Pharmacoepidemiology and Drug Safety

WILEY

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Warfarin-Associated Bleeding and Thromboembolic Events in Sub-Saharan Africa: A Systematic Review and Meta-Analysis

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Received: 15 December 2024 | **Revised:** 4 June 2025 | **Accepted:** 13 September 2025

Funding: The authors received no specific funding for this work.

Keywords: bleeding | Sub-Saharan Africa | thromboembolic event | warfarin

ABSTRACT

Background: Warfarin use in Sub-Saharan Africa is associated with elevated risks of thromboembolic events and bleeding, but precise prevalence estimates are lacking. This systematic review and meta-analysis aimed to quantify the prevalence of bleeding and thromboembolic events among patients on warfarin in Sub-Saharan Africa.

Methods: Comprehensive searches were conducted in MEDLINE via Ovid, PubMed, Embase via Ovid, Scopus, and Google Scholar to identify relevant studies. Primary outcomes included major and minor bleeding events, while thromboembolic events were secondary outcomes. Meta-analysis was conducted using RStudio version 4.3.3 with the meta and `metaprop` packages. Proportions were transformed using the Freeman–Tukey double arcsine method, and meta-regression was performed with the `metafor` package's `escal`, `rma`, and `res` functions. Publication bias was assessed via funnel plots and Egger's test, with a p value <0.05 indicating potential bias. Sensitivity analysis was conducted through leave-one-out analysis. The review was performed in adherence to PRISMA guidelines.

Results: We identified 10 observational studies for inclusion in this systematic review and meta-analysis. Egger's test indicated no publication bias. Meta-regression analysis showed that moderators (publication year, sample size, setting, and follow-up duration) did not significantly impact bleeding risk. The pooled prevalence of major and minor bleeding was 18% (95% CI: 0.10–0.27; I^2: 96%, prediction interval: 0.00–0.53), with rates ranging from 4% to 46%. Thromboembolic events occurred in 7% of warfarin users (95% CI: 0.01–0.07).

Conclusion: Warfarin therapy in Sub-Saharan Africa is associated with considerable bleeding and thromboembolic risks. The robustness of these findings was confirmed through meta-regression and sensitivity analyses, underscoring the need for improved therapeutic monitoring and safety strategies in this population.

1 | Introduction

Globally, rates of thromboembolic events (TEEs) and bleeding are rising in community and hospitalized patients, and they have turned out to be a major public health problem [1–6]. Anticoagulation decreases the risk of TEEs, leading to a notable reduction in associated morbidity and mortality [7–11]. In a meta-analysis of randomized controlled trials, vitamin K antagonists

Summary

- The overall proportion of bleeding events was 18% with a confidence interval ranging from 10% to 27%.
- The lowest reported bleeding rate was 4% among all studies.
- The highest reported bleeding rate reached 46%.
- Bleeding proportions across studies showed significant variation, ranging from 4% to 46%.
- In Sub-Saharan Africa, 3% of warfarin users experienced TEEs.

(VKAs) and antiplatelets reduced the risk of stroke by 64% and 22%, respectively [12]., while a separate systematic review and meta-analysis suggested that anticoagulants demonstrate efficacy and safety in patients with cerebral venous thrombosis [13].

However, the benefits of VKAs have been questioned due to ongoing concerns about their effectiveness and safety. Specifically, warfarin use, whether in general medical settings or specialized anticoagulation centers, has been linked to high risks of bleeding, thromboembolism, recurrent venous thromboembolism, and increased all-cause mortality [14–16]. In a propensity weighted nationwide study, a trend of higher rates of ischemic stroke/systemic embolism [17] and 4.5%–46% of bleeding risk was observed among African warfarin users [2, 5, 11, 18]. Also, in other studies, this drug was associated with the risk of TEEs, with up to 22.5% of Sub-Saharan patients developing TEE [18].

In Sub-Saharan African countries, the problem of anticoagulation is exacerbated by limited anticoagulation centers, access to safe alternatives, experienced personnel, and pharmacovigilance services. Despite these existing challenges and the rising concern over the safety and effectiveness of the drug in various settings [11, 19–21], the pooled estimate of bleeding and TEEs has not been reported. This study not only highlights the scope of these challenges but also serves as an input for the identification of gaps for improvement in warfarin therapy across the region. The findings would pave the way for the development of tailored, region-specific guidelines aimed at enhancing anticoagulation management, contributing to reducing complications, improving patient safety, and supporting better clinical outcomes for individuals on warfarin therapy.

Thus, the aim of this systematic review and meta-analysis was to assess the pooled prevalence of bleeding risk and TEE with warfarin in Sub-Saharan Africa.

2 | Methods

2.1 | Data Sources and Search Strategy

We searched MEDLINE via Ovid, Embase via Ovid, and Scopus, and citation analysis from Google Scholar from the inception to July 31, 2024. Furthermore, we hand-searched of reference lists of the retrieved articles to locate any potential studies not captured in the database searches. The search strategy employed a comprehensive approach, utilizing both Medical Subject Heading (MeSH) terms and a range of relevant keywords for warfarin and anticoagulation control (Supporting Information: Tables). This systematic review and meta-analysis was not registered in any registration databases.

2.2 | Eligibility Criteria

Although the eligibility criteria allowed for inclusion of case–control studies and clinical trials, only prospective and retrospective studies were identified during the search period. The criteria included studies that reported the proportion of patients with major and/or minor bleeding and TEEs. Exclusive consideration was accorded to articles published in English. In a deliberate exclusionary approach, studies delving into the effects of anticoagulation arising from the concomitant use of warfarin and other medications were excluded. Moreover, a refined focus on the scope of safety-related outcomes led to the exclusion of reports addressing aspects beyond anticoagulation control. This exclusion encompassed pharmacogenomic analyses, qualitative studies, review articles, and unpublished works.

2.3 | Process for Screening Studies

Two researchers (C.T. and Z.D.A.) independently screened articles for compliance with eligibility criteria among the retrieved studies. The initial selection was based on the title and abstract. Subsequently, especially when the title and abstract provided insufficient information, the full text of studies was reviewed to assess the relevance of the papers. In instances of disagreements, the other author (B.B.) facilitated a discussion to resolve conflicting ideas. If a consensus could not be reached, additional independent adjudication involving all authors was considered.

3 | Data Extraction

Data extraction was independently performed by two reviewers (C.T. and Z.D.A.) using a standardized template. Extracted variables included study characteristics, sample size, outcomes, and risk of bias.

3.1 | Outcome Measurement and Quality Assessment of Studies

The Newcastle-Ottawa Scale (NOS) for cross-sectional and cohort studies was employed to assess the quality of observational studies. This critical appraisal tool evaluates studies across three domains: the selection of participants, the comparability of study groups, and the measurement of outcomes. The NOS assigns a maximum of four stars for the selection domain, two for comparability, and three for outcome assessment, totaling a maximum score of nine. Each criterion within these domains is rated with up to one star. Studies scoring 7–9 were rated as high quality, 5–6 as moderate, and 0–4 as low quality [22].

The primary outcomes assessed in this review were minor and/or major bleeding events, while TEEs were considered secondary outcomes. Major bleeding was defined as any clinically overt bleeding that was fatal, occurred in a critical anatomical site (e.g., intracranial, intraspinal, intraocular with vision changes, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome), or resulted in a hemoglobin drop of ≥1.24 mmol/L or required transfusion of ≥2 units of whole blood or red blood cells [23]. In contrast, minor bleeding was defined as any bleeding episode that did not meet the criteria for major bleeding or intracranial hemorrhage (ICH) (https://www.ncbi.nlm.nih.gov/books/NBK169813/table/T15/).

3.2 | Meta Regression and Sensitivity Analysis

To explore sources of heterogeneity in clinical outcomes among patients using warfarin, we employed a meta-regression. This model assesses the influence of publication year, sample size, clinical setting (cardiac center vs. medical clinic), and follow-up duration. To further evaluate the robustness of our findings, we conducted a sensitivity analysis using a leave-one-out approach. This technique systematically excludes each study one at a time to assess its influence on the overall pooled estimate. The sensitivity analysis report examines the robustness of the meta-analysis findings by sequentially omitting each study to observe the impact on the overall proportion estimate.

Initially, we performed a meta-analysis using the inverse variance method combined with the Freeman–Tukey double arcsine transformation to generate pooled outcome estimates. Subsequently, we applied the *metainf* function to iteratively omit individual studies and produce a series of forest plots. These plots allowed us to visually inspect for any significant changes in the pooled estimates, thereby gauging the stability and reliability of our meta-analysis results.

3.3 | Heterogeneity and Publication Bias

Prediction intervals (PIs) were employed in meta-analysis to estimate the range within which the true effect sizes of future studies are likely to fall, incorporating both the uncertainty in the pooled effect estimate and the variability among study results. For interpretation, a wide PI suggests high heterogeneity, indicating that future studies may report a broad range of effect sizes, while a narrow interval reflects greater consistency across studies. Additionally, I^2 values were used to quantify the level of heterogeneity, although they provide less reliable evidence compared to PIs. Heterogeneity was determined as low, moderate, and high using *I*-square (I^2) values of $I^2 < 25\%$, $25\% < I^2 < 50\%$, $I^2 > 50\%$, respectively. We evaluated publication bias using funnel plots and Egger's test, considering a p value below 0.05 as indicative of publication bias.

3.4 | Statistical Analysis

All statistical analyses were performed using R version 4.3.3. To estimate the pooled proportions of bleeding risk and TEEs across studies, we utilized the `metaprop()` function from the *meta* package. This approach allowed us to input the number of events and total participants from each study, enabling the calculation of pooled proportions. The inverse-variance method (`method = "inverse"`) was employed to weight studies based on their sample size and variance, while the Freeman–Tukey double arcsine transformation (PFT) was applied to stabilize variances, particularly for studies reporting extreme proportions.

Given the anticipated variability across studies, a random-effects model was selected to account for between-study heterogeneity. This model provided not only an overall pooled estimate but also a PI, which reflects the expected range of effect sizes in future studies.

To visually summarize the findings, we generated forest plots using the `forest()` function in the *meta* package. Each study was depicted by a red square, scaled to its relative weight, with horizontal lines indicating 95% confidence intervals. The overall pooled estimate was represented by a diamond, and PIs were also displayed.

To evaluate the robustness of the meta-analysis findings, a sensitivity analysis was conducted using the `metainf()` function. Following the sensitivity analysis, we further explored potential sources of between-study heterogeneity through meta-regression. Using the *metafor* package, we applied the `rma()` function to examine how moderator variables—such as publication year, sample size, clinical setting (e.g., cardiac center vs. medical clinic), and follow-up duration—were associated with variations in effect sizes across studies. These variables were selected based on their potential to affect bleeding risk estimates. Publication year was included to account for temporal changes in clinical practice and reporting standards. Sample size was considered to capture the influence of study precision on effect variability. Clinical setting was examined to reflect differences in healthcare infrastructure, protocols, and patient populations that might influence outcomes. Follow-up duration was included as longer observation periods could increase the likelihood of detecting bleeding events. Together, these moderators aimed to explain some of the substantial heterogeneity observed in the pooled estimates.

Finally, to assess the risk of publication bias, we performed Egger's test using the `metabias()` function. Complementing this test, a funnel plot was generated via the `funnel()` function to visually examine asymmetry in the distribution of study estimates, which may suggest potential bias in the reporting of results.

4 | Results

4.1 | Study Identification and Selection

From a total of 11 567 articles retrieved, 10 observational studies fulfilled our inclusion criteria, Figure 1. Each of these selected studies provided valuable insights into outcomes related to TEEs, major or minor bleeding, international normalized ratio, and time in therapeutic range.

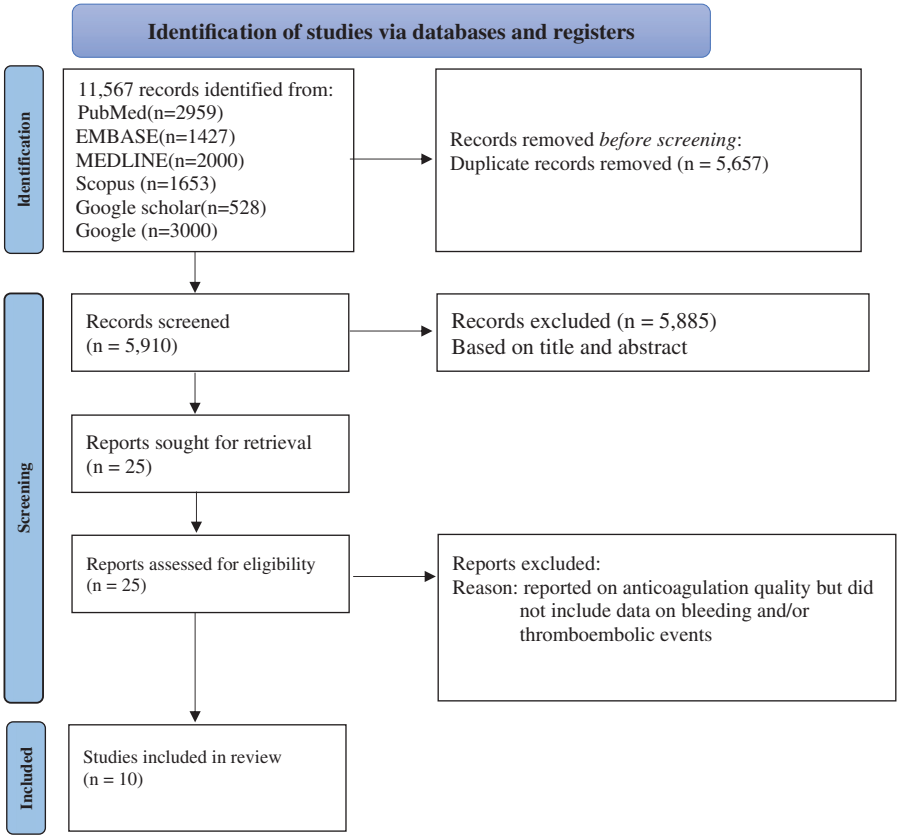

FIGURE 1 | Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

4.2 | Study Characteristics

The reviewed studies employed both retrospective and prospective designs across various African countries, with adult patient populations, diverse follow-up durations, and varying sample sizes. Most studies were retrospective and conducted in Ethiopia. Getachew et al. [24], Yimer et al., Liyew et al., and Masresha et al. examined cohorts ranging from 202 to 347 patients, with follow-up durations between 3 months and 2 years, primarily in outpatient, cardiology, and anticoagulation clinic settings.

Additional retrospective studies from Nigeria, South Africa, and Sudan also contributed important observational evidence. In Nigeria, Anakwue et al. followed 26 patients over 5 years in a teaching hospital. In South Africa, Jacobs et al. and Sonuga et al. studied 126 and 136 patients, respectively, with follow-up periods of 6 to 12 months. Sudanese studies by Ahmed et al. and Salaheldin included 135 and 21 patients, respectively, monitored over 12 to 14 months. Notably, the only prospective study was conducted in Tunisia by Ouali et al., involving a large cohort of 915 patients followed for 1 year in a cardiac clinic.

Bleeding event rates demonstrated notable variability across the included studies. The highest rates were reported by Jacobs et al. at 46%, Ahmed et al. at 39%, and Liyew et al. at 25%. Moderate bleeding rates were observed in the studies conducted by Yimer et al. (21%), Getachew et al. [24] (17%), Anakwue et al. (12%), and Salaheldin (10%). In contrast, lower rates were reported by Sonuga et al. (14%), Ouali et al. (6%), and Masresha et al. (4%) (Table 1).

4.3 | Quality Assessment and Publication Bias

As illustrated in Figure 2, funnel plot asymmetry was observed, potentially suggesting small studies or unreported studies might be missed, but Egger's test yielded statistically insignificant results for bleeding (Egger's test: $p = 0.19$) and TEE (Egger's test: $p = 0.51$). Seven studies were considered to be of high quality (Newcastle–Ottawa score ≥ 7 (Supporting Information: Tables)).

4.4 | Meta-Analysis

4.4.1 | Meta-Regression

The meta-regression analysis of bleeding risk across 11 studies showed substantial unexplained variability. Key model fit statistics were a log-likelihood of 2.1256, AIC of 7.7489, and BIC of 6.4994. The residual heterogeneity (τ^2) was estimated at 0.0270 (SE = 0.0170), with a high I^2 of 94.20% and an H^2 of 17.26, indicating considerable heterogeneity not explained by the model. The model explained none of the heterogeneity ($R^2 = 0\%$).

The test for residual heterogeneity was significant (QE = 111.36, $p < 0.0001$), while the test of moderators (QM = 3.41, $p = 0.4914$) was not, suggesting that the moderators—publication year, sample size, cardiac center, and follow-up duration—did not significantly account for variability in bleeding risk. The intercept (estimate = 52.42, $p = 0.3245$) and all moderators had non-significant effects, indicating high uncertainty and no meaningful contribution to explaining heterogeneity (Supporting Information).

TABLE 1 | Demographic and methodological characteristics of included studies.

Author and year	Country	Study design	study Population	Follow-up time	Setting	Sample size	Bleeding	TEE
[24]	Ethiopia	Retrospective	Adult patients (≥18 years)	3 months and above	Private cardiac centers	374	17.11	
[25]	Nigeria	Retrospective	Adult patients	5 years	Teaching Hospital	26	11.5	
[2]	South Africa	Retrospective	Adult patients (≥18 years)	One-year period	Teaching Hospital	126	46	
[21]	South Africa	Retrospective	Adult patients	6 months	INR clinic	136	14	
[26]	Ethiopia	Retrospective	Adult outpatients	2 years	Anticoagulation clinic	300	20.67	4.67
[27]	Ethiopia	Retrospective	Adults	≥6 months	Cardiology and Hematology clinics	338	25	
[28]	Sudan	Retrospective	Private cardiology clinic attendants	14 months	Cardiology clinic	21	9.5	
[18]	Sudan	Retrospective	Adult patients	12 months	Anticoagulation clinic	135	39.2	
[5]	Ethiopia	Retrospective	Adult patients	2 years	Outpatient department	202	4.5	7.4
[11]	Tunisia	Prospective	≥18 years	1 year	Cardiac clinic	915	5.8	1.64

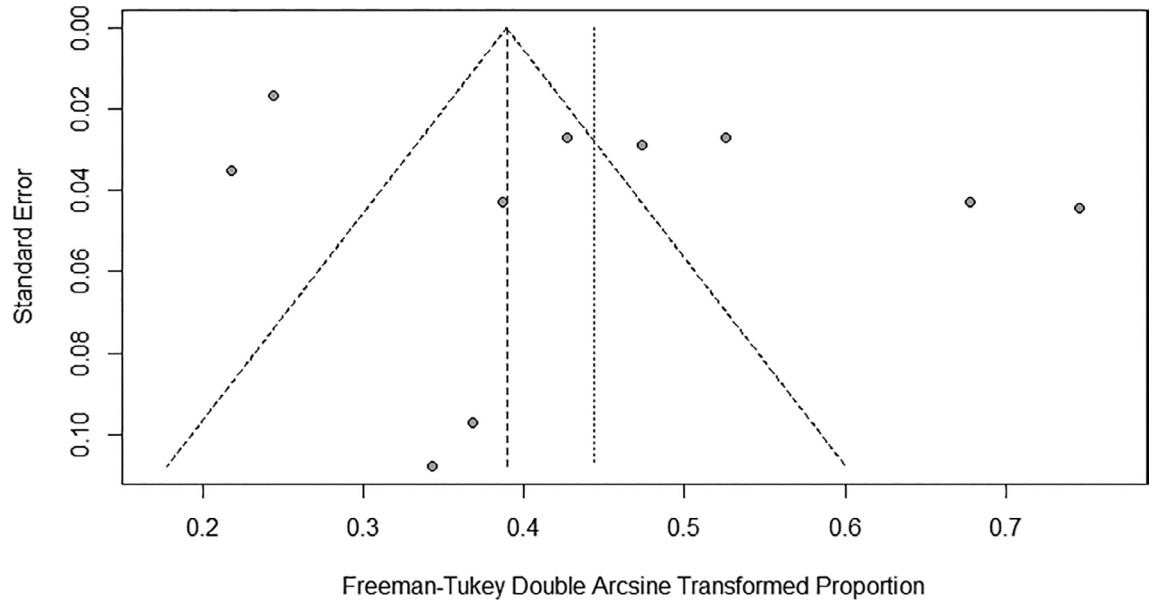

FIGURE 2 | Funnel plot for bleeding.

4.4.2 | Sensitivity Analysis

The sensitivity analysis of bleeding risk indicated that the pooled proportion of bleeding events across the included studies was 0.14 (95% CI: 0.13–0.15), with an I^2 value of 97%. For each omitted study, the proportion remained between 0.12 and 0.20 (Figure 3). For TEE, two proportions of 0.02 and one proportion of 0.05 were recorded (Figure 4).

4.4.3 | Proportion of Bleeding and Thromboembolic Events

The forest plot illustrates the proportions of bleeding events reported across the included studies, encompassing a total of 403 bleeding events among 2546 patients. The pooled proportion of bleeding was 0.18 (95% CI: 0.10–0.27), indicating that, on average, 18% of patients experienced bleeding. However,

there was considerable variation across individual studies, with reported proportions ranging from as low as 0.04 in the study by Masresha et al. to as high as 0.46 in Jacobs [29]. This wide variability is further reflected in the substantial heterogeneity among studies, as indicated by an I^2 value of 96%. Additionally, the PI, estimated at 0.00 to 0.57, suggests that future studies could observe bleeding rates anywhere within this broad range, highlighting the inconsistency of findings across the existing literature (Figure 5).

In Sub-Saharan Africa, 3% of warfarin users experienced TEEs (95% CI: 0.01–0.17; Figure 6), with substantial heterogeneity ($I^2 = 87\%$) and a PI ranging from 0.00 to 0.93.

5 | Discussion

This systematic review and meta-analysis, synthesizing data from 10 observational studies, assessed the clinical outcomes of warfarin anticoagulation, focusing on bleeding risk and TEE rates as key safety parameters. The meta-analysis showed a pooled bleeding proportion of 0.18 (95% CI: 0.10–0.27) across 11 studies, with substantial heterogeneity ($I^2 = 96\%$). The PI ranged from 0.00 to 0.57, indicating considerable variability in bleeding risk across settings. Notably, Jacobs, 2017 reported the highest bleeding proportion (0.46), which is markedly above the pooled estimate and may have disproportionately influenced both the overall effect size and the observed

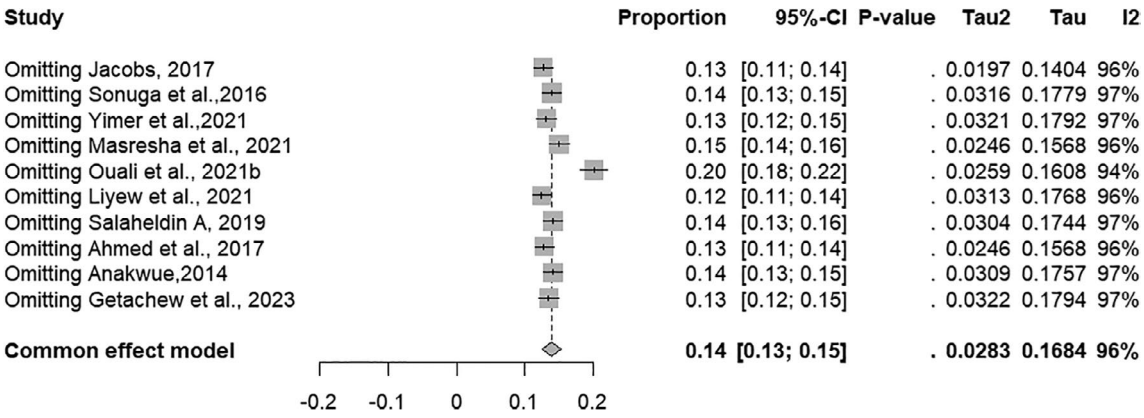

FIGURE 3 | Sensitivity analysis for bleeding.

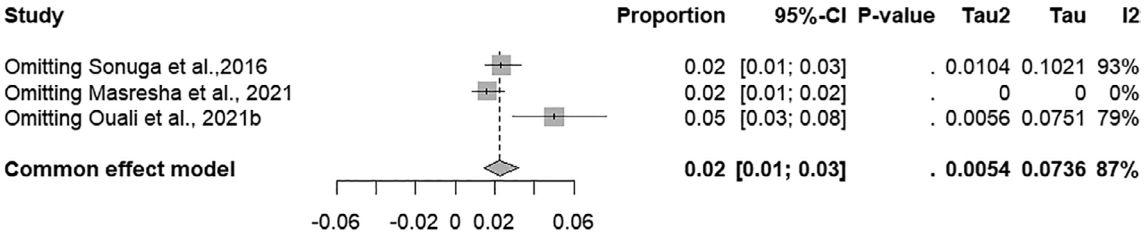

FIGURE 4 | Sensitivity analysis for thromboembolic events.

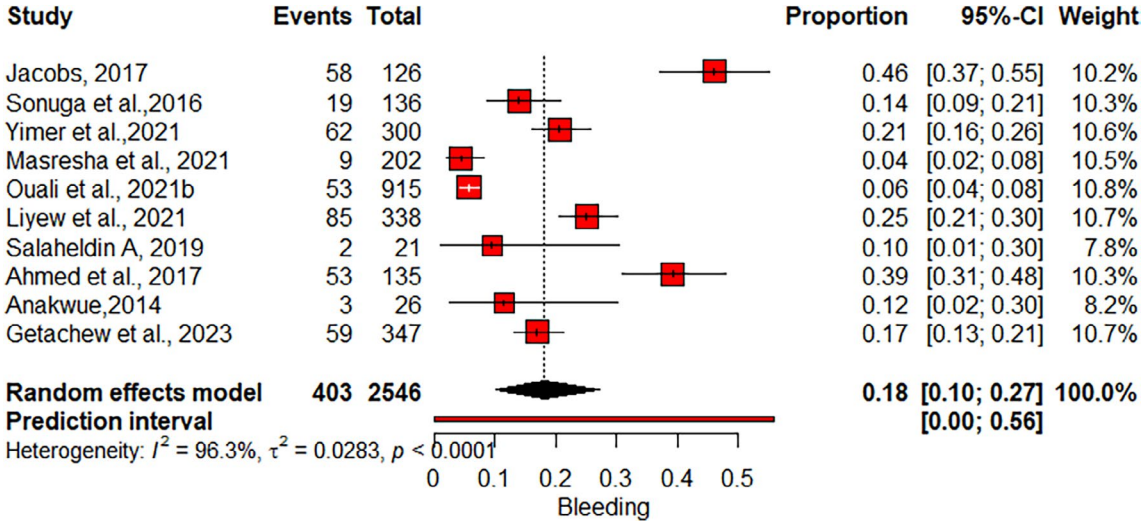

FIGURE 5 | Forest plot of bleeding risk.

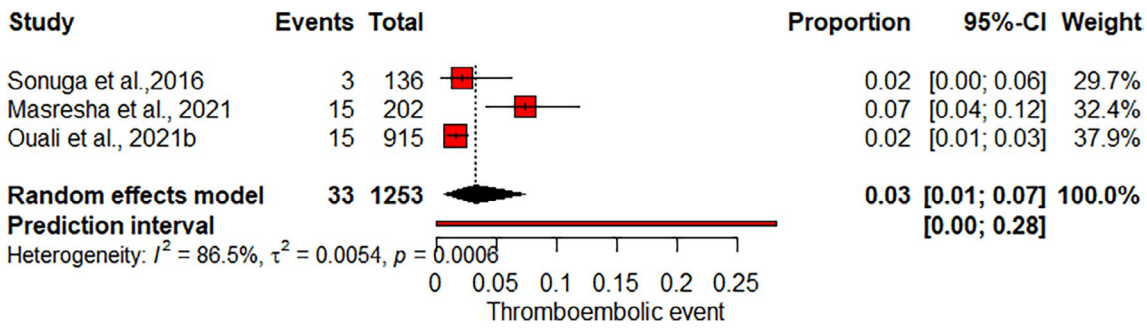

FIGURE 6 | Forest plot of thromboembolic events.

heterogeneity. In contrast, Masresha et al. and Ouali et al. reported the lowest proportions (0.04 and 0.06, respectively), potentially contributing to the wide range and heterogeneity. The extreme values reported by these studies suggest they may be outliers and primary drivers of the variability seen in the meta-analysis.

The pooled proportion of bleeding risk was comparatively higher than previous studies; for example, Mihm et al. [10] reported a 10% bleeding risk among warfarin users, and Lorenz and Linneman [9] found a 17.1% incidence. Additionally, a Japanese prospective cohort by Hosokawa et al. observed a 6.4% three-year clinically relevant bleeding rate [30]. In Turkey, a study reported a 15.23% bleeding incidence among warfarin users [31]. Meanwhile, a multinational study across nine countries indicated a bleeding rate of 20%, highlighting a higher bleeding risk across diverse populations [32].

The current study also reported a 7% rate of TEEs, which contrasts with a lower TEE rate of 3.7% in a pooled analysis by Cardoso et al. [33] and an even lower rate of 2.7% in the work by Holbrook et al. [34]. However, Willeford et al. [35] documented a markedly higher TEE incidence of 54.3%, underscoring the variability in thromboembolic outcomes.

The disparities in anticoagulation quality and TEE incidence highlight the need to consider regional factors, variations in study populations, and methodological differences [36–38]. Variations in bleeding rates may result from sub-therapeutic INR levels, such as the 42% of patients with INR values <2 in the study by Masresha et al., and small sample sizes in studies like Salaheldin [28] with 21 patients and Anakwue et al. [25] with 26, possibly due to limited warfarin use. Additionally, higher bleeding risks (46%) may stem from potential drug–drug interactions (DDIs) with warfarin, as 77% of patients experienced DDIs due to concurrent medications like antimicrobials and CNS agents [2]. Limited physician awareness about these interactions may further elevate bleeding risks [5], while lack of alternative dosage forms complicates dose adjustments [2].

The control of anticoagulation directly influences bleeding risks. In Sub-Saharan African studies, where a 25% bleeding prevalence was observed, only 13% of patients achieved a therapeutic time in range (TTR) of $\geq 65\%$, with therapeutic INR (2.0 to 3.0) attainment at 33%. Supratherapeutic INR values (>3.0) can increase bleeding risk, while sub-therapeutic INR values (<2.0), often due to undertreatment from fear of bleeding, may lead to lower effectiveness and heightened thromboembolic risk. Patient compliance is also crucial; Liyew et al. [27] found a 24% non-adherence rate among warfarin users, potentially linked to low awareness of oral anticoagulant benefits. This indicates gaps in healthcare systems in Sub-Saharan Africa, where specialized anticoagulation centers, self-care initiatives, and adequate follow-up are limited.

The narrow therapeutic index of warfarin and its unpredictable pharmacokinetics further challenge anticoagulation safety. Patient-specific factors, including age, weight, and pharmacogenomics, play a role in reducing the risk of suboptimal anticoagulation [16, 39]. Genetic variations, particularly in cytochrome P450 enzymes (e.g., CYP2C9, VKORC1, and CYP4F2), affect warfarin metabolism. Variants like CYP2C9*2* and *CYP2C9*3 can lower warfarin dose requirements by 39% [40]. The limited application of pharmacogenomics in African settings emphasizes the need for genetic profiling to optimize anticoagulant safety [41].

Healthcare systems should prioritize addressing anticoagulation safety, especially in regions with high TEE and bleeding risks, such as Sub-Saharan Africa [42]. Close monitoring and dose adjustments to maintain INR ≥ 1.8 within the first 6 days of therapy can reduce hospitalization duration and improve patient safety [43]. This approach aligns with findings that adjusted-dose warfarin therapy can decrease stroke risk by nearly 60% [12].

Improving anticoagulation in resource-limited settings requires a multifaceted approach, including decentralization of care, increased anticoagulant availability, and enhanced support for both healthcare providers and patients. Developing dosing protocols for initiation and maintenance that consider locally relevant factors is crucial [44]. Other supportive measures include raising public awareness, improving healthcare financing, expanding access to health facilities, and overcoming language barriers to enhance patient safety [45]. Monitoring DDIs and comorbidities is essential for optimal anticoagulation; an Ethiopian study found that coadministration of warfarin with multiple drugs reduced TTR, and Yimer et al. [26] noted heart failure as a contributing factor to suboptimal anticoagulation. Establishing anticoagulation management centers and incorporating NOACs could improve outcomes, but many Sub-Saharan clinics lack routine NOAC availability, necessitating policies for affordable access and staff training [46].

In conclusion, our systematic review and meta-analysis highlight safety challenges in warfarin use, with high bleeding and

TEE rates in Sub-Saharan Africa. Improved monitoring, dose management, and supportive healthcare infrastructure are essential to enhance warfarin safety and effectiveness, leading to better outcomes for anticoagulation-reliant patients in the region. Further research and tailored healthcare interventions are necessary to ensure safe and effective warfarin therapy.

6 | Strength and Limitations of the Study

A key strength of this systematic review and meta-analysis is its comprehensive assessment of warfarin safety across multiple Sub-Saharan African contexts, providing insights into bleeding and TEE rates. Furthermore, the review adhered to PRISMA reporting standards, which supports methodological transparency and rigor. However, several limitations exist. Primarily, the reliance on cross-sectional studies restricts causal inferences and limits understanding of anticoagulation outcomes over time. Small sample sizes introduce selection bias, reducing generalizability and the ability to detect rare, clinically significant events. Another limitation is that the exclusion of grey literature and unpublished studies could contribute to bias. Most of the included studies reported bleeding as a dichotomous outcome (yes/no) without detailed follow-up data. As a result, key longitudinal indicators—such as TTR, bleeding recurrence, or time to bleeding event—were often unreported or inconsistently measured, precluding their inclusion in the analysis. These outcomes are important for understanding bleeding dynamics over time but were beyond the scope of the available data. We acknowledge this as a limitation and recommend that future studies provide standardized and time-based bleeding outcomes to facilitate more comprehensive analyses. Variations in healthcare infrastructure across study settings, such as the presence or absence of specialized anticoagulation clinics, likely contributed to differences in anticoagulation quality and, consequently, bleeding or TEE rates. These disparities may have affected key aspects of the studies, including INR monitoring quality, outcome definitions, follow-up duration, and reporting standards, thereby challenging data consistency and depth. Future research should prioritize robust, multicenter longitudinal studies across diverse regions, enhancing the representativeness of findings and offering actionable insights to strengthen anticoagulation management and patient safety in resource-limited settings. The health care system in Sub-Saharan Africa should also emphasize the application of cross-country or inter-institutional collaboration to mitigate resource constraints.

6.1 | Plain Language Summary

Warfarin is a widely prescribed blood thinner, but its use in Sub-Saharan Africa is associated with risks of bleeding and thromboembolic events, with unclear prevalence rates. This systematic review and meta-analysis aimed to quantify the occurrence of these events among patients on warfarin in the region. We reviewed data from 10 studies involving 2546 patients, conducting a meta-analysis using RStudio to estimate the prevalence of bleeding and thromboembolic events. We assessed major and minor bleeding as primary outcomes and thromboembolic events as secondary outcomes. To account for variations across studies, we used the Freeman–Tukey double arcsine method and conducted meta-regression. Publication bias was assessed using funnel plots and Egger's test, with sensitivity analysis performed through leave-one-out testing. Our analysis revealed that 18% of patients experienced bleeding events, with a range from 4% to 46%. Additionally, 6% of patients had thromboembolic events. These findings highlight the importance of regular monitoring for warfarin users in Sub-Saharan Africa, as the risks can vary widely. The study underscores the need for personalized treatment plans to balance warfarin's effectiveness with its potential risks, providing valuable insights for healthcare providers and policymakers.

Author Contributions

Conceptualization: D.G.D., C.T., and Z.D.A. Formal analysis: D.G.D. and C.T. Methodology: B.B, and M.B.Y. Supervision, D.G.D., C.T., and B.B. Writing – original draft: D.G.D. and G.M. Writing – review and editing: D.F.B. and C.T. All authors have read and agreed to the final version of the manuscript.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** pds70225-sup-0001-supinfo.docx. **Data S2:** pds70225-sup-0002-supinfo.docx.