# Quality Improvement Initiatives to Reduce Anticoagulation-related Harm:

# A review of literature and practice

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## Abbreviations

ACS Anticoagulation stewardship

ACSQHC Australian Commission for Safety and Quality in Healthcare

ADE Adverse drug event

AF Atrial fibrillation

AHRQ Agency for Health Research and Quality

AI Artificial intelligence

AMS Antimicrobial stewardship

CDSS Clinical decision support system

CI Confidence interval

CPOE Computerised physician order entry

DHB District Health Board

DOAC Direct oral anticoagulant

DVT Deep vein thrombosis

ECMO Extracorporeal membrane oxygenation

ED Emergency department

EHR Electronic health record

EMR Electronic medical record

FDA Federal Drug Administration

GI Gastrointestinal

GP General Practitioner

GPT-3 Generative pre-trained transformer

HIT Heparin-induced thrombocytopenia

INR International normalised ratio

ISMP Institute for Safe Medical Practices

IT Information technology

LMWH Low molecular weight heparin

MHRA Medicines and Healthcare Products Regulatory Agency

MIDAS Mentored Implementation and Dissemination of Anticoagulation Stewardship

NHS National Health Service (UK)

NICE National Institute for Health and Care Excellence

NPSG National Patient Safety Goal

OR Odds ratio

PE Pulmonary embolism

PGY1/PGY2 Post-graduate year 1/2 (junior doctors)

QI Quality improvement

RCT Randomised controlled trial

SPSP Scottish Patient Safety Programme

TTR Time in therapeutic range

UK United Kingdom

US United States

VTE Venous thromboembolism

WHO World Health Organization

## Executive Summary

The clinical benefits of anticoagulants come with risks and significant anticoagulant-related harm has been described. Despite these risks the use of anticoagulants is not always based on guidelines. In New Zealand, common errors in the prescribing of anticoagulants include medication interactions, incorrect dosing and timing around dosing, patients not being monitored, and prescribers not taking renal function into account. Additionally, anticoagulation must be appropriately managed before and after procedures and across transitions of care.

The Health Quality & Safety Commission (The Commission) is undertaking a quality improvement (QI) project with the aim of reducing harm from the use of anticoagulants. This report presents the findings of a commissioned review of hospital QI initiatives that aim to reduce anticoagulant-related harm. The aim was to identify academic literature, institutional guidance, and New Zealand QI initiatives including systems, processes, or practices, relevant to the safe use of anticoagulants.

Anticoagulation stewardship programmes were found to show promise for improving adherence to guidelines, more appropriate prescribing, improved institutional processes, with potential cost-savings, and possible trends towards reduction in adverse events.

Evidence indicates there are benefits of increasing pharmacist involvement in prescribing, review of prescriptions, management of anticoagulation, and education and counselling for patients taking anticoagulants.

Technological interventions such as electronic alerts have been associated with improved prescribing quality, and the use of app-based guidance or electronic clinical decision support systems (CDSS) may be associated with fewer emergency department visits or decreased rates of venous thromboembolism, however the evidence is weak.

Institutional advice supports the use of anticoagulation stewardship, monitoring and evaluation and continuous quality improvement.

In New Zealand, DHBs have implemented a range of ad hoc approaches to ensuring the safe use of anticoagulants. However, most of these approaches have not been audited, evaluated, or systematically deployed. One notable exception is a peri-procedural anticoagulation bridging service at Capital and Coast DHB.

Based on the evidence sourced, this report concludes that three areas of apparent utility stand out. These are:

* Expanding the role of pharmacists
* Anticoagulation stewardship programmes
* Improved use of the electronic health record and CDSS to support the above and facilitate efficient audit and evaluation

The discussion that follows describes specific details of suggested evidence-based interventions, the core components of stewardship programmes, and links to case studies and step-by-step approaches, as well tools for organisational self-assessment guidance.

## Introduction and Aims

Anticoagulants include unfractionated and low molecular weight heparins (LMWH), vitamin K antagonists such as warfarin, as well as direct oral anticoagulants (DOACs). These medicines are commonly used by individuals with cardiac and vascular conditions. Uses include stroke prevention for those with atrial fibrillation (AF) and prosthetic heart valves, as well as to reduce the risk of venous thromboembolism (VTE) in those with pulmonary embolism (PE) or deep vein thrombosis (DVT). The use of anticoagulants in the inpatient setting is very common with up to 40 per cent of medical inpatients warranting VTE prophylaxis (Anticoagulation Forum 2019b). Despite these benefits, anticoagulants are used less commonly than evidence-based practice guidelines recommend.

However, the use of anticoagulants is also associated with risks. There is an elevated risk of bleeding, and this can be exacerbated by patient factors such as poor renal function, or other factors such as drug-drug interactions. Despite these risks the use of anticoagulants does not always adhere to guideline recommended cautions.

Evidence has described under and over-utilisation of anticoagulants, inappropriate prescribing, inappropriate laboratory testing and diagnostics, suboptimal management of adverse drug reactions (ADEs), suboptimal care transitions, and excessive adverse event rates including bleeding and thrombosis. In New Zealand, common errors in the prescribing of anticoagulants include medication interactions, incorrect dosing and timing around dosing, patients not being monitored, and prescribers not taking renal function into account (Savage and Kunac 2016).

Analysis of anticoagulation-related adverse events has shown that prescribers’ active errors rather than latent system factors are often a root cause of DOAC-related incidents. This may reflect lack of awareness of guidelines, or insufficient prescriber education, and may suggest avenues for quality improvement, such as increasing the role of pharmacists (Haque et al 2021). As many as one in six DOAC prescriptions do not follow guideline recommendations (Vazquez and Barnes 2022).

The situation is complicated by the fact that recent years have seen the introduction of the new direct oral anticoagulants. These DOACs require less monitoring but remain very high-risk medications (Frazer et al 2019). The DOACs require different dosing regimens, have different indications for use, along with expanding indications for anticoagulation use, new specific reversal agents, and the fact that many people taking anticoagulants need to undergo invasive procedures requiring an interruption to anticoagulation. There are few hospital anticoagulation monitoring services (Ahuja, Raco, Papadopoulos, and Green 2021), and although some jurisdictions have community anticoagulation monitoring services, these don’t always include the DOACs (Sylvester et al 2018), although it has been argued that they should (Clark 2018).

The Health Quality & Safety Commission (The Commission) is undertaking a quality improvement (QI) project with the aim of reducing harm from the use of anticoagulants. The Commission worked with the sector to identify a specific area for focus. The Commission has also identified (by survey of the DHB Quality and Risk leads) several projects across New Zealand relevant to this aim. The present work seeks to identify national and international work on QI to reduce anticoagulant harm and to understand the efficacy of different approaches and interventions.

### Aim and Scope

The aim of the following review was to identify academic literature, institutional guidance, and New Zealand QI initiatives including systems, processes, or practices, relevant to the safe use of anticoagulants. The focus was on evidence since 2015, in a public hospital setting, where there has been a change or adjustment in anticoagulants, including reversal of anticoagulation, treatment planning, procedure or surgery postponement, and at discharge. The focus was adult consumers and identified QI should be able to be applied nationally. Anticoagulants of interest included the use of LMWHs, unfractionated heparin, vitamin K antagonists, and DOACs.

## Methods

The literature scan consisted of a non-systematic, time-limited search. The search comprised three parts (1) a review of the academic literature since 2015, (2) a review of advice published by international institutions, (3) a survey of activities occurring at DHBs around New Zealand.

### Academic Literature Review

The Ministry of Health conducted a literature search in December 2021 on, ‘Quality improvement activities to reduce harm from anticoagulant/antiplatelets’ (see Appendix B for detailed search strategy). This review provided the basis for an extended and targeted search with the aim of complementing the sources identified in the Ministry’s search and the following databases were further examined: PubMed, Cochrane, Google Scholar, MedRxiv, and SafetyLit.

Targeted supplementary searches were undertaken on PubMed on 19 and 20 May 2022. Five targeted search queries are described in Appendix B. In total 2,183 titles were screened, and 94 abstracts were obtained.

Review of the Cochrane Database provided 3 additional sources, Google Scholar returned 6 in the first ten pages that were not duplicates of sources already obtained, MedRxiv and SafetyLit both returned no additional results.

A new semantic artificial intelligence (AI) search assistant called ‘Elicit’ was tested. Elicit is a semantic AI assistant that identifies relevant literature using GPT-3 (an AI language model).[[1]](#footnote-1) Search queries are phrased in natural language rather than keywords. The search engine uses semantic structure to infer the papers of interest, results are refined by iteratively selecting results of interest and searching for ‘more like these’. Elicit was deployed on 19 May 2022 with the following query:

Query:‘Reviews or randomised trials or studies that report on interventions or initiatives to reduce harm from anticoagulants or improve patient safety when anticoagulation is used. The studies should focus on human factors or systems interventions or quality improvements’

When limited to papers since 2015 and following ten iterations of selecting in-scope sources and instructing ‘more like these’, the Elicit search returned 19 additional sources that were not duplicates of sources already obtained.

Results from the Ministry’s search were screened by abstract. Of 82 abstracts retained, 36 were out-of-scope (often because they focused on primary care or were primarily reporting on strategies to increase anticoagulation use in AF), 11 had already been obtained in the searches above, and of 33 not already obtained 6 sources were relevant.

In total 58 full-text papers were obtained from the academic literature.

### Search for Institutional Guidance

The grey literature was searched by scanning the websites of the following organisations, searching for ‘anticoagulant’ or ‘anticoagulation’:

* UK National Institute for Health and Care Excellence (NICE)
* UK Medicines and Healthcare Products Regulatory Agency (MHRA)
* NHS Improvement
* Scottish Patient Safety Programme (SPSP)
* Agency for Health Research and Quality (AHRQ)
* Australian Commission for Safety and Quality in Healthcare (ACSQHC)
* Health Excellence Canada (previously the Canadian Patient Safety Institute)
* Institute for Safe Medical Practices (ISMP)

### New Zealand Initiatives

In 2021 the Health Quality & Safety Commission conducted a survey of DHB Quality and Risk Leads. This revealed several projects possibly relevant to the present review. These projects are listed in Appendix Table A5 (see section on ‘New Zealand Initiatives’ under ‘Findings’ below). Contact details of pertinent staff (eg medication safety pharmacists, clinical effectiveness or quality facilitators, haematologist) were obtained and a total of 15 individuals from 10 DHBs provided additional information about these projects. Information was obtained by email answers to questions, by phone interviews (n = 6), and by Zoom meetings (n = 1).

## Findings

The following section describes the findings of the review. Academic literature on safety and quality initiatives aimed at reducing anticoagulation-related harm is described first, followed by institutional advice, case studies, and current New Zealand initiatives.

### Academic Literature

A total of 48 sources from the academic literature were retained following full-text review. These were organised by study type and are tabulated in Appendix A. Appendix Table A1 displays meta-analyses and reviews (n = 8). Appendix Table A2 catalogues individual studies arranged by intervention type: anticoagulation stewardship (n = 6), discharge protocols and follow-up (n = 4), pharmacist interventions (n = 11), e-prescribing, electronic health record, clinical decision support systems (CDSS), and apps (n = 8), and ‘other’ interventions (n = 4). Appendix Table A3 presents high-level commentaries, consensus statements and interpretations of the literature (n = 7). The individual studies comprise a mixture of randomised controlled trials as well as non-randomised and observational studies.

#### Reviews of the Literature

Eight reviews of the literature were obtained. Details of these reviews are presented in Appendix Table A1. One systematic review included meta-analysis and evaluated the role of technology-based interventions in the management of oral anticoagulants (Zheng et al 2020). Five systematic reviews examined: EMR interventions to improve safety and quality of anticoagulation (Austin, Barras, and Sullivan 2020), interventions to improve safety and quality of anticoagulant prescribing for therapeutic interventions (Frazer et al 2019), system-wide interventions to improve VTE prophylaxis (Kahn et al 2018), the effect of education on mortality, thromboembolic events, and bleeding in patients taking oral anticoagulants (Paquette et al 2019), and the impact of computerized CDSS on prescribing of oral anticoagulants (Sennesael, Krug, Sneyers, and Spinewine 2020). Two narrative reviews examined patient-focused interventions trialled to support vulnerable patient populations taking oral anticoagulants (Yiu and Bajorek 2019), and pharmacist-led inpatient anticoagulation services (Lee, Davis, and Kielly 2016).

In general, these published reviews rated the quality of research evidence they evaluated to be of insufficiently high quality to make concrete recommendations.

Physician led anticoagulation consultation services may reduce bleeding rates in high-risk patients (based on one study where in-hospital bleeding rates were 58% lower in the physician-led intervention group compared with standard care (95% CI 2–82%; p = 0.03). Decision-supported warfarin dosing, such as the use of dosing nomograms, led to more time with INR in the therapeutic range, but systematic education and feedback programmes for medical prescribers were not effective (Frazer et al 2019).

Supplemental education for patients was evaluated in one systematic review, with findings indicating only low or very-low certainty that patient-important outcomes were improved with serious risk of bias and spurious imprecision in studies (Paquette et al 2019). A narrative review examined patient education, written information, patient decision aids, videos, pharmacist counselling, medication instructions, and multiple-component interventions, specifically aimed at patients with limited health literacy or from culturally and linguistically diverse backgrounds. Studies of several of these interventions reported positive impact in knowledge, reduction in bleeding events, and better INR control (Yiu and Bajorek 2019), however, follow-up timeframes were often short, knowledge alone was assessed in some studies, and studies outside the review criteria were included.

E-health interventions were found to be generally underwhelming or under-studied. Some limited benefits were found for four major EMR interventions including computerised physician order entry (CPOE), clinical decision support systems (CDSS), dashboard utilisation, and EMR implementation in general. However, research investigating clinical impact to the patient was lacking (Austin et al 2020). Nevertheless, alerts increased the proportion of patients who received VTE prophylaxis and decreased the incidence of symptomatic VTE, additionally computer alerts were more effective than human alerts (Kahn et al 2018). A further systematic review focusing just on CDSS for the initiation and monitoring of oral anticoagulants found evidence of significant improvements in practice (in 9 out of 16 studies), however clinical outcomes were poorly reported, the prevalence of CDSS use was low, and the risk of bias precluded general conclusions (Sennesael et al 2020). Meta-analysis evaluating ‘technology-based’ interventions generally to manage warfarin (including telephone), found that the time in therapeutic range was improved, however, there was no statistically significant difference in safety (Zheng et al 2020).

Pharmacist management of heparin and warfarin was found to provide some benefits in surrogate outcomes (greater time in therapeutic INR range, greater INR stability, decreased length of stay, and reduced major drug interactions) and may be associated with reduced patient mortality (Lee et al 2016). However, conclusions were limited by small, poorly designed studies lacking statistical power, and measurement of surrogate outcomes.

#### Individual Studies

The 33 individual studies retained following full-text review are described in Appendix Table A2. The table organises studies first by intervention type and within each type studies are listed very roughly according to quality of the evidence they provide, with more robust studies listed first.

### Anticoagulation Stewardship

Anticoagulation stewardship programmes have been evaluated in several locations. These programmes usually consist of a multicomponent approach involving leadership, guidelines, protocols, anticoagulation services such as pharmacist screening or expert consultation, medication review/reconciliation, education, patient counselling, measurement, and are based on principles imported from antimicrobial stewardship programmes.

In the Netherlands, a prospective, non-randomised, pre-/post- study included 1,886 patients who started anticoagulation therapy in hospital and evaluated a multidisciplinary antithrombotic stewardship programme against usual care (Dreijer, Diepstraten, Leebeek, Kruip, and van den Bemt 2019). Implementation of the programme was associated with significantly greater adherence to guidelines (adjusted OR 1.58, 95% CI 1.21–2.05) with improved practice largely seen with low molecular weight heparins. A composite endpoint of bleeding or thrombosis by three months after hospitalisation showed a trend of reducing by 1.83% per two months (Jan–Dec 2017) following intervention (95% CI -2.58 to -1.08). However, there was no difference for in-hospital bleeding or thrombosis events. All-cause mortality was lower in the intervention period [8.6% (81/945)] compared to the usual care period [11.5% (108/941)] OR 0.72 (0.53 to 0.98). Analysis of causes of death indicated that bleeding and thrombosis were not the driving factors (Dreijer et al 2020).

In the United States, a pre-/post- intervention study evaluated an anticoagulation stewardship programme in which pharmacists and haematologists provided oversight of anticoagulant use, high-cost reversal agents and management of heparin-induced thrombocytopenia. Assessment was triggered by daily review of EMR generated reports. The comparator was usual care. Of 19,445 charts reviewed 1,930 contained a stewardship opportunity. Recommended interventions were accepted 83–91% of the time. Inappropriate use of prothrombin complex concentrate fell from 55.8% pre- to 2.6% post-intervention. The intervention was estimated to be cost-saving (-US$799,690) (Wychowski, Ruscio, Kouides, and Sham 2017). A study in Israel of pharmacist-led anticoagulation stewardship similarly reported high rates of potentially inappropriately prescribed DOACs (one in three), with a high rate of physician acceptance of pharmacist recommendations (70%) (Perlman et al 2019). Another real-time clinical surveillance and management study evaluated a haemostatic and antithrombotic stewardship programme focused on HIT, haemophilia A/B, ECMO, and patients with mechanical cardiac assist devices also found cost-savings (-US$1,449,417 in one financial year) (Reardon et al 2015).

In Australia, a pre-/post- study evaluated a public metropolitan tertiary referral hospital’s implementation of an anticoagulation and analgesic stewardship programme. The programme was based on antimicrobial management services principles and was led by a senior clinical pharmacist and clinical haematologist. It included multidisciplinary governance, clinical education, data and monitoring, QI initiatives and activities, and lead pharmacist involvement in patient-centred care. Hospital acquired VTE, as measured by coded data, reduced by 33% in the following year. Hospital-wide anticoagulant-related bleeds twelve months after programme implementation showed a 20% reduction in events. However, no statistical analysis was presented (Bui et al 2021).

In lower quality evidence, a multi-site hospital system in the United States reported its use of a multidisciplinary anticoagulant taskforce to address anticoagulation-related issues. Institutional self-assessment using the Institute for Safe Medical Practice antithrombotic self-assessment score (see below) rose from 67% to 87% (Attia et al 2022).

Overall, the evidence sourced indicates that anticoagulation stewardship programmes may show some promise with evidence indicating improvements in adherence to guidelines, more appropriate prescribing, improved institutional processes, with potential cost-savings, and possible trends towards some reduction in adverse events. These findings are consistent with the Anticoagulation Forum’s advocacy and evidence for anticoagulation stewardship programmes and the Forum provides extensive resources to support implementation of stewardship programmes (see below).

### Discharge protocols and follow-up

Interventions at the time of discharge, described in the sources identified, include system alerts, pharmacist follow-up by phone or home visit, patient educational resources, and structured clinical summaries.

In a small pre-/post- single centre study a Lean Six Sigma approach was implemented to reduce omission of warfarin at discharge. A system alert was created to identify patients who received warfarin during admission, but who had no warfarin prescription at discharge. Across 96 alerts, the rate of warfarin omission reduced from 10.5% to 0% (p = 0.03) following intervention (Kallal, Griffen, and Jaeger 2020).

However, the other studies sourced demonstrated no benefits resulting from interventions at discharge or follow-up. In an RCT, patients (n = 361) who received multifaceted pharmacist-led follow-up and were visited at home by a clinical pharmacist within four days of being discharged on a high risk medicine, exhibited no difference in adverse drug-related events (although few total events were reported) (Gurwitz et al 2021). In another RCT, patients newly diagnosed with VTE and prescribed anticoagulation reported a ‘high quality care transition’ when they received a pharmacist home visit and subsequent anticoagulation expert consultation, however, their knowledge remained low (Kapoor et al 2020). Additionally, a concise discharge report with the aim of improving timeliness of INR testing and quality of warfarin management post-hospital, had no effect on frequency of appropriate INR management (Dunn et al 2015). However, the authors did note that such an intervention likely needed to be a component of a broader multifaceted intervention to be effective.

Overall, the evidence sourced provides little evidence for meaningful impact of the discharge protocols and follow-up regimens described.

### Pharmacist Interventions

Of the 11 studies retrieved that described pharmacist interventions to reduce anticoagulant harm, 4 described patient education or counselling, 4 evaluated pharmacist prescribing or oversight of anticoagulation use, 2 assessed routine pharmacist review of DOAC prescriptions, and one described routine inclusion of pharmacists on ward rounds.

#### Education/Counselling by Pharmacist

An RCT (n = 200) examining those discharged on an oral anticoagulant and followed-up by phone at day 3 and day 30, found that pharmacist counselling plus nursing counselling compared with nursing counselling alone, led to significantly increased patient communication with their providers as well as increased awareness of their next appointment date. However, there were no differences in bleeding rates (Karaoui, Ramia, Mansour, Haddad, and Chamoun 2021).

Another RCT (n = 152) that studied pharmacist-led education (15 min, one-on-one) and follow-up (by phone, day 30 and 90) for patients newly started on warfarin, prior to discharge found that the intervention group spent more time in the extended target range than the control group (54.4% vs 42.0%, p = 0.024), and also had better warfarin knowledge (p = 0.003). No major bleeding events were observed and incidence of VTE was similar between groups (Liang et al 2020).

A retrospective analysis of 174 patients discharged from the emergency department with a new prescription for an anticoagulant, found that those who had not received pharmacist counselling and phone follow-up, needed more intervention at follow-up, and were more likely to be readmitted to hospital or return to the ED within 90 days for an anticoagulation-related problem (12.1% vs 1.9%, p = 0.0069) (Zdyb, Courtney, Malik, Schmidt, and Lyden 2017). There may be some systematic difference between cases and controls since controls were largely out-of-hours patients.

A small retrospective cohort study (n = 57) of pharmacist education or counselling for inpatients with non-valvular AF and heart failure found that time in therapeutic range was higher in the intervention group (those instructed only by physicians) (An, Kose, Kikkawa, and Hayashi 2017).

#### Pharmacist Prescribing or Oversight

A retrospective single-centre cohort pre-/post- study (n = 502 inpatients) assessed a pharmacist-driven DOAC protocol allowing pharmacists to order and monitor DOACs prescribed for hospital inpatients for indications of VTE and AF. The comparator was usual care and in the post-phase there were significantly fewer medication errors (8.9% vs 16%, p = 0.017) (Willeford, Leiman, and Noel 2021). Similarly, fewer medication errors were observed in low risk VTE patients discharged from ED when a pharmacist was involved at the time of diagnosis than in those patients without pharmacist involvement. However, this was a small study with only 14 patients in the intervention cohort (Bakey and Nguyen 2021). A cost-effectiveness study, based on a 2013 RCT, evaluated pharmacist VTE risk assessment and prescribing of usual medications along with VTE prophylaxis in pre-admission clinics. Pharmacist prescribing increased the proportion of patients adequately treated and decreased VTE incidence. Although the authors conclude there were cost-savings, the 95% confidence intervals include zero, indicating that the study was potentially underpowered to detect a relevant difference (Hale, Merlo, Nissen, Coombes, and Graves 2018).

#### Pharmacist Review of Prescriptions

Pharmacist review of ED discharge prescriptions triggered by a real-time notification system in the EHR, identified 158 of 378 discharge prescriptions as having at least one problem. The intervention rate on anticoagulation prescriptions was 15.4% (Lineberry, Rozycki, Jordan, Mellett, and North 2021). Comparable results were observed in a pre-/post- study of adult patients admitted to a community teaching hospital who received DOAC therapy. A pharmacist-driven DOAC service, including review of all patients on DOACs, was associated with a fall in inappropriate prescriptions compared with usual care (34% to 13.8%, p = 0.039) (Miele, Taylor, and Shah 2017). Low quality descriptive evidence identified medication errors picked up by pharmacists accompanying internal medicine ward rounds (Sharma, Krishnamurthy, Snyder, and Mauro 2017), and on surgical inpatient floors (Tavakoli, Adams-Sommer, Frendak, Kiehle, and Dalpoas 2022).

Overall, most of the studies obtained indicate possible benefits of pharmacist involvement in prescribing, review of prescriptions, or education and counselling of patients taking anticoagulants. Pharmacist involvement in patient education appeared to lead to increased awareness of the care plan, increased time in therapeutic range, and possibly reduces return to ED. Pharmacist prescribing and oversight was associated with fewer medication errors, and pharmacist review of prescriptions can prevent medication errors. However, little evidence was sourced that reported on clinical outcomes.

### E-prescribing, EHR, CDSS, and Apps

The systematic reviews evaluating technological interventions discussed above found only limited evidence of benefit. Primary sources obtained for the present review included seven studies published recently (after 2018, with four published in 2021 or 2022). These recent studies evaluated: an app, clinical rule alerts, CDSSs, and a checklist automatically printed at the time of dispensing.

A prospective two cohort comparison study (n = 642 adults on oral anticoagulation undergoing elective procedures) evaluated an app to support management of anticoagulation in the peri-procedural period. The app recommended evidence-based guidance. Acceptance of app-based guidance was significantly associated with fewer ED visits within 30 days post-procedure (4.0% vs 8.3%, p = 0.0205). However, acceptance was more common in patients who were also younger, on anticoagulants other than warfarin, and for procedures with high bleeding risk (Spyropoulos et al 2020).

A Belgian study of 39,481 clinical rule-based alerts reviewed by pharmacists found that pharmacists sent 2,568 electronic notes and made 637 phone calls as a result. Anticoagulants were the medicine class for which actions were most commonly carried out and 69% of actions were accepted by physicians (Quintens et al 2019). The same group reported additional follow-up across two years, finding a relative reduction in anticoagulant-related potentially inappropriate prescriptions of 70% (95% CI, 54–81) (Quintens et al 2022).

In a prospective observational study of 1,086 alerts, pharmacists generated an intervention 51% of the time. Of these 66% required a documented modification to therapy due to prescription error. The positive predictive value of adjustment in anticoagulation therapy resulting from alerts was 0.24 (Ibáñez-Garcia et al 2019). A check sheet set to print automatically at the time of DOAC dispensing in hospital pharmacies was associated with an increase in pharmacist inquiries to prescribers from 0.6% to 2.3% (p = 0.0089), however clinical impacts were not measured (Ishikawa et al 2021).

In a retrospective pre-/post- study of Australian inpatients prescribed a DOAC (n = 100), tailored electronic patient-specific physiological alerts improved the appropriateness of DOAC prescribing from 48% to 91% (p < 0.05). However, the impact on hospital acquired complications was not statistically significant (Khalil 2021).

A single centre pre-/post- implementation study evaluated the use of use of a multifunctional CDSS based on national and international guidelines for VTE prevention. Implementation of the CDSS was associated with a decrease in the rate of hospital acquired VTE (11.71 per 1000 hospitalizations to 4.84, p = 0.0068) (Nazarenko et al 2015). However, in another study, retrospective review of 121 randomly selected inpatients indicated that computerised CDSS tools to enhance safety when DOACs are used did not correlate with bleeding events (Ahuja et al 2021).

Consistent with the systematic reviews reported above, the individual studies obtained suggest that electronic alerts lead to improved prescribing quality, and that use of app-based guidance or electronic CDSS may be associated with fewer ED visits or decreased VTE rates. However, most studies did not report hard clinical outcomes, and most were low quality, uncontrolled, non-randomised studies.

### Other Interventions

Other interventions described in the sources obtained include use of a shared decision-making tool, a specialist perioperative bridging service, a QI intervention bundle, and a surgical ward round checklist.

In an RCT, n = 922 (including hospital inpatients), the use of the ‘Anticoagulation Choice’ shared decision-making tool had no impact on anticoagulation adherence or clinical safety outcomes (Noseworthy et al 2022).

A QI intervention bundle aimed to increase guideline compliance with prophylactic doses of anticoagulation in gynaecological oncological procedures. Compliance improved from 73% to 96% (n = 100, p < 0.001) when compared to historical controls (n = 182). The rate of VTE remained unchanged (Pelkofski, Baker, Rowlingson, Cantrell, and Duska 2019).

A surgical ward round checklist was implemented at Christchurch Hospital and evaluated over a two-week period. After the intervention anticoagulation/antiplatelet treatment increased from 32% to 58.1% (p < 0.05) (Tranter-Entwistle et al 2020).

A specialist perioperative anticoagulation bridging service was developed at Capital and Coast DHB. The aim was to devise individualised plans for interruption of anticoagulation and have these plans managed by the specialist service. A single-centre, prospective analysis of 566 consecutive patients who underwent a procedure found low rates of major bleeding (1.9%) and thrombosis (0.8%) at day 30. These rates were comparable to those in RCTs, however, the study itself included no comparator group (Ruell, Smith, Perera, and Carter 2019).

Overall, evidence suggests these other interventions might have some impact on guideline compliance, however there was scant evidence for any impact on clinical outcomes.

#### High-level Consensus or Commentary

High-level consensus statements of summaries obtained are described in Appendix Table A3. Most of the high-level statements obtained pertained to the United States context. The Joint Commission’s National Patient Safety Goal NPSG.03.05.01 aims to ‘Reduce the likelihood of patient harm associated with the use of anticoagulant therapy’. Commentary on this goal from the Anticoagulation Forum (Dager et al 2020), notes the rapid evolution of medical evidence and best practices means that organisations must undertake serial re-evaluation of their guidance. The Anticoagulation Forum itself provides continually updated materials at their ‘Centers of Excellence’ website. However, to achieve safe use of anticoagulants institutions need high level buy in, appropriate resourcing, clear communication, engagement of multidisciplinary teams, easily retrievable policies and procedures, involvement from pharmacy and informatics, continuous redesign and evaluation.

Picking up on the theme of involving pharmacists, the International Pharmacists Anticoagulation Taskforce issued a Position Statement that identified seven steps on the patient care pathway where pharmacy input could be beneficial (Alves da Costa, Rydant, and Antoniou 2020). The statement cites research literature pertaining to all steps, however only one step is based in the hospital context. Pharmacists could contribute to:

* dosing and monitoring checking
* integrated medicines management
* pharmacokinetics monitoring
* monitoring off-label prescribing (where there is no evidence-based benefit)
* ensuring appropriate dosing (including renal function adjustment)
* monitoring for excess anticoagulant perioperatively, and insufficient at discharge
* educating patients at discharge (often there are three or more changed medications)
* improving transfer of information

Accompanying NPSG.03.05.01, the Joint Commission provides a ‘List of Resources’[[2]](#footnote-2) organised around six elements of performance. These elements include:

* EPs 1 through 3 include the use of approved protocols and evidence-based practice guidelines for medication selection, reversal and management of bleeding, and perioperative care.
* EP 4 requires a written policy about laboratory testing to monitor and adjust anticoagulation.
* EP 5 addresses institutional safety practices, including the development of processes for identifying and responding to adverse drug events.
* EP6 focuses on patient education, ensuring that patients are aware of medication dose and schedule, follow-up plan, and potential drug interactions and adverse reactions

Commentary on the List of Resources argues that there is an opportunity to implement ‘systems-based haematologists’, who are specialty-trained physicians, employed by a hospital, *or health system*, to optimize individual patient care, as well as the overall system of health care delivery (May and Moll 2019).

Two relevant consensus statements of the New York State Anticoagulation Task Force were obtained.

* The first of these provided consensus on features of electronic health records necessary to deliver optimised anticoagulation therapy. The multidisciplinary panel of anticoagulation experts generated 78 recommended EHR features across 20 key discrete areas and 425 individual logic steps. These features are detailed in Table 5 of Spyropoulos et al, p.118-120, (Spyropoulos et al 2015).
* The second consensus statement emerged from the premise that anticoagulated patients are vulnerable to adverse drug events when they experience transitions in care or changes to medication. There are 12 general data elements and three that are specific to warfarin, which should accompany all anticoagulated patients undergoing care transitions. Triller et al 2018, Table 1, lists these 15 requisite data elements (Triller et al 2018).

The Health and Human Services Office of Disease Prevention and Health Promotion published a ‘National Action Plan for Adverse Drug Prevention’ in 2014 (Dept Health and Human Services 2014). Anticoagulants are one of three medication classes targeted. Opportunities to prevent anticoagulation adverse drug events in the inpatient setting include: improving provider knowledge, improving dissemination of evidence-based tools, and development of guidelines, along with effective communication and coordination of care: such as improved EHR tools to integrate pharmacy and laboratory data, electronic flowsheets, CDSS, and integrating anticoagulation-specific targets into care transition models (Harris et al 2015). A range of ‘Federal Assets’ exist to support these activities including: anticoagulation protocols, a national anticoagulation training program, education for providers, the chronic disease self-management program, patient education sheets and video, medication guides, ‘Project Red’ including medicines reconciliation, anticoagulant electronic flowsheet, medication use tracker, CDSS, and a shared resource centre. Page 58–66 of the National Action Plan details the interventions relevant to anticoagulation in the inpatient setting.

The Michigan Anticoagulation Quality Improvement Initiative Toolkit Recommends a range of quality improvement measures for anticoagulation safety (Barnes and Kline-Rogers 2015). These include measuring:

* clinical events (bleeding, stroke/VTE, ED visits, hospitalizations, death)
* surrogate measures (TTR, INR variability, percent in/out of range INRs, percent missed or late INR test, adherence)
* process measures (INR in first 2 weeks, time from warfarin initiation to first INR, time from out-of-range INR to patient contact)
* population focused measures (percent of patients receiving guideline-based appropriate care, percent of patients receiving appropriate education, patients with drug-drug interactions at risk for GI bleeding)

### Institutional Advice

Search of institutional websites revealed a wealth of advice and guidance about stroke prevention in atrial fibrillation, and recommendations to increase the proportion of patients with AF who are anticoagulated. However, there was considerably less guidance aimed at reducing harm from anticoagulants. Information obtained from six institutions is highlighted in Appendix Table A4. The institutions are the Agency for Healthcare Research and Quality (AHRQ), the Anticoagulation Forum, the Australian Commission for Safety and Quality in Healthcare (ACSQHC), the Institute for Safe Medical Practices (ISMP), the UK National Institute for Health and Care Excellence (NICE), and the Scottish Patient Safety Programme (SPSP).

#### AHRQ

There were 115 results for a search for ‘anticoagulation filetype:PDF’ on the AHRQ website. Users were directed to the Anticoagulation Forum’s ‘MIDAS Programme’ (see below). The AHRQ website also hosted a 2008 Institute for Healthcare Improvement Anticoagulation Toolkit, which advised that, ‘Adverse drug events (ADEs) associated with anticoagulants can be reduced by implementing recognized safe practices in high-risk areas, redesigning care processes, partnering with patients and families, and maximizing communications within and across the care continuum’. However, the more recent ‘Making Healthcare Safer III’ resource contained a chapter specifically on anticoagulants (AHRQ 2020). The most relevant recommendation was for pharmacist-provided anticoagulation management services (largely in the ambulatory care setting). It was noted that other interventions such as dosing protocols or nomograms for DOACs, as well as interventions supporting safe transitions of care lacked a high-quality evidence base.

#### Anticoagulation Forum

The Anticoagulation Forum, with funding support from the FDA, leveraging off the Joint Commission’s updated national patient safety goal that now includes DOACs, produced an Anticoagulation Stewardship Guide (Anticoagulation Forum 2019b). The guide uses much of the same language and many concepts based on the practice of antibiotic stewardship. An associated overview slide presentation is freely available.[[3]](#footnote-3) The guide is intended for all care settings and all anticoagulation populations. Additionally, a ‘how to’ guide published in the peer-reviewed academic literature describes the justification for anticoagulation stewardship and a step-by-step approach that has been successful at Johns Hopkins Hospital and can be deployed by any healthcare organisation (Dane et al 2022).

The Anticoagulation Forum promotes the Mentored Implementation and Dissemination of Anticoagulation Stewardship (MIDAS) programme. The recommended anticoagulation stewardship consists of seven core elements (the guide expands on all of these):

1. **Secure Administrative Leadership Commitment:**Dedicating necessary human, financial, and technology resources
2. **Establish Professional Accountability and Expertise:** Appointing a single leader responsible for program outcomes, supported by at least one clinician with expertise in anticoagulation management
3. **Engage Multidisciplinary Support:** Involving key specialists and disciplines to obtain perspective from all domains of the care delivery system
4. **Perform Data Collection, Tracking, and Analysis:** Defining the population, objectively evaluating performance, and guiding decision-making
5. **Implement Systematic Care:** Implementing sustainable, efficient, evidence-based action(s) at the system level to assure the safety and quality of anticoagulation management
6. **Facilitate Transitions of Care:** Creating systems to optimize communication and ensure safe transitions between care settings
7. **Advance Education, Comprehension, and Competency:** Assuring that clinicians, patients, and others have the knowledge and skills necessary to optimize outcomes

The MIDAS programme runs across 24 months and pairs nationally recognized anticoagulation experts with hospitals. The experts assist hospitals to deploy the Core Elements of Anticoagulation Stewardship. The programme will result in an ‘Implementation Playbook’ by the end of 2022. Evaluation of stewardship implementation is ongoing, and case studies are presented below (see ‘Case Studies’).

The Forum provides supporting resources including a Core Elements of Anticoagulation Stewardship Programmes guidebook (Anticoagulation Forum 2019b) and the Administrative Oversight Gap Analysis: Hospitals and Skilled Nursing Facilities (Anticoagulation Forum 2019a). Organisations can self-assess using the ‘Checklist of Core Elements’[[4]](#footnote-4) and access the supporting resources at the Anticoagulation Forum’s ‘Centers of Excellence Resource Center’.[[5]](#footnote-5)

The Forum has published an evidence summary (Anticoagulation Forum 2022a) and supporting bibliography.[[6]](#footnote-6) The evidence cited by the Forum suggests benefits in proportion of appropriate dosing, reduction in dosing errors, decrease in major bleeding, decrease in death, improved medication adherence, reduced inappropriate aspirin-anticoagulation combination, and improved warfarin control, among other outcomes. The programme may also be cost-saving (Anticoagulation Forum 2022b), with North Carolina Medical Center reporting US$4million in annual cost-savings driven largely by reduced use of recombinant Factor VIIa and reduced length of stay.

In addition to the comprehensive advice published by the Anticoagulation Forum, Dane et al describe the approach to anticoagulation stewardship at Johns Hopkins Hospital in detail (Dane et al 2022). These authors note the high risks associated with antithrombotic medicines and the high cost of associated haemostatic medications. This article first reviews the evidence for the effectiveness and cost-savings of established programmes. Noting the significant impact of several established haemostatic/antithrombotic stewardship programmes the authors then explain exactly how organisations can develop and implement their own programme. The toolkit provided covers three phases and is explicit in its instructions (Table 2 in the paper details 23 discrete practical steps across the three phases):

1. **Phase One** focuses on establishing the programme infrastructure, defining the current state of practice, and identifying opportunities for QI intervention. All existing stewardship programmes have been at least co-led by pharmacists and haematologists.
2. **Phase Two** consists of identifying targeted interventions and broadly implementing them as well as developing materials needed to standardise clinical practices for haemostatic and antithrombotic use.
3. **Phase Three** provides ongoing assessment of adherence to implemented policies, guidelines, and targeted interventions, as well as identifying new opportunities.

#### ACSQHC

Five relevant results were returned on the ACSQHC website. Many resources pre-dated 2015 and were, therefore, out-of-scope. However, ACSQHC directed users a document detailing ‘Medication without harm WHO Global Patient Safety Challenge Australia’s response’ (ACSQHC 2020), as well as to the National Quality Use of Medicines Indicators in Australian Hospitals. The indicators for antithrombotic therapy are:

1.1 Antithrombotic therapy – Percentage of hospitalised adult patients that are assessed for risk of venous thromboembolism

1.2 Antithrombotic therapy – Percentage of hospitalised adult patients that receive venous thromboembolism prophylaxis appropriate to their level of risk

1.3 Antithrombotic therapy – Percentage of patients prescribed enoxaparin whose dosing schedule is appropriate

1.4 Antithrombotic therapy – Percentage of patients prescribed hospital initiated warfarin whose loading doses are consistent with a drug and therapeutics committee

1.5 Antithrombotic therapy – Percentage of patients with an INR above 4 whose dosage has been adjusted or reviewed prior to the next warfarin dose

1.6 Antithrombotic therapy – Percentage of patients with atrial fibrillation that are discharged on oral anticoagulants

5.4 Continuity of care – Percentage of patients on warfarin that receive written information regarding warfarin management prior to discharge

#### ISMP

ISMP recommends that organisations use the ISMP Medication Safety Self-Assessment for antithrombotic therapy,[[7]](#footnote-7) which covers 11 ‘core characteristics’ across 8 domains and includes 115 items:

1. Patient information
2. Drug information
3. Communication
4. Drug storage
5. Medication devices
6. Competency/Education
7. Patient education
8. Quality processes

#### NICE

NICE provides quality standards and guidance for several anticoagulation-related aspects of care including the diagnosis and management of VTE (for example, QS-201 and NG-158).

NICE guidance NG158 states in sections 1.2 and 1.5 that patients should be discharged with adequate monitoring of anticoagulant treatment and should be provided with sufficient information and education. However, mostly this guidance is not specific to anticoagulation-related harm quality initiatives. The NICE website does however host case studies in shared learning, and two of these are detailed below (see ‘Case Studies’).

#### SPSP

The Scottish Patient Safety Programme supports a Warfarin Care Bundle (Health Improvement Scotland 2015), which is largely targeted at primary care. The Warfarin Bundle consists of:

**Measure 1:** Warfarin dose is prescribed according to local guidance.

**Measure 2:** Is the target INR and duration of treatment clearly documented in the notes?

**Measure 3:** Patient complying with dosage instructions.

**Measure 4:** INR is taken according to previous recommendation. INR is taken within 7 days of planned repeat INR?

**Measure 5:** Patient receives regular education. Patient has received education in the last 6 months.

**Measure 6:** Have all Measures been met?

The programme was evaluated in 2015 and the evaluation found improvements in: mean time in therapeutic range, good control, and excellent control, as well as fewer very abnormal results and patient attendances (McNab, McKay, and Bowie 2015).

### Case Studies

In addition to the detailed case study of anticoagulation stewardship provided in Dane et al (see ‘Institutional Advice’ above), the following examples illustrate the development and implementation of QI initiatives to reduce harm associated with anticoagulant use.

#### Capital and Coast District Health Board: Periprocedural Bridging Service (Ruell et al 2019)

Following multiple procedure cancellations due to issues with patients’ anticoagulation status, Wellington Hospital initiated a wraparound peri-procedure anticoagulation bridging service. This was setup by professional agreement with all involved clinicians and was to be run by the hospital thrombosis service. Everyone involved recognised the importance of optimal bridging for patient safety and the scheduling of services. The intention was to provide individual bridging assessments including implementation of the appropriate management, communication, and education. The thrombosis service (which included expert thrombosis nurses) would contact patients, provide key reminders about stopping and starting medications, ensure documentation was complete, and manage a safe return to the previous anticoagulant. Once established the service was evaluated and the overall incidence of major bleeding was 1.9% at day 30 (rate of thrombosis was 0.8%). This figure compares favourably with the BRIDGE study where rates of bleeding were 1.3% in the no bridging group and 3.2% in the bridging group.

#### Western Sussex NHS Foundation Trust: Pharmacists on ward rounds[[8]](#footnote-8)

The Western Sussex NHS Foundation Trust recognised that the UK Carter Report (2016) recommended deploying more clinical pharmacists, including pharmacist prescribers. The aim was to derive value from medicines as well as optimising their use through medicines review and reconciliation. Western Sussex integrated pharmacists into the ward multidisciplinary team, particularly on surgical wards, ensuring that decision support is present at the point of prescribing. Venous thromboembolism prophylaxis is one of the most common prescriptions on surgical wards and the presence of the pharmacist was intended to improve compliance with relevant guidelines and ensure prescribing was correct and appropriate as soon as possible after admission. Independent Prescribing pharmacists could also help facilitate timely discharge. The pharmacists scan electronic drug charts and note potential issues, such as potential interactions or dosing. Being physically present on the ward round means that access to the prescriber is ensured and notes in the medical record are not unintentionally overlooked. Baseline audit showed that up to 33% of surgical patients did not have full VTE assessment and 20% did not have appropriate prophylaxis. At first the role of the pharmacist on the ward rounds was not fully understood, but after a trial consultants described the pharmacist as essential and asked for their presence at every ward round. Pharmacists suggested on average 1.3 interventions per patient.

#### Anticoagulation Forum (US): Profiles of stewardship(Anticoagulation Forum 2022b)

The Anticoagulation Forum has collected examples of hospitals that have deployed anticoagulation stewardship models. These programmes are multidisciplinary and/or pharmacy-driven, often targeting dose minimisation of clotting factor use and reducing need for high-cost reversal. Programmes have also aimed to reduce HIT antibody testing through use of the 4T pre-test probability score. Hospitals implementing these programmes include: Johns Hopkins Hospital, North Carolina Medical Center, Tufts Medical Center, and Rochester General Hospital, among others. The impact across eight profiled hospitals included cost savings and cost avoidance ranging from tens of thousands to millions of dollars, reductions in length of stay, reduced use of reversal agents, and identification of patients inappropriately on some treatments.

*Alfred Hospital, Melbourne: Anticoagulation stewardship*(Bui et al 2021)

The Alfred is a tertiary referral hospital network with more than 600 beds across three campuses. In 2011 Alfred Health launched an antimicrobial stewardship (AMS) programme led by a full-time senior clinical pharmacist with part-time support from infectious disease physicians. Key components of the AMS programme included regular review of antimicrobial use, feedback and education to prescribers, antimicrobial formulary restriction, research, and ongoing improvement initiatives. The programme led to reduction in antimicrobial use and improved patient outcomes. Alfred Health took the core elements of their well-established AMS programme and developed anticoagulation and analgesic stewardship programmes with the same philosophy and components. Critical aspects included multidisciplinary hospital-wide stakeholder engagement, clinician education, monitoring outcomes supported by access to data, quality improvement activities, and involvement of the lead pharmacist in patient-centred care. Implementation followed key stages of exploring the current situation, planning, implementation, monitoring, evaluation, and iterated change. It was important to have dedicated expertise and resources, including identified champions and engagement with end-users. The ACS programme aims to improve institution-wide management and oversight of anticoagulation across all settings with a focus on appropriateness rather than minimisation of use. Quality improvement activities included audit of VTE prophylaxis, increased prescribing of pharmacological prophylaxis for high-risk

patients and access to intermittent pneumatic compression, a VTE information leaflet to provide patient education, and quality assurance reviews investigating special populations such as bariatric and burns patients. Hospital acquired VTE decreased by 33% and anticoagulation-related bleeds decreased by 20%.

#### Erasmus University Medical Center and the Reinier de Graaf Hospital, Netherlands: Antithrombotic stewardship (Dreijer et al 2019; Dreijer et al 2020)

These two Dutch hospitals implemented an anticoagulation stewardship programme based upon the formation of a multidisciplinary antithrombotic team. At Erasmus, the team consisted of a specialised thrombosis nurse (the case manager), as well as haematologist, paediatric haematologist, head haematologist, hospital pharmacist, cardiologist, anaesthetist, pulmonary physician, neurologist, vascular surgeon and a quality officer. These teams focused on providing hospital-wide education about antithrombotic therapy, medication reviews by hospital pharmacists (this included dosing, duplicate medication, drug-drug interactions, contraindications, and perioperative bridging), drafting of antithrombotic guidelines and a uniform policy, patient counselling daily, medication reconciliation (at admission data from the thrombosis service was handed to the responsible physician, at discharge pharmacotherapy advice/medication review were handed to the thrombosis service or GP, and community pharmacist). This initiative led to a statistically significant increase in adherence to anticoagulant guidelines. This was largely due to improved use of LMWH with respect to renal function and bodyweight. Additionally, there was some indication of a reduction in bleeding and thrombotic events, but this trend was not apparent immediately following intervention, rather it increased across time (change in trend -1.83% per 2 months). However, all-cause mortality was lower in the intervention period [8.6% (81/945)] compared to the usual care period [11.5% (108/941)] OR 0.72 (0.53 to 0.98). Analysis of causes of death indicated that bleeding and thrombosis were not the driving factors. However, a generalised improvement in care cannot be ruled out. The cost per admission of anticoagulant users decreased by EUR790 (p = 0.27) at one hospital and by EUR480 (p = 0.09) at the other, although neither was statistically significant.

#### Nottingham Universities Hospitals Trust: Discharge follow-up[[9]](#footnote-9)

Nottingham Universities Hospitals Trust began looking at how to improve the discharge process for patients with a PE. This was an especially pressing issue given recent trends towards managing haemodynamically stable patients with PE as outpatients. NICE provided guidance about adequate monitoring of anticoagulation treatment and patient necessary education/information. British Thoracic Society Guidelines 2018 state that a patient should be formally reviewed during the first week after discharge. A multidisciplinary panel decided that anticoagulation nurse specialists would contact patients within a week and a protocol was created. A PE pathway and electronic referral was developed to be in line with all guidelines. A new DVD was commissioned for patient information and rolled out on wards. During the initial roll-out of the new system it became clear that about 20% of patients had not been given advice on what to do if their condition deteriorates and 47% had not been given a card to alert others to their new anticoagulant medication. The new follow-up process should help prevent these omissions.

### New Zealand Initiatives

Ten DHBs provided information pertaining to initiatives for reducing anticoagulation-related harm in response to the Commission’s survey of Quality and Risk Leads. Survey responses are summarised in the second column of Appendix Table A5. Additional information provided by the targeted individuals who were additionally approached is also presented in Appendix Table A5.

DHB responses indicate some activities taking place are aimed at reducing harm from anticoagulants, but responses also highlight several needs and opportunities.

Guidelines and protocols for the use of anticoagulants and for VTE prophylaxis are common, however, many are ad hoc with different guidelines in different clinical areas and there appears to be little evaluation and infrequent audit of adherence. Partly the lack of audit has been attributed to disruptions from the Covid-19 pandemic. Even when audit takes place, however, it is unclear what the gold standard is because there is no national approach or agreed standard of care.

Requiring electronic documentation of VTE assessment and the use of post-take ward round forms is helping to ensure that risk information is recorded.

Additional guidance for the use of anticoagulants has been provided through development of apps (including warfarin reversal and rivaroxaban use) that make guidelines accessible, however, these are not yet integrated into common apps used by medical staff such as MedApp or EHRs. Other cognitive aids in use include lanyards providing readily available information on anticoagulant use.

Alerts exist to flag double-charting of anticoagulants, but alerts regarding renal function are generally not integrated with laboratory results, and therefore do not offer patient-specific clinical decision support.

Education has commonly been deployed, largely focussed on PGY1 and PGY2, but also for trainee interns, including low fidelity simulation activities. Presentations have been made at grand rounds, and posters developed guiding safe DOAC use, as well as adverse event updates. However, some education initiatives were obstructed by failure of e-learning platforms, or because information was not kept up to date. There has been no real evaluation of education initiatives beyond participant opinions.

Coloured bracelets identifying patients on warfarin don’t appear to have prevented reportable events, although this was possibly because photocopies of an out-of-date form were concurrently in use.

Separate anticoagulant/antiplatelet and heparin medication charts have been used. However, the mix of paper and electronic, or the need to look at additional charts, risks confusion.

Heparin safety has been addressed by providing heparin in pre-filled bags.

A specialist anticoagulation bridging service operates at one DHB, this is detailed in the section on ‘Case Studies’ above (Ruell et al 2019). This programme was formally evaluated and found to have outcomes comparable to those of published randomized controlled trials. This programme is in part facilitated by specialist thrombosis nurses.

Specialist thrombosis services also exist at Auckland, Counties Manukau, Waitemata, Mid-Central, Canterbury, and Capital and Coast DHBs. Such services support important interventions at the time of discharge for patients with VTE. Clinical nurse specialists liaise with a haematologist/thrombosis specialist and educate patients about their VTE and medications, and often follow up by phone.

Pharmacist rounding provides some oversight of anticoagulation use and pharmacists are also providing one-on-one education to patients on the ward prior to discharge. Without evaluation it is unclear whether this education is opportunistic or systematic.

At discharge, warfarin-specific fields on discharge paperwork provide information to GPs and ensure follow-up INR testing is arranged. However, barriers to getting even relatively small changes to discharge forms were also reported. There are also barriers to referring patients directly to community anticoagulation management services where GPs must make this referral.

Expert DHB informants suggested that the following would all be useful to pursue: Systematic e-prescribing, clinical decision support systems that include learning opportunities, universal electronic notes, integration of renal function alerts with laboratory data (linked to individual patients), the ability to identify patients coming for outpatient procedures who are taking anticoagulants, national rather than ad hoc guidelines on VTE prophylaxis, automated audits with clear criteria, more pharmacists, and the use of electronic forms to prevent photocopying old documents.

## Discussion and Recommendations

The evidence presented above includes surprisingly few high-quality studies, especially given the long history of anticoagulation-related harm, and efforts dedicated to reducing harm from other medicines such as antibiotics or opiates. Nevertheless, interpreting the evidence described above, and tabulated in Appendix A below, three areas of apparent utility stand out. These are:

* Expanding the role of pharmacists
* Anticoagulation stewardship programmes
* Improved use of the EHR and CDSS to support the above and facilitate efficient audit and evaluation

Additionally, the institutional advice identified in this study provided recommendations in favour of pharmacist-provided anticoagulation management services, anticoagulation stewardship programmes, the measurement of performance indicators, institutional self-assessment using published tools, and widespread use of clinical guidelines. Pursuing the three avenues of QI above should facilitate these recommendations.

It is also noted that an additional literature review was undertaken for the Commission by a pharmacy student in 2019 (Zhang 2019, unpublished). Although this review focused on evidence of anticoagulation-related harm, it had a secondary purpose to identify interventions for the safer use of anticoagulants. This earlier review identified potential QI avenues as follows: pharmacist identification of errors, education for patients and prescribers, anticoagulation stewardship programmes, and active encouragement of adverse event reporting. These findings are consistent with the three areas listed above since anticoagulation stewardship programmes generally include education for staff as well as reporting of adverse events.

### Expanding the Role of Pharmacists

The role of pharmacists in improving management of anticoagulation has been well-studied in the community setting with many benefits identified (Entezari-Maleki, Dousti, Hamishehkar, and Gholami 2016). The narrative review by Lee et al described previous (out-of-scope) evidence of a possible reduction in mortality in hospitals with pharmacist managed warfarin or heparin therapy (Lee et al 2016). Additionally, several of the studies identified provide low to moderate quality evidence that pharmacist prescribing privileges, pharmacist review of prescribing, or other forms of pharmacist oversight, improve the quality of anticoagulation prescription with respect to guideline adherence, adjustment for patient-specific factors, and appropriateness of prescription. Pharmacist counselling of patients may increase time in therapeutic range, and possibly reduces the frequency of return to ED.

Efforts could be made to systematically incorporate pharmacists in decisions to use anticoagulants, their prescription, monitoring, adjustment, and to support patients in their use. Pharmacist review can be automatically triggered by EMR reports, clinical rule alerts, and pharmacists can contribute as active team members on multidisciplinary rounds, in pre-admission, perioperatively, or by reviewing discharge prescriptions. It is likely that an expanded pharmacy workforce enabling systematic oversight of the prescribing and monitoring of anticoagulants both in hospital and via community monitoring services, including both warfarin and the DOACs, with appropriate systematic electronic alerts of anticoagulant use, would lead to safer use of these medicines. The intermediate step of patients needing a GP referral following discharge from hospital to access anticoagulation monitoring services may be a barrier to appropriate and systematic monitoring.

### Anticoagulant Stewardship

Stewardship of anticoagulants derives support from several areas: the fact that guideline-based physician-led anticoagulation consultation services have been found to reduce bleeding rates, in high-risk patients (Frazer et al 2019), combined with the totality of evidence demonstrating improved outcomes with some kinds of pharmacist-led anticoagulation services, as well as successes with the model of antimicrobial stewardship, and the apparent cost-effectiveness of these approaches. A key benefit of stewardship programmes is that individual organisations can take a systematic approach and prioritise where, locally, action is most warranted. This provides the benefits of a national programme (of stewardship) with locally tailored interventions.

Hospital-wide studies of stewardship programmes provide good evidence for improved guideline compliance (Dreijer et al 2019; Wychowski et al 2017), and provide suggestions of trends toward improved endpoints such as reduced incidence of VTE and bleeding (Bui et al 2021; Dreijer et al 2020), and reduced all-cause mortality (Dreijer et al 2020). However, the evidence for these patient outcomes is not as robust, or not fully explained, and further ongoing study is warranted.

Anticoagulation stewardship is recommended by several institutions including the Anticoagulation Forum (Anticoagulation Forum 2019b), on the basis of a wide range of evidence supporting the individual components of such programmes. These programmes effectively take the philosophy around consistent and expert management of anticoagulation use which underpins current community pharmacy anticoagulation management services and expand it across the entire healthcare organisation or system.

Stewardship may be more difficult to implement at smaller sites, and cost-effectiveness considerations will be important. However, evidence suggests that stewardship programmes in several settings are demonstrably cost-saving, particularly when applied to the use of high-cost reversal agents and the management of HIT (Anticoagulation Forum 2022b).

Stewardship could be integrated with other possible solutions, relevant in defined areas, and a multidisciplinary governance team for stewardship could prioritise which interventions to implement and in which order. Stewardship could oversee the integration of approaches such as discharge prescription checking, referral to community ambulatory anticoagulation management services, specialist periprocedural bridging services (managing those on anticoagulants pre-, during, and post- procedures), and roll-out of supporting e-prescribing, CDSS, and audit tools. Notably, evaluation of the impact of the periprocedural bridging in avoiding procedure cancellation should be undertaken, along with ongoing measurement of clinical outcomes as already described (Ruell et al 2019).

Advice for developing and optimising anticoagulation stewardship programmes has been provided by the Anticoagulation Forum, along with self-assessment guides for organisations, and by the Johns Hopkins Hospital programme (Dane et al 2022). Descriptions of successful anticoagulation stewardship programmes are available in the literature, and a selection of these studies are highlighted in Appendix Table A2. In general, such programmes require sophisticated multidisciplinary governance and oversight, dedicated resourcing, as well as continuous audit and redesign (see Box 1), but the potential clinical benefits and possible cost-savings could make programmes worthwhile. It appears that no systematic review of anticoagulation stewardship programmes exists, and this shortcoming should be remedied.

**Box 1: Key components of anticoagulation stewardship programmes**

* High level buy-in from administrative leadership
* Budgeted resources for development and ongoing support
* Identify a champion to serve as programme leader
* Identify anticoagulation expert(s) to support leader
* Engage multidisciplinary support across key areas
* Establish a mechanism to obtain multidisciplinary input
* Deploy IT resources to develop necessary tools
* Track processes and outcomes: adherence to guidelines, documentation, quality of anticoagulation management, adverse events, education (staff/patient), safety and effectiveness of care transitions (see ‘Measurement’ below)
* Identify opportunities for improvement
* Feedback to administrators
* Develop policy and evidence-based guidelines/protocols and ensure these are easy to retrieve at point of care
* Implement pharmacist-driven interventions (see above)
* Implement standardised processes for: identifying patients receiving anticoagulation therapy, managing periprocedural anticoagulation, identifying anticoagulant users transitioning to other care settings
* Ensure adequate staff training
* Ensure adequate patient/whānau education
* Continuous redesign based on evaluation and measurement
* Institutional self-assessment using published tools, eg:
  + Anticoagulation Forum ‘Checklist for Core Elements of Anticoagulation Stewardship Programmes’ (Anticoagulation Forum 2019b)
  + ISMP Medication Safety Self-Assessment for antithrombotic therapy (ISMP 2017)
  + ‘Table 2’ and ‘Table 3’ in (Dane et al 2022)

### Electronic Solutions

Several DHB key informants spoken to for this project mentioned the shortcomings of paper workflow, which included information not being available to those who need it, as well as possible benefits of electronic prescribing, electronic health records, and better integration of laboratory data with patient-specific prescribing guidance.

The impact of pharmacists and multidisciplinary stewardship teams would likely be enhanced by systematic implementation of electronic systems that allow daily reports, clinical-rule based alerts to pharmacists and other healthcare team members, and automated audit and evaluation of progress to facilitate ongoing QI.

The literature sourced, and described above, did not provide strong evidence about a range of electronic solutions when deployed in isolation, but in their systematic review Austin et al concluded that computerised physician order entry needs to be combined with computerised CDSSs to ensure effectiveness (Austin et al 2020). Furthermore, studies of several interventions demonstrated that the possible utility of an expanded role for pharmacists depends in part on universal implementation of electronic prescribing systems and the ability to run reports and program clinical alerts, which in some cases could be stealth alerts notifying pharmacists, or other members of a stewardship team about relevant patients, or context-aware alerts, thereby overcoming alert fatigue. Prescribing alerts need to be integrated with laboratory systems to provide patient-specific decision support. This is particularly pressing given the very high proportion of inappropriate prescriptions described in the studies sourced.

Overall, although the evidence for electronic solutions (including apps, CDSS, e-prescribing, EMRs, and other digital solutions) is generally of low quality these systems may be needed to effectively support programmes to utilise the knowledge and expertise of pharmacists, and multidisciplinary teams. A key barrier to the effectiveness of CDSS is their low use (Sennesael et al 2020), which might reflect poor user experience and underscores the need for effective implementation. Nonetheless, low rates of adherence to guidelines suggests that the benefit of clinical research is being lost because it is not being incorporated into practice. Well-designed CDSS should help address this problem (Nazarenko et al 2015) and should probably employ a modern user interface and the familiar ease of an app.

### Measurement

Quality improvement initiatives must be monitored and evaluated to ensure benefits are realised. However, a national approach and standard of care would likely help facilitate meaningful and comparable audit and evaluation. In the case of anticoagulation-related harm, a range of clinical and non-clinical metrics have been proposed. The following list includes examples of metrics, those advocated in the Michigan Anticoagulation Quality Improvement Toolkit (Barnes and Kline-Rogers 2015), the National Quality Use of Medicines Indicators in Australian Hospitals (ACSQHC 2020), and the Scottish Patient Safety Programme Warfarin Bundle (Health Improvement Scotland 2015). Some selection of these measures could be employed to monitor progress (along with institutional self-assessments as discussed above), ideally those that can be automatically captured and monitored through electronic systems:

* Michigan:
  + Clinical events (bleeding, stroke/VTE, ED visits, hospitalizations, death)
  + Surrogate measures (TTR, INR variability, percent in/out of range INRs, percent missed or late INR test, adherence)
  + Process of care (INR in first 2 weeks, time from warfarin initiation to first INR, time from out-of-range INR to patient contact)
  + Population focused (percent of patients receiving guideline-based appropriate care, percent of patients receiving appropriate education, patients with drug-drug interactions at risk for GI bleeding)
* Australia:
  + Percentage of hospitalised adult patients that are assessed for risk of venous thromboembolism
  + Percentage of hospitalised adult patients that receive venous thromboembolism prophylaxis appropriate to their level of risk
  + Percentage of patients prescribed enoxaparin whose dosing schedule is appropriate
  + Percentage of patients prescribed hospital initiated warfarin whose loading doses are consistent with a drug and therapeutics committee
  + Percentage of patients with an INR above 4 whose dosage has been adjusted or reviewed prior to the next warfarin dose
  + Percentage of patients with atrial fibrillation that are discharged on oral anticoagulants
  + Percentage of patients on warfarin that receive written information regarding warfarin management prior to discharge
* Scotland:
  + Warfarin dose is prescribed according to local guidance.
  + Is the target INR and duration of treatment clearly documented in the notes?
  + Patient complying with dosage instructions.
  + INR is taken according to previous recommendation/INR is taken within 7 days of planned repeat INR?
  + Patient receives regular education/Patient has received education in the last 6 months.
  + Have all Measures been met?

## Limitations of this Study

This study has some limitations. Firstly, it was not a systematic review, but rather a time-limited evidence scan, which aimed to find the most relevant evidence, not necessarily all the evidence. It is expected that there will be evidence that exists but is not described in this report. Additionally, the organisations’ whose websites were searched are those thought *a priori* to have been most likely to have published relevant information. Hence, the search of institutional websites was not systematic or exhaustive. Furthermore, key informants at DHBs were selectively approached, based on information received suggesting who might have the relevant knowledge for each DHB. Time constraints meant that only a selected group of key informants could be interviewed, and it is possible that other informants may have been able to provide additional information. The DHB findings are, therefore, illustrative rather than comprehensive. Finally, the overall quality of literature and evidence sourced was low, which means that these findings should be seen as provisional, pending the publication of results from larger, or more methodologically robust research and evaluation.

## Conclusion

This study sought to identify academic literature, institutional guidance, and New Zealand QI initiatives relevant to the safe use of anticoagulants in hospital settings. Most evidence obtained was of low quality, however, there were some promising findings. These findings largely focus on increasing the role of pharmacists, in all settings (including wards, ED, preadmission clinics, anticoagulation management services, and other settings), as well as anticoagulation stewardship programmes, and some electronic interventions in conjunction with the above. Institutional guidance obtained largely concurred with this assessment of the evidence and anticoagulation stewardship programmes are enthusiastically promoted by the Anticoagulation Forum in particular, along with a wealth of supporting materials.

Transitions of care have been identified as points at which management of anticoagulation is susceptible to discontinuity, error, or oversight. In the above evidence and discussion, change ideas have been identified that are pertinent to every care transition. These include pharmacist involvement (along with specialist thrombosis nurses) in pre-admissions, anticoagulation bridging services to manage the interruption of anticoagulation for elective procedures, systematic pharmacist oversight of anticoagulation prescriptions on the wards, at ED discharge, and inpatient discharge to the community, with potential for direct referral of those on anticoagulation to community anticoagulation management services, including patients taking DOACs. Anticoagulation management services could be established where these do not already exist.

These interventions can be governed by multidisciplinary anticoagulation stewardship programmes, that assess current practice, and prioritise interventions appropriate and specific to local context. Interventions at transitions of care, as well as stewardship programmes, can be supported using e-prescribing, with patient-context-specific CDSS and systems of alerts so that the right individuals are notified of patients relevant to their expertise and scope of practice. Systematic use of electronic systems would support monitoring, audit, and evaluation. A national programme could be established that pairs ‘systems haematologists’, or others with relevant expertise, with hospitals to help develop these programmes. Nationally consistent standards of care and guidelines could help reduce complexity and make audit comparable across providers.

The above can be achieved by following the step-by-step toolkits that exist to support initiatives aimed at reducing anticoagulant-related harm.

## Appendices

### Appendix A: Tabulation of Sources Obtained (Tables A1 – A5)

**Table A1: Anticoagulant harm QI initiatives - Meta-analyses & reviews** (arranged alphabetically by first author)

| **Authors/link** | **Design** | **Population** | **Intervention** | **Comparator** | **Outcome** | **Quality of Evidence** |
| --- | --- | --- | --- | --- | --- | --- |
| Austin et al 2020 | Systematic review of literature (to Sept 2018) to determine which EMR interventions improved safety and quality of anticoagulation.  27 studies (including 3 RCTs, 4 cohort studies and 20 pre/post observational studies) | Inpatient hospital setting | **4 major EMR interventions**: computerised  physician order entry (CPOE) (n = 4 studies), clinical decision support system (CDSS) methods (n = 21),  dashboard utilisation (n = 1) and EMR implementation in general (n = 1) | Business as usual | **Some limited benefits** have been demonstrated to date across 7 outcomes:  Prescribing or documentation  compliance (n = 18), medication errors (n = 9), adverse drug events (n = 5), patient outcomes (morbidity/mortality/length of hospital stay/re-hospitalisation) (n = 5), quality use of anticoagulant (n = 4), end-user acceptance (n = 4), cost effectiveness (n = 1).  **Research investigating clinical impact to the patient is scarce**, with only 5 studies reviewing ADEs and 5 investigating morbidity/mortality/LOS/re-hospitalisation outcomes  “It appears healthcare organisations are yet to determine optimal, evidence-based-methods to improve EMR utilisation” | No papers assessed the effectiveness of EMR strategies on improving the quality and safety of use of DOACs  The 3 RCTs were designed and conducted to reduce bias.  Other studies lacked robust allocation method |
| Frazer et al (2019) | Systematic review of literature (to March 2018) on interventions to improve safety or quality of anticoagulant prescribing  (19 controlled trials included, n = 12,742) | Hospital inpatients | **Interventions to improve safety and quality of anticoagulant prescribing** for therapeutic interventions | No intervention, usual care, or another intervention | **Physician-led anticoagulation consultation services** may reduce bleeding rates in high-risk patients.  Meta-analysis found **decision supported warfarin dosing** resulted in higher proportion of time with INR in therapeutic range (p = 0.0007).  Other CDSS and heparin monitoring systems did not demonstrate improved safety, and quality findings were inconsistent.  **Systematic education and feedback programs were not efficacious**.  The authors noted that: “While there is insufficient evidence to recommend widespread implementation of inpatient anticoagulation consultation services on the basis of this single study (**Landefeld et al 1992**), support from observational studies, and high-level evidence of the utility of consultation systems in other contexts (such as outpatient-based anticoagulation clinics and antimicrobial stewardship) suggest further RCTs are warranted. Establishing an anticoagulation consultation service is resource intensive, may only be viable in larger centres and cost-effectiveness is uncertain.” (p.1654) | No study evaluated prescribing of LMWH or DOACs  Authors state: “There is currently **insufficient high-quality evidence** to recommend any reviewed intervention, though several  warrant closer evaluation.” |
| Kahn et al 2018 (full text)  &  Kahn et al 2019 (abridged version) | Cochrane systematic review of RCTs  (13 studies included, n = 33,207) | Hospitalized surgical and medical patients at risk of VTE | **System-wide interventions** such as alerts, multifaceted interventions, education, pre-printed orders | No intervention, existing policy, or another intervention | Alerts increased the proportion of patients who received prophylaxis and appropriate prophylaxis and decreased the incidence of symptomatic VTE. **Computer alerts were more effective than human alerts**.  Multifaceted interventions increased the proportion of patients who received prophylaxis but were less effective than alerts  There was **absolute increase in the prescription of prophylaxis associated with alerts** (21% increase, 95% CI [15% to 275%]) and multifaceted interventions (4% increase, 95% CI [3% to 11%]), absolute increase in the prescription of appropriate prophylaxis associated with alerts (16% increase, 95% CI [12% to 20%]) and relative risk reductions (risk ratio 64%, 95% CI [47% to 86%]) in the incidence of symptomatic VTE associated with alerts | Authors state: “The quality of evidence for improvement in outcomes was judged to be low to moderate certainty.” |
| Lee et al 2016 | Narrative review of literature on clinical impact of pharmacist-led anticoagulation services to evaluate efficacy and safety | Patient populations varied among studies (eg, elderly patients, post valve replacement surgery patients, and orthopaedic surgery patients) | **Pharmacist-led inpatient anticoagulation services** | Usual or physician-managed care | 26 studies included.  Divided into two categories:  1) autono­mous pharmacist-managed anticoagulation programs (PMAPs)  2) pharmacist recommen­dation  **Pharmacist management of heparin and warfarin appears to result in improvements in some surrogate outcomes** (international normalized ratio [INR] stability and time in INR goal range).  There is also some indication that pharmacist management **may be associated with reduced patient mortality**.  For direct thrombin inhibitors, there seems to be a shorter time to therapeutic aPTT and a greater percentage of time in the therapeutic range, as well as a decrease in the frequency of medication errors.  Pharmacist recommendation services have generally resulted in a greater time in therapeutic INR range, greater INR stability, decreased length of stay, and reduced major drug interactions, with no significant differences in safety outcomes (see Table 1, p.55-56 in the paper for list of individual studies and results).  Authors’ conclusion, “Pharmacist-led inpatient anticoagulation management seems to result in superior outcomes, as compared to usual or physician-managed care.” | Non-systematic review of literature to 2015.  Conclusions were limited by small, poorly designed studies lacking statistical power, focusing mainly on surrogate outcomes. No meta-analysis conducted. |
| Paquette et al 2019 | Systematic review to assesses the effect of education on mortality,  thromboembolic events (TEEs) including venous thromboembolism (VTE), and bleeding in patients taking OACs (9 RCTs, n = 1,366) | 3 studies included inpatient setting | **Supplemental education for patients** (explaining incorrect JAKQ responses; or daily visits by nurses and physicians emphasizing education, visual material; or 5-min educational video) | Usual care | Authors conclusion: “Despite additionally searching the 6 most recent research intensive years and including additional studies, there was **low to very low certainty in the evidence for improving patient-important outcomes with supplemental education**. Although absolute risk of harm with education tended to be lower with supplemental education, we were uncertain about this effect on critically important outcomes. The small magnitude of improvement (<3%) on TTR alone is unlikely to be sufficient to improve critical” | Authors state, “The certainty of evidence was low to very low because of serious risk of bias and serious imprecision”  Small number of events and limited follow-up raises serious concern with overall precision. Difficult to draw conclusions with any certainty. |
| Sennessael et al 2020 | Systematic review of impact of computerized CDSS on prescribing of OACs and features associated with success or failure (16 studies included) | 6 studies were in hospitals | **CDSS for**  **the initiation or monitoring of oral anticoagulants** | Routine care | Most CDSS were integrated  in electronic records or prescribing and provided support automatically at the point of care.  **Significant improvements in practitioner performance** were found in 9 out of 16 studies (eg not reordering interacting medicines following alert, reduced medication errors, proportion of AF on OAC).  Clinical outcomes were poorly reported.  Low usage of CDSS noted (5-30%).  The only study that found a reduced risk of bleeding (in the CDSS group) was in primary care setting: Karlsson et al. (12 vs. 16 events per 1000 patients, p = 0.04) | Authors state: “the small number and heterogeneity  of studies, the limited impact and the **risk of bias preclude general conclusions** regarding the impact of CDSS on oral anticoagulant prescribing. Moreover, the effect on clinical outcomes remains unclear.” |
| Yiu and Bajorek 2019 | Narrative review with aim to identify patient-focused interventions  trialled to support vulnerable patient populations taking oral anticoagulants and outcomes | Oral anticoagulants (warfarin and DOACs), older persons (65 years and over),  those with limited health literacy, and those from culturally and linguistically diverse (CALD)  backgrounds | **Monitoring using INR** (n = 20 studies), **patient education**: written information (n = 2), decision aids (DAs) (n = 6), videos (n = 3), pharmacist counselling (n = 1), medication instructions (n = 1), and programs with multiple components (n = 4). | Often usual care | 41 studies were identified (37 were studies of older people taking warfarin).  A variety of outcomes were assessed including knowledge, anticoagulation control, adverse effects, decisional conflict, mortality, QOL, and patient satisfaction and persistence with warfarin therapy.  **Many interventions reported a significant positive impact on patients’ knowledge, reduction in the number of AEs caused by haemorrhage, and better INR control**.  One RCT (n = 125) found benefits of education alone in improving TTR (Khan 2004)  A post-discharge home-based service decreased AEs from warfarin | Non-systematic narrative review of literature to June 2017, many studies were RCTs or prospective, however timeframe of some outcomes as short as 28 days (only knowledge assessed in one study), some studies included because they fit the search criteria, not because they studied the vulnerable groups of interest. Heterogeneous methods and outcomes, no meta-analysis performed. |
| Zheng et al 2020 | Systematic review and meta-analysis to evaluate the role of technology-based interventions in the management  of OACs (15 RCTs included, n = 2,218) | Multiple settings, including discharge from hospital, mean age >60 years in all studies.  Inclusion criteria:  (1) RCT  (2) taking warfarin  (3) technology-based  interventions used to manage OACs;  (4) results report TTR, bleeding, and  VTE events  (5) English | **Technology-based intervention** to manage warfarin, telephone included. | Usual care | **Technology-based interventions significantly improved the effectiveness of oral anticoagulation management,** as measured by TTR (mean difference [MD]=6.07; 95% CI 0.84-11.30; I2=72%; P=.02).  The safety of oral anticoagulation management was also improved, but the results were **not statistically significant**. Bleeding events were reduced (major bleeding events MD=1.02; 95% CI 0.78-1.32; I2=0%; P=.90; minor bleeding events MD=1.06, 95% CI 0.77-1.44; I2=41%; P=.73) and thromboembolism events were reduced (MD=0.71; 95% CI 0.49-1.01; I2=0%; P=.06).  In general, patients were more satisfied with technology-based interventions, which could also improve their knowledge of anticoagulation management, improve their quality of life, and reduce mortality and hospitalization events. | Included studies had relatively small sample sizes and varying  follow-up times, with some as short as 1 month.  Authors state, “the Cochrane  systematic evaluation method was used for quality evaluation, and overall, the included studies had **low risk of bias and were**  **high quality**.” |

**Table A2: Anticoagulant harm QI initiatives - Individual studies** (arranged by intervention type: anticoagulation stewardship, interventions at discharge, pharmacist interventions, electronic interventions and CDSS, and other interventions)

| **Authors/link** | **Design** | **Population** | **Intervention** | **Comparator** | **Outcome** | **Quality of Evidence** |
| --- | --- | --- | --- | --- | --- | --- |
| **Anticoagulation Stewardship** |  |  |  |  |  |  |
| Dreijer et al 2019  AND  Dreijer et al 2020 | Two hospitals, prospective non-randomised before-and-after study (n = 1,886) | Netherlands, patients hospitalized between October 2015 and December 2017 and treated with anticoagulant therapy | Hospital-based  **multidisciplinary antithrombotic stewardship programme** (education, medication reviews, drafting of local anticoagulant therapy protocols, patient counselling and medication reconciliation  at admission and discharge).  The pharmacotherapy review focused on dosing (i.e., in relation to decreased renal function, body weight and age), duplicate medication, drug–drug interactions,  contraindications and perioperative bridging of  anticoagulants | Business as usual pre-intervention | **Adherence was observed significantly more often during the intervention period** (adjusted odds ratio [ORadj] 1.58, 95% confidence interval [95% CI] 1.21–2.05). The significantly higher overall adherence in the intervention period was attributed to dosing of LMWHs (odds ratio [OR] 1.58, 95% CI 1.16–2.14).  “Introduction of a multidisciplinary  antithrombotic stewardship leads to a significantly higher overall adherence to anticoagulant guidelines.”  Dreijer et al 2020 additionally examined a **composite endpoint: one or more bleeding episodes or one or more thrombotic event** from hospitalization until three months after hospitalization in patients using anticoagulant drugs, this **reduced in the intervention group (-1.83% (-2.58% to -1.08%) per 2 month period).**  **All-cause mortality was significantly lower in the intervention period [8.6% (81/945)] compared**  **to the usual care period [11.5% (108/941)] OR 0.72 (0.53 to 0.98).**  **Economic evaluation showed that total costs decreased at both sites, although not statistically significantly.** | Moderate quality (multi-site, large population, composite endpoint measured, as well as all-cause mortality), but nonrandomised, and some variation in before and after patient populations, including that more intervention patients were on NOACs and fewer on warfarin |
| Wychowski et al 2017 | Pre-/post- intervention study | USA, inpatient, hospital-wide | **Anticoagulation stewardship programme** (consisting of two clinical pharmacists and haematologists to provide oversight of anticoagulants, high-cost reversal agents,  and heparin-induced thrombocytopenia (HIT) management) | Usual care pre-intervention | 19,445 patient charts were reviewed, and **1930 (10%) contained stewardship**  **opportunity**.  Of the interventions, 71% were provided to the medical service and 22% to surgical services with  acceptance rates of 91 and 83%, respectively.  Intervention cost-avoidance calculated to be $694,217.  55.8% of PCC orders were considered inappropriate in the pre-invention period versus 2.6% post-intervention.  Appropriate PCC doses per month post-intervention were consistent  with pre-intervention doses (7.67 vs. 6.73, respectively).  Overall **estimated financial impact is $799,690 saved**. Implementation of an anticoagulation stewardship  program reduced costs and improved clinical outcomes. | Moderate quality, large study with associated budget impact calculation |
| Reardon et al 2015 | Single institution case study | Hospital inpatients with focus on  (1) management of heparin-induced thrombocytopenia (HIT)  (2) management of patients with Hemophilia A/B with inhibitors and acquired Factor VIII deficiency due to inhibitors  (3) oversight of anticoagulation in patients on  extracorporeal membrane oxygenation  (4) assistance with anticoagulation management for patients with mechanical cardiac assist devices. | A **haemostatic and antithrombotic stewardship programme** to provide real time clinical surveillance and management  Programme staffed daily by an interdisciplinary team. | Previous financial year | Cost per patient savings of $1141 or an estimated $228,200 for fiscal year 2014 (FY14) in patients treated for HIT  Annual cost of stewardship $175,000, which accounts for the pharmacist salary and a portion of the attending Hematologist and Medical Director’s  salary. **Economic impact of the stewardship for FY14 is estimated $1,449,417, based on cost avoidance** and an overall decrease in expenditure for DTIs for the treatment of HIT. | Low quality, retrospective, non-randomized, pre-post design |
| Perlman et al 2019 | Single institution (2 hospitals), retrospective, n = 585 | All hospital inpatients with DOAC orders, mean age 78 years. | **Anticoagulant stewardship**, a hospital-wide program, for monitoring and promoting  safe and effective prescription of DOAC during hospitalization. Electronic medical records throughout the hospital were screened for DOAC orders. All DOAC orders were assessed by a clinical pharmacist for potentially-inappropriate prescribing. When potentially-inappropriate prescribing or a drug-related problem was identified, the clinical pharmacist provided consultation on management  options | No comparator | Most patients (63%) received “reduced dose” DOAC regimens. Clinical pharmacists provided 258  consultations for 210 patients, regarding anticoagulation management, **more than one in three patients on DOAC had potentially inappropriate prescribing or drug related problems**. Consultations included alerts regarding potentially inappropriate DOAC doses and recommendations to increase (29%) or decrease (5%) the  dose, potentially inappropriate concomitant antiplatelet agents (20%), need for DOAC level monitoring (23%), and  alerts regarding other drug related problems (23%).  **More than 70% of recommendations were accepted by the attending physician**. | Low, non-randomized, no comparator, no outcomes measured. |
| Bui et al 2021 | Single institution case study of development of AAA (including anticoagulation) stewardship programme | Australian public metropolitan tertiary referral hospital  network with over 600 overnight beds across three  campuses | Implementation  of **anticoagulation and analgesic stewardship programs**, based on local AMS program principles (Antimicrobial, Anticoagulation, Analgesic (AAA) program) led by a full-time Senior  Clinical Pharmacist and a Clinical Haematologist  Core elements (see Table 1, p.343 for more details):  1. Structure and governance, with multidisciplinary, hospital-wide stakeholder engagement  2. Clinician education  3. Monitoring of stewardship program outcomes, supported by access to data  4. Implementation of quality improvement activities and initiatives  5. Involvement of the lead pharmacist in patient-centred clinical care | Pre-post design Data gathered from year following implementation | Coded data for hospital acquired **VTE in the subsequent year demonstrated a 33% reduction in events. Follow-up data for hospital-wide anticoagulant-related bleeds 12 months after ACS program implementation showed a 20% reduction** in events. | Very low quality, single institution before and after study, **no statistical analysis provided**. |
| Attia et al 2022 | Description of development of an intervention. Multi-site (hospital system, which includes 1 academic  medical centre, 6 community hospitals, and 1 long-term care facility) | Hospital system processes targeted | **Multidisciplinary anticoagulant safety taskforce** (ASTF) to address anticoagulation-related issues  across the medication-use system, **used the 2017 Institute for Safe Medication Practices (ISMP) Medication Safety Self-Assessment for Antithrombotic Therapy** to review current practice, performing gap analysis,  and identify opportunity. 8 best practice elements were identified for initial efforts of  ASTF activity.  Error mitigation occurred through policy revisions, order set development and modification, and implementation of practice changes to comply with each best practice | Baseline score on the ISMP antithrombotic self-assessment score. | The **ISMP antithrombotic self-assessment score improved from 67% to 87%,** surpassing the initially targeted score of 75%. | Very low quality, descriptive case study, with self-reporting, no outcome data measured |
| **Discharge Protocols or Follow-up** |  |  |  |  |  |  |
| Gurwitz et al 2021 (RCT) | RCT (n = 361) | USA, large  multidisciplinary group practice, patients >50 years (mean 69 years)  discharged from hospital and prescribed at least 1 high-risk medication | **Multifacted pharmacist-directed follow-up** on discharge from hospital, included in-home clinical pharmacist assessment (<4 days), evidence-based educational resources, communication with the primary  care team, and telephone follow-up. | Participants in the control group were provided  educational materials via mail. | Assessed across 45 days post-discharge.  81 ADEs in the intervention group and 72 in the control group.  44 clinically important medication errors in the intervention group and 45 in the control group.  **The intervention did not significantly alter the per-patient rate of adverse drug-related incidents** (unadjusted incidence rate ratio, 1.13; 95%CI, 0.83-1.56) or clinically important medication errors (unadjusted incidence rate ratio, 0.99; 95%CI, 0.65-1.49). | Moderate quality, randomized, but possibly underpowered, there were study recruitment challenges and lower than expected numbers of  events among the study population. Some possibility of bias towards an effect. |
| Kapoor et al 2020 | Randomized, controlled study, n = 163 | Adults 18 years and older diagnosed with a new episode of VTE and prescribed anticoagulation | A care transition intervention with **pharmacist home visit and subsequent anticoagulation expert consultation** for patients with new episode of venous thromboembolism. At home visit: assessed medication management proficiency, asked open-ended questions to discuss knowledge gaps, and distributed illustrated medication instructions. Subsequent consultation  with anticoagulation expert further filled knowledge gaps. | Usual care | The mean ± SD time required to conduct home visits was 52 min. Most patients agreed that the intervention was helpful. In general, **patients reported a high-quality care transition**. Despite that, mean percentage of knowledge items answered correctly among  patients was low (51.5 versus 50.7 for intervention and controls, respectively). | Moderate quality, randomized, controlled, but no outcomes measured, focus on knowledge & beliefs. |
| Kallal, Griffen, and Jaeger 2020 | Single institution, pre-post study of a Lean Six Sigma intervention to reduce warfarin omission at discharge | Inpatients started on warfarin therapy, managed with one-time  warfarin orders and warfarin indicated at discharge | A system alert that fires to providers at chart closing after discharge medication reconciliation is completed. The **alert identifies patients**  **that received warfarin during admission but without warfarin prescription** at discharge. | Incidence of warfarin omission pre-intervention | Three months post-implementation,  96 alerts fired to 42 providers on 40  patients. The **rate of intended warfarin prescriptions at discharge that were omitted decreased** from 1 omission per  month to 0 omissions per month or 10.5% (4/38) to 0% (0/40) (two proportion test, p=0.03). | Low quality, small single centre study, no control group. |
| Dunn et al 2015  [*see also Day 2016: no statistical analysis*] | Pre/post- retrospective administrative database review (n = 797) | Hospital inpatients who were discharged on warfarin and were established patients at an affiliated ambulatory practice. | ‘Safe transitions’ discharge form, **a concise discharge report** to improve the timeliness  of international normalized ratio (INR) testing and quality  of warfarin management post-hospitalization. | Usual care pre-intervention | There was no change in the frequency of obtaining an INR value within 10 days of discharge (41.4% and 47.6%, respectively, P = 0.09), and no increase in attaining a therapeutic INR level within 10 days of discharge (17.0% and 21.2%, respectively, P = 0.14). Ambulatory clinicians reported that the STAR improved “workflow and efficiency” (58%) and “patient safety” (77%), and led to an altered warfarin dose for 34% of survey respondents.  A concise anticoagulation report embedded in the discharge summary was perceived by ambulatory physicians as improving patient safety, but had **no impact on clinical outcomes**. | Low quality, single centre, retrospective, non-randomized |
| **Pharmacist Interventions** |  |  |  |  |  |  |
| Karaoui et al 2021 | Randomized, non-blinded interventional study (RCT) (n = 200) | Lebanon, inpatients ≥18 years discharged on an oral  anticoagulant for treatment. | Standard nursing counselling plus **pharmacy counselling**: Phone call follow-ups on day 3 and 30 post-discharge | Standard nursing counselling | Pharmacist education **significantly increased patient communication with their providers** in the early days post-discharge.  In the pharmacist-counselled group, more patients contacted their physician within 3 days (14% versus  4%; p = 0.010), received explicit elements of education (p < 0.001) and documentation in the chart was better (p < 0.05).  In the standard of care group, patients were more aware of their next physician appointment date (52% versus 31%, p < 0.001).  **No difference in bleeding rates** at day 3 and 30 post-discharge was observed between the groups. | Moderate quality, randomized, but single-centre design, lack of power calculation and small sample size may have decreased  the possibility of detecting statistically significant difference  in bleeding rates between groups. |
| Liang et al 2020 | RCT, n = 152 | China, adult inpatients newly  initiated on warfarin with intended treatment 3 months or more | **Pharmacist-led education and follow-up service**, Prior to discharge, each participant  in the PEFS group was provided with a standardised, one-on-one warfarin education session, which lasted for 15 min on average, patient education booklet and two phone follow-up sessions (day 30, 90), pharmacists did not adjust dosing. | Usual care | Within 180 days after hospital discharge, **the PEFS group spent more time in extended target range than the UC group** (54.4% versus 42.0%; P = 0.024),  whereas the difference in TTR did not reach statistical significance (35.9% versus 29.5%; P = 0.203).  No major bleeding events were observed, and the cumulative  incidences of major thromboembolic events (6.5% versus 9.3%) and  mortality (1.3% versus 1.3%) were similar between the two groups (P> 0.05).  At 30 days post-discharge, the PEFS group had **better warfarin knowledge** answering 57.5% of questions correctly, compared with the UC group (43.0%) (P = 0.003). | Moderate quality, randomised, but physicians might have dosed too conservatively. Mean TER was  only 54.4% in the PEFS group, which was considerably  lower than that reported in the previous studies (78–82%  of TER). |
| Hale et al 2018 | Cost-effectiveness decision tree modelling study informed by the RCT of Hale et al 2013 | High risk surgical patients at pre-admission clinic | **Pharmacist pre-admission prescribing**: prescribes usual medications, assesses VTE risk and prescribes VTE prophylaxis | RMO assessment and prescribing | Pharmacist prescribing increased the proportion of patients adequately treated and decreased incidence of VTE resulting in cost savings and improved quality of life.  **Cost savings** were $31 (95% CI: -$97, $160) per patient in the base scenario and $12 (95% CI: -$131, $155) per patient in the alternative scenario.  In both scenarios the pharmacist-doctor prescribing resulted in an **increase in QALYs** of 0.02 (95% CI: -0.01, 0.005) per patient. | Moderate quality, cost analysis applied to findings of an RCT. However, null finding is possible, as **CIs include zero for both costs and QALYs**. |
| Willeford et al 2021 | Retrospective, single-centre cohort study, pre-post design, n = 502 | Hospital inpatients, but excluded if  DOAC was for an indication other than VTE or AF. | A **pharmacist-driven DOAC protocol** that permitted pharmacists to independently order and monitor DOACs pursuant to a consult order. | Business as usual pre-intervention | 41 patients in the pre-phase received a medication error involving a DOAC compared with 22 patients in the post-phase (16% vs 8.9%; **relative risk reduction 44%; P = 0.017).** Rates of near misses were numerically higher in the post-phase group (7.4% vs 11.8%; P = .1), and rates of discharge DOAC errors were numerically lower (8.5% vs 4.9%; P = .1). The most common error was underdosing (N = 31).  Authors state: “These findings underscore the impact of a protocolized approach to DOAC management, as well as the role of pharmacists in overseeing inpatient DOAC use.” | Low quality, retrospective, single centre, no outcomes measured. |
| Zdyb et al 2017 | Single centre (tertiary 900 beds),  retrospective analysis, n = 174 | Patients discharged from the ED between May 2013 and May 2016 with a new anticoagulant  prescription. | Patients discharged with a new prescription for any anticoagulant receive **education from an ED pharmacist** when on-site, plus, they received follow-up phone calls from an ED pharmacist within 72 hours of discharge. Counselling was supported by a written e-form, and auto triggering of pharmacy consult upon prescription of an anticoagulant. | Physician and nursing-driven  discharge measures (usually provided out of pharmacist hours) | Patients who did not receive pharmacist education required more  intervention during call-back versus those who did (36.4% vs. 12.9%, p = 0.0005) related to adherence, inappropriate administration, and continued use of interacting medications or supplements.  In addition, **patients who had not received pharmacist counselling**  **were more likely to be readmitted to a hospital or return to the ED** within 90 days for an anticoagulation-related problem (12.12% vs. 1.85%, p = 0.0069). | Low quality, retrospective, potential differences between cases and controls (eg out-of-hours) |
| Bakey and Nguyen 2021 | Single centre, retrospective cohort study, n = 58 | Low-risk VTE patients discharged from the ED | Protocol for **pharmacist involvement at the time of VTE diagnosis** (cohort with pharmacist involvement) | Cohort without pharmacist involvement | 14 patients had a pharmacist directly involved with their care in the ED while 44 patients did not. **The rate of medication errors was lower when a pharmacist was involved**, 7.1% (n = 1), compared to when a pharmacist was not involved, 36.4% (n = 16), (p = 0.046). All patients in the pharmacist involvement group received anticoagulation counselling prior to discharge compared to only 56.8% of patients in the non-pharmacist involvement group (p = 0.002). | Low quality, single centre, non-randomized, small study |
| Miele et al 2017 | Single centre (504 bed teaching hospital), pre-/post- study, n = 50 pre- and 85 post- | USA, Adult patients admitted to a community teaching hospital who received >= 2 days DOAC therapy January to March 2015 (pre-intervention  group) and January to March 2016 (post-intervention group). | **Pharmacist-driven DOAC service** including an evidence-based prescribing table to guide appropriate DOAC therapy, daily reports and review of all patients on DOACs. | Usual care pre-intervention | A total of 333 (pre-) and 816 (post-) doses were administered. Of the total doses, **32.4% were considered inappropriate in the pre-intervention group compared with 13.8% in the post-intervention group** (adjusted odds ratio [OR], 0.42, 95% CI,  0.19-0.96; p = 0.039). | Low quality, small study, single-centre, non-randomized |
| Lineberry et al 2021 | Single centre, retrospective review, n = 378 prescriptions | ED discharge prescriptions containing pre-specified high-alert medications, over a 12-week period from February 19th, 2018 to May 14th, 2018 | **Pharmacist review of ED discharge prescriptions** triggered by real-time notification system in EHR | No comparator | Pharmacists reviewed 378 discharge prescriptions and a total of 158 prescriptions were identified as having at least one problem. Of these **anticoagulation prescriptions had a 15.4% intervention rate**. | Low quality, single-centre, non-randomized, no comparator |
| An et al 2017 | Single centre, retrospective cohort study, n = 57 | Non-valvular AF patients with HF admitted and discharged from CV internal medicine ward March 2011 to July 2013 | **Patients instructed by hospital pharmacists** and physicians | Patients instructed by physicians only (usual care) | **TTR within therapeutic range was significantly higher in intervention group**.  Time in sub-therapeutic range was significantly lower in intervention group. | Low quality, small study, single centre, not randomized. |
| Tavakoli et al 2022 | Brief (2 week) observational study | Postsurgical  non-intensive care patients | **A clinical pharmacist provided care for 2 postsurgical inpatient floors** for 2 weeks | No comparator | The **clinical pharmacist made 218 interventions, including 26 recommendations for**  **anticoagulation optimization**, and provided education for 20 patients planned for discharge on high-risk medications | Very low quality, no comparator, brief study, single site, not randomized. |
| Sharma et al 2017 | Retrospective review of medical records (community teaching hospital) | Internal medicine ward rounds, n = 41 identified medication errors | Incorporation of **clinical pharmacist on daily rounds** | No comparator | Of **41 medication errors described** most were related to LMWH (20 cases) followed by 10 cases of medication errors related to NOACs, 9 cases where appropriate anticoagulation was not initiated and 2 cases involved errors with warfarin. Inaccurate renal dose adjustment was common (15). | Very low quality, descriptive, only errors included, no comparator |
| **E-prescribing, Electronic Health Record, Clinical Decision Support Systems (CDSS), and Apps** |  |  |  |  |  |  |
| Spyropoulos et al 2020 | Prospective, 2 cohort comparison study, n = 642 | Adults, creatinine clearance >=15 mL/min, on chronic OAC, undergoing elective procedures, mean age 73 years | The MAPPP (management of anticoagulation in the peri-procedural period) app was integrated into the electronic health record (EHR), and the end user was free to accept or decline **app/EHR recommended**  **evidence-based perioperative anticoagulation management guidance**. | Non-acceptance of MAPPP recommended guidance | Acceptance of recommended guidance was more common in  younger patients (P = 0.0137), patients on oral anticoagulants other than warfarin (P < 0.0001), and patients undergoing increased  bleeding risk procedures (P = 0.0068). Acceptance of the MAPPP app recommendation was significantly associated with fewer ED visits (acceptance group: 4.0% vs rejection group: 8.3%, P = 0.0205). Logistic regression showed that **intervention acceptance and**  **female gender were significantly associated with fewer 30-day ED visits.** | Low to moderate quality, single institution, prospective study with comparator, not randomized. |
| Quintens et al 2019 | Single centre (1995 bed academic tertiary hospital), 18-month retrospective, observational study | Belgium, 39,481 clinical rule alerts | A back-office clinical pharmacy service, called “Check of Medication Appropriateness” (CMA),  consisting of **clinical rule-based screening (daily) for medication inappropriateness** | No comparator | 39,481 clinical rule alerts were checked, 2568 (7%) electronic notes were sent and 637 (1.6%) phone calls performed. 37,782 (96%) alerts were checked within four pharmacotherapeutic categories: drug use in renal insufficiency (25%), QTc interval prolonging drugs (11%), drugs with a restricted indication or dosing (14%)  and overruled very severe drug-drug interactions (50%).  **Anticoagulants were drug class for which actions are most frequently carried out, eg** overruled combination of DOACs with other anticoagulants (often LMWHs) was the most frequent alert for which a phone call was carried out (37%) or an electronic note was sent (15%). 57% of electronic notes about renal insufficiency were sent for direct oral anticoagulants (DOACs).  69% of actions were accepted by physicians. | Low quality, retrospective, observational, no comparator |
| Quintens et al 2022 | Before and after  implementation, quasi-experimental interrupted time series analysis | Belgium, non-critically ill inpatients | Clinical decision rules (implemented in electronic system) to promote judicious medication use: ‘Check of Medication Appropriateness’ (CMA), **a pharmacist led review service, targeting potentially inappropriate prescriptions** (PIPs), including anticoagulants, comprising 13 clinical rules pertaining to anticoagulation therapies (Table 3 in Quintens et al 2022 displays the rules). | Usual care | Pre-implementation, 501 PIPs in 466 inpatients on 36 days, with a median proportion of 78.5% (range: 46.2%–100%) residual PIPs per day. Most frequently in geriatrics. Postimplementation (36 days),  538 PIPs were detected in 485 patients over the same number of days.  The CMA intervention reduced the median proportion to 18.2% (range: 0–100%) per day. The effect coincided with **an immediate relative reduction of 70% (95%CI 0.19–0.46) in anticoagulant-related residual PIPs**.  In observational study across 2-years **post-implementation, 2778 recommendations were provided and 75.1% were accepted** | Low to moderate quality, pre-/post- study, with 2 years additional follow-up |
| Ibanez-Garcia et al 2019 | 6-month, single centre (1,300 bed tertiary), observational  prospective study | Inpatients whose prescriptions violate one of 211 clinical rules | **CDSS (HIGEA), which generates alerts based on predefined clinical rules** to  identify patients at risk of an ADE. Specialist pharmacists review all alerts. | No comparator | HIGEA generated 1,086 alerts (8.9 alerts per working day), which were reviewed by pharmacists. **Fifty-one percent (554/1,086) of alerts generated an intervention to prevent a possible ADE**; of these, 66% (368/554) required a documented modification to therapy owing to a real prescription error intercepted. The highest number of modifications to therapy was in dose adjustment for renal impairment program (PPV = 0.51), followed by the **adjustment of anticoagulation/antiplatelet therapy program (PPV = 0.24).**  HIGEA could be highly effective in preventing potential ADEs at the prescription stage.  When specialist pharmacists examine the alerts generated daily, **the system identifies a large number of potential ADEs that go unnoticed by the physician** and led to a change in the clinician’s decision (368/554; 66%) | Low quality, not randomized, no comparator, no outcomes measured. |
| Ahuja et al 2021 | Single institution case study (725 bed tertiary academic), retrospective review, n = 121 patients | Randomly selected adult inpatients, who received at least two doses of a DOAC from January 2013 to July 2014, median age 73 years | Antithrombotic stewardship team developed guidelines  and implemented **CCDS tools to enhance medication and patient safety related**  **to the DOAC** (including alerts, dosage information, contraindications/interactions), a clinical pharmacotherapy specialist performs a daily review of patients prescribed a DOAC to ensure the dose is appropriate for acute phase hospitalisation. | No comparator | Adherence to CCDS was 80% (n = 24), 75% (n = 46), and 87% (n = 27) in the dabigatran, apixaban, and rivaroxaban group, respectively. **Bleeding events did not correlate with nonadherence to CCDS recommendations.** | Low quality, uncontrolled, retrospective, small sample |
| Nazarenko et al 2015 | Single-centre, pre-/post- study. | VTE cases and pulmonary embolism in 2014 before and after CDSS implementation, as well as in the first half of 2015. Patients with VTE in first 48 hours of hospitalization or receiving anticoagulants in therapeutic doses  were excluded. | A multifunctional **CDSS based on national and international guidelines** on VTE prevention was developed and implemented in the Medical Center of the Bank of Russia | Business as usual for 6 months prior to intervention | The **rate of hospital-acquired VTE significantly decreased after CDSS implementation** and was 11.71, 8.28 and 4.84 per 1,000 hospitalizations in the first and second half of 2014 and in the first half of 2015, respectively (χ2 = 7.325, df = 1, p = 0.0068). The rate of postoperative VTE for the same period amounted to 8.76, 3.39 and 4.17 per 1,000 operations, respectively (χ2 = 7.266, df = 1, p = 0.007).  Coverage of hospitalized patients with documented VTE risk assessment gradually increased after the CDSS implementation, but remained at a low level (19% of eligible patients).  Deviations from clinical guidelines or anticoagulant package inserts were revealed in 74% of VTE cases. | Low quality, single centre, non-randomized study. |
| Khalil et al 2021 | Pre-/post- retrospective study at a multi-site teaching hospital (650 beds), n = 100 | Australia, inpatients, prescribed a NOAC for AF, PE, DVT, AVR. | **Tailored electronic patient specific physiological alerts** (such as age, renal function weight and drug interactions) built in EMS to improve the appropriateness of NOAC prescribing | Usual care pre-implementation | Redesign of computerised decision support in EMS **improved appropriateness of NOAC prescribing from 48 % to 91 %, P *<* 0.05.**  Implementation of NOAC alerts reduced inappropriately prescribed high doses of NOACs (39 % vs 2%, P = 0.003) and inappropriately prescribed low doses of NOACs (P = 0.002), but did not prevent the incorrect type (as suited to the patient comorbidities) of NOAC being prescribed (4% vs 1%, p = 0.72).  A total of 67 prescribers accepted the invitation to participate in the qualitative satisfaction study. Half the respondents (n = 33, 50 %) answered positively to a question assessing the usefulness of implementing NOAC alerts in the EMS in improving their practice and patient safety  The number of hospital acquired complications trended downward, and may have reduced costs, but not statistically significant. | Low quality, not randomized, possibly underpowered to demonstrate reduction in complications. |
| Ishikawa et al 2021 | Pre-/post- design with evaluation survey, descriptive | Prescriptions containing DOACs dispensed by hospital pharmacists | A system for dispensing  DOACs using **a check sheet automatically printed at the time of dispensing** | Usual care | There were 4/642 (0.6%) inquiries from pharmacists to physicians regarding DOAC prescriptions, such as the dose  introduced before DOAC check sheet utilization and **increased to** **21/905 inquiries (2.3%) when the DOAC check sheet was used (p = 0.0089).**  After introduction, overdoses of DOACs were identified at the time of dispensing.  51/52 pharmacists who responded to the questionnaire stated that the check sheet was useful. | Low quality, small number of ‘inquiries’, self-report questionnaire. |
| **Other interventions** |  |  |  |  |  |  |
| Noseworthy et al 2022 | RCT, n = 922 | Patients cared for in EDs, outpatient safety net, primary  care and cardiology clinics, **and inpatient hospital**  **services**, a suburban group practice, and an urban safety-net  health system. Two cohorts: starting anticoagulation cohort and reviewing anticoagulation cohort. | Use of the Anticoagulation  Choice tool (**shared decision-making tool**) | Usual care | “In this large, randomized trial comparing UC with a tool to promote SDM against UC alone, we found **no significant differences** between arms in primary or secondary adherence to anticoagulation or in clinical safety outcomes.” | High quality, large and randomised, although enrolled fewer women and minorities. |
| Ruell et al 2019 | Single centre (**CCDHB)** prospective, consecutive patients, n = 566 (that underwent procedure) | All patients who required a surgical procedure or intervention that required  interruption of anticoagulation  between May 2015 and February 2017. | **Specialist perioperative anticoagulation bridging service** devised an individualised plan based on their anticoagulation,  surgical procedure, and indication for anticoagulation | Bleeding and thrombosis rates in existing RCTs | **Low rates of major bleeding 1.9% and thrombosis 0.8% at day**  **30 were comparable to RCTs**.  Zero of 222 patients taking dabigatran experienced major bleeding events.  Authors state, “We believe using a specialist coagulation service  is optimal to ensure surgery can proceed safely” | Low quality, no comparator, not randomized. |
| Pelkofski et al 2019 | Pre-/post- intervention study, (n = 100 intervention, 182 historical controls) | Women undergoing gynaecological oncology surgical procedures. | **QI intervention bundle:** Reasons for non-compliance identified, and then bundle to address this including: education, morale, documentation, communication, visibility, momentum (see Figure 1 in Pelkofski et al 2019 for details). | Cases in the year prior to intervention | Compliance was defined as the receipt of a prophylactic dose of anticoagulant within 1 hour after NA or before skin incision regardless of anesthesia type.  **Overall compliance improved (96% QI v 73% Control; P < 0.001).** This difference was marked in cases with neuroaxial anaesthesia (95% QI v 40% Control; P < 0.001) and remained stable in non-neuroaxial anaesthesia cases (97% QI v 91% HC; P = 0.29). Overall rate of VTE, independent of anesthesia type, remained unchanged (2.1% HC v 0% QI; P = 0.3). | Low quality, non-randomized, non-synchronous controls, outcome of VTE measured but probably underpowered. |
| Tranter-Entwistle et al 2020 | Single centre (**CDHB**) Pre- / post- intervention study, 233 patient consultations recorded (60 pre- introduction  and 89 and 84 during each post-introduction period) | All vascular inpatients seen on ward round during the assessed periods were included | Surgical **ward round checklist** based on WHO Surgical Safety Checklist | Usual care in the two weeks prior to intervention | **20 of 21 ward round quality indicators showed statistically significant improvement**, including anticoagulation/ antiplatelet treatment (32% to 61% to 58.1%) (P < 0.05). | Low quality, single centre, no outcomes measured, short timeframe |

**Table A3: Anticoagulant harm QI initiatives - High-level commentary and consensus** (arranged alphabetically by first author)

| **Authors/link** | **Article type** | **Population/setting** | **Intervention/Recommendations** | **Quality of Evidence** |
| --- | --- | --- | --- | --- |
| Alves da Costa et al 2020 | **Position statement from the International Pharmacists for Anticoagulation Care Taskforce** | Identifies seven steps on the patient care pathway, literature identified pertaining to all steps, one step is hospital care. | **Secondary care pharmacist role in anticoagulation**:   * Dosing and monitoring can be checked * Pharmacists can play a role in integrated medicines management * Pharmacokinetics monitoring * Monitor off-label prescribing (for no benefit) * Ensure appropriate dosing (including renal function adjustment) * Monitor for excess anticoagulant perioperatively, and insufficient at discharge * Educate patients at discharge (often 3 or more changed medications) * Improve transfer of information | Non-systematic review and high-level interpretation of evidence.  However, focus was on where pharmacist intervention is possible, less focus on what specific interventions might look like |
| Barnes and Kline-Rogers 2015 | Review **summarizing the justification for engaging in QI for anticoagulation management**, describes several programs (covering warfarin and DOACs), also details potential quality measures and provider resources | Michigan Anticoagulation Quality Improvement Initiative (Multi-centre, collaborative quality initiative); 6 anticoagulation management services in Michigan (mostly ambulatory care) | **Collaborative QI initiative**:  - Reduce inappropriate use of warfarin  - Develop more effective patient education materials  - Perform regular root-cause-analyses of AEs  - Reduce unnecessary lab testing, inappropriate aspirin use, and off-label dosing.  Collect data on patients taking oral anticoagulants from 6 participating Michigan health systems and entered into a data registry.  Collect information on each site’s protocols, processes, and structure to link outcomes with variations in clinic operations  **Michigan Anticoagulation Quality Improvement Initiative Toolkit**  <https://anticoagulationtoolkit.org/>  - Risk evaluation guides  - Initiation/management guides  - Patient education resources (includes email to referrer aiming to reduce duration of treatment for provoked VTE, extended INR interval)  - Adverse event reviews  **Recommended QI measures:**  Clinical events (bleeding, stroke/VTE, ED visits, hospitalizations, death), surrogate measures (TTR, INR variability, percent in/out of range INRs, percent missed or late INR test, adherence), process of care (INR in first 2 weeks, time from warfarin initiation to first INR, time from out-of-range INR to patient contact), population focused (percent of patients receiving guideline-based appropriate care, percent of patients receiving appropriate education, patients with drug-drug interactions at risk for GI bleeding) | Non-systematic expert interpretation of pre-2015 evidence |
| Dager et al 2020 | **Commentary from the Anticoagulation Forum on the Joint Commission’s NPSG.03.05.01** (see May & Moll 2019 below) | NPSG.03.05.01 is the National Patient Safety Goal for anticoagulation therapy: Reduce the likelihood of patient harm associated with the use of anticoagulant therapy | Rapid evolution of medical evidence and best practices requires serial re-evaluation of organizational guidance.  The Anticoagulation Forum provides continually updated guidance materials available at their Centers of Excellence website.  **Institutions need**:   * High-level buy in * Financial and personal resources * Clear communication * Multidisciplinary engagement * Policies and procedures must be easy to retrieve * Pharmacy and informatics involvement * Continuous redesign * Evaluation of performance | Authors’ Commentary on Joint Commission and Anticoagulation Forum initiatives |
| Harris et al 2015  see also the actual action plan (Dept Health and Human Services 2014) | Commentary on: ‘**National Action Plan for Adverse Drug Prevention 2014**’ (HHS Office of Disease Prevention and Health Promotion)  Anticoagulants are one of 3 medication classes targeted. Evidence-based prevention is one of 4 key areas. | p.58–66 of the action plan details interventions relevant to anticoagulation and hospital inpatients | **Existing ‘federal assets’**: Anticoagulation protocols, national anticoagulation training program, education for providers, chronic disease self-management program, patient education sheet and video, medication guides, ‘Project Red’ including medicines reconciliation, anticoagulant electronic flowsheet, medication use tracker, CDSS, shared resource centre  **Inpatient setting opportunities to prevent anticoagulation ADEs**:  Safer care: improve provider knowledge, improve dissemination of evidence-based tools, develop guidelines  Effective communication and coordination of care: improve EHR tools to integrate pharmacy/laboratory data, electronic flowsheets, CDSS, integrate anticoagulation-specific targets into care transition models  Science-Driven prevention and treatment: multidisciplinary, coordinated, systematic approach, eg anticoagulation rounds, pharmacist/nurse services, anticoagulation stewardship, culture of safety, guidelines  Promotion of best practices: eg anticoagulation centre of excellence, disseminate results of large-scale QI initiatives | High-level institutional guidance based on totality of evidence to 2014 |
| May and Moll 2019 | **Commentary on Joint Commission’s ‘list of Resources’ to accompany NPSG.03.05.01** | Health systems | [Joint Commission list of Resources](https://www.jointcommission.org/-/media/tjc/documents/standards/national-patient-safety-goals/historical/npsg_030501_resources.pdf?db=web&hash=F6DCAA29747C1586309C3557E72959FF&hash=F6DCAA29747C1586309C3557E72959FF) (organised by ‘element of performance’, EP1-EP6, as prescribed in NPSG.03.05.01).  EPs 1 through 3 include the use of approved protocols and evidence-based practice guidelines for medication selection, reversal and management of bleeding, and perioperative care.  EP 4 requires a written policy about laboratory testing to monitor and adjust anticoagulation.  EP 5 addresses institutional safety practices, including the development of processes for identifying and responding to adverse drug events.  EP6 focuses on patient education, ensuring that patients are aware of medication dose and schedule, follow-up plan, and potential drug interactions and adverse reactions  May & Moll note **an opportunity to implement a “systems-based haematologist,”,** a specialty-trained physician, employed by a hospital, *or health system*, who optimizes individual patient care, as well as the overall system of health care delivery. | Authors’ commentary on Joint Commission and Anticoagulation Forum initiatives |
| Spyropoulos et al 2015 | Consensus statement on ‘**Features of Electronic Health Records**  **Necessary for the Delivery of Optimized**  **Anticoagulant Therapy**’ with objective to generate a comprehensive, consensus-based list of EHR features clinically necessary to  deliver optimized AC management | EHRs generally | Electronic health records (EHRs) have the potential to improve safety and quality but have not yet incorporated specialized features necessary to optimize therapy. A multidisciplinary panel of AC specialists utilized the framework of a previously published consensus statement A finalized list of proposed features was ranked according to perceived clinical necessity by physician, pharmacist, and nurse panellists.  The task force generated **78 recommended EHR features across 20 key discrete areas** and 425 individual logic steps (detailed in Table 5 of Spyropoulos, p.118-120) | Expert Consensus of New York State Anticoagulation Taskforce, no implementation, outcomes measurement or evaluation undertaken. |
| Triller et al 2018 | Anticoagulated patients are particularly vulnerable to ADEs when they experience changes in medical acuity, pharmacotherapy, or care setting. New York State Anticoagulation Coalition task force developed a **consensus list of requisite data elements (RDEs)** | Data elements should accompany all anticoagulated patients undergoing care transitions | **Consensus on 15 requisite data elements** (RDEs) (12 general, 3 specific to warfarin)  See Triller et al 2018, Table 1, for a list of the 15 RDEs | Expert Consensus of New York State Anticoagulation Taskforce (15 member, multidisciplinary, Delphi process, blinded electronic polling) |

**Table A4: Institutional Guidance** (examples, arranged alphabetically)

| **Institution/Programme** | **Recommendations** | **Supporting resources** | **Evaluation** |
| --- | --- | --- | --- |
| Agency for Healthcare Research and Quality (AHRQ) | **Pharmacist-provided anticoagulation management services** (largely in ambulatory community care setting) | *Making Healthcare Safer III,* Chapter 7: Anticoagulants (AHRQ 2020) | Other interventions such as dosing protocols or nomograms for NOACs, and interventions to support safe transitions of care suffer a paucity of high-quality evidence. |
| Anticoagulation Forum (MIDAS Programme) | **Anticoagulation Stewardship** Programmes:  7 Core Elements   1. Secure Administrative Leadership Commitment 2. Establish Professional Accountability and Expertise 3. Engage Multidisciplinary Support 4. Perform Data Collection, Tracking, and Analysis 5. Implement Systematic Care 6. Facilitate Transitions of Care 7. Advance Education, Comprehension, and Competency | *Core Elements of Anticoagulation Stewardship Programmes* guidebook (Anticoagulation Forum 2019b)  *Administrative Oversight Gap Analysis: Hospitals and Skilled Nursing Facilities* (Anticoagulation Forum 2019a)  Checklist of core elements: <https://acforum-excellence.org/Resource-Center/resource_files/1392-2019-09-18-110525.pdf>  Anticoagulation Forum Centers of Excellence Resource Center: <https://acforum-excellence.org/> | Improved processes, outcomes, and cost-savings  ‘Anticoagulation Stewardship Evidence of Impact’ infographic (Anticoagulation Forum, 2022a)  ‘Anticoagulation Stewardship: Profiles in Progress’ – eight case studies of success (Anticoagulation Forum, 2022b) |
| Australian Commission for Safety and Quality in Healthcare | The National Quality Use of Medicines Indicators in Australian hospitals:  1.1 Antithrombotic therapy – Percentage of hospitalised adult patients that are assessed for risk of venous thromboembolism  1.2 Antithrombotic therapy – Percentage of hospitalised adult patients that receive venous thromboembolism prophylaxis appropriate to their level of risk  1.3 Antithrombotic therapy – Percentage of patients prescribed enoxaparin whose dosing schedule is appropriate  1.4 Antithrombotic therapy – Percentage of patients prescribed hospital initiated warfarin whose loading doses are consistent with a drug and therapeutics committee  1.5 Antithrombotic therapy – **Percentage of patients with an INR above 4 whose dosage has been adjusted or reviewed prior to the next warfarin dose**  1.6 Antithrombotic therapy – Percentage of patients with atrial fibrillation that are discharged on oral anticoagulants  5.4 Continuity of care – **Percentage of patients on warfarin that receive written information regarding warfarin management prior to discharge** | *Medication without harm WHO Global Patient Safety Challenge Australia’s response* (ACSQHC 2020) |  |
| Institute for Safe Medical Practices (ISMP) | Recommends that institutions use the ISMP **Medication Safety** **Self-Assessment** for antithrombotic therapy  Self-assessment covers 11 ‘core characteristics’ across 8 domains and includes 115 items:   1. Patient information 2. Drug information 3. Communication 4. Drug storage 5. Medication devices 6. Competency/Education 7. Patient education 8. Quality processes | ISMP Medication Safety Self-Assessment for Antithrombotic Therapy:  <https://www.ismp.org/sites/default/files/attachments/2017-11/2017_ISMP_Antithrombotic_Self_Assessment.pdf> |  |
| National Institute for Health and Care Excellence UK (NICE) guidance | NICE provides **quality standards** and guidance for a number of anticoagulation-related aspects of care including: diagnosis and management of VTE, mostly this is not specific to anticoagulation-related harm QI | Venous thromboembolism in adults quality standard (QS-201)  Venous thromboembolic diseases: diagnosis, management and thrombophilia testing (NG-158) | Case studies in ‘Shared Learning Database’, eg:  [Improving the care of patients discharged following a pulmonary embolism, in line with NICE Guidelines (NG158)](https://www.nice.org.uk/sharedlearning/improving-the-care-of-patients-discharged-following-a-pulmonary-embolism-in-line-with-nice-guidelines-ng158) Nottingham Universities Hospital Trust  [Utilising the skills of the clinical pharmacist within the MDT for improved medicines optimisation](https://www.nice.org.uk/sharedlearning/utilising-the-skills-of-the-clinical-pharmacist-within-the-mdt-for-improved-medicines-optimisation) Western Sussex NHS Foundation Trust |
| Scottish Patient Safety Programme | **Warfarin bundle** (largely ambulatory community care setting):  **Measure 1:** Warfarin dose is prescribed according to local guidance.  **Measure 2:** Is the target INR and duration of treatment clearly documented in the notes?  **Measure 3:** Patient complying with dosage instructions.  **Measure 4:** INR is taken according to previous recommendation. INR is taken within 7 days of planned repeat INR?  **Measure 5:** Patient receives regular education. Patient has received education in the last 6 months.  **Measure 6:** Have all Measures been met? | SPSP Warfarin Bundle Rationale (Health Improvement Scotland 2015) | The programme was evaluated in 2015 (McNab et al 2015).  Evaluation found improvements in mean time in therapeutic range, good control, and excellent control, as well as fewer very abnormal results and patient attendances. |

**Table A5: Examples of Local QI Initiatives**: Anticoagulation, New Zealand

|  |  |  |
| --- | --- | --- |
| **DHB** | **Anticoagulation harm reduction initiatives identified in survey responses** | **Follow-up with individuals (what, why, who, how, where, outcomes?) – the roles of specific individuals contacted varied by DHB** |
| Northland DHB | Adverse event bulletins to staff  Education to prescribing teams | Increasing VTE rates indicated poor VTE assessment processes. Now an electronic VTE assessment is mandated, this might lead to some duplication, but ensures information is recorded  Education module for medical staff had stopped working (e-learning), also no mechanism to see who had completed the education and the course had aged a bit. A new education package for PGY1 is about to be delivered (and possible extension to all RMOs) this will also cover the new VTE assessment form  Adverse events bulletin went out March 2020  Pharmacists are supposed to see each person started on warfarin on the ward for education (‘red book’)  Heparin is now in pre-filled bags, a standard ampule is supplied to start heparin, then a standard bag  Needs identified:   * E-prescribing would be ideal, with alerts, and CDSS * Some way to screen outpatient procedure patients, eg endoscopy, to see if they’re on anticoagulation * Electronic notes because paper notes go disappearing on the surgical ward (eg pharmacists can’t access when needed) * There’s not really a mechanism for picking up renal function alerts * With Health New Zealand coming a national VTE guideline would be useful (prophylaxis, TEDs, etc), perhaps supported by an online ‘Hub’ (eg New South Wales has this) |
| Waitemata DHB | Red flag education campaign about novel oral anticoagulants  Pharmacist lead education workshops for all PGY1s | ‘Top 10 Red Flag campaign’ including education for specific teams, grand rounds, posters, which included DOACs, eg ‘know your DOAC’ poster.  Joint pharmacy/medical approach to training of medical students and prevocational doctors (PGY1 and 2). Anticoagulant training is incorporated at each level of training (trainee intern, PGY1, PGY2), includes low-fidelity simulation.  All new start doctors are given the VTE risk assessment and warfarin lanyard.  E-prescribing requires warfarin be charted daily, prompts the loading dose, and alerts any interactions. There is also information/alerts about renal function, double prescribing, multiple anticoagulants, and INR already therapeutic (for enoxaparin).  Discharge summary includes a section for warfarin.  Issues identified:   * Double charting of anticoagulants on admission can be a problem, the system will alert with a warning if double prescribed. * Heparin prescribing is still on a separate paper chart, this can cause problems of omission/lack of awareness * Discharge summary for warfarin does not include forcing function * E-prescribing alerts are not linked to patient laboratory data |
| Waikato DHB | Guidelines: acute & perioperative  Discharge document: warfarin  Project on postponement and reversal of anticoagulants is planned | Acute and perioperative anticoagulation guidelines (sporadic auditing)  **Guidelines**: cover VTE prevention, anticoagulation with DOACs, Anticoagulation with warfarin (including nomogram and discharge checklist)  **Policy**: VTE risk assessment and prophylaxis  **Protocols**: eg for specific procedures under anticoagulation, for heparin infusions  **Audits:** 16 over several years, 1/3 were in obstetrics  **Upcoming**: VTE prophylaxis in patients with neck of femur fractures  Warfarin discharge document: indication, target INR, duration, dose, testing, education, referral, GP  Education for PGY1 on ‘approach to anticoagulation’ and on bridging (no evaluation or assessment)  Issues identified:   * There are no forcing functions * There is a lack of electronic processes or focus on local issues * Audits are labour intensive, not automated * Need audit criteria that are clear and measurable * Electronic prescribing opportunity, ideally linked to the discharge summary |
| Lakes DHB | Specialist drug rounds  Separate anticoagulant prescription section added to national prescription chart | An additional 1 page in the medication chart after the prn 2 pages, dedicated to anticoagulants and antiplatelets so they are not overlooked (requires education, but there is an orientation package)  The DHB has tried pharmacy only dispensing of anticoagulants, but this was not successful (it was reported that it is possible staff sourced anticoagulants from other wards, or pharmacists did not pay enough attention to the prescriptions)  ‘Special medication safety walkarounds’ where a pharmacist, QI member, nurse, house surgeon, etc check charts and discuss whether prescribed medications meet guidance and protocols. These are moments for reinforcement. But they are not systematic.  Medication chart ‘change cards’ indicate when an order has been altered (by the pharmacist, eg for renal impairment)  A discharge summary project has ensured that there are different sections on the d/c summary, eg ‘old meds’ that GPs may not be interested in, and ‘new meds’ that are highlighted, also sections for meds to be weaned.  Needs identified:   * More pharmacists * E-prescribing and CDSS systems that offer learning opportunities * Education about electronic prescribing * Pharmacist access to the adverse drug reaction fields so they can be recorded properly (correct wording etc) * Better review of Datix errors (in the UK NHS they had a template for ‘reflecting on it’, eg about systems problems, eg rushing, not identifying patient etc) |
| Taranaki DHB | Warfarin counselling clinic, now includes newer anticoagulants | Ward pharmacists aim to counsel all patients newly commenced on oral anticoagulants one-on-one (and whanau if appropriate), includes video and/or health navigator information leaflet on DOACs – however coverage is not known.  Warfarin Counselling and Newer Anticoagulant Clinics on Monday and Thursday in the pharmacy reception (changed to the inpatient bedside during Covid-19 pandemic) |
| Whanganui DHB | Post-take ward round form (includes anticoagulation considered, bloods, prophylaxis). Currently in trial.  Finalising a VTE procedure for Surgical and orthopaedic patients | Post-take ward round form being trialled by junior doctors, which includes VTE prophylaxis.  Initiatives to close the loop on things that get missed at afterhours admissions, ensuring consistent approached to VTE in surgical/orthopaedic patients. VTE prophylaxis was ad-hoc, so a registrar put together guideline for surgical/ortho patients.  No initiatives are yet evaluated.  Issues identified:   * When the VTE box was on the National medication chart it was very poorly utilised |
| Mid-Central DHB | Monitoring use of prophylactic anticoagulants, VTE prophylaxis audits monthly    Developed smart phone apps to help medical staff use anticoagulants  Possibly an app to help manage the areas of concern would be helpful. It could make guidelines more accessible. Junior staff use MedApp, it may be useful to add additional information to this. | VTE prophylaxis audits, but infrequent during Covid-19 (check inpatients for risks of bleeding, adequate prophylaxis etc, however there is no consensus on what ‘appropriate’ prophylaxis is, so hard to audit)  Bespoke apps (these make guidelines accessible): NZ Blood App, Managing/Reversing Warfarin Apps, Rivaroxaban/Dabigatran App, etc.  PGY1 education includes cards that are handed out with VTE risk assessment information  Needs identified:   * A national approach would be useful, eg for Apps, audits (orthopaedics are often outliers, need a standard of care) * Basic knowledge of anticoagulation could be improved * Discharge planning is a future project (transition to community is a problem because only the GP can refer the patient to community management of anticoagulation service, but is not necessarily aware), along with e-prescribing * Approval barriers prevented getting a ‘does this patient need anticoagulation, who is responsible for follow-up’ item on the discharge summary * Apps could perhaps be integrated into the MedApp that the doctors tend to use. |
| Wairarapa DHB | Patients admitted on warfarin have an extra Blue bracelet attached (new initiative not evaluated yet) | Introduced the Blue Bracelet for 'Patients admitted on warfarin’.  Reportable events have occurred since introduction, leading to follow up review of current practice (reviewing current documentation used and the charting of medication)  Needs identified:   * An out-of-date document was in use that had been photocopied, this could have led to some of the issuesseen in the reportable events. |
| Capital & Coast DHB | [Not from survey response]  CCDHB developed a specialist anticoagulation bridging service | Specialist anticoagulation bridging service described and evaluated in ‘The Role of a specialist bridging service. A New Zealand prospective study of 600 patients’ (Ruell et al 2019). The service was developed because of ad hoc approaches across various departments.  Pathway in place where anyone who is anticoagulated and is being admitted for an elective procedure is referred to the thrombosis service. An assessment looking at both thrombotic and haemorrhagic risk is completed, and a plan recommended based on international guidelines. Face-to-face meeting with the patient if required, copy of the plan on the hospital system so is available to clinicians, including GPs. The patient received reminder texts/calls or emails at each key stage, i.e.: last dose of warfarin or last dose of enoxaparin. Post procedure the patient would remain under the care of thrombosis service until INR is therapeutic and enoxaparin can be stopped, then transferred back to primary care for management.  Some warfarin management is undertaken by the thrombosis service, generally the high-risk patients for example, MVR patient who has also had a CVA. The service also provides advice or management for patients whose INR’s have become erratic for whatever reason. |
| South Canterbury DHB | Medical department teaching to house surgeons  Review by pharmacy team | Teaching to PGY1/2 through Grand Rounds, complex cases presented to illustrate issues around renal function, obesity, clexane, indications, etc  Pharmacy team systematically reviews medication of all patients on anticoagulation, including those already taking at admission. Pharmacists are alerted to anticoagulation at dispensing, but also undertake non-systematic checks on surgical wards. Also one-on-one patient education.  No audits or evaluations.  Suggestions:   * Alerts would be useful: more sophisticated than ‘have you considered?’ for VTE risk assessment, thromboprophylaxis, gastroprotection, requiring a comment, and re-alert after 24/48 hours is nothing charted. * “We’re behind where we ought to be (internationally)” |

### Appendix B: Search Strategies

Ministry of Health Search (2021)

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R) <1946 to December 13, 2021>, adapted for Scopus, Embase, Cochrane, OVID Nursing

Search Strategy:

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1 Anticoagulants/ or anticoagulant\*.mp.

2 antiplatelet\*.mp. (31186)

3 1 or 2 (142060)

4 (care adj3 transition\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (9904)

5 (discharg\* adj3 (counsel\* or educat\*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1092)

6 Decision Making, Shared/ (1334)

7 (shared adj3 decision\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (12533)

8 (medic\* adj3 manag\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (62584)

9 (reduc\* adj3 harm\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (12200)

10 (collab\* adj3 project\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3872)

11 ((home adj3 hospital\*) or "team to team").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (11587)

12 "team to team” or multidisc\* or shared decision\* or "decision aid\*" or "decision support\*" or interdisc\*

13 Patient Transfer/ or patient transfer\*.mp. (10372)

14 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 (121177)

15 3 and 14 (1569)

16 15 and (anticoag\* or anti-coag\* or antiplatelet\* or anti-platelet\*).ti. (334)

17 limit 16 to (english language and yr="2016 -Current") (189)

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

#### Supplementary PubMed Strategies

**PubMed**

Search: (((Anticoagula\*) AND ((harm OR safety OR adverse))) AND ((intervention OR initiative OR policy OR protocol OR guideline OR system OR QI OR quality OR process OR practice))) AND ((hospital OR surgery OR procedure OR transition OR handover OR handoff OR discharge OR decision))

* 2015 - 2022
* 15,757 results
* Restricted to RCTs
* 1,223 RCTs screened by title
* **10 retained**

Search: ((anticoagula\*[Title/Abstract]) AND (quality[Title/Abstract] OR harm[Title/Abstract])) AND ("hospital"[Title/Abstract])

Results:

* 2015 - 2022
* 477 results
* **44 retained**

Search: ((("adverse event" OR "adverse outcome" OR "patient harm" OR safety OR quality)) AND ((communication OR transition OR handover OR discharge))) AND ((anticoagula\* OR enoxaparin OR dalteparin OR heparin OR warfarin OR phenindione OR dabigatran OR rivaroxaban OR apixaban))

* 2015 - 2022
* Limit to RCTs & systematic reviews
* 89 results
* **2 retained**

Search: (stewardship OR education OR "medication chart" OR "EMR" OR "EHR" OR "electronic medical record") AND anticoagula\* AND (harm OR safety OR quality OR adverse)

* 2015 - 2022
* 1,680 results
* Limited to RCTs & systematic reviews
* 229 results
* **7 retained**

Search: Pharmacist AND anticoagula\* AND hospital\* AND (safety OR quality)

* 2015 - 2022
* 165 Results
* **31 retained**

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