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ORIGINAL RESEARCH ARTICLE

Warfarin for Prevention of Thrombosis Among Long-Term Care Residents with Atrial Fibrillation: Evidence of Continuing Low Use Despite Consideration of Stroke and Bleeding Risk

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Abstract
Objectives The aims of the study were to evaluate usage rates of warfarin in stroke prophylaxis and the association with assessed stages of stroke and bleeding risk in long-term care (LTC) residents with atrial fibrillation (AFib).
Methods A cross-sectional analysis of two LTC databases (the National Nursing Home Survey [NNHS] 2004 and an integrated LTC database: AnalytiCare) was conducted. The study involved LTC facilities across the USA (NNHS) and within 19 states (AnalytiCare). It included LTC residents diagnosed with AFib (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnostic code 427.3X). Consensus guideline algorithms were used to classify residents by stroke risk categories: low (none or 1+ weak stroke risk factors), moderate (1 moderate), high (2+ moderate or 1+ high). Residents were also classified by number of risk factors for bleeding (0–1, 2, 3, 4+). Current use of warfarin was assessed. A logistic regression model predicted odds of warfarin use associated with the stroke and bleeding risk categories.
Results The NNHS and AnalytiCare databases had 1,454 and 3,757 residents with AFib, respectively. In all, 34 % and 45 % of residents with AFib in each respective database were receiving warfarin. Only 36 % and 45 % of high-stroke-risk residents were receiving warfarin, respectively. In the logistic regression model for the NNHS data, when compared with those residents having none or 1+ weak stroke risk and 0–1 bleeding risk factors, the odds of receiving warfarin increased with stroke risk (odds ratio [OR] = 1.93, $p = 0.118$ [1 moderate risk factor]; OR = 3.19, $p = 0.005$ [2+ moderate risk factors]; and OR = 8.18, $p \leq 0.001$ [1+ high risk factors]) and decreased with bleeding risk (OR = 0.83, $p = 0.366$ [2 risk factors]; OR = 0.47, $p \leq 0.001$ [3 risk factors]; OR = 0.17, $p \leq 0.001$ [4+ risk factors]). A similar directional but more constrained trend was noted for the AnalytiCare data: only 3 and 4+ bleeding risk factors were significant.
Conclusions The results from two LTC databases suggest that residents with AFib have a high risk of stroke. Warfarin use increased with greater stroke risk and declined with greater bleeding risk; however, only half of those classified as appropriate warfarin candidates were receiving guideline-recommended anticoagulant prophylaxis.

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1 Introduction

Atrial fibrillation (AFib), a condition that becomes more prevalent with advancing age [1], is the most common sustained cardiac arrhythmia [1, 2]. Lifetime risks for developing AFib are 1 in 4 for men and women ≥40 years of age [3]. AFib is a major independent risk factor for stroke; patients with this condition have a nearly fivefold excess in age-adjusted incidence of stroke [4].

The potential benefit of stroke risk reduction from warfarin prophylaxis is substantial. In a meta-analysis of clinical trials, when compared with no antithrombotic,

adjusted-dose warfarin reduced stroke in AFib by 64 % and death by 26 %, and compared with antiplatelet therapy, it reduced stroke in AFib by 39 % (all significant at 95 % confidence interval (CI); a 9 % reduction in death for warfarin vs. antiplatelets was not significant) [5]. Recent evidence suggests that net clinical benefit (annual rate of ischaemic strokes and systemic emboli prevented by warfarin minus intracranial haemorrhages attributable to warfarin, then multiplied by an impact weight) is clear among patients having a Cardiac Failure, Hypertension, Age, Diabetes, [and] Stroke [Doubled] [6] ($CHADS_2$) score of ≥ 2 [7, 8].

Prescribing guidelines for antithrombotic (anticoagulant and antiplatelet) prophylaxis in patients with AFib were issued by the American College of Cardiology (ACC) and the American Heart Association (AHA) jointly with the European Society of Cardiology (ESC) in 2006 [1], by the ESC alone in 2010 [9], and by the American College of Chest Physicians (ACCP) in 2008 [10] and were updated by the ACCP in 2012 [11]. The American Medical Directors Association (AMDA) recently released an updated stroke management guideline that addresses, in part, the use of anticoagulant therapy in nursing home residents with AFib [12].

The guidelines above state that AFib patients with moderate or high risk factors for stroke are candidates for warfarin therapy. Although specific, listed stroke and bleeding risk factors vary somewhat among guidelines, ACC/AHA/ESC (2006), ACCP (2008) and ESC (2010) recommend long-term use of aspirin in patients with no stroke risk factors (ACCP 2012 recommends no use of antithrombotics), aspirin or oral anticoagulation in patients with 1 moderate risk factor (ACCP 2012 recommends oral anticoagulation as preferred), and oral anticoagulation as preferred in patients with 1+ high risk factor(s) or 2+ moderate risk factors. The AMDA 2011 guidelines recommend using $CHADS_2$, but do not link specific scores with a recommendation for warfarin use.

All guidelines above recommend that oral anticoagulation prophylaxis be considered on the basis of degree of stroke risk, but also with consideration of the risk of bleeding. In both the ACC/AHA/ESC 2006 and the ACCP 2008 guidelines, studies regarding bleeding risk and warfarin use are discussed, but no systematic scoring algorithm is recommended. The ESC 2010, AMDA 2011 and ACCP 2012 guidelines specifically demonstrate the use of various algorithms for scoring bleeding risk. However, in contrast to the evaluation of stroke risk, none of these guidelines specifically suggests when to withhold warfarin on the basis of a particular assessment of bleeding risk.

Previous local and regional long-term care (LTC) studies have shown that warfarin was used in only 17–57 % of residents with AFib [13–17]. Lau et al. [16] further found that warfarin was often inconsistently prescribed in LTC when considering resident risk factors for stroke and bleeding, where many optimal candidates for warfarin therapy received suboptimal treatment and residents at high risk for bleeding received excessive treatment. In a recent study, Ghaswalla et al. [18] examined the US National Nursing Home Survey (NNHS) database and concluded that 54 % of US residents with AFib who had indications for, but no contraindications against, warfarin use were prescribed neither warfarin nor antiplatelet agents, suggesting underuse of antithrombotic therapy. In an earlier study, McCormick et al. [17] found that warfarin use increased with magnitude of overall stroke risk and decreased with overall bleeding risk in all residents with AFib, but that this relationship was significant only for high bleeding risk (having 2+ risk factors).

The aim of the current study was to expand the method used by McCormick et al. [17] to quantify, by assignment to stages of increasing severity, combined assessment of overall bleeding risk and stroke risk among all LTC residents with AFib (i.e. without removal of subjects from the analysis who had been screened as candidates for or against warfarin use). In this updated approach we examined the relationship of warfarin use with these risk stages during a period following publication of $CHADS_2$ and release of formalized guidelines for assessing the risk and benefit of warfarin for stroke prevention in AFib. At the time of the current study, warfarin was the only prescribed oral anticoagulant in the USA. We assessed whether warfarin use increases and declines, respectively, across stages of increasing stroke and bleeding risk. We further evaluated rates of warfarin use among stroke risk and bleeding risk category combinations and compared overall usage rates with earlier studies.

2 Methods

2.1 Study Design

This study applied a retrospective cross-sectional analysis of residents across multiple LTC facilities. Two databases were analysed: the publicly available cross-sectional NNHS database and the proprietary longitudinal AnalytiCare database.

2.2 National Nursing Home Survey Database

The NNHS is currently administered by the US Centers for Disease Control and Prevention (CDC; http://www.cdc.gov/nchs/nnhs.htm). This database consists of a continuing series of national sample surveys of nursing homes, their residents and their staff. Eligible facilities consisted of

those having three or more beds that are certified to provide reimbursable services by Medicare or Medicaid or that are licensed by an individual state. In the most recent survey year, calendar year 2004, 1,500 facilities were randomly drawn from 17,000 nursing homes listed in either the Centers for Medicare and Medicaid Services file of US nursing homes (skilled and other nursing facilities) or state nursing home licensing lists. De-identified, public-use, single-point-in-time data were obtained through computer-assisted personal interviews with facility administrators and designated staff. Interviewees used administrative records to answer questions about the facilities, staff, services and programmes, and used medical records to answer questions about the residents. Data for residents were drawn by simple random sampling in facilities that agreed to participate.

For the current study, eligible residents included those of the 13,507 sampled residents in the NNHS database who had an open-ended entry for AFib (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnostic code 427.3X) in any of the 15 available current diagnosis fields on the resident questionnaire. In the most recent 2004 release, current drug therapy was available and was used in this study. This included all agents taken the day before the resident questionnaire was completed or recorded as 'regularly scheduled'. Resident demographics, comorbid conditions, activities of daily living (ADL) assessments, history of falling, and specific stroke and bleeding risk assessments were obtained from the resident data file.

2.3 AnalytiCare Long-Term Care Database

The AnalytiCare study database (http://www.analyticare.com) was drawn from a universe of ~100,000 LTC residents of ~200 nursing homes in 19 states over the study period 1 January 2007–30 June 2009. Available data included all elements from the Minimum Data Set (MDS) version 2.0 [19] and pharmacy dispensing records. The MDS, which is used in the USA, Canada and more than 20 other countries, is a detailed collection of measures and indicators (including assessments of physical and cognitive functioning, listings of current conditions, assessment of pain, among many others) that are completed by LTC staff to provide a comprehensive assessment of each resident's functional capabilities and to identify health problems. In the USA, the MDS is mandated to be completed for all residents in federally certified facilities at least once quarterly, and also upon admission, discharge or a significant change in resident health status (version 3.0 was implemented in October 2010). Prior to their release for the study, data were de-identified by AnalytiCare according to *Health Insurance Portability and Accountability Act*–compliant safe harbour rules and were exempt from the requirement of review by an internal review board.

The MDS was used to identify chronic resident conditions, including AFib. AFib is not one of the listed 'checkbox' conditions in MDS Sect. I1, but is identified in the section permitted for open-ended entry of conditions in Sect. I3 [19]. Eligible residents in the current study (1) had complete pharmacy data, ≥2 MDS assessments, and an entry for AFib (ICD-9-CM diagnostic code 427.3X) in any MDS assessment completed during the study period (these were the minimum criteria for production of the de-identified database released by AnalytiCare); (2) had an MDS assessment at least 1 year prior to the end of the study period (to assure adequate follow-up was not constrained by the study database); (3) had a diagnosis for AFib within 1 year of the earliest MDS assessment; (4) had a complete admission or annual assessment within 1 year of the earliest MDS assessment (since these forms provide space for up to five open-ended ICD-9 code entries vs. only two for quarterly assessments); and (5) were ≥18 years of age on 1 January 2007 and his/her sex was known. For study residents, current drug therapy included all agents dispensed 30 days before through to 60 days after the earliest AFib entry described in item 3 above (to establish a limited date range to evaluate concurrent drug use with a single indexed notation of the AFib condition). Comorbid condition data were obtained on all MDS (checkbox) or open-ended entries during the 1-year period starting from the earliest MDS assessment.

2.4 Measurement of Stroke and Bleeding Risk

For the NNHS, data from the single-point-in-time survey and, for AnalytiCare, from a summary of the 90-day drug therapy period and the 1-year MDS assessment period (noted above) were used to identify stroke and bleeding risk factors for individual residents. Specific stroke risk factors (listed in Table 1), based primarily on $CHADS_2$ [6] were obtained directly from AHA/ACC/ESC [1] and ACCP [10] guidelines and were stratified by 'high risk' for stroke and 'moderate risk' for stroke. Fuster et al. [1] also listed some factors with 'less validated' or 'weak association' with stroke. In the current study, residents were assigned to one of the following stroke-risk categories: low (none or 1+ weak stroke risk factors), moderate (1 moderate), high (2+ moderate or 1+ high).

At the time this study was designed, the AFib risk-specific HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly [>65 years], Drugs/alcohol concomitantly) [20] and atherothrombotic risk-specific REACH (REduction of Atherothrombosis for Continued Health) [21] bleeding algorithms had not yet

Table 1 Assessment of stroke and bleeding risk among residents with atrial fibrillation: warfarin users and non-users

Risk factor	NNHS[a]			AnalytiCare		
	User ($n = 502$) (%)	Non-user ($n = 952$) (%)	p value[b]	User ($n = 1,674$) (%)	Non-user ($n = 2,083$) (%)	p value[b]
Stroke risk factors						
High risk factors						
Previous stroke[c] [1, 10]	20	12	0.001	24	23	0.405
TIA [1, 10]	5	3	0.079	4	3	0.110
Systemic embolism [1, 10]	0	0	0.140	0	0	0.441
Mitral stenosis [1]	1	0	0.046	0	0	0.177
Prosthetic heart valve [1]	0	0	0.139	0	0	0.704
Moderate risk factors						
Age ≥75 years [1, 10]	89	88	0.636	80	83	0.003
Hypertension [1, 10]	61	59	0.399	75	73	0.168
Congestive heart failure[c] [1, 10]	41	38	0.266	47	40	<0.001
Diabetes mellitus [1, 10]	24	23	0.667	38	34	0.026
Less-validated or weaker risk factors						
Female sex [1]	72	69	0.344	64	63	0.273
Age 65–74 years [1]	9	8	0.675	15	12	0.002
Coronary artery disease [1]	26	25	0.694	13	12	0.346
Thyrotoxicosis [1]	5	4	0.633	0	0	0.502
Bleeding risk factors						
AFFIRM study bleeding risk factors [22][d]						
Older age[e]	n/a	n/a	n/a	n/a	n/a	n/a
Aspirin use	11	48	<0.001	5	8	<0.001
Liver disease	0	0	0.128	0	1	0.344
Renal disease	2	4	0.056	14	14	0.750
Diabetes mellitus	24	23	0.667	38	34	0.026
Congestive heart failure	41	38	0.266	47	40	<0.001
Other bleeding risk factors						
Age ≥65 years [23]	98	96	0.073	95	95	0.655
Previous gastrointestinal bleed [23]	2	4	0.153	2	3	0.029
Previous stroke or TIA [23]	24	14	<0.001	26	25	0.211
Dementia or cognitive impairment [24]	12	17	0.042	24	40	<0.001
Anaemia [23]	17	21	0.063	26	30	0.011
NSAID use	2	3	0.251	4	5	0.209
Antiplatelet use	11	55	<0.001	10	22	<0.001
History of falls (in last 180 days) [24]	41	37	0.225	42	44	0.249
Internal bleeding (in last 7 days) [24]	n/a	n/a	n/a	1	1	0.492

LVEF left ventricular ejection fraction, *n/a* not applicable, *NNHS* National Nursing Home Survey, *NSAID* nonsteroidal anti-inflammatory drug, *TIA* transient ischaemic attack

[a] Sampling weights were applied to NNHS data to determine population estimates and frequencies

[b] Chi-square test

[c] Fuster et al. [1] list "previous stroke," whereas Singer et al. [10] list "prior ischemic stroke." Data did not distinguish between ischaemic and haemorrhagic stroke; therefore, haemorrhagic stroke is included in these percentages. Fuster et al. [1] lists "LV [left ventricular] ejection fraction [EF] [of] 35% or less" as a separate moderate risk factor besides heart failure, whereas Singer et al. [10] lists "moderately or severely impaired left ventricular systolic function and/or heart failure." Impaired LVEF was unavailable in the data unless the resident had a diagnosis of congestive heart failure

[d] AFFIRM study hazard ratios for covariates associated with major bleeding (with adjustment): age, 1.05 per year; aspirin use, 2.01; hepatic or renal disease, 1.93; warfarin use, 1.78; diabetes, 1.44; congestive heart failure, 1.43; first episode of atrial fibrillation, 1.30

[e] See "Age ≥65 years" in "Other bleeding risk factors" category for older age as a bleeding risk factor. The AFFIRM study reported that bleeding risk increased with age when age is expressed as a continuous variable. Age categories were not evaluated. The average age of study participants experiencing a major bleeding episode was 72.3 years

Table 2 Application of inclusion criteria to obtain eligible residents for analysis

Database	Application of inclusion criteria to resident population	Number excluded [population estimate][a]	Number retained [population estimate][a]
NNHS	All residents who were included in the NNHS database	n/a	13,507 [1,492,207]
	Had an open-ended entry for AFib (ICD-9-CM diagnostic code 427.3X) in any of the 15 available current diagnosis fields on the resident questionnaire	12,053 [1,330,146]	1,454 [162,061]
	Eligible residents retained for analysis	n/a	1,454 [162,061]
AnalytiCare	All residents who had complete pharmacy data, ≥2 MDS assessments, and an entry for AFib (ICD-9-CM diagnostic code 427.3X) in any MDS assessment completed during the study period 1 January 2007–30 June 2009	n/a	6,391
	Had an MDS assessment at least 1 year prior to the end of the study period	1,830	4,561
	Had a diagnosis for AFib within 1 year of the earliest MDS assessment	343	4,218
	Had a complete admission or annual assessment within 1 year of the earliest MDS assessment	456	3,762
	Was ≥18 years of age on 1 January 2007 and his/her sex was known	5	3,757
	Eligible residents retained for analysis	n/a	3,757

AFib atrial fibrillation, *ICD-9-CM* International Classification of Diseases, Ninth Revision, Clinical Modification, *MDS* Minimum Data Set, *n/a* not applicable, *NNHS* National Nursing Home Survey

[a] NNHS-provided sampling weights were applied to derive population estimates

been published. Bleeding risk factors were identified from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study [22] and from other studies [23, 24]. Bleeding risk factors (listed in Table 1) were tallied by count and assigned to one of four levels: 0–1, 2, 3 and 4+.

Available ADL measures were comparable between NNHS and AnalytiCare databases, because these were derived from the same source: the MDS 2.0. The method of Carpenter et al. [25] was used to derive a single ADL functioning score from seven physical function assessment items. Logistic regression models were used to predict the odds of being prescribed warfarin by including, for each resident, only stroke-risk and bleeding-risk category assignments (no other resident characteristics). NNHS-provided sampling weights were applied to derive all estimates from that database. Intercooled Stata version 8.0 (Stata Corporation, College Station, TX, USA) was used for all analyses.

3 Results

3.1 Resident Characteristics

After applying inclusion criteria, NNHS had 1,454 eligible residents with AFib (Table 2), representing (after applying sampling weights) an LTC population of 162,061 having AFib in the year 2004 (55,061 warfarin users and 107,000 non-users). The AnalytiCare database had 3,757 eligible residents with AFib.

Table 3 shows characteristics of residents with AFib. In the NNHS, the median age was 85 years; 70 % were female. In AnalytiCare, median age was 83 years; 63 % were female. In the NNHS, age and sex distributions were similar between residents having AFib who were receiving warfarin therapy and those who were not. In AnalytiCare, a smaller proportion of residents over 85 years of age (37 %) were receiving warfarin compared with those not receiving warfarin (50 %; $p < 0.001$ for age distribution); the sex distribution was similar between these groups.

In both the NNHS and AnalytiCare, residents receiving warfarin had a more favourable distribution of ADL functioning (less physical dependence; $p = 0.050$ and $p < 0.001$, respectively, Table 3) compared with non-users. In both databases, warfarin users had a higher mean $CHADS_2$ score (indicating greater stroke risk) than non-users, although group differences in scores were small: 0.2 (NNHS; $p = 0.001$) and 0.1 (AnalytiCare; $p = 0.003$) points. Except for deep vein thrombosis, rates of common chronic conditions (excluding stroke or bleeding risk factors) were generally similar among warfarin users and non-users in both databases (Table 3).

3.2 Individual Stroke and Bleeding Risk Factors

Table 1 compares the proportion of residents having each of the individual stroke risk factors. The distribution of high risk factors was similar among warfarin users and non-users in AnalytiCare. In the NNHS, warfarin users had higher rates of previous stroke ($p = 0.001$) and mitral stenosis ($p = 0.046$) than non-users (previous stroke is also

Table 3 Characteristics of residents with atrial fibrillation: warfarin users and non-users

Characteristics	NNHS[a]			AnalytiCare		
	User ($n = 502$) (%)	Non-user ($n = 952$) (%)	p value[b]	User ($n = 1,674$) (%)	Non-user ($n = 2,083$) (%)	p value[b]
Demographics						
Age, year (<75 year referent)	11	12	0.615	20	17	<0.001
75–84	33	30		43	33	
≥85	57	58		37	50	
Female	72	69	0.344	64	63	0.273
Race/ethnicity (White referent)	92	89	0.010	85	81	0.006
Black	4	7		8	10	
Hispanic	3	1		6	7	
Other	1	3		2	2	
Physical functioning						
ADL assessment from MDS using Carpenter score[c] [25] (independent, score <14 referent)	41	35	0.050	29	26	<0.001
Moderate (score ≥14 and <21)	33	33		55	51	
Dependent (score ≥21)	26	32		16	22	
Hospice/<6 months to live	1	4	0.005	1	3	<0.001
$CHADS_2$ stroke risk index [6]						
0	1	3	0.021	1	1	0.044
1	17	21		10	13	
2	31	35		28	31	
3	30	26		29	28	
4	13	11		19	16	
5	6	4		9	8	
6	2	1		3	3	
Mean (±SE) $CHADS_2$ score	2.6 (0.07)	2.4 (0.04)	0.001	2.9 (0.03)	2.8 (0.03)	0.003
Comorbid conditions not elsewhere listed as a stroke or bleeding risk factor						
Deep vein thrombosis	6	2	0.004	7	4	<0.001
Peripheral vascular disease	11	12	0.671	19	18	0.200
Depression	35	33	0.374	47	49	0.148
Emphysema/COPD	18	20	0.390	30	29	0.288
Cancer	6	9	0.053	10	9	0.385

ADL activities of daily living, *CHADS$_2$* Cardiac Failure, Hypertension, Age, Diabetes, [and] Stroke [Doubled], *COPD* chronic obstructive pulmonary disease, *MDS* Minimum Data Set, *NNHS* National Nursing Home Survey, *SE* standard error

[a] Sampling weights were applied to NNHS data to determine population estimates and frequencies

[b] Chi-square test (proportions), t test (mean)

[c] Score range 0–28, where a higher score indicates greater physical functioning dependence (i.e. worsened ADL performance)

listed in combination with transient ischaemic attack [TIA] as a bleeding risk factor). For moderate stroke risk factors, warfarin users and non-users in the NNHS had similar distributions. However, in AnalytiCare, compared with non-users, a lower proportion of warfarin users were aged ≥75 years ($p = 0.003$), a larger proportion had diabetes mellitus ($p = 0.026$), and a larger proportion had congestive heart failure (CHF) ($p < 0.001$) (diabetes mellitus and CHF are also listed as bleeding risk factors). The distribution of less validated or weak association factors was similar between warfarin users and non-users between databases, except for a higher proportion of residents in the 65–74 age group among warfarin users in AnalytiCare ($p = 0.002$).

Table 1 also compares the proportion of residents having each of the individual bleeding risk factors. In the NNHS, a lower proportion of warfarin users (11 %) were taking aspirin compared with non-warfarin users (48 %; $p < 0.001$). Similarly, in AnalytiCare, a lower proportion of warfarin users (5 %) were taking aspirin compared with

non-warfarin users (8 %; $p < 0.001$), although under-reporting of over-the-counter aspirin use is noted as a limitation of the latter database. In both databases, compared with non-users, a significantly smaller proportion of warfarin users had dementia or cognitive impairment ($p = 0.042$ NNHS; $p < 0.001$ AnalytiCare) or were currently using antiplatelet therapy ($p < 0.001$ for both databases). In AnalytiCare only, a smaller percentage of warfarin users were anaemic when compared with non-users ($p = 0.011$).

3.3 Rate of Warfarin Use by Bleeding and Stroke Risk Category

Table 4 shows the rate of warfarin use for each combination of stroke risk and bleeding risk category for residents in each database. In the NNHS, 34 % of all residents with AFib were receiving warfarin (95 % CI 31.1–36.8). Thirty-six per cent of all AFib residents with high stroke risk (2+ moderate or 1+ high risk factors) were receiving warfarin. Findings were similar in the AnalytiCare database: a minority (45 % of all residents with AFib) were currently receiving warfarin (95 % CI 43.0–46.1) and 45 % of residents with high stroke risk were receiving warfarin. In both databases, warfarin use generally increased with higher stroke risk among residents in the same bleeding risk category.

3.4 Distribution of Resident Counts by Stroke and Bleeding Risk

Figure 1 shows the distribution of residents in each category of stroke and bleeding risk, without regard to warfarin use. Findings were similar among both databases. A majority of all residents with AFib in the NNHS database (78 %) and in the AnalytiCare database (87 %) were classified as having high stroke risk. In both databases, approximately three out of every four of these high-stroke-risk residents had at least three or more bleeding risk factors.

3.5 Modelling Warfarin Use from Stroke and Bleeding Risk

Figure 2 shows, from the single logistic regression model within each database, the odds of a resident being prescribed warfarin according to stroke and bleeding risk category.

In the NNHS, compared with the 'none or 1+ weak' stroke risk factor(s) and '0–1' bleeding risk factors' referent categories (odds ratio [OR] = 1), the odds of receiving warfarin consistently increased with greater stroke risk: 1 moderate, OR = 1.93 ($p = 0.118$, 95 % CI 0.85–4.38); 2+ moderate, OR = 3.19 ($p = 0.005$, 95 % CI 1.42–7.17); and 1+ high, OR = 8.18 ($p \leq 0.001$, 95 % CI 3.49–19.16). The odds of receiving warfarin consistently decreased with greater bleeding risk: 2 risk factors, OR = 0.83 ($p = 0.366$, 95 % CI 0.56–1.24); 3 risk factors, OR = 0.47 ($p \leq 0.001$, 95 % CI 0.31–0.70); and 4+ risk factors, OR = 0.17 ($p \leq 0.001$, 95 % CI 0.11–0.26).

A similar, consistent trend was observed for AnalytiCare, although only two risk factors were significant. For stroke risk: 1 moderate, OR = 0.99 ($p = 0.973$, 95 % CI 0.55–1.78); 2+ moderate, OR = 1.55 ($p = 0.138$, 95 % CI 0.87–2.75); and 1+ high, OR = 1.79 ($p = 0.052$, 95 % CI <1.0–3.23). For bleeding risk: 2 risk factors, OR = 0.91 ($p = 0.479$, 95 % CI 0.69–1.19); 3 risk factors, OR = 0.68 ($p = 0.004$, 95 % CI 0.52–0.88); and 4+ risk factors, OR = 0.54 ($p \leq 0.001$, 95 % CI 0.41–0.70).

Table 4 Rates of warfarin use by stroke and bleeding risk category

Database	Bleeding risk factors	Stroke risk factors (%)					All stroke risks (%)
		None or 1+ weak	1 moderate	2+ moderate	1+ high	2+ moderate or 1+ high (combined)	
NNHS	0–1	20	43	55	80	56	45
	2	11	41	51	78	54	50
	3	0	31	37	60	42	40
	4+	0[a]	7	17	32	21	19
	All bleeding risks	17	30	32	46	36	34
AnalytiCare	0–1	41	44	56	55	56	49
	2	43	47	50	59	52	51
	3	50[a]	37	44	53	46	45
	4+	0[a]	14	42	41	42	41
	All bleeding risks	42	39	45	46	45	45

NNHS National Nursing Home Survey

[a] Small counts (sample, $n < 10$); age ≥75 years was considered a bleeding risk

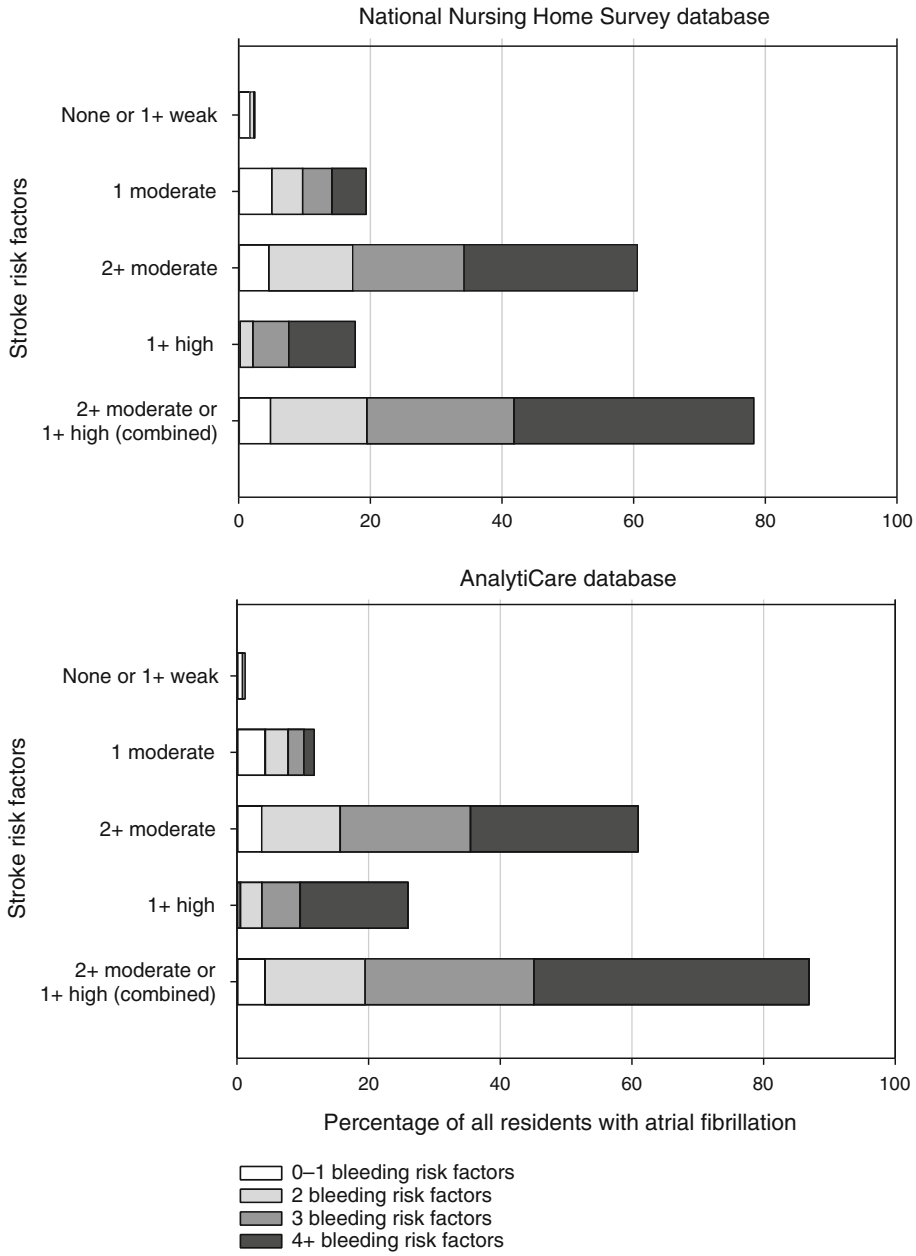

Fig. 1 Percentage of all residents with atrial fibrillation by stroke and bleeding risk

4 Discussion

Our study showed that of every ten LTC residents with AFib, eight (NNHS) and nine (AnalytiCare) were at a high risk for stroke (i.e. had 2+ moderate or 1+ high stroke risk factors). A majority of residents (six and seven of every ten, respectively) had high stroke risk combined with 3+ bleeding risk factors. This is not unexpected, since several key risk factors listed are common to both stroke and bleeding risk assessments (e.g. previous stroke or TIA, CHF and diabetes mellitus). An earlier study of Canadian LTC residents with AFib by Lau et al. [16], using ACCP guidelines [10] to define risk, found that nearly 97 % had high stroke risk. Thus our study affirms Lau et al.'s [16] finding of a high and continuing level of need for consideration for stroke risk reduction in the LTC population.

4.1 Rates of Warfarin Use

Findings from the present study also revealed that fewer than half of all residents with AFib (including fewer than half of all residents with high stroke risk) were receiving warfarin prophylaxis. Although warfarin usage increased from 34 % in the 2004 NNHS database to 45 % in the

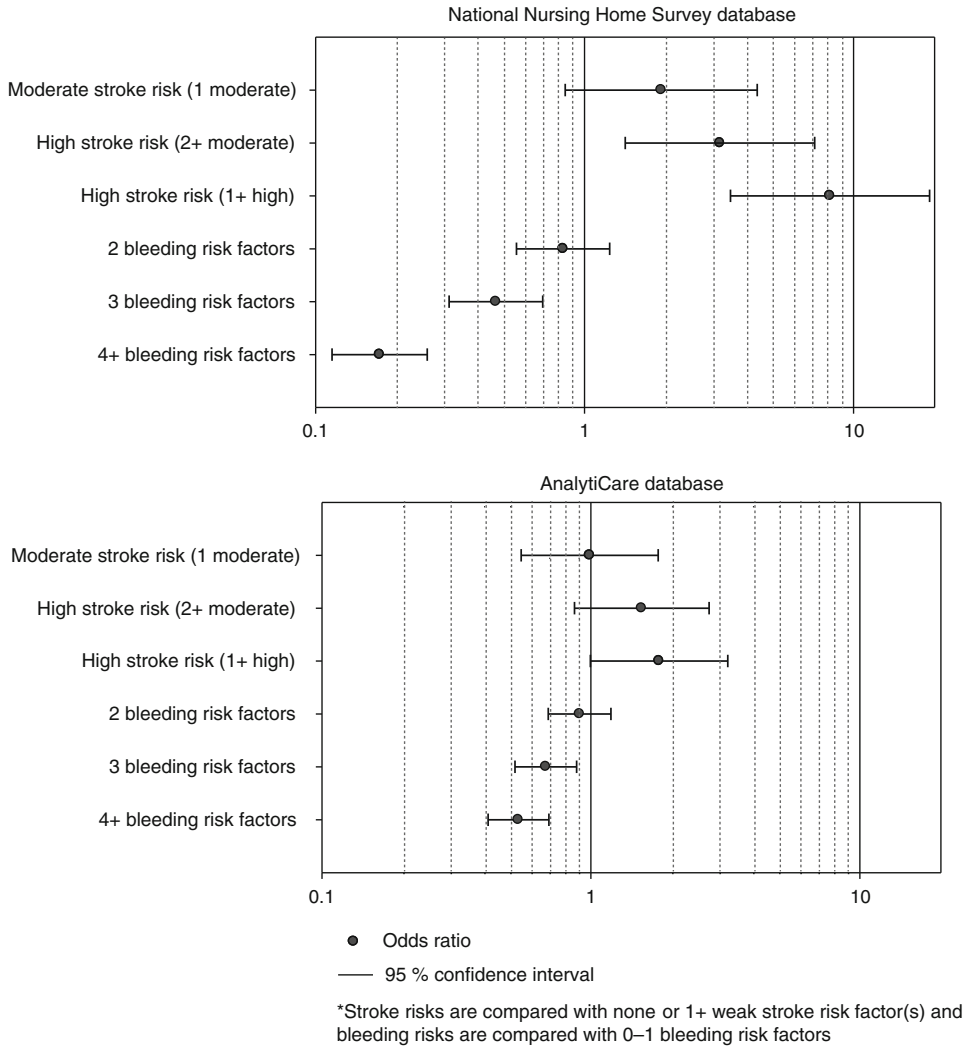

Fig. 2 Odds of being prescribed warfarin according to stroke and bleeding risk category

2007–2009 AnalytiCare database, overall usage of warfarin in residents with AFib remains low. These findings are generally consistent with five earlier regional LTC studies that evaluated the use of warfarin in AFib among US and Canadian nursing home facilities prior to 2004 [13–17] and one that examined the same NNHS database used in the current study [18]. Abdel-Latif et al. [13] found that 46 % of residents with AFib were using warfarin, and Gurwitz et al. [14] found that 32 % were. Three of these studies also evaluated the use of warfarin when patients were stratified by stroke and bleeding risk. Lau et al. [16] found that warfarin was prescribed for 57 % of AFib residents. Among high-stroke-risk/low-bleeding-risk candidates, the warfarin prescribing rate remained similar at 60 %. Lackner and Battis [15] found that only 17 % of patients with non-valvular AFib received warfarin, whereas among residents with 1+ additional risk factor for stroke and no contraindication, 20 % received warfarin. McCormick et al. [17] reported that although 42 % of residents with AFib received warfarin, only 53 % of 'ideal' candidates for warfarin therapy (i.e. no bleeding risk factors) received oral anticoagulant prophylaxis. Ghaswalla et al. [18] found usage of warfarin among only 30 % of appropriate candidates in the NNHS database (residents who had an indication for warfarin and no contraindications against its use); these authors further found that of the remaining 70 % not receiving warfarin, only 23 % had been placed on antiplatelet therapy (aspirin or clopidogrel). Findings regarding low anticoagulant usage have also been noted within non-LTC community settings. In a recent systematic review, Ogilvie et al. [26] found suboptimal (<70 %) anticoagulant usage in seven of nine studies of patients who had both AFib and a $CHADS_2$ score of ≥2.

4.2 Modelling of Stroke and Bleeding Risk

Findings from our logistic regression analysis showed that stroke and bleeding risk components, when evaluated together within the same resident with AFib, have a consistent, directional relationship with warfarin use.

Increased stroke risk and reduced bleeding risk are associated with greater odds of receiving warfarin; the converse also applies. This finding contrasts with Lau et al.'s [16] earlier finding of discordance between antithrombotic use and relative risk of bleeding but agrees with McCormick et al.'s [17] finding of lower warfarin use among residents with 2+ bleeding risk factors. An unexpected finding in the NNHS data is that residents with high stroke risk classified as having 1+ high stroke risk factor(s) usually had greater odds of receiving warfarin than those with high stroke risk classified as 2+ moderate risk factors, despite the risk equivalence of these categories.

Despite consistency in the stroke–bleeding risk relationship with warfarin use, we found evidence of an upper limit or plateau in usage—a finding also noted in earlier studies [15–17] and in a recent systematic review that concluded that bleeding risk alone may not explain low rates of warfarin use for AFib in LTC [27]. Except for the small number of residents with a combination of 0–2 bleeding risk factors and 1+ high stroke risk factors in the NNHS database (who had a 78–80 % rate of warfarin use), warfarin use did not otherwise exceed 60 % among residents with AFib in either database, and was typically lower, regardless of which category of combined stroke and bleeding risk was evaluated (Table 4).

4.3 Potential Reasons for Limits in Warfarin Use

Addressing similar limits to warfarin use as observed among residents with higher stroke risk, McCormick et al. [17] and Lau et al. [16] cited the potential unavailability of patient preferences, care directives, or other data from the medical records they examined as possible explanations for the low rate of warfarin use in AFib. Additional reasons for warfarin underuse included difficulty in monitoring anticoagulation therapy [17], concerns about the risk of bleeding complications that outweigh concerns about the risk of stroke [17], knowledge deficits regarding risk factors for stroke and the effectiveness of warfarin for stroke prevention in older patients with AFib [16, 17], underrecognition of AFib [16], and past experiences with antithrombotics [16].

Two studies of physicians who responded to hypothetical AFib case studies in LTC settings showed that they were most concerned about the risk of falls [28, 29], dementia [28], limited life expectancy [28], a history of gastrointestinal (GI) bleeding and non-CNS bleeding [29], and a history of ischaemic stroke [29]. We found no effect on warfarin use from a history of falling (Table 1), but our findings support many of these physician-reported factors, including a strong effect of dementia or cognitive impairment (both databases), effects due to limited life expectancy (both databases), and GI bleeding (AnalytiCare).

Both databases revealed that LTC residents receiving warfarin appeared to have better physical functioning (i.e. lower ADL dependence). Although it has not been reported to be a bleeding risk factor, poor physical functioning can be added to the list of factors that might negatively influence the use of warfarin in the LTC facility.

4.4 Limitations

A primary source of data in both the NNHS and AnalytiCare databases was the MDS 2.0. Although the validity and reliability of the MDS can vary by a given indicator [30], the MDS 2.0 has been reported to generally have moderate, or moderate to high, validity and reliability [31]. In both study databases, current medication use was evaluated by temporal proximity to the AFib diagnosis (under-reporting of aspirin use in the AnalytiCare database was described above). Other non-AFib indications for warfarin use, such as post-myocardial infarction secondary prevention, were possible. No distinction was made by type of AFib (e.g. valvular/non-valvular, paroxysmal/persistent), although warfarin is used for stroke prophylaxis among AFib variants [9]. Specific stroke and bleeding risk factors identified in consensus guidelines have not been validated against stroke and bleeding outcomes in the LTC setting. Our model tested an amalgam of summary measures of stroke and bleeding risk taken from AFib guidelines and medical literature. Other risk factors considered in new models may have been relevant but were not included (e.g. bleeding risk factors: some items listed in HAS-BLED [20] [such as hypertension and poor International Normalised Ratio (INR) control] and some items listed in REACH [21] [e.g. smoking and hypercholesterolaemia]). As noted, several factors in our list are counted as both stroke and bleeding risks, and this remains a limitation even among newer models such as HAS-BLED and REACH. Although a difficult issue to reconcile, this degree of overlap limits the ability of models to discriminate among summary stroke and bleeding categories when these are considered together.

5 Conclusion

Although our two study databases differed in design, scope and time period of data collection, findings from the analysis of each appear similar. High-stroke-risk patients, who are known to have the greatest net clinical benefit from warfarin use [5, 29], comprised approximately 80 % or more of AFib residents in our two databases. Consistent with our findings and those from earlier research [15, 16, 21], warfarin use continues to appear low among residents with AFib in the LTC setting. Further research is needed to evaluate the degree to which this low usage rate represents

appropriate balancing of stroke and bleeding risk or other concerns in these unique patients, or whether this represents a potentially large lost clinical benefit from otherwise preventable stroke.

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