Impact of Spontaneous Extracranial Bleeding Events on Health State Utility in Patients with Atrial Fibrillation: Results from the ENGAGE AF-TIMI 48 Trial

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Background—The impact of different types of extracranial bleeding events on health-related quality of life and health-state utility among patients with atrial fibrillation is not well understood.

Methods and Results—The ENGAGE AF-TIMI 48 (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48) Trial compared edoxaban with warfarin with respect to the prevention of stroke or systemic embolism in atrial fibrillation. Data from the EuroQol-5D (EQ-5D-3L) questionnaire, prospectively collected at 3-month intervals for up to 48 months, were used to estimate the impact of different categories of bleeding events on health-state utility over 12 months following the event. Longitudinal mixed-effect models revealed that major gastrointestinal bleeds and major nongastrointestinal bleeds were associated with significant immediate decreases in utility scores (−0.029 [−0.044 to −0.014; P<0.001] and −0.029 [−0.046 to −0.012; P=0.001], respectively). These effects decreased in magnitude over time, and were no longer significant for major nongastrointestinal bleeds at 9 months, but remained borderline significant for major gastrointestinal bleeds at 12 months. Clinically relevant nonmajor and minor bleeds were associated with smaller but measurable immediate impacts on utility (−0.010 [−0.016 to −0.005] and −0.016 [−0.024 to −0.008]; P=0.001 for both), which remained relatively constant and statistically significant over the 12 months following the bleeding event.

Conclusions—All categories of bleeding events were associated with negative impacts on health-state utility in patients with atrial fibrillation. Major bleeds were associated with relatively large immediate decreases in utility scores that gradually diminished over 12 months; clinically relevant nonmajor and minor bleeds were associated with smaller immediate decreases in utility that persisted over 12 months.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov/. Unique identifier: NCT00781391. (J Am Heart Assoc. 2017;6: e006703. DOI: 10.1161/JAHA.117.006703.)

Key Words: anticoagulation • bleeding • quality of life • utility

Contemporary management of atrial fibrillation (AF) imposes many challenges. Anticoagulation in patients with AF involves a careful balance between maximizing the benefit with respect to the prevention of stroke while minimizing the bleeding risk. Several novel oral anticoagulants have been approved and released on the market as...
Clinical Perspective

What Is New?

- The impact of different types of extracranial bleeding events on health-state utility among patients with atrial fibrillation was examined using data from the ENGAGE AF-TIMI 48 (Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48) trial.
- Compared with clinically relevant nonmajor and minor bleeds, major gastrointestinal and nongastrointestinal bleeds were associated with larger immediate decrements in utility scores that decreased gradually over the year following the bleeding event and were no longer statistically significant at 12 months.
- In contrast, clinically relevant and minor bleeding events were associated with smaller but statistically significant initial decreases in utility that persisted for 12 months.

What Are the Clinical Implications?

- These findings have potential use in future studies of the net clinical benefit and cost-effectiveness of alternative strategies for stroke prevention in patients with atrial fibrillation.

Few studies have examined the impact of adverse events such as bleeding on utility among patients with atrial fibrillation. In contrast, clinically relevant and minor bleeding events were associated with smaller but statistically significant initial decreases in utility that persisted for 12 months. In contrast, clinically relevant and minor bleeding events were associated with smaller but statistically significant initial decreases in utility that persisted for 12 months.

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Methods

Study Population

The design, methods, and clinical results of the ENGAGE AF-TIMI 48 trial have been described previously. Briefly, patients from 1393 centers in 46 countries were enrolled between November 2008 and November 2010. Eligible patients were randomly assigned in a 1:1:1 ratio to receive warfarin, dose-adjusted to achieve an international normalized ratio of 2.0 to 3.0 or to receive higher-dose 60 mg, or lower-dose 30-mg edoxaban regimens; the dose of edoxaban in each arm was reduced by 50% in patients with anticipated increased exposure based on creatinine clearance, body weight, and concomitant permeability glycoprotein inhibitor use. Patients with a high risk of bleeding such as history of prior ICH, major bleeding or peptic ulcer disease within 1 year, hemorrhagic disorders, thrombocytopenia, need for dual antiplatelet therapy, severe renal failure, moderate or severe hepatic insufficiency, active infective endocarditis, uncontrolled hypertension (blood pressure >170/100 mm Hg), or recent severe trauma, major surgery, or deep organ biopsy within the previous 10 days, were all excluded. The study was approved by the institutional review board at each site, and all patients provided written informed consent before participation.

Quality of Life Assessments

Quality of life was assessed using the self-administered EuroQol 5 Dimension questionnaire, which was completed at baseline and at 3-month intervals for up to 4 years (median 2.8 years) by a subsample of ≈80% of patients from the overall trial population. The EuroQol 5 Dimension questionnaire is a generic health status measure consisting of 5 domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) that can be converted to utilities using an algorithm developed for the US population. Utilities are preference-based health status measures and range from 0 to 1, with 1 representing perfect health and 0 corresponding to the worst imaginable health state. The EuroQol 5 Dimension questionnaire has been extensively validated and frequently used to assess health-state utility and health-related QOL in health economic studies for patients with cardiovascular disease. For the purposes of this study, only patients who had baseline and at least 1 follow-up QOL assessment were included in the study population.
Bleeding End Points
The primary safety end point in ENGAGE AF–TIMI 48 was adjudicated major bleeding. Spontaneous bleeding events requiring medical attention were adjudicated by an independent and blinded clinical events committee, according to prespecified criteria as defined by the International Society on Thrombosis and Haemostasis. The specific event categories included major gastrointestinal bleeding, major nongastrointestinal bleeding, and clinically relevant nonmajor (CRNM) bleeding. Major bleeds include symptomatic bleeding in a critical area or organ, such as intraspinal, intraocular, retroperitoneal, intraarticular, or pericardial, or intramuscular with compartment syndrome and/or bleeding causing a decrease in hemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of 2 or more units of whole blood or red blood cells. CRNM bleeds are acute or subacute clinically overt bleeds that do not meet the criteria for major bleed but prompt a clinical response, in that they lead to at least 1 of the following: a hospital admission for bleeding; a physician-guided medical or surgical treatment for bleeding; or a change in antithrombotic therapy (including interruption or discontinuation of study drug). Bleeding events that did not require medical attention were classified as minor bleeding, without clinical events committee adjudication.

Statistical Analysis
Baseline clinical and demographic characteristics and QOL scores were compared between patients included versus excluded from this QOL study, and within the QOL study between those with versus without bleeding events, using 2-sample Student t tests for continuous variables and P2 or Fisher exact tests for categorical variables. Standardized differences, assuming a threshold of 10% for a clinically meaningful difference, were calculated for the comparison of baseline characteristics in the study sample versus those patients excluded from the analysis, in order to evaluate the importance of statistically significant differences given the large sample sizes in both groups. Longitudinal mixed effect models were used to examine the impact of different categories of bleeding events on QOL scores by modeling bleeding events as time-varying covariates. These models incorporate all available health status data from all follow-up time points, and accommodate missing data under the assumption of missing at random. Variables included in the models were baseline QOL score, bleeding status, and time relative to the bleeding event. Linear, quadratic, and cubic effects of follow-up time were considered, as well as all corresponding interactions between follow-up time and bleeding status. The interactions between bleeding status and time elapsed since the bleeding events were added to the models to assess any changes in the impact of bleeding events over time. In addition, age, sex, and all other baseline clinical characteristics listed in Table were included in the model development. The models were optimized using a backward selection process and only variables with P<0.1 were retained.

To avoid potential confounding of other vascular events on the estimated impact of bleeding events on QOL outcomes, patients who experienced any stroke, transient ischemic attack, myocardial infarction, or systemic embolic event were censored on the date of the first thrombotic event. In addition, patients who experienced multiple bleeding events of either the same or different types were censored on the date of the second bleeding event. Any QOL measures on or after the date of censoring were thereby excluded from the analysis.

All analyses were performed using SAS for Windows version 9.4 (SAS Institute, Cary, NC), and a 2-tailed P<0.05 was considered statistically significant for all comparisons.

Results
Patient Population and Baseline QOL
A total of 21105 patients were enrolled in the ENGAGE AF–TIMI 48 trial, of whom 10706 had baseline and at least 1 follow-up EQ-5D collected. Most of the standardized differences between the patients included versus excluded from the QOL study were <10%; only the standardized differences in creatinine clearance, CHADS2 score, dyslipidemia, and hypertension were slightly higher than 10% (Table S1). These results suggest no substantial difference between the 2 cohorts. Patients excluded specifically because of having no follow-up QOL assessments (n=236) had lower mean baseline EQ-5D utility scores than those included in the analysis (0.836 versus 0.808, P=0.004); because the analysis adjusts for baseline score, this is unlikely to impact our findings. There were 2492 patients in the QOL study population for whom a spontaneous nonintracranial bleed was reported as a first event; 207 of these were major gastrointestinal bleeds, and 152, 1419, and 714 were major nongastrointestinal, CRNM, and minor bleeds, respectively. One hundred thirty-seven ICH events were observed in the study population, though only 23 of these ICH events were the first event for the patient; therefore, ICH bleed was not analyzed because of small sample size.

For each bleeding category, patients with versus without a bleeding event were older and more likely to have a history of non-ICH bleeding history and prior coronary artery bypass graft at baseline (Table). Baseline EQ-5D utility scores did not differ for patients with versus without a bleeding event. Completeness of QOL data collection was high (>90%)
Table. Demographic and Clinical Characteristics of the Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Major GI Bleeding</th>
<th>Major Non-GI Bleeding</th>
<th>CRNM Bleeding</th>
<th>Minor Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Event (N=207)</td>
<td>No Event † (N=9801)</td>
<td>P Value</td>
<td>Event (N=1419)</td>
</tr>
<tr>
<td>Age, y, mean±SD</td>
<td>74.6±8.6</td>
<td>70.3±9.5</td>
<td>&lt;0.001</td>
<td>72.1±9.2</td>
</tr>
<tr>
<td>Male</td>
<td>61.4</td>
<td>61.5</td>
<td>0.974</td>
<td>60.2</td>
</tr>
<tr>
<td>Previous use of vitamin K antagonist</td>
<td>64.7</td>
<td>58.8</td>
<td>0.084</td>
<td>62.6</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>38.2</td>
<td>36.6</td>
<td>0.639</td>
<td>38.3</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>57.5</td>
<td>54.7</td>
<td>0.421</td>
<td>58.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>95.2</td>
<td>95.0</td>
<td>0.933</td>
<td>93.9</td>
</tr>
<tr>
<td>Prior MI</td>
<td>13.5</td>
<td>11.3</td>
<td>0.328</td>
<td>11.6</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>16.4</td>
<td>18.3</td>
<td>0.485</td>
<td>18.3</td>
</tr>
<tr>
<td>Prior transient ischemic attack</td>
<td>11.1</td>
<td>12.2</td>
<td>0.649</td>
<td>12.5</td>
</tr>
<tr>
<td>Prior PAD</td>
<td>7.7</td>
<td>4.2</td>
<td>0.014</td>
<td>4.2</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>61.8</td>
<td>60.0</td>
<td>0.584</td>
<td>51.2</td>
</tr>
<tr>
<td>Prior CAD</td>
<td>38.8</td>
<td>33.5</td>
<td>0.106</td>
<td>35.5</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>14.0</td>
<td>7.3</td>
<td>&lt;0.001</td>
<td>10.0</td>
</tr>
<tr>
<td>History of ICH bleed</td>
<td>0.0</td>
<td>0.1</td>
<td>1.000</td>
<td>0.2</td>
</tr>
<tr>
<td>History of non-ICH bleed</td>
<td>17.4</td>
<td>9.0</td>
<td>&lt;0.001</td>
<td>16.8</td>
</tr>
<tr>
<td>History of gastrointestinal bleed</td>
<td>5.8</td>
<td>3.0</td>
<td>0.018</td>
<td>5.1</td>
</tr>
<tr>
<td>Creatinine clearance in mg/dL, mean±SD</td>
<td>69.4±28.4</td>
<td>79.1±32.4</td>
<td>&lt;0.001</td>
<td>76.1±31.0</td>
</tr>
<tr>
<td>CHADS2 score (0-6), mean±SD</td>
<td>3.0±1.1</td>
<td>2.8±1.0</td>
<td>0.004</td>
<td>2.9±1.0</td>
</tr>
<tr>
<td>EuroQol-5D utility, mean±SD</td>
<td>0.821±0.166</td>
<td>0.837±0.152</td>
<td>0.147</td>
<td>0.843±0.147</td>
</tr>
</tbody>
</table>

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; CHADS2, scoring system for the long-term risk of stroke in atrial fibrillation; acronym stands for Congestive heart failure, Hypertension, Age≥75y, Diabetes mellitus, and prior Stroke; CRNM, clinically relevant nonmajor; EuroQol 5 Dimension questionnaire; GI, gastrointestinal; ICH intracranial hemorrhage; MI, myocardial infarction; PAD, peripheral arterial disease.

*Only extracranial bleeds are included.

†The sample sizes for the “no event” categories differ according to the category of bleed because of censoring in data selection. All results are % of patients unless otherwise specified.
throughout the entire study period among the 10,706 patients who were included in this analysis (Table S2), although it tended to be slightly lower for patients with versus without major gastrointestinal bleeding events beginning at the 6-month follow-up and thereafter.

Impact of Bleeding on Quality of Life

After adjusting for baseline score and clinical and demographic characteristics, results from the longitudinal mixed effect models revealed that all categories of bleeding events were associated with a significant immediate reduction in EQ-5D utility (Figure). Major gastrointestinal and nongastrointestinal bleeding events had similar immediate impacts on utility (−0.029 [95% CI: −0.044 to −0.014; \(P<0.001\)] and −0.029 [95% CI: −0.046 to −0.012; \(P=0.001\)], respectively). CRNM and minor bleeding events were associated with smaller but measurable immediate impacts on utility (−0.010 [95% CI: −0.016 to −0.005; \(P<0.001\)] and −0.016 [95% CI: −0.024 to −0.008; \(P<0.001\)], respectively).

Figure demonstrates the estimated impact of bleeding over time, for each of the categories of bleeding events. For major gastrointestinal and nongastrointestinal bleeds, the impact on utility scores consistently decreased in magnitude over time; while the impact of major nongastrointestinal bleeds was no longer statistically significant at 9 months, the impact of major gastrointestinal bleeds on utility scores remained borderline significantly (−0.011 points, \(P=0.058\)) at 12 months. The impacts of CRNM and minor bleeding events on utility were smaller but persisted throughout 12 months with no clear temporal trend.

Discussion

Bleeding is the most common complication associated with anticoagulation management in patients with AF. The frequent (3-month intervals) assessment of QOL with the EQ-5D questionnaire in the ENGAGE AF—TIMI 48 trial allowed us to estimate the impact of extracranial bleeding events on health-state utility over the course of 12 months following the event. All categories of bleeding events were associated with significant immediate decreases in EQ-5D utility. Compared with CRNM and minor bleeds, major gastrointestinal and nongastrointestinal bleeds were associated with larger immediate decrements in utility scores that decreased gradually over the year following the bleeding event and were no longer statistically significant at 12 months. In contrast, CRNM and minor bleeding events were associated with smaller but statistically significant initial decreases in utility that persisted for 12 months. The persistence of this decrease is unexpected, and may be because of unmeasured confounding in the population that experiences minor bleeds. The larger relative magnitude of the impact of minor versus CRNM bleeds on utility may be related to the fact that by definition, CRNM bleeding events require some degree of medical intervention, whereas minor bleeding events do not.

To put the estimated immediate disutilities associated with major, CRNM, and minor bleeding events of −0.020, −0.010, and −0.016 from our study in context, a study of complication-specific changes in utility based on longitudinal data from patients with type 2 diabetes mellitus reported decreases in EQ-5D-derived utility scores ranging from −0.026, −0.045, and −0.049 for myocardial infarction, congestive heart failure, and renal failure, to −0.083, −0.099, and −0.122 for
bleeding, stroke, and amputation, respectively.\textsuperscript{17} The estimated immediate decreases in EQ-5D utility scores with bleeding events from our study are comparable to estimates reported in other studies involving other patient populations. For example, using data from the TRANSLATE-ACS (Treatment With Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome) study, Amin et al\textsuperscript{18} reported that among patients who underwent percutaneous coronary intervention for acute myocardial infarction, bleeding events, classified according to the Bleeding Academic Research Consortium (BARC) criteria, that occurred between discharge and 6 months postacute myocardial infarction were associated with a mean reduction in utility scores of 0.033 points at 6 months. More severe bleeding events (BARC types 3 or 4) were associated with larger decrements in utility (−0.045 points), whereas even minor bleeds (BARC type 1) were associated with smaller but still detectable decreases in utility. A similar finding was observed for patients with acute myocardial infarction with respect to nuisance bleeding, which was found to be independently associated with worse QOL at 1 month.\textsuperscript{19} Our study is unique, however, given its examination of the trajectory of QOL outcomes over 12 months following the bleeding event. The lack of statistical significance with respect to the estimated utility decrements at 9 months for major nongastrointestinal bleeds and at 12 months for major gastrointestinal and major nongastrointestinal bleeds may be because of the relatively small number of events (207 and 152 major gastrointestinal and nongastrointestinal bleeds, respectively, as compared with 1419 and 714 CRNM and minor bleeds, respectively) or survivor bias resulting from a higher death rate for patients with more severe bleeds.

These estimates of the pattern of utility changes over time for bleeding events in patients with AF have implications for the estimation of quality-adjusted life years in cost-effectiveness studies. In recent years, studies of the cost-effectiveness of anticoagulation or other approaches to stroke prevention in patients with AF have generally applied utility estimates from a limited number of available sources including the Beaver Dam Health Outcomes Study and the national catalog of preference-based scores for chronic conditions in the United States.\textsuperscript{20–26} However, both of these sources are based on data obtained from general community populations, and therefore the utility/disutility estimates may not pertain to patients with AF. Moreover, in cost-effectiveness analyses, the impact of bleeding events is often assumed to be transient.\textsuperscript{23,24,27} For example, published cost-effectiveness analyses comparing apixaban and edoxaban versus warfarin assumed disutilities of −0.1511 lasting 2 weeks for major extracranial hemorrhage, −0.0582 lasting 2 days for CRNM bleeds, and −0.013 lasting 2 days for minor bleeds.\textsuperscript{28,29} Even with the assumption of no impact on utility beyond 1 year for all categories of extracranial bleeds, results from the current study suggest that disutilities for all categories of bleeds from the patient’s perspective may be greater in magnitude than previously assumed. This could have an impact for the evaluation of net clinical benefit, comparative effectiveness, and cost-effectiveness evaluation of alternative anticoagulation strategies, for which chronic utility and temporary disutility weights are or might be used to combine different clinical events into a common metric.

Results from an analysis of data from the RE-LY trial examining the impact of therapy with dabigatran versus warfarin on health-state utility in patients with no major clinical events found no evidence to suggest that the relative complexity and inconveniences of management with warfarin versus dabigatran yielded any measurable decrement in health-state utility.\textsuperscript{30} The double-blind double-dummy design of the ENGAGE AF-TIMI 48 trial precluded us from exploring the impact of international normalized ratio monitoring and dose adjustment on QOL in our analysis.

**Study Limitations**

This study should be considered in light of several important limitations. The ENGAGE AF-TIMI 48 trial enrolled subjects with AF at medium or high risk of thromboembolic events, and excluded subjects with AF caused by a reversible disorder, severe renal dysfunction, a high risk of bleeding, and moderate or severe mitral stenosis. Our results may not apply to patients outside of the select enrolled trial population. The EuroQol 5 Dimension questionnaire is a simple, generic health status questionnaire, for which each of the 5 component domains is measured on a 3-level scale (indicating no problem, some or moderate problem, and extreme problem); as a result it may have limited ability to delineate minor but important clinical differences in health status. Despite adjustment for potential confounders in all models, there remains the possibility of unmeasured confounding. The exclusion of patients with no or limited QOL information might introduce the possibility of selection bias. Since we observed slightly more missing data in patients with a major gastrointestinal bleed, it is possible that the missing data could affect our results if the assumption of missing at random does not hold, though this seems unlikely given the high rate of QOL data collection across all bleeding categories and follow-up time points. This study considered only the first bleeding event within a patient; thus the results may not accurately relate to the impact of a second bleeding event of either the same or different type on health-state utility.

**Conclusions**

In summary, in this large-scale prospective study of patients with AF, we found that all categories of bleeding events were
associated with measurable immediate decreases in health-state utility. Major gastrointestinal and nongastrointestinal bleeds had relatively large immediate decrements, which decreased in magnitude over time and were no longer statistically significant at 12 months. CRNM and minor bleeding events were associated with smaller initial decrements in utility that remained statistically significant and relatively consistent in magnitude through 12 months after the bleeding event. Collectively, these findings have potential use in future studies of the net clinical benefit and cost-effectiveness of alternative strategies for stroke prevention in patients with AF.

Sources of Funding
The study was funded by a grant from Daiichi Sankyo, Inc.

Disclosures
Dr Kwong is an employee of Daiichi Sankyo. Dr Antman reports receiving grant support through his institution from Daiichi Sankyo. Dr Ruff reports receiving consulting fees from Daiichi Sankyo, Bristol-Myers Squibb, and Boehringer Ingelheim and grant support from his institution from Daiichi Sankyo. Dr Giugliano reports receiving consulting fees from Bristol-Myers Squibb, Daiichi Sankyo, Merck, Janssen Pharmaceuticals, and Merck; lecture fees from Bristol-Myers Squibb, Daiichi Sankyo, Merck, and Sanofi; and grant support through his institution from Daiichi Sankyo, Merck, Johnson & Johnson, Sanofi, and AstraZeneca. Dr Cohen reports receiving institutional grant support from Daiichi Sankyo. Dr Magnuson reports receiving institutional grant support and consulting fees from Daiichi Sankyo. The remaining authors have no disclosures to report.

References
Supplemental Material
Table S1. Demographic and clinical characteristics between patients in the study population and those excluded from analysis*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study population (N=10706)</th>
<th>Patients excluded (N=10399)</th>
<th>Standardized Difference (%)</th>
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<tbody>
<tr>
<td>Age, years, (mean ± SD)</td>
<td>70.6 ± 9.5</td>
<td>70.6 ± 9.3</td>
<td>0.8</td>
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<tr>
<td>Male</td>
<td>61.4</td>
<td>62.4</td>
<td>2.0</td>
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<tr>
<td>Previous use of vitamin K antagonist</td>
<td>59.1</td>
<td>58.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>36.7</td>
<td>35.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>55.1</td>
<td>49.6</td>
<td>11.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>94.9</td>
<td>92.3</td>
<td>10.8</td>
</tr>
<tr>
<td>Prior MI</td>
<td>11.6</td>
<td>11.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Prior Stroke</td>
<td>18.3</td>
<td>19.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Prior transient ischemic attack</td>
<td>12.4</td>
<td>10.9</td>
<td>4.7</td>
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<tr>
<td>Prior PAD</td>
<td>4.3</td>
<td>3.7</td>
<td>3.2</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>59.5</td>
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<td>8.2</td>
</tr>
<tr>
<td>Prior CAD</td>
<td>34.1</td>
<td>32.5</td>
<td>3.4</td>
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<tr>
<td>Prior CABG</td>
<td>8.0</td>
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<td>8.6</td>
</tr>
<tr>
<td>History of ICH bleed</td>
<td>0.1</td>
<td>0.2</td>
<td>1.6</td>
</tr>
<tr>
<td>History of non-ICH bleed</td>
<td>9.9</td>
<td>9.8</td>
<td>0.2</td>
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<tr>
<td>History of gastrointestinal bleed</td>
<td>3.2</td>
<td>2.8</td>
<td>8.1</td>
</tr>
<tr>
<td>Creatinine clearance in mg/dL, (mean ± SD)</td>
<td>78.6 ± 32.4</td>
<td>74.9 ± 30.4</td>
<td>11.8</td>
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<td>CHADS2 score (0-6) , (mean ± SD)</td>
<td>2.9 ± 1.0</td>
<td>2.8 ± 0.9</td>
<td>10.2</td>
</tr>
</tbody>
</table>

*All results are % of patients unless otherwise specified.

GI indicates gastrointestinal; CRNM, clinically relevant non-major; SD, standard deviation; PAD, peripheral arterial disease; CAD, coronary artery disease; CABG, coronary artery bypass graft; ICH intracranial hemorrhage, CHADS2, scoring system for the long-term risk of stroke in atrial fibrillation, acronym stands for Congestive heart failure, Hypertension, Age>75, Diabetes mellitus, and prior Stroke
Table S2. Quality of life compliance by bleeding status

<table>
<thead>
<tr>
<th>Time (month)</th>
<th>Major GI bleeding</th>
<th>Major non-GI bleeding</th>
<th>CRNM bleeding</th>
<th>Minor bleeding</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Event (N=207)</td>
<td>No event* (N=9801)</td>
<td>p-value</td>
<td>Event (N=1419)</td>
</tr>
<tr>
<td>3</td>
<td>100.0</td>
<td>100.0</td>
<td>1.000</td>
<td>100.0</td>
</tr>
<tr>
<td>6</td>
<td>86.5</td>
<td>93.9</td>
<td>&lt; 0.001</td>
<td>93.4</td>
</tr>
<tr>
<td>9</td>
<td>86.8</td>
<td>93.4</td>
<td>&lt; 0.001</td>
<td>91.3</td>
</tr>
<tr>
<td>12</td>
<td>89.7</td>
<td>93.8</td>
<td>0.015</td>
<td>93.2</td>
</tr>
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<td>100.0</td>
<td>84.6</td>
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* the sample sizes for the “no event” categories differ according to the category of bleed due to censoring at the time of events. All results are % of patients.

GI indicates gastrointestinal, CRNM, clinically relevant non-major
Appendix

The members of the Operations, Executive, Steering, Data Monitoring, Clinical Events Committees, countries, participating centers, Principal Investigators, and Primary Study Coordinators of the ENGAGE AF-TIMI 48 trial were as follows:

**Operations Committee:** TIMI Study Group, Brigham and Women’s Hospital, Boston, MA – E. Braunwald (Study Chair), E.M. Antman (Principal Investigator), R.P. Giugliano (Co-Principal Investigator), C.T. Ruff (Investigator), S.E. Morin (Director), E.B. Hoffman (Lead Biostatistician), S.A. Murphy (Biostatistician), N. Deenadayalu (Biostatistician), L. Grip (Project Director); **Sponsor** – Daiichi Sankyo Pharma Development, Edison, NJ – M. Mercuri (Vice President, Clinical Development), H. Lanz (Executive Director, Clinical Development), I. Patel (Executive Director, Clinical Development), V. Curt (Senior Director, Clinical Development), A. Duggal (Senior Director, Clinical Development), J. Hanyok (Senior Director, Clinical Development), J. Davé (Associate Director, Clinical Development), D. Morgan (Executive Director, Regulatory Affairs), Y. Choi (Senior Director, Clinical Safety), M. Shi (Senior Director, Biostatistics), J. Jin (Senior Biostatistician), J. Xie (Biostatistician); **Contract Research Organization** – Quintiles, Research Triangle Park, NC – M. Skinner (Global Operations Head), S. Patel (Project Director) J. Betcher (Biostatician), G. Selicato (Biostatician), C. Otto Jr. (Project Manager), C. Reissner (Clinical Director), K. Smith (Project Manager), J. Ostroske (Project Manager), A. Ron (Project Manager).

**Executive Committee:** TIMI Study Group, Brigham and Women’s Hospital, Boston, MA – E. Braunwald, E.M. Antman, R. P. Giugliano; **Daiichi Sankyo** – M. Mercuri; **Canada** – S. Connolly; **United Kingdom** – J. Camm; **United States** – M. Ezekowitz, J. Halperin, A. Waldo.

**Steering Committee:** Argentina – E. Paolasso (deceased); **Australia** – P. Aylward; **Belgium** – H. Heidbuchel; **Brazil** – J.C. Nicolau; **Bulgaria** – A. Goudev; **Canada** – D. Roy, J. Weitz; **Chile** – R. Corbalán; **China** – Y. Yang; **Colombia** – R. Botero; **Croatia** – M. Bergovec; **Czech Republic** – J. Špinar; **Denmark** – P. Grande, C. Hassager; **Estonia** – J. Voitk; **Finland** – H. Huikuri, M. Nieminen; **France** – J.J. Blanc, J.Y. LeHeuzey; **Germany** – V. Mitrovic; **Greece** – D. Alexopoulos; **Guatemala** – G. Sotomora; **Hungary** – R. Kiss; **India** – B. Somaraju; **Israel** – B. Lewis; **Italy** – P. Merlini, M. Metra; **Japan** – Y. Koretsune, T. Yamashita; **Mexico** – A. Garcia-Castillo; **Netherlands** – T. Oude Ophuis; **New Zealand** – H. White; **Norway** – D. Atar; **Peru** – M. Horna; **Philippines** – N. Babilonia; **Poland** – W. Ruzylo; **Portugal** – J. Morais; **Romania** – M. Dorobantu; **Russian Federation** – M. Ruda; **Serbia** – M. Ostojic; **Slovakia** – T. Duris; **South Africa** – A. Dalby; **South Korea** – N. Chung; **Spain** – J.L. Zamorano; **Sweden** – S. Juul-Möller; **Switzerland** – T. Moccetti; **Taiwan** – S.A. Chen; **Thailand** – P. Sritara; **Turkey** – A. Oto; **Ukraine** – A. Parkhomenko; **United Kingdom** – R. Senior.

**Data Monitoring Committee:** F. Verheugt (Chair), A. Skene (Statistician), J. Anderson, K. Bauer, J.D. Easton, S. Goto.

**Clinical Events Committee:** S. Wiviott (Chair), C. Lowe (Director), E. Awtry, C.J. Berger, K. Croce, A. Desai, E. Gelfand, W. Goessling, N.J. Greenberger, C. Ho, D.E. Leeman, M.S. Link, A.D. Norden, A. Pande, N. Rost, F. Ruberg, S. Silverman, A. Singhal, J.A. Vita.
Participating Countries, Centers, and Investigators (National Lead Investigator in Bold)

Argentina- 1059 subjects 58 centers

O Vogelmann, C Gonzalez, Hospital de Alta Complejidad Presidente Juan Domingo Peron, Formosa, FOR; R Ahuad Guerrero, M Rodriguez, Corporación Médica de Gral. San Martín S.A., San Martín, BUE; J Albisu, E Rosales, Instituto Cardiovascular de San Luis, San Luis, SLS; O Allall, M Reguero, Hospital Cordoba, Cordoba, CRD; C Alvarez, M Garcia, Hospital Italiano Regional del Sur, Bahia Blanca, BUE; S Ameriso, P Ameriso, Instituto de Investigaciones Neurologicas Raúl Carrea FLENI, Capital Federal, BUE; M Amuchastegui, M Caceres, Hospital Privado Centro Médico de Córdoba, Cordoba, CRD; J Beloscar, J Petrucci, Hospital Provincial del Centenario, Rosario, SFE; M Berli, M Berli, Cedir, Santa Fe, SFE; N Budassi, M Valle, Hospital Interzional General de Aguados Dr Jose Penna, Bahia Blanca, BUE; G Bustamante Labarta, M Saravia, Sanatorio Nuestra Señora del Rosario, San Salvador de Jujuy, JUJ; A Caccavo, V Fracaro, Clínica Coronel Suarez, Coronel Suarez, BUE; L Cartasegna, V Novas, Hospital Italiano de La Plata, La Plata, BUE; O Caruso, R Saa Zarandon, Hospital Central Mendoza, Mendoza, MEN; H Colombo, M Morandini, Clínica Colombo, Cordoba, CRD; J Cuello, M Rosell, Instituto de Investigaciones Clínicas - Bahia Blanca, Bahia Blanca, BUE; C Cuneo, M Bocanera, Hospital San Bernardo, Salta, SAL; A D’Amico, G Cendali, Cedin Clínica Privada, Ramos Mejia, BUE; R Dran, V Moreno, Centro de Salud Norte, Munro, Buenos Aires, BUE; C Estol, M Davolos, STAT Research, Ciudad Autonoma de Bs. As., CBA; A Facello, M Facello, Centro Privado de Tomografía Computada Cordoba S.A., Cordoba, CRD; E Falu, M Iriarte, Sanatorio del Carmen, Salta; F Femenia, M Arrieta, Hospital Español de Mendoza, Godoy Cruz, MEN; J Fuselli, A Zanotti, Cemic Saavedra, Ciudad Autonoma de Bs. As., CBA; J Gant Lopez, F Meiller, Hospital Aleman, Ciudad Autonoma de Bs. As., CBA; R Garcia Duran, D Perlo, Instituto de Investigaciones Clínicas San Nicolas, San Nicolas, BUE; M Garrido, C Ceirano, Clínica Privada Provincial S.A., Merlo Buenos Aires, BUE; G Giacomi, M Eden, Unidad de Cardiología Clinica, Mar del Plata, BUE; R Giannaula, M Huerta, Hospital Español, Buenos Aires, CBA; R Goicoechea, M von Wulffen, Hospital Jose Maria Ramos Mejia, Capital Federal, BUE; M Hominal, M Bianchini, Centro de Investigaciones Clínicas del Litoral SRL, Santa Fe, SFE; H Jure, D Jure, Clínica Chutro SRL, Cordoba, CRD; R Kevorkian, F Monaco, Hospital General de Aguados Donacion Francisco Santojanni, Capital Federal, CBA; G Lanternier, M Belcuore, Azira Clinical Research, Pergamino, BUE; G Liniado, M Iglesias, ALPI-Inst. de Rehabilitacion Marcelo Fitte, C.A.B.A., BUE; B Litvak, A Nigro, Servicios Hospitalarios San Justo S.A., Buenos Aires, BUE; J Llanos, S Vignau, Instituto de Investigaciones Clínicas de Rosario, Rosario, SFE; C Lorente, K Shatsky, Sanatorio Julio Corzo, Rosario, SJN; J Lotti, G Raimondi, Sanatorio Plaza, Rosario, SFE; I Mackinnon, M Carne, Instituto de Investigaciones Clínicas-Mar del Plata, Mar del Plata, BUE; O Manuale, M Calderon, Hospital Britanico de Buenos Aires, Capital Federal, CBA; J Marino, I Funes, Centro Medico Alcorta, Ciudad Autonoma de Bs. As., CBA; J Muntaner, H Gandur, Centro Mod de Cardiología, San Miguel de Tucuman; D Nul, E Verdini, Clinica Constituyentes, Moron, BUE; D Piskorz, A Tommasi, Sanatorio Britanico S.A., Rosario, SFE; G Povedano, E Casares, Complejo Medico de la PFA Churruca Vizca, CABA, CBA; D Pozzer, E Fernandez, Inst. de Cardiología de Corrientes Juana Francisca Cabral, Corrientes, COR; A Prado, C Venturini, Inves Clinicas Tucuman, San Miguel de Tucuman, TUC; H Ramos, S Navarrete, Clinica Privada Caraffa, Cordoba, CRD; M Rodriguez, M Alvarez, Clinica y Maternidad Colon SA, Mar del Plata, BUE; A Sanchez, L Bowen, Instituto Investigaciones Clinicas Cipolletti, Cipolletti, RIO; M Sanjurjo, O Codutti, Cordis-Instituto del Corazón, Resistencia, CHA; S Saravia Toledo, I Formoso, Instituto de Medicina Cenesa, Salta, SAL; J Schmidberg, A Goloboulicz, Instituto
Medico Aguero, Moron, BUE; P Schygiel, C Buzzetti, Clinica Instituto Medico Adrogue, Adrogue, BUE; P Severino, P Morara, Clinica Independencia, Munro, BUE; M Sosa Liprandi, M Teves, Sanatorio Guemes, Ciudad Autonoma de Bs As, BUE; M Vico, Y Morell, Instituto Investigaciones Clinicas Zarate, Zarate, BUE.

**Australia** - 102 subjects 13 centers
C Anderson, T Paraskevaidis, Royal Prince Alfred Hospital, Camperdown NSW, NSW; M Arstall, B Hoffmann, Lyell McEwin Hospital, Elizabeth Vale, SA; D Colquhoun, S Price-Smith, Core Research Group, QLD; D Crimmins, A Slattery, Central Coast Neuroscience Research, East Gosford, NSW; A Dart, S Kay, Baker Heart Research Institute, Melbourne, VIC; S Davis, G Silver, Royal Melbourne Hospital, Parkville, VIC; S Flecknoe-Brown, J Roberts, Broken Hill Hospital, Broken Hill, NSW; P Gates, S Jones, Geelong Hospital, Geelong, VIC; R Lehman, H Morrison, Adelaide Medical Research, Ashford, SA; M McKeirnan, J Li, Brisbane South Clinical Research Centre, Carina Heights, QLD; V Paul, C Batta, Royal Perth Hospital, Perth, WA; P Purnell, L Perrett, Joondalup Cardiovascular Trials Foundation, Joondalup, WA; G Szto, V O'Shea, Peninsula Private Hospital, Frankston, VIC.

**Belgium** - 149 subjects 15 centers
L Capiau, F Banaeian, Wetteren; J De Bleecker, K de Koning, AZ Sint-Lucas, Gent; M De Tollenaere, L De Bruyne, Sint Augustinusikliniek, Veurne; P Desfontaines, G Tincani, CHC - Cliniques de l'Espérance, Montegnée; H Heidbuchel, K Meeusen, UZ Leuven, Leuven; J Herzet, D Malmendier, Centre Hospitalier Régional de la Citadelle (Psychiatry), Liege; G Mairessé, M Raepers, Clinique Saint-Joseph, Arlon; J Parqué, N Clinckemaille, Parqué Jean-Luc, Mouscron; C Scavée, D Huyberechts, Cliniques Universitaires Saint-Luc, Bruxelles; D Stockman, C Jacobs, ZNA Middelheim, Antwerpen; Y Vandekerckhove, K Derycker, A.Z St. Jan, Brugge; J Vanwelden, J van Welden, A.Z Jan Palfijn, Merksem; G Vervoort, I Mestdagh, AZ Sint-Maarten - Campus Leopoldstraat, Mechelen; M Vrolix, C Beerts, Z.O.L - Campus St. Jan, Genk; B Wollaert, D Denie, ZNA Stuivenberg, Antwerpen.

**Brazil** - 707 patients 37 centers
A Amato Vincenzo de Paola, E Coutinho, Universidade Federal de Sao Paulo - UNIFESP, Sao Paulo, SP; P Andrade Lotufo, R Ferreira de Melo, Hospital Universitário da FMUSP, Sao Paulo, SP; J Atie, C Motta, SMO Brazil, Rio de Janeiro, RJ; F Augusto Alves da Costa, R Franchin Ferraz, FGM Clin Paulista de Doenças Cardio LTDA, Sao Paulo, SP; D Bertolim Precoma, E Sehnem, Hospital Angelina Caron, Campina Grande do Sul, PR; R Botelho, S Cunha, Instituto do Coração do Triângulo Mineiro, Uberlândia, MG; R Brondani, N Fleck, Hospital das Clinicas de Porto Alegre, Porto Alegre, RS; H Chaves Junior, J Silva, Hospital as Clinicas da Universidade Federal de Pernambuco, Recife, PE; C Costantini, D Barroso, Hospital Cardiologico Costantini, Curitiba, PR; M De Patra, V Pereira, Instituto de Cardiologia de Santa Catarina, San Jose, SC; N Duda, R Laimer, Hospital Sao Vicente de Paulo, Passo Fundo, RS; O Dutra, S Morgado, Instituto de Cardiologia do Rio Grande do Sul, Porto Alegre, RS; W Faustino Saporito, M Seroqui, Hospital Estadual Mario Covas- SP, Santo Andre, SP; L Ferreira, E Araújo, Instituto de Cardiologia do Distrito Federal, Brasília, DF; H Finimundi, C Daityz, Instituto de Pesquisa de Estudos Multicentricos, Caxias do Sul, RS; R Gagliardi, G Pereira, Santa Casa de Misericordia de Sao Paulo, Sao Paulo, SP; M Gomes, A Gomes, Clínicor - Hospital do Coracao de Alagoas, Maceio, AL; A Guimarães, L Ninho, Hospital Geral de Bonsucesso, Rio de Janeiro, RJ; C Jaeger, L Pereira, Hospital Mae de Deus, Porto Alegre, RS; J Jorge, C Cury, Santa Casa de Misericordia de Curitiba - PUCPR, Curitiba, PR; S Kaiser, A Almeida, CCBR Brasil, Rio de Janeiro, RJ; E Bittencourt, M Carreiro, Hospital de Clínicas da Universidade Federal de São Paulo, São Paulo, SP; V Moreira, E Almeida, Hospital das Clínicas da Universidade Federal de Uberlândia, Uberlândia, MG; H Correa, M Refúgio, Hospital Universitário de Uberlândia, Uberlândia, MG; R Colucci, E Meira, Hospital Regional de Uberlândia, Uberlândia, MG; D Vaz, J Mendonça, Hospital dos Proveedores de Uberlândia, Uberlândia, MG; M Carvalho, M Lopes, Hospital da Consolação, São Paulo, SP; S Ribeiro, E Azevedo, Hospital do Coração, São Paulo, SP; J Souza, M Faria, Hospital das Clínicas, São Paulo, SP; L Caires, M Vale, Hospital São Luiz, São Paulo, SP; F Bueno, H Marins, Hospital São Francisco, São Paulo, SP; L Andrade, H Almeida, Hospital São Joaquim, São Paulo, SP; G Souza, C Mussa, Hospital São José, São Paulo, SP; V Vilela, F Peres, Hospital São Lucas, São Paulo, SP.
Janeiro, RJ; C Kalil, G Radaelli, Hospital Sao Lucas - PUCRS, Porto Alegre, RS; W Kunz Sebba Barroso de Souza, K Morales, Via Médica - Centro Clinico, Goiania, GO; P Leaes, R Osorio Luiz, Santa Casa de Porto Alegre, Porto Alegre; J Pimenta Almeida, A Gozalo, Hospital do Servidor Publico Estadual de Sao Paulo, Sao Paulo, SP; G Reis, K Avellar, Santa Casa de Misericordia de Belo Horizonte, Belo Horizonte, MG; L Reis Katz Weiand, J Leipelt, Hospital Bruno Born, Lajeado, RS; J Rocha, R Barros, Hospital Centro Medico de Campinas, Campinas, SP; L Rodrigues, M Rubia Rocha, Encore Cardiologia e Radiologia Intervencionista, Aparecida de Goiânia, GO; A Rodrigues, D Rodrigues, ICM - Instituto do Coracao de Marilia, Marilia, SP; F Rossi dos Santos, L Goncalves Pagnan, Loema - Instituto de Pesquisa Clinica, Campinas, SP; R Sampaio, R do Val, Instituto do Coracao - Incor, Sao Paulo, SP; J Saraiva, C Vicente, Hospital Espanhol Salvador, Salvador, BA; S Zimmermann, E Burger Zimmermann, Clinica Procardio, Blumenau, SC.

**Bulgaria-** 520 patients 17 centers
B Chompalova, G Parishev, MHAT - Plovdiv AD, Plovdiv; S Denchev, N Milcheva, UMHAT Alexandrovskaya EAD, Sofia; T Donova, V Gergova, UMHAT Alexandrovskaya EAD, Sofia; B Georgiev, E Kostova, MHAT-National Heart Hospital EAD, Sofia; A Goudev, E Kinova, UMHAT Tzaritza Yoanna - ISUL EAD, Sofia; V Hergeldjieva, P Kamenova, MHAT - Ruse AD, Ruse; A Manolova, I Vasilev, MHAT - Haskovo AD, Haskovo; A Mihov, B Miteva, MHAT Sveti Ekaterina EOOD, Dimitrovgrad; V Mincheva, V Stoyanovski, UNMTHAT Tzar Boris III - Sofia, Sofia; F Nikolov, D Vasilev, UMHAT Sv. Georgi EAD, Plovdiv; G Pencheva, K Kostov, Fourth MHAT- Sofia AD, Sofia; S Petranov, T Milusheva, MHAT – Burgas AD, Burgas; A Popov, I Vasilev, Diagnostic Consultative Center Sveti Georgi EOOD, Varna; M Tzekova, M Kitova, E Manoylov, UMHAT Dr. Georgi Stranski EAD, Pleven.

**Canada-** 774 patients 54 centers
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Chile- 254 patients 14 centers

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China- 469 patients 33 centers

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1st Affiliated Hospital of Harbin Medical University, Harbin; ZQ Li, Y Liu, People's Hospital of Liaoning Province, Shenyang; DN Liao, XJ Gu, Changzheng Hospital, The Second Military Medical University, Shanghai; L Liu, ZH Lu, The People’s Hospital of Guangxi Zhuang Autonomous Region, Nanning; SM Ma, ZY Yang, Shengjing Hospital of China Medical University, Shenyang; DM Wang, SY Qi, Bethune International Peace Hospital, Shijiazhuang; GP Wang, XJ Shi, The First Hospital Affiliated to Liaoning Medical College, Jinzhou; M Wei, D Huang, Shanghai No.6 People's Hospital, Shanghai; SL Wu, YE Li, Guangdong Provincial People's Hospital, Guangzhou; JH Xu, JY Gu, Tong Ji Hospital of Tongji University, Shanghai; YM Xu, YZ Liang, The 2nd Hospital of Tianjin Medical University, Tianjin; K Yang, AY Li, The Third Xiangya Hospital of Central South University, Changsha; YJ Yang, X Zheng, Cardiovascular Institute & Fuwai Hospital Chinese Academy of Medical Sciences, Beijing; Y Zheng, M Gao, The First Hospital of Jilin University, Changchun; YH Yin, YP Xu, The Second Affiliated Hospital of Chongqing Medical University, Chongqing; B Yu, LL Li, The 2nd Affiliated Hospital of Harbin Medical University, Harbin; ZY Yuan, H Qiang, The 1st Hospital Affiliated to Xi'an Medical University, Xian; HQ Zhang, YN Lin, The 1st Affiliated Hospital of Wenzhou Medical College, Wenzhou; Z Zhang, H Kang, The 1st Hospital Affiliated to Lanzhou University, Lanzhou; RP Zhao, RJ Han, Baotou Central Hospital, Baotou; XL Zhao, JQ Wang, Beijing Tong Ren Hospital Affiliated to Capital Medical University, Beijing; ZQ Zheng, BG Li, The First Affiliated Hospital of NanChang University, Nanchang; SX Zhou, YL Zhang, The Second Affiliated Hospital of Zhongshan University, Guangzhou.

Colombia- 141 patients 11 centers
J Accini, M Accini, Consultorio Privado-Jose Luis Accini, Baranquilla; N Cano, L León Pineda, Hospital Santa Sofía, Manizales; J Delgado Restrepo, C Arroyave, Instituto Corbic, Medellín; R Fernández Ruiz, I Aldana Diaz, Clínica Cardiovascular Santa María, Medellín; H Hernandez, P Delgado, Instituto Corazon de Bucaramanga, Bucaramanga; C Jaramillo Muñoz, A Builes, Promotora Medica Las Americas SA, Medellín; F Manzur, E Rivera Rodriguez, Centro de diagnostico cardiologico Ltda, Cartagena; M Moncada Corredor, D Lopez Giraldo, Fundacion Centro de Investigacion Clinica CIC, Medellín; L Orozco Linares, J Fonseca, Foqus LTDA, Bogotá Cundinamarca; A Quintero, C Gonzales, Fundación del Caribe para la Investigación Biomédica, Barranquilla; G Sanchez Vallejo, I Perdomo Mejia, Centro de Estudios Clinicos del Quindio, Armenia.

Croatia- 127 patients 11 centers
J Bagatin, V Carevic, Clinical Hospital Centre Split, Split; S Car, M Jeric, General Hospital Varazdin, Varazdin; N Ciglenecki, S Tusek, Special Hospital for Medical Rehabilitation, Krapinske Toplice; J Ferri Ćertic, I Romic, General Hospital Dubrovnik, Dubrovnik; I Francetic, K Makar Ausperger, University Hospital Center Zagreb, Zagreb; V Jelic, S Jaksic Jurinjak, General Hospital Karlovac, Karlovac; A Knezevic, B Buksa, General Hospital Zadar, Zadar; P Samardzic, K Cvitkusic Lukenda, General Hospital Dr. J. Bencevic, Slavonski Brod; R Steiner, D Kirner, Clinical Hospital Osijek, Osijek; K Sutalo, Z Bakliza, General Hospital Dr.Tomislav Bardek, Koprivnica; H Vrazic, M Bergovec, T Lucijanic, University Hospital Dubrava, Zagreb.

Czech Republic- 1173 patients 39 centers
M Bar, P Brodova, Neurologicka ambulance Bormed, Ostrava- Trebovice; L Berka, V Kunkelova, Ordinace pro choroby srdece a cev, Jindrichuv Hradec; M Brtko, M Brtko, Fakultni nemocnice Hradec Králova, Hradec Královo; H Burianova, H Burianova, Poliklinika Humanitas, Bilovec; O Cermak, O Cermak, Nemocnice Slany, Slany; L Elbl, L Elbl, Kardiologicka

**Denmark- 219 patients 11 centers**

K Dodt, Horsens Sygehus, Horsens; H Christensen, L Christensen, Bispebjerg Hospital, København NV; C Hassager, A Loof, Rigshospitalet, København Ø; H Ibsen, H Madsen, Holbaek Sygehus, Holbaek; H Iversen, T Veng-Olsen, Glosstrup Hospital, Glosstrup; H Nielsen, R Olsen, Bispebjerg Hospital, København NV; K Overgaard, V Petrovic, Herlev Hospital, Herlev; I Raymond, D Rae, Frederiksberg Hospital, Frederiksberg; N Sand, A Svenningsen, Sydvestyds Sygehus Esbjerg, Esbjerg; C Torp-Pedersen, U Jakobsen, Gentofte Hospital, Hellerup; H Wiggers, K Serup-Hansen, Skejby Sygehus- Aarhus University Hospital, Aarhus N.

**Estonia- 191 patients 6 centers**

J Kaik, A Stern, Fertilitas AS, Haabneeme; R Kolk, R Kolk, Tartu University Hospital, Tartu; E Laane, L Rivis, Orthopaedic and Clinical Research Center, Tartu; M Paumets, J Voitk, M Laheläär, North Estonia Medical Centre Foundation, Tallinn; A Rosenthal, R Rajasalu, Tallinn; V Vahula, E Ratnik, Pärnu Hospital, Pärnu.

**Finland- 42 patients 7 centers**


**France- 110 patients 14 centers**

J Le Heuzey, Hôpital Européen Georges Pompidou, Paris, 75; B Agraou, F El Jarroudi, Centre Hospitalier Général, Valenciennes, 59; P Amarenco, P Boursin, Hopital Bichat, Paris, 75; D Babuty, M Boyer, Hospital Trousseau, Tours Cedex, 37; A Belhassane, F El Jarroudi, Centre
Hôpital de Cambrai, Cambrai, 59; H Berbari, H Berbari, Hôpital d'Instruction des Armees Percy, Clamart Cedex, 92; J Blanc, P Dias, Chu de Brest- Hôpital de la Cavale Blanche, Brest Cedex, 29; D Coisne, N Berger, Chu Poitiers- Hôpital de la Milètrie, Poitiers, 86; E Decoulx, M El Jarroudi, CH Chatiliez Tourcoing, Tourcoing, 59; S Dinanian, M Arfaoui, Hôpital Antoine Beclere, Clamart, 92; J Hermida, E Deruche, Centre Hospitalier Sud, Amiens, 80; S Kacet, S Corbut, Hospital Cardiologique Chru Lille, Lille Cedex, 59; J Poulard, S Leparree, Centre Hospitalier d'Abbeville, Abbeville, 80; R Roudaut, C Duprat, Hôpital du Haut l'Eveque (Cardiologie), Pessac, 33.

Germany- 913 patients 55 centers


Greece- 51 patients 7 centers
D Alexopoulos, E Mavronasiou, Patras University Hospital, Patra; P Bourlios, A Tziortziotis, General Prefectural Hospital of Trikala, Trikala; C Karamitsos, E Exarchou, General Hospital of Larissa, Larissa; K Kifnidis, A Daskalaki, General Hospital of Athens Asklipio Voulas, Athens; N Moschos, K Dimitra, General Hospital of Rhodes, Rhodes; C Olympios, E Kartasgkoulis, General Hospital of Elefsina Attikis Thriasio, Athens; V Pyrgakis, K Korantanis, General Hospital of Athens G. Gennimatas, Athens.

Guatemala- 136 patients 7 centers
O Ayau Milla, V de Leon Ramirez, Zacapa; I Guzman Melgar, T Jimenez, Edificio Plaza Dorada, Guatemala City; A Ovando Lavagnino, S Guevara, Liga del Corazon, Guatemala City; M Rodas Estrada, T Jimenez, Clinica Privada Dr. Rodas Estrada, Guatemala City; M Sanchez, J Mayen Pozuelos, CardioQuetzal, Quetzaltenango; C Sanchez Samayoa, L Guerra, Clinicas Hospital Centro Medico, Guatemala City; L Velasquez Camas, S Padilla Almaraz, Unicar, Guatemala.

Hungary- 464 patients 21 centers

India- 690 patients 65 centers
S Malhan, Sheth Vadilal Sarabhai Hospital and Municipal Medical College, Ahmedabad, Gujarat; J Abdullakutty, N.H., Lissie Hospital, Cochin, Kerala; D Agarwal, R Ranka, S. P. Medical College & Associated Group of Hospitals, Bikaner, Rajasthan; J Arneja, A Memon, Arneja Heart Institute, Nagpur, Mahara; V Arora, R Shree, Max Devki Devi Heart & Vascular Institute, New Delhi, Delhi; G Avvaru, A Shaikh, Yashoda Hospital, Hyderabad, Andh Prad; P Babu, B Rao, Dr. Ramesh Cardiac and Multi Speciality Hospital Ltd., Vijayawada, Andh Prad; R Babu, J Reddy, Medwin Hospital, Hyderabad, Andh Prad; D Banker, T Sheth, Banker’s Heart Institute, Vadodara, Gujarat; P Benjarge, S Surushe, Krishna Hospital & I. C. U., Aurangabad, Mahara; A Bharani, R Solanki, MGM Medical College and MY Hospital, Indore, Madh Prad; V Bhargava,
A Rathi, Care Hospital (Nagpur), Nagpur, Mahara; A Biniwale, M Bhuti, Biniwale Clinic, Pune, Mahara; N Calambur, B Somaraju, N Karnwal, Care Hospital, Hyderabad, Andh Prad; M Chopda, N Mali, Chopda Medicare & Research Centre, Nashik, Mahara; N Goyal, A Saini, Speciality Clinic, New Delhi, Delhi; J Gupta, P Singh, S. R. Kalla Memorial General Hospital, Jaipur, Rajasthan; S Hadan, P Savanth, Yenepoya Speciality Hospital, Mangalore, Karna; S Hardas, G Thakor, Ruby Hall Clinic, Pune, Mahara; J Hiremath, A Ghume, Poona Hospital and Research Centre, Pune, Mahara; R Jain, M Pahuja, CHL - Apollo Hospital, Indore, Madh Prad; S Joseph, D Oommen, Little Flower Hospital, Cochin, Kerala; J Joseph, R Thomas, Caritas Hospital, Kottayam, Kerala; H Joshi, Iby, Apollo Hospitals International Ltd., Gandhinagar, Gujarat; V Kale, N Raut, Lokmanya Hospital, Pune, Mahara; B Kandekar, S Kandekar, Nobel Hospital, Ahmednagar, Mahara; R Kishore, H Krishnan, Narayana Hrudayalaya Institute of Medical Sciences, Bangalore, Karna; V Kotiwale, V B, Kles's Dr. Prabhakar Kore Hospital and Med. Res. Centre, Belgaum, Karna; R Kulkarni, M Deokar, Moraya Multispeciality Hospital, Pune, Mahara; G Kulkarni, A Lawande, Shree Hospital, Pune, Mahara; P Kumar, M Karpuram, Osmania General Hospital, Hyderabad, Andh Prad; A Kumar, J Francis, Lakeshore Hospital and Research Centre, Cochin, Kerala; M Kumbla, A Anthony, Omega Hospital, Mangalore, Karna; P Lavhe, M Kale, Avanti Institute of Cardiology, Nagpur, Mahara; H Mardikar, P Bhaskarwar, Spandan Heart Institute, Nagpur, Mahara; A Mathur, P Sharma, Escorts Heart Institute & Research Centre, New Delhi, Delhi; J Menon, V Francis, Mar Augustine Golden Jubilee Hospital, Ernakulam, Kerala; D Namjoshi, S Shelke, Criti Care Hospital, Mumbai, Mahara; J Narendra, P J, S. A. T. Hospital, Shimoga, Karna; S Natarajan, V Francis, G. Kupuswami Naidu Memorial Hospital, Coimbatore, Tamilnadu; A Oomaan, P Gurusamy, Apollo Hospitals, Chennai, Tamilnadu; B P. R., J Angel, Frontier Lifeline & Dr. K.M. Cherian Heart Foundation, Chennai, Tamilnadu; M Padinhare Purayil, S Shams, West Fort Hi-Tech Hospital Ltd., Thrissur, Kerala; U Pandurangi, R Sababathi, Institute of Cardiovascular Diseases Madras Medical Mission, Chennai, Tamilnadu; P Parekh, B Jasani, Care Hospital, Surat, Gujarat; N Patki, A Babbar, Deenanath Mangeshkar Hospital and Research Centre, Pune, Mahara; B Pinto, H Kharalkar, Bandra Holy Family Hospital and Research Center, Mumbai, Mahara; R Premchand, H Jambula, Krishna Institute of Medical Sciences, Hyderabad, Andh Prad; M Rao, A Vuriya, Queen's NRI Hospital, Vishakhapatnam, Andh Prad; A Ravi Shankar, R E R, Mysore Medical College and Research Institute, Mysore, Karna; R Reddy, S Bekal, Mediciti Hospital, Hyderabad, Andh Prad; D Roy, A Barai, Rabindranath Tagore International Institute of Cardiac Scien, Kolkata, W Bengal; D Saha, R Gadeppalli, Nizam's Institute of Medical Sciences, Hyderabad, Andh Prad; H Sant, D Jadhav, Medipoint Hospital Pvt Ltd, Pune, Mahara; M Sarna, T Arora, Monilek Hospital and Research Centre, Jaipur, Rajasthan; J Sawhney, R Singh, Dharmavira Heart Centre, New Delhi, Delhi; K Sethi, N Bansal, Delhi Heart and Lung Institute, New Delhi, Delhi; A Sethia, S Sethia, Indore, Madh Prad; G Shetty, R Sudheer, St.John’s Medical College and Hospital, Bangalore, Karna; G Singh, R Gupta, Dayanand Medical College and Hospital, Ludhiana, Punjab; A Srinivas, V G, Vikram Hospital & Heart Care, Mysore, Karna; A T.P., L thankaraj, Sri Gokulam Heart Centre, Trivandum, Kerala; S Varma, A Kaur, Sadbhavna Medical and Heart Institute, Patiala, Punjab; M Vijan Vinod, B Thakur, Vijan Cardiac Center, Nashik, Mahara; I Zanwar, A Dharmaraao, Hardas Heart Centre, Pune, Mahara.

Israel- 283 patients 20 centers
S Atar, E Lasri, Western Galilee Hospital- Nahariya, Nahariya; D Dicker, D Marcovicu, Rabin Medical Center, Petach Tikva; M Elias, G Avraham Ron, HaEmek Medical Center, Afula; a Francis, R Ghantous, Holy Family Hospital, Nazareth; A Goldhaber, M Goldhaber, Shuali Community Clinic- Clalit Health Services, Ra’anana; S Gottlieb, S Rouwaida, Bikur Cholim
Hospital, Jerusalem; E Grossman, T Dagan, Chaim Sheba Medical Center, Tel-Hashomer; Y Hasin, M Roshrosh, Poriya Government Hospital, Tiberias; T Hayek, A Majdoub, Rambam Health Care Campus, Haifa; E Klainman, I Genin, Gefen-Cardiac Center, Givatayim; M Lahav, T Gilat, Rabin Medical Center, Petach Tikva; B Lewis, M Ben Ari, The Lady Davis Carmel Medical Center, Haifa; M Lishner, M Karny, Sapir Medical Center Meir Hospital, Kfar Saba; E Ouzan, H Givoni, Hadassah University Hospital- Ein Kerem, Jerusalem; Y Rozenman, S Logvinenko, Wolfson Medical Center, Holon; E Schiiff, J Sterlin, Bnai Zion Medical Center, Haifa; M Shochat, I Aloni, Hillel Yaffé Medical Center, Hadera; M Swissa, V Belatsky, Kaplan Medical Center, Rechovot; D Tsalihin, D Kisos, Ben Yair Community Clinic- Clalit Health Services, Beer-Sheva; D Zeltser, N Platner, Tel-Aviv Sourasky Medical Center, Tel-Aviv.

**Italy- 169 patients 24 centers**

A Berni, F Giovannelli, Azienda Ospedaliera Sant Andrea, Roma, RM; G Boriani, E Cervi, Ospedale S. Orsola-Malpighi, Bologna; G Comi, L Peruzzotti, Fondazione San Raffaele del Monte Tabor, Milano, MI; C Cuccia, C Forgione, Fondazione Poliambulanza Istituto Ospedaliero, Brescia, BS; R De Caterina, D De Pace, Azienda Ospedaliera Universitaria G. D'Annunzio, Chieti, CH; S De Servi, M Mariani, A.O. Ospedale Civile di Legnano, Legnano, MI; A Di Lenarda, C Mazzone, ASS I Triestina, Trieste, TS; G Di Pasquale, M Di Niro, Ospedale Maggiore C.A. Pizzardi, Bologna, BO; L Fattore, B Bosco, Ospedale San Giuseppe e Melorio, Santa Maria Capua Vetere, CE; V Grassia, E Murena, Ospedale Santa Maria Delle Grazie, Pozzuoli, NA; Laffi, G Gaggioli, Azienda Ospedaliera Villa Scassi, Genova, GE; G Lo Pinto, F Raggi, Ente Ospedaliero Ospedali Galliera, Genova, GE; P Marino, F Francalacci, A.O. Maggiore della Carità di Novara, Novara, NO; P Merlini, M Babbolin, Azienda Ospedaliera Ospedale Niguarda Cà Granda -2, Milano, MI; M Metra, M Bulgari, Spedali Civili di Brescia, Brescia; M Penco, E Lioy, Policlinico Casilino, Roma, RM; P Perrone Filardi, C Marciano, Università degli Studi di Napoli-Federico II, Napoli, NA; S Pirelli, G Paradiso, Azienda Ospedaliera Istituti Ospitalieri di Cremona, Cremona, CR; G Piseddu, L Fenu, Ospedale Ss. Annunziata Az. USL 1, Sassari, SS; A Raisaro, K Granzow, IRCCS Policlinico San Matteo, Pavia, PV; M Rausa, C Cannes, Università La Sapienza-Ospedale Sant Andrea, Roma, RM; S Severi, M Breschi, Ospedale della Misericordia, Grosseto, GR; V Toschi, M Gagliano, A.O. Ospedale San Carlo Borromeo, Milano, MI; V Zacà, F Furiozzi, A.O.U. Senese Policlinico Santa Maria alle Scorte, Siena, SI.

**Japan- 1010 patients 99 centers**

T Hirahara, U Akihisa, W Masaki, Kumamoto University Hospital, Kumamoto-shi Kumamoto; M Ajioka, C Matsushita, Tosei General Hospital, Seto-shi Aichi-ken; T Anzai, K Mino, NHO Hakodate National Hospital, Hakodate-shi Hokkaido; S Arakawa, A Tsukimine, JHWO Kyushu Rosai Hospital, Kitakyushu-shi Fukuoka; H Endo, M Fujiwara, Clinic Horikawa, Kyoto-shi Kyoto; K Fujii, S Kozeni, Watanabe Igakukai Sakurabashi Watanabe Hospital, Osaka-shi Osaka; E Fujii, M Kotera, Mie University Hospital, Tsu-shi Mie; S Fujimoto, K Omae, Nippon Steel Yawata Memorial Hospital, Kitakyushu-shi Fukuoka; K Fujimoto, Y Ichishita, NHO Kumamoto Medical Center, Kumamoto-shi Kumamoto; T Fujita, Y Ito, Nagaoka Red Cross Hospital, Nagaoka-shi Niigata; S Fukamizu, J Harada, Tokyo Metropolitan Hiroo Hospital, Shibuya-ku Tokyo; N Fukuda, C Fujimoto, NHO Zentsuji National Hospital, Zentsuji-shi Kagawa; T Funazaki, A Yamaguchi, Saiseikai Kawaguchi General Hospital, Kawaguchi-shi Saitama; Y Furukawa, C Kamitake, Kobe City Medical Center General Hospital, Kobe-shi Hyogo; N Hagiwara, M Nagaruma, Tokyo Women's Medical University Hospital, Shinjuku-ku Tokyo; S Harai, S Kumagai, Iida Hospital, Iida-shi Nagano; K Harada, Y Fuki,
Tokyo Metropolitan Geriatric Hospital, Itabashi-ku Tokyo;  T Haruna, Y Nakahara, TazukeKoufukai Igakuenkyuyo Kitano Hospital, Osaka-shi Osaka;  Y Hashimoto, Y Shimazu, Tesshokai Kameda Clinic, Kamogawa-shi Chiba;  Y Hiasa, Y Oga, Tokushima Red Cross Hospital, Komatsushima-shi Tokushima;  T Higashikata, Y Nakagawa, Komatsu Municipal Hospital, Komatsu-shi Ishikawa;  A Hirayama, A Kawaguchi, Nihon University Itabashi Hospital, Itabashi-ku Tokyo;  Y Iesaka, C Miyamoto, Tsuchiura Kyodo General Hospital, Tsuchiura-shi Ibaraki;  T Iijima, K Higuchi, Fujioka General Hospital for outpatient, Fujioka-shi Gunma;  H Ino, H Noguchi, Kanazawa University Hospital, Kanazawa-shi Ishikawa;  T Inomata, K Nakamura, Kitasato University Hospital, Sagamihara-shi Kanagawa;  Y Ishibashi, T Nozaki, Iwate Medical University Hospital, Morioka-shi Iwate;  Y Ishii, H Tomita, Asahikawa City Hospital, Asahikawa-shi Hokkaido;  S Ishimaru, M Ise, Hokkaido Social Insurance Hospital, Sapporo-shi Hokkaido;  K Itamoto, T Ito, Teine Keijinkai Hospital, Sapporo-shi Hokkaido;  Y Ito, M Onishi, TOYOTA Memorial Hospital, Toyota-shi Aichi;  K Iwade, Y Sakuma, NHO Yokohama Medical Center, Yokohama-shi Kanagawa;  T Iwasaki, H Nagatome, Cardiovascular Hospital of Central Japan, Shibukawa-shi Gunma;  S Kinoki, C Adachi, Otaru Kyoikai Hospital, Otaru-shi Hokkaido;  S Kamakura, F Nakahara, National Cerebral and Cardiovascular Center, Suita-shi Osaka;  M Kamijo, S Iida, Chubu Rosai Hospital, Nagoya-shi Nagoya;  K Kamiyama, R Fujii, Iijinkai Nakamura Memorial Hospital, Sapporo-shi Hokkaido;  K Kato, A Ishida, JLWHO Yokohama Rosai Hospital, Yokohama-shi Kanagawa;  Y Kazatani, Y Ichikawa, Ehime Prefectural Central Hospital, Matsuyama-shi Ehime;  H Kitazawa, C Igarashi, Tachikawa General Hospital, Nagoaka-shi Niigata;  Y Kobayashi, R Kikuchi, Showa University Hospital, Shinagawa-ku Tokyo;  M Kohno, S Tamura, Kagawa University Hospital, Kita-gun Kagawa;  Y Koretsune, I Yamoto, NHO Osaka National Hospital, Osaka-shi Osaka;  M Kurabayashi, E Koya, Gunma University Hospital, Maebashi-shi Gunma;  T Masuyama, Y Kaneno, Hyogo College of Medicine Hospital, Nishinomiya-shi Hyogo;  K Matsuda, E Ebina, MATSUDA Med Clinic, Sapporo-shi Hokkaido;  H Meno, M Satake, Japanese Red Cross Fukuoka Hospital, Fukuoka-shi Fukuoka;  T Mita, M Takeda, Mita Medical-Cardiovascular Clinic, Sapporo-shi Hokkaido;  N Miyamoto, T Kimizu, Saino Clinic, Tokorozawa-shi Saitama;  Y Miyachi, S Sakamoto, Nippon Medical School Hospital, Bunkyo-ku Tokyo;  M Munemasa, J Murata, NHO Okayama Medical Center, Okayama-shi Okayama;  Y Nagai, Y Sakata, Rinku General Medical Center, Izumi-shi Osaka;  S Naito, H Oya, Gunma prefectural Cardiovascular Center, Maebashi-shi Gunma;  Y Nishi, T Nagase, Seiwakai Nagata Hospital, Yanagawa-shi Fukuoka;  Y Ochiai, H Junko, Nagoya Ekisaikai Hospital, Nagoya-shi Nagoya;  T Ogawa, M Sugeno, Fukushima Koseikai Fukushima Dai Hospital, Fukushima-shi Fukushima;  H Oguro, M Tanabe, Shimane University Hospital, Izumo-shi Shimane;  K Okada, Y Moriyama, Ohda Municipal Hospital, Ohda-shi Shimane;  K Okajima, M Nakashima, Hyogo Brain and Heart Center, Himeji-shi Hyogo;  O Okazaki, H Wada, National Center for Global Health and Medicine Hospital, Shinjuku-ku Tokyo;  K Okishige, S Kitani, Yokohama City Minato Red Cross Hospital, Yokohama-shi Kanagawa;  K Okumura, Y Narita, Hirosaki University School of Medicine & Hospital, Hirosaki-shi Aomori;  H Onaka, H Moriyama, Takatsuki Red Cross Hospital, Takatsuki-shi Osaka;  Y Ozaki, I Tanikawa, Fujita Health University Hospital, Toyoake-shi Aichi;  S Sakagami, A Nakano, Kanazawa Medical Center, Kanazawa-shi Ishikawa;  S Sakuragi, N Hayashi, NHO Ikwanuki Clinical Center, Iwakuni-shi Yamaguchi;  S Sakurai, H Ooki, Aizawa Hospital, Matsumoto-shi Nagano;  T Sasaki, N Oosawa, NHO Takasaki General Medical Center, Takasaki-City Gunma;  A Satoh, E Fujimoto, Shunkaihakai Nagasaki Kita Hospital, Nishinogigu-gun Nagasaki;  Y Seino, M Narumi, Nippon Medical School Chiba Hokushoh Hospital, Inzai-shi Chiba;  T Shirai, M Shigenari, Tokyo Metropolitan Police Hospital, Nakano-ku Tokyo;  Y Shoji, J Ueda, Makabe Hospital, Higashimatsushima-shi Miyagi;  K Sugi,
Mexico- 190 patients 13 centers
E Bayram Llamas, A Hurtado, Fundacion Cardiovascular de Aguascalientes A.C, Aguascalientes, AGS; C Calvo Vargas, M Cedano Limon, Unidad de Investigacion Medica, Guadalajara, JAL; E Cardona Munoz, S Hernandez, ICLE S.A., Guadalajara, JAL; J Carrillo, T Delgadillo, Hospital Central Dr. Ignacio Morones Prieto, San Luis Potosi, SLP; M Casares Ramirez, J Franco Valles, Hospital General de Durango, Durango, DGO; N Garcia, M Alcantara Colin, Hospital Mocel, Mexico City, DF; A Garcia-Castillo, A Jaramillo, Cardiolink, Monterrey, NL; J Leiva-Pons, S de la Mora, Hospital Lomas de San Luis, San Luis Potosi, SLP; G Llamas Esperon, A Grajales, Hospital Cardiologica Aguascalientes, Aguascalientes, AGS; G Mendez-Machado, H Avila, Hospital Angeles Xalapa, Xalapa, VER; L Nevarez Ruiz, G Magallanes, Hospital CIMA Chihuahua, Chihuahua, CHIH; C Sanchez Diaz, A Ortiz, Unidad de Investigacion Clinica en Medicina S.C., Monterrey, NL; R Velasco Sanchez, E Moran Velazquez, Hospital General Dr. Angel Leano, Zapopan, JAL.

Netherlands- 153 patients 10 centers
M Alhakim, I van Welsen, Flevoresearch, Almere; T Bruning, A Jones, Maasstad Ziekenhuis Zuider, Rotterdam; C Buiks, C Buiks, Huisartsenpraktijk Buiks, Ewijk; J de Groot, I Radder, Academisch Medisch Centrum, Amsterdam; R de Vos, R de Vos, Huisartsenpraktijk de Vos, Dordrecht; R Hazeleger, R Daniels, VieCuri Medisch Centrum Venlo, Venlo; B Kietseelaer, LMuijs, Maastricht University Medical Center, Maastricht; H Mannaerts, E Kooiman, Ziekenhuis Amstelland, Amstelveen; H Mevissen, H Mevissen, Huisartsenpraktijk Westerhave, Wildervank; D van der Heijden, H Hofmeyer, Rijnland Ziekenhuis Leiderdorp, Leiderdorp.
New Zealand- 131 patients 10 centers
R Anscombe, T O'Meeghan, M Kjentjes, Hutt Valley Health Hospital, Lower Hutt; J Benatar, H White, L Borthwick, Auckland City Hospital, Auckland; R Doughty, M Copley, Auckland City Hospital, Auckland; R Fisher, R Monkley, Waikato Hospital, Hamilton; B Green, D Scott, Dunedin Hospital, Dunedin; A Hamer, J Tomlinson, Nelson Hospital, Nelson; H Hart, A Turner, North Shore Hospital, Auckland; D Scott, R Cammell, Middlemore Hospital, Otahuhu; R Troughton, L Skelton, Christchurch Hospital, Christchurch; C Young, K Kennett, P3 Research Limited (Tauranga), Tauranga.

Norway- 34 patients 4 centers

Peru- 173 patients 11 centers
G Bustamante, M Tejada Guillen, Clinica San Borja, Lima 41; J Cabrera, R Esteves Mendoza, Clínica Vésalio, Lima; C Chavez, C Luna, Hospital Nacional Daniel Alcides Carrion, Callao; J Lema, A Carrion, Hospital Nacional Arzobispo Loayza, Lima; N Llerena, S Araoz Bedregal, Consultorio Privado Dr. Nassil Llerena Navarro, Arequipa; F Medina Palomino, J Rodriguez, Clinica Medica Cayetano Heredia, Lima; J Minchola, C Bautista, Clinica San gabriel, Lima; S Negron Miguel, B Honores Armas, Centro Medico Naval Cirujano Mayor Santiago Tavara, San Borja; A Rodriguez, N Romero, Hospital Nacional Alberto Sabogal Sologuren, Callao; P Torres, K Fernandez Rodriguez, Consultorio Privado Dr Pedro Torres, Arequipa; P Yanac Chavez, M Horna, S Delgado, Hospital Alberto Sabogal Sologuren, Callao.

Philippines- 125 patients 8 centers
N Babilonia, CM Sambaz, Philippine Heart Center, Quezon; R Barcinas, M Zapanta, Alexian Brothers Health and Wellness Center, Davao; R Coching, M Vallenas, Davao Doctors Hospital, Davao; G Matiga, C Enad, Perpetual Succour Hospital - Cebu, Cebu; G Rogelio, F Joaquin, St. Luke's Medical Center, Quezon; A Roxas Jr., L Gilo, The Medical City, Pasig; R To, M Aquino, The Medical City, Pasig; L Villamor, K Nario, Cebu Doctors’ University Hospital, Cebu.

Poland- 1278 patients 49 centers
Portugal—180 patients 10 centers
F Matias, Cruz Vermelha Portuguesa- Sociedade de Gestão Hospitalar SA, Lisboa; J Correia, J Correia, Hospital de Santo André EPE, Leiria; V Gil, S Lopes, Hospital Fernando da Fonseca (Amadora Sintra), Amadora; J Madeira, D Maymone, Hospital de São Bernardo, Setúbal; D Martins, E Neves, Hospital do Divino Espírito Santo, Ponta Delgada; P Monteiro, D Oliveira, Hospitais da Universidade de Coimbra, Coimbra; P Monteiro, A Leitão Marques, C Castro, Centro Hospitalar de Coimbra, Coimbra; A Salgado, A Gonçalves, H. Sao Marcos, Braga; O Santos, L Veiga Pais Nunes, H Sao Teotonio, Viseu; J Santos, D Soares, Hospital Infante D. Pedro S.A., Aveiro.

Romania—410 patients 23 centers
P Albulescu, M Ciortea, Spitalul Clinic Judetean de Urgenta Ilfov, Bucuresti; E Apetrei, C Matei, Institutul de Boli Cardiovasculare Prof. Dr. C.C. Iliescu, Bucuresti; D Bartos, E Badila, Spitalul Clinic de Urgenta Floreasca Bucuresti, Bucuresti; C Bengus, V Ochean, Spitalul Judetean de Urgenta Sf. Pantelimon Focsani, Focsani; E Bobescu, B Doka, Spitalul Clinic Judetean de Urgenta Brasov, Brasov; F Bolohan, F Bolohan, Centrul Clinic de Urgenta de Boli Cardiovasculare al Armatei, Bucuresti; G Ciobotaru, M Andor, Centrul Medical Privat
Russian Federation- 1151 patients 66 centers

M Ruda, N Zhukova, FSBI Russian Cardiology Research and Production Complex, Moscow; G Arutyunov, T Chernyavskaya, Russian State Medical University, Moscow; M Ballyuzek, L Alexandrova, St-Petersburg Clinical Hospital of Russian Academy of Science, Saint-Petersburg; O Barbarash, A Bashkireva, MIH Kemerovo Cardiology Dispensary, Kemerovo; B Bart, V Larina, SBEU Russia National RMU n.a. N.I. Pirogov of MoH of RF, Moscow; D Belenky, Y Kosolapov, SBIH of Novosibirsk Region Clinical Emergency Hospital 2, Novosibirsk; S Berns, E Yukhno, SI SRI of Complex Problems of Cardio-Vascular Diseases of SB, Kemerovo; I Bokarev, T Khlevchuk, Moscow City Clinical Hospital 20, Moscow; G Chumakova, O Pokutneva, TSIH Altay Territorial Cardiology Dispensary, Barnaul; A Demko, A Masin, Dep. Clin. Hosp. on Station Kemerovo of OAO Russian Railway, Kemerovo; P Dovgalevsky, N Puchinaya, Saratov Institute of Cardiology, Saratov; O Drapkina, E Zyatenkova, First Moscow State Medical University n.a. I.M. Sechenov, Moscow; L Egorova, L Egorova, StP SHI Clinical hospital of St. Luka, Saint-Petersburg; V Esip, N Kirichek, St. Petersburg State Healthcare Institution Diagnostic Cent, St. Petersburg; A Filatov, I Soin, State healthcare facility Tula Regional Hospital, Tula; O Gilinskaya, E Valuyshkih, SI SRI of Physiology SB RAMS, Novosibirsk; M Glezer, S Valovyeva, SBHI City Clinical Hospital 59 of HD of city of Moscow, Moscow; S Golitsyn, T Kratskina, FSBI Russian Cardiology Research and Production Complex, Moscow; B Goloshchekin, I Laptev, St-Petersburg SIH City Hospital 15, St-Petersburg; N Gratsiansky, O Mazovets, SIH of Moscow City Clinical Hospital 29 n.a. Baymana, Moscow; Y Karpov, V Buza, FSBI Russian Cardiology Research and Production Complex, Moscow; Y Karpov, B Kosenko, Emergency Medical Care Hospital 1, Voronezh; V Khirmanov, I Kireenkov, All-Russian Center of Emergency and Radiation Medicine MCRS, St-Petersburg; A Khokhlov, O Sinitsina, Municipal MI Clinical Hospital 2, Yaroslavl; R Khoklov, E Tsareva, Voronezh regional clinical hospital 1 Interregional cardio, Voronezh; O Khrustalev, A Khrustalev, Yaroslavl Regional SBHI Regional Clinical Hospital, Yaroslavl; V Kostenko, S Karabaliaeva, St. Petersburg SHI City Polyclinic 109, St. Petersburg; N Koziolova, E Polyanskaya, SHI Perm Regional Hospital of War Veteran’s, Perm; O Kozyrev, O Kostenko, Smolensk State Medical Academy of Roszdrav, Smolensk; V Kuznetsov, A Rychkov, SRI of Cardiology of SB of RAMS br Tumen cardiology Center, Tumen; O Lavrova, L Tereschenko, Pavlov State Medical University of St.Petersburg, St. Petersburg; S Levashov, E Volkova, SBHI Regional Clinical Hospital 3, Chelyabinsk; R Libis, A Maslova, Orenburg State Medical Academy of RosZdrav, Orenburg; I Libov, Y Moiseeva, City Clinical Hospital named after S.P.Botkin, Moscow; A Lila, L Belousova, SBEI HPE NWSMU n.a.I.I.Mechnikov MoH RF, St.
Petersburg; Y Lukyanov, D Lamden, SEIHPE SPb SMU n.a. Pavlov affiliate 1 of FAHSD, St. Petersburg; K Nikolaev, A Nikolaev, SBIH of Novosibirsk Region City Clinical Hospital 19, Novosibirsk; I Nikolskaya, O Khromova, MBHI of Novosibirsk City Clinical Hospital 25, Novosibirsk; N Novikova, S Patrusheva, Central Clinical Hospital of Siberian branch of RAOS, Novosibirsk; E Panchenko, P Laguta, FSBI Russian Cardiology Research and Production Complex, Moscow; A Panov, R Nikl, FSI FC of Heart Blood and Endocrinology n.a. Almazov, St. Petersburg; E Polkanova, I Matveeva, SHI Center of Occupational Pathology, St-Petersburg; N Poluyanova, N Pikalova, FSI Outpatient Clinic 3 President of RF, Moscow; T Raskina, M Letaeva, SBHII of Kem. Regional Clinical Hospital for War Veterans, Kemerovo; A Rebrov, N Karoli, SEIHPE Saratov State Medical University, Saratov; M Repin, N Rodina, LLC Institute of Medical Investigations, St. Petersburg; I Shaposhnik, E Lebedev, City Hospital 1, Chelyabinsk; Z Shogenov, M Agirov, CityClinicalHospital81, Moscow; B Sidorenko, S Vorontsova, FSD ESMC of GMD of the president of RF Central Clinical Hospital, Moscow; I Sinitsina, V Orlov, M Golshmid, RMA of Post Graduate Education of MoH and SD of RF, Moscow; Z Sizova, N Lapidus, State Healthcare Institution of city of Moscow Cardiologic, Moscow; K Sobolev, S Erofeeva, City Clinical Hospital No.61, Moscow; E Suprun, D Dronov, Municipal Healthcare Institution MedicoInstitutionalMedicosanitaryUnit 9, Omsk; N Tarasov, L Isaak, FGHI MSU of the MoA of the RF for the Kemerovo Region, Kemerovo; S Tereshenko, I Kositsyna, Moscow State Medico-stomat. Hospital University City Hospital 68, Moscow; E Tikhonova, A Solovyev, JSC Med. Scient. Production Association Clinic Dvizhenie, Volgograd; A Timofeev, S Bulygin, MIH City Hospital 1, Barnaul; S Ustyugov, M Rossosyakaya, MBHI City Clinical Emergency Hospital n/a N.S. Karpovich, Krasnoyarsk; A Vishnevsky, A Krigizova, SPb SIH Pokrovskaya City Hospital, St-Petersburg; D Volkov, N Rodina, Medical Institute on Krestovsky, St. Petersburg; V Yakusevich, A Petrochenko, SHI Clinical Hospital for Emergency Medical Care n.a N.V. Solovyev, Niska Banja; S Yakushin, N Nikulina, Ryazan Regional Clinical Cardiology Dispensary, Ryazan; D Zateyshchikov, I Zotova, SBIH of city of Moscow City Hospital 17, Moscow; A Zateyshchikova, B Mankhaeva, SBHI City Clinical Hospital 51 of Hd of Moscow city, Moscow; S Zenin, O Kononenko, SBIH Novosibirsk Regional clinical cardiology Dispensary, Novosibirsk; G Zubeeva, I Motylev, Municipal Medicoprophylactic Institution City Hospital 33, Nizhny Novgorod.

Serbia- 277 patients 14 centers
S Apostolovic, D Djordjevic-Radojkovic, Clinical Center of Nis, Nis; V Celic, A Majstorovic, Clinical Center Dragisa Misovic, Belgrade; N Cemerlic Adjic, M Bjelobrk, Institute of Cardiovascular Diseases Sremska Kamenica, Sremska Kamenica; N Despotovic, P Erceg, Clinical Center Zvezdara, Belgrade; S Ilic, B Ilic, Institute for Treatment and Rehabilitation Niska Banja, Niska Banja; M Krotin, A Djokovic, Clinical Center Bezanijska Kosa, Zemun; V Miloradovic, I Djokic, Clinical Center Kragujevac, Kragujevac; P Otasevic, N Tasic, Dedine Cardiovascular Institute, Belgrade; T Potpara, M Polovina, Clinical Center of Serbia, Belgrade; B Putnikovic, T Kalezic, Clinical Center Zemun, Zemun; P Seferovic, I Milinkovic, Institute of CV Disease Clinical Center of Serbia, Belgrade; D Tavciiovski, Z Davicevic, Military Medical Academy, Belgrade; Z Vasiljevic-Pokrajic, P Mitrovic, Clinical Center of Serbia, Belgrade; B Vujisic Tesic, M Ostojic, M Tesic, Institute of CV Diseases Clinical Center of Serbia, Belgrade.

Slovakia- 405 patients 15 centers
V Ambrovicova, I Ambrovic, CELL B s.r.o., Levice; A Banikova, A Banikova, Kardiomed s.r.o., Lucenec; A Dukat, V Kosmalova, Univerzitna nemocnica Bratislava Nemocnica Stare Mesto, Bratislava; K Dulkova, T Dulka, Kardiovaskularne centrum s.r.o., Bratislava; T Duris, L
Vankova, FNsP Nove Zamky, Nove Zamky; A Dzupina, M Dzupinova, Alian s.r.o., Bardejov; K Hatalova, R Hatala, Cardioconsult s.r.o., Bratislava; M Hranai, J Hofmanova, Kardiocentrum Nitra s.r.o., Nitra; V Kasperova, A Reptova, Univerzitna nemocnica Bratislava Nemocnica Stare Mesto, Bratislava; J Mazur, J Mazur, Kardioonkologia s.r.o., Dolny Kubin; D Pella, J Fedacko, Cardio D&R s.r.o., Kosice; L Ruffini, J Morsky, Nestatna kardiologicka ambulancia, Rimavská Sobota; M Slanina, J Kmec, FNsP J. A. Reimana, Presov; A Zachar, M Kokles, Univerzitna nemocnica Bratislava Nemocnica ak. L. Derera, Bratislava; P Zareczky, D Bollova, Cardio s.r.o., Galanta.

South Africa- 277 patients 15 centers
J Badenhorst, L Erasmus, Unitas Hospital, Lyttelton, Gauteng; M Basson, M Poynton, Tierveli Trial Centre, Belville, W Cape; A Dalby, J Allman, Millpark Hospital, Parktown West, Gauteng; G Ellis, L Botha, Helderberg Clinical Trials, Somerset West Western Cape, W Cape; J Engelbrecht, M Mostert, Somerset West, W Cape; M Essop, T Nunkoo, Chris Hani Baragwanath Hospital, Diepkloof, Gauteng; M Gani, L Wilson, GCT- Mercantile CTC, Port Elizabeth, E Cape; Y Kelfkens, Y Kelfkens, Potchefstroom, NW; I Mitha, J Taljaard, Worthwhile Clinical Trials, Benoni, Gauteng; D Naaidoo, Y Duki, Research Clinic, Durban, KZ-Natal; F Snyders, M Munnik, Wilgers Medical Consortium, Pretoria, Gauteng; P Soma, H Johnston, University of Pretoria Clinical Trial Unit, Pretoria, Gauteng; N van der Merwe, Y Goosen, Medi-Clinic Bloemfontein, Bloemfontein, Free State; L van Zyl, M le Roux, Clinical Project Research, Worcester; T Venter, L Wessels, Union Hospital, Alberton, Gauteng.

South Korea- 230 patients 23 centers
HJ Bae, MG Han, Seoul National University Bundang Hospital, Gyeonggi-do; JK Cha, DH Kim, Dong-A University Medical Center, Busan; BR Cho, DR Ryu, Kangwon National University Hospital, Gangwon-do; HH Choi, KS Hong, Chuncheon Sacred Heart Hospital, Gangwon-do; WS Chung, YS Oh, The Catholic University of Korea Seoul St. Mary Hospital, Seoul; SH Han, KH Lee, Gachon University Gil Hospital, Incheon; TJ Hong, HW Lee, Pusan National University Hospital, Busan; MS Hyon, JW Jung, Soonchunhyang University Hospital, Seoul; HK Jeon, JM Lee, The Catholic University of Korea Uijeongbu St.Mary's Hospital, Gyeonggi-do; DH Kang, KJ Choi, Asan Medical Center, Seoul; CJ Kim, ES Jin, Kyung Hee University Hospital at Gangdong, Seoul; DS Kim, JS Seo, Inje University Busan Paik Hospital, Busan; HS Kim, MJ Cha, Seoul National University Hospital, Seoul; JT Kim, MS Park, Chonnam National University Hospital, Gwangju; JH Kim, JH Park, Chungnam National University Hospital, Daejeon; JS Kim, SJ Park, Samsung Medical Center, Seoul; SH Kim, JB Seo, Seoul Metropolitan Government Seoul National University Hospital, Seoul; YJ Kim, MY Chun, Ewha Womans University Mokdong Hospital, Seoul; MH Lee, BY Joung, Severance Hospital Yonsei University College of Medicine, Seoul; SH Lee, DG Shin, Yeungnam University Hospital, Daegu; J Namgung, JI Kwak, Inje University Ilsan Paik Hospital, Gyeonggi-do; SW Rha, JO Na, Korea University Guro Hospital, Seoul; SJ Rim, JY Kim, Gangnam Severance Hospital, Seoul.

Spain- 166 patients 14 centers
M Arcocha Torres, A Manzanal Rey, Hospital de Basurto, Bilbao, 48; J Blanco Coronado, I Puertas, Hospital Virgen del Mar, Almeria, 4; J Bruguera Cortada, P Cabero, H del Mar, Barcelona, 8; C Calvo, G Calvo, HCU de Santiago, La Coruna, 15; A de Arce Borda, A Asensio, Hospital de Donostia, San Sebastian, 20; E Diez Tejedor, M Pérez Guevara, HGU La Paz, Madrid, 28; J Gonzalez Juanatey, M Moure, HCU de Santiago, Santiago de Compostela, 15; A

Sweden- 252 patients 16 centers

Switzerland- 5 patients 1 center
T Moccetti, I Petrova Slater, Cardio Centro Ticino, Lugano.

Taiwan- 234 patients 15 centers
CC Cheng, WS Wu, Chi-Mei Medical Center - Yongkang, Tainan; CE Chiang, WC Yu, Taipei Veterans General Hospital, Taipei; FT Chiang, YW Wu, National Taiwan University Hospital, Taipei; CW Chiu, TC Yeh, Kaohsiung Veterans General Hospital, Kaohsiung; CH Hsia, YP Chen, Changhua Christian Hospital, Changhua; JL Huang, YF Chen, Taichung Veterans General Hospital, Taichung; CT Kuo, CL Wang, Chang Gung Memorial Hospital - Linkou, Taoyuan; WT Lai, TH Lin, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung; JT Lee, CC Cheng, Tri-Service General Hospital, Taipei; PY Pai, KH Lin, China Medical University Hospital, Taichung; KG Shyu, CZ Chiu, Shin Kong Wu Ho-Su Memorial Hospital, Taipei; WK Tseng, YF Pan, E-Da Hospital, Kaohsiung; KC Ueng, SC Lee, Chung-Shan Medical University Hospital, Taichung; JH Wang, WC Tsai, Hualien Tzu Chi Hospital, Hualien; HI Yeh, JY Kuo, Mackay Memorial Hospital - Tamsui, New Taipei.

Thailand- 115 patients 8 centers
K Jirasirirojanakorn, K Pornchayaisit, Bhumibol Adulyadej Hospital, Bangkok; P Kaewsawanna, W Sinthusopa, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima; S Kiatchoosakun, S Sriprasert, Siriraj Hospital, Khon Kaen; P Laothavorn, P Bamrunpong, Phramongkutkla Hospital, Bangkok; D Piyayotai, A Sripintra, Thammasat Chalerm-Prakiat Hospital, Pathumthani; P Sritara, P Panpunuan, Ramathibodi Hospital, Bangkok; A Sukonthasarn, W Mekara, Maharaj Nakorn Chiang Mai Hospital, Chiang Mai; Y Vorassatatarnjik, E Puripun, King Chulalongkorn Memorial Hospital, Bangkok.

Turkey- 111 patients 17 centers
M Acikel, M Acikel, Ataturk University Medical Faculty, Erzurum; H Akilli, H Demir, Konya Necmettin Erbakan University Meram Faculty of Medicine, Konya; N Ata, N Ata, Osmangazi University Tip Faculty Hospital, Eskisehir; S Bayata, S Bayata, Izmir Ataturk Training and
Research Hospital, Izmir; N Cakmak, A Calik, Siyami Ersek Hospital, Istanbul; M Cayli, M Cayli, Adana Numune Training and Research Hospital, Adana; C Ceyhan, C Ceyhan, Adnan Menderes University Medical Faculty, Aydin; D Erdogan, D Erdogan, Suleyman Demirel University Medical Faculty, Isparta; C Ermis, C Ermis, Akdeniz University Medical Faculty, Antalya; K Kabul, H Demir, GATA (Gulhane Military Medical School), Ankara; M Kanadasi, M Kanadasi, Cukurova University Medical Faculty, Adana; A Oto, A Oto, Hacettepe University School of Medicine, Ankara; O Turgut, I Tandogan, Cumhuriyet University Medical Faculty, Sivas; R Yalcin, R Yalcin, Gazi University, Ankara; F Yigit, F Yigit, Baskent University Medical Faculty, Adana; Z Yigit, Z Yigit, Istanbul University Cardiology Institute, Istanbul; M Zoghi, M Zoghi, Ege University Medical Faculty Hospital, Izmir.

Ukraine- 1148 patients 46 centers
V Batushkin, M Azhdari, Kyiv City Clinical Hospital 5, Kyiv; A Bazylevych, Z Vlasyuk, City Communal Clinical Hospital #5, Outpatient Department, Danylo Galyskiv Lviv National Medical University, Lviv; I Bereznjakov, M Lebedynskaya, City Clinical Multifield Hospital #25, Cardiology Department; Kharkiv Medical Academy of Postgraduate Education, Kharkiv; S Dotsenko, R Kulynych, Communal Institution Zaporizhzhya Regional Clinical Hospital, Zaporizhzhya State Medical University, Chair of Internal Diseases #3, Zaporizhzhya; G Dzyak, L Vasylieva, Communal Institution Dnipropetrovsk Regional Clinical Centre of Cardiology and Cardiosurgery of Dnipropetrovsk Regional Council, Department of Electrophysiological Research and Anaesthesiological Care, State Institution Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine, Dnipropetrovsk; A Faynyk, M Sorokivskyy, Lviv Regional State Clinical Medical and Diagnostic Cardiology Centre, Lviv; V Gavrysky, Y Dzublik, SI National Institute of Phthisiology and Pulmonology named after F.G.Yanovsky AMS of Ukraine, Kyiv; L Horbach, V Husyev, Communal City Clinical Hospital 8, Lviv; O Godlevska, Y Samburg, City Clinical Emergency Hospital named after O.I. Meshchaninov, Department of Therapy #1, Kharkiv Medical Academy of Postgraduate Education, Kharkiv; O Karpenko, I Nevolina, Kiyv Municipal Clinical Hospital 1, Kyiv; Y Karpenko, O Biha, Odesa Regional Clinical Hospital, Department of Cardiology, Odesa State Medical, Odesa; I Kaydashyev, N Gerasimenko, City Clinical Hospital #1, Therapeutic Department; Ukrainian Medical Stomatological Poltava; S Kolomyyits, V Vasylets, Odesa Municipal Clinical Hospital 9, Odesa; M Kopytsya, O Petrunina, State Institution Institute of Therapy named after L.T. Malaya of Academy of Medical Sciences of Ukraine, Kharkiv; V Kotseruba, M Dvoieglazova, Chernigiv City Hospital 1, Chernigiv; V Koval, O Ohirko, Communal City Clinical Hospital 8, Lviv; O Koval', P Kaplan, Communal Institution Dnipropetrovsk Clinical Association of Emergency Medical Care of Dnipropetrovsk Regional Council, Department of Cardiology for Treatment of Patients with Myocardial Infarction #2, State Institution Dnipropetrovsk Medical Academy of the Ministry of Health of Ukraine, Dnipropetrovsk; I Kraiz, N Usan, Kharkiv Central Clinical Hospital Ukrzaliznitsi, Kharkiv; O Kraydashyev, R Stets, Zaporizhzhya State Medical University, Communal Institution City Clinical Hospital #6, chair of clinical pharmacology and pharmacotherapy, Zaporizhzhia; I Kupnovytska, I Kupnovytska, Iv-Frank. Ivano-Frankivsk Regional Clinical Cardiological Center, Department of Arterial Hypertension, Ivano-Frankivsk State Medical University, Ivano-Frankivsk; Y Kyyak, Y Kyyak, Communal City Clinical Emergency Hospital, Cardiology Department, Danilo Galyskiv Lviv State Medical University, Lviv; V Lizogub, O Gorna, Kyiv City Clinical Hospital #12, Department of Cardiology, O.O. Bogomolets National Medical University, Kyiv; Y Malynovsky, S Fedotov, MI RMC of Cardiovascular Diseases of Zaporizhzhia RC, Zaporizhzhia; L Ostrovska, L Ushakova-Sokolova, Kherson Municipal Clinical Hospital, Kherson; A Parkhomenko, N Dovgan, National Scientific
United Kingdom—400 patients 31 centers

R Aggarwal, S Smith, Basildon University Hospital, Basildon, Essex; I Beeton, S Dunn, St Peter's Hospital, Chertsey, Surrey; M Blagden, R Price, Avondale Surgery, Chesterfield, Derby; J Camm, K Dougal, St Georges Hospital, London, GT LON; O Chapman, D Davies, University Hospital of Coventry and Warwickshire, Coventry, Warwks; A Choy, J Duff, Ninewells Hospital, Dundee; A Cohen, R Wilmott, King's College Hospital, London, GT LON; D D'Costa, M Green, New Cross Hospital, Wolverhampton, WSTMD; H Douglas, D Dickinson, University Hospital Aintree, Liverpool, MERSYD; F Lie, V Ramasamy, Whipps Cross Hospital, London, GT LON; S Lindsay, C Atkinson, Bradford Royal Infirmary, Bradford, WYORKS; N Linker, M Finlayson, James Cook Hospital, Middlesborough, T&W; G Lip, R Brown, City Hospital, Birmingham; P MacCallum, P Ebano, Barts and the London NHS Trust, London; P MacCallum, P Ebano, Wolfson Institute of Preventive Medicine, London, GT LON; M MacLeod, C McGhee, Forth Valley Royal Hospital, Larbert, AYR; P Marazzi, D Jones, East Horsley Medical Centre, East Horsley, Surrey; T Maxwell, C Isted, Little Common Surgery, Bexhill on Sea, E.SUSX; R More, L Helliwell, Lancashire Cardiac Centre, Blackpool, LANCS; A Moriarty, A Mackin, Craigavon Area Hospital, Belfast, BFS; D Murdoch, A Andrews, Southern General Hospital NHS Trust, Glasgow, STRATH; D Newby, L Flint, Edinburgh Royal Infirmary, Edinburgh,
LOT; M Pye, L Wright, York Hospital, York, E YORK; J Roberts, D Avery, Mayfield Medical Centre, Paignton, DEVON; R Senior, G Young, Northwick Park Hospital, Middlesex, MDDSX; M Sopher, S Kennard, Royal Bournemouth Hospital, Bournemouth, Dorset; R Storey, C Bridge, University of Sheffield SOM & Biomed Sciences, Sheffield, SYORKS; W Turner, M Walker, The Burbage Surgery, Leicester, LEICS; A Venkataraman, M Gilchrist, George Eliot Hospital, Nuneaton, Warwks; R Watkin, A Chung, Good Hope District General Hospital, Birmingham, WSTMID; A Wright, J Wright, Hathaway Medical Centre, Swindon, WILTS.

United States- 3907 patients 336 centers
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*J Am Heart Assoc.* 2017;6:e006703; originally published August 11, 2017; doi: 10.1161/JAHA.117.006703

The *Journal of the American Heart Association* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Online ISSN: 2047-9980

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