Medication incidents and pharmacist interventions in relation to directly acting oral anticoagulants in hospital settings: evaluation using Reason's Accident Causation Theory

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Research Article

Abstract

Background

Direct oral anticoagulants (DOACs) have revolutionised anticoagulant pharmacotherapy. However DOACs medication incidents are known to be common.

Objective

To assess medication incidents associated with DOACs using an error theory and to analyse pharmacists' contributions in minimising medication incidents in secondary care settings.

Setting

A large University tertiary academic hospital in the West Midlands of England.

Methods

Medication incident data from the incident reporting system (48-months period) and pharmacist interventions data from the prescribing system (26-month period) were extracted. Reason's Accident Causation Model was used to identify potential causality of the incidents. Pharmacists' intervention data was thematically analysed.

Main outcome measure

(a) Frequency, type and potential causality of DOACs incidents, (b) Nature of pharmacists' interventions.

Results

A total of 812 DOACs reports were included in the study (124 medication incidents and 688 intervention reports). Missing drug/omission was the most common incident type (26.6%,n = 33) followed by wrong drug (16.1%,n = 20) and wrong dose/strength (11.3%,n = 14). A high majority (89.5%,n = 111) of medication incidents were caused by active failures. Patient discharge without anticoagulation supply and failure to restart DOACs post procedure/scan were commonly recurring themes. The majority of (38.1%,n = 262) the pharmacist interventions were related to pharmacological strategy (i.e., drug or dose changes or discontinuation). Impaired renal function was the most common reason for dose adjustments.

Conclusion

Prescribers' active failure rather than system errors (i.e. latent failures) are contributing to DOACs incidents. Rreinforcement of guideline adherence, prescriber education, harnessing pharmacists' roles and mandating renal function information in prescriptions are likely to improve patient safety.

Impact Of Findings On Practice Statements

- Further strategies are required to improve patient safety related to direct oral anticoagulants as mistakes and guideline violations are common.
- Mandating renal function information on prescriptions may help avoid DOACs incidents.
- Pharmacists' clinical checks on DOACs are vital as this study shows many errors and potential harms being avoided due to their interventions.

Introduction

Thromboembolic events present major clinical concern. Consequences can be serious, resulting in morbidity or mortality [1]. It is estimated that one in five people die due to causes involving clots [2]. Anticoagulants are first-line therapy for thromboembolic events. They are indicated for prophylaxis and treatment of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE). Additionally, they are used to reduce the risk of secondary complications such as stroke in patients with atrial fibrillation (AF) [3,4]. In recent years, the traditionally used vitamin K antagonist (VKA), warfarin has been gradually replaced by direct oral anticoagulants (DOACs), previously known as novel oral anticoagulants (NOACs).

Currently, there are four DOACs licensed in the United Kingdom (UK) including: apixaban, rivaroxaban, dabigatran and edoxaban [3]. The approval of this drug class has revolutionised oral anticoagulation pharmacotherapy and considerably expanded clinical use [5]. DOACs display a preferred safety profile; they have fewer problematic interactions, a fixed-dose regimen and do not require routine international normalised ratio (INR) monitoring, unlike VKAs. Moreover, DOACs have a faster onset effect and a relatively short half-life compared to VKAs. Therefore, anticoagulation outcomes are achieved quicker whilst still reaching the desired effectiveness [6,7]. These advantages have encouraged a shift in favour of DOACs in treatment guidelines, consequently increasing national prescribing rates [8].

Despite wide use, research studying DOAC-related medication incidents is lacking. Though reports of adverse events relating to DOACs and the wider anticoagulant class are available [5,9-11], analysis of error cause is limited. As they continue to be integrated into clinical practice, a better understanding of the DOAC-related incident types and what entails occurrence is required. Determination of causes will help identify risk reduction strategies and allow further guidance from regulatory bodies to ultimately reduce medication incidents associated with DOACs.

In this study, a medication incident is defined as "a medication related incident or event which actually resulted in or had the potential for a detrimental result consequence to a patient" [12]. It is important to understand that the outcome of a medication incident is not always harmful, but rather risks patient safety. Incidents can occur at any stage of the medication process: prescribing, transcribing, dispensing, administering and monitoring [13]. Previous studies have detected and quantified error types according to the medication process stages [14-16]. Inappropriate prescribing due to incorrect dosing has been

highlighted in literature as a major issue in relation to DOAC prescribing [17,18]. Patient height and weight, baseline activated partial prothrombin time, INR, haemoglobin, urea, electrolytes, liver function tests and creatinine clearance (CrCl) are imperative assessments before DOAC initiation [19].

Reason's Accident Causation Model is a widely used theoretical framework. This model can be applied to identify potential causality of errors [20]. Fig. 1 displays a simplified diagram of the model categories. Errors can be classified into active and latent failures. Active failures are defined as unsafe acts carried out by individuals in direct contact with the patient or system. These can be sub-classified into slips (action-related execution error), lapses (memory-related execution error), mistakes (planning error) and violations (rule-breaking error). Latent failures are system failures that arise from high level organisation decisions [21]. Application of this model and subsequent identification of incident causes will stimulate the basis for future interventions in minimising medication incidents.

Aim of the study

The aims of this study were to assess medication incidents associated with DOACs in the hospital setting using Reason's Accident Causation Model and to evaluate the nature of pharmacists' interventions in minimising DOACs medication incidents.

Ethics approval

This study was approved by the University of Birmingham School of Pharmacy Research Ethics Panel in October 2020 (UoB/SoP/2020-03) (see Appendix 1). The NHS Foundation Trust approved this study as an audit (CARMS-16618) and no further NHS ethical approval was required.

Method

A two-part data analysis study was conducted. Firstly, medication incidents reported to DATIX by healthcare professionals was analysed over a 48-month period (September 2016 – September 2020). DATIX is a widely used, web-based, voluntary incident reporting and risk management system. This database collates occurrence of all events that have resulted in or have the potential to result in patient safety violation [23]. Next, pharmacist interventions submitted to the Prescribing Information and Communications System (PICS) were reviewed over a 26-month period (August 2018 to September 2020). PICS is an electronic clinical decisions support system, specific to the study setting. The system is designed to minimise medication related errors via various automatic rule-based prescribing checks. PICS is also a communication platform; it allows healthcare professionals to voluntarily log occurrence of events/interventions [24].

Setting

Both databases, DATIX and PICS were obtained from one of the largest tertiary teaching hospitals in England. The patient population across the hospital sites is estimated to be 2.2 million [25].

Data processing and analysis

Search terms (DOAC, NOAC, apixaban, rivaroxaban, dabigatran, edoxaban and anticoagulant) were used to extract relevant data from both databases in the preceding five years up to 30/09/2020. The acquired data was processed on Microsoft Excel in an anonymous form. Then, data was filtered according to the inclusion criteria: adult patients (≥18 years old) who were prescribed a DOAC. Data cleaning was used to remove duplicate records, incomplete and unclear information. Quantitative analysis was used to investigate the identified medication incidents from DATIX. Categorisation according to incident type was conducted primarily by one author followed by independent checks by two authors (VP and ZJ). Classification of categories was determined by identifying the common reoccurring events. Descriptive statistics including frequency and percentages were used to analyse this data.

Reason's Accident Causation Model was used to determine the contributory factors associated with medication incidents and to ultimately establish potential causality. The free text data from the DATIX database were examined to classify cause of medication incident according to the model categories. Organisation into sub-categories dependent on the most common themes was conducted to enable further investigation. Quantitative analysis via descriptive statistics was performed to determine the major cause of medication incidents.

Data from the PICS database in relation to pharmacist interventions and associated rationale was classified as per nature of clinical interventions. The classification system used was adapted from a previously reported study [26]. Two additional categories: 'documentation' and 'other' were also added. Sub-categories were included as appropriate.

Results

Evaluation of DOAC incidents

A total of 419 incidents were identified over a 48-month period from the initial DATIX system search. 241 reported incidents were excluded. Reasons include not DOAC-related (i.e., regarding warfarin, enoxaparin, tinzaparin), duplicate records and incomplete information (i.e., DOAC unspecified, use of unclear abbreviations). Of the remaining 178 DOAC-related incidents, a further 54 cases were excluded as they were not deemed as medication incidents. For instance, these were concerning access, transfer and cancellation of procedures. Hence, 124 reports were included in this study following inclusion and exclusion filtering.

A number of factors resulted in medication incidents as shown in Fig. 2. The majority of the incidents occurred during the prescribing and administration stage of the medication process. The most common errors resulting in an incident were missing drug/omission (26.6%, n=33), wrong drug (16.1%, n=20) and wrong dose/strength (11.3%, n=14). Table 1 shows the contributory factors that resulted in medication incidents in line with Reason's Accident Causation Model. Almost all (89.5%, n=111) medication incidents were classified as active failures. The active failures comprised of lapses (29.8%, n=37), slips (24.2%,

n=30), mistakes (22.6%, n=28) and violations (12.9%, n=16). The rest of the incidents were classified as latent failures (10.5%, n=13). These categories were sub-categorised, as summarised in Table 1.

Missing drug/omission

Various scenarios resulted in drug dose omission, each with differing error causes as defined by Reason's Accident Causation Model (see Table 1). The majority of drug omission incidents were due to lapses including lack of plan adherence (48.6%, n=18). A reoccurring theme was patient discharge from hospital without anticoagulation supply. Failure to restart DOAC post procedure/scan was also a common cause resulting in drug omission (10.8%, n=4). This indicates lack of staff awareness of the importance of missed DOAC doses and effect on anticoagulation. A few cases of drug omission due to violation concerned to take out (TTO) prescriptions which had inadvertently not been updated by the prescriber prior to patient discharge (18.8%, n=3). Latent failures resulting in drug dose omission involved insufficient team communication/handover (7.7%, n=1).

Wrong drug

Medication incidents due to wrong drug supply comprised a high percentage of incidents. Causes of error were largely due to slips and mistakes (see Table 1). Slips involved dispensing errors such as selecting the wrong drug due to incorrect system/clerking documentation (16.7%, n=5). There were two reported cases where the look-alike, sound-alike drug rosuvastatin was dispensed instead of rivaroxaban (6.7%, n=2). A large proportion of slips involved drug supply to the incorrect patient (26.7%, n=8).

Wrong dose/strength

The most common dose/strength related medication incident was the prescribing of wrong dose for indication (28.6%, n=8). This error is classified as a mistake (see Table 1). For example, a patient diagnosed with left leg DVT was commenced on rivaroxaban 15mg once daily. However, the patient should have been prescribed 15mg twice daily for the first 21 days as per national guidance [3]. Latent failures resulting in wrong dose/strength supply involved the double dose administration of DOAC to overcome the effect of missed doses (15.4%, n=2).

Evaluation of pharmacist interventions

Following the initial PICS database search, 1024 pharmacist interventions were identified over a 26-month period. 336 intervention cases were excluded from the study due to the same reasons for exclusion of reported incidents as aforementioned (i.e., not DOAC related, unclear, incomplete text). The remaining 688 submitted interventions specific to DOACs formed the data sample included in this study.

Changes in pharmacological strategy comprised the highest proportion (38.1%, n=262). Interventions related to quantity of drug followed (26.5%, n=182) and then those related to patient education (14.5%, n=100) (see Fig. 3). Start/restart DOAC accounted for more than half of the pharmacological strategy interventions (51.5%, n=135) (see Table 2). Drug change was the second most common pharmacological

strategy intervention (21.0%, n=55). Almost all of the quantity of drug interventions were associated with DOAC dose changes (91.2%, n=166). The rationale for the interventions varied, as shown in Table 2.

Dose change

Pharmacist-led interventions owing to inappropriate dose prescribing contributed to the largest overall percentage of recorded interventions (see Table 2). In many circumstances, multifactorial rationale including age, weight and renal function were assessed to establish suitable doses. Renal function was the most common reason for dose adjustment (29.4%, n=67). The majority of these cases involved renally impaired patients requiring dose reduction and a few increased doses as renal function improved. Age and weight were also highlighted as important considerations when determining the appropriate patient dose (16.7%, n=38 and 18.0%, n=41 respectively). 13.2% (n=30) of dose modification interventions were related to indication and/or treatment guidelines such as the switch from initiation to maintenance doses or changing between prophylactic and therapeutic doses.

Start/restart medication

Key rationale for this intervention included the initiation or re-initiation of DOAC therapy on discharge (22.2%, n=30). A common scenario involved inpatient low molecular weight heparin therapy and re-initiation of DOAC on discharge, in line with the hospital Trust policy guidelines [27]. New diagnosis of thromboembolic indications, such as AF and PE resulted in the initiation of appropriate DOAC therapy (7.4%, n=10). Anticoagulation is contraindicated during state of active bleeding. Restarting anticoagulation post-procedure or post-scan comprised of 6.7% (n=9) and 3.0% (n=4) respectively (see Table 2).

Drug change

Foundation for changes in anticoagulation therapy involved drug-drug interactions (12.7%, n=7). Concurrent use with antibiotics (i.e., rifampicin) or antifungals (i.e., voriconazole) comprised almost all of the recorded DOAC interactions. A total of 12.7% (n=7) of drug change interventions involved contraindication due to renal impairment. Further significant rationale included dysphagia (3.6%, n=2), surgical purpose (5.5%, n=3) and more effective treatment (3.6%, n=2), as summarised in Table 2.

Patient education

General counselling formed the majority of patient education interventions (79%, n=79). Also, 19% (n=19) were related to patients newly initiated on a DOAC. The remaining 2% (n=2) concentrated on enhancing patient compliance (see Table 2).

Discussion

Key findings

This study shows that the majority of the DOAC-related incidents in a secondary care setting occurred in the prescribing and administration stages of the medication process. This is in line with previous studies which reported a high degree of anticoagulant incidents due to inappropriate prescribing and administration [10,28]. This demonstrates a need for further education surrounding DOACs and other anticoagulants for all staff groups. By contrast, a Danish study showed that most of the incidents occurred largely in the prescribing phase, suggesting a problem specifically correlating the incidents to physicians and prescribers rather than the nursing staff [29].

Key medication incidents associated with DOACs were missing drug/omission, wrong drug and wrong dose/strength. Omissions accounted for a considerably high percentage, more than a quarter of the incidents in this study. Past research reviewing all medication incidents reported to the National Reporting and Learning System (NRLS) in England over a 6-year period (2005-2010) found that the most frequent incident type was those relating to drug dose omissions [30]. Targeted implementation of preventative strategies is required to reduce this incident type.

The application of Reason's Accident Causation Model in this study showed that most of the errors were due to active failures (slips, lapses, mistakes and violations). Lapses were the most common of the active failure category, closely followed by slips and mistakes. Causes of the medication incidents were largely due to the performance of the healthcare professionals, rather than faults in system organisation. Hence, it is vital that staff adhere to guidelines.

Our findings show that pharmacists play an integral role in minimising medication incidents. Some key interventions include dose and drug alterations, stopping and starting treatment, documentation and patient counselling. Overall, dose changes contributed to the highest percentage of recorded interventions. This is consistent with several published studies investigating pharmacist interventions in other therapeutic areas [31-34]. Hence, this demonstrates lack of prescriber familiarity with dosing regimens and necessitates for further prescriber education.

A closer look at dose change rationale reveals renal function as the top cause. The National Patient Safety Agency (NPSA) in the UK has warranted a safety alert with regard to inappropriate anticoagulant dose prescribing, particularly concerning renal function [4]. Dose adjustment according to renal function is highly important to ensure optimal thromboembolic therapy whilst reducing the associated bleeding risks. The Medicines and Healthcare products Regulatory Agency (MHRA) advises calculation of CrCl prior to making dosing decisions [35]. These incorporated measures stress the frequency of inappropriate renal dosing and suggest the need for further implementation to reduce related incidents.

Recommendations for practice

With regards to prescribing errors, there are two distinct ways in lowering them: reducing errors during prescribing and reducing errors after prescribing [36]. The latter focuses on the pharmacist's role. As shown in this study and previous studies, pharmacist interventions are significant in identifying and minimising medication incidents. It is imperative that pharmacists continue reviewing drug charts and

conducting patient medicine reconciliations, but on a larger scale. The involvement of more clinical pharmacists throughout the medication process increases the chance of error identification; therefore, implementation is recommended. Only a small percentage of incidents were due to latent system failures; the main cause of error consisted of active failures. This demonstrates that the causes are mainly due to errors in task execution and planning by healthcare professionals. Pharmacist participation in the training process will assist education of other multidisciplinary team members such as prescribers and nurses. Annual assessments in relation to the correct prescribing and administration process of DOACs specific to staff groups are needed. Furthermore, we recommend mandating renal function information on prescriptions as priority [14]. This will allow ease of checking by the prescriber and the pharmacist.

In this study, medication incidents due to wrong/omitted verbal patient directions were identified as a significant issue. Thus, it is necessary to understand deficiencies in current counselling and cooperate with patients to implement effective counselling practices.

Strengths and Limitations

Large, comprehensive data samples were extracted over a substantial timeframe using sophisticated incident and intervention reporting databases. The commonly applied framework, Reason's Accident Causation Model was used providing indication of error causality allowing identification of areas of improvement for patient safety. However, both reporting systems operate voluntary. Underreporting, selective and incomplete reporting are recognised; our results are likely to be underestimated compared to the true values. In addition, data was obtained from only one large hospital Trust in the UK limiting generalisability. This study used a theoretical model to allow analysis and interpretation of the data in a structured way, which may enable other researchers to classify DOACs incidents and interventions accordingly.

Recommendations for research

Future observational research can be conducted to overcome bias in the voluntary reporting system. Qualitative studies consisting of semi-structured interviews of patients, nurses, prescribers and pharmacists to determine medication incidents and actioned interventions are needed. Additional research should aim to extend the scope of this study to incident severity and its impact on patient health outcomes. Development and evaluations of interventions to minimise errors are needed. Research should be extended to non-hospital settings.

Conclusion

DOACs related medication incidents commonly occur in hospital settings due to varying factors. It is important to stress on the healthcare professionals around the importance of guideline adherence, in particular renal function assessment to determine appropriate dosing schedules. Mandating renal function information on prescriptions is recommended to allow ease of checking. Whilst pharmacists play a crucial role in minimising incidents at present, additional strategies such as strengthening clinical

governance, pharmacist involvement in the on-going training of staff and annual staff assessments are required to improve patient safety in relation to DOACs.

Declarations

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Conflicts of interest

None declared.

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Tables

Table 1: Contributory factors to medication incidents based on Reason's Accident Causation Model

Error cause, n=124	Error	% (n)*
Active failures (slips), n=30	*Dispensing error*	
	Look-alike sound-alike medications	6.7 (2)
	Selecting wrong drug	16.7 (5)
	Selecting wrong dose	13.3 (4)
	Wrong labeling	10 (3)
	Wrong quantity	6.6 (2)
	Incorrect patient	26.7 (8)
	Others	20 (6)
Active failures (lapses), n=37	*Lack of plan adherence*	
	Omission	48.6 (18)
	Failure to restart drug	10.8 (4)
	Failure to discontinue drug	10.8 (4)
	Omitted verbal patient directions	16.2 (6)
	Others	13.5 (5)
Active failures (mistakes), n=28	*Drug prescribing error*	
	Contraindication	14.3 (4)
	Unlicensed indication	3.6 (1)
	No clear indication	7.1 (2)
	Allergic reaction	3.6 (1)
	Duplicate therapy	14.3 (4)
	Dose prescribing error	
	Contraindication	10.7 (3)
	Wrong dose on admission	3.6 (1)
	Wrong dose for indication	28.6 (8)
	Drug administration despite procedure booking	7.1 (2)
	Others	7.1 (2)
Active failures (violations), n=16	*Non-compliance to policy*	
	Prescribing without confirmed diagnosis	6.3 (1)
	Not using the most up to date TTO	18.8 (3)
	Not sending RICaD** to anticoagulation team	12.5 (2)
	Others	12.5 (2)
	Patient related	
	Medication stoppage	12.5 (2)
	Unauthorised self-medication	31.3 (5)
	Not taking as instructed	6.3 (1)
Latent failures, n=13	*Inadequate training/knowledge*	
	Failure to administer as unaware of stock storage	15.4 (2)
	Wrong patient directions	46.2 (6)
	Duplicate dose to overcome missed dose	7.7 (1)
	Insufficient communication/handover	
	Duplicate dose administration	15.4 (2)
	Missed dose	7.7 (1)
	Duplicate therapy	7.7 (1)

*Rounding to one decimal place, therefore may not exactly add to 100%

** Rationales for Initiation, Continuation and Discontinuation (RICaD) form

Table 2: Rationale for pharmacist interventions

on y	Subcategory	Reasons for intervention	n (%)	Examples
drug,	Dose change	Age	38 (16.7)	• Apixaban dose change to 2.5mg as per patient's age and weight • Dabigatran dose reduction due to age
		Renal function	67 (29.4)	• Spoke to doctor regarding rivaroxaban dose and poor renal function, eGFR 29 (CrCl 49) and recommended consider reduce dose 15mg OD. Doctor has reduced dose • Discussed with Dr, edoxaban dose increased to 60mg OD as GFR improved (eGFR 62, CrCl >50ml/min) • Edoxaban dose corrected according to GFR • Advised Dr renal function declined CrCl 27ml/min. Advised to review apixaban dosing - he will change to 2.5mg BD for AF as per BNF guidance
		Weight	41 (18.0)	• Apixaban changed to 2.5mg BD as weight <60kg and age >80 years • Advised 60mg edoxaban based on weight and renal function • Apixaban dose increased as per weight, creatinine level and age
		Adverse effect (bleeding)	2 (0.9)	• Discussed with Dr regarding apixaban dosing as patient's characteristics would allow a dose increase to 5mg BD however recently reduced in April 2020 due to varicose veins bleeding
		Pre-admission dose	9 (3.9)	• Dabigatran changed to BD by Dr as per pre-admission
		Indication/per guidelines	30 (13.2)	• Apixaban increased to 5mg BD for PE treatment • Apixaban dose increased as per guidelines for AF • Spoke to Dr to discuss dose of apixaban who agreed to change it to licensed dose for DVT prophylaxis
		To match medicine reconciliation	10 (4.4)	• Changed from dabigatran 150mg to 110mg to match med rec • Rivaroxaban amended to match med rec dose
		Not specified	31 (13.6)	• Rivaroxaban changed to 20mg • Apixaban dose changed
		Total	228*	
	Change schedule	Total	1	• Apixaban timings altered. Previously patient was to be missing a day of treatment

	Change duration of treatment	Per guidelines	7 (46.7)	• Apixaban loading 4 days instead of 7. Dr should have prescribed as 7 days at 10mg bd – been changed • Discussed with Dr regarding Apixaban. Apixaban confirmed 3 months following DVT diagnosis so end date amended to 18/2/19 as per protocol
		Not specified	8 (53.3)	• Apixaban changed from 7 weeks to 7 days
		Total	15	
gical	Drug change	Interaction	7 (12.7)	• Interaction between voriconazole and apixaban. Discussed with team, patient to be switched to warfarin • Discussed interaction between apixaban and rifampicin with Dr. Advised a few options, consider changing apixaban to warfarin as treatment with rifampicin is long term
		Surgical purpose	3 (5.5)	• Plan for apixaban to start post-surgery, still not started, queried this. Enoxaparin stopped and apixaban restarted
		More effective	2 (3.6)	• Advised Dr that apixaban less effective if weight >120kg. Advised that warfarin more suitable
		Renal function	7 (12.7)	• Rivaroxaban changed to enoxaparin as CrCl<15 • Advised Dr to consider switching apixaban to enoxaparin due to renal function • Rivaroxaban contraindicated in renal impairment, paused and changed to renal enoxaparin dosing for the time being
		Per history (Hx)	6 (10.9)	• Apixaban changed to edoxaban as per history • Apixaban switched back to rivaroxaban as per Hx
		Dysphagia	2 (3.6)	• Apixaban switched to enoxaparin due to swallowing issues
		Aid compliance	1 (1.8)	• Tinzaparin prescribed for discharge, discussion had with Dr. To aid compliance have advised to switch to edoxaban as only once daily regime, no need to inject, carry around numerous boxes.
		Not specified	27 (49.1)	• Dr will add apixaban and end enoxaparin • Tinzaparin ended and apixaban started new
		Total	55	
	Change administration	Dysphagia	4 (66.7)	• Dysphagia, apixaban to be crushed and dispersed in water • Rivaroxaban was paused due to swallowing difficulties however advised can continue - crushed and dispersed in

			water/puree
	Other	2 (33.3)	• Advised nurse rivaroxaban can be crushed to ease administration
	Total	6	
Start/restart medication	Pre-admission	25 (18.5)	• Proposed pre-admission dabigatran • Prescribed pre-admission dose of apixaban • Pre-admission apixaban 2.5mg BD started
	Discharge	30 (22.2)	• Confirmed with Dr - apixaban to restart on discharge • Spoken to Dr to highlight to patient that rivaroxaban to be restarted 1 week after discharge • Confirmed with Dr that patient is to resume apixaban on discharge
	Post-procedure	9 (6.7)	• Spoke to Dr - apixaban to restart - tunnelled line done - paused prior to placement of line • Proposed rivaroxaban to start 3/11/18 (72 hours post-surgery) as per procedure noting
	Diagnosis	10 (7.4)	• Discussion with vascular team for anticoagulation. Newly diagnosed AF with CHADSVASc score of 3. Team to consider starting apixaban + anticoagulation referral • Edoxaban not on patient history but is prescribed on PICs. Discussed with Dr, he reviewed and states this is newly prescribed as patient has fast AF
	Post-scan	4 (3.0)	• Apixaban restarted due to clear CT head
	Not specified	57 (42.2)	• Rivaroxaban commenced • Apixaban restarted
	Total	135	
Medication paused	Surgical purpose	9 (31.0)	• Discussed thrombosis with Dr - patient usually on edoxaban for recurrent DVT - currently not on any cover - due procedure today - to review post procedure • Discussed with Dr - patient due procedure, apixaban paused and to be restarted after • Advised to stop edoxaban for 24-48hrs prior to surgery - actioned
	Reduced renal function	5 (17.2)	• Discussed thromboprophylaxis with Dr- rivaroxaban paused due to AKI • Apixaban paused whilst poor renal function - current GFR 13

	Active bleeding	3 (10.3)	• Queried with Dr what the plan was to restart patients Apixaban. Dr confirmed that the Apixaban is being withheld as patient has a subdural haematoma • Apixaban paused due to bleed
	Fall risk	2 (6.9)	• Confirmed with Dr - patient is at high risk of falling - apixaban is paused at present
	Vomiting	1 (3.4)	• Discussion with Dr - regards to restarting rivaroxaban. Currently held off due to vomiting. Therefore, advised to increase enoxaparin to 40mg OD as per weight/renal function. When swallow is OK recommence rivaroxaban
	Not specified	9 (31.0)	• Apixaban currently paused • Edoxaban to pause and resume when appropriate
	Total	29	
Discontinue medication	Interaction	1 (3.4)	• Asked Dr to remove Ibuprofen from TTO due to high risk of bleeding with Apixaban
	Duplicate therapy	3 (10.3)	• Confirmed with the GP Dr. that patient was on rivaroxaban. Community pharmacy had stock issues thus prescribed apixaban instead. Patient states taking both. Confirmed that GP would like apixaban to end
	Active bleeding	4 (13.8)	• Apixaban stopped due to small subarachnoid haemorrhage - any further interventions to be discussed with haematology • Patient started bleeding from mouth again - advised Dr to stop rivaroxaban and to consider tranexamic acid mouthwash
	Bleeding risk	2 (6.9)	• I have asked Dr to review enoxaparin/apixaban plan - patient will be reviewed in best interests meeting. Patient has high risk of bleeds and doctor states likely apixaban and enoxaparin stopped
	Fall risk	1 (3.4)	• Rivaroxaban stopped in June due to risk of falls - spoken to ward Drs who have now ended rivaroxaban
	Renal impairment	3 (10.3)	• Informed Dr - edoxaban should be stopped (when CrCl<15ml/min) as patient currently CrCL 14ml/min • Advised Dr that apixaban is contraindicated if GFR <15ml/min, have advised to contact haematology/anticoagulant department for advice on alternative
	Not indicated	3 (10.3)	• Apixaban 10mg BD prescribed on TTO - no clear indication. Dr ended
	Not specified	12	

		(41.4)	• Rivaroxaban stopped • Apixaban not to continue
	Total	29	
Monitoring	Interaction	3 (37.5)	• Fluoxetine has the potential to increase bleeding risk when administered with apixaban. Advice from manufacturer - caution or avoid. Monitor closely for any signs of bleeding • Discuss with Dr interaction between Apixaban + Duloxetine (increased risk of bleeding). Dr has discussed with anticoagulant nurse who has advised to continue with Apixaban and monitor patient closely as benefits outweigh the risks
	Liver impairment	1 (12.5)	• Apixaban needs reviewing, patient's LFTs not within range – Dr to monitor
	Monitor renal function	1 (12.5)	• Advised advanced nurse practitioner to review rivaroxaban and add note to GP to review renal function in one week's time to check GFR. Currently it is 52 so 20mg appropriate, if drops below 49ml/min then dose needs adjusting to 15mg daily for AF
	Intolerance	1 (12.5)	• Summary care record states intolerance to apixaban. Mentioned to Dr to monitor as patient needs apixaban
	Other	2 (25.0)	• Discussed this patient with Dr. Not a straightforward case and there are several treatment options for patient. Dr happy to stick to apixaban 5mg BD, monitor and review with anticoagulant team
	Total	8	
Enhance compliance	Change dosing regime	1 (50.0)	• Flagged up to Dr that at home patient has been taking apixaban 10mg OD. Advised to discuss patient with haematology and see if switching to rivaroxaban is an option to help with compliance without imposing a risk
	Patient refusal to take medicine	1 (50.0)	• Have informed Dr that patient has refused every dose of apixaban - he states he will have a discussion with patient
	Total	2	
Newly initiated	Diagnosis	3 (15.8)	• Counselled on newly started edoxaban for PE • Patient counselled on newly started apixaban for AF
	Drug change	2 (10.5)	• Counselled patient on apixaban (switched from rivaroxaban) • Conversation about change from apixaban to edoxaban, patient was hesitant to make switch because she thought 60mg (edoxaban) was too high a dose in comparison to 5mg (apixaban)

		Not specified	14 (73.7)	• Apixaban new – counselled • Counselled patient on newly started rivaroxaban
		Total	19	
	General counselling	Total	79	• Edoxaban counselling • Counselled patient on rivaroxaban • Apixaban counselling • Patient counselled on the use of dabigatran
ion,	Update drug record	Document end date	1 (6.3)	• Apixaban end date not stated on TTO, Dr informed and amended
		Amend drug	2 (12.5)	• Informed Dr of 'rivaroxaban' in noting is documented as edoxaban in patient drug history • Advised Dr that patient was on apixaban 2.5mg BD pre-admission, not rivaroxaban (this was taken from last admission in 2016)
		Amend dose	4 (25.0)	• Informed Dr that Edoxaban dose is normally 60mg, amended on chart as per med rec • Informed Dr that Rivaroxaban is usually 15mg, amended on chart as per med rec
		Drug missing from chart	5 (31.3)	• Missing apixaban - informed team and added on to chart • Rivaroxaban missing from chart, added by Dr as per med rec • Informed Dr that Apixaban missing from chart, Dr will look into this and take appropriate action
		Other	4 (25.0)	• Informed Dr of patient's regular medications to be charted, including apixaban
		Total	16	
	Update discharge letter	Drug change	4 (30.8)	• Advised discharge letter needs to be updated to include that Warfarin has been switched to apixaban, need anticoagulation follow up and to state ranitidine stopped • Advised Dr to update discharge letter as not clear regarding: apixaban and edoxaban (patient to continue with edoxaban and to stop apixaban)
		Amend dose	3 (23.1)	• Discharge letter updated to match haematology plan for Apixaban BD as previously written OD • Apixaban prescribed as 2.5mg BD. Discharge letter states OD will be amended to BD
		Other	6 (46.2)	• Dr to update discharge letter regarding: Why patient on low dose apixaban for AF - due to risk of bleeding from

			varicose veins
			• Amended apixaban on discharge letter to correct dose and asked Dr confirm all medication changes
	Total	13	
Indication	Total	23	• Confirm with Dr regarding: apixaban indication as not clearly documented in the discharge letter – confirmed for prophylaxis of recurrent PE
			• Apixaban indication added (as per clinical noting)
			• Called GP to find out indication of apixaban. Informed Dr, confirmed to be discussed on ward round tomorrow
			• Rivaroxaban indication added
Thrombosis assessment update	Total	15	• Thrombosis assessment completed to include contraindication to enoxaparin as patient now on rivaroxaban
			• Enoxaparin prescribed alongside dabigatran - informed Dr and he stopped enoxaparin and updated thrombosis assessment
			• Thrombosis assessment changed to include contraindication to enoxaparin as patient now on apixaban
Book follow-up appointment	Total	5	• Advised Dr patient is new to apixaban and will need anticoagulation appointment referral on discharge - Dr will arrange
			• Communicated with on-call Dr regarding patient apixaban bleeding risk - require follow-up with GP
Check dose	Doesn't comply with guidelines	4 (18.2)	• To discuss with consultant rational behind apixaban being 2.5mg BD as it should be 5mg BD as per guidelines for AF
			• To clarify who advised dose apixaban prescribed at 5mg BD (dose for prophylaxis DVT/PE = 2.5mg BD)
	Subtherapeutic	7 (31.8)	• Queried apixaban dose with Dr and anticoagulation team. Currently prescribed 2.5mg BD which is a subtherapeutic dose for treatment of PE. Anticoagulation team suggested either dose increase to 5mg BD OR prescribe edoxaban 30mg OD
			• Queried why lower dose of apixaban prescribed as patient does not meet criteria for dose reduction in AF - will query with Dr
	Renal function	4 (18.2)	• Rivaroxaban dose queried as renally impaired - but for DVT advised Drs to carry out risk/benefit, they would like to continue at 20mg OD as patient at high risks of clots
			• Spoken to Dr regarding considering reducing rivaroxaban due to decline in renal function

			• Discussed with Dr about apixaban dose – patient with declining renal function. Dr advised to propose to the team to discuss with haematology and consider doing an apixaban level
	Other	7 (31.8)	• Queried with Dr whether patient needs a higher dose of apixaban for AF. Pt only has one risk factor for dose reduction >80yrs. Renal function okay and weight, so could have 5mg BD. Dr would like to continue at 2.5mg BD • Asked Dr to review Apixaban dose
	Total	22	
Consult prescriber	Rational for drug change	2 (4.0)	• Asked Dr to review - can enoxaparin be switched to edoxaban, as per anticoagulation note? Doctor will review
	When to restart drug	14 (28.0)	• Queried when plan is to restart rivaroxaban – Dr said bleeding has settled so will confirm when to start • Discussed with Dr when to restart apixaban - renal function shows slight improvement, above threshold of 15ml.min (currently GFR 21) - asked to review when will be restarted
	Rational for drug choice	4 (8.0)	• Spoke to Dr to query the choice of anticoagulant for this patient. Stated consultant intentionally picked apixaban
	Rational for drug discontinuation	3 (6.0)	• Confirmed reason for rivaroxaban stopping
	Rational for duplicate therapy	12 (24.0)	• Asked Dr to review rivaroxaban and tinzaparin as both prescribed together • Queried use of clopidogrel and apixaban - apixaban to be started 4 days after discharge and patient is to continue both clopidogrel and apixaban - confirmed with ward Dr
	Query drug duration	1 (2.0)	• Apixaban prescribed for 7 days, called Dr to check if wanted as unlimited
	Review plan	14 (28.0)	• Asked Dr to review apixaban plan - paused 48 hours pre-operation and not resumed or paused - Dr is to review plan • Discussed edoxaban - needs review prior to discharge • Unclear why rivaroxaban paused - team to review
	Total	50	

* The total number of reasons for dose change does not equal the number of dose change intervention cases (n=166) due to multifactorial rationale (i.e., dose change for one patient due to both age and weight)