Temporal trends in anticoagulation management for US active duty personnel with atrial fibrillation

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Objectives This study aims to investigate US active duty (AD) military members diagnosed with atrial fibrillation (AF) and the temporal trends of systemic anticoagulation (AC). Our secondary objective is to study the AC prescriptions in AD military members diagnosed with AF and associated military dispositions and deployment rates.

Design and setting A retrospective investigation of Tricare pharmacy AC prescriptions within the San Antonio Military Health System from January 2004 to July 2019 for AD individuals diagnosed with AF was performed.

Participants 386 AD personnel with non-valvular AF were analysed (mean age 35.0±9.4 years; mean body mass index, 28.3±4.3 kg/m²; 93% male; 57% Caucasian, 94% paroxysmal AF).

Outcomes The temporal trends of systemic AC prescriptions were the primary outcome measures. The association between AC prescriptions and military dispositions and deployments were secondary outcomes of interest.

Statistical analysis The association between AC management, future deployments and military disposition was analysed using χ² and Fisher’s exact test for categorical variables. The t-test was used for comparison of continuous variables.

Results CHA₂DS₂-VASC and HAS-BLED scores were low (0.39±0.65 and 0.86±0.63, respectively). 127 (33%) members received warfarin and 58 (15%) received direct oral anticoagulants (DOACs). Rates of military retention were not different between AC histories (no AC (64%) vs warfarin (75%) vs DOAC (65%); p=0.425). There was a significant trend of more recent utilisation of DOACs compared with warfarin (p<0.0001). When adjusted for temporal changes in deployment rates, there was no significant difference in deployment between AC groups (no AC (39%) vs warfarin (49%) vs DOAC (27%); p=0.9472).

Conclusions This is the first report describing AC utilisation in US AD military members with AF. Young AD personnel with low stroke and bleeding risks do not commonly receive AC prescriptions. DOAC prescription rates are increasing and predominate over warfarin for AC indications.

INTRODUCTION

US military personnel diagnosed with atrial fibrillation (AF) are under-reported in the literature and often present without traditional cardiovascular or AF risk factors.2 The prevalence of AF diagnosed in US military personnel has not been previously described, but a retrospective cohort study of approximately 1.5 million Swedish military conscripts from 1969 to 1997 demonstrated a prevalence of 23,600 (1.5%).3 In comparison, the prevalence of AF in the Swedish population as a whole is estimated at 3.0% based on the National Patient Register data from 2004 to 2010.4

Thromboembolic disease secondary to AF is a disqualifying condition for flying and special duty personnel and has morbid impacts on many military occupations.5-7 For decades, the vitamin K antagonist warfarin was preferred for the prevention of thromboembolism associated with non-valvular AF.8,9 In 2010, dabigatran was the first approved direct oral anticoagulant (DOAC) after the results of the RE-LY trial demonstrated superior endpoints in stroke and systemic embolism reduction when compared with warfarin.10,12 Intracranial bleeding and life-threatening events with dabigatran were significantly decreased with both the 110 mg and 150 mg trial dosages.10,11 Rivaroxaban was the second DOAC approved in 2011 by the Food and Drug Administration (FDA) for the reduction of strokes and
systemic emboli in patients with non-valvular AF after the ROCKET AF trial showed that it was non-inferior in the primary endpoints of stroke and systemic embolism when compared with warfarin. Overall major bleeding events were similar between rivaroxaban and warfarin, but there were lower life-threatening bleeding and intracranial bleeds in those treated with rivaroxaban. Apixaban was the third DOAC that became FDA approved after the results of the ARISTOTLE trial were published. The landmark ARISTOTLE trial demonstrated that apixaban was significantly associated with fewer strokes (ischaemic and haemorrhagic), systemic emboli, and major bleeding.

| Table 1 Demographic characteristics of active duty military servicemembers diagnosed with atrial fibrillation (AF) and relationship to anticoagulation (AC) prescriptions |
|---------------------------------------------------------------|
| Demographics | All (n=386) | No AC (n=201) | Warfarin (n=127) | DOAC (n=58) | P value |
| Demographics | | | | | |
| Age, years | 35.0±9.4 | 33.7±8.9 | 35.5±9.5 | 38.7±9.7 | 0.0008 |
| Male, no (%) | 360 (93) | 182 (91) | 123 (97) | 55 (95) | 0.0620 |
| BMI, kg/m² | 28.3±4.3 | 27.9±3.9 | 28.1±4.1 | 29.9±5.3 | 0.0037 |
| Race | | | | | |
| Caucasian, no (%) | 219 (57) | 110 (55) | 76 (60) | 33 (57) | N/A |
| African American, no (%) | 81 (21) | 45 (22) | 23 (18) | 13 (22) | N/A |
| Asian/Pacific Islander, no (%) | 9 (2) | 3 (2) | 4 (3) | 2 (3) | N/A |
| Native American, no (%) | 1 (0.3) | 1 (0.5) | 0 (0) | 0 (0) | N/A |
| Hispanic, no (%) | 3 (0.8) | 3 (2) | 0 (0) | 0 (0) | N/A |
| Other race/unknown, no (%) | 73 (19) | 39 (19) | 24 (19) | 10 (17) | N/A |
| Military Branch | | | | | |
| US Army, no (%) | 246 (64) | 127 (63) | 86 (68) | 33 (57) | N/A |
| US Air Force, no (%) | 119 (31) | 65 (32) | 34 (27) | 20 (34) | N/A |
| US Navy, no (%) | 21 (5) | 9 (4) | 7 (6) | 5 (9) | N/A |
| Comorbidities | | | | | |
| Hypertension, no (%) | 91 (24) | 36 (18) | 40 (31) | 15 (26) | 0.0173 |
| Obstructive sleep apnoea, no (%) | 75 (19) | 34 (17) | 21 (17) | 20 (34) | 0.0129 |
| Diabetes mellitus, no (%) | 6 (2) | 2 (1) | 1 (0.8) | 3 (5) | N/A |
| Vascular disease, no (%) | 4 (1) | 0 (0) | 2 (2) | 2 (3) | N/A |
| History of VTE, no (%) | 5 (1) | 0 (0) | 5 (4) | 0 (0) | N/A |
| Prior TIA or CVA, no (%) | 5 (1) | 1 (0.5) | 4 (3) | 0 (0) | N/A |
| Coronary artery disease, no (%) | 8 (2) | 1 (0.5) | 5 (4) | 2 (3) | N/A |
| History of heart failure, no (%) | 12 (3) | 1 (0.5) | 10 (8) | 1 (2) | N/A |
| Laboratory data | | | | | |
| Glucose, mg/dL | 95.9±16.4 | 96.5±15.3 | 93.6±16.3 | 98.8±19.3 | 0.1122 |
| Total cholesterol, mg/dL | 181.6±37.7 | 182.2±40.6 | 182.7±34.3 | 177.5±5.0 | 0.6897 |
| LDL, mg/dL | 112.4±46.8 | 114.9±59.5 | 111.3±28.5 | 107.1±33.7 | 0.5636 |
| HDL, mg/dL | 47.4±13.8 | 48.8±13.5 | 46.0±14.0 | 46.4±13.7 | 0.2196 |
| Triglycerides, mg/dL | 121.8±88.8 | 115.2±88.0 | 131.0±95.6 | 121.1±72.6 | 0.2934 |
| Risk Scores | | | | | |
| Median CHA2DS2-VASc | 0 | 0 | 0 | 0 | N/A |
| CHA2DS2-VASc<2 | 364 (94) | 197 (98) | 113 (89) | 54 (93) | N/A |
| CHA2DS2-VASc≥2 | 22 (6) | 4 (2) | 14 (11) | 4 (7) | N/A |
| Median HAS-BLED | 1 | 0 | 0 | 0 | N/A |
| HAS-BLED<3 | 385 (99) | 201 (100) | 126 (99) | 58 (100) | N/A |
| HAS-BLED≥3 | 1 (1) | 0 (0) | 1 (1) | 0 (0) | N/A |
| AF classification | | | | | |
| Paroxysmal, no (%) | 361 (94) | 198 (98) | 114 (90) | 49 (84) | <0.0001 |
| Persistent, no (%) | 21 (5) | 1 (0.5) | 11 (9) | 9 (16) | <0.0001 |
| Permanent, no (%) | 4 (1) | 2 (1) | 2 (2) | 0 (0) | <0.0001 |

Values are number (%), mean (±1 SD), BMI, body mass index; CVA, cerebrovascular accident; HDL, high-density lipoprotein; LDL, low-density lipoprotein; N/A, not applicable; TIA, transient ischaemic attack; VTE, venous thromboembolism.
events when compared with warfarin therapy. Edoxaban has limited availability within US military treatment facility pharmacies but also has literature demonstrating non-inferior outcomes when compared with warfarin. The DOACs overall present advantages over warfarin due to their favourable pharmacokinetics, reduced burden of routine laboratory monitoring, fewer drug–drug interactions, absence of major dietary impacts and lower risk of intracranial haemorrhages.

There is a paucity of literature describing active duty (AD) US military personnel with AF and systemic anticoagulation (AC) prescriptions provided for the reduction of stroke and systemic embolism despite there being robust literature describing veterans in the Veterans Health Administration. One limited retrospective study published shortly after the DOAC FDA approvals in 2014 from the British Royal Air Force reports on just 6 of 23 military aircrew diagnosed with AF being treated with systemic AC or antiplatelet therapy. Five individuals were reported as having a CHA₂DS₂-VASc score of 1 and three members with a score of 0. One individual with a score of 1 and three members with a score of 0 were prescribed aspirin. Two aircrew members with a score of 0 were treated with warfarin. Aside from this study, there are no other widely published reports describing military personnel with AF and the systemic AC provided despite the associated mission-related consequences. In the UK Armed Forces and US Armed Forces, long-term warfarin and DOAC therapy are incompatible with most flying duties and service in deployed environments due to the associated increased risk of haemorrhage in individuals whose duties require participation in high risk activities such as combat situations, jumping from aircraft or high performance flying. Further, the temporal trends of oral AC prescription patterns in military treatment facilities in the post-DOAC approval period have never been reviewed and reported despite consensus guidelines reflecting the effectiveness and safety of DOACs in routine clinical practice for non-valvular AF. This study aims to investigate US AD military members diagnosed with AF and the temporal trends of military treatment facility systemic AC prescriptions. Our secondary objective is to evaluate the AC prescriptions in AD military members diagnosed with AF and association with military dispositions and deployment rates.

**METHODS**

**Study design**

A retrospective analysis of all AD AF diagnoses within the San Antonio Military Health System from 1 January 2004 to 30 June 2019 was performed. Patients met inclusion criteria if they were AD personnel in the US Air Force, Army or Navy and had a confirmed 12-lead electrocardiographic diagnosis of AF by a board-certified cardiologist. AF was classified as paroxysmal (duration less than 7 days), persistent (duration more than 7 days) or permanent. There were no patients with valvular AF. Available clinical, demographic, deployment and military disposition information was collected through review of the electronic medical record. AC prescriptions were electronically reviewed based on evidence of Tricare covered prescriptions. Duration of systemic AC treatment was not available from this retrospective analysis. This retrospective research protocol was approved by the institutional review board of San Antonio Military Medical Center, which waived the need for informed consent because the research involved no more than minimal risk to the patients.
participants and the waiver did not adversely affect their rights and welfare.

Statistical analysis
The association between management therapies, deployment history and military disposition was analysed using $\chi^2$ and Fisher’s exact test for categorical variables. The t-test was used for comparison of continuous variables. Due to the sample size, we relied on central limit theorem and did not test normality assumption. A one way analysis was performed to assess temporal trends in AC use and Tukey-Kramer HSD was used to compare all groups. Data analysis was performed using JMP statistical analysis software V.15 (SAS Institute).

Patient and public involvement
Patients and the public were not directly involved in the research process given the retrospective, observational nature of the study.

RESULTS
There were 386 AD personnel with a diagnosis of non-valvular AF treated within the San Antonio Military Health System during the study period who met inclusion criteria. The study population had a mean age of 35.0±9.4 years and mean body mass index (BMI) of 28.3±4.3 kg/m$^2$. 93% were male and 57% were described as Caucasian. Most members were in the Army (246 (64%)) and paroxysmal AF was most common (361 (94%)). Hypertension and obstructive sleep apnoea were the most common AF risk factors observed, present in 91 (24%) and 75 (19%), respectively. Overall CHA$_2$DS$_2$-VASc and HAS-BLED scores were low with medians of 0 and 1, respectively.

The majority of AD servicemembers received no AC (201 (52%)) throughout their AD careers. Of those who received any AC, 127 (69%) members received warfarin and 58 (31%) members received DOACs (table 1).

Individuals who received DOACs had a greater mean age (no AC (33.7±8.9) vs warfarin (35.5±9.5) vs DOAC (38.7±9.7); p=0.0008) and greater mean BMI compared with those who did not (no AC (27.9±3.9) vs warfarin (28.1±4.1) vs DOAC (29.9±5.3); p=0.0037). Personnel treated with AC statistically trended to have higher CHA$_2$DS$_2$-VASc scores (no AC (0.28±0.49) vs warfarin (0.57±0.78) vs DOAC (0.41±0.75); p=0.0003). There was a significant difference in HAS-BLED averages between AC strategies, with the lowest averages observed in DOAC treatment group and highest in the warfarin group (no AC (0.82±0.66) vs warfarin (1.01±0.55) vs DOAC (0.68±0.66); p=0.0038).

There was a significant trend for more recent utilisation of DOACs compared with warfarin between 2004 and 2019 (p<0.0001) (Figure 1). Among the DOACs, dabigatran utilisation was more frequent earlier in the study period (figure 2). Apixaban and rivaroxaban were used more frequently in more recent years when compared with warfarin (p<0.0001) (figure 2).

In a subgroups analysis (n=365), many individuals who had a history of AC prescriptions were able to participate in future deployments and meet military retention standards (table 2). Of those who received any systemic AC, 72 (39%) deployed and 123 (66%) remained on AD.

| Table 2 | Military deployment and retention rates in a subgroup of active duty military servicemembers after atrial fibrillation diagnosis comparing anticoagulation prescriptions |
|---------|----------------------------------------------------------------------------------------------------------------------------------|
|         | All (n=365) | Deployed (n=147) | Non-deployed (n=218) | Retained (n=248) | Discharged (n=117) |
| No anticoagulation | 194 (53%) | 75 (51%) | 119 (55%) | 125 (50%) | 69 (59%) |
| Any anticoagulation | 171 (47%) | 72 (49%) | 99 (45%) | 123 (50%) | 48 (41%) |
| Warfarin | 119 (70%) | 58 (81%) | 61 (62%) | 89 (72%) | 30 (63%) |
| DOAC | 52 (30%) | 14 (19%) | 38 (38%) | 34 (28%) | 18 (38%) |
| Dabigatran | 8 (15%) | 3 (21%) | 5 (13%) | 4 (12%) | 4 (22%) |
| Apixaban | 25 (48%) | 6 (43%) | 19 (50%) | 18 (53%) | 7 (39%) |
| Rivaroxaban | 19 (37%) | 5 (36%) | 14 (37%) | 12 (35%) | 7 (39%) |

Values are number, (%).

DOAC, direct oral anticoagulant.

Figure 3 | Bar graph showing the change in deployment rate of active duty military servicemembers after atrial fibrillation diagnosis over time.
Individuals with a history of AC deployed at similar rates compared with those who were never anticoagulated (no AC (51%) vs any AC (49%); p=0.5030). Personnel with a history of warfarin prescriptions deployed more commonly than those who did not receive AC and those who received DOACs (no AC (39%) vs warfarin (49%) vs DOAC (27%); p=0.0207). Deployment rates were significantly higher in those with a history of warfarin utilisation directly compared with those with a history of DOAC utilisation (warfarin (49%) vs DOAC (27%); p=0.0058). Figure 3 demonstrates the temporal trends in deployments of military members diagnosed with AF in this cohort and shows the highest prevalence of deployment rates between the years 2001 and 2012. The higher deployment rate associated with a history of warfarin use compared with other AC strategies was not independently and statistically significant when adjusted for the primary deployment rates as noted in figure 3 (p=0.9472). Military retention rates were not influenced by historical AC strategy (no AC (64%) vs warfarin (75%) vs DOAC (65%), p=0.1418).

DISCUSSION
This is the first report describing AC utilisation in a cohort of US AD military members with AF. Our study showed AD military personnel to be generally younger than the traditional at risk population with low stroke and bleeding risks by CHA2DS2-VASc and HAS-BLED scores, respectively. In addition, this population carried a lower burden of comorbidities in comparison to other contemporary AF studies such as the CABANA trial and studies evaluating the Veterans Health Administration population.\(^{18,21}\) As expected, CHA2DS2-VASc scores were higher in those who were previously provided AC therapy but not as a whole greater than the standard score of 2 needed to substantiate long-term AC according to AF guidelines.\(^ {16}\) Nearly half (47.9%) of this military cohort was previously treated with systemic AC. The combination of the high AC prescriptions in nearly half of personnel diagnosed with AF and the overall low stroke risk leads us to postulate that the majority of the military personnel who received systemic AC may have been treated for procedural and temporary reasons such as AF ablations or cardioversions. This similar trend in AC management has been recommended and demonstrated in other younger and athletic populations of similar demographics and profiles.\(^ {22}\)

At the beginning of our study and prior to the first DOAC FDA approval in 2010, warfarin utilisation was higher (figure 1) in military personnel. More recently, DOAC prescriptions in the military population predominate with an initial uptrend in dabigatran prescriptions followed by an increase in prescriptions of apixaban and rivaroxaban after 2011. These data highlight military practice pattern changes in the AD population following the introduction of DOACs, in line with their proven efficacy and safety in previous studies and endorsement by the guidelines.\(^ {14,16,17}\) This occurred shortly after their initial approval despite reversal agents not being available at that time, suggesting the progressive nature of military prescriptions in this arena within the largest military healthcare systems.\(^ {23,24}\) These temporal trends of DOAC prescriptions are comparable with US registry data, showing that the majority of new prescriptions for non-valvular AF are for a DOAC.\(^ {25}\) Overall though, the percentage of DOAC prescriptions in servicemembers with AF is still low compared with warfarin prescriptions, 15% vs 33%, respectively. This particular percentage endpoint suggests that there is still a role for increasing the prescription rates of DOACs within the military population with an effort to optimise medical therapy for stroke prevention in relevant cases.

Deployment rates were initially significantly higher in those who had previously received warfarin than those previously treated with a DOAC. However, this was driven by the independent and overall cohort higher deployment rates that occurred earlier in the study period as demonstrated by figure 3. Decreasing servicemember deployment rates after 2013, as demonstrated in figure 3 likely coincide with the withdrawal of US troops from Iraq just prior to this in 2011.\(^ {26}\) We can conclude that military members diagnosed with AF were eligible for deployment even if they had a history of systemic AC utilisation for non-valvular AF when the deployment tempo was steady during significant wartimes. As a limitation of this study, we are unable to make conclusions about whether or not individual members deployed while actively maintained on systemic AC and a prospective study would be needed in order to clarify this information. Currently, Department of Defence policies prohibit deployment of an AD servicemember while being maintained on therapeutic AC in most situations.\(^ {7}\)

The overall military retention rates in AD persons were not independently influenced by utilisation of AC or the AC strategy provided. The relatively high retention rates (66% of military personnel with AF diagnoses and a history of AC met military retention standards) could be explained by (1) short-term AC utilisation for AF ablations or cardioversions, (2) low AF-related comorbidities in this population with low stroke risk of whom most would not be candidates for long-term AC and (3) this group of servicemembers having low risk military occupations that are amenable to AC. Furthermore, one could also postulate that the identified personnel prescribed AC represent servicemembers who required active management in the form of cardioversion, catheter ablation or an elevated stroke risk. This is a clinical management profile contrast relative to an identified servicemember with AF who has no history of AC and presumably required less intensive management during the study period.

The limitations of this study are anchored on the retrospective study design and unavailable information regarding the duration of systemic AC utilisation. Our study cohort is limited in racial and gender diversity. Further, our study was not designed to assess for medication compliance and long-term prescription rates in
those patients with elevated stroke risks requiring chronic AC. Despite these limitations, we believe our study pres-
ents novel information that is valuable to providers who could be faced with having to care for servicemen
with AF or government organisations tracking the care of this mission critical population.

In conclusion, young AD military personnel with low stroke and bleeding risks are commonly not prescribed AC. DOAC prescription therapy has more recently increased over warfarin, and a history of AC utilisation does not independently influence military deployment or retention rates.

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Contributors The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. ANK, JMS, and KNVB conceived the idea for the study and drafted the protocol. ANK, ASW, AY, and JMS completed data collection. Data analysis was completed by ANK, JMS, and KNVB. ANK and ASW composed the initial manuscript draft, however, all authors provided critical feedback and contributed to the final manuscript. KNVB supervised the study and is the guarantor of the manuscript.

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Data availability statement Data are available on reasonable request. The full dataset is available from the corresponding author (kelvin.n.bush@mail.mil) on request. Participant consent for data sharing was not obtained but the presented data are anonymised and risk of identification is low.

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REFERENCES

1. Nesheiwat Z, Goyal A, Rhythm JM, A Fib StatPears. 2019; 10, 1–7, https://www.ncbi.nlm.nih.gov/books/NBK526072/
2. Nanda A, Kabra R. Racial differences in atrial fibrillation epidemiology, management, and outcomes. Curr Treat Options Cardiovasc Med 2019;21:1–11 https://link.springer.com/article/10.1007/s11939-019-00104-7
3. Crump C, Sundquist J, Winkleby MA, et al. Height, weight, and aerobic fitness level in relation to the risk of atrial fibrillation. Am J Epidemiol 2018;187:417–26 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6075081/
4. Norberg J, Bäckström S, Jansson JH. Estimating the prevalence of atrial fibrillation in a general population using validated electronic health data. Clin Epidemiol 2013;2013:475–81.
5. Staerk L, Shiner JA, Ko D, et al. Atrial fibrillation: epidemiology, pathophysiology, and clinical outcomes. Circ Res 2017;120:1501–17 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5500874/
6. Dod instruction 6130.03 medical standards for appointment, Enlistment or Induction Into The Military Services20181118
7. U.S. Air Force. Air force instruction 48-123: medical examinations and standards. Washington, DC: US government printing office, 2013;24–50.
8. Fuster V, Rydén LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: Executive summary. A report of the American College of Cardiology/American heart association Task force on practice guidelines and the European Society of cardiology Committee for practice guidelines and policy conferences (Committee to develop guidelines for the management of patients with atrial fibrillation): developed in collaboration with the North American Society of pacing and electrophysiology. J Am Coll Cardiol 2001;38:1231–66 https://www.sciencedirect.com/science/article/pii/S073510970101587X?via%3Dihub
9 . Fuster V, et al, European Heart Rhythm Association, Heart Rhythm Society. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation—executive summary; a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). J Am Coll Cardiol 2006;48:854–906 https://www.sciencedirect.com/science/article/pii/S073510970601816X?via%3Dihub
10 Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139–51 https://www.nejm.org/doi/full/10.1056/NEJMoa0905654?url=ver-398.88-2003&frr_dar=cr_pub%20200pubmed
11 Barnes GD, Lucas E, Alexander GC, et al. National trends in ambulatory oral anticoagulant use. Am J Med 2015;128:1300–5 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4658248/
12. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014;383:955–62 https://www.thelancet.com/journals/lancet/article/PIIS1470-211X(14)00123-6/fulltext
13. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365:883–91 https://www.nejm.org/doi/full/10.1056/NEJMoa1100938?url=ver-398.88-2003&frr_dar=orcid.crossref.org&rfr_dar=cr_pub%20200pubmed
14. Wann LS, Curtis AB, Ellenbogen KA. ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (update on dabigatran). A report of the American College of cardiology Foundation/American heart association Task force on practice guidelines. Heart Rhythm 2011;2011;3:1–8 https://www.heartrhythmjournal.com/article/S1547-5271(11)00050-6/fulltext
15 Granger CB, Alexander JH, McMurray JvJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011;365:981–92 https://www.nejm.org/doi/full/10.1056/NEJMoa1107039?url=ver-398.88-2003&frr_dar=cr_pub%20200pubmed
16. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American heart association Task force on practice guidelines and the heart rhythm society. Circulation 2014;130:e199–267 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4670681/
17. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American heart association Task force on clinical practice guidelines and the heart rhythm society. Circulation 2019;140;104–32 https://www.sciencedirect.com/science/article/abs/pii/S000287031930209X?via%3Dihub
18. Rose AJ, Goldberg R, McNamaras DD, et al. Anticoagulant prescribing for Non-Valvular atrial fibrillation in the Veterans health administration. J Am Heart Assoc 2019;8:e012646 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6758851/
19. Hunter AH, Timperley AC, Reid ANC, et al. A 5-year review of atrial fibrillation in military aircrew. Aviat Space Environ Med 2013;84:1249–54.
20. Hunter AH, Cox AT, D’Arcy J, et al. Atrial fibrillation in the military patient: a review. J R Army Med Corps 2015;161:237–43 https://milcare.health.mil/journals/161/3/237.long
21. Packer DL, Mark DB, Robb RA, et al. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and
cardiac arrest among patients with atrial fibrillation: the CABANA randomized clinical trial. *JAMA* 2019;321:1261–74. / https://www.ncbi.nlm.nih.gov/pmc/articles/

22 Turagam MK, Flaker GC, Velagapudi P, et al. Atrial fibrillation in athletes: pathophysiology, clinical presentation, evaluation and management. *J Atr Fibrillation* 2015;8:1309. / https://www.ncbi.nlm.nih.gov/pmc/articles/

23 Praxbind. *Idarucizumab injection for intravenous use prescribing information*. Ridgefield, Connecticut: Boehringer Ingelheim Pharmaceuticals, Inc, 2015. https://docs.boehringer-ingelheim.com/Prescribing%20Information/Pis/Praxbind/Praxbind.pdf

24 Baker DE. Coagulation factor Xa (recombinant), Inactivated-zhzo (Andexanet alfa). *Hosp Pharm* 2018;53:286–91 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6130111/

25 Marzec LN, Wang J, Shah ND, et al. Influence of Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation. *J Am Coll Cardiol* 2017;69:2475–84 https://www.sciencedirect.com/science/article/pii/S0735109717367165?via%3Dihub

26 Arango T, Schmidt MS. “Last Convoy of American Troops Leaves Iraq,” New York Times. 2011, Available: https://www.nytimes.com/2011/12/19/world/middleeast/last-convoy-of-american-troops-leaves-iraq.html