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Association of body mass index with outcomes in patients with newly diagnosed atrial fibrillation: GARFIELD-AF

Christian Fielder Camm ,[1,2] Saverio Virdone,[3] Shinya Goto,[4] Jean-Pierre Bassand,[3,5] Martin van Eickels,[6] Sylvia Haas,[7] Bernard J Gersh,[8] Karen Pieper,[3] Keith A A Fox,[9,10] Frank Misselwitz,[11] Alexander G G Turpie,[12] Samuel Z Goldhaber,[13] Freek Verheugt,[14] John Camm,[15] Gloria Kayani,[3] Elizaveta Panchenko,[16] Seil Oh,[17] Hector Lucas Luciardi,[18] Jitendra Pal Singh Sawhney,[19] Stuart J Connolly,[20] Pantep Angchaisuksiri,[21] Hugo ten Cate,[22,23] John W Eikelboom,[20] Ajay K Kakkar,[3,24] on behalf of the GARFIELD-AF investigators

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For numbered affiliations see end of article.

Correspondence to
Dr Christian Fielder Camm; cfcamm@gmail.com

ABSTRACT

Objective While greater body mass index (BMI) is associated with increased risk of developing atrial fibrillation (AF), the impact of BMI on outcomes in newly diagnosed AF is unclear. We examine the influence of BMI on outcomes and whether this is modified by sex and evaluate the effect of non-vitamin K oral anticoagulants (NOACs) in patients with high BMI.

Methods GARFIELD-AF is a prospective registry of 52 057 newly diagnosed AF patients. The study population comprised 40 482 participants: 703 underweight (BMI <18.5 kg/m^2), 13 095 normal (BMI=18.5–24.9 kg/m^2), 15 043 overweight (BMI=25.0–29.9 kg/m^2), 7560 obese (BMI=30.0–34.9 kg/m^2) and 4081 extremely obese (BMI ≥35.0 kg/m^2). Restricted cubic splines quantified the association of BMI with outcomes. Comparative effectiveness of NOACs and vitamin K antagonists (VKAs) by BMI was performed using propensity score overlap-weighted Cox models.

Results The median age of participants was 71.0 years (Q1; Q3 62.0; 78.0), and 55.6% were male. Those with high BMI were younger, more often had vascular disease, hypertension and diabetes. Within 2-year follow-up, a U-shaped relationship between BMI and all-cause mortality was observed, with BMI of ~30 kg/m^2 associated with the lowest risk. The association with new/worsening heart failure was similar. Only low BMI was associated with major bleeding and no association emerged for non-haemorrhagic stroke. BMI was similarly associated with outcomes in men and women. BMI did not impact the lower rate of all-cause mortality of NOACs compared with VKAs.

Conclusions In the GARFIELD-AF registry, underweight and extremely obese AF patients have increased risk of mortality and new/worsening heart failure compared with normal or obese patients.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Evidence supports an association between high body mass index and risk of atrial fibrillation (AF). However, the evidence of an association between BMI and AF-related outcomes remains unclear.

WHAT THIS STUDY ADDS

⇒ A U-shaped association between BMI and all-cause mortality and heart failure in AF patients is revealed, indicating that underweight or extremely obese patients have a significantly higher risk of mortality and heart failure in comparison with those with normal body weight, overweight or obese patients. BMI, however, does not significantly impact the benefits of non-vitamin K oral anticoagulants (NOACs) versus vitamin K antagonists therapy.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In clinical practise, BMI should be measured and considered as a risk factor for outcomes in AF. NOACs could be considered for the treatment of all patients regardless of associated BMI.

INTRODUCTION

Atrial fibrillation (AF) is a common arrhythmia associated with significant risk of mortality, cardioembolic stroke and heart failure.[1] Evidence supports an association between higher body mass index (BMI) and risk of AF as well as other anthropometric measures including waist circumference, weight and height.[2] The association of higher BMI with risk of AF-related outcomes is unclear, with some studies suggesting an inverse relationship.[3 4] As obesity is generally considered detrimental to health, this inverse

relationship has been described as an 'obesity paradox'.[5] However, this finding has not been consistent.[6]

Significant sex-based differences exist for both the incidence of AF and the risk of AF-related outcomes.[7] Additionally, anthropometric measures differ between men and women.[8] In particular, body fat distribution differs substantially.[2 9] At present, it is unclear whether the association between anthropometric measures and the risk of AF-related outcomes is similar in men and women.

Given the higher risk of non-haemorrhagic stroke in patients with AF, treatment with oral anticoagulation is often recommended.[10] However, concerns have been raised regarding the safety and efficacy of non-vitamin K oral anticoagulants (NOACs) in obese and extremely obese populations.[11]

This study evaluates a large international cohort of participants with new-onset AF in GARFIELD-AF. The three principal aims were to: (1) assess associations between BMI, weight and height and the risk of AF-associated outcomes; (2) explore sex-based differences in these associations; and (3) examine the association of obesity with the impact of NOAC therapy in patients with AF.

METHODS

Study design and participants

The GARFIELD-AF design has been previously published (ClinicalTrials.gov identifier: NCT01090362).[12 13] Eligible participants (≥18 years) required a recent diagnosis of new onset non-valvular AF and ≥1 further stroke risk factor. Patients (n=52 057) were enrolled prospectively and consecutively from 35 countries globally into five cohorts from 2010 to 2016, without exclusions according to treatment or comorbidities. Study sites were computationally selected at random from a list of representative care settings. Treatment and therapy decisions were at the discretion of the physician and patient.

Patients <20 years of age, without BMI data or for whom follow-up information was unavailable were omitted from the analysis. Those with a BMI of <15 kg/m^2 or >60 kg/m^2 were excluded due to likely measurement error in the calculation of height or weight.

Data collection

Data were collected using electronic case report forms that were securely submitted electronically to the registry-coordinating centre Dendrite Clinical Systems Ltd (Henley-on-Thames, UK). Accuracy and completeness of data was ensured by the coordinating centre, the Thrombosis Research Institute (London, UK). Data were extracted from the study data base on 30 June 2019.

Ethics

The GARFIELD-AF registry is conducted in accordance with the principles of the Declaration of Helsinki, local regulatory requirements and International Conference on Harmonization–Good Pharmacoepidemiological and Clinical Practice guidelines.

Patient and public involvement statement

Written informed consent was obtained from all study participants. There was no public or patient involvement in the design or execution of the GARFIELD-AF study design. Investigators from representative investigator sites in each participating country were involved in data collection. Confidentiality and anonymity were maintained through assigned unique identifiers. Independent ethics committee and hospital-based institutional review board approvals were obtained. A full list of ethics committees is provided in the online supplemental material 1.

BMI categories

Patients were categorised into five BMI groups according to the WHO definitions: underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), obese (30–34.9 kg/m^2) and extremely obese (≥35.0 kg/m^2).[14]

Clinical characteristics and outcomes

Demographic and clinical characteristics were recorded at baseline. The primary clinical outcomes included the rate of mortality, non-haemorrhagic stroke/systemic embolism (SE), major bleeding and new/worsening heart failure according to BMI. These outcomes were also analysed according to BMI and sex. Major bleeding was defined as clinically overt bleeding associated with a critical site, a fall in haemoglobin (≥2 g/dL), transfusion of packed red blood cells (≥2 units), haemorrhagic stroke or fatal outcome.

Statistical analysis

Continuous variables are reported using medians and IQR. Categorical variables are presented as percentages and frequency counts. Data for the CHA_2DS_2-VASc and HAS-BLED risk scores were collected; the latter was calculated excluding labileinternational normalized ratios (INRs) as this was not recorded at baseline. Clinical outcomes are described by number of events, event rate per 100 person-years estimated via a Poisson model and 95% CIs. Only the first occurrence of each event was considered. Survival differences across BMI groups were examined using Kaplan-Meier curves.

To identify non-linear association between the continuous variables BMI, weight and height with outcome events, analyses of restricted cubic splines were performed by generating restricted cubic splines with four knots and applying a separate Cox multivariable model for each studied endpoint.

Covariate adjustments for Cox models were selected by avoiding the inclusion of factors in the mediating pathway between BMI and clinical outcomes. Apart from the selected demographic characteristic, smoking status and alcohol consumption were included because of their established relationship with BMI. Chronic kidney disease (CKD) was also considered a possible confounder, as CKD often causes weight loss in later stages.[15 16]

Three sensitivity analyses were performed; the first analysed the rate of new/worsening heart failure in patients without baseline heart failure. The second examined the association of BMI and AF outcomes in patients with ≥6 months of follow-up. The third adjusted associations for a broader range of covariates.

Comparative effectiveness analyses of NOAC versus VKA were performed in a study population restricted to anticoagulated patients at baseline with a CHA_2DS_2-VASc score ≥2 (excluding sex) enrolled in GARFIELD-AF cohorts 3–5 (NOACs were not widely available for patients enrolled in earlier cohorts). Analyses were performed for patients with a normal/overweight BMI (18.5–29.9 kg/m^2) and separately for those with an obese/extremely obese BMI (≥30 kg/m^2). Patients with a BMI <18.5 were not included. HRs for NOAC versus VKA were obtained using a Cox proportional hazards model via a propensity method of overlap weighting to balance covariates in the population. Treatment was defined as the first treatment received at the time of enrolment, approximating 'intention-to-treat'. Absolute standardised differences for NOAC versus VKA comparison before and after propensity score weighting among normal weight or overweight patients (BMI 18.5–29.9 kg/m^2) and obese or extremely obese patients (BMI ≥30 kg/m^2) have been presented in online supplemental figure S1a and S1b, respectively.

Only complete cases are presented in descriptive tables. Multiple imputation was applied in the derivation for the modelling process for the estimation of the BMI effect; coefficients and SEs for the risk models were obtained by combining estimates across five imputed datasets. Single imputation was applied for the NOAC versus VKA comparison. P<0.05 were considered statistically significant. Statistical analyses were carried out using SAS (V.9.4).

RESULTS

Baseline characteristics

A total of 40 482 participants were eligible for inclusion within the main analysis: underweight (n=703), normal weight (n=13 095), overweight (15,043), obese (n=7560) and extremely obese (n=4081). The median age of participants was 71.0 years (Q1; Q3: 62.0; 78.0) and slightly over half of the participants were male (n=22 881, 56.5%). Median BMI was 26.9 kg/m2 (Q1; Q3: 24.0; 30.7 kg/m^2), and median weight was 75.0 kg (Q1; Q3: 65.0; 88.0 kg). Those with higher BMI were generally younger, more often had diabetes mellitus, hypertension and vascular disease at enrolment and were more likely to have been diagnosed with permanent AF. Baseline demographic characteristics are provided in table 1). Baseline anticoagulation patterns differed significantly among BMI categories; underweight patients were less likely to receive anticoagulation treatment at baseline compared with other groups (60.3% vs 67.9%, p<0.0001, table 1), even when considering only patients at high risk of stroke (ie, CHA_2DS_2-VASc≥2, 62.1% vs 70.1%, p<0.0001, online supplemental figure S2). Medical history at baseline is provided in table 2.

Events

During a 2-year follow-up, 2805 participants (6.9%) died, 770 (1.9%) suffered a non-haemorrhagic stroke/SE, 730 (1.8%) had a major bleeding event and 589 (1.5%) had a new or worsening heart failure event (online supplemental table S1). Cumulative survival at 6 months, and past 6 month, according to BMI category is shown in figure 1.

BMI association with outcomes

After adjustment, restricted cubic spline regression demonstrated a U-shaped relationship between BMI and all-cause mortality and new/worsening heart failure; both low and high BMI were positively associated with events (figure 2). The lowest risk of all-cause mortality was observed at a BMI of ~30 kg/m^2. Below 30 kg/m^2, there was a 32% higher risk of mortality per 5 kg/m^2 lower BMI (95% CI 25% to 40%). Above 30 kg/m^2, there was a 16% higher risk of mortality per 5 kg/m^2 higher BMI (95% CI 9% to 23%). The lowest risk of new/worsening heart failure was at ~25 kg/m^2. Above 25 kg/m^2, each 5 kg/m^2 higher BMI was associated with a 23% higher risk (95% CI 14% to 33%). For major bleeding, there was a positive association only in those with low BMI. There was no association between non-haemorrhagic stroke and BMI.

Association of height and weight with outcomes

As with BMI, weight showed similar associations with AF outcomes. A U-shaped relationship was observed between weight and all-cause mortality and new/worsening heart failure, with both low and high weight being positively associated (figure 3). The lowest risk for both outcomes was at ~75 kg. Below 75 kg, there was a 15% higher risk of all-cause mortality per 5 kg lower weight (95% CI 12% to 18%). For every 5 kg higher weight above 75 kg, there was a 1% higher risk of all-cause mortality (95% CI 0% to 3%) and 6% higher risk of new/worsening heart failure (95% CI 3% to 9%). No significant association was observed between weight and the risk of major bleeding or non-haemorrhagic stroke. There was no association between height and AF outcomes (figure 4).

Association between BMI and AF outcomes by sex

BMI showed similar association in both men and women with all-cause mortality; however, there were apparent differences in the strengths of association, p value for interaction assuming a linear trend: 0.01 (figure 5). While higher BMI appeared numerically more strongly associated with all-cause mortality in women (20%, 95% CI 11% to 30% increase per 5 kg/m^2 higher BMI above 30 kg/m^2) compared with men (11%, 95% CI 0% to 22% increase per 5 kg/m^2 higher BMI above 30 kg/m^2), the difference in this specific BMI range was not significant (p-interaction 0.32). Conversely, lower BMI (<30 kg/m^2) was similarly associated with risk of all-cause mortality in

Table 1 Baseline characteristics by BMI category

Baseline characteristics	BMI category				
	Underweight (n=703)	Normal weight (n=13 095)	Overweight (n=15 043)	Obese (n=7560)	Extremely obese (n=4081)
Male, n (%)	275 (39.1)	7228 (55.2)	9276 (61.7)	4195 (55.5)	1907 (46.7)
Age, median (Q1; Q3), years	77.0 (68.0–84.0)	73.0 (64.0–80.0)	71.0 (62.0–78.0)	69.0 (61.0–76.0)	66.0 (59.0–73.0)
Age, n (%), years					
<65	117 (16.6)	3485 (26.6)	4583 (30.5)	2599 (34.4)	1823 (44.7)
65–69	88 (12.5)	1795 (13.7)	2354 (15.6)	1314 (17.4)	751 (18.4)
70–74	95 (13.5)	2215 (16.9)	2638 (17.5)	1340 (17.7)	636 (15.6)
≥75	403 (57.3)	5600 (42.8)	5468 (36.3)	2307 (30.5)	871 (21.3)
Ethnicity, n (%)					
Caucasian	204 (29.5)	5710 (44.3)	9684 (65.4)	5786 (78.0)	3309 (82.6)
Hispanic/Latino	20 (2.9)	654 (5.1)	1042 (7.0)	628 (8.5)	330 (8.3)
Asian	463 (66.9)	6353 (49.2)	3783 (25.6)	791 (10.7)	196 (4.9)
Afro-Caribbean/mixed/other	5 (0.7)	185 (1.4)	297 (2.0)	210 (2.8)	163 (4.1)
Weight, median (Q1–Q3), kg	45.0 (40.0–49.0)	62.0 (55.0–69.0)	77.0 (70.0–84.0)	90.0 (82.0–98.0)	108.0 (96.0–120.0)
Height, median (Q1–Q3), cm	160.0 (154.0–168.0)	165.0 (158.0–172.0)	168.0 (161.0–175.0)	168.0 (160.0–175.0)	166.0 (159.0–174.0)
SBP, median (Q1–Q3), mm Hg	126.0 (112.0–140.0)	130.0 (119.0–140.0)	131.0 (120.0–144.0)	135.0 (121.0–148.0)	136.0 (123.0–149.0)
DBP, median (Q1–Q3), mm Hg	74.0 (66.0–80.0)	79.0 (70.0–85.0)	80.0 (70.0–88.0)	80.0 (73.0–90.0)	80.0 (74.5–90.0)
Pulse, median (Q1–Q3), bpm	85.0 (70.0–103.0)	81.0 (70.0–100.0)	81.0 (70.0–100.0)	84.0 (70.0–104.0)	88.0 (73.0–110.0)
Type of AF, n (%)					
Permanent	66 (9.4)	1610 (12.3)	2027 (13.5)	1050 (13.9)	584 (14.3)
Persistent	127 (18.1)	1979 (15.1)	2454 (16.3)	1232 (16.3)	686 (16.8)
Paroxysmal	260 (37.0)	4378 (33.4)	4210 (28.0)	1884 (24.9)	839 (20.6)
New onset (unclassified)	250 (35.6)	5128 (39.2)	6352 (42.2)	3394 (44.9)	1971 (48.3)
Specialty at diagnosis, n (%)					
Internal medicine/neurology/ geriatrics	144 (20.5)	2404 (18.4)	2958 (19.7)	1520 (20.1)	891 (21.8)
Cardiology	503 (71.6)	9419 (71.9)	10 017 (66.6)	4793 (63.4)	2446 (60.0)
Primary care/general practice	56 (8.0)	1272 (9.7)	2068 (13.7)	1247 (16.5)	743 (18.2)
Care setting at diagnosis, n (%)					
Hospital	439 (62.4)	8039 (61.4)	8806 (58.5)	4106 (54.3)	2215 (54.3)
Office/anticoagulation clinic/ thrombosis centre	224 (31.9)	4021 (30.7)	4799 (31.9)	2550 (33.7)	
Emergency room	40 (5.7)	1035 (7.9)	1438 (9.6)	904 (12.0)	479 (11.7)
Heavy alcohol use, n (%)	12 (1.9)	287 (2.5)	303 (2.3)	151 (2.2)	64 (1.8)
Current smoker, n (%)	79 (11.9)	1542 (12.6)	1568 (11.1)	694 (9.7)	380 (9.8)
Treatment, n (%)					
NOAC±AP	185 (26.5)	3739 (28.9)	4137 (27.9)	2048 (27.6)	1184 .6)
VKA±AP	235 (33.7)	4502 (34.8)	5952 (40.2)	3265 (44.0)	1770 .3)
AP only	146 (20.9)	2906 (22.5)	3190 (21.5)	1466 (19.7)	675 (16.9)
None	131 (18.8)	1787 (13.8)	1545 (10.4)	644 (8.7)	367 (9.2)

AF, atrial fibrillation; AP, antiplatelet; BMI, body mass index; DBP, diastolic blood pressure; NOAC, non-oral anticoagulant; SBP, systolic blood pressure; VKA, vitamin K antagonist.

Table 2 Medical history by BMI category

Baseline comorbidity or risk score/tool, n (%)	BMI category				
	Underweight (n=703)	Normal weight (n=13 095)	Overweight (n=15 043)	Obese (n=7560)	Extremely obese (n=4081)
Heart failure	203 (28.9)	2972 (22.7)	3281 (21.8)	1969 (26.0)	1221 (29.9)
Acute coronary syndromes	64 (9.1)	1269 (9.7)	1706 (11.4)	935 (12.4)	429 (10.6)
Vascular disease*	147 (21.0)	2960 (22.8)	3877 (25.9)	2182 (29.1)	1106 (27.3)
Carotid occlusive disease	22 (3.2)	397 (3.1)	525 (3.5)	219 (2.9)	87 (2.2)
VTE	9 (1.3)	213 (1.6)	362 (2.4)	245 (3.3)	200 (4.9)
Prior stroke/TIA/SE	101 (14.5)	1575 (12.1)	1693 (11.3)	756 (10.1)	356 (8.8)
Prior bleeding	28 (4.0)	326 (2.5)	384 (2.6)	197 (2.6)	107 (2.6)
Hypertension	388 (55.3)	8945 (68.5)	11 816 (78.7)	6490 (86.0)	3603 (88.5)
Hypercholesterolaemia	157 (23.1)	4216 (33.0)	6481 (44.3)	3821 (52.3)	2088 (52.7)
Diabetes	69 (9.8)	2099 (16.0)	3190 (21.2)	2238 (29.6)	1590 (39.0)
Cirrhosis	7 (1.0)	83 (0.6)	81 (0.5)	50 (0.7)	28 (0.7)
Moderate to severe CKD	95 (14.1)	1455 (11.4)	1456 (10.0)	783 (10.7)	449 (11.4)
Dementia	31 (4.4)	265 (2.0)	169 (1.1)	71 (0.9)	28 (0.7)
CHA_2DS_2-VASc score, median (Q1–Q3)	4.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)
HAS-BLED score†, median (Q1–Q3)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)
GARFIELD-AF death score‡, median (Q1–Q3)	9.1 (4.8–16.9)	5.2 (2.9–10.1)	4.4 (2.5–8.1)	4.5 (2.6–7.6)	4.1 (2.4–6.9)
GARFIELD-AF stroke score§, median (Q1–Q3)	2.1 (1.4–3.0)	1.7 (1.1–2.5)	1.5 (1.1–2.3)	1.5 (1.0–2.2)	1.4 (0.9–2.1)
GARFIELD-AF bleeding score¶, median (Q1–Q3)	1.9 (1.2–3.1)	1.6 (1.0–2.5)	1.6 (1.0–2.4)	1.5 (1.0–2.3)	1.4 (0.9–2.1)

*Defined as peripheral artery disease and/or coronary artery disease.
†The risk factor 'Labile INRs' is not included in the HAS-BLED score as it is not collected at baseline. As a result, the maximum HAS-BLED score at baseline is 8 points (not 9).
‡Represent the risk of mortality within 2 years.
§Represent the risk of non-haemorrhagic stroke within 2 years.
¶Represent the risk of major bleeding within 2 years.
CKD, chronic kidney disease; SE, systemic embolism; TIA, transient ischaemic attack; VTE, venous thromboembolism.

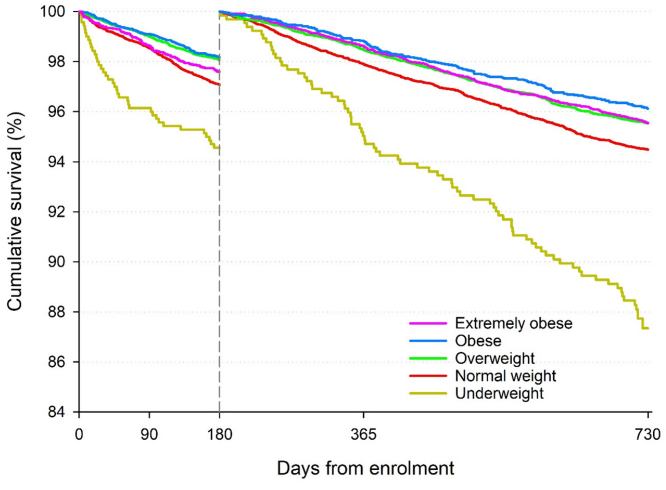

Figure 1 Cumulative survival at 6 months and conditional at having survived 6 months by BMI category. BMI, body mass index.

women (15%, 95% CI 7% to 24% increase per 5 kg/m^2 lower BMI below 30 kg/m^2) and men (16%, 95% CI 8% to 25% decrease per 5 kg/m^2 lower BMI below 30 kg/m^2 (p-interaction 0.88).

Sensitivity analysis

In patients without baseline heart failure, the association between BMI and weight and risk of new heart failure (330 events) was similar (online supplemental figure S3). No association was observed between height and risk of new heart failure. Age did not impact the association between BMI and risk of all-cause mortality or new/worsening heart failure with similar risk of outcomes observed in both younger and older participants (online supplemental figure S4).

Limiting the analysis to participants with at ≥6 months of follow-up (n=39 081) did not affect the association between BMI and AF outcomes (online supplemental figure S5). Furthermore, adjusting for baseline treatment

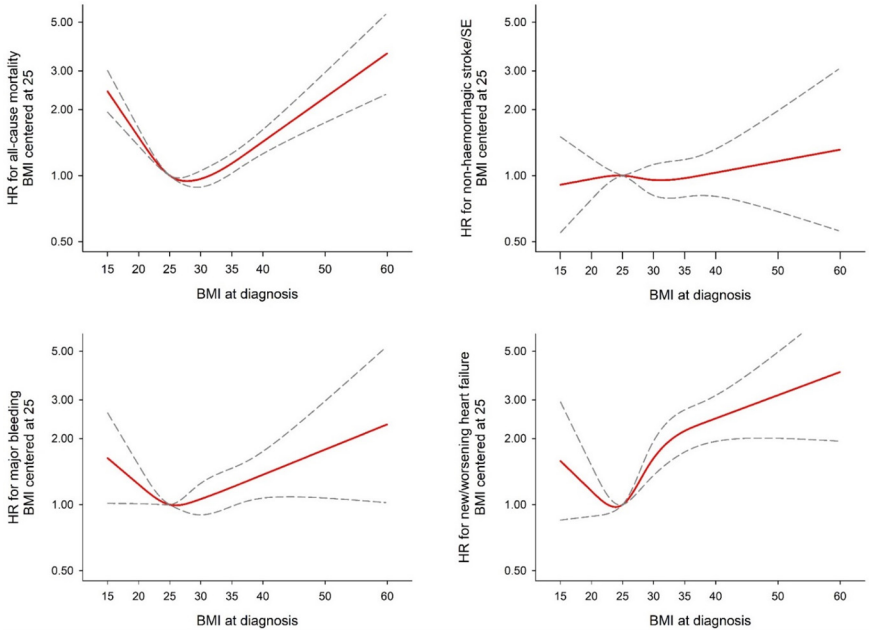

Figure 2 Adjusted* associations through 2-year follow-up between BMI and selected endpoints based on a restricted cubic spline model. *Adjusted by age, sex, ethnicity, smoking status, alcohol use and moderate to severe CKD. BMI, body mass index; CKD, chronic kidney disease.

did not alter these results (online supplemental figure S6).

Additional adjustment for a broader range of covariates (model 1: age, sex, ethnicity, smoking status, alcohol use and moderate to severe CKD; model 2: as model 1, plus hypertension, heart failure, diabetes, vascular disease, prior stroke/TIA/SE, history of bleeding and baseline anticoagulation) included suspected mediators of the association between higher BMI and risk of AF outcomes. This led to a substantial attenuation of the association between higher BMI and risk of all-cause mortality (4%, 95% CI −2 to 12% increase per 5 kg/m^2 increase). Conversely, there was no meaningful difference in the negative association between low BMI (<30 kg/m^2) and all-cause mortality (39%, 95% CI 31% to 47% increase per 5 kg/m^2 decrease, online supplemental table S2).

Effects of BMI in relation to NOAC therapy

Participants were separated into two groups: patients with a normal or overweight BMI (BMI 18.5–29.9 kg/m^2, VKA

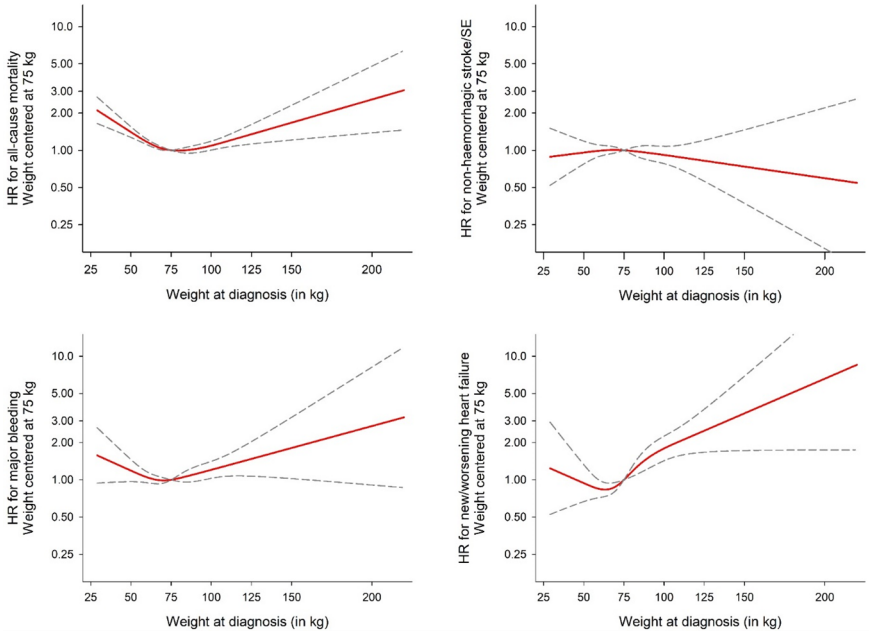

Figure 3 Adjusted* associations through 2-year follow-up between weight and selected endpoints based on a restricted cubic spline model. *Adjusted by age, sex, ethnicity, smoking status, alcohol use and moderate to severe CKD. CKD, chronic kidney disease.

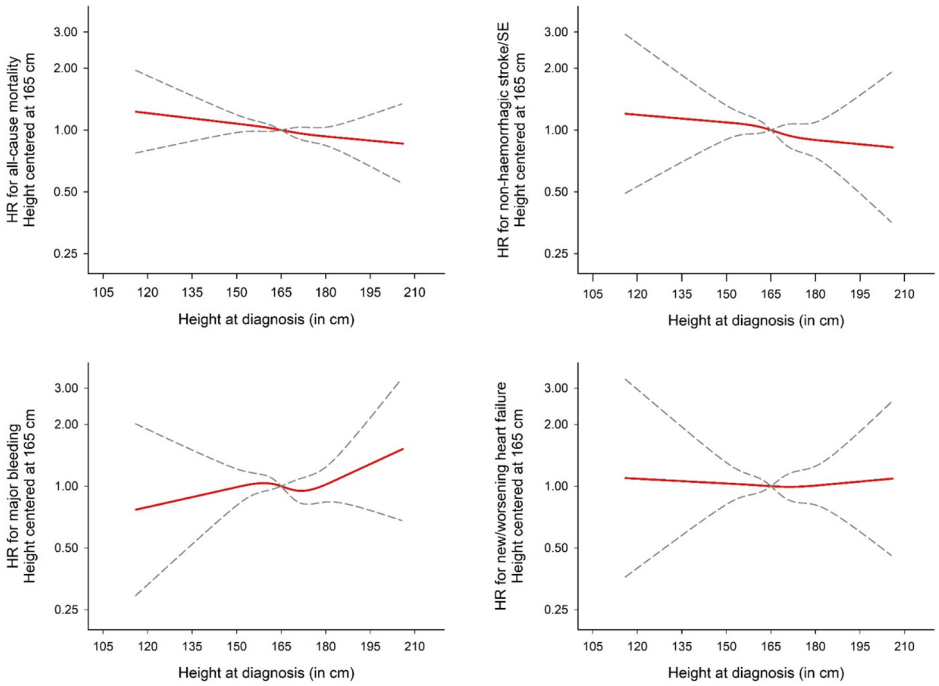

Figure 4 Adjusted* associations through 2-year follow-up between height and selected endpoints based on a restricted cubic spline model.*Adjusted by age, sex, ethnicity, smoking status, alcohol use, and moderate to severe CKD.

participants=5051, NOAC participants=5612) and those with an obese/extremely obese BMI (BMI ≥30.0 kg/m^2, VKA participants=2549, NOAC participants=2298). No significant difference was observed in the effect of NOAC therapy between BMI groups (figure 6). NOAC therapy was associated with lower all-cause mortality in both the normal/overweight group (HR 0.77, 95% CI 0.65 to 0.90) and the obese/extremely obese group (HR 0.77, 95% CI 0.60 to 0.99). There were no substantial differences in the impact of NOAC therapy on non-haemorrhagic stroke or major bleeding event risk between BMI groups.

DISCUSSION

This study demonstrated a non-linear association between BMI and weight, with risk of all-cause mortality and new/worsening heart failure. This suggested that those with both low and high values were at higher risk of these AF outcomes. There was no association of obesity/extreme obesity with the efficacy of NOACs versus VKAs when compared with a normal/overweight group.

Previously, an inverse relationship has been demonstrated between BMI and mortality in AF. Post hoc analysis of 21 028 ENGAGE TIMI-48 trial participants showed a ~10% lower risk of death and stroke per 5 kg/m^2 higher BMI.[3] Conversely a 6% higher risk of bleeding was demonstrated per 5 kg/m^2 higher BMI. Similar findings have been reported from post hoc analysis of AFFIRM (n=2492) and ORBIT-AF participants (n=9513).[4 17] Interestingly, results from GARFIELD-VTE similarly supported an 'obesity paradox' with all-cause mortality was lowest in obese patients.[18] In contrast, Overvad *et al*[6] analysed a subgroup of the Danish Diet, Cancer, and Health cohort and, similar to our results, demonstrated a positive association with higher BMI and, intriguingly, a U-shaped relationship, which was particularly pronounced in women. Our findings support an inverse relationship between BMI and risk of death in AF but only for BMI <~30 kg/m^2. Above this level, a strong positive association existed. While not in keeping with most studies examining AF patients, it is consistent with the association between BMI and mortality in the general population.[19]

The association of BMI with the risk of heart failure in AF has not been well established. Schnabel *et al* demonstrated a 6% higher risk of heart failure per 1 kg/m^2 higher BMI in those with AF (AF cases=725).[20] Assessment of the ORBIT-AF cohort, however, revealed no significant association between BMI and risk of heart failure.[17] Our results demonstrated that both low and high BMI are associated with risk of new/worsening heart failure. Given the potential for reverse causation, we confirmed this when patients with events in the first 6 months of follow-up were excluded and in those without baseline heart failure.

Reasoning for the difference in our findings compared with prior groups is unclear. This study was limited to new-onset AF. Inclusion of participants previously diagnosed with AF, such as in ORBIT-AF and AFFIRM,[4 17] may have led to a selection bias with those dying shortly after diagnosis being excluded. Additionally, previous studies have often adjusted for variables which may mediate relationships between BMI and mortality in patients with AF, such as hypertension/blood pressure, diabetes or history of ischaemic heart disease. Adjustment for variables involved in mediating pathways will necessarily

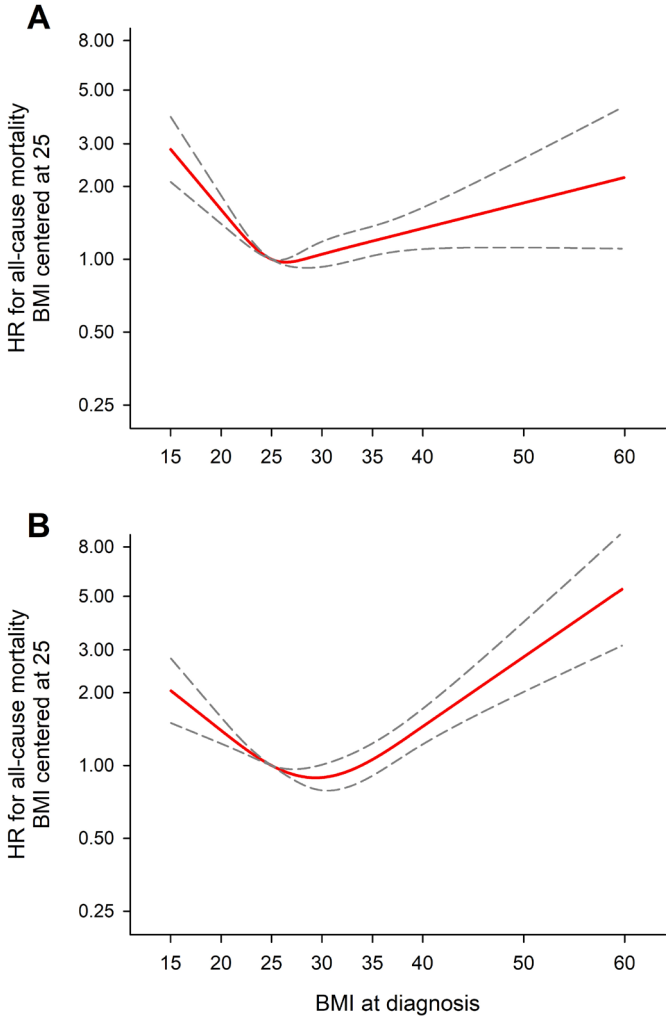

Figure 5 Adjusted[1] associations through 2-year follow-up between BMI and selected endpoints based on a restricted cubic spline model in (A) male and (B) female patients.[1] Adjusted by age, ethnicity, smoking status, alcohol use and moderate to severe CKD. BMI, body mass index; CKD, chronic kidney disease.

bias results.[21] Additional adjustments made in our analysis mitigated the positive association with higher BMI (>30 kg/m^2), suggesting that over adjustment may have produced the previously reported negative association between BMI and mortality.

The mechanisms underlying the association between BMI and AF outcomes are not clearly established. Greater BMI has been associated with higher risk of hypertension,[22] diabetes[23] and coronary heart disease,[24] which are established risk factors for mortality and heart failure. However, these comorbidities are associated with risk of ischaemic stroke,[25] which was not associated with BMI in our analysis. As such, the mediating pathway between BMI and mortality/heart failure in AF may partially lie outside these established risk factors. Increasing adiposity has been associated with higher levels of epicardial fat and atrial fibrosis both of which are risk factors for AF.[26] Further exploration into the role of cardiac factors in the association between BMI and AF outcomes may therefore be warranted.

Trend differences were observed in the BMI association with outcomes between sexes; high BMI was more strongly associated with mortality among women. However, the observed differences were numerically small, and more research is required to identify significant effect modifications between sexes.

Despite a strong association between height and risk of AF, there has been limited assessment of the association of height with AF-related outcomes. Height has previously been shown to be inversely associated with risk of stroke and cardiovascular disease.[27 28] However, the association of height with cardioembolic stroke is not clear. A small case–control study in South Korea suggested a possible inverse association between height and stroke in those with AF.[29] However, our findings have suggested no association between height and AF-related outcomes. Height is often considered a surrogate marker for lean mass. As such, these results may suggest that fat mass, rather than lean mass, is associated with higher mortality and heart failure in those with AF. This would contrast with AF risk itself where both lean and fat mass are associated.[2] Our findings suggest a need for assessment of the association of lean and fat mass with risk of AF outcomes.

The causal relevance of this association between BMI and AF outcomes is not clear. However, previous trials of weight loss in patients with AF have demonstrated substantial improvements in symptoms and AF burden.[30] To date, no randomised trial of weight loss in AF has been powered to detect meaningful changes in AF outcomes. Our results suggest that further assessment of weight loss in overweight/obese individuals with AF should be considered to determine the impact on reduced mortality and heart failure.

The potential detrimental effects of raised BMI on the efficacy of NOAC therapy have been raised previously.[11] Robust pharmacokinetic and pharmacodynamics data in obesity and extreme obesity are lacking. Piran *et al*[31] suggested that one-fifth of extremely obese patients have a peak NOAC plasma concentration below the expected range. A meta-analysis of randomised controlled trials also suggested a similar rate of stroke and major bleeding in obese patients treated NOACs and warfarin.[32] In line with this, our findings suggested there is no difference between NOAC and VKA therapy on the risk of non-haemorrhagic stroke or major bleeding in obese/extremely obese participants. In contrast, our results demonstrated substantially lower all-cause mortality with NOAC compared with VKA therapy in both normal/overweight and obese/extremely obese participants. This suggests that while there may be differences in the pharmacokinetics/pharmacodynamics of NOACs in obese/extremely obese individuals, NOAC therapy is likely more beneficial than VKA therapy in those with higher BMI.

This study has several strengths, including its large size, data on a broad range of major potential confounders and excellent participant follow-up. However,

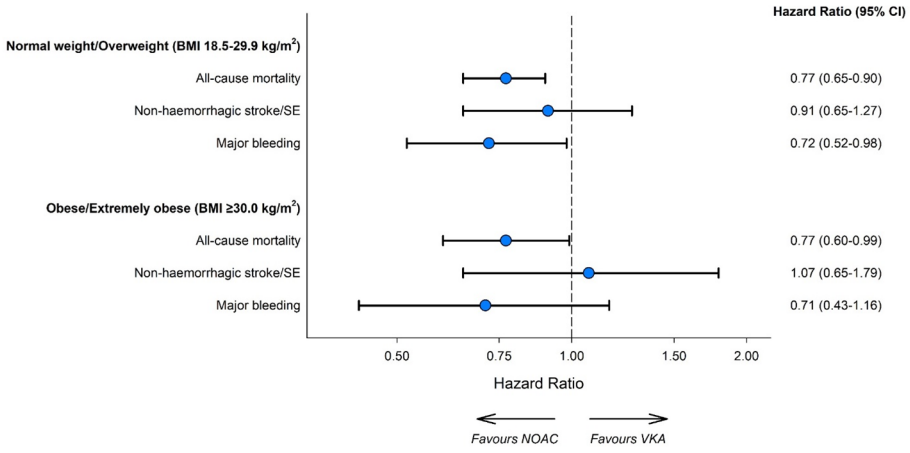

Figure 6 Propensity score weighted HRs* for NOAC versus VKA treatment through 2-year follow-up by BMI group. The reference category is patients treated with VKA treatment. *Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: country and cohort enrolment, sex, age, ethnicity, type of AF, care setting specialty and location, congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolaemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, heart rate, systolic and diastolic blood pressure at diagnosis and baseline antiplatelet use. AF, atrial fibrillation; CKD, chronic kidney disease; NOAC, non-vitamin K oral anticoagulants; SE, systemic embolism; TIA; transient ischaemic attack; VKA, vitamin K antagonist.

observational associations can be subject to uncontrolled residual confounding. Additionally, the lack of more detailed anthropometric measures limits our ability to make mechanistic inferences. As AF development is casually linked to BMI and a series of clinical endpoints, by restricting enrolment to AF patients, the obtained associations between BMI and clinical endpoints are possibly subject to collider stratification bias. Studies that collect longitudinal BMI measurements preceding AF incidence and the application of time-varying exposure methods would help quantify the magnitude of this bias.

CONCLUSIONS

Our findings from this large-scale observational cohort suggest important associations between both high and low BMI and risk of mortality and new/worsening heart failure in those with AF. These findings are not in line with the so-called 'obesity paradox' and suggest that further investigation of weight management strategies in those with AF may reduce mortality and heart failure risk.

Author affiliations
[1]Keble College, University of Oxford, Oxford, UK
[2]Cardiology Department, Royal Berkshire NHS Foundation Trust, Reading, UK
[3]Thrombosis Research Institute, London, UK
[4]School of Medicine Graduate School of Medicine, Tokai University, Isehara, Japan
[5]Universite de Besancon, Besancon, France
[6]Bayer AG, Leverkusen, Germany
[7]Haemostasis and Thrombosis Research Group, Institute for Experimental Oncology and Therapy Research, Technical University of Munich, Munich, Germany
[8]Mayo Clinic, Rochester, Minnesota, USA
[9]The University of Edinburgh School of Clinical Sciences, Edinburgh, UK
[10]Royal Infirmary of Edinburgh, Edinburgh, UK
[11]Bayer AG, Berlin, Germany
[12]Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[13]Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA
[14]Department of Cardiology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands
[15]Department of Cardiology, St George's University of London, London, UK
[16]Ministry of Health of the Russian Federation, Moskva, Russian Federation
[17]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea (the Republic of)
[18]National University of Tucuman, San Miguel de Tucuman, Tucumán, Argentina
[19]Sir Ganga Ram Hospital, Lahore, Pakistan
[20]McMaster University, Hamilton, Ontario, Canada
[21]Department of Medicine, Mahidol University, Salaya, Thailand
[22]Maastricht University Cardiovascular Research Institute Maastricht, Maastricht, The Netherlands
[23]Maastricht University Medical Centre+, Maastricht, The Netherlands
[24]Department of Surgery, University College London, London, UK

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Collaborators Global Steering Committee: GARFIELD-AF Registry Investigators: Ajay K Kakkar (UK) (Chair), Jean-Pierre Bassand (France), A John Camm (UK), David A Fitzmaurice (UK), Keith A A Fox (UK), Bernard J Gersh (USA), Samuel Z Goldhaber (USA), Shinya Goto (Japan), Sylvia Haas (Germany), Werner Hacke (Germany), Lorenzo G Mantovani (Italy), Frank Misselwitz (Germany), Karen S Pieper (USA), Alexander G G Turpie (Canada), Martin van Eickels (Germany) and Freek W A Verheugt (the Netherlands). Audit Committee: Keith A A Fox (UK) and Bernard J Gersh (USA). GARFIELD-AF National Coordinators: Hector Lucas Luciardi (Argentina), Harry Gibbs (Australia), Marianne Brodmann (Austria), Frank Cools (Belgium), Antonio Carlos Pereira Barretto (Brazil), Stuart J Connolly, John Eikelboom (Canada), Ramon Corbalan (Chile), Zhi-Cheng Jing (China), Petr Jansky (Czech Republic), Jørn Dalsgaard Nielsen (Denmark), Hany Ragy (Egypt), Pekka Raatikainen (Finland), Jean-Yves Le Heuzey (France), Harald Darius (Germany), Matyas Keltai (Hungary), Jitendra Pal Singh Sawhney (India), Giancarlo Agnelli and Giuseppe Ambrosio (Italy), Yukihiro Koretsune (Japan), Carlos Jerjes Sánchez Díaz (Mexico), Hugo Ten Cate (the Netherlands), Dan Atar (Norway), Janina Stepinska (Poland), Elizaveta Panchenko (Russia), Toon Wei Lim (Singapore), Barry Jacobson (South Africa), Seil Oh (South Korea), Xavier Viñolas (Spain), Marten Rosenqvist (Sweden), Jan Steffel (Switzerland), Pantep Angchaisuksiri (Thailand), Ali Oto (Turkey), Alex Parkhomenko (Ukraine), Wael Al Mahmeed (United Arab Emirates), David Fitzmaurice (UK) and Samuel Z Goldhaber (USA). GARFIELD-AF National

Investigators: China: Dayi Hu, Kangning Chen, Yusheng Zhao, Huaiqin Zhang, Jiyan Chen, Shiping Cao, Daowen Wang, Yuejin Yang, Weihua Li, Hui Li, Yuehui Yin, Guizhou Tao, Ping Yang, Yingmin Chen, Shenghu He, Yong Wang, Guosheng Fu, Xin Li, Tongguo Wu, Xiaoshu Cheng, Xiaowei Yan, Ruiping Zhao, Moshui Chen, Longgen Xiong, Ping Chen, Yang Jiao, Ying Guo, Li Xue and Zhiming Yang. India: Praveen Jadhavm, Raghava Sarma, Govind Kulkarni, Prakash Chandwani, Rasesh Atulbhai Pothiwala, Mohanan Padinhare Purayil, Kamaldeep Chawla, Veerappa Annasaheb Kothiwale, Bagirath Raghuraman, Vinod Madan Vijan, Jitendra Sawhney, Ganapathi Bantwal, Aziz Khan, Ramdhan Meena, Manojkumar Chopada, Sunitha Abraham, Vikas Bisne, Govindan Vijayaraghavan, Debabrata Roy, Rajashekhar Durgaprasad, A G Ravi Shankar, Sunil Kumar, Dinesh Jain, Kartikeya Bhargava, Vinay Kumar, Udigala Madappa Nagamalesh and Rajeeve Kumar Rajput. 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Ikeda, Kazuo Maeda, Tomohiro Shinozuka, Takeshi Inoue, Koichi Kawakami, Hiromichi Kitazumi, Tsutomu Takagi, Mamoru Hamaoka, Jisho Kojima, Akitoshi Sasaki, Yoshihiro Tsuchiya, Tetsuo Betsuyaku, Koji Higuchi, Masaaki Honda, Koichi Hasegawa, Takao Baba, Kazuaki Mineoi, Toshihiko Koeda, Kunihiko Hirasawa, Toshihide Kumazaki, Akira Nakagomi, Eiji Otaki, Takashi Shindo, Hiroyoshi Hirayama, Chikako Sugimoto, Takashi Yamagishi, Ichiro Mizuguchi, Kazunori Sezaki, Isamu Niwa, Ken Takenaka, Osamu Iiji, Koichi Taya, Hitoshi Kitazawa, samu Ueda, Hirokazu Kakuda, Takuya Ono, Seizo Oriso, Junya Kamata, Toshihiko Nanke, Itaru Maeda, Yoshifusa Matsuura, Hiroki Teragawa, Yasuyuki Maruyama, Kazuo Takei, Hajime Horie, Tetsutaro Kito, Hiroshi Asano, Koji Matsushita, Masaichi Nakamura, Takashi Washizuka, Tomoki Yoshida, Masato Sawano, Shinichi Arima, Hidekazu Arai, Hisanori Shinohara, Hiroyuki Takai, Nobufusa Furukawa, Akira Ota, Kentaro Yamamoto, Kenji Aoki, Taku Yamamoto, Takeaki Kasai, Shunji Suzuki, Shu Suzuki, Nitaro Shibata, Masayuki Watanabe, Yosuke Nishihata, Toru Arino, Masaki Okuyama, Tetsushi Wakiyama, Tomoko Kato, Yasuo Sasagawa, Takeshi Tana, Yoshihito Hayashi, Shinichi Hirota, Yukihiko Abe, Yoshihiro Saito, Hirohide Uchiyama, Hiroshi Takeda, Hiroshi Ono, Shuichi Tohyo, Naoto Hanazono, Seiichi Miyajima, Hisashi Shimono, Takuma Aoyama, Yasunobu Shozawa, Yawara Niijima, Osamu Murai, Osamu Murai, Hideko Inaba, Katsumasa Nomura, Masatsugu Nozoe, Kazuo Suzuki, Toshiyuki Furukawa, Toshihiko Shiraiwa, Nobuhisa Ito, Shunichi Nagai, Kiyoharu Sato, Shiro Nakahara, Yujin Shimoyama, Naoko Ohara, Teruhiko Kozuka, Hideaki Okita, Masato Endo, Tsutomu Goto, Makoto Hirose, Emiko Nagata, Noriyuki Nakanishi, Toshizumi Mori, Shuichi Seki, Katsuhiro Okamoto, Osamu Moriai, Yoko Emura, Tsuyoshi Fukuda, Haruhiko Date, Shuichi Kawakami, Sho Nagai, Yuya Ueyama, Tetsuro Fudo, Mitsuru Imaizumi, Takuo Ogawa, Shunsuke Take, Hideo Ikeda, Hiroaki Nishioka, Norihiko Sakamoto, Kiyomitsu Ikeoka, Nobuo Wakaki, Masatake Abe, Junji Doiuchi, Tetsuya Kira, Masato Tada, Ken Tsuzaki, Naoya Miura, Yasuaki Fujisawa, Wataru Furumoto, Susumu Suzuki, Akinori Fujisawa, Ryosai Nakamura, Hiroyasu Komatsu, Rei Fujiki, Shuichi Kawano, Keijiro Nishizawa, Yoji Kato, Junya Azuma, Kiyoshi Yasui,Toshio Amano, Yasuhiro Sekine, Tatsuo Honzawa, Yuichiro Koshibu, Yasuhide Sakamoto, Yukihiro Seta, Shingo Miyaguchi, Kojuro Morishita, Yasuko Samejima, Toyoshi Sasaki, Fumiko Iseki, Toshiyuki Kobayashi, Hiroshi Kano, Jaeyoung Kim, Hiroshi Yamaguchi, Yoichi Takagi, Yoko Onuki Pearce, Yasuyuki Suzuki, Takayuki Fukui, Toru Nakayama, Hideaki Kanai, Yoshiyuki Kawano, Tetsuji Ino, Hironori Miyoshi, Yasufumi Miyamoto, Masahito Shigekiyo, Shimato Ono, Yoshiyuki Kawano, Yutaka Okamoto, Satoshi Ubukata, Kojiro Kodera, Tatsuo Oriuchi, Naoki Matsumoto, Koichi Inagaki, Atsushi Iseki, Tomohiro Yoshida, Toshihiro Goda, Tsukasa Katsuki, Atsushi Sato, Etsuo Mori, Toshio Tsubokura, Hiroshi Shudo, Shunichi Fujimoto, Tomohiro Katsuya, 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Nava, Jesus David Morales Cerda, Pedro Fajardo Campos and Mario Benavides Gonzalez. Austria: Marianne Brodmann, Kurt Lenz, Claus Hagn, Johannes Foechterle, Heinz Drexel, Kurt Huber, Andrea Podczeck- Schweighofer, Michael Winkler, Bruno Schneeweiss, Alfons Gegenhuber, Wilfried Lang, Sabine Eichinger-Hasenauer, Peter Kaserer, Josef Sykora, Heribert Rasch and Bernhard Strohmer. Belgium: Luc Capiau, Geert Vervoort, Bart Wollaert, Frank Cools, Geert Hollanders, Jan Vercammen, Dirk Faes, Yohan Balthazar, Marc Delforge, Olivier Xhaet, Harry Striekwold, John Thoeng, Kurt Hermans, Georges Mairesse, Wim Anné, Ivan Blankoff, Michel Beutels, Stefan Verstraete, Peter Vandergoten, Philippe Purnode, Pascal Godart, Tim Boussy, Philippe Desfontaines, Alex Heyse, Joeri Voet and Axel De Wolf. Czech Republic: Eva Zidkova, Petr Jansky, Rudolf Spacek, Vilma Machova, Ondrej Ludka, Josef Olsr, Lubos Kotik, Blazej Racz, Richard Ferkl, Jan Hubac, Ilja Kotik, Zdenek Monhart, Hana Burianova, Ondrej Jerabek, Jana Pisova, Iveta Petrova, Vratislav Dedek, Michaela Honkova, Petr Podrazil, Petr Reichert, Jindrich Spinar, Miroslav Novak, Vaclav Durdil, Katarina Plocova and Jiri Lastuvka. Denmark: Jørn Nielsen, Steen Husted, Helena Dominguez, Ulrik Hintze, Søren Rasmussen, Næstved Sygehus, Arne Bremmelgaard, John Markenvard, Jan Børger, Jorgen Solgaard, Ebbe Eriksen, Thomas Løkkegaard, Michael Bruun, Jacob Mertz, Morten Schou, Helena Dominguez and Michael Olsen. Finland: Pekka Raatikainen, Carmela Viitanen. 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Poland: Janina Stepinska, Andrzej Gieroba, Malgorzata Biedrzycka, Michal Ogorek, Beata Wozakowska-Kaplon, Krystyna Loboz-Grudzien, Jaroslaw, Wieslaw Supinski, Jerzy Kuzniar, Roman Zaluska, Jaroslaw Hiczkiewicz, Lucyna Swiatkowska-Byczynska, Lech Kucharski, Marcin Gruchala, Piotr Minc, Maciej Olszewski, Grzegorz Kania, Malgorzata Krzciuk, Zbigniew Lajkowski, Bozenna Ostrowska-Pomian, Jerzy Lewczuk, Elzbieta Zinka, Agnieszka Karczmarczyk, Malgorzata Chmielnicka-Pruszczynska, Iwona Wozniak-Skowerska, Grzegorz Opolski, Marek Bronisz, Marcin Ogorek, Grazyna Glanowska, Piotr Ruszkowski, Grzegorz Skonieczny, Ryszard Sciborski, Boguslaw Okopien, Piotr Kukla, Krzysztof Galbas, Krzysztof Cymerman, Jaroslaw Jurowiecki, Pawel Miekus, Waldemar Myszka, Stanislaw Mazur, Roman Lysek, Jacek Baszak, Teresa Rusicka-Piekarz, Grzegorz Raczak, Ewa Domanska, Jadwiga Nessler and Jozef Lesnik. Russia: Vera Eltishcheva, Roman Libis, Gadel Kamalov, Dmitry Belenky, Liudmila Egorova, Alexander Khokhlov, Eduard Yakupov, Dmitry Zateyshchikov, Olga Barbarash, Olga Miller, Evgeniy Mazur, Konstantin Zrazhevskiy, Tatyana Novikova, Yulia Moiseeva, Elena Polkanova, Konstantin Sobolev, Maria Rossovskaya, Yulia Shapovalova, Alla Kolesnikova, Konstantin Nikolaev, Oksana Zemlianskaia, Anna Zateyshchikova, Victor Kostenko, Sergey Popov, Maria Poltavskaya, Anton Edin, Elena Aleksandrova, Oksana Drapkina, Alexander Vishnevsky, Oleg Nagibovich, Petr Chizhov, Svetlana Rachkova, Mikhail Sergeev, Borys Kurylo and Alexey Ushakov. Spain: Xavier Vinolas, Pere Alvarez Garcia, Maria Fernanda Lopez Fernandez, Luis Tercedor Sanchez, Salvador Tranche Iparraguirre, Pere Toran Monserrat, Emilio Marquez Contreras, Jordi Isart Rafecas, Juan Motero Carrasco, Pablo Garcia Pavia, Casimiro Gomez Pajuelo, Luis Miguel Rincon Diaz, Luis Fernando Iglesias Alonso, Angel Grande Ruiz, Jordi Merce Klein, Jose Ramon Gonzalez Juanatey, Ines Monte Collado, Herminia Palacin Piquero, Carles Brotons Cuixart, Esther Fernandez Escobar, Joan Bayo i Llibre, Cecilia Corros Vicente, Manuel Vida Gutierrez, Francisco Epelde Gonzalo, Carlos Alexandre Almeida Fernandez, Encarnacion Martinez Navarro, Jordi Isart Rafecas, Juan Jose Montero Alia, Maria Barreda Gonzalez, Maria Angels Moleiro Oliva, Jose Iglesias Sanmartin, Mercedes Jimenez Gonzalez, Maria del Mar Rodriguez Alvarez, Juan Herreros Melenchon, Tomas Ripoll Vera, Manuel Jimenez Navarro, Maria Vazquez Caamano, Maria Fe Arcocha Torres, Gonzalo Marcos Gomez, Andres Iniguez Romo and Miguel Angel Prieto Diaz. 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UK: Will Murdoch, Naresh Chauhan, Daryl Goodwin, Louise Lumley, Ramila Patel, Philip Saunders, Bennett Wong, Alex Cameron, Philip Saunders, Niranjan Patel, P Jhittay, Andrew Ross, M S Kainth, Karim Ladha, Kevin Douglas, Gill Pickavance, Joanna McDonnell, Laura Handscombe, Trevor Gooding, Helga Wagner, Cumberlidge, Colin Bradshaw, Catherine Bromham, Kevin Jones, Shoeb Suryani, Richard Coates, Bhupinder Sarai, W Willcock, S Sircar, John Cairns, A Gilliand, Roman Bilas, E Strieder, Peter Hutchinson, Anne Wakeman, Michael Stokes, Graham Kirby, Bhaskhar Vishwanathan, Nigel Bird, Paul Evans, M Clark, John Bisatt, Jennifer Litchfield, E Fisher, Tim Fooks, Richard Kelsall, Neil Paul, Elizabeth Alborough, Michael Aziz, C Ramesh, Pete Wilson, Simon Franklin, Sue Fairhead, Julian Thompson, Hasan Chowan, Gary Taylor, Dawn Tragen, Matt Parfitt, Claire Seamark, Carolyn Paul, Mark Richardson, Angus Jefferies, Helen Sharp, Hywel Jones, Claire Giles, Matthew Bramley, Philip Williams, Jehad Aldegather, Simon Wetherell, William Lumb, Phil Evans, Frances Scouller, Neil Macey, Stephen Rogers, Yvette Stipp, Richard West, Philip Pinney, Paul Wadeson, John Matthews, Preeti Pandya, Andrew Gallagher, T Railton, Emyr Davies, Jonathan McClure, Marc Jacobs, Claire Hutton, R Thompson, Bijoy Sinha, Keith Butter, Susan Barrow, Helen Little, David Russell, Ulka Choudhary, Ikram Haq, Paul Ainsworth, Claire Jones, Phil Weeks, Jane Eden, Lisa Gibbons, Janet Glencross, Alison MacLeod, K Poland, Conor Mulolland, A Warke, Paul Conn, D Burns, R Smith, R Kamath, Jonathan Webster, Ian Hodgins, Stephen Vercoe, Paul Roome, Hilary Pinnock, Jayesh Patel, Amar Ali, Nigel Hart, Richard Davies, Nigel De-Sousa, Catherine Neden, Mark Danielsen, Purnima Sharma, Sophia Galloway, Charlotte Hawkins, Raife Oliver, Martin Aylward, Mira Pattni, Gordon Irvine, Shahid Ahmad, Catherine Rothwell, Fiaz Choudhary, Sabrina Khalaque, Stephanie Short, Sharon Peters, Warwick Coulson, Neil Roberts, Amy Butler, Steven Coates, Ben Ward, Daniel Jackson, Steve Walton, Diane Shepherd, Toh Wong, Mark Boon, Melanie Deacon, David Cornelius, Sarah Davies, Ben Frankel, Nick Hargreaves, Henry Choi, Jon Sumner, Tim Myhill, Salah Estifanos, Diane Geatch, Justin Wilkinson, Richard Veale, Karen Forshaw, Rob Hirst, Kashif Zaman, Catherine Liley, Rebecca Wastling, Paul McEleny, Andre Beattie, Philip Cooke, Mike Wong, Mark Pugsley, Chaminda Dooldeniya, Greg Rogers, James Bennett, Polly Jacobs, Rajesh Muvva, Matthew Adam, Robin Fox, Nicolas Thomas,

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Ethics approval This study involves human participants and was approved by Independent ethics committee and hospital-based institutional review board approvals were obtained.The GARFIELD-AF registry is conducted in accordance with the principles of the Declaration of Helsinki, local regulatory requirements and International Conference on Harmonization–Good Pharmacoepidemiological and Clinical Practice guidelines. Written informed consent was obtained from all study participants. There was no public or patient involvement in the design or execution of the GARFIELD-AF study design. Investigators from representative investigator sites in each participating country were involved in data collection. Confidentiality and anonymity were maintained through assigned unique identifiers. Independent ethics committee and hospital-based institutional review board approvals were obtained. A full list of ethics committees are provided in the supplemental material. Participants gave informed consent to participate in the study before taking part.

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ORCID iD

Christian Fielder Camm http://orcid.org/0000-0003-2122-4225

REFERENCES

1 Benjamin EJ, Levy D, Vaziri SM, *et al*. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham heart study. *JAMA* 1994;271:840–4.
2 Camm CF, Lacey B, Massa MS. Independent effects of adiposity measures on risk of atrial fibrillation in men and women: a study of 0.5 million individuals. *Int J Epidemiol* 2021.
3 Boriani G, Ruff CT, Kuder JF, *et al*. Relationship between body mass index and outcomes in patients with atrial fibrillation treated with edoxaban or warfarin in the engage AF-TIMI 48 trial. *Eur Heart J* 2019;40:1541–50.
4 Badheka AO, Rathod A, Kizilbash MA, *et al*. Influence of obesity on outcomes in atrial fibrillation: yet another obesity paradox. *Am J Med* 2010;123:646–51.
5 Sandhu RK, Ezekowitz JA, Hijazi Z, *et al*. Obesity paradox on outcome in atrial fibrillation maintained even considering the prognostic influence of biomarkers: insights from the ARISTOTLE trial. *Open Heart* 2018;5:e000908.
6 Overvad TF, Rasmussen LH, Skjøth F, *et al*. Body mass index and adverse events in patients with incident atrial fibrillation. *Am J Med* 2013;126:640.e9–640.e17.
7 Chugh SS, Havmoeller R, Narayanan K, *et al*. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. *Circulation* 2014;129:837–47.
8 Wells JCK. Sexual dimorphism of body composition. *Best Pract Res Clin Endocrinol Metab* 2007;21:415–30.
9 Schorr M, Dichtel LE, Gerweck AV, *et al*. Sex differences in body composition and association with cardiometabolic risk. *Biol Sex Differ* 2018;9:28.

10 Hindricks G, Potpara T, Dagres N. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European association of Cardio-Thoracic surgery (EACTS). *Eur Heart J* 2020.
11 Moll S, Crona DJ, Martin K. Direct oral anticoagulants in extremely obese patients: OK to use? *Res Pract Thromb Haemost* 2019;3:152–5.
12 Kakkar AK, Mueller I, Bassand J-P, *et al*. International longitudinal registry of patients with atrial fibrillation at risk of stroke: global anticoagulant registry in the field (Garfield). *Am Heart J* 2012;163:13–19.
13 Fox KAA, Gersh BJ, Traore S, *et al*. Evolving quality standards for large-scale registries: the GARFIELD-AF experience. *Eur Heart J Qual Care Clin Outcomes* 2017;3:114–22.
14 Obesity: preventing and managing the global epidemic. Report of a who consultation. *World Health Organ Tech Rep Ser* 2000;894:1–253.
15 Mak RH IA, Kovesdy CP, Raj DS. Kalantar-Zadeh wasting in chronic kidney disease. *J Cachexia Sarcopenia Muscle* 2011;2:9–25.
16 Friedman AN, Kaplan LM, le Roux CW, *et al*. Management of obesity in adults with CKD. *JASN* 2021;32:777–90.
17 Pandey A, Gersh BJ, McGuire DK, *et al*. Association of Body Mass Index With Care and Outcomes in Patients With Atrial Fibrillation: Results From the ORBIT-AF Registry. *JACC Clin Electrophysiol* 2016;2:355–63.
18 Weitz JI, Farjat AE, Ageno W, *et al*. Influence of body mass index on clinical outcomes in venous thromboembolism: insights from GARFIELD-VTE. *J Thromb Haemost* 2021;19:3031–43.
19 Sun Y-Q, Burgess S, Staley JR, *et al*. Body mass index and all cause mortality in HUNT and UK Biobank studies: linear and non-linear Mendelian randomisation analyses. *BMJ* 2019;364:l1042.
20 Schnabel RB, Rienstra M, Sullivan LM, *et al*. Risk assessment for incident heart failure in individuals with atrial fibrillation. *Eur J Heart Fail* 2013;15:843–9.
21 Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiologic studies. *Epidemiology* 2009;20:488–95.
22 Gelber RP, Gaziano JM, Manson JE, *et al*. A prospective study of body mass index and the risk of developing hypertension in men. *Am J Hypertens* 2007;20:370–7.
23 Schienkiewitz A, Schulze MB, Hoffmann K, *et al*. Body mass index history and risk of type 2 diabetes: results from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study. *Am J Clin Nutr* 2006;84:427–33.
24 Flint AJ, Rexrode KM, Hu FB, *et al*. Body mass index, waist circumference, and risk of coronary heart disease: a prospective study among men and women. *Obes Res Clin Pract* 2010;4:e171–81.
25 Boehme AK, Esenwa C, Elkind MS. Genetics, and prevention. *Circ Res* 2017;120:472–95.
26 Nalliah CJ, Sanders P, Kottkamp H, *et al*. The role of obesity in atrial fibrillation. *Eur Heart J* 2016;37:1565–72.
27 Njølstad I, Arnesen E, Lund-Larsen PG. Body height, cardiovascular risk factors, and risk of stroke in middle-aged men and women. A 14-year follow-up of the Finnmark study. *Circulation* 1996;94:2877–82.
28 Emerging Risk Factors Collaboration. Adult height and the risk of cause-specific death and vascular morbidity in 1 million people: individual participant meta-analysis. *Int J Epidemiol* 2012;41:1419–33.
29 Moon J, Lee H-J, Kim YJ, *et al*. Short stature and ischemic stroke in nonvalvular atrial fibrillation: new insight into the old observation. *Int J Cardiol* 2014;174:541–4.
30 Abed HS, Wittert GA, Leong DP, *et al*. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial. *JAMA* 2013;310:2050–60.
31 Piran S, Traquair H, Chan N, *et al*. Peak plasma concentration of direct oral anticoagulants in obese patients weighing over 120 kilograms: a retrospective study. *Res Pract Thromb Haemost* 2018;2:684–8.
32 Proietti M, Guiducci E, Cheli P, *et al*. Is there an obesity paradox for outcomes in atrial fibrillation? A systematic review and meta-analysis of non-vitamin K antagonist oral anticoagulant trials. *Stroke* 2017;48:857–66.

The association of body mass index with outcomes in patients with newly diagnosed atrial fibrillation – GARFIELD-AF

C. Fielder Camm[1], BM BCh, Saverio Virdone[2], MSc, Shinya Goto[3], MD, Jean-Pierre Bassand[2,4], MD, Martin van Eickels[5], MD, Sylvia Haas[6], MD, PhD, Bernard J. Gersh[7], MB, Karen S. Pieper[2], PhD, Keith A.A. Fox[8], MBChB, Frank Misselwitz[9], MD, PhD, Alexander G.G. Turpie[10], MD, Samuel Z. Goldhaber[11], MD, Freek W.A. Verheugt[12], MD, PhD, A. John Camm[13], MD, Gloria Kayani[2], BSc, Elizaveta Panchenko[14], PhD, Seil Oh[15], MD, Hector Lucas Luciardi[16], MD, Jitendra Pal Singh Sawhney[17], MD, Stuart Connolly[18], MD, Pantep Angchaisuksiri[19], MD, Hugo ten Cate[20], MD, PhD, John Eikelboom[21], MBBS, Ajay K. Kakkar, PhD[2,22] on behalf of the GARFIELD-AF investigators*

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Supplemental Material

Supplementary Table S1. Event rates (per 100 person-years) through 2-years of follow-up by BMI category.

Outcome	Events	Event Rate (95% CI)
All-cause mortality		
Underweight	117	9.62 (8.03-11.53)
Normal weight	1052	4.38 (4.13-4.66)
Overweight	927	3.28 (3.07-3.49)
Obese	460	3.21 (2.93-3.52)
Extremely Obese	249	3.22 (2.84-3.65)
Non-haemorrhagic stroke/SE		
Underweight	12	0.99 (0.56-1.75)
Normal weight	267	1.12 (1.00-1.27)
Overweight	295	1.05 (0.94-1.18)
Obese	130	0.91 (0.77-1.09)
Extremely Obese	66	0.86 (0.68-1.09)
Major bleeding		
Underweight	23	1.92 (1.28-2.89)
Normal weight	241	1.01 (0.89-1.15)
Overweight	258	0.92 (0.81-1.04)
Obese	137	0.97 (0.82-1.14)
Extremely Obese	71	0.93 (0.73-1.17)
New/worsening heart failure		
Underweight	13	1.08 (0.63-1.86)
Normal weight	142	0.60 (0.51-0.70)
Overweight	193	0.69 (0.60-0.79)
Obese	143	1.01 (0.86-1.19)
Extremely Obese	98	1.29 (1.06-1.57)

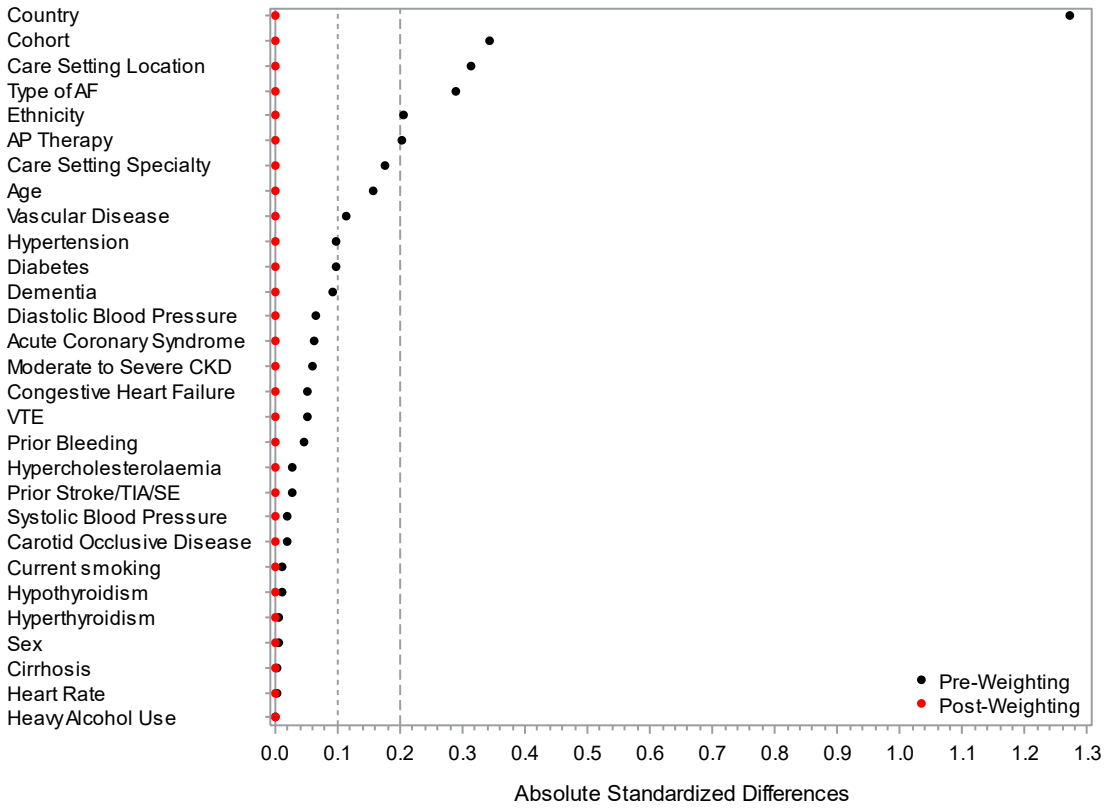
Supplementary Table S2. BMI effects (HR and 95% CI per 5kg/m^2 increase) on selected outcomes using Cox models with different sets of adjustments.

Outcomes	**Model 1[1]**		**Model 2[2]**	
All-cause mortality	**<30 kg/m^2**	**≥30 kg/m^2**	**<30 kg/m^2**	**≥30 kg/m^2**
	1.32 (1.25-1.40)	1.16 (1.09-1.23)	1.39 (1.31-1.47)	1.04 (0.98-1.12)
Non-haemorrhagic stroke/SE	**Linear**		**Linear**	
	1.01 (0.94-1.07)		1.00 (0.93-1.07)	
Major bleeding	**<30 kg/m^2**	**≥30 kg/m^2**	**<30 kg/m^2**	**≥30 kg/m^2**
	1.12 (1.01-1.26)	1.10 (0.97-1.24)	1.17 (1.04-1.31)	1.07 (0.95-1.22)
New/worsening HR	**<25 kg/m^2**	**≥25 kg/m^2**	**<25 kg/m^2**	**≥25 kg/m^2**
	1.12 (0.96-1.32)	1.23 (1.14-1.33)	1.15 (0.99-1.36)	1.18 (1.09-1.29)

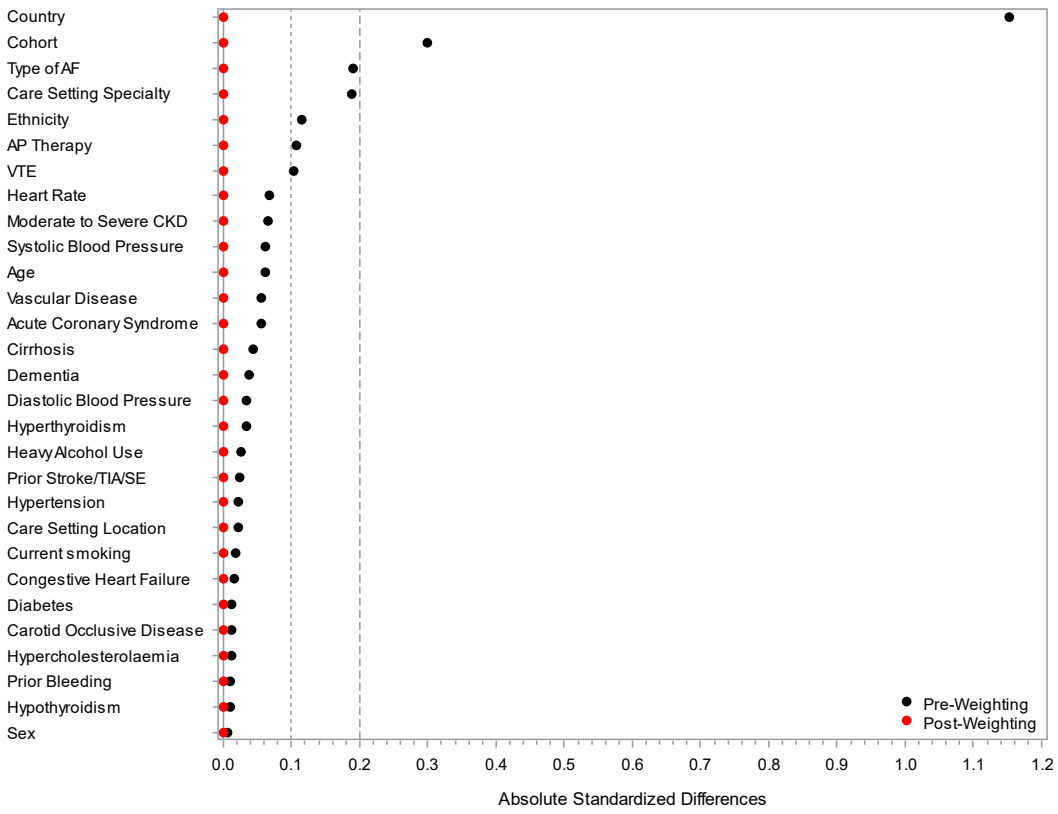
[1]Adjustments: age, sex, ethnicity, smoking status, alcohol use, and moderate to severe CKD;

[2]Adjustments: age, sex, ethnicity, smoking status, alcohol use, moderate to severe CKD, hypertension, heart failure, diabetes, vascular disease, prior stroke/TIA/SE, history of bleeding, baseline anticoagulation

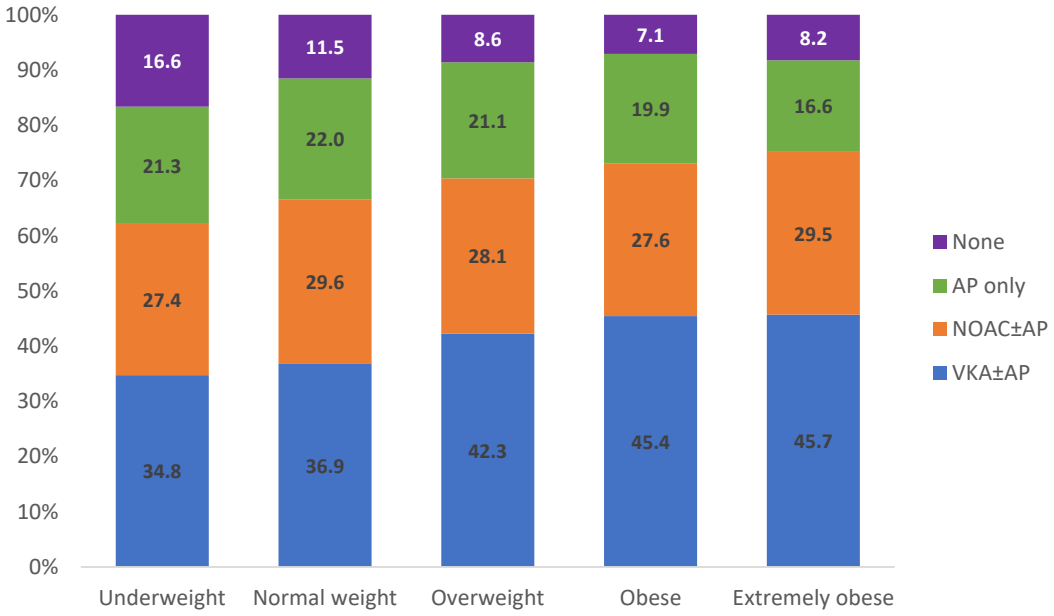
Supplementary Figure S1a. Absolute standardised differences for NOAC vs VKA comparison before and after propensity score weighting among patients with normal weight or overweight (BMI 18.5-29.9 kg/m^2)



Supplementary Figure S1b. Absolute standardised differences for NOAC vs VKA comparison before and after propensity score weighting among patients obese or extremely obese (BMI ≥30 kg/m^2)

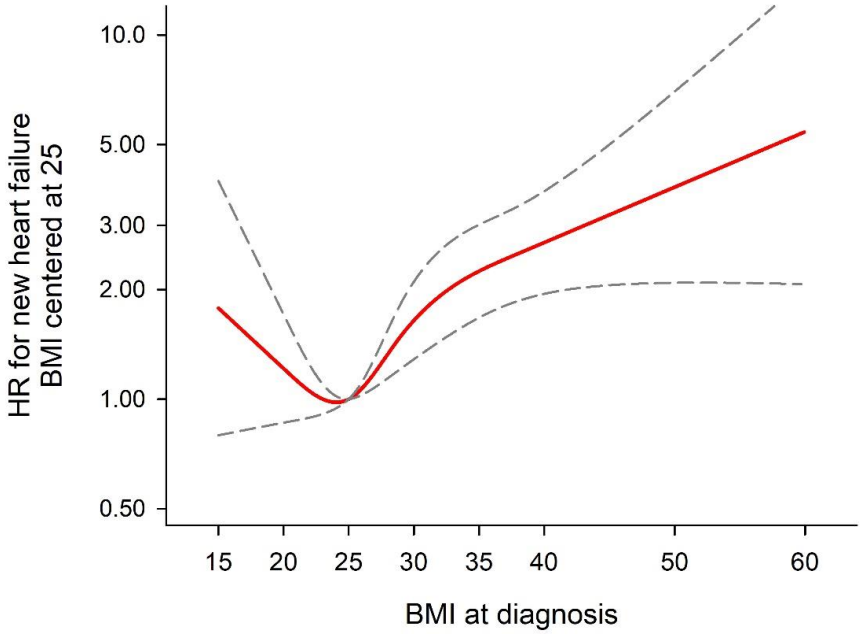


Supplementary Figure S2. Baseline treatment distribution[1] by BMI category among patients with CHA_2DS_2VASc score of ≥2.



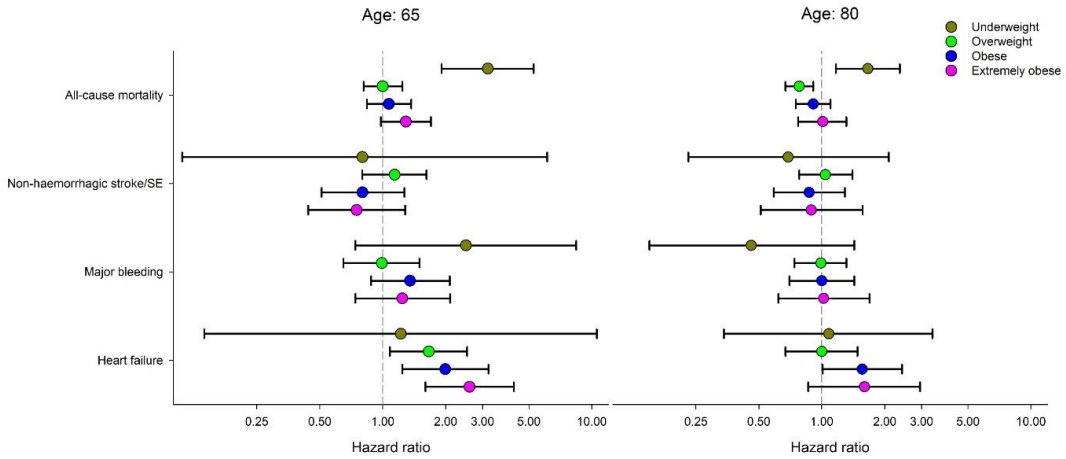
[1]A total of 518 patients were excluded from this analysis because of missing baseline treatment information

Supplementary Figure S3. Adjusted[1] associations through 2-years follow-up between BMI and new heart failure based on a restricted cubic spline model.



[1]Adjusted by age, sex, ethnicity, smoking status, alcohol use, and moderate to severe CKD.

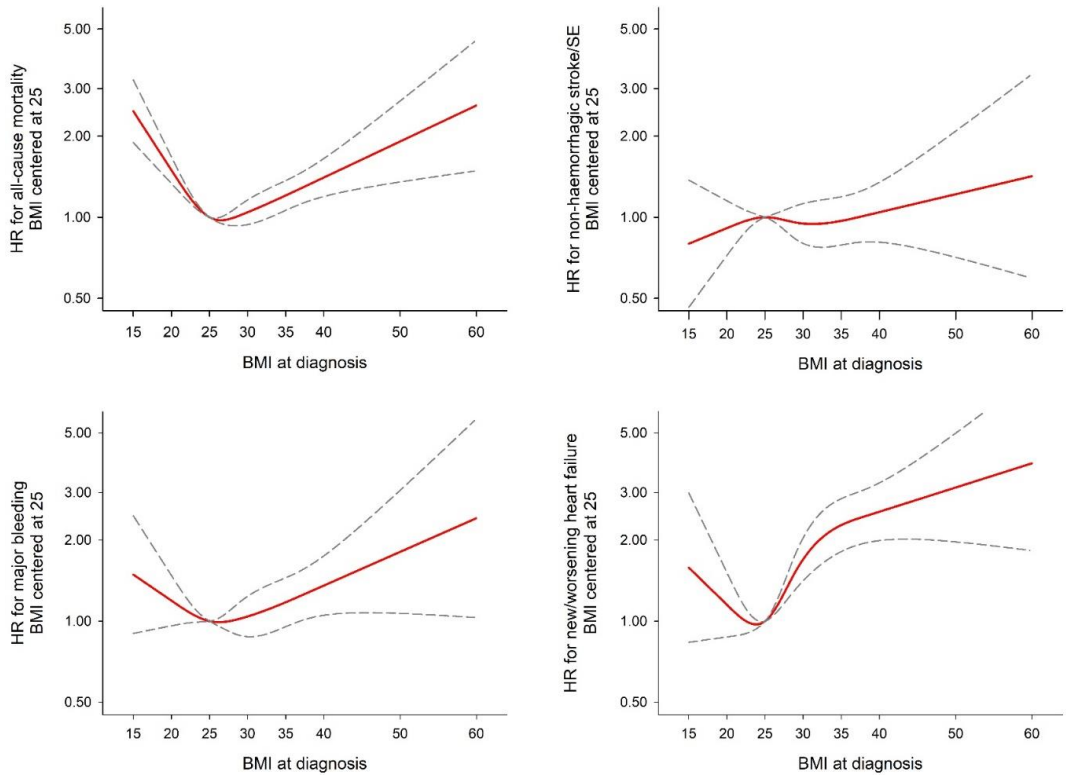
Supplementary Figure S4. Adjusted[1] hazard ratios through 2-years follow-up by BMI category for ages 65 and 80. The reference category is normal weight



[1]Adjusted by age, sex, ethnicity, smoking status, alcohol use, and moderate to severe CKD. Age included using restricted cubic spline with 4 knots.

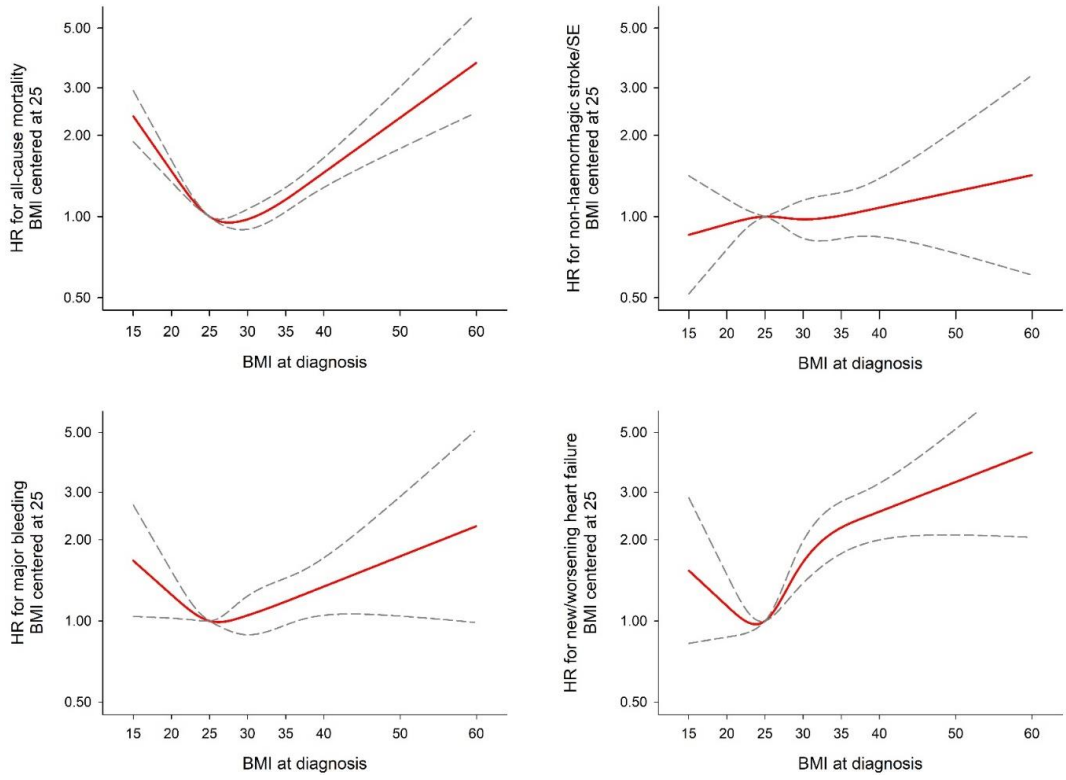
Supplementary Figure S5. Adjusted[1] associations through 2-years follow-up between BMI and selected endpoints based on a restricted cubic spline model in patients with at least 6 months of follow-up (n=39,081).

[1]Adjusted by age, sex, ethnicity, smoking status, alcohol use, and moderate to severe CKD.



Supplementary Figure S6. Adjusted[1] associations through 2-years follow-up between BMI and selected endpoints based on a restricted cubic spline model

[1]Adjusted by age, sex, ethnicity, baseline treatment, smoking status, alcohol use, and moderate-to-severe CKD.



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GARFIELD-AF National Investigators:

China

Dayi Hu, Kangning Chen, Yusheng Zhao, Huaiqin Zhang, Jiyan Chen, Shiping Cao, Daowen Wang, Yuejin Yang, Weihua Li, Hui Li, Yuehui Yin, Guizhou Tao, Ping Yang, Yingmin Chen, Shenghu He, Yong Wang, Guosheng Fu, Xin Li, Tongguo Wu, Xiaoshu Cheng, Xiaowei Yan, Ruiping Zhao, Moshui Chen, Longgen Xiong, Ping Chen, Yang Jiao, Ying Guo, Li Xue, Zhiming Yang.

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Praveen Jadhavm, Raghava Sarma, Govind Kulkarni, Prakash Chandwani, Rasesh Atulbhai Pothiwala, Mohanan Padinhare Purayil, Kamaldeep Chawla, Veerappa Annasaheb Kothiwale, Bagirath Raghuraman, Vinod Madan Vijan, Jitendra Sawhney, Ganapathi Bantwal, Aziz Khan, Ramdhan Meena, Manojkumar Chopada, Sunitha Abraham, Vikas Bisne, Govindan Vijayaraghavan, Debabrata Roy, Rajashekhar Durgaprasad, A.G. Ravi Shankar, Sunil Kumar, Dinesh Jain, Kartikeya Bhargava, Vinay Kumar, Udigala Madappa Nagamalesh, Rajeeve Kumar Rajput.

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Hiroshi Kubo, Mizuho Imamaki, Masahiro Akiyama, Takashi Ueda, Hironori Odakura, Masahiko Inagaki, Yoshiki Katsube, Atsuyuki Nakata, Shinobu Tomimoto, Mitsuhiro Shibuya, Masayuki Nakano, Kenichiro Ito, Masahiro Matsuta, Motoyuki Ishiguro, Taro Minagawa, Masamichi Wada, Hiroaki Mukawa, Masato Mizuguchi, Fumio Okuda, Teruaki Kimura, Kuniaki Taga, Masaaki Techigawara, Morio Igarashi, Hiroshi Watanabe, Toshihiko Seo, Shinya Hiramitsu, Hiroaki Hosokawa, Mitsumoto Hoshiai, Michitaka Hibino, Koichi Miyagawa, Hideki Horie, Nobuyoshi Sugishita, Yukio Shiga, Akira Soma, Kazuo Neya, Tetsuro Yoshida, Kunio Akahane, Sen Adachi, Chiei Takanaka, Takashi Ueda, Saori Matsui, Hirofumi Kanda, Masanori Kaneko, Shiro Nagasaka, Atsushi Taguchi, Shuta Toru, Kazuyuki Saito, Akiko Miyashita, Hiroki Sasaguri, Jin Nariyama, Taketo Hatsuno, Takash Iwase, Kazuki Sato, Kazuya Kawai, Tomobumi Kotani, Tsuyoshi Tsuji, Hirosumi Sakai, Kiyoshi Nishino, Kenichi Ikeda, Kazuo Maeda, Tomohiro Shinozuka, Takeshi Inoue, Koichi Kawakami, Hiromichi Kitazumi, Tsutomu Takagi, Mamoru Hamaoka, Jisho Kojima, Akitoshi Sasaki, Yoshihiro Tsuchiya, Tetsuo Betsuyaku, Koji Higuchi, Masaaki Honda, Koichi Hasegawa, Takao Baba, Kazuaki Mineoi, Toshihiko Koeda, Kunihiko Hirasawa, Toshihide Kumazaki, Akira Nakagomi, Eiji Otaki, Takashi Shindo, Hiroyoshi Hirayama, Chikako Sugimoto, Takashi Yamagishi, Ichiro Mizuguchi, Kazunori Sezaki, Isamu Niwa, Ken Takenaka, Osamu Iiji, Koichi Taya, Hitoshi Kitazawa, samu Ueda, Hirokazu Kakuda, Takuya Ono, Seizo Oriso, Junya Kamata, Toshihiko Nanke, Itaru Maeda, Yoshifusa Matsuura, Hiroki Teragawa, Yasuyuki Maruyama, Kazuo Takei, Hajime Horie, Tetsutaro Kito, Hiroshi Asano, Koji Matsushita, Masaichi Nakamura, Takashi Washizuka, Tomoki Yoshida, Masato Sawano, Shinichi Arima, Hidekazu Arai, Hisanori Shinohara, Hiroyuki Takai, Nobufusa Furukawa, Akira Ota, Kentaro Yamamoto, Kenji Aoki, Taku Yamamoto, Takeaki Kasai, Shunji Suzuki, Shu Suzuki, Nitaro Shibata, Masayuki Watanabe, Yosuke Nishihata, Toru Arino, Masaki Okuyama, Tetsushi Wakiyama, Tomoko Kato, Yasuo Sasagawa, Takeshi Tana, Yoshihito Hayashi, Shinichi Hirota, Yukihiko Abe, Yoshihiro Saito, Hirohide Uchiyama, Hiroshi Takeda, Hiroshi Ono, Shuichi Tohyo, Naoto Hanazono, Seiichi Miyajima, Hisashi Shimono, Takuma Aoyama, Yasunobu Shozawa, Yawara Niijima, Osamu Murai, Osamu Murai, Hideko Inaba, Katsumasa Nomura, Masatsugu Nozoe, Kazuo Suzuki, Toshiyuki Furukawa, Toshihiko Shiraiwa, Nobuhisa Ito, Shunichi Nagai, Kiyoharu Sato, Shiro Nakahara, Yujin Shimoyama, Naoko Ohara, Teruhiko Kozuka, Hideaki Okita, Masato Endo, Tsutomu Goto, Makoto Hirose, Emiko Nagata, Noriyuki Nakanishi, Toshizumi Mori, Shuichi Seki, Katsuhiro Okamoto, Osamu Moriai, Yoko Emura, Tsuyoshi Fukuda, Haruhiko Date, Shuichi Kawakami, Sho Nagai, Yuya Ueyama, Tetsuro Fudo, Mitsuru Imaizumi, Takuo Ogawa, Shunsuke Take, Hideo Ikeda, Hiroaki Nishioka, Norihiko Sakamoto, Kiyomitsu Ikeoka, Nobuo Wakaki, Masatake Abe, Junji Doiuchi, Tetsuya Kira, Masato Tada, Ken Tsuzaki, Naoya Miura, Yasuaki Fujisawa, Wataru Furumoto, Susumu Suzuki, Akinori

Fujisawa, Ryosai Nakamura, Hiroyasu Komatsu, Rei Fujiki, Shuichi Kawano, Keijiro Nishizawa, Yoji Kato, Junya Azuma, Kiyoshi Yasui,Toshio Amano, Yasuhiro Sekine, Tatsuo Honzawa, Yuichiro Koshibu, Yasuhide Sakamoto, Yukihiro Seta, Shingo Miyaguchi, Kojuro Morishita, Yasuko Samejima, Toyoshi Sasaki, Fumiko Iseki, Toshiyuki Kobayashi, Hiroshi Kano, Jaeyoung Kim, Hiroshi Yamaguchi, Yoichi Takagi, Yoko Onuki Pearce, Yasuyuki Suzuki, Takayuki Fukui, Toru Nakayama, Hideaki Kanai, Yoshiyuki Kawano, Tetsuji Ino, Hironori Miyoshi, Yasufumi Miyamoto, Masahito Shigekiyo, Shimato Ono, Yoshiyuki Kawano, Yutaka Okamoto, Satoshi Ubukata, Kojiro Kodera, Tatsuo Oriuchi, Naoki Matsumoto, Koichi Inagaki, Atsushi Iseki, Tomohiro Yoshida, Toshihiro Goda, Tsukasa Katsuki, Atsushi Sato, Etsuo Mori, Toshio Tsubokura, Hiroshi Shudo, Shunichi Fujimoto, Tomohiro Katsuya, Yoshiyuki Furukawa, Hiroshi Hosokawa, Jun Narumi, Kiichiro Yamamoto, Masaki Owari, Takuya Inakura, Takafumi Anno, Kazuyuki Shirakawa.

Singapore

Chi Keong Ching, Toon Wei Lim, David Foo, Kelvin Wong, Tan Yuyang.

South Korea

Seil Oh, Hui Nam Park, Woo-Shik Kim, HyeYoung Lee, Sung-Won Jang, Dae Hyeok Kim, Jun Kim, DongRyeol Ryu, Jaemin Shim, Dae-Kyeong Kim, Dong Ju Choi, Yong Seog Oh, Myeong-Chan Cho, Hack-Lyoung Kim, Hui-Kyung Jeon, Dong-Gu Shin, Sang Weon Park, Hoon Ki Park, Sang-Jin Han, Jung Hoon Sung, Hyung-Wook Park, Gi-Byoung Nam, Young Keun On, Hong Euy Lim, JaeJin Kwak, Tae-Joon Cha, Taek Jong Hong, Seong Hoon Park, Jung Han Yoon, Nam-Ho Kim, Kee-Sik Kim, Byung Chun Jung, Gyo-Seung Hwang, Chong-Jin Kim.

Thailand

Sakda Rungaramsin, Peerapat Katekangplu, Porames Khunrong, Thanita Bunyapipat, Wanwarang Wongcharoen, Pinij Kaewsuwanna, Khanchai Siriwattana, Waraporn Tiyanon, Supalerk Pattanaprichakul, Khanchit Likittanasombat, Doungrat Cholsaringkarl, Warangkana Boonyapisit, Sirichai Cheewatanakornkul, Songkwan Silaruks, Pisit Hutayanon, Seksan Chawanadelert, Pairoj Chattranukulchai, Boonsert Chatlaong, Yingsak Santanakorn, Khompiya Kanokphatcharakun, Piya Mongkolwongroj, Sasivimon Jai-Aue, Ongkarn Komson.

Turkey

Armagan Altun, Ali Aydinlar, Ramazan Topsakal, Zeki Ongen, Sadik Acikel, Durmus Yildiray Sahin, Ozcan Yilmaz, Mehmet Birhan Yilmaz, Hasan Pekdemir, Mesut Demir, Murat Sucu, Levent Sahiner, Ali Oto, Murat Ersanli, Ertugrul Okuyan, Dursun Aras.

Argentina

Florencia Rolandi, Adrian Cesar Ingaramo, Gustavo Alberto Sambadaro, Vanina Fernandez Caputi, Hector Luciardi, Sofia Graciela Berman, Pablo Dragotto, Andres Javier Kleiban, Nestor Centurion, Rodolfo Andres Ahuad Guerrero, Leonel Adalberto Di Paola, Ricardo Dario Dran, Javier Egido, Matias Jose Fosco, Victor Alfredo Sinisi, Luis Rodolfo Cartasegna, Oscar Gomez Vilamajo, Jose Luis Ramos, Sonia Sassone, Gerardo Zapata, Diego Conde, Guillermo Giacomi, Alberto Alfredo Fernandez, Mario Alberto Berli, Fabian Ferroni.

Brazil

Dário Celestino Sobral Filho, Jefferson Jaber, Luciana Vidal Armaganijan, Costantino Roberto Frack Costantini, André Steffens, Weimar Kunz Sebba Barroso de Souzaem, João David de Souza Neto, José Márcio Ribeiro, Marcelo Silveira Teixeira, Paulo Rossi, Leonardo Pires, Daniel Moreira, José Carlos Moura Jorge, Adalberto Menezes Lorga Filho, Luiz Bodanese, Marcelo Westerlund Montera, Carlos Henrique Del Carlo, Jamil Abdalla Saad, Fernando Augusto Alves da Costa, Renato Lopes, Gilson Roberto de Araújo, Euler Roberto Manenti, Jose Francisco Kerr Saraiva, João Carlos Ferreira Braga, Alexandre Negri, Carlos Moncada, Dalton Precoma, Fernando Roquette, Gilmar Reis, Roberto Álvaro Ramos Filho,: Estêvão Lanna Figueiredo, Roberto Vieira Botelho, Cláudio Munhoz da Fontoura Tavares, Helius Carlos Finimundi, Adriano Kochi, César Cássio Broilo França, Fábio Alban, Guido Bernardo Aranha Rosito, João Batista de Moura Xavier Moraes Junior, Rogério Tadeu Tumelero, Lilia Maia,: Roberto Simões de Almeida, Ney Carter do Carmo Borges, Luís Gustavo Gomes Ferreira.

Chile

Ramón Corbalán, Benjamin Aleck Joseh Stockins Fernandez, Humberto Montecinos, Fernando Lanas, Martín Larico Gómez, Carlos Astudillo, Carlos Conejeros, Patricio Marin Cuevas, Alejandro Forero, Claudio Bugueño Gutiérrez, Juan Aguilar, Sergio Potthoff Cardenas, German Eggers, Cesar Houzvic, Carlos Rey, Germán Arriagada, Gustavo Charme Vilches.

Mexico

Carlos Jerjes Sanchez Diaz, Jesus Jaime Illescas Diaz, Raul Leal Cantu, Maria Guadalupe Ramos Zavala, Ricardo Cabrera Jardines, Nilda Espinola Zavaleta, Enrique Lopez Rosas, Guillermo Antonio Llamas Esperón, Gerardo Pozas, Ernesto Cardona Muñoz, Norberto Matadamas Hernandez, Adolfo Leyva Rendon, Norberto Garcia Hernandez, Manuel de los Rios Ibarra, Luis Ramon Virgen Carrillo,

David Lopez Villezca, Carlos Hernandez Herrera, Juan Jose Lopez Prieto, Rodolfo Gaona Rodriguez, Efrain Villeda Espinosa, David Flores Martinez, Jose Velasco Barcena, Omar Fierro Fierro, Ignacio Rodriguez Briones, Jose Luis Leiva Pons, Humberto Alvarez Lopez, Rafael Olvera Ruiz, Carlos Gerardo Cantu Brito, Eduardo Julian Jose Roberto Chuquiure Valenzuela, Roxana Reyes Sanchez, Alberto Esteban Bazzoni Ruiz, Oscar Martin Lopez Ruiz, Roberto Arriaga Nava, Jesus David Morales Cerda, Pedro Fajardo Campos, Mario Benavides Gonzalez.

Austria

Marianne Brodmann, Kurt Lenz, Claus Hagn, Johannes Foechterle, Heinz Drexel, Kurt Huber, Andrea Podczeck-Schweighofer, Michael Winkler, Bruno Schneeweiss, Alfons Gegenhuber, Wilfried Lang, Sabine Eichinger-Hasenauer, Peter Kaserer, Josef Sykora, Heribert Rasch, Bernhard Strohmer.

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Luc Capiau, Geert Vervoort, Bart Wollaert, Frank Cools, Geert Hollanders, Jan Vercammen, Dirk Faes, Yohan Balthazar, Marc Delforge, Olivier Xhaet, Harry Striekwold, John Thoeng, Kurt Hermans, Georges Mairesse, Wim Anné, Ivan Blankoff, Michel Beutels, Stefan Verstraete, Peter Vandergoten, Philippe Purnode, Pascal Godart, Tim Boussy, Philippe Desfontaines, Alex Heyse, Joeri Voet, Axel De Wolf.

Czech Republic

Eva Zidkova, Petr Jansky, Rudolf Spacek, Vilma Machova, Ondrej Ludka, Josef Olsr, Lubos Kotik, Blazej Racz, Richard Ferkl, Jan Hubac, Ilja Kotik, Zdenek Monhart, Hana Burianova, Ondrej Jerabek, Jana Pisova, Iveta Petrova, Vratislav Dedek, Michaela Honkova, Petr Podrazil, Petr Reichert, Jindrich Spinar, Miroslav Novak, Vaclav Durdil, Katarina Plocova, Jiri Lastuvka.

Denmark

Jørn Nielsen, Steen Husted, Helena Dominguez, Ulrik Hintze, Søren Rasmussen, Næstved Sygehus, Arne Bremmelgaard, John Markenvard, Jan Børger, Jorgen Solgaard, Ebbe Eriksen, Thomas Løkkegaard, Michael Bruun, Jacob Mertz, Morten Schou, Helena Dominguez, Michael Olsen.

Finland

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Germany

Sebastien Schellong, Harald Darius, Georg Koeniger, Andreas Kopf, Uwe Gerbaulet, Bernd-Thomas Kellner, Thomas Schaefer, Jan Purr, Enno Eißfeller, Heinz-Dieter Zauzig, Peter Riegel, Christoph Axthelm, Gerd-Ulrich Heinz, Holger Menke, Andreas Pustelnik, Stefan Zutz, Wolfgang Eder, Guenter Rehling, Dirk Glatzel, Norbert Ludwig, Petra Sandow, Henning Wiswedel, Cosmas Wildenauer, Steffen Schoen, Toralf Schwarz, Adyeri Babyesiza, Maximilian Kropp, Hans-Hermann Zimny, Friedhelm Kahl, Andreas Caspar, Sabine Omankowsky, Torsten Laessig, Hermann-Josef Hartmann, Gunter Lehmann, Hans-Walter Bindig, Gunter Hergdt, Dietrich Reimer, Joachim Hauk, Holger Michel, Praxis Dres. Werner Erdle, Wilfried Dorsch, Janna Dshabrailov, Karl-Albrecht Rapp, Reinhold Vormann, Thomas Mueller, Peter Mayer, Uwe Horstmeier, Volker Eissing, Heinz Hey, Heinz Leuchtgens, Volker Lilienweiss, Heiner Mueller, Christian Schubert, Herrmann Lauer, Thomas Buchner, Gunter Brauer, Susanne Kamin, Karsten Mueller, Sylvia Baumbach, Muwafeg Abdel-Qader, Hans-Holger Ebert, Carsten Schwencke, Peter Bernhardt, Laszlo Karolyi, Britta Sievers, Wilhelm Haverkamp, Jens-Uwe Roehnisch.

Hungary

Andras Vertes, Gabor Szantai, Andras Matoltsy, Nikosz Kanakaridisz, Zoltan Boda, Erno Kis, Balazs Gaszner, Ferenc Juhasz, Gizella Juhasz, Sandor Kancz, Zoltan Laszlo, Zsolt May, Bela Merkely, Ebrahim Noori, Tamas Habon, Peter Polgar, Gabriella Szalai, Sandor Vangel, Andras Nagy, Gabriella Engelthaler, Judit Ferenczi, Mihaly Egyutt.

Italy

Giuliana Martini, Leone Maria Cristina, Eros Tiraferri, Rita Santoro, Sophie Testa, Giovanni Di Minno, Marco Moia, Teresa Maria Caimi, Maria Tessitori, Giancarlo Agnelli, Roberto Cappelli, Daniela Poli, Roberto Quintavalla, Franco Cosmi, Raffaele Fanelli, Vincenzo Oriana, Raffaele Reggio, Roberto Santi, Leonardo Pancaldi, Raimondo De Cristofaro, Giuliana Guazzaloca, Angelo De Blasio, Jorge Salerno Uriate, Flavia Lillo, Enrico Maria Pogliani, Grzegorz Bilo, Michele Accogli, Antonio Mariani, Mauro Feola, Arturo Raisaro, Luciano Fattore, Andrea Mauric, Fabrizio Germini, Luca Tedeschi, Maria Settimi, Sergio Nicoli, Paolo Ricciarini, Antonio Argena, Paolo Ronchini, Claudio Bulla, Filippo Tradati, Massimo Volpe, Maria D'Avino, Maria Grazia Bongiorni, Silva Severi, Alessandro Capucci, Corrado Lodigiani, Enrico Salomone, Gaetano Serviddio, Claudio Tondo, Giuseppe Ambrosio, Paolo Golino, Carmine Mazzone, Saverio Iacopino.

The Netherlands

Hugo ten Cate, J.H. Ruiter, Andreas Lucassen, Henk Adriaansen, Maarten Bongaerts, Mathijs Pieterse, Coen van Guldener, Johannes Herrman, S.H.K. P.R. Nierop, Pieter Hoogslag, Walter Hermans, B.E. Groenemeijer, W. Terpstra, Cees Buiks, L.V.A. Boersma.

Norway

Eivind Berge, Per Anton Sirnes, Erik Gjertsen, Torstein Hole, Knut Erga, Arne Hallaråker, Gunnar Skjelvan, Anders Østrem, Beraki Ghezai, Arne Svilaas, Peter Christersson, Torbjørn Øien, Svein Høegh Henrichsen, Jan Erik Otterstad, Jan Berg-Johansen.

Poland

Janina Stepinska, Andrzej Gieroba, Malgorzata Biedrzycka, Michal Ogorek, Beata Wozakowska-Kaplon, Krystyna Loboz-Grudzien, Jaroslaw, Wieslaw Supinski, Jerzy Kuzniar, Roman Zaluska, Jaroslaw Hiczkiewicz,

Lucyna Swiatkowska-Byczynska, Lech Kucharski, Marcin Gruchala, Piotr Minc, Maciej Olszewski, Grzegorz Kania, Malgorzata Krzciuk, Zbigniew Lajkowski, Bozenna Ostrowska-Pomian, Jerzy Lewczuk, Elzbieta Zinka, Agnieszka Karczmarczyk, Malgorzata Chmielnicka-Pruszczynska, Iwona Wozniak-Skowerska, Grzegorz Opolski, Marek Bronisz, Marcin Ogorek, Grazyna Glanowska, Piotr Ruszkowski, Grzegorz Skonieczny, Ryszard Sciborski, Boguslaw Okopien, Piotr Kukla, Krzysztof Galbas, Krzysztof Cymerman, Jaroslaw Jurowiecki, Pawel Miekus, Waldemar Myszka, Stanislaw Mazur, Roman Lysek, Jacek Baszak, Teresa Rusicka-Piekarz, Grzegorz Raczak, Ewa Domanska, Jadwiga Nessler, Jozef Lesnik.

Russia

Vera Eltishcheva, Roman Libis, Gadel Kamalov, Dmitry Belenky, Liudmila Egorova, Alexander Khokhlov, Eduard Yakupov, Dmitry Zateyshchikov, Olga Barbarash, Olga Miller, Evgeniy Mazur, Konstantin Zrazhevskiy, Tatyana Novikova, Yulia Moiseeva, Elena Polkanova, Konstantin Sobolev, Maria Rossovskaya, Yulia Shapovalova, Alla Kolesnikova, Konstantin Nikolaev, Oksana Zemlianskaia, Anna Zateyshchikova, Victor Kostenko, Sergey Popov, Maria Poltavskaya, Anton Edin,
Elena Aleksandrova, Oksana Drapkina, Alexander Vishnevsky, Oleg Nagibovich, Petr Chizhov, Svetlana Rachkova, Mikhail Sergeev, Borys Kurylo, Alexey Ushakov.

Spain

Xavier Vinolas, Pere Alvarez Garcia, Maria Fernanda Lopez Fernandez, Luis Tercedor Sanchez, Salvador Tranche Iparraguirre, Pere Toran Monserrat, Emilio Marquez Contreras, Jordi Isart Rafecas, Juan Motero Carrasco, Pablo Garcia Pavia, Casimiro Gomez Pajuelo, Luis Miguel Rincon Diaz, Luis Fernando Iglesias Alonso, Angel Grande Ruiz, Jordi Merce Klein, Jose Ramon Gonzalez Juanatey, Ines Monte Collado, Herminia Palacin Piquero, Carles Brotons Cuixart, Esther Fernandez Escobar, Joan Bayo i Llibre, Cecilia Corros Vicente, Manuel Vida Gutierrez, Francisco Epelde Gonzalo, Carlos Alexandre Almeida Fernandez, Encarnacion Martinez Navarro, Jordi Isart Rafecas, Juan Jose Montero Alia, Maria Barreda Gonzalez, Maria Angels Moleiro Oliva, Jose Iglesias Sanmartin, Mercedes Jimenez Gonzalez, Maria del Mar Rodriguez Alvarez, Juan Herreros Melenchon, Tomas Ripoll Vera, Manuel Jimenez Navarro, Maria Vazquez Caamano, Maria Fe Arcocha Torres, Gonzalo Marcos Gomez, Andres Iniguez Romo, Miguel Angel Prieto Diaz.

Sweden

Mårten Rosenqvist, Alexander Wirdby, Centrumkliniken, Jan Lindén, Kerstin Henriksson, Micael Elmersson, Arnor Egilsson, Ulf Börjesson, Gunnar Svärd, Bo Liu, Anders Lindh, Lars-Bertil Olsson, Mikael Gustavsson, Lars Andersson, Lars Benson, Claes Bothin, Ali Hajimirsadeghi, Björn Martinsson, Marianne Ericsson, Åke Ohlsson, Håkan Lindvall, Peter Svensson, Katarina Thörne, Hans Händel, Pyotr Platonov, Fredrik Bernsten, Ingar Timberg, Milita Crisby, Jan-Erik Karlsson, Agneta Andersson, Lennart Malmqvist, Johan Engdahl, Jörgen Thulin, Aida Hot-Bjelak, Steen Jensen, Per Stalby.

Switzerland

Jan Steffel, Johann Debrunner, Juerg H. Beer, Dipen Shah.

Ukraine

Iurii Rudyk, Vira Tseluyko, Oleksandr Karpenko, Svitlana Zhurba, Igor Kraiz, Oleksandr Parkhomenko, Iryna Kupnovytska, Nestor Seredyuk, Yuriy Mostovoy, Oleksiy Ushakov, Olena Koval, Igor Kovalskiy, Yevgeniya Svyshchenko, Oleg Sychov, Mykola Stanislavchuk, Andriy Yagensky, Susanna Tykhonova, Ivan Fushtey.

United Kingdom

Will Murdoch, Naresh Chauhan, Daryl Goodwin, Louise Lumley, Ramila Patel, Philip Saunders, Bennett Wong, Alex Cameron, Philip Saunders, Niranjan Patel, P Jhittay, Andrew Ross, M S Kainth, Karim Ladha, Kevin Douglas, Gill Pickavance, Joanna McDonnell, Laura Handscombe, Trevor Gooding, Helga Wagner, Cumberlidge, Colin Bradshaw, Catherine Bromham, Kevin Jones, Shoeb Suryani, Richard Coates, Bhupinder Sarai, W Willcock, S Sircar, John Cairns, A Gilliand, Roman Bilas, E Strieder, Peter Hutchinson, Anne Wakeman, Michael Stokes, Graham Kirby, Bhaskhar Vishwanathan, Nigel Bird, Paul Evans, M Clark, John Bisatt, Jennifer Litchfield, E Fisher, Tim Fooks, Richard Kelsall, Neil Paul, Elizabeth Alborough, Michael Aziz, C Ramesh, Pete Wilson, Simon Franklin, Sue Fairhead, Julian Thompson, Hasan Chowan, Gary Taylor, Dawn Tragen, Matt Parfitt, Claire Seamark, Carolyn Paul, Mark Richardson, Angus Jefferies, Helen Sharp, Hywel Jones, Claire Giles, Matthew Bramley, Philip Williams, Jehad Aldegather, Simon Wetherell, William Lumb, Phil Evans, Frances Scouller, Neil Macey, Stephen Rogers, Yvette Stipp, Richard West, Philip Pinney, Paul Wadeson, John Matthews, Preeti Pandya, Andrew Gallagher, T Railton, Emyr Davies, Jonathan McClure, Marc Jacobs, Claire Hutton, R Thompson, Bijoy Sinha, Keith Butter, Susan Barrow, Helen Little, David Russell, Ulka Choudhary, Ikram Haq,

Paul Ainsworth, Claire Jones, Phil Weeks, Jane Eden, Lisa Gibbons, Janet Glencross, Alison MacLeod, K Poland, Conor Mulolland, A Warke, Paul Conn, D Burns, R Smith, R Kamath, Jonathan Webster, Ian Hodgins, Stephen Vercoe, Paul Roome, Hilary Pinnock, Jayesh Patel, Amar Ali, Nigel Hart, Richard Davies, Nigel De-Sousa, Catherine Neden, Mark Danielsen, Purnima Sharma, Sophia Galloway, Charlotte Hawkins, Raife Oliver, Martin Aylward, Mira Pattni, Gordon Irvine, Shahid Ahmad, Catherine Rothwell, Fiaz Choudhary, Sabrina Khalaque, Stephanie Short, Sharon Peters, Warwick Coulson, Neil Roberts,

Amy Butler, Steven Coates, Ben Ward, Daniel Jackson, Steve Walton, Diane Shepherd, Toh Wong, Mark Boon, Melanie Deacon, David Cornelius, Sarah Davies, Ben Frankel, Nick Hargreaves, Henry Choi, Jon Sumner, Tim Myhill, Salah Estifanos, Diane Geatch, Justin Wilkinson, Richard Veale, Karen Forshaw, Rob Hirst, Kashif Zaman, Catherine Liley, Rebecca Wastling, Paul McEleny, Andre Beattie, Philip Cooke, Mike Wong, Mark Pugsley, Chaminda Dooldeniya, Greg Rogers, James Bennett, Polly Jacobs, Rajesh Muvva, Matthew Adam, Robin Fox, Nicolas Thomas, Simon Cartwright, Rory Reed, Simon Randfield, Christine A'Court, Ann Flynn, Andrew Halpin, Shoeb Suryani, Simon Dobson, Louise Lomax, Minnal Nadaph, Iain Munro, Jane Goram, Helen Stoddart, Phil Simmons, John Shewring, Emma Bowen-Simpkins, Mark Rickenbach, Polly Jacobs.

Australia

Adam Blenkhorn, Bhuwanendu Singh, Penny Astridge, William van Gaal, Walter Abhayaratna, Philip Thomson, Ron Lehman, Jens Kilian, David Coulshed, Andrei Catanchin, David Colquhoun, Hosen Kiat, David Eccleston, John French, Bronte Ayres, Peter Blombery, Thanh Phan, James Rogers, David O'Donnell, Sang Cheol Bae, Harry Gibbs, Patrick Carroll, Greg Starmer, Margaret Arstall, Maurits Binnekamp, Astin Lee.

Canada

John Eikelboom, Robert Luton, Milan Gupta, Amritanshu Shekhar Pandey, Stephen Cheung, Rolland Leader, Philippe Beaudry, Félix Ayala-Paredes, Joseph Berlingieri, John Heath, Germain Poirier, Miranda du Preez, Bradley Schweitzer, Reginald Nadeau, Ripple Dhillon, Tomasz Hruczkowski, Andrea Lavoie, Ratika Parkash, James Cha, Benoit Coutu, Paul MacDonald, Brian Ramjattan, Jorge Bonet, Saul Vizel, Paul Angaran, Sameh Fikry.

Egypt

Ahmed Mowafy, Azza Katta, Mazen Tawfik, Moustafa Nawar, Mohamed Sobhy, Seif Kamal Abou Seif, Tarek Khairy, Ahmed Abd El-Aziz, Nasser Taha, Ashraf Reda, Atef Elbahry, Mohamed Setiha, Mohamed Gamal El Din, Magdi Elkhadem, Adel El-Etreby.

South Africa

David Kettles, Junaid Bayat, Heidi Siebert, Adrian Horak, Ynez Kelfkens, Riaz Garda, Barry Jacobson, Thayabran Pillay, Michele Guerra, Louis van Zyl, Hendrik Theron, Andrew Murray, Rikus Louw, Deon Greyling, Pindile Mntla, Siddique Ismail, Fayzal Ahmed, Johannes Engelbrecht, Shambu Maharajh, Wessel Oosthuysen, Rehana Loghdey, Veronica Ueckermann.

United Arab Emirates

Wael Al Mahmeed, Abdullah Al Naeemi, Ghazi Yousef, Nooshin Bazargani, Munther AlOmairi, Rajan Maruthanayagam, Rupesh Singh, Ahmed Naguib, Mohamed Ibrahim, Amrish Agrawal, Mukesh Nathani, Ehab M. Esheiba, Adel Wassef, Rajeev Gupta.

United States

Michael Cox, Scott Beach, Peter Duffy, Stephen Falkowski, Kevin Ferrick, Miguel Franco, W. Michael Kutayli, Annette Quick, Niraj Sharma, Vance Wilson, Stephen Miller, Mark Alberts, Edwin Blumberg, Roddy Canosa, Ted Gutowski, Rodney Ison, Jorge Garcia, Paul Mullen, Howard Noveck, Pamela Rama, Rajneesh Reddy, Marcus Williams, Daniel Nishijima, Keith Ferdinand, Ihsan Haque, Robert Mendelson, Sridevi Pitta, Daniel Theodoro, Charles Treasure, Moustafa Moustafa, Cas Cader, Walter Pharr, Alisha Oropallo, George Platt, Jaspal Gujral, James Welker, Firas Koura.

1 **GARFIELD-AF Ethics Committee List**

Sponsor	Protocol #	Project Code	Region	Sub-Region	Country	Submission Requirement Type	Authority/Committee Name
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	CEC	Comite Independiente de Etica
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	CEC	Comite Independiente de Etica
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	CEC	Comite Independiente de Etica
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	CEC	Comite Independiente de Etica
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	RA	CCIS Comision Conjunta de Investigacion en Salud
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	CEC	Comite Independiente de Etica
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	RA	CCIS Comision Conjunta de Investigacion en Salud
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	RA	CCIS Comision Conjunta de Investigacion en Salud
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	RA	CCIS Comision Conjunta de Investigacion en Salud
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	CEC	Comite Independiente de Etica
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Argentina	Others	
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Australia & New Zealand	Australia	Central IRB	Metro South Health Service District Human Research Ethics Committee
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Australia & New Zealand	Australia	Central IRB	University of Wollongong & Illawarra HREC
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Australia & New Zealand	Australia	Central IRB	
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Australia & New Zealand	Australia	Central IRB	Metro South Health Service District Human Research Ethics Committee
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Austria	CEC	Ethikkommission der Medizinischen Universität Graz

Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Belgium	CEC	Ethisch Comité UZA
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Brazil	CEC	
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Brazil	CEC	
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Brazil	CEC	
Thrombosis Research Institute	TRI08888	IPAA4663	USA/Canada	Canada	Canada	Central IRB	WIRB
Thrombosis Research Institute	TRI08888	IPAA4663	USA/Canada	Canada	Canada	Central IRB	WIRB
Thrombosis Research Institute	TRI08888	IPAA4663	USA/Canada	Canada	Canada	Central IRB	WIRB
Thrombosis Research Institute	TRI08888	IPAA4663	USA/Canada	Canada	Canada	Central IRB	WIRB

Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	South America	Chile	RA	Instituto de Salud Pública de Chile
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Czech Republic	RA	Statni ustav pro kontrolu leciv
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Czech Republic	RA	Statni ustav pro kontrolu leciv
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Denmark	CEC	De Videnskabsetiske Komitéer for Region Hovedstaden
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Denmark	CEC	De Videnskabsetiske Komitéer for Region Hovedstaden
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Denmark	CEC	De Videnskabsetiske Komitéer for Region Hovedstaden
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Denmark	CEC	De Videnskabsetiske Komitéer for Region Hovedstaden
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Denmark	CEC	De Videnskabsetiske Komitéer for Region Hovedstaden
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Denmark	CEC	De Videnskabsetiske Komitéer for Region Hovedstaden
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Finland	CEC	Pirkanmaan sairaanhoitopiirin eettinen toimikunta
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Finland	CEC	Pirkanmaan sairaanhoitopiirin eettinen toimikunta
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Finland	CEC	Pirkanmaan sairaanhoitopiirin eettinen toimikunta
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Finland	CEC	Pirkanmaan sairaanhoitopiirin eettinen toimikunta
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé

Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	France	CEC	Comité Consultatif sur le Traitement de l'information Recherche/Santé
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag

Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	CEC	Egeszsegugyi Tudomanyos Tanacs Tudomanyos es Kutatasetikai Bizottsag
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	Orszagos Gyogyszereszteti es Elelmezes-egszsegugyi Intezet
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Hungary	RA	
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	India Region	India	RA	Directorate General of Health Services (India)
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	India Region	India	RA	Directorate General of Health Services (India)
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Italy	CEC	Comitato Etico delle Aziende Sanitarie dell'Umbria di Perugia
Thrombosis Research Institute	TRI08888	IPAA4663	Japan	Japan	Japan	RA	

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Thrombosis Research Institute	TRI08888	IPAA4663	Japan	Japan	Japan	RA	
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Southeast Asia	Korea, Republic of	RA	
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)

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Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
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Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
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Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)

Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
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Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Latin America	Central America	Mexico	RA	COFEPRIS - Comision de Autorizacion Sanitaria (Mexico)
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Netherlands	CEC	
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Norway	CEC	REK Sør-øst
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Norway	CEC	REK Sør-øst
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii

Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Poland	CEC	Terenowa Komisja Bioetyczna przy Instytucie Kardiologii
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Russian Federation	CEC	IIC of Ethic Assessment of Clinical Researches
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Southeast Asia	Singapore	RA	
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Africa	South Africa	RA	MCC - Medicines Control Council (South Africa)
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Africa	South Africa	RA	MCC - Medicines Control Council (South Africa)
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Africa	South Africa	RA	MCC - Medicines Control Council (South Africa)
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Spain	CEC	CEIC Hospital Universitario Virgen de la Victoria
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Spain	CEC	CEIC Hospital Universitario Virgen de la Victoria

Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Sweden	CEC	Regionala etikprövningsnämnden i Stockholm
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Western Europe	Switzerland	RA	
Thrombosis Research Institute	TRI08888	IPAA4663	Asia Pacific	Southeast Asia	Thailand	RA	

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Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Turkey	CEC	Malatya Klinik Arastirmalar Etik Kurulu
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Turkey	RA	Turkish Ministry of Health
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Turkey	CEC	Malatya Klinik Arastirmalar Etik Kurulu
Thrombosis Research Institute	TRI08888	IPAA4663	Europe/Middle East/Africa-EMEA	Eastern Europe/Middle East	Ukraine	CEC	Central Ethics Commission of the Ministry of Health of Ukraine

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