- We aimed to identify predictors of ICH in patients with AF on anticoagulation therapy.

1. Fang MC et al. Am J Med 2007;120:700–5.
2. Held C et al. Eur Heart J 2015;36:1264–72.

Methods—GARFIELD-AF and ORBIT-AF



ORBIT-AF (USA)
N = 23,500

GARFIELD-AF
N = 52,000

Methods—potential predictors of ICH

Demographics
- Sex, age, ethnicity

Vital signs
- BMI, heart rate, SBP / DBP

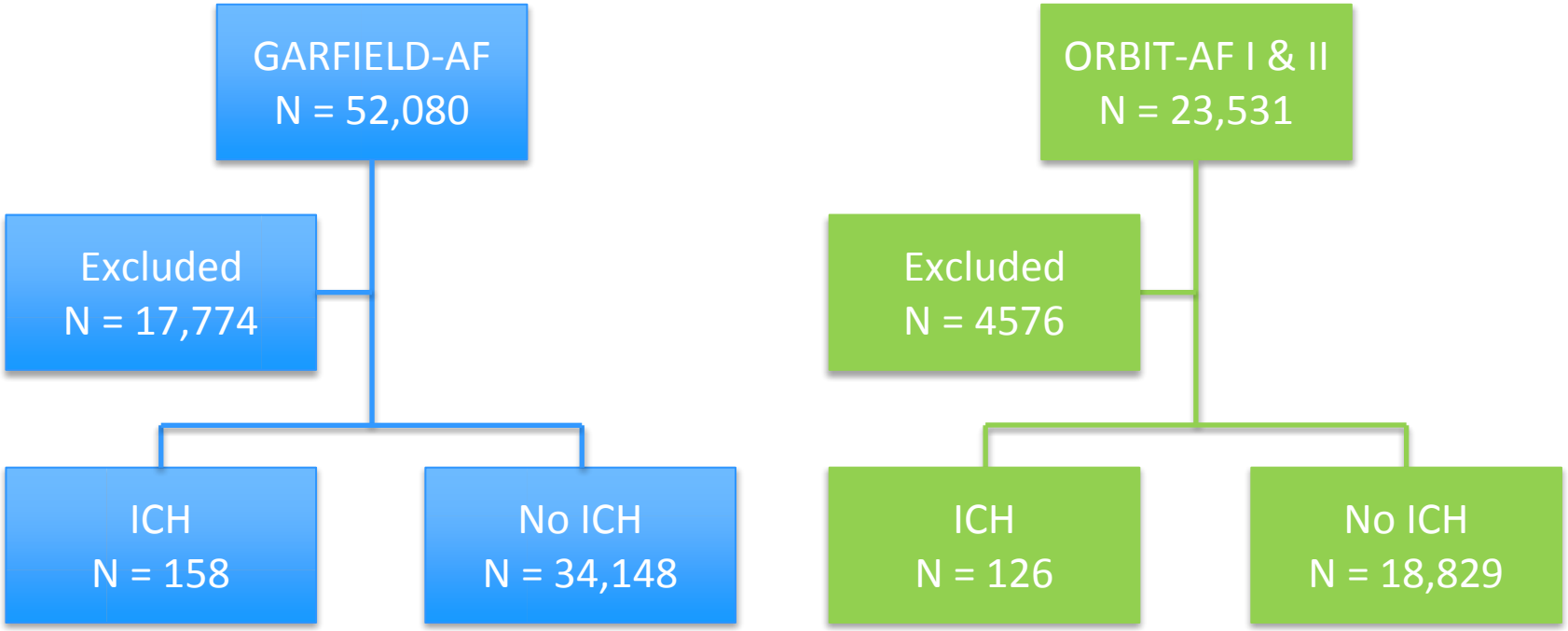
Type of AF

Treatment
- NOAC, VKA, AP therapy

Lifestyle factors
- Smoker, heavy alcohol consumption

Medical history
- Hypertension
- Diabetes
- CKD
- History of bleeding
- CHF
- ACS
- Vascular disease
- Prior stroke / TIA
- Hyperlipidaemia
- Cirrhosis / liver disease
- Hyperthyroidism / hypothyroidism
- Dementia

Results—study population



Baseline characteristics

Variable	ICH (N = 284)	No ICH (N = 52,977)
Sex male, n (%)	149 (52.5)	29,913 (56.5)
Age, median (IQR), years	77 (71–83)	72 (64–79)
Type of AF, n (%)		
Persistent/permanent	90 (31.7)	16,551 (31.2)
Paroxysmal	90 (31.7)	16,329 (30.8)
New onset	104 (36.6)	20,095 (37.9)
NOAC use, n (%)	87 (30.6)	24,246 (45.8)
VKA use, n (%)	197 (69.4)	28,731 (54.2)
Concomitant AP, n (%)	98 (34.5)	13,352 (25.2)
CHA_2DS_2-VASc score, median (IQR)	3 (2–4)	4 (3–5)
HAS-BLED score, median (IQR)	1 (1–2)	2 (1–3)

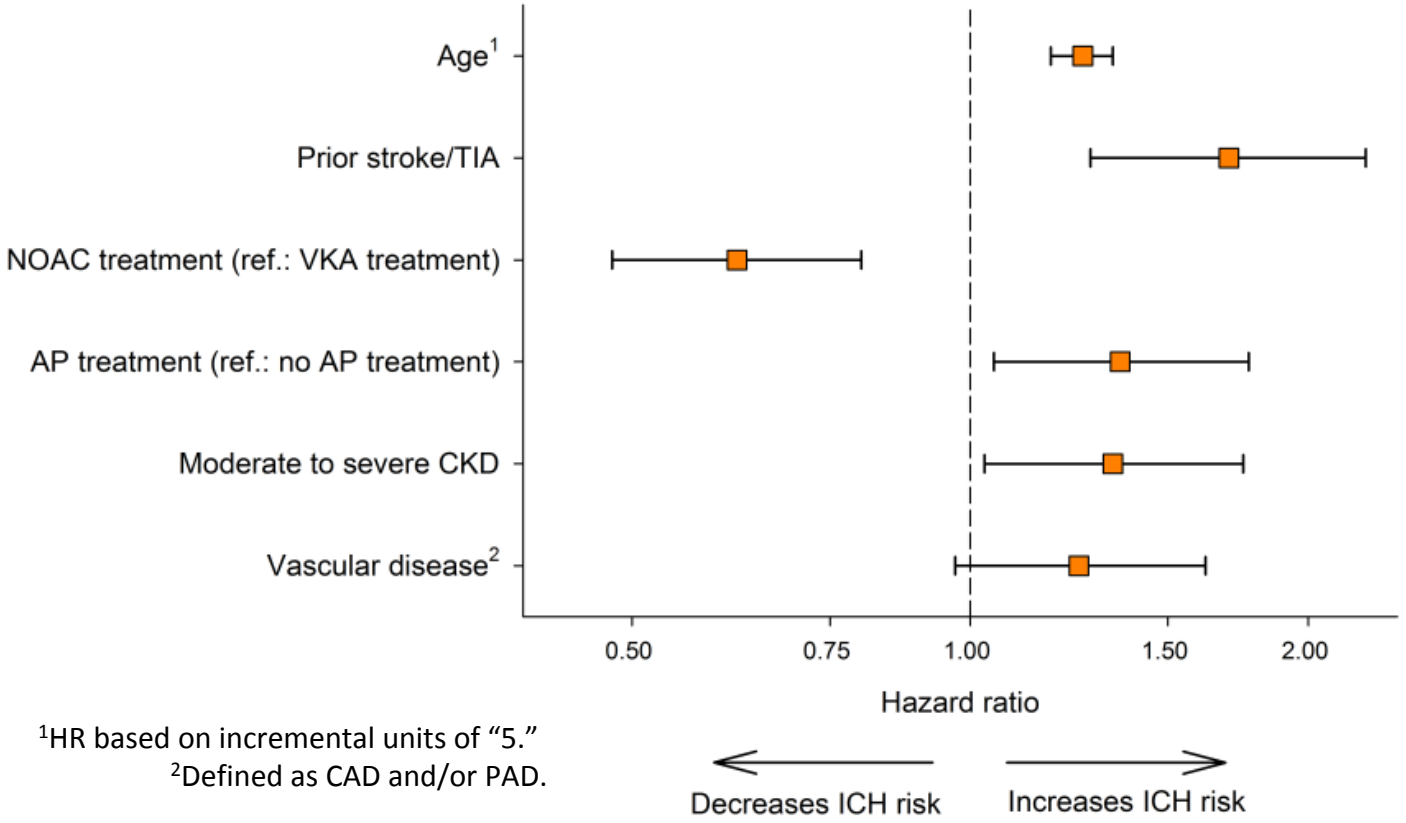
Results—ICH events

	Events/100 P-Y	Rate (95% CI)[1]
GARFIELD-AF (N = 34,306)	158	0.25 (0.21–0.29)
ORBIT-AF (N = 18,955)	126	0.46 (0.39–0.55)
Overall (N = 53,261)	284	0.31 (0.28–0.35)

[1]Event rates/100 person-years calculated over 2-year follow-up.

Results—final predictors of ICH

χ^2	P-value
47	<0.0001
14	0.0002
14	0.0002
5	0.0212
5	0.0296
3	0.0845



[1]HR based on incremental units of "5."
[2]Defined as CAD and/or PAD.

Results—model C-index

Study population	ICH model	CHA_2DS_2-VASc	HAS-BLED	GARFIELD score
GARFIELD-AF (N = 34,306)	0.67 (0.63–0.71)	0.60 (0.56–0.64)	0.60 (0.56–0.64)	0.64 (0.60–0.68)
ORBIT-AF (N = 18,955)	0.70 (0.65–0.75)	0.66 (0.61–0.71)	0.63 (0.58–0.67)	0.67 (0.62–0.72)
Overall (N = 53,261)	0.68 (0.65–0.71)	0.63 (0.60–0.66)	0.62 (0.59–0.65)	0.66 (0.63–0.69)

Strengths and limitations

- By combining data from two large registries (GARFIELD-AF and ORBIT-AF) more than 75,000 AF patients were studied
- However, because ICH is a rare event we were unable to validate the model in an external dataset
- Type of ICH (intraparenchymal, subdural, etc.) was not recorded

Summary of findings

- This study looked at predictors of ICH in a large cohort of AF patients
- Older age was by far the most highly significant risk factor for experiencing an ICH event
  - Prior stroke/TIA also important risk factor
- Treatment with NOAC versus VKA reduced ICH risk
- Concurrent use of AP increased ICH risk

Conclusions

- This study identified major risk factors associated with anticoagulant-associated ICH.
  - These include older age, prior stroke/TIA, AP use, CKD
- NOAC associated with lower ICH risk than VKA
- Minimize concomitant AP use in AF patients on OAC

Acknowledgements

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