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ORIGINAL RESEARCH

AIM-AF: A Physician Survey in the United States and Europe

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BACKGROUND: Guideline recommendations are the accepted reference for selection of therapies for rhythm control of atrial fibrillation (AF). This study was designed to understand physicians' treatment practices and adherence to guidelines.

METHODS AND RESULTS: The AIM-AF (Antiarrhythmic Medication for Atrial Fibrillation) study was an online survey of clinical cardiologists and electrophysiologists that was conducted in the United States and Europe (N=629). Respondents actively treated ≥30 patients with AF who received drug therapy, and had received or were referred for ablation every 3 months. The survey comprised 96 questions on physician demographics, AF types, and treatment practices. Overall, 54% of respondents considered guidelines to be the most important nonpatient factor influencing treatment choice. Across most queried comorbidities, amiodarone was selected by 60% to 80% of respondents. Other nonadherent usage included sotalol by 21% in patients with renal impairment; dofetilide initiation (16%, United States only) outside of hospital; class Ic agents by 6% in coronary artery disease; and dronedarone by 8% in patients with heart failure with reduced ejection fraction. Additionally, rhythm control strategies were frequently chosen in asymptomatic AF (antiarrhythmic drugs [AADs], 35%; ablation, 8%) and subclinical AF (AADs, 38%; ablation, 13%). Despite guideline algorithms emphasizing safety first, efficacy (48%) was selected as the most important consideration for AAD choice, followed by safety (34%).

CONCLUSIONS: Despite surveyed clinicians recognizing the importance of guidelines, nonadherence was frequently observed. While deviation may be reasonable in selected patients, in general, nonadherence has the potential to compromise patient safety. These findings highlight an underappreciation of the safe use of AADs, emphasizing the need for interventions to support optimal AAD selection.

Key Words: atrial fibrillation ■ antiarrhythmic drug ■ physician

Atrial fibrillation (AF) is the most common sustained tachyarrhythmia and is associated with a 5-fold increased relative risk of stroke,[1] a 3-fold increased relative risk of heart failure (HF),[2] and a doubled relative risk of mortality.[3] The prevalence of AF is increasing worldwide, predicted to affect 6 to 12 million people in the United States by 2050 and 18 million people in Europe by 2060.[4]

For the past 2 decades, the European Society of Cardiology (ESC)[5] and the American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS)[6,7] have provided physicians with guidelines to direct the management of patients with AF. Both recommend the use of antiarrhythmic drugs (AADs) for rhythm control in patients with symptomatic AF only.[5–7] Additionally, both guidelines indicate that selection of antiarrhythmic therapies should consider arrhythmia burden, presence of underlying heart disease, severity of symptoms, and risk of side effects.[5–7]

Since the publication of the Etude en Activité Libérale de la Fibrillation Auriculaire study over 2 decades ago,[8] the clinical landscape of AF treatment has evolved considerably, as have the guidelines. Two new AADs, dofetilide and dronedarone, are now available (although dofetilide is available in the United States only[9]), and the use of ablation therapy has become increasingly widespread.

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CLINICAL PERSPECTIVE

What Is New?

- This survey extensively explored treatment practices and attitudes toward antiarrhythmic therapies for atrial fibrillation among cardiologists and electrophysiologists in the United States and Europe.
- Despite 97% of respondents reporting that they follow treatment guidelines, there was a high level of deviation, of varying degrees, from recommendations in the 2020 European Society of Cardiology and 2014/2019 American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines.

What Are the Clinical Implications?

- While deviations from guidelines may be reasonable in select clinical circumstances, a high degree of nonadherence raises concerns regarding patient safety.
- As the clinical presentations of AF evolve over time, and guidelines are regularly updated in line with new evidence, important safety questions arise over the extent to which physicians are keeping abreast of such updates, particularly with regard to antiarrhythmic drug use.

Nonstandard Abbreviations and Acronyms

AFFIRM	Atrial Fibrillation Follow-up Investigation of Rhythm Management
AIM-AF	Antiarrhythmic Medication for Atrial Fibrillation
GWTG-AFib	Get With The Guidelines – Atrial Fibrillation
HFrEF	heart failure with reduced ejection fraction
ORBIT-AF	Outcomes Registry for Better Informed Treatment of Atrial Fibrillation
SHD	structural heart disease

Real-world data from the United States indicated that between 1990 and 2005, there was a 13-fold increase in the proportion of patients with AF who received ablation ($P < 0.001$)[10]; a 12.5% annual rate of increase worldwide is predicted from 2019 to 2025.[11] However, in the current clinical landscape, prescribing practices of physicians and their attitudes toward the management of patients with AF are poorly understood. Accordingly, the AIM-AF (Antiarrhythmic Interventions for Managing Atrial Fibrillation) study was designed to explore cardiologist and electrophysiologist antiarrhythmic treatment practices in patients with AF. The results of the study are reported in the context of the 2020 ESC guidelines,[5] and the 2014 and 2019 AHA/ACC/HRS guidelines.[6,7]

METHODS

Qualified researchers may request access to data including the study summary, study questionnaire with any amendments, and data set specifications for validation purposes. Only fully anonymized data will be provided.

Study Design

The AIM-AF study was an exploratory, online physician survey, designed by a steering committee of 9 global experts in AF. Practicing physicians from the M3 Global International Market Research Panel were invited to complete the survey, with a geographical spread across the United States and European countries involved, to avoid potential selection bias. Ethics approval was obtained from the Western Institutional Review Board committee (Ref: 1-1337237-1), and from the local ethics committee in Uppsala, Sweden; participants provided informed consent in accordance with institutional guidelines.

Study Population

The survey aimed to recruit 600 clinical cardiologists, including clinical electrophysiologists and interventional electrophysiologists from the United States, Germany, Italy, Sweden, and the United Kingdom. These countries were selected to ensure that physicians from Central, Northern, Southern, and Western Europe were represented. Inclusion criteria were as follows: qualification in their specialty for >3 years and <40 years; >40% of their time spent actively treating patients; ≥30 new or existing patients with AF seen within a 3-month period (before the COVID-19 pandemic); and management of patients with AF who have received ablation or have been referred for ablation.

Data Collection and Analysis

The survey was conducted between October 2, 2020, and February 12, 2021, and was intended to take 60 minutes to complete. Respondents were asked to complete 96 questions (Table S1), including a set of screening questions to ascertain demographics and eligibility. Questions were grouped on the basis of topics such as physician setting and patient caseload; treatment journey, with a focus on oral AADs; prescribing/treatment practices; and use/referral of ablation. The survey predominantly comprised closed questions,

with a small number of open-ended questions to probe physician perceptions and behaviors. Survey questions were designed to understand physicians' general approaches to the management of patients with AF.

The survey was performed in compliance with the European Pharmaceutical Market Research Association code of conduct and in full accordance with the US Health Insurance Portability and Accountability Act of 1996.

Since no formal hypothesis was tested, data analyses are descriptive in nature. Univariate tests were conducted for comparisons between the 2 groups (United States versus Europe) and the *Z* test was applied to determine statistical significance (*P* value boundary of <0.05); however, *P* values should be considered notional since no adjustment was made for multiple testing.

To distinguish the degree of nonadherence between survey responses and recommendations from the 2020 ESC[5] and 2014/2019 AHA/ACC/HRS guidelines,[6,7] we established 4 definitions to describe adherence: compliance with guidelines (AAD use aligns with guideline recommendations); noncompliance with guidelines (AAD use contradicts guideline recommendations); deviation from guidelines (guidelines recommend use of an alternative therapy or alternative practice in this setting); and potential noncompliance with guidelines (use in this setting *could* contradict guideline recommendations, but clinical thresholds differed between the survey questions and the guidelines, preventing absolute certainty). Estimated percentage of nonadherence was calculated for each AAD, which described the proportion of physicians who selected an AAD in at least 1 clinical circumstance that fell into any of the "noncompliance with guidelines," "deviation from guidelines," or "potential noncompliance with guidelines" definitions.

RESULTS

Survey Response and Physician Profiling

The survey completion rate (all questions answered) was 7% in the United States and 16% in Europe (Table 1). A total of 629 physicians completed the survey, of 6428 approached, with similar characteristics between the global population, the United States, and Europe (Table 2). Overall, the proportion of cardiologists (57%) was higher than that of electrophysiologists (43%), with 80% reporting a specialization in AF. At the time of the survey, respondents had been qualified in their specialty for an average of 14.5 years. The most common clinical practice setting was a university hospital/clinic (40% global; 31% United States, 49% Europe) or a general community hospital/clinic (37% global; 33% United States, 40% Europe). Over a typical 3-month period (before the COVID-19 pandemic), the average total cardiology patient caseload, including all diagnoses and conditions, was 549; the average caseload of follow-up patients was greater than the average caseload of new patients with AF (158 versus 94, respectively). Most respondents referred patients for ablation, rather than performing ablations themselves (55% versus 45%, respectively).

Physicians' Attitudes Toward Guideline Use

Overall, 97% of respondents stated that they follow guidelines for their treatment decisions. Approximately half (49%) of the respondents primarily referred to the AHA/ACC/HRS guidelines[6,7] for their decision making, with 43% referring to the ESC guidelines.[5] Overwhelmingly, US respondents chose the AHA/ACC/HRS guidelines[6,7] as their primary reference (96%), although 20% also referred to the ESC guidelines.[5] European respondents generally chose the ESC guidelines[5] as their primary reference (82%), with 32% also referring to the AHA/ACC/HRS guidelines.[6,7] Guidelines were chosen as the first and second most important nonpatient factor that influenced treatment strategy by 54% and 28% of respondents, respectively; other scientific literature was chosen by 23% and 41%, respectively. Most respondents (65%), including 58% of European respondents, were unsure whether the 2020 ESC guideline[5] update had influenced their survey responses.

AAD Choice in Specific Clinical Circumstances

AADs were chosen as a typical treatment choice across multiple patient comorbidity categories, with extensive use of amiodarone (selected by 60% to 80% of respondents across most queried comorbidities), despite guidelines recommending alternative first-line agents in most

Table 1. Survey Response and Completion Rates

	United States			Europe		
	Total	Cardiologists	Interventional electrophysiologists	Total	Cardiologists	Interventional electrophysiologists
Invitations sent, n	4428	3382	1046	2000	1266	734
Responses,* n (%)	1075 (24)	721 (21)	354 (34)	716 (36)	423 (33)	293 (40)
Completed survey, n (%)	308 (7)	168 (5)	140 (13)	321 (16)	210 (17)	111 (15)

*Respondents who started the survey, including those who did not complete all questions.

Table 2. Physician Profiling and Demographics

Category	Global (N=629)	United States (n=308)	Europe (n=321)
Physician type, n (%)			
Cardiologist	360 (57)	168 (55)	192 (60)
Interventional electrophysiologist	269 (43)	140 (45)	129 (40)
Subspecialty, n (%)			
AF	501 (80)	231 (75)	270 (84)
Other	52 (8)	22 (7)	30 (9)
None	76 (12)	55 (18)	21 (7)
Length of time qualified in specialty			
3–25 y, n (%)	565 (90)	265 (93)	300 (86)
26–40 y, n (%)	64 (10)	43 (7)	21 (14)
Mean, y	14.5	15.0	14.0
Time spent on physician-related activities, %			
Actively treating patients	89	93	86
Academia/research	6	4	8
Administration/other	5	3	7
Main clinical practice setting, n (%)			
General community hospital/clinic	230 (37)	102 (33)	128 (40)
University hospital/clinic	251 (40)	95 (31)	156 (49)
Primary outpatient practice/clinic	93 (15)	74 (24)	19 (6)
Private hospital/clinic	53 (8)	37 (12)	16 (5)
Other	2 (<1)	0	2 (1)
Typical patient caseload over 3 mo,* n			
Total cardiology patient caseload†	549	619	481
New patients with AF	94	82	105
Follow-up patients with AF	158	175	141
Clinical activities, n (%)			
Prescribe drug treatments and perform ablation	284 (45)	150 (49)	134 (42)
Prescribe drug treatments and refer for ablation	345 (55)	158 (51)	187 (58)

Due to rounding, not all percentages add up to 100%. AF indicates atrial fibrillation.

*Before the COVID-19 pandemic.

†Including all cardiology diagnoses and conditions.

settings. Sotalol use ranged from 18% to 46% between comorbidity categories, and dronedarone was used by 8% to 27% of respondents, while use of class Ic drugs was generally low. Estimated percentage of nonadherence for each agent was 93% for amiodarone, 61% for flecainide, 60% for sotalol, 48% for propafenone, 40% for dronedarone, and 25% for dofetilide.

No or Minimal Structural Heart Disease

In patients with no or minimal structural heart disease (SHD), 25% of respondents selected amiodarone as a typical treatment option (Figure 1A). Despite guidelines recommending that alternative agents should be considered first, class Ic agents were selected by the highest number of respondents (54%) in this patient group.

SHD With Preserved Ejection Fraction

Sotalol and class Ic agents were selected as a typical treatment choice in left ventricular hypertrophy (LVH) by 33% and 12%, respectively (Figure 1B). This could indicate potential noncompliance, as these agents are not recommended in patients with severe LVH (ESC guidelines[5]) or significant LVH (wall thickness >1.5 cm; AHA/ACC/HRS guidelines[6,7]). In patients with HF with preserved ejection fraction, guidelines do not recommend use of class Ic agents, yet they were selected by 18% of respondents, indicating noncompliance (Figure 2).

Coronary Artery Disease

The guideline-preferred AADs for use in patients with coronary artery disease (CAD) are dronedarone (IA) and sotalol (IIbA in ESC guidelines),[5] plus dofetilide in the United States. However, class Ic agents were selected as a typical treatment choice in CAD (average across myocardial infarction presentations and revascularized CAD; Figure 1C) by 6% of respondents (numbers reported are the average use of flecainide and propafenone; Figure 2), indicating noncompliance with guidelines.

SHD With Reduced Ejection Fraction

Amiodarone is recommended for use in patients with HF with reduced ejection fraction (HFrEF) by both sets of guidelines and AHA/ACC/HRS recommendations[6,7] also include dofetilide in this setting. Dronedarone may be used in patients with mildly impaired but stable left ventricular function according to the ESC guidelines[5] and was used by 9% of respondents. Notably, sotalol was selected by 18% of respondents, despite ESC guidelines[5] not recommending it and AHA/ACC/HRS guidelines[6,7] advising to exclude or use with caution in this setting. Class Ic agents were used by 6% for patients with HFrEF (Figure 1D), which directly contradicts guidelines, indicating noncompliance (Figure 2).

Other Comorbidities

Class Ic drugs (43%) and sotalol (29%) were selected as typical choices in chronic lung disease (Figure 1A), which could indicate potential noncompliance, as guidelines recommend avoiding use in patients with asthma. In patients with renal impairment (estimated glomerular filtration rate <60 mL/min per 1.73 m^2), sotalol was selected by 21% of respondents, which contradicts AHA/ACC/HRS guidelines[6,7] and may indicate

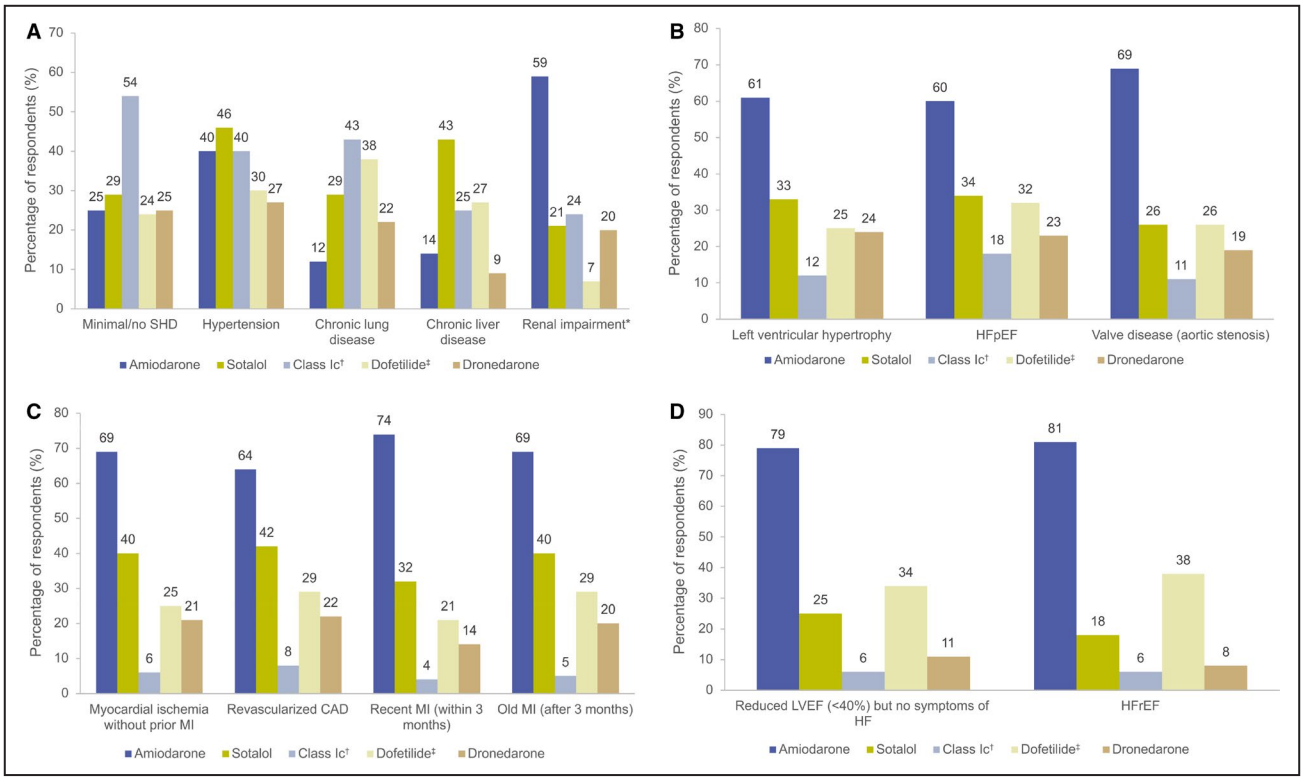

Figure 1. Proportion of respondents who selected AADs as a typical treatment choice in patients with specific comorbidities. **A**, Patients with minimal/no SHD and comorbidities unrelated to SHD. **B**, Patients with SHD and preserved ejection fraction. **C**, Patients with CAD. **D**, Patients with SHD and reduced ejection fraction. *Renal impairment defined as eGFR <60 mL/min per 1.73 m^2; †Average individual use of flecainide and propafenone; ‡US respondents only. AAD indicates antiarrhythmic drug; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and SHD, structural heart disease.

potential noncompliance with ESC guidelines,[5] which state that sotalol should not be used if creatinine clearance is <30 mL/min. Responses also suggested potential noncompliant use of class Ic drugs in chronic liver disease (25%) and renal impairment (24%) (Figure 2).

Initiation of AAD Therapy

A notable number of respondents indicated they initiated sotalol therapy outside a hospital setting (53%). While this does not directly contradict recommendations, the 2014 AHA/ACC/HRS guidelines[6] state that hospital initiation of sotalol should be considered. As such, these responses suggest deviation from guidelines.

A number of respondents (United States only) initiated dofetilide outside a hospital setting (16%). This does not follow the 2014 AHA/ACC/HRS guidelines[6] or the US Food and Drug Administration labeling for this agent,[9] which recommend inpatient initiation of dofetilide because of QT prolongation and risk of torsades de pointes.

Monitoring of Patients Receiving AADs

Guidelines recommend close monitoring of proarrhythmic risk factors in individuals using AADs. In general, respondents requested routine investigations (at least annually) most often with amiodarone (Figure 3). ECGs were routinely requested by 80% of respondents with amiodarone, sotalol, and class Ic drugs. Routine requests for electrolyte monitoring was similar between all AADs, but notably low for sotalol (52%) and class Ic drugs (50%). Renal function monitoring was also notably low with sotalol (57%) and dofetilide (US respondents only; 62%), despite both guidelines recommending electrolyte and renal function monitoring for all patients receiving sotalol. Respiratory function monitoring was requested by 64% of respondents with amiodarone and 14% with dronedarone. Monitoring of hepatic function with amiodarone, dronedarone, and class Ic drugs was requested by 84%, 57%, and 27% of respondents, respectively.

Use of Rhythm and Rate Control Strategies Across AF Subtypes

Survey responses indicated notable variation in control strategy, dependent on AF subtype (Figure 4). Use of rate control agents was most frequent for asymptomatic and subclinical AF (57% and 56%, respectively).

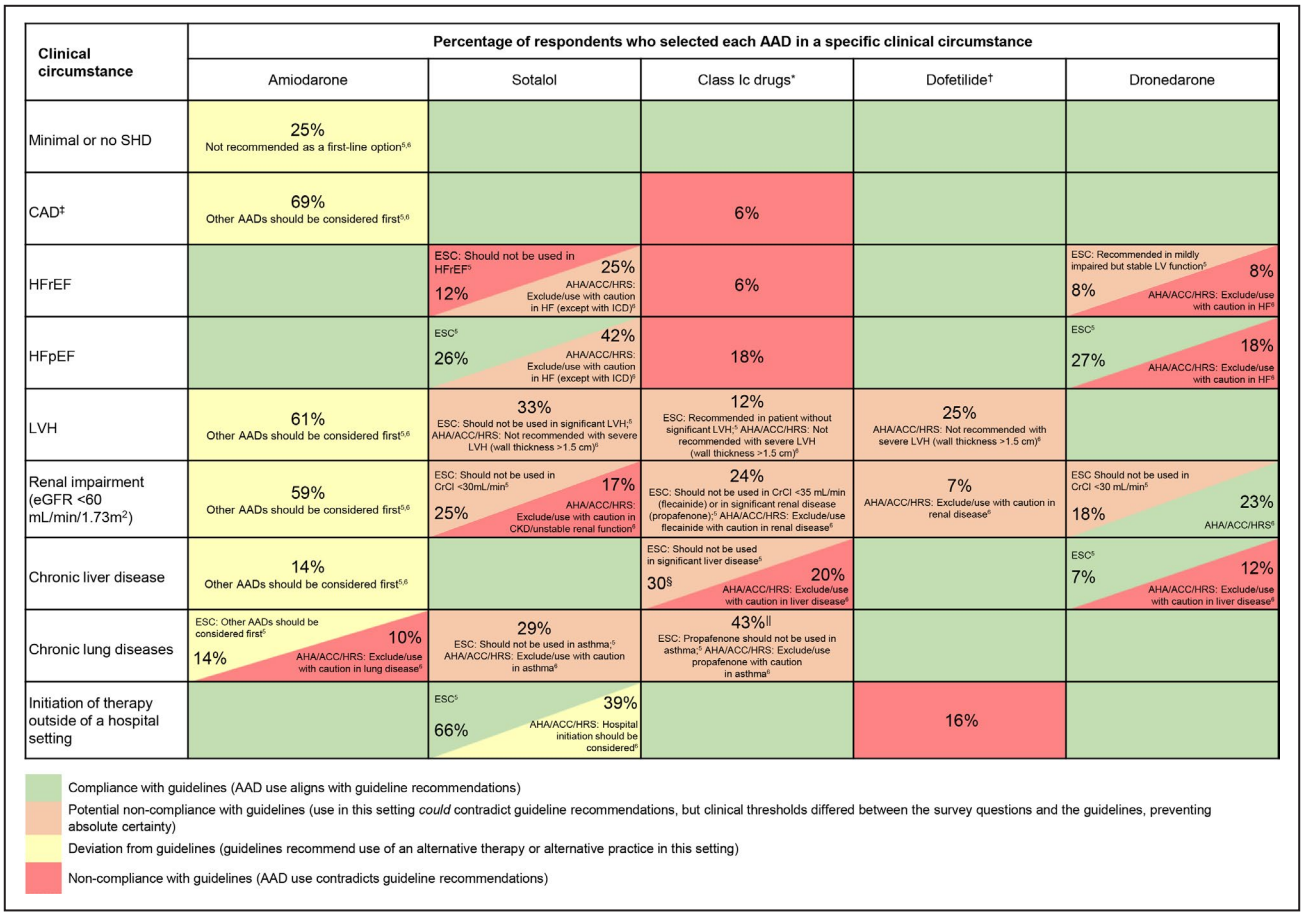

Figure 2. Degree of nonadherence to guidelines based on selection of AADs under specific clinical circumstances.
Data shown describe the percentage of respondents who selected each AAD in specific clinical circumstances. The color codes describe the degree of adherence or nonadherence between survey responses and the 2014/2019 AHA/ACC/HRS[6,7] and 2020 ESC guideline recommendations.[5] The text in the boxes corresponds to recommendations in the AHA/ACC/HRS[6,7] and ESC guidelines.[5] Global data are shown for instances in which the AHA/ACC/HRS[6,7] and ESC[5] guideline recommendations align. For instances in which AHA/ACC/HRS[6,7] and ESC[5] guidelines have differing recommendations, both the US and European data are shown. *Average individual use of flecainide and propafenone (unless otherwise indicated); †US respondents only (agent is not available in Europe and does not appear in ESC guidelines[5]); ‡Average use across myocardial ischemia, MI, and revascularized CAD; §Flecainide 41%, propafenone 19%; ‖Data shown for propafenone only. AAD indicates antiarrhythmic drug; ACC, American College of Cardiology; AF, atrial fibrillation; AHA, American Heart Association; CAD, coronary artery disease; CKD, chronic kidney disease; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; ESC, European Society of Cardiology; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HRS, Heart Rhythm Society; ICD, implantable cardioverter defibrillator; LV, left ventricular; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; MI, myocardial infarction; and SHD, structural heart disease.

However, rhythm control strategies were also reported in these 2 AF groups, using AADs (35% and 38%, respectively) and performing ablation (8% and 13%, respectively). Ablation was the most common treatment strategy for recurrent episodes of symptomatic AF (61%), and its use increased with the prior failure of single (62%) or multiple AADs (74%) in preventing AF recurrence, as well as with prior failure of AAD combinations (71%) (Figure 4).

On average, AADs were primarily used more often as a first-line strategy than rate control agents in paroxysmal AF (in 60% versus 32% of patients, respectively). For the management of persistent AF, rate control agents were primarily used over AADs (in 51% versus 42% of patients, respectively).

Use of Drug Combinations

Beta blockers (90%) were the most frequently used rate control agent in combination with an AAD for rhythm control, followed by calcium channel blockers (32%), and digitalis (19%). Drug combinations were most frequently used for the treatment of persistent AF (in 36% of patients), mixed persistent/paroxysmal AF (in 34% of patients) and paroxysmal AF (in 32% of patients). Amiodarone was the AAD most frequently selected in combination with a rate control agent, used by 66% of

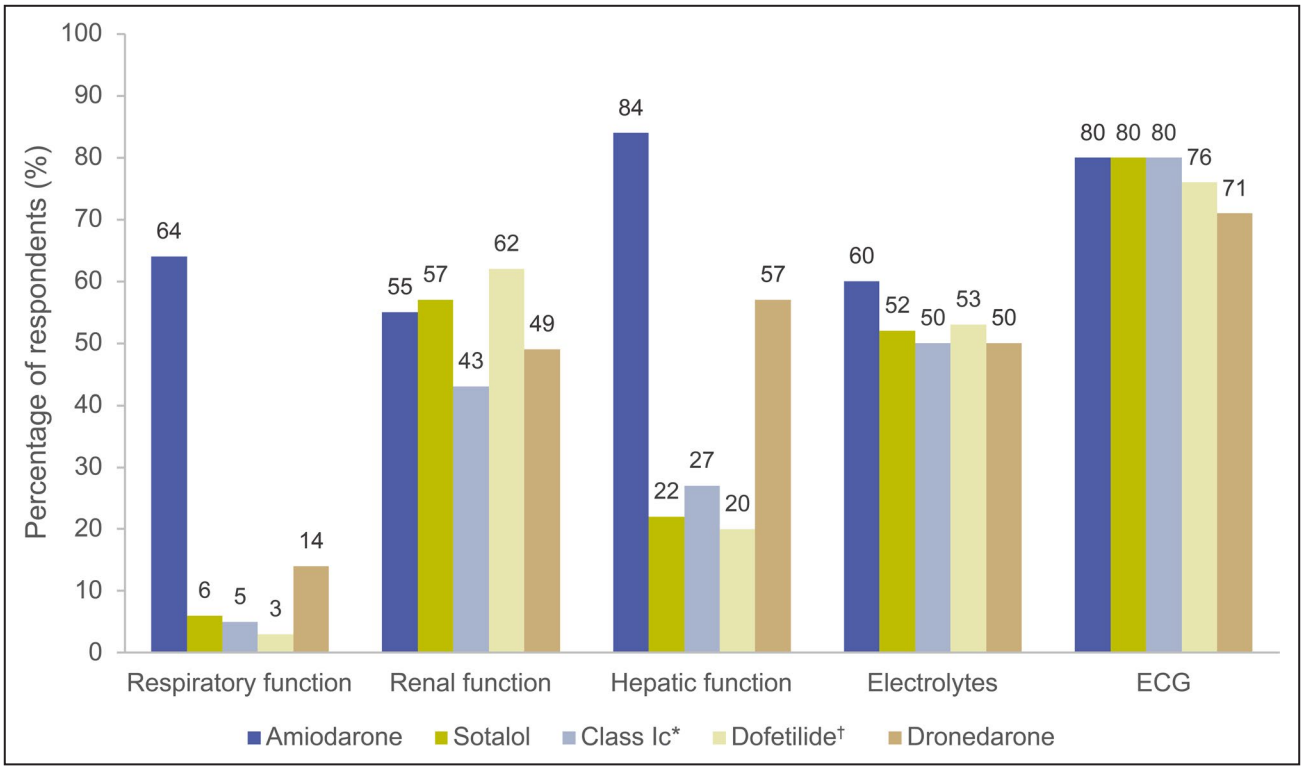

Figure 3. Proportion of respondents who routinely (at least annually) request investigations in patients with AF receiving AADs.
Total respondent numbers varied slightly between drugs. *Average individual use of flecainide and propafenone; †US respondents only. AAD indicates antiarrhythmic drug; and AF, atrial fibrillation.

respondents in combination with digitalis, 44% with a beta blocker, and 42% with a calcium channel blocker (Figure 5).

The ESC guidelines[5] recommend avoiding combinations of >1 AAD to minimize proarrhythmic risk. However, 10% reported that this was the most common type of combination regimen used for rhythm control. On average, respondents would try combinations of AADs (add-on) in 20% of patients if they experienced a recurrence while receiving an AAD.

Factors Influencing Therapy Selection

Despite guideline algorithms emphasizing safety first, efficacy was felt to be the most important nonpatient factor for selection of rhythm control therapy (48% ranked it first from a list of 9 general considerations; data not shown), while safety was considered the second most important factor (34%). Symptomatic status was ranked by 38% as the most important patient factor in guiding the choice of rhythm control therapy (data not shown). Overall, the combination of both antiarrhythmic properties and rate control properties in a single drug with multichannel effects, such as amiodarone, dronedarone, or sotalol, influenced 68% of respondents regarding their choice of AAD; 23% felt that their AAD choice was not influenced, and 9% were unsure.

Regional Differences in Treatment Practices and Guideline Adherence

The largest difference in treatment practice overall between US and European respondents was the use of dofetilide in the United States (selected across patient subgroups, by 7% to 38% of respondents), whereas this agent is not marketed for use in Europe and was not selected by European respondents. This is likely to have led to regional disparities in the selection of other agents, most notably amiodarone, which was selected by significantly more European respondents ($P < 0.05$) across all SHD subgroups apart from in patients with LVH. However, sotalol was used more frequently by US respondents across most comorbidity categories, including LVH and HFrEF. Across all AADs used in both regions, routine investigations were generally requested by fewer US respondents than European respondents.

Regional differences were also seen in the degree of adherence to specific guideline recommendations (Table 3). Considering AAD usage clearly noncompliant with guidelines, class Ic agents were selected in

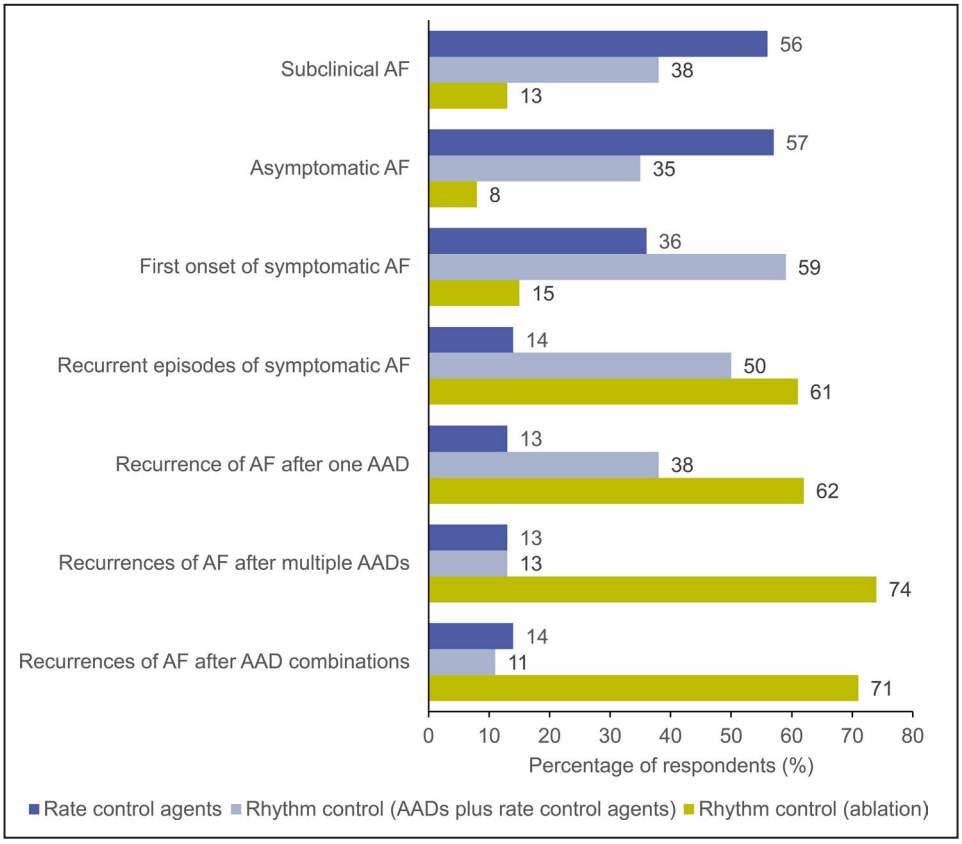

Figure 4. Proportion of respondents who selected rhythm and rate control strategies across AF subtypes.
AAD indicates antiarrhythmic drug; and AF, atrial fibrillation.

HFrEF, and propafenone was selected in LVH by significantly more US than European respondents ($P < 0.05$). Additionally, significantly more European than US respondents selected flecainide in LVH (19% versus 11%, $P < 0.05$). Renal function monitoring with sotalol, which is recommended by guidelines, was performed by statistically significantly more US respondents than European respondents (64% versus 50%, respectively; $P < 0.05$), against the general trend for US practitioners to request fewer routine follow-up investigations. Use of AADs for rhythm control was statistically significantly lower in US respondents than European respondents for asymptomatic AF (31% versus 39%, respectively; $P < 0.05$) and subclinical AF (33% versus 43%, respectively; $P < 0.05$), both deviating from guideline recommendations.

DISCUSSION

The AIM-AF physician survey extensively explored cardiologist and electrophysiologist treatment decisions regarding antiarrhythmic treatment for AF in 629 respondents. The response rate seen was in line with those previously reported from online physician surveys.[12–14] The major finding from this study is that there is a high level of deviation, of varying degrees, from the 2020 ESC[5] and 2014/2019 AHA/ACC/HRS guidelines[6,7]; a particularly surprising result, since 97% of respondents stated that they follow guidelines and 54% felt that guidelines were the most important nonpatient factor influencing their treatment decisions. It is not possible to determine from these data whether this degree of deviation results from an unexpectedly high level of adaptation of treatment to suit individual patients or reflects a serious knowledge gap among treating physicians. However, the survey questions were worded to ascertain general treatment practices, so respondents would not be expected to select answers based on individual patient circumstances.

While deviations from guidelines may be reasonable in select clinical circumstances, a high degree of nonadherence raises concerns regarding patient safety.[15,16] Despite the growing use of ablation, appropriate AAD use is an increasingly important issue in clinical practice, as one study found that antiarrhythmic prescriptions nearly tripled between 2004 and 2016 in the United States, with the most substantial increases observed for amiodarone, sotalol, flecainide,

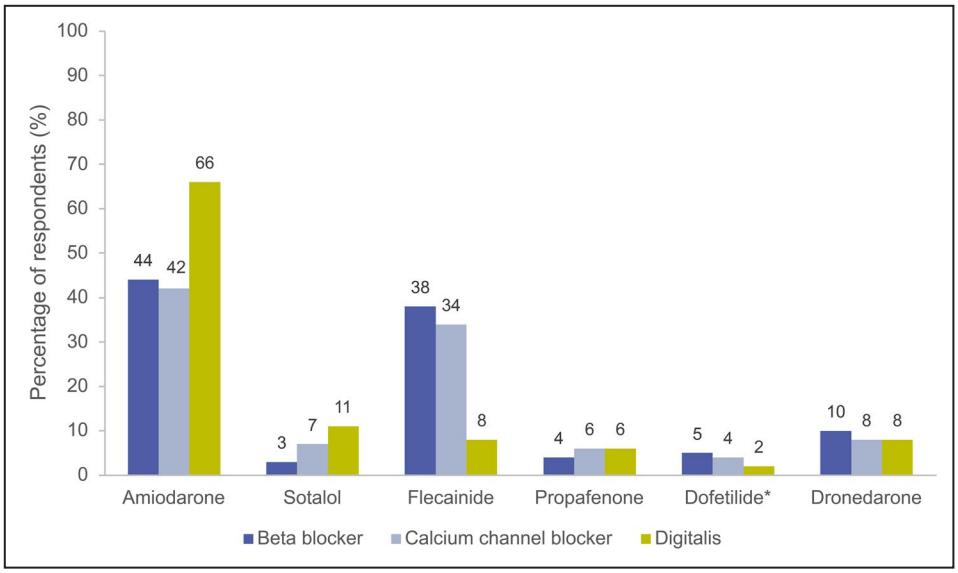

Figure 5. Proportion of respondents who selected different AADs in combination with rate control agents.
Total respondent numbers varied slightly between each rate control agent. *US respondents only. AAD indicates antiarrhythmic drug.

and dofetilide.[17] As the clinical presentations of AF evolve over time, and guidelines are regularly updated in line with new evidence, important safety questions arise over the extent to which physicians are keeping abreast of such updates, particularly with regard to AAD use.

The choice between rate control and rhythm control in the treatment of patients with AF was widely debated until the publication of the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study, which found no clear survival advantage when using a rhythm control strategy compared with rate control.[18] However, more recent data have shown greater improvement in quality of life,[19] functional status,[19–22] exercise tolerance,[23] and also reductions in both symptoms[24] and symptomatic HF incidence[25] with restoration of sinus rhythm (using ablation or AADs) compared with rate-controlled AF. Moreover, The Early Treatment of Atrial Fibrillation for Stroke Prevention Trial found that early comprehensive rhythm control reduced the risk of adverse cardiovascular outcomes (a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of HF or acute coronary syndrome) versus usual care, demonstrating that AADs remain an important treatment option for many patients with AF.[26]

A key finding in this survey was the factors that drive contemporary AAD selection. Both the ESC[5] and AHA/ACC/HRS guidelines[6,7] advocate a safety-based algorithm for AAD selection; however, almost half (48%) of respondents in our survey considered efficacy to be the most important consideration for selection of rhythm control. This finding has implications for patient management and likely explains the high use of amiodarone regardless of the clinical scenario.

Despite the well-known organ toxicity and complex drug interaction profile associated with its use, amiodarone was frequently chosen as a typical treatment across multiple patient comorbidity categories, although both guidelines recommend consideration of other AADs first. However, routine monitoring via all queried parameters was considerably higher with amiodarone than other AADs, suggesting that respondents were aware of the increased safety considerations related to amiodarone. While class Ic drugs were mainly used in patients with minimal or no SHD, a notable proportion were also used in patients with CAD, HFrEF/HF with preserved ejection fraction, or LVH, which is contrary to guidelines and increases the risk of potentially life-threatening proarrhythmia. In the ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation), 44% of investigators used a class Ic agent in patients with CAD, representing documented noncompliance with guidelines. Additionally, 35% used amiodarone as a first-line therapy in patients without HF or LVH, representing the second most common instance of noncompliance in the ORBIT-AF registry.[27]

In our study, the extent to which sotalol was selected as a typical treatment in patients with LVH (33%), renal impairment (21%), and HFrEF (18%) was of concern. Similar results were seen in the GWTG-AFib (Get With The Guidelines—Atrial Fibrillation) study, where 20% and 17% of patients, respectively,

Table 3. Survey Responses Indicating Significant* Differences Between Proportions of US and European Respondents Reporting Specific Cases of Guideline Nonadherent Practice

Treatment practices, n (%)	United States (n=308)	Europe (n=321)
Treatments typically selected for patients with specific comorbidities		
HFrEF		
Class Ic*	24 (8)	12 (4)
Sotalol	77 (25)	38 (12)
CAD‡		
Amiodarone	186 (77)	248 (60)
LVH		
Class Ic*	36 (12)†	41 (13)†
Flecainide	35 (11)	60 (19)
Propafenone	36 (12)	22 (7)
Chronic liver disease		
Amiodarone	33 (11)	53 (17)
Dronedarone	37 (12)	21 (7)
Class Ic*	60 (20)	97 (30)
Renal impairment‡		
Class Ic*	62 (20)	88 (28)
Sotalol	52 (17)	80 (25)
Chronic lung disease		
Class Ic*	124 (40)	146 (46)
Sotalol	105 (34)	75 (23)
Routine investigations§ (at least annually)		
Electrolytes		
Flecainide	130 (44)	189 (60)
Propafenone	122 (41)	158 (53)
Hepatic function		
Dronedarone	134 (46)	206 (67)
Renal function		
Sotalol	191 (64)	152 (50)
Initiation of AADs outside of a hospital inpatient setting		
Sotalol	121 (39)	212 (66)
Use of AADs for rhythm control		
In asymptomatic AF	96 (31)	125 (39)
In subclinical AF	101 (33)	138 (43)

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; CAD, coronary artery disease; HFrEF, heart failure with reduced ejection fraction; LVH, left ventricular hypertrophy; and MI, myocardial infarction.

*$P < 0.05$.

†Average individual use of flecainide and propafenone.

‡Average use across myocardial ischemia, MI and revascularized CAD.

§Overall use of class Ic agents in this subgroup was similar across regions, but differences were seen in use of the individual agents.

‖Defined as eGFR<60 ml/min/1.73 m^2.

#Total respondent numbers in US and Europe varied between all drugs.

received sotalol in the presence of HF and LVH.[28] In the 2020 update to the ESC guidelines,[5] sotalol was downgraded from a class I to a class IIb recommendation on the basis of evidence of increased mortality compared with placebo[29] and other AADs.[30,31] There was no downgrading of sotalol in the 2019 update to the AHA/ACC/HRS guidelines,[7] perhaps a contributing factor to greater overall use of sotalol in the United States than in Europe, but close monitoring in line with the ESC guidelines is advised.[5] The 2020 update to the ESC guidelines include no specific recommendations with regard to sotalol initiation in hospital[5]; however, according to the AHA/ACC/HRS guidelines, hospital initiation of sotalol should be considered, although it is acknowledged that there is considerable experience of sotalol initiation in patients with a low risk of torsades de pointes outside of a hospital.[6,7] It is perhaps unsurprising, therefore, that our study found that statistically significantly fewer US respondents initiated sotalol outside of a hospital compared with European respondents (39% versus 66%; $P < 0.05$). With dofetilide, however, despite the clear guideline recommendation for hospital initiation, 16% of US respondents still initiated dofetilide outside of hospital. Although a recent study found that safe outpatient initiation of dofetilide was possible with intensive monitoring,[32] this involved a very small patient cohort and should not yet inform clinical practice.

Our survey results revealed that a rhythm control strategy is being frequently used to treat asymptomatic and subclinical AF, with only 38% of respondents ranking symptomatic status as the top factor for influencing selection of rhythm control rather than rate control. While the use of early rhythm control is gaining more interest and supporting evidence,[26] the ESC and AHA/ACC/HRS guidelines recommend that rhythm control should be confined only to otherwise symptomatic patients.[5–7] Of note, the Euro Heart Survey also found that rhythm control strategies were used in 44% to 46% of asymptomatic patients.[33]

This study extensively explored physicians' attitudes toward antiarrhythmic therapies and their treatment practices in patients with AF. Strengths of the AIM-AF study include the fact that responses were gathered from cardiology physicians across several countries, the majority of whom considered AF to be their subspecialty. Additionally, the survey explored physicians' attitudes to therapy selection, which provided a better understanding of physicians' decision-making processes.

A key limitation of the study is that data were dependent on the accurate reporting of information by the respondents, which may have been subject to recall bias. Additionally, the survey sample was taken from physicians who were part of the M3 Global International Market Research Panel, and only from 4 European countries. The survey completion rate was rather low (7% in the United States and 16% in Europe), as is often the case with wide-reaching surveys such as the one used in this study; as such, the respondents may not be wholly representative of the general population of

physicians treating AF. However, it is likely that physicians who did respond to the survey were more representative of high-quality standards of care, which is particularly noteworthy in this context, given that adherence to guidelines was unsatisfactory. Another study limitation lies in the fact that this survey did not consider AAD dosing, which can condition both safety and efficacy of therapy and, as such, could have influenced physician responses. Furthermore, the threshold values assigned for certain questions were different than thresholds cited in the guidelines; for instance, guidelines recommend against using sotalol in patients with creatinine clearance <30 mL/min, while the survey classified renal impairment as estimated glomerular filtration rate <60 mL/min per 1.73 m^2. Results were not stratified by degree of renal impairment; therefore, it remains difficult to accurately estimate the number of respondents who are noncompliant in this regard. Both the lack of information on dosing and the inclusion of data on potential noncompliant prescribing could have had the effect of overinflating the nonadherence rates calculated for each agent, as each could result in compliant practice being scored as nonadherent. Furthermore, these rates do not include any weighting for the degree of deviation from the guidelines or the potential outcomes of nonadherence; for example, the use of a contraindicated agent in a patient with HF, which could severely compromise patient safety, has the same weight as a guideline-compliant dose reduction in a patient with renal impairment.

CONCLUSIONS

Across the United States and Europe, many physicians considered guidelines to be the most important nonpatient factor influencing treatment decisions with regard to AAD use. However, nonadherence with guideline recommendations was common, and responses indicated notable noncompliance and potential noncompliance, which may compromise patient safety. Further research to better understand physicians' reasons for nonadherence and interventional opportunities to improve adherence to guidelines is warranted.

ARTICLE INFORMATION

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Supplemental Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. List of survey questions in the AIM-AF study

Question number	Question	Responses
Screening/physician demographics		
S1	Firstly, in which country is your practice located? *Please select one*	1. US 2. UK 3. Germany 4. Italy 5. Sweden Other
S2a	What is your current primary medical interest? *Please select all that apply*	1. Clinical cardiologist (non-interventional) 2. Non-interventional cardiac electrophysiologist 3. Interventional cardiac electrophysiologist Other
S2b	Do you have any sub-specialty or areas of special interest? *Please select one*	1. Atrial fibrillation (AF) 2. Other, please specify None
S3	How many years have you been qualified in your specialty? *Please indicate to the nearest year*	_____years
S4	Approximately what percentage of your time is spent in the following activities? *Please type % for each row*	_____% actively treating patients _____% academic / research _____% admin / other
S5	In a typical 3 months (i.e. prior to the COVID-19 pandemic), how many patients with AF do you see? *Please specify both new and existing AF patients*	_____new patients _____existing/ongoing patients

S7a&b	In a typical 3-month period, on how many patients with AF do you conduct / refer an ablation procedure? Roughly what proportion of your total caseload of AF patients does this represent? *Please type in number*	____ per month ____% of my AF patients
S8	Which of the following best describes your role in the treatment of patients with AF? *Please select one only*	1. I prescribe drug treatments and ablate 2. I prescribe drug treatments and refer for ablation 3. I do not prescribe drug treatments nor perform ablation
S9	Do you agree with these terms and conditions? *Please select one*	1. I agree 2. I do not agree
S10	***Adverse event reporting*** This study is funded by a pharmaceutical company and for this reason we are required to pass on any possible Adverse Events, Product Complaints and Special Reporting Situations. The details of these will be reported anonymously unless you agree to disclose your personal details, only and exclusively for the purpose of follow-up by the client's drug safety team. Please select one of the options below: *Please select one*	1. I would like to proceed and agree to be contacted by the drug safety team for follow-up 2. I would like to proceed but do not wish to be contacted by the drug safety team for follow-up 3. I do not wish to proceed
S11	Please select which region/area you work in. *Please select one*	Options were provided in an appendix
Section A: Setting and caseload		
A1	A1a Which health care settings do you spend your time at? *Please tick all that apply* A1b Please indicate your main practice setting.	1. General community hospital/clinic (i.e. public or government hospital) 2. University hospital/clinic 3. Primary outpatient practice/clinic 4. Private hospital/clinic 5. Other (please specify)
A2a	For your main practice setting, approximately how many practitioners (including yourself) are there in your department?	1. Clinical cardiologists 2. Non-invasive cardiac electrophysiologist 3. Cardiac invasive electrophysiologists 4. Internists

	Type in number for each row	5. Fellows 6. Clinical pharmacologists 7. Physician assistants/nurse practitioners
A2b	How are physician assistants/nurse practitioners primarily involved in the treatment of AF patients in your practice? *Select all that apply*	1. Initiation of rate control treatments 2. Initiation of antiarrhythmic drugs (AADs) 3. Repeat prescriptions 4. Ongoing follow-up of patients 5. No role
A3a A3b A3c	Thinking about the patients you would see in a typical <u>three-month</u> period (i.e. prior to the COVID-19 pandemic): What is your typical total cardiology patient caseload? *This should be overall and include all diagnoses and conditions* What is your typical caseload of new patients with AF? And what is your typical caseload of follow-up patients with AF? *Please type number below:*	In a typical three-month period… ____ total cardiology patient caseload ____ new patients with AF ____follow-up patients with AF
A4	Thinking about your AF patient caseload ([pipe number from A3b&c "AF patients"] patients), what percentage fall into each of the following subgroups? *Please type % for each row*	1. First onset AF: AF presenting for the first time and not yet classified as paroxysmal, persistent, or permanent 2. Paroxysmal AF: Self-terminating, in most cases within 48 hours. Some AF paroxysms may continue for up to 7 days. AF episodes that are cardioverted within 7 days should be considered paroxysmal 3. Persistent AF: AF that lasts longer than 7 days, including episodes that are terminated by cardioversion, either with drugs or by direct current cardioversion, after 7 days or more 4. Mixed paroxysmal and persistent

		5. Long-standing persistent AF: Where the patient has had continuous AF for a year or longer, but rhythm control will be tried 6. Permanent AF: Where AF is present continuously for more than one year but no rhythm control will be attempted
A5	Thinking about your AF patient caseload [pipe number from A3b&c "AF patients"] patients, what percentage would you define as subclinical AF detected on an implantable device (pacemaker, implantable cardioverter defibrillator, loop recorder) or a wearable device (watch, phone, etc.)? *Please type % for each row*	1. Implantable device-detected subclinical AF ____% 2. Wearable device-detected subclinical AF ____%
A6	Of your AF patient caseload [pipe number from A3b&c "AF patients"] patients, approximately what percentage fits into the following categories when you first see them? *Please type % for each row*	1. Inpatient __% 2. Day case (in hospital)__% 3. Outpatient (clinic) __%
Section B: Treatment journey		
Information	**Questions designed to identify the typical treatment approaches of physicians for their patients with AF, with a focus on the use of oral antiarrhythmic drugs (AADs) and what influences their decision making.**	
B1	In what percentage of your patients with AF do you opt for each main strategy as first-line (after dealing with anticoagulation)? *Please type % for each row*	COLUMNS: 1. Paroxysmal AF 2. Persistent AF ROWS: 1. Primarily heart rate control only 2. Primarily rhythm control (with drugs) 3. Other, please specify
B2	What factors influence/guide your choice of rhythm control rather than rate control? *Please rank all options within each category*	<u>Non-patient factors:</u> 1. Guidelines 2. Previous personal experience 3. Scientific literature 4. Advice from colleagues 5. Other, please specify

		<u>Patient factors:</u> 1. Age of patient 2. Early onset of AF 3. Symptomatic status 4. Paroxysmal rather than persistent AF 5. Absence of structural heart disease 6. Presence of heart failure 7. Co-morbidities 8. Compliance 9. Patient preference 10. Other, please specify _____
B3	For what types of AF do you prefer to use (oral) antiarrhythmic drugs (AADs) as first line rather than ablation therapy? *Please select all that apply*	1. Asymptomatic recurrent AF 2. Mildly symptomatic but infrequent paroxysmal AF 3. Highly symptomatic infrequent paroxysmal AF patient 4. Frequent symptomatic paroxysmal AF 5. Infrequent symptomatic persistent AF 6. Frequent symptomatic persistent AF (2 or more cardioversions in the past year) 7. Long-standing symptomatic persistent AF (a year or longer) 8. Other, please specify ____ 9. No types of AF in particular
B4	How would you typically treat patients with subclinical (asymptomatic, detected by chance) AF, if at all? *Please select one answer*	1. Primarily rate control 2. Primarily rhythm control (with drugs) 3. No rate or rhythm treatment
B5	What factors influence your preference for (oral) AADs rather than the alternative of ablation therapy? *Please rank the top 5 influences.* *Click or drag to place your top 5 in rank order, where 1=most influential* *If any items do not influence you, do not rank them*	1. Presence of heart failure (HFrEF) 2. Other severe comorbidities 3. Potential for procedure-related complications 4. Old age of the patient 5. Patient preference 6. Cost/reimbursement 7. Concerns about ablation efficacy in general (dilated left atrium, time in persistent AF) 8. Long AF duration 9. ESC and ACC/AHA/HRS algorithms emphasize safety first over efficacy

		10. Need for medication for other conditions (patient is taking medication anyway) 11. Comorbidities that shorten survival 12. Other, please specify____
B6	When choosing a particular (oral) AAD, please rank the top 5 considerations that broadly influence your choice of AAD. *Click or drag to place your top 5 in rank order, where 1=most important* *If any items do not influence you, do not rank them*	1. Efficacy 2. Safety 3. No need for hospitalization at initiation 4. Comfort with the drug based on prior experience 5. Drug–drug interaction 6. Cost/reimbursement 7. Patient comorbidities 8. Patient preference 9. Need for ongoing electrocardiogram or laboratory monitoring 10. Other, please specify _____
B7	When prescribing an AAD, does the regulatory agency approval of a drug for a specific rhythm control indication influence your decision regarding the use of that drug? *Please select one*	1. Yes 2. No 3. Not sure
B8	Thinking in more detail about efficacy and safety considerations when prescribing an AAD, please rank the top 5 considerations that influence your choice of AAD. *Click or drag to place your top 5 in rank order, where 1=most important* *If any items do not influence you, do not rank them*	1. Efficacy in reducing mortality and CV hospitalizations 2. Efficacy in terms of % of sinus rhythm maintenance at long term after electrical CV event 3. Low risk of atrial proarrhythmia (e.g. 1:1 atrial flutter) 4. Low risk of ventricular proarrhythmia 5. Low risk of major cardiovascular adverse effects 6. Low risk of major non-cardiovascular adverse effects (pulmonary, hepatic, thyroid, neurologic) 7. Other, please specify _____
B9	Does the combination of both antiarrhythmic and rate control properties in a single drug influence your choice of AAD?	1. Yes 2. No 3. Not sure
B10	When do you consider an AAD as not working? *Please select all that apply*	1. Single recurrence 2. Multiple recurrences of symptomatic episodes 3. Need for hospitalizations 4. High daily burden

		5. Other, specify _____
B11	In some cases, ablation may take place first-line prior to prescribing any AAD (Class I and III AADs). Why is this? *Please select all that apply*	1. Prefer to conduct ablation as early as possible to prevent progression of AF 2. I would never conduct ablation first line *(exclusive)* 3. Concerns about AAD efficacy/belief of higher efficacy with ablation 4. Concerns about AAD safety 5. Best treatment for paroxysmal AF 6. Avoiding anticoagulation 7. Special conditions: Comorbidities e.g. heart failure 8. Special conditions: Sinus node dysfunction 9. Special conditions: Age of the patient 10. Drug–drug interaction 11. Special conditions: Exercise/athletic considerations 12. Avoidance of long-term drug therapy 13. Patient preference 14. Cost/reimbursement/beneficial economic profile for practice or hospital 15. Other, please specify___
B12	Of the answers you selected, please pick the top 3 reasons for why ablation may take place first-line prior to prescribing any AAD (Class I and III AADs)? *Click or drag to place your top 3 in rank order, where 1=most important* *If any items do not influence you, do not rank them*	1. [Answers piped from B11]
B13	Does your center focus on ablation or AADs as a first-line treatment recommendation, or are both drugs and ablation options used as first-line? *Select one*	1. Focus on ablation first-line 2. Focus on AAD as first-line 3. Offer both drugs and ablation first-line
B14a B14b	Thinking about the following circumstances/comorbidities that AF patients often present with…	COLUMNS (DRUG SHORT LIST): 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone

	Which AAD(s) would you typically use in these patients? *Select all per row* And of the ones you use, which do you use most of all? *Please select which of the AAD(s) you are most likely to prescribe for each comorbidity*	5. Sotalol 6. Dofetilide (US only) 7. Other AAD, please specify ROWS: AF patients with… 1. Minimal or no structural heart disease 2. Heart failure with reduced left ventricular function (with LVEF <40%) 3. Heart failure with preserved left ventricular function 4. Reduced left ventricular function (LVEF <40%) but no symptoms of heart failure 5. Left ventricular hypertrophy 6. Hypertension 7. Valve disease i.e. aortic stenosis 8. Myocardial ischemia without prior myocardial infarction 9. Revascularized coronary artery disease patient 10. Recent myocardial infarction (within 3 months) 11. Old myocardial infarction (after 3 months) 12. Renal impairment (eGFR <60mL/min/1.73m^2) 13. Chronic lung diseases 14. Chronic liver disease
B15	How would you manage most patients in the following categories? *Please select all that apply in each row (for each patient type)*	ROWS: 1. Implantable-device-detected or subclinical AF 2. Asymptomatic AF 3. First attack of symptomatic AF 4. Recurrent episodes of symptomatic AF 5. Recurrence after one AAD 6. Recurrences after multiple AADs 7. Recurrences after AAD combinations COLUMNS: 1. Drug rate control alone (no rhythm control) 2. Ablation for rate control (AV node ablation) and pacemaker implantation 3. Drug rhythm control (plus rate control with drugs)

		4. Ablation for rhythm control
B16a B16b	Which of the following guidelines do you follow for the treatment of patients with AF? *Select all that apply* Which is the MAIN one that you follow / that is most important for your decision making? *Select one*	1. American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) 2. Canadian Cardiovascular Society (CCS) 3. European Society of Cardiology (ESC) 4. National Institute for Health and Care Excellence (NICE) guidelines 5. Other national/local guidelines, please specify _____ 6. Hospital guidance/protocol 7. I do not follow any particular treatment guidelines
B17	Of the following AAD drugs, which method of initiation do you use in most of your patients? 1. Typically initiate in hospital 2. Outpatient initiation with intensive ECG monitoring 3. Initiate out of hospital with only a routine clinic appointment after initiation *Select one option per drug*	ROWS: 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) COLUMNS: 1. Typically initiate in hospital 2. Outpatient initiation with intensive ECG monitoring 3. Initiate out of hospital with only a routine clinic appointment after initiation
B18	In what proportion of patients do you use these methods to monitor for recurrences? *Please type % for each (several methods may be used, i.e. does not need to add up to 100%)*	1. Symptoms 2. Patient self-check of pulse 3. 12-lead ECGs in the clinic 4. Ambulatory Holter recordings or patch ECG recordings 5. Loop recorders 6. Watch plethysmographs 7. Watch ECGs 8. Smart phone ECGs 9. Event recorders (Zio, Bardy, etc) 10. Other, please specify _____ 11. No routine monitoring for recurrence

B19	How often do you use an implantable loop recorder for monitoring in each of the following situations? *Please select one per row*	ROWS: 1. Documentation of AF burden pre-ablation 2. Assessment of AT/AF occurrence/recurrence post-ablation 3. Symptom diagnosis 4. Assessment of AAD efficacy 5. Evaluation of rate control COLUMNS: 1. Always (76–100% of patients) 2. Often (51–75%) 3. Sometimes (26–50%) 4. Rarely (1–25%) 5. Never (0%)
B20	How do you routinely verify a) heart failure and b) ischemic heart disease before undertaking AF AAD treatment? *Select all that apply*	COLUMNS: a) Heart failure b) Ischemic heart disease ROWS: 1. Functional stress testing 2. Echocardiography e.g. for assessment of LA size and LVEF, etc., 3. Other imaging (cardiac CT, MRI, coronary angiography) 4. Other, please specify _____ 5. Do not routinely verify [exclusive]
Section C: Prescribing/treatment practices		
Information	**Questions designed to focus in more detail on specific treatment practices.**	
C1	Please indicate the % of your patients with AF who would receive each treatment approach as first-line treatment. *Please type % of patients for each column* *Keep thinking about your [A3b+c] patients as your total AF population*	COLUMNS (pipe in numbers in each subgroup from A4/A5): 1. First onset AF (unclassified) 2. Paroxysmal AF 3. Persistent AF 4. Mixed paroxysmal and persistent 5. Long-standing persistent AF 6. Permanent AF 7. Device/wearable-detected asymptomatic AF

		ROWS: 1. Drug rate control alone (no rhythm control) 2. Ablation for rate control (AV node ablation) and pacemaker implantation 3. Drug rhythm control (plus rate control with drugs) 4. Ablation for rhythm control 5. Other 6. None of the above
C2a	How often do you use beta-blockers for a) rate control and b) rhythm control? *Please select one per row*	COLUMNS: a) Rate control b) Rhythm control ROWS: 1. Always (76–100% of patients) 2. Often (51–75%) 3. Sometimes (26–50%) 4. Rarely (1–25%) 5. Never (0%)
C2b	Of the beta-blockers listed, please rank the <u>top three</u> that you use for rhythm control and rate control? *Please rank your top three with 1 being most preferred.*	COLUMNS 1. Rhythm control 2. Rate control ROWS: Beta-blockers: 1. Acebutolol 2. Atenolol 3. Betaxolol 4. Bisoprolol 5. Carvedilol 6. Labetalol 7. Metoprolol succinate 8. Metoprolol tartrate 9. Nadolol 10. Nebivolol

		11. Penbutolol 12. Pindolol 13. Propranolol 14. Timolol
C3a	How often do you use non-dihydropyridine calcium antagonist/channel blocker (CCB) for a) rate control and b) rhythm control? *Please select one per column*	COLUMNS: a) Rate control b) Rhythm control ROWS: 1. Always (76–100% of patients) 2. Often (51–75%) 3. Sometimes (26–50%) 4. Rarely (1–25%) 5. Never (0%)
C3b	Which non-dihydropyridine calcium antagonist/channel blocker (CCB) do you prefer to use? *Please select one*	1. Diltiazem 2. Verapamil
C4	How often do you use digitalis glycosides for a) rate control and b) rhythm control? *Please select one per column*	COLUMNS: a) Rate control b) Rhythm control ROWS: 1. Always (76–100% of patients) 2. Often (51–75%) 3. Sometimes (26–50%) 4. Rarely (1–25%) 5. Never (0%)
C5	Of the following sodium channel blockers, which have you used for patients with AF for long-term use in the last 12 months? *Please select all that apply*	1. Quinidine 2. Propafenone 3. Flecainide 4. Disopyramide 5. Antazoline 6. Cibenzoline

		7. Ranolazine 8. Other, please specify _____ 9. None
C6	Of the following potassium or multichannel K channel blockers, which have you used for patients with AF for long term use in the last 12 months? *Please select all that apply*	1. Amiodarone 2. Dronedarone 3. Sotalol 4. Other, please specify _____ 5. None
C7a and b	Which drug combinations for rhythm control do you use most often, if any? *Please select all that apply* For, each combination, please specify which drugs you most commonly use: *Please use the drop-down menus*	Category (multi select): 1. AAD + beta blocker 2. AAD + calcium channel blocker (CCB) 3. AAD + digitalis 4. Combinations of AADs 5. Other combination 6. I do not use drug combinations [exclusive] [masked from items selected at above] For, each combination, please specify which drugs you most commonly use: 1. AAD + beta blocker, please specify: ____ + _____ 2. AAD + CCB, please specify: ____ + _____ 3. AAD + digitalis, please specify: ____ + _____ 4. Combinations of AADs, please specify: ____ + _____ 5. Other combination, please specify: ____ + _____
C8	In what percentage (%) of your AF patients overall do you use drug combinations? *Please estimate the % for each of the AF patient subtypes*	1. First onset AF (unclassified) 2. Paroxysmal AF 3. Persistent AF 4. Mixed paroxysmal and persistent 5. Long-standing persistent AF 6. Permanent AF
C9	In patients with AF on an AAD who experience a recurrence, in what percentage do you: *Please type in % per row*	1. Try another AAD (switch) 2. Try combinations of AADs (add-on) 3. Move to ablation 4. Other, please specify

C10	Now we will focus on your use of AADs in patients with AF in four different patient types. 1. Thinking of patients with AF who have no or minimal structural heart disease… Which AAD drug do you most commonly use in each of these patient sub-groups? *Select one drug per column*	COLUMNS: 1. First onset AF (unclassified) 2. Paroxysmal AF 3. Persistent AF 4. Mixed paroxysmal and persistent 5. Long-standing persistent AF 6. Permanent AF ROWS: (short drug list) 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) 7. Other AAD, please specify _____ None
C11	2. <u>For patients with AF who have coronary artery disease...</u> Which AAD drug do you most commonly use in each of these patient sub-groups? *Select one drug per column*	Same options as C10
C12	3. <u>For patients with AF who have heart failure…</u> Which AAD drug do you most commonly use in each of these patient sub-groups? *Select one drug per column*	Same options as C10
C13	4. <u>For patients with AF who have left ventricular hypertrophy (>1.4 cm)…</u> Which AAD drug do you most commonly use in each of these patient sub-groups?	Same options as C10

	Select one drug per column	
C14	In what % of your patients with paroxysmal or persistent AF do you use the “pill-in-the-pocket approach”, as opposed to a daily AAD regimen? *Type in %*	COLUMNS: 1. Paroxysmal AF 2. Persistent AF ROWS: 1. Minimal or no heart disease 2. Structural heart disease
C15	When you use “pill-in-the-pocket”, do you: *Please select one*	1. Use it without rate control 2. Use it only in patients taking regular rate control therapy 3. Add rate control medication to the “pill-in-the-pocket” therapy
C16	Which rate control therapy do you prefer to use with “pill-in-the-pocket” therapy? *Please select one*	1. Beta-blockers 2. CCBs 3. Digitalis glycosides
C17	Which AAD drug(s) do you use for the “pill-in-the-pocket” approach? *Please select all that apply*	COLUMNS: 1. Minimal or no heart disease 2. Structural heart disease ROWS: (short drug list) 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) 7. Other, please specify ___
C18	What arrhythmia frequency seems appropriate to you to use the “pill-in-the-pocket” approach? *Please select one*	1. About once a month or more 2. Once every 2–3 months 3. Every 4–6 months 4. Every 7–12 months 5. Yearly or more
C19	What investigations do you request routinely (at least yearly) in your patients who are taking each of the following AADs?	COLUMNS: 1. Amiodarone 2. Dronedarone

	Please select all that apply	3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) ROWS: 1. ECG 2. Renal function 3. Electrolytes 4. Hepatic function 5. Echocardiogram 6. Plasma concentration 7. Chest x-ray 8. Stress (exercise) test/assessment heart rate control 9. Thyroid function 10. Respiratory function 11. Visual/ophthalmology 12. Other, please specify _____ 13. No routine investigations
C20	What, if any, are the main reasons in general for not using the following AADs, in your opinion? *Please select all that apply* *Please note, do not report any individual patient experience encountered while being treated with a product*	COLUMNS: 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) ROWS: 1. Poor efficacy 2. Increased mortality 3. Ventricular proarrhythmic effects 4. Aggravation of heart failure 5. Other side effects 6. Specific comorbidity, please specify _____ 7. Poor general health status of patient

<table>
<tr><td></td><td></td><td>8. Specific patient characteristic, please specify: _____
9. Other, please specify _____
10. None</td></tr>
<tr><td>C21a, b, c</td><td>In your opinion, which of the following safety concerns would you associate with these AADs, if any?

Please select all that apply</td><td>COLUMNS:
1. Amiodarone
2. Dronedarone
3. Flecainide
4. Propafenone
5. Sotalol
6. Dofetilide (US only)

ROWS:
1. Mortality
2. Heart failure
3. Ventricular proarrhythmia
4. Atrial flutter with 1:1 conduction
5. Systemic toxicity (e.g. liver, lung, renal etc.)
6. Bradycardia/conduction system disease
7. No safety risks</td></tr>
<tr><td>C22</td><td>In your opinion, for patients with recurrent AF treated with the following AADs, what is an approximate estimate of drug withdrawal rates at long term (2 years) for safety reasons or side effects in general?

Please think hypothetically</td><td>
<table>
<tr><th></th><th>0%</th><th>1–2%</th><th>3–10%</th><th>11–25%</th><th>26–40%</th><th>>40%</th></tr>
<tr><td>Amiodarone</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Dronedarone</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Flecainide</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Propafenone</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Sotalol</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Dofetilide (US only)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>C23</td><td>In your opinion, for patients with recurrent AF treated with the following AADs, what is an approximate estimate of drug withdrawal rates at long term (2 years) for efficacy reasons (i.e. lack of a satisfactory clinical effect, even if no complete efficacy)?</td><td>
<table>
<tr><th></th><th>0%</th><th>1–5%</th><th>6–15%</th><th>16–30%</th><th>31–50%</th><th>>50%</th></tr>
<tr><td>Amiodarone</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Dronedarone</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Flecainide</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Propafenone</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Sotalol</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>
</td></tr>
</table>

	Please think hypothetically	Dofetilide (USA only) | | | | | | |
C24	Do you have concerns using any of the following drugs with: - Apixaban - Dabigatran - Edoxaban - Rivaroxaban - Vitamin K antagonist e.g. warfarin *Select all that apply for each column*	COLUMNS (AADs): 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) 7. Beta blockers 8. Non-dihydropyridine calcium antagonist/channel blocker (CCB) 9. Digitalis ROWS: 1. Apixaban 2. Dabigatran 3. Edoxaban 4. Rivaroxaban 5. Vitamin K antagonists e.g. warfarin and phenprocoumon 6. I don't have any concerns
Section D: Ablation		
Information	**Questions designed to focus on the use/recommendation of ablation procedures.**	
D1: alternative wording was used dependent on specialty	Now we will focus on your use of ablation as first procedure (de novo) for rhythm control. Which ablation procedure do you most commonly recommend in each of these patient sub-groups? *Single select*	COLUMNS: 1. Paroxysmal AF 2. Persistent AF 3. Long-standing persistent AF 4. Permanent AF ROWS: 1. PVI alone 2. PVI plus other additional ablation lesions

		Cardiologists only: show “Don’t know”
D2	Which patient types are you more likely to refer for ablation, rather than initiation of AAD drug treatment? *Please put the options into rank order, where 1=most likely* *If you are not likely to refer these patients for ablation, do not rank them*	1. Subclinical AF 2. Asymptomatic recurrent AF 3. Mildly symptomatic but infrequent paroxysmal AF 4. Frequent symptomatic paroxysmal AF 5. Infrequent persistent AF 6. Persistent AF (2 or more cardioversions in the past year) 7. Long-standing persistent AF (a year or longer) 8. Recurrence of AF post-ablation 9. Other, please specify____
D3	Are there any patient characteristics that would preclude attempts at ablation? *Please select all that apply*	1. Over a specific age, specify _____ 2. Specific comorbidities 3. Left atrial diameter, please specify mm____ 4. Left ventricular impairment 5. Other, specify ____ 6. None of the above
D4	What percentage of your ablation patients have previously tried an AAD? *Type in % for each row*	1. ____% have not previously tried any AAD 2. ____% have previously tried one AAD 3. ____% have previously tried more than one AAD 4. ____% don’t know
D5	In what % of your patients in the following groups do you use an AAD after the ablation procedure: *Type in % per row*	1. Directly after the ablation procedure in all patients irrespective of symptoms/recurrences until first post-ablation visit after 3–6 months ___% 2. Directly after ablation procedure in all patients irrespective of symptoms/recurrences for 1–2 months post-ablation ___% 3. Any time post-ablation if symptomatic AF recurrences ___% 4. Short term if AF recurrence and a re-ablation is planned ___% 5. Long term if AF recurrence and a re-ablation is not planned ___%
D6ai D6aii	1. <u>Thinking about your patients with paroxysmal AF:</u> Which AAD drugs do you tend to use in patients after ablation at the following time points:	COLUMNS: 1. Directly after the ablation procedure in all patients irrespective of symptoms/recurrences until first post-ablation visit after 3–6 months

	- Directly after the ablation procedure in all patients irrespective of symptoms/recurrences until first post-ablation visit after 3–6 months - Directly after ablation procedure in all patients irrespective of symptoms/recurrences for 1–2 months post-ablation - Any time post-ablation if symptomatic AF recurrences - Short term if AF recurrence and a re-ablation is planned - Long term if AF recurrence and a re-ablation is not planned *Select one drug per column*	2. Directly after ablation procedure in all patients irrespective of symptoms/recurrences for 1–2 months post-ablation 3. Any time post-ablation if symptomatic AF recurrences 4. Short term if AF recurrence and a re-ablation is planned 5. Long term if AF recurrence and a re-ablation is not planned ROWS: 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) 7. Other AAD, please specify ____ 8. No drug treatment D6aii: FOR EACH TIME POINT, TICK BOX: Is this drug used for recurrence or prophylactically? a) For recurrence b) Prophylactically c) No drug treatment
D6bi D6bii	2. <u>Thinking about your patients with non-paroxysmal AF:</u> Which AAD drug do you tend to use in patients after ablation at the following time points? 1. Directly after the ablation procedure in all patients irrespective of symptoms/recurrences until first post-ablation visit after 3–6 months	COLUMNS: 1. Directly after the ablation procedure in all patients irrespective of symptoms/recurrences until first post-ablation visit after 3–6 months 2. Directly after ablation procedure in all patients irrespective of symptoms/recurrences for 1–2 months post-ablation 3. Any time post-ablation if symptomatic AF recurrences 4. Short term if AF recurrence and a re-ablation is planned 5. Long term if AF recurrence and a re-ablation is not planned

	2. Directly after ablation procedure in all patients irrespective of symptoms/recurrences for 1–2 months post-ablation 3. Any time post-ablation if symptomatic AF recurrences 4. Short term if AF recurrence and a re-ablation is planned 5. Long term if AF recurrence and a re-ablation is not planned *Select one drug per column*	ROWS: 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) 7. Other AAD, please specify ____ 8. No drug treatment D6bii - FOR EACH TIME POINT, TICK BOX: Is this drug used for recurrence or prophylactically? a) For recurrence b) Prophylactically c) No drug treatment
D7	Which AAD do you generally use in a hypothetical patient who has an atrial tachyarrhythmia directly after the ablation procedure? *Select one drug per column*	COLUMNS: Arrhythmias seen after the ablation procedure (not the primary ablated arrhythmia) 1. Paroxysmal AF 2. Persistent AF 3. Atrial tachycardia/atypical flutter 4. Common atrial flutter ROWS: 1. Amiodarone 2. Dronedarone 3. Flecainide 4. Propafenone 5. Sotalol 6. Dofetilide (US only) 7. Other AAD, please specify 8. No AAD drug treatment D7i - FOR EACH TIME POINT, TICK BOX:

		Is this drug used for recurrence or prophylactically? a) For recurrence b) Prophylactically c) No drug treatment
D8	In general, for those patients who receive an AAD directly after the ablation procedure (i.e. within first 3-6 months), do you tend to use a new AAD or one that the patient previously received prior to ablation? *Select one option*	1. AAD that was unsuccessful prior to ablation 2. AAD that was partially successful following first ablation 3. AAD that was not used before 4. Drug combination that was not used before 5. Rate controlling drug 6. Other, please specify _____
D9	Does the energy source (cryo or RFA) influence AAD therapy after PVI? *Select one option*	1. Yes, with cryo I use ____ 2. Yes, with RFA I use ____ 3. No 4. Don't know
D10	How do you judge the efficacy of ablation? *Please select all that apply*	1. Recurrence of any atrial fibrillation irrespective of duration or associated symptoms 2. Single symptomatic AF/atrial tachycardia 3. High burden of AF 4. Need for hospitalization 5. Other, specify _____
D11	What percentage of your patients referred for ablation have a clinically significant recurrence that mandates a re-ablation within 1 year? *Please type % for each column*	ROW: 1. Paroxysmal AF 2. Persistent AF 3. Long-standing persistent /permanent AF COLUMN: __% patients who undergo re-ablation
D12	And in patients who receive an AAD after ablation, do you tend to use a new AAD or one that the patient previously received prior to ablation, or is rate control sufficient? *Select one option*	1. AAD that was unsuccessful prior to ablation 2. AAD that was partially successful following first ablation 3. AAD that was not used before 4. Drug combination that was not used before 5. Rate controlling drug 6. Other, please specify _____

Section E: Patient types/scenarios		
Information	**Questions based on several different AF patient profiles, allowing physicians to consider how they would treat these patients. Physicians were encouraged to draw on experiences with real patients where possible.**	
E1a-j	In a patient with recurrent symptomatic AF in whom AF ablation is deferred or not planned, what is your first pharmacological option with AAD if the hypothetical patient … a. ...has no or minimal signs for structural heart disease (i.e. no left ventricular hypertrophy nor LV dilatation, and no ischemic heart disease)? b. …has history of coronary artery disease (MI 5 years ago, no active ischemia), normal left ventricular EF, with no current signs/symptoms of ischemia? c. …has history of mild stable heart failure, NYHA II, LVEF 45%, no hospitalization during the least two years? d. …has mild left ventricular hypertrophy (<14 mm LV thickness at echocardiogram)? e. …has hypertensive moderate/severe left ventricular hypertrophy (≥14mm LV thickness at echocardiogram)? f. …has heart failure with preserved ejection fraction (>50%)? g. … has major comorbidities but without severe heart failure?	[short DRUG LIST] plus beta blockers And other and none

	h. …is an asymptomatic patient with evidence of CAD on a cardiac CT scan, but no IHD history and a negative stress test? i. …has bradycardia tendency or intraventricular conduction defects? j. …has paroxysmal AF and sinus node dysfunction? k. …has moderate chronic kidney disease (eGFR 30–60 ml/min/1.73m^2)? l. … has severe chronic kidney disease (<30 ml/min/1.73m^2) m. … has hypertrophic cardiomyopathy and AF?	
E2	What are the general differences in how you treat men versus women? *Please select all that apply, and explain your response(s)*	1. Rate control vs rhythm control, please explain _____ 2. Ablation vs AADs, please explain _____ 3. Choice of AAD, please explain _____ 4. Choice of AAD dose, please explain _____ 5. I don't treat men and women differently
E3	What is your age limit for rhythm control with drugs, if any? *Select one option*	1. >65 years of age 2. >70 years of age 3. >75 years of age 4. >80 years of age 5. No limit
E4	What is your age limit for rhythm control with ablation, if any? *Select one option*	1. >65 years of age 2. >70 years of age 3. >75 years of age 4. >80 years of age 5. No limit
Section F: Future AF landscape		
Information	**Questions designed to investigate physician opinions on the future for management of patients with AF**	

F1a	Thinking ahead… Do you think the uptake of first-line ablation will change in the next 3–5 years? *Select one option*	1. No change 2. Decrease 3. Increase 4. Don't know
F1b	You stated the uptake of ablation will decrease in the next 3–5 years. Please tell us the approximate decrease. *Please select one*	1. 10% 2. 25% 3. 50% 4. >50%
F1c	You stated the uptake of ablation will increase in the next 3–5 years. Please tell us the approximate increase. *Please select one*	5. 10% 6. 25% 7. 50% 8. >50%
F2	Thinking about the new AADs that will be coming to market in the next 5–10 years, what changes or improvements in AADs would you LIKE to see, ideally? *Please rank these in terms of what you would like to see*	1. Greater antiarrhythmic efficacy 2. Drugs that reverse remodelling 3. Less proarrhythmia 4. Less effect on ventricular function 5. Fewer complications 6. New modes of action 7. Other, please specify _____
F3	Where do you see as the most important indications/situations for AADs in the future? *Select top 3*	1. For prevention of AF recurrence 2. For prevention of post-ablation AF recurrence 3. Whilst waiting for an ablation 4. For ablation failure or as hybrid therapy 5. For patients not willing or with high risk of ablation 6. For patients due to health care limitations 7. For patients unable to afford an ablation 8. Other, please specify _____ 9. No place for AADs in the future [exclusive]
F4	In your opinion, is there a need for clinical trials of AADs post-ablation that were ineffective prior to ablation? *Select one option*	1. Yes 2. No 3. Not sure
F5	Did the recent 2020 ESC Guidelines on AF influence your responses to this survey?	1. Yes

		2. No 3. Not sure (if yes/no): Please explain: _____
F6a	Are you aware of the EAST study presented at the European Society of Cardiology 2020 congress?	1. Yes 2. No 3. Not sure
F6b and c (2 questions on 1 page)	a) Did the results of the EAST study influence your choice between rate and rhythm control? b) Has it influenced the choice of AAD versus ablation?	1. Yes 2. No 3. Not sure (if yes/no): Please explain: _____