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ORIGINAL REPORT

Trends in the outpatient treatment of atrial fibrillation in the USA from 2001 to 2010†

Amarsinh M. Desai[1], Teresa M. Cavanaugh[1], Vibha C. A. Desai[1], Pamela C. Heaton[1] and Christina M. L. Kelton[1,2]*

[1] *James L. Winkle College of Pharmacy, University of Cincinnati Academic Health Center, Cincinnati, OH, 45267, USA*
[2] *Carl H. Lindner College of Business, University of Cincinnati, Cincinnati, OH, 45221, USA*

ABSTRACT

Purpose Several clinical trials have shown that rhythm-control drugs have serious adverse events and no survival advantage over rate-control drugs in patients with atrial fibrillation. The objectives were to determine and explain the recent trends in outpatient prescribing of both drug classes.

Methods Data were obtained over 10 years from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. Visits by patients with atrial fibrillation were identified by ICD-9 diagnosis code 427.31. Trend lines were estimated for drug prescribing and comorbidities. A multinomial logistic model was estimated to predict treatment on the basis of visit characteristics.

Results The percentage of visits mentioning only a rate-control medication trended upward ($p = 0.07$) from 41.9% in 2001 to 47.3% in 2010; the percentage mentioning both rhythm-control and rate-control drugs also had an upward trend ($p < 0.05$) from 3.1% to 12.5%; finally, the percentage mentioning rhythm-control drugs alone remained steady ($p = 0.37$). Consistent with the increase ($p = 0.10$) in the percentage of visits mentioning hypertension, there was a statistically significant ($p < 0.01$) rise in the prescribing of β-blockers from 20.5% to 43.4%. The odds that a patient aged 65 years or younger was prescribed a rhythm-control medication were significantly higher ($p < 0.01$) than those for a patient older than 65 years. The estimated odds that a diabetic patient was prescribed both rhythm-control and rate-control medications was only 0.269 ($p < 0.05$).

Conclusions This study documents change in the outpatient treatment of atrial fibrillation in the USA from 2001–2010. In clinical practice, there has been a growing reliance on rate-control medications. Copyright © 2014 John Wiley & Sons, Ltd.

KEY WORDS—atrial fibrillation; outpatient treatment; rhythm-control medications; rate-control drugs; beta-blockers; calcium channel blockers; pharmacoepidemiology

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INTRODUCTION

Atrial fibrillation (AF), the most common form of cardiac arrhythmia, is characterized by chaotic, irregular beating of the atria and an increased ventricular rate. Treatment for AF depends on a number of factors, including how long the patient has had the disease, how severe the symptoms are, and the underlying cause of AF. Treatment strategies include conversion to normal sinus rhythm, if possible, while preventing blood clots through the concomitant use of anticoagulants.[1,2] Restoring the heart's rhythm pharmacologically can be accomplished through blocking sodium channels or potassium channels. Amiodarone, a multi-channel blocker, has been shown to be effective in patients with persistent AF.[3] In patients with a cardiac comorbidity condition such as coronary artery disease (CAD) or congestive heart failure (CHF), amiodarone is the drug of choice because of its lowering proarrhythmic effects as compared with other anti-arrhythmic agents, such as sotalol.[4–6] Alternatively, some patients may undergo electrical cardioversion, which stops the heart's electrical activity momentarily and then restores it to its normal rhythm. After the procedure, the patient may take a rhythm-control drug to prevent a future AF episode.[1,7]

If the heart's rhythm cannot be restored, the goal in treating AF becomes to slow the heart rate to between 60 and 100 beats a minute using a rate-control therapy.[7]

*Correspondence to: C. M. L. Kelton, Professor of Economics and Adjunct Professor of Clinical Pharmacy, University of Cincinnati, Carl H. Lindner College of Business, 414 Lindner Hall, 2925 Campus Green Drive, Cincinnati, OH 45221, USA. E-mail: chris.kelton@uc.edu.

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Pharmacologic agents used for rate control include digoxin, beta- (β-) blockers (BBs), and calcium channel blockers (CCBs). Digoxin is a cardiac glycoside that binds to the sodium and potassium adenosine triphosphatase pump in the membranes of heart cells. BBs work by blocking β-receptors predominantly found on the heart. The CCBs used in the treatment of AF are nondihydropyridines, including verapamil, which is relatively selective for calcium channels in cardiac tissue, and diltiazem, which blocks calcium channels in cardiac tissue and modestly blocks calcium channels in blood vessels.[8]

Despite some general treatment principles, pharmacological treatment of AF remains controversial. Of primary concern is that rhythm-control agents are associated with significant adverse effects including organ toxicity.[9] Rate-control drugs are generally better tolerated. Over the last decade, a number of clinical trials have studied the relative safety and efficacy of rate-control versus rhythm-control medications. Indeed, PIAF, RACE, AFFIRM, STAF, and HOT-CAFÉ showed that rate-control drugs were equally as effective as rhythm-control drugs in terms of mortality.[10–17] The trials that have compared safety and efficacy of BBs versus CCBs have been inconclusive, offering no clear evidence-based guidance on the selection of an appropriate rate-control therapy.[18]

To determine the extent to which the evidence over the last decade on rate-control versus rhythm-control drugs has influenced clinical practice, this study examined outpatient-prescribing trends for AF patients, from 2001 to 2010, for both classes of drugs nationwide. There has been only one prior study with this particular objective. Whereas the Fang *et al.* study (2004) showed that the prescribing of rhythm-control medications remained fairly constant over the 1990s decade,[19] we hypothesize that the data from the more recent trials may result in a fall in their prescribing and a concurrent increase in the prescribing of rate-control alternatives. A secondary objective was to detect any change in the prescribing of BBs versus CCBs in controlling heart rate.

METHODS

Data source

Data were obtained over 10 years, 2001 through 2010, from two large national surveys administered by the National Center for Health Statistics and the Centers for Disease Control and Prevention (CDC). The first, the National Ambulatory Medical Care Survey (NAMCS), is based on a random sample of all US non-federally employed physicians who are primarily engaged in office-based patient care.[20] The second, the National Hospital Ambulatory Medical Care Survey (NHAMCS), includes hospital outpatient departments, which we considered, as well as emergency departments, which we did not.[21] The patient visit is the unit of observation for both NAMCS and NHAMCS. The data can generate, through visit weights, reliable national estimates of certain outcomes, for example, prescribing of a particular drug, provided that the sample size (number of visits during which that drug was mentioned) is ≥ 30.[20,21] The data are de-identified and publicly accessible.

Visit selection

Visits were selected from the NAMCS/NHAMCS database for 2001–2010 if they included an International Classification of Diseases, Ninth Revision (ICD-9) code of 427.31 (AF) as one of the three listed diagnoses for the visit. Demographic data for race, age, and gender were collected for each AF visit. Patient payer type and geographic location of the physician's office were also identified.

The AF visits were then subcategorized according to one of the following five comorbidities, if relevant: hypertension (HTN, ICD-9 codes 401–405), CAD (ICD-9 codes 410–414), CHF (ICD-9 codes 428.1–428.4 and 428.9), chronic kidney disease (CKD, ICD-9 code 585), and diabetes (ICD-9 code 250).

Drug identification

Rhythm-control and rate-control agents, both branded and generic, were identified by name, from an initial list obtained from Facts and Comparisons 4.0.[22] Mexiletine was then excluded from the initial list because current guidelines favor the use of other antiarrhythmic agents.[1] The AF visits were searched, by drug codes provided by NAMCS/NHAMCS, for any mention of any of the branded or generic drugs listed in the Appendix. The AF visits were categorized as follows: those involving a rhythm-control drug only, those involving a rate-control drug (BB, nondihydropyridine CCB, and/or digoxin) only, those with both rhythm-control and rate-control medications, and those mentioning neither type of medication. Each patient visit record could contain mention of up to eight medications.

Statistical analysis

Using ordinary-least-squares regression, linear trends from 2001 to 2010 were estimated for the visit shares of rhythm-control drugs only, rate-control drugs only, both rhythm-control and rate-control medications, and neither. Trend lines were also estimated for all additional variables considered: age, gender, race, region, payer type, and comorbidities. Although we could not

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obtain treatment trend lines while stratifying by covariate, we were able to obtain average frequencies and percentage shares (along with 95% confidence intervals, CIs) for treatments by pooling the annual data. Finally, with patient visit as the unit of observation and pooling data across the years, a multinomial logistic regression to predict treatment was estimated. All data analyses were conducted using the SAS software package for Windows (Version 9.2, SAS Institute Inc., Cary, NC) and Microsoft Excel 2010.

RESULTS

An estimated 81.9 million visits with AF as a diagnosis were identified over the decade 2001–2010. The first four columns of Table 1 describe the visit characteristics. Because there was no statistically significant trend in covariate shares over time ($p > 0.10$ in each case), only full-period descriptive statistics are shown. The mean patient age was 73.9 years old, and the majority (63.8%) of patient visits occurred among patients aged 66–85 years. Visits were essentially equally divided between men and women. Visits by white patients accounted for slightly over 90% of the visits, and Medicare was the payer for approximately 70% of the visits.

The last four columns in Table 1 categorize patient visits by drug mentions. On average, over the decade, the breakdown was 6.6% (95%CI: 5.6%–7.5%), 50.2% (95%CI: 47.4%–53.1%), 8.0% (95%CI: 6.8%–9.3%), and 35.2% (95%CI: 32.5%–37.9%) of visits mentioning only rhythm-control drugs, only rate-control drugs, both rhythm-control and rate-control medications, and neither type of medication, respectively.

Out of the 81.9 million visits with an AF diagnosis, 26.9% (95%CI: 24.5%–29.2%) had a diagnosis for HTN as well (Table 2). Similarly, 9.4% (95%CI: 7.9%–10.9%), 12.6% (95%CI: 10.9%–14.2%), and 7.5% (95%CI: 5.8%–9.1%) had diagnoses for CHF, CAD, and diabetes, respectively. Only 10.6% (95%CI: 8.2%–13.0%) of the visits had no other diagnosis besides AF recorded. Whereas an estimated 10.5% (95%CI: 7.3%–13.7%) of patients with no comorbidity were prescribed only rhythm-control medication, that percentage was 4.7% (95%CI: 2.8%–6.6%) for patients with CHF. Because of a low raw visit count (<30 occurrences between 2001 and 2010), drug prescribing for patients with CKD could not be effectively captured.

Annual percentages of comorbidity diagnoses for visits involving AF are depicted in Figure 1, along with fitted trend lines. As expected from the literature, the NAMCS/NHAMCS database revealed a rising trend in visits involving HTN as a diagnosis.[23] Over the decade, there was a marginally significant ($p = 0.10$) increase in the percentage of visits mentioning HTN, from 19.5% (95%CI: 13.3%–25.5%) in 2001 to 24.1% (95%CI: 17.3%–30.8%) in 2010. There was no significant trend detected for diabetes ($p = 0.25$), CAD ($p = 0.22$), or CHF ($p = 0.37$).

Figure 2 shows trends in the outpatient prescribing of rhythm-control and rate-control medications over the last decade. The percentage of visits mentioning only a rate-control medication trended upward ($p = 0.07$) from 41.9% (95%CI:34.1%–49.7%) in 2001 to 47.3% (95% CI:38.3%–56.2%) in 2010 while the percentage of visits mentioning both rhythm-control and rate-control drugs had a statistically significant upward trend ($p = 0.01$) from 3.1% (95%CI:1.2%–5.0%) to 12.5% (95%CI: 7.9%–17.1%). There was a statistically significant ($p < 0.01$) rise in the prescribing of BBs from 20.5% (95%CI: 15.0%–25.9%) to 43.4% (95%CI: 36.9%–49.9%). The prescribing of CCBs remained steady ($p = 0.33$). Digoxin mentions experienced a statistically significant ($p < 0.01$) decline from 28.6% (95%CI: 22.0%–35.2%) in 2001 to 14.5% (95%CI: 10.0%–19.0%) in 2010. A non-significant ($p = 0.37$) negative time-trend coefficient was estimated for the mention of rhythm-control medication by itself. Finally, there was a statistically significant ($p = 0.01$) decrease in the percentage of visits mentioning neither rhythm-control nor rate-control medications from 49.6% (95%CI: 40.5%–58.8%) in 2001 to 34.4% (95%CI: 26.8%–42.1%) in 2010.

Among the rhythm-control medications in the Appendix, amiodarone was mentioned the most often, in 5.7 million visits over the 10-year period (Table 3). Among the BBs, metoprolol was the most widely prescribed. It was mentioned in 18.7 million visits, representing approximately 23% of all AF visits. Both atenolol and carvedilol were also widely prescribed for AF patients. Diltiazem, with 8.0 million mentions, had substantially higher prescribing than verapamil, with 1.8 million mentions over the decade.

Table 4 presents the odds-ratio results from the multinomial logistic regression for which drug treatment (rhythm only, rate only, or rhythm and rate) was regressed on visit characteristics. Consistent with the frequencies shown in Table 1, the odds of a younger patient's being prescribed a rhythm-control medication, either alone or concomitantly with a rate-control drug, were statistically higher ($p < 0.01$) than those of an older patient. Compared with patients without hypertension, patients with this comorbidity were more likely ($p < 0.01$) to be prescribed rate-control medication alone, whereas diabetics were less likely ($p = 0.01$) to be prescribed both rhythm-control and rate-control medications. Again consistent with results in Table 1, some practice variation was observed,

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Table 1. Visit characteristics for patients with atrial fibrillation: 2001–2010 combined (95%CI in parentheses)

		All visits		Drug class mentioned (% of visit number)			
	Group	Percent of total (%)	Visit number	Rhythm only	Rate only	Rhythm and rate	None
Characteristic	Estimated national visit total	100.00	81 871 906*	6.6 (5.6–7.5)	50.2 (47.4–53.1)	8.0 (6.8–9.3)	35.2 (32.5–37.9)
Age (years; mean age 73.9 years (73.6–74.3))	≤55	7.3 (5.8–8.8)	6 010 465	6.4 (3.5–9.3)	49.8 (40.7–58.9)	16.4 (9.7–22.9)	27.4 (21.5–33.4)
	56–65	13.8 (12.2–15.3)	11 277 510	13.4 (9.4–17.3)	48.9 (43.1–54.6)	9.3 (6.4–12.2)	28.4 (23.3–33.5)
	66–75	28.2 (26.1–30.3)	23 087 226	6.5 (4.8–8.2)	47.1 (42.6–51.6)	8.2 (6.0–10.3)	38.2 (33.8–42.7)
	76–85	35.6 (32.9–38.2)	29 146 317	5.3 (3.7–6.8)	53.0 (48.8–57.3)	6.9 (5.1–8.7)	34.8 (30.7–38.8)
	>85	15.1 (13.3–16.9)	12 350 388	3.6 (1.6–5.5)	51.3 (46.5–56.2)	4.9 (2.3–7.6)	40.2 (35.3–45.1)
Sex	Female	49.9 (47.7–52.1)	40 840 820	6.9 (5.4–8.3)	47.8 (44.1–51.5)	7.9 (6.2–9.5)	37.4 (33.8–41.1)
	Male	50.1 (47.9–52.3)	41 031 086	6.2 (5.0–7.4)	52.7 (49.1–56.4)	8.2 (6.3–9.9)	32.9 (29.7–36.1)
Race	White	90.3 (88.4–92.1)	73 887 895	6.7 (5.7–7.7)	50.8 (47.9–53.8)	8.3 (6.9–9.6)	34.2 (31.5–36.9)
	Black	6.9 (5.4–8.4)	5 622 852	7.2 (3.4–10.9)	43.3 (36.3–50.3)	5.5 (3.1–7.7)	44.0 (35.5–52.5)
	Other	2.8 (1.9–3.9)	2 361 159	1.4 (0.4–2.3)	48.7 (34.1–63.4)	5.8 (1.9–9.8)	44.1 (31.6–56.4)
Region	Northeast	21.1 (16.3–26.0)	17 309 954	4.2 (2.6–5.7)	59.9 (54.4–65.4)	6.3 (3.7–8.9)	29.6 (24.4–34.7)
	Midwest	23.6 (17.9–29.1)	19 286 386	6.8 (4.5–9.0)	49.9 (44.4–55.4)	9.1 (6.9–11.4)	34.2 (28.4–39.8)
	South	36.1 (30.5–41.6)	29 514 022	8.0 (6.2–9.9)	45.9 (41.5–50.3)	8.7 (6.5–10.8)	37.4 (33.1–41.7)
	West	19.2 (14.7–23.8)	15 761 544	6.1 (4.1–8.0)	48.4 (40.5–56.4)	7.2 (3.8–10.4)	38.3 (31.5–45.2)
Payer type	Private insurance	21.7 (19.5–23.9)	17 771 062	9.8 (7.3–12.3)	47.6 (42.8–42.7)	11.3 (8.1–14.3)	31.3 (26.9–35.6)
	Medicare	69.5 (66.9–72.1)	56 926 088	5.5 (4.3–6.7)	50.6 (47.1–53.9)	7.1 (5.7–8.4)	36.8 (33.8–39.9)
	Medicaid/SCHIP	3.7 (2.8–4.7)	3 035 467	5.5 (1.1–9.9)	52.5 (42.1–62.9)	7.0 (1.3–12.8)	35.0 (26.2–43.6)
	Other†	5.1 (3.8–6.4)	4 139 289	7.6 (2.1–12.9)	55.9 (46.7–66.1)	8.1 (2.1–13.3)	28.4 (20.2–36.5)

*Based on a raw count of 4076.
†Other includes workers' compensation, self-pay, no charge, and charity.

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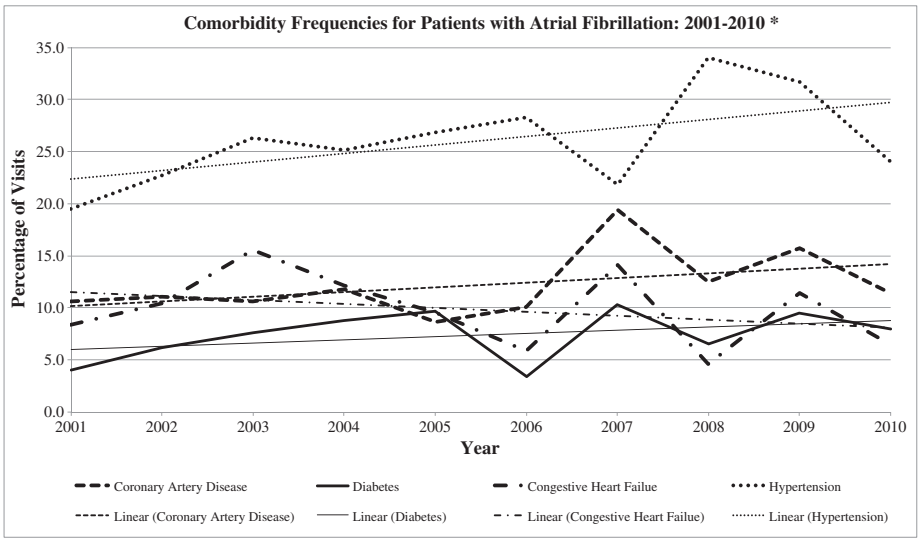
Table 2. Visit characteristics for patients with atrial fibrillation stratified by comorbidity: 2001–2010 combined (95%CI in parentheses)

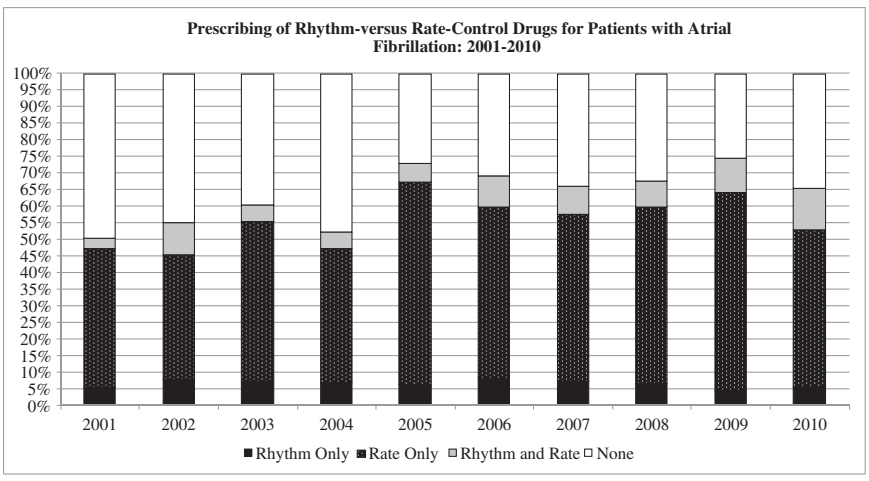
	All visits		Drug class mentioned (% of visit number)			
Comorbidity	Percent of total* (%)	Visit number*	Rhythm only	Rate only	Rhythm and rate	None
Hypertension	26.9 (24.5–29.2)	22 016 735	8.1 (5.5–10.6)	55.7 (50.4–61.5)	9.2 (6.0–11.9)	27.0 (21.8–32.1)
Congestive heart failure	9.4 (7.9–10.9)	7 689 601	4.7† (2.8–6.6)	46.9 (39.9–54.2)	7.3 (3.5–11.0)	41.1 (33.4–48.5)
Coronary artery disease	12.6 (10.9–14.2)	10 275 158	8.3 (4.6–11.9)	55.4 (49.5–60.9)	8.9 (6.6–11.0)	27.4 (23.3–32.1)
Diabetes	7.5 (5.8–9.1)	6 118 811	7.8† (4.3–11.3)	56.6 (48.9–64.4)	2.2† (1.0–3.5)	33.4 (25.7–41.1)
Other comorbidity	41.2 (38.3–43.9)	33 642 345	4.4 (3.2–5.6)	48.4 (44.5–52.4)	8.7 (6.5–10.8)	38.5 (34.7–42.3)
No comorbidity	10.6 (8.2–13.0)	8 690 265	10.5 (7.3–13.7)	38.4 (33.6–43.5)	7.2 (5.0–9.1)	43.9 (38.6–49.3)

*Based on estimated national visit total of 81 871 906. Visit numbers do not sum to 81 871 906 due to multiple comorbidities mentioned for some visits. Similarly, percentages do not sum to 100%.
†Estimate based on a raw visit count <30.



* The estimated slope coefficients for the plotted linear time trends were 0.4436 (p=0.22), 0.3139 (p=0.25), -0.3770 (p=0.37), and 0.4315 (p=0.10) for coronary artery disease, diabetes, congestive heart failure, and hypertension, respectively.

Figure 1. Comorbidity frequencies for patients with atrial fibrillation: 2001–2010*



* The estimated slope coefficients for linear time trends were -0.1249 (p=0.37) for rhythm only, 1.4988 (p=0.07) for rate only, 0.7139 (p=0.01) for rhythm and rate, and -2.0879 (p=0.01) for none.

Figure 2. Prescribing of rhythm-control versus rate-control drugs for patients with atrial fibrillation: 2001–2010

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Table 3. Prescribing of individual drugs: 2001–2010 combined (95%CI in parentheses)

Drug	Visit number *	Percent of total* (%)
Total	81 871 906	100.0
Rhythm control		
Amiodarone	5 663 270	6.9 (5.7–8.1)
Flecainide	1 018 427	1.2 (0.8–1.7)
Propafenone	1 247 111	1.5 (1.0–2.0)
Sotalol	3 569 560	4.4 (3.5–5.3)
Other rhythm control†	489 354	0.6 (0.3–0.9)
Rate control		
β-blocker		
Atenolol	7 234 644	8.8 (7.6–10.1)
Carvedilol	5 949 896	7.3 (5.8–8.8)
Metoprolol	18 740 084	22.9 (20.7–25.0)
Other β-blocker ‡	1 640 639	2.0 (1.2–2.8)
Calcium channel blocker		
Diltiazem	8 039 107	9.8 (8.3–11.3)
Verapamil	1 808 992	2.2 (1.6–2.8)
Cardiac glycoside		
Digoxin	17 398 819	21.3 (19.1–23.4)

*Visit numbers do not sum to 81 871 906 as a result of multiple drugs mentioned for some visits as well as no drugs mentioned for some visits. Similarly, percentages do not sum to 100%.
†Other rhythm control includes dofetilide, dronedarone, disopyramide, ibutilide, procainamide, and quinidine. Estimate based on a combined raw visit count <30.
‡Other β-blocker includes acebutolol, bisoprolol, esmolol, nadolol, nebivolol, and propranolol, each individually with a raw visit count <30.

with visits in the Midwest, South, and West shown to be statistically ($p < 0.05$ in each case) less likely to be characterized by only a rate-control drug.

DISCUSSION

Compared with the 1990s, the past decade has witnessed significant change in the prescribing of rhythm-control and rate-control medications for AF patients. Whereas Fang *et al*. showed that there was no statistically significant difference between 1991–1992 and 1999–2000,[19] this study showed a statistically significant rise in the share of rate-control drugs, especially BBs, as well as rhythm-and-rate-control combinations over the period 2001 through 2010.

The results from this study are consistent with the conclusions from several randomized controlled trials, comparing rhythm-control versus rate-control medications, which were published between 2000 and 2004.[11–17] The trials indicated no difference in mortality or stroke rate between the two strategies and non-inferiority of rate-control relative to rhythm-control medications for prevention of morbidity. Hence, it is not surprising that we have witnessed rising outpatient prescriptions for rate-control drugs. Indeed, on the basis of the clinical trial data, the 2006 US AF Guideline was updated in 2011, putting more emphasis on the use of rate-control medications. A rate-control medication is suggested for all patients with persistent or permanent AF, except in those cases in which the patient does not have an accessory pathway.[1] The Clinical Guidelines for AF put out by the National Institute for Health and Clinical Excellence (NICE) recommend rate control as first-line therapy for patients with persistent AF who are 65 years old and older, patients with CAD, patients with contraindications to antiarrhythmic agents, and patients not suited for cardioversion.[24] The NICE Guidelines recommend rhythm-control medication as first-line therapy for patients who are symptomatic, younger than 65 years, presenting for the first time with lone AF, and with AF secondary to a treated/corrected precipitant.[24] Evidence from this study indicates a higher likelihood of a rhythm-control prescription for a younger than older patient, as the guidelines recommend.

The controversy surrounding rhythm-control versus rate-control strategies continues to evolve. A large observational study in 2012 found a lower risk of death, after both 5 and 8 years of treatment, for patients taking rhythm-control medication relative to those taking a rate-control drug (HR = 0.89, 95%CI: 0.81–0.96; and HR = 0.77, 95%CI: 0.60–0.95, after 5 and 8 years, respectively).[25] Because the results of this observational study are contrary to what was learned from the clinical trials, future study is warranted.

The rising number of prescriptions for BBs in particular is consistent with the comorbidity trends (Figure 1), especially the rise in HTN diagnoses, over the last decade. The cardioselective nature of certain BBs coupled with an additional survival benefit for BBs in other cardiovascular states give BBs an advantage over CCBs for the treatment of AF with a comorbid cardiovascular condition.[26] A BB is also the preferred rate-control medication for AF patients experiencing liver disease or mild hypotension.[27] CCBs, however, are preferred for patients with pulmonary disease because of the bronchoconstriction associated with BBs.[28]

Some patients were prescribed a rhythm-control medication along with a BB or CCB. Patients already taking a BB for HTN may be prescribed a rhythm-control medication after developing AF.[23] Alternatively, for acute management of AF, patients may be prescribed both types of medication, followed by either rhythm-control or rate-control therapy for long-term management.[1] In 2010, 34.4% of visits had no mention of either a rhythm-control or rate-control medication. Because not all of a patient's medications may have been listed on the survey forms, which have a limit of eight medications, the number of mentions of AF medications may be biased downward. Moreover, an AF medication from the Appendix may not have been recorded if the patient was being seen post-cardioversion

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Table 4. Odds-ratio estimates from multinomial logistic regression: 2001–2010 combined (reference group or 95%CI in parentheses)

	Drug class					
	Rhythm only		Rate only		Rhythm and rate	
Visit characteristic	Odds ratio	*p*-value*	Odds ratio	*p*-value*	Odds ratio	*p*-value*
Patient age ≤ 65	2.52	< 0.01	1.32	0.12	2.09	< 0.01
(Patient age > 65)	(1.60–3.96)		(0.93–1.86)		(1.21–3.61)	
Female	1.07	0.70	0.86	0.17	0.95	0.74
(Male)	(0.75–1.54)		(0.69–1.07)		(0.68–1.31)	
Black	0.72	0.40	0.69	0.13	0.43	0.05
(White)	(0.33–1.56)		(0.43–1.12)		(0.19–0.99)	
Other race	0.14	0.01	0.65	0.20	0.48	0.09
(White)	(0.03–0.64)		(0.34–1.26)		(0.21–1.13)	
Midwest	1.53	0.20	0.69	0.05	1.12	0.71
(Northeast)	(0.80–2.94)		(0.48–0.99)		(0.61–2.06)	
South	1.63	0.07	0.60	< 0.01	1.02	0.95
(Northeast)	(0.96–2.76)		(0.43–0.85)		(0.58–1.79)	
West	1.26	0.43	0.63	0.02	0.79	0.48
(Northeast)	(0.71–2.25)		(0.42–0.94)		(0.40–1.53)	
Medicare	0.74	0.20	1.04	0.84	0.77	0.41
(Private insurance)	(0.47–1.17)		(0.73–1.47)		(0.42–1.43)	
Medicaid/SCHIP	0.57	0.30	1.06	0.82	0.71	0.53
(Private insurance)	(0.20–1.66)		(0.62–1.82)		(0.24–2.09)	
Other†	0.90	0.81	1.36	0.24	0.87	0.76
(Private insurance)	(0.37–2.16)		(0.82–2.27)		(0.34–2.22)	
Hypertension	1.72	0.16	1.82	< 0.01	1.77	0.12
	(0.81–3.65)		(1.16–2.85)		(0.87–3.61)	
Congestive heart failure	0.53	0.11	1.19	0.47	1.17	0.64
	(0.24–1.16)		(0.75–1.89)		(0.60–2.28)	
Coronary artery disease	1.75	0.10	1.60	0.08	1.50	0.25
	(0.90–3.40)		(0.95–2.70)		(0.75–3.01)	
Diabetes	1.12	0.79	1.14	0.64	0.27	0.01
	(0.48–2.64)		(0.66–1.96)		(0.10–0.76)	
Other comorbidity‡	0.75	0.51	1.11	0.68	1.11	0.81
	(0.33–1.74)		(0.68–1.81)		(0.48–2.56)	
2002	1.42	0.38	1.00	0.99	3.36	< 0.01
(2001)	(0.65–3.09)		(0.58–1.73)		(1.49–7.61)	
2003	1.75	0.18	1.44	0.23	2.22	0.13
(2001)	(0.78–3.94)		(0.80–2.61)		(0.80–6.19)	
2004	1.23	0.63	0.95	0.85	1.64	0.26
(2001)	(0.53–2.82)		(0.58–1.58)		(0.69–3.90)	
2005	1.86	0.16	2.59	< 0.01	3.07	0.02
(2001)	(0.78–4.45)		(1.36–4.93)		(1.24–7.59)	
2006	2.29	0.05	1.94	0.02	4.69	< 0.01
(2001)	(0.99–5.31)		(1.11–3.41)		(1.99–11.04)	
2007	1.74	0.18	1.71	0.03	3.91	< 0.01
(2001)	(0.77–3.94)		(1.05–2.79)		(1.65–9.27)	
2008	1.60	0.26	1.84	0.02	3.84	< 0.01
(2001)	(0.71–3.62)		(1.09–3.10)		(1.60–9.25)	
2009	1.39	0.47	2.65	< 0.01	6.31	< 0.01
(2001)	(0.57–3.39)		(1.58–4.45)		(2.72–14.68)	
2010	1.36	0.44	1.66	0.07	5.73	< 0.01
(2001)	(0.62–2.99)		(0.97–2.83)		(2.58–12.76)	

Number of (unweighted) observations: 4076.
Number of (weighted) observations: 81 871 906.

*p-value for the Wald chi-square test that the multinomial logistic coefficient = 0.
†Other includes workers' compensation, self-pay, no charge, and charity.
‡Other comorbidity includes any other diagnosis code for the visit besides HTN, CHF, CAD, and Diabetes.

or was being prescribed an anticoagulant. When AF was the secondary, rather than primary, diagnosis for the visit, an AF medication may not have been listed.

Among rhythm-control drugs, amiodarone was the most frequently prescribed throughout the decade. Amiodarone is often used as a medication of last resort, in the most refractory patients because of its effectiveness and in patients with CHF. It is also used in older patients for whom duration of exposure will be shorter.[29] Although many BBs were mentioned in

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the database, only a few were heavily prescribed. The high use of metoprolol may be explained by its cardioselective β_1 receptor blockade, its being well tolerated by most patients, and its association with lower hospitalization rates than other BBs.[30] Among CCBs, diltiazem was most frequently prescribed, perhaps because cardiac side effects, when they develop in elderly patients, are less intense than with verapamil.[31] The prescribing trends were generally consistent with utilization patterns from several recent studies.[32–34]

Although this study tried to capture national outpatient prescription trends, it was limited by the nature of the NAMC/NHAMCS database. Results depend on consistently accurate ICD-9 coding over the decade. To the extent that coding became more or less accurate between 2001 and 2010, any detected trends in drug prescribing would be biased. Because up to only three diagnoses were available in the database, the study may not have captured all AF patients nor is there sufficient detail to determine a patient's type of AF, for example, paroxysmal or persistent. Because severity of illness may be correlated with visiting a physician, more severely ill patients are more likely to be captured in the database than those with less severe AF. Lacking longitudinal data, no patient's medication use over time could be observed. Because visits, not patients, were the units of observation, it is possible that one individual had >1 visit. For example, if a patient visited both a primary-care physician and cardiac specialist, both visits might be captured in the database. Moreover, because NAMCS and NHAMCS data were pooled, the odds of a patient's being observed more than once were even higher because of the potential of a hospital outpatient visit as well.

Nevertheless, despite these limitations, the NAMCS/NHAMCS database allows observation of clinical practice nationwide over time. Although it was not possible to determine whether patients actually filled the prescription or took the medication, the data do accurately reflect the prescribing behavior of the physicians. The results of this study suggest that healthcare providers over the last decade, by holding fairly steady their prescribing of rhythm-control drugs by themselves and increasing their prescribing of rate-control drugs, have adhered to evidence from clinical trials that rate-control medications may be as effective as rhythm-control drugs in the treatment of AF without the organ toxicity associated with the latter drugs. Hence, we speculate that some movement back to rhythm-control drugs will occur in response to the Ionescu-Ittu *et al.* large observational study (2012) with new evidence of lower mortality among patients using rhythm-control drugs.[25] An aging population suggests a continuing upward trend in cardiovascular comorbidities associated with AF, leading us to expect, in the future, even more reliance on BBs.

CONCLUSION

This study documents substantial changes in the treatment of AF in the USA over the last decade. In clinical practice nationally, there has been no trend in the prescribing of rhythm-control drugs by themselves accompanied by a rise in rate-control medication prescriptions. This change in clinical practice is consistent with clinical trial evidence from the early 2000s. Although there is no evidence of increased reliance on CCBs in the treatment of AF, the prescribing of BBs has risen dramatically, most likely at least in part because of the rise in cardiovascular comorbidities, especially HTN, associated with AF.

CONFLICT OF INTEREST

The authors received no funding and have no conflict of interest to disclose.

KEY POINTS

- Over the last decade, there has been a change in clinical practice nationwide, with a rise in the prescribing of rate-control agents for patients with atrial fibrillation.
- The increased outpatient prescribing of β-blockers far exceeded that of calcium channel blockers, consistent with the rising prevalence of cardiovascular comorbidities, particularly hypertension.
- Nationwide, the most widely prescribed rhythm-control agent over the last decade was amiodarone. The β-blocker and calcium channel blocker most prescribed were metoprolol and diltiazem, respectively.

ETHICS STATEMENT

The authors state that no ethical approval was needed.

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