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ORIGINAL ARTICLE

# Systematic review of cost-effectiveness analyses of novel oral anticoagulants for stroke prevention in atrial fibrillation☆

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**KEYWORDS**
Novel oral anticoagulants;
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Atrial fibrillation

**Abstract**
*Introduction and Objectives:* Novel oral anticoagulants are emerging options for the prevention and treatment of thromboembolic diseases. They are increasingly used in clinical practice due to their simplicity of use and clinical benefits, but an important step is to evaluate their cost-effectiveness. The aim of the AFFORD study (A Review of Cost EFFectiveness of Novel ORal Anticoagulant Drugs) was to perform a systematic review of cost-effectiveness studies of novel oral anticoagulants for stroke prevention in non-valvular atrial fibrillation (AF).
*Methods:* A systematic review of the literature was conducted by searching the PubMed, Embase, Scopus, Cochrane and Web of Knowledge databases to identify all cost-effectiveness studies of novel oral anticoagulants for stroke prevention in AF.
*Results:* The search identified 27 studies, 18 with dabigatran, three with apixaban, two with rivaroxaban and four with at least two of these drugs. The incremental cost-effectiveness ratios were 30 405±16 101 euros per quality-adjusted life-year (QALY) for dabigatran 110 mg, 17 566±16 902 euros/QALY for dabigatran 150 mg, 8102±3252 euros/QALY for age-adjusted dabigatran, 11 897±3341 euros/QALY for apixaban and 17 960±12 005 euros/QALY for rivaroxaban.
*Conclusion:* The present systematic review demonstrates that novel oral anticoagulants are cost-effective for stroke prevention in AF.


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**PALAVRAS-CHAVE**
Novos anticoagulantes orais;
Apixabano;
Dabigatrano;
Edoxabano;
Rivaroxabano;
Custo-efetividade;
Fibrilhação auricular

**Revisão sistemática das análises custo-efetividade dos novos anticoagulantes orais na prevenção do acidente vascular cerebral na fibrilhação auricular: estudo AFFORD**

**Resumo**
*Introdução e objetivos:* Os novos anticoagulantes orais são opções emergentes para a prevenção e tratamento das doenças tromboembólicas. São cada vez mais usados na prática clínica pela facilidade do seu uso e pelos seus benefícios clínicos, mas a sua utilização mais generalizada carece de demonstração de custo-efetividade. O objetivo do estudo A Review of Cost EFFectiveness of Novel ORal Anticoagulant Drugs (AFFORD) consistiu na realização de uma revisão sistemática dos estudos de custo-efetividade dos novos anticoagulantes orais na prevenção do acidente vascular cerebral (AVC) na fibrilhação auricular não valvular (FA).
*Métodos:* Foi realizada uma revisão sistemática da literatura nas bases de dados Pubmed, Embase, Scopus, Cochrane e Web of Knowledge para identificar todos os estudos de custo-efetividade dos novos anticoagulantes orais na prevenção do AVC na FA.
*Resultados:* A pesquisa selecionou 27 estudos, 18 com dabigatrano, três com apixabano, dois com rivaroxabano e quatro com pelo menos dois destes fármacos. Os rácios custo-efetividade incremental por anos de vida ajustados para qualidade foram de 30.405 ± 16.101 euros para o dabigatrano 110 mg, 17.566 ± 16.902 euros para o dabigatrano 150 mg, 8.102 ± 3.252 euros para o dabigatrano ajustado à idade, 11.897 ± 3.341 euros para o apixabano e 17.960 ± 12.005 euros para o rivaroxabano.
*Conclusões:* A presente revisão sistemática demonstra que os novos anticoagulantes orais são custo-efetivos para a prevenção do AVC na FA.


**List of abbreviations**

| | |
|---|---|
| AF | atrial fibrillation |
| CAD | Canadian dollar |
| CHF | Swiss franc |
| EUR | euro |
| GBP | UK pound |
| ICER | incremental cost-effectiveness ratio |
| INR | international normalized ratio |
| OAC | oral anticoagulants |
| QALY | quality-adjusted life years |
| USD | US dollar |
| VKA | vitamin K antagonists |
| WTPT | willingness-to-pay threshold |
| ZAR | South African rand |

## Introduction

Health expenditure is growing faster than wealth creation in most developed countries. In Portugal, per capita state health expenditure rose from 0.3 euros in 1972 to 989.4 euros in 2012, while total expenditure increased from 2.8 million euros (0.2% of gross domestic product) in 1972 to 10 430.5 million euros (6.3%) in 2012.[1] State expenditure on drugs, which in 2010 accounted for 17% of total health spending, has risen in parallel with overall health expenditure.[1]

This investment has led to improvements in health indicators, notably increased life expectancy.[2] However, there is growing awareness that the available resources for medical treatments, including drug therapy, are increasingly limited. Economic evaluations are designed to rationalize the use of these resources and to direct them where they are most needed.

In this context, cost-effectiveness analyses are a valuable tool to compare the cost of a health intervention with the expected health gains.[3] Interventions include any action intended to improve health that uses financial and/or human resources.

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice,[4] and results in a considerable burden in economic terms as well as in morbidity and mortality. Stroke prevention by anticoagulant therapy is the mainstay of AF treatment.[5]

AF is associated with a prothrombotic state caused by atrial blood stasis and structural heart disease, which predispose to thrombus formation, particularly in the left atrial appendage, and to cardiac embolism. As a result, AF patients have a fivefold greater risk of stroke and systemic embolism than those without AF.[5]

Anticoagulant therapy is the cornerstone of prevention and treatment of thromboembolic disease.[6] Novel oral anticoagulants (OAC) represent a step forward, being easier to use and presenting a more favorable pharmacological profile than vitamin K antagonists (VKA). They also have more rapid onset of action and a more predictable anticoagulant response, eliminating the need for monitoring.[6]