PICO Search Assignment Worksheet **Name** Rachel Freundlich

Brief description of patient problem/setting:
67 y/o F presented to the Emergency Department with complaints of URI symptoms. While auscultating the patient's heart during my physical exam, I learned that the patient had atrial fibrillation. I questioned the patient whether she took any medications for her atrial fibrillation (AF) and she informed me that she takes Rivaroxaban. She noted that she did not have any history of valve repair. At the end of the interview, she let me know that her friend was taking Warfarin for AF and she was wondering why she was taking Rivaroxaban as opposed to Warfarin.

Search Question:
For patients with nonvalvular AF that are treated with anticoagulation, are Direct Oral Anticoagulants associated with fewer complications such as bleeding and occurrence of ischemic stroke compared to Warfarin?

Question Type: What kind of question is this?

☐Prevalence ☐Screening ☐Diagnosis
☐Prognosis ☒Treatment ☐Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)? **Please explain your choices.**

- If meta-analysis and systematic review are not available, I would use randomized controlled trials because they are high quality experiments which allow for control groups to be compared to the group receiving the treatment or medication of interest. It also reduces bias which makes it a good study to use. One group of patients with atrial fibrillation would be treated with Warfarin while the other group would receive treatment with a DOAC.
- A cohort study can also be used as it looks at the outcomes of two groups that received different treatment / interventions - in this case DOACs compared to Warfarin.

PICO search terms:

P	**I**	**C**	**O**
Patients with nonvalvular afib	DOAC	Warfarin	Complications
Nonvalvular Atrial fibrillation	Rivaroxaban	Vitamin K antagonist	Bleeding
Patients with nonvalvular Atrial fibrillation	Dabigatran	Coumadin	Thrombosis
Nonvalv afib	Apixaban		Clot
Nonvalvular afib	Eliquis		Emboli
	Xarelto		Ischemic stroke
	Pradaxa		Mortality
	NOAC		

	Direct Oral Anticoagulant		

Search tools and strategy used:

Results found:

PubMed:

- Warfarin for nonvalvular Afib (Best Match) – 2,246
- Warfarin for nonvalvular Afib (Best Match, 5 years publication) – 603
- Warfarin for nonvalvular Afib (Best Match, 5 years publication, Systematic Review) – 39

Google Scholar:

- DOAC for nonvalv Afib (since 2024, sort by relevance) – 9
- DOAC for nonvalvular Afib (Any time, sort by relevance) – 6,500
- DOAC for nonvalvular Afib (since 2024, sort by relevance) – 421

ScienceDirect:

- Nonvalvular Afib and Warfarin (any time, best match) – 96
- Nonvalvular Afib and Warfarin (since 2022, best match) – 21

- When I was looking for articles I was most interested in articles that asked the same question that I wanted to answer with my mini CAT. I used search terms that I thought would generate appropriate results and I then added search filters to narrow down the articles that populated. For the search results on Google Scholar I focused on skimming the titles as a significant number of articles populated even after I added filters. I found it interesting that so many articles appeared that were published within the year and therefore I chose to read through the titles. For the other databases, I read through the article titles, years the articles were published, and the location of the study. I would scan the abstract to ensure that the article had similar study goals as my mini CAT. Lastly, I would read the article in its entirety to confirm that I wanted to include the article in my mini CAT. I prioritized articles that have a high level of evidence such as Meta Analyses and Systematic Reviews.

Results found:

Title: Real-world evidence comparing oral anticoagulants in non-valvular atrial fibrillation: a systematic review and network meta-analysis
Citation: Deitelzweig S, Bergrath E, di Fusco M, et al. Real-world evidence comparing oral anticoagulants in non-valvular atrial fibrillation: a systematic review and network meta-analysis. *Future Cardiol*. 2022;18(5):393-405. doi:10.2217/fca-2021-0120
Type of article: Systematic Review and Meta Analysis

Abstract:
Aim: To compare real-world effectiveness/safety of non-vitamin K antagonist oral anticoagulants and vitamin K antagonists (VKA) among patients with non-valvular atrial fibrillation.
Materials & Methods: A systematic review of electronic databases yielded 7661 citations published from January 2013 to January 2020. Fifty-five studies were included in Bayesian network meta-analyses of hazard ratios.
Results & Conclusion: In comparison with vitamin K antagonists, apixaban, dabigatran and rivaroxaban were associated with a reduced risk of stroke or systemic embolism, ischemic stroke, intracranial hemorrhage and all-cause mortality. Apixaban, dabigatran and edoxaban, but not rivaroxaban, were associated with a reduced risk of major bleeding. This study confirmed the effectiveness and safety of non-vitamin K antagonist oral anticoagulants for the treatment of non-valvular atrial fibrillation in real- world settings, consistent with clinical trial evidence.

Key points:

- Articles from January 2013-January 2020 were reviewed and assessed to be qualified for this systematic review and meta analysis
- Primary outcomes such as stroke, bleeding and systemic embolism were analyzed
- 143 research articles were included in this review
- NOACs were all found to be associated with a reduced risk of stroke or systemic embolism compared with Vitamin K anticoagulant/
- Apixaban and Dabigatran were found to be associated with reduced risk of bleeding compared to VKA.
- NOACs were found to be associated with reduced risk of intracranial hemorrhage and ischemic stroke compared to VKA
- Rivaroxaban and Edoxaban were associated with lower risks of GI bleeding compared to VKAs

Why I chose it:
I chose this article because it represents a high level of evidence and was published within the last 5 years. I felt that these combined factors made this paper a compelling piece to include in my mini CAT. I appreciated that the study was American and therefore more likely to easily translate into practice as a provider functioning within the US.

Title: Effectiveness and Safety of Non-vitamin K Antagonist Oral Anticoagulants for Atrial Fibrillation and Venous Thromboembolism: A Systematic Review and Meta-analyses

Citation:
Almutairi AR, Zhou L, Gellad WF, et al. Effectiveness and Safety of Non-vitamin K Antagonist Oral Anticoagulants for Atrial Fibrillation and Venous Thromboembolism: A Systematic Review and Meta-analyses. *Clin Ther*. 2017;39(7):1456-1478.e36. doi:10.1016/j.clinthera.2017.05.358

Type of article:
Meta Analysis and Systematic Review

Abstract:
Purpose: The findings from the observational studies comparing the effectiveness and safety of non-vitamin K antagonist oral anticoagulants (NOACs) versus vitamin K antagonists (VKAs) for atrial fibrillation (AF) and venous thromboembolism (VTE) are inconsistent. We conducted separate meta-analyses examining the efficacy/effectiveness and safety of NOACs versus VKAs by disease (AF vs VTE), study design (randomized controlled trials [RCTs] vs observational studies), and NOAC (dabigatran, rivaroxaban, apixaban, and edoxaban).
Methods: The main data sources included PubMed/MEDLINE, EMBASE, Web of Science, CINAHL, and Scopus from January 1, 2005, to February 15, 2016. We searched for Phase III RCTs and observational studies comparing NOACs versus VKAs. The primary outcomes were stroke/systemic embolism (SE) for AF; recurrent VTE/fatal pulmonary embolism (PE) for VTE; and major bleeding for both conditions. Secondary outcomes included stroke and myocardial infarction (MI) for AF, recurrent deep vein thrombosis (DVT)/PE for VTE, and mortality, intracranial hemorrhage (ICH), and gastrointestinal bleeding for both conditions. Pooled hazard ratios (HRs) were reported by using inverse variance-weighted random effects models.
Findings: A total of 13 RCTs and 27 observational studies (AF, n = 32; VTE, n = 8) were included. For AF, dabigatran and VKAs were comparable for stroke/SE risk in 1 RCT (HR, 0.77 [95% CI, 0.57-1.03]) and 6 observational studies (HR, 1.03 [95% CI, 0.83-1.27]). Rivaroxaban had a 20% decreased risk of stroke/SE in 3 RCTs (HR, 0.80 [95% CI, 0.67-0.95]) compared with VKA, but the effect was nonsignificant in 3 observational studies (HR, 0.78 [95% CI, 0.59-1.04]). Apixaban decreased stroke/systemic embolism risk (HR, 0.79 [95% CI, 0.66-0.95]) compared with VKA in 1 RCT, but edoxaban was comparable to VKA (HR, 0.99 [95% CI, 0.77-1.28]) in 1 RCT (no observational studies available for apixaban/edoxaban). Dabigatran, apixaban, and edoxaban decreased the risk of hemorrhagic stroke, mortality, major bleeding, and ICH by 10% to 71% compared with VKAs but not rivaroxaban. For VTE, NOACs and VKAs were comparable for recurrent VTE/fatal PE/DVT/PE risk in 7 RCTs and 1 observational study. The 7 RCTs demonstrated a 32% to 69% decreased risk of major bleeding for dabigatran, rivaroxaban, and apixaban compared with VKAs. No difference was shown in 1 rivaroxaban observational study (HR, 0.77 [95% CI, 0.40-1.49]) and 1 edoxaban RCT (HR, 0.84 [95% CI, 0.59-1.20]). Except for dabigatran, the NOACs had a 61% to 86% decreased risk of ICH and gastrointestinal bleeding.
Implications: Overall, NOACs were comparable or superior to VKAs. Although no observational studies are currently available for apixaban/edoxaban, a few notable inconsistencies exist for dabigatran (ischemic stroke, MI) and rivaroxaban (stroke/SE, major bleeding in VTE) between RCTs and observational studies. Individualizing NOAC/VKA therapy based on benefit/safety profiles and patient characteristics is suggested.

Key points:

- 40 articles were included in this Meta Analysis and Systematic Review conducted between January 2005 - February 2016
- 32 of these articles specifically looked at AF while 8 studies focused on VTE
- Dabigatran and VKAs had similar risks of stroke/systemic embolism while Rivaroxaban had a 20% less chance of causing these adverse effects
- Apixaban had a 21% reduced risk of causing stroke and systemic embolism compared to Warfarin
- Apixaban had a 31% reduced risk of major bleeding compared to VKAs while Dabigatran, Rivaroxaban, and Edoxaban had no significantly reduced risk compared to VKAs
- Dabigatran, Apixaban, Edoxaban had a 10-34% decreased risk of mortality compared to VTEs when taken for AF
- Overall, NOACs were found to be just as effective and safe, if not more, than VKAs when treating patients with AF

Why I chose it:
I chose this article because it is a meta analysis and systematic review which is a high level of evidence. I also chose to include this article because it was published relatively recently (within the last 10 years). This article looks at multiple outcomes associated with the use of NOACs and VKAs and provides extensive statistics regarding the benefits and advantages of the different drug choices. I also appreciated that this Meta Analysis includes 40 studies.

Title: Meta-Analysis Comparing Left Atrial Appendage Occlusion, Direct Oral Anticoagulants, and Warfarin for Nonvalvular Atrial Fibrillation

Citation:
Abdelfattah OM, Sayed A, Munir M, et al. Meta-analysis comparing left atrial appendage occlusion, direct oral anticoagulants, and warfarin for Nonvalvular Atrial Fibrillation. *The American Journal of Cardiology*, Volume 186, 2023, Pages 117-125, ISSN 0002-9149, https://doi.org/10.1016/j.amjcard.2022.08.012.

Type of article:
Meta Analysis

Abstract:
Randomized trials have shown that direct oral anticoagulants (DOACs) are superior to warfarin in patients with nonvalvular atrial fibrillation. However, long-term use of anticoagulation carries an inherent risk of bleeding and nonadherence. Although the use of percutaneous left atrial appendage occlusion (LAAO) has become readily available, its effectiveness relative to oral anticoagulants is still unclear. The present study aimed to compare the outcomes of warfarin, DOACs, and LAAO in patients with atrial fibrillation. Medline, Embase, CENTRAL, and Web of Science were systematically searched through December 2021 for randomized controlled trials comparing warfarin, DOACs, or LAAO, reporting on all-cause mortality, stroke, and clinically relevant bleeding. A random-effects model was used to assess the safety and efficacy outcomes of these 3 treatments relative to each other in a Bayesian network meta-analysis. A total of 40 trials with 95,469 patients (LAAO: 5 trials, 3,032 patients; DOAC: 36 trials, 54,327 patients; warfarin: 37 trials, 38,110 patients) were included. LAAO was associated with significantly lower mortality than warfarin (odds ratio [OR] 0.68; 95% credible interval [CrI] 0.50 to 0.90) and DOACs (OR 0.75, 95% CrI 0.55 to 0.99). LAAO was the best-ranked treatment with respect to mortality reduction (surface under the cumulative ranking curve [SUCRA] 98.77%) and bleeding avoidance (SUCRA 72.26%). Compared with warfarin, DOACs significantly reduced mortality (OR 0.91, 95% CrI 0.85 to 0.97), stroke (OR 0.80, 95% CrI 0.63 to 0.93), and bleeding (OR 0.78, 95% CrI 0.63 to 0.95) and were ranked as the best option at preventing stroke (SUCRA 82.63%). In conclusion, LAAO was associated with lower mortality compared with DOACs, and both LAAO and DOACs significantly reduce mortality compared with warfarin. Future trials are needed to rule out a significant inferiority of LAAO compared with DOACs in terms of stroke and bleeding risks.

Key points:
- This meta analysis included 40 Randomized Controlled Trials and compared the risks and outcomes such as bleeding, stroke and mortality between Warfarin, DOACs and Left Atrial Appendage Occlusion
- DOACs and LAAO were associated with reduced mortality compared to treatment with Warfarin. Most notably, DOACs reduced mortality by 0.7% compared to Warfarin
- LAAO was deemed the best choice of treatment in regards to reducing mortality, while Warfarin was deemed the worst
- DOACs significantly reduced the risk of stroke by 0.6% compared to Warfarin while LAAO did not significantly reduce the risk of stroke compared to Warfarin
- DOACs significantly reduced the risk of bleeding by 2.3% compared to Warfarin

Why I chose it:
I chose this article because it is a Meta Analysis which is the highest level of evidence. This Meta Analysis also included 40 articles which I thought was a significant number of articles. I thought it was interesting that the Meta Analysis compares DOACs to Warfarin, a Vitamin K Antagonist as well as Left Atrial Appendage Occlusion. Although this was not the focus of my mini- CAT I thought it provided a well-rounded approach to the various treatment/prevention options and emphasized the benefits and risks of VKAs and DOACs.

Title: Efficacy and Safety of Direct Oral Anticoagulants Compared to Warfarin in Prevention of Thromboembolic Events Among Elderly Patients with Atrial Fibrillation

Citation:
Kailas SD, Thambuluru SR. Efficacy and Safety of Direct Oral Anticoagulants Compared to Warfarin in Prevention of Thromboembolic Events Among Elderly Patients with Atrial Fibrillation. *Cureus*. 2016;8(10):e836. Published 2016 Oct 18. doi:10.7759/cureus.836

Type of article:
Systematic Review

Abstract:
Direct oral anticoagulants (DOACs), previously also known as novel oral anticoagulants (NOACs), have increased the therapeutic options for stroke prevention in atrial fibrillation (AF). Previous studies comparing their relative efficacy and safety do not address age-related differences, such as comorbidities and physical and social boundaries. This review aimed to summarize and compare the clinical and safety outcomes of DOACs and warfarin for stroke prevention in AF in the elderly population (≥ 65 years). We searched PubMed for randomized controlled trials and meta-analyses that compared DOACs and warfarin in elderly patients with AF. Stroke and systemic embolism (SSE) and major bleeding (MB) were primary outcomes. Secondary outcomes included ischemic stroke, all-cause mortality, intracranial bleeding, and gastrointestinal bleeding. Of 66 studies identified, one randomized control trial (RCT) and one meta-analysis were included. DOACs were at least as effective at reducing the risk of SSE as warfarin. DOACs demonstrated a minimal benefit for ischemic stroke (dabigatran, 110 mg, relative risk (RR) 1.08; edoxaban, 60 mg, RR 1.00; and apixaban, 5 mg, RR 0.99). DOACs associated with decreased risk of MB relative to warfarin include dabigatran, 110 mg; apixaban, 5 mg; and edoxaban, 60 mg (RR 0.80, 0.70, and 0.80, respectively), while dabigatran, 150 mg, and rivaroxaban, 20 mg, increased risk (RR 0.79 - 0.83, respectively). Dabigatran, 110 mg and 150 mg doses, and edoxaban increased the risk of gastrointestinal bleeding (RR 1.04, 1.12, and 1.23, respectively). Lower rates of SSE and intracranial bleeding were seen with DOACs compared to warfarin. Dabigatran, 150 mg, and rivaroxaban, 20 mg, were associated with higher MB in older elderly compared to warfarin. DOACs may be attractive alternatives to warfarin, but further studies are needed to make clinical recommendations.

Key points:

- This Systematic Review included one Randomized Controlled Trial and one Meta Analysis
- The rate of stroke occurrence for patients on Rivaroxaban was 2.29% compared to 2.85% for patients taking Warfarin
- No significant difference was noted in the development of stroke and systemic embolism amongst patients taking Rivaroxaban, Dabigatran, Apixaban or Edoxaban and those taking Warfarin
- No significant decrease in mortality was noted amongst those taking DOACs or those treated with Warfarin
- DOACs reduced the risk of bleeding (3%) compared to Warfarin (22%), however this was not reported to be statistically significant

- Dabigatran and Rivaroxaban were found to have increasing benefit compared to Warfarin in regards to reducing the risk of ischemic stroke in the older population
- However, Dabigatran and Rivaroxaban were found to have increasing risk of bleeding in the older population compared to Warfarin

Why I chose it:
I chose this article because it is a Systematic Review which is a high level of evidence. I appreciated that this Systematic Review specifically was interested in the effects of Warfarin and DOACs in the older population. The majority of patients that I have seen treated with an anticoagulant for AF have been elderly and I was particularly interested in the outcomes associated with these medications in this population.

Summary of the Evidence:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/ studies, cohort definition etc.)	Outcome(s) studied	Key Findings	Limitations and Biases
Deitelzweig S, Bergrath E, di Fusco M, et al. 2022	Systematic review and Meta analysis	A literature search was conducted using MEDLINE, MEDLINE In-Process and Embase. The Risk of Bias in Non-Randomized Studies of Interventions tool was used to evaluate the risk of bias. Inclusion Criteria: • Articles published from January 2013-January 2020 • >1 outcome of interest	The outcomes studied included the following: • Risk of ischemic and hemorrhagic stroke • Incidence of systemic embolism • Incidence of major bleeding Secondary outcomes included • GI bleeding • Intracranial	• NOACs were all found to be associated with a reduced risk of stroke or systemic embolism compared with Vitamin K anticoagulant/ - Apixaban and Dabigatran were found to be associated with reduced risk of bleeding compared to VKA. - NOACs were	• While the articles included in this Systematic Review and Meta analysis were all published in English, they may not have originally been conducted in America. This limits the application of the results to the American population due to differing standards

		studied including ischemic or hemorrhagic stroke, systemic embolism and major bleeding and all cause mortality • >2 of the following were compared: Apixaban, Dabigatran, Edoxaban, Rivaroxaban and VKAs • 7,661 articles resulted following duplicate removal • 879 full-text articles were evaluated for	hemorrhage • All-cause mortality These outcomes were analyzed when Apixaban, Dabigatran, Edoxaban, Rivaroxaban and VKAs were administered.	found to be associated with reduced risk of intracranial hemorrhage and ischemic stroke compared to VKA - Rivaroxaban and Edoxaban were associated with lower risks of GI bleeding compared to VKAs	of care, baseline health, and availability of healthcare and follow up. • Dosing of VKAs vs non-VKAs may have differed in the various studies which may alter research findings. • Warfarin was the VKA studied in the majority of included articles

		inclusion • 143 articles were included in this Systematic review and Meta analysis			
Almutairi AR, Zhou L, Gellad WF, et al. 2017	Systematic Review and Meta Analysis	A literature search was conducted using National Library of Medicine PubMed/MEDLINE, Elsevier EMBASE, Thomson Reuters Web of Science, Science Citation Index Expanded, Social Sciences Citation Index and Arts and Humanities Citation Index, Cumulative Index to Nursing and Allied Health Literature, Ebsco Academic Search Complete, Wiley Cochrane Libraries, Elsevier Scopus, Clinical Trial Registries and ProQuest's Dissertations and Theses Inclusion Criteria:	The primary outcomes studied include the following: • Stroke and/or systemic embolism for anticogaulant use in AF Secondary outcomes included: • Ischemic and hemorrhagic stroke, MI, all-cause mortality for AF This Systematic Review and Meta analysis also looked at the efficacy of NOACs compared to VKAs for VTE. The primary outcomes	• The efficacy of each NOAC compared to VKAs was assessed separately, as well as each outcome of interest. • Dabigatran and VKAs did not have statistically significant differences in risk for stroke and systemic embolism • Rivaroxaban was shown to have a 20% reduced risk of stroke and systemic embolism in RCTs, however the observational studies	• The follow up duration ranged widely amongst different study groups • There is not equal information regarding the different NOACs and therefore the findings for each of the NOACs is based on varying amount of data • Various articles included did not include blinding or adjust for bias which increases the likelihood of bias

		- January 1, 2005 - February 15, 2016 - Phase III Randomized Controlled Trials and Observational studies comparing NOACs (Apixaban, Dabigatran, Edoxaban, Rivaroxaban) and Vitamin K Agonists Exclusion Criteria: - Studies that looked at NOAC use for short-term anticoagulation • 21,869 articles resulted • 56 articles were evaluated for inclusion • 40 articles were included	looked at for this included • Recurrent VTE or fatal PE for VTE	utilized did not show a statistically significant reduction in risk • APixaban had a 21% reduced risk of stroke and systemic embolism in one RCT when compared with warfarin • Edoxaban was not associated with a reduced risk of stroke and systemic embolism compared to Warfarin • Safety outcomes for NOACs and VKAs were comparable	
Abdelfattah OM, Sayed A, Munir M,	Meta analysis	A literature search was conducted using MEDLINE/PubMed,	The primary outcomes studied included:	• DOACs were associated with 0.7% reduced	• Patients included in these studies had various

et al. 2023		EMBASE/Ovid, Web of Science, and the Cochrane Central Register of Controlled Trials Inclusion Criteria: • The final date articles were accepted from was December 29, 2021 • RCTs that looked at incidence of stroke, mortality and bleeding among patients with AF that used DOACs, Warfarin or received Left Atrial Appendage Occlusion (LAAO) Texts Included • 3,703 records results	• Mortality • Stroke • Bleeding Each of these was analyzed in regards to the risks attributed to DOACs, Warfarin and LAAO	risk of mortality compared to Warfarin • DOACs reduced the risk of stroke by 0.6% when compared with Warfarin • In regards to bleeding, DOACs reduced the risk by 2.3% when compared with Warfarin	comorbidities which may have affected outcomes • Length of follow up varied among groups • This study did not differentiate between the various DOACs and therefore does not report on the efficacy and risks associated with each individual DOAC

		• 40 RCTs met inclusion criteria			
Kailas SD, Thambururu SR. 2016	Systematic Review	A literature search was conducted using PubMed Inclusion Criteria: • Articles published from January 2000 through November 2015 were included • Texts Included: • 92 articles resulted • One RCT and one Systematic Meta analysis was included	Primary outcomes: • Stroke • Systemic Embolism • All-cause mortality • Major bleeding These outcomes were assessed for patients < 65 and >75 years old.	RCT: • The rate of stroke and systemic embolism for Rivaroxaban was 2.29% compared to 2.85% for Warfarin • The event rate of intracranial bleeding for Rivaroxaban was 0.66% for Rivaroxaban and 0.83% for Warfarin Systematic Review: • DOACs were not associated with significant reduction in risks of stroke and systemic embolism compared to Warfarin (22% vs 18%) • DOACs were not associated with significantl	• Nonrandomized studies were used in this article which increases the risk of bias • The only Vitamin K agonist observed is Warfarin • Various doses of DOACs were used across the articles studies in the Systematic Review

				y reduced mortality compared to Warfarin • Dabigatran, Edoxaban and Apixaban were associated with reduced risks of bleeding • DOACs were associated with reduced risk of intracranial bleeding compared to warfarin although Rivaroxaban was found to have the least benefit • DOACs were associated with a lower risk of ischemic stroke more significantly in the older population (>75 years) than the younger elderly population (<65 years..	

Conclusions:

Article #1: This Systematic Review and Meta analysis concludes that NOACs are associated with reduced risk of stroke, systemic embolism, intracranial hemorrhage and ischemic stroke when compared to VKAs. Rivaroxaban, however, was not associated with reduced risk of bleeding. The study suggests that NOACs are associated with a better safety profile compared to VKAs and may be the preferred choice. It is important to note however that choosing a NOAC other than Rivaroxaban may be preferred when there is reason to believe a patient is at increased risk of bleeding.
Article #2: The findings of this Systematic Review and Meta analysis suggest that NOACs can be considered equally as effective and perhaps safer when compared to VKAs. While this article looked at the outcomes when used for both AF and VTE, for the purposes of this mini-CAT the findings analyzed focus on the outcomes associated with AF. Dabigatran and Edoxaban were associated with similar risk for stroke and systemic embolism compared to VKAs. Although Rivaroxaban was associated with a 20% reduced risk, the observational studies analyzed for this article did not observe the same results and therefore it is not possible to conclude this finding definitively. Apixaban was associated with a 20% reduced risk compared to Warfarin. These findings suggest that using NOACs to prevent stroke and systemic embolism rather than VKAs is an appropriate and possibly superior drug choice.
Article 3: This study concludes that DOACs yield lower risks of adverse events such as stroke, bleeding and mortality when compared to Warfarin. In regards to bleeding, DOACs were associated with a 2.3% decreased risk compared to Warfarin. DOACs also reduced the risk of stroke when compared to Warfarin by 0.6% as well as reduced the risk of mortality by 0.7%. DOACs were found to be superior to Warfarin across all outcomes studied in this article.
Article 4: This study looked at the associated risk of DOACs compared to Warfarin in the elderly population. Rivaroxaban, a DOAC, was associated with reduced rate of stroke and systemic embolism (2.29%) compared to Warfarin (2.85%) in the RCT analyzed. However, the Systematic Review included in this study did not find a significantly reduced risk. While DOACs were associated with reduced risks of bleeding, it's important to note that not all DOACs are associated with equal safety outcomes. The article also looked at the outcomes associated with different age groups - those <65 and those >75. The older elderly group seem to be the most likely to benefit from DOACs as they were associated with a lower risk of ischemic stroke compared to the younger elderly population.

Overarching Conclusions: Research suggests that DOACs are associated with an equal if not superior safety profile compared to VKAs. Risks such as bleeding, stroke and systemic embolism, and mortality were evaluated and appear to be a viable replacement for patients with AF in need of anticoagulation.

Weight of Evidence:

Article #1: I ranked this article as #1. This article is a Systematic Review and Meta analysis which is the highest level of evidence. This article was published in 2022 which is within the last 5 years. This makes the article more relevant to current practice. This article specifically looks at the efficacy of Vitamin K agonists in comparison with non-Vitamin K agonists in patients with nonvaluvular AF. This is consistent with my search question and answers it directly.
Article #2: I ranked this article as #2. This article is also a Systematic Review and Meta analysis which is the highest level of evidence. This article was published within the last 10 years and includes a substantial number of articles which are analyzed. I chose this article as #2 because it directly addresses my question. I appreciated that it compared each DOAC individually with Vitamin K agonists, which provided even more specific information that VKAs compared with DOACs in general.
Article #3: I ranked this article as #4. This article is a Meta analysis which is the highest level of evidence. I appreciate that this article was published within the last 5 years which makes it relevant. While this article did directly analyze my research question, it also looked at the efficacy of LAAO which was not part of my question. However, it did add an interesting element to my research.

Article #4: I ranked this article as #3. This article is a Systematic Review, although it does not include as many articles as the other Systematic Reviews included in this mini-CAT. One of the most significant differentiating factors between this article and others is that this review specifically looked at the effects of VKAs compared to DOACs among the elderly. As the majority of patients that are treated with anticoagulation for AF are >65, I thought that this was an appropriate study to include.

Magnitude of Effects:
All of the articles included conclude with a similar recommendation. The research analyzed in this mini-CAT reports that DOACs are similar in efficacy to Vitamin K agonists, while some may even have additional benefits such as reducing the risk of mortality and stroke. Therefore, these articles have a high magnitude of effect as they can be translated into clinical practice.

Clinical Bottom Line:
The articles included show that when analyzing the safety profiles of DOACs and Vitamin K agonists when treating nonvalvular AF, DOACs are a comparable and possibly more desired treatment option. The first article concludes that DOACs were found to be associated with reduced risk of stroke and systemic embolism, intracranial bleeding and GI hemorrhage compared to Vitamin K agonists. The second article differentiated between the various DOACs and compared them to VKAs. While Dabigatran was found to have similar risks of stroke and systemic embolism, both Rivaroxaban and Apixaban were shown to reduce the risk of these adverse events (reducing the risk by 20% and 21% respectively). Apixaban was also found to reduce the risk of major bleeding by 31% compared to VKAs. The third article concluded that DOACs reduced mortality and stroke by 0.7% and 0.6% respectively compared to VKAs. Each of the articles presented represent a high level of evidence and have been published within the last 10 years. Both of these factors represent strengths of the articles chosen. While the third article looked at an additional treatment option, the main question was directly addressed and therefore the appropriate results were able to be extracted from the article. The fourth article aimed to answer the research question for a specific age group which strengthened its ability to be applied to clinical practice as this age group is most commonly treated with anticoagulants for AF. Therefore, after analyzing the research presented, I would be inclined to suggest that patients requiring anticoagulation for nonvalvular AF should be treated with a DOAC rather than VKA.

Referring back to the original clinical scenario presented, the research presented concludes that the woman in the vignette was appropriately prescribed Rivaroxaban, a DOAC. Although continued research is indicated to further ascertain the benefits of each individual DOAC, I would prescribe a DOAC rather than a VKA for a patient presenting with nonvalvular AF.