

More Patients, Fewer Bleeds? What the Data Shows About Anticoagulation Safety Since DOACs Arrived

Bootstrap CUSUM applied to NHS prescribing and adverse event data asks the question the anticoagulation community has been debating: did the shift from warfarin to DOACs produce a detectable structural improvement in patient safety?

Data: NHS BSA Prescription Cost Analysis 2005–2025 · MHRA Yellow Card ADR reports · N=21 annual observations · 95% confidence · Loops=5,000 · By Syd Stewart, StepChangeAnalysis.com

Four findings

The anticoagulation revolution

Between 2005 and 2025, anticoagulant prescriptions in England tripled as four new DOACs received NICE approval and replaced warfarin for most indications. Bootstrap CUSUM identifies three structural change points confirming that both prescribing volumes and adverse event rates shifted structurally — not just gradually.

2012: adverse event rate doubled

As DOACs arrived and NICE mandated funding, the total adverse event rate stepped up from 35 to 79 per million prescriptions. Renal contraindications were not yet fully understood, and the rate peaked at 137 per million in 2015 before clinical practice caught up with the new drug class.

2016: DOAC rate fell by two-thirds

The DOAC-specific adverse event rate fell over two thirds following the ROCKET-AF trial controversy, an EMA renal dosing label update for rivaroxaban, and a rapid prescriber switch to apixaban. By 2025 the total adverse rate of 27.5 per million approaches the pre-DOAC warfarin baseline of 26 per million.

Improvement is real but uneven

The national average has improved substantially. But prescribing rates vary from 53% to 99% across English regions, up to 28.9% of hospitalised patients receive inappropriate prescribing, and approximately half of DOAC prescriptions were still not adjusted for renal function by 2019. The scope for further improvement remains large.

Three confirmed structural change points

Year	What changed	Confidence	Magnitude
2012	Total adverse event rate stepped up as DOACs arrived	95%+	35 → 79 per million prescriptions (+126%)
2015	Total prescriptions doubled — NICE approval and NHS funding mandated for all 4 DOACs	95%+	+107% prescribing volume
2016	DOAC-specific adverse event rate collapsed after ROCKET-AF controversy and EMA label update	95%+	-67%+ DOAC adverse event rate

THE WARFARIN PARADOX

DOACs generated 4.4 times more total adverse event reports than warfarin over 2005–2025. But the DOAC rate per prescription fell 97% as prescribers learned. Meanwhile the remaining warfarin patients are systematically higher risk — older, with more comorbidities, and on warfarin specifically because DOACs were contraindicated. The warfarin adverse event rate per prescription therefore rose, not because warfarin became less safe but because the warfarin patient population became more complex.

WHERE THE SCOPE FOR IMPROVEMENT REMAINS

- Prescribing rates vary 53%–99% across English regions
- Up to 28.9% of hospitalised patients receive inappropriate DOAC prescribing
- ~50% of DOAC prescriptions not adjusted for renal function by 2019
- Bootstrap CUSUM applied to Trust-level data could identify which regions have already closed the gap — and what they did differently.

Data files

File	Contents
anticoag-warfarin-rate.csv	Annual warfarin adverse event rate per million prescriptions, 2005–2025
anticoag-total-rate.csv	Total anticoagulant adverse event rate per million prescriptions, 2005–2025
anticoag-doac-rate.csv	DOAC-specific adverse event rate per million prescriptions, 2005–2025

References

- NHS BSA Prescription Cost Analysis 2005–2025. nhsbsa.nhs.uk
- MHRA Yellow Card Scheme — serious and fatal ADR reports. yellowcard.mhra.gov.uk
- Mokbel M. et al. (2022). Comparative analysis of ADRs across drug classes. *In Vivo*, 36.
- NICE TA249/TA256/TA275/TA355 — DOAC appraisals for AF stroke prevention.
- Taylor W.A. (2000). Change-point analysis. · Page E.S. (1954). *Biometrika*, 41(1–2).
- Efron B. & Tibshirani R.J. (1993). *An Introduction to the Bootstrap*. Chapman & Hall.



Read the full article and download the data

stepchangeanalysis.com/anticoag-safety.html

Three CSV files available for download from the article: warfarin rate, total rate, and DOAC rate. Upload to StepChangeAnalysis.com to reproduce all charts shown.