Sheffield Teaching Hospitals NHS
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Bridging anticoagulation: the peri-procedural management of patients on oral anticoagulants

Reference Number	Version	Status	Executive Lead(s) Name and Job Title	Author(s) Name and Job Title	
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Version History

Version	Date Issued	Brief Summary of amendments	Owner's Name:
7.4	July 2019	Amendment regarding peri-operative guidance for cardiac surgery	Joost van Veen Jannat Muen
7.3	May 2019	Amendment to appendix 5: guidance for renal bridging	Joost van Veen Jannat Muen
7.2	September 2018	Addition of guidance regarding peri-operative management of patients taking treatment dose LMWH	Joost van Veen Jannat Muen
7.1	January 2017	Amendments to include new guidance regarding peri-operative management of patients taking DOACs	Joost Van Veen Jannat Muen
6.1	December 2015	Amendment to include neurosurgical patients. Amendment to guideline to include management of patients on edoxaban	Joost Van Veen Jannat Muen
5.1	November 2014	Amendments to appendix 3 regarding cancellation of surgery and amendment to guidance to include near patient testing.	Joost Van Veen Jannat Muen
4.1	July 2014	Amendments to guideline to include management of patients on apixaban and long term dalteparin. Amendments to guidance for bridging patients with renal impairment	Joost Van Veen Jannat Muen
3.1	April 2013	Amendments to guideline for pulmonary hypertension and urology procedures. Amendment to advice following cardiac surgery. Amendments to include management of patients on rivaroxaban and dabigatran.	Joost Van Veen Jannat Muen
2.1	January 2012	Major review following STH switch of LMWH from enoxaparin to dalteparin. Title amended. Introduction of prescription chart.	Joost Van Veen Rebecca Ellis
1.1	August 2009	New guideline "Bridging anticoagulation: The Peri-Operative Management of patients on Oral Anticoagulant Therapy (excluding neurosurgery)"	Joost Van Veen

Document Imprint

Executive Summary

Bridging anticoagulation: the peri-procedural management of patients on oral anticoagulants

Document Objectives:	To provide a standardised approach to the peri-procedural management of patients on oral anticoagulants.
Group/Persons Consulted:	Departments of haematology, cardiology and cardiovascular surgery, anaesthesia and surgery.
Monitoring Arrangements and Indicators:	Regular audits through haematology.
Training Implications:	
Equality Impact Assessment:	An equality impact assessment has been undertaken and will be published on the Trust website
Resource implications:	None
Intended Recipients:	All medical and nursing staff who work in surgical and medical departments where invasive procedures are undertaken. All anaesthetists and nursing staff working in pre-assessment clinics. All clinical pharmacists. All anticoagulation clinic staff
Who should:-	All the above.
➢ be **aware** of the document and where to access it	
➢ **understand** the document	Junior and Senior doctors working in medical/surgical/anaesthetic/haematology clinical areas. All clinical pharmacists. Pre-assessment nursing staff and anticoagulation nursing staff.
➢ have a **good working knowledge** of the document	Junior and Senior doctors working in medical/surgical/anaesthetic/haematology clinical areas, pre-assessment nursing and medical staff involved with pre-operative bridging and anticoagulation clinic staff involved with post-operative bridging.

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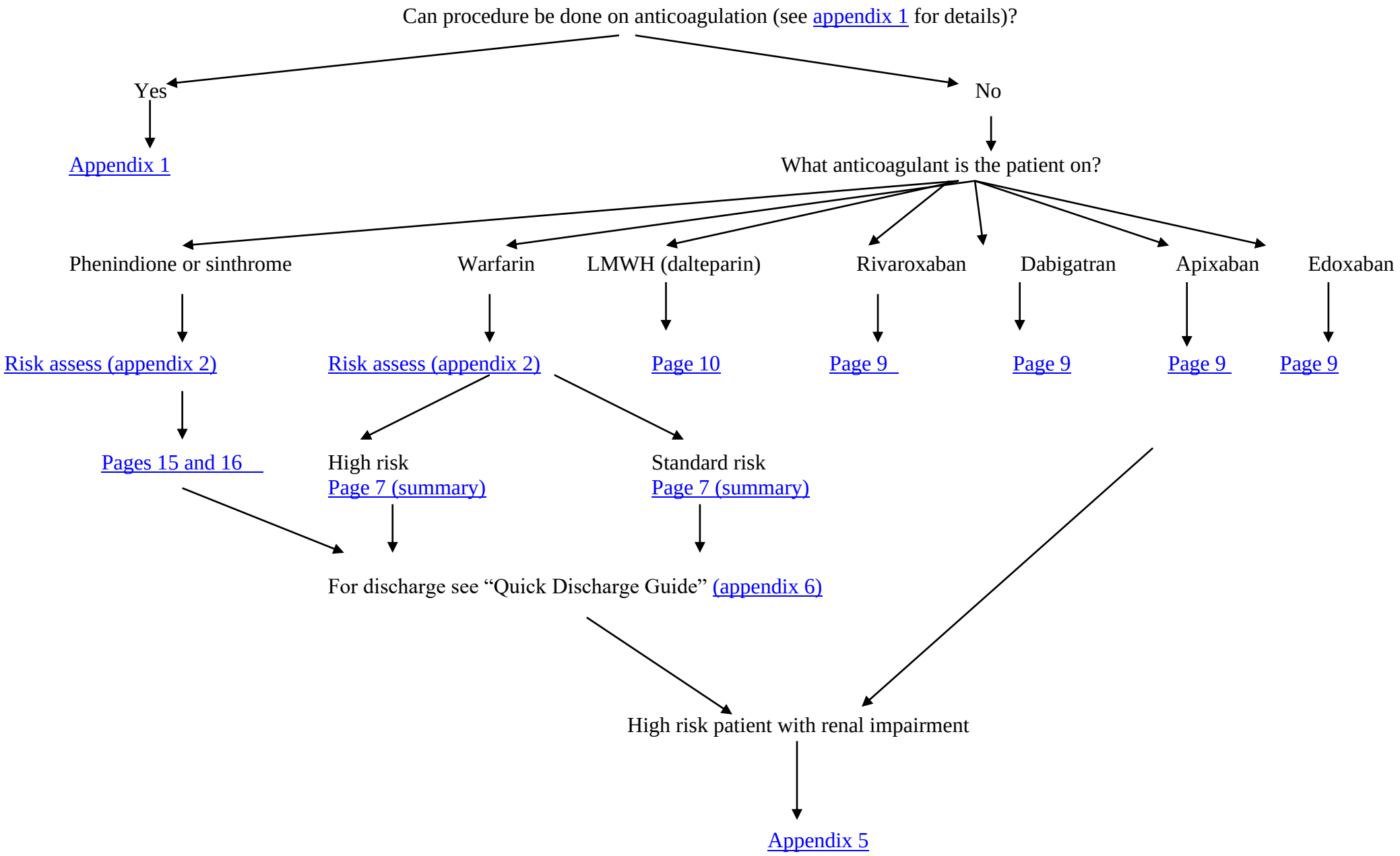
A sample of the prescription chart to be used with this guideline is available on the STH intranet:
Peri-procedural Bridging Anticoagulation Prescription Chart
The prescription chart is controlled stationary and should be ordered from pharmacy

GPs should not be asked to prescribe or monitor bridging anticoagulation.
Prior to the procedure, management should be by the medical/surgical team looking after the patient (maybe via pre-op assessment clinic if applicable). Following discharge from hospital, the patient should be referred to the STH Anticoagulation Clinic.
There may be exceptions to this if the patient lives outside the Sheffield area: see specific guidance within this document.


Can procedure be done on anticoagulation (see appendix 1 for details)?
Yes
No
Appendix 1
What anticoagulant is the patient on?
Phenindione or sinthrome
Warfarin
LMWH (dalteparin)
Rivaroxaban
Dabigatran
Apixaban
Edoxaban
Risk assess (appendix 2)
Risk assess (appendix 2)
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High risk
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Standard risk
Page 7 (summary)
For discharge see "Quick Discharge Guide" (appendix 6)
High risk patient with renal impairment
Appendix 5

For patients on warfarin, the following groups are at high risk for thrombotic events and should be considered for bridging with therapeutic doses of dalteparin (See also appendix 2):

VTE	Patients with a VTE within previous 3 months. Very high risk patients such as patients with a previous VTE whilst on therapeutic anticoagulation who now have a target INR of 3.5.
AF	Patients with a previous stroke/TIA in last three months. Patients with a previous stroke/TIA and three or more of the following risk factors: • Congestive cardiac failure • Hypertension (> 140/90 mmHg or on medication) • Age >75 years • Diabetes mellitus
MHV	MHV patients other than those with a bileaflet aortic valve and no other risk factors

SUMMARY OF BRIDGING ANTICOAGULATION FOR PATIENTS ON WARFARIN

Pre-operative summary for patients on warfarin

Preoperative management for patients at **standard thrombotic risk**

Day -5	Day -4	Day -3	Day -2	Day -1	Surgery
Last dose of warfarin				Check INR: if greater than 1.4 give 1mg oral vitamin K. Prophylactic dalteparin at least 12 hours before surgery	Check INR if greater than 1.4 on day -1

Pre-operative management for patients at **high thrombotic risk**

Day -5	Day -4/-3	Day -2	Day -1	Surgery
Last dose of warfarin	Omit warfarin	**Check INR:** If greater than 2 give 1mg vit K orally and recheck day -1 - If 1.5 – 2.0 give 1mg oral vit K and recheck day -1. Start on twice daily dalteparin. - If less than 1.5 start twice daily dalteparin.	Recheck INR if greater than 1.4 on day -2 and give 1mg vit K if greater than 1.4 Last dose of therapeutic dalteparin in the morning (24 hours pre-op)	Check INR if greater than 1.4 on day -1

Post-operative summary for patients on warfarin*:*

Post-operative warfarin management for patients at **standard thrombotic risk**

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
Prophylactic dalteparin OD 6 – 8 hrs post op	Warfarin at usual dose. Continue prophylactic dalteparin	VTE patients: Continue warfarin at usual doses **and** prophylactic dalteparin until INR is greater than 2.0. Patients with AF without previous stroke/TIA: continue warfarin at usual doses, no need to give dalteparin on discharge even if INR ≤2.0 **unless** extended prophylaxis is indicated e.g. hip/knee arthroplasty, fractured neck of femur, major cancer surgery in abdomen or pelvis.				

Post-operative warfarin management for patients at **high thrombotic risk**

Surgery	D +1	D+2	D+3	D+4	D+5	D + 6
Prophylactic dalteparin OD 6 – 8 hrs post op	Warfarin at usual dose Continue prophylactic dalteparin		Warfarin at usual dose. Increase prophylactic dalteparin as per bridging prescription chart		Warfarin at usual dose. Increase dalteparin as per bridging prescription chart. Continue until INR is greater than 2.0	

Treatment should be reviewed daily. Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with a haematologist. After minor procedures *with* low bleeding risk, high dose LMWH and warfarin may be restarted **at earliest** 24 hours after the procedure

SUMMARY OF BRIDGING ANTICOAGULATION FOR PATIENTS TAKING DOACs (rivaroxaban, apixaban, dabigatran, edoxaban)

Pre-operative summary for patients on DOACs

Creatinine Clearance (ml/min)	Low bleeding risk procedure	High bleeding risk procedure (including spinal/epidural anaesthesia)
Rivaroxaban/Apixaban/Edoxaban:		
>30 ml/min	**Omit for at least 24 hours**	**Omit for at least 48 hours**
<15 - 30ml/min	**Omit for at least 48 hours**	**Omit for at least 72 hours**
< 15ml/min: contra-indictated.	**Discuss with Haematology**	**Discuss with Haematology**
Dabigatran:		
>80 ml/min	**Omit for at least 24 hours**	**Omit for at least 48 hours**
50-80 ml/min	**Omit for at least 24-48 hours**	**Omit for at least 48-72 hours**
30-50 ml/min	**Omit for at least 48-72 hours**	**Omit for at least 96 hours**
< 30ml/min: contra-indicated	**Discuss with Haematology**	**Discuss with Haematology**

Post-operative summary for patients on DOACs for procedures with major bleeding risk

Surgery (D 0)	D +1	D+2	D+3	D+4	D+5	D + 6
Prophylactic dose dalteparin starting 6 – 8 hrs post op			Restart DOAC at the earliest on day +3, depending on bleeding tendency. Check U&E/LFT and do not restart if epidural *in situ.* Administer last dose of dalteparin the day **before** restarting DOAC.			

Post-operative management of DOACs after minor procedures and low bleeding risk

- DOACs may be restarted at earliest 24 hours post-procedure.
- If there is concern about absorption of DOAC, dalteparin may be continued longer at a dose depending on the thrombotic risk group.
- Prophylactic doses of rivaroxaban (10mg OD) and dabigatran (150/220mg OD) may be restarted 6-8 hours post op.

Treatment should be reviewed daily. Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with a haematologist.

SUMMARY OF BRIDGING ANTICOAGULATION FOR PATIENTS TAKING LOW MOLECULAR WEIGHT HEPARIN (dalteparin)

Patients on prophylactic doses of dalteparin (according to their weight and renal function) can have their last dose at least 12 hours before any procedure and can be re-started at earliest 6 – 8 hours post-operatively provided there is no concern about bleeding.

Pre-operative management of patients on therapeutic doses of dalteparin who are at high risk of thrombotic events

Creatinine Clearance (ml/min)	**Last dose**	**Restart for low bleeding risk procedure**
Treatment dose dalteparin ***>20ml/min***	Omit for at least 24 hours	Prophylactic weight adjusted dalteparin 6 – 8 hours post-op and therapeutic doses at earliest 24 hours post-op
Less than 20ml/min or patients with AKI and CrCl 20 – 30ml/min	Discuss with Specialist Anticoagulation Nurses	Discuss with Specialist Anticoagulation Nurses

Post-operative management of patients on therapeutic doses of dalteparin who are at high risk of thrombotic events

Re-starting therapeutic dalteparin after high bleeding risk procedures			
Surgery (D 0)	**D +1 to D+4**	**D+5**	**D + 6**
Prophylactic dose dalteparin starting 6 – 8 hrs post op Use weight adjusted doses as on the high risk bridging prescription chart.		Restart therapeutic dalteparin at the earliest on day +5, depending on bleeding tendency. Check U&E/LFT and do not restart if epidural *in situ*	
Creatinine Clearance less than 30ml/min or AKI, see appendix 5 of the bridging protocol			

INTRODUCTION

When patients on anticoagulation require surgery or an invasive procedure, the risks and benefits of stopping or continuing anticoagulation must be considered. In many cases it is necessary to stop the oral anticoagulant (most commonly warfarin) and replace it with low molecular weight heparin (LMWH) until after the procedure. This is known as "bridging anticoagulation".

SITUATIONS COVERED BY THIS GUIDELINE

This guideline provides recommendations for the management of peri-procedural anticoagulation for patients on warfarin, rivaroxaban (Xarelto®), dabigatran (Pradaxa®), apixaban (Eliquis®), edoxaban (Lixiana®**), acenocoumarol (Sinthrome®) or phenindione (Dindevan®),** who need interruption of anticoagulant therapy (with an INR of less than 1.5 if on a vitamin K antagonist) for a procedure. Additional advice may be required from a haematologist regarding acenocoumarol or phenindione.

This guideline may also be used as guidance for the management of patients who are on long term treatment with low molecular weight heparin (LMWH).

This guideline does not cover the management of the following groups of patients:

- **Pregnant patients:** advice should always be sought from a haematologist.
- **Pulmonary hypertension patients:** patients on the pulmonary vascular diseases unit should be managed according to the Sheffield pulmonary vascular disease unit bridging guideline
- **Urology day case and outpatient procedure patients:** this group of patients should be managed according to the Urology day case and outpatient procedure guidance on bridging anticoagulation.

This document provides guidance only. In all cases, the risks of stopping anticoagulant therapy to prevent procedure related bleeding must be balanced against the risk of a further thromboembolic event.

If there are any uncertainties/concerns regarding these recommendations, discuss with a haematologist (RHH bleep 2132 / NGH bleep 2916 / on-call haematologist out of hours). The on-call anaesthetist can be contacted via switchboard.

Throughout this guideline, the terms "Standard risk" and "High risk" refer to a patient's thrombotic risk

PRE-OPERATIVE ASSESSMENT AND MANAGEMENT

Assessment of elective patients should be carried out at pre-operative assessment clinic. Where the procedure does not warrant a formal pre-operative assessment, the clinician ordering the procedure should ensure that the guidance is followed.

Certain procedures **may** be done whilst on therapeutic anticoagulation - see appendix 1 for further guidance.

If anticoagulation is to be interrupted, patients will need to be given clear instructions about when to take their last dose of anticoagulant:

1. **Pre-op assessment: assess whether anticoagulation needs to be interrupted for the procedure.** Certain procedures **may** be done whilst on rivaroxaban, dabigatran, apixaban, edoxaban and warfarin with an INR of less than 3.0 - see appendix 1 for further guidance.

2. **If anticoagulation needs to be interrupted, use the *peri-procedural bridging anticoagulation prescription chart* to determine whether a patient is in the Standard risk or High risk category** (see appendix 2 for criteria for stratification of thrombotic risk).
   2.1. Use the peri-procedural bridging anticoagulation prescription chart to prescribe the appropriate treatments.
   2.2. If there is any uncertainty as to which category a patient should be assigned, discuss with the cardiothoracic team (mechanical valve patients), cardiology/relevant medical team (AF and risk factors for stroke) or haematology/relevant medical team (venous thromboembolic disease patients) prior to admission. It may be appropriate to involve a senior anaesthetist at this stage.

3. **Certain patients should be discussed with senior clinicians before commencing bridging:**

   3.1. **Patients who are at particularly high risk of thrombosis** should be discussed with the senior clinician and anaesthetist involved; these include
      3.1.1. patients with a venous thrombosis in the last 3 months
      3.1.2. patients with recent stroke (within the previous 6 months) or any history of cardiac thromboembolism
      3.1.3. patients with a left-ventricular assist device
      3.1.4. patients within 1 month of a bare-metal stent insertion or 3 months of a drug-eluting stent insertion

   3.2. **Procedures which carry a very high bleeding risk**: these patients can follow the pre-operative bridging guideline but post-operative bridging may need to be individualised (e.g. spinal surgery, cardiac surgery, radical prostatectomy). All patients undergoing cardiac or thoracic procedures should have their last dose of LMWH no later than 0800 hours on the day before procedure (-1). They must not receive a dose of LMWH on the evening prior to surgery.

   3.3. **Patients with antithrombin deficiency** should be discussed with a haematologist as treatment with antithrombin concentrates may be required.

   3.4. Where there is uncertainty about the management of any patient, discuss with the senior clinician and anaesthetist involved.

4. Patients without any complicating factors (e.g. renal impairment, weight greater than 150kg, etc) should follow the treatment plans as described on the peri-procedural bridging anticoagulation prescription chart and in appendix 3.

5. Patients on therapeutic treatment with LMWH should have their dalteparin discontinued at least 24 hours prior to surgery. Post procedure patients should follow the treatment plan as described on the peri-procedural bridging anticoagulation prescription chart according to their risk (standard/high).

6. **"High risk" patients who are expected to require epidural/spinal anaesthesia or analgesia for more than 48 hours post-operatively** should be considered for an alternative method of analgesia, as high dose dalteparin and therapeutic doses of rivaroxaban, dabigatran apixaban or edoxaban are incompatible with safe removal of epidural catheters. If no other mode of anaesthesia/analgesia is suitable, the patient must be discussed with a haematologist.

7. **Patients with renal impairment**
   7.1. **Standard risk patients on dalteparin should have the dose reduced if their eGFR is less than 20ml/min/1.73m^2**. eGFR should only be used to dose dalteparin for standard risk patients and must NOT be used to dose dalteparin for high risk patients. Dose reductions are advised on the *peri-procedural bridging anticoagulation prescription chart*.
   7.2. **High risk patients on dalteparin should have the dose reduced if their calculated creatinine clearance (CrCl) is less than 30ml/min.** These patients should be discussed with a haematologist before bridging is commenced. Renal function for high risk patients should be estimated using the following calculation:

$$\text{CrCl} = \frac{(140 - \text{age}\_\_\_) \times \text{weight}\ \_\_\_(\text{kg})}{\text{Serum Creatinine (micromol/L)}\ \_\_\_} \times \begin{cases} 1.04 & \text{(female)} \\ 1.23 & \text{(male)} \end{cases} = \_\_\_\_\_\ \text{(mL/min)}$$

   High risk patients with a creatinine clearance of 20-30ml/min may be managed according to guidance in appendix 5. These patients *must* be discussed individually with haematology, for advice regarding anti-Xa monitoring. Renal transplant patients, irrespective of creatinine clearance *must* be discussed with haematology for suitability of dalteparin.

   7.3. **Patients on rivaroxaban, dabigatran apixaban, or edoxaban with renal impairment should be managed according to the guidance given on page 7 to 10 respectively**. Renal function for all patients on rivaroxaban, dabigatran apixaban or edoxaban should be estimated using the above equation; eGFR should not be used to estimate renal function.

8. **Patients weighing more than 150kg should be discussed with a haematologist** as dose adjustments of dalteparin and monitoring of anti-Xa activity may be required.

9. **GPs should not normally be asked to prescribe or monitor bridging anticoagulation.**
   9.1. Prior to the procedure, management should be by the medical/surgical team looking after the patient (may be via pre-op assessment clinic if applicable).
   9.2. Following discharge from hospital, follow the guidance later in this document.

10. **If surgery is cancelled see advice in appendix 3**. It is the responsibility of the person cancelling the patient to inform pre-assessment clinic staff as patients will need advice regarding their bridging therapy.

11. **Guidance for pre-operative assessment clinics / waiting list staff / secretaries is in appendix 4**

PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF PATIENTS TAKING VITAMIN K ANTAGONISTS (warfarin, acenocoumarol (Sinthrome®) or phenindione (Dindevan®))

Pre-Operative Management:

Pre-operative investigations

- A full blood count must be taken in the week prior to surgery (this may be performed at the same time as the pre-op INR). If the patient has acute or chronic thrombocytopenia (platelets less than 150 x10^9/L) then discussion with a haematologist is recommended.
- A U&E must be taken within 6 weeks prior to surgery. This should be repeated in the week prior to surgery for accurate assessment of renal function (calculated creatinine clearance).
- Obtain an accurate weight for the patient so that dosing can be carried out correctly.
- For those patients who are anticoagulated with warfarin:
    - High risk patients: an INR will be required on day -2 and again on day -1 if INR was greater than 1.4 on day -2
    - Standard risk patients: an INR will be required on day -1
    - Near patient testing is acceptable however, the patient must have a venous INR on either day -1 or -2 pre-operatively. Post operatively the patient must have venous samples undertaken whilst an inpatient but may return to near patient testing once discharged.

Warfarin: Patients should be instructed to take their last dose 5 days pre-operatively (i.e. 4 clear days before surgery) and attend for INR checks as appropriate. Patients should be advised that they may need to continue receiving injections of dalteparin after discharge from hospital until their INR is therapeutic. Patients or carers should be trained to inject dalteparin wherever possible.

Phenindione (Dindevan®) and acenocoumarol (Sinthrome®): These agents have shorter half-lives than warfarin, hence a shorter duration of action and more rapid onset of action. Patients should be advised to take their last dose 3 days pre-operatively (i.e. 2 clear days before surgery) and attend for INR checks as appropriate. As above these patients should be advised that they may need to continue receiving injections of dalteparin after discharge from hospital until their INR is therapeutic.

Pre-operative management of emergency patients taking vitamin K antagonists
For emergency procedures consider **warfarin/phenindione/acenocoumarol** reversal with vitamin K and/or prothrombin complex concentrate (Beriplex™) pre-operatively. Further guidance can be found on the back of the STH Warfarin Prescription and Monitoring Chart. Consider discussing warfarin/phenindione/acenocoumarol reversal with a haematologist.

Post-procedure follow the guidance below.

Post-Operative Management:

1. **Follow the appropriate treatment plan according to the patient's thrombotic risk.**
    1.1. Treatment should be reviewed daily. Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with a haematologist.
    1.2. Dalteparin doses should be adjusted according to the patient's weight and renal function – refer to specific guidance on the *peri--procedural bridging anticoagulation prescription chart*. High risk patients with renal impairment (CrCl less than 30ml/min) should be discussed with a haematologist
    1.3. Patients undergoing cardiac surgery should not be given dalteparin on the day of surgery.
    1.4. Neurosurgical patients may have the initiation of their dalteparin delayed according to bleeding risk at the discretion of the Consultant Neurosurgeon.
    1.5. **Patients or their carers should be trained to inject dalteparin whilst they are in hospital**
    Many patients are capable of self-injecting dalteparin after discharge, and failure to train them appropriately places an unnecessary burden on the community nursing service. Training should be carried out in accordance with the STH Self-Administration Policy.
    1.5. Patients with atrial fibrillation without prior stroke/TIA and no other risk factors for stroke may be discharged before their INR is therapeutic without continuing dalteparin if they are medically fit and would not otherwise be a candidate for extended thromboprophylaxis (see STH Guidelines for the Prevention of Venous Thromboembolic Disease)

1.6. **Post-operative summary for patients on warfarin:**

Post-operative warfarin management for patients at **standard thrombotic risk**

Surgery	**D +1**	**D+2**	**D+3**	**D+4**	**D+5**	**D + 6**
Dalteparin prophylaxis 6 – 8 hrs post op	Warfarin at usual dose. Continue dalteparin	Continue warfarin at usual doses **and** prophylactic dalteparin until INR is greater than 2.0 in patients with VTE, or until discharge in patients with standard risk AF.				

Post-operative warfarin management for patients at **high thrombotic risk**

Surgery	**D +1**	**D+2**	**D+3**	**D+4**	**D+5**	**D + 6**
Prophylactic dalteparin OD 6 – 8 hrs post op	Warfarin at usual dose Continue prophylactic dalteparin		Warfarin at usual dose. Increase prophylactic dalteparin as per bridging prescription chart		Warfarin at usual dose. Increase dalteparin as per bridging prescription chart. Continue until INR is greater than 2.0	

Warfarin should be re-started at the patient's usual dose on the first day post-procedure. It will take up to 2 weeks for the INR to become therapeutic. Additional loading or boost doses of warfarin are not recommended. Dalteparin should be continued until the INR is greater than 2 for **all patients** including those with a higher INR target range. After minor procedures *with* low bleeding risk, high dose LMWH and warfarin may be restarted **at earliest** 24 hours after the procedure.

1.6. **Post-operative summary for patients on phenindione (Dindevan®) and acenocoumarol (Sinthrome®):**

Post-operative phenindione/acenocoumarol management for patients at **standard** thrombotic risk

Surgery	**D +1 to +2**	**D +3/4/5**
Dalteparin prophylaxis 6 – 8 hrs post op	Continue prophylactic dalteparin	Restart phenindione/acenocoumarol at usual doses between day 3-5 (at earliest day 3) **and** continue prophylactic dalteparin until INR is greater than 2.0 in patients with VTE or until discharge in patients with standard risk AF. May be restarted day +1 following very minor procedures (discuss with Haematologist)

Post-operative phenindione/acenocoumarol management for patients at **high** thrombotic risk

Surgery	**D +1**	**D+2**	**D+3/4/5**
Prophylactic dalteparin OD 6 – 8 hrs post op	Continue prophylactic dalteparin		Increase dose of dalteparin as per bridging prescription chart. Continue until INR is greater than 2.0. Restart phenindione/ acenocoumarol at usual dose between day 3-5 (at earliest day 3).

PRE-OPERATIVE & POST-OPERATIVE MANAGEMENT OF PATIENTS TAKING RIVAROXABAN (XARELTO®), DABIGATRAN (PRADAXA®), APIXABAN (ELIQUIS®) & EDOXABAN (LIXIANA®)

Pre-Operative Management:

Pre-operative investigations:

- A full blood count must be taken in the week prior to surgery. If the patient has acute or chronic thrombocytopenia (platelets less than 150 $x10^9$/L) then discussion with a haematologist is recommended.
- A U&E must be taken within 6 weeks prior to surgery. This should be repeated in the week prior to surgery for accurate assessment of renal function (calculated creatinine clearance).
- Obtain an accurate weight for the patient so that post-operative dalteparin dosing can be carried out correctly.

Pre-operative summary for patients on DOACs

Creatinine Clearance (ml/min)	Low bleeding risk procedure	High bleeding risk procedure (including spinal/epidural anaesthesia)
Rivaroxaban/Apixaban/Edoxaban:		
>30 ml/min	**Omit for at least 24 hours**	**Omit for at least 48 hours**
<15 - 30ml/min	**Omit for at least 48 hours**	**Omit for at least 72 hours**
< 15ml/min: contra-indictated.	**Discuss with Haematology**	**Discuss with Haematology**
Dabigatran:		
>80 ml/min	**Omit for at least 24 hours**	**Omit for at least 48 hours**
50-80 ml/min	**Omit for at least 24-48 hours**	**Omit for at least 48-72 hours**
30-50 ml/min	**Omit for at least 48-72 hours**	**Omit for at least 96 hours**
< 30ml/min (contra-indicated)	**Discuss with Haematology**	**Discuss with Haematology**

Pre-operative management of emergency patients taking rivaroxaban, dabigatran, apixaban or edoxaban:
For patients on **rivaroxaban**, please refer to the "Guidelines for management of rivaroxaban-bleeding" **and** discuss with haematology.

For patients on **dabigatran**, please refer to the "Guidelines for management of dabigatran-related bleeding" **and** discuss with haematology.

For patients on **apixaban**, please refer to the "Guidelines for the management of apixaban-related bleeding" **and** discuss with haematology.

For patients on edoxaban, please refer to the "Guidelines for the management of edoxaban-related bleeding" **and** discuss with haematology.

Post-procedure follow the guidance below

Post-Operative Management:

2. **Follow the appropriate treatment plan according to the patient's thrombotic risk.**
   2.1. Treatment should be reviewed daily. Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with a haematologist.
   2.2. Dalteparin doses should be adjusted according to the patient's weight and renal function – refer to specific guidance on the *peri--procedural bridging anticoagulation prescription chart*. High risk patients with renal impairment (CrCl less than 30ml/min) should be discussed with a haematologist
   2.3. Patients undergoing cardiac surgery should not be given dalteparin on the day of surgery.

Post-operative summary for patients on DOACs for procedures with major bleeding risk

Surgery (D 0)	**D +1**	**D+2**	**D+3**	**D+4**	**D+5**	**D + 6**
Prophylactic dose dalteparin starting 6 – 8 hrs post op			Restart DOAC at the earliest on day +3, depending on bleeding tendency. Check U&E/LFT and do not restart if epidural *in situ.* Administer last dose of dalteparin the day **before** restarting DOAC.			

Post-operative management of DOACs after minor procedures and low bleeding risk

- DOACs may be restarted at earliest 24 hours post-procedure.
- If there is concern about absorption of DOAC, dalteparin may be continued longer at a dose depending on the thrombotic risk group.
- Prophylactic doses of rivaroxaban (10mg OD) and dabigatran (150/220mg OD) may be restarted 6-8 hours post op.

Treatment should be reviewed daily. Doses should only be escalated when haemostasis is secure. Pay particular attention if the patient is at high bleeding risk and seek advice if there are any concerns. If overt bleeding is present, stop anticoagulation and discuss with a haematologist.

3.0 MONITORING FOR HEPARIN-INDUCED THROMBOCYTOPENIA (HIT)

All patients receiving dalteparin must have a full blood count performed in the week prior to starting treatment. Full blood counts must be repeated every 3 to 4 days (i.e. twice weekly) for the first two weeks of treatment with dalteparin as inpatients. Patients discharged from hospital on LMWH only require HIT monitoring if they have undergone cardiothoracic surgery or they have received unfractionated heparin (prophylactic or treatment doses) within the last 100 days. If the platelet count falls by 30-50% from baseline or to less than $150x10^9$/L, and/or the patient develops new signs of thrombosis, suspect HIT: contact a haematologist for advice.

MANAGEMENT OF SPINAL OR EPIDURAL ANAESTHESIA OR ANALGESIA

The risks of spinal haematoma with spinal/epidural anaesthesia are greatest at times of needle/catheter insertion and removal.

1.1 Patients on low dose dalteparin (i.e. any "standard risk" patients, or "high risk" patients receiving treatment on days 0, 1 or 2 post-operatively):

1.1.1 Spinal/epidural catheters must be inserted or removed at least 12 hours after the last dose of prophylactic dalteparin

1.1.2 The next dose of dalteparin must be given at least 4 hours after inserting or removing a spinal/epidural catheter

1.1.3 If a patient is on twice daily dosing of low dose dalteparin, a dose should be delayed by 4 hours to allow removal of the spinal/epidural catheter

1.2. **Patients on high dose dalteparin (i.e. "high risk" patients from day 3 post-operatively)**
If a "high risk" patient is expected to require spinal/epidural analgesia for more than 48 hours post-operatively then an alternative route of analgesia should be considered. High dose dalteparin is incompatible with safe removal of spinal/epidural catheters.

1.2.1 If a patient receiving high dose dalteparin still has a spinal/epidural catheter in situ, advice should be sought from a haematologist and anaesthetist regarding management of the patient.

1.2.2 Spinal/epidural catheters must be inserted or removed at least 24 hours after the last dose of high dose dalteparin.

1.2.3 High dose dalteparin must not be administered within 12 hours of insertion or removal of a spinal/epidural catheter.

1.3 **Patients taking rivaroxaban, dabigatran, apixaban or edoxaban (DOACs).**
Patients taking a DOAC should be managed according to the DOAC bridging protocol when spinal/epidural catheters are to be removed or inserted as below.

Creatinine Clearance (ml/min)	Interval between inserting or removing spinal/epidural catheter
Rivaroxaban:	
>30ml/min	48 hours
<30ml/min	72 hours
Apixaban:	
>30ml/min	48 hours
<30ml/min	72 hours
Edoxaban:	
>30ml/min	48 hours
<30ml/min	72 hours
Dabigatran:	
>80ml/min	48 hours
50-80ml/min	48-72 hours
30-50ml/min	96 hours

1.4 **Patients taking warfarin should have an INR of 1.4 or less when epidural catheters are inserted or removed**.

1.5 Be vigilant for the signs of spinal cord compression due to spinal haematoma: backache, leg weakness, loss of perineal and leg sensation, loss of bladder control. These must be acted upon promptly with urgent referral to the on-call anaesthetist

DISCHARGING PATIENTS

1. **Patients taking warfarin: Standard risk patients with atrial fibrillation can stop dalteparin on discharge provided continuing thromboprophylaxis for other reasons is not indicated. All other standard and high risk patients should remain on dalteparin until their INR is greater than 2.0**

   If the patient's INR is greater than 2.0 at the time of discharge, patients should be referred back to their usual anticoagulation provider using the STH Anticoagulation Referral Form. Patients must have an INR check within 7 days of discharge (sooner if clinically indicated).
   If the INR is 2.0 or less, the discharge arrangements differ depending on where the patient lives:

   - **Patients registered with a Sheffield GP:**

   These patients can be discharged before the INR is therapeutic if they are medically fit.
   They must be referred to STH Anticoagulation Clinic for outpatient bridging management, using the STH Anticoagulation Referral Form. These patients should **not** be referred to their GP.
   Patients should be prescribed a 10 day supply of dalteparin on their TTO. The patient or their carer should be trained to administer dalteparin wherever possible; if this is not possible they should be referred to the community nursing team.

   - **Patients registered with a non-Sheffield GP:**

   These patients should remain in hospital until the INR is greater than 2.0 unless discussion on an individual basis with the patient's usual anticoagulation provider has been undertaken and the following agreed and understood:
   - the hospital and anticoagulation provider's responsibilities for prescribing warfarin and dalteparin
   - the correct dosing of warfarin and dalteparin, and the correct time to discontinue dalteparin
   - the monitoring requirements (INR and HIT monitoring, where applicable)

Patients with atrial fibrillation without prior stroke/TIA and no other risk factors for stroke may be discharged without dalteparin before their INR is therapeutic if they are medically fit. The patient's warfarin should be restarted at their usual dose and they MUST be referred to their regular anticoagulation provider for INR monitoring. These patients do not need to be "bridged" with dalteparin on discharge from hospital. For further guidance, see appendix 6.

2. **Patients taking DOACs (rivaroxaban, dabigatran, apixaban or edoxaban):**
   - Patients taking DOACs should be managed according to the peri-operative guidance within this guideline.
   - Dalteparin MUST be **discontinued** the day before rivaroxaban, dabigatran, apixaban or edoxaban is restarted.
   - INR monitoring is not required in patients who are taking rivaroxaban, dabigatran, apixaban or edoxaban and there is no referral required on discharge.

BACKGROUND AND RATIONALE FOR RECOMMENDATIONS

Introduction

The purpose of this document is to provide recommendations for the management of peri-procedural anticoagulation for patients on oral anticoagulant therapy who need to stop anticoagulation prior to surgery (INR of less than 1.5 prior to the procedure or interruption of dabigatran/rivaroxaban/apixaban/edoxaban). They are part of a trust wide initiative to implement NPSA guidance for safer anticoagulation and are adapted from the guidelines by the American College of Chest Physicians (Douketis *et al*, 2012) and the British Committee for Standards in Haematology (refer to: Peri-operative management of anticoagulation and antiplatelet therapy . Keeling, Campbell Tait, Watson, and on behalf of the British Committee of Standards for Haematology. BJHaem 2016 Volume 175, Pages 602–613)

There are an estimated 500,000 patients in the UK using oral anticoagulants, the majority for atrial fibrillation (AF) and mechanical heart valves (Baglin *et al*, 2007). In the USA approximately 10% of patients on oral anticoagulants are thought to require surgery or invasive procedures annually (Douketis *et al*, 2012) making peri-operative bridging anticoagulation a common occurrence. A risk assessment by the National Patient Safety Agency demonstrated wide variation in practice of the peri-operative management of patients on oral anticoagulation both between and within hospital trusts as well as deficiencies in training of staff dealing with anticoagulation issues (National Patient Safety Agency, 2006). This can lead to potentially unnecessary admissions for pre-procedural anticoagulation, delays in discharge because of unstable anticoagulation, and unsafe anticoagulation management with potentially increased morbidity and mortality.

For patients on oral anticoagulant therapy requiring invasive procedures, the risk of a thromboembolic event in the peri-operative period when anticoagulation is interrupted must be balanced against the risk of bleeding when these are continued. If the risk of procedure-related bleeding whilst continuing oral anticoagulation is thought to be small, anticoagulation may be continued. This applies to some minor dental (Douketis *et al*, 2012;Perry *et al*, 2007), ophthalmic (Douketis *et al*, 2012) and dermatological (Douketis *et al*, 2012) procedures and should be discussed with the relevant team. Recent guidelines from the British Society of Gastroenterology suggest that diagnostic endoscopic procedures with or without biopsy, biliary or pancreatic stenting and diagnostic endoscopic ultrasound can also be performed whilst the patient is on therapeutic anticoagulation (Veitch *et al*, 2008). Similarly, patients requiring invasive cardiology procedures may be at low risk of bleeding and these procedures can be done whilst anticoagulated. These patients should be discussed with the cardiology team before anticoagulation is altered. Patients requiring diagnostic angiography also have a low risk of bleeding and procedures can generally be done on warfarin provided the INR is less than 3 and the guidance as given by vascular radiology should be followed. A list of procedures that may be undertaken whilst a patient's INR is less than 3 is given below, and in appendix 1 of this document.

If the risk of procedure-related bleeding is thought to outweigh the risk of thromboembolic events, anticoagulation should be stopped and bridging anticoagulation considered depending on the thrombotic risk. If bridging anticoagulation is instituted, this should be done in a manner whereby both the time without anticoagulation and the bleeding risk are minimised. The peri-procedural management therefore depends both on individual patient characteristics and the type of procedure done.

Bleeding risk associated with procedures

Note that this list is not comprehensive and is intended as guidance only.

Very high risk[1]	High risk	Low risk[2]	Procedures which may be performed on warfarin [3]
Cardiac surgery	Major orthopaedic surgery	Minor procedures as specified by treating surgeon/physician	Diagnostic GI endoscopic procedures ± biopsy (Veitch *et al*, 2008)
Neurosurgery	Major vascular surgery		Biliary or pancreatic stenting (Veitch *et al*, 2008)
Spinal surgery	Major gynaecological and urological surgery		Diagnostic EUS (Veitch *et al*, 2008) minor dermatological surgery (Douketis *et al*, 2012)
Radical prostatectomy	Major cancer surgery		Minor dental surgery (Perry *et al*, 2007) Minor ophthalmological surgery (cataract extraction) (Douketis *et al*, 2012)
	Other major abdominal and thoracic surgery		
	Renal biopsy		

[1] Procedures with very high bleeding risk can follow this guideline pre-operatively. Post operative dalteparin should not be escalated before day +3 and some may need an individualised decision.

[2] Minor procedures at low risk of bleeding but where warfarin needs to be stopped should be identified by the treating physician or surgeon. In patients with a high thrombotic risk undergoing a low risk procedure high dose dalteparin **may** be restarted **at earliest** 24 hours after the procedure. Caution may be needed with procedures that appear to have a low bleeding risk but have been associated with higher bleeding rates. These include resection of large pedunculated polyps or broad based flat (sessile) polyps requiring EMR and pacemaker or defibrillator implantation.

[3] Guidelines on selected procedures that may be done whilst on warfarin are available from the British Society for Gastroenterology (Veitch *et al*, 2008), ACCP (Douketis *et al*, 2012) and British Committee for Standards in Haematology (Perry *et* al, 2007) (Keeling *et al*, 2011). Other minor vascular and cardiological procedures may also be possible whilst on warfarin but should be discussed with the relevant team.

Assessment of thrombotic risk

This guideline recommends stratification of thrombotic risk as Standard risk or High risk. Bridging with therapeutic doses dalteparin should be considered in those at highest thrombotic risk (Keeling et al 2016):

VTE	Patients with a VTE within previous 3 months. Very high risk patients such as patients with a previous VTE whilst on therapeutic anticoagulation who now have a target INR of 3.5.
AF	Patients with a previous stroke/TIA in last three months. Patients with a previous stroke/TIA and three or more of the following risk factors: • Congestive cardiac failure • Hypertension (> 140/90 mmHg or on medication) • Age >75 years • Diabetes mellitus
MHV	MHV patients other than those with a bileaflet aortic valve and no other risk factors

Mechanical heart valves
The risk of thrombosis is highest in mechanical mitral valve prosthesis and aortic valve prosthesis using caged ball or tilting disc devices. The risk is lower in modern bileaflet aortic valves. Most studies assessing the use of low molecular weight heparin (LMWH) as bridging anticoagulation have used therapeutic dose regimens (for a review see Douketis *et al*, 2012). Two studies have used low dose LMWH (including patients with mitral valve prosthesis) but it is not clear if this is sufficient as it can be argued that higher doses of LMWH are needed for the prevention of arterial thrombosis. The latter however is also not established.

This guideline therefore classifies all patients with mechanical valve prosthesis as high risk **except** those with bileaflet aortic valves without any other risk factors for stroke.

Atrial Fibrillation
Patients at highest risk for stroke are those with a previous stroke/TIA in the last 3 months, patients with rheumatic valvular heart disease and patients who suffered a previous TIA/stroke over 3 months ago and who have 3 of the following risk factors:

- Congestive cardiac failure
- Hypertension (>140/90mmHg or on medication)
- Age >75 years
- Diabetes mellitus

These patients should be bridged according to the high risk guideline (BCSH guidelines). The BRIDGE trial showed that bridging is associated with a significant risk of major bleeding whilst it does not reduce the risk of stroke in patients with a CHADS2 score of up to and including 4. There were too few patients to draw conclusions with a CHADS2 score of 5 and 6 (Douketis et al 2015).

For all other patients with AF this guideline recommends using prophylactic doses of LMWH whilst an inpatient. If there is any uncertainty as to which category a patient should be assigned, this should be discussed with the cardiology team/relevant medical team prior to admission.

Previous venous thrombotic events (VTE)
In contrast to arterial thrombotic events, there is evidence that prophylactic dose LMWH therapy decreases the post-operative thrombotic risk. Therefore there is a clear role for the use of prophylactic

dose LMWH in patients with a previous VTE who are on long term anticoagulation with warfarin and have a target INR of 2 – 3.

Patients with VTE in the previous 3 months are at high risk of recurrence and any procedures (for which interruption of anticoagulation is necessary) should preferably be delayed for 3 months. If this is not possible, a temporary IVC filter should be considered after discussion with a Haematologist or Coagulation Consultant prior to admission.

Patients with antiphospholipid syndrome (who have had either arterial or venous thrombotic events) and those with recurrent thrombosis whilst on warfarin (who are managed with a target INR of 3.5) are at high risk of recurrence: they should be managed according to the high risk guideline. Patients with antithrombin deficiency may require peri-procedural antithrombin concentrate and should also be discussed with a Haematology Coagulation Consultant prior to admission.

The use of low molecular weight heparin (LMWH) for bridging anticoagulant therapy
LMWH given subcutaneously has a 90 – 100% bioavailability and a more predictable anticoagulant response than unfractionated heparin (UFH). It has a half life of approximately 4 hours and is given in weight adjusted doses. Dosage monitoring is generally not necessary except in patients with renal failure, at extremes of body weight, and during pregnancy. Compared to unfractionated heparin, it has a favourable benefit to risk ratio in animal models and when used to treat VTE (Hirsh *et al*, 2008). In addition LMWH can be given in the outpatient setting. Because of these advantages LMWH is recommended in preference to unfractionated heparin (UFH) for anticoagulation bridging.

Standard risk patients should receive prophylactic doses of LMWH until oral anticoagulation with warfarin has become therapeutic (INR greater than 2.0). In patients taking rivaroxaban, apixaban, edoxaban or dabigatran, the last LMWH dose should be 24 hours before restarting rivaroxaban, apixaban, edoxaban or dabigatran.

High risk patients should receive LMWH with the dose increasing at increments post-operatively until full therapeutic doses have been achieved. LMWH should continue in patients taking warfarin until it has become therapeutic (INR greater than 2.0). In patients taking rivaroxaban, dabigatran, edoxaban or apixaban, the last LMWH dose should be 24 hours before restarting dabigatran, rivaroxaban, edoxaban or apixaban. Both the creatinine clearance and liver function tests should be checked before restarting rivaroxaban, dabigatran, edoxaban or apixaban and their doses checked against these parameters.

Dose adjustments for LMWH are necessary for patients with renal impairment. Patients requiring low "prophylactic" doses of dalteparin should have doses reduced if their eGFR is less than 20ml/min/1.73m^2, and additional monitoring of anti-Xa levels carried out. Advice should be sought from a Haematologist regarding the management of these patients.

For patients who require high dose ("therapeutic dose") LMWH and who have renal impairment (creatinine clearance less than 20 ml/min), the use of unfractionated heparin infusion may be preferable. Patients requiring therapeutic doses of dalteparin and who have a CrCl between 20-29 ml/min can have reduced doses of dalteparin as outlined in appendix 5. These patients ***must*** be discussed with a Haematologist and additional monitoring of anti-Xa levels will be required. Alternatively unfractionated heparin infusion may be considered.

Timescale for peri-operative anticoagulation

Stopping warfarin

Prospective cohort studies stopped warfarin 5 – 6 days prior to surgery (for a review see Douketis *et al*, 2008). One study stopping anticoagulation 5 days before surgery found that 7% of patients had an INR greater than 1.5 the day before surgery which was corrected with 1mg oral vitamin K (Kovacs *et al*, 2004). In another retrospective study including 43 patients with an INR of 1.5 – 1.9, administration of 1mg oral vitamin K resulted in INR normalisation in 91% of the patients (Woods *et al*, 2007). An INR greater than 1.5 on the day of operation is more likely in patients with a higher INR target (e.g. mechanical heart valves and patients with recurrent VTE whilst on warfarin) and elderly patients. This guideline recommends taking the last dose of warfarin 5 days prior to surgery (4 clear days), checking the INR the day prior to surgery and giving 1mg oral vitamin K if INR greater than 1.5. Patients at high thrombotic risk should have their INR checked on day -2 and should be started on LMWH; their INR should be rechecked on day -1 if INR was greater than 1.4 on day -2. Advice on starting LMWH is detailed below.

Other vitamin K antagonists (i.e. phenindione and acenocoumarol) have shorter half-lives and a shorter duration of action. They should be stopped closer to the date of surgery; as per guidance outlined above.

Other oral anticoagulants (e.g. rivaroxaban, dabigatran, apixaban, edoxaban)

Renal Function CrCl ml/min	Estimated half-life (hours)	Low bleeding risk	High bleeding risk
Dabigatran			
>80	13	24 hours	48 hours
>50 to <80	15	24-48 hours	48-72 hours
>30 to <50	18	48-72 hours	96 hours
Rivaroxaban			
>30	9	24 hours	48 hours
<30		48 hours	72 hours
Apixaban			
>30	8	24 hours	48 hours
<30		48 hours	72 hours
Edoxaban			
>30	10-14	24 hours	48 hours
<30		48 hours	72 hours

The newer oral anticoagulants have a different mode of action to vitamin K antagonists, and require different management. They are renally excreted and therefore the timescale for stopping and re-starting peri-operatively is partly dependent on renal function.

Rivaroxaban, dabigatran, edoxaban and apixaban have shorter half-lives in comparison to warfarin and an onset of action within 2 hours if intestinal absorption is normal. As a result, it can be assumed that interrupting anticoagulation with dabigatran, apixaban, edoxaban or rivaroxaban is sufficient to ensure haemostasis and that surgery is safe (Schulman & Crowther 2012).

Rivaroxaban, edoxaban & apixaban
This guideline recommends that for patients taking therapeutic doses of rivaroxaban, edoxaban and apixaban and who have a creatinine clearance of greater than 30 ml/min and are to undergo major surgery or procedures with high bleeding risk, Should omit these drugs for at least 48 hours.
In patients with a creatinine clearance <30ml/min undergoing a major procedure or procedures with high bleeding risk should omit these drugs for at least 72 hours.
Patients who are to undergo minor procedures with a low bleeding risk and a creatinine clearance greater than 30 ml/min whilst taking therapeutic rivaroxaban, apixaban or edoxaban, should omit these drugs for at least 24 hours.
Patients who are to undergo minor procedures with a low bleeding risk and a creatinine clearance of <30 ml/min should omit these drugs for at least 48 hours.
Patients taking prophylactic doses of rivaroxaban (10mg OD) must have taken their last dose of rivaroxaban at least 18 hours prior to the procedure (Keeling et al 2016). These drugs are contraindicated in a creatinine clearance of less that 15ml/min and these patients should be discussed with haematology.

Dabigatran
Patients taking therapeutic doses of dabigatran who have a creatinine clearance of greater than 80ml/min who require major surgery or a procedure with a high bleeding tendency should omit dabigatran for at least 48 hours.
Those with a creatinine clearance of 50-80ml/min should omit dabigatran for at least 48 – 72 hours and those patients with a creatinine clearance 30 – 50 ml/min should omit dabigatran for at least 96 hours.
Those requiring minor surgery with low bleeding risk and who have a creatinine clearance of greater than 80 ml/min should omit dabigatran 24 hours and those with a creatinine clearance of 50 – 80 ml/min for at least 24 – 48 hours and those with a creatinine clearance of 30 – 50 ml/min for at least 48 – 72 hours (Keeling et al 2016). Dabigatran is contra-indicated in patients with a creatinine clearance of less than 30ml/min and these patients should be discussed with Haematology.

Influence of rivaroxaban, dabigatran, apixaban and edoxaban on routine coagulation testing.
A normal thrombin time effectively excludes the presence of dabigatran but a normal APTT and PT do not exclude significant concentrations of apixaban, rivaroxaban or edoxaban in a sample (Keeling et al 2016). Specific drug level measurements may be considered after discussion with haematology for example for emergency surgery when omission of the drug by the timescales in this guidance is not feasible or acute renal failure when there is concern about drug accumulation.

Restarting anticoagulation and bleeding risk
When to restart anticoagulation after a procedure depends on the bleeding risk associated with the type of procedure and the proximity of surgery. The ultimate dose is dependent on the thrombotic risk of the patient. The risk of bleeding is highest in patients who receive therapeutic doses of anticoagulation in the immediate post-operative period. The ACCP and BCSH guidelines suggest that therapeutic-dose LMWH should not be restarted within 24 hours of minor procedures with a low bleeding risk and not within 48 – 72 hours of surgery with a high bleeding risk.

Very little data are available on surgery with a very high bleeding risk. There continue to be concerns about potential high bleeding rates in patients where therapeutic anticoagulation has been started post-operatively. Studies are underway randomising patients with high risk AF and mechanical heart valves to bridging with low molecular weight heparin versus no bridging and PERIOP-2 study (http://clinicaltrials.gov/ct2/show/NCT00432796)].

Provided surgical haemostasis is secure, low dose prophylactic LMWH can usually be restarted 6 – 8 hours after surgery. Patients at high risk of thrombosis should initially be started on low-dose LMWH; the dose can subsequently be escalated at 72 hours provided haemostasis is secure and full dose LMWH can be given on day 5 and continued until the INR is greater than 2.

Warfarin can be restarted at the patient's usual dose on the day after surgery (day +1) provided haemostasis is secure. Loading or boost doses of warfarin should be avoided as these increase the risk of over-anticoagulation. It will take 1 to 2 weeks for the patient's INR to become therapeutic. LMWH should be continued until the INR is greater than 2.0, irrespective of the target INR. LMWH can be discontinued in standard risk patients with AF provided there is no indication for prolonged thromboprophylaxis (see STH guidelines for prevention of venous thromboembolism for a list of procedures where extended thromboprophylaxis is indicated)

Prophylactic doses of rivaroxaban (10mg OD) and dabigatran (150/220mg OD) may be restarted 6-8 hours post-op provided haemostasis is secure. Patients who normally take therapeutic doses of rivaroxaban (15 OD or BD or 20mg OD), dabigatran (110 or 150mg BD), apixaban (2.5/5mg BD) or edoxaban (30 or 60mg OD) should receive LMWH for at least 48 hours, at which point their normal dose of anticoagulant can be resumed provided there is no concern about bleeding at that point. LMWH MUST be discontinued once rivaroxaban/dabigatran/apixaban/edoxaban have been restarted.

Other oral anticoagulants (i.e. phenindione and acenocoumarol) should be re-started later after surgery due to their short half-lives and more rapid onset of action as by the tables above.

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Appendix 1

PROCEDURES WHICH MAY BE PERFORMED ON WARFARIN WITH AN INR LESS THAN 3.0

Diagnostic angiographic procedures by vascular radiology: guidance given in the vascular handbook should be followed, i.e.

Check INR in pre-assessment clinic
If INR less than 3.0, check the INR on the day-ward, proceed with angiography and discharge on usual dose of warfarin
If the INR is greater than 3.0 and the patient is non-urgent, adjust dose accordingly and proceed when the INR is less than 3.0
If the INR is greater than 3.0 and the patient is urgent discuss with Radiologist and a Haematologist

Some invasive cardiology procedures may be done whilst the patient is anticoagulated on warfarin: these patients should be discussed with the cardiology team before anticoagulation is altered.

Minor dental, ophthalmic, (cataract surgery) and dermatological surgery: these patients should be discussed with the relevant team before anticoagulation is altered.

Diagnostic GI endoscopies, biliary or pancreatic stenting and diagnostic endoscopic ultrasound: these patients should be discussed with the relevant team before anticoagulation is altered.

PROCEDURES WHICH MAY BE PERFORMED ON RIVAROXABAN, DABIGATRAN APIXABAN AND EDOXABAN

Minor procedures with low bleeding risk for which clear guidelines exist to be done whilst on warfarin may also be possible to do on rivaroxaban, dabigatran, edoxaban and apixaban. Although this is recommended internationally (Spyropoulos 2012), evidence of safety is lacking. These procedures include:

Dental procedures including minor oral surgery or up to 3 dental extractions, Prosthodontics, conservation, endodontics, hygiene phase therapy and orthodontics.

Minor ophthalmic, (cataract surgery) and dermatological surgery.

Diagnostic GI endoscopies.

In patients taking rivaroxaban, dabigatran, edoxaban or apixaban we suggest omitting the dose taken in the morning of the procedure and restarting/ continuing after the procedure, provided there are no concerns about bleeding.

Appendix 2
ASSESSMENT OF THROMBOTIC RISK

Reason for being on oral anticoagulants	STANDARD RISK	HIGH RISK
Prosthetic heart valve	● Bileaflet mechanical aortic valve and no other risk factors for stroke and more than 3 months after implantation	● ● Any mechanical mitral valve ● Caged ball or tilting disc aortic valve ● Bileaflet mechanical aortic valve ***and*** one or more of the following stroke risk factors: chronic atrial fibrillation left ventricular dysfunction age over 75 years hypertension diabetes prior stroke or TIA ● Any mechanical valve within 3 months of implantation
	● Bioprosthetic valves with no other risk factors for stroke – anticoagulation not required. Thromboprophylaxis if indicated.	
Chronic atrial fibrillation	● Atrial fibrillation without prior stroke/TIA or rheumatic valvular heart disease	● Atrial fibrillation with previous stroke/TIA within the last 3 months. • Atrial fibrillation with previous stroke/TIA & 3 or more of following risk factors: - age >75 - congestive cardiac failure - hypertension (>140/90mmHg or on medication) - diabetes mellitus ● Atrial fibrillation with rheumatic valvular heart disease
Venous thromboembolism or antiphospholipid syndrome	● Previous VTE and now on long term anticoagulant therapy (target INR 2.5) *(Patients with previous VTE who are no longer on oral anticoagulation should be treated according to the STH Guidelines for the Prevention of Venous Thromboembolic Disease)*	● Recent episode of VTE (within 3 months) – discuss with senior clinician and anaesthetist: consider postponing surgery or placing an IVC filter ● Antiphospholipid syndrome with a history of venous or arterial thrombosis ● Recurrence of VTE on oral anticoagulation (target INR 3.5) • Patients with anti-thrombin deficiency should be discussed with haematology.

Pulmonary hypertension (undergoing a procedure that is *not* for investigation or management of PH)	● **PH patients with chronic thromboembolic pulmonary hypertension or IVC filter in situ:** discuss with PH consultants regarding risk stratification, then manage according to this guideline. ● **Pulmonary hypertension patients with other risk factors:** risk stratify according to the risk factors as above ● **Pulmonary hypertension patients who are on warfarin for survival benefit only:** anticoagulation bridging is not required.
Antithrombin deficiency	**All patients with antithrombin deficiency should be discussed with a Haematologist before bridging is commenced, as some may require antithrombin replacement.**

Appendix 3
CANCELLATION OF SURGERY

Patients on warfarin
Cancellation of surgery will lead to an increased period of bridging (even if warfarin is restarted). There is the potential for patients to receive inadequate anticoagulation or no anticoagulation during this time. This would put them at increased risk of thromboembolic events.

- Cancellation should be avoided if at all possible.
- If cancellation is unavoidable, postpone the surgery or procedure for a **maximum** of 1 week.
- The person cancelling the surgery or procedure must inform the relevant pre-assessment clinic immediately:
  - On weekdays contact pre-assessment clinic immediately
  - If a patient is cancelled at the weekend, ensure pre-assessment clinic is informed by 9.00am on Monday morning. Provide high risk patients with dalteparin (see doses below) and ask them to attend pre-assessment clinic at 8.00 am on Monday morning.
- Teach patients or carers to inject dalteparin wherever possible, to avoid unnecessary community nurse workload.
- If surgery is to be postponed for more than 1 week, contact a Haematologist for advice: a decision on an individual basis should be made.

Dalteparin dosing for HIGH RISK PATIENTS & STANDARD RISK AF PATIENTS who have been cancelled and rescheduled within 1 week with calculated Creatinine Clearance 30ml/min or greater					
less than 46kg	**46-65 kg**	**66-99 kg**	**100-120 kg**	**121-150 kg**	**greater than 150kg**
5,000 units am 2,500 units pm	5,000 units BD	7,500 units BD	10,000 units BD	12,500 units BD	Discuss with a Haematologist
The last dose should be given in the morning on the day prior to procedure/surgery					

Dalteparin dosing for HIGH RISK PATIENTS & STANDARD RISK AF who have been cancelled with calculated Creatinine Clearance less than 30ml/min
Discuss with a Haematologist.

Dalteparin dosing for STANDARD RISK PATIENTS with previous venous thrombosis with eGFR 20ml/min/1.73m^2 or greater **who have been cancelled and rescheduled within 1 week**			
Weight less than 45kg	**Weight 45 – 100kg**	**Weight 101 – 150kg**	**Weight greater than 150kg**
Dalteparin 2,500 units **once daily** in the evening	Dalteparin 5,000 units **once daily** in the evening	Dalteparin 7,500 units **once daily** in the evening	Dalteparin 5,000 units **twice daily** in the evening
The last dose should be given in the evening on the day prior to procedure/surgery			

Dalteparin dosing for STANDARD RISK PATIENTS who have been cancelled with eGFR less than 20 ml/min/1.73m^2 Anti-Xa monitoring may be required: discuss with a Haematologist
Dalteparin 2,500 units **once daily** in the evening
The last dose should be given in the evening on the day prior to procedure/surgery

Patients on rivaroxaban, dabigatran, edoxaban or apixaban

If surgery is cancelled for patients on rivaroxaban, dabigatran, edoxaban or apixaban and either drug has been stopped, it should be re-started as soon as possible. Dalteparin is not necessary given the short onset of action of these drugs.

Appendix 4
NOTES FOR PRE-OPERATIVE ASSESSMENT CLINICS / WAITING LIST STAFF / SECRETARIES

Patients on anticoagulants should be assessed for thrombotic risk using the Peri-procedural bridging anticoagulation prescription chart. This chart should then be placed in the patient's notes with the pre-assessment prescription chart.

Pre-assessment clinic staff will ensure the last three INR results are included in the pre-operative document, along with the current dose of warfarin.

Pre-assessment clinic staff will identify on the feedback sheet that is returned to each secretary/waiting list co-ordinator which patients need to have U&E and INR checks and when.

When patients are dated for surgery the waiting list coordinator / secretary will book patients for INR checks in either pre-assessment clinic, or the designated area at the weekends and the notes will be sent to the relevant area.

Arrangements **must** be made to ensure that the patient knows when to take their last dose of warfarin, rivaroxaban. dabigatran or apixaban. In addition to this, patients **must** be informed on when they are to restart taking their anticoagulant.

Patients will have an appointment made on PFI or Patient Centre to attend the pre-assessment clinic and will be entered as a ward attender when they return to the main hospital for checks.

Where INR checks will take place:
NGH:
Monday to Friday patients to attend central pre-assessment clinic
Weekends: patients to attend Surgical Assessment Centre
RHH:
Every day: patients to attend appropriate ward according to specialty

Appointment Times:
Standard risk patients will attend the day prior to surgery at 10.00am (to give Vitamin K the necessary time to take effect if it is necessary). Any necessary treatment will be given at this time.

High risk patients will attend 48 hours pre-surgery date at 07.30 for bloods and treatment as identified on the prescription chart and again at 19.30 for the 2nd dose of dalteparin (if patient is not self-administering dalteparin). Pre-assessment clinic staff will make individual patient arrangements for the 19.30 injection. If patient or carer is administering the dalteparin they must be trained and provided with a sharps bin.

High risk patients may need to return for a further INR check on the day prior to surgery at 08.00 (depending on the previous day's INR) and again any necessary treatment will be given.

Prescriptions
The Peri-procedural anticoagulation bridging prescription chart sets out what treatment is required. It should be used to prescribe vitamin K (if required) and dalteparin.
The STH Warfarin Prescription and Monitoring Chart should be used to prescribe the patient's warfarin.

Prescriptions for dalteparin
All prescriptions will be completed on receipt of U&E (within last 6 weeks) and INR result.
Between Monday and Friday all prescriptions will be completed by the anaesthetists in pre-assessment clinic. On the weekend prescriptions to be completed by F1 doctors (house officers).

Pre-assessment clinic and ward areas to keep stock of dalteparin 2,500 units and dalteparin 5,000 units and Vitamin K 1mg (phytomenadione 2mg/0.2mL).
Dalteparin for high risk patients will need to be ordered from pharmacy on an individual basis.

If there are any questions/queries when patient attends for INR check these should be discussed with the attendant anaesthetist first. If needed, advice can be sought from a Haematologist.

Admission Plan
All patients can be admitted on the day of surgery, unless they have other co-morbidities that require them to be admitted earlier.

All patients will need to have their INR checked on day of surgery and bridging therapy continued as per the treatment plan throughout admission.

Notes for waiting list staff/secretaries.
NGH:
Patients attending pre-assessment for INR checks: please ring 66235 for appointment to be made and a letter to be sent to patient. Medical notes will then be sent to pre-assessment clinic for these appointments. On completion of treatment the notes will be returned to admissions so they can be distributed to the TAU for admission.

To book patients into the ward areas; please ring the wards direct and book into their diary. Secretaries/ waiting list co-ordinators need to send out a letter for these patients and the notes should then be taken to the ward area. Notes will need to be taken to designated ward by 3pm on the Friday before the weekend. On Monday morning notes will need to be taken to TAU by the relevant wards for admission at 7am.

RHH:
To book patients into the ward areas; please ring the wards direct and book into their diary. Secretaries/waiting list co-ordinators need to send out a letter for these patients and the notes should then be taken to the ward area. Notes will need to be taken to designated ward by 3pm on the day before the patient attends.

Notes will need to be taken to the admitting ward before 7am on the day of admission

Cancellations:
It is the responsibility of the person cancelling the patient to inform pre-assessment clinic staff as patients will need advice regarding their bridging therapy.
Please remember patients will have stopped their warfarin 5 days prior to their day of surgery.

Avoid cancellation if at all possible: patients are to be given some priority by general managers/bed managers when considering which patients to cancel due to lack of beds. This will be managed by the individual specialities.

See Appendix 3 for further advice regarding cancellation.

Other issues
Out-of-Sheffield patients and patients needing transport will be assessed for suitability of being admitted for bridging therapy or attending on an outpatient basis. This should be discussed at their pre-assessment appointment and an agreed plan documented on the pre-assessment document.

Appendix 5

PERI-OPERATIVE MANAGEMENT OF HIGH RISK PATIENTS WITH CREATININE CLEARANCE 20-30ML/MIN UNDERGOING PROCEDURES WITH MAJOR BLEEDING RISK						
Pre-Operative dalteparin dosing for HIGH RISK PATIENTS with creatinine clearance 20- 30ml/min						
Day	**Weight less than 56kg**	**Weight 57-68kg**	**Weight 69-82kg**	**Weight 83-100kg**	**Weight 101-115kg**	**Weight 115-150kg**
-5	Last dose of warfarin (4 days clear) ensure patient has clear instructions					
-2	**Check INR:** if greater than 1.5 give 1mg oral vitamin K and recheck day -1. Start twice daily dalteparin if INR less than 2.0.					
	5000 units OM & 2500 units pm	5000 units BD	7500 units OM & 5000 units PM	7500 units BD	10,000 units OM & 7500 units PM	10,000 units BD
-1	5000 units OM	5000 units OM	7500 units OM	7500 units OM	10,000 units OM	10,000 units OM
Post-Operative dalteparin dosing for HIGH RISK PATIENTS with creatinine clearance 20-30ml/min						
Day	**Weight less than 56kg**	**Weight 57-68kg**	**Weight 69-82kg**	**Weight 83-100kg**	**Weight 101-115kg**	**Weight 115-150kg**
0	2500 units OD	5000 units OD	5000 units OD	5000 units OD	7500 units OD	7500 units OD
+1	2500 units OD	5000 units OD	5000 units OD	5000 units OD	7500 units OD	7500 units OD
+2	2500 units OD	5000 units OD	5000 units OD	5000 units OD	7500 units OD	7500 units OD
+3	2500 units BD	5000 units OM & 2500 units PM	5000 units BD	7500 units OM & 5000 units PM	7500 units BD	10,000 units OM & 7500 units PM
+4	2500 units BD	5000 units OM & 2500 units PM	5000 units BD	7500 units OM & 5000 units PM	7500 units BD	10,000 units OM & 7500 units PM
+5 onwards	5000 units OM & 2500 units PM	5000 units BD	7500 units OM & 5000 units PM	7500 units BD	10,000 units OM & 7500 units PM	10,000 units BD

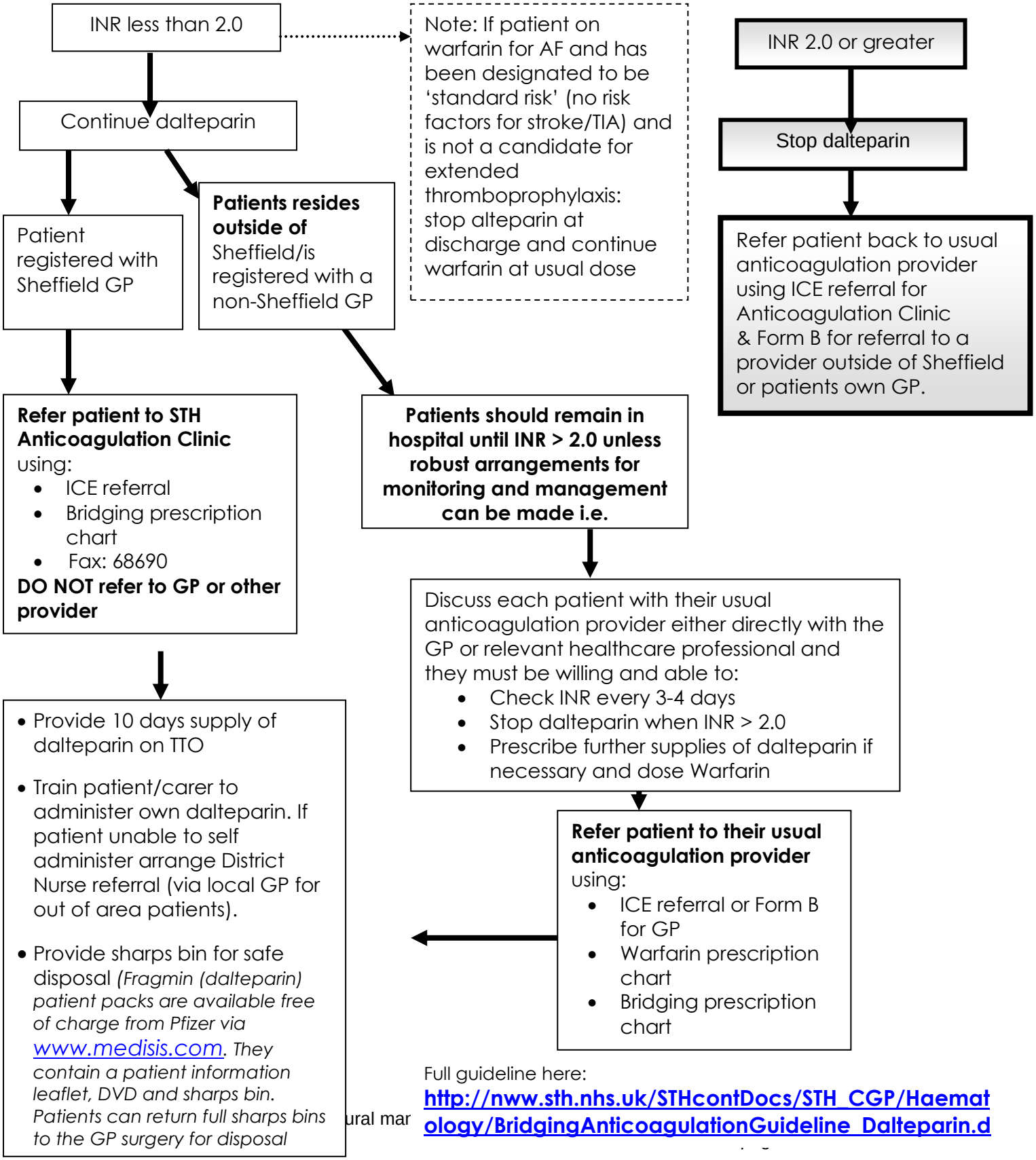
- **Pre-operatively:** no anti-Xa monitoring is required provided the patient is not taking for longer than 3 days. Cancellations should be avoided in this patient cohort
- **Post-operatively:** peak anti-Xa monitoring is required from day +5 onwards once the patient has received 3 – 5 doses. Samples should be taken 3-4 hours post dose and levels discussed with haematology. Warfarin should be restarted at the patient's usual dose on day +1.
- **PATIENTS UNDEROGING MINOR BLEEDING RISK PROCEDURES: P**re-operatively follow the advice for patients undergoing major surgery as above. Post-operatively day +5 doses may be commenced 24 hours post-procedure with anti Xa levels after 3 – 5 doses.

Day	PERI-OPERATIVE MANAGEMENT OF HIGH RISK PATIENTS WITH CREATININE CLEARANCE LESS THAN 20ML/MIN OR ON HAEMODIALYSIS UNDERGOING PROCEDURES WITH A MAJOR BLEEDING RISK					
Pre-Operative dalteparin dosing for HIGH RISK PATIENTS with Creatinine Clearance less than 20ml/min or haemodialysis						
-5	Last dose of warfarin (4 days clear) ensure patient has clear instructions					
-2	**Check INR:** if greater than 1.5 give 1mg oral vitamin K and recheck day -1. Admit patient and initiate unfractionated heparin if INR less than 2.0					
-1	**Re-Check INR** only if INR greater than 1.5 on day -2 and give further 1mg oral vitamin K if INR > 1.5. If INR less than 2.0 start unfractionated heparin.					
Creatinine Clearance less than 20ml/min or haemodialysis Stop unfractionated heparin 6 hours before the procedure						
Day	**Weight less than 56kg**	**Weight 57-68kg**	**Weight 69-82kg**	**Weight 83-100kg**	**Weight 101-115kg**	**Weight 115-150kg**
0	2500 units OD	5000 units OD	5000 units OD	5000 units OD	7500 units OD	7500 units OD
+1	2500 units OD	5000 units OD	5000 units OD	5000 units OD	7500 units OD	7500 units OD
+2	2500 units OD	5000 units OD	5000 units OD	5000 units OD	7500 units OD	7500 units OD
+3 onwards	**Commence unfractionated heparin until INR ≥ 2.0**					

Appendix 6

Quick Guide to DISCHARGING ON PERI-PROCEDURAL ANTICOAGULATION BRIDGING

(Restart patient on usual dose of Warfarin: do NOT give loading or boost doses)



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Full guideline here:
http://nww.sth.nhs.uk/STHcontDocs/STH_CGP/Haematology/BridgingAnticoagulationGuideline_Dalteparin.d