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Derleme Makalesi / Review

Antikoagülasyon Tedavisinde Sosyal Belirleyicilerin Kanama Sonuçları Üzerindeki Etkisinin İncelenmesi: Kapsam İncelemesi

Examining The Influence of Social Determinants on Bleeding Outcomes in Anticoagulation Therapy: A Scoping Review

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ÖZET

Giriş: Oral antikoagülasyon (OAK) kontrolü, istenmeyen kanama olasılığını azaltır ve hastanın kanının pıhtılaşmasını geciktirir. Sosyal belirleyiciler, örneğin sosyoekonomik durum, cinsiyet, yaş, ırk/etnik köken, alkol kullanımı gibi faktörler ile oral antikoagülanların reçetelenme alışkanlıkları ve kanama olaylarında farklılıklar gözlemlenmiştir.

Amaç: Çalışmanın amacı, oral antikoagülan kullanan hastalarda sosyal belirleyicilerin kanama üzerindeki etkisini incelemektir.

Sonuç: Düşük sosyoekonomik durum, bu hastalar arasında kanamaya bağlı ölümlerde önemli bir belirleyicidir. Düşük gelirli bireylerin ve siyahi hastaların oral antikoagülan tedaviye erişme olasılığı daha düşüktür. İleri yaş, antikoagülan tedavide kanama riskinin önemli bir sosyal belirleyicisidir ve yaş ilerledikçe kanama riski artar. Cinsiyet değişkeninin, Uluslararası Normalleştirilmiş Oran (INR) kontrolü ve kanama riski açısından anlamlı bir etkisi olmamıştır. Genel alkol kullanımı kanama riskini belirlemede sosyal bir belirleyici olarak görülmemektedir. Ancak kanama riskinin belirlenmesinde hastaların ağır alkol kullanımı ve sosyoekonomik durumları değerlendirilmelidir.

Klinik çıkarımlar: Etnik köken ve sosyoekonomik durum, sağlık profesyonelleri tarafından hasta bakımının yönetilmesinde ve antikoagülan tedavi kullanan hastalarda kanama riskinin değerlendirilmesinde önemli parametrelerdir. Hemşireler, hasta öyküsünü dikkatlice değerlendirmeli ve bu hastalarda daha sık INR izlemesi yapılmalıdır. Literatür, özellikle farklı ırk ve alkol gibi sosyal belirleyicileri olan hastalar arasında oral antikoagülan tedavisindeki eşitsizlikleri ele almak için daha fazla araştırma yapılması gerektiğini belirtmektedir.

Anahtar kelimeler: Antikoagülan, Kanama, Cinsiyet, Tromboz, Etnisite

ABSTRACT

Background: Oral anticoagulation (OAC) control reduces the likelihood of unwanted bleeding and delays the patient's blood clotting. Differences in prescription patterns and bleeding events of oral anticoagulants have already been observed concerning social determinants, such as socioeconomic status, gender, age, race/ethnicity, alcohol use, etc.

Objective: The objective of the study is to examine the effect of social determinants on bleeding in patients using oral anticoagulants.

Conclusions: Low socioeconomic status is a significant determinant in bleeding-related deaths among these patients. Low-income individuals and black patients are less likely to access oral anticoagulant therapy. Older age is a crucial social determinant of bleeding with anticoagulant therapy, and the bleeding risk rises with advancing age. Although the gender variable did not have a significant effect in terms of International Normalized Ratio (INR) control and bleeding risk. General alcohol use is not a social determinant in determining the risk of bleeding. However, the heavy alcohol use and socioeconomic status of the patients should be assessed in determining the risk of bleeding.

Clinical implications: Ethnicity and socioeconomic status are important parameters in the management of patient care by healthcare professionals and in evaluating the risk of bleeding in patients using anticoagulant therapy. Patient history should be carefully evaluated by nurses and more frequent INR monitoring should be done in these patients. The literature indicates that more research is needed to understand underlying factors and develop strategies to address disparities in the use of oral anticoagulant therapy among patients of especially different racial and alcohol social determinants.

Keywords: Anticoagulant, Bleeding, Gender, Thrombosis, Ethnicity

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INTRODUCTION

The risk of thrombosis increases due to common heart diseases and anticoagulant treatment is applied to the patients. These drugs choice for preventing stroke in people with atrial fibrillation, valve replacement, and bypass. Oral anticoagulation (OAC) control reduces the likelihood of unwanted bleeding and delays the patient's blood clotting. OAC can be grouped into two classes of oral anticoagulants to prevent a thromboembolic event: vitamin K antagonists (VKA-coumadin, warfarin) and direct oral anticoagulants (DOAC- dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban or the novel oral anticoagulants (NOAC). VKAs require frequent monitoring, are effective in preventing strokes, increase the risk of bleeding, can be used in people with any degree of renal impairment, and are less expensive than DOACs. DOACs do not require frequent monitoring, are effective in preventing strokes, and also increase the risk of bleeding, particularly intracranial hemorrhage, although to a lesser extent than VKAs.

Despite the importance of these therapies, approximately half of the patients are unaware of critical aspects such as bleeding risks, drug/food interactions, and their INR values, which heightens the risk of adverse outcomes (İlçe et al., 2022). The cost and follow-up of a particular treatment may affect patient prescription differently depending on certain factors. Prescribing may be influenced by sociodemographic and economic factors unrelated to drug eligibility criteria (Maguire et al., 2007). There are studies examining significant disparities in access to new anticoagulant therapies and disparities in prescribing oral anticoagulants among socioeconomically disadvantaged patients (Essien et al., 2020; Nathan et al., 2019).

Differences in prescription patterns of DOACs have been observed concerning social determinants, such as socioeconomic status (SES), gender, age, race/ethnicity, and alcohol use. One of the most significant adverse effects of anticoagulants are bleeding and bleeding-related death. However, there is currently insufficient information about the impact of social determinants on oral anticoagulant prescribing and their effect on bleeding (Essien et al., 2020).

This scoping review undertakes a comprehensive examination of how social determinants impact bleeding incidents as a result of anticoagulation therapy. Its objective is to examine deeper into the interplay between various social determinants and the bleeding outcomes experienced by individuals undergoing anticoagulation treatment. Considering the rapid increase in oral anticoagulant use in healthcare services due to heart diseases, it is crucial to examine these social determinants to reduce bleeding and bleeding-related deaths, thereby promoting greater equality in healthcare services.

The objective of the study is to examine the effect of social determinants on bleeding in patients using oral anticoagulants and to emphasize the need for a multi-faceted approach that includes not only traditional parameters such as INR and Time in Therapeutic Range (TTR) but also an examination of social determinants impacting the patient's response to anticoagulant therapy.

Design

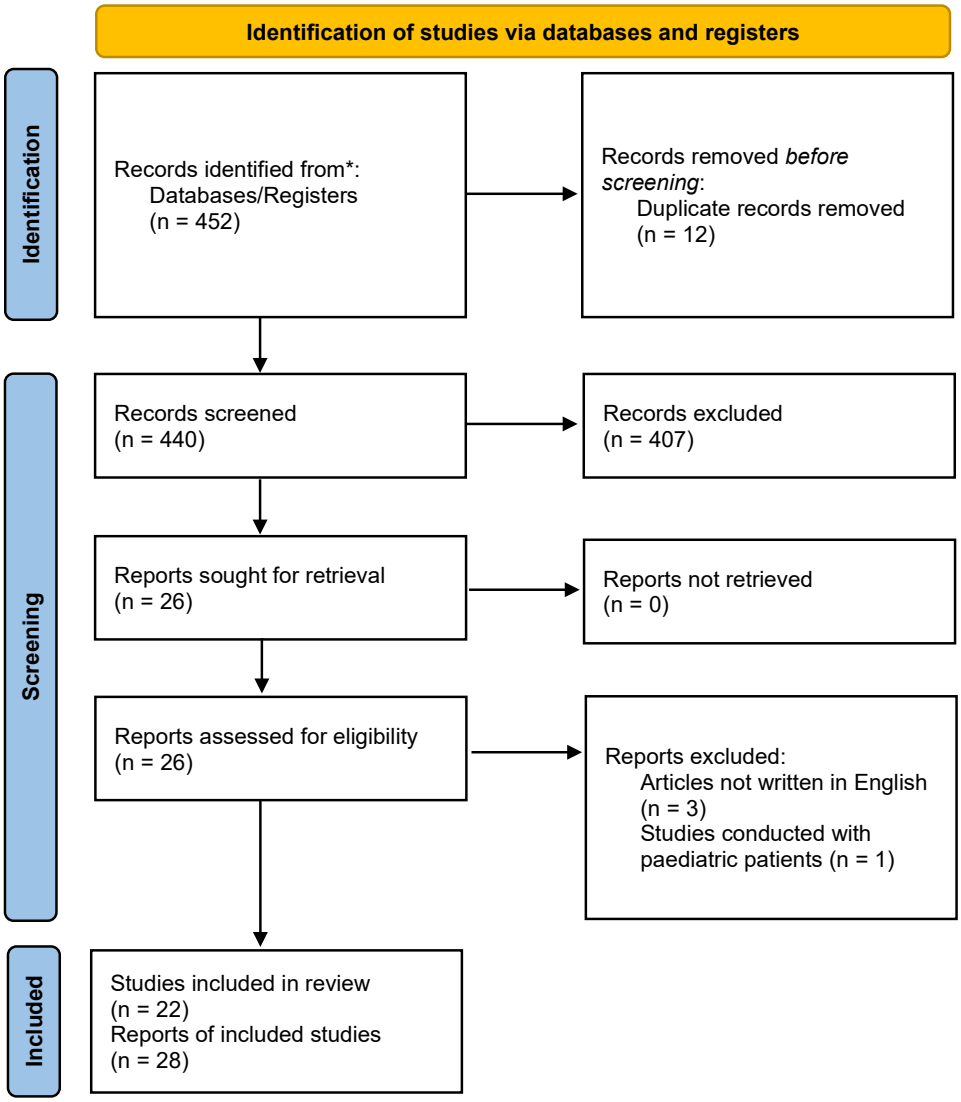
A scoping review was conducted according to Arksey & O'Malley's (2005)(Arksey et al., 2007) methodological framework and further refined by the Joanna Briggs Institute (Peters et al., 2020), to examine existing knowledge about social determinants affecting bleeding in patients using oral anticoagulants obtain a broad and comprehensive view and summarise the evidence and identify gaps in the literature. Preferred Reporting Items for Analyses extension for Scoping Reviews (PRISMA-ScR) were used (Figure 1) to ensure reporting standards (Tricco et al., 2018).

Research questions

We sought to answer the following questions: What can be found in the international literature? Does SES

affect bleeding in patients using anticoagulants? Does SES affect the risk of bleeding-related death in patients using anticoagulants? Does gender affect bleeding in patients using anticoagulants? Does age affect bleeding in patients using anticoagulants? Does race/ethnicity affect bleeding in patients using anticoagulants? Does alcohol affect bleeding in patients using anticoagulants?

Figure 1. PRISMA 2020 flow diagram for systematic reviews



Search methods

The authors designed the review protocol and agreed on its details. A librarian assisted with the definition of the search strategy and database identification. The search was performed in Pubmed, CINAHL, Web of Science, Sciences Direct, Scopus, and Cochrane databases for January 2007-June 2024. The terms used were “anticoagulant”, “social or social determinants: socioeconomic/income/age/race/ethnicity/gender/ sex/tobacco/alcohol/marriedstatus”, “bleeding/hemorrhage” and “VKA/DOAC/NOAC” with their respective synonyms, combined with the Boolean operators “AND” and “OR”. To improve sensitivity and avoid omission of relevant articles, MeSH terms and keywords identified in the existing literature were used. Studies were selected based on the application of the inclusion and exclusion criteria presented in Table 1.

Table 1. Selection criteria

Inclusion criteria	Exclusion criteria
• Adults over 18 years old • Studies in patients with cardiological problems (valve replacement, bypass surgery, Venous Thromboembolism, rhythm disorders (AF, VF,..) who reported bleeding using OAC/ NOAC) • Studies in patients with cerebrovascular disease SVD who reported bleeding using OAC/ NOAC • Clinical/ cohort studies • Qualitative, quantitative, mixed, and grey literature studies • Studies covering the social determinants/factors (social and economic status, alcohol use, age, gender, education, ethnicity, social relations, profession…) in the above headings. • English language studies • 2007-2024 period	• Pediatric studies • In vivo studies • Studies carried out in a laboratory environment • Articles written in languages other than English

Data extraction

Results were collated using reference software (Mendeley Reference Manager 1.19.8) and duplicates were removed. Titles and abstracts were screened for eligibility independently by all team members. The second screening involved a full-text read conducted independently by all team members. Data extraction was conducted by reviewing by all team members. Data extracted were author, year, study type, country, objectives, methodology, sample, social determinants, and main results The extracted data was recorded and summarised using Microsoft Excel and was reviewed by all team members.

Main results of the studies

The results of the comprehensive analysis of the identified studies are presented below. Table 2 shows a representation of the main results of this study.

Table 2. Data extraction table

Author, year, country	Objectives	Methodology	Sample	Social determinant	Main results
Vitry et al. (Vitry et al., 2007) USA	The study aimed to quantify the excess risk of bleeding-related hospitalization when warfarin was co-dispensed with potentially interacting medicines.	Retrospective cohort study	Patients 65 years and older. n= 17,661	Age	The overall incidence rate was lower in the 65–74 age group than in those aged 85yrs or older.
Rohla et.al. (Rohla et al., 2019) Austria, France, Germany, Italy, Spain, Switzerland, and the UK	To determine factors associated with thromboembolic and bleeding events (gastrointestinal bleeding, intracerebral hemorrhage, and other life-threatening bleeding) in two contemporary cohorts of anticoagulated patients with atrial fibrillation (AF), treated with either vitamin K antagonists (VKA) or non-VKA oral anticoagulants (NOACs).	Prospective, multicentre observational study	Patients 18 years and older. n= 7243	Age	A substantial number of thromboembolic and major bleeding events in anticoagulated patients with AF can be attributed to a few modifiable risk factors. For each single point (age ≥ 75 years) decrease on an adjusted modifiable bleeding risk scale, we observed an approximately 30% reduction in both major bleeding and thromboembolic events.
Büchele et al. (Büchele et al., 2020) Germany	The aim of this study was to estimate the incremental risk of a traumatic intracranial haemorrhages associated with OAC in older people.	A cohort study	Patients 65 years and older. n= 1,089,004	Age	Older people exposed to oral anticoagulants containing phenprocoumon, as warfarin, have an almost three times higher risk to sustain traumatic intracranial hemorrhage compared to controls.
Šinigoj et al. (Šinigoj et al., 2020) Slovenia	The aim of this study was to evaluate the safety of direct oral anticoagulants in the oldest old patients with atrial fibrillation and assess the impact of age on major bleeding events.	Prospective clinical study	Patients 65 years and older. n= 2260	Age	The oldest old patients have the highest risk of major bleeding, which is further increased with a patient's history of bleeding.
Erquicia et al. (Domínguez-Erquicia et al., 2021) Spain	To contribute to increasing the knowledge regarding anticoagulation (with vitamin K antagonists (VKAs) and direct oral anticoagulants (DOAC)) in elderly patients by analyzing the incidence, predictors and prognosis of major bleeding in anticoagulated nonagenarian patients with nonvalvular atrial fibrillation (NVAF).	Prospective cohort study	Patients 90 years and older. n= 1216 patient	Age	The results we did not find significant differences regarding the incidence rate of major bleeding between patients treated with VKAs and those treated with DOAC. We found an association between the male sex and the risk of major bleeding in DOAC group.

Author, year, country	Objectives	Methodology	Sample	Social determinant	Main results
Herrera et al. (Adrianzen-Herrera et al., 2024) USA	To assess the incidence of severe (hospitalized) bleeding due to thromboprophylaxis in patients undergoing treatment for multiple myeloma and to identify clinical risk factors for bleeding in this group.	A cohort study	Patients aged 18 to 99 years old. n= 6656	Age	Older age was significantly associated with a higher risk of bleeding, with a hazard ratio of 1.38 per 10-year increase.
Kefale et al. (Kefale et al., 2023) Australia	This study aimed to evaluate the prescription rate of OACs and identify factors associated with their use in patients with AF and a low risk of stroke. Additionally, we investigated bleeding events and their risk factors.	Retrospective cohort study	Patients 18 years and older. n= 61,361	Age, Gender and Socioeconomic status	Age: Increasing age was associated with a higher likelihood of OAC use and an increased risk of bleeding. Gender: Female patients had lower odds of receiving OAC despite a higher stroke risk compared to males. Socioeconomic Status: Better SES was linked to lower odds of receiving OAC.
Nilsson et al. (Nilsson et al., 2014) Netherlands	The objective is to evaluate the sex-dependent effectiveness of (Patient-self-management) PSM of oral anticoagulant therapy in everyday clinical practice.	Case study.	Patients who could self-manage their OAT, as shown by passing the final exam. n= 2068	Gender	Importantly, death, bleeding and thromboembolism were not significantly different between females and males.
Božić et al. (Bozic et al., 2021) Croatia	To investigate the demographic characteristics (sex, age), comorbidities and mortality rate of patients with gastrointestinal bleeding related to anticoagulant (warfarin and NOACs including (apixaban, rivaroxaban, and dabigatran) or antiplatelet therapy.	Retrospective cohort study	Patients 65 years and older. n= 1367	Gender and age	Older age was the main predictors of death, regardless of the drug type (anticoagulant and antiplatelet therapy) or bleeding localization or cause. There was no significant difference in overall mortality according to sex.
Carnicelli et al. (Carnicelli et al., 2022) USA	To determine the effects of age and sex variables on standard-dose DOAC, lower-dose DOAC and warfarin treatments.	Meta-Analyse *(Meta-Analyses of Randomized Clinical Trials)*	Patients 18 years and older. n= 71,683	Gender and age	Younger patients showed a greater benefit from standard-dose DOAC versus warfarin for major bleeding with each 10-year increase in age. No significant interaction for major bleeding by sex was observed for either treatment strategy.

Author, year, country	Objectives	Methodology	Sample	Social determinant	Main results
Khatib, R. et al. (Khatib et al., 2022) USA	Evaluate the impact of between social determinants of health (SDOH) on anticoagulant prescriptions in patients with atrial fibrillation (DOAC).	Systemic review and meta-analysis.	They included 13 studies; 11 were meta-analyzed, covering 9 of the 14 SDOH.	Gender	It has been observed that there exists a disparity in the level of acceptance towards the utilization of anticoagulants between the two genders. There are preconceived concerns about the risk of bleeding in women.
Matsumura et al. (Matsumura et al., 2022) Japan	To investigate sex difference in patient characteristics and clinical outcomes of the (non-valvular atrial fibrillation) NVAF patients treated with DOAC.	Prospective observational study	Women n: 806 Men n= 1410	Gender	Patients treated with DOAC showed that Japanese women experienced comparable bleeding events as compared to men despite the higher bleeding risk estimates.
Essien et al. (Essien et al., 2020) USA	To assess racial/ethnic differences in the use of oral anticoagulants, particularly DOACs, in patients with atrial fibrillation.	Cohort study	Patients 21 years and older. n= 12,417	Race/Ethnicity	Black patients and Hispanic patients were more likely to have a high bleeding risk.
Tedla et al. (Tedla et al., 2020) USA	Our primary aim was to examine racial disparity in the prescription of any OAC in general and NOACs in particular in newly diagnosed AF patients who visited a health care setting. Our secondary aim was to investigate whether race modifies the association between prescription of NOACs (as compared to VKA) and incidence of stroke (a composite of ischemic and hemorrhagic stroke and cerebral embolism) and major bleeding in newly diagnosed AF patients who had at least two visits to a health care setting.	Retrospective cohort study	Patients 30 to 80 years old. n= 11,575	Race/Ethnicity	When stratified by race, crude rates of bleeding were also higher among patients on VKAs than those on NOACs in both whites and blacks. Use of NOACs as compared to VKA significantly lowered the risk of bleeding independent of other risk factors only in whites.
Essien et al. (Essien et al., 2022) USA	To compare OAC use at discharge among different races and ethnicities in the Get With The Guidelines-Atrial Fibrillation registry, and explore trends and postdischarge outcomes like ischemic stroke, major bleeding, and mortality.	Cohort study	Patients 65 years and older. n= 69,553	Race/Ethnicity	Overall, the 1-year cumulative incidence of major bleeding was found to be higher in Black and Hispanic patients compared to White patients. Black patients had a significantly higher bleeding risk than White patients, especially when discharged without any OAC or while taking warfarin or DOAC.

Author, year, country	Objectives	Methodology	Sample	Social determinant	Main results
Abdullah Haddad et al.(Haddad et al., 2021) USA	The objective of the study was to investigate underrepresentation and racial disparities in left atrial appendage occlusion (LAAO) management among black patients.	Comparative Study	Patients 65 years and older. n= 109	Race/Ethnicity and Socioeconomic status	White patients were nearly five times more likely to be discharged on OAC versus dual antiplatelet therapy compared to black patients. Among patients with a history of gastrointestinal bleeding, OAC was more frequently used among White individuals than black individuals. Although there was a substantial disparity in income between White and black individuals, this difference in income was not found to be a significant contributing factor to the association between race and the prescribing of OAC therapy at discharge.
Tse et al. (Tse et al., 2021) New Zealand	The purpose of this study was to determine whether ethnicity and/or socioeconomic status are also independent risk factors for a major bleed among people with a history of cardiovascular disease (CVD) or AF. (Warfarin therapy).	Prospective cohort study	Men aged 45 years or older, women aged 55 years or older. n= 488,107	Ethnicity and socioeconomic status	An increased risk of intracranial bleeds was observed among Chinese and Other Asian people and, in the CVD and no CVD/AF subgroups, among Indian people. Increasing socioeconomic deprivation was also associated with increased risk of a major bleed in all three subgroups, respectively, for each increase in socioeconomic deprivation quintile.
Cressman et al. (Cressman et al., 2015) UK	To examined the extent to which socioeconomic status influences the risk of hemorrhage in older individuals newly commencing warfarin therapy for atrial fibrillation.	Prospective cohort study	Patients 66 years and older. n= 166,742	Socioeconomic status	Among older individuals receiving warfarin therapy for atrial fibrillation, lower socioeconomic status is a risk factor for hemorrhage (GİS) and hemorrhage-related mortality. Socioeconomic status was not associated with intracranial hemorrhage.
Ravvaz et al. (Ravvaz et al., 2021) USA	To evaluate the impact of socioeconomic status (SES), measured by ADI, on patients' risk of stroke and bleeding in newly diagnosed AF patients started on warfarin therapy.	Retrospective cohort study	Patients 18 years and older. n= 7274	Socioeconomic status	Regardless of age, patients in low SES areas are more likely to experience bleeding on warfarin, though age-specific results vary for bleeding and efficacy. Patients in very low socioeconomic status areas required a significantly higher number of INR checks than patients in higher SES areas.

Author, year, country	Objectives	Methodology	Sample	Social determinant	Main results
Dalen et al. (Dalén et al., 2022) Sweden	To examine sought to investigate the impact of patients' socioeconomic status on the risk of bleeding after mechanical aortic valve replacement (AVR). (Warfarin therapy)	Retrospective cohort study	Patients 18 to 70 years old. n= 5974	Socioeconomic status	The socioeconomic status and risk of bleeding in that the risk of bleeding decreased with increasing income level. The risk of death from intracranial hemorrhage was five times higher in the lowest income quartile than the age- and sex-matched general Swedish population.
Roth, J. A. et al. (Roth et al., 2018) USA	Alcohol misuse and the risk of major bleeding in a community sample of patients using warfarin.	Case and control study	Patients 18 years and older. n= 570	Alcohol use	Among 265 cases and 305 controls, AUDIT-C scores indicative of moderate/severe alcohol misuse and heavy episodic drinking were associated with increased risk of major bleeding.
Reddiess et al. (Reddiess et al., 2021) Switzerland	The main aim of the current study was to investigate the associations of regular alcohol intake with incident stroke or systemic embolism in patients with established AF oral anticoagulants.	Prospective cohort studies.	Patients 65 years and older. n= 3852	Alcohol use	There was no significant association between alcohol consumption and bleeding.

Age

Age was evaluated in 7 studies investigating the relationship between age and the incidence of bleeding in patients treated with oral anticoagulants. Bozik et al. (2021) found that older age was a significant predictor of death, regardless of the type of drug used, the location of bleeding, or the cause of bleeding (Bozic et al., 2021). Similarly, Carnicelli et al. (2022) found that the incidence of major bleeding increased with increasing age in a group of patients treated with lower doses of DOACs compared to warfarin (Carnicelli et al., 2022).

Rohla et al. (2019) found that age was associated with a reduction in major bleeding of approximately 30% (Rohla et al., 2019). Büchele et al. (2020) found that older people exposed to oral anticoagulants containing phenprocoumon, such as warfarin, had an almost three times higher risk of sustaining a traumatic intracranial bleeding compared to controls (Büchele et al., 2020). Kefale et al. (2023) in their study also revealed that increasing age was linked to a higher likelihood of receiving OACs. Moreover, older age was associated with an increased risk of bleeding (Kefale et al., 2023).

Sinigoj et al. (2020) found that the oldest old patients (≥ 85 years) had the highest risk of any major bleeding, and intracranial bleeding compared to the group of patients aged 65–74 years, even though the majority of them were treated with reduced doses of DOACs. Significant predictors for major bleeding were age ≥ 85 years and a history of bleeding (Šinigoj et al., 2020). Similarly, a study by Adrianzen-Herrera (2024) found that increasing age is a significant clinical risk factor for bleeding, with the risk increasing by a factor of 1.38 for every 10-year increment in age (Adrianzen-Herrera et al., 2024).

These studies collectively suggest that older age is a significant predictor of bleeding in patients treated with oral anticoagulants and highlight the need for careful monitoring and individualized dosing in this population. Therefore, it is important for healthcare providers to carefully evaluate and closely monitor the potential risks and benefits of oral anticoagulant therapy in elderly patients, particularly those aged 85 years and older and those using DOACs even if the dose is reduced.

Gender

Gender was evaluated in 6 studies conducted on the effects of anticoagulant therapy on bleeding, with a focus on the potential differences between genders. et al. (2007)found a higher risk of atrial fibrillation-related thromboembolism in women not receiving oral anticoagulation, emphasizing the importance of considering gender in treatment strategies. Božić et al. (2021) found that the bleeding caused by these therapies was not affected by the gender variable (Bozic et al., 2021). Similarly, Carnicelli et al. (2022) found no significant differences between standard-dose DOAC, lower-dose DOAC and warfarin treatments in terms of gender (Carnicelli et al., 2022).

A study by Matsumura et al. (2014) showed that Japanese women treated with DOAC experienced comparable bleeding events as men despite the higher bleeding risk estimates. The higher thromboembolic risk estimates in women resulted in higher thromboembolic event rates (Matsumura et al., 2022).

In the study by Kefale et al. (2023), it was observed that female patients had lower odds of being prescribed oral anticoagulants (OAC) compared to males. Despite gender differences in OAC prescription patterns, no significant disparity in bleeding risk between females and males was found, suggesting that gender may not directly impact bleeding outcomes in the context of anticoagulation therapy (Kefale et al., 2023).

A study by Nillson et al. (2015) found that males achieved better TTR control than females but death, bleeding and thromboembolism were not significantly different between females and males. The study also found that oral anticoagulant initiation was lower in women, but Japanese women experienced comparable bleeding events as men (Nilsson et al., 2014). Additionaly, Khatib et al. (2022) noted that there appears to be a marked difference in the level of

acceptance towards the utilization of anticoagulants between male and female populations. The reason for this has been shown to be prejudiced about bleeding risk in women.

Overall, these studies suggest that there is no significant difference in the effects of anticoagulant and antiplatelet therapy on bleeding based on gender, although some differences in TTR control and risk assessment tool performance have been noted.

Race and etnicity

Race and etnicity were evaluated in 5 studies. The studies highlight the disparities in OAC therapy among racial minorities and individuals. Tedla (2020) found that minorities were less likely to receive any OAC, specifically VKAs and DOACs, in comparison to whites, despite accounting for insurance status, income, and stroke risk factors. The study also found that the use of DOACs as compared to VKA therapy was associated with a significantly lower risk of stroke and bleeding in white patients, but not in black patients (Tedla et al., 2020).

A study by Haddad et al. (2021) investigated the association between race and the prescribing of OAC therapy at discharge among individuals with a prior gastrointestinal (GI) bleed. The study found that among those with a prior GI bleed, white patients were nearly five-times more likely to be discharged on OAC therapy than black patients, independent of income. This finding highlights the potential disparities in healthcare access and outcomes for racial and ethnic minorities. Additionally, the study found that although there was a substantial disparity in income between white and black individuals, this difference in income was not found to be a significant contributing factor to the association between race and the prescribing of OAC therapy at discharge. This suggests that other factors, such as systemic biases in healthcare access and treatment, may play a larger role in determining prescribing patterns for OAC therapy (Haddad et al., 2021).

Tse (2021) emphasized the importance of considering ethnicity and socioeconomic status in bleeding risk assessments to guide the use of antithrombotic medication for the management of CVD (Tse et al., 2021).

The study by Essien et al. (2018) found that black individuals were less likely to receive any oral anticoagulant and specifically to receive DOAC therapy compared to white individuals, even after adjusting for clinical features and socioeconomic factors. Furthermore, black and Hispanic individuals treated with DOACs were found to have a higher risk of inappropriate dosing than white individuals. The study also found that black and Hispanic individuals treated with warfarin had a lower median time in TTR compared to white individuals (Essien et al., 2021). Similarly, in a subsequent study, Essien et al. (2022) reported that Black and Hispanic patients were less likely to be prescribed anticoagulation at discharge than White patients, with significant disparities in the prescription of DOACs. This study also revealed that Black patients had higher rates of AF-related adverse outcomes, such as stroke, major bleeding, and mortality (Essien et al., 2022).

These studies indicate that there is a need for further research to understand the underlying factors contributing to these disparities and to develop strategies to address these disparities in the utilization of oral anticoagulant therapy from different racial and ethnic backgrounds. Furthermore, these studies emphasize the importance of considering ethnicity in the assessment of bleeding risk to guide the use of antithrombotic medication for the management of CVD.

Socioeconomic status

Socioeconomic status impacts individual health, even within a universal health care system. This may be partly explained by differences in exposure to risk factors for cardiovascular and other disease, differences in disease severity, inequitable access to health services, and other determinants of health such

as social and physical environments (Addo et al., 2012; Adler, N. E. et al., 1994; Kondo et al., 2009; Mackenbach et al., 2003; Manrique-Garcia et al., 2011)

Socioeconomic status was evaluated in 5 studies. These studies have highlighted the correlation between socioeconomic status and the risk of bleeding among patients undergoing warfarin therapy. A study conducted by Cresman et al. (2015) analyzed the cumulative incidence of bleeding among patients commencing warfarin therapy for atrial fibrillation, stratified by neighborhood-level income quintile. The results showed that the 5-year estimates were 11.5%, 11.2%, 10.6%, 10.3%, and 9.6% for income quintiles 1 (lowest) through 5 (highest), respectively. Additionally, the study identified a similar association between socioeconomic status and risk of fatal bleeding, with patients in the lowest-income quintile 28% more likely to die of warfarin-associated bleeding than those in the highest-income quintile. These findings align with those of a recent study from the United Kingdom, which suggests that social deprivation is associated with an elevated risk of bleeding in anticoagulant recipients (Hippisley-Cox, 2014).

A separate study by Dalen et al. (2022) investigates the association between individual-level socioeconomic status and the risk of bleeding, ischemic stroke/ transient ischemic attack/ embolism, all-cause mortality, and the combined outcome after weighting (Dalén et al., 2022). The results of the study show that the absolute risk of bleeding after 20 years of follow-up was 20% in the lowest income quartile and 16% in the highest income quartile. The study found a significantly higher risk of bleeding in the lowest income quartile than in the highest quartile. Moreover, the risk of death due to intracranial bleeding was strongly related to income level, and the standardized mortality ratio was 5.0 in the lowest income quartile and decreased to 1.3 in the highest income quartile. This implies that the risk of death due to intracranial bleeding was five times higher in patients in the lowest income quartile than in individuals in the age- and gender-matched general Swedish population.

A study by Kefale et al. (2023) shows that higher socioeconomic status was associated with a reduced likelihood of being prescribed OACs. This connection implies that socioeconomic status influenced OAC prescription patterns, which could indirectly affect bleeding risk through factors like medication adherence or access to healthcare resources (Kefale et al., 2023).

The study by Ravvaz (2021) suggests that patients living in very low socioeconomic status areas require more frequent INR checks, particularly beyond 180 days post warfarin initiation, as well as compliance counseling and educational interventions to improve their TTR and decrease the risk of stroke and bleeding. However, these interventions may present additional logistical and financial challenges for these patients (Ravvaz et al., 2021).

Erquicia (2021) conducted a study and found that there were no significant differences in the incidence rate of major bleeding between patients treated with VKAs and those treated with DOACs (Domínguez-Erquicia et al., 2021).

These studies have shown a correlation between socioeconomic status and the risk of bleeding among patients undergoing warfarin therapy. These findings indicate that patients from lower-income backgrounds are at a higher risk of bleeding and bleeding-related death. Furthermore, access to warfarin therapy for stroke prevention varies among those of different social deprivation levels.

Alcohol use

Alcohol use was evaluated in 2 studies. The study conducted by Philip et al. (2021) found that there was no significant association between alcohol consumption and bleeding (Reddiess et al., 2021).

Another study by Roth (2011) found that patients who screened positive for moderate to severe alcohol misuse or heavy drinking had approximately two-fold increased odds of major bleeding. The association between moderate to severe alcohol misuse and major

bleeding was similar for both gastrointestinal and other types of bleeding, while the association between heavy drinking and major bleeding was stronger for gastrointestinal bleeding. The association between moderate to severe alcohol misuse and major bleeding risk was significant in patients on warfarin therapy for one year and those with some genetic variants (Roth et al., 2018).

The findings from these studies indicate that moderate to severe alcohol misuse and heavy drinking is correlated with an elevated risk of major bleeding in individuals who use anticoagulants. However, the data does not demonstrate a significant relationship between general alcohol consumption and bleeding events in anticoagulant recipients.

DISCUSSION

This scoping review has provided a better understanding of the comprehensive examination of the impact that social determinants have on bleeding incidents as a result of anticoagulation therapy. Through this analysis, it was sought to examine deeper into the interplay between various social determinants and the bleeding outcomes experienced by individuals undergoing anticoagulation treatment.

Patients who are older have been reluctant to adhere to recommendations on anticoagulation. This situation, accompanying diseases and the drugs they use may increase the predisposition to bleeding in patients (Bozic et al., 2021). Bozic et al. al, in the study in which they examined the causes of major bleeding and bleeding sites in patients over the age of 65 using anticoagulant and antiplatelet therapy. They stated that aging is an important determinant (Bozic et al., 2021). In another study examining the risk factors of thromboembolic and bleeding events in patients with atrial fibrillation, individuals aged 75 and over were at risk for bleeding (Rohla et al., 2019). Carnicelli et. al. examined at the effect of age on bleeding in the comparison of warfarin and DOAC. In their study, which included patients over the age of 18 using anticoagulants, they reported that being younger is more beneficial in terms of major bleeding (Carnicelli et al., 2022).Older age is a significant determinant of bleeding in patients treated with oral anticoagulants and highlight the need for careful monitoring and individualized dosing in this elderly patients.

In terms of gender, it can be said that there is no difference between men and women in terms of bleeding in patients using anticoagulants. There are studies showing that death, bleeding, and thromboembolism are not significantly different between men and women.(Bozic et al., 2021; Carnicelli et al., 2022; Nilsson et al., 2014) However, Japanese women appear to experience similar bleeding patterns as men, despite having a higher risk of bleeding.(Matsumura et al., 2022) This may be due to higher rates of thromboembolic events in women. It is stated that the prejudice of women about the risk of bleeding increases this risk(Khatib et al., 2022). Although the incidence of stroke is higher in women, it is also known that the probability of receiving oral anticoagulant (OAC) therapy is lower than in men.(Pilcher et al., 2020; Tamirisa et al., 2022a) According to these results the bleeding events of why women are more symptomatic, have a higher risk of side effects with antiarrhythmic drugs is unclear.(Tamirisa et al., 2022b)

Minority populations have persistent disparities in the use of OAC therapy, with minorities less likely to receive OAC therapy, particularly DOACs, compared to white individuals (Essien et al., 2020; Haddad et al., 2021; Tse et al., 2021). The reasons behind this disparity could be due to lack of access to healthcare, lack of knowledge about treatment options, or discrimination based on race or ethnicity. The studies show that white patients are more likely to be prescribed OAC therapy than black patients, even after controlling for income (Tedla et al., 2020). Black individuals are less likely to receive any oral anticoagulant or DOAC therapy compared to white individuals and are at a higher risk of inappropriate dosing. These findings show that there is a need for further examination to address the racial disparities in CVD management. Healthcare providers need to be

aware of these disparities to ensure all individuals have access to effective CVD management.

We review that lower socioeconomic status is a risk factor for bleeding and bleeding-related death. Some studies included within the limitations of the study because they could not distinguish intracranial hemorrhage from fall events (Cressman et al., 2015). As compared with a younger, older patients typically exhibit more risk factors for falls and intracranial hemorrhage (Gage et al., 2005). Up to 80% of older patients have inadequate knowledge of anticoagulant therapy (Nasser et al., 2012), and lower socioeconomic status impacts health literacy, understanding of warfarin therapy, and access to educational and information resources (Hu et al., 2006; Nasser et al., 2012).

We found that alcohol misuse may play a role in increasing the risk of major bleeding, particularly in patients on anticoagulant therapy and those with specific genetic predispositions. However, further research is necessary to fully understand the relationship between alcohol consumption and bleeding risk, as well as the mechanisms underlying this association. These studies highlight the importance of considering alcohol use in bleeding risk assessments and anticoagulant management for patients (Reddiess et al., 2021; Roth et al., 2018).

CONCLUSIONS

The literature review shows that social determinants of health, such as socioeconomic status, race, ethnicity, age, and gender, significantly impact bleeding outcomes in patients undergoing anticoagulant therapy. Specifically, low socioeconomic status is a significant determinant, with low-income individuals and Black patients being less likely to access oral anticoagulant therapy. Notably, there is a lack of comprehensive qualitative studies that explore the systemic barriers to equitable healthcare access, particularly for minority populations, who are less likely to receive OAC despite having similar or higher risks of adverse outcomes compared to individuals of different racial or ethnic backgrounds. This disparity highlights inequalities in access to health services. Additionally, older age is associated with an increased risk of bleeding in patients on anticoagulants and the risk increases with age. While gender does not significantly affect INR control and bleeding risk, variations in the diseases for which anticoagulants are prescribed may influence outcomes. General alcohol use does not appear to be a social determinant of bleeding risk, but moderate to severe alcohol misuse and heavy drinking are correlated with an increased risk of major bleeding and should be considered in patient assessments.

Socioeconomic status and ethnicity are important factors in managing patient care and assessing bleeding risk. For these patients, nurses should take thorough patient histories and monitor INR more frequently. Further research is essential to uncover the underlying factors contributing to disparities in oral anticoagulant therapy and to develop strategies to address these disparities, particularly among different racial and ethnic groups. Individualized dosing, along with close observation, is recommended for elderly patients, particularly those aged 85 years and older, due to the increased risk of bleeding. Additionally, nursing care for elderly patients should include a careful assessment of both the benefits and risks of oral anticoagulant therapy, along with close monitoring for signs of bleeding.

Further research is needed to investigate both the individual and combined effects of social determinants of health on outcomes and processes related to oral anticoagulant therapy. To address these gaps, it is essential to focus on developing targeted educational interventions aimed at improving health literacy and adherence to anticoagulation therapy among socioeconomically disadvantaged populations. Additionally, longitudinal studies that track the long-term outcomes of patients across diverse demographic groups are crucial for better understanding the effectiveness of treatment protocols and informing tailored approaches that consider individual risk factors.

REFERENCES

Addo, J., Ayerbe, L., Mohan, K. M., Crichton, S., Sheldenkar, A., Chen, R., Wolfe, C. D. A., & McKevitt, C. (2012). Socioeconomic status and stroke: An updated review. *Stroke*, *43*(4), 1186–1191. https://doi.org/10.1161/STROKEAHA.111.639732

Adler, N. E., Boyce, T., Chesney, M. A., Cohen, S., Folkman, S., Kahn, R. L., & Syme, S. L. (1994). Socioeconomic status and health: The challenge of the gradient. *American Psychologist*, *49*(1), 15–24. https://doi.org/https://doi.org/10.1037/0003-066X.49.1.15

Adrianzen-Herrera, D., Giorgio, K., Walker, R. F., Sparks, A. D., Gergi, M., Zakai, N. A., & Lutsey, P. L. (2024). Bleeding risk from anticoagulant thromboprophylaxis in patients with multiple myeloma: a MarketScan analysis. *Research and Practice in Thrombosis and Haemostasis*, *8*(4). https://doi.org/10.1016/j.rpth.2024.102418

Arksey, H., Malley, L. O., Arksey, H., & Malley, L. O. (2007). *Scoping studies : towards a methodological framework Scoping Studies : Towards a Methodological Framework*. *5579*. https://doi.org/10.1080/1364557032000119616

Bozic, D., Vukovic, J., Mustapic, I., Cindro, P. V., Bozic, J., Kardum, G., Puljiz, Z., Hadjina, I. T., & Tonkic, A. (2021). Characteristics and clinical outcomes of patients with acute gastrointestinal bleeding related to anticoagulant or antiplatelet therapy: A retrospective study. *Croatian Medical Journal*, *62*(5), 488–494. https://doi.org/10.3325/cmj.2021.62.488

Büchele, K., Rapp, G., Jaensch, J. M. B. A., & Petra, C. B. (2020). Risk of traumatic intracranial haemorrhage is increased in older people exposed to oral anticoagulation with phenprocoumon. *Aging Clinical and Experimental Research*, *32*(3), 441–447. https://doi.org/10.1007/s40520-019-01215-5

Carnicelli, A., Hong, H., Connolly, S. J., Eikelboom, J., Giugliano, R. P., Morrow, D. A., Patel, M. R., Wallentin, L., Alexander, J. H., Cecilia Bahit, M., Benz, A. P., Bohula, E. A., Chao, T.-F., Dyal, L., Ezekowitz, M., A.A. Fox, K., Gencer, B., Halperin, J. L., Hijazi, Z., … Granger, C. B. (2022). Direct Oral Anticoagulants Versus Warfarin in Patients With Atrial Fibrillation: Patient-Level Network Meta-Analyses of Randomized Clinical Trials With Interaction Testing by Age and Sex. *Circulation*, *145*(4), 242–255. https://doi.org/10.1161/circulationaha.121.056355

Cressman, A. M., MacDonald, E. M., Yao, Z., Austin, P. C., Gomes, T., Paterson, J. M., Kapral, M. K., Mamdani, M. M., & Juurlink, D. N. (2015). Socioeconomic status and risk of hemorrhage during warfarin therapy for atrial fibrillation: A population-based study. *American Heart Journal*, *170*(1), 133-140.e3. https://doi.org/10.1016/j.ahj.2015.03.014

Dagres, N., Nieuwlaat, R., Vardas, P. E., Andresen, D., Lévy, S., Cobbe, S., Kremastinos, D. T., Breithardt, G., Cokkinos, D. V., Crijns, H. J. G. M., Camm, A. J., Davies, W., Capucci, A., Olsson, B., Aliot, E., Le Heuzey, J. Y., Santini, M., Manini, M., Bramley, C., … Randjelovic, M. (2007). Gender-Related Differences in Presentation, Treatment, and Outcome of Patients With Atrial Fibrillation in Europe. A Report From the Euro Heart Survey on Atrial Fibrillation. *Journal of the American College of Cardiology*, *49*(5), 572–577. https://doi.org/10.1016/j.jacc.2006.10.047

Dalén, M., Persson, M., Glaser, N., & Sartipy, U. (2022). Socioeconomic Status and Risk of Bleeding After Mechanical Aortic Valve Replacement. *Journal of the American College of Cardiology*, *79*(25), 2502–2513. https://doi.org/10.1016/j.jacc.2022.04.030

Domínguez-Erquicia, P., Raposeiras-Roubín, S., Abu-Assi, E., Cespón-Fernández, M., Alonso-Rodríguez, D., Camacho-Freire, S. J., Cubelos-Fernández, N., López-Masjuán Ríos, Á., Melendo-Viu, M., & Íñiguez-Romo, A. (2021). Incidence, predictors of bleeding and prognosis of bleeding

in anticoagulated nonagenarian patients with atrial fibrillation. *International Journal of Cardiology*, *327*, 217–222. https://doi.org/10.1016/j.ijcard.2020.11.023

Essien, U. R., Chiswell, K., Kaltenbach, L. A., Wang, T. Y., Fonarow, G. C., Thomas, K. L., Turakhia, M. P., Benjamin, E. J., Rodriguez, F., Fang, M. C., Magnani, J. W., Yancy, C. W., & Piccini, J. P. (2022). Association of Race and Ethnicity With Oral Anticoagulation and Associated Outcomes in Patients With Atrial Fibrillation. *JAMA Cardiology*, *7*(12), 1207. https://doi.org/10.1001/jamacardio.2022.3704

Essien, U. R., Kim, N., Hausmann, L. R. M., Mor, M. K., Good, C. B., Magnani, J. W., Litam, T. M. A., Gellad, W. F., & Fine, M. J. (2021). Disparities in Anticoagulant Therapy Initiation for Incident Atrial Fibrillation by Race/Ethnicity among Patients in the Veterans Health Administration System. *JAMA Network Open*, *4*(7), 1–14. https://doi.org/10.1001/jamanetworkopen.2021.14234

Essien, U. R., Magnani, J. W., Chen, N., Gellad, W. F., Fine, M. J., & Hernandez, I. (2020). Race/Ethnicity and Sex-Related Differences in Direct Oral Anticoagulant Initiation in Newly Diagnosed Atrial Fibrillation: A Retrospective Study of Medicare Data. *Journal of the National Medical Association*, *112*(1), 103–108. https://doi.org/10.1016/j.jnma.2019.10.003

Gage, B. F., Birman-Deych, E., Kerzner, R., Radford, M. J., Nilasena, D. S., & Rich, M. W. (2005). Incidence of intracranial hemorrhage in patients with atrial fibrillation who are prone to fall. *The American Journal of Medicine*, *118*(6), 612–617. https://doi.org/10.1016/j.amjmed.2005.02.022

Haddad, A., Bocchese, M., Garber, R., O'Neill, B., Yesenosky, G. A., Patil, P., Keane, M. G., Islam, S., Sherrer, J. M., Basil, A., Gangireddy, C., Cooper, J. M., Cronin, E. M., & Whitman, I. R. (2021). Racial and ethnic differences in left atrial appendage occlusion wait time, complications, and periprocedural management. *PACE - Pacing and Clinical Electrophysiology*, *44*(7), 1143–1150. https://doi.org/10.1111/pace.14255

Hippisley-Cox, J. (2014). Predicting risk of upper gastrointestinal bleed and intracranial bleed with anticoagulants: Cohort study to derive and validate the QBleed scores. *BMJ (Online)*, *349*(July), 1–21. https://doi.org/10.1136/bmj.g4606

Hu, A., Chow, C., Dao, D., Errett, L., & Mary Keith. (2006). of Warfarin Therapy After Mechanical Heart Valve Replacement. *Journal of Cardiovascular Nursing*, *21*(3), 169–175.

İlçe A., Yiğit, Ü., Soysal, G.E. (2022). Determination of Drug-Related Risk Behaviours of Patients Using Oral Anticoagulants and Innovative Solutions. Journal of Health Care and Rehabilitation, 1(1), 1-11.

Kefale, A. T., Bezabhe, W. M., & Peterson, G. M. (2023). Oral Anticoagulant Use in Patients with Atrial Fibrillation at Low Risk of Stroke and Associated Bleeding Complications. *Journal of Clinical Medicine*, *12*(19). https://doi.org/10.3390/jcm12196182

Khatib, R., Glowacki, N., Byrne, J., & Brady, P. (2022). Impact of social determinants of health on anticoagulant use among patients with atrial fibrillation: Systemic review and meta-analysis. *Medicine (United States)*, *101*(35), E29997. https://doi.org/10.1097/MD.0000000000029997

Kondo, N., Sembajwe, G., Kawachi, I., Van Dam, R. M., Subramanian, S. V., & Yamagata, Z. (2009). Income inequality, mortality, and self rated health: Meta-analysis of multilevel studies. *BMJ (Online)*, *339*(7731), 1178–1181. https://doi.org/10.1136/bmj.b4471

Mackenbach, J. P., Bos, V., Andersen, O., Cardano, M., Costa, G., Harding, S., Reid, A., Hemström, Ö., Valkonen, T., & Kunst, A. E. (2003). Widening socioeconomic inequalities in mortality in six Western European countries. *International Journal of Epidemiology*, *32*(5), 830–837. https://doi.org/10.1093/ije/dyg209

Maguire, A., Douglas, I., Smeeth, L., & Thompson, M. (2007). Determinants of cholesterol and triglycerides recording in patients treated with lipid lowering therapy in UK primary care. *Pharmacoepidemiol Drug Saf.*, *16*(August), 228–228. https://doi.org/doi:10.1002/pds

Manrique-Garcia, E., Sidorchuk, A., Hallqvist, J., & Moradi, T. (2011). Socioeconomic position and incidence of acute myocardial infarction: a meta-analysis. *Journal of Epidemiology and Community Health*, *65*(4), 301 LP – 309. https://doi.org/10.1136/jech.2009.104075

Matsumura, M., Sotomi, Y., Hirata, A., Sakata, Y., Hirayama, A., & Higuchi, Y. (2022). Sex-related difference in bleeding and thromboembolic risks in patients with atrial fibrillation treated with direct oral anticoagulants. *Heart and Vessels*, *37*(3), 467–475. https://doi.org/10.1007/s00380-021-01931-x

Nasser, S., Mullan, J., & Bajorek, B. (2012). Challenges of Older Patients' Knowledge About Warfarin Therapy. *Journal of Primary Care and Community Health*, *3*(1), 65–74. https://doi.org/10.1177/2150131911416365

Nathan, A. S., Geng, Z., Dayoub, E. J., Khatana, S. A. M., Eberly, L. A., Kobayashi, T., Pugliese, S. C., Adusumalli, S., Giri, J., & Groeneveld, P. W. (2019). Racial, ethnic, and socioeconomic inequities in the prescription of direct oral anticoagulants in patients with venous thromboembolism in the United States. *Circulation: Cardiovascular Quality and Outcomes*, *12*(4), 1–7. https://doi.org/10.1161/CIRCOUTCOMES.119.005600

Nilsson, H., Grove, E. L., Larsen, T. B., Nielsen, P. B., Skjøth, F., Maegaard, M., & Christensen, T. D. (2014). Sex differences in treatment quality of self-managed oral anticoagulant therapy: 6,900 patient-years of follow-up. *PLoS ONE*, *9*(11), 1–15. https://doi.org/10.1371/journal.pone.0113627

Pham MT, Greig JD, Sargeant JM, Mcewen SA. A scoping review of scoping reviews: advancing the approach and enhancing the consistency. *Res Synth Methods*. 2015;(January 2014):71-385. doi:10.1002/jrsm.1123

Peters, M., Godfrey, C., McInerney, P., Munn, Z., Tricco, A., & Khalil, H. (2020). Chapter 11: Scoping Reviews (2020 version). In E. Aromataris & Z. Munn (Eds.), *JBI Manual for Evidence Synthesis*.

Pilcher, S. M., Alamneh, E. A., Chalmers, L., & Bereznicki, L. R. (2020). The Tasmanian Atrial Fibrillation Study (TAFS): Differences in Stroke Prevention According to Sex. *Annals of Pharmacotherapy*, *54*(9), 837–845. https://doi.org/10.1177/1060028020904969

Ravvaz, K., Weissert, J. A., Jahangir, A., & Ruff, C. T. (2021). Evaluating the effects of socioeconomic status on stroke and bleeding risk scores and clinical events in patients on oral anticoagulant for new onset atrial fibrillation. *PLoS ONE*, *16*(3 March), 1–13. https://doi.org/10.1371/journal.pone.0248134

Reddiess, P., Aeschbacher, S., Meyre, P., Coslovsky, M., Kühne, M., Rodondi, N., Baretella, O., Beer, J. H., Kobza, R., Moschovitis, G., Di Valentino, M., Müller, C., Steiner, F., Bonati, L. H., Sticherling, C., Osswald, S., & Conen, D. (2021). Alcohol consumption and risk of cardiovascular outcomes and bleeding in patients with established atrial fibrillation. *Cmaj*, *193*(4), E117–E123. https://doi.org/10.1503/cmaj.200778

Rohla, M., Weiss, T. W., Pecen, L., Patti, G., Siller-matula, J. M., Schnabel, R. B., Schilling, R., Kotecha, D., Lucerna, M., Huber, K., Caterina, R. De, & Kirchhof, P. (2019). Risk factors for thromboembolic and bleeding events in anticoagulated patients with atrial fibrillation : the prospective , multicentre observational PREvention oF thromboembolic events - European Registry in Atrial Fibrillation (PREFER in AF). *BMJ*, 1–8. https://doi.org/10.1136/bmjopen-2018-022478

Roth, J. A., Bradley, K., Thumme, K. E., Veenstra, D. L., & Boudreau, D. (2018). Alcohol misuse, genetics,

and major bleeding among warfarin therapy patients in a community setting. *Physiology & Behavior*, *176*(1), 139–148. https://doi.org/10.1002/pds.3769

Šinigoj, P., Vene, N., Košmelj, K., & Mavri, A. (2020). Risk of major bleeding in elderly patients with atrial fibrillation on direct oral anticoagulants: real world experience. *International Journal of Clinical Pharmacy*, *42*(2), 445–452. https://doi.org/10.1007/s11096-020-01008-1

Tamirisa, K. P., Dye, C., Ekeruo, I., & Volgman, A. S. (2022a). Atrial Fibrillation in Women: from Epidemiology to Treatment. *Current Cardiovascular Risk Reports*, *16*(12), 207–217. https://doi.org/10.1007/s12170-022-00707-w

Tedla, Y. G., Schwartz, S. M., Silberman, P., Greenland, P., & Passman, R. S. (2020). Racial Disparity in the Prescription of Anticoagulants and Risk of Stroke and Bleeding in Atrial Fibrillation Patients. *Journal of Stroke and Cerebrovascular Diseases*, *29*(5), 104718. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104718

Tricco, A. C., Lillie, E., Zarin, W., Brien, K. K. O., Colquhoun, H., Levac, D., Moher, D., Peters, M. D. J., Ma, Q., Horsley, T., Weeks, L., Hartling, L., Aldcroft, A., Hons, B. A., Wilson, M. G., & Garritty, C. (2018). *R ESEARCH AND R EPORTING M ETHODS PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation*. https://doi.org/10.7326/M18-0850

Tse, W. C., Grey, C., Harwood, M., Jackson, R., Kerr, A., Mehta, S., Poppe, K., Pylypchuk, R., Wells, S., & Selak, V. (2021). Risk of major bleeding by ethnicity and socioeconomic deprivation among 488,107 people in primary care: a cohort study. *BMC Cardiovascular Disorders*, *21*(1), 1–11. https://doi.org/10.1186/s12872-021-01993-9

Vitry, A., Roughead, E. E., Ramsay, E. N., Preiss, A. K., Ryan, P., & Andrew L. Gilbert. (2007). Determinants of cholesterol and triglycerides recording in patients treated with lipid lowering therapy in UK primary care. *Pharmacoepidemiology and Drug Safety*, *16*(August), 228–228. https://doi.org/10.1002/pds.2219