# Supplementary Online Content

Barnett AS, Lewis WR, Field ME, et al. Quality of evidence underlying the American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines on the management of atrial fibrillation. *JAMA Cardiol*. Published online December 14, 2016. doi:10.1001/jamacardio.2016.4936



This supplementary material has been provided by the authors to give readers additional information about their work.

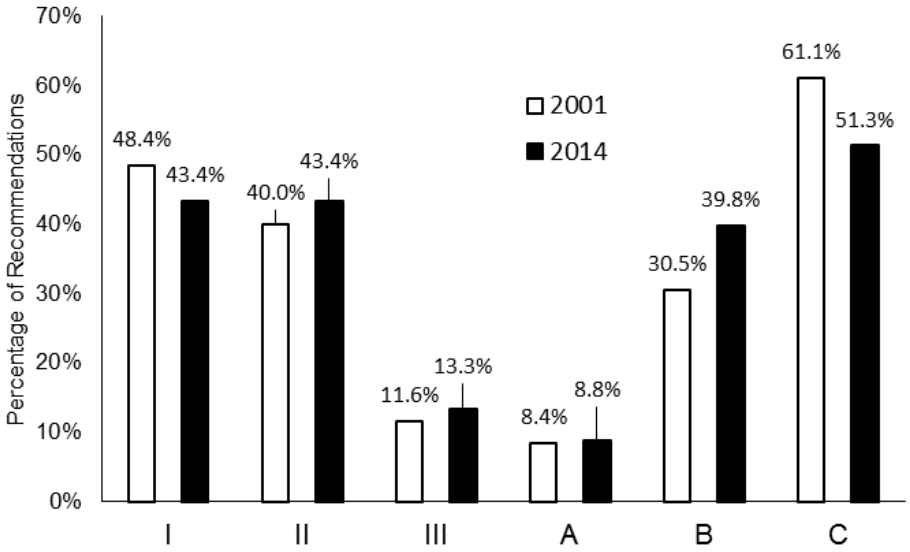
**eAppendix.** Complete Methods

The AHA/ACC/HRS practice guidelines on AF from 2001,[2] 2006,[3] 2011,[4] and 2014[5] were abstracted. Guidelines were obtained from the AHA website (http://my.americanheart.org/professional/StatementsGuidelines) with the exception of the 2001 guideline, which was obtained from the original journal article. For each guideline document, all recommendations were extracted with the corresponding class of recommendation (COR) and level of evidence (LOE). Class IIa and IIb were grouped into one class II for the analysis. The category of each recommendation as specified in the guideline document was also recorded, including antithrombotic therapy, rate control, maintenance of sinus rhythm (including cardioversion, antiarrhythmic drugs, and ablation), as well as miscellaneous recommendations. Approval of the institutional review board and informed consent were not obtained because this study did not involve human subjects.

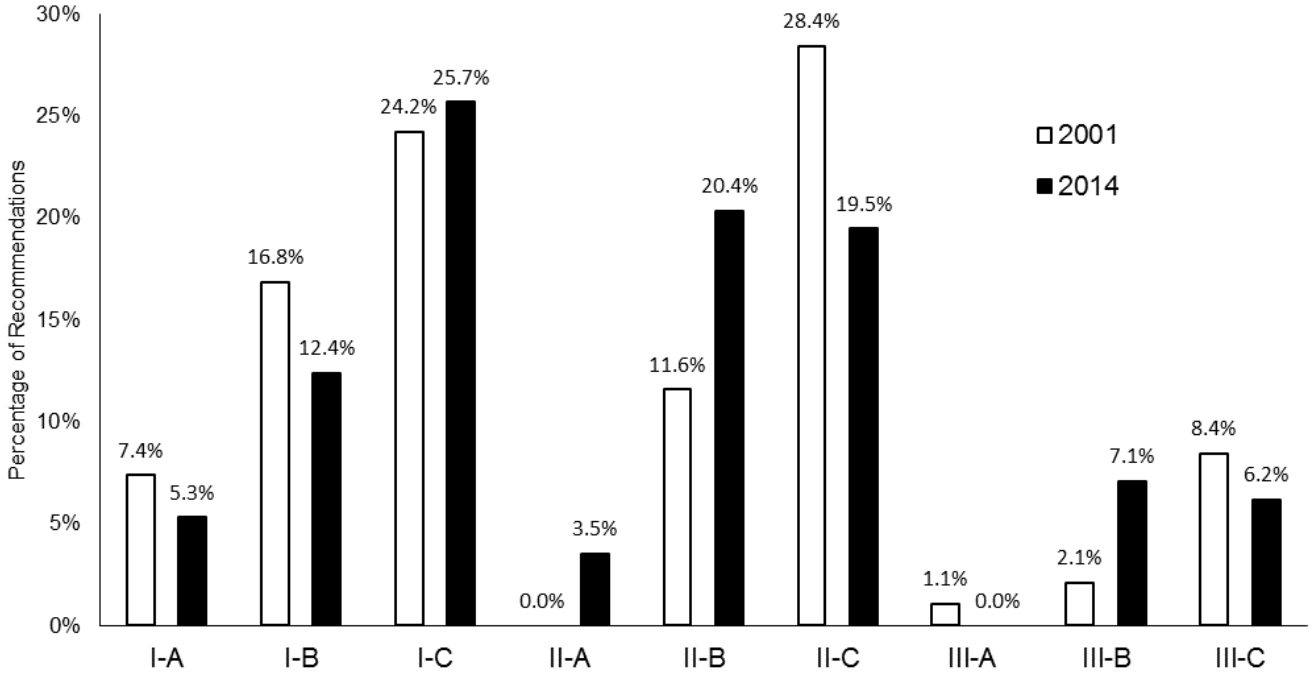
For each guideline version, the proportion of recommendations falling under each COR and LOE was determined. The percentage change in the proportion of recommendations within each category between the 2001 and 2014 guideline versions was then calculated. Similar calculations were performed with recommendations grouped by specific COR – LOE combinations and by AF categories. P values were calculated using a two proportion z-test using data from the 2001 and 2014 guideline editions. In addition, we recorded recommendation class and level of evidence for 21 individual recommendations that were present in both the 2001 and 2014 guideline editions. All calculations were performed in Microsoft Excel.

To quantify the amount of clinical research in AF since the guideline was first published, we conducted a search of the MEDLINE database for studies on AF from 2001 to 2014. The number of annual publications on AF in humans was determined by searching for all publications with the Medical Subject Headings (MeSH) terms “atrial fibrillation” and “humans” each year from 2001 to 2014. This search was then repeated with the additional filter of publication type “randomized clinical trial.” Both searches were performed on November 29, 2015.

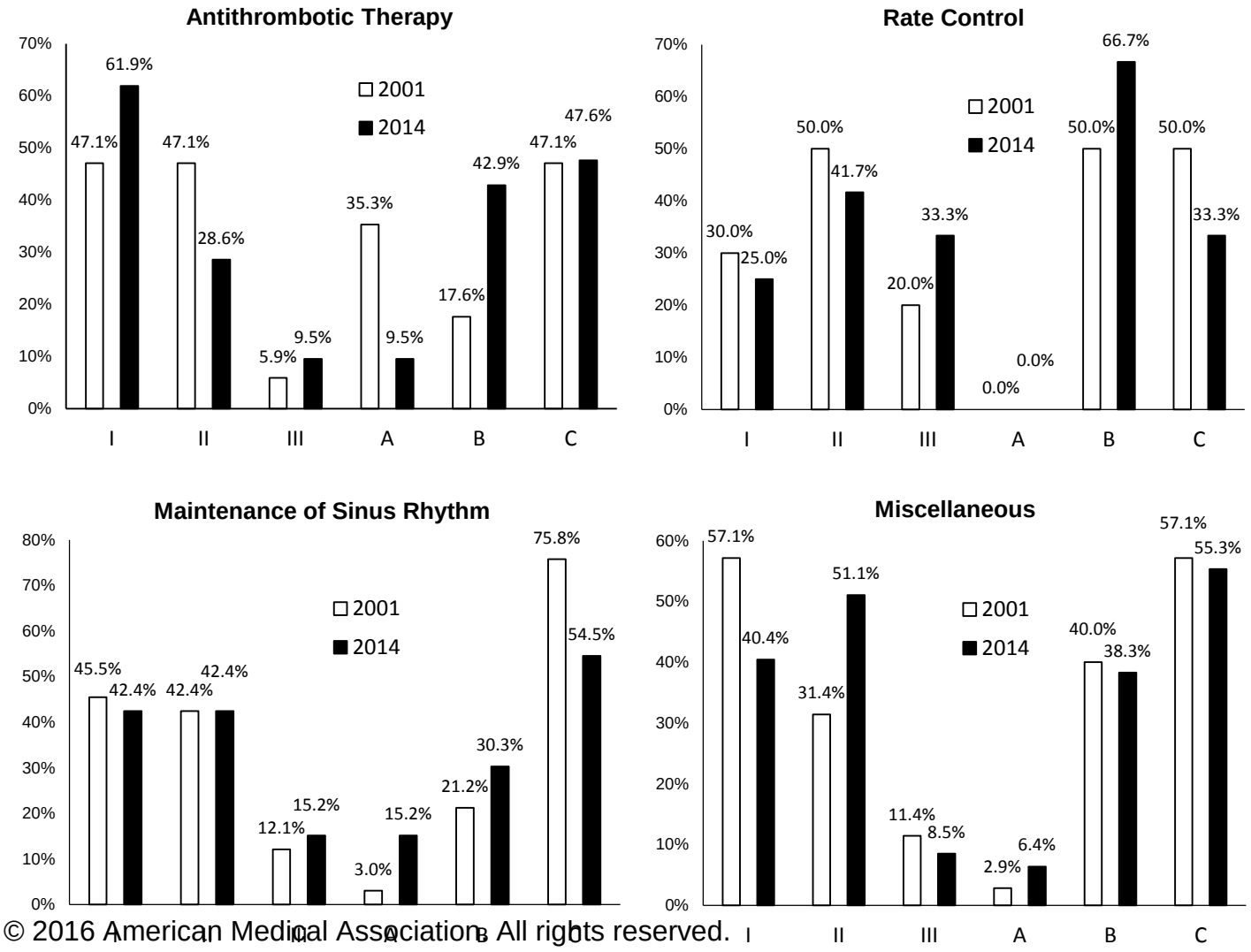
**eFigure 1.** Distribution of Recommendations Assigned as Class I, II, or III and Level of Evidence A, B, or C in 2001 and 2014



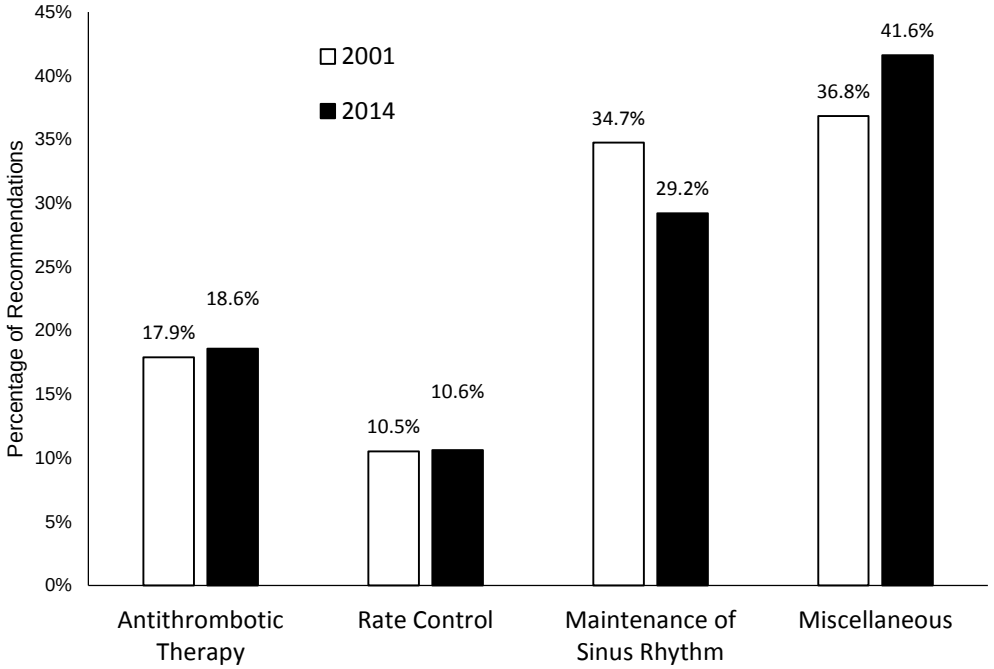
**eFigure 2.** Distribution of Recommendations Across Specific Class Of Recommendation–Level of Evidence Combinations in 2001 and 2014



**eFigure 3.** Distribution of Recommendation Class and Level of Evidence in 2001 and 2014 By Category of Recommendation as follows: Antithrombotic therapy (top left), Rate control (top right), Rhythm control (bottom left), Miscellaneous (bottom right)



**eFigure 4.** Distribution of Recommendations Across Atrial Fibrillation Treatment Categories in 2001 and 2014



| **eTable.** Class of Recommendation and Level of Evidence for 21 Recommendations in 2001 and 2014 | | | | | |
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| **2001** | | | **2014** | | |
| **COR** | **LOE** | **Text** | **COR** | **LOE** | **Text** |
| I | C | Immediate electrical cardioversion in patients with paroxysmal AF and a rapid ventricular response who have ECG evidence of acute MI or symptomatic hypotension, angina, or HF that does not respond promptly to pharmacological measures. (Level of Evidence: C) | I | C | Cardioversion is recommended when a rapid ventricular response to AF or atrial flutter does not respond promptly to pharmacological therapies and contributes to ongoing myocardial ischemia, hypotension, or HF. ***(Level of Evidence: C)*** |
| I | C | Treat precipitating or reversible causes of AF before initiating antiarrhythmic drug therapy. | I | C | Before initiating antiarrhythmic drug therapy, treatment of precipitating or reversible causes of AF is recommended. |
| I | B | Base selection of pharmacological therapy to maintain sinus rhythm in patients with disabling or otherwise troublesome symptoms during AF predominantly on safety. | I | C | The risks of the antiarrhythmic drug, including proarrhythmia, should be considered before initiating therapy with each drug. |
| I | B | Administer intravenous beta-blockers or calcium channel antagonists (verapamil, diltiazem) in the acute setting to slow the ventricular response to AF in the absence of conduction over an accessory pathway, exercising caution in patients with hypotension or HF. (Level of Evidence: B) | I | B | Intravenous administration of a beta blocker or nondihydropyridine calcium channel blocker is recommended to slow the ventricular heart rate in the acute setting in patients without pre-excitation. In hemodynamically unstable patients, electrical cardioversion is indicated (96–99). ***(Level of Evidence: B)*** |
| I | C | Measure heart rate response both at rest and during exercise in patients with persistent or permanent AF and control the rate with pharmacological agents (using a beta-blocker or calcium channel antagonist in most cases) to the physiological range. | I | B | Control of the ventricular rate using a beta blocker or nondihydropyridine calcium channel antagonist is recommended for patients with paroxysmal, persistent, or permanent AF |
| III | C | Catheter ablation without prior medical therapy to control AF. | III | C | AV nodal ablation with permanent ventricular pacing should not be performed to improve rate control without prior attempts to achieve rate control with medications. ***(Level of Evidence: C)*** |
| I | A | Individualize the selection of the antithrombotic agent based on assessment of the absolute risks of stroke and bleeding and the relative risk and benefit for a particular patient. | I | C | In patients with AF, antithrombotic therapy should be individualized based on shared decision making after discussion of the absolute and relative risks of stroke and bleeding and the patient's values and preferences. |
| I | A | The need for anticoagulation should be reevaluated at regular intervals. (Level of Evidence: A) | I | C | Reevaluation of the need for and choice of antithrombotic therapy at periodic intervals is recommended to reassess stroke and bleeding risks. |
| II | B | Select antithrombotic therapy by the same criteria irrespective of the pattern of AF (ie, for patients with paroxysmal, persistent, or permanent AF). | I | B | Selection of antithrombotic therapy should be based on the risk of thromboembolism irrespective of whether the AF pattern is paroxysmal, persistent, or permanent (64–67). |
| I | B | Anticoagulate patients with AF lasting more than 48 h or | I | B | For patients with AF or atrial flutter of 48 hours' duration or longer, or |

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| | | of unknown duration for at least 3 to 4 weeks before and after cardioversion (INR 2 to 3). | | | when the duration of AF is unknown, anticoagulation with warfarin (INR 2.0 to 3.0) is recommended for at least 3 weeks before and 4 weeks after cardioversion, regardless of the CHA2DS2-VASc score and the method (electrical or pharmacological) used to restore sinus rhythm |
| I | B | Screening for the presence of thrombus in the LA or LAA by TEE is an alternative to routine preanticoagulation in candidates for cardioversion of AF. | I | B | For patients with AF or atrial flutter of 48 hours' duration or longer or of unknown duration who have not been anticoagulated for the preceding 3 weeks, it is reasonable to perform transesophageal echocardiography before cardioversion and proceed with cardioversion if no left atrial thrombus is identified, including in the left atrial appendage, provided that anticoagulation is achieved before transesophageal echocardiography and maintained after cardioversion for at least 4 weeks |
| II | B | Restore sinus rhythm in patients who develop postoperative AF by pharmacological cardioversion with ibutilide or direct-current cardioversion, as recommended for nonsurgical patients. | I | B | It is reasonable to restore sinus rhythm pharmacologically with ibutilide or direct-current cardioversion in patients who develop postoperative AF, as advised for nonsurgical patients |
| I | C | Electrical cardioversion for patients with severe hemodynamic compromise or intractable ischemia. | I | C | Urgent direct-current cardioversion of new-onset AF in the setting of acute coronary syndromes (ACS) is recommended for patients with hemodynamic compromise, ongoing ischemia, or inadequate rate control. |
| I | C | Intravenous beta-blockers to slow a rapid ventricular response in patients without clinical LV dysfunction, bronchospastic disease, or AV block. | I | C | Intravenous beta blockers are recommended to slow a rapid ventricular response to AF in patients with ACS who do not display HF, hemodynamic instability, or bronchospasm. |
| I | B | Immediate electrical cardioversion to prevent ventricular fibrillation in patients with WPW in whom AF occurs with a rapid ventricular response associated with hemodynamic instability. | I | C | Direct-current cardioversion should be attempted in patients with pulmonary disease who become hemodynamically unstable as a consequence of new-onset AF. |
| I | C | Intravenous procainamide or ibutilide in an attempt to restore sinus rhythm in patients with WPW in whom AF occurs without hemodynamic instability in association with a wide QRS complex on the ECG (greater than or equal to 120 ms in duration). | I | C | Intravenous procainamide or ibutilide to restore sinus rhythm or slow the ventricular rate is recommended for patients with pre-excited AF and rapid ventricular response who are not hemodynamically compromised |
| III | B | Intravenous administration of beta-blocking agents, digitalis glycosides, diltiazem, or verapamil in patients with WPW syndrome who have preexcited ventricular activation in AF. | III | B | Administration of intravenous amiodarone, adenosine, digoxin (oral or intravenous), or nondihydropyridine calcium channel antagonists (oral or intravenous) in patients with Wolff-Parkinson-White syndrome who have pre-excited AF is potentially harmful because these drugs accelerate the ventricular rate |
| I | B | Administer a beta-blocker as necessary to control the rate of ventricular response in patients with AF complicating thyrotoxicosis, unless contraindicated. | I | C | Beta blockers are recommended to control ventricular rate in patients with AF complicating thyrotoxicosis unless contraindicated. |
| I | B | In circumstances when a beta-blocker cannot be used, | I | C | In circumstances in which a beta blocker cannot be used, |

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| | | administer a calcium channel antagonist (diltiazem or verapamil) to control the ventricular rate. | | | a nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate. |
| I | C | In circumstances in which a beta blocker cannot be used, a nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate. | I | C | A nondihydropyridine calcium channel antagonist is recommended to control the ventricular rate in patients with AF and chronic obstructive pulmonary disease. |
| I | C | Attempt electrical cardioversion in patients with pulmonary disease who become hemodynamically unstable due to AF. | I | C | Direct-current cardioversion should be attempted in patients with pulmonary disease who become hemodynamically unstable as a consequence of new-onset AF. |

Abbreviations: COR, class of recommendation. LOE, level of evidence.