

# Warfarin

## Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Management of Atrial Fibrillation and Venous Thromboembolism

Source: Adam SS, McDuffie JR, Ortel TL, Williams JW. *Ann Intern Med.* 2012;157:796-807  
 Conflicts of Interest: Ortel: consultancy (Boehringer Ingelheim; Bristol-Myers-Squibb), grant (Eisai), trial participation (Pfizer; Daiichi Sankyo), Williams: grant (VA Health Services Research.)

### CLINICAL SUMMARY

#### EFFECTIVE

●●○ Atrial fibrillation: patients taking direct thrombin and factor Xa inhibitors had lower all-cause mortality compared with patients taking warfarin.

●●○ Risk of fatal bleeding was lower with direct thrombin and factor Xa inhibitors compared with patients taking warfarin.

●●○ Subgroup analysis suggested a higher risk of myocardial infarction with direct thrombin inhibitors than with factor Xa inhibitors.

#### UNKNOWN EFFECT

- Nothing to report.

#### UNLIKELY EFFECTIVE

- Venous thromboembolism: direct thrombin and factor Xa inhibitors did not differ for mortality, recurrent deep vein thrombosis, or pulmonary embolism compared with warfarin.

#### POSSIBLY INEFFECTIVE OR HARMFUL

- Nothing to report.

### REVIEW INFORMATION

|                      |   |
|----------------------|---|
| <b>Participants</b>  | Adults, ≥18 years with history of chronic nonvalvular atrial fibrillation (AF), deep venous thromboembolism (VTE), or mechanical valve replacement (excludes pregnant population) |
| <b>Interventions</b> | NOAC compared to warfarin and low molecular weight heparin  |
| <b>Outcomes</b>      | Primary: thromboembolic event   |
| <b>Study Types</b>   | Randomized controlled trials (RCTs)   |
| <b>Limitations</b>   | No head-to-head comparisons of NOACs; limited data on harms   |

| CLINICAL CONDITION     | TREATMENTS  | # months follow-up in trial participants | # trials | OUTCOMES  | ADVERSE EVENTS  |
|------------------------|---|--|----------|---|---|
|                        |   |  |          |   |   |
| Atrial Fibrillation    | Direct thrombin inhibitor (DTI) / factor Xa (FXa) inhibitors compared with warfarin<br><br>Participants: 22,256 (DTI / FXa inhibitors); 22,185 (warfarin) | 21-24                                    | 3        | <b>Outcome: Death</b><br>●●○<br>Favours DTI / FXa inhibitors<br>RR: 0.88; 95% CI: 0.82-0.96<br><br><b>Outcome: Hemorrhagic Stroke</b><br>●●○<br>Favours DTI / FXa inhibitors<br>RR: 0.48; 95% CI: 0.36-0.92<br><br><b>Outcome: Hemorrhagic Stroke</b><br>●●○<br>Favours DTI / FXa inhibitors<br>RR: 0.48; 95% CI: 0.36-0.92   | <b>Fatal Bleeding</b><br>●●○<br>Risk of fatal bleeding: lower with DTI / FXa inhibitors when compared with warfarin<br>RR: 0.60; 95% CI 0.46-0.77<br><br><b>Major Bleeding</b><br>●●○<br>Risk of fatal bleeding: lower with DTI / FXa inhibitors when compared with warfarin<br>RR: 0.60; 95% CI 0.46-0.77  |
| Venous thromboembolism | Direct thrombin inhibitor (DTI) / factor Xa (FXa) inhibitors compared with warfarin<br><br>Participants: 5417 (DTI / FXa); 5388 (warfarin)                | 3-12                                     | 3        | <b>Outcome: Death</b><br>●●○<br>No statistically significant difference in the effects of DTI / FXa inhibitors when compared with warfarin<br>RR: 0.97; 95% CI: 0.72-1.30<br><br><b>Outcome: Recurrent Deep vein thrombosis / Pulmonary embolism</b><br>●●○<br>No statistically significant difference in the effects of DTI / FXa inhibitors when compared with warfarin<br>RR: 0.95; 95% CI: 0.71-1.27<br><br><b>Outcome: Thromboembolism death</b><br>●●○<br>No statistically significant difference in the effects of DTI / FXa inhibitors when compared with warfarin<br>RR: 1.00; 95% CI: 0.48-2.10 | <b>Gastrointestinal Bleeding</b><br>●○○<br>Risk of gastrointestinal bleeding: increased with DTI / FXa inhibitors when compared with warfarin<br>RR: 1.30; 95% CI 0.97-1.73<br><br><b>Myocardial Infarction</b><br>●○○<br>Risk for myocardial infarction: no statistically significant differences between DTI / FXa inhibitors when compared with warfarin<br>RR: 0.95; 95% CI 0.81-1.11<br><br><b>Liver Dysfunction</b><br>●○○<br>Risk for liver dysfunction: no statistically significant differences between DTI / FXa inhibitors when compared with warfarin<br>RR: 0.82; 95% CI 0.56-1.18 |

#### RISK RATIOS (RR)

Probability that member of exposed group will develop a disease relative to probability that member of unexposed group will develop the same disease.

|          |  |
|----------|--|
| RR = 1.0 | No association between risk factor and disease |
| RR > 1.0 | Risk is increased                              |
| RR < 1.0 | Risk is decreased                              |

#### STRENGTH OF RESEARCH EVIDENCE

Ratings are based on the overall quantity and quality of clinical evidence.

●●●  
**STRONG**

Results consistent from high quality studies. Conclusions unlikely to change with further research.

●●○  
**MODERATE**

Current research supports findings, however conclusions could change with further research.

●○○  
**WEAK**

Limited studies available for drawing conclusions, or existing studies have significant limitations.